DEDICATION

The past years have seen the loss of two staunch champions for the both of us — the late Athel L.J. Beckwith FAA, FRS from the Research School of Chemistry, ANU (scientist extraordinaire, mentor and friend) as well as Mrs Joan E. Smith, Research School of Chemistry ANU (a dedicated and amazing librarian, and a strong supporter of this book and its previous editions. In her eyes, we could do no wrong). The world is a little less bright in their absence. We dedicate this book to their memories.

W.L.F. Armarego & C.L.L. Chai

Purification of Laboratory Chemicals

Seventh Edition

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Butterworth-Heinemann is an imprint of Elsevier
The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, UK
225 Wyman Street, Waltham, MA 02451, USA

Sixth edition 2008
Seventh edition 2013

British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library

Library of Congress Cataloging-in-Publication Data
A catalog record for this book is available from the Library of Congress

ISBN: 978-0-12-382161-4

Printed and bound in the US

12 13 14 15 16 10 9 8 7 6 5 4 3 2 1

Preface to the Seventh Edition

THE SALES of the sixth edition, which appeared in April 2009, were high by about October 2009, and one of us (WLFA) was approached by Ms Melanie Benson, Editorial Project Manager of Elsevier Science & Technology Books (who was mainly responsible for the production of the 6th edition), about writing a 7th edition within 2–3 years. In the past, 6–9 years were allowed to lapse between editions. However, the attraction this time, was that we were allowed to increase the size of the work by up to 249 pages. This has given us the opportunity to update all the previous chapters in the light of current thinking on safety (personal and environmental), and to introduce two new chapters. The award of five Nobel Prizes in the past ten years or so in Chemistry and one in Physics, of which three were awarded for work on *Catalysis* and *the catalytic process* (2001, 2005 and 2010), and two for work on *Nanomaterials and Nanotechnology* (1996, 2010) have prompted us to write a new chapter on *Catalysts* and a new chapter on *Nanomaterials and Nanotechnology*. Chemical suppliers have now made commercially available a large number of catalysts as well as many nanomaterials of various sorts. Since the number of commercially available catalysts are currently considerably larger than that of nanomaterials, the chapter on Catalysts is larger than that on Nanomaterials and Nanotechnology, and had to be divided into two parts. The availability, preparation and purification of a large range of these, are presented in these chapters. The other chapters have been updated and expanded, also in keeping with the purpose of all previous editions which is to provide information for the purification of commercially available laboratory materials. Of course, the General Subjects Index and the Chemical Abstracts Registry Numbers (CASRNs) Index increased in size accordingly. Much of the cross-referencing is done *via* CASRNs and a page of how to use this book through these is included before Chapter 1 to assist the reader, not only to locate the pages where the required CASRNs are to be found, but also to let the reader know whether a particular substance is included in this work. CASRNs can be readily obtained from chemical catalogues or from SciFinder.

We would like to acknowledge Professor Martin Banwell FAA (Director, Research School of Chemistry, ANU) for his generosity in allowing the use of IT services, and to Dr Emil Mittag (Research School of Chemistry, ANU) for editing and updating the *Macro* program used for making the CASRNs Index.

We are greatly indebted to many people who have made valuable and constructive comments, and indicated errors, in previous editions. The continued help from Joe Papa of BS MS (EXAXOL in Clearwater, Florida, USA) with the preparation and purification of several inorganic compounds, particularly beryllium and cerium, is appreciated and gratefully acknowledged.

One of us (W.L.F.A) owes a debt of gratitude to Professor Jill E. Gready (John Curtin School of Medical Research, ANU) for her continued encouragement and for strongly supporting a Visiting Fellowship over a period of many years.

We thank Dr Pauline M. Armarego for assistance in the painstaking task of proofreading and correcting typographical errors as well as checking the General Index and the CASRNs Index.

We thank the ANU library and its staff, both on campus and at the ANU Print Repository, for their prompt and unfailing assistance.

W.L.F. Armarego & C.L.L. Chai

May 2012

Preface to the First Edition

WE BELIEVE that a need exists for a book to help the chemist or biochemist who wishes to purify the reagents she or he uses. This need is emphasised by the previous lack of any satisfactory central source of references dealing with individual substances. Such a lack must undoubtedly have been a great deterrent to many busy research workers who have been left to decide whether to purify at all, to improvise possible methods, or to take a chance on finding, somewhere in the chemical literature, methods used by some previous investigators.

Although commercially available laboratory chemicals are usually satisfactory, as supplied, for most purposes in scientific and technological work, it is also true that for many applications further purification is essential.

With this thought in mind, the present volume sets out, first, to tabulate methods, taken from the literature, for purifying some thousands of individual commercially available chemicals. To help in applying this information, two chapters describe the more common processes currently used for purification in chemical laboratories and give fuller details of new methods which appear likely to find increasing application for the same purpose. Finally, for dealing with substances not separately listed, a chapter is included setting out the usual methods for purifying specific classes of compounds.

To keep this book to a convenient size, and bearing in mind that its most likely users will be laboratory-trained, we have omitted manipulative details with which they can be assumed to be familiar, and also detailed theoretical discussion. Both are readily available elsewhere, for example in Vogel's very useful book **Practical Organic Chemistry** (Longmans, London, 3rd ed., 1956), or Fieser's **Experiments in Organic Chemistry** (Heath, Boston, 3rd ed., 1957).

For the same reason, only limited mention is made of the kinds of impurities likely to be present, and of the tests for detecting them. In many cases, this information can be obtained readily from existing monographs.

By its nature, the present treatment is not exhaustive, nor do we claim that any of the methods taken from the literature are the best possible. Nevertheless, we feel that the information contained in this book is likely to be helpful to a wide range of laboratory workers, including physical and inorganic chemists, research students, biochemists, and biologists. We hope that it will also be of use, although perhaps to only a limited extent, to experienced organic chemists.

We are grateful to Professor A. Albert and Dr D.J. Brown for helpful comments on the manuscript.

D.D.P., W.L.F.A. & D.R.P.
1966

Preface to the Second Edition

SINCE the publication of the first edition of this book, there have been major advances in purification procedures. Sensitive methods have been developed for the detection and elimination of progressively lower levels of impurities. Increasingly stringent requirements for reagent purity have gone hand-in-hand with developments in semiconductor technology, in the preparation of special alloys and in the isolation of highly biologically active substances. The need to eliminate trace impurities at the micro- and nanogram levels has placed greater emphasis on ultrapurification technique. To meet these demands the range of purities of laboratory chemicals has become correspondingly extended. Purification of individual chemicals thus depends more and more critically on the answers to two questions-Purification from what, and to what permissible level of contamination. Where these questions can be specifically answered, suitable methods of purification can usually be devised.

Several periodicals devoted to ultrapurification and separations have been started. These include "Progress in Separation and Purification" (vol. 1) Ed. E.S. Perry, Wiley-Interscience, New York, vols. 1-4, 1968-1971, and **Separation and Purification Methods**, Ed. E.S.Perry and C.J.van Oss, Marcel Dekker, New York, vol. 1, 1973. Nevertheless, there still remains a broad area in which a general improvement in the level of purity of many compounds can be achieved by applying more or less conventional procedures. The need for a convenient source of information on methods of purifying available laboratory chemicals was indicated by the continuing demand for copies of this book even though it had been out of print for several years.

We have sought to revise and update this volume, deleting sections that have become more familiar or less important, and incorporating more topical material. The number of compounds in Chapters 3 and 4 have been increased appreciably. Also, further details in purification and physical constants are given for many compounds that were listed in the first edition.
We take this opportunity to thank users of the first edition who pointed out errors and omissions, or otherwise suggested improvements or additional material that should be included. We are indebted to Mrs S.Schenk who emerged from retirement to type this manuscript.

D.D.P., W.L.F.A. & D.R.P.
1980

Preface to the Third Edition

THE CONTINUING demand for this monograph and the publisher's request that we prepare a new edition are an indication that **Purification of Laboratory Chemicals** fills a gap in many chemists' reference libraries and laboratory shelves. The present volume is an updated edition that contains significantly more detail than the previous editions, as well as an increase in the number of individual entries and a new chapter.

Additions have been made to Chapters 1 and 2 in order to include more recent developments in techniques (e.g. Schlenk-type, *cf* p. 10), and chromatographic methods and materials. Chapter 3 still remains the core of the book, and lists in alphabetical order relevant information on *ca* 4000 organic compounds. Chapter 4 gives a smaller listing of *ca* 750 inorganic and metal-organic substances, and makes a total increase of ca 13% of individual entries in these two chapters. Some additions have also been made to Chapter 5.
We are currently witnessing a major development in the use of physical methods for purifying large molecules and macromolecules, especially of biological origin. Considerable developments in molecular biology are apparent in techniques for the isolation and purification of key biochemicals and substances of high molecular weight. In many cases something approaching homogeneity has been achieved, as evidenced by electrophoresis, immunological and other independent criteria. We have consequently included a new section, Chapter 6, where we list upwards of 100 biological substances to illustrate their current methods of purification. In this chapter the details have been kept to a minimum, but the relevant references have been included.

The lists of individual entries in Chapters 3 and 4 range in length from single-line entries to *ca* one page or more for solvents such as acetonitrile, benzene, ethanol and methanol. Some entries include information such as likely contaminants and storage conditions. More data referring to physical properties have been inserted for most entries [i.e. melting and boiling points, refractive indexes, densities, specific optical rotations (where applicable) and UV absorption data]. Inclusion of molecular weights should be useful when deciding on the quantities of reagents needed to carry out relevant synthetic reactions, or preparing analytical solutions. The Chemical Abstracts registry numbers have also been inserted for almost all entries and should assist in the precise identification of the substances.

In the past ten years laboratory workers have become increasingly conscious of safety in the laboratory environment. We have therefore in three places in Chapter 1 (pp. 3 and 33, and bibliography p. 52) stressed more strongly the importance of safety in the laboratory. Also, where possible, in Chapters 3 and 4 we draw attention to the dangers involved with the manipulation of some hazardous substances.

The worldwide facilities for retrieving chemical information provided by the Chemical Abstract Service (CAS on-line) have made it a relatively easy matter to obtain CAS registry numbers of substances, and most of the numbers in this monograph were obtained *via* CAS on-line. We should point out that two other available useful files are CSCHEM and CSCORP, which provide, respectively, information on chemicals (and chemical products) and addresses and telephone numbers of the main branch offices of chemical suppliers.

The present edition has been produced on an IBM PC and a Laser Jet printer using the **Microsoft Word (4.0)** word-processing program with a set stylesheet. This has allowed the use of a variety of fonts and font sizes which has made the presentation more attractive than in the previous edition. Also, by altering the format and increasing slightly the sizes of the pages, the length of the monograph has been reduced from 568 to 391 pages. The reduction in the number of pages has been achieved in spite of the increase of *ca* 15% of total text.

We extend our gratitude to the readers whose suggestions have helped to improve the monograph, and to those who have told us of their experiences with some of the purifications stated in the previous editions, and in particular with the hazards that they have encountered. We are deeply indebted to Dr M.D. Fenn for the several hours that he has spent on the terminal to provide us with a large number of CAS registry numbers.

This monograph could not have been produced without the expert assistance of Mr David Clarke who has spent many hours loading the necessary fonts in the computer, and for advising one of the authors (W.L.F.A.) on how to use them together with the idiosyncrasies of Microsoft Word.

D.D.P. & W.L.F.A.
1988

Preface to the Fourth Edition

THE AIMS of the first three editions, to provide purification procedures of commercially available chemicals and biochemicals from published literature data, are continued in this fourth edition. Since the third edition in 1988 the number of new chemicals and biochemicals that have been added to most chemical and biochemical catalogues have increased enormously. Accordingly there is a need to increase the number of entries with more recent useful reagents and chemical and biochemical intermediates. With this in mind, together with the need to reorganise and update general purification procedures, particularly in the area of biological macromolecules, as well as the time lapse since the previous publication, this fourth edition of **Purification of Laboratory Chemicals** has been produced. Chapter 1 has been reorganised with some updating, and by using a smaller font it was kept to a reasonable number of pages. Chapters 2 and 5 were similarly altered and have been combined into one chapter. Eight hundred and three hundred and fifty entries have been added to Chapters 3 (25% increase) and 4 (44% increase), respectively, and four hundred entries (310% increase) were added to Chapter 5 (Chapter 6 in the Third Edition), making a total of 5700 entries-all resulting in an increase from 391 to 529 pages, i.e., by *ca* 35%.

Many references to the original literature have been included remembering that some of the best references happened to be in the older literature. Every effort has been made to provide the best references, but this may not have been achieved in all cases. Standard abbreviations, listed on page 1, have been used throughout this edition to optimise space, except where no space advantage was achieved, in which cases the complete words have been written down to improve the flow of the sentences.

With the increasing facilities for information exchange, chemical, biochemical and equipment suppliers are making their catalogue information available on the Internet; e.g., Aldrich-Fluka-Sigma catalogue information is available on the World Wide Web by using the address http://www.sigma.sial.com and GIBCO BRL catalogue information from http://www.lifetech.com as well as on CD-ROMS which are regularly

updated. Facility for enquiring about, ordering and paying for items is available *via* the Internet. CAS on-line can be accessed on the Internet, and CAS data is available now on CD-ROM. Also biosafety bill boards can similarly be obtained by sending SUBSCRIBE SAFETY John Doe at the address "listserv@uvmvm.uvm.edu", SUBSCRIBE BIOSAFETY at the address "listserv@mitvma.mit.edu", and SUBSCRIBE RADSAF at the address "listserv@romulus.ehs.uiuc.edu"; and the Occupational, Health and Safety information (Australia) is available at the address "http://www. safework.gov.au/". Sigma-Aldrich provided Material Safety data sheets on CD-ROMs.

It is with much sadness that Dr Douglas D. Perrin was unable to participate in the preparation of the present edition due to illness. His contributions towards the previous editions have been substantial, and his drive and tenacity have been greatly missed.

The Third Edition was prepared on an IBM-PC, and the previous IBM files were converted into Macintosh files. These have now been reformatted on a Macintosh LC575 computer, and all further data to complete the Fourth Edition were added to these files. The text was printed with a Hewlett-Packard 4MV -600dpi Laser Jet printer, which gives a clearer resolution.

I thank my wife Dr Pauline M. Armarego, also an organic chemist, for the arduous and painstaking task of entering the new data into the respective files, and for the numerous hours of proofreading as well as the corrections of typographic errors in the files. I should be grateful to my readers for any comments, suggestions, amendments and criticisms which could, perhaps, be inserted in the second printing of this edition.

W.L.F. Armarego, 30 June 1996

Preface to the Fifth Edition

THE DEMAND for **Purification of Laboratory Chemicals** has not abated since the publication of the fourth edition as evidenced by the number of printings and the sales. The request by the Editor for a fifth edition offered an opportunity to increase the usefulness of this book for laboratory purposes. It is with deep regret that mention should be made that Dr Douglas D. Perrin had passed away soon after the fourth edition was published. His input in the first three editions was considerable, and his presence has been greatly missed. A fresh, new and young outlook was required in order to increase the utility of this book, and it is with great pleasure that Dr Christina L.L. Chai, a Reader in Chemistry and leader of a research group in organic and bio-organic chemistry, has agreed to coauthor this edition. The new features of the fifth edition have been detailed below.

Chapters 1 and 2 have been reorganised and updated in line with recent developments. A new chapter on the Future of Purification has been added. It outlines developments in syntheses on solid supports, combinatorial chemistry as well as the use of ionic liquids for chemical reactions and reactions in fluorous media. These technologies are becoming increasingly useful and popular, so much so that many future commercially available substances will most probably be prepared using these procedures. Consequently, knowledge of their basic principles will be helpful in many purification methods of the future.

Chapters 4, 5 and 6 (3, 4 and 5 in the 4th ed.) form the bulk of the book. The number of entries has been increased to include the purification of many recent commercially available reagents that have become more and more popular in the syntheses of organic, inorganic and bio-organic compounds. Several purification procedures for commonly used liquids, e.g., solvents, had been entered with excessive thoroughness, but in many cases the laboratory worker only requires a simple, rapid but effective purification procedure for immediate use. In such cases a **rapid purification** procedure has been inserted at the end of the respective entry, and should be satisfactory for most purposes. With the increased use of solid phase synthesis, even for small molecules, and the use of reagents on solid support (e.g., on polystyrene) for reactions in liquid media, compounds on solid support have become increasingly commercially available. These have been inserted at the end of the respective entry and have been listed in the General Index together with the above rapid purification entries.

A large number of substances are ionisable in aqueous solutions, and knowledge of their ionisation constants, stated as pK (pKa) values, can be of importance not only in their purification but also in their reactivity. Literature values of the pK's have been inserted for ionisable substances, and where values could not be found they were estimated (pK_{Est}). The estimates are usually so close to the true values as not to affect the purification process or the reactivity seriously. The book will thus be a good compilation of pK values for ionisable substances.

Almost all the entries in Chapters 4, 5 and 6 have CAS (Chemical Abstract Service) Registry Numbers to identify them, and these have been entered for each substance. Unlike chemical names which may have more than one synonymous name, there is only one CAS Registry Number for each substance (with only a few exceptions, e.g., where a substance may have another number before purification, or before determination of absolute configuration). To simplify the method for locating the purification of a substance, a CAS Registry Number Index with the respective page numbers has been included after the General Index at the end of the book. This will also provide the reader with a rapid way to see if the purification of a particular substance has been reported in the book. The brief General Index includes page references to procedures and equipment, page references to abbreviations of compounds, e.g., TRIS, as well as the names of substances for which a Registry Number was not found.

Website references for distributors of substances or/and of equipment have been included in the text. However, since these may be changed in the future we must rely on the suppliers to inform users of their change in website references.

We wish to thank readers who have provided advice, constructive criticism and new information for inclusion in this book. We should be grateful to our readers for any further comments, suggestions, amendments and criticisms which could, perhaps, be inserted in a second printing of this edition. In particular, we thank Professor Ken-chi Sugiura (Graduate School of Science, Tokyo Metropolitan University, Japan) who has

provided us with information on the purification of several organic compounds from his own experiences, and Joe Papa BS MS (EXAXOL in Clearwater, Florida, USA) who has provided us not only with his experiences in the purification of many inorganic substances in this book, but also gave us his analytical results on the amounts of other metal impurities at various stages of purification of several salts. We thank them graciously for permission to include their reports in this work. We express our gratitude to Dr William B. Cowden for his generous advice on computer hardware and software over many years and for providing an Apple LaserWriter (16/600PS) which we used to produce the master copy of this book. We also extend our sincere thanks to Dr Bart Eschler for advice on computer hardware and software and for assistance in setting up the computers (iMac and eMac) used to produce this book.

We thank Dr Pauline M. Armarego for assistance in the painstaking task of entering data into respective files, for many hours of proofreading, correcting typographical errors and checking CAS Registry Numbers against their respective entries.

One of us (W.L.F.A) owes a debt of gratitude to Dr Desmond (Des) J. Brown of the Research School of Chemistry, ANU, for unfailing support and advice over several decades and for providing data that was difficult to acquire not only for this edition but also for the previous four editions of this book.

One of us (C.L.L.C) would especially like to thank her many research students (past and present) for their unwavering support, friendship and loyalty, which enabled her to achieve what she now has. She wishes also to thank her family for their love, and would particularly like to dedicate her contribution towards this book to the memory of her brother Andrew who had said that he should have been a scientist.

We thank Mrs. Joan Smith, librarian of the Research School of Chemistry, ANU, for her generous help in many library matters, which has made the tedious task of checking references more enduring.

W.L.F. Armarego & C.L.L. Chai
November 2002

Preface to the Sixth Edition

THERE IS a continuing demand for the **Purification of Laboratory Chemicals** book, to the extent that the 5th edition which was published in early 2003 was carefully translated into Chinese (ISBN 978-7-5025-94367) by Ying-Jie Lin, Wei Liu, Hui-Ping Wang, Xiao-Bo Sun, Qing-Shan Li and Jun-Gang Cao from Jilin University (People's Republic of China) in 2007. In response to the demand, it was timely to update the 5th edition to include the more recently developed purification procedures, as well as add to the list of compounds for purification. The latter comprise some commercially available compounds that have gained usefulness and popularity in the past few years.

The first two chapters have been updated, sections of current interest have been expanded and new sections added. Chapter 3 has been rewritten so that areas of work that have lost popularity have been reduced in size or deleted and sections on recent, and now commonly adopted, technologies have been inserted. Chapters 4, 5 and 6 are now completely reorganized, and each is subdivided into several sections which will make it easier for the reader to locate compounds of similar classification. Chapter 4 is subdivided into aliphatic, alicyclic, aromatic and heterocyclic compounds, Chapter 5 has been subdivided into inorganic and metal-organic compounds, and Chapter 6 has been subdivided into amino acids and peptides, proteins, enzymes, DNA and RNA, carotenoids, carbohydrates, steroids and a miscellaneous section which includes small biologically active substances such as antibiotics, coenzymes, co-factors, lipids, phospholipids, polynucleotides and vitamins. Some useful compounds that have been added recently to commercial catalogues have been included in these three chapters. A large number of derivatives of previous entries with their physical properties and purifications have been inserted together with extensive referencing to the original literature including *Beilstein* references. This resulted in an increase in size of the 5th edition, in text and number of compounds, by over 20%. The purifications of some 7400 substances are described. As in the 5th edition, substance entries are in alphabetical order within subsections and each substance is defined by its Chemical Abstracts Service (CAS) Registry Number. An index of these numbers with their respective page numbers at the end of the book will make it possible to locate the purification of a desired substance readily and to check if the substance is contained in the book. For this purpose we thank Rodney Armarego for setting up a *Macro* on the MacBook Pro computer used for collating the CAS Registry Numbers for the index. There is also a General Index of Contents.

Website references of distributors of substances and/or of equipment have been included in the text. However, since these may change in the future, users should check for current websites of suppliers. The bibliographies have been updated, and websites of a few publishers and book suppliers have been included. Several texts with publication dates older than fifteen years have been deleted except for a few very useful textbooks which are out of print and where recent editions have not been produced. In these cases it is usually possible to obtain used copies from good suppliers of old books, for which there are several websites, e.g. visit Google under "old books suppliers"; also visit websites such as <http//www.abebooks.com>, <http//www.betterworld.com/usedbooks>, <http//www.booksandcollectibles.com.au/index>, <http//www.ebay.com.au/>. Further information for almost every entry in Chapters 4, 5 and 6 of the 6th edition can be obtained from the references to the original literature, which are cited under each entry together with their respective *Beilstein* reference(s).

We thank readers who have provided advice, constructive criticism and new information. We are grateful for any further comments, suggestions, amendments and criticisms which could, perhaps, be inserted in a second printing of this edition. We thank Joe Papa BS MS (EXAXOL in Clearwater, Florida, USA) in particular for sharing his experiences on the purification of several inorganic substances in this and previous editions, and also for allowing us to use his analytical results on the amounts of metal impurities at various stages of purification of several salts.

We thank Dr Pauline M. Armarego for assistance in the painstaking task of entering data into respective files, for many hours of proofreading, correcting typographical errors and checking CAS Registry Numbers against their respective entries.

One of us (W.L.F.A) owes a debt of gratitude to Dr Desmond (Des) J. Brown of the Research School of Chemistry, ANU, for unfailing support and advice over several decades and for providing data that was difficult to acquire not only for this edition but also for the previous five editions of this book.

One of us (C.L.L.C) would like to acknowledge the support and friendship of her many research staff and students (past and present at ANU and A*STAR). She especially thanks Drs Paul Huleatt, Paul Bernardo, Felicity Moore and Brendan Burkett for their unfailing faith in her, through chemical and personal journeys both in Singapore and Australia. The legacy of this book is for Kimberley and Victoria Tse because it is cool to be a scientist!

We thank Mrs Joan Smith, librarian of the Research School of Chemistry, ANU, for her generous help in many library matters which made the tedious task of checking references more enduring.

W.L.F. Armarego & C.L.L. Chai

November 2008

HOW THIS BOOK SHOULD BE USED

Substances have been entered under their respective chapters, sections and subsections. In these sections compounds have been entered in alphabetical order according to the more commonly used name. However, because compounds can be named differently (some of these other names have been included in brackets after their entries) and may be difficult to find, it is advisable to obtain the page number of the entry from the Chemical Abstracts Registry Numbers (CASRNs) Index at the end of the book. CASRNs of substances are readily obtained from "SciFinder", or better, from any commercial catalogue that sells these compounds, as almost all of these have CASRNs inserted after the names of their products. Also, in this book we could not insert some substances that can be formally included in more than one section without repeating the entry. In such cases the compounds are entered in a preferred section and are cross-referenced by inserting "see [CASRN]" or just "[CASRN]". Thus the cross-reference is its CASRN. The CASRNs Index provides the page numbers in bold/italic type. If the CASRN of a desired substance is not in the CASRN Index, or its full or abbreviated name is not in the General Index, then it will not be present in this book.

CASRNs are unique for each chemical substance and are such that they are internally consistent. They are set up according to a specific formula. Refer to the first page of the CASRNs Index to calculate the formula in order to check whether the number is a valid number or not.

W.L.F.A. & C.L.L.C.

ABOUT THE AUTHORS

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Wilfred L.F. Armarego graduated BSc (Hons) in 1953 and PhD from the University of London in 1956 and came to Australia in that year. After two years at the Central Research Laboratories (ICIANZ) in Melbourne, where he worked on plant growth substances, and one year on potentially carcinogenic polycyclic aromatic hydrocarbons at the University of Melbourne as Senior Demonstrator in Organic Chemistry, he joined the Department of Medical Chemistry as a Research Fellow in 1960. He became a Fellow in 1963 and was awarded a DSc degree (London) in 1968. He was promoted to Senior Fellow in 1967 and began research work on the biochemistry and molecular biology of pteridine-requiring enzymes related to the inherited metabolic disease phenylketonuria and its variants. He was head of the Protein Biochemistry Group and Pteridine Biochemistry Laboratory and is now a visiting fellow at the John Curtin School of Medical Research, and member of the editorial boards of 'Medicinal Research Reviews' and 'Pteridines' journals. He is a Chartered Chemist, a Fellow of the Royal Society of Chemistry and a Fellow of the Royal Australian Chemical Institute.

Christina L.L. Chai

Department of Pharmacy, National University of Singapore and Institute of Chemical and Engineering Sciences, Agency for Science Technology and Research, Singapore.

Christina Li Lin Chai obtained her BSc (Hons) from the University of Canterbury, Christchurch, New Zealand and her PhD in synthetic organic chemistry from the Research School of Chemistry, Australian National University, Canberra, Australia. Upon completion of her PhD, she was awarded a Samuel-Glasstone Research Fellowship tenable at the Dyson Perrins Laboratory, University of Oxford, UK. Her first faculty position was at the Department of Chemistry, Victoria University of Wellington in 1991–1993, followed by a second faculty position at the Australian National University (1994–2004) where she was an Associate Professor. She moved to the Institute of Chemical and Engineering Sciences, Agency for Science Technology and Research (A*STAR), Singapore as a Principal Scientist and Programme Manager in Dec 2004 and held various co-appointments as Director of Graduate Affairs at the Science and Engineering Council (SERC), A*STAR as well as an honorary adjunct appointment at Nanyang Technological University, Singapore. Since August 2011, Dr Chai holds a joint appointment as Associate Professor in the Department of Pharmacy, National University of Singapore and as Principal Scientist in the Institute of Chemical and Engineering Sciences.

CHAPTER 1

COMMON PHYSICAL TECHNIQUES USED IN PURIFICATION

INTRODUCTION

Purity is a matter of degree. Other than contaminants such as dust, paper fibres, wax, cork, etc., that may have been inadvertently introduced into the sample during manufacture, all commercially available chemical substances are in some measure impure. Any amounts of unreacted starting material, intermediates, by-products, isomers and related compounds may be present depending on the synthetic or isolation procedures used for preparing the substances. Inorganic reagents may deteriorate because of defective packaging (glued liners affected by sulfuric acid, zinc extracted from white rubber stoppers by ammonia), corrosion or prolonged storage. Organic molecules may undergo changes on storage. In extreme cases the container may be incorrectly labelled or, where compositions are given, they may be misleading or inaccurate for the proposed use. Where any doubt exists, it is usual to check for impurities by appropriate spot tests, or by recourse to tables of physical or spectral properties such as the extensive infrared and NMR libraries published by the Sigma-Aldrich Chemical Co.

The important question, then, is not whether a substance is pure but whether a given sample is sufficiently pure for some intended purpose. That is, are the contaminants likely to interfere in the process or measurement that is to be studied? By suitable manipulation it is often possible to reduce levels of impurities to acceptable limits, but absolute purity is an ideal which, no matter how closely approached, can never be attained. A *negative* physical or chemical test indicates only that the amount of an impurity in a substance lies below a certain sensitivity level; no test can demonstrate that a likely impurity is entirely absent.

When setting out to purify a laboratory chemical, it is desirable that the starting material is of the best grade commercially available. Particularly among organic solvents there is a range of qualities varying from *laboratory chemical* to *spectroscopic* and *chromatographic* grades. Many of these are suitable for use as received. With the more common reagents it is usually possible to obtain from the current literature some indications of likely impurities, their probable concentrations and methods for detecting them. However, in many cases complete analyses are not given so that significant concentrations of unspecified impurities may be present.

THE QUESTION OF PURITY

Solvents and substances that are specified as *pure* for a particular purpose may, in fact, be quite impure for other uses. Absolute ethanol may contain traces of benzene, which makes it unsuitable for ultraviolet spectroscopy, or plasticizers which make it unsuitable for use in solvent extraction. See also the section on “Criteria of Purity” in Chapter 2.

Irrespective of the grade of material to be purified, it is essential that some criteria exist for assessing the degree of purity of the final product. The more common of these include:

1. Examination of physical properties such as:
   (a) Melting point, freezing point, boiling point, and the freezing curve (i.e. the variation, with time, in the freezing point of a substance that is being slowly and continuously frozen).
   (b) Density.

Purification of Laboratory Chemicals. http://dx.doi.org/10.1016/B978-0-12-382161-4.00001-7

(c) Refractive index at a specified temperature and wavelength. The sodium D line at 589.26 nm (weighted mean of the D_1 and D_2 lines) is the usual wavelength used but the refractive index values at other wavelengths can often be interpolated from a plot of refractive index versus $1/(\text{wavelength})^2$.
(d) Specific conductivity (This can be used to detect, for example, water, salts, inorganic and organic acids and bases, in non-electrolytes).
(e) Optical rotation, optical rotatory dispersion and circular dichroism.

2. Empirical analysis, for C, H, N, ash, etc.

3. Chemical tests for particular types of impurities, e.g. for peroxides in aliphatic ethers (with acidified KI), or for water in solvents (quantitatively by the Karl Fischer method, see Fieser and Fieser, *Reagents for Organic Synthesis*, J. Wiley & Sons, NY, Vol 1 pp. 353, 528 *1967*, Library of Congress Catalog Card No 66-27894, also see Karl Fischer titrant or Hydranal® –Titrant type 5E [64-17-5] and other types in Fluka and Sigma-Aldrich Catalogue.

4. Physical tests for particular types of impurities:
Emission and atomic absorption spectroscopy for detecting organic impurities and determining metal ions.
Chromatography, including paper, thin layer, liquid (high, medium and normal pressure), flash and vapour phase.
Electron spin resonance for detecting free radicals.
Other spectroscopic methods (see 5 below).

5. Examination of spectroscopic properties
Nuclear Magnetic Resonance (^{1}H, ^{13}C, ^{31}P, ^{19}F, ^{11}B NMR, etc.)
Infrared spectroscopy (IR and Fourier Transform IR)
Ultraviolet (UV), visible and fluorescence spectroscopy
X-ray photoelectron spectroscopy (XPS)
Atomic absorption spectroscopy (AAA)
Mass spectroscopy [electron ionisation (EI), chemical ionisation (CI), electrospray ionisation (ESI), fast atom bombardment (FAB), matrix-associated laser desorption ionisation (MALDI), inductively coupled plasma-mass spectrometry (ICP-MS)

6. Electrochemical methods (see Chapter 6 for macromolecules).

7. Nuclear methods which include a variety of radioactive elements as in organic reagents, complexes or salts.

A substance is usually taken to be of an acceptable purity when the measured property is unchanged by further treatment (especially if it agrees with a recorded value). In general, at least two different methods, such as recrystallisation and distillation, should be used in order to ensure maximum purity. Crystallisation may be repeated (from the same solvent or better from different solvents) until the substance has a constant melting point, and until it distils repeatedly within a narrow specified temperature range. The purified product should have spectroscopic properties which indicate that the traces of impurities left in the sample are of acceptable levels for the intended purpose.

With liquids, the refractive index at a specified temperature and wavelength is a sensitive test of purity. Note however that this is sensitive to dissolved gases such as O_2, N_2 or CO_2. Under favourable conditions, freezing curve studies are sensitive to impurity levels of as little as 0.001 moles percent. Analogous fusion curves or heat capacity measurements can be up to ten times as sensitive as this. With these exceptions, most of the above methods are rather insensitive, especially if the impurities and the substances in which they occur are chemically similar. In some cases, even an impurity comprising many parts per million of a sample may escape detection.

The common methods of purification, discussed below, comprise distillation (including fractional distillation, distillation under reduced pressure, sublimation and steam distillation), crystallisation, extraction, chromatographic, electrophoresis and other methods. In some cases, volatile and other impurities can be removed simply by heating. Impurities can also sometimes be eliminated by the formation of derivatives from which the purified material is regenerated (see Chapter 2).

Common techniques used for determining the purity of a specimen and for following the purification procedure are described below (p. 33).

SOURCES OF IMPURITIES

Some of the more obvious sources of contamination of solvents arise from storage in metal drums and plastic containers, and from contact with grease and screw caps. Many solvents contain water. Others have traces of acidic materials such as hydrochloric acid in chloroform. In both cases this leads to corrosion of the drum and contamination of the solvent by traces of metal ions, especially Fe^{3+}. Grease, for example on stopcocks of separating funnels and other apparatus, e.g. greased ground joints, is also likely to contaminate solvents during extractions and chemical manipulation. Oxygen from the air is also a source of contamination by virtue of its ability to produce small or large amounts of oxidation products (see section on the *Solubilities of gases in liquids* below).

A much more general source of contamination that has not received the consideration it merits comes from the use of plastics for tubing and containers. Plasticisers can readily be extracted by organic solvents from PVC and other plastics, so that most solvents, irrespective of their grade (including spectrograde and ultrapure), have been reported to contain 0.1 to 5ppm of plasticiser [de Zeeuw, Jonkman and van Mansvelt *Anal Biochem* **67** 339 *1975*]. Where large quantities of solvent are used for extraction followed by evaporation, this can introduce significant amounts of impurity, even exceeding the weight of the genuine extract and giving rise to spurious peaks in gas chromatography, for example of fatty acid methyl esters [Pascaud, *Anal Biochem* **18** 570 *1967*]. Likely contaminants are di(2-ethylhexyl)phthalate and dibutyl phthalate, but upwards of 20 different phthalate esters are listed as plasticisers as well as adipates, azelates, phosphates, epoxides, polyesters and various heterocyclic compounds. These plasticisers would enter the solvent during passage through plastic tubing or from storage in containers or from plastic coatings used in cap liners for bottles. Such contamination could arise at any point in the manufacture or distribution of a solvent. The problem with cap liners is avoidable by using corks wrapped in aluminium foil, although even in this case care should be taken because aluminium foil can dissolve in some liquids, e.g. benzylamine and propionic acid. Polycarbonate containers invariably leach out the 'estrogenic chemical' **Bisphenol A** (see Chapter 4, Aromatic Compounds) into the liquid in the container [Fiona Case *Chemistry World* **5** (No. 4) 12 *2008*, Rebecca Trager *Chemistry World* **5** (No. 5) 8 *2008*].

Solutions in contact with polyvinyl chloride can become contaminated with trace amounts of lead, titanium, tin, zinc, iron, magnesium or cadmium from additives used in the manufacture and moulding of PVC.

N-Phenyl-2-naphthylamine is a contaminant of solvents and biological materials that have been in contact with black rubber or neoprene (in which it is used as an antioxidant). Although this naphthylamine was only an artifact of the isolation procedures, it was at first thought to be a genuine component of vitamin K preparations, extracts of plant lipids, algae, butter, animal livers, eye tissue and kidney tissue [Brown *Chem Br* **3** 524 *1967*].

Most of the above impurities can be removed by prior distillation of the solvent, and care should be taken to avoid further contact with plastic or black rubber materials.

PRACTICES TO AVOID IMPURITIES

Cleaning practices

Laboratory glassware and Teflon equipment can be cleaned satisfactorily for most purposes by careful immersion into a solution of sodium dichromate in concentrated sulfuric acid, followed by draining, and rinsing copiously with distilled water. This is an exothermic reaction and should be carried out **very** cautiously in an efficient fume cupboard. [To prepare the chromic acid bath, dissolve 5 g of sodium dichromate (CARE: cancer suspect agent) in 5 ml of water. The dichromate solution is then cooled and stirred while 100 ml of concentrated sulfuric acid is added slowly. Store it in a glass bottle.] Where traces of chromium (adsorbed on the glass) must be avoided, a 1:1 mixture of concentrated sulfuric and nitric acid is a useful alternative. (*Use in a fumehood to remove vapour and with adequate face protection.*) Acid washing is also suitable for polyethylene ware, but prolonged contact (some weeks) leads to severe deterioration of the plastic. Alternatively an alcoholic solution of sodium hydroxide (alkaline base bath) can be used. This strongly corrosive solution (CAUTION: alkali causes serious burns) can be made by dissolving 120 g of NaOH in 120 ml of water, followed by dilution to 1 L with 95% ethanol.

This solution is conveniently stored in suitable alkali-resistant containers (e.g. Nalgene heavy duty rectangular tanks) with lids. Glassware can be soaked overnight in the base bath and rinsed thoroughly after soaking. For much glassware, washing with hot detergent solution, using tap water, followed by rinsing well with distilled water and acetone, and heating to 200–300° overnight, is adequate. (Volumetric apparatus should not be heated: after washing it is rinsed with acetone, then pure diethyl ether, and air-dried. Prior to use, equipment can be rinsed with acetone, then with petroleum ether or pure diethyl ether, to remove the last traces of contaminants.)
Teflon equipment should be soaked, first in acetone, then in petroleum ether or pure diethyl ether for ten minutes, then dried in a vacuum or flushed with dry nitrogen prior to use.
For trace metal analyses, prolonged soaking of equipment in 1M nitric acid may be needed to remove adsorbed metal ions.
Soxhlet thimbles and filter papers may contain traces of lipid-like materials. For manipulations with highly pure materials, as in trace-pesticide analysis, thimbles and filter papers should be thoroughly extracted with pure diethyl ether before use.
Trace impurities in silica gel for TLC can be removed by heating at 300° for 16 hours or by Soxhlet extraction for 3 hours with distilled chloroform, followed by 4 hours extraction with distilled pure diethyl ether and drying in a vacuum.

Silylation of glassware and plasticware

Silylation of apparatus makes it repellant to water and hydrophilic materials. It minimises loss of solute by adsorption onto the walls of the container. The glassware is placed in a desiccator containing dichloromethyl silane (1ml) in a small beaker and evacuated for 5 minutes. The vacuum is turned off and air is introduced into the desiccator, which allows the silylating agent to coat the glassware uniformly. The desiccator is then evacuated, closed and set aside for 2 hours. The glassware is removed from the desiccator and baked at 180° for 2 hours before use.

Fluka supplies a variety of silylating mixtures including (a) Silanization solution I (Fluka gel repel I: ~5% dimethyldichlorosilane in hexane, (b) Silanization solution II (Fluka gel repel II: ~2% dimethyldichlorosilane in 1,1,1-trichloroethane) for silanizing micro electrode, (c) Silanization solution III (Selectophore: 10% hexamethyldisilazane and 6% trimethylchlorosilane in 1-chloronaphthalene), (d) Silanization solution IV (Selectophore: ~4% trimethylchlorosilane in *o*-xylene, (e) Silanization solution V (Selectophore: ~5% dimethyldichlorosilane in *o*-xylene, and (f) Silanization solution VI (Selectophore: ~3% tributylchlorosilane in 1-chloronaphthalene for silanizing micropipette electrodes by the dip-and-bake method. Most powerful general silylating mixtures among many others are also available from Fluka (see catalogue).

Plasticware is treated similarly except that it is rinsed well with water before use instead of baking. Note that dichloromethyl silane is highly **TOXIC** and **VOLATILE**, and the whole operation should be carried out in an efficient fume cupboard.
An alternative procedure used for large apparatus is to rinse the apparatus with a 5% solution of dichloromethyl silane in chloroform, followed by several rinses with water before baking the apparatus at 180°/2 hours (for glass) or drying in air (for plasticware).
A solution of 2% w/v of dichloromethyl silane in octamethyl cyclooctasilane or octmethylcyclotetrasiloxane is used to inhibit the sticking of polyacrylamide gels, agarose gels and nucleic acids to glass surfaces and these chemicals are available commercially [from Fluka (Riedel-deHaën)].

SAFETY PRECAUTIONS ASSOCIATED WITH THE PURIFICATION OF LABORATORY CHEMICALS

Although most of the manipulations involved in purifying laboratory chemicals are inherently safe, care is necessary if hazards are to be avoided in the chemical laboratory. In particular there are dangers inherent in the inhalation of vapours and absorption of liquids and low melting solids through the skin. In addition to the toxicity of solvents there is also the risk of their flammability and the possibility of eye damage. Chemicals, particularly in admixture, may be explosive. Compounds may be carcinogenic or otherwise deleterious to health. Present-day chemical catalogues specifically indicate the particular dangerous properties of the individual chemicals they list, and these should be consulted whenever the use of commercially available chemicals is contemplated. Radioisotopic labeled compounds pose special problems of human exposure and of disposal of laboratory waste.

Hazardous purchased chemicals are accompanied by detailed MSDS (Material Safety Data Sheets), which contain information regarding their toxicity, safety handling procedures and the necessary precautions to be taken. These should be read carefully and filed for future reference. In addition, chemical management systems such as Chem-ChemWatch, which include information on hazards, handling and storage, are commercially available. There are a number of websites which provide selected safety information: these include the Sigma-Aldrich website <www.sigmaaldrich.com> and other chemical websites, e.g. <www.ilpi.com/msds>.

The most common hazards are:

(1) Explosions due to the presence of peroxides formed by aerial oxidation of ethers and tetrahydrofuran, decahydronaphthalene, acrylonitrile, styrene and related compounds.
(2) Compounds with low flash points (below room temperature). Examples are acetaldehyde, acetone, acetonitrile, benzene, carbon disulfide, cyclohexane, diethyl ether, ethyl acetate and *n*-hexane.
(3) Contact of oxidising agents ($KMnO_4$, $HClO_4$, chromic acid) with organic liquids.
(4) Toxic reactions with tissues (Me_2SO_4).

The laboratory should at least be well-ventilated and safety glasses should be worn, particularly during distillations and manipulations carried out under reduced pressure or elevated temperatures. With this in mind we have endeavoured to warn users of this book whenever greater than usual care is needed in handling chemicals. As a general rule, however, **all chemicals which users are unfamiliar with should be treated with extreme care and assumed to be highly flammable and toxic.** The safety of others in a laboratory should always be foremost in mind, with ample warning whenever a potentially hazardous operation is in progress. Also, unwanted solutions or solvents should never be disposed of *via* the laboratory sink. The operator should be aware of the usual means for disposal of chemicals in her/his laboratories, and she/he should remove unwanted chemicals accordingly. **Organic liquids for disposal should be temporarily stored, as is practically possible, in respective containers. Avoid placing all organic liquids in the same container particularly if they contain small amounts of reagents which could react with each other. Halogenated waste solvents should be kept separate from other organic liquids.**
Laboratory coats, disposable aprons, caps, sleeves, dust/mist respirators and foot protection, hearing protection as well as a variety of safety glasses, goggles, face and body shields should be used when the demand arises and are available commercially (see e.g. the Sigma-Aldrich Labware catalogue).

SOME HAZARDS OF CHEMICAL MANIPULATION IN PURIFICATION AND RECOVERY OF RESIDUES

Performing chemical manipulations calls for some practical knowledge if danger is to be avoided. However, with care, hazards can be kept to an acceptable minimum. A good general approach is to consider every operation as potentially perilous and then to adjust one's attitude as the operation proceeds. A few of the most common dangers are set out below. For a larger coverage of the following sections, and of the literature, the bibliography at the end of this chapter should be consulted.

Perchlorates and perchloric acid. At 160° perchloric acid is an exceedingly strong oxidising acid and a strong dehydrating agent. Organic perchlorates, such as methyl and ethyl perchlorates, are unstable and are violently explosive compounds. A number of heavy-metal perchlorates are extremely prone to explode. The use of anhydrous magnesium perchlorate, *Anhydrone*, *Dehydrite*, as a drying agent for organic vapours is **not** recommended. Desiccators which contain this drying agent should be adequately shielded at all times and kept in a cool place, i.e. **never** on a window sill where sunlight can fall on it.
No attempt should be made to purify perchlorates, except for ammonium, alkali metal and alkaline earth salts which, in water or aqueous alcoholic solutions are insensitive to heat or shock. Note that perchlorates react relatively slowly in aqueous organic solvents, but as the water is removed there is an increased possibility of an explosion. Perchlorates, often used in non-aqueous solvents, are explosive in the presence of even small amounts of organic compounds when heated. Hence stringent care should be taken when purifying perchlorates, and direct flame and infrared lamps should be avoided. Tetra-alkylammonium perchlorates should be dried below 50° under vacuum (and protection). Only very small amounts of such materials should be prepared, and stored, at any one time.

Peroxides. These are formed by aerial oxidation or by autoxidation of a wide range of organic compounds, including diethyl ether, allyl ethyl ether, allyl phenyl ether, dibenzyl ether, benzyl butyl ether, *n*-butyl ether, *iso*-butyl ether, *t*-butyl ether, dioxane, tetrahydrofuran, olefins, and aromatic and saturated aliphatic hydrocarbons. They accumulate during distillation and can detonate violently on evaporation or distillation when their concentration becomes high. If peroxides are likely to be present materials should be tested for peroxides before distillation (for tests see entry under "Ethers", in Chapter 2). Also, distillation should be discontinued when at least one quarter of the residue is left in the distilling flask.

Heavy-metal-containing explosives. Ammoniacal silver nitrate, on storage or treatment, will eventually deposit the highly explosive silver nitride *fulminating silver*. Silver nitrate and ethanol may give silver fulminate (see Chapter 5), and in contact with azides or hydrazine and hydrazides may form silver azide. Mercury can also form such compounds. Similarly, ammonia or ammonium ions can react with gold salts to form *"fulminating gold"*. Metal fulminates of cadmium, copper, mercury and thallium are powerfully explosive, and some are detonators [Luchs, *Photog Sci Eng* **10** 334 *1966*]. Heavy-metal-containing solutions, particularly when organic material is present, should be treated with great respect and precautions towards possible explosion should be taken.

Strong acids. In addition to perchloric acid (see above), extra care should be taken when using strong mineral acids. Although the effects of concentrated sulfuric acid are well known, these cannot be stressed strongly enough. Contact with tissues will leave irreparable damage. **Always dilute the concentrated acid by carefully adding the acid down the side of the flask which contains the water, and the process should be carried out under cooling. This solution is not safe to handle until the acid has been thoroughly mixed (care) with the water. Protective face, and body coverage should be used at all times.** Fuming sulfuric acid and chlorosulfonic acid are even more dangerous than concentrated sulfuric acid, and adequate precautions should be taken. Chromic acid cleaning mixture contains strong sulfuric acid and should be treated in the same way; and in addition the mixture is potentially ***carcinogenic.***
Concentrated and fuming nitric acids are also dangerous because of their severe deleterious effects on tissues.

Picric acid. This acid and related nitro compounds, e.g. styphnic acid, are explosive and should **not** be kept dry. The acid is generally stored wet by covering the crystals with water. Solutions in ethanol and benzene are used occasionally. They should be stored in the cold (to minimise evaporation), and a rubber or plastic stopper (**not a ground glass stopper**) should be used. **Note** that picric acid and picrates stain skin protein with a yellow colour that is not readily washed off. This can be avoided by wearing rubber gloves.

Reactive halides and anhydrides. Substances like acid chlorides, low-molecular-weight anhydrides and some inorganic halides (e.g. PCl_3) can be **highly toxic and lachrymatory, affecting mucous membranes and lung tissues. Utmost care should be taken when working with these materials. Work should be carried out in a very efficient fume cupboard.**

Salts and organic esters of some inorganic acids. In addition to the dangers of perchlorate salts, other salts such as nitrates, azides, diazo salts, organic nitrates, organic azides and picrates (see above) can be hazardous, and due care should be taken when these are dried. Large quantities should never be prepared or stored for long periods.

Solvents. The flammability of low-boiling organic liquids cannot be emphasised strongly enough. These invariably have very low flash points and can ignite spontaneously. Special precautions against explosive flammability should be taken when recovering such liquids. Care should be taken with small volumes (*ca* 250ml) as well as large volumes (> 1L), and the location of all the fire extinguishers, and fire blankets, in the immediate vicinity of the apparatus should be checked. The fire extinguisher should be operational. The following flammable liquids (in alphabetical order) are common fire hazards in the laboratory: acetaldehyde, acetone, acrylonitrile, acetonitrile, benzene, carbon disulfide, cyclohexane, diethyl ether, ethyl acetate, hexane, low-boiling petroleum ether, tetrahydrofuran and toluene. Toluene should always be used in place of benzene wherever possible due to the potential *carcinogenic* effects of the liquid and vapour of the latter.
The drying of flammable solvents with sodium or potassium metal and metal hydrides poses serious potential fire hazards, and adequate precautions should be stressed.

SAFETY DISCLAIMER

Experimental chemistry is a very dangerous occupation, and extreme care and adequate safety precautions should be taken at all times. Although we have stated the safety measures that have to be taken under specific entries, these are by no means exhaustive and some may have been unknowingly or accidentally omitted. The experimenter without prior knowledge or experience must seek further safety advice on reagents and procedures from experts in the field before undertaking the purification of any material. *We take no responsibility whatsoever if any mishaps occur when using any of the procedures described in this book.*

METHODS OF PURIFICATION OF REAGENTS AND SOLVENTS

Many methods exist for the purification of reagents and solvents. A number of these methods are routinely used in synthetic as well as analytical chemistry and biochemistry. These techniques, outlined below, will be discussed in greater detail in the respective sections in this chapter. It is important to note that more than one method of purification may need to be implemented in order to obtain compounds of highest purity.
Common methods of purification are:

Solvent Extraction and Distribution
Distillation
Recrystallisation
Sublimation
Electrophoresis
Chromatography

For substances contaminated with water or solvents, drying with appropriate absorbents and desiccants may be sufficient.

SOLVENT EXTRACTION AND DISTRIBUTION

Extraction of a substance from suspension or solution into another solvent can sometimes be used as a purification process. Thus, organic substances can often be separated from inorganic impurities by shaking an aqueous solution or suspension with suitable immiscible solvents such as benzene, carbon tetrachloride, chloroform, diethyl ether, diisopropyl ether or petroleum ether. After several such extractions, the combined organic phase is dried and the solvent is evaporated. Grease from the glass taps of conventional separating funnels is invariably soluble in the solvents used. Contamination with grease can be very troublesome particularly when the amounts of material to be extracted are very small. Instead, the glass taps should be lubricated with the extraction solvent; or better, the taps of the extraction funnels should be made of the more expensive material *Teflon*. Immiscible solvents suitable for extractions are given in Table 1. Addition of electrolytes (such as ammonium sulfate, calcium chloride or sodium chloride) to the aqueous phase helps to ensure that the organic layer separates cleanly and also decreases the extent of extraction into the latter. Emulsions can also be broken up by filtration (with suction) through Celite, or by adding a little diethyl ether, octyl alcohol or some other paraffinic alcohol. The main factor in selecting a suitable immiscible solvent is to find one in which the material to be extracted is readily soluble, whereas the substance from which it is being extracted is not. The same considerations apply irrespective of whether it is the substance being purified, or one of its contaminants, that is taken into the new phase. (The second of these processes is described as washing.)

Common examples of washing with aqueous solutions include the following:

Removal of acids from water-immiscible solvents by washing with aqueous alkali, sodium carbonate or sodium bicarbonate.
Removal of phenols from similar solutions by washing with aqueous alkali.
Removal of organic bases by washing with dilute hydrochloric or sulfuric acids.
Removal of unsaturated hydrocarbons, of alcohols and of ethers from saturated hydrocarbons or alkyl halides by washing with cold concentrated sulfuric acid.

This process can also be applied to purification of the substance if it is an acid, a phenol or a base, by extracting into the appropriate aqueous solution to form the salt which, after washing with pure solvent, is again converted to the free species and re-extracted. Paraffin hydrocarbons can be purified by extracting them with phenol (in which aromatic hydrocarbons are highly soluble) prior to fractional distillation.

For extraction of solid materials with a solvent, a *Soxhlet* extractor is commonly used. This technique is applied, for example, in the alcohol extraction of dyes to free them from insoluble contaminants such as sodium chloride or sodium sulfate.
Acids, bases and amphoteric substances can be purified by taking advantage of their ionisation constants (see below).
The recovery of some fifty more commonly used solvents from water, other solvents, residues etc. have been discussed, together with information on their behaviour before and after use, by I.M. Smallwood in the *Solvent Recovery Handbook*, Blackwood Science Publ Ltd, *2001*, ISBN 9780632056477.

DISTILLATION

One of the most widely applicable and most commonly used methods of purification of liquids or low melting solids (especially of organic chemicals) is fractional distillation at atmospheric, or some lower, pressure. Almost without exception, this method can be assumed to be suitable for all organic liquids and most of the low-melting organic solids. For this reason it has been possible, e.g. in Chapter 4, to omit many procedures for purification of organic chemicals when only a simple fractional distillation is involved-the suitability of such a procedure is implied from the boiling point.
The boiling point of a liquid varies with the 'atmospheric' pressure to which it is exposed. A liquid boils when its vapour pressure is the same as the external pressure on its surface, its normal boiling point being the temperature at which its vapour pressure is equal to that of a standard atmosphere (760 mmHg). Lowering the external pressure lowers the boiling point. For most substances, boiling point and vapour pressure are related by an equation of the form,

$$\log p = A + B/(t + 273),$$

where p is the pressure in mmHg, t is in ^{o}C, and A and B are constants. Hence, if the boiling points at two different pressures are known, the boiling point at another pressure can be calculated from a simple plot of $\log p$ *versus* $1/(t + 273)$. For organic molecules that are not strongly associated, this equation can be written in the form,

$$\log p = 8.586 - 5.703\ (T + 273)/(t + 273)$$

where T is the boiling point in ^{o}C at 760 mmHg. Tables 2A and 2B give computed boiling points over a range of pressures. Some examples illustrate its application. Ethyl acetoacetate, **b** 180^{o} (with decomposition) at 760 mmHg has a predicted **b** of 79^{o} at 16 mm; the experimental value is 78^{o}. Similarly 2,4-diaminotoluene, **b** 292^{o} at 760mm, has a predicted **b** of 147^{o} at 8mm; the experimental value is 148–150^{o}. For self-associated molecules the predicted **b** are lower than the experimental values. Thus, glycerol, **b** 290^{o} at 760mm, has a predicted **b** of 146^{o} at 8mm: the experimental value is 182^{o}.

Similarly an estimate of the boiling points of liquids at reduced pressure can be obtained using a nomogram (see Fig. 1).

For pressures near 760mm, the change in boiling point is given approximately by

$$\delta t = a(760 - p)(t + 273)$$

where a = 0.00012 for most substances, but a = 0.00010 for water, alcohols, carboxylic acids and other associated liquids, and a = 0.00014 for very low-boiling substances such as nitrogen or ammonia [Crafts *Chem Ber* **20** 709 *1887*]. When all the impurities are non-volatile, simple distillation is adequate purification. The observed boiling point remains almost constant and approximately equal to that of the pure material. Usually, however, some of the impurities are appreciably volatile, so that the boiling point progressively rises during the distillation because of the progressive enrichment of the higher-boiling components in the distillation flask. In such cases, separation is effected by fractional distillation using an efficient column. [For further reading see section on "Variation of Boiling Points with Pressure" on pp. 15–26 in *CRC—Handbook of Chemistry and Physics 88th Edition*, David R Lide (Editor–in-Chief) CRC Press, Boca Raton, Florida *2007–2008*, ISBN 0849304881.]

Techniques

The distillation apparatus consists basically of a distillation flask, usually fitted with a vertical fractionating column (which may be empty, or packed with suitable materials such as glass helices or stainless-steel wool) to which is attached a condenser leading to a receiving flask. The bulb of a thermometer projects into the vapour phase just below the region where the condenser joins the column. The distilling flask is heated so that its contents are steadily vaporised by boiling. The vapour passes up into the column where, initially, it condenses and runs back into the flask. The resulting heat transfer gradually warms the column so that there is a progressive movement of the vapour phase-liquid boundary up the column, with increasing enrichment of the more volatile component. Because of this fractionation, the vapour finally passing into the condenser (where it condenses and flows into the receiver) is commonly that of the lowest-boiling components in the system. The conditions apply until all of the low-boiling material has been distilled, whereupon distillation ceases until the column temperature is high enough to permit the next component to distil. This usually results in a temporary fall in the temperature indicated by the thermometer.

Distillation of liquid mixtures

The principles involved in fractional distillation of liquid mixtures are complex but can be seen by considering a system which approximately obeys *Raoult's law*. (This law states that the vapour pressure of a solution at any given temperature is the sum of the vapour pressures of each component multiplied by its mole fraction in the solution.) If two substances, A and B, having vapour pressures of 600 mmHg and 360 mmHg, respectively, were mixed in a molar ratio of 2:1 (i.e. 0.666:0.333 mole ratio), the mixture would have (ideally) a vapour pressure of 520 mmHg (i.e. 600 x 0.666 + 360 x 0.333, or 399.6 + 119.88 mmHg) and the vapour phase would contain 77% (399.6 x 100/520) of A and 23% (119.88 x 100/520) of B. If this phase was now condensed, the new liquid phase would, therefore, be richer in the volatile component A. Similarly, the vapour in equilibrium with this phase is still further enriched in A. Each such liquid-vapour equilibrium constitutes a "theoretical plate". The efficiency of a fractionating column is commonly expressed as the number of such plates to which it corresponds in operation. Alternatively, this information may be given in the form of the height equivalent to a theoretical plate, or HETP. The number of theoretical plates and equilibria between liquids and vapours are affected by the factors listed to achieve maximum separation by fractional distillation in the section below on techniques.

In most cases, systems deviate to a greater or lesser extent from Raoult's law, and vapour pressures may be greater or less than the values calculated. In extreme cases (e.g. azeotropes), vapour pressure-composition curves pass through maxima or minima, so that attempts at fractional distillation lead finally to the separation of a constant-boiling (azeotropic) mixture and one (but not both) of the pure species if either of the latter is present in excess.

Elevation of the boiling point by dissolved solids. Organic substances dissolved in organic solvents cause a rise in boiling point which is proportional to the concentration of the substance, and the extent of rise in temperature is characteristic of the solvent. The following equation applies for dilute solutions and non-associating substances:

$$\frac{M\,\Delta t}{c} = K$$

where M is the molecular weight of the solute, Δt is the elevation of boiling point in ^{o}C, c is the concentration of solute in grams for 1000 gm of solvent, and K is the *Ebullioscopic Constant* (molecular elevation of the boiling point) for the solvent. K is a fixed property (constant) for the particular solvent. This has been very useful for the determination of the molecular weights of organic substances in solution.

The efficiency of a distillation apparatus used for purification of liquids depends on the difference in boiling points of the pure material and its impurities. For example, if two components of an ideal mixture have vapour pressures in the ratio 2:1, it would be necessary to have a still with an efficiency of at least seven plates (giving an enrichment of $2^7 = 128$) if the concentration of the higher-boiling component in the distillate was to be reduced to less than 1% of its initial value. For a vapour pressure ratio of 5:1, three plates would achieve as much separation.

In a fractional distillation, it is usual to reject the initial and final fractions, which are likely to be richer in the lower-boiling and higher-boiling impurities respectively. The centre fraction can be further purified by repeated fractional distillation.

To achieve maximum separation by fractional distillation:

1. The column must be flooded initially to wet the packing. For this reason it is customary to operate a still at reflux for some time before beginning the distillation.

2. The reflux ratio should be high (i.e. the ratio of drops of liquid which return to the distilling flask and the drops which distil over), so that the distillation proceeds slowly and with minimum disturbance of the equilibria in the column.

3. The hold-up of the column should not exceed one-tenth of the volume of any one component to be separated.

4. Heat loss from the column should be prevented but if the column is heated to offset this, its temperature must not exceed that of the distillate in the column.

5. Heat input to the still-pot should remain constant.

6. For distillation under reduced pressure there must be careful control of the pressure to avoid flooding or cessation of reflux.

Types of distillation

The distilling flask. To minimise superheating of the liquid (due to the absence of minute air bubbles or other suitable nuclei for forming bubbles of vapour), and to prevent bumping, one or more of the following precautions should be taken:

(a) The flask is heated uniformly over a large part of its surface, either by using an electrical heating mantle or, by partial immersion in a bath above the boiling point of the liquid to be distilled (Table 3).

(b) Before heating begins, small pieces of unglazed fireclay or porcelain (porous pot, boiling chips), pumice, diatomaceous earth, or platinum wire are added to the flask. These act as sources of air bubbles.

(c) The flask may contain glass siphons or boiling tubes. The former are inverted J-shaped tubes, the end of the shorter arm being just above the surface of the liquid. The latter comprise long capillary tubes sealed above the lower end.

(d) A steady slow stream of inert gas (e.g. N_2, Ar or He) is passed through the liquid.

(e) The liquid in the flask is stirred mechanically. This is especially necessary when suspended insoluble material is present.

For simple distillations a Claisen flask is often used. This flask is, essentially, a round-bottomed flask to the neck of which is joined another neck carrying a side arm. This second neck is sometimes extended so as to form a Vigreux column [a glass tube in which have been made a number of pairs of indentations which almost touch each other and which slope slightly downwards. The pairs of indentations are arranged to form a spiral of glass inside the tube].

For heating baths, see Table 3. For distillation apparatus on a macro, semi-micro or micro scale see Aldrich and other glassware catalogues. Alternatively, visit some useful websites for suppliers of laboratory glassware, e.g. <www.wheatonsci.com>; <www.sigmaaldrich.com> and <www.kimble-kontes.com>.

Types of columns and packings. A slow distillation rate is necessary to ensure that equilibrium conditions operate and also that the vapour does not become superheated so that the temperature rises above the boiling point. Efficiency is improved if the column is heat insulated (either by vacuum jacketing or by lagging) and, if necessary, heated to just below the boiling point of the most volatile component. Efficiency of separation also improves with increase in the heat of vaporisation of the liquids concerned (because fractionation depends on heat equilibration at multiple liquid-gas boundaries). Water and alcohols are more easily purified by distillation for this reason.

Columns used in distillation vary in their shapes and types of packing. Packed columns are intended to give efficient separation by maintaining a large surface of contact between liquid and vapour. Efficiency of separation is further increased by operation under conditions approaching total reflux, i.e. under a high reflux ratio. However, great care must be taken to avoid flooding of the column during distillation. The minimum number of theoretical plates for satisfactory separation of two liquids differing in boiling point by δt is approximately $(273 + t)/3\delta t$, where t is the average boiling point in ^{o}C.

Some of the commonly used *columns* are:

Bruun column. A type of all-glass bubble-cap column.

Bubble-cap column. A type of plate column in which inverted cups (bubble caps) deflect ascending vapour through reflux liquid lying on each plate. Excess liquid from any plate overflows to the plate lying below it and ultimately returns to the flask. (For further details, see Bruun & Faulconer *Ind Eng Chem (Anal Ed)* **9** 247 *1937*). Like most plate columns, it has a high through-put, but a relatively low number of theoretical plates for a given height.

Dufton column. A plain tube, into which fits closely (preferably ground to fit) a solid glass spiral wound round a central rod. It tends to choke at temperatures above 100^{o} unless it is lagged (Dufton *J Soc Chem Ind* (London) **38** 45T *1919*).

Hempel column. A plain tube (fitted near the top with a side arm) which is almost filled with a suitable packing, which may be of rings or helices.

Oldershaw column. An all-glass perforated-plate column. The plates are sealed into a tube, each plate being equipped with a baffle to direct the flow of reflux liquid, and a raised outlet which maintains a definite liquid level on the plate and also serves as a drain on to the next lower plate [see Oldershaw *Ind Eng Chem (Anal Ed)* **11** 265 *1941*].

Podbielniak column. A plain tube containing "Heli-Grid" Nichrome or Inconel wire packing. This packing provides a number of passage-ways for the reflux liquid, while the capillary spaces ensure very even spreading of the liquid, so that there is a very large area of contact between liquid and vapour while, at the same time, channelling and flooding are minimised. A column 1m high has been stated to have an efficiency of 200-400 theoretical plates (for further details, see Podbielniak *Ind Eng Chem (Anal Ed)* **13** 639 *1941*; Mitchell & O'Gorman *Anal Chem* **20** 315 *1948*).

Stedman column. A plain tube containing a series of wire-gauze discs stamped into flat, truncated cones and welded together, alternatively base-to-base and edge-to-edge, with a flat disc across each base. Each cone has a hole, alternately arranged, near its base, vapour and liquid being brought into intimate contact on the gauze surfaces (Stedman *Can J Research B* **15** 383 *1937*).

Todd column. A column (which may be a Dufton type, fitted with a Monel metal rod and spiral, or a Hempel type, fitted with glass helices) which is surrounded by an open heating jacket so that the temperature can be adjusted to be close to the distillation temperature (Todd *Ind Eng Chem (Anal Ed)* **17** 175 *1945*).

Vigreux column. A glass tube in which have been made a number of pairs of indentations which almost touch each other and which slope slightly downwards. The pairs of indentations are arranged to form a spiral of glass inside the tube.

Widmer column. A Dufton column, modified by enclosing within two concentric tubes the portion containing the glass spiral. Vapour passes up the outer tube and down the inner tube before entering the centre portion. Thus flooding of the column, especially at high temperatures, is greatly reduced (Widmer *Helv Chim Acta* **7** 59 *1924*).

The packing of a column greatly increases the surface of liquid films in contact with the vapour phase, thereby increasing the efficiency of the column, but reducing its capacity (the quantities of vapour and liquid able to flow in opposite directions in a column without causing flooding). Material for packing should be of uniform size, symmetrical shape, and have a unit diameter less than one-eighth that of the column. (Rectification efficiency increases sharply as the size of the packing is reduced but so, also, does the hold-up in the column.) It should also be capable of uniform, reproducible packing.

The usual ***packings*** are:

(a) **Rings.** These may be hollow glass or porcelain (Raschig rings), of stainless steel gauze (Dixon rings), or hollow rings with a central partition (Lessing rings) which may be of porcelain, aluminium, copper or nickel.

(b) **Helices.** These may be of metal or glass (Fenske rings), the latter being used where resistance to chemical attack is important (e.g. in distilling acids, organic halides, some sulphur compounds, and phenols). Metal single-turn helices are available in aluminium, nickel or stainless steel. Glass helices are less efficient, because they cannot be tamped to ensure uniform packing.

(c) **Balls.** These are usually glass.

(d) **Wire packing.** For use of "Heli-Grid" and "Heli-Pak" packings, see references given for Podbielniak column. For Stedman packing, see entry under Stedman column.

Types of condensers:

Air condenser. A glass tube such as the inner part of a Liebig condenser. Used for liquids with boiling points above 90^{o}. Can be of any length.

Allihn condenser. The inner tube of a Liebig condenser is modified by having a series of bulbs to increase the condensing surface. Further modifications of the bubble shapes give the Julian and Allihn-Kronbitter condensers.

Bailey-Walker condenser. A type of all-metal condenser fitting into the neck of extraction apparatus and being supported by the rim. Used for high-boiling liquids.

Coil condenser. An open tube, into which is sealed a glass coil or spiral through which water circulates. The tube is sometimes also surrounded by an outer cooling jacket.

Double surface condenser. A tube in which the vapour is condensed between an outer and inner water-cooled jacket after impinging on the latter. Very useful for liquids boiling below 40°.

Friedrichs condenser. A "cold-finger" type of condenser sealed into a glass jacket open at the bottom and near the top. The cold finger is formed into glass screw threads.

Graham condenser. A type of coil condenser.

Hopkins condenser. A cold-finger type of condenser resembling that of Friedrichs.

Liebig condenser. An inner glass tube surrounded by a glass jacket through which water is circulated.

Othmer condenser. A large-capacity condenser which has two coils of relatively large bore glass tubing inside it, through which the water flows. The two coils join at their top and bottom.

West condenser. A Liebig condenser with a light-walled inner tube and a heavy-walled outer tube, with only a narrow space between them.

Wiley condenser. A condenser resembling the Bailey-Walker type.

Vacuum distillation. This expression is commonly used to denote a distillation under reduced pressure lower than that of the normal atmosphere. As the boiling point of a substance depends on the pressure, it is often possible to distil materials at a temperature low enough to avoid partial or complete decomposition by lowering the pressure, even if they are unstable when boiled at atmospheric pressure.

Sensitive or high-boiling liquids should invariably be distilled or fractionally distilled under reduced pressure. The apparatus is essentially as described for distillation except that ground joints connecting the different parts of the apparatus should be air tight by using grease, or better Teflon sleeves. For low, moderately high, and very high temperatures Apiezon L, M and T greases, respectively, are very satisfactory. Alternatively, it is often preferable to avoid grease and to use thin Teflon sleeves in the joints. The distilling flask, must be supplied with a capillary bleed (which allows a fine stream of air, nitrogen or argon into the flask), and the receiver should be of the fraction collector type. When distilling under vacuum it is very important to place a loose packing of glass wool above the liquid to buffer sudden boiling of the liquid. The flask should be not more than two-thirds full of liquid. The vacuum must have attained a steady state, i.e. the liquid has been completely degassed, before the heat source is applied, and the temperature of the heat source must be raised *very slowly* until boiling is achieved.

If the pump is a filter pump off a high-pressure water supply, its performance will be limited by the temperature of the water because the vapour pressure of water at 10°, 15°, 20° and 25° is 9.2, 12.8, 17.5 and 23.8 mmHg, respectively. The pressure can be measured with an ordinary manometer. For vacuums in the range 10^{-2} mmHg to 10 mmHg, rotary mechanical pumps (oil pumps) are used and the pressure can be measured with a Vacustat McLeod-type gauge. If still higher vacuums are required, for example for high vacuum sublimations, a mercury diffusion pump is suitable. Such a pump can provide a vacuum up to 10^{-6} mmHg. For better efficiencies, the diffusion pump can be backed up by a mechanical pump. In all cases, the mercury pump is connected to the distillation apparatus through several traps to remove mercury vapours. These traps may operate by chemical action, for example the use of sodium hydroxide pellets to react with acids, or by condensation, in which case empty tubes cooled in solid carbon dioxide-ethanol or liquid nitrogen (contained in wide-mouthed Dewar flasks) are used.

Special oil or mercury traps are available commercially, and a liquid-nitrogen (**b** –209.9°C) trap is the most satisfactory one to use between these and the apparatus. It has an advantage over liquid air or oxygen in that it is non-explosive if it becomes contaminated with organic matter. Air should not be sucked through the apparatus before starting a distillation because this will cause liquid oxygen (**b** –183°C) to condense in the liquid nitrogen trap, and this is potentially explosive (especially in mixtures with organic materials). Due to the potential lethal consequences of liquid oxygen/organic material mixtures, care must be exercised when handling liquid nitrogen. Hence, it is advisable to degas the system for a short period before the trap is immersed into the liquid nitrogen (which is kept in a Dewar flask).

Spinning-band distillation. Factors which limit the performance of distillation columns include the tendency to flood (which occurs when the returning liquid blocks the pathway taken by the vapour through the column) and the increased hold-up (which decreases the attainable efficiency) in the column that should, theoretically, be highly efficient. To overcome these difficulties, especially for distillation under high vacuum of heat sensitive or high-boiling highly viscous fluids, spinning band columns are commercially available. In such units, the distillation columns contain a rapidly rotating, motor-driven, spiral band, which may be of polymer-coated metal, stainless steel or platinum. The rapid rotation of the band in contact with the walls of the still gives intimate mixing of descending liquid with ascending vapour while the screw-like motion

of the band drives the liquid towards the still-pot, helping to reduce hold-up. There is very little pressure drop in such a system, and very high throughputs are possible, with high efficiency. For example, a 765-mm long 10-mm diameter commercial spinning-band column is reported to have an efficiency of 28 plates and a pressure drop of 0.2 mmHg for a throughput of 330ml/hour. The columns may be either vacuum jacketed or heated externally. The stills can be operated down to 10^{-5} mmHg. The principle, which was first used commercially in the Podbielniak Centrifugal Superfractionator, has also been embodied in descending-film molecular distillation apparatus.

Steam distillation. When two immmiscible liquids distil, the sum of their (independent) partial pressures is equal to the atmospheric pressure. Hence in steam distillation, the distillate has the composition

$$\frac{\text{Moles of substance}}{\text{Moles of water}} = \frac{P_{substance}}{P_{water}} = \frac{760 - P_{water}}{P_{water}}$$

where the *P*'s are vapour pressures (in mmHg) in the boiling mixture.

The customary technique consists of heating the substance and water in a flask (to boiling), usually with the passage of steam, followed by condensation and separation of the aqueous and non-aqueous phases in the distillate. Its advantages are those of selectivity (because only some water-insoluble substances, such as naphthalene, nitrobenzene, phenol and aniline are volatile in steam) and of ability to distil certain high-boiling substances well below their boiling point. It also facilitates the recovery of a non-steam-volatile solid at a relatively low temperature from a high-boiling solvent such as nitrobenzene. The efficiency of steam distillation is increased if superheated steam is used (because the vapour pressure of the organic component is increased relative to water). In this case the flask containing the material is heated (without water) in an oil bath and the steam passing through it is superheated by prior passage through a suitable heating device (such as a copper coil heated electrically or an oil bath).

Azeotropic distillation. In some cases two or more liquids form constant-boiling mixtures, or azeotropes. Azeotropic mixtures are most likely to be found with components which readily form hydrogen bonds or are otherwise highly associated, especially when the components are dissimilar, for example an alcohol and an aromatic hydrocarbon, but have similar boiling points.

Examples where the boiling point of the distillate is a minimum (less than either pure component) include:
Water with ethanol, *n*-propanol and isopropanol, *tert*-butanol, propionic acid, butyric acid, pyridine,
methanol with methyl iodide, methyl acetate, chloroform,
ethanol with ethyl iodide, ethyl acetate, chloroform, benzene, toluene, methyl ethyl ketone,
benzene with cyclohexane,
acetic acid with toluene.
Although less common, azeotropic mixtures are known which have higher boiling points than their components. These include water with most of the mineral acids (hydrofluoric, hydrochloric, hydrobromic, perchloric, nitric and sulfuric) and formic acid. Other examples are acetic acid-pyridine, acetone-chloroform, aniline-phenol, and chloroform-methyl acetate.

The following azeotropes are important commercially for drying ethanol:

ethanol 95.5% (by weight) - water 4.5%	**b** 78.1°
ethanol 32.4% - benzene 67.6%	**b** 68.2°
ethanol 18.5% - benzene 74.1% - water 7.4%	**b** 64.9°

Materials are sometimes added to form an azeotropic mixture with the substance to be purified. Because the azeotrope boils at a different temperature, this facilitates separation from substances distilling in the same range as the pure material. (Conversely, the impurity might form the azeotrope and be removed in this way.) This method is often convenient, especially where the impurities are isomers or are otherwise closely related to the desired substance. Formation of low-boiling azeotropes also facilitates distillation.

One or more of the following methods can generally be used for separating the components of an azeotropic mixture:

1. By using a chemical method to remove most of one species prior to distillation. (For example, water can be removed by suitable drying agents; aromatic and unsaturated hydrocarbons can be removed by sulfonation).
2. By redistillation with an additional substance which can form a ternary azeotropic mixture (as in the ethanol-water-benzene example given above).
3. By selective adsorption of one of the components. (For example, of water on to silica gel or molecular sieves, or of unsaturated hydrocarbons onto alumina).
4. By fractional crystallisation of the mixture, either by direct freezing or by dissolving in a suitable solvent.

Kügelrohr distillation. The Aldrich Kügelrohr Distillation Apparatus (see Aldrich-Sigma Labware catalogue) is made up of small glass bulbs (*ca* 4–5cm diameter) which are joined together *via* Quickfit joints at each pole of the bulbs. The liquid (or low melting solid) to be purified is placed in the first bulb of a series of bulbs joined end to end, and the system can be evacuated. The first bulb is heated in a furnace (e.g. Büchi Kügelrohr micro distillation oven from Sigma-Aldrich Labware catalogue) at a high temperature whereby most of the material distils into the second bulb (which is outside of the furnace). The second bulb is then moved into the furnace and the furnace temperature is reduced by *ca* 5º whereby the liquid in the second bulb distils into the third bulb (at this stage the first bulb is now out at the back of the furnace, and the third and subsequent bulbs are outside the front of the furnace). The furnace temperature is lowered by a further *ca* 5º, and the third bulb is moved into the furnace. The lower boiling material will distil into the fourth bulb. The process is continued until no more material distils into the subsequent bulb. The vacuum (if applied) and the furnace are removed, the bulbs are separated and the various fractions of distillates are collected from the individual bulbs. For volatile liquids, it may be necessary to cool the receiving bulb with solid CO_2 held in a suitable container (a Kügelrohr distillation apparatus with an integrated cooling system is available). This procedure is used for preliminary purification and the distillates are then redistilled or recrystallised.

Isopiestic or isothermal distillation. This technique can be useful for the preparation of metal-free solutions of volatile acids and bases for use in trace metal studies. The procedure involves placing two beakers, one of distilled water and the other of a solution of the material to be purified, in a desiccator. The desiccator is sealed and left to stand at room temperature for several days. The volatile components distribute themselves between the two beakers whereas the non-volatile contaminants remain in the original beaker. This technique has afforded metal-free pure solutions of ammonia, hydrochloric acid and hydrogen fluoride.

RECRYSTALLISATION

Techniques

The most commonly used procedure for the purification of a solid material by recrystallisation from a solution involves the following steps:

(a) The impure material is dissolved in a suitable solvent, by shaking or vigorous stirring, at or near the boiling point, to form a near-saturated solution.
(b) The hot solution is filtered to remove any insoluble particles. To prevent crystallisation during this filtration, a heated filter funnel can be used, or the solution can be diluted with more of the solvent.
(c) The solution is then allowed to cool so that the dissolved substance crystallises out.
(d) The crystals are separated from the mother liquor, either by centrifuging or by filtering, under suction, through a sintered glass, a Hirsch or a Büchner, funnel. Usually, centrifugation is preferred because of the greater ease and efficiency of separating crystals and mother liquor, and also because of the saving of time and effort, particularly when very small crystals are formed or when there is entrainment of solvent.
(e) The crystals are washed free from mother liquor with a little fresh cold solvent, then dried.

If the solution contains extraneous coloured material likely to contaminate the crystals, this can often be removed by adding some activated charcoal (decolorising carbon) to the hot, but not boiling, solution which is then shaken frequently for several minutes before being filtered. (The large active surface of the carbon makes it a good adsorbent for this purpose.) In general, the cooling and crystallisation steps should be rapid so

as to give small crystals which occlude less of the mother liquor. This is usually satisfactory with inorganic material, so that commonly the filtrate is cooled in an ice-water bath while being vigorously stirred. In many cases, however, organic molecules crystallise much more slowly, so that the filtrate must be set aside to cool to room temperature or left in the refrigerator. It is often desirable to subject material that is very impure to preliminary purification, such as steam distillation, Soxhlet extraction, or sublimation, before recrystallising it. A greater degree of purity is also to be expected if the crystallisation process is repeated several times, especially if different solvents are used. The advantage of several crystallisations from different solvents lies in the fact that the material sought, and its impurities, are unlikely to have similar solubilities as solvents and temperatures are varied.

For the final separation of solid material, sintered-glass discs are preferable to filter paper. Sintered glass is unaffected by strongly acidic solutions or by oxidising agents. Also, with filter paper, cellulose fibres are likely to become included in the sample. The sintered-glass discs or funnels can be readily cleaned by washing in freshly prepared *chromic acid cleaning mixture*. This mixture is made by adding 100ml of concentrated sulfuric acid slowly with stirring to a solution of 5g of sodium dichromate (CARE: cancer suspect) in 5ml of water. (The mixture warms to about 70°, and sulfuric acid becomes hot when water is added to it; see p 3).

For materials with very low melting points it is sometimes convenient to use dilute solutions in acetone, methanol, pentane, diethyl ether or $CHCl_3/CCl_4$. The solutions are cooled to –78° in a dry-ice/acetone bath, to give a slurry which is filtered off through a precooled Büchner funnel. Experimental details, as applied to the purification of nitromethane, are given by Parrett and Sun [*J Chem Educ* **54** 448 *1977*].

Where substances vary little in solubility with temperature, *isothermal crystallisation* may sometimes be employed. This usually takes the form of a partial evaporation of a saturated solution at room temperature by leaving it under reduced pressure in a desiccator.

However, in rare cases, crystallisation is not a satisfactory method of purification, especially if the impurity forms crystals that are isomorphous with the material being purified. In fact, the impurity content may even be greater in such recrystallised material. For this reason, it still remains necessary to test for impurities and to remove or adequately lower their concentrations by suitable chemical manipulation prior to recrystallisation.

Filtration. Filtration removes particulate impurities rapidly from liquids and is also used to collect insoluble or crystalline solids which separate or crystallise from solution. The usual technique is to pass the solution, cold or hot, through a fluted filter paper in a conical glass funnel.

If a solution is hot and needs to be filtered rapidly, a Büchner funnel and flask are used and filtration is performed under a slight vacuum (water pump), the filter medium being a circular cellulose filter paper wet with solvent. If filtration is slow, even under high vacuum, a pile of about twenty filter papers, wet as before, are placed in the Büchner funnel and, as the flow of solution slows down, the upper layers of the filter paper are progressively removed. Alternatively, a filter aid, e.g. Celite, Florisil or Hyflo-supercel, is placed on top of a filter paper in the funnel. When the flow of the solution (under suction) slows down, the upper surface of the filter aid is scratched gently. Filter papers with various pore sizes are available covering a range of filtration rates. Hardened filter papers are slow filtering, but they can withstand acidic and alkaline solutions without appreciable hydrolysis of the cellulose (see Table 4). When using strong acids it is preferable to use glass micro fibre filters, which are commercially available (see Tables 4 and 5).

Freeing a solution from extremely small particles [e.g. for optical rotatory dispersion (ORD) or circular dichroism (CD) measurements] requires filters with very small pore size. Commercially available (Millipore, Gelman, Nucleopore) filters other than cellulose or glass include nylon, Teflon, and polyvinyl chloride, and the pore diameter may be as small as 0.01 micron (see Table 9). Special containers are used to hold the filters, through which the solution is pressed by applying pressure, e.g. from a syringe. Some of these filters can be used to clear strong sulfuric acid solutions.

As an alternative to the Büchner funnel for collecting crystalline solids, a funnel with a sintered glass-plate under suction may be used. Sintered-glass funnels with various porosities are commercially available and can be easily cleaned with warm chromic or nitric acid (see above).

When the solid particles are too fine to be collected on a filter funnel because filtration is extremely slow, separation by **centrifugation** should be used. Bench-type centrifuges are most convenient for this purpose. The solid is placed in the centrifuge tube, the tubes containing the solutions on opposite sides of the rotor should be balanced accurately (at least within 0.05 to 0.1g), and the solutions are spun at maximum speed for as long as it takes to settle the solid (usually *ca* 3–5 minutes). The solid is washed (by shaking) with cold solvent by centrifugation, and finally twice with a pure volatile solvent in which the solid is insoluble,also by centrifugation.

After decanting the supernatant, the residue is dried in a vacuum, at elevated temperatures if necessary. In order to avoid "spitting" and contamination with dust while the solid in the centrifuge tube is dried, the mouth of the tube is covered with aluminium foil and held fast with a tight rubber band near the lip. The flat surface of the aluminium foil is then perforated in several places with a pin, and the tube and contents are dried in a vacuum desiccator over a desiccant.

Solvents

Choice of solvents. The best solvents for recrystallisation have the following properties:

(a) The material is much more soluble at higher temperatures than it is at room temperature or below.
(b) Well-formed (but not large) crystals are produced.
(c) Impurities are either very soluble or only sparingly soluble.
(d) The solvent must be readily removed from the purified material.
(e) There must be no reaction between the solvent and the substance being purified.
(f) The solvent must not be inconveniently volatile or too highly flammable. (These are reasons why diethyl ether and carbon disulfide are not commonly used in this way.)

The following generalisations provide a rough guide to the selection of a suitable solvent:

(a) Substances usually dissolve best in solvents to which they are most closely related in chemical and physical characteristics. Thus, hydroxylic compounds are likely to be most soluble in water, methanol, ethanol, acetic acid or acetone. Similarly, petroleum ether might be used with water-insoluble substances. However, if the resemblance is too close, solubilities may become excessive.
(b) Higher members of homologous series approximate more and more closely to their parent hydrocarbon.
(c) Polar substances are more soluble in polar than in non-polar solvents.

Although Chapters 4, 5 and 7 provide details of the solvents used for recrystallising a large portion of commercially available laboratory chemicals, they cannot hope to be exhaustive, nor need they necessarily be the best choice, but they are the solvents reported in the literature. In other cases where it is desirable to use this process, it is necessary to establish whether a given solvent is suitable. This is usually done by taking only a small amount of material in a small test-tube and adding enough solvent to cover it. If it dissolves readily in the cold or on gentle warming, the solvent is unsuitable. Conversely, if it remains insoluble when the solvent is heated to boiling (adding more solvent if necessary), the solvent is again unsuitable. If the material dissolves in the hot solvent but does not crystallise readily within several minutes of cooling in an ice-salt mixture, another solvent should be tried.

Water

The properties and purification of water are described in the “Inorganic Compounds” section of Chapter 5. Fluka (Riedel-de Haën) supply purified water prepared specifically for a variety of uses, e.g. LC-MS, HPLC, gradient elution, for cell biology which is freed from enterotoxins by ultrafiltration and autoclaving, for organic and for inorganic trace analysis, for residue analysis and other analytical purposes. Some of these have been prepared by reverse osmosis, or ultrafiltration, under clean room conditions and filtered through 0.2 μm membranes into bottles of high purity glass under inert gas. They have a limited shelf life once opened most probably because O_2 from the air dissolves readily in the water. The solubility of O_2 in 100 ml of water is ~1.02 ml (0.455 mM) at 0°, 0.68 ml (0.282 mM) at 20°, 0.63 ml (0.258 mM) at 25°, 0.63 ml (0.237 mM) at 30°, and 0.12 ml (0.033 mM) at 100°, all at ~760 mmHg in equilibrium with air (see Tables 20–23). This is in comparison with the concentration of O_2 of 0.23 mM in 0.1M Tris HCl buffer at pH 7.2 and 25° in equilibrium with air at 760 mmHg. Routinely, water is best purified by redistilling it twice in an all glass apparatus, storing it under N_2 or He in stoppered glass containers and, if necessary, preferably subjected to ultrafiltration through a single or multistage 0.2 μm membrane system or reverse osmosis (visit <www.millipore.com>). If oxygen-free water is required, N_2 or argon should be bubbled through a sintered glass frit in the highly purified water for 2–3 hours, and stoppered immediately. It is best to use a glass container from which the water can be withdrawn without it coming into contact with air. Note that boiling and distilling water, and condensing it in an inert atmosphere should de-gas it.

Petroleum ethers are commercially available fractions of refined petroleum and are sold in fractions of about 20° boiling ranges. This ensures that little of the hydrocarbon ingredients boiling below the range is lost during standing or boiling when recrystallising a substance. Petroleum ethers with boiling ranges (at 760 mm pressure) of 35–60°, 40–60°, 60–80°, 80–100°, and 100–120° are generally free from unsaturated and aromatic hydrocarbons. The lowest boiling petroleum ether commercially available has **b** 30–40°/760 mm and is mostly *n*-pentane. The purer spectroscopic grades are almost completely free from olefinic and aromatic hydrocarbons. ***Petroleum spirit*** (which is sometimes used synonymously with petroleum ether or light petroleum) is usually less refined petroleum, and ***ligroin*** is used for fractions boiling above 100°. The lower boiling fractions consist of mixtures of *n*-pentane (**b** 36°), *n*-hexane (**b** 68.5°) and *n*-heptane (**b** 98°), and some of their isomers in varying proportions. For purification see petroleum ether b 35–60° in "Aliphatic Compounds", chapter 4, which is typical.

Solvents commonly used for recrystallisation, and their boiling points, are given in Table 6.
For comments on the toxicity and use of **benzene** see the "Introduction" pages of Chapters 4, 5 and 6.

Mixed Solvents. Where a substance is too soluble in one solvent and too insoluble in another, for either to be used for recrystallisation, it is often possible (provided the solvents are miscible) to use them as a mixed solvent system. (In general, however, it is preferable to use a single solvent if this is practicable.) Table 7 contains many of the common pairs of miscible solvents.
Several procedures with mixed solvents have been used successfully for crystallisation. These include the following:
(a) The material is dissolved in the solvent in which it is more soluble at room temperature, then the second solvent (heated to near boiling) is added cautiously to the cold solution until a slight turbidity persists or crystallisation begins. The turbidity is cleared by warming or by adding several drops of the first solvent, and the clear solution is allowed to cool slowly for crystallisation to occur. The supernatant is decanted off carefully (do not disturb the crystals unduly) and more of the second solvent is added to the clear decanted supernatant until turbidity begins again, and is set aside for further crystals to form. The procedure is repeated until no more crystals separate.
(b) A variation of the procedure in (a) is simply to precipitate the material in a microcrystalline form from solution in one solvent at room temperature, by adding a little more of the second solvent also at room temperature, filtering off the crystals, adding a little more of the second solvent and repeating the process. This ensures, at least in the first or last precipitation, a material which contains as little as possible of the impurities, which may also be precipitated in this way. With inorganic salts or metal salts of organic acids, the first solvent is commonly water, and the second solvent is alcohol or acetone. With salts of organic bases and inorganic acids, e.g. hydrochloride, or salts of organic acids and organic bases, the first solvent is usually an alcohol or acetone, in which the salt is very soluble and the second solvent is dry diethyl ether.
(c) A very concentrated solution of the compound in the first solvent in one beaker, and a second beaker containing the second solvent in which the compound is insoluble are placed in a desiccator. As the vapours of the two solvents equilibrate in the desiccator, and crystals separate in the first beaker that contains the compound.
(d) This procedure is best carried out in a cold room (at *ca* 4°). A strong solution of the solid in the solvent in which it is very soluble is *layered* carefully with the second solvent. As the second solvent diffuses and dissolves into the solution, crystals begin to form at the 'interface'. When separation of crystals is complete and the solvent mixture is homogeneous, another layer of the second solvent is applied and the process is repeated.
Seeding is well known to initiate the crystallisation process. A good way to procure seed crystals is to dissolve the crystals in the minimum amount of solvent, place the solution in a watch glass, then blow a fine stream of dry N_2 or argon gently over the surface of the solution until seed crystals are formed. Alternatively, the inert gas is allowed to evaporate all the solvent, and the residual crystals or fine powder are used for seeding. The seeds are applied in the above procedures at the appropriate time, e.g. when first turbidity appears, or placed onto the tip of a glass rod which is then rubbed against the sides of the container of the solution until crystallisation begins.

Recrystallisation from the melt

A crystalline solid melts when its temperature is raised sufficiently for the thermal agitation of its molecules or ions to overcome the restraints imposed by the crystal lattice. Usually, impurities weaken crystal structures, and hence lower the melting points of solids (or the freezing points of liquids). If an impure material is melted and cooled slowly (with the addition, if necessary, of a trace of solid material near the freezing point to avoid supercooling), the first crystals that form will usually contain less of the impurity, so that fractional solidification by partial freezing can be used as a purification process for solids with melting points lying in a convenient temperature range (or for more readily frozen liquids). Some examples of cooling baths that are

useful in recrystallisation are summarised in Table 8. In some cases, impurities form higher melting eutectics with substances to be purified, so that the first material to solidify is less pure than the melt. For this reason, it is often desirable to discard the first crystals and also the final portions of the melt. Substances having similar boiling points often differ much more in melting points, so that fractional solidification can offer real advantages, especially where ultrapurity is sought. For further information on this method of recrystallisation, consult the earlier editions of this book as well as references by Schwab and Wichers (*J Res Nat Bur Stand* **25** 747 *1940*). This method works best if the material is already nearly pure, and hence tends to be a final purification step.

Zone refining. Zone refining (or zone melting) is a particular development for fractional solidification and is applicable to all crystalline substances that show differences in the concentrations of impurities in liquid and solid states at solidification. The apparatus used in this technique consists essentially of a device in which the crystalline solid to be purified is placed in a glass tube (set vertically) which is made mechanically to move slowly upwards while it passes through a fixed coil (one or two turns) of heated wire. A narrow zone of molten crystals is formed when the tube is close to the heated coil. As the zone moves away from the coil the liquid crystallises, and a fresh molten zone is formed below it at the coil position. The machine can be set to recycle repeatedly. At its advancing side, the zone has a melting interface with the impure material whereas on the upper surface of the zone there is a constantly growing face of higher-melting, resolidified purer material. This leads to a progressive increase in impurity in the liquid phase which, at the end of the run, is discarded from the bottom of the tube. Also, because of the progressive increase in impurity in the liquid phase, the resolidified material contains correspondingly less of the impurites. For this reason, it is usually necessary to make several zone-melting runs before a sample is satisfactorily purified. This is also why the method works most successfully if the material is already fairly pure. In all these operations the zone must travel slowly enough to enable impurities to diffuse or be convected away from the area where resolidification is occurring.
The technique finds commercial application in the production of metals of extremely high purity (tubes other than glass are used in these cases, and impurities are reduced down to 10^{-9} ppm), in purifying refractory oxides, and in purifying organic compounds, using commercially available equipment. Criteria for indicating that definite purification is achieved include elevation of melting point, removal of colour, fluorescence or smell, and a lowering of electrical conductivity. Difficulties likely to be found with organic compounds, especially those of low melting points and low rates of crystallisation, are supercooling and, because of surface tension and contraction, the tendency of the molten zone to seep back into the recrystallised areas. The method is likely to be useful in cases where fractional distillation is not practicable, either because of unfavourable vapour pressures or ease of decomposition, or where super-pure materials are required. The method has been used for the latter purpose for purifying anthracene, benzoic acid, chrysene, morphine, 1,8-naphthyridine and pyrene to name a few. [See E.F.G. Herington, *Zone Melting of Organic Compound*s, Wiley & Sons, NY, 1963; W. Pfann, *Zone Melting*, 2nd edn, Wiley, NY, 1966; H. Schildknecht, *Zonenschmelzen*, Verlag Chemie, Weinheim, 1964; W.R. Wilcox, R.Friedenberg et al. *Chem Rev* **64** 187 *1964*; M. Zief and W.R. Wilcox (Eds), *Fractional Solidification*, Vol I, M Dekker Inc. NY, 1967.]

SUBLIMATION

Sublimation differs from ordinary distillation because the vapour condenses to a solid instead of a liquid. Usually, the pressure in the heated system is diminished by pumping, and the vapour is condensed (after travelling a relatively short distance) onto a cold finger or some other cooled surface. This technique, which is applicable to many organic solids, can also be used with inorganic solids such as aluminium chloride, ammonium chloride, arsenious oxide and iodine to name a few. In some cases, passage of a stream of inert gas over the heated substance secures adequate vaporisation and reduces oxidation. This procedure has the added advantage of removing occluded solvent used for recrystallising the solid.

CHROMATOGRAPHY

Chromatography is often used with advantage for the purification of small, and large, amounts of complex organic mixtures. Chromatography techniques all rely on the differential distribution of the various components in the solution, between the mobile phase and the stationary phase. The mobile phase can either be a gas or a liquid, whereas the stationary phase can either be a solid or a non-volatile liquid adsorbed on a solid surface.

The major chromatographic techniques can also be categorised according to the nature of the mobile phase used – vapour phase chromatography for when a gas is the mobile phase and liquid chromatography for when a liquid is the mobile phase.
The suppliers of chromatography equipment for every need are too numerous to list here but can be viewed on the internet under "Chromatography products". Details and orders can be obtained from the respective websites listed at the end of the section on HPLC below.

Vapour phase chromatography (GC or gas-liquid chromatography)

The mobile phase in vapour phase chromatography is a gas (e.g. hydrogen, helium, nitrogen or argon), and the stationary phase is a non-volatile liquid impregnated onto a porous material. The mixture to be purified is injected into a heated inlet whereby it is vaporised and taken into the column by the carrier gas. It is separated into its components by partition between the liquid on the porous support and the gas. For this reason vapour-phase chromatography is sometimes referred to as gas-liquid chromatography (g.l.c). Vapour phase chromatography is very useful for the resolution of a mixture of volatile compounds. This type of chromatography uses either packed or capillary columns. Packed columns have internal diameters of 3–5 mm with lengths of 2–6 metres. These columns can be packed with a range of materials including firebrick derived materials (chromasorb P, for separation of non-polar hydrocarbons) or diatomaceous earth (chromasorb W, for separation of more polar molecules such as acids, amines). Capillary columns have stationary phase bonded to the walls of long capillary tubes. The diameters of capillary columns are less than 0.5 mm, and the lengths of these columns can go up to 50 metres! These columns have much superior separating powers than the packed columns. Elution times for equivalent resolutions with packed columns can be up to ten times shorter. It is believed that almost any mixture of compounds can be separated using one of the four stationary phases, OV-101, SE-30, OV-17 and Carbowax-20M. Capillary columns for analysis in gas chromatography are now routinely used. An extensive range of packed and capillary columns is available from chromatographic specialists such as Supelco, Alltech, Hewlett-Packard, Phenomenex (for stainless steel capillary columns see <phenomenex.com>, etc. (see above and at the end of the section on HPLC below).
Table 9 shows some typical liquids used for stationary phases in gas chromatography.
Although gas chromatography is routinely used for the analysis of mixtures, this form of chromatography can also be used for separation/purification of substances. This is known as preparative GC. In preparative GC, suitably packed columns are used, and as substances emerge from the column, they are collected by condensing the vapour of these separated substances in suitable traps. The carrier gas blows the vapour through these traps; hence these traps have to be very efficient. Improved collection of the effluent vaporised fractions in preparative work is attained by strong cooling, increasing the surface of the traps by packing them with glass wool, and/or by applying an electrical potential which neutralises the charged vapour and causes it to condense.
When the gas chromatograph is attached to a mass spectrometer, a very powerful analytical tool (*gas chromatography-mass spectrometry*; **GC-MS**) is produced. Gas chromatography allows the separation of mixtures but does not allow the definitive identification of unknown substances, whereas mass spectrometry is good for the identification of individual compounds of the mixtures of compounds. This means that with GC-MS, both separation *and* identification of substances in mixtures can be achieved. The spectrometer can be connected to a computer that has a library from which the mass peaks can be compared and is a very powerful analytical tool. Because of the relatively small amounts of material required for mass spectrometry, a splitting system is inserted between the column and the mass spectrometer. This enables only a small fraction of the effluent to enter the spectrometer; the rest of the effluent is usually collected or vented to the air.
For more detail on apparatus and chromatographic columns see http://www.sigmaaldrich.com/analytical-chromatography/gas-chromatography.html and websites at the end of the section on HPLC below.

Liquid chromatography

In contrast to vapour phase chromatography, the mobile phase in liquid chromatography is a liquid. In general, there are four main types of liquid chromatography: *adsorption*, *partition*, *ion-chromatography*, and *gel filtration*.

Adsorption chromatography is based on the difference in the extent to which substances in solution are adsorbed onto a suitable surface. The main techniques in adsorption chromatography are TLC (thin layer chromatography), paper and column chromatography.

Thin layer chromatography **(TLC)**. In thin layer chromatography, the mobile phase, i.e. the solvent, creeps up the stationary phase (the absorbent) by capillary action. The adsorbent (e.g. silica, alumina, cellulose) is spread on a rectangular glass plate (or solid inert plastic sheet or aluminium foil). Some adsorbents (e.g. silica) are mixed with a setting material (e.g. $CaSO_4$) by the manufacturers which causes the film to set hard on drying. The adsorbent can be activated by heating at 100–110° for a few hours. Other adsorbents (e.g. celluloses) adhere on glass plates without a setting agent. Thus some grades of absorbents have prefixes; e.g. prefix G means that the absorbent can cling to a glass plate and is used for TLC (e.g. silica gel GF_{254} is for TLC plates which have a dye that fluoresces under 254nm UV light). Those lacking this binder have the letter H after any coding and is suitable for column chromatography e.g. silica gel 60H. The materials to be purified or separated are spotted in a solvent close to the lower end of the plate and allowed to dry. The spots will need to be placed at such a distance so as to ensure that when the lower end of the plate is immersed in the solvent, the spots are a few mm above the eluting solvent. The plate is placed upright in a tank containing the eluting solvent. Elution is carried out in a closed tank to ensure equilibrium. Good separations can be achieved with square plates if a second elution is performed at right angles to the first using a second solvent system. For rapid work, plates of the size of microscopic slides or even smaller are used which can decrease the elution time and cost without loss of resolution. The advantage of plastic backed and aluminium foil backed plates is that the size of the plate can be made as required by cutting the sheet with scissors or a sharp guillotine. Visualisation of substances on TLC can be carried out using UV light if they are UV absorbing or fluorescing substances or by spraying or dipping the plate with a reagent that gives coloured products with the substance (e.g. iodine solution or vapour gives brown colours with amines), or with dilute sulfuric acid (organic compounds become coloured or black when the plates are heated at 100° if the plates are of alumina or silica, but not cellulose). (See Table 10 for some methods of visualisation.) Some alumina and silica powders are available with fluorescent materials in them, in which case the whole plate fluoresces under UV light. Non-fluorescing spots are thus clearly visible, and fluorescent spots invariably fluoresce with a different colour. The colour of the spots can be different under UV light at 254 nm and at 365 nm. Another useful way of showing up non-UV absorbing spots is to spray the plate with a 1–2% solution of Rhodamine 6G in acetone. Under UV light the dye fluoresces and reveals the non-fluorescing spots. For preparative work, if the material in the spot or fraction is soluble in ether or petroleum ether, the desired substance can be extracted from the absorbent with these solvents which leave the water soluble dye behind.

TLC can be used as an analytical technique, or as a guide to establishing conditions for column chromatography or as a preparative technique in its own right.

The thickness of the absorbent on the TLC plates could be between 0.2 mm to 2 mm or more. In preparative work, the thicker plates are used and hundreds of milligrams of mixtures can be purified conveniently and quickly. The spots or areas are easily scraped off the plates and the desired substances extracted from the absorbent with the required solvent. For preparative TLC, non-destructive methods for visualising spots and fractions are required. As such, the use of UV light is very useful. If substances are not UV active, then a small section of the plate (usually the right or left edge of the plate) is sprayed with a visualising agent while the remainder of the plate is kept covered.

Thin layer chromatography has been used successfully with ion-exchange celluloses as stationary phases and various aqueous buffers as mobile phases. Also, gels (e.g. Sephadex G-50 to G-200 superfine) have been adsorbed on glass plates and are good for fractionating substances of high molecular weights (1500 to 250,000). With this technique, which is called *thin layer gel filtration* (**TLG**), molecular weights of proteins can be determined when suitable markers of known molecular weights are run alongside (see Chapter 6).

Commercially available pre-coated plates with a variety of adsorbents are generally very good for quantitative work because they are of a standard quality. Plates of a standardised silica gel 60 (as medium porosity silica gel with a mean porosity of 6 mm) released by Merck have a specific surface of 500 m^2/g and a specific pore volume of 0.75 ml/g. They are so efficient that they have been called *high performance thin layer chromatography* (**HPTLC**) plates (Ropphahn & Halpap *J Chromatogr* **112** 81 *1975*). In another variant of thin layer chromatography the adsorbent is coated with an oil as in gas chromatography thus producing *reverse-phase thin layer chromatography*. Reversed-phase TLC plates e.g. silica gel RP-18 are available from Fluka and Merck.

A very efficient form of chromatography makes use of a circular glass plate (rotor) coated with an adsorbent (silica, alumina or cellulose). As binding to a rotor is needed, the sorbents used may be of a special quality and/or binders are added to the sorbent mixtures. For example when silica gel is required as the absorbent, silica gel 60 PF-254 with calcium sulfate (Merck catalog 7749) is used. The thickness of the absorbent (1, 2 or 4mm) can vary depending on the amount of material to be separated. The apparatus used is called a **Chromatotron** (available from Harrison Research, USA). The glass plate is rotated by a motor, and the sample followed by the eluting solvent is allowed to drip onto a central position on the plate. As the plate rotates the solvent elutes the

mixture, centrifugally, while separating the components in the form of circular bands radiating from the central point. The separated bands are usually visualised conveniently by UV and as the bands approach the edge of the plate, the eluent is collected. The plate with the adsorbent can be re-used many times if care is employed in the usage, and hence this form of chromatography utilises less absorbents as well as solvents.
Recipes and instructions for coating the rotors are available from the Harrison website <http://www.harrisonresearch.com/chromatotron/>. In addition, information on how to regenerate the sorbents and binders is also included.

Paper chromatography. This is the technique from which thin layer chromatography was developed. It uses cellulose paper (filter paper) instead of the TLC adsorbent and does not require a backing like the plastic sheet in TLC. It is used in the **ascending procedure** (like in TLC) whereby a sheet of paper is hung in a jar, and the materials to be separated are spotted (after dissolving in a suitable solvent and drying) near the bottom of the sheet which dips into the eluting solvent just below the spots. As the solvent rises up the paper the spots are separated according to their adsorption properties. A variety of solvents can be used, the sheet is then dried in air (fume cupboard), and can then be run again with the solvent running at right angles to the first run to give a two-dimensional separation. The spots can then be visualised as in TLC or can be cut out and analysed as required. A **descending procedure** had also been developed where the material to be separated is spotted near the top of the paper and the top end is made to dip into a tray containing the eluting solvent. The whole paper is placed in a glass jar, and the solvent then runs down the paper causing the materials in the spots to separate also according to their adsorption properties and to the eluting ability of the solvent. This technique is much cheaper than TLC and is still used (albeit with thicker cellulose paper) with considerable success for the separation of protein hydrolysates for sequencing analysis and/or protein identification. However, modern and more efficient technologies are available for analysing proteins and their hydrolysates although the equipment is expensive. (Whatman papers for chromatography and electrophoresis are available also from Sigma-Aldrich Labware.)

Column Chromatography. The substances to be purified are usually placed on the top of the column and the solvent is run down the column. Fractions are collected and checked for compounds using TLC (UV and/or other means of visualisation). The adsorbent for chromatography can be packed dry and solvents to be used for chromatography are used to equilibrate the adsorbent by flushing the column several times until equilibration is achieved. Alternatively, the column containing the adsorbent is packed wet (slurry method), and pressure is applied at the top of the column until the column is well packed (i.e. the adsorbent is settled).

Graded Adsorbents and Solvents. Some materials used in columns for adsorption chromatography are grouped in Table 11 in an approximate order of effectiveness. Other adsorbents sometimes used include barium carbonate, calcium sulfate, calcium phosphate, charcoal (usually mixed with Kieselguhr or other form of diatomaceous earth, for example, the filter aid Celite) and cellulose. The alumina can be prepared in several grades of activity (see below).
In most cases, adsorption takes place most readily from non-polar solvents such as petroleum ether and least readily from polar solvents such as alcohols, esters, and acetic acid. Common solvents, arranged in approximate order of increasing eluting ability are also given in Table 11. Eluting power roughly parallels the dielectric constants of solvents. The series also reflects the extent to which the solvent binds to the column material, thereby displacing the substances that are already adsorbed. This preference of alumina and silica gel for polar molecules explains, for example, the use of percolation through a column of silica gel for the following purposes-drying of ethylbenzene, removal of aromatics from 2,4-dimethylpentane and of ultraviolet absorbing substances from cyclohexane.
Mixed solvents are intermediate in strength, and so provide a finely graded series. In choosing a solvent for use as an eluent it is necessary to consider the solubility of the substance in it and the ease with which it can subsequently be removed.

Preparation and Standardisation of Alumina. The activity of alumina depends inversely on its water content, and a sample of poorly active material can be rendered more active by leaving for some time in a round bottomed flask heated up to about 200^{o} in an oil bath or a heating mantle while a slow stream of a dry inert gas is passed through it. *Alternatively*, it is heated to red heat (380–400^{o}) in an open vessel for 4–6 hours with occasional stirring and then cooled in a vacuum desiccator: this material is then of grade I activity. Conversely, alumina can be rendered less active by adding small amounts of water and thoroughly mixing for several hours. Addition of about 3% (w/w) of water converts grade I alumina to grade II.

Used alumina can be regenerated by repeated extraction, first with boiling methanol, then with boiling water, followed by drying and heating. The degree of activity of the material can be expressed conveniently in terms of the scale due to Brockmann and Schodder (*Chem Ber* B **74** 73 *1941*).

Alumina is normally slightly alkaline. A (less strongly adsorbing) neutral alumina can be prepared by making a slurry in water and adding 2M hydrochloric acid until the solution is acid to Congo red. The alumina is then filtered off, washed with distilled water until the wash water gives only a weak violet colour with Congo red paper, and dried.
Alumina used in TLC can be recovered by washing in ethanol for 48 hours with occasional stirring, to remove binder material and then washed with successive portions of ethyl acetate, acetone and finally with distilled water. Fine particles are removed by siphoning. The alumina is first suspended in 0.04M acetic acid, then in distilled water, siphoning off 30 minutes after each wash. The process is repeated 7–8 times. It is then dried and activated at 200° [Vogh & Thomson *Anal Chem* **53** 1365 *1981*].

Preparation of other adsorbents

Silica gel can be prepared from commercial water-glass by diluting it with water to a density of 1.19 and, while keeping it cooled to 5°, adding concentrated hydrochloric acid with stirring until the solution is acid to thymol blue. After standing for 3 hours, the precipitate is filtered off, washed on a Büchner funnel with distilled water, then suspended in 0.2M hydrochloric acid. The suspension is set aside for 2–3 days, with occasional stirring, then filtered, washed well with water and dried at 110°. It can be activated by heating up to about 200° as described for alumina.
Powdered commercial silica gel can be purified by suspending and standing overnight in concentrated hydrochloric acid (6 ml/g), decanting the supernatant and repeating with fresh acid until the latter remains colourless. After filtering with suction on a sintered-glass funnel, the residue is suspended in water and washed by decantation until free of chloride ions. It is then filtered, suspended in 95% ethanol, filtered again and washed on the filter with 95% ethanol. The process is repeated with anhydrous diethyl ether before the gel is heated for 24 hours at 100° and stored for another 24 hours in a vacuum desiccator over phosphorus pentoxide.
To buffer silica gel for flash chromatography (see later), 200g of silica is stirred in 1L of 0.2M NaH_2PO_4 for 30 minutes. The slurry is then filtered with suction using a sintered glass funnel. The silica gel is then activated at 110°C for 16 hours. The pH of the resulting silica gel is ~4. Similar procedures can be utilised to buffer the pH of the silica gel at various pHs (up to pH ~8: pH higher than this causes degradation of silica) using appropriate phosphate buffers.
Commercial silica gel has also been purified by suspension of 200g in 2L of 0.04M ammonia, and stood for 5minutes before siphoning off the supernatant. The procedure was repeated 3–4 times, before rinsing with distilled water and drying, and activating the silica gel in an oven at 110° [Vogh & Thomson, *Anal Chem* **53** 1345 *1981*].
Although silica gel is not routinely recycled after use (due to fear of contamination as well as the possibility of reduced activity), the costs of using new silica gel for purification may be prohibitive. In these cases, recycling may be achieved by stirring the used silica gel (1 kg) in a mixture of methanol and water (2L MeOH/4L water) for 30–40 minutes. The silica gel is filtered (as described above) and reactivated at 110°C for 16 hours.

Diatomaceous earth (Celite 535 or 545, Hyflo Super-cel, Dicalite, Kieselguhr) is purified before use by washing with 3M hydrochloric acid, then water, or it is made into a slurry with hot water, filtered at the pump and washed with water at 50° until the filtrate is no longer alkaline to litmus. Organic materials can be removed by repeated extraction at 50° with methanol or chloroform, followed by washing with methanol, filtering and drying at 90-100°.

Charcoal is generally satisfactorily activated by heating gently to red heat in a crucible or quartz beaker in a muffle furnace, finally allowing to cool under an inert atmosphere in a desiccator. Good commercial activated charcoal is made from wood, e.g. *Norit* (from Birch wood), *Darco* and *Nuchar*. If the cost is important, then the cheaper *animal charcoal* (bone charcoal) can be used. However, this charcoal contains calcium phosphate and other calcium salts and cannot be used with acidic materials. In this case the charcoal is boiled with dilute hydrochloric acid (1:1 by volume) for 2–3 hours, diluted with distilled water and filtered through a fine grade paper on a Büchner flask, washed with distilled water until the filtrate is almost neutral, and dried first in air, then in a vacuum, and activated as above. To improve the porosity, charcoal columns are usually prepared in admixture with diatomaceous earth.

Cellulose for chromatography is purified by sequential washing with chloroform, ethanol, water, ethanol, chloroform and acetone. More extensive purification uses aqueous ammonia, water, hydrochloric acid, water, acetone and diethyl ether, followed by drying in a vacuum. Trace metals can be removed from filter papers by washing for several hours with 0.1M oxalic, citric acid, or 0.1M EDTA solution, followed by repeated washing with distilled water.

Supelco supply a variety of "solvent desorption tubes", which are cartridges that remove specific impurities (e.g. LpDNPH cartridges which contain a high purity silica adsorbent coated with 2,4-dinitrophenylhydrazine and remove carbonyl compounds; ozone scrubbers which eliminate ozone). Other cartridges such as the "ORBO charcoal" cartridges contain various beds such as *activated coconut charcoal, activated petroleum charcoal, HBr on petroleum charcoal or 4-tert-butyl catechol on charcoal* and are used for specific or for general purposes. Other ORBO cartridges contain activated silica gel and coated silica gel, Florisil, Carboxen, Carbosieve and carbon-coated traps, as well as a variety of ORBO porous polymers, polyurethane, and glass fibre coated with 1-(2-pyridyl)piperazine (which is specific for sampling diisocyanates). They also supply filter cartridges for trapping aerosols and particulate forms of semivolatiles.

Flash Chromatography (FC and HPFC)

A faster method of separating components of a mixture is *flash chromatography* (see Still et al. *J Org Chem* **43** 2923 *1978*). Flash chromatography has become an extremely useful and popular means of purification of small as well as large quantities of compounds. In flash chromatography the eluent flows through the column under a pressure of *ca* 1 to 4 atmospheres. The lower end of the chromatographic column has a relatively long taper closed with a tap. The upper end of the column is connected through a ball joint to a tap. Alternatively a specially designed chromatographic column with a solvent reservoir can also be used (for an example, see the Aldrich Chemical Catalog-glassware section). The tapered portion is plugged with cotton, or quartz, wool and *ca* 1 cm length of fine washed sand (the latter is optional). The adsorbent is then placed in the column as a dry powder or as a slurry in a solvent and allowed to fill to about one-third of the column. A fine grade of adsorbent is required in order to slow the flow rate at the higher pressure, e.g. Silica 60, 230 to 400 mesh with particle size 0.040-0.063mm (e.g. from Merck). The top of the adsorbent is layered with *ca* 1 cm length of fine washed sand. The mixture in the smallest volume of solvent is applied at the top of the column and allowed to flow into the adsorbent under gravity by opening the lower tap momentarily. The top of the column is filled with eluent, the upper tap is connected by a tube to a nitrogen supply from a cylinder, or to compressed air, and turned on to the desired pressure (monitor with a gauge). The lower tap is turned on and fractions are collected rapidly until the level of eluent has reached the top of the adsorbent (do not allow the column to run dry). If further elution is desired then both taps are turned off, the column is filled with more eluting solvent and the process repeated. The top of the column can be modified so that gradient elution can be performed. Alternatively, an apparatus for producing the gradient is connected to the upper tap by a long tube and placed high above the column in order to produce the required hydrostatic pressure. Much better resolution is obtained by dry loading the sample for purification rather than loading the sample as a solution. Flash chromatography is more efficient and gives higher resolution than conventional chromatography at atmospheric pressure and is completed in a relatively shorter time. A successful separation of components of a mixture by TLC using the same adsorbent is a good indication that flash chromatography will give the desired separation on a larger scale.

Very elaborate equipment is now available for FC and HPFC (high-performance flash chromatography), which may include a pump, facility for gradient elution, UV detection and fraction collection of effluent. A large variety of columns (disposable cartridges) with packings such as silicate, carbon, reverse phases for a wide range of applications are commercially available. In addition a plethora of cartridges are available for preliminary purification, prior to FC or HPFC, packed with adsorbents which can remove specific impurities, e.g. unwanted reaction products such as aldehydes or ketone which may be suspected by-products and/or starting materials See

Supelco online catalog http://sigma-aldrich.dirxion.com/WebProject.asp?BookCode=chr09flx#

Sigma Aldrich: http://www.sigmaaldrich.com/analytical-chromatography/analytical-chromatography-catalog.html

Biotage: *Synthesis and Purification* Catalogue and the *Analytical Sample Preparation* Catalogue contain details on available FC and HPFC equipment, accessories and consumables, as well as means of optimising purification, see <www.biotage.com>.

Paired-ion Chromatography (PIC)

Mixtures containing ionic compounds (e.g. acids and/or bases), non-ionisable compounds, and zwitterions can be separated successfully by paired-ion chromatography (PIC). It utilises the "reverse-phase" technique (Eksberg & Schill *Anal Chem* **45** 2092 *1973*). The stationary phase is lipophilic, such as μ-BONDAPAK C_{18} or any other adsorbent that is compatible with water. The mobile phase is water or aqueous methanol containing the acidic or basic counter ion. Thus the mobile phase consists of dilute solutions of strong acids (e.g. 5mM

1-heptanesulfonic acid) or strong bases (e.g. 5 mM tetrabutylammonium phosphate) that are completely ionised at the operating pH values which are usually between 2 and 8. An equilibrium is set up between the neutral species of a mixture in the stationary phase and the respective ionised (anion or cation) species which dissolve in the mobile phase containing the counter ions. The extent of the equilibrium will depend on the ionisation constants of the respective components of the mixture, and the solubility of the unionised species in the stationary phase. Since the ionisation constants and the solubility in the stationary phase will vary with the water-methanol ratio of the mobile phase, the separation may be improved by altering this ratio gradually (gradient elution) or stepwise. If the compounds are eluted too rapidly, the water content of the mobile phase should be increased, e.g. by steps of 10%. Conversely, if components do not move, or move slowly, the methanol content of the mobile phase should be increased by steps of 10%.

The application of pressure to the liquid phase in liquid chromatography generally increases the separation (see HPLC). In PIC also, improved efficiency of the column is observed if pressure is applied to the mobile phase (Wittmer et al. *Anal Chem* **47** 1422 *1975*). [See the Fluka (Riedel-deHaën) catalogue and Supelco catalogue, <http://sigma-aldrich.dirxion.com/WebProject.asp?BookCode=chr09flx#> for IPC reagents for the separation of cations and anions,]

Ion-exchange Chromatography

Ion-exchange chromatography involves an electrostatic process which depends on the relative affinities of various types of ions for an immobilised assembly of ions of opposite charge. The mobile phase is an aqueous buffer with a fixed pH or an aqueous mixture of buffers in which the pH is continuously increased or decreased as the separation may require. This form of liquid chromatography can also be performed at high inlet pressures of liquid with increased column performances.

Ion-exchange Resins. An ion-exchange resin is made up of particles of an insoluble elastic hydrocarbon network to which is attached a large number of ionisable groups. Materials commonly used comprise synthetic ion-exchange resins made, for example, by crosslinking polystyrene to which has been attached non-diffusible ionised or ionisable groups. Resins with relatively high crosslinkage (8–12%) are suitable for the chromatography of small ions, whereas those with low cross linkage (2–4%) are suitable for larger molecules. Applications to hydrophobic systems are possible using aqueous gels with phenyl groups bound to the rigid matrix (Phenyl-Superose/Sepharose, Pharmacia-Amersham Biosciences) or neopentyl chains (Alkyl-Superose, Pharmacia-Amersham Biosciences). (Superose is a cross-linked agarose-based medium with an almost uniform bead size.) These groups are further distinguishable as strong [$-SO_2OH$, $-NR_3^+$] or weak [$-OH$, $-CO_2H$, $-PO(OH)_2$, $-NH_2$]. Their charges are counterbalanced by diffusible ions, and the operation of a column depends on its ability and selectivity to replace these ions. The exchange that takes place is primarily an electrostatic process but adsorptive forces and hydrogen bonding can also be important. A typical sequence for the relative affinities of some common anions (and hence the inverse order in which they pass through such a column) is the following, obtained using a quaternary ammonium (strong base) anion-exchange column:

Fluoride < acetate < bicarbonate < hydroxide < formate < chloride < bromate < nitrite < cyanide < bromide < chromate < nitrate < iodide < thiocyanate < oxalate < sulfate < citrate.

For an amine (weak base) anion-exchange column in its chloride form, the following order has been observed:

Fluoride < chloride < bromide = iodide = acetate < molybdate < phosphate < arsenate < nitrate < tartrate < citrate < chromate < sulfate < hydroxide.

With strong cation-exchangers (e.g. with SO_3H groups), the usual sequence is that polyvalent ions bind more firmly than mono- or di- valent ones, a typical series being as follows:

$Th^{4+} > Fe^{3+} > Al^{3+} > Ba^{2+} > Pb^{2+} > Sr^{2+} > Ca^{2+} > Co^{2+} > Ni^{2+} = Cu^{2+} > Zn^{2+} = Mg^{2+} > UO_2^{+} = Mn^{2+} > Ag^{+} > Tl^{+} > Cs^{+} > Rb^{+} > NH_4^{+} = K^{+} > Na^{+} > H^{+} > Li^{+}$.

Thus, if an aqueous solution of a sodium salt contaminated with heavy metals is passed through the sodium form of such a column, the heavy metal ions will be removed from the solution and will be replaced by sodium ions from the column. This effect is greatest in dilute solution. Passage of sufficiently strong solutions of alkali metal salts or mineral acids readily displaces all other cations from ion-exchange columns. (The regeneration of columns depends on this property.) However, when the cations lie well to the left in the above series it is often advantageous to use a complex-forming species to facilitate removal. For example, iron can be displaced from ion-exchange columns by passage of sodium citrate or sodium ethylenediaminetetraacetate.

Some of the more common commercially available resins are listed in Table 12.
Ion-exchange resins swell in water to an extent which depends on the amount of crosslinking in the polymer, so that columns should be prepared from the wet material by adding it as a suspension in water to a tube already partially filled with water. (This also avoids trapping air bubbles.) The exchange capacity of a resin is commonly expressed as mg equiv/ml of wet resin. This quantity is pH-dependent for weak-acid or weak-base resins but is constant at about 0.6–2 for most strong-acid or strong-base types.
Apart from their obvious applications to inorganic species, sulfonic acid resins have been used in purifying amino acids, aminosugars, organic acids, peptides, purines, pyrimidines, nucleosides, nucleotides and polynucleotides. Thus, organic bases can be applied to the H^+ form of such resins by adsorbing them from neutral solution and, after washing with water, they are eluted sequentially with suitable buffer solutions or dilute acids. Alternatively, by passing alkali solution through the column, the bases will be displaced in an order that is governed by their pK values. Similarly, strong-base anion exchangers have been used for aldehydes and ketones (as bisulfite addition compounds), carbohydrates (as their borate complexes), nucleosides, nucleotides, organic acids, phosphate esters and uronic acids. Weakly acidic and weakly basic exchange resins have also found extensive applications, mainly in resolving weakly basic and acidic species. For demineralisation of solutions without large changes in pH, mixed-bed resins can be prepared by mixing a cation-exchange resin in its H^+ form with an anion-exchange resin in its OH– form. Commercial examples include Amberlite MB-1 (IR-120 + IRA-400) and Bio-Deminrolit (Zeo-Karb 225 and Zerolit FF). The latter is also available in a self-indicating form.

Ion-exchange Celluloses and Sephadex. A different type of ion-exchange column that finds extensive application in biochemistry for the purification of proteins, nucleic acids and acidic polysaccharides derives from cellulose by incorporating acidic and basic groups to give ion-exchangers of controlled acid and basic strengths. Commercially available cellulose-type resins are listed in Tables 13 and 14. AG 501 x 8 (Bio-Rad) is a mixed-bed resin containing equivalents of AG 50W-x8 H^+ form and AG 1-x8 HO^- form, and Bio-Rex MSZ 501 resin. A dye marker indicates when the resin is exhausted. Removal of unwanted cations, particularly of the transition metals, from amino acids and buffer can be achieved by passage of the solution through a column of Chelex 20 or Chelex 100. The metal-chelating abilities of the resin reside in the bonded iminodiacetate groups. Chelex can be regenerated by washing in two bed volumes of 1M HCl, two bed volumes of 1M NaOH and five bed volumes of water.
Ion-exchange celluloses are available in different particle sizes. It is important that the amounts of ‘fines’ are kept to a minimum otherwise the flow of liquid through the column can be extremely slow to the point of no liquid flow. Celluloses with a large range of particle sizes should be freed from 'fines' before use. This is done by suspending the powder in the required buffer and allowing it to settle for one hour and then decanting the ‘fines’. This separation appears to be wasteful, but it is necessary for reasonable flow rates without applying high pressures at the top of the column. Good flow rates can be obtained if the cellulose column is packed dry whereby the ‘fines’ are evenly distributed throughout the column. Wet packing causes the ‘fines’ to rise to the top of the column, which thus becomes clogged.
Several ion-exchange celluloses require recycling before use, a process which must be applied for recovered celluloses. Recycling is done by stirring the cellulose with 0.1M aqueous sodium hydroxide, washing with water until neutral, then suspending in 0.1M hydrochloric acid and finally washing with water until neutral. When regenerating a column it is advisable to wash with a salt solution (containing the required counter ions) of increasing ionic strength up to 2M. The cellulose is then washed with water and recycled if necessary. Recycling can be carried out more than once if there are doubts about the purity of the cellulose and when the cellulose had been used previously for a different purification procedure than the one to be used. The basic matrix of these ion-exchangers is cellulose and it is important not to subject them to strong acid (> 1M) and strongly basic (> 1M) solutions.
When storing ion-exchange celluloses, or during prolonged usage, it is important to avoid growth of microorganisms or moulds which slowly destroy the cellulose. Good inhibitors of microorganisms are phenyl mercuric salts (0.001%, effective in weakly alkaline solutions), chlorohexidine (Hibitane at 0.002% for anion exchangers), 0.02% aqueous sodium azide or 0.005% of ethyl mercuric thiosalicylate (Merthiolate); these are most effective in weakly acidic solutions for cation exchangers. Trichlorobutanol (Chloretone, at 0.05% is only effective in weakly acidic solutions) can be used for both anion and cation exchangers. Most organic solvents (e.g. methanol) are effective antimicrobial agents but only at high concentrations. These inhibitors must be

removed by washing the columns thoroughly before use because they may have adverse effects on the material to be purified (e.g. inactivation of enzymes or other active preparations).

Sephadex. Other carbohydrate matrices such as *Sephadex* are a bead form of cross-linked gels (based on dextran) which have more uniform particle sizes. Their advantages over the celluloses include faster and more reproducible flow rates and they can be used directly without removal of 'fines'. *Sephadex*, which can also be obtained in a variety of ion-exchange forms (see Table 14) consists of beads of a cross-linked dextran gel which swells in water and aqueous salt solutions. The smaller the bead size, the higher the resolution that is possible but the slower the flow rate. Typical applications of Sephadex gels are the fractionation of mixtures of polypeptides, proteins, nucleic acids, polysaccharides and for desalting solutions.
Sephadex ion-exchangers, unlike celluloses, are available in narrow ranges of particle sizes. These are of two medium types**,** the G-25 and G-50, and their dry bead diameter sizes are *ca* 50 to 150 microns. They are available as cation and anion exchange Sephadex. One of the disadvantages of using Sephadex ion-exchangers is that the bed volume can change considerably with alteration of pH. *Ultragels* also suffer from this disadvantage to a varying extent, but ion-exchangers of the bead type have been developed e.g. *Fractogels, Toyopearl*, which do not suffer from this disadvantage.

Sepharose (e.g. *Sepharose CL and Bio-Gel A*) is a bead form of agarose gel which is useful for the fractionation of high molecular weight substances, for molecular weight determinations of large molecules (molecular weight > 5000), and for the immobilisation of enzymes, antibodies, hormones and receptors usually for affinity chromatography applications.

In preparing any of the above for use in columns, the dry powder is evacuated, then mixed under reduced pressure with water or the appropriate buffer solution. Alternatively it is stirred gently with the solution until all air bubbles are removed. Because some of the wet powders change volumes reversibly with alteration of pH or ionic strength (see above), it is imperative to make allowances when packing columns (see above) in order to avoid overflowing of packing when the pH or salt concentrations are altered.

Cellex CM ion-exchange cellulose can be purified by treatment of 30–40g (dry weight) with 500ml of 1mM cysteine hydrochloride. It is then filtered through a Büchner funnel and the filter cake is suspended in 500ml of 0.05M NaCl/0.5M NaOH. This is filtered and the filter cake is resuspended in 500ml of distilled water and filtered again. The process is repeated until the washings are free from chloride ions. The filter cake is again suspended in 500ml of 0.01M buffer at the desired pH for chromatography, filtered, and the last step repeated several times.

Cellex D and other anionic celluloses are washed with 0.25M NaCl/0.25M NaOH solution, then twice with deionised water. This is followed with 0.25M NaCl and then washed with water until chloride-free. The *Cellex* is then equilibrated with the desired buffer as above.

Crystalline Hydroxylapatite is a structurally organised, highly polar material which, in aqueous solution (in buffers) strongly adsorbs macromolecules such as proteins and nucleic acids, permitting their separation by virtue of the interaction with charged phosphate groups and calcium ions, as well by physical adsorption. The procedure therefore is not entirely ion-exchange in nature. Chromatographic separations of singly and doubly stranded DNA are readily achievable, whereas there is negligible adsorption of low-molecular-weight species.

Gel Filtration

The gel-like, bead nature of wet Sephadex enables small molecules such as inorganic salts to diffuse freely into it while, at the same time, protein molecules are unable to do so. Hence, passage through a Sephadex column can be used for complete removal of salts from protein solutions. Polysaccharides can be freed from monosaccharides and other small molecules because of their differential retardation. Similarly, amino acids can be separated from proteins and large peptides.
Gel filtration using Sephadex G-types (50 to 200) is essentially useful for fractionation of large molecules with molecular weights above 1000. For Superose, the range is given as 5000 to 5 x 10^6. Fractionation of lower molecular weight solutes (e,g, ethylene glycols, benzyl alcohols) can now be achieved with Sephadex G-10 (up to Mol.Wt 700) and G-25 (up to Mol.Wt 1500). These dextrans are used only in aqueous solutions. In contrast, Sephadex LH-20 and LH-60 (prepared by hydroxypropylation of Sephadex) are used for the separation of small molecules (Mol.Wt less than 500) using most of the common organic solvents as well as water.
Sephasorb HP (ultrafine, prepared by hydroxypropylation of crossed-linked dextran) can also be used for the separation of small molecules in organic solvents and water, and in addition it can withstand pressures up to

1400 psi making it useful in HPLC. These gels are best operated at pH values between 2 and 12, because solutions with high and low pH values slowly decompose them (see further in Chapter 7).
Supelco (see catalogue) supply a variety of SUPELCOGEL columns (for small molecule separations), TSK-GEL columns (for large molecules separation) and guard columns for gel permeation chromatography. They have columns of the latter type (e.g. TSL-GEL column G4000SW) which can separate globular proteins of 20–10,000 x 10^3 Daltons in molecular weight. They also supply "Ascentis HPLC Applications CDs" containing a comprehensive library of their columns and possible applications.

High Performance Liquid Chromatography (HPLC)

When pressure is applied at the inlet of a liquid chromatographic column the performance of the column can be increased by several orders of magnitude. This is partly because of the increased speed at which the liquid flows through the column and partly because fine column packings which have larger surface areas can be used. Because of the improved efficiency of the columns, this technique has been referred to as high performance, high pressure, or high speed liquid chromatography and has found great importance in chemistry and biochemistry.

The equipment consists of a hydraulic system to provide the pressure at the inlet of the column, a column, a detector, data storage and output, usually in the form of a computer. The pressures used in HPLC vary from a few psi to 4000–5000 psi. The most convenient pressures are, however, between 500 and 1800psi. The plumbing is made of stainless steel or non-corrosive metal tubing to withstand high pressures. Plastic tubing and connectors are used for low pressures, e.g. up to ~500psi. Increase of temperature has a very small effect on the performance of a column in liquid chromatography. Small variations in temperatures, however, do upset the equilibrium of the column, hence it is advisable to place the column in an oven at ambient temperature in order to achieve reproducibility. The packing (stationary phase) is specially prepared for withstanding high pressures. It may be an adsorbent (for adsorption or solid-liquid HPLC), a material impregnated with a high boiling liquid (e.g. octadecyl sulfate, in *reverse-phase* or *liquid-liquid or paired-ion* HPLC), an ion-exchange material (in *ion-exchange* HPLC), or a highly porous non-ionic gel (for high performance *gel filtration* or *permeation*). The mobile phase is water, aqueous buffers, salt solutions, organic solvents or mixtures of these.

Detectors

The more commonly used detectors for column chromatography in general have UV, visible, diode array or fluorescence monitoring for light absorbing substances in the effluent, and refractive index monitoring and evaporative light scattering for transparent compounds in the effluent. UV detection is not useful when molecules do not have UV absorbing chromophores, and solvents for elution should be carefully selected when UV monitoring is used so as to ensure the lack of background interference in detection. The sensitivity of the refractive index monitoring is usually lower than the light absorbing monitoring by a factor of ten or more. It is also difficult to use a refractive index monitoring system with gradient elution of solvents. When substances have readily oxidised and reduced forms, e.g. phenols, nitro compounds, heterocyclic compounds etc. then electrochemical detectors are useful. These detectors oxidise and/or reduce these substances and make use of this process to provide a peak on the recorder.
The cells of the monitoring devices are very small (*ca* 5 µl) and the detection is very good. The volumes of the analytical columns are quite small (*ca* 2ml for a 1 metre column); hence the result of an analysis is achieved very quickly. Larger columns have been used for preparative work and can be used with the same equipment. Most machines have solvent mixing chambers for solvent gradient or ion gradient elution. The solvent gradient (for two solvents) or pH or ion gradient can be adjusted in a linear, increasing or decreasing exponential manner. Splitters can be used, whereby very small volumes of the effluent are directed through the detectors so that the whole effluent does not pass through the detector.

Columns for HPLC

In general two different types of HPLC columns are available. Prepacked columns are those with metal casings with threads at both ends onto which capillary connections are attached. The cartridge HPLC columns are cheaper and are used with cartridge holders. As the cartridge is fitted with a groove for the holding device, no threads are necessary and the connection pieces can be reused.
A large range of HPLC columns (including guard columns, i.e. small pre-columns) are available from Supelco < http://sigma-aldrich.dirxion.com/WebProject.asp?BookCode=chr09flx# >, Waters <www.waters.com>, Agilent Technologies <www.chem.agilent.com>, Phenomenex <www.phenomenex.com>, YMC <www.ymc.co.jp/en/>, Merck <www.merck.de>, SGE <www.sge.com>, GE Healthcare

<www.gehealthcare.com>, and other leading companies. It is not possible to list the range of columns here that are commercially available because the numbers are too large and include prepared columns for the type of chromatography described below in the *Other Types of Liquid Chromatography* such as Monolithic Chromatography and UPLC (see below). Also, in this range of columns are columns with chiral bonded phases capable of separating enantiomeric mixtures. The number of these, on the other hand, is relatively smaller and some *chiral* columns are listed in Table 15.

Other Types of Liquid Chromatography

New stationary phases for specific purposes in chromatographic separation are being continually developed. *Charge transfer adsorption chromatography* makes use of a stationary phase which contains immobilised aromatic compounds and permits the separation of aromatic compounds by virtue of the ability to form charge transfer complexes (sometimes coloured) with the stationary phase. The separation is caused by the differences in stability of these complexes (Porath and Dahlgren-Caldwell *J Chromatogr* **133** 180 *1977*).

In *metal chelate adsorption chromatography* a metal is immobilised by partial chelation on a column which contains bi- or tri- dentate ligands. Its application is in the separation of substances which can complex with the bound metals and depends on the stability constants of the various ligands (Porath et al. *Nature* **258** 598 *1975*; Loennerdal et al. *FEBS Lett* **75** 89 *1977*).

An application of chromatography which has found extensive use in biochemistry and has brought a new dimension in the purification of enzymes is *affinity chromatography*. A specific enzyme inhibitor is attached by covalent bonding to a stationary phase (e.g. AH-Sepharose 4B for acidic inhibitors and CH-Sepharose 4B for basic inhibitors, Phenyl-Sepharose for hydrophobic proteins), and will strongly bind only the specific enzyme which is inhibited or preferentially bound, allowing all other proteins to flow through the column. The enzyme is then eluted with a solution of high ionic strength (e.g. 1M sodium chloride) or a solution containing a substrate or reversible inhibitor of the specific enzyme. (The ionic medium can be removed by gel filtration using a mixed-bed gel.) Similarly, an immobilised lectin may interact with the carbohydrate moiety of a glycoprotein. The most frequently used matrixes are cross-linked (4-6%) agarose and polyacrylamide gel. Many adsorbents are commercially available for nucleotides, coenzymes and vitamins, amino acids, peptides, lectins and related macromolecules and immunoglobulins. Considerable purification can be achieved by one passage through the column and the column can be reused several times.

The affinity method may be *biospecific*, for example as an antibody-antigen interaction, or chemical as in the chelation of boronate by *cis*-diols, or of unknown origin as in the binding of certain dyes to albumin and other proteins.

Hydrophobic adsorption chromatography takes advantage of the hydrophobic properties of substances to be separated and has also found use in biochemistry (Hoftsee *Biochem Biophys Res Commun* **50** 751 *1973*; Jennissen & Heilmayer Jr *Biochemistry* **14** 754 *1975*). Specific covalent binding with the stationary phase, a procedure that was called *covalent chromatography*, has been used for the separation of compounds and for immobilising enzymes on a support: the column was then used to carry out specific bioorganic reactions (Mosbach *Method Enzymol* **44** 1976; A. Rosevear et al. *Immobilised Enzymes and Cells: A Laboratory Manual*, Adam Hilger, Bristol, 1987, ISBN 085274515X). See Bibliography for further literature.

More recently ***Monolithic Chromatography*** has been introduced which is a new type of high-performance liquid chromatography in which the columns are a 'one-piece porous solid', or *monolith*, instead of particles. These columns take a variety of forms for use in adsorption, ion exchange (weak and strong, cation and anion), reverse phase, and are for use in the separation of small and large molecules. The mobile phase in these columns flows through the whole of the stationary phase. [P. Wang ed., *Monolithic Chromatography and its Modern Applications* ILM Publications, pp 648 *2010*, ISBN 9781906799038, 1906799032; and for columns see BIA Separations <www.biaseparations.com>.

Ultra performance Liquid chromatography **(UPLC)** affords a considerable improvement by bringing high performance liquid chromatography to a new level. Great improvements in analysis and purification of amino acids, peptides, proteins, oligonucleotides and glycans can be accomplished. This has been achieved by packing columns with smaller sized particles (1.7–1.8μm) and applying pressures of ~15,000psi (~1030 bar) to the mobile phase. NanoACQUITY UPLC trapping and nanoflow columns have been specifically designed for use on Waters nanoACQUITY systems that can be integrated with MS components [see www.waters.com].

Automated column chromatography

Most of the above methods of column chromatography have been, or can be, automated. Devices are available for the automated injection of samples to columns which are useful for analytical evaluation of samples, for

repeated analyses, or for repeated separations to obtain larger amounts of material. The specific fractions of the effluent can be collected. Equipment for these purposes can be obtained from several of the suppliers listed at the end of the HPLC section above with the corresponding websites. GC systems coupled with mass spectrometers (GC-MS) and HPLC systems coupled to mass spectrometers (LC-MS) are extremely important methods for the separation and identification of substances. These are invariably linked to a computer with internal libraries which can identify the peaks, and the libraries can be continually updated (see above). With more elaborate equipment LC-MS-MS where the peaks from the first spectrometer are further analysed by a second mass spectrometer provide a wealth of information. If not for the costs involved in GC-MS, GC-MS-MS, LC-MS and LC-MS-MS equipment, these systems would be more commonly found in analytical and research laboratories. [For further reading see Bibliography.]

ELECTROPHORESIS

Ionisable substances such as organic and inorganic acids, bases and salts migrate to their respective electrodes (anode or cathode) if a voltage is applied. When they are placed onto a matrix, e.g. paper or gel, then their rate of migration to the electrodes will vary with the charge, nature and structure of the substance. This phenomenon is known as electrophoresis and is very useful for separating and purifying substances. Capillary techniques have been adapted to electrophoresis and "capillary electrophoresis", and "capillary zone electrophoresis" are finding wide use for identification, separation and isolation of ionisable substances (see text in the Bibliography under "electrophoresis" and the "Introduction" in Chapter 7). The method is used extensively for biological substances, e.g. proteins, polypeptides, DNA, RNA, (see Introduction in Chapter 7) but has been used to a limited extent for identifying and purifying small molecules. Elaborate equipment is available commercially which contains essentially an electrolytic cell and a power supply which provides variable voltage for the process. The use of paper (Whatman of various thicknesses) as the matrix on a flat bed or in a vertical descending mode has been completely superseded with polyacrylamide or agarose flat bed gels. These are routinely used mainly for the separation of proteins and nucleic acids. Also capillary electrophoresis (CE) is now widely used for the analysis and detection of biological substances. It is used for the separation and purification of carbohydrates, nucleic acids, proteins and peptides and for chiral analysis and separations [see Bibliography].

DRYING

Removal of Solvents

Where substances are sufficiently stable, removal of solvent from recrystallised materials presents no problems. The crystals, after filtering at the pump (and perhaps air-drying by suction), are heated in an oven above the boiling point of the solvent (but below the melting point of the crystals), followed by cooling in a desiccator. Where this treatment is inadvisable, it is still often possible to heat to a lower temperature under reduced pressure, for example in an Abderhalden pistol. This device consists of a small chamber which is heated externally by the vapour of a boiling solvent. Inside this chamber, which can be evacuated (pump) is placed a small boat containing the sample to be dried and also a receptacle with a suitable drying agent. Convenient liquids for use as boiling liquids in an Abderhalden pistol, and their boiling temperatures, are given in Table 16. Alternatively an electrically heated drying pistol can also be used. In cases where heating above room temperature cannot be used, drying must be carried out in a vacuum desiccator containing suitable absorbents. For example, hydrocarbons, such as cyclohexane and petroleum ether, can be removed by using shredded paraffin wax, and acetic acid and other acids can be absorbed by pellets of sodium or potassium hydroxide. However, in general, solvent removal is less of a problem than ensuring that the water content of solids and liquids is reduced below an acceptable level.

Removal of Water

Methods for removing water from solids depend on the thermal stability of the solids or the time available. The safest way is to dry in a vacuum desiccator over concentrated sulfuric acid, phosphorus pentoxide, silica gel, calcium chloride, or some other desiccant. Where substances are stable in air and melt above 100^{o}, drying in an air oven may be adequate. In other cases, use of an Abderhalden pistol may be satisfactory.

Often, in drying inorganic salts, the final material that is required is a hydrate. In such cases, the purified substance is left in a desiccator to equilibrate above an aqueous solution having a suitable water-vapour pressure. A convenient range of solutions used in this way is given in Table 17.

The choice of desiccants for drying liquids is more restricted because of the need to avoid all substances likely to react with the liquids themselves. In some cases, direct distillation of an organic liquid is a suitable method

for drying both solids and liquids, especially if low-boiling azeotropes are formed. Examples include acetone, aniline, benzene, chloroform, carbon tetrachloride, heptane, hexane, methanol, nitrobenzene, petroleum ether, toluene and xylene. Addition of benzene can be used for drying ethanol by distillation. In carrying out distillations intended to yield anhydrous products, the apparatus should be fitted with guard-tubes containing calcium chloride or silica gel to prevent entry of moist air into the system. (Many anhydrous organic liquids are appreciably hygroscopic.)

Traces of water can be removed from solvents such as benzene, 1,2-dimethoxyethane, diethyl ether, pentane, toluene and tetrahydrofuran by refluxing under nitrogen a solution containing sodium wire and benzophenone, and fractionally distilling. Drying with, and distilling from CaH_2 is applicable to a number of solvents including aniline, benzene, *tert*-butylamine, *tert*-butanol, 2,4,6-collidine, diisopropylamine, dimethylformamide, hexamethyl-phosphoramide, dichloromethane, ethyl acetate, pyridine, tetramethylethylene diamine, toluene, triethylamine.

Removal of water from gases may be by physical or chemical means, and is commonly by adsorption on to a drying agent in a low-temperature trap. The effectiveness of drying agents depends on the vapour pressure of the hydrated compound - the lower the vapour pressure the less the remaining moisture in the gas.

The most usually applicable of the specific methods for detecting and determining water in organic liquids is due to Karl Fischer. (See J. Mitchell & D.M. Smith, *Aquametry*, 2nd Ed, J Wiley & Sons, New York, *1977–1984*, ISBN 0471022640; Fieser & Fieser, *Reagents for Organic Synthesis*, J.Wiley & Sons, NY, Vol 1, 528 *1967*, ISBN 0271616X), also see Karl Fischer titrant or Hydranal® –Titrant Type 5E [64-17-5] and other types in the Fluka and <http://www.sigmaaldrich.com/analytical-chromatography/titration/hydranal.html>.

Other techniques include electrical conductivity measurements and observation of the temperature at which the first cloudiness appears as the liquid is cooled (applicable to liquids in which water is only slightly soluble). Addition of anhydrous cobalt (II) iodide (blue) provides a convenient method (colour change to pink on hydration) for detecting water in alcohols, ketones, nitriles and some esters. Infrared absorption measurements of the broad band for water near 3500 cm^{-1} can also sometimes be used for detecting water in non-hydroxylic substances.

Cartridges for the removal not only water from solvents or solutions but other specific impurities, e.g. acids, amines , aldehydes, are now commercially available [see supplies listed at the end of the HPLC section together with their respective websites].

For further useful information on mineral adsorbents and drying agents, go to the SigmaAldrich website <sigmaaldrich.com>, under technical library (Aldrich) for technical bulletin AL-143.

Intensity and Capacity of Common Desiccants

Drying agents are conveniently grouped into three classes, depending on whether they combine with water reversibly, they react chemically (irreversibly) with water, or they are molecular sieves. The first group varies in their drying intensity with the temperature at which they are used, depending on the vapour pressure of the hydrate that is formed. This is why, for example, drying agents such as anhydrous sodium sulfate, magnesium sulfate or calcium chloride should be filtered off from the liquids before the latter are heated. The intensities of drying agents belonging to this group fall in the sequence:

P_2O_5 >> BaO > $Mg(ClO_4)_2$, CaO, MgO, KOH (fused), conc H_2SO_4, $CaSO_4$, Al_2O_3 > KOH (pellets), silica gel, $Mg(ClO_4)_2.3H_2O$ > NaOH (fused), 95% H_2SO_4, $CaBr_2$, $CaCl_2$ (fused) > NaOH (pellets), $Ba(ClO_4)_2$, $ZnCl_2$, $ZnBr_2$ > $CaCl_2$ (technical) > $CuSO_4$ > Na_2SO_4, K_2CO_3.

Where large amounts of water are to be removed, a preliminary drying of liquids is often possible by shaking with concentrated solutions of sodium sulfate or potassium carbonate, or by adding sodium chloride to salt out the organic phase (for example, in the drying of lower alcohols), as long as the drying agent does not react (e.g. $CaCl_2$ with alcohols and amines, see below).

Drying agents that combine irreversibly with water include the alkali metals, the metal hydrides (discussed in Chapter 2), and calcium carbide.

Suitability of Individual Desiccants

Alumina. (Preheated to 175^{o} for about 7 hours). Mainly as a drying agent in a desiccator or as a column through which liquid is percolated.

Aluminium amalgam. Mainly used for removing traces of water from alcohols *via* refluxing followed by distillation.

Barium oxide. Suitable for drying organic bases.

Barium perchlorate. Expensive. Used in desiccators (*covered with a metal guard*). Unsuitable for drying solvents or organic material where contact is necessary, because of the danger of **EXPLOSION.**

Boric anhydride. (Prepared by melting boric acid in an air oven at a high temperature, cooling in a desiccator, and powdering.) Mainly used for drying formic acid.

Calcium chloride (anhydrous). Cheap. Large capacity for absorption of water, giving the hexahydrate below 30^{o}, but is fairly slow in action and not very efficient. Its main use is for preliminary drying of alkyl and aryl halides, most esters, saturated and aromatic hydrocarbons and ethers. Unsuitable for drying alcohols and amines (which form addition compounds), fatty acids, amides, amino acids, ketones, phenols, or some aldehydes and esters. Calcium chloride is suitable for drying the following gases: hydrogen, hydrogen chloride, carbon monoxide, carbon dioxide, sulfur dioxide, nitrogen, methane, oxygen, also paraffins, ethers, olefins and alkyl chlorides.

Calcium hydride. See Chapter 2.

Calcium oxide. (Preheated to 700–900^{o} before use.) Suitable for alcohols and amines (but does not dry them completely). Need not be removed before distillation, but in that case the head of the distillation column should be packed with glass wool to trap any calcium oxide powder that might be carried over. Unsuitable for acidic compounds and esters. Suitable for drying gaseous amines and ammonia.

Calcium sulfate (anhydrous). (Prepared by heating the dihydrate or the hemihydrate in an oven at 235^{o} for 2–3 hours; it can be regenerated.) Available commercially as *Drierite*. It forms the hemihydrate, $2CaSO_4.H_2O$, so that its capacity is fairly low (6.6% of its weight of water), and hence is best used on partially dried substances. It is very efficient (being comparable with phosphorus pentoxide and concentrated sulfuric acid). Suitable for most organic compounds. Solvents boiling below 100^{o} can be dried by direct distillation from calcium sulfate.

Copper (II) sulfate (anhydrous). Suitable for esters and alcohols. Preferable to sodium sulfate in cases where solvents are sparingly soluble in water (for example, benzene or toluene). The colourless to fawn coloured powder turns blue as it absorbs water

Lithium aluminium hydride. See Chapter 2.

Magnesium amalgam. Mainly used for removing traces of water from alcohols by refluxing the alcohol in the presence of the Mg amalgam followed by distillation.

Magnesium perchlorate (anhydrous). (Available commercially as *Dehydrite*. Expensive.) Used in desiccators. Unsuitable for drying solvents or any organic material where contact is necessary, because of the danger of **EXPLOSION**.

Magnesium sulfate (anhydrous). (Prepared from the heptahydrate by drying at 300^{o} under reduced pressure.) More rapid and effective than sodium sulfate but is slightly acidic. It has a large capacity, forming $MgSO_4.7H_2O$ below 48^{o}. Suitable for the preliminary drying of most organic compounds.

Molecular sieves. See below.

Phosphorus pentoxide. Very rapid and efficient, but difficult to handle and should only be used after the organic material has been partially dried, for example with magnesium sulfate. Suitable for anhydrides, alkyl and aryl halides, ethers, esters, hydrocarbons and nitriles, and for use in desiccators. Not suitable with acids, alcohols, amines or ketones, or with organic molecules from which a molecule of water can be eliminated. Suitable for drying the following gases: hydrogen, oxygen, carbon dioxide, carbon monoxide, sulfur dioxide, nitrogen, methane, ethene and paraffins. It is available on a solid support with an indicator under the name *Sicapent* (from Merck). The colour changes in Sicapent depend on the percentage of water present (e.g. in the absence of water, Sicapent is colourless but becomes green with 20% water and blue with 33% w/w water). When the quantity of water in the desiccator is high, a crust of phosphoric acid forms a layer over the phosphorus pentoxide powder and decreases its efficiency. The crust can be removed with a spatula to expose the dry powder and restore the desiccant property.

Potassium (metal). Properties and applications are similar to those for sodium but as the reactivity is greater than that of sodium, the hazards are greater than those of sodium. **Handle with extreme care**.

Potassium carbonate (anhydrous). Has a moderate efficiency and capacity, forming the dihydrate. Suitable for an initial drying of alcohols, bases, esters, ketones and nitriles by shaking with them, then filtering off. Also suitable for salting out water-soluble alcohols, amines and ketones. Unsuitable for acids, phenols, thiols and other acidic substances.

Potassium carbonate. Solid potassium hydroxide is very rapid and efficient. Its use is limited almost entirely to the initial drying of organic bases. Alternatively, sometimes the base is shaken first with a concentrated solution of potassium hydroxide to remove most of the water present. Unsuitable for acids, aldehydes, ketones, phenols, thiols, amides and esters. Also used for drying gaseous amines and ammonia.

Silica gel. Granulated silica gel is a commercially available drying agent for use with gases, in desiccators, and (because of its chemical inertness) in physical instruments (pH meters, spectrometers, balances). Its drying action depends on physical adsorption, so that silica gel must be used at room temperature or below. By incorporating cobalt chloride into the material it can be made self indicating (blue when dry, pink when wet), re-drying in an oven at 110^{o} being necessary when the colour changes from blue to pink.

Sodium (metal). Used as a fine wire or as chips, for more completely drying ethers, saturated hydrocarbons and aromatic hydrocarbons which have been partially dried (for example with calcium chloride or magnesium sulfate). Unsuitable for acids, alcohols, alkyl halides, aldehydes, ketones, amines and esters. Reacts violently if water is present and can cause a fire with highly flammable liquids.

Sodium hydroxide. Properties and applications are similar to those for potassium hydroxide.

Sodium-potassium alloy. Used as lumps. Lower melting than sodium, so that its surface is readily renewed by shaking. Properties and applications are similar to those for sodium.

Sodium sulfate (anhydrous). Has a large capacity for absorption of water, forming the decahydrate below 33°, but drying is slow and inefficient, especially for solvents that are sparingly soluble in water. It is suitable for the preliminary drying of most types of organic compounds.

Sulfuric acid (concentrated). Widely used in desiccators. Suitable for drying bromine, saturated hydrocarbons, alkyl and aryl halides. Also suitable for drying the following gases: hydrogen, nitrogen, carbon dioxide, carbon monoxide, chlorine, methane and paraffins. Unsuitable for alcohols, bases, ketones or phenols. Also available on a solid support with an indicator under the name *Sicacide* (from Merck) for desiccators. The colour changes in Sicacide depends on the percentage of water present (e.g. when dry Sicacide is red-violet but becomes pale violet with 27% water and pale yellow to colourless with 33% w/w water).

For convenience, many of the above drying agents are listed in Table 18 under the classes of organic compounds for which they are commonly used.

Molecular sieves

Molecular sieves are types of adsorbents composed of crystalline zeolites (sodium and calcium aluminosilicates). By heating them, water of hydration is removed, leaving holes of molecular dimensions in the crystal lattices. These holes are of uniform size and allow the passage into the crystals of small molecules, but not of large ones.

This *sieving* action explains their use as very efficient drying agents for gases and liquids. The pore size of these sieves can be modified (within limits) by varying the cations built into the lattices. The four types of molecular sieves currently available are:

Type 3A sieves. A crystalline potassium aluminosilicate with a pore size of about 3 Angstroms. This type of molecular sieves is suitable for drying liquids such as acetone, acetonitrile, methanol, ethanol and 2-propanol, and drying gases such as acetylene, carbon dioxide, ammonia, propylene and butadiene. The material is supplied as beads or pellets.

Type 4A sieves. A crystalline sodium aluminosilicate with a pore size of about 4 Angstroms, so that, besides water, ethane molecules (but not butane) can be adsorbed. This type of molecular sieves is suitable for drying chloroform, dichloromethane, diethyl ether, dimethylformamide, ethyl acetate, cyclohexane, benzene, toluene, xylene, pyridine and diisopropyl ether. It is also useful for low pressure air drying. The material is supplied as beads, pellets or powder.

Type 5A sieves. A crystalline calcium aluminosilicate with a pore size of about 5 Angstroms, these sieves adsorb larger molecules than type 4A. For example, as well as the substances listed above, propane, butane, hexane, butene, higher *n*-olefins, *n*-butyl alcohol and higher *n*-alcohols, and cyclopropane can be adsorbed, but not branched-chain C_6 hydrocarbons, cyclic hydrocarbons such as benzene and cyclohexane, or secondary and tertiary alcohols, carbon tetrachloride or boron trifluoride. This is the type generally used for drying gases, though organic liquids such as THF and dioxane can be dried with this type of molecular sieves.

Type 13X sieves. A crystalline sodium aluminosilicate with a pore size of about 10 Angstroms which enables many branched-chain and cyclic compounds to be adsorbed, in addition to all the substances removed by type 5A sieves.

They are unsuitable for use with strong acids but are stable over the pH range 5–11.

Because of their selectivity, molecular sieves offer advantages over silica gel, alumina or activated charcoal, especially in their very high affinity for water, polar molecules and unsaturated organic compounds. Their relative efficiency is greatest when the impurity to be removed is present at low concentrations. Thus, at 25° and a relative humidity of 2%, type 5A molecular sieves adsorb 18% by weight of water, whereas for silica gel and alumina the figures are 3.5 and 2.5% respectively. Even at 100° and a relative humidity of 1.3%, molecular sieves adsorb about 15% by weight of water.

The greater preference of molecular sieves for combining with water molecules explains why this material can be used for drying ethanol and why molecular sieves are probably the most universally useful and efficient drying agents. Percolation of ethanol with an initial water content of 0.5% through a 144 cm long column of type 4A molecular sieves reduced the water content to 10ppm. Similar results have been obtained with pyridine.

The main applications of molecular sieves to purification comprise:

1. Drying of gases and liquids containing traces of water.
2. Drying of gases at elevated temperatures.
3. Selective removal of impurities (including water) from gas streams.

(For example, carbon dioxide from air or ethene; nitrogen oxides from nitrogen; methanol from diethyl ether. In general, carbon dioxide, carbon monoxide, ammonia, hydrogen sulfide, mercaptans, ethane, ethene, acetylene (ethyne), propane and propylene are readily removed at 25°. In mixtures of gases, the more polar ones are preferentially adsorbed).

The following applications include the removal of straight-chain from branched-chain or cyclic molecules. For example, type 5A sieves will adsorb *n*-butyl alcohol but not its branched-chain isomers. Similarly, it separates *n*-tetradecane from benzene, or *n*-heptane from methylcyclohexane.
The following liquids have been dried with molecular sieves: acetone, acetonitrile, acrylonitrile, allyl chloride, amyl acetate, benzene, butadiene, *n*-butane, butene, butyl acetate, *n*-butylamine, *n*-butyl chloride, carbon tetrachloride, chloroethane, 1-chloro-2-ethylhexane, cyclohexane, dichloromethane, dichloroethane, 1,2-dichloropropane, 1,1-dimethoxyethane, dimethyl ether, 2-ethylhexanol, 2-ethylhexylamine, *n*-heptane, *n*-hexane, isoprene, isopropyl alcohol, diisopropyl ether, methanol, methyl ethyl ketone, oxygen, *n*-pentane, phenol, propane, *n*-propyl alcohol, propylene, pyridine, styrene, tetrachloroethylene, toluene, trichloroethylene and xylene. In addition, the following gases have been dried: acetylene, air, argon, carbon dioxide, chlorine, ethene, helium, hydrogen, hydrogen chloride, hydrogen sulfide, nitrogen, oxygen and sulfur hexafluoride.
After use, molecular sieves can be regenerated by heating at between 300–350° for several hours, preferably in a stream of dry inert gas such as nitrogen or preferably under vacuum, then cooling in a desiccator. Special precautions must be taken before regeneration of molecular sieves used in the drying of flammable solvents.
However, care must be exercised in using molecular sieves for drying organic liquids. Appreciable amounts of impurities were *formed* when samples of acetone, 1,1,1-trichloroethane and methyl-*t*-butyl ether were dried in the liquid phase by contact with molecular sieves 4A (Connett *Lab Pract* **21** 545 *1972*). Other, less reactive types of sieves may be more suitable but, in general, it seems desirable to make a preliminary test to establish that no unwanted reaction takes place. Useful comparative data for Type 4A and 5A sieves are in Table 19.
With the advent of nanotechnology, nanoparticles are finding use as porous materials for a variety of purposes [see J.A. Schwartz & C. Contescu (Eds), *Surfaces of Nanoparticles & Porous Materials*, Marcel Dekker Inc, *1999*. ISBN 9780824719333].

PROPERTIES USEFUL IN PURIFICATION

Spectroscopic

Spectroscopic instruments of one sort or another are generally available in laboratories and useful for providing some idea of the purity of the specimen in question. Among these are IR, UV-VIS, fluorescence, NMR and mass spectrometers.
Infrared spectra [IR or FT(Fourier Transformed)-IR with frequency range of ν from ~ 600 to 3400 cm^{-1}], generally of the solid grounded in a large excess of KBr, or in a mull by grinding into an oil, e.g. Nujol, or in solution, e.g. $CHCl_3$, provide a 'fingerprint' of the substance. The KBr spectrum, or the spectrum of a film between NaCl plates if the substance is a liquid, are more useful as they give detailed information without interfering signals from Nujol or solvent which may mask important signals. Since the IR spectra consist of several signals many of which are sharp, impurities show up clearly. However, if the impurities are less than say 10% it may be difficult to say how impure the sample is, or what impurities are present in it. On the other hand, if the sample is very pure then its spectrum will be superimposable on that of the pure authentic sample.
Ultraviolet Spectra (with wavelength range of λ form ~ 200 to 400 mμ) are measured in dilute solution and are generally broad bands. Although the broadness of the bands make it difficult to identify impurities, the values of the molecular absorption extinction coefficients ε ($M^{-1}cm^{-1}$) at all wavelengths, but usually measured at the peaks or troughs, are characteristics of the substance in the particular solvent used, and would be different if the sample was impure. Glass cuvettes cannot be used as they are not transparent to UV radiation, and quartz cells should be used. However, quartz cells need only be on the two opposite faces of the four sided cuvette through which the light passes; the other two faces being made of glass. Similarly in the *visible* spectra (wavelength range of λ form ~ 400 to 800 mμ) the ε values are characteristics of the substance in the solvent used. In this case the cheaper glass cuvettes may be used as they are transparent to visible light.
Fluorescence Spectra are measured in the wavelength range similar to the *visible* range, but from light that is scattered at right angles to the incident excitation (UV) wavelength. Thus at a set excitation wavelength λ_{ex}, the fluorescence spectrum is scanned and the peak maximum λ_{em} and its ε_{em} are recorded. In this case the cuvettes generally have quartz faces on all four sides, as the UV light has to go through adjacent sides of the cell. This spectroscopy is useful as sometimes impurities in a sample may fluoresce at a particular wavelength. Generally, dyes have fluorescent properties and are identified in this way. Substances with strongly fluorescing properties have found considerable use in biology. Here they have been tagged to biological molecules and their movement into particular tissues and cells has been traced through their fluorescence. Table 20 lists a number

of *Fluorochromes* which have found many applications in analytical chemistry (by tagging to non-fluorescent compounds) and in biology. By selecting a mixture of two fluorochromes it is possible to obtain a desired emission wavelength. In this case the emitted fluorescence energy from the excitation of the first fluorochrome is transferred to the second fluorochrome to provide the desired fluorescence.
For other than macromolecules it is important that *at least* the ^{1}H NMR spectrum and/or the mass spectrum of the substance should be measured routinely. These measurements require no more than one to three milligrams of material and provide a considerable amount of information about the substance. The ^{1}H NMR and ^{13}C NMR spectra are measured to assess the purity of hydrogen and carbon containing samples. The use of very high magnetic field NMR spectrometers is especially useful for detecting impurities in such samples. The signals and their relative heights can provide valuable information not only about the extent of the impurities, but also some indications about the nature of the impurities. A variety of NMR solvents are available for dissolving the samples, and the hydrogen atoms of the solvents are replaced by deuterium which does not interfere with the ^{1}H or ^{13}C spectra. However, deuteration is generally just under 100% and signals from residual H in the solvent may appear in the spectrum and need to be identified. Similarly ^{13}C signals from solvents also should be identified. Common solvents and reagents that contain trace impurities will also show minor signals in the NMR spectra. The ^{1}H NMR signals of trace impurities in some common organic solvents (including water) and some reagents are presented in Tables 21 and 22. Similarly presented in Table 23 are the ^{13}C NMR signals of some common solvents and reagents. In some instances these minor signals have been very useful as internal standards for reporting the chemical shifts of substances, thus avoiding contamination from other added standards, particularly if the samples need to be used for further studies. The NMR spectra of other nuclei such as ^{11}B and ^{31}P are currently also measured routinely for boron and phosphorus containing compounds. Since the compounds invariably have only a small number of these atoms in their molecules, boron or phosphorus containing impurities are readily identified in the ^{11}B or ^{31}P NMR spectra.

References in the bibliography at the end of this chapter to the Aldrich-Sigma catalogues of NMR, IR and mass spectral data for a large number of the compounds are listed. These collections of spectra are extremely useful for identifying compounds and impurities. If the material appears to have several impurities, these spectra should be valuable for identifying the impurities as much as possible. Preliminary chromatographic (e.g. TLC) and spot tests could be devised to monitor the material and its impurities. Purification methods can then be devised to remove these impurities, and a monitoring method will have already been established.

Ionisation Constants — pK

When substances ionize, their neutral species produce positive and negative species. The ionisation constants are those constant values (equilibrium constants) for the equilibria between the charged species and the neutral species, or species with a larger number of charges (e.g. between mono and dications). These ionisation constants are given as **pK** values where **pK = -log K**, and **K** is the dissociation constant for the equilibrium between the species [Albert and Serjeant, *The Determination of Ionisation Constants*, A Laboratory Manual, 3rd Edition, Chapman & Hall, New York, London, 1984, ISBN 0412242907].

The advantage of using pK values (instead of K values) is that theory (and practice) states that the pK values of ionisable substances are numerically equal to the pH of the solution at which the concentrations of ionised and neutral species are equal. For example acetic acid has a pK^{25} value of 4.76 at 25^{o} in H_2O; then at pH 4.76 the aqueous solution contains equal amounts of acetic acid [AcOH] and acetate anion [AcO^{-}], i.e. [AcOH]/[AcO^{-}] of 50/50. At pH 5.76 (pK + 1) the solution contains [AcOH]/[AcO^{-}] of 10/90, at pH 6.76 (pK + 2) the solution contains [AcOH]/[AcO^{-}] of 1/99 etc; conversely at pH 3.76 (pK – 1) the solution contains [AcOH]/[AcO^{-}] of 90/10, and at pH 2.76 (pK – 2) the solution contains [AcOH]/[AcO^{-}] of 99/1.

One can readily appreciate the usefulness of pK value in purification procedures, e.g. as when purifying acetic acid. If acetic acid is placed in aqueous solution and the pH adjusted to 7.76 {[AcOH]/[AcO^{-}] with a ratio of 0.1/99.9}, and extracted with say diethyl ether, neutral impurities will be extracted into diethyl ether leaving almost all the acetic acid in the form of AcO^{-} in the aqueous solution. If then the pH of the solution is adjusted to 1.67 where the acid is almost all in the form AcOH, almost all of it will be extracted into diethyl ether.

Aniline will be used as a second example. It has a pK^{25} of 4.60 at 25° in H_2O. If it is placed in aqueous solution at pH 1.60 it will exist almost completely (99.9%) as the anilinium cation. This solution can then be extracted with solvents e.g. diethyl ether to remove neutral impurities. The pH of the solution is then adjusted to 7.60 whereby aniline will exist as the free base (99.9%) and can be extracted into diethyl ether in order to give purer aniline.

See Table 24 for the pH values of selected buffers.

A knowledge of the pK allows the adjustment of the pH without the need of large excesses of acids or base. In the case of inorganic compounds, knowledge of the pK is useful for adjusting the ionic species for making metal complexes which could be masked or extracted into organic solvents [Perrin and Dempsey, *Buffers for pH and Metal ion Control*, Chapman & Hall, New York, London, 1974, ISBN 0412117002], or for obtaining specific anionic species in solution e.g. $H_2PO_4^-$, HPO_4^{2-} or PO_4^{3-}.

The **pK** values that have been entered in Chapters 4, 5 and 6 have been collected directly from the literature or from compilations of literature values for organic bases [Perrin, *Dissociation Constants of Organic Bases in Aqueous Solution*, Butterworths, London, 1965, Supplement 1972, ISBN 040870408X; Albert and Serjeant, *The Determination of Ionisation Constants*, A Laboratory Manual, 3rd Edition, Chapman & Hall, London, New York, 1984, ISBN 0412242907]; organic acids [Kortum, Vogel and Andrussow, *Dissociation Constants of Organic Acids in Aqueous Solution,* Butterworth, London, 1961; Serjeant and Dempsey, *Dissociation Constants of Organic Acids in Aqueous Solution,* Pergamon Press, Oxford, New York, 1979, ISBN 0080223397; and inorganic acids and bases [Perrin, *Ionisation Constants of Inorganic Acids and Bases in Aqueous Solution*, Second Edition, Pergamon Press, Oxford, New York, 1982, ISBN 0080292143]. Where literature values were not available, values have been predicted and assigned $\mathbf{pK_{Est}}$ ~. Most predictions should be so close to true values as to make very small difference for the purposes intended in this book. The success of the predictions, i.e. how close to the true value, depends on the availability of pK values for closely related compounds because the effect of substituents or changes in structures are generally additive [Perrin, Dempsey and Serjeant, *pKa Prediction for Organic Acids and Bases*, Chapman & Hall, London, New York, 1981, ISBN 041222190X].

All the pK values in this book are pKa values, the acidic pK, i.e. dissociation of H^+ from an acid (AH) or from a conjugate base (BH^+). Occasionally pKb values are reported in the literature but these can be converted using the equation **pKa + pKb = 14**. For strong acids e.g. sulfuric acid, and strong bases, e.g. sodium hydroxide, the pK values lie beyond the 1 to 11 pH scale and have to be measured in strong acidic and basic media. In these cases appropriate scales e.g. the H_o (for acids) and H_- (for bases) have been used [see Katritzky & Waring, *J Chem Soc* 1540 *1962*]. These values will be less than 1 (and negative) for acids and >11 for bases. They are rough guides to the strengths of acids and bases. Errors in the stated pK and pK_{Est} ~ values can be judged from the numerical values given. Thus pK values of 4.55, 4.5 and 4 mean that the respective errors are better than ± 0.05, ± 0.3 and ± 0.5. Values taken from the literature are written as **pK**, and all the values that were estimated because they were not found in the literature are written as $\mathbf{pK_{Est}}$.

pK and Temperature

The temperatures at which the literature measurements were made are given as superscripts, e.g. pK^{25}. Where no temperature is given, it is assumed that the measurements were carried out at room temperature, e.g. 15–25°. No temperature is given for estimated values ($\mathbf{pK_{Est}}$ ~), and these have been calculated from data at room temperature. The variation of pK with temperature is given by the equation:

$$- \delta(pK)/ \delta T = (pK + 0.052\Delta S^o)/T$$

where T is in degrees Kelvin and ΔS^o is in Joules deg^{-1} mol^{-1}. The $\delta(pK)/dT$ in the range of temperatures between 5 to 70° is generally small (e.g. between ~0.0024 and ~0.04), and for chemical purification purposes is not a seriously deterring factor. It does, however, vary with the compound under study because ΔS^o varies from compound to compound. The following are examples of the effect of temperature on pK values: for imidazole the pK values are 7.57 (0°), 7.33 (10°), 7.10 (20°), 6.99 (25°), 6.89 (30°), 6.58 (40°) and 6.49 (50°), and for 3,5-di-nitrobenzoic acid they are 2.60 (10°), 2.73 (20°), 2.85 (30°), 2.96 (40°) and 3.07 (40°), and for *N*-acetyl-β-

alanine they are 4.4788 (5°), 4.4652 (10°), 4.4564 (15°), 4.4488 (20°), 4.4452 (25°), 4.4444 (30°), 4.4434 (35°) and 4.4412 (40°).

pK and solvent

All stated pK values in this book are for data in dilute aqueous solutions unless otherwise stated, although the dielectric constants, ionic strengths of the solutions and the method of measurement, e.g. potentiometric, spectrophotometric etc., are not given. Estimated values are also for dilute aqueous solutions whether or not the material is soluble enough in water. Generally the more dilute the solution the closer is the pK to the real thermodynamic value. The pK in mixed aqueous solvents can vary considerably with the relative concentrations and with the nature of the solvents. For example the pK^{25} values for *N*-benzylpenicillin are 2.76 and 4.84 in H_2O and H_2O/EtOH (20:80) respectively; the pK^{25} values for (–)-ephedrine are 9.58 and 8.84 in H_2O and $H_2O/MeOCH_2CH_2OH$ (20:80), respectively; and for cyclopentylamine the pK^{25} values are 10.65 and 4.05 in H_2O and H_2O/EtOH (50:50) respectively. pK values in acetic acid or aqueous acetic acid are generally lower than in H_2O.

The dielectric constant of the medium affects the equilibria where charges are generated in the dissociations e.g. $AH \leftrightarrows A^- + H^+$ and therefore affects the pK values. However, its effect on dissociations where there are no changes in total charge such as $BH^+ \leftrightarrows B + H^+$ is considerably less, with a slight decrease in pK with decreasing dielectric constant.

Solubilities of Gases in Liquids

There are two ways to define the solubilites of gases in water.

The first is the *Bunsen coefficient* (β), which is the ratio of the volume of gas corrected to STP (0°C and 1atm, i.e. 760 mmHg) that dissolves in unit volume of solvent at the temperature of the experiment in equilibrium with the gas at 1atm. The second is the *Ostwald coefficient* (*l*) which is the ratio of the volume of gas that dissolves in unit volume of solvent at the temperature of the experiment in equilibrium with the gas at 1atm.

The latter is a more convenient ratio to use because no correction for volume is required. Note that the volume of an ideal gas occupied by one molecular weight in grams of element or compound is ~22.4L at STP (e.g. 32g of oxygen occupy 22.4L at STP). The discussion will be limited to the solubilites of oxygen, nitrogen and air (which behave almost as ideal gases) in water, water containing salts, and in some organic solvents. Generally the solubility of these three gases in water decreases with increase of temperature and can be "boiled out" of the liquid. Their solubilities in organic liquids, on the other hand, generally increase with increase of temperature. The presence of salts in water tends to decrease the solubilities of these gases, i.e. a salting out effect, and increase in pressure increases their solubilities. These properties have to be noted in liquid chromatography at atmospheric and at high pressures. They become important when purifying small amounts of compounds by crystallisation or chromatography when large amounts of solvents are used. One must be wary of the presence of oxygen in solution, particularly in the presence of organic matter. Also the formation of reactive oxygen species e.g. "singlet" oxygen, superoxide and hydroxyl radicals, especially in the presence of trace metals such as iron, and/or of ultraviolet light can result in the formation of impurities.

The composition of air is: 78.08% of N_2, 20.95% of O_2, 0.03% of CO_2, 0.93% of Ar and less than 0.01% of other gases. Although the partial pressure of O_2 in air at 1atm is ~0.20, it has a higher solubility in H_2O than N_2. At STP the solubility of O_2 by volume in H_2O is 34.9% when in equilibrium with excess of air. Thus by successively dissolving air in H_2O, expelling it, and redissolving the expelled air six to seven times it is possible to increase the concentration of oxygen by volume in the expelled air to 90%. The (β) values for O_2 and N_2 in H_2O at STP are 0.028 and 0.014 respectively. There are 55.5 moles of H_2O in 1L of H_2O, so the molar ratios of O_2 to H_2O can be calculated. Note that the concentration of O_2 in liquids is higher when the liquids are in equilibrium with excess O_2 than when they are with excess of air.

The solubility coefficients (β) and/or (*l*) of some gases in liquids are give in Tables 25–28. Tables of the solubilities of HCl and NH_3 (g/100g of solution) at 760 mm (Table 29) and the boiling points of some useful gases at 760 mm (Table 30) are included.

MISCELLANEOUS TECHNIQUES

Freeze-pump-thaw and purging

Volatile contaminants, e.g. traces of low boiling solvent residue or oxygen, in liquid samples or solutions can be very deleterious to the samples on storage. These contaminants can be removed by repeated freeze-pump-thaw cycles. This involves freezing the liquid material under high vacuum in an appropriate vessel (which should be large enough to avoid contaminating the vacuum line with liquid that has bumped) connected to the vacuum line *via* efficient liquid nitrogen traps. The frozen sample is then thawed until it liquefies, kept in this form for some time (*ca* 10–15 minutes), refreezing the sample and the cycle repeated several times without interrupting the vacuum. This procedure applies equally well to solutions, as well as purified liquids, e.g. as a means of removing oxygen from solutions for NMR and other measurements. If the presence of nitrogen, helium or argon, is not a serious contaminant then solutions can be freed from gases, e.g. oxygen, carbon dioxide, and volatile impurities by purging with N_2, He or Ar at room, or slightly elevated, temperature. The gases used for purging are then removed by freeze-pump-thaw cycles or simply by keeping in a vacuum for several hours. Special NMR tubes with a screw cap thread and a PTFE valve (Wilmad) are convenient for freeze thawing of NMR samples. Alternatively NMR tubes with "J Young" valves (Wilmad) can also be used.

Vacuum lines, Schlenk and glovebox techniques

Manipulations involving materials sensitive to air or water vapour can be carried out by these procedures. Vacuum line methods make use of quantitative transfers, and **P**(pressure)-**V**(volume)-**T**(temperature) measurements, of gases, and trap-to-trap separations of volatile substances.

It is usually more convenient to work under an inert-gas atmosphere using **Schlenk** type apparatus. The *principle* of Schlenk methods involve all-glass tubes, flasks or vessels which have standard ground-glass joints with one or more side-arms, one of which may have a tap. The system can be purged by evacuating and flushing with an inert gas (usually dry nitrogen, or in some cases, argon or helium), repeating the process until the contaminants, e.g. O_2, H_2O or CO_2 in the vapour phases have been diminished to acceptable limits. Many of the reactions using Schlenk equipment require anhydrous conditions and in this case the equipment should be heated in an oven slightly above 100^o for 1 to 2 hours (preferably with dry N_2, He or argon flushing), and allowed to cool to room temperature in the presence of a desiccant. A large range of Schlenk glassware is commercially available. Schlenk equipment in which refluxing of liquids is possible without contact with the atmosphere outside of the apparatus is available commercially. With these, and tailor-made pieces of glassware, inert atmospheres can be maintained during transfer of material, crystallisation, reflux, filtration, and sublimation. Where addition of a solid sample should be made, an L-tube, or a small bulb with a bent neck, with a glass joint is used in which the solid is placed, and can be transferred to the main reaction vessel by simply rotating the tube or bulb. In the case of a liquid, a separating funnel with an equalising tube can be used to allow equilibration of pressure. Also, liquids can be injected, *via* a syringe through "Sure/Seal" caps which can be stretched over, or insert nicely into, the ground joint necks of the main reaction container.

Syringe techniques have been developed for small volumes, while for large volumes or where much manipulation is required, dryboxes (*glove boxes*) or dry chambers should be used. Disposable glove bags (e.g. Atmosbags see Sigma-Aldrich Labware of various dimensions) with two or four hands which can be sealed, purged and inflated with an inert gas are available and are relatively cheap and disposable. They are useful not only for handling moisture-sensitive substances, but also for toxic materials.

CHEMICAL AND BIOCHEMICAL SOURCES

Apart from wishing to obtain a pure substance there are many reasons for wanting to purify a substance. For example the substance may have been in the store for too long and has deteriorated to a smaller or larger extent and needs to be used. Large quantities may be required, so bulk amounts, less pure but of cheaper grade could serve the purpose if they can be purified readily and cheaply. The cost consideration is very important. Substances that are available commercially can be of varying grades of purity and the purer the grade the higher the price. Biological substances may be only available in crude form, e.g. acetone powders for enzymes. There are a large number of suppliers of substances for chemical, biochemical and for biological requirements and they are continually improving quality, increasing their range and introducing recently developed substances. The following is a website list of the more commonly used suppliers from which almost all the substances and equipment described in this book can be purchased. The list also contains suppliers of laboratory ware as well as of scientific instruments. The list is not exhaustive.

USEFUL WEBSITES
http://www.

chemsupply.com.au [organics, inorganics & equipment]
sigmaaldrich.com/ [organics, inorganics, lifescience materials & equipment]
wilmad-labglass.com. [glass ware & equipment]
merck-chemicals.com/ [organics, inorganics & equipment]
acros.com/ [organics (Acros organics, inorganics & equipment]
alfa.com/ [organics, inorganics & equipment]
strem.com/ [general inorganics, metal-organics, catalysts, nanomaterials]
tci-asiapacific.com/ [Tokyo Chemical Industry, chemicals, lab equipment]
thermofisher.com/global/en/home.asp [instruments, chemicals, custom products]
https://au.vwr.com/app/Home [VWR International- chemicals/laboratory scientific supplies]
quantumscientific.com/ [chemical, biochemical & lab equipment]
gelifesciences.com [GE Healthcare, chemicals, biochemicals & life science products]
bio-strategy.com [Laboratory technology]
glschina.com [GL biochemical products]
invitrogen.com [Invitrogen, life science products]
lifetechnologies.com [molecular biology products and equipment]
promega.com [Promega, life science products]
tocris.com [Tocris Bioscience products, i.e. neurochemicals, biochemical, peptides, DNA]
novachem.com.au
scilabware.com [plastic labware]
waters.com [Waters, chromatography materials]
biaseparations.com [chromatography materials]
daicel.co.jp/indexe.html [chromatography materials]
restekcorp.com [chromatography materials]
winlab.com.au/ [chromatography materials]
Fritsch-laser.com [for up to nano particle size and milling]
retsch-technology.com [for up to nano particle size]
haverstandard.com [for up to nano particle size]
perkinelmer.com [spectral and other instruments]
agilent.com/chem/atomicspec/ap
betterworld.com [books]
abebooks.com [books]
booksandcollectibles.com.au [books, collectibles]
ebay.com.au/ [books, etc]

For high purity inorganic compounds, NIST Traceable inorganic reference standards/calibrants and aqueous standard solutions for ICP, ICP-MS, AA, GFAA and IC visit <www.exaxol.com>. Note that all the trace metal analyses in the "Inorganic Compounds" section of Chapter 5 are by courtesy of Joe Papa (EXAXOL see Preface).

TABLES

TABLE 1. SOME COMMON IMMISCIBLE OR SLIGHTLY MISCIBLE PAIRS OF SOLVENTS AT AMBIENT TEMPERATURES

Acetonitrile with hexane, heptane, iso-octane, cyclohexane.

Benzene with water, brine and aqueous solutions generally.

Butanol with water, brine and aqueous solutions generally.

Carbon tetrachloride with ethanolamine, ethylene glycol, formamide, water or brine.

Chloroform with glycerol, ethylene glycol, water, aqueous solutions generally

Cyclohexane with alohols, dimethyl formamide, dimethyl sulfoxide, glycerol, pyridine.

Cyclopropyl methyl ether same as ethyl ether but less so.

Dimethyl formamide or **dimethyl acetamide** with cyclohexane, pentane, petroleum ether, xylene.

Dimethyl sulfoxide with ethyl ether, pentane, petroleum ethers, cyclohexane, xylene.

Ethyl acetate with aqueous solutions generally or petroleum ethers.

Ethyl ether with ethanolamine, dimethyl sulfoxide, ethylene glycol, glycerol, water or aqueous solutions generally.

Ethanol with carbon disulfide, petroleum ethers, cyclohexanes.

Glyerol with benzene, ether, chloroform, carbon tetrachloride, carbon disulfide, petroleum ethers, oils.

Iso-octane with acetonitrile, dimethyl formamide, dimethyl sulfoxide, methanol, water.

Methanol with carbon disulfide, hexane, heptane, cyclohexane or petroleum ethers.

***N*-Methylpyrrolidone** with petroleum ethers, cyclohexanes.

Petroleum ether(s) with aniline, benzyl alcohol, dimethyl formamide, dimethyl sulfoxide, formamide, phenol or water and aqeuous solutions generally.

Phenol with petroleum ethers, cyclohexanes.

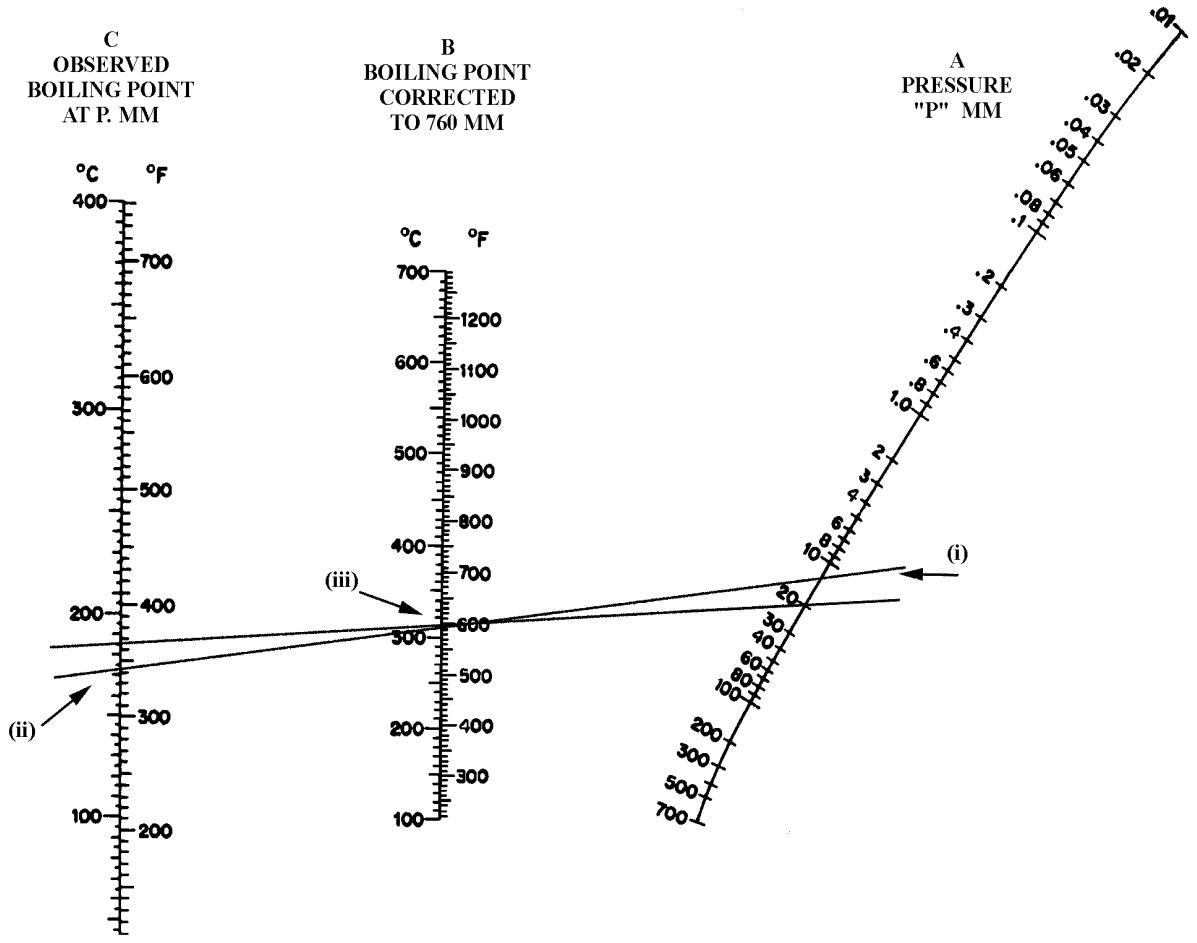
Pyridine with petroleum ethers, hexanes.

Toluene with water, brine, aqueous solutions generally, glycerol but less so than benzene.

Water with aniline, benzene, benzyl alcohol, carbon disulfide, carbon tetrachloride, chloroform, cyclohexane, cyclohexanol, cyclohexanone, diethyl ether, ethyl acetate, isoamyl alcohol, methyl ethyl ketone, nitromethane, tributyl phosphate or toluene.

Xylene with water, brine, aqueous solutions generally, glycerol, dimethyl formamide, dimethyl sulfoxide.

FIGURE 1: NOMOGRAM



How to use Figure 1:

You can use a nomogram to estimate the boiling points of a substance at a particular pressure. For example, the boiling point of 4-methoxybenzenesulfonyl chloride is 173°C/14mm. Thus to find out what the boiling point of this compound will be at 760 mm (atmospheric), draw a point on curve A (pressure) at 14mm (this is shown in (i). Then draw a point on curve C (observed boiling point) corresponding to 173° (or as close as possible). This is shown in (ii). Using a ruler, find the point of intersection on curve B, drawing a line between points (i) and (ii). This is the point (iii) and is the boiling point of 4-methoxybenzenesulfonyl chloride (i.e. approx. 310°C) at atmospheric pressure. If you want to distil 4-methoxybenzenesulfonyl chloride at 20 mm, then you will need to draw a point on curve A (at 20 mm). Using a ruler, find the point of intersection on curve C drawing through the line intersecting (iii, curve B, i.e. 310°C) and the point in curve A corresponding to 20 mm. You should have a value of 185°C; that is, the boiling point of 4-methoxybenzenesulfonyl chloride is estimated to be at 185°C at 20 mm.

TABLE 2A. PREDICTED EFFECT OF PRESSURE ON BOILING POINT*

	Temperature in degrees Centigrade									
760 mmHg	0	20	40	60	80	100	120	140	160	180
0.1	-111	-99	-87	-75	-63	-51	-39	-27	-15	-4
0.2	-105	-93	-81	-69	-56	-44	-32	-19	-7	5
0.4	-100	-87	-74	-62	-49	-36	-24	-11	2	15
0.6	-96	-83	-70	-57	-44	-32	-19	-6	7	20
0.8	-94	-81	-67	-54	-41	-28	-15	-2	11	24
1.0	-92	-78	-65	-52	-39	-25	-12	1	15	28
2.0	-85	-71	-58	-44	-30	-16	-3	11	25	39
4.0	-78	-64	-49	-35	-21	-7	8	22	36	51
6.0	-74	-59	-44	-30	-15	-1	14	29	43	58
8.0	-70	-56	-41	-26	-11	4	19	34	48	63
10.0	-68	-53	-38	-23	-8	7	22	37	53	68
14.0	-64	-48	-33	-23	-2	13	28	44	59	74
16.0	-61	-45	-29	-14	2	17	33	48	64	79
20.0	-59	-44	-28	-12	3	19	35	50	66	82
30.0	-54	-38	-22	-6	10	26	42	58	74	90
40.0	-50	-34	-17	-1	15	32	48	64	81	97
50.0	-47	-30	-14	3	19	36	52	69	86	102
60.0	-44	-28	-11	6	23	40	56	73	86	107
80.0	-40	-23	-6	11	28	45	62	79	97	114
100.0	-37	-19	-2	15	33	50	67	85	102	119
150.0	-30	-12	6	23	41	59	77	95	112	130
200.0	-25	-7	11	29	47	66	84	102	120	138
300.0	-18	1	19	38	57	75	94	113	131	150
400.0	-13	6	25	44	64	83	102	121	140	159
500.0	-8	11	30	50	69	88	108	127	147	166
600.0	-5	15	34	54	74	93	113	133	152	172
700.0	-2	18	38	58	78	98	118	137	157	177
750.0	0	20	40	60	80	100	120	140	160	180
770.0	0	20	40	60	80	100	120	140	160	180
800.0	1	21	41	61	81	101	122	142	162	182

* *How to use the Table*: Take as an example a liquid with a boiling point of 80°C at 760 mmHg. The Table gives values of the boiling points of this liquid at pressures from 0.1 to 800 mmHg. Thus at 50 mmHg this liquid has a boiling point of 19°C, and at 2 mmHg its boiling point would be –30°C.

TABLE 2B. PREDICTED EFFECT OF PRESSURE ON BOILING POINT*

	Temperature in degrees Centigrade										
760 mmHg	200	220	240	260	280	300	320	340	360	380	400
0.1	8	20	32	44	56	68	80	92	104	115	127
0.2	17	30	42	54	67	79	91	103	116	128	140
0.4	27	40	53	65	78	91	103	116	129	141	154
0.6	33	40	59	72	85	98	111	124	137	150	163
0.8	38	51	64	77	90	103	116	130	143	156	169
1.0	41	54	68	81	94	108	121	134	147	161	174
2.0	53	66	80	94	108	121	135	149	163	176	190
4.0	65	79	93	108	122	136	151	156	179	193	208
6.0	72	87	102	116	131	146	160	175	189	204	219
8.0	78	93	108	123	137	152	167	182	197	212	227
10.0	83	98	113	128	143	158	173	188	203	218	233
14.0	90	105	120	136	151	166	182	197	212	228	243
18.0	95	111	126	142	157	173	188	204	219	235	251
20.0	97	113	129	144	160	176	191	207	223	238	254
30.0	106	123	139	155	171	187	203	219	235	251	267
40.0	113	130	146	162	179	195	211	228	244	260	277
50.0	119	135	152	168	185	202	218	235	251	268	284
60.0	123	140	157	174	190	207	224	241	257	274	291
80.0	131	148	165	182	199	216	233	250	267	284	301
100.0	137	154	171	189	206	223	241	258	275	293	310
150.0	148	166	184	201	219	237	255	273	290	308	326
200.0	156	174	193	211	229	247	265	283	302	320	338
300.0	169	187	206	225	243	262	281	299	318	337	355
400.0	178	197	216	235	254	273	292	311	330	350	369
500.0	185	205	224	244	263	282	302	321	340	360	379
600.0	192	211	231	251	270	290	310	329	349	368	388
700.0	197	217	237	257	277	296	316	336	356	376	396
750.0	200	220	239	259	279	299	319	339	359	279	399
770.0	200	220	241	261	281	301	321	341	361	381	401
800.0	202	222	242	262	282	302	322	342	262	382	403

**How to use the Table*: Taking as an example a liquid with a boiling point of 340°C at 760 mmHg, the column headed 340°C gives values of the boiling points of this liquid at each value of pressures from 0.1 to 800 mmHg. Thus, at 100 mmHg its boiling point is 258°C, and at 0.8mm Hg its boiling point will be 130°C.

TABLE 3. HEATING BATHS

Up to 100°	Water baths
20 to 200°	Glycerol or di-*n*-butyl phthalate
Up to about 200°	Medicinal paraffin
Up to about 250°	Hard hydrogenated cotton-seed oil (**m** 40–60°) or a 1:1 mixture of cotton-seed oil and castor oil containing about 1% of hydroquinone.
40 to 250° (to 400° under N_2)	D.C. 550 silicone fluid
Up to about 260°	A mixture of 85% orthophosphoric acid (4 parts) and metaphosphoric acid (1 part)
Up to 340°	A mixture of 85% orthophosphoric acid (2 parts) and metaphosphoric acid (1 part)
60 to 500°	Fisher bath wax (highly unsaturated)
73 to 350°	Wood's Metal*
250 to 800°	Solder*
350 to 800°	Lead*

* In using metal baths, the container (usually a metal crucible) should be removed while the metal is still molten.

TABLE 4. WHATMAN FILTER PAPERS

Grade No.	1	2	3	4	5	6	113
Particle size retained (in microns)	11	8	5	12	2.4	2.8	28
Filtration speed*(sec/100ml)	40	55	155	20	<300	125	9

Routine ashless filters

Grade No.	40	41	42	43	44
Particle size retained (in microns)	7.5	12	3	12	4
Filtration speed* (sec/100ml)	68	19	200	38	125

	Hardened			**Hardened ashless**		
Grade No.	50	52	54	540	541	542
Particle size retained(in microns)	3	8	20	9	20	3
Filtration speed* (sec/100ml)	250	55	10	55	12	250

Glass microfilters

Grade No	GF/A	GF/B	GF/C	GF/D	GF/F
Particle size retained (in microns)	1.6	1.0	1.1	2.2	0.8
Filtration speed (sec/100ml)*	8.3	20.0	8.7	5.5	17.2

*Filtration speeds are rough estimates of initial flow rates and should be considered on a relative basis.

TABLE 5. MICRO FILTERS*

Nucleopore (polycarbonate) Filters

Mean Pore Size (microns)	8.0	2.0	1.0	0.1	0.03	0.015
Av. pores/cm^2	10^5	2×10^6	2×10^7	3×10^8	6×10^8	$1–6\times10^9$
Water flow rate(ml/min/cm^2)	2000	2000	300	8	0.03	0.1–0.5

Millipore Filters

Type	*Cellulose ester*		*Teflon*		*Microweb*#	
	MF/SC	MF/VF	LC	LS	WS	WH
Mean Pore Size (microns)	8	0.01	10	5	3	0.45
Water flow rate (ml/min/cm^2)	850	0.2	170	70	155	55

Gelman Membranes

Type	*Cellulose ester*				*Copolymer*	
	GA-1	T CM-450	VM-1	DM-800	AN-200	Tuffryn-450
Mean Pore Size (microns)	5	0.45	5	0.8	0.2	0.45
Water flow rate (ml/min/cm^2)	320	50	700	200	17	50

Sartorius Membrane Filters (SM)

Application	Gravi-metric	Biological clarifica-tion	Sterili-sation	Particle count in H_2O	For acids & bases
Type No.	11003	11004	11006	11011	12801
Mean PoreSize (microns)	1.2	0.6	0.45	0.01	8.0
Water flow rate (ml/min/cm^2)	300	150	65	0.6	1100

* Only a few representative filters are tabulated (available ranges are more extensive). # Reinforced nylon.

TABLE 6. COMMON SOLVENTS USED IN RECRYSTALLISATION

Acetic acid (118°)	*Cyclohexane (81°)	*Methanol (64.5°)
*Acetone (56°)	Dichloromethane (41°)	*Methyl ethyl ketone (80°)
Acetylacetone (139°)	*Diethyl ether (34.5°)	Methyl isobutyl ketone (116°)
Acetonitrile (82°C)	Dimethyl formamide (76°/39mm)	Nitrobenzene (210°)
*Benzene (80°)	*Dioxane (101°)	Nitromethane (101°)
Benzyl alcohol (93°/10mm)	*Ethanol (78°)	*Petroleum ether (various)
n-Butanol (118°)	2-Ethoxyethanol (cellosolve 135°)	Pyridine (115.5°)
Butyl acetate (126.5°)	*Ethyl acetate (78°)	Pyridine trihydrate (93°)
n-Butyl ether (142°)	Ethyl benzoate (98°/19mm)	*Tetrahydrofuran (64-66°)
γ-Butyrolactone (206°)	Ethylene glycol (68°/4mm)	Toluene (110°)
Carbon tetrachloride (77°)	Formamide (110°/10mm)	Trimethylene glycol (59°/11mm)
Chlorobenzene (132°)	Glycerol (126°/11mm)	Water (100°)
Chloroform (61°)	Isoamyl alcohol (131°)	Xylenes (*o* 143-145°, *m* 138-139°, *p* 138°)

***Highly flammable, should be heated or evaporated on steam or electrically heated water baths only (preferably under nitrogen). None of these solvents should be heated over a naked flame.**

TABLE 7. PAIRS OF MISCIBLE SOLVENTS

Acetic acid: with chloroform, ethanol, ethyl acetate, acetonitrile, petroleum ether, or water.
Acetone: with benzene, butyl acetate, butyl alcohol, carbon tetrachloride, chloroform, cyclohexane, ethanol, ethyl acetate, methyl acetate, acetonitrile, petroleum ether or water.
Ammonia: with ethanol, methanol, pyridine.
Aniline: with acetone, benzene, carbon tetrachloride, ethyl ether, *n*-heptane, methanol, acetonitrile or nitrobenzene.
Benzene: with acetone, butyl alcohol, carbon tetrachloride, chloroform, cyclohexane, ethanol, acetonitrile, petroleum ether or pyridine.
Butyl alcohol: with acetone or ethyl acetate.
Carbon disulfide: with petroleum ether.
Carbon tetrachloride: with cyclohexane.
Chloroform: with acetic acid, acetone, benzene, ethanol, ethyl acetate, hexane, methanol or pyridine.
Cyclohexane: with acetone, benzene, carbon tetrachloride, ethanol or diethyl ether.
Diethyl ether: with acetone, cyclohexane, ethanol, methanol, methylal (dimethoxymethane), acetonitrile, pentane or petroleum ether.
Dimethyl formamide: with benzene, ethanol or ether.
Dimethyl sulfoxide: with acetone, benzene, chloroform, ethanol, diethyl ether or water.
Dioxane: with benzene, carbon tetrachloride, chloroform, ethanol, diethyl ether, petroleum ether, pyridine or water**.**
Ethanol: with acetic acid, acetone, benzene, chloroform, cyclohexane, dioxane, ethyl ether, pentane, toluene, water or xylene.
Ethyl acetate: with acetic acid, acetone, butyl alcohol, chloroform, or methanol.
Glycerol: with ethanol, methanol or water.
Hexane: with benzene, chloroform or ethanol.
Methanol: with chloroform, diethyl ether, glycerol or water.
Methylal: with diethyl ether.
Methyl ethyl ketone: with acetic acid, benzene, ethanol or methanol.
Nitrobenzene: with aniline, methanol or acetonitrile.
Pentane: with ethanol or diethyl ether.
Petroleum ether: with acetic acid, acetone, benzene, carbon disulfide or diethyl ether.
Phenol: with carbon tetrachloride, ethanol, diethyl ether or xylene.
Pyridine: with acetone, ammonia, benzene, chloroform, dioxane, petroleum ether, toluene or water.
Toluene: with ethanol, diethyl ether or pyridine.
Water: with acetic acid, acetone, ethanol, methanol, or pyridine.
Xylene: with ethanol or phenol.

TABLE 8. MATERIALS FOR COOLING BATHS

Temp. (°)	Composition	Temp. (°)	Composition
0	Crushed ice	–72	Solid CO_2 with ethanol
–5 to –20	Ice-salt mixtures	–77	Solid CO_2 with chloroform or acetone
Up to –20	Ice-MeOH mixtures	–78	Solid CO_2 (powdered; CO_2 snow)
–33	Liquid ammonia	–100	Solid CO_2 with diethyl ether
–40 to –50	Ice (3.5–4 parts) - $CaCl_2 \cdot 6H_2O$ (5 parts)	–196	liquid nitrogen (see footnote*)

Alternatively, the following liquids can be used, partially frozen, as cryostats, by adding solid CO_2 from time to time to the material in a Dewar-type container and stirring to make a slush:

13	*p*-Xylene	–55	Diacetone
12	Dioxane	–56	*n*-Octane
6	Cyclohexane	–60	Di-isopropyl ether
5	Benzene	–73	Trichloroethylene or isopropyl acetate
2	Formamide	–74	*o*-Cymene or *p*-cymene
–8.6	Methyl salicylate	–77	Butyl acetate
–9	Hexane-2,5-dione	–79	Isoamyl acetate
–10.5	Ethylene glycol	–83	Propylamine
–11.9	*tert*-Amyl alcohol	–83.6	Ethyl acetate
–12	Cycloheptane or methyl benzoate	–86	Methyl ethyl ketone
–15	Benzyl alcohol	–89	*n*-Butanol
–16.3	*n*-Octanol	–90	Nitroethane
–18	1,2-Dichlorobenzene	–91	Heptane
–22	Tetrachloroethylene	–92	*n*-Propyl acetate
–22.4	Butyl benzoate	–93	2-Nitropropane or cyclopentane
–22.8	Carbon tetrachloride	–94	Ethyl benzene or hexane
–24.5	Diethyl sulfate	–94.6	Acetone
–25	1,3-Dichlorobenzene	–95.1	Toluene
–29	*o*-Xylene or pentachloroethane	–97	Cumene
–30	Bromobenzene	–98	Methanol or methyl acetate
–32	*m*-Toluidine	–99	Isobutyl acetate
–32.6	Dipropyl ketone	–104	Cyclohexene
–38	Thiophene	–107	Isooctane
–41	Acetonitrile	–108	1-Nitropropane
–42	Pyridine or diethyl ketone	–116	Ethanol or diethyl ether
–44	Cyclohexyl chloride	–117	Isoamyl alcohol
–45	Chlorobenzene	–126	Methylcyclohexane
–47	*m*-Xylene	–131	*n*-Pentane
–50	Ethyl malonate or *n*-butylamine	–160	Isopentane
–52	Benzyl acetate or diethylcarbitol		

For other organic materials used in low temperature slush-baths with liquid nitrogen see R.E.Rondeau [*J Chem Eng Data* **11** 124 *1966*]. ***NOTE**: Use high quality pure nitrogen; do not use liquid air or liquid nitrogen that has been in contact with air for a long period (due to the dissolution of oxygen in it) as this could EXPLODE in contact with organic matter.

TABLE 9. LIQUIDS FOR STATIONARY PHASES IN GAS CHROMATOGRAPHY*

Material	Temp. (°)	Retards
Dimethylsulfolane	0–40	Olefins and aromatic hydrocarbons
Di-*n*-butyl phthalate	0–40	General purposes
Squalane	0–150	Volatile hydrocarbons and polar molecules
Silicone oil or grease	0–250	General purposes
Diglycerol	20–120	Water, alcohols, amines, esters, and aromatic hydrocarbons
Dinonyl phthalate	20–130	General purposes
Polydiethylene glycol succinate	50–200	Aromatic hydrocarbons, alcohols, ketones, esters
Polyethylene glycol	50–200	Water, alcohols, amines, esters and aromatic hydrocarbons
Apiezon grease	50–200	Volatile hydrocarbons and polar molecules
Tricresyl phosphate	50–250	General purposes

* See Suppliers at the end of section on HPLC and E.F. Barry and R.L. Grob, *Columns for Gas Chromatography*, J. Wiley and Sons NY, *2007*, ISBN 9780471740438.

TABLE 10. METHODS OF VISUALISATION OF TLC SPOTS

Reagent	Compound	Preparation	Observations
Iodine	General	Iodine crystals in a closed chamber or spray 1% methanol solution of Iodine	Brown spots which may disappear upon standing
H_2SO_4	General	50% solution, followed by heating to 150°C	Black or coloured spots
Molybdate	General	5% $(NH_4)_6Mo_7O_{24}$ + 0.2% $Ce(SO_4)_2$ in 5% H_2SO_4, followed by heating to 150°C	Deep blue spots
Vanillin	General	0.5g vanillin, 0.5 ml H_2SO_4, 9 ml ethanol	various coloured spots
Ammonia	phenols	Ammonia vapour in a closed chamber	various coloured spots
$FeCl_3$	phenols, enols	1% aqueous $FeCl_3$	various coloured spots
2,4-DNP	aldehydes, ketones	0.5% 2,4-dinitrophenylhydrazine/2M HCl	red to yellow spots
HCl	aromatic acids and amines	HCl vapour in a closed chamber	various coloured spots
Ninhydrin	amino acids, and amines	0.3% ninhydrin in *n*-BuOH with 3% AcOH, followed by heating to 125°C/10 min	blue spots
$PdCl_2$	S and Se compds	0.5% aq. $PdCl_2$ + few drops of conc. HCl	red and yellow spots
Anisaldehyde	carbohydrates	0.5 ml anisaldehyde in 0.5 ml conc H_2SO_4 + 95% EtOH + a few drops of AcOH Heat at 100–110°C for 20–30 minutes	various blue spots

TABLE 11. GRADED ADSORBENTS AND SOLVENTS FOR CHROMATOGRAPHY

Adsorbents (decreasing effectiveness)	**Solvents** (increasing eluting ability)
Fuller's earth (hydrated aluminosilicate)	Petroleum ether, b. 40–60°.
Magnesium oxide	Petroleum ether, b. 60–80°.
Charcoal	Carbon tetrachloride
Alumina	Cyclohexane
Magnesium trisilicate	Benzene
Silica gel	Diethyl ether
Calcium hydroxide	Chloroform
Magnesium carbonate	Ethyl acetate
Calcium phosphate	Acetone
Calcium carbonate	Ethanol
Sodium carbonate	Methanol
Talc	Pyridine
Inulin	Acetic acid
Sucrose = starch	

TABLE 12. REPRESENTATIVE ION-EXCHANGE RESINS USED IN CHROMATOGRAPHY

Sulfonated polystyrene	**Aliphatic amine-type**
Strong-acid cation exchanger	**weak base anion exchangers**
AG 50W-x8	Amberlites IR-45 and IRA-67
Amberlite IR-120	Dowex 3-x4A
Dowex 50W-x8	Permutit E
Duolite 225	Permutit A 240A
Permutit RS	
Permutite C50D	
Carboxylic acid-type	**Strong Base, anion exchangers**
Weak acid cation exchangers	AG 2x8
Amberlite IRC-50	Amberlite IRA-400
Bio-Rex 70	Dowex 2-x8
Chelex 100	Duolite 113
Duolite 436	Permutit ESB
Permutit C	Permutite 330D
Permutits H and H-70	

TABLE 13. MODIFIED FIBROUS CELLULOSES FOR ION-EXCHANGE CHROMATOGRAPHY

Cation exchange	**Anion exchange**
CM cellulose (carboxymethyl)	DEAE cellulose (diethylaminoethyl)
CM 22, 23 cellulose	DE 22, 23 cellulose
P cellulose (phosphate)	PAB cellulose (*p*-aminobenzyl)
SE cellulose (sulfoethyl)	TEAE cellulose (triethylaminoethyl)
SM cellulose (sulfomethyl)	ECTEOLA cellulose

SE and SM are much stronger acids than CM, whereas P has two ionisable groups (pK 2–3, 6–7)*, one of which is stronger, the other weaker, than for CM* (3.5–4.5). For basic strengths, the sequence is: TEAE » DEAE (pK 8-95) > ECTEOLA (pK 5.5-7) > PAB. **Their exchange capacities lie in the range 0.3 to 1.0 mg equiv/g.**

TABLE 14. BEAD FORM ION-EXCHANGE PACKAGINGS FOR CHROMATOGRAPHY[1]

Cation exchange	Capacity (meq/g)	Anion exchange	Capacity (meq/g)
CM-Sephadex C-25, C-50.[2](weak acid)	4.5±0.5	DEAE-Sephadex A-25, A-50.[7] (weak base)	3.5±0.5
SP-Sephadex C-25, C-50.[3](strong acid)	2.3±0.3	QAE-Sephadex A-25, A-50.[8] (strong base)	3.0±0.4
CM-Sepharose CL-6B.[4]	0.12±0.02	DEAE-Sepharose CL-6B.[4]	0.13±0.02
		DEAE-Sephacel.[9]	1.4±0.1
Fractogel EMD,CO_2^- ($pK \sim 4.5$), SO_3^{2-} ($pK \sim < 1$).[5]		Fractogel EMD, DMAE (pK ~9), DEAE (pK ~10.8), TMAE (pK >13).[5]	
CM-32 Cellulose.		DE-32 Cellulose.	
CM-52 Cellulose.[6]		DE-52 Cellulose	

[1]May be sterilised by autoclaving at pH 7 and below 120°. [2]Carboxymethyl. [3]Sulfopropyl. [4]Crosslinked agarose gel, no pre-cycling required, pH range 3-10. [5]Hydrophilic methacrylate polymer with very little volume change on change of pH (equivalent to *Toyopearl,* Sigma), available in superfine 650S, and medium 650M particle sizes. [6]Microgranular, pre-swollen, no pre-cycling required. [7]Diethylaminoethyl. [8]Diethyl(2-hydroxy-propyl)aminoethyl. [9]Bead form cellulose, pH range 2–12, no pre-cycling required. Sephadex and Sepharose from GE Healthcare, Fractogel from Merck, Cellulose from Whatman.

TABLE 15 SELECTED CHIRAL COLUMNS FOR CHROMATOGRAPHY*

Column name	Chiral ligand	Attributes	Manufacture
CHIRA-chrom-1 CHIRA-chrom-2	*R*- or *S*- phenylglycine *S*-leucine dinitrophenyl tartramide	High capacity & efficiency	HICHROM
CHIRAL-AGP CHIRAL-CBH CHIRAL-HAS	α 1-acid glycoprotein cellobiohydrolase human serum albumin	Used in wide pH range	CHROM TECH
CHIRALCEL OD/OJ CHIRALPAK AD/AS/H CHIRALPAK 1A CHIRALPAK 1B CROWNPAK	cellulose derivative amylose derivative immobilised amylose immobilised cellulose 18-crown 6 type ether	Particular separations versatile broad range broad range for amino acids and primary amines	DIACEL
CHIROSIL	(18-crown 6)$(CO_2H)_4$	for amino acids and primary amines	RStech

(continued)

TABLE 15 (Continued) SELECTED CHIRAL COLUMNS FOR CHROMATOGRAPHY*

Column name	Chiral ligand	Attributes	Manufacture
CHIROBIOTIC R	Ristocetin A	Broad selectivity	
CHIROBIOTIC T	Teicoplanin	Broad selectivity	Astech 1
CHIROBIOTIC V	Vancomycin	Broad selectivity	
CYCLOBOND I	β-cyclodextrin	form chiral	Astech 1
CYCLOBOND II	γ-cyclodextrin	inclusion complexes	
KROMASIL DMB	Acetylated *N*,*N'*-diallyl	stable, high capacity	Eka Chemicals
KROMASIL TBB	*S*-tartardiamide	for large prep work	
NUCLEODEX β-OH	β-cyclodextrin	reverse phase work	
NUCLEODEX α-, β-	permethylated α-, β- and	reverse phase work	Macherey–
and γ-PM	γ-cyclodextrins	reverse phase work	Nagel
NUCLEOSIL Chiral-1	*S*-hydroxyproline-Cu^{2+} complex	ligand exchange, e.g. α-amino acids	
RESOLVOSIL BSA-7PX	bovine serum albumen	various applications	
ULTRON ES-OVM	ovomucoid protein	stable phase	Shinwa Chem
ULTRON ES-Pepsin	pepsin protein	stable phase	Industries
DACH-DNB	3,5-dinitrobenzoyl derivs	π-electron acceptor/	
ULMO	3,5-dinitrobenzoyl derivs	donor — widely used	
α-Burke 2	3,5-dinitrobenzoyl derivs	π-electron acceptor	
β-GEM 1	3,5-dinitrobenzoyl derivs	π-electron acceptor	
Leucine	3,5-dinitrobenzoyl derivs	π-electron acceptor	REGIS
Phenyglycine	β-lactamase chiral selector	π-electron acceptor	
PIRKLE-1J	*S*-naphthylleucine	π-electron donor	
Naphthylleucine	ligand exchange	good for underivatised	
DAVAKOV	ligand exchange	amino acids	

* These data were generously provided by Gordon Wingate, Operational Director of Winlab Pty Ltd., POBox 5007, Brendale, Queensland 4500, Australia. Further details about these and other chromatographic columns may be obtained from him, and at < http://www.winlab.com.au/>.

TABLE 16. LIQUIDS FOR DRYING PISTOLS

Boiling points (760 mm)	(°)	Boiling points (760 mm)	(°)
Ethyl chloride	12.2	Toluene	110.5
Dichloromethane	39.8	Tetrachloroethylene	121.2
Acetone	56.1	Chlorobenzene	132.0
Chloroform	62.0	*m*-Xylene	139.3
Methanol	64.5	Isoamyl acetate	142.5
Carbon tetrachloride	76.5	Tetrachloroethane	146.3
Ethanol	78.3	Bromobenzene	155.0
Benzene	79.8	*p*-Cymene	176.0
Trichloroethylene	86.0	*o*-Chlorobenzene	180.5
Water	100.0	Tetralin	207.0

TABLE 17. VAPOUR PRESSURES (mm Hg) OF SATURATED AQUEOUS SOLUTIONS IN EQUILIBRIUM WITH SOLID SALTS

Salt	Temperature					% Humidity
	10^o	15^o	20^o	25^o	30^o	at 20^o
$LiCl.H_2O$			2.6			15
$CaBr_2.6H_2O$	2.1	2.7	3.3	4.0	4.8	19
KOAc			3.5			20
$CaCl_2.6H_2O$	3.5	4.5	5.6	6.9	8.3	20
CrO_3			6.1			32
$Zn(NO_3)_2.6H_2O$			7.4			42
$K_2CO_3.2H_2O$			7.7	10.7		44
KCNS			8.2			47
$Na_2Cr_2O_7.2H_2O$			9.1			52
$Ca(NO_3)_2.4H_2O$	6.0	7.7	9.6	11.9	14.2	55
$Mg(NO_3)_2.6H_2O$			9.8			56
$NaBr.2H_2O$	5.8	7.8	10.3	13.5	17.5	58
$NaNO_2$			11.6			66
NaCl	6.9	9.6	13.2	17.8	21.4	75
NaOAc			13.3			76
NH_4Cl			13.8			79
$(NH_4)_2SO_4$			14.2			81
KBr			14.7			84
$KHSO_4$			15.1			86
KCl			15.1	20.2	27.0	86
K_2CrO_4			15.4			88
$ZnSO_4.7H_2O$			15.8			90
$NH_4.H_2PO_4$			16.3			93
KNO_3			16.7	22.3	29.8	95
$Pb(NO_3)_2$			17.2			98
H_2O	9.21	12.79	17.53	23.76	31.82	100

TABLE 18. DRYING AGENTS FOR CLASSES OF COMPOUNDS

Class	Dried with
Acetals	Potassium carbonate.
Acids (organic)	Calcium sulfate, magnesium sulfate, sodium sulfate.
Acyl halides	Magnesium sulfate, sodium sulfate.
Alcohols	Calcium oxide, calcium sulfate, magnesium sulfate, potassium carbonate, followed by magnesium and iodine.
Aldehydes	Calcium sulfate, magnesium sulfate, sodium sulfate.
Alkyl halides	Calcium chloride, calcium sulfate, magnesium sulfate. phosphorus pentoxide, sodium sulfate.
Amines	Barium oxide, calcium oxide, potassium hydroxide, sodium carbonate, sodium hydroxide.
Aryl halides	Calcium chloride, calcium sulfate, magnesium sulfate, phosphorus pentoxide, sodium sulfate.
Esters	Magnesium sulfate, potassium carbonate, sodium sulfate.
Ethers	Calcium chloride, calcium sulfate, magnesium sulfate, sodium, lithium aluminium hydride.
Heterocyclic bases	Magnesium sulfate, potassium carbonate, sodium hydroxide.
Hydrocarbons	Calcium chloride, calcium sulfate, magnesium sulfate, phosphorus pentoxide, sodium (not for olefins).
Ketones	Calcium sulfate, magnesium sulfate, potassium carbonate, sodium sulfate.
Mercaptans	Magnesium sulfate, sodium sulfate.
Nitro compounds and Nitriles	Calcium chloride, magnesium sulfate, sodium sulfate.
Sulfides	Calcium chloride, calcium sulfate.

TABLE 19. STATIC DRYING FOR SELECTED LIQUIDS (25°C)

Liquid	Water	Linde Type 4 A	Linde Type 5 A	Activated Alumina	Silicic Acid Gel
MeOH	Residual H_2O % Wt % absorbed	0.54 2.50	0.55 1.50	— —	0.60 —
EtOH	Residual H_2O % Wt % absorbed	0.25 7.00	0.25 6.80	0.45 1.50	0.68 —
1-Butylamine	Residual H_2O % Wt % absorbed	1.65 10.40	1.31 18.20	1.93 3.40	2.07 —
2-Ethyl-hexylamine	Residual H_2O % Wt % absorbed	0.25 15.10	0.08 21.10	0.43 6.10	0.53 1.70
Diethyl ether	Residual H_2O % Wt % absorbed	0.001 9.50	0.013 9.20	0.16 6.20	0.27 4.30
Amyl acetate	Residual H_2O % Wt % absorbed	0.002 9.30	— —	0.33 7.40	0.38 1.80

TABLE 20 FLUOROCHROMES*

	CAS registry No	λ_{ex} (nm) #	λ_{em} (nm)#	Applications
Acriflavin	[8048-52-0]	463	490	Stains many compounds
Allophycocyanin (APC)		604 (650)	650 (660)	Polypeptide with exceptional Fluorescence for cytometry
3-Aminocoumarin	[1635-31-0]	350	445	Forms fluorescent derivatives *via* reaction with the 3-NH_2 group
Auramine O (basic yellow 2)	[2465-27-2]	440	530	Fluorescent stain for bacteria and probe for certain enzymes, e.g. alcohol dehydrogenases
4-Bromomethyl-7-methoxycoumarin	[35231-44-8]	360 (340)	410 (421)	Forms fluorescent probes with various compds for TLC/HPLC
Chromomycin A_3	[7059-24-7]	445	575	Stains DNA
Ethidium bromide	[1239-45-8]	493	620	Stains DNA
Fluorescamine	[38183-12-9]			Reacts with various R-NH_2 to form fluorescent compds
Fluorescein	[2321-07-5]	490	514	Fluorescent nucleus for staining a Variety of compounds
Fluorescein-Isothiocyanate (FITC)	[3326-32-7]	492	518	Microsequencing of peptides & proteins, makes fluorescent Amino acids
Hoechst H 2495 (benzoxanthene yellow)	[72845-94-4]			Fluorochrome for various compds
Hoechst H33342 (bisBenzimide 3HCl)	[23491-52-3]	346	640	Intercalates DNA for cytometry and fluorescence microscopy
R-Phycoerythrin	[11016-17-4]	488	572	Forms fluorescent probes with proteins
PKH 2 and 72 (green)		490	504	A Protein Kinase polypeptide that links to cells causing fluorescence
PKH 26 (red)		557	567	Used for labeling cells. (cf PKH 2 or 72)
Tetramethyl rhodamine Isothiocyanate (TRITC)	[95197-95-8]	529 (492)	596 (518)	Protein fluorochrome, used for immunofluorescence

** Of the many fluorochromes reported in this book only a very small selection is tabulated here. # These wavelengths may vary somewhat depending on the solvent used, and on the pH if measured in aqueous solutions.

TABLE 21. RESIDUAL SOLVENT SIGNALS OF COMMON NMR SOLVENTS
(Adapted from Gottieb et al. *J Org Chem* **62** 7512 *1997*, Fulmer et al. *Organometallics* **29**, 2176 *2010.*)

Solvents	**^{1}H NMR**	**^{13}C NMR**
Deuterated chloroform , $CDCl_3$	7.26	77.16
Deuterated dichloromethane CD_2Cl_2	5.32	53.84
Deuterated benzene, C_6D_6	7.16	128.06
Deuterated acetone, $(CD_3)_2CO$	2.05	29.84; 206.26
Deuterated dimethylsulfoxide, $(CD_3)_2SO$	2.50	35.52
Deuterated acetonitrile, CD_3CN	1.94	1.32; 118.26
Deuterated methanol, CD_3OD	3.31	49.00
Deuterated water, D_2O	4.79	–

TABLE 22. ^{1}H NMR CHEMICAL SHIFTS OF TRACE IMPURITIES OF COMMON SOLVENTS AND REAGENTS

	$CDCl_3$	**CD_2Cl_2**	**C_6D_6**	**$(CD_3)_2CO$**	**$(CD_3)_2SO$**	**CD_3CN**	**CD_3OD**	**D_2O**
H_2O	1.56	1.52	0.40	*2.84*	*3.33*	2.13	4.87	4.79
Acetone	2.17	2.12	1.55	2.05	2.09	2.09	2.15	2.22
Acetonitrile	2.10	1.97	0.58	2.05	2.07	1.94	2.03	2.06
Chloroform	7.26	7.32	6.15	8.02	8.32	7.58	7.90	-
Dichloromethane	5.30	5.33	4.27	5.63	5.76	5.44	5.49	-
Diethyl ether	1.21 (t), 3.48 (q)	1.15 (t), 3.43 (q)	1.11 (t), 3.26 (q)	1.11 (t), 3.41 (q)	1.09 (t), 3.38 (q)	1.12 (t), 3.42 (q)	1.18 (t), 3.49 (q)	1.17 (t), 3.56 (q)
DMF	8.02, 2.96, 2.88	7.96, 2.91, 2.82	7.63, 2.36, 1.86	7.96, 2.94, 2.78	7.95, 2.89, 2.73	7.92, 2.89, 2.77	7.97, 2.99, 2.86	7.92, 3.01, 2.85
DMSO	2.62		1.68	2.52	2.50	2.50	2.65	2.71
Dioxane	3.71	3.65	3.35	3.59	3.57	3.60	3.66	3.75
Ethanol*	1.25 (t), 3.72 (q), 1.32 (s, OH)	1.19 (t), 3.66 (q), 1.33 (s, OH)	0.96 (t), 3.34 (q), 0.50 (s, OH)	1.12 (t), 3.57 (q), 3.39 (s, OH)	1.06 (t), 3.44 (q), 4.63 (s, OH)	1.12 (t), 3.54 (q), 2.47 (s, OH)	1.19 (t), 3.60 (q)	1.17 (t), 3.65 (t)
Ethyl acetate	2.05 (s), 4.12 (q), 1.26 (t)	2.00 (s), 4.08 (q), 1.23 (t)	1.65 (s), 3.89 (q), 0.92 (t)	1.97 (s), 4.05 (q), 1.20 (t)	1.99 (s), 4.03 (q), 1.17 (t)	1.97 (s), 4.06 (q), 1.20 (t)	2.01 (s), 4.09 (q), 1.24 (t)	2.07 (s), 4.14 (q), 1.24 (t)
Methanol*	3.49 (s), 1.09 (s, OH)	3.42 (s), 1.09 (s, OH)	3.07 (s)	3.31 (s), 3.12 (s, OH)	3.16 (s), 4.01 (s, OH)	3.28 (s), 2.16 (s, OH)	3.31	3.34
pyridine	8.62 (m), 7.29 (m), 7.68 (m)	8.59 (m), 7.28 (m), 7.68 (m)	8.53 (m), 6.66 (m), 6.98 (m)	8.58 (m), 7.35 (m), 7.76 (m)	8.58 (m), 7.39 (m), 7.79 (m)	8.57 (m), 7.33 (m), 7.73 (m)	8.53 (m), 7.44 (m), 7.85 (m)	8.52 (m), 7.45 (m), 7.87 (m)
Silicon grease	0.07 (s)	0.09 (s)	0.29 (s)	0.13 (s)	-0.06 (s)	0.08	0.10	-
THF	3.76 (m), 1.85 (m)	3.69 (m), 1.82 (m)	3.57 (m), 1.40 (m)	3.63 (m), 1.79 (m)	3.60 (m), 1.76 (m)	3.64 (m), 1.80 (m)	3.71 (m), 1.87 (m)	3.74 (m), 1.88 (m)
Toluene	2.36 (s), 7.17 (m), 7.25 (m)	2.34 (s), 7.15 (m), 7.24 (m)	2.11 (s), 7.02 (m), 7.13 (m)	2.32 (s), 7.10-7.20 (m), 7.10-7.20 (m)	2.30 (s), 7.18 (m), 7.25 (m)	2.33 (s), 7.10-7.30 (m), 7.10-7.30 (m)	2.32 (s), 7.16 (m), 7.16 (m)	-
Triethylamine	1.03 (t), 2.53 (q)	0.99 (t), 2.48 (q)	0.96 (t), 2.40 (q)	0.96 (t), 2.45 (q)	0.93 (t), 2.43 (q)	0.96 (t), 2.45 (q)	1.05 (t), 2.58 (q)	0.99 (t), 2.57 (q)
Silicon grease	0.07	0.09	0.29	0.13	-0.06	0.08	0.10	-

Shaded region denotes residual undeuterated solvent. Multiplicities are singlet unless denoted otherwise (s=singlet, t=triplet, m=multiplet).
. The multiplicities of trace impurities maybe different for methanol and ethanol if coupling with the OH proton is observed.

TABLE 23. ^{13}C NMR CHEMICAL SHIFTS OF TRACE IMPURITIES OF COMMON SOLVENTS AND REAGENTS

	$CDCl_3$	CD_2Cl_2	C_6D_6	$(CD_3)_2CO$	$(CD_3)_2SO$	CD_3CN	CD_3OD	D_2O
Acetone	30.92 207.07	31.00 206.78	30.14 204.43	30.60 205.87	30.56 206.31	30.91 207.43	30.67 209.67	30.89 215.94
Acetonitrile	1.89 116.43	2.03 116.92	0.20 116.02	1.12 117.60	1.03 117.91	1.79 118.26	0.85 118.06	1.47 119.68
Chloroform	77.36	77.99	77.79	79.19	79.16	79.17	79.44	-
Dichloromethane	53.52	54.24	53.46	54.95	54.84	55.32	54.78	-
Diethyl ether	15.20 65.91	15.44 66.11	15.46 65.94	15.78 66.12	15.12 62.05	15.63 66.32	15.46 66.88	14.77 66.42
DMF	31.45 36.50 162.62	31.39 36.56 162.57	30.72 35.25 162.13	31.03 36.15 162.79	30.73 35.73 162.29	31.32 36.57 163.31	31.61 36.89 164.73	32.03 37.54 165.53
DMSO	40.76		40.03	41.23	40.45	41.31	40.45	39.39
Dioxane	67.14	67.47	67.16	67.60	66.36	67.72	68.11	67.19
Ethanol	18.41 58.28	18.69 58.57	18.72 57.86	18.89 57.72	18.51 56.07	18.80 57.96	18.40 58.26	17.47 58.05
Ethyl acetate	14.19 21.04 60.49 171.36	14.37 21.15 60.63 171.24	14.19 20.56 60.21 170.44	14.50 20.83 60.56 170.96	14.40 20.68 59.74 170.31	14.54 21.16 60.98 171.68	14.49 20.88 61.50 172.89	13.92 21.15 62.32 175.26
Methanol	50.41	50.45	49.97	49.77	48.59	49.90	49.86	49.50
Pyridine	123.75 135.96 149.90	124.06 136.16 150.27	123.58 135.28 150.27	124.57 136.56 150.67	123.84 136.05 149.58	127.76 136.89 150.76	125.53 138.35 150.05	125.12 138.27 149.18
THF	25.62 67.97	25.98 68.16	25.72 67.80	26.15 68.07	25.14 67.03	26.27 68.33	26.48 68.83	25.67 68.68
Toluene	21.46 125.33 128.26 129.07 137.89	21.53 125.62 128.54 129.35 138.36	21.10 125.68 128.56 129.33 137.91	21.46 126.12 129.03 129.76 138.48	20.99 125.29 128.18 128.88 137.35	21.50 126.28 129.23 129.94 138.90	21.50 126.29 129.20 129.91 138.85	
Triethylamine	11.61 46.25	12.12 46.75	12.35 46.77	12.49 47.07	11.74 45.74	12.38 47.10	11.09 46.96	9.07 47.19
Silicon grease	1.19	1.22	1.38	1.40			2.10	

TABLE 24. AQUEOUS BUFFERS

Approx. pH	Composition
0	2N sulfuric acid or N hydrochloric acid
1	0.1N hydrochloric acid or 0.18N sulfuric acid
2	**Either** 0.01N hydrochloric acid or 0.013N sulfuric acid **Or** 50 ml of 0.1M glycine (also 0.1M NaCl) + 50 ml of 0.1N hydrochloric acid
3	**Either** 20 ml of the 0.2M Na_2HPO_4 + 80 ml of 0.1M citric acid **Or** 50 ml of 0.1M glycine + 22.8 ml of 0.1N hydrochloric acid in 100 ml
4	**Either** 38.5 ml of 0.2M Na_2HPO_4 + 61.5 ml of 0.1M citric acid **Or** 18 ml of 0.2M NaOAc + 82 ml of 0.2M acetic acid
5	**Either** 70 ml of 0.2M NaOAc + 30 ml of 0.2M acetic acid **Or** 51.5 ml of 0.2M Na_2HPO_4 + 48.5 ml of 0.1M citric acid
6	63 ml of 0.2M Na_2HPO_4 + 37 ml of 0.1M citric acid
7	82 ml of M Na_2HPO_4 + 18 ml of 0.1M citric acid
8	**Either** 50 ml of 0.1M Tris buffer + 29 ml of 0.1N hydrochloric acid, in 100 ml **Or** 30 ml of 0.05M borax + 70 ml of 0.2M boric acid
9	80 ml of 0.05M borax + 20 ml of 0.2M boric acid
10	**Either** 25 ml of 0.05M borax + 43 ml of 0.1N NaOH, in 100 ml **Or** 50 ml of 0.1M glycine + 32 ml of 0.1N NaOH, in 100 ml
11	50 ml of 0.15M Na_2HPO_4 + 15 ml of 0.1N NaOH
12	50 mL of 0.15M Na_2HPO_4 + 75 ml of 0.1N NaOH
13	0.1N NaOH or KOH
14	N NaOH or KOH

These buffers are suitable for use in obtaining ultraviolet spectra. Alternatively, for a set of accurate buffers of low, but constant, ionic strength (I = 0.01) *covering a pH range 2.2 to 11.6 at 20*°, *see* Perrin *Aust J Chem* **16** 572 *1963.* "In 100 ml" means that the solution is made up to 100 ml with pure water.

TABLE 25. SOLUBILITY COEFFICIENTS OF AIR AT 1atm IN WATER

T °C	$(\beta)_{air}$	$(l)_{air}$	% O_2 (by vol)	$(l)_{O_2}$	Conc of O_2 in H_2O
0	0.0292	0.0292	34.91	0.0102	0.455mM
20	0.0187	0.0199	34.03	0.0068	0.282mM
25	0.0171	0.0187	33.82	0.0063	0.258mM
30	0.0156	0.0173	33.62	0.0060	0.237mM

(β) is the Bunsen coeff. in ml gas/ml H_2O at STP. (*l*) is the Ostwald coeff. in ml gas/ml H_2O at stated temp.
Adapted from W.F. Linke, *A. Seidell's Solubilities of Inorganic and Metal-organic Compounds*, American Chemical Society, 1965.

TABLE 26. SOLUBILITY COEFFICIENTS OF O_2 AT 1atm IN WATER

T °C	(β)	(*l*)	Conc of O_2 in H_2O
0	0.047	0.047	2.10mM
20	0.031	0.033	1.37mM
25	0.028	0.0306	1.25mM
30	0.026	0.0289	1.16mM
50	0.021	0.0248	0.94mM

(β) is the Bunsen coeff. in ml gas/ml H_2O at STP. (*l*) is the Ostwald coeff. in ml gas/ml H_2O at stated temp.
Adapted from W.F. Linke, *A. Seidell's Solubilities of Inorganic and Metal-organic Compounds*, American Chemical Society, 1965.

TABLE 27. BUNSEN COEFFICIENTS (β) OF GASES AT 1atm IN ORGANIC SOLVENTS AT 20°C

Solvent	H_2	He	N_2	O_2	CO	CO_2
H_2O	0.017	0.009	0.015	0.031	0.025	0.88
CS_2	0.031	—	0.049	—	0.076	0.83
$CHCl_3$	—	—	0.120	0.205	0.177	0.345
EtOH	0.080	0.028	0,130	0.143	0.177	3.0
Me_2CO	0.065	0.030	0.129	0.207	0.198	6.5
Et_2O	0.12	—	0.24	0.415	0.38	5.0
C_6H_6	0.066	0.018	0.104	0.163	0.153	—

(β) is the Bunsen coeff. in ml gas/ml H_2O at STP.
Adapted from S. Glasstone, *Textbook of Physical Chemistry*, Macmillan & Co Ltd, London, 1951.

TABLE 28. OSTWALD COEFFICIENTS (*l*)/L OF O_2 AT 1atm IN AQUEOUS SOLUTIONS AT 25°C

	(*l*)/L		(*l*)
0.125N NH_4Cl	2,31	0.5M HCl	0.0296
0.25N NH_4Cl	1.60	1.0M HCl	0.0287
1.0N NH_4Cl	0.07	2.0M HCl	0.0267
0.125N NaCl	5.52	0.25M H_2SO_4	0.0288
0.025N NaCl	5,30	0.5M H_2SO_4	0.0275
0.50N NaCl	4.92	1.0M H_2SO_4	0.0251
1.0N NaCl	4.20	1.5M H_2SO_4	0.0229
2.0N NaCl	3.05	2.0M H_2SO_4	0.0209
4.0N NaCl	1.62	2.5M H_2SO_4	0.0194
0.125N NaBr	5.65	0.5M HNO_3	0.0302
0.5N NaBr	5.15	1.0M HNO_3	0.0295
1.0N NaBr	4.47	2.0M HNO_3	0.0284
6.0N NaBr	1.28		
0.125N KCl	5.52	0.5M NaOH	0.0250
0.25N KCl	5.30	1.0M NaOH	0.0204
1.0N KCl	4.26	2.0M NaOH	0.0133
4.0N KCl	1.17		
0.125N K_2SO_4	5.11	0.5M KOH	0.0252
0.25N K_2SO_4	4.66	1.0M KOH	0.0206
0.05N K_2SO_4	3.89		
0.125N $BaCl_2$	5.40	0.125N Sucrose	0.00540
0.25N $BaCl_2$	5.04	0.5N Sucrose	0.00438
1.0N $BaCl_2$	3.10	1.0N Sucrose	0.00320
		2.0N Sucrose	0.00184

The Ostwald coefficient (*l*)/L is for ml of gas in 1L of solution, and (*l*) is for ml of gas in 1ml of solution. Adapted from W.F. Linke, *A. Seidell's Solubilities of Inorganic and Metal-organic Compounds*, American Chemical Society, 1965.

TABLE 29. SOLUBILITIES OF HCl AND NH_3 AT 760mm (g/100g OF SOLUTION)

Gas	Temperature °C	MeOH	EtOH	Et_2O
Hydrogen Chloride*	–10 0 20 30	54.6 51.3 47.0 (18°) 43.0	— 45.4 41.0 38.1	37.5 (–9.2°) 35.6 24.9 19.47
Ammonia	15 25	21.6 (27.6g/100g MeOH) 16.5 (19.8g/100g MeOH)	13.2 (9.2g/100ml soln) 10.0 (6.0g/100ml soln)	— —

* Saturated EtOH with HCl is ~ 5.7M at 25°C, i.e. 21.5g/100ml of solution.

TABLE 30. BOILING POINTS OF SOME USEFUL GASES AT 760 mm

Argon	–185.6°	Krypton	–152.3°
Carbon dioxide (sublimes)	–78.5°	Methane	–164.0°
		Neon	–246.0°
Carbon monoxide	–191.3°	Nitrogen	–209.9°
Ethane	–88.6°	Nitrous oxide	–88.5°
Helium	–268.6°	Nitric oxide	–195.8°
Hydrogen	–252.6°	Oxygen	–182.96°

TABLE 31. PREFIXES FOR QUANTITIES

Fractional	deci (d) = 10^{-1}	centi (c) = 10^{-2}	milli (m) = 10^{-3}	micro (μ) = 10^{-6}	nano (n) = 10^{-9}	pico (p) = 10^{-12}	femto (f) = 10^{-15}	atto (atto) = 10^{-18}
Multiple	deca (d) = 10^{1}	hecto (h) = 10^{2}	kilo (k) = 10^{3}	mega (M) = 10^{6}	giga (G) = 10^{9}	tera (T) = 10^{12}	penta (P) = 10^{15}	eka (E) = 10^{18}

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CHAPTER 2

CHEMICAL METHODS USED IN PURIFICATION

GENERAL REMARKS

Greater selectivity in purification can often be achieved by making use of differences in chemical properties between the substance to be purified and the contaminants. Unwanted metal ions may be removed by precipitation in the presence of a *collector* (see below). Sodium borohydride and other metal hydrides transform organic peroxides and carbonyl-containing impurities such as aldehydes and ketones in alcohols and ethers. Many classes of organic chemicals can be purified by conversion into suitable derivatives, followed by regeneration. This chapter describes relevant procedures.

REMOVAL OF TRACES OF METALS FROM REAGENTS

METAL IMPURITIES

The presence of metal contaminants in reagents may sometimes affect the chemical or biochemical outcomes of an experiment. In these cases, it is necessary to purify the reagents used. Metal (and other) impurities can be determined qualitatively and quantitatively by atomic absorption spectroscopy (AAA), x-ray photoelectron spectroscopy (XPS), various mass spectrometric methods and/or inductively coupled plasma mass spectrometry (ICP-MS) (see Chapter 1, Question of Purity) and the required purification procedures can be formulated. Metal impurities in organic compounds are usually in the form of ionic salts or complexes with organic compounds and very rarely in the form of free metal. If they are present in the latter form then they can be removed by crystallising the organic compound (whereby the insoluble metal can be removed by filtration), or by distillation in which case the metal remains behind with the residue in the distilling flask. If the impurities are in the ionic or complex forms, then extraction of the organic compound in a suitable organic solvent with aqueous acidic or alkaline solutions will reduce their concentration to acceptable levels.

When the metal impurities are present in inorganic compounds as in metals or metal salts, then advantage of the differences in chemical properties should be taken. Properties of the impurities like the solubility, the solubility product (product of the metal ion and the counter-ion concentrations), the stability constants of the metal complexes with organic complexing agents and their solubilities in organic solvents should be considered. Alternatively the impurities can be masked by the addition of complexing agents which could lower the concentration of the metal ion impurities to such low levels that they would not interfere with the main compound (see **complexation** below). Specific procedures and examples are provided below.

DISTILLATION

Reagents such as water, ammonia, hydrochloric acid, nitric acid, perchloric acid, and sulfuric acid can be purified *via* distillation (preferably under reduced pressure and particularly with perchloric acid) using an all-glass still. Isothermal distillation is convenient for ammonia: a beaker containing concentrated ammonia is placed alongside a beaker of distilled water for several days in an empty desiccator so that some of the ammonia distils over into the water. The redistilled ammonia should be kept in polyethylene or paraffin-waxed bottles. Hydrochloric acid can be purified in the same way. To ensure the absence of metal contaminants from some salts (e.g. ammonium acetate), it may be more expedient to synthesise the salts using distilled components rather than to attempt to purify the salts themselves.

Purification of Laboratory Chemicals. http://dx.doi.org/10.1016/B978-0-12-382161-4.00002-9

SCAVENGER RESINS AND OTHER SUPPORTS

There is now an extensive range of supported reactants that use resins, silica, carbons etc, to clean up reactions prior to final purification which is gaining favour in the laboratory. [See section on "Scavenger Resins" in Chapter 3, at the end of the sections on "*Preparation of other adsorbents"*, "FPLC" and "HPLC".]

USE OF ION-EXCHANGE RESINS

Application of ion-exchange columns has greatly facilitated the removal of heavy metal ions such as Cu^{2+}, Zn^{2+} and Pb^{2+} from aqueous solutions of many reagents. Thus, sodium salts and sodium hydroxide can be purified by passage through a column of a cation-exchange resin in its sodium form, prepared by washing the resin with 0.1M aqueous NaOH then washing with water until the pH of the effluent is ~7. Similarly, for acids, a resin in its H^+ form [prepared by washing the column with 0.1M aqueous mineral acid (HCl, H_2SO_4) followed by thorough washing with water until the effluent has pH ~7 is used]. In some cases, where metals form anionic complexes, they can be removed by passage through an anion-exchange resin. Iron in hydrochloric acid solution can be removed in this way.

Ion-exchange resins are also useful for demineralising biochemical preparations such as proteins. Removal of metal ions from protein solutions using polystyrene-based resins, however, may lead to protein denaturation. This difficulty may be avoided by using a weakly acidic cation exchanger such as Bio-Rex 70.

Heavy metal contamination of pH buffers can be removed by passage of the solutions through a Chelex X-100 column. For example when a solution of 0.02M HEPES [4-(2-Hydroxyethyl)piperazine-1-ethanesulfonic acid] containing 0.2M KCl (1L, pH 7.5) alone or with calmodulin, is passed through a column of Chelex X-100 (~60g) in the K^+ form, the level of Ca^{2+} ions falls to less than 2×10^{-7} M as shown by atomic absorption spectroscopy. Such solutions should be stored in polyethylene containers that have been washed with boiling deionised water (5 minutes) and rinsed several times with deionised water. TES [*N*,*N*,*N*′,*N*′-Tetraethylsulfamide] and TRIS [Tris-(hydroxymethyl)aminomethane] have been similarly decontaminated from metal ions.

Water, with very low concentrations of ionic impurities (and approaching conductivity standards), is very readily obtained by percolation through alternate columns of cation- and anion-exchange resins, or through a mixed-bed resin, and many commercial devices are available for this purpose. For some applications, this method is unsatisfactory because the final deionised water may contain traces of organic material after passage through the columns. However, organic matter can be removed by using yet another special column in series for this purpose (see Water Purification Systems-Pure and Ultrapure in <www.millipore.com>).

PRECIPITATION

In removing traces of impurities by precipitation, it is necessary to include a material to act as a *collector* of the precipitated substance so as to facilitate its removal by filtration or decantation. The following are a few examples.

Removal of lead contaminants

Aqueous hydrofluoric acid can be freed from lead by adding 1ml of 10% strontium chloride per 100ml of acid, lead being co-precipitated as lead fluoride with the strontium fluoride. If the hydrofluoric acid is decanted from the precipitate and the process repeated, the final lead content in the acid is less than 0.003ppm. Similarly, lead can be precipitated from a nearly saturated sodium carbonate solution by adding 10% strontium chloride dropwise (1–2ml per 100ml) followed by filtration. (If the sodium carbonate is required as a solid, the solution can be evaporated to dryness in a platinum dish.) Removal of lead from potassium chloride uses precipitation as lead sulfide by bubbling H_2S, followed, after filtration, by evaporation and recrystallisation of the potassium chloride.

Removal of iron contaminants

Iron contaminants have been removed from potassium thiocyanate solutions by adding a slight excess of an aluminium salt, then precipitating aluminum and iron as their hydroxides by adding a few drops of ammonia. Iron is also carried down on the hydrated manganese dioxide precipitate formed in cadmium chloride or cadmium sulfate solutions by adding 0.5% aqueous potassium permanganate (0.5ml per 100ml of solution), sufficient ammonia to give a slight precipitate, and 1ml of ethanol. The solution is heated to boiling to coagulate the precipitate, then filtered. Ferrous ion can be removed from copper solutions by adding some hydrogen peroxide to the solution to oxidise the iron, followed by precipitation of ferric hydroxide by adding a small amount of sodium hydroxide.

Removal of other metal contaminants

Traces of calcium can be removed from solutions of sodium salts by precipitation at pH 9.5–10 as the 8-hydroxyquinolinate. The excess 8-hydroxyquinoline acts as a *collector* and is extracted out with an organic solvent.

EXTRACTION

In some cases, a simple solvent extraction is sufficient to remove a particular impurity. For example, traces of gallium can be removed from titanous chloride in hydrochloric acid by extraction with diisopropyl ether. Similarly, ferric chloride can be removed from aluminium chloride solutions containing hydrochloric acid by extraction with diethyl ether. Usually, however, it is necessary to extract an undesired metal with an organic solvent in the presence of a suitable complexing agent such as dithizone (diphenylthiocarbazone) or sodium diethyl dithiocarbamate. When the former is used, weakly alkaline solutions of the substance containing the metal impurity are extracted with dithizone in chloroform (at about 25mg/L of chloroform) or carbon tetrachloride until the colour of some fresh dithizone solution remains unchanged after shaking. Dithizone complexes metals more strongly in weakly alkaline solutions. Excess dithizone in the aqueous medium is removed by extracting with the pure solvent (chloroform or carbon tetrachloride), the last traces of which, in turn, are removed by aeration. This method has been used to remove metal impurities from aqueous solutions of ammonium hydrogen citrate, potassium bromide, potassium cyanide, sodium acetate and sodium citrate. The advantage of dithizone for such a purpose lies in the wide range of metals with which it combines under these conditions. 8-Hydroxyquinoline (oxine) can also be used in this way. Sodium diethyl dithiocarbamate has been used to remove metals from aqueous hydroxylamine hydrochloride (made just alkaline to thymol blue by adding ammonia) from copper and other heavy metals by repeated extraction with chloroform until no more diethyl dithiocarbamate remained in the solution (which was then acidified to thymol blue by adding hydrochloric acid).

COMPLEXATION

Although not strictly a removal of an impurity, addition of a suitable complexing agent such as ethylenediaminetetraacetic acid often overcomes the undesirable effects of contaminating metal ions by reducing the concentrations of the free metal species to very low levels, i.e. sequestering metal ions by complexation. For a detailed discussion of this *masking*, see *Masking and Demasking of Chemical Reactions*, D.D.Perrin, Wiley-Interscience, New York, 1970.

USE OF METAL HYDRIDES

This group of reagents is commercially available in large quantities; some of its members-notably lithium aluminium hydride ($LiAlH_4$), calcium hydride (CaH_2), sodium borohydride ($NaBH_4$) and potassium borohydride (KBH_4)-have found widespread use in the purification of chemicals.

LITHIUM ALUMINIUM HYDRIDE

This solid is stable at room temperature and is soluble in ether-type solvents. It reacts violently with water, liberating hydrogen, and is a powerful drying and reducing agent for organic compounds. It reduces aldehydes, ketones, esters, carboxylic acids, peroxides, acid anhydrides and acid chlorides to the corresponding alcohols. Similarly, amides, nitriles, aldimines and aliphatic nitro compounds yield amines, while aromatic nitro compounds are converted to azo compounds. For this reason it finds extensive application in purifying organic chemical substances by the removal of water and carbonyl containing impurities as well as peroxides formed by autoxidation. Reactions can generally be carried out at room temperature, or in refluxing diethyl ether, at atmospheric pressure. *When drying organic liquids with this reagent it is important that the concentration of water in the liquid is below 0.1% - otherwise a violent reaction or* **EXPLOSION** *may occur. $LiAlH_4$ should be added cautiously to a cooled solution of organic liquid in a flask equipped with a reflux condenser.*

CALCIUM HYDRIDE

This powerful drying agent is suitable for use with hydrogen, argon, helium, nitrogen, hydrocarbons, chlorinated hydrocarbons, esters and higher alcohols.

SODIUM BOROHYDRIDE

This solid, which is stable in dry air up to 300°, is a less powerful reducing agent than lithium aluminium hydride, from which it differs also by being soluble in hydroxylic solvents and to a lesser extent in ether-type solvents. Sodium borohydride forms a dihydrate melting at 36–37°, and its aqueous solutions decompose slowly unless stabilised to above pH 9 by alkali. (For example, a useful sodium borohydride solution is one that is nearly saturated at 30–40° and containing 0.2% sodium hydroxide.) Its solubility in water is 25, 55 and 88g per 100ml of water at 0, 25 and 60°, respectively. Boiling or acidification rapidly decomposes aqueous sodium borohydride solutions. The reagent, available either as a hygroscopic solid or as an aqueous sodium hydroxide solution, is useful as a water soluble reducing agent for aldehydes, ketones and organic peroxides. This explains its use for the removal of carbonyl-containing impurities and peroxides from alcohols, polyols, esters, polyesters, amino alcohols, olefins, chlorinated hydrocarbons, ethers, polyethers, amines (including aniline), polyamines and aliphatic sulfonates.

Purifications using sodium borohydride can be carried out conveniently using alkaline aqueous or methanolic solutions of sodium borohydride, allowing the reaction mixture to stand at room temperature for several hours. Other solvents that can be used with this reagent include isopropyl alcohol (without alkali), amines (including liquid ammonia, in which its solubility is 104g per 100g of ammonia at 25°, and ethylene diamine), diglyme, formamide, dimethylformamide and tetrahydrofurfuryl alcohol. Alternatively, the material to be purified can be percolated through a column of the borohydride. In the absence of water, sodium borohydride solutions in organic solvents such as dioxane or amines decompose only very slowly at room temperature. Treatment of ethers with sodium borohydride appears to inhibit peroxide formation.

POTASSIUM BOROHYDRIDE

Potassium borohydride is similar in properties and reactions to sodium borohydride, and can similarly be used as a reducing agent for removing aldehydes, ketones and organic peroxides. It is non-hygroscopic and can be used in water, ethanol, methanol or water-alcohol mixtures, provided some alkali is added to minimise decomposition, but it is somewhat less soluble than sodium borohydride in most solvents. For example, the solubility of potassium borohydride in water at 25° is 19g per 100ml of water (as compared to 55g of sodium borohydride).

PURIFICATION *via* DERIVATIVES

Relatively few derivatives of organic substances are suitable for use as aids to purification. This is because of the difficulty in regenerating the starting material. For this reason, we list below the common methods of preparation of derivatives that can be used in this way.

Whether or not any of these derivatives is likely to be satisfactory for the use of any particular case will depend on the degree of difference in properties, such as solubility, volatility or melting point, between the starting material, its derivative and likely impurities, as well as on the ease with which the substance can be recovered. Purification *via* a derivative is likely to be of most use when the quantity of pure material that is required is not too large. Where large quantities (for example, more than 50g) are available, it is usually more economical to purify the material directly (for example, in distillations and recrystallisations).

The most generally useful purifications *via* derivatives are as follows.

ALCOHOLS

Aliphatic or aromatic alcohols are converted to solid esters. *p*-Nitrobenzoates are examples of convenient esters to form because of their sharp melting points, and the ease with which they can be recrystallised as well as the ease with which the parent alcohol can be recovered. The *p*-nitrobenzoyl chloride used in the esterification is prepared by refluxing dry *p*-nitrobenzoic acid with a 3 molar excess of thionyl chloride for 30minutes on a steam bath (*in a fume cupboard*). The solution is cooled slightly and the excess thionyl chloride is distilled off under vacuum, keeping the temperature below 40°. Dry toluene is added to the residue in the flask, then distilled off under vacuum, the process being repeated two or three times to ensure complete removal of thionyl chloride, hydrogen chloride and sulfur dioxide. (This freshly prepared *p*-nitrobenzoyl chloride cannot be stored without decomposition; it should be used directly.) A solution of the acid chloride (1mol) in dry toluene or alcohol-free chloroform (distilled from P_2O_5 or by passage through an activated Al_2O_3 column) under a reflux condense is cooled in an ice bath while the alcohol (1mol), with or without a solvent (preferably miscible

with toluene or alcohol-free chloroform), is added dropwise to it. When addition is over and the reaction subsides, the mixture is refluxed for 30minutes and the solvent is removed under reduced pressure. The solid ester is then recrystallised to constant melting point from toluene, acetone, low boiling point petroleum ether or mixtures of these, but not from alcohols (due to unwanted trans-esterifiction).
Hydrolysis of the ester is achieved by refluxing in aqueous N or 2N NaOH solution until the insoluble ester dissolves. The solution is then cooled, and the alcohol is extracted into a suitable solvent, e.g. ether, toluene or alcohol-free chloroform. The extract is dried ($CaSO_4$, $MgSO_4$) and distilled, then fractionally distilled if liquid or recrystallised if solid. (The *p*-nitrobenzoic acid can be recovered by acidification of the aqueous layer.) In most cases where the alcohol to be purified can be readily extracted from ethanol, the hydrolysis of the ester is best achieved with N or 2N ethanolic NaOH or 85% aqueous ethanolic N NaOH. The former is prepared by dissolving the necessary alkali in a minimum volume of water and diluting with absolute alcohol. The ethanolic solution is refluxed for one to two hours and hydrolysis is complete when an aliquot gives a clear solution on dilution with four or five times its volume of water. The bulk of the ethanol is distilled off and the residue is extracted as above. Alternatively, use can be made of ester formation with benzoic acid, toluic acid or 3,5-dinitrobenzoic acid, by the above method.
Other derivatives can be prepared by reaction of the alcohol with an acid anhydride. For example, phthalic or 3-nitrophthalic anhydride (1 mol) and the alcohol (1mol) are refluxed for half to one hour in a non-hydroxylic solvent, e.g. toluene or alcohol-free chloroform, and then cooled. The phthalate ester crystallises out, is precipitated by the addition of low boiling petroleum ether or is isolated by evaporation of the solvent. It is recrystallised from water, 50% aqueous ethanol, toluene or low boiling petroleum ether. Such an ester has a characteristic melting point and the alcohol can be recovered by acid or alkaline hydrolysis.

ALDEHYDES

The best derivative from which an aldehyde can be recovered readily is its bisulfite addition compound, the main disadvantage being the lack of a sharp melting point. The aldehyde (sometimes in ethanol) is shaken with a cold saturated solution of sodium bisulfite until no more solid adduct separates. The adduct is filtered off, washed with a little water, followed by alcohol. A better reagent to use is a freshly prepared saturated aqueous sodium bisulfite solution to which 75% ethanol is added to near-saturation. (Water may have to be added dropwise to render this solution clear.) With this reagent the aldehyde need not be dissolved separately in alcohol and the adduct is finally washed with alcohol. The aldehyde is recovered by dissolving the adduct in the least volume of water and adding an equivalent quantity of sodium carbonate (not sodium hydroxide) or concentrated hydrochloric acid to react with the bisulfite, followed by steam distillation or solvent extraction.
Other derivatives that can be prepared are the Schiff bases and semicarbazones. Condensation of the aldehyde with an equivalent of primary aromatic amine yields the Schiff base, for example aniline at 100° for 10–30minutes.
Semicarbazones are prepared by dissolving semicarbazide hydrochloride (*ca* 1g) and sodium acetate (*ca* 1.5g) in water (8–10ml) and adding the aldehyde or ketone (0.5–1g) with stirring. The semicarbazone crystallises out and is recrystallised from ethanol or aqueous ethanol. These are hydrolysed by steam distillation in the presence of oxalic acid or better by exchange with pyruvic acid (Hershberg *J Org Chem* **13** 542 *1948*) [see entry under Ketones].

AMINES

Picrates

The most versatile derivative from which the free base can be readily recovered is the picrate. This is very satisfactory for primary and secondary aliphatic amines and aromatic amines and is particularly so for heterocyclic bases. The amine, dissolved in water or alcohol, is treated with excess of a saturated solution of picric acid in water or alcohol, respectively, until separation of the picrate is complete. If separation does not occur, the solution is stirred vigorously and warmed for a few minutes, or diluted with a solvent in which the picrate is insoluble. Thus, a solution of the amine and picric acid in ethanol can be treated with petroleum ether to precipitate the picrate. Alternatively, the amine can be dissolved in alcohol and aqueous picric acid added. The picrate is filtered off, washed with water or ethanol and recrystallised from boiling water, ethanol, methanol, aqueous ethanol, methanol or chloroform. The solubility of picric acid in water and ethanol is 1.4 and 6.23% respectively at 20°.
It is not advisable to store large quantities of picrates for long periods, *particularly when they are dry due to their potential* **EXPLOSIVE** *nature*. Also this method is not advised when large quantities of amines (e.g. >25g) are to be purified. The free base should be recovered as soon as possible. The picrate is suspended in an

excess of 2N aqueous NaOH and warmed a little. Because of the limited solubility of sodium picrate, excess hot water must be added. Alternatively, because of the greater solubility of lithium picrate, aqueous 10% lithium hydroxide solution can be used. The solution is cooled, the amine is extracted with a suitable solvent such as diethyl ether or toluene, washed with 5N NaOH until the alkaline solution remains colourless, then with water, and the extract is dried with anhydrous sodium carbonate. The solvent is distilled off and the amine is fractionally distilled (under reduced pressure if necessary) or recrystallised.
If the amines are required as their hydrochlorides, picrates can often be decomposed by suspending them in acetone and adding two equivalents of 10N HCl. The hydrochloride of the base is filtered off, leaving the picric acid in the acetone. Dowex No 1 anion-exchange resin in the chloride form is useful for changing solutions of the more soluble picrates (for example, of adenosine) into solutions of their hydrochlorides, from which sodium hydroxide precipitates the free base.

Salts

Amines can also be purified *via* their salts, e.g. hydrochlorides. A solution of the amine in dry toluene, diethyl ether, dichloromethane or chloroform is saturated with dry hydrogen chloride (generated by addition of concentrated sulfuric acid to dry sodium chloride, or to concentrated HCl followed by drying the gas through sulfuric acid, or the HCl gas is obtained from a hydrogen chloride cylinder) and the insoluble hydrochloride is filtered off and dissolved in water. The solution is made alkaline and the amine is extracted, as above. Hydrochlorides can also be prepared by dissolving the amine in ethanolic HCl and adding diethyl ether. Where hydrochlorides are too hygroscopic or too soluble for satisfactory isolation, other salts, e.g. nitrate, sulfate, bisulfate or oxalate, can be used.

Double salts

The amine (1mol) is added to a solution of anhydrous zinc chloride (1mol) in concentrated HCl (42ml) in ethanol (200ml, or less depending on the solubility of the double salt). The solution is stirred for 1 hour and the precipitated salt is filtered off and recrystallised from ethanol. The free base is recovered by adding excess of 5-10N NaOH (to dissolve the zinc hydroxide that separates) and is steam distilled. Mercuric chloride (highly poisonous) in hot water can be used instead of zinc chloride and the salt is crystallised from 1% hydrochloric acid. Other double salts have been used, e.g. cuprous salts, but are not as convenient as the above salts.

***N*-Acetyl derivatives**

Purification as their *N*-acetyl derivatives is satisfactory for primary, and to a limited extent, secondary amines. Tertiary amines are not acetylated. The base is refluxed with slightly more than one equivalent of acetic anhydride for half to one hour, cooled and poured into ice-cold water. The insoluble derivative is filtered off, dried, and recrystallised from water, ethanol, aqueous ethanol or benzene (CAUTION **toxic**!). The derivative can be hydrolysed to the parent amine by refluxing with 70% sulfuric acid for a half to one hour. The solution is cooled, poured onto ice, and made alkaline. The amine is steam distilled or extracted as above. Alkaline hydrolysis is very slow.

***N*-Tosyl derivatives**

Primary and secondary amines are converted into their tosyl derivatives by mixing equimolar amounts of amine and *p*-toluenesulfonyl chloride in dry pyridine (*ca* 5–10mols) and allowing to stand at room temperature overnight. The solution is poured into ice-water and the pH adjusted to 2 with HCl. The solid derivative is filtered off, washed with water, dried (vacuum desiccator) and recrystallised from an alcohol or aqueous alcohol solution to a sharp melting point. The derivative is decomposed by dissolving in liquid ammonia (*fume cupboard*) and adding sodium metal (in small pieces with stirring) until the blue colour persists for 10–15 minutes. Ammonia is allowed to evaporate (*fume cupboard*), the residue treated with water and the solution checked that the pH is above 10. If the pH is below 10, then the solution has to be basified with 2N NaOH. The mixture is extracted with diethyl ether or toluene, the extract is dried (K_2CO_3), evaporated and the residual amine recrystallised if solid or distilled if liquid.

AROMATIC HYDROCARBONS

Adducts

Aromatic hydrocarbons can be purified as their picrates using the procedures described for amines. Instead of picric acid, 1,3,5-trinitrobenzene or 2,4,7-trinitrofluorenone can also be used. In all these cases, following recrystallisation, the hydrocarbon can be isolated either as described for amines or by passing a solution of the adduct through an activated alumina column and eluting with toluene or petroleum ether. The picric acid and nitro compounds are more strongly adsorbed on the column.

Sulfonation

Naphthalene, xylenes and alkyl benzenes can be purified by sulfonation with concentrated sulfuric acid and crystallisation of the sodium sulfonates. The hydrocarbon is distilled out of the mixture with superheated steam.

CARBOXYLIC ACIDS

4-Bromophenacyl esters

A solution of the sodium salt of the acid is prepared. If the salt is not available, the acid is dissolved in an equivalent of aqueous NaOH and the pH adjusted to 8–9 with this base. A solution of one equivalent of 4-bromophenacyl bromide (for a monobasic acid, two equivalents for a dibasic acid, etc) in ten times its volume of ethanol is then added. The mixture is heated to boiling, and, if necessary, enough ethanol is added to clarify the solution which is then refluxed for half an hour to three hours depending on the number of carboxylic groups that have to be esterified. (One hour is generally sufficient for monocarboxylic acids.) On cooling, the ester should crystallise out. If it does not, then the solution is heated to boiling, and enough water is added to produce a slight turbidity. The solution is again cooled. The ester is collected, and recrystallised or fractionally distilled.

The ester is hydrolysed by refluxing for 1–2 hours with 1–5% of barium carbonate suspended in water or with aqueous sodium carbonate solution. The solution is cooled and extracted with diethyl ether, toluene or chloroform. It is then acidified and the acid is collected by filtration or extraction, and recrystallised or fractionally distilled. 4-Bromophenylphenacyl esters are used similarly.

p-Nitrobenzyl esters can be prepared in an analogous manner using the sodium salt of the acid and *p*-nitrobenzyl bromide. They are readily hydrolysed.

Alkyl esters

Of the alkyl esters, methyl esters are the most useful because of their rapid hydrolysis. The acid is refluxed with one or two equivalents of methanol in excess alcohol-free chloroform (or dichloromethane) containing about 0.1g of *p*-toluenesulfonic acid (as catalyst), using a Dean-Stark apparatus. (The water formed by the esterification is carried away into the trap.) When the theoretical amount of water is collected in the trap, esterification is complete. The chloroform solution in the flask is washed with 5% aqueous sodium carbonate solution, then water, and dried over anhydrous sodium sulfate or magnesium sulfate. The chloroform is distilled off and the ester is fractionally distilled through an efficient column, or recrystallised if it is a solid. The ester is hydrolysed by refluxing with 5–10% aqueous NaOH solution until the insoluble ester has completely dissolved. The aqueous solution is concentrated a little by distillation to remove almost all of the methanol. It is then cooled and acidified. The acid is either extracted with diethyl ether, toluene or chloroform, or filtered off and isolated as above. Other methods for preparing esters are available, e.g. addition of an ethereal solution of diazomethane (yellow in colour, poisonous, use a fume cupboard. CARE: Use diazomethane with extreme care as the reagent is POISONOUS and HIGHLY explosive; special precautions MUST be used; see *Fieser and Fieser's Reagents for Organic Synthesis* **1** pp. 191–195 *1967*) to the acid which dissolves as the acid is esterified, liberating N_2 and the yellow colour. The methyl ester so produced is obtained by evaporating the ethereal solution.

Salts

The most useful salt derivatives for carboxylic acids are the isothiouronium salts. These are prepared by mixing almost saturated solutions containing the acid (carefully neutralised with N NaOH using phenolphthalein indicator) then adding two drops of N HCl and an equimolar amount of *S*-benzylisothiouronium chloride in ethanol and filtering off the salt that crystallises out. After recrystallisation from water, alcohol or aqueous alcohol the salt is decomposed by suspending or dissolving in 2N HCl and extracting the carboxylic acid from aqueous solution into diethyl ether, chloroform or toluene.

HYDROPEROXIDES

These can be converted to their sodium salts by precipitation below 30º with aqueous 25% NaOH. The salt is then decomposed by addition of solid (powdered) carbon dioxide and extracted with low-boiling petroleum ether. The solvent should be removed under reduced pressure below 20º. **The manipulation should be adequately shielded at all times to guard against EXPLOSIONS for the safety of the operator.**

KETONES

Bisulfite adduct

The adduct can be prepared and decomposed as described for aldehydes. Alternatively, because no Cannizzaro reaction is possible, it can also be decomposed with 0.5N NaOH.

Semicarbazones

A powdered mixture of semicarbazide hydrochloride (1mol) and anhydrous sodium acetate (1.3mol) is dissolved in water by gentle warming. A solution of the ketone (1mol) in the minimum volume of ethanol needed to dissolve it is then added. The mixture is warmed on a water bath until separation of the semicarbazone is complete. The solution is cooled, and the solid filtered off. After washing with a little ethanol followed by water, it is recrystallised from ethanol or dilute aqueous ethanol. The derivative should have a characteristic melting point. The semicarbazone is decomposed by refluxing with excess of oxalic acid or with

aqueous sodium carbonate solution. The ketone (which steam distils) is distilled off. It is extracted or separated from the distillate (after saturating with NaCl), dried with $CaSO_4$ or $MgSO_4$ and fractionally distilled using an efficient column (under vacuum if necessary). [See entry under Aldehydes.]

PHENOLS

The most satisfactory derivatives for phenols that are of low molecular weight or monohydric are the benzoate esters. (Their acetate esters are generally liquids or low-melting solids.) Acetates are more useful for high molecular weight and polyhydric phenols.

Benzoates

The phenol (1mol) in 5% aqueous NaOH is treated (while cooling) with benzoyl chloride (1mol) and the mixture is stirred in an ice bath until separation of the solid benzoyl derivative is complete. The derivative is filtered off, washed with alkali, then water, and dried (in a vacuum desiccator over NaOH). It is recrystallised from ethanol or dilute aqueous ethanol. The benzoylation can also be carried out in dry pyridine at low temperature (*ca* 0°) instead of in NaOH solution, finally pouring the mixture into water and collecting the solid as above. The ester is hydrolysed by refluxing in an alcohol (for example, ethanol, *n*-butanol) containing two or three equivalents of the alkoxide of the corresponding alcohol (for example, sodium ethoxide or sodium *n*-butoxide) and a few (*ca* 5–10) millilitres of water, for half an hour to three hours. When hydrolysis is complete, an aliquot will remain clear on dilution with four to five times its volume of water. Most of the solvent is distilled off. The residue is diluted with cold water and acidified, and the phenol is steam distilled. The latter is collected from the distillate, dried and either fractionally distilled or recrystallised. It can also be isolated by extraction from a slightly acidified (pH ~3) aqueous solution with diethyl ether.

Acetates

These can be prepared as for the benzoates using either acetic anhydride with 3N NaOH or acetyl chloride in pyridine. They are hydrolysed as described for the benzoates. This hydrolysis can also be carried out with aqueous 10% NaOH solution, completion of hydrolysis being indicated by the complete dissolution of the acetate in the aqueous alkaline solution. On steam distillation, acetic acid also distils off, but in these cases the phenols (see above) are invariably solids which can be filtered off and recrystallised.

PHOSPHATE AND PHOSPHONATE ESTERS

These can be converted to their uranyl nitrate addition compounds. The crude or partially purified ester is saturated with uranyl nitrate solution and the adduct is filtered off. It is recrystallised from *n*-hexane, toluene or ethanol. For the more soluble members crystallisation from hexane using low temperatures (–40°) has been successful. The adduct is decomposed by shaking with sodium carbonate solution and water, the solvent is steam distilled (if hexane or toluene is used) and the ester is collected by filtration. Alternatively, after decomposition, the organic layer is separated, dried with $CaCl_2$ or BaO, filtered, and fractionally distilled under high vacuum.

MISCELLANEOUS

Impurities can sometimes be removed by conversion to derivatives under conditions where the major component does not react or reacts much more slowly. For example, normal (straight-chain) paraffins can be freed from unsaturated and branched-chain components by taking advantage of the greater reactivity of the latter with chlorosulfonic acid or bromine. Similarly, the preferential nitration of aromatic hydrocarbons can be used to remove e.g. benzene or toluene from cyclohexane by shaking for several hours with a mixture of concentrated nitric acid (25%), sulfuric acid (58%), and water (17%).

GENERAL METHODS FOR THE PURIFICATION OF CLASSES OF COMPOUNDS

Chapters 4, 5 and 6 list a large number of individual compounds, with a brief statement of how each one may be purified. For substances that are not included in these chapters the following procedures may prove helpful.

PROCEDURES

If the laboratory worker does not know of a reference to the preparation of a commercially available substance, he/she may be able to make a reasonable guess at the synthetic methods used from published laboratory syntheses.

This information, in turn, can simplify the necessary purification steps by suggesting probable contaminants.
Physical methods of purification depend largely on the melting and boiling points of the materials. For gases and low-boiling liquids use is commonly made of the *freeze-pump-thaw* procedure. Gas chromatography is also useful, especially for low-boiling point liquids. Liquids are usually purified by refluxing with drying agents, acids or bases, reducing agents, charcoal, etc., followed by fractional distillation under reduced pressure. For solids, general methods include fractional freezing of the melted material, taking the middle fraction. Another procedure is sublimation of the solid under reduced pressure. The other commonly used method for purifying solids is by recrystallisation from a solution in a suitable solvent, by cooling with or without the prior addition of a solvent in which the solute is not very soluble (see Chapter 1).

The nature of the procedure will depend to a large extent on the quantity of purified material that is required. For example, for small quantities (50–250mg) of a pure volatile liquid, preparative gas chromatography is probably the best method. Two passes through a suitable column may well be sufficient. Similarly, for smaller amounts (100–500 mg) of an organic solid, column chromatography is likely to be satisfactory, the eluate being collected as a number of separate fractions (*ca* 5–10 ml) which are examined by FT-IR, NMR or UV spectroscopy, TLC or by some other appropriate analytical technique. (For information on suitable adsorbents and eluents the texts referred to in the bibliography at the end of Chapters 1 and 2 should be consulted.) Preparative thin layer chromatography or HPLC, FC and HPFC can also be used successfully for purifying up to 500 mg of solid. The latter chromatographic techniques (see Chapter 1) are more and more commonly used procedures for the purification of small molecules as well as large molecules such as polypeptides and DNA.

Where larger quantities (upwards of 1g) are required, most of the impurities should be removed by preliminary treatments, such as solvent extraction, liquid-liquid partition, or conversion to a derivative (*vide supra*) which can be purified by crystallisation or fractional distillation before being reconverted to the starting material. The substance is then crystallised or distilled. If the final amounts must be in excess of 25 g, preparation of a derivative is sometimes omitted because of the cost involved. In all of the above cases, purification is likely to be more laborious if the impurity is an isomer or a derivative with closely similar physical properties.

CRITERIA OF PURITY

Purification becomes meaningful only insofar as adequate tests of purity are applied: the higher the degree of purity that is sought, the more stringent these tests must be. For this, the experimenter has to resort, in the first place, to preliminary physical methods such as melting and boiling points, chromatographic and spectroscopic procedures which are described in detail in Chapter 1. If the material is an organic solid, its melting point should first be taken and compared with the recorded value. *Note that the melting points of most salts, organic or inorganic, are generally decomposition points and are not reliable criteria of purity.* As part of the preliminary examination, the sample might be examined by thin layer chromatography in several different solvent systems and in high enough concentrations to facilitate the detection of minor components. On the other hand, if the substance is a liquid, its boiling point should be measured. If, further, the boiling point of the liquid is too high, or it decomposes on heating, then its purity should be assessed by high pressure liquid chromatography. Liquids, especially volatile ones, can be studied very satisfactorily by gas chromatography, preferably using at least two different stationary and/or mobile phases. Spectroscopic methods, if facilities are available, such as atomic absorption spectroscopy (AAA), and inductively coupled plasma mass spectrometry (ICP-MS) are useful and sensitive methods for detecting metal impurities and the concentrations of metals and metal salts or complexes.
Application of these tests at successive steps will give a good indication of whether or not the purification is satisfactory and will also show when adequate purification has been achieved. Finally elemental analyses, e.g. of carbon, hydrogen, nitrogen, sulfur, metals etc., are very sensitive to impurities (other than with isomers), and are good criteria of purity.
There are certain requirements for purity of new compounds in most journals. This is especially so for samples which are shown to have biological activity. See instructions to authors for ACS journals especially in *J. Med. Chem* (see "Guidelines for Authors under *Purity Criteria of Tested Compounds* <http://pubs.acs.org/journal/jmcmar>.)

GENERAL PROCEDURES FOR THE PURIFICATION OF SOME CLASSES OF ORGANIC COMPOUNDS

In the general methods of purification described below, it is assumed that the impurities belong essentially to a class of compounds different from the one being purified. They are suggested for use in cases where substances are not listed in Chapters 4, 5 and the low-molecular-weight compounds in Chapter 6. In such cases, the experimenter is advised to employ them in conjunction with information given in these chapters for the purification of suitable analogues. Also, for a wider range of drying agents and the use of cartridges (e.g. Na_2SO_4 for removal of H_2O, or Celite for removal of tar), solvents for extraction and solvents for recrystallisation, the reader is referred to Chapter 1. A common method of purification of organic compounds is to convert them to a suitable derivative which is purified (with the assumption that the impurity does not form a similar derivative, or if it does its properties are different), and then regenerate the original compound and purify it further. Various derivatives are described for different classes of compounds below, but many more can be considered, and the reader is referred to texts on "Protecting Groups" which describe ways of selectively protecting functional groups and facile means of deprotecting them, i.e. regenerating the unprotected group [P.J. Kocienski *Protecting Groups* Thieme International Publisher, 2005, ISBN 9783131356031; J.R. Hanson *Protecting Groups in Organic Synthesis* Sheffield Academic Press, 1999, ISBN 9781850759577, or J. Wiley & Sons Inc, 1999, ISBN 980632045068]. See Chapter 6 for general purification procedures used for macromolecules.

ACETALS

These are generally diethyl or dimethyl acetal derivatives of aldehydes. They are more stable to alkali than to acids. Their common impurities are the corresponding alcohol, aldehyde and water. Drying with sodium wire removes alcohols and water, and polymerizes aldehydes so that, after decantation, the acetal can be fractionally distilled. In cases where the use of sodium is too drastic, aldehydes can be removed by shaking with alkaline hydrogen peroxide solution and the acetal is dried with sodium carbonate or potassium carbonate. Residual water and alcohols (up to *n*-propyl) can be removed with Linde type 4A molecular sieves. The acetal is then filtered and fractionally distilled. Solid acetals (i.e. acetals of high-molecular-weight aldehydes) are generally low-melting and can be recrystallised from low-boiling petroleum ether, toluene or a mixture of both.

ACIDS

Carboxylic acids

Liquid carboxylic acids are first freed from neutral and basic impurities by dissolving them in aqueous alkali and extracting with diethyl ether. (The pH of the solution should be at least three units above the pK_a of the acid, see pK in Chapter 1). The aqueous phase is then acidified to a pH at least three units below the pK_a of the acid and again extracted with ether. It is quite unnecessary to add large excesses of mineral acid (e.g. HCl) to liberate the organic acid, as mineral acids dissolve appreciably in organic solvents such as diethyl ether. The extract is dried with magnesium sulfate or sodium sulfate and the ether is distilled off. The acid is fractionally distilled through an efficient column. It can be further purified by conversion to its methyl or ethyl ester (*vide supra*) which is then fractionally distilled. Hydrolysis yields the original acid which is again purified as above.
Acids that are solids can be purified in this way, except that distillation is replaced by repeated crystallisation (preferable from at least two different solvents such as water, alcohol or aqueous alcohol, toluene, toluene/petroleum ether or acetic acid.) Water-insoluble acids can be partially purified by dissolution in N sodium hydroxide solution and precipitation with dilute mineral acid. If the acid is required to be free from sodium ions, then it is better to dissolve the acid in hot N ammonia, heat to *ca* 80°, adding slightly more than an equal volume of N formic acid and allowing to cool slowly for crystallisation. Any ammonia, formic acid or ammonium formate that adhere to the acid are removed when the acid is dried in a vacuum — these are volatile.
Cartridges and columns are available (e.g. the Isolute SCX-2 made of polysulfonic acid bonded to silica as an ion exchange column developed by Biotage Inc (<www.biotage.com>), particularly for the purification of acids using flash chromatography.
The separation and purification of naturally occurring fatty acids, based on distillation, salt solubility and low temperature crystallisation, are described by K.S. Markley (Ed.), *Fatty Acids*, 2nd Edn, part 3, Chap. 20, Interscience, New York, 1964, see also N. Reavley *Essential Fatty Acids* Book Media Publ, 2002, ISBN 9780958157643; G. Grati and K. Sato (Eds) *Crystallisation and Polymorphism of Fats and Fatty Acids* Marcel Dekker, 1988, ISBN 9780824778750.
Aromatic carboxylic acids can be purified by conversion to their sodium salts, recrystallisation from hot water, and reconversion to the free acids.

Sulfonic acids

The low solubility of sulfonic acids in organic solvents and their high solubility in water makes necessary a treatment different from that for carboxylic acids. Sulfonic acids are strong acids, they have the tendency to hydrate, and many of them contain water of crystallisation. The lower-melting and liquid acids can generally be purified with only slight decomposition by fractional distillation, preferably under reduced pressure. A common impurity is sulfuric acid, but this can be removed by recrystallisation from concentrated aqueous solutions. The wet acid can be dried by azeotropic removal of water with toluene, followed by distillation. The higher-melting acids, or acids that melt with decomposition, can be recrystallised from water or, occasionally, from ethanol. For a typical purification of aromatic sulfonic acids using their barium salts refer to benzenesulfonic acid in the "Aromatic Compounds" section in Chapter 4.

Sulfinic acids

These acids are less stable, less soluble and less acidic than the corresponding sulfonic acids. The common impurities are the respective sulfonyl chlorides from which they have been prepared, and the thiolsulfonates (neutral) and sulfonic acids into which they decompose. The first two of these can be removed by solvent extraction from an alkaline solution of the acid. On acidification of an alkaline solution, the sulfinic acid crystallises out leaving the sulfonic acid behind. The lower molecular weight members are isolated as their metal (e.g. ferric) salts, but the higher members can be crystallised from water (made slightly acidic), or alcohol.

ACID CHLORIDES

The corresponding acid and hydrogen chloride are the most likely impurities. Usually these can be removed by efficient fractional distillation. Where acid chlorides are not readily hydrolysed (e.g. aryl sulfonyl chlorides) the compound can be freed from contaminants by dissolving in a suitable solvent such as alcohol-free chloroform, dry toluene or petroleum ether and shaking with dilute sodium bicarbonate solution. The organic phase is then washed with water, dried with anhydrous sodium sulfate or magnesium sulfate, and distilled or recrystallised. This procedure is *hazardous* with readily hydrolysable *carboxylic* acid chlorides such as acetyl chloride and benzoyl chloride. Solid acid chlorides should be thoroughly dried *in vacuo* over strong drying agents and are satisfactorily recrystallised from toluene, toluene-petroleum ether, petroleum ethers, alcohol-free chloroform/toluene, and, occasionally, from dry diethyl ether. Hydroxylic or basic solvents should be strictly avoided. *All operations should be carried out in a fume cupboard because of the* ***irritant*** *nature of these compounds which also attack the skin.*

ALCOHOLS

Monohydric alcohols

The common impurities in alcohols are aldehydes or ketones, and water. [*Ethanol* in Chapter 4 is typical.] Aldehydes and ketones can be removed by adding a small amount of sodium metal and refluxing for 2 hours, followed by distillation. Water can be removed in a similar way but it is preferable to use magnesium metal instead of sodium because it forms a more insoluble hydroxide, thereby shifting the equilibrium more completely from metal alkoxide to metal hydroxide. The magnesium should be activated with iodine (or a small amount of methyl iodide), and the water content should be low, otherwise the magnesium will be deactivated. If the amount of water is large, it should be removed by azeotropic distillation (see below), or by drying over anhydrous $MgSO_4$ (not $CaCl_2$ which combines with alcohols). Acidic materials can be removed by treatment with anhydrous Na_2CO_3, followed by a suitable drying agent, such as calcium hydride, and fractional distillation, using gas chromatography to establish the purity of the product (Ballinger & Long, *J Am Chem Soc* **82** 795 *1960*). Alternatively, the alcohol can be refluxed with freshly ignited CaO for 4hours and then fractionally distilled (McCurdy & Laidler, *Can J Chem* **41** 1867 *1963*).

With higher-boiling alcohols it is advantageous to add some freshly prepared magnesium ethoxide solution (only slightly more than required to remove the water), followed by fractional distillation. Alternatively, in such cases, water can be removed by azeotropic distillation with toluene. Higher-melting alcohols can be purified by crystallisation from methanol or ethanol, toluene/petroleum ether or petroleum ether. Sublimation in vacuum, molecular distillation and gas and liquid chromatographic methods are also useful means of purification. For purification *via* derivatives, *vide supra*.

Polyhydric alcohols

These alcohols are more soluble in water than are monohydric alcohols. Liquids can be freed from water by shaking with type 4A Linde molecular sieves and can safely be distilled only under high vacuum. Carbohydrate alcohols can be crystallised from strong aqueous solution or, preferably, from mixed solvents such as ethanol/petroleum ether or dimethyl formamide/toluene. Crystallisation usually requires seeding and is extremely slow. Further purification can be effected by conversion to the acetyl or benzoyl derivatives which are much less soluble in water and which can readily be recrystallised, e.g. from ethanol. Hydrolysis of the acetyl derivatives, followed by removal of acetate or benzoate and metal ions by ion-exchange chromatography, gives the purified material. On no account should solutions of carbohydrates be concentrated above 40° because of darkening and formation of *caramel*. Ion exchange, charcoal or cellulose column chromatography has been used for the purification and separation of carbohydrates.

ALDEHYDES

Common impurities found in aldehydes are the corresponding alcohols, aldols and water from self-condensation, and the corresponding acids formed by autoxidation. Acids can be removed by shaking with aqueous 10% sodium bicarbonate solution. The organic liquid is then washed with water. It is dried with anhydrous sodium sulfate or magnesium sulfate and then fractionally distilled. Water soluble aldehydes must be dissolved in a suitable solvent such as diethyl ether before being washed in this way. Further purification can be effected *via* the bisulfite derivative (see above) or the Schiff base formed with aniline or benzidine. Solid aldehydes can be dissolved in diethyl ether and purified as above. Alternatively, they can be steam distilled, then sublimed and crystallised from toluene or petroleum ether.

AMIDES

Amides are stable compounds. The lower-melting members (such as acetamide) can be readily purified by fractional distillation. Most amides are solids which have low solubilities in water. They can be recrystallised from large quantities of water, ethanol, ethanol/ether, aqueous ethanol, chloroform/toluene, chloroform or acetic acid. The likely impurities are the parent acids or the alkyl esters from which they have been made. The former can be removed by thorough washing with aqueous ammonia followed by recrystallisation, whereas elimination of the latter is by trituration or recrystallisation from an organic solvent. Amides can be freed from solvent or water by drying below their melting points. These purifications can also be used for sulfonamides and acid hydrazides.

AMINES

The common impurities found in amines are nitro compounds (if prepared by reduction), the corresponding halides (if prepared from them) and the corresponding carbamate salts. Amines are dissolved in aqueous acid, the pH of the solution being at least three units below the pK_a value of the base to ensure almost complete formation of the cation. They are extracted with diethyl ether to remove neutral impurities and to decompose the carbamate salts. The solution is then made strongly alkaline and the amines that separate are extracted into a suitable solvent (ether or toluene) or steam distilled. The latter process removes coloured impurities. Note that chloroform cannot be used as a solvent for primary amines because, in the presence of alkali, poisonous carbylamines (isocyanides) are formed. However, chloroform is a useful solvent for the extraction of heterocyclic bases. In this case it has the added advantage that while the extract is being freed from the chloroform most of the moisture is removed with the solvent.

Alternatively, the amine may be dissolved in a suitable solvent (e.g. toluene), and dry HCl gas is passed through the solution to precipitate the amine hydrochloride. This is purified by recrystallisation from a suitable solvent mixture (e.g. ethanol/diethyl ether). The free amine can be regenerated by adding sodium hydroxide and isolated as above. Cartridges and columns are available (e.g. KP-NH silica column with slightly nitrogenous alkaline chemistry developed by Biotage Inc (<www.biotage.com>) for the purification of amines using flash chromatography.

Liquid amines can be further purified *via* their acetyl or benzoyl derivatives (*vide supra*). Solid amines can be recrystallised from water, alcohol, toluene or toluene-petroleum ether. *Care should be taken in handling large quantities of amines because their vapours are* ***harmful (possibly carcinogenic)*** *and they are readily absorbed through the skin.*

AMINO ACIDS

Because of their zwitterionic nature, amino acids are generally soluble in water. Their solubility in organic solvents rises as the fat-soluble portion of the molecule increases. The likeliest impurities are traces of salts, heavy metal ions, proteins and other amino acids. Purification of these is usually easy, by recrystallisation from water or ethanol/water mixtures. The amino acid is dissolved in the boiling solvent, decolourised if necessary by boiling with 1g of acid-washed charcoal/100g amino acid, then filtered hot, chilled, and set aside for several hours to crystallise. The crystals are filtered off, washed with ethanol, then ether, and dried.

Amino acids have high melting or decomposition points and are best examined for purity by paper or thin layer chromatography. The spots are developed with ninhydrin. Customary methods for the purification of small quantities of amino acids obtained from natural sources (i.e. 1–5g) are ion-exchange chromatography (see Chapter 1). For general treatment of amino acids see Greenstein and Winitz [*The Amino Acids*, Vols 1–3, J.Wiley & Sons, New York 1961] and individual amino acids in Chapters 4 and 7.

A useful source of details such as likely impurities, stability and tests for homogeneity of amino acids is *Specifications and Criteria for Biochemical Compounds*, 3rd edn, National Academy of Sciences, USA, 1972.

ANHYDRIDES

The corresponding acids, resulting from hydrolysis, are the most likely impurities. Distillation from phosphorus pentoxide, followed by fractional distillation, is usually satisfactory. With high boiling or solid anhydrides, another method involves boiling under reflux for 0.5–1 hours with acetic anhydride, followed by fractional distillation. Acetic acid distils first, then acetic anhydride and finally the desired anhydride. Where the anhydride is a solid, removal of acetic acid and acetic anhydride at atmospheric pressure is followed by heating under vacuum. The solid anhydride is then either crystallised as for acid chlorides or (in some cases) sublimed in a vacuum. A preliminary purification when large quantities of acid are present in a solid anhydride (such as phthalic anhydride) is by preferential solvent extraction of the (usually) more soluble anhydride from the acid (e.g. with $CHCl_3$ in the case of phthalic anhydride). *All operations with liquid anhydrides should be carried out in a fume cupboard because of their* **LACHRYMATORY** *properties. Almost all anhydrides attack skin.*

CAROTENOIDS

These usually are decomposed by light, air and solvents, so that degradation products are probable impurities. Chromatography and adsorption spectra permit the ready detection of coloured impurities, and separations are possible using solvent distribution, chromatography or crystallisation. Thus, in partition between immiscible solvents, xanthophyll remains in 90% methanol while carotenes pass into the petroleum ether phase. For small amounts of material, thin-layer or paper chromatography may be used, while column chromatography is suitable for larger amounts. Colourless impurities may be detected by IR, NMR or mass spectrometry. The more common separation procedures are described by P. Karrer and E. Jucker in *Carotenoids*, E.A. Braude (translator), Elsevier, NY, 1950.

Purity can be checked by chromatography (on thin-layer plates, Kieselguhr, paper or columns), by UV or NMR procedures. See "Carotenoids" in Chapter 7.

ESTERS

The most common impurities are the corresponding acid and hydroxy compound (i.e. alcohol or phenol), and water. A liquid ester from a carboxylic acid is washed with 2N sodium carbonate or sodium hydroxide to remove acid material, then shaken with calcium chloride to remove ethyl or methyl alcohols (if it is a methyl or ethyl ester). It is dried with potassium carbonate or magnesium sulfate, and distilled. Fractional distillation then removes residual traces of hydroxy compounds. This method does not apply to esters of inorganic acids (e.g. dimethyl sulfate) which are more readily hydrolysed in aqueous solution when heat is generated in the neutralisation of the excess acid. In such cases, several fractional distillations, preferably under vacuum, are usually sufficient.

Solid esters are easily crystallisable materials. It is important to note that esters of alcohols must be recrystallised either from non-hydroxylic solvents (e.g. toluene) or from the alcohol from which the ester is derived. Thus methyl esters should be crystallised from methanol or methanol/toluene, but not from ethanol, *n*-butanol or other alcohols, in order to avoid alcohol exchange and contamination of the ester with a second ester. Useful solvents for crystallisation are the corresponding alcohols or aqueous alcohols, toluene, toluene/petroleum ether, and chloroform (ethanol-free)/toluene. Esters of carboxylic acids derived from phenols are more difficult to hydrolyse and exchange, hence any alcoholic solvent can be used freely. Sulfonic acid esters of phenols are even more resistant to hydrolysis: they can safely be crystallised not only from the above solvents but also from acetic acid, aqueous acetic acid or boiling *n*-butanol. Note that sulfonic esters of lower alcohols, e.g. methanol, are good alkylating agents.

Fully esterified phosphoric acid and phosphonic acids differ only in detail from the above mentioned esters. Their major contaminants are alcohols or phenols, phosphoric or phosphonic acids (from hydrolysis), and (occasionally) basic material, such as pyridine, which is used in their preparation. Water-insoluble esters are washed thoroughly and successively with dilute acid (e.g. 0.2N sulfuric acid), water, 0.2N sodium hydroxide and water. After drying with calcium chloride they are fractionally distilled. Water-soluble esters should first be dissolved in a suitable organic solvent and, in the washing process, water should be replaced by saturated aqueous sodium chloride. Some esters (e.g. phosphate and phosphonate esters) can be further purified through their uranyl adducts (*vide supra*). Traces of water or hydroxy compounds can be removed by percolation through, or shaking with, activated alumina (about 100g/L of liquid solution), followed by filtration and fractional distillation in a vacuum. For high molecular weight esters (which cannot be distilled without some decomposition) it is advisable to carry out distillation at as low a pressure as possible. Solid esters can be crystallised from toluene or petroleum ether. Alcohols can be used for recrystallising phosphoric or phosphonic esters of phenols.

ETHERS

The purification of diethyl ether (see Chapter 4) is typical of liquid ethers. The most common contaminants are the alcohols or hydroxy compounds from which the ethers are prepared, their oxidation products (e.g. aldehydes), peroxides and water. Dialkyl ethers form peroxides much more readily than other ethers, e.g. ethyl phenyl ethers, on standing in air. Peroxides, aldehydes and alcohols can be removed by shaking with alkaline potassium permanganate solution for several hours, followed by washing with water, concentrated sulfuric acid [CARE], then water. After drying with calcium chloride, the ether is distilled. It is then dried with sodium or with lithium aluminium hydride, redistilled and given a final fractional distillation. The drying process is repeated if necessary.

Alternatively, methods for removing peroxides include leaving the ether to stand in contact with iron filings or copper powder, shaking with a solution of ferrous sulfate acidified with N sulfuric acid, shaking with a copper-zinc couple, passage through a column of activated alumina, and refluxing with phenothiazine. Cerium(III) hydroxide has also been used.

A simple test for ether peroxides is to add 10ml of the ether to a stoppered cylinder containing 1ml of freshly prepared 10% solution of potassium iodide containing a drop of starch indicator. No colour should develop during one minute if free from peroxides. Alternatively, a 1% solution of ferrous ammonium sulfate, 0.1M in sulfuric acid and 0.01M in potassium thiocyanate should not increase appreciably in red colour when shaken with two volumes of the ether. Merck-Chemicals supply peroxide test kits (Perex Test) which use a colorimetric method with test strips which can be used to estimate the amount of hydrogen peroxide, from as low a concentration as 0.2mg/L to as high as1000mg/L. They are very convenient as they can give an indication of the concentration of peroxide rapidly <see http://www.merck-chemicals.com>. As a safety precaution against **EXPLOSION** in case purification from peroxides has been insufficiently thorough, at least a quarter of the total volume of liquid ether should remain in the distilling flask when the distillation is discontinued, as the peroxides are generally higher boiling than the corresponding ethers. To minimise peroxide formation, ethers should be stored in dark bottles and, if they are liquids, they should be left in contact with type 4A Linde molecular sieves, in a cold place, over sodium amalgam. The rate of formation of peroxides depends on storage conditions and is accelerated by metal impurities, heat, light, air and moisture. Always be vigilant and test for peroxides. The formation of peroxides is inhibited in the presence of diphenylamine, di-*tert*-butylphenol, or other antioxidants which can be used as stabilisers.

Ethers that are solids (e.g. phenyl ethers) can be steam distilled from an alkaline solution which will hold back any phenolic impurity. After the distillate is made alkaline with sodium carbonate, the insoluble ether is collected either by extraction (e.g. with chloroform, diethyl ether or toluene) or by filtration. It is then crystallised from alcohols, alcohol/petroleum ether, petroleum ether, toluene or mixtures of these solvents, sublimed in a vacuum and recrystallised if necessary.

HALIDES

Aliphatic halides are likely to be contaminated with halogen acids and the alcohols from which they have been prepared, whereas in aromatic halides the impurities are usually aromatic hydrocarbons, amines or phenols. In both groups the halogen is less reactive than it is in acid halides. Purification is by shaking with concentrated hydrochloric acid, followed by washing successively with water, 5% sodium carbonate or bicarbonate, and water. After drying with calcium chloride, the halide is distilled and then fractionally distilled using an efficient column. For a solid halide the above purification is carried out by dissolving it in a suitable solvent such as toluene. Solid halides can also be purified by chromatography using an alumina column and eluting with toluene or petroleum ether.

They can be crystallised from toluene, petroleum ethers, toluene/petroleum ether or toluene/chloroform/petroleum ether. Care should be taken when handling organic halogen compounds because of their HIGH **TOXICITY**. It should be noted that methyl iodide is a cancer suspect.
Liquid aliphatic halides are obtained alcohol-free by distillation from phosphorus pentoxide. They are stored in dark bottles to prevent oxidation and, in some cases, the formation of phosgene.
A general method for purifying *chlorohydrocarbons* uses repeated shaking with concentrated sulfuric acid [CARE] until no further colour develops in the acid, then washing with water followed by a solution of sodium bicarbonate, then with water again. After drying with calcium chloride, the chlorohydrocarbon is fractionally redistilled to constant boiling point or recrystallised.

HYDROCARBONS

Gaseous hydrocarbons are best freed from water and gaseous impurities by passage through suitable adsorbents and (if olefinic material is to be removed) oxidants such as alkaline potassium permanganate solution, followed by fractional cooling (see Chapter 1 for cooling baths) and fractional distillation at low temperature. To effect these purifications and also to store the gaseous sample, a vacuum line is necessary.
Impurities in hydrocarbons can be characterised and evaluated by gas chromatography and mass spectrometry. The total amount of impurities present can be estimated from the thermometric freezing curve.
Liquid aliphatic hydrocarbons are freed from aromatic impurities by shaking with concentrated sulfuric acid [CARE] whereby the aromatic compounds are sulfonated. Shaking is carried out until the sulfuric acid layer remains colourless for several hours. The hydrocarbon is then freed from the sulfuric acid and the sulfonic acids by separating the two phases and washing the organic layer successively with water, 2N sodium hydroxide, and water. It is dried with $CaCl_2$ or Na_2SO_4, and then distilled. The distillate is dried with sodium wire, P_2O_5, or metallic hydrides, or passage through a dry silica gel column, or preferably, and more safely, with molecular sieves (see Chapter 1) before being finally fractionally distilled through an efficient column. If the hydrocarbon is contaminated with olefinic impurities, shaking with aqueous alkaline permanganate is necessary prior to the above purification. Alicyclic and paraffinic hydrocarbons can be freed from water, non-hydrocarbon and aromatic impurities by passage through a silica gel column before the final fractional distillation. This may also remove isomers. (For the use of chromatographic methods to separate mixtures of aromatic, paraffinic and alicyclic hydrocarbons see references in the bibliography in Chapter 1 under *Liquid and Flash Chromatography, Gas Chromatography and High Performance Liquid and Flash Chromatography*).
Another method of removing branched-chain and unsaturated hydrocarbons from straight-chain hydrocarbons depends on the much faster reaction of the former with chlorosulfonic acid.
Isomeric materials which have closely similar physical properties can be serious contaminants in hydrocarbons. With aromatic hydrocarbons, e.g. xylenes and alkyl benzenes, advantage is taken of differences in ease of sulfonation. If the required compound is sulfonated more readily, the sulfonic acid is isolated, crystallised (e.g. from water), and decomposed by passing superheated steam through the flask containing the acid. The sulfonic acid undergoes hydrolysis, and the liberated hydrocarbon distils with the steam. It is separated from the distillate, dried, distilled and then fractionally distilled. For small quantities (10–100mg), vapour phase chromatography is the most satisfactory method for obtaining a pure sample (for column materials for packings see Chapter 1).
Azeotropic distillation with methanol or 2-ethoxyethanol (cellosolve) has been used to obtain highly purified saturated hydrocarbons and aromatic hydrocarbons such as xylenes and isopropylbenzenes.
Carbonyl-containing impurities can be removed from hydrocarbons (and other oxygen-lacking solvents such as $CHCl_3$ and CCl_4) by passage through a column of Celite 545 (100g) mixed with concentrated sulfuric acid (60ml). After first adding some solvent and about 10g of granular Na_2SO_4, the column is packed with the mixture and a final 7-8cm of Na_2SO_4 is added at the top [Hornstein & Crowe, *Anal Chem* **34** 1037 *1962*]. Alternatively, Celite impregnated with 2,4-dinitrophenylhydrazine can be used.
With solid hydrocarbons such as naphthalene and polycyclic hydrocarbons, preliminary purification by sublimation in vacuum (or high vacuum if the substance is high melting) is followed by zone refining and finally by chromatography (e.g. on alumina) using low-boiling liquid hydrocarbon eluents. These solids can be recrystallised from alcohols, alcohol/petroleum ether or from liquid hydrocarbons (e.g. toluene) and dried below their melting points. Aromatic hydrocarbons that have been purified by zone melting include anthracene, biphenyl, fluoranthrene, naphthalene, perylene, phenanthrene, pyrene and terphenyl, among others. Some polycyclic hydrocarbons, e.g. benzopyrene, are CARCINOGENIC.
Olefinic hydrocarbons have a very strong tendency to polymerise, and commercially available materials are generally stabilised, e.g. with hydroquinone. When distilling compounds such as vinylpyridine or styrene, the stabiliser remains behind and the purified olefinic material is more prone to polymerisation. The most common impurities are higher-boiling dimeric or polymeric compounds. Vacuum distillation in a nitrogen

atmosphere not only separates monomeric from polymeric materials but in some cases also depolymerises the impurities. The distillation flask should be charged with a polymerisation inhibitor, and the purified material should be used immediately or stored in the dark and mixed with a small amount of stabiliser (e.g. 0.1% of hydroquinone or di-*tert*-butylcatechol). It is also advisable to add to the flask a small amount (*ca* 5-10% by volume of liquid in the flask) of a ground mixture of Kieselguhr and NaCl which will provide nuclei for facilitating boiling and finally for cleaning the flask from insoluble polymeric residue (due to the presence of the water soluble NaCl).

IMIDES

Imides (e.g. phthalimide) can be purified by conversion to their potassium salts by reaction in ethanol with ethanolic potassium hydroxide. The imides are regenerated when the salts are hydrolysed with water or dilute acid. Like amides, imides readily crystallise from alcohols and, in some cases (e.g. quinolinic imide), from glacial acetic acid.

IMINO COMPOUNDS

These substances contain the -C=NH group and, because they are strong, unstable bases, they are kept as their more stable salts, such as the hydrochlorides. (The free base usually hydrolyses to the corresponding oxo compound and ammonia.) Like amine hydrochlorides, the salts are purified by solution in alcohol containing a few drops of hydrochloric acid. After treatment with charcoal, and filtering, dry diethyl ether (or petroleum ether if ethanol is used) is added until crystallisation sets in. The salts are dried and kept in a vacuum desiccator.

KETONES

Ketones are more stable to oxidation than aldehydes and can be purified from oxidisable impurities by refluxing with potassium permanganate until the colour persists, followed by shaking with sodium carbonate (to remove acidic impurities) and distilling. Traces of water can be removed with type 4A Linde molecular sieves. Ketones which are solids can be purified by crystallisation from alcohol, toluene, or petroleum ether, and are usually sufficiently volatile for sublimation in vacuum. Ketones can be further purified *via* their bisulfite, semicarbazone or oxime derivatives (*vide supra*). The bisulfite addition compounds are formed only by aldehydes and methyl ketones but they are readily hydrolysed in dilute acid or alkali.

MACROMOLECULES See Chapter 7.

NITRILES

All purifications should be carried out in an efficient fume cupboard because of the **TOXIC** *nature of these compounds*.

Nitriles are usually prepared either by reacting the corresponding halide or diazonium salts with a cyanide salt or by dehydrating an amide. Hence, possible contaminants are the respective halide or alcohol (from hydrolysis), phenolic compounds, amines or amides. Small quantities of phenols can be removed by chromatography on alumina. More commonly, purification of liquid nitriles or solutions of solid nitriles in a solvent such as diethyl ether is by shaking with dilute aqueous sodium hydroxide, followed by washing successively with water, dilute acid and water. After drying with sodium sulfate, the solvent is distilled off. Liquid nitriles are best distilled from a small amount of P_2O_5 which, besides removing water, dehydrates any amide impurity to the nitrile. About one-fifth of the nitrile should remain in the distilling flask at the end of the distillation (*the residue may contain some inorganic cyanide*). This purification also removes alcohols and phenols. Solid nitriles can be recrystallised from ethanol, toluene or petroleum ether, or a mixture of these solvents. They can also be sublimed under vacuum. Preliminary purification by steam distillation is usually possible.

Strong alkali or heating with dilute acids may lead to hydrolysis of the nitrile and should be avoided.

NITRO COMPOUNDS

Aliphatic nitro compounds are generally acidic. They are freed from alcohols or alkyl halides by standing for a day with concentrated sulfuric acid, then washed with water, dried with magnesium sulfate followed by calcium sulfate and distilled. The principal impurities are isomeric or homologous nitro compounds. In cases where the nitro compound was originally prepared by vapour phase nitration of the aliphatic hydrocarbon, fractional distillation should separate the nitro compound from the corresponding hydrocarbon. Fractional crystallisation is more effective than fractional distillation if the melting point of the compound is not too low.

The impurities present in aromatic nitro compounds depend on the aromatic portion of the molecule. Thus, benzene, phenols or anilines are probable impurities in nitrobenzene, nitrophenols and nitroanilines, respectively.

Purification should be carried out accordingly. Isomeric compounds are likely to remain as impurities after the preliminary purifications to remove basic and acidic contaminants. For example, *o*-nitrophenol may be found in samples of *p*-nitrophenol. Usually, the *o*-nitro compounds are more steam volatile than the *p*-nitro isomers and can be separated in this way. Polynitro impurities in mononitro compounds can be readily removed because of their relatively lower solubilities in solvents. With acidic or basic nitro compounds which cannot be separated in the above manner, advantage may be taken of their differences in pK values (see Chapter 1). The compounds can thus be purified by preliminary extractions with several sets of aqueous buffers of known pH (see for example Table 24, Chapter 1) from a solution of the substance in a suitable solvent such as diethyl ether. This method is more satisfactory and less laborious the larger the difference between the pK value of the impurity and the desired compound. Heterocyclic nitro compounds require similar treatment to the nitroanilines. Neutral nitro compounds can be steam distilled.

NUCLEIC ACIDS See Chapter 7.

PHENOLS

Because phenols are weak acids, they can be freed from neutral impurities by dissolution in aqueous N sodium hydroxide (cf pK) and extraction with a solvent such as diethyl ether, or by steam distillation to remove the non-acidic material. The phenol is recovered by acidification of the aqueous phase with 2N sulfuric acid, and either extracted with ether or steam distilled. In the second case the phenol is extracted from the steam distillate after saturating it with sodium chloride (salting out). A solvent is necessary when large quantities of liquid phenols are purified. The phenol is fractionated by distillation under reduced pressure, preferably in an atmosphere of nitrogen to minimise oxidation. Solid phenols can be crystallised from toluene, petroleum ether or a mixture of these solvents, and can be sublimed under vacuum. Purification can also be effected by fractional crystallisation or zone refining. For further purification of phenols *via* their acetyl or benzoyl derivatives *vide supra*.

POLYPEPTIDES AND PROTEINS See Chapter 7.

QUINONES

These are neutral compounds which are usually coloured. They can be separated from acidic or basic impurities by extraction of their solutions in organic solvents with aqueous basic or acidic solutions, respectively. Their colour is a useful property in their purification by chromatography through an alumina column with, e.g. toluene, as eluent. They are volatile enough for vacuum sublimation, although with high-melting quinones a very high vacuum is necessary. *p*-Quinones are stable compounds and can be recrystallised from water, ethanol, aqueous ethanol, toluene, petroleum ether or glacial acetic acid. *o*-Quinones, on the other hand, are readily oxidised. They should be handled in an inert atmosphere, preferably in the absence of light.

SALTS

With metal ions

Water-soluble salts are best purified by preparing a concentrated aqueous solution to which, after decolourising with charcoal and filtering, ethanol or acetone is added so that the salts crystallise. They are collected, washed with aqueous ethanol or aqueous acetone, and dried. In some cases, water-soluble salts can be recrystallised satisfactorily from alcohols. With very water-soluble salts, pure crystals are best obtained by dissolving them in water and allowing the solution to evaporate slowly in a desiccator over a suitable desiccant in a cold room. When crystals are formed they are removed, e.g. by centrifugation, washed with a little ice-cold water and dried in a vacuum. Water-insoluble salts are purified by Soxhlet extraction, first with organic solvents and then with water, to remove soluble contaminants. The purified salt is recovered from the thimble.

With organic cations

Organic salts (e.g. trimethylammonium benzoate) are usually purified by recrystallisation from polar solvents (e.g. water, ethanol or dimethyl formamide). If the salt is too soluble in a polar solvent, its concentrated solution should be treated dropwise with a miscible non-polar, or less polar, solvent (see Table 8, Chapter 1) until crystallisation begins.

With sodium alkane sulfonates

These are purified from sulfites by boiling with aqueous HBr. They are purified from sulfates by adding $BaBr_2$. Sodium alkane disulfonates are finally precipitated by addition of MeOH (Pethybridge & Taba *J Chem Soc Faraday Trans 1* **78** 1331 *1982*).

SULFUR COMPOUNDS

Disulfides

These can be purified by extracting acidic and basic impurities with dilute aqueous base or acid, respectively. However, they are somewhat sensitive to strong alkali which slowly cleaves the disulfide bond. The lower-melting members can be fractionally distilled under vacuum. The high members can be recrystallised from alcohol, toluene or glacial acetic acid.

Sulfones

Sulfones are neutral and very stable compounds that can be distilled without decomposition. They are freed from acidic and basic impurities in the same way as disulfides. The low-molecular-weight members are quite soluble in water, but the higher members can be recrystallised from water, ethanol, aqueous ethanol or glacial acetic acid.

Sulfoxides

These are odourless, rather unstable compounds because they oxidise to sulfones, and should be distilled under vacuum in an inert atmosphere. They are generally water-soluble but can be extracted from aqueous solution with a solvent such as diethyl ether.

Thioethers (sulfides)

Thioethers are neutral stable compounds that can be freed from acidic and basic impurities as described for disulfides. They can be recrystallised from organic solvents and distilled without decomposition. They have sulfurous odours.

Thiols

Thiols, or mercaptans, are stronger acids than the corresponding aliphatic hydroxy or phenolic compounds, but can be purified in a similar manner. However, care must be exercised in handling thiols to avoid their oxidation to disulfides. For this reason, purification is best carried out in an inert atmosphere in the absence of oxidising agents. Similarly, thiols should be stored out of contact with air. They can be distilled without change, and the higher-melting thiols (which are usually more stable) can be crystallised, e.g. from water or dilute alcohol. They oxidise readily in alkaline solution but can be separated from the disulfide which is insoluble in this medium. They should be stored in the dark below 0^o. *All operations with thiols should be carried out in an efficient fume cupboard because of their very unpleasant odour and their* **TOXICITY**.

Thiolsulfonates (disulfoxides)

Thiolsulfonates are neutral and are somewhat light-sensitive compounds. Their most common impurities are sulfonyl chlorides (neutral) or the sulfinic acid or disulfide from which they are usually derived. The first can be removed by partial freezing or crystallisation, the second by shaking with dilute alkali, and the third by recrystallisation because of the higher solubility of the disulfide in solvents. Thiolsulfonates decompose slowly in dilute, or rapidly in strong, alkali to form disulfides and sulfonic acids. Thiolsulfonates also decompose on distillation but they can be steam distilled. The solid members can be recrystallised from water, alcohols or glacial acetic acid.

PURIFICATION *via* FLUOROCHROMES

If the purification procedure is proving difficult then by tagging the desired molecule in a mixture with a fluorochrome (see Table 20, Chapter 1) can provide a means of following the substance through the purification process. The fluorochrome should have a group which can react with the desired compound, and it should be possible to remove the fluorochromic group after purification. Such groups are present for example in fluorescein-isothiocyanate (FITC), where the SCN group can react with an RNH_2 compound to form fluorescent thioureas; 4-bromomethyl-7-methoxycoumarin, which can react with R-OH or R-COONa compounds to form fluorescent ether or ester links with the desired compound; or 3-aminocoumarin, which reacts through its NH_2 group to form fluorescent amides. The fluorescent products can then be readily identified by their fluorescence, separated from impurities, and it should be possible to recover the purified compound after chemically separating it from the fluorescent tag. Such procedures can also be used as analytical tools for detecting specific substances (see *fluorescence spectra* in Chapter 1 and Table 20).

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CHAPTER 3

THE FUTURE OF PURIFICATION

INTRODUCTION

The essence of research is to seek answers wherever there are questions. Regardless of what the answers are, the experiments to be conducted must be carried out with utmost care. For this, one must ensure that the quality of the reactants used and the products obtained are of the highest possible purity. In general terms, one can broadly categorise experimental chemistry and biological chemistry into the following areas:

> Isolation and identification of substances (natural products from nature, protein purification and characterisation, etc).
> Synthesis of substances (organic, or inorganic in nature; these substances may be known substances or new compounds).
> Analysis of substances (this is a key process in the identification of new or known chemical and biological substances. Methods of analysis include spectroscopic methods, derivatisation and sequencing methods).
> Measurements of particular properties of a compound or substance (enzyme kinetics, reaction kinetics, FACS, fluorescence-activated cell sorting, assay).

Impressive and sophisticated strategies, in the form of new reagents, catalysts and chemical transformations, are currently available for the synthesis of molecules. In recent years there has been a deviation in focus from developing new synthetic routes and reactions to improving methods for carrying out reactions. In particular, traditional reactions are carried out in new ways such that the efficiencies of reactions are greatly improved. Emphasis on "Green Technologies" and "Green Chemistry" is continually being stressed to the experimenter and will be for many years to come. Included in this is the movement towards the development of "greener" technologies. Although there is continual debate over the definition of "green" technologies, for our intent and purpose we consider these to include methodologies that are developed to reduce waste and energy, improve on atom economy and are environmentally benign. [Anastas & Kirchhoff *Acc Chem Res* **35** 686 *2002*; *Benign by Design*; American Chemical Society: Washington, DC, *1994*; Constable et al, *Green Chem* **9** 411 *2007*; Li & Trost *PNAS* **105** 13197 *2008*; Anastas & Eghbali, *Chem Soc. Rev*. **39** 301 *2010*]. This may mean that there will be a new world order for carrying out synthesis, which in turn will change the way that one approaches purification. Hence the future of purification very much depends on future methods and trends in synthesis. In the previous edition of this book, some improved methods of synthesis which seek to minimise purification steps were outlined. These included the use of solid phase synthesis, fluorous chemistry as well as ionic liquids. Although some of these methods are still important in some areas of research, other trends have emerged. In this chapter, a brief survey of the emerging trends is presented.

Safety is another issue that goes hand in hand with "Green Science", and cannot be emphasised enough. It should be the first consideration when planning a scientific operation. Safety issues have already been discussed in Chapter 1, and should never be considered a *nuisance*, or an aspect which hampers procedures. This is no longer a *local* or a *regional* issue, but is becoming more and more a *global* problem. It is true that it means more effort should be put in planning an operation, but this is something that the worker should get used to. It is totally *unacceptable* today, and certainly will be in the future, not to take safety very seriously. Questions to be addressed include: Could this procedure be carried out in a safer way with respect not only to the operator but also to those around him or her? How does it affect the immediate as well as the extended environment around the operation? Could the operation be performed in an alternative way that can better satisfy these criteria? Safety now goes well beyond the laboratory and all should be consciously aware of the consequences of a potentially unsafe situation.

Purification of Laboratory Chemicals. http://dx.doi.org/10.1016/B978-0-12-382161-4.00003-0

ATOM ECONOMY

Atom economic chemistry seeks to maximise the incorporation of starting materials into the final product of any given reaction and thus reduce side products or waste formed in a chemical transformation. [Trost *Angew Chem, Int Ed* **34** 259 *2005*.] Thus in an ideal atom economic reaction, all the atoms present in the starting materials are present in the product. Ways to achieve atom economy or efficient reactions include the use of catalysts to enable transformations that will otherwise utilise multiple steps or are impossible to perform. Cross coupling reactions to form C-N, C-O, C-C bonds can now be achieved with relative ease. Despite the progress in the area of catalysis, there are continual challenges to reduce the number of steps needed to achieve the desired transformations. For example, direct methods for C-H functionalisation in a selective and predictable fashion can dramatically alter the way organic molecules are assembled, negating multi-step chemical processes and rendering functional group interconversion steps obsolete. To date, there are numerous reported protocols, with new catalyst systems and designs, for the direct transformation of C-H bond to C-C or C-heteroatom bonds [for a sample of articles on C-H functionalisation, see the special issue on C-H functionalisation in organic synthesis themed issue, Eds. Davies, Du Bois & Yu, in *Chem Soc Rev* Issue 4, *2011*]. This field is an emerging, highly competitive area of research and a comprehensive review of C-H functionalisation is beyond the scope of this book.

Even a seemingly 'simple' transformation such as amide bond formation warrants investigation of new atom economic methods. This is because 'traditional' methods for amide formation suffer from the drawback of producing a stoichiometric amount of waste. Advances in this area are metal catalysed approaches to amide bond formation that includes oxidative amidation of alcohols [for examples, see Taylor et al. *Synlett* 1293 *2002*; Owston et al. *Org. Lett*. **9** 73 *2007*; Zweifel et al. *Angew Chem, Int Ed* **48** 559 *2009*] and amines [e.g. Kim et al. *Angew Chem, Int Ed* **47** 9249 *2008*], aminocarbonylation of aryl halides, [for example, Ueda et al. *J Am Chem Soc* **122** 10722 *2000*; Schnyder, et al. *J Org Chem* **66** 4311 *2001*; Wu et al. *Chem Asian J* **5** 2168 *2010*], rearrangement of aldoximes [e.g. Shie & Fang *J Org Chem* **68** 1158 *2003*; Owston et al. *Org Lett* **9** 3599 *2007*], and direct amidation of aldehydes [e.g. Ali & Punniyamurthy *Adv Synth Catal* **352** 288 *2010*; Shie & Fang *J Org Chem* **68** 1158 *2003*; Yoo & Li *J Am Chem Soc* **128** 13064 *2006*].

Improved atom efficiency can also be achieved if it was possible to carry out synthesis without the use of protecting groups. The protection-deprotection sequence of functional groups increases the number of steps in the synthesis of target compounds. As such, novel chemistry is needed to overcome this. In elegant work reported by Baran et al. [*Nature* **446** 404 *2007*], a total synthesis of a natural product was achieved without any protecting groups.

ORGANOCATALYSIS

One of the major areas of chemical research is in the development of efficient catalysts for carrying out organic transformations. Traditionally this field is dominated by metal mediated catalysis, although increasingly biocatalysis and organocatalysis are gaining prominence. Organocatalysts are defined as catalysts (usually small organic molecules) with low molecular weights (<1000g/mol) where a metal is not part of the active principle. The potential advantages that organocatalysts can offer over metal catalysts include the ease of handling, good stability, low costs and the environmentally benign nature of the former. A major disadvantage of organocatalysis is the limited substrate scope for a particular organocatalyst in a particular transformation. It should be added that the field of organocatalysis was in its relative infancy and stunning progress has been made in the last ten years or so. For example, readily available organic compounds have been found to be capable of catalysing a range of reactions. These include carbon-carbon bond forming reactions (Aldol, Mannich, Diels-Alder, alkylations, cyclopropanations, etc), epoxidation reactions, desymmetrisation reactions and so on [for an excellent book, see Berkessel and Gröger, in the bibliography]. Classes of compounds that have demonstrated applications as organocatalysts include α-amino acids [Jarvo & Miller *Tetrahedron* **58** 2481 *2002*], *N*-heterocyclic carbenes [Marion et al. *Angew Chem, Int Ed* **46** 2988 *2007*], thioureas [Connon *Chemistry-A Eur J* **12** 5419 *2006*], cinchona alkaloids [Dalaigh *Syn Lett* 875 *2005*] and so on. One of the earliest practical demonstrations of the use of organocatalysts is exemplified by the Hajos-Parrish-Eder-Sauer-Wiechert reaction which was patented as early as 1971 [Eder, Sauer & Wiechert DE 2014757 1971, Eder, Sauer & Wiechert *Angew Chem, Int Ed* **10** 496 *1971*, Hajos & Parrish DE 2102623 1971, Hajos & Parrish *J Org Chem* **39** 1612 *1974*]. The Robinson aldol annulation reaction utilised the humble proline molecule as the organocatalyst, and is the *first* example of a highly enantioselective carbon-carbon bond forming reaction. Recently, advances in organocatalysis have progressed to the level of sophistication that has enabled the synthesis of relatively complex organic molecules with multiple stereocentres in high chemical and optical yields. There are many excellent reviews and monographs on organocatalysis, and some of these are listed in the bibliography. Also see ChemFiles, Vol 6, no 4 from Sigma-Aldrich for a compilation of some commercially

available organocatalysts. Another class of organocatalysts are the Phase Transfer Catalysts (PTCs) which have been used for quite some time, and chiral PTCs have more recently been used to catalyse reactions stereospecifically. Sections on "Organocatalysts" and "Phase Transfer Catalysts" are presented in Chapter 6, Part 1 and Part 2, respectively.

MICROWAVE TECHNOLOGIES

The first reports of the use of microwave technologies to accelerate organic reactions were published in 1986 [Gedye et al. *Tetrahedron Lett* **27** 279 *1986,* Giguere et al. *Tetrahedron Lett.* **27** 4945 *1986*]. These days, dedicated microwave instrumentation for carrying out organic synthesis is an almost indispensable piece of equipment in chemical laboratories. Microwave assisted organic synthesis have several advantages over conventional heating methods in that the reaction times are greatly reduced, yields are increased, side reactions are decreased and reactions have greater reproducibility. Microwave irradiation produces efficient internal heating due to the direct coupling of the microwave energy with the reactants and solvents. Inverted temperature gradients in microwave *versus* traditional oil-bath heating have been demonstrated. Although there is still some controversy regarding the "special" effects of microwave assisted technologies, it is generally accepted that microwave technologies provide "specific microwave effects" – that resulting due to thermal effects. The microwave thermal effect may be different to thermal effects from conventional heating methods in view of the inverted temperature gradient leading to direct "in-core" heating, or superheating effects of solvents at atmospheric pressure, or selective heating by strongly absorbing components of some of the reactants. Microwave-assisted organic synthesis has been demonstrated in a number of reactions: from transition metal catalysed reactions to solid phase synthesis to polymerisation reactions. For online resources on microwave chemistry, go to http://www.milestonesci.com (and follow the links to the resource library). Some excellent reviews and books on this topic are listed in the bibliography. It should be noted that microwave technologies have been touted as an important development towards "green" technologies in terms of reduction in energy and waste as well as improved efficiencies. In many instances, solventless reactions under microwave conditions have also been developed and reported [see e.g. Varma *Green Chem* **1** 43 *1999*].

There are a number of commercial microwaves for carrying out synthesis. Mono-mode (single mode) reactors direct electromagnetic irradiation onto a reaction vessel which is mounted at a fixed position. In these reactors, only one vessel can be used at any one time. In contrast, a multi-mode reactor can accommodate several reaction vessels which can be irradiated simultaneously. The choice of solvent for microwave reactions is dependent on the loss factor "tan δ". A reaction medium with a high "tan δ" is required for efficient absorption of electromagnetic energy from the microwave and hence leads to rapid heating. High microwave absorbing solvents include ethanol, DMSO, methanol, 1-butanol ("tan δ" >0.5), while medium solvent absorbers ("tan δ" between 0.1–0.5) include water and DMF. Poor absorbers are solvents like hexane, dichloromethane, chloroform, THF, acetone and ethyl acetate. Common solvents without a permanent dipole, e.g. carbon tetrachloride and *benzene are more or less microwave transparent. Solvents with low "tan δ" values can still be used in microwave reactions as the other components present are likely to be polar and can allow enough heating by microwaves. Alternatively, practices such as doping the reaction with solvents with high "tan δ" values have also been successful. Of note, ionic liquids (which have high "tan δ" values) have been used successfully [see Leadbeater, Torenius & Tye *Comb Chem High Throughput Screening* **7** 511 *2004*, for a review].

FLOW CHEMISTRY

The traditional way of carrying out synthesis utilises batch chemistry, with chemistry occurring inside flasks or reaction vessels. Although there are limitations with batch chemistry, especially in the scale-up of reactions, this has been the mainstay of organic synthesis. In recent years, continuous flow chemistry, an old process concept, has gained increasing attention as an alternative technology to batch chemistry. This will clearly have an impact on the way we carry out synthesis or think about synthesis. The advantages of continuous flow chemistry are improved safety and process reliability, reproducibility and facile automation. Continuous flow chemistry can be carried out on different scales, from using microfluidics (miniaturisation) to large continuous reactors found in chemical plants. In a research laboratory setting, there are advantages and disadvantages in using microfluidics *versus* minifluidic reactors as is summarised by Kirschning et al. [*Chem Commun* **47** 4583 *2011*]. There are a number of vendors that offer flow chemistry equipment, with varying capabilities and price ranges [e.g. http://www.vapourtec.co.uk/; http://www.syrris.com/.] One of the hurdles to the ready adoption of flow chemistry in a research laboratory setting is the need to consider physical chemistry and engineering principles such as mixing times, residence time, flow rates, etc. when designing an experiment. This can initially be a daunting task to a traditional organic chemist. One of the early pioneers of flow chemistry in organic

synthesis is S.V. Ley, University of Cambridge, UK. The reader is advised to refer to his numerous, elegant work in this area – from the development of solid supported reagents and scavengers to applications to complex natural product synthesis. Many types of reactions can be carried out using flow chemistry, and flow chemistry has particular advantage when carrying out "dangerous" reactions such as oxidations. Also see Aldrich Chem Files, Vol 5, no 7 for enabling technologies: Microreactor Technology.

SOLID PHASE SYNTHESIS

The promise of cleaner, more rapid and efficient chemistries *via* solid phase synthesis (SPS) was the driving force behind the huge body of research that emerged. The ease of work-up and purification procedures in solid phase as compared to solution phase chemistry, as well as the scope for combinatorial chemistry provided impetus for further development in this field. The earliest studies on solid phase chemistry were focused on solid phase peptide synthesis (SPPS). The concept of carrying out reactions on a polymer support as distinct to reactants in solution, was conceived by R.B. Merrifield who received the Nobel Prize in Chemistry in 1984 for his pioneering work. However, since the mid-1990s, advances in solid phase chemistry have moved beyond the routine (often robotic) synthesis of small to medium sized peptides and oligonucleotides. SPOS (solid phase organic synthesis) gained much prominence due to the wealth of compounds (combinatorial libraries) that can be synthesised rapidly. This is especially important for pharmaceutical companies screening for compounds with certain biological profiles, or for chemical companies screening for new catalysts or reagents. However, the lack of generality of reactions carried out on solid support as well as the difficulties in monitoring reactions on solid phase has limited the synthetic applications of SPOS. The legacy from solid phase synthesis that is more widely adopted in recent times is the use of solid supported reactants and reagents for carrying out synthesis and for scavenging and purification purposes. The more common methods of SPS are outlined here. For a more complete treatise, readers are encouraged to consult the 5th and 6th editions of this book.

SOLID PHASE PEPTIDE SYNTHESIS (SPPS)

Extensive studies on the synthesis of peptides on solid phase have been carried out, so much so that the technique of SPPS can be reliably and routinely used for the synthesis of short peptides by novices in the field. A large number of resins and reagents have been developed specifically for this purpose, and much is known about problems and avoidance of racemisation, difficult couplings, compatibility of reagents and solvents. Methods for monitoring the success of coupling reactions are available. Automated synthesisers are available commercially (e.g. from Protein Technologies, Rainin Inst Inc, Tuscon AZ; See Google) which can carry out as many as a dozen polypeptide syntheses simultaneously. A more recent advance is in the use of microwave energy to carry out the reactions (e.g. Liberty™ Microwave Peptide Synthesis, cf http://www.cem.com). By using different solid supports, protected amino acids and slightly different chemistry but the same equipment, peptide synthesis can be accomplished from the carboxy or the amino terminal with equal success [refer to CEM Corporation catalogues]. The most satisfactory chemistry currently used is FMOC (9-fluorenylmethoxycarbonyl) chemistry whereby the amino group of the individual amino acid residues is protected as the FMOC. A large number of Fmoc-amino acids are commercially available as well as polymer resins to which the specific Fmoc-amino acid (which will eventually become the carboxy terminal residue of the peptide) is attached. With automated synthesisers, the solvent used is *N*-methylpyrrolidone and washings are carried out with dimethylformamide. A cycle for one residue varies with the residue but can take an hour or more. This means that 70–80 mer polypeptides could take more than a week to prepare. This is not a serious drawback because several different polypeptides can be synthesised simultaneously. The success of the synthesis is dependent on the amino acid sequence since there are some twenty or more different amino acids and the facility of forming a peptide bond varies with the pair of residues involved. However, generally 70 to 80 mers are routinely prepared, and if the sequence is favourable, up to 120-mer polypeptides can be synthesised. After deprotection, the polypeptide is usually purified by HPLC using a C18 column with reverse phase chromatography. A new paradigm in solid phase peptide synthesis developed by A.G. Livingston and co-workers [So et al. *Organic Process Research and Development* **14** 1313 *2010*] is the use of solvent resistant nano filters (SRNFs) which adopt the newly emerging technology of organic solvent nanofiltration (OSN). Thus after the activation and coupling reactions, reagents and unreacted compounds are removed by nanofiltration, and then again after deprotection, reaction products other than the support-bound peptide are removed by SRNF (see SRNFs in Chapter 8). There are many commercial firms that will supply custom-made polypeptides at a price depending on the degree of purity required.

SOLID PHASE DEOXYRIBONUCLEOTIDE SYNTHESIS

The need for oligodeoxyribonucleotides mainly as primers for the preparation of deoxyribonucleic acids (DNA) and for DNA sequencing has resulted in considerable developments in oligo-deoxyribonucleotide synthesis. The solid phase procedure is the method commonly used. Automated synthesisers are commercially available, but with the increase in the number of firms that will provide custom-made oligo-deoxyribonucleotides, it is often not economical to purchase a synthesiser to make one's own oligo-deoxyribonucleotides. Unlike in polypeptide synthesis where there are some twenty different residues to "string" together, in DNA synthesis there are only four deoxyribonucleotides. Consequently there is usually little difficulty in synthesising 100-mers in quantities from 10 μg to 10 milligrams of material. The deprotected deoxyribonucleic acid which is separated from the solid support is purified on an anion exchange column followed by reverse phase HPLC using C8 to C18 columns for desalting. As for the polypeptides, the cost of DNA will depend on the purification level required.

POLYMER SUPPORTED REACTANTS

These have become of increasing importance in synthesis, and a broad classification of polymer supported reactants is as follows: Polymer bound bases (e.g. dimethylaminopyridine, morpholine, piperidine); Polymer supported catalysts (e.g. Grubbs catalyst for metathesis reactions, palladium for hydrogenation reactions, tributylmethylammonium chloride for phase transfer reactions); Polymer supported condensation reagents {e.g. DEAD (diethyl azodicarboxylate) for Mitsonobu reactions, DEC [1-(3-dimethylamino-propyl)-3-ethyl-carbodiimide hydrochloride] {or EDCI [1-ethyl-3-(3-di-methylaminopropyl) carbodiimide HCl]} for peptide synthesis, HOBt (1-hydroxybenzotriazole) for peptide synthesis; Polymer supported oxidising agents (e.g. osmium tetroxide, perruthenate, pyridinium chlorochromate); Polymer supported reducing agents (e.g. borohydride, tributyltin fluoride); Polymer-supported phosphines (for miscellaneous applications depending on the structure) and so on. Commercially available polymer supported catalysts and reagents can be purchased from a number of companies including Sigma-Aldrich (see Chem Files, Vol 5, issue 11 as well as the main catalog), Biotage, Alfa-Aesar, TCI.

SCAVENGER RESINS

The use of resins to clean up reactions has gained much importance over the years. The type of commercially available scavenger resins are electrophilic scavenger resins (e.g. benzaldehyde derivatised resins to scavenge amines; isocyanate resins to scavenge amines, anilines and hydrazines; tosyl chloride resins to scavenge nucleophiles) and nucleophilic scavenger resins (e.g. diethylenetriamine resins to scavenge acids, acid chlorides, anhydrides; sulfonyl amide resins to scavenge acids, acid chlorides, aldehydes, isocyanates and chloroformates) [e.g. see Bhattacharyya *Comb Chem High Throughput Screening* **3** 65 *2000*, Bhattacharyya *Curr Opin Drug Disc Dev* **7** 752 *2004*].

Specific scavengers that use purified silica support (e.g. LpDNPH cartridges which contain a high purity silica adsorbent coated with 2,4-dinitrophenylhydrazine to remove carbonyl compounds), charcoal in various forms and Florisil etc. for particular purposes are available commercially (see Biotage: the *Synthesis and Purification* Catalogue and the *Analytical Sample Preparation* Catalogue and <www.biotage.com> which contain details of such resins, and Supelco: *the Chromatographic Products for Analysis & Purification* Catalogue <www.sigmaaldrich.com/supelco/analytical> for various supports). General types of scavenger resins are also available from a number of companies including Sigma-Aldrich and Biotage.

COMBINATORIAL CHEMISTRY

The major impetus for the development of solid phase synthesis centers on applications in combinatorial chemistry. The notion that new drug leads and catalysts can be discovered in a high throughput fashion has been demonstrated many times over as is evidenced from the number of publications that have arisen (see references at the end of this chapter). A number of approaches to combinatorial chemistry exist. These include the split-mix method, serial techniques and parallel methods to generate libraries of compounds. The advances in combinatorial chemistry are also accompanied by sophisticated methods in deconvolution and identification of compounds from libraries. In a number of cases, innovative hardware and software have been developed for these purposes.

Depending on the size of the combinatorial library to be generated as well as the scale of the reactions to be carried out, a wide range of specialised glassware and equipment is commercially available. For example, in order to carry out parallel combinatorial synthesis, reaction stations equipped with temperature and stirring control are available from a number of sources (e.g. www.fisher.co.uk; www.radleys.com). These reaction stations are readily adapted, using appropriate modules, for conditions under reflux or under inert atmosphere. For automated synthesis of large libraries of compounds, reactions can be carried out using reaction blocks on microtiter plates.

ALTERNATIVE SOLVENTS

The bulk of a reaction medium usually comprises the solvent for reaction. It has been estimated that generally solvents account for 80–90% of the mass utilisation in a typical batch reaction. In view of this, one of the greatest challenges to the 'greening' of chemistry is to consider the 'greening' of solvents. In this regard, issues such as environmental toxicities, waste minimisation, recyclability or the use of renewable solvents are considered in the greening of solvents. A number of publications have provided a framework for the environmental assessment of solvents [Capello et al. *Green Chem* **8** 927 *2007*, Alfonsi et al. *Green Chem* **10** 31 *2008*]. Some approaches to the replacement of conventional solvents include the use of supercritical fluids, e.g. carbon dioxide, ionic liquids, perfluorohydrocarbons. The use of water as an environmentally friendly reaction media has also been the focus of study by several groups [Dallinger & Kappe *Chem Rev* **107** 2563 *2007*, Hailes *Org Proc Res Dev* **11** 114 *2007*, Li & Chen *Chem Soc Rev* **35** 68 *2006*, Leadbeater *J Chem Soc, Chem Commun* 2881 *2005*] as is the study of solvent-less reactions [Polshettiwar & Varma *Pure Appl Chem* **80** 777 *2008*].

SUPERCRITICAL FLUIDS

Supercritical fluids (SCF) are defined as substances that are above their critical temperatures and pressures such that at this critical point, this is the highest temperature and pressure at which the substance can exist as a vapour and liquid in equilibrium. The commonly used SCF in chemistry is that of supercritical carbon dioxide ($scCO_2$), which has a critical point at 31.1°C and a pressure of 73.8 Bar. The density of CO_2 at this critical point is approximately 0.4g/mL. CO_2 is potentially an ideal green solvent–it is non-toxic to the environment and at atmospheric pressure, CO_2 is a gas and hence does not require any waste treatment. It has a high gas-dissolving ability, a low solvation ability, good mass transfer properties and high diffusion rates. CO_2 is inexpensive, non-flammable, environmentally benign and can be removed completely from products. Although CO_2 is a greenhouse gas, CO_2 is naturally occurring as well as obtained as a byproduct of many processes, and the use of CO_2 as solvent is to use a "renewable" resource. In this respect, CO_2 is easily recovered either by cooling (condensing) or absorption by aqueous alkaline solutions and re-used. The disadvantages of using $scCO_2$ are the specialised and expensive equipment needed to achieve the critical conditions, the low dielectric constant and low dissolving abilities. In addition, $scCO_2$ cannot be used in reactions with strong nucleophiles. Applications with $scCO_2$ as solvent has been demonstrated, in extractions (e.g. of caffeine), dry-cleaning, polymerisation reactions, pharmaceutical processing. The use of $scCO_2$ in organic synthesis has also been demonstrated in a number of reactions including hydrogenation reactions, Diels-Alder chemistry, free radical reactions, Friedel Crafts reactions and so on [S. Hadlington *Chem Br* **39** 21 *2003*, Liu & Xiao, *J Mol Cat A: Chem* **270** 1 *2007*]. The solvent properties of $scCO_2$ can be tuned by adjusting the temperature and pressure. Liquids and solid solutes are surprisingly soluble in $scCO_2$ though it is generally true that the solubility of non-polar substances is higher than the polar ones because CO_2 is a non-polar molecule. The solubility can be tuned by changing the bulk densities of CO_2 or by adding a co-solvent or modifying the solute. Other fluids that have been used in this way are ammonia and SO_2, although they do not have the many advantages of CO_2, especially those pertaining to its low reactivity under "normal" reaction conditions.

IONIC LIQUIDS

Ionic liquids (ILs) are organic or inorganic salts that are liquids at room or reaction temperatures. Although ionic liquids are themselves not new discoveries (e.g. the ionic liquid $[EtNH_3]$ $[NO_3]$ was described in 1914), the use of ionic liquids in synthesis is relatively recent. In particular, the potential applications of ionic liquids as solvents in synthesis and in catalysis have been achieved. They have high mechanical, thermal and electrochemical stability. Their physical properties make them unique solvents for synthesis, and are 'green' alternatives to volatile organic solvents, though there has been some debate on whether ionic liquids can be considered as 'green' solvents. [R. Sanghi & M.M. Srivasatava, *Green Chemistry: Environment Friendly Alternatives*, Alpha Science International, *2003*, ISBN 9781842651735; C. Alfonso, A.M. Crespo & P.S.G. Joao, *Green Separation Processes: Fundamentals and Applications*, VCH-Wiley Publishing, *2005*, ISBN 978357309856; J. Clark & J. Hardy, *Green Chemistry in Undergraduate Practical Classes (with CD-ROM)*, Royal Society of Chemistry, *2006*, ISBN 978054042784]. The impact of ILs on health and environment is not known. In addition to this, many ILs are difficult to prepare and can be expensive if bulk, high purity ILs are needed. Ionic liquids are good solvents for both organic and inorganic substances and hence can be used to bring reagents into the same phase for reaction. Ionic liquids are also immiscible with a number of organic solvents and thus provide a non-aqueous, polar alternative for two-phase extraction systems. As ionic liquids are non-flammable and non-volatile (with hardly any measurable vapour pressure), they can be used in high vacuum systems without the possibility of loss or contaminants. In addition, this also facilitates the isolation of products as products can be distilled from the ionic liquid or alternatively extracted with an organic solvent that is immiscible with the ionic liquid. Although ionic liquids are frequently composed of poorly coordinating ions,

they are highly polar which are important characteristics in the activation of catalysts. For example the 1-butyl-3-methylimidazolinium salt with $AlCl_3$ is a very good catalyst for the Friedel-Crafts reaction, and varying the ratio of salt to $AlCl_3$ produces a more or less acidic medium. ILs are used successfully in organic reactions which are mediated by microwaves. ILs have found uses in phase-separation processes, in electrochemical processes, as heat storage media, lubricants and additives.

A large variety of ILs of high purity with water content below 100ppm and halide content below 10ppm are now available commercially. These include numerous *N*-alkylpyridinium, *N,N'*-dialkylimidazolium, alkylammonium and alkylphosphonium salts, covalent hydrophobic ILs (e.g. 1,2-dimethyl-3-propylimidazolium bis(trifluoromethylsulfonyl)imide, task-specific ILs, Brønsted acidic ILs (e.g. 3-[triphenylphosphonio]propane-1-sulfonic acid tosylate), nitrile-functionalised ILs, perfluorinated ILs (e.g. tetrabutylammonium nonafluorobutane sulfonate, BASF Basionics (e.g. 1,2,3-trimethylimidazolium methyl sulfate), and TOMATS for heavy metal extraction (e.g. methyltrioctylammonium thiosalicylate)

A number of reactions have been carried out in ionic liquids; for examples see Dell'Anna et al. *J Chem Soc, Chem Commun* 434 *2002*, Nara et al. *Tetrahedron Lett* **43** 1127 *2002*, Semeril et al. *J Chem Soc, Chem Commun* 146 *2002*, Buijsman et al. *Org Lett* **3** 3785 *2001*. These include Diels-Alder reactions, Friedel-Crafts (above), transition-metal mediated catalysis, e.g. Heck and Suzuki coupling reactions, and olefin metathesis reactions. An example of ionic liquid acceleration of reactions carried out on solid phase is given by Revell & Ganesan [*Org Lett* **4** 3071 *2002*]. [See also Fluka, Riedel-deHaën, Catalogue 2007–2008, and <www.sigmaaldrich.com/ionicliquids>, with or without Basionics™ and Cytec (Cytos®); Chem Files (Sigma-Aldrich) Vol 6, No 9 *2006*, Ghassemi et al. Application Note 48 in Synthesis and Purification Catalog 2007, <www.Biotage.com>.]

FLUOROUS CHEMISTRY

Fluorous chemistry is defined as chemistry that is related to highly fluorinated sp^3-hybridised carbon containing compounds. The seminal work by Horvath and Rabai (*Science* **266** 72 *1994*) described the applications of fluorous biphasic catalysis and applied it to Rh catalysed hydroformylation reactions. To date the scope of fluorous chemistry has expanded to include applications in organic synthesis and material science, separation, extraction and chromatography. For example, fluorous phase labels can be attached to substrates such that the subsequent fluorinated products can be extracted into the fluorous phase. This has applications in liquid-liquid extractions (typical work-up procedures) where a three-phase extraction is now possible (organic, fluorous and aqueous phases). As organic and inorganic compounds have little or no tendency to dissolve in highly fluorinated solvents and compounds, phase labelling a compound as fluorous will enable successful extraction into the fluorous phase. However, in order to carry out homogenous reactions with these fluorinated compounds, organic solvents with a good dissolving power for fluorous compounds or miscible organic and fluorous solvents can be used. Alternatively organic solvents with a few fluorine atoms, e.g. trifluoroethanol, benzotrifluoride ("hybrid solvents") will dissolve both organic and fluorous compounds. A number of synthetic applications utilising fluorous chemistry have been reported in the literature. [For examples, see Schneider & Bannwarth *Helv Chim Acta* **84** 735 *2001*, Galante et al. *Tetrahedron Lett* **42** 5425 *2001*, Studer & Curran *Tetrahedron* **53** 6681 *1997*, Studer et al. *J Org Chem* **62** 2917 *1997*, Crich & Neelamkavil *Tetrahedron* **58** 3865 *2002*.] For some fluorous compounds for synthesis and separation, see Chem Files from Sigma-Aldrich, Supplement II, 2008. One potential limitation of fluorous solvents is their cost.

BIOMASS DERIVED ORGANIC SOLVENTS

Biomass derived organic solvents are solvents that are obtained from renewable resources, which is in contrast to the traditional petrochemical based solvents that are limited in resource. These solvents are gaining traction as green solvents, though the scope of the reaction transformations and other solvent replacement applications have not been fully studied. Examples of such biomass derived solvents are 2-methyltetrahydrofuran [96-47-9], glycerol [56-81-5], glycerol ethers, ethyl lactate and cyclopentylmethyl ethers. 2-Methyltetrahydrofuran is an aprotic ether which has polarity and Lewis base strengths between that for diethyl ether and THF [Aycock *Org Proc Res Dev* **11** 156 *2007*; Ripin & Vetelino *Syn Lett* 2353 *2003*]. It had been used as a replacement solvent for THF [109-99-9] in organometallic reactions (e.g. Grignard, lithiation, hydride reduction, coupling reactions) with the advantage that MeTHF is only partially water miscible and hence can be conveniently used to recover reaction products [Comanita & Aul *Chimica Oggi* **25** 26 *2007*; Pace et al. *Tetrahedron* **67** 2670 *2011*]. Cyclopentylmethyl ether has been used as an alternative to ethereal solvents such as THF [109-99-0], 1,4-dioxane [123-91-1], 1,2-dimethoxyethane [110-71-4] [Watanabe et al. *Org Proc Res Dev* **11** 251 *2007*]. The formation of peroxides is suppressed in cyclopentylmethyl ether [5614-37-9] and this solvent has a narrow explosion range and can be easily dried. The use of cyclopentylmethyl ether as solvent has also been demonstrated in a number of reactions including organometallic reactions, oxidation and reduction reactions

and reactions with transition metal catalysts. Interestingly, a promising new sustainable solvent is glycerol. Glycerol is an organic waste product from biodiesel production and hence is cheap, readily available and is renewable. Glycerol is a non-toxic polar solvent that is able to dissolve inorganic salts, acids, bases, transition metal complexes as well as organic compounds that are poorly miscible in water [Diaz-Alvarez *Chem Commun* **47** 6208 *2011*; Gu & Jerome *Green Chem* **12** 1127 *2010*]. The disadvantages of using glycerol as solvent are the high viscosity as well as the possible reactivity of the hydroxyl groups in chemical transformations. Nevertheless, the use of glycerol as solvent in a variety of organic transformations has been demonstrated. In some cases, glycerol as solvent has a beneficial effect on reaction rates and selectivity. Due to glycerol's immiscibility with non-polar solvents, the use of glycerol facilitates isolation of reaction products and has been used in separation processes.

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CHAPTER 4

PURIFICATION OF ORGANIC CHEMICALS

INTRODUCTION

The general principles, techniques and methods of purification in Chapters 1 and 2 are applicable to this chapter. Most organic liquids and a number of solids can readily be purified by fractional distillation, usually at atmospheric pressure. Sometimes, particularly with high boiling or sensitive liquids, or when in doubt about stability, distillation or fractionation under as low a pressure as possible should be carried out. To save space, the present chapter omits many substances for which the published purification methods involve simple distillation. Where boiling points are given, purification by distillation is another means of removing impurities. Literature references, and in particular Beilstein references, are included for most entries which refer the reader directly or indirectly to the original sources. Substances are listed alphabetically in each section, usually with some criteria of purity, giving brief details of how they can be purified. Also noted are the molecular weights (to the first decimal place), melting points and/or boiling points together with the respective densities and refractive indexes for liquids, and optical rotations for chiral compounds. All temperatures are in centigrade unless stated otherwise. When temperatures and/or wavelengths are not given for the last three named properties, then they should be assumed to be 20°C and the average of the wavelengths of the sodium D lines respectively; and most densities are relative to water at 4°C.

Ionisation constants of ionisable compounds are given as **pK** values (published in the literature) and refer to the **pKa** values at room temperature (~15°C to 25°C). Values at other temperatures are given as superscripts, e.g. $\mathbf{pK^{30}}$ for 30°C. Estimated values are entered as $\mathbf{pK_{Est}}$ (see Chapter 1**,** pp 34–36).

The present chapter includes commercially available organic chemicals. Most of the inorganic, metal-organic, organo- bismuth, boron, phosphorus, selenium, silicon and alkali metal compounds and metal ion salts of organic acids are in Chapter 5. Naturally occurring commercially available organic compounds for use in biochemistry, molecular biology and biology are in Chapter 6. Commercially available polymer supported reagents are indicated with **§** under the appropriate reagent.

Rapid purification procedures are included for commonly used solvents and reagents which make them suitable for general use in synthetic chemistry.

Abbreviations of titles of periodicals are defined as in the Chemical Abstracts Service Source Index (CASSI) except that punctuation is deleted. Other abbreviations are self evident.

As a good general rule, all low boiling (<100°) organic liquids should be treated as highly flammable and toxic (because they can be inhaled in large quantities) and the necessary precautions should be taken (see Safety precautions associated with the purification of laboratory chemicals in Chapter 1, p 4).

Benzene has been used as a solvent successfully and extensively in the past for reactions and purification by chromatography and crystallisation but is now considered a **very dangerous substance**. It should be used with extreme care. We emphasise that an alternative solvent to benzene (e.g. toluene, toluene-petroleum ether, or a petroleum ether to name a few) should be used first. However, if no other solvent system can be found, then all operations involving benzene (and storage) have to be performed in an efficiently running fumehood, and precautions must be taken to avoid inhalation and contact with skin and eyes. An asterisk has been inserted in the text, e.g. $^{*}C_6H_6$ or *benzene, to remind the user that special precautions should be adopted.

This chapter consists of five sections *viz*: **Aliphatic Compounds, Alicyclic Compounds, Aromatic Compounds, Heterocyclic Compounds** and **Miscellaneous As, B, P, Si, S, Se, and Te Compounds.**

Purification of Laboratory Chemicals. http://dx.doi.org/10.1016/B978-0-12-382161-4.00004-2

ALIPHATIC COMPOUNDS

Acetal (acetaldehyde diethylacetal) *[105-57-7]* **M 118.2, b 103.7-104°, d $_4^{20}$ 0.831, n $_D^{25}$ 1.38054, n^{25} 1.3682.** Dry acetal over Na to remove alcohols and H_2O, and to polymerise aldehydes, then fractionally distil. Or, treat it with alkaline H_2O_2 at 40-45° to remove aldehydes, then saturate with NaCl, separate, dry with K_2CO_3 and distil it from Na [Vogel *J Chem Soc* 616 *1948*]. [*Beilstein* **1** IV 3103.]

Acetaldehyde *[75-07-0]* **M 44.1, b 20.2°, d $_4^{20}$ 0.788, n $_D^{25}$ 1.33113, pK^{25} 13.57 (hydrate).** Acetaldehyde is usually purified by fractional distillation in a glass helices-packed column under dry N_2, discarding the first portion of distillate. Or, it is shaken for 30 minutes with $NaHCO_3$, dried with $CaSO_4$ and fractionally distilled at 760mm through a 70cm Vigreux column. The middle fraction is collected and further purified by standing for 2 hours at 0° with a small amount of hydroquinone (free radical inhibitor), followed by distillation [Longfield & Walters *J Am Chem Soc* **77** 810 *1955*]. [*Beilstein* **1** IV 3094.]

Acetaldehyde dimethyl acetal (1,1-dimethoxyethane) *[534-15-6]* **M 90.1, b 63-65°, d $_4^{20}$ 0.852, n $_D^{25}$ 1.36678.** Distil the dimethyl acetal through a fractionating column and fraction boiling at 63.8°/751mm is collected. It forms an azeotrope with MeOH. *Alternatively*, purify it as for *acetal* above. It has been purified by GLC. [*Beilstein* **1** IV 3103.]

Acetamide *[60-35-5]* **M 59.1, m 81°, pK $_1^{25}$ -1.4, pK $_2^{25}$ +0.37.** Acetamide is crystallised by dissolving in hot MeOH (0.8ml/g), diluting with Et_2O and allowing to stand [Wagner *J Chem Edu* **7** 1135 *1930*]. Alternate crystallisation solvents are acetone, *benzene, chloroform, dioxane, methyl acetate or *benzene/ethyl acetate mixtures (3:1 and 1:1). It has also been recrystallised from hot water after treating with HCl-washed activated charcoal (which had been repeatedly washed with water until free from chloride ions), then crystallised again from hot 50% aqueous EtOH and finally twice from hot 95% EtOH [Christoffers & Kegeles *J Am Chem Soc* **85** 2562 *1963*]. Finally it is dried in a vacuum desiccator over P_2O_5. Acetamide is also purified by distillation (**b** 221-223°) or by sublimation *in vacuo*. It has also been purified by two recrystallisations from cyclohexane containing 5% (v/v) of *benzene. Needle-like crystals separate and are filtered, washed with a small volume of distilled H_2O and dried with a flow of dry N_2. [Slebocka-Tilk et al. *J Am Chem Soc* **109** *4620 1987*, *Beilstein* **2** H 175, **2** I 80, **2** II 177, **2** III 384, **2** IV 399.]

Acetamidine hydrochloride *[124-42-5]* **M 94.5, m 164-166°, 165-170°(dec), 174°, pK^{25} 12.40.** The hydrochloride can be recrystallised from small volumes of EtOH. *Alternatively*, it is dissolved in EtOH, filtered, Et_2O is added; filter the crystalline salt off under N_2 and dry it in a vacuum desiccator over H_2SO_4. The salt is deliquescent and should be stored in a tightly stoppered container. Its solubility in H_2O is 10% at room temperature and it is soluble in Me_2CO. The *free base* reacts strongly alkaline in H_2O. It has λ_{max} 224nm (ε 4000) in H_2O. The *picrate* has **m** 252° (sintering at ~245°). [Dox *Org Synth* Coll Vol **I** 5 *1941*, Davies & Parsons *Chem Ind (London)* 628 *1958*, Barnes et al. *J Am Chem Soc* **62** 1286 *1940* give **m** 177-178°, *Beilstein* **2** H 185, **2** I 85, **2** II 183, **2** III 416, **2** IV 428.]

***N*-(2-Acetamido)-2-aminoethanesulfonic acid (ACES)** *[7365-82-4]* **M 182.2, m > 220°(dec), pK$_{Est}$ ~1.5, pK$_2$ 6.9.** Recrystallise ACES from hot aqueous EtOH. [Perrin & Dempsey *Buffers for pH and Metal Ion Control* Chapman & Hall, London *1974*, *Beilstein* **4** III 1707.]

***N*-(2-Acetamido)iminodiacetic acid (ADA)** *[26239-55-4]* **M 190.2, m 219°(dec), pK$_1$ ~2.3, pK$_2$ 6.6.** Dissolve ADA in water, add one equivalent of NaOH solution (to final pH of 8-9), then acidify with HCl to precipitate the free acid. This is filtered off, washed with water and dried *in vacuo*. [*Beilstein* **4** IV 2441.]

Acetamidomethanol *[625-51-4]* **M 89.1, m 47-50°, 54-56°, 55°.** Recrystallise it from freshly distilled Me_2CO, wash the crystals with dry Et_2O and dry them in a vacuum desiccator over P_2O_5. R_F 0.4 on paper chromatography with $CHCl_3$/EtOH (2:8) as solvent and developed with ammoniacal $AgNO_3$. It also crystallises in needles from EtOAc containing a few drops of Me_2CO. It is *hygroscopic* and should be stored under dry conditions. [Bachmann et al. *J Am Chem Soc* **73** 2775 *1951*, Walter et al. *Chem Ber* **99** 3204 *1966*, Einhorn &

Ladisch *Justus Liebigs Ann Chem* **343** 265 *1905*, *Beilstein* **2** IV 405.]

Acetic acid (glacial) *[64-19-7]* **M 60.1, m 16.6°, b 118°, d $_4^{20}$ 1.049, n $_D^{25}$ 1.37171, n^{25} 1.36995, pK^{25} 4.76.** Usual impurities are traces of acetaldehyde and other oxidisable substances and water. (Glacial acetic acid is very *hygroscopic*. The presence of 0.1% water lowers its **m** by 0.2°.) Purify it by adding some acetic anhydride to react with water present, heat it for 1 hour to just below boiling in the presence of 2g CrO_3 per 100ml and then fractionally distil it [Orton & Bradfield *J Chem Soc* 960 *1924*, Orton & Bradfield *J Chem Soc* 983 *1927*]. Instead of CrO_3, use 2-5% (w/w) of $KMnO_4$, and boil under reflux for 2-6 hours. Traces of water have been removed by refluxing with tetraacetyl diborate (prepared by warming 1 part of boric acid with 5 parts (w/w) of acetic anhydride at 60°, cooling, and filtering off, followed by distillation [Eichelberger & La Mer *J Am Chem Soc* **55** 3633 *1933*].
Refluxing with acetic anhydride in the presence of 0.2g % of 2-naphthalenesulfonic acid as catalyst has also been used [Orton & Bradfield *J Chem Soc* 983 *1927*]. Other suitable drying agents include anhydrous $CuSO_4$ and chromium triacetate: P_2O_5 converts some acetic acid to the anhydride. Azeotropic removal of water by distillation with thiophene-free *benzene or with butyl acetate has been used [Birdwhistell & Griswold *J Am Chem Soc* **77** 873 *1955*]. An alternative purification uses fractional freezing. [*Beilstein* **2** H 96, **2** IV 94.]
Rapid procedure: Add 5% acetic anhydride, and 2% of CrO_3. Reflux and fractionally distil.

Acetic anhydride *[108-24-7]* **M 102.1, b 138°, d $_4^{20}$ 1.082, n $_D^{25}$ 1.3904.** Adequate purification can usually be achieved by fractional distillation through an efficient column. Acetic acid can be removed by prior refluxing with CaC_2 or with coarse Mg filings at 80-90° for 5 days, or by distillation from a large excess of quinoline (1% AcOH in quinoline) at 75mm pressure. Acetic anhydride can also be dried by standing with Na wire for up to a week, removing the Na and distilling it under vacuum. (Na reacts vigorously with acetic anhydride at 65-70°). Dippy & Evans [*J Org Chem* **15** 451 *1950*] let the anhydride (500g) stand over P_2O_5 (50g) for 3 hours, then decanted it and stood it with ignited K_2CO_3 for a further 3 hours. The supernatant liquid was distilled and the fraction **b** 136-138° was further dried with P_2O_5 for 12 hours, followed by shaking with ignited K_2CO_3, before two further distillations through a five-section Young and Thomas fractionating column. The final material distilled at 137.8-138.0°. It can also be purified by azeotropic distillation with toluene: the azeotrope boils at 100.6°. After removal of the remaining toluene, the anhydride is distilled [sample had a specific conductivity of 5×10^{-9} ohm^{-1}cm^{-1}]. [*Beilstein* **2** H 96, **2** I 39, **2** II 91, **2** III 134, **2** IV 94.]
Rapid procedure: Shake with P_2O_5, separate, shake with dry K_2CO_3 and fractionally distil.

Acetic hydrazide *[1068-57-1]* **M 74.1, m 67°, b 127°/18mm.** Acetic hydrazide crystallises as needles from EtOH. It reduces $NH_3/AgNO_3$. [*Beilstein* **2** H 191, **2** IV 435.]

Acetoacetamide *[5977-14-0]* **M 101.1, m 54-55°, 54-56°**. Recrystallise the amide from $CHCl_3$, or Me_2CO/petroleum ether. It also crystallises from pyridine with 4mols of solvent. It is slightly soluble in H_2O, EtOH and AcOH but is insoluble in Et_2O. The *phenylhydrazone* has **m** 128°. [Kato *Chem Pharm Bull Jpn* **15** 921 923 *1967*, Claisen & Meyer *Chem Ber* **35** 583 *1902*, *Beilstein* **3** H 659, **3** I 231, **3** III 1204, **3** IV 1545.]

Acetone *[67-64-1]* **M 58.1, b 56.2°, d $_4^{20}$ 0.791, n $_D^{25}$ 1.35880, pK $_1^{25}$ –6.1 (basic, mono-protonated), pK $_2^{25}$ 20.0 (acidic)** The commercial preparation of acetone by catalytic dehydrogenation of isopropyl alcohol gives relatively pure material. Analytical reagent quality generally contains less than 1% of organic impurities but may have up to about 1% of H_2O. Dry acetone is appreciably *hygroscopic*. The main organic impurity in acetone is mesityl oxide, formed by aldol condensation. It can be dried with anhydrous $CaSO_4$, K_2CO_3 or type 4A Linde molecular sieves, and then distilled. Silica gel and alumina, or mildly acidic or basic desiccants cause acetone to undergo the aldol condensation, so that its water content is increased by passage through these reagents. This also occurs to some extent when P_2O_5 or sodium amalgam is used. Anhydrous $MgSO_4$ is an inefficient drying agent, and $CaCl_2$ forms an addition compound. Drierite (anhydrous $CaSO_4$) offers minimum acid and base catalysis for aldol formation and is the recommended drying agent for this solvent [Coetzee & Siao *Inorg Chem* **14** 2 *1987*, Riddick & Bunger *Organic Solvents* Wiley-Interscience, N.Y., 3rd edn, *1970*]. Acetone can be shaken with Drierite (25g/L) for several hours before it is decanted and distilled from fresh Drierite (10g/L) through an efficient column, maintaining atmospheric contact through a Drierite drying tube.

The equilibrium water content is about 10^{-2}M. Anhydrous $Mg(ClO_4)_2$ **should not be used as drying agent as there is a high risk of EXPLOSION with acetone vapour.**
Organic impurities have been removed from acetone by adding 4g of $AgNO_3$ in 30ml of water to 1L of acetone, followed by 10ml of M NaOH, shaking for 10 minutes, filtering, drying with anhydrous $CaSO_4$ and distilling [Werner *Analyst (London)* **58** 335 *1933*]. *Alternatively*, successive small portions of $KMnO_4$ have been added to acetone at reflux, until the violet colour persists, followed by drying and distilling. Refluxing with chromium trioxide (CrO_3) has also been used. Methanol has been removed from acetone by azeotropic distillation (at 35°) with methyl bromide, and treatment with acetyl chloride.
Small amounts of acetone can be purified as the NaI addition compound, by dissolving 100g of finely powdered NaI in 400g of boiling acetone, then cooling in ice and salt to –8°. Crystals of $NaI.3Me_2CO$ are filtered off and, on warming in a flask, acetone distils off readily. [This method is more convenient than the one using the bisulfite addition compound.] It has also been purified by gas chromatography on a 20% free fatty acid phthalate (on Chromosorb P) column at 100°.
For efficiency of desiccants in drying acetone see Burfield and Smithers [*J Org Chem* **43** 3966 *1978*]. The water content of acetone can be determined by a modified Karl Fischer titration [Koupparis & Malmstadt *Anal Chem* **54** 1914 *1982*]. [*Beilstein* **1** IV 3180.]
Rapid procedure: Dry over anhydrous $CaSO_4$ and distil.

Acetone cyanohydrin *[75-86-5]* **M 85.1, b 48°/2.5mm, 68-70°/11mm, 78-82°/15mm, d_4^{20} 0.93.** Dry the cyanohydrin with Na_2SO_4, and distil it as rapidly as possible under vacuum to avoid decomposition. Discard fractions boiling below 78-82°/15mm. Store it in the dark. **USE AN EFFICIENT FUME HOOD as HCN (POISONOUS) is always present.** [Cox & Stormont *Org Synth* Coll.Vol. **II** 7 *1940*, *Beilstein* **3** H 316, **3** IV 785.]

Acetonedicarboxylic acid (3-oxoglutaric acid) *[542-05-2]* **M 146.1, m 138°(dec), pK^{25} 3.10.** Crystallise it from ethyl acetate and store it over P_2O_5. It decarboxylates in hot water. [*Beilstein* **3** IV 1816.]

Acetone semicarbazone *[110-20-3]* **M 115.1, m 187°, pK^{25} 1.33.** Acetone semicarbazone crystallises from water or from aqueous EtOH. [*Beilstein* **3** H 101, **3** I 48, **3** II 81, **3** III 189, **3** IV 179.]

Acetonitrile (methyl cyanide) *[75-05-8]* **M 41.1, b 81.6°, d^{25} 0.77683, n_D^{20} 1.3441, n^{25} 1.34163.** Commercial acetonitrile is a by-product of the reaction of propylene and ammonia to acrylonitrile. The following procedure that significantly reduces the levels of acrylonitrile, allyl alcohol, acetone and *benzene was used by Kiesel [*Anal Chem* **52** 2230 *1988*]. Methanol (300ml) is added to 3L of acetonitrile fractionated at high reflux ratio until the boiling temperature rises from 64° to 80°, and the distillate becomes optically clear down to λ = 240nm. Add sodium hydride (1g) free from paraffin, to the liquid, reflux for 10 minutes, and then distil rapidly until about 100ml of residue remains. Immediately pass the distillate through a column of acidic alumina, discarding the first 150ml of percolate. Add 5g of CaH_2 and distil the first 50ml at a high reflux ratio. Discard this fraction, and collect the following main fraction. The best way of detecting impurities is by gas chromatography.
Usual contaminants in commercial acetonitrile include H_2O, acetamide, NH_4OAc and NH_3. Anhydrous $CaSO_4$ and $CaCl_2$ are inefficient drying agents. Preliminary treatment of acetonitrile with cold, saturated aqueous KOH is undesirable because of base-catalysed hydrolysis and the introduction of water. Drying by shaking with silica gel or Linde 4A molecular sieves removes most of the water in acetonitrile. Subsequent stirring with CaH_2 until no further hydrogen is evolved leaves only traces of water and removes acetic acid. The acetonitrile is then fractionally distilled at high reflux, taking precaution to exclude moisture by refluxing over CaH_2 [Coetzee *Pure Appl Chem* **13** 429 *1966*]. *Alternatively*, 0.5-1% (w/v) P_2O_5 is often added to the distilling flask to remove most of the remaining water. Excess P_2O_5 should be avoided because it leads to the formation of an orange polymer. Traces of P_2O_5 can be removed by distilling from anhydrous K_2CO_3.
Kolthoff, Bruckenstein and Chantooni [*J Am Chem Soc* **83** 3297 *1961*] removed acetic acid from 3L of acetonitrile by shaking for 24 hours with 200g of freshly activated alumina (which had been reactivated by heating at 250° for 4 hours). The decanted solvent was again shaken with activated alumina, followed by five batches of 100-150g of anhydrous $CaCl_2$. (Water content of the solvent was then less than 0.2%.) It was shaken for 1 hour with 10g of P_2O_5, twice; and distilled in a 1m×2cm column, packed with stainless steel wool and

protected from moisture by $CaCl_2$ tubes. The middle fraction had a water content from 0.7 to 2mM. Traces of unsaturated nitriles can be removed by initially refluxing with a small amount of aqueous KOH (1ml of 1% solution per L). Acetonitrile can be dried by azeotropic distillation with dichloromethane, *benzene or trichloroethylene. Isonitrile impurities can be removed by treatment with conc HCl until the odour of isonitrile has gone, followed by drying with K_2CO_3 and distilling.
Acetonitrile is refluxed with, and distilled from alkaline $KMnO_4$ and $KHSO_4$, followed by fractional distillation from CaH_2. (This is better than fractionation from molecular sieves or passage through a type H activated alumina column, or refluxing with KBH_4 for 24 hours and fractional distillation) [Bell et al. *J Chem Soc, Faraday Trans 1* **73** 315 *1977*, Moore et al. *J Am Chem Soc* **108** 2257 *1986*].
Material suitable for polarography is obtained by refluxing over anhydrous $AlCl_3$ (15g/L) for 1 hour, distilling, refluxing over Li_2CO_3 (10g/L) for 1 hour and redistilling. It is then refluxed over CaH_2 (2g/L) for 1 hour and fractionally distilled, retaining the middle portion. The product is not suitable for UV spectroscopy use. A better purification procedure uses refluxing over anhydrous $AlCl_3$ (15g/L) for 1 hour, distilling, refluxing over alkaline $KMnO_4$ (10g $KMnO_4$, 10g Li_2CO_3/L) for 15 minutes, and distilling. A further reflux for 1 hour over $KHSO_4$ (15g/L), then distillation, is followed by refluxing over CaH_2 (2g/L) for 1 hour, and fractional distillation. The product is protected from atmospheric moisture and stored under nitrogen [Walter & Ramalay *Anal Chem* **45** 165 *1973*]. Purificaton of "General Purity Reagent" for this purpose is not usually satisfactory because very large losses occur at the $KMnO_4/LiCO_3$ step. For electrochemical work involving high oxidation fluorides, further reflux over P_2O_5 (1g/ml for 0.5 hours) and distilling (discarding 3% of first and last fractions) and repeating this step is necessary. The distillate is kept over molecular sieves *in vacuo* after degassing, for 24 hours and distilling in a vacuum onto freshly activated 3A molecular sieves. The MeCN should have absorption at 200nm of <0.05 (H_2O reference) and UV cutoff at *ca* 175nm. Also the working potential range of purified $Et_4N^+ BF_4^-$ (0.1mol.dcm^{-3} in the MeCN) should be +3.0 to –2.7V *vs* Ag^+/Ag^o. If these criteria are not realised then further impurities can be removed by treatment with activated neutral alumina (60 mesh) *in vacuo* before final molecular sieves treatment [Winfield *J Fluorine Chem* **25** 91 *1984*].
Acetonitrile has been distilled from $AgNO_3$, Payecting the middle fraction over freshly activated Al_2O_3. After standing for two days, the liquid is distilled from the activated Al_2O_3. The specific conductivity should be 0.8-1.0 × 10^{-8} mhos [Harkness & Daggett *Can J Chem* **43** 1215 *1965*]. *Acetonitrile* ^{14}C is best purified by gas chromatography and is water free, and distils at 81°. [*Beilstein* **2** H 183, **2** IV 419.]
Rapid procedure: Dry over anhydrous K_2CO_3 for 24 hours, followed by further drying for 24 hours over 3A molecular sieves or boric anhydride, followed by distillation. *Alternatively*, stir over P_2O_5 (5% w/v) for 24 hours then distil. However, this last method is not suitable for reactions with very acid sensitive compounds.

Acetonylacetone (2,5-hexanedione) *[110-13-4]* **M 114.2, m –9°, b 76-78°/13mm, 88°/25mm, 137°/150mm, 188°/atm, d $_4^{20}$ 0.9440, n $_D^{20}$ 1.423, pK^{25} 18.7.** Purify it by dissolving in Et_2O, stiring with K_2CO_3 (a quarter of the weight of dione), filtering, drying over anhydrous Na_2SO_4 (**not $CaCl_2$**), filtering again, evaporating the filtrate and distilling it in a vacuum. It is then redistilled through a 30cm Vigreux column (oil bath temperature 150°). It is miscible with H_2O and EtOH. The *dioxime* has **m** 137° (plates from *C_6H_6), the *mono-oxime* has **b** 130°/11mm, and the *2,4-dinitrophenylhydrazone* has **m** 210-212° (red needles from EtOH). It forms complexes with many metals. [Werner et al. *Chem Ber* **22** 2100 *1989*, for enol content see Gero *J Org Chem* **19** 1960 *1954*, *Beilstein* **1** IV 3688.]

Acetoxime (acetone oxime) *[127-06-0]* **M 73.1**, **m 63°, b 135°/760mm, d $_4^{20}$ 0.901, pK^{40} 0.99.** It crystallises from petroleum ether (b 40-60°) and can be sublimed. [*Beilstein* **1** H 649, **1** IV 3202.]

Acetoxyacetone (acetonyl acetate, acetol acetone) *[592-20-1]* **M 116.1, b 65°/11mm, 73-75°/17mm, 174-176°/atm, d $_4^{20}$ 1.0757, n $_D^{20}$ 1.4141.** Distil it in a vacuum, then redistil it at atmospheric pressure. It is miscible with H_2O, but is slowly decomposed by it. Store it in a dry atmosphere. The *2,4-dinitrophenylhydrazone* has **m** 115-115.5° (from $CHCl_3$/hexane). [Perkin Jr *J Chem Soc* **59** 789 *1891*, Reich & Samuels *J Org Chem* **21** 68 *1956*, Nef *Justus Liebigs Ann Chem* **335** 260 *1904*, *Beilstein* **2** IV 297.]

1-Acetoxy-1,3-butadiene (1,3-butadienyl acetate) ***cis-trans*** mixture *[1515-76-0]* **M 112.1, b 42-43°/16mm, 51-52°/20mm, 60-61°/40mm, d $_4^{20}$ 0.9466, n $_D^{20}$ 1.4622.** The commercial sample is stabilised with 0.1% of *p*-

tert-butylcatechol. If the material contains crotonaldehyde (by IR, used in its synthesis), it should be dissolved in Et_2O, shaken with 40% aqueous sodium bisulfite, then 5% aqueous Na_2CO_3, water, dried (Na_2SO_4) and distilled several times in a vacuum through a Widmer [*Helv Chim Acta* **7** 59 *1924*] or Vigreux column [Wicterle & Hudlicky *Col Czech Chem Commun* **12** 564 *1947*, Hagemeyer & Hull *Ind Eng Chem* **41** 2920 *1949*]. [*Beilstein* **2** III 295.]

1-Acetoxy-2-butoxyethane (2-butyloxyethyl acetate) *[112-07-2]* **M 160.2, b 61-62°/0.2mm, 75-76°/12mm, 185.5°/740mm, 188-192°/atm, d_4^{20} 0.9425, n_D^{20} 1.4121.** Shake the ester with anhydrous Na_2CO_3, filter and distil it in a vacuum. Redistillation can then be carried out at atmospheric pressure. [Dunbar & Bolstad *J Org Chem* **21** 1041 *1956*, *Beilstein* **2** IV 215.]

2-Acetoxyethanol (2-hydroxyethyl acetate) *[542-59-6]* **M 104.1, b 61°/1mm, 79-81°/12mm, 187°/761mm, d_4^{20} 1.108, n_D^{20} 1.42.** Dry the ester over K_2CO_3 (**not $CaCl_2$**), and distil it. [Davis & Ross *J Chem Soc* 3061 1950, rate of hydrolysis: Davis & Ross *J Chem Soc* 2706 *1951*, *Beilstein* **2** H 141, **2** I 66, **2** II 154, **2** III 303, **2** IV 214.]

1-Acetoxy-2-ethoxyethane *[111-15-9]* **M 132.2, b 30°/3mm, 49-50°/12mm, 156-159°, d_4^{20} 0.97, n_D^{20} 1.406.** Shake the ethoxy-ethane with anhydrous Na_2CO_3, filter and distil it in a vacuum. Redistillation can then be carried out at atmospheric pressure. [Dunbar & Bolstad *J Org Chem* **21** 1041 *1956*, *Beilstein* **2** IV 214.]

1-Acetoxy-2-methoxyethane *[110-49-6]* **M 118.1, b 30°/6mm, 40-41°/12mm, 140-144°/760mm, d_4^{20} 1.009, n_D^{20} 1.4011.** Shake the methoxy-ethane with anhydrous Na_2CO_3, filter and distil it in a vacuum. Redistillation can be then be carried out at atmospheric pressure. [Dunbar & Bolstad *J Org Chem* **21** 1041 *1956*, *Beilstein* **2** IV 214.]

***S*-(-)-2-Acetoxypropionyl chloride** *[36394-75-9]* **M 150.6, b 51-53°/11mm, d_4^{20} 1.19, n_D^{20} 1.423, $[\alpha]_D^{27}$ -33°, (c 4, $CHCl_3$), $[\alpha]_{546}^{20}$ –38° (c 4, $CHCl_3$).** It is moisture sensitive and is hydrolysed to the corresponding acid. Check the IR spectrum. If the OH band above 3000cm^{-1} is too large and broad then the mixture should be refluxed with pure acetyl chloride for 1 hour, evaporated and distilled under reduced pressure. [Julia & Sans *J Chromatographic Sci* **17** 651 *1979*, Dolittle & Heath *J Org Chem* **49** 5041 1984, *Beilstein* **3** II 189.]

***S*-Acetoxysuccinic anhydride** *[59025-03-5]* **M 158.1, m 58° (*RS* 81.5-82.5°, 86-87°), $[\alpha]_D^{20}$ –26.0° (c 19, Me_2CO), $[\alpha]_D^{20}$ –28.4° (c 13, Ac_2O).** Recrystallise it from Ac_2O and dry it in a vacuum over KOH, or by washing it with dry Et_2O due to its deliquescent nature. [Jones *J Chem Soc* 788 *1933,* Henrot et al. *Synth Commun* **16** 183 *1986*, Shiuey et al. *J Org Chem* **52** 1040 *1988*, *RS*: Cohen et al. *J Am Chem Soc* **88** 5306 *1966*.]

Acetylacetone (2,4-pentanedione, acac) *[123-54-6]* **M 100.1, m –23°, 45°/30mm, b 140.4°/atm, $d^{30.2}$ 0.9630, $n^{18.5}$ 1.45178, pK_1^{25} –5.0 (enol), –6.6 (keto), pK_2^{25} 8.95.** Small amounts of acetic acid are removed by shaking with small portions of 2M NaOH until the aqueous phase remains faintly alkaline. The sample, after washing with water, is dried with anhydrous Na_2SO_4, and distilled through a modified Vigreux column [Cartledge *J Am Chem Soc* **73** 4416 *1951*]. An additional purification step is fractional crystallisation from the liquid. *Alternatively*, there is less loss of acetylacetone if it is dissolved in four volumes of *benzene and the solution is shaken three times with an equal volume of distilled water (to extract acetic acid): the *benzene is then removed by distillation at 43-53° and 20-30mm through a helices-packed column. It is then refluxed over P_2O_5 (10g/L) and fractionally distilled under reduced pressure. The distillate (sp conductivity 4×10^{-8} $ohm^{-1}cm^{-1}$) is suitable for polarography [Fujinaga & Lee *Talanta* **24** 395 *1977*]. To recover used acetylacetone, metal ions are stripped from the solution at pH 1 (using 100ml 0.1M H_2SO_4/L of acetylacetone). The acetylacetone is then washed with (1:10) ammonia solution (100ml/L) and with distilled water (100ml/L, twice), then treated as above. It complexes with Al, Be, Ca, Cd, Ce , Cu, Fe^{2+}, Fe^{3+}, Mn, Mg, Ni, Pb and Zn. [*Beilstein* **1** H 777, **1** I 401, **1** II 831, **1** III 3113, **1** IV 3662.]

Acetyl bromide *[506-96-7]* **M 123.0, b 76-77°, d_4^{20} 1.65.** Boil acetyl bromide with PBr_3/Ac_2O for 1 hour, then distil the latter off and redistil it. Store it dry. [Burton & Degering *J Am Chem Soc* **62** 227 *1940*, *Beilstein* **2** IV

398.] **LACHRYMATORY.**

2-Acetylbutyrolactone *[517-23-7]* **M 128.1, b 105°/5mm, 120-123°/11mm, 142-143°/30mm, d_4^{20} 1.1846, n_D^{20} 1.459.** Purify the lactone by distillation, which will convert any free acid to the lactone, *alternatively* dissolve it in Et_2O, wash well with 0.5N HCl, dry the organic layer and distil it. Its solubility in H_2O is 20% v/v. The *2,4-dinitrophenylhydrazone* forms orange needles from MeOH, **m** 146°. The lactone hydrolyses in mineral acid to 2-acetyl-4-hydroxybutyric acid which can be converted to the *di-n-propylamine salt* with **m** 68-70°. The lactone is a **SKIN IRRITANT**. [Matsuhawa *Yakugaku Zasshi (J Pharm Soc Jpn)* **62** 417 *1942*, Willman & Schinz *Helv Chim Acta* **35** 2401 *1952*, *Beilstein* **17/11** V 16.]

Acetyl chloride *[75-36-5]* **M 78.5, b 52°, d_4^{20} 1.1051, n_D^{20} 1.38976.** Reflux acetyl chloride with PCl_5 for several hours to remove traces of acetic acid, then distil it. Redistil it from one-tenth its volume of dimethylaniline or quinoline to remove free HCl. A.R. quality is freed from HCl by pumping it for 1 hour at –78° and distilling it into a trap at –196°. [*Beilstein* **2** IV 395.] **LACHRYMATORY.**

Acetylene *[74-86-2]* **M 26.0, m –80.8°, b –84°, pK^{25} ~25.** If very impure, acetylene should be purified by successive passage through spiral wash bottles containing, in this order, saturated aqueous $NaHSO_4$, H_2O, 0.2M iodine in aqueous KI (two bottles), sodium thiosulfate solution (two bottles), alkaline sodium hydrosulfite with sodium anthraquinone-2-sulfonate as indicator (two bottles), and 10% aqueous KOH solution (two bottles). The gas is then passed through a Dry-Ice trap and two drying tubes, the first containing $CaCl_2$, and the second, Dehydrite [$Mg(ClO_4)_2$] [Conn et al. *J Am Chem Soc* **61** 1868 *1939*]. Acetone vapour can be removed from acetylene by passage through H_2O, then conc H_2SO_4, or by passage through two gas traps at –65° and –80°, conc H_2SO_4 and a soda lime tower, a tower of 1-mesh Al_2O_3 then through H_2SO_4 [Reichert & Nieuwland *Org Synth* Coll Vol **I** 229 *1941*, Wiley *Org Synth* Coll Vol **III** 853 *1955*, Jones & Whiting *Org Synth* Coll Vol **IV** 793 *1963*]. Sometimes it contains acetone and air. These can be removed by a series of bulb-to-bulb distillations, e.g. a train consisting of a conc H_2SO_4 trap and a cold EtOH trap (–73°), or passage through H_2O and H_2SO_4, then over KOH and $CaCl_2$. [See Brandsma *Preparative Acetylenic Chemistry,* 1st Edn Elsevier 1971 p15, for pK, ISBN 0444409475, 2nd Edn Elsevier 1988, ISBN 0444429603, and below for sodium acetylide.] It is also available commercially as 10ppm in helium, and several concentrations in N_2 for instrument calibration. [*Beilstein* **1** IV 939.]
Sodium acetylide *[1066-26-8]* M 48.0, is prepared by dissolving Na (23g) in liquid NH_3 (1L) and bubbling acetylene until the blue colour is discharged (ca 30 minutes) and evaporated to dryness [Saunders *Org Synth* Coll Vol **III** 416 *1955*], and is available commercially as a suspension in xylene/light mineral oil. [See entry in "Metal-organic Compounds", Chapter 5.]

Acetylenedicarboxamide (Aquamycin, Cellocidin) *[543-21-5]* **M 112.1, m 216-218°(dec), 219-221°(dec).** Acetylenedicarboxamide crystallises from MeOH and H_2O [**m** 190-192°(dec) as *hemihydrate*]. When prepared from the ester + NH_3 it has **m** 213°(dec). Also a melting point of 290-292°(dec) has been reported. [Saggimo *J Org Chem* **22** 1171 *1857*, Kharash et al. *J Org Chem* **10** 392 *1945*, Blomquist & Winslow *J Org Chem* **10** 156 *1945*, *Beilstein* **2** I 317, **2** III 1995, **2** IV 2295.]

Acetylenedicarboxylic acid (butynedioic acid) *[142-45-0]* **M 114.1, m 179°(anhydrous), pK_1^{19} 1.04, pK_2^{19} 2.50.** The acid is soluble in Et_2O and crystallises from Et_2O/petroleum ether (**m** 183-183.5°), or H_2O as the *dihydrate* which dehydrates in a desiccator over conc H_2SO_4 in a vacuum. The *dipicrate* crystallises from aqueous ether. For the mono K salt see entry in "Metal-organic Compounds", Chapter 5. [Abbott et al. *Org Synth* Coll Vol **II** 10 *1943*, Huntress et al. *Org Synth* Coll Vol **IV** 329 *1963*, *Beilstein* **2** H 801, **2** I 317, **2** II 670, **2** III 1991, **2** IV 2290.]

***N*-Acetylethylenediamine** *[1001-53-2]* **M 102.1, m 50-51°, 51°, b 128°/3mm, 125-130°/5mm, 133-139°/27mm, pK^{25} 9.28.** The acetyl-diamine has been fractionated under reduced pressure and fraction **b** 125-130°/5mm was refractionated, fraction **b** 132-135°/4mm was collected and solidified. It is a low melting *hygroscopic* solid which can be recrystallised from dioxane/Et_2O. It is soluble in H_2O, Et_2O and $*C_6H_6$. The *p-toluenesulfonate salt* can be recrystallised from EtOH/EtOAc (1:8), has **m** 125-126°, but the free base cannot be recovered from it by basifying and extracting with CH_2Cl_2. The *picrate* has **m** 175° (from EtOH) [Aspinall *J*

Am Chem Soc **63** 853 *1941*, Hall *J Am Chem Soc* **78** 2570 *1956*]. [*Beilstein* **4** IV 1193.]

Acetyl fluoride *[557-99-3]* **M 62.0, b 20.5°/760mm, d_4^{20} 1.032.** Purify acetyl fluoride by fractional distillation. It attacks glass and is sold in steel cylinders. [*Beilstein* **2** H 172, **2** I 79, **2** II 175, **2** III 385, **2** IV 393.] **TOXIC and LACHRYMATORY.**

Acetyl iodide *[507-02-8]* **M 170.0, b 39.5-40°/64mm, 108°/760mm.** Purify it by fractional distillation. [*Beilstein* **2** H 174, **2** I 80, **2** II 177, **2** III 393, **2** IV 399.] **TOXIC and LACHRYMATORY.**

3-(S-Acetylmercapto)isobutyric acid *[RS 33325-40-5]* **M 162.2, m 40-40.5°, b *ca* 120°/1.25mm, pK_{Est} ~4.0.** Distil the acid under high vacuum and recrystallise it from $*C_6H_6$. [Fredga & Mastersson *Chem Abstr* **38** 3616 *1944*.]

Acetyl methanesulfonate *[5539-53-7]* **M 170.2, b <120°/<0.01mm.** The main impurity is methanesulfonic acid. Reflux it with redistilled acetyl chloride for 6-10 hours, i.e. until no further HCl is absorbed in a trap, and exclude moisture. Distil off excess of AcCl and carefully distil it below 0.001mm with the bath temperature below 120° to give the anhydride as a pale yellow oil which solidifies below 0°. Below ~130° it gives the disulfonic anhydride, and above ~130° polymers are formed, and it is used for cleaving ethers [Preparation, IR, NMR: Karger & Mazur *J Org Chem* **36** 528, 532 *1971*]. [*Beilstein* **2** H 166, **2** III 349.]

3-(Acetylthio)propionic acid *[41345-70-4]* **M 148.2, m 48-52°, 52-54°, b 127-128°/3mm, pK_{Est} ~4.2.** Purify the propionic acid by distillation in a vacuum. It has λ_{max} at 231nm (ε 4200). It is a potential enzyme inhibitor [Noda et al. *J Am Chem Soc* **75** 914 *1953*, Clegg et al. *J Am Chem Soc* **121** 5319 *2004*, Clegg & Hutchinson *Angew Chem, Int Edn* **43** 3716 *2005*]. [*Beilstein* **3** III 551, **3** IV 731.]

***N*-Acetylthiourea** *[591-08-2]* **M 118.2, m 164-165°, 166-168°**. Recrystallise the thiourea from AcOH; the solid is washed with Et_2O and dried in air then at 100°. [Zahradnik *Col Czech Chem Commun* **24** 3678 *1959*, *Beilstein* **3** IV 354.]

***cis*-Aconitic acid** *[585-84-2]* **M 174.1, m 126-129°(dec).** Crystallise the *cis*-acid from water by cooling (solubility is 1g in 2ml of water at 25°). Dry it in a vacuum desiccator. [*Beilstein* **2** IV 2405.]

***trans*-Aconitic acid (1,2,3-propenetriscarboxylic acid)** *[4023-65-8]* **M 174.1, m 195°(dec), m 198-199°(dec), 204-205°(dec), pK_1^{25} 2.81, pK_2^{25} 4.46.** Purify the *trans*-acid by dissolving it in AcOH (77g/150ml), filtering and cooling. The acid separates (55g) as colourless needles. A further quantity (10g) can be obtained by reducing the volume of the filtrate. The acid is dried in air then in a vacuum desiccator over NaOH. The acid can be recrystallised from $Me_2CO/CHCl_3$. The highest melting point is obtained with the very dry acid. A melting point of 209° was obtained on a Dennis bar [Dennis & Shalton *J Am Chem Soc* **52** 3128 *1930*, Bruce *Org Synth* Coll Vol **II** 12 *1943*]. [*Beilstein* **2** IV 2405.]

cis*-Aconitic anhydride** *[6318-55-4]* **M 156.1, m 75°, 76-78°, 78-78.5°.** Reflux it in xylene (7.5 parts) for 1 hour, then evaporate and recrystallise the residue from $*C_6H_6$. *Alternatively*, reflux it in Ac_2O, evaporate and recrystallise from $*C_6H_6$. It is sensitive to moisture, store dry. [IR: Groth & Dahlén *Acta Chem Scand* ***21 291 *1967*, Malachowski & Maslowski *Chem Ber* **61** 2523 *1928*, NMR: Gawron & Mahajan *Biochemistry* **5** 2335 *1966*.] [*Beilstein* **18/8** V 530.]

Acrolein (acraldehyde, 2-propenal) *[107-02-8]* **M 56.1, fp –86.95°, b 25°/100mm, 52.69°/760mm (dt/dp 0.0355°/mm, d_4^{20} 0.839, n^{25} 1.3992**. Purify acrolein by fractional distillation, under nitrogen, drying with anhydrous $CaSO_4$ and then distilling under vacuum. Blacet, Young and Roof [*J Am Chem Soc* **59** 608 *1937*] distilled it under nitrogen through a 90cm column packed with glass rings. To avoid formation of diacryl, the vapour is passed through an ice-cooled condenser into a receiver cooled in an ice-salt mixture and containing 0.5g catechol. The acrolein is then distilled twice from anhydrous $CuSO_4$ at low pressure, catechol being placed in the distilling flask and the receiver to avoid polymerisation. [*Alternatively*, hydroquinone (1% of the final

solution) can be used.] **Respiratory irritant, work in an efficient fume cupboard.** [*Beilstein* **1** IV 3435.]

Acrolein diacetyl acetal (1,1-diacetoxy-2-propene). *[869-29-4]* **M 158.2, b 75°/10mm, 184°/atm, d $_4^{20}$ 1.08, n $_D^{20}$ 1.4203.** Check the NMR spectrum. If it is not satisfactory, then add Ac_2O and a drop of conc H_2SO_4 and heat at 50° for 10 minutes. Then add anhydrous NaOAc (*ca* 3g/100g of liquid) and fractionate. Note that it forms an azeotrope with H_2O, so do not add H_2O at any time. It is a **highly flammable and TOXIC** liquid; use protective gloves. [Smith et al. *J Am Chem Soc* **73** 5282 *1951*, *Beilstein* **2** H 154, **2** I 72, **2** III 356, **2** IV 291.]

Acrolein diethyl acetal (3,3-diethoxy-I-propene or 1,1-diethoxy2-propene) *[3054-95-3]* **M 130.2, b 120-125°/atm, n $_D^{20}$ 1.398-1.407**. Add Na_2CO_3 (*ca* 3.5%) and distil it using an efficient column, or better use a spinning band column. [Witzemann et al. *Org Synth* Coll Vol **II** 17 *1943*, *Beilstein* **1** H 727, **1** I 378, **1** III 2960, **1** IV 3437.]

Acrolein dimethyl acetal (1,1-dimethoxy-2-propene) *[6044-68-4]* **M 102.1, b 87.5-88°/750mm, 89-90°/760mm, d $_4^{20}$ 0.86, n $_D^{20}$ 1.3962.** Fractionally distil it (after adding 0.5g of hydroquinone) under reduced pressure through an all glass column (40 cm × 2.5 cm) packed with glass helices and provided with a heated jacket and a total reflux variable take-off head. Stainless steel Lessing rings (1/8 x 1/8 in) or gauze have also been used as packing. It is a **highly flammable and TOXIC** liquid; keep away from the skin. [Hall & Stern *J Chem Soc* 2657 *1955*, *Beilstein* **1** IV 3437.]

Acrolein semicarbazone *[6055-71-6]* **M 113.1, m 171°**. It crystallises from water in needles. [Auwers & Heineke *Justus Liebigs Ann Chem* **458** 202 *1927*, *Beilstein* **1** II 785.]

Acrylamide *[79-06-1]* **M 71.1, m 84°, b 125°/25mm**. Crystallise acrylamide from acetone, chloroform, ethyl acetate, methanol or *benzene/chloroform mixture, then vacuum dry and store it in the dark under vacuum. Recrystallise it from $CHCl_3$ by dissolving 200g in 1L, heating to boiling and filtering without suction in a warmed funnel through Whatman 541 filter paper; allowing to cool to room temperature and keeping at –15° overnight. The crystals are collected with suction in a cooled funnel and washed with 300ml of cold MeOH. The crystals are air-dried in a warm oven. [Dawson et al. *Data for Biochemical Research*, Oxford Press 1986 p. 449, *Beilstein* **2** IV 1471.]
CAUTION: *Acrylamide is extremely* **TOXIC (neurotoxic),** *and precautions must be taken to avoid skin contact or inhalation. Use gloves and handle in a well-ventilated fume cupboard.*

Acrylic acid *[79-10-7]* **M 72.1, m 13°, b 30°/3mm, 70°/50mm, d $_4^{20}$ 1.051, pK^{25} 4.25.** It can be purified by steam distillation, or vacuum distillation through a column packed with copper gauze to inhibit polymerisation. (This treatment also removes inhibitors such as methylene blue that may be present.) Azeotropic distillation of the water with *benzene converts aqueous acrylic acid to the anhydrous material. [*Beilstein* **2** H 397, **2** I 186, **2** II 383, **2** III 1215, **2** IV 1455.]

Acrylonitrile *[107-13-1]* **M 53.1, b 78°, d $_4^{20}$ 0.806, n^{25} 1.3886**. Wash acrylonitrile with dilute H_2SO_4 or dilute H_3PO_4, then with dilute Na_2CO_3 and water. Dry it with Na_2SO_4, $CaCl_2$ or (better) by shaking with molecular sieves. Fractionally distil it under N_2. It can be stabilised by adding 10ppm *tert*-butyl catechol. Immediately before use, the stabiliser can be removed by passage through a column of activated alumina (or by washing with 1% NaOH solution if traces of water are permissible in the final material), followed by distillation. *Alternatively*, shake it with 10% (w/v) NaOH to extract inhibitor, and then wash it in turn with 10% H_2SO_4, 20% Na_2CO_3 and distilled water. Dry for 24 hours over $CaCl_2$ and fractionally distil under N_2 taking fraction boiling at 75.0-75.5°C (at 734mm). Store it with 10ppm *tert*-butyl catechol. Acrylonitrile is distilled off when required. [Burton et al. *J Chem Soc, Faraday Trans 1* **75** 1050 *1979*, *Beilstein* **2** IV 1473.]

Acryloyl chloride *[814-68-6]* **M 90.5, b 72-74°/740mm, 74°/760mm, d $_4^{20}$ 1.1127, n $_D^{20}$ 1.4337.** Distil acryloyl chloride rapidly through an efficient 25cm column after adding 0.5g of hydroquinone/200g of chloride, and then redistil it carefully at atmospheric pressure preferably in a stream of dry N_2. [Stempel et al. *J Am Chem Soc* **72** 72 *1950*, Gresham et al. *J Am Chem Soc* **72** 2299 *1950*, *Beilstein* **2** IV 1471.] **The liquid is an irritant and is**

TOXIC.

Adipic acid *[124-04-9]* **M 146.1, m 154-154.5°, b 159.5°/0.1mm, 191°/5mm, 205.5°/10mm, 222.5°/20mm, 337.5°/760mm, pK_1^{20} 4.42, pK_2^{20} 5.41; pK_1^{25} 4.44, pK_2^{25} 5.45; pK_1^{40} 4.54, pK_2^{40} 5.59.** For use as a volumetric standard, adipic acid is crystallised once from hot water with the addition of a little animal charcoal, dried at 120° for 2 hours, then recrystallised from acetone and again dried at 120° for 2 hours. Other purification procedures include crystallisation from ethyl acetate and from acetone/petroleum ether, fusion, followed by filtration and crystallisation from the melt, and preliminary distillation under vacuum. [*Beilstein* **2** H 649, **2** I 277, **2** II 572, **2** III 1705, **2** IV 1956.]
Diethyl adipate *[141-28-6]* **M 202.3, m –20°** to **–19°, b 111°/5mm, 125°/10mm, 133°/15mm, 251°/atm, d^{25} 1.0034, n_D^{20} 1.42776**, is prepared in the usual way by boiling the acid and excess EtOH in the presence of a catalytic amount of H_2SO_4 and distilled. [*Beilstein* **2** H 652, 2 I 277, **2** II 574, **2** III 1721, **2** IV 1960.]

Adiponitrile (1,4-dicyanobutane) *[111-69-3]* **M 108.14, m 2.4°, b 123°/0.5mm, 153°/6mm, 175°/26mm, 184°/30mm, 295°/atm, d_4^{20} 0.9396, n_D^{20} 1.4371.** Reflux adiponitrile over P_2O_5 and $POCl_3$, and fractionally distil it, then fractionate it through an efficient column. **The liquid is TOXIC and is an IRRITANT.** [Braun & Rudolph *Chem Ber* **67** 1770 *1934*, Reppe et al. *Justus Liebigs Ann Chem* **596** 127 *1955*, Gagnon et al. *Can J Chem* **34** 1662 *1956*, Copley et al. *J Am Chem Soc* **62** 228 *1940*, *Beilstein* **2** IV 1947.]

Agaricic acid [1-(*n*-hexadecyl)citric acid] *[666-99-9]* **M 416.6, m 142°(dec), $[\alpha]_D$ –9.8° (in NaOH), $pK_{Est(1)}$ ~2.7, $pK_{Est(2)}$ ~4.2, $pK_{Est(3)}$ ~5.5.** Crystallise the acid from EtOH. The *trihydrazide* has **m** 170°(dec) (from EtOH). [Brandänge et al. *Acta Chem Scand B* **31** 307 *1977*, *Beilstein* **3** I 186, **3** II 372, **3** III 1109, **3** IV 1284.]

Agmatine sulfate [5-guanidinopent-1-ylamine sulfate] *[2482-00-0]* **M 228.3, m 231°, $pK_{Est(1)}$ ~9.1, $pK_{Est(2)}$ ~13.0.** Crystallise the salt from aqueous MeOH. The *free base* has **m** 101.5-103°, the *gold chloride hydrochloride* crystallises from H_2O with **m** 223°(dec), and the *picrate* has **m** 236-238°. [Odo *J Chem Soc Jpn* **67** 132 *1946*, *Beilstein* **4** I 420, **4** II 703, **4** III 575, **4** IV 1291.]

Aldol (3-hydroxybutanal) *[107-89-1]* **M 88.1, b 80-81°/20mm, d^{16} 1.109.** An ethereal solution of aldol is washed with a saturated aqueous solution of $NaHCO_3$, then with water. The non-aqueous layer is dried with anhydrous $CaCl_2$ and distilled immediately before use. The fraction, **b** 80-81°/20mm, is collected as a thick liquid which decomposes at 85°/atm. It is a sedative and a hypnotic, but is used in perfumery. [Mason et al. *J Am Chem Soc* **76** 2255 *1954*]. [*Beilstein* **1** H 824, **1** I 419, **1** II 868, **1** III 3195, **1** IV 3984.]

Aleuritic acid [*RS-erythro*-9,10,16-trihydroxyhexadecanoic acid] *[533-87-9]* **M 304.4, m 100-101°, pK_{Est} ~4.9.** Crystallise this *RS*-acid from aqueous EtOH. It is soluble in MeOH, and forms a less soluble crystalline sodium salt. The *methyl ester* **m** 72-73°, **b** 235°/0.2mm, is best prepared by reaction with diazomethane and forms fine feathery needles; it is soluble in MeOH, EtOH, $CHCl_3$, Me_2CO, slightly soluble in $*C_6H_6$ and insoluble in petroleum ether. The *ethyl ester [6003-09-4]* **m** 59°, crystallises in needles from EtOH. The *hydrazide [6003-10-7]* crystallises from EtOH and has **m** 139-140°.
The *RS-acid* has been isolated from Shellac although it has two asymmetric carbon atoms, and possibly contains the *RS-erythro* or *RS-cis form* [Gidvani *J Chem Soc* 306 *1944*, Sengupta & Bose *J Sci Ind Res* (India) **11B** 458 *1952*]. A stereoisomer have been synthesised [Hunsdieker *Chem Ber* **76** 142 *1943*, Hunsdieker *Chem Ber* **77** 185 *1944*]. [*Beilstein* **3** III 901.]

***n*-Alkylammonium chloride *n*=2,4,6**. Recrystallise them from EtOH or an EtOH/Et_2O mixture. [Hashimoto & Thomas *J Am Chem Soc* **107** 4655 *1985,* Chu & Thomas *J Am Chem Soc* **108** 6270 *1986*.]

***n*-Alkyltrimethylammonium bromide *n*=10,12,16**. Recrystallise them from an EtOH/Et_2O mixture. [Hashimoto & Thomas *J Am Chem Soc* **107** 4655 *1985*.]

Allene (propadiene) *[463-49-0]* **M 40.1, m –146°, b –32°**. Freeze allene in liquid nitrogen, evacuate, then thaw out. This cycle is repeated several times, then the allene is frozen in a methylcyclohexane/liquid nitrogen bath and pumped for some time. It has also been purified by HPLC. [Cripps & Kiefer *Org Synth* **42** 12 *1962*,

Beilstein **1** IV 966.]

***neo*-Alloocimene (allocimene B, *tc*-2,6-dimethyl-2,4,6-octatriene)** *[7216-56-0; cis/trans mixture 673-84-7; trans/trans 3016-19-1]* **M 136.2, b 80°/13mm, 196-198°/atm, d $_4^{20}$ 0.8161, n $_D^{20}$ 1.5437.** Fractionally distil allocimene through an efficient column and repeatedly distil it at 15mm through a long column of glass helices, with a final distillation from sodium under nitrogen. It should be stabilised with *ca* 0.1% of hydroquinone. Its UV has λ_{max} nm(ε $M^{-1}cm^{-1}$) at 290 (32 500), 279 (41,900) and 278 (42,870). [Alder et al. *Justus Liebigs Ann Chem* **609** 1 *1957*, O'Connor & Goldblatt *Anal Chem* **26** 1726 *1954*, *Beilstein* **1** IV 1106.]

Allyl acetate *[591-87-7]* **M 100.1, b 103°, d $_4^{20}$ 0.928, n $_D^{17}$ 1.4004, n $_D^{20}$ 1.4040.** The ester is freed from peroxides by standing with crystalline ferrous ammonium sulfate, then washed with 5% $NaHCO_3$, followed by saturated $CaCl_2$ solution. Dry it with Na_2SO_4 and fractionally distil it in an all-glass apparatus. **FLAMMABLE LIQUID.** [*Beilstein* **2** H 136, **2** IV 180.]

Allylacetic acid (pent-4-enoic acid) *[591-80-0]* **M 100.1, m –22.5°, b 83-84°/12mm, 90°/15mm, 187-189°/~760mm, d $_4^{20}$ 0.9877, n $_D^{20}$ 1.4280, pK^{25} 4.68.** Distil the acid through an efficient column (allyl alcohol has **b** 95-97°). It is characterised as the S-*benzylisothiouronium salt* **m** 155-158° (from 96% EtOH, or aqueous EtOH) [Friediger & Pedersen *Acta Chem Scand* **9** 1425 *1955*], and the *4-bromophenacyl ester* has **m** 59.5-60.5° (from 90% EtOH). Its solubility at 18° in solvents is: pyridine (57%), AcOH (7.3%), MeOH (5.4%), Me_2CO (3.2%), MeOAc (2.8%), EtOH (5.4%), H_2O (1.8%), PrOH (1.6%), isoPrOH (0.27%). [Brown & Berkowski *J Am Chem Soc* **74** 1894 *1952*, *Beilstein* **2** IV 1542.]

Allyl alcohol *[107-18-6]* **M 58.1, b 98°, d $_4^{20}$ 0.857, n $_D^{20}$ 1.4134.** It can be dried with K_2CO_3 or $CaSO_4$, or by azeotropic distillation with *benzene followed by distillation under nitrogen. It is difficult to obtain it free of peroxide. It has also been refluxed with magnesium and fractionally distilled [Hands & Norman *Ind Chem* **21** 307 *1945*]. [*Beilstein* **1** IV 2079.]

Allylamine *[107-11-9]* **M 57.1, b 52.9°, d $_4^{20}$ 0.761, n $_D^{20}$ 1.42051, pK^{25} 9.49.** Purify allylamine by fractional distillation from calcium chloride. It causes sneezing and tears. [*Beilstein* **4** IV 1057.]

Allyl bromide *[106-95-6]* **M 121, b 70°, d $_4^{20}$ 1.398, n $_D^{20}$ 1.46924.** Wash the bromide with $NaHCO_3$ solution then distilled water, dry ($CaCl_2$ or $MgSO_4$), and fractionally distil. Protect it from strong light. [*Beilstein* **1** IV 754.] **LACHRYMATORY, HIGHLY TOXIC and FLAMMABLE.**

Allyl butyl ether *[3739-64-8]* **M 114.2, b 64-65°/120mm, 117.8-118°/763mm, d $_4^{20}$ 1.4057, n $_D^{20}$ 0.7829.** Check the IR for the presence of OH str vibrations; if so then wash it well with H_2O, dry it with $CaCl_2$ and distil it through a good fractionating column. **The liquid is an irritant.** [Watanabe et al. *J Org Chem* **23** 1666 *1958*, Schueler & Hanna *J Am Chem Soc* **73** 3528 *1951*, *Beilstein* **1** IV 2084.]

Allyl chloride *[107-05-1]* **M 76.5, b 45.1°, d $_4^{20}$ 0.939, n $_D^{20}$ 1.4130.** Likely impurities include 2-chloropropene, propyl chloride, *iso*-propyl chloride, 3,3-dichloropropane, 1,2-dichloropropane and 1,3-dichloropropane. Purify it by washing with conc HCl, then with Na_2CO_3 solution, dry it with $CaCl_2$, and distil it through an efficient column [Oae & Vanderwerf *J Am Chem Soc* **75** 2724 *1953*]. [*Beilstein* **1** IV 738.] **LACHRYMATORY, TOXIC.**

Allyl chloroformate *[2937-50-0]* **M 120.5, b 56°/97mm, 109-110°/atm, d $_4^{20}$ 1.14, n $_D^{20}$ 1.4223.** Wash the chloroformate several times with cold H_2O to remove alcohol and HCl and dry it over $CaCl_2$. It is **important** to dry well before distilling *in vacuo*. Note that the receiver should be cooled in ice to avoid loss of distillate into the trap and vacuum pump. The liquid is **highly TOXIC and flammable.** [Fierz-David & Müller *J Chem Soc* **125** 26 *1924*, Strain et al. *J Am Chem Soc* **72** 1254 *1950*, *Beilstein* **3** IV 29.]

Allyl cyanide (3-butene nitrile) *[109-75-1]* **M 67.1, b –19.6°/1.0mm, 2.9°/5mm, 14.1°/5mm, 26.6°/20mm, 48.8°/60mm, 60.2°/100mm, 98°/400mm, 119°/760mm, d $_4^{20}$ 0.8341, n $_D^{20}$ 1.406.** The nitrile should be redistilled at atmospheric pressure, then distilled under a vacuum to remove the final traces of HCN from the

residue. Note that the residue from the first distillation may be difficult to remove from the flask and should be treated with conc HNO_3 then H_2O and finally hot EtOH **(CARE)**. Allyl cyanide has an onion-like odour and is stable to heat. It forms a complex with $AlCl_3$ (2:2) **m** 41°, and (3:2) **m** 120°. **All operations should be done in an efficient fume hood as the liquid is flammable, may contain cyanide and is HIGHLY TOXIC.** [Supniewski et al. *Org Synth* Coll Vol **I** 46 *1941*, *Beilstein* **2** IV 1491.]

Allyl disulfide (diallyl disulfide) *[2179-57-9]* **M 146.3, b 58-59°/5mm, 79-81°/20mm, 138-139°/atm, d_4^{20} 1.01, n_D^{20} 1.541.** Purify the disulfide by fractional distillation until the molar refractivity is in uniformly good agreement with the calculated value [Small et al. *J Am Chem Soc* **69** 1710 *1947*]. It has also been purified by gas chromatography [retention times: Carson & Wong *J Org Chem* **24** 175 *1959*, UV: Koch *J Chem Soc* 395 *1949*]. It is present in garlic. [*Beilstein* **1** IV 2098.]

Allyl iodide (3-iodopropene) *[556-56-9]* **M 167.7, b 103°/760mm, d^{12} 1.848.** Purify allyl iodide in a dark room by washing with aqueous Na_2SO_3 to remove free iodine, then dry with $MgSO_4$ and distil at 43°/90 mm or at atmospheric pressure to give a very pale yellow liquid. (This material, dissolved in hexane, can be stored in a light-protected tight container at –5° for up to three months before free iodine can be detected, by its colour in the solution.) Store it away from light. [Sibbett & Noyes *J Am Chem Soc* **75** 761 *1953*, *Beilstein* **1** H 202, **1** I 84, **1** II 172, **1** III 714, **1** IV 761.]

Allylisocyanate *[1476-23-9]* **M 83.1, b 84°/atm, 87-89°/atm, d_4^{20} 0.94, n_D^{20} 1.417.** Purify it as for allylisothiocyanate below and it is **TOXIC**. [*Beilstein* **4** IV 1081.]

Allylisothiocyanate *[57-06-7]* **M 99.2, m –80°, b 84-85°/80mm, 150°/760mm, 151°/atm, d_4^{20} 1.017, n_D^{20} 1.5268.** Fractionate the isothiocyanate using an efficient column, preferably in a vacuum. It is a yellow **pungent, irritating and TOXIC (suspected CARCINOGEN) liquid.** Store it in a sealed tube under N_2. The *N'-benzylthiourea* derivative has **m** 94.5° (from aqueous EtOH) [Weller et al. *J Am Chem Soc* **74** 1104 *1952*]. [*Beilstein* **4** IV 1081.]

***N*-Allylthiourea (thiosinamine)** *[109-57-9]* **M 116.2, m 70-73°, 78°.** Recrystallise it from H_2O. It is soluble in 30 parts of cold H_2O, and it is soluble in EtOH but insoluble in $*C_6H_6$. It has also been recrystallised from acetone, EtOH or ethyl acetate, after decolorising with charcoal. The white crystals have a bitter taste with a slight garlic odour and are **TOXIC**. An unstable crystalline form is obtained by recrystallising from the melt. [McCrone et al. *Anal Chem* **21** 421 *1949*, *Beilstein* **4** IV 1072.]

***N*-Allylurea** *[557-11-9]* **M 100.1, m 85°.** It crystallises from EtOH, EtOH/ether, EtOH/chloroform or EtOH/toluene. [*Beilstein* **4** IV 1070.]

Aminoacetaldehyde dimethyl acetal (2,2-dimethoxyethylamine) *[22483-09-6]* **M 105.1, m <–78°, b 139.5°/768mm, 137-139°/atm, d_4^{20} 0.9676 n_D^{20} 1.4144.** Dry the acetal over KOH pellets and distil it through a 30cm vacuum jacketed Vigreux column. [Lawson *J Am Chem Soc* **75** 3398 *1953*, Erickson et al. *J Am Chem Soc* **77** 6640 *1955*, *Beilstein* **4** IV 1918.]

Aminoacetonitrile bisulfate *[151-63-3]* **M 154.1, m 125°(dec), pK^{25} 5.34 (NH_2).** Recrystallise the hydrogensulfate (1:1) from EtOH/Et_2O (hygroscopic leaflets). The ***Sulfate* (2:1)** [5466-22-8] crystallises as flat prisms from H_2O/EtOH with **m** 166°(dec). [Stephen *J Chem Soc* 871 *1931*, Anslow & King *J Chem Soc* 2465 *1929*, *Beilstein* **4** III 1120.]

Aminoacetonitrile hydrochloride *[6011-14-9]* **M 92.5, m 166-167°, 172-174°, pK^{25} 5.24 (NH_2).** The salt recrystallises from dilute EtOH as *hygroscopic* leaflets. It is best to crystallise it from absolute EtOH/Et_2O (1:1) and then recrystallise it from absolute EtOH. The melting point recorded ranges from 144 to 174°. The *free base* has **b** 58°/15mm with partial decomposition. [Klages *J Prakt Chem* **[2] 65** 189 *1902*, Mange *J Am Chem Soc* **56** 2197 *1934*, Goldberg & Kelly *J Chem Soc* 1371 *1947*, *Beilstein* **4** H 344, **4** I 468, **4** II 783, **4** III 1120, **4** IV 2363.]

2-Amino-1-butanol *[RS(±) 96-20-8, R(–) 5856-63-3, S(+) 5856-62-2]* **M 89.1, m ~ -2°, b 78-80°/10mm and 179-183°/atm for (±), 172-174°/atm for (+) or (–), pK^{0} 10.353, pK^{20} 9.672, pK^{60} 8.555.** They are purified by shaking with solid NaOH, filtering and distilling through a short column. The *oxalate salt* of the racemate has **m** 176°. They are strong bases and should be stored under N_2 in the absence of CO_2. The *enantiomers* have $[\alpha]_D^{20}$ +12.5° and –12.5° (c 2, EtOH). [Johnson & Degering *J Org Chem* **8** 7 *1943*, Nagao et al. *J Org Chem* **51** 2392 *1986*, Santaniello et al. *J Chem Soc, Perkin Trans 1* 919 *1985*, *Beilstein* **4** H 291, **4** IV 1705.]

2-Aminoethanol (ethanolamine) *[141-43-5]* **M 61.1, f 10.5°, b 72-73°/12mm, 171.1°/760mm, d_4^{20} 1.012, n_D^{20} 1.14539, pK^{25} 9.51.** It decomposes slightly when distilled at atmospheric pressure, with the formation of conducting impurities. Fractional distillation at about 12mm pressure is most satisfactory. After distillation, 2-aminoethanol is further purified by repeated washing with ether and crystallising from EtOH (at low temperature). After fractional distillation in the absence of CO_2, it is twice crystallised by cooling, followed again by distillation. It is *hygroscopic*, and absorbs CO_2 from the atmosphere. [Reitmeier et al. *J Am Chem Soc* **62** 1943 *1940*.] It can be dried by azeotropic distillation with dry *benzene. [*Beilstein* **4** IV 1406.]

2-Aminoethanol hydrochloride *[2002-24-6]* **M 97.6, m 75-77°.** Recrystallise the salt from EtOH. It is deliquescent; store it dry. [*Beilstein* **4** IV 1406.]

2-Aminoethyl hydrogen sulfate (sulfuric acid mono-2-aminoethyl ester) *[926-39-6]* **M 141.1, m 285-287° (chars at 275°).** Crystallise the sulfate ester from water or dissolve it in water and add EtOH. Wash this with Et_2O and dry it *in vacuo*. [*Beilstein* **4** III 1414.]

S-(2-Aminoethyl)isothiouronium bromide hydrobromide *[56-10-0]* **M 281.0, m 194-195°**. Crystallise the salt from absolute EtOH/ethyl acetate or MeOH. Store dry as it is *hygroscopic* in a humid atmosphere. It is a radioprotective agent. When refluxed in EtOH for 16 hours or H_2O for 30 minutes, it decomposes to *2-amino-4(5H)-thiazoline hydrobromide* which on recrystallisation from isoPrOH/EtOAc has **m** 175-176° [Doherty et al. *J Am Chem Soc* **79** 5667 *1957*].

(2-Aminoethyl)trimethylammonium chloride hydrochloride (chloramine chloride hydrochloride) *[3399-67-5]* **M 175.1, m 268°(dec).** Crystallise the hydrochloride from EtOH. The material is very soluble in H_2O. [*Beilstein* **4** II 690.]

Aminomalononitrile toluene-4-sulfonate *[5098-14-6]* **M 253.4, m 168-170°, 172°(dec), pK_{Est} ~ 1.3.** It forms colourless crystals on recrystallisation from MeCN (1.8g in 100mL) using activated charcoal. Wash the crystals with dry Et_2O and dry them at 25°/1mm. Recovery is ~80%. [Ferris et al. *Org Synth* Coll Vol **V** 32 *1973*.]

(±)-2-Amino-4-methylhexane (Forthane, 1,3-dimethylpentylamine) *[105-41-9]* **M 115.2, b 131-133°/atm, 130-135°/atm, 135-136°/atm, d_4^{20} 0.760, n_D^{15} 1.4160, n_D^{24} 1.4160, pK^{25} 10.54.** This strong base is obtained by catalytic hydrogenation of 4-methylhexan-2-one oxime (57g) in EtOH (50ml) with Raney Ni (6g) in a bomb at 75-80° and 1000psi of H_2, cool, filter off the catalyst, acidify with HCl, and evaporate to dryness. Basify the residue with aqueous NaOH, extract it with Et_2O, dry the extract ($MgSO_4$), filter, evaporate, and distil to give the base in 75-80% yield. It forms a *sulfate salt* **m 215-220°(dec)**, and it readily forms a *carbonate salt*, hence it should be stored in the absence of CO_2. It is physiologically active as an opium pressor and is adrenergic. [Rohrmann & Shonle *J Am Chem Soc* **66** 1516 *1944*, Chiang *J Clin Chem Soc* **18** 65 *1951*, USP to E. Lilly 2350318 (1943) *Chem Abstr* **39** 1510 *1945*, USP 2386273 (1943) *Chem Abstr* **40** 598 *1946*, *Beilstein* **4** III 378, **4** IV 747.]

2-Amino-2-methyl-1,3-propanediol *[115-69-5]* **M 105.1, m 111°, b 151-152°/10mm, pK^{25} 8.80.** Crystallise the diol three times from MeOH, dry in a stream of dry N_2 at room temperature, then in a vacuum oven at 55°. Store it over $CaCl_2$ [Hetzer & Bates *J Phys Chem* **66** 308 *1962*]. [*Beilstein* **4** IV 1881.]

2-Amino-2-methyl-1-propanol (β-aminoisobutanol) *[124-68-5]* **M 89.4, m 24°, 31°, b 67°/10mm, 164-166°/760mm, d_4^{20} 0.935, n_D^{20} 1.45, pK^{25} 9.71.** Purify it by distilling and fractional freezing. The *hydrochloride* [3207-12-3] has **m** 204°-206°. [*Beilstein* **4** III 783, **4** IV 1740.]

***n*-Amyl acetate (*n*-pentyl acetate)** *[628-63-7]* **M 130.2, b 149.2°, d_4^{20} 0.876, n_D^{20} 1.40228.** Shake the ester with saturated $NaHCO_3$ solution until neutral, washed it with water, dry with $MgSO_4$ and distil it. The ester has also been purified by repeated fractional distillation through an efficient column or spinning band column. [Timmermann & Hennant-Roland *J Chim Phys* **52** 223 *1955*, Mumford & Phillips *J Chem Soc* 75 *1950*, ^{1}H NMR: Crawford & Foster *Can J Phys* **34** 653 *1956*, *Beilstein* **2** IV 152.]

***n*-Amyl alcohol (1-pentanol)** *[71-41-0]* **M 88.2, b 138.1°, d^{15} 0.818, n_D^{20} 1.4100.** Dry 1-pentanol with anhydrous K_2CO_3 or $CaSO_4$, filter and fractionally distil it. It has also been treated with 1-2% of sodium and heated at reflux for 15 hours to remove water and chlorides. Traces of water can be removed from the near-dry alcohol by refluxing it with a small amount of sodium in the presence of 2-3% *n*-amyl phthalate or succinate followed by distillation (see *ethanol*).
Small amounts of amyl alcohol have been purified by esterifying with *p*-hydroxybenzoic acid, recrystallising the ester from CS_2, saponifying with ethanolic-KOH, drying with $CaSO_4$ and fractionally distilling [Olivier *Rec Trav Chim Pays Bas* **55** 1027 *1936*]. [*Beilstein* **1** IV 1640.]

***tert*-Amyl alcohol (2-methyl-2-butanol)** *[75-85-4]* **M 88.2, m –12°, b 102.3°, d^{15} 0.8135, n_D^{20} 1.4058.** Reflux it with K_2CO_3, CaH_2, CaO or sodium, then fractionally distil. The near-dry alcohol is further dried by refluxing with Mg activated with iodine, as described for *ethanol*. Further purification is possible using fractional crystallisation and zone refining at <–10° or preparative gas chromatography. [*Beilstein* **1** IV 1668.]

***n*-Amylamine [1-aminopentane]** *[110-58-7]* **M 87.2, b 105°, d_4^{20} 0.752, pK^{25} 10.63.** Dry it by prolonged shaking with NaOH pellets, then distilling. Store it in a CO_2-free atmosphere. [*Beilstein* **4** IV 674.]

***n*-Amyl bromide (*n*-pentylbromide)** *[110-53-2]* **M 151.1, b 129.7°, d_4^{20} 1.218, n_D^{20} 1.445.** Wash the bromide with conc H_2SO_4, then water, 10% Na_2CO_3 solution, again with water, dry with $CaCl_2$ or K_2CO_3, and fractionally distil it just before use. [*Beilstein* **1** IV 312.]

***n*-Amyl chloride (1-chloropentane)** *[543-59-9]* **M 106.6, b 107.8°, d_4^{20} 0.882, n_D^{20} 1.41177.** Purify as for *sec*-amyl chloride. [*Beilstein* **1** IV 309.]

***sec*-Amyl chloride (1-chloro-2-methylbutane)** *[616-13-7]* **M 106.6, b 52.2°/150mm, 96-97° (100°)/760mm, d_4^{20} 0.886, n_D^{20} 1.412.** Purify the chloride by stirring vigorously with 95% H_2SO_4, replacing the acid when it becomes coloured, until the layer remains colourless after 12 hours stirring. The amyl chloride is then washed with saturated Na_2CO_3 solution, then distilled water, and dried with anhydrous $MgSO_4$, followed by filtration, and distillation through a 10-in Vigreux column. *Alternatively*, a stream of oxygen containing 5% ozone is passed through the amyl chloride for three times as long as it takes to cause the first coloration of starch iodide paper by the exit gas. The liquid is washed with $NaHCO_3$ solution to hydrolyse the ozonides and remove organic acids prior to drying and fractional distillation [Chien & Willard *J Am Chem Soc* **75** 6160 *1953*]. The *S*(+)-*enantiomer* has **b** 50-51°/140mm, 100°/760, mm, $[\alpha]_D^{20}$ +1.64° (neat) [Brown et al. *J Am Chem Soc* **62** 3437 *1940*]. [*Beilstein* **1** H 134, **1** I 46, **1** III 356, **1** IV 326.]

***tert*-Amyl chloride (2-chloro-2-methylbutane)** *[594-36-5]* **M 106.6, b 86°, d_4^{20} 0.866.** Methods of purification commonly used for other alkyl chlorides lead to decomposition. Unsaturated contaminants are removed by chlorination with a small amount of chlorine in bright light, followed by distillation [Chien & Willard *J Am Chem Soc* **75** 6160 *1953*]. [*Beilstein* **1** H 134, **1** I 46, **1** II 100, **1** III 357, **1** IV 324.]

Amylene (β-*iso*-amylene, 2-methyl-2-butene) *[513-35-9]* **M 70.1, b 37-38°/~760mm, d_4^{20} 0.663, n_D^{20} 1.387.** Distil amylene and collect the distillate at low temperature. It has also been distilled from sodium. **FLAMMABLE.** It is available in steel cylinders and has a short shelf life. [*Beilstein* **1** H 211, **1** I 87, **1** II 187, **1** III 788, **1** IV 820.]

Amyl ether (dipentyl ether) *[693-65-2]* **M 158.3, b 186.8°, d_4^{20} 0.785, n_D^{20} 1.41195.** Repeatedly reflux amyl ether over sodium and distil it. [*Beilstein* **1** IV 1643.]

Arachidic (eicosanoic C_{20}) acid *[506-30-9]* **M 312.5, m 77°, pK_{Est} ~5.0.** Crystallise the C_{20} acid from absolute EtOH. [*Beilstein* **2** IV 1276.]

Arachidic alcohol (1-eicosanol C_{20}) *[629-96-9]* **M 298.6, m 65.5° (71°), b 200°/3mm.** Crystallise the C_{20} alcohol from *benzene or *benzene/petroleum ether. [*Beilstein* **1** IV 1900.]

Azelaic acid (1,9-nonanedioic acid, heptane-1,7-dicarboxylic acid) *[123-99-9]* **M 188.2, m 105-106°, b 225°/10mm, 256°/50mm, pK_1^{25} 4.53, pK_2^{25} 5.33.** Recrystallise it from H_2O (charcoal) or thiophene-free *benzene. The acid can be dried by azeotropic distillation with toluene, the residual toluene solution is then cooled and filtered, and the precipitate is dried in a vacuum oven. It has been purified by zone refining or by sublimation onto a cold finger at 10^{-3}torr. It distils above 360° with partial formation of the anhydride. The *dimethyl ester* has **m** –3.9° and **b** 140°/8mm. [Hill & McEwen *Org Synth* Coll Vol **II** 53 *1943*, *Beilstein* **2** IV 2055.]

2,2'-Azobis(isobutyronitrile) (α,α'bis-azo-[2-methylpropionitrile], AIBN) *[78-61-1]* **M 164.2, m 102.1-103.2°, 103°, 103-104°.** Crystallise the nitrile from Et_2O, Me_2CO, $CHCl_3$, aqueous EtOH or MeOH. It has also been crystallised from absolute EtOH below 40° in subdued light. Dry it under vacuum at room temperature over P_2O_5 and store it under vacuum in the dark at <–10° until required. Also crystallise it from $CHCl_3$ solution by addition of petroleum ether (b <40°). It is a radical inhibitor. [Askham et al. *J Am Chem Soc* **107** 7423 *1985*, Ennis et al. *J Chem Soc, Dalton Trans* 2485 *1986*, Inoue & Anson *J Phys Chem* **91** 1519 *1987,* Tanner *J Org Chem* **52** 2142 *1987*.] It is prepared by the oxidation of *N,N'-bis(isobutyronitrile)hydrazine* by addition of the solid hydrazine (4.15g, 0.025mole) to a solution of HNO_3 (100%, 6.5g, 0.1mol) and Ac_2O (30ml) (0.1mole) which are previously mixed at -30°. As the temperature rises to –20° the solid begins to dissolve and the colour of the solution turns to green, and dissolution is complete at ~5°. After stirring at 25° for 0.5 hours, the solution is poured onto cracked ice and H_2O (100ml), the product separates out, is filtered off, washed free from acid with H_2O. The solid (m 95-100°) is dried *in vacuo,* recrystallised from 50% EtOH and from Et_2O to give pure *AIBN* (2.5g, 60%), m 105°. [Picard & Boivin *Can J Chem* **29** 223 *1951*.] *Alternatively*, the *hydrazine* (0.989g, 6mmol) is added to a solution of glacial acetic acid (40ml) and concentrated H_2SO_4 (3ml) at ~0°, followed by addition of $NaMnO_2.3H_2O$ (1.8g) in H_2O (25ml). MnO_2 separates immediately, excess of $NaMnO_2$ and MnO_2 are reduced with aqueous sodium bisulfite and poured into H_2O. AIBN separates, is filtered off, washed with H_2O, dried in a vacuum desiccator and recrystallised as above to give pure *azo* compound (0.61g, 63%). [Overberger & Lebovitz *J Am Chem Soc* **76** 2722 *1954*, Overberger et al. *J Am Chem Soc* **71** 2661 *1949*.] [*Beilstein* **4** H 563, **4** I 566, **4** III 1750, **4** IV 3377.]

Azomethane (dimethyldiimide) *[503-28-6]* **M 58.1, m –78°, b 1.5°, d_0^{15} 0.981, n_D^{19} 1.3933.** Purify azomethane by distillation in a vacuum line and store it in the dark at –80°. It is soluble in EtOH, Et_2O and EtOAc. It can be **EXPLOSIVE.** [*Beilstein* **4** H 562, **4** I 566, **4** II 966, **4** III 1747, **4** IV 3366.]

B.A.L. (British Anti-Lewesite) see 2,3-dimercapto-1-propanol.

Batyl alcohol (*rac*-3-[1-octadecyloxy]-1,2-propanediol) *[544-62-7]* **M 344.6, m 70.5-71°.** Batyl alcohol crystallises from aqueous Me_2CO, EtOH or petroleum ether (b 40-60°). [Taguchi & Armarego *Med Res Rev* **18** pp43-88 *1998*, *Beilstein* **1** IV 2758.]

Behenoyl chloride (docosanoyl chloride) *[21132-76-3]* **M 359.0, m 40°.** If the IR shows OH bands, then it should be dissolved in oxalyl chloride in *C_6H_6 solution and warmed at 35° for 24 hours in the absence of moisture, evaporated and distilled in a vacuum of 10^{-5}mm. It is soluble in *C_6H_6 and Et_2O. It is moisture sensitive and is **LACHRYMATORY**. [Francis et al. *J Chem Soc* 1001 *1937*, Levene & Taylor *J Biol Chem* **59** 905 *1924*, *Beilstein* **2** III 1076.]

Biacetyl (butan-2,3-dione) *[431-03-8]* **M 86.1, b 88°, d_4^{20} 0.981, $n^{18.5}$ 1.3933.** Dry biacetyl over anhydrous $CaSO_4$, $CaCl_2$ or $MgSO_4$, then distil it in a vacuum under nitrogen, taking the middle fraction and storing it at Dry-Ice temperature in the dark (to prevent polymerisation). [*Beilstein* **1** IV 3644.]

Biguanide *[56-03-1]* **M 101.1, m 130° pK_1^{25} 3.1, pK_2^{25} 12.8.** Crystallise biguanide from EtOH. It gives a red Cu derivative, and it forms salts with many metals. The *monohydrochloride* has **m** 235° [38664-03-8] and the *dihydrochloride* forms plates with **m** 248° (213-214°, also reported) [25836-74-2]. [*Beilstein* **3** H 93, **3** I 44, **3** II 76, **3** III 171, **3** IV 162.]

Bis-acrylamide (*N,N'*-methylene bisacrylamide) *[110-26-9]* **M 154.2, m >300°.** Recrystallise the amide from MeOH (100g dissolved in 500ml boiling MeOH) and filter without suction in a warmed funnel. Allow to stand at room temperature and then at –15°C overnight. The crystals are collected with suction in a cooled funnel and washed with cold MeOH. The crystals are air-dried in a warm oven. [*Beilstein* **2** IV 1472.] **VERY TOXIC (neurotoxic).**

Bis(β-chloroethyl)amine hydrochloride *[821-48-7]* **M 178.5, m 214-215°, 216-217°, pK_{Est} ~5.8 (free base).** Crystallise the salt from Me_2CO or MeOH/Et_2O. The *picrate* has **m** 112-113° (from EtOH or Me_2CO). [Mann *J Chem Soc* 464 *1934*, Ward *J Am Chem Soc* **57** 915 *1935*, *Beilstein* **4** III 238.]

Bis(β-chloroethyl) ether *[111-44-4]* **M 143.0, b 94°/33mm, 178.8°, d_4^{20} 1.220, n_D^{20} 1.45750.** Wash the ether with conc H_2SO_4, then Na_2CO_3 solution, dry with anhydrous Na_2CO_3, and finally pass it through a 50cm column of activated alumina before distillation. *Alternatively*, wash it with 10% ferrous sulfate solution to remove peroxides, then H_2O, dry with $CaSO_4$, and distil it in a vacuum. Add 0.2% of catechol to stabilise it. [*Beilstein* **1** IV 1375, Kamm & Waldo *J Am Chem Soc* **43** 2223 *1921*.] **VERY TOXIC**.

2,2'-Bis[di-(carboxymethyl)-amino]diethyl ether, $(HOOCCH_2)_2NCH_2CH_2OCH_2CH_2N-(CH_2COOH)_2$ *[923-73-9]* **M 336.3, pK_1^{20} 1.8, pK_2^{20} 2.76, pK_3^{20} 8.84, K_4^{20} 9.47.** Crystallise it from EtOH.

Bis(2-ethylhexyl) sebacate ['dioctyl' sebacate, di(2-ethylhexyl) 1,8-octanedicarboxylate] *[122-62-3]* **M 426.7, b 212°/1mm, d_4^{25} 1.914, n_D^{20} 1.4496.** If it is acidic due to hydrolysis (effervesces with $NaHCO_3$), then purify by dissolving in Et_2O, shaking with aqueous Na_2CO_3, dry (Na_2SO_4), filter, evaporate and distil the residue at a high vacuum. Note that 2-ethylhexan-1-ol has **b 184-185°/760mm** with estimated **b ~40-50°/1mm** (see Figure 1, and Table 2A, Chapter 1) and will distil at a much lower temperature than the ester. Otherwise it should be distilled through a short column under high vacuum and the higher boiling fraction is redistilled. This vacuum pump oil can be prepared by esterifying decanedioic acid with 2-ethylhexanoic acid by Fischer-Speier's method (Fiscer & Speier *Chem Ber* **28** 1150 *1895*], whereby dry HCl gas is bubbled through the alcohol until its weight is increased by ~10%, the acid is added, the mixture is heated at 100° until esterification is complete (~2-3 hours), and purified as above. [Bruno USPat 2628249 *1953*, GBPat 747260 *1956*, *Beilstein* **2** IV 2803.]

***N,N*-Bis(2-hydroxyethyl)-2-aminoethanesulfonic acid (BES)** *[10191-18-1]* **M 213.3, m 150-155°, pK^{25} 7.17.** Crystallise BES from aqueous EtOH. [*Beilstein* **4** IV 3290.]

Bis(2-hydroxyethyl)amino-*tris*-(hydroxymethyl)methane (BIS-TRIS) *[6976-37-0]* **M 209.2, m 89°, 104°, pK^{20} 6.46.** Crystallise BIS-TRIS from hot 1-butanol and dry it in a vacuum at 25°.

***N,N*-Bis(2-hydroxyethyl)glycine** (BICINE) See in "Amino Acids and Peptides", Chapter 7.

Bis(2-mercaptoethyl)sulfone (BMS) *[145626-87-5]* **M 186.3, m 57-58°, pK_1^{25} 7.9, pK_2^{25} 9.0**. BMS recrystallises from hexane as white fluffy crystals. Large amounts are best recrystallised from de-oxygenated H_2O (charcoal). It is a good alternative reducing agent to dithiothreitol. Its IR (film) has ν_{max} □□ 2995, 2657, 1306, 1248, 1124 and 729 cm^{-1}. The synthetic intermediate *thioacetate* has **m** 82-83° (white crystals from CCl_4). The *disulfide* is purified by flash chromatography on SiO_2 and elution with 50% EtOAc/hexane, recrystallised from hexane, and has **m** 137-139°. [Lamoureux & Whitesides *J Org Chem* **58** 633 *1993*, *Beilstein* **1** IV 2455.]

Bis(trichloromethyl) carbonate (triphosgene) *[32315-10-9]* **M 296.8, m 79-83°, 81-83°, b 203-206°(slight dec).** It is a good solid substitute for phosgene (using a third mol per mol). Crystallise it from petroleum ether (b 60-80°), wash it with anhydrous cold Et_2O, de-gas it at 200mm then dry at 0.1mm (over H_2SO_4). It has IR with ν_{max} at 900 and 1900 cm^{-1}. It is a **lachrymator**, is **TOXIC**, and should be handled with gloves and in an efficient fume hood. [Hales et al. *J Chem Soc* 620 *1957*, Eckert & Forster *Angew Chem, Int Ed Engl* **26** 894 *1987*, *Aldrichimica Acta* **21** 47 *1988*, *Beilstein* **3** H 17, **3** I 8, **3** II 16, **3** III 36, **3** IV 33.]

Bistrifluoroacetamide (BTFA) *[407-24-9]* **M 209.1, m 85°, b 135-136°/744mm, 141°/760mm.** A major impurity is trifluoroacetamide. Add trifluoroacetic anhydride to BTFA, reflux for 2 hours and fractionate using a Vigreux column at atmospheric pressure. [Donike *J Chromatogr* **78** 273 *1973*, *Beilstein* **2** IV 471.]

Biuret (allophanic acid amide, carbamoylurea) *[108-19-0]* **M 103.1, sinters at 218° and chars at 270°, pK_1^{25} –0.88, pK_2^{25} >4.** Crystallise biuret from EtOH. [*Beilstein* **3** IV 141.]

***N*-Bromoacetamide** *[79-15-2]* **M 138.0, m 102-105°, 107-109°, 108°(anhydrous).** A possible contaminant is CH_3CONBr_2. Recrystallise it from $CHCl_3$/hexane (1:1, seed if necessary) or water and dry over $CaCl_2$. It is a brominating agent. [Oliveto & Gerold *Org Synth* Coll Vol **IV** 104 *1963*.] *Alternatively*, dissolve it in the minimum volume of warm H_2O (60°), then cool in an ice bath, collect the crystals and dry them in an anhydrous atmosphere, dissolve in Et_2O, chill and evaporate till crystallisation. Dry the crystals *in vacuo* at 25°, then at 45° (**m** 108°). Crystallise from $CHCl_3$ (**m** 103°). Estimate the available Br iodometrically [Buckles et al. *J Org Chem* **23** 483 *1958*]. [*Beilstein* **2** H 181, **2** I 82, **2** II 180, **2** III 406, **2** IV 417.]

Bromoacetic acid *[79-08-3]* **M 138.9, m 50°, b 118°/15mm, 208°/760mm, d^{25} 1.93, pK^{25} 2.92.** Crystallise bromoacetic acid from pet ether (b 40-60°). A diethyl ether solution of it is passed through an alumina column, and the ether is evaporated at room temperature under vacuum. It is best obtained by distillation from a Claisen (flask immersed in an oil bath) fitted with an insulated Vigreux column and the fraction **b** 108-110°/30mm is collected. It is light and moisture sensitive. [Natelson & Gottfried *Org Synth* Coll Vol **III** 381 *1955*, *Beilstein* **2** IV 526.] **LACHRYMATORY and is a skin IRRITANT**.

Bromoacetone *[598-31-2]* **M 137.0, b 31.5°/8mm, 63.5-64°/50mm, 137°/atm, d^{23} 1.643.** Stand bromoacetone over anhydrous $CaCO_3$, filter, distil it under low vacuum, and store it with $CaCO_3$ in the dark at 0°. [Levene *Org Synth* Coll Vol **II** 88 *1943*.] **Violently LACHRYMATORY and skin IRRITANT.**

2-Bromobutane *[78-76-2]* **M 137.0, b 91.2°, d_4^{20} 1.255, n_D^{20} 1.4367, n^{25} 1.4341.** Wash 2-bromobutane with conc HCl, water, 10% aqueous $NaHSO_3$, and then water. Dry it with $CaCl_2$, Na_2SO_4 or anhydrous K_2CO_3, and fractionally distil it through a 1m glass helices packed column. [*Beilstein* **1** IV 261.]

Bromoform *[75-25-2]* **M 252.8, m 8.1°, 55-56°/35mm, 149.6°/760mm, d^{15} 2.9038, d^{30} 2.86460, n^{15} 1.60053, n_D^{20} 1.5988.** The storage and stability of bromoform and chloroform are similar. Ethanol, added as a stabiliser, is removed by washing with H_2O or with saturated $CaCl_2$ solution, and the $CHBr_3$, after drying with $CaCl_2$ or K_2CO_3, is fractionally distilled. Prior to distillation, $CHBr_3$ has also been washed with conc H_2SO_4 until the acid layer is no longer coloured, then dilute NaOH or $NaHCO_3$, and H_2O. A further purification step is fractional crystallisation by partial freezing. [*Beilstein* **1** IV 82.]

(±)-2-Bromohexadecanoic acid (2-bromopalmitic acid) *[18263-25-7]* **M 335.3, m 51-53°, 52.3-52.5°, 53°, pK_{Est} ~3.2.** Recrystallise the acid from petroleum ether (b 60-80°, charcoal) and finally from EtOH. The *ethyl ester* has **b** 177-178°/2mm, d_{28}^{28} 1.0484, n_D^{20} 1.4560. [IR: Sweet & Estes *J Org Chem* **21** 1426 *1956*, *Beilstein* **2** IV 1184.]

6-Bromohexanoic acid (6-bromocaproic acid) *[4224-70-8]* **M 195.1, m 32-33°, 35°, 34-36°, b 129-130°/5mm.** It has been prepared by the oxidation of 6-bromohexanol with concentrated HNO_3 (sp. gr. 1.42, one hour for addition at 25-30°, stir at ~25° for 4 hours then at 100° for 45 minutes) [Degering & Boatright *J Am Chem Soc* **72** 5137]. It is made more conveniently by oxidation of cyclohexanone (174 g) with Caro's acid (using a mixture prepared from 919g of potassium persulfate for 10-15 minutes as in Barger et al. *J Chem Soc*

718 *1937*), and the crude lactones (200g) are treated with a cooled mixture of 48% HBr (1L) and concentrated H_2SO_4 (240ml). After standing at ~25° for 2 hours, then for 4 hours at 100°, the mixture is cooled, poured into H_2O, the organic layer is separated, the aqueous layer is saturated with $(NH_4)_2SO_4$, and is extracted with Et_2O. The combined organic layers and extracts are washed with saturated $(NH_4)_2SO_4$, dried (Mg_2SO_4), evaporated and distilled in a vacuum. [See Brown & Partridge *J Am Chem Soc* **66** 839 *1944*, Degering & Boatright *J AmChem Soc* **72** 5137 *1950*]. [*Beilstein* **2** II 287, **2** III 737, **2** IV 940.] When the acid is refluxed with $SOCl_2$ in the absence of moisture until all the HCl and SO_2 have evolved, then evaporated, and the residue is distilled in a vacuum, it provides **6-bromohexanoyl chloride** *[22809-37-6]* **M 213.5, b 130°/20mm, d ^{25} 1.395, n $^{20}_{D}$ 1.486** as an almost colourless oil which is typically reactive and corrosive like most acid chlorides. [Osmond *J Chem Soc* 3469 *1951*]. *6-Bromohexanamide* has **m 107-108°**, and the *anilide* has **m 84°**. [*Beilstein* **2** IV 940.]

***S*-(+)-1-Bromo-2-methylbutane** *[534-00-9]* **M 151.1, b 38.2°/39mm, 49°/62mm, 60.8°(57-58°)/100mm, 65-65.6°/140mm, 116-122°/atm, d $^{20}_{4}$ 1.2232, n $^{20}_{D}$ 1.4453, [α] $^{20}_{D}$ +5.1° (c 5, $CHCl_3$) (neat, +5.8°).** Wash the bromobutane with ice-cold H_2O, dry by freezing, shake it twice with an equal volume of H_2SO_4 at 0°, and twice with an equal volume of H_2O at 0°. Freeze-dry and keep over freshly heated (and then cooled) K_2CO_3, and distil it through a vacuum jacketed column of broken glass. *Alternatively*, dissolve it in petroleum ether (b 40-60°), wash it with 5% NaOH, conc H_2SO_4 (at 0°), then H_2O, dry ($CaCl_2$), evaporate it and distil. [Heller *J Am Chem Soc* **74** 4858 *1952*, Foley *J Am Chem Soc* **81** 2779 *1959*, Easton & Hargreaves *J Chem Soc* 1413 *1959*, Crombie & Harper *J Chem Soc* 2685 *1950*, *Beilstein* **1** IV 327.]

2-Bromo-2-methylpropane *[507-19-7]* **M 137.0, b 71-73°, d $^{20}_{4}$ 1.218, n $^{20}_{D}$ 1.429.** Neutralise the bromomethylpropane with K_2CO_3, distil, and dry it using molecular sieves (5A), then distil it in a vacuum and degas it by the freeze-pump-thaw technique. Seal it under vacuum. [*Beilstein* **1** IV 295.]

1-Bromooctadecane *[112-89-0]* **M 333.4, m 26°, 27.3°, 28-30°, b 178-179°/2mm, 214-218°/15mm, d $^{20}_{4}$ 0.976, n $^{20}_{D}$ 1.461.** Twice recrystallise bromooctadecane from the melt, then distil it under vacuum three times taking the middle cut. *Alternatively*, wash the oil with aqueous Na_2SO_4, then conc H_2SO_4 (cool) and again with aqueous Na_2SO_4, and then fractionally distil it. [Meyer & Ried *J Am Chem Soc* **55** 1574 *1933*, Hoffmann & Smyth *J Am Chem Soc* **72** 171 *1950*, IR: LeFévre et al. *Aust J Chem* **12** 743 *1959*, IR: Brini-Fritz *Bull Soc Chim Fr* 516 *1957*, *Beilstein* **1** IV 555.]

(±)-2-Bromopentane *[107-81-3]* **M 151.1, b 117.2°/753mm, 116-117°/atm, 117.5°/740mm, d $^{20}_{4}$ 1.2190, n $^{20}_{D}$ 1.4401.** Dry it over K_2CO_3 and distil it through a short Vigreux column. [IR: Pines et al. *J Am Chem Soc* **74** 4063 *1952*, Brown & Wheeler *J Am Chem Soc* **78** 2199 *1956*, *Beilstein* **1** IV 312.]

Bromopicrin (tribromonitromethane) *[464-10-8]* **M 297.8, m 10.2-10.3°, b 85-87°/16mm, d $^{20}_{4}$ 2.788, n $^{20}_{D}$ 1.579.** Steam distil it, dry it with anhydrous Na_2SO_4 and distil it again in a vacuum. **HIGHLY TOXIC.** [*Beilstein* **1** H 77, **1** I 21, **1** II 43, **1** III 115, **1** IV 106.]

***R*-(+)-2-Bromopropionic acid** *[10009-70-8]* **M 153.0, b 78°/4mm, d $^{20}_{4}$ 1.474, [α] $^{25}_{D}$ +27.2° (neat), pK^{25} 4.07.** Dissolve it in Et_2O, dry ($CaCl_2$), evaporate and distil it through a short column. Distillation through a Podbielniak column (see *S*-(–)-2-chloropropionic acid below) led to decomposition. Store it in the dark under N_2, preferably in sealed ampoules. Even at –10° it slowly decomposes. **LACHRYMATORY.** [Fuet et al. *J Am Chem Soc* **76** 6054 *1954*, *Beilstein* **2** IV 761.]

3-Bromopropionic acid *[590-92-1]* **M 153.0, m 62.5°, 62.5-63.5°, 63-64°, pK^{25} 4.01.** The acid crystallises as plates from CCl_4. It is soluble in organic solvents and H_2O. Its *methyl ester* has **b** 65°/18mm and 80°/27mm. The *S-benzylisothiouronium salt* has **m** 136°. [Kendall & McKenzie *Org Synth* Coll Vol **I** 131 *1941*, *Beilstein* **2** IV 764.]

Bromopyruvic acid (3-bromo-2-oxopropionic acid) *[1113-59-3]* **M 167.0, m 79-82°, pK$_{Est}$ ~1.6.** Dry it by azeotropic distillation (with toluene), and then recrystallise it from dry $CHCl_3$. Dry for 48 hours at 20° (0.5 torr) over P_2O_5. Store it at 0°. [Labandiniere et al. *J Org Chem* **52** 157 *1987*, *Beilstein* **3** III 1167.]

***N*-Bromosuccinimide** *[128-08-5]* **M 178.0, m 183-184°(dec).** *N*-Bromosuccinimide (30g) is purified by dissolving rapidly in boiling water (300ml) and filtering through a fluted filter paper into a flask immersed in an ice bath, and left for 2 hours. The crystals are filtered off, washed thoroughly with of ice-cold water (*ca* 100ml) and drained on a Büchner funnel before drying under vacuun over P_2O_5 or $CaCl_2$ [Dauben & McCoy *J Am Chem Soc* **81** 4863 *1959*]. This *brominating agent* has also been recrystallised from acetic acid or water (10 parts see above), washed in water and dried *in vacuo* [Wilcox et al. *J Am Chem Soc* **108** 7693 *1986,* Shell et al. *J Am Chem Soc* **108** 121 *1986*, Phillips & Cohen *J Am Chem Soc* **108** 2013 *1986*, *Beilstein* **21/9** V 543.]

Bromotetronic acid (2-bromo-4-hydroxyacetoacetic lactone) *[21151-51-9]* **M 179.0, m 182.8°, pK^{25} 2.23.** Decolourise with Norit in EtOAc, evaporate, and crystallise from EtOAc or $*C_6H_6$. [Schuler et al. *J Phys Chem* **78** 1063 *1974*, Gillespie & Price *J Org Chem* **22** 782 *1957*, *Beilstein* **17** III/IV 5819.]

Bromotrichloromethane *[75-62-7]* **M 198.5, f –5.6°, m 21°, b 104.1°, d $_{D}^{20}$ 2.01, n $_{D}^{20}$ 1.5061.** Wash it with aqueous NaOH solution or dilute Na_2CO_3, then with H_2O, and dry with $CaCl_2$, BaO, $MgSO_4$ or P_2O_5 before distilling in diffuse light and storing in the dark. It has also been purified by treatment with charcoal and fractional crystallisation by partial freezing. It is purified also by vigorous stirring with portions of conc H_2SO_4 until the acid does not discolour during several hours stirring. Wash with Na_2CO_3 and water, dry with $CaCl_2$ and then illuminate it with a 1000W projection lamp at 15cm for 10 hours, after making it 0.01M in bromine. Pass it through a 30 × 1.5cm column of activated alumina and fractionally redistil it through a 12-in Vigreux column. [Firestone & Willard *J Am Chem Soc* **83** 3511 *1961*; see also Cadogan & Duell *J Chem Soc* 4154 *1962*, *Beilstein* **1** IV 77.]

1-Bromo-2,2,2-trifluoroethane *[421-06-7]* **M 163.0, m –94°, b 26-27°, d $_{4}^{20}$ 1.788, n $_{D}^{20}$ 1.332.** Wash it with water, dry ($CaCl_2$) and distil it. [*Beilstein* **1** III 179, **1** IV 154.]

Bromotrifluoromethane (Freon 13B1) *[75-63-8]* **M 148.9, b –59°, d $_{4}^{20}$ 1.590.** Purify the gas by passing it through a tube containing P_2O_5 on glass wool into a vacuum system where it is frozen out in a quartz tube and degassed by cycles of freezing, evacuating and thawing. [*Beilstein* **1** III 83, **1** IV 73.]

5-Bromovaleric (γ–bromopentanoic) acid *[2067-33-6]* **M 181.0, m 40°, pK$_{Est}$ ~4.6.** Crystallise the acid from petroleum ether. [*Beilstein* **2** IV 883.]

(±)-Bromural [*N*-(aminocarbonyl)-2-bromo-3-methylbutanamide, bromisovalum] *[496-67-3]* **M 223.1, m 154-155°.** Crystallise it from aqueous EtOH or toluene, and dry it in air. [*Beilstein* **3** H 63, **3** I 29, **3** II 51, **3** III 123, **3** IV 117.]

1,3-Butadiene *[106-99-0]* **M 54.1, b –2.6°.** Dry the gas by condensing it into a solution of triethylaluminium in decahydronaphthalene, then it is flash distilled. It has also been dried by passage over anhydrous $CaCl_2$ or distilled from $NaBH_4$. Also purify by passing through a column packed with molecular sieves (4A), followed by cooling in a Dry-ice/MeOH bath overnight, filtering off the ice and drying over CaH_2 at –78° then distilling in a vacuum line. [*Beilstein* **1** IV 976.]

***n*-Butane** *[106-97-8]* **M 58.1, m –135°, b –0.5°.** Dry by passing over anhydrous $Mg(ClO_4)_2$ and molecular sieves type 4A. Air is removed by prolonged and frequent degassing at –107°. [*Beilstein* **1** IV 236.]

1,4-Butanediol (tetramethylene glycol) *[110-63-4]* **M 90.1, f 20.4°, b 107-108°/4mm, 127°/20mm, d $_{4}^{20}$ 1.02, n $_{D}^{20}$ 1.4467.** Distil the glycol and store it over Linde type 4A molecular sieves, or crystallise it twice from anhydrous diethyl ether/acetone, and redistil it. It has been recrystallised from the melt and doubly distilled *in vacuo* in the presence of Na_2SO_4. [*Beilstein* **1** IV 2515.]

***erythro*-2,3-Butanediol (*meso*-2,3-butylene glycol)** *[5341-95-7]* **M 90.1, m 32-34°, 34.4°, b 89°/16mm, 181.7°/742mm, d $_{4}^{20}$ 0.9939, n $_{D}^{20}$ 1.443, n $_{D}^{25}$ 1.4324.** The *meso*-form is prepared from *trans*-2,3-epoxybutane and is recrystallised from isopropyl ether at low temperature. [Wilson & Lucas *J Am Chem Soc* **58** 2396 *1936*, *Beilstein* **1** II 546, 1 III 2178, **1** IV 2524.]

***threo*-2,3-Butanediol (*rac* ±-2,3-butylene glycol)** *[513-85-9]* **M 90.1, m 7.6°, b 86°/16mm, 172.7°/742mm, 183-184°/760mm, d_4^{25} 0.995, n_D^{20} 1.443, n_D^{25} 1.4310.** The ±-*threo*-form is prepared from *cis*-2,3-epoxybutane and is recrystallised from isopropyl ether at low temperature. [*Beilstein* **1** II 546, **1** III 2180, **1** IV 2525.]

***threo*-2,3-Butanediol** *[R,R(–) 24347-58-8, S,S(+) 19132-06-0]* **M 90.1, m 16-19°, 19.7°, b 77.5-78°/10mm, 179-180°/atm, d_4^{25} 0.987, n_D^{20} 1.443, n_D^{25} 1.4310, $[\alpha]_D^{20}$ (–) or (+) 13.1° (neat).** Purify by fractional distillation. The *bis-(p-nitrobenzoate) ester* has **m** 141-142°, and $[\alpha]_D^{20}$ (–) or (+) 52° (c 4, $CHCl_3$). [Ghirardelli & Lucas *J Am Chem Soc* **79** 734 *1957*, Rubin et al. *J Am Chem Soc* **74** 425 *1952*, Neish *Can J Res* **27** 6 *1949*, Neish & Ledingham *Can J Res* **27** 694 *1949*, *Beilstein* **1** IV 2524-2525.] When (-)-*2R,3R*-butane-2,3-diol (22g, 21ml, 244.5mmol) is added slowly to a stirred mixture of toluene-*p*-sulfonyl chloride (100g, 525mmol) in dry pyridine at 0° (ice-water bath), kept thus for 20 minutes, and the semi-solid mixture is set aside at ~25° overnight, then is shaken vigorously with crushed ice-water for 2 hours, poured rapidly with stirring into a mixture of concentrated HCl (70ml) and crushed ice, and the slurry is filtered gives solid **(+)-*2R,3R*-butane-2,3-diol bis(tosylate)** after washing thoroughly with H_2O and drying (91.0g, 93.5%). *Alternatively*, the crude dry ester is dissolved in CH_2Cl_2, dried ($MgSO_4$), evaporated *in vacuo*, and the residue is washed with petroleum ether (b 20-60°), and stored over solid KOH in a desiccator. It has **m 62-64° (65.1-65.5°), $[\alpha]_D^{20}$ +37.2° (c 2.105, $CHCl_3$)**. [Corey & Mitra *J Am Chem Soc* **84** 2938 *1962*, Lucas et al. *J Am Chem Soc* **72** 2138 *1950*, Fryzuk & Bosnich *J Am Chem Soc* **99** 6262 *1977*.] This (+)-*2R,3R*-ditosylate provides the chiral ligand (–)-*S,S*-CHIRAPHOS [cf 64896-28-2] after reaction with 2 mols of Ph_2PLi, *via* inversion of configuration at the two chiral centres. **(+)-*2R,3R*-butane-2,3-diol bis(methanesulfonate)** has **m 123-125°, $[\alpha]_D^{22}$ +2° (c 1, $CHCl_3$)**. [*Beilstein* **1** I 250, **1** II 547, **1** III 2181-3, **1** IV 2525.]

1-Butanesulfonyl chloride *[2386-60-9]* **M 156.6, b 75-76°/7mm, 98°/13mm, 100-103°/27-28mm, d_4^{20} 1.2078, n_D^{20} 1.4559**. It has a pungent odour and is **LACHRYMATORY.** If IR shows OH bands, then dissolve in Et_2O, wash with cold saturated aqueous $NaHCO_3$ (care since CO_2 will be generated) then H_2O, dry it over solid Na_2SO_4, filter, evaporate and distil the residue twice. Characterise it by shaking a solution in Et_2O or $*C_6H_6$ with aqueous NH_3, collect the solid *1-butanesulfonamide* with **m** 48° after recrystallisation from $CHCl_3$, CCl_4 or Et_2O/petroleum ether. [Douglass & Johnson *J Am Chem Soc* **60** 1488 *1938*, Lee & Dougherty *J Org Chem* **5** 83 *1940*, *Beilstein* **4** IV 45.]

1-Butanethiol *[109-79-5]* **M 90.2, b 98.4°, d^{25} 0.837, n_D^{20} 1.443, n^{25} 1.440, pK_{Est} ~11.3.** Dry the thiol with $CaSO_4$ or Na_2SO_4, then reflux it over magnesium, or dry with, and distil it from CaO, under nitrogen [Roberts & Friend *J Am Chem Soc* **108** 7204 *1986*.] It has been separated from hydrocarbons by extractive distillation with aniline.
Dissolve it also in 20% NaOH, extract with a small amount of $*C_6H_6$, then steam distil it until clear. The distillate is then cooled and acidified slightly with 15% H_2SO_4. The thiol is distilled out, dried with $CaSO_4$ or $CaCl_2$, and fractionally distilled under N_2 [Mathias & Filho *J Phys Chem* **62** 1427 *1958*]. It has also been purified by precipitation as the lead mercaptide from alcoholic solution, then regeneration by addition of dilute HCl to the residue followed by steam distillation. *All operations should be carried out in a fume cupboard due to the* **TOXICITY** *and obnoxious odour of the thiol.* [*Beilstein* **1** IV 1555.]

2-Butanethiol *[513-53-1]* **M 90.2, b 37.4°/134mm, d^{25} 0.846, n^{25} 1.4338, pK_{Est} ~11.4.** Purify it as for 1-butanethiol. [*Beilstein* **1** IV 1584.]

***n*-Butanol** *[71-36-3]* **M 74.1, b 117.7°, d^{25} 0.80572, n_D^{20} 1.39922, n^{15} 1.40118.** Dry it with $MgSO_4$, CaO, K_2CO_3, or solid NaOH, followed by refluxing with, and distilling from, small amounts of calcium, magnesium activated with iodine, or aluminium amalgam. It can also be dried with molecular sieves, or by refluxing with *n*-butyl phthalate or succinate. (For method, see *Ethanol*.) *n*-Butanol can also be dried by efficient fractional distillation, water passing over in the first fraction as a binary azeotrope (contains about 37% water). An ultraviolet-transparent distillate has been obtained by drying with magnesium and distilling from sulfanilic acid. To remove bases, aldehydes and ketones, the alcohol is washed with dilute H_2SO_4, then $NaHSO_4$ solution; esters are removed by boiling for 1.5 hours with 10% NaOH.
It has also been purified by adding $NaBH_4$ (2g) to butanol, (1.5L) gently bubbling under argon and a reflux con-

denser for 1 day at 50°. Then add freshly cut sodium (2g, washed with butanol) and reflux 1 day. Distil, and collect the middle fraction [Jou & Freeman *J Phys Chem* **81** 909 *1977*]. [*Beilstein* **1** IV 1506.]

2-Butanone (methyl ethyl ketone, MEK) *[78-93-0]* **M 72.1, b 79.6°, d $_4^{20}$ 0.853, n $_D^{20}$ 1.37850, n^{25} 1.37612, pK^{25} –7.2 (aqueous H_2SO_4).** In general, purification methods are the same as for acetone. Aldehydes can be removed by refluxing with $KMnO_4$ + CaO, until the Schiff aldehyde test is negative, prior to distillation. Shaking with saturated K_2CO_3, or passing through a small column of activated alumina, removes cyclic impurities. The ketone can be dried by careful distillation (an azeotrope containing 11% water boils at 73.4°), or over $CaSO_4$, P_2O_5, Na_2SO_4, or K_2CO_3, followed by fractional distillation. Purification as the bisulfite addition compound is achieved by shaking with excess saturated Na_2SO_3, cooled to 0°, filtering off the precipitate, washing with a little ethyl ether and drying in air; this is followed by decomposition with a slight excess of Na_2CO_3 solution and steam distillation, the distillate being saturated with K_2CO_3 so that the ketone can be separated, dried with K_2CO_3, filtered, and distilled. Purification as the *NaI addition compound* (**m** 73-74°) is more convenient. (For details, see *Acetone*.) Small quantities of 2-butanone can be purified by conversion to the semicarbazone, recrystallisation to constant melting point, drying under vacuum over $CaCl_2$ and paraffin wax, refluxing for 30 minutes with excess oxalic acid, followed by steam distillation, salting out, drying and distilling. [Cowan et al. *J Chem Soc* 171 *1940*]. [*Beilstein* **1** IV 3243.]

***cis*-2-Butene** *[590-18-1]* **M 56.1, b 2.95-3.05°/746mm.** The gas is dried with CaH_2 and purified by gas chromatography. [*Beilstein* **1** H 205, **1** II 176, **1** III 728, **1** IV 778.] **HIGHLY FLAMMABLE.**

***trans*-2-Butene** *[624-64-6]* **M 56.1, b 0.3-0.4°/744mm.** The gas is dried with CaH_2 and purified by gas chromatography. [*Beilstein* **1** H 205, **1** II 176, **1** III 730, **1** IV 781.] **HIGHLY FLAMMABLE.**

2-Butene-1,4-dicarboxylic acid (*trans*-3-hexenedioic acid, *trans*-ß-hydromuconic acid) *[4436-74-2]* **M 144.1, m 194-197°, 195-196°, $pK_{Est(1)}$ ~4.2, $pK_{Est(2)}$ ~5.00.** Crystallise the acid from boiling water, then dry it at 50-60° in a vacuum oven. [*Beilstein* **2** IV 2237.]

2-Butoxyethanol (butyl cellosolve) *[111-76-2]* **M 118.2, b 171°/745mm, d $_4^{20}$ 0.903, n $_D^{20}$ 1.4191.** Peroxides can be removed by refluxing with anhydrous $SnCl_2$ or by passage under slight pressure through a column of activated alumina. Dry with anhydrous K_2CO_3 and $CaSO_4$, filter and distil, or reflux with, and distil from NaOH. [*Beilstein* **1** IV 2380.]

***n*-Butyl acetate** *[123-86-4]* **M 116.2, b 126.1°, d $_4^{20}$ 0.882, n $_D^{20}$ 1.394.** Distil, reflux with successive portions of $KMnO_4$ until the colour persists, dry with anhydrous $CaSO_4$, filter and redistil. [*Beilstein* **2** IV 143.]

***tert*-Butyl acetate** *[540-88-5]* **M 116.2, b 97-98°, d $_4^{20}$ 0.866, n $_D^{20}$ 1.387.** Wash the ester with 5% Na_2CO_3 solution, then saturated aqueous $CaCl_2$, dry with $CaSO_4$ and distil it. [McClosky et al. *Org Synth* Coll Vol **IV** 263 *1963,* Mangia et al. *Org Prep Proc Int* **18** 13 *1986*, *Beilstein* **2** IV 151.]

***tert*-Butyl acetoacetate** *[1694-31-1]* **M 158.2, b 71°/10mm, 85°/20mm, d $_4^{20}$ 0.954, n $_D^{20}$ 1.42.** Distil it under reduced pressure through a short column. [Lawesson et al. *Org Synth* Coll Vol **V** 155 *1973*, Lawesson et al. *Org Synth* **42** 28 *1962*, *Beilstein* **3** IV 1536.] **HARMFUL VAPOUR.**

***tert*-Butylacetyl chloride** *[7065-46-5]* **M 134.6, b 68-71°/100mm, 81°/180mm, 128-132°/atm, d $_4^{20}$ 0.964, n $_D^{20}$ 1.423.** Distil it under vacuum. If IR shows OH group, then treat with thionyl chloride or oxalyl chloride at *ca* 50° for 30 minutes, evaporate and fractionate the residue using a short column. Strongly **LACHRYMATORY**, use a good fume hood. [Berliner & Berliner *J Am Chem Soc* **72** 222 *1950*, Traynham & Battiste *J Org Chem* **22** 1551 *1957*, *Beilstein* **2** IV 956.]

Butyl acrylate *[141-32-2]* **M 128.2, b 59°/25mm, d $_4^{20}$ 0.894, n^{12} 1.4254.** Wash it repeatedly with aqueous NaOH to remove inhibitors such as hydroquinone, then with distilled water. Dry with $CaCl_2$. Fractionally distil under reduced pressure in an all-glass apparatus. The middle fraction is sealed under N_2 and stored at 0° in the dark until required or with a stabiliser [Mallik & Das *J Am Chem Soc* **82** 4269 *1960*]. [*Beilstein* **2** IV 1463.]

***tert*-Butyl acrylate** *[1663-39-4]* **M 128.2, b 30.0-30.8°/26mm, 61-63°/15mm, 117-120°/760mm, d^{25} 0.875, n_D^{20} 1.410.** Purify the ester by fractional distillation. If it contains acid (OH bands in the IR), then dissolve it in Et_2O, wash it with aqueous $NaHCO_3$, dry the organic layer (Na_2SO_4), filter it and distil it under reduced pressure. Stabilise it by adding hydroquinone monomethyl ether (~0.05%). It forms a crystalline *tert*-butyl acrylate polymer which is soluble in organic solvents [Garrett et al. *J Am Chem Soc* **81** 1007 *1959*]. [*Beilstein* **2** IV 1465.] For other alkyl acrylates see Rehberg *Org Synth Coll Vol* **3** 146 *1955*.

(±)-*sec*-Butyl alcohol (± 2-butanol) *[78-92-2; 15892-23-6]* **M 74.1, b 99.4°, d_4^{20} 0.808.** Purification methods are the same as for *n*-Butanol. These include drying with K_2CO_3 or $CaSO_4$, followed by filtration and fractional distillation, refluxing with CaO, distillation, then refluxing with magnesium and redistillation, and refluxing with, then distilling from CaH_2. Calcium carbide has also been used as a drying agent. The anhydrous alcohol is obtained by refluxing with *sec*-butyl phthalate or succinate. (For method see *Ethanol*.) Small amounts of alcohol can be purified *via* conversion to the alkyl hydrogen phthalate and recrystallisation [Hargreaves *J Chem Soc* 3679 *1956*]. For purification of optical isomers, see Timmermans and Martin [*J Chem Phys* **25** 411 *1928*]. [*Beilstein* **2** III 1566.]

***tert*-Butyl alcohol** *[75-65-0]* **M 74.1, m 23-25°, 25.7°, b 28.3°/60mm, 43.3°/123.8mm, 61.8°/315mm, 72.5°/507mm, 82.45°/760mm, d_4^{20} 0.7858, n_D^{20} 1.3878.** It is synthesised commercially by the hydration of 2-methylpropene in dilute H_2SO_4. Dry it with CaO, K_2CO_3, $CaSO_4$ or $MgSO_4$, filter and fractionally distil it. Dry further by refluxing with, and distilling from, either magnesium activated with iodine, or small amounts of calcium, sodium or potassium, under nitrogen. Passage through a column of type 4A molecular sieve is another effective method of drying; as well as refluxing with *tert*-butyl phthalate or succinate. (For method see *Ethanol*.) Other methods include refluxing with excess aluminium *tert*-butylate, or standing with CaH_2, and distilling as needed. Further purification is achieved by fractional crystallisation by partial freezing, taking care to exclude moisture. *tert*-Butyl alcohol samples containing much water can be dried by adding *benzene, so that the water distils off as a tertiary azeotrope, **b** 67.3°. Traces of isobutylene have been removed from dry *tert*-butyl alcohol by bubbling dry pre-purified nitrogen through for several hours at 40-50° before using. It forms azeotropic mixtures with a large number of compounds. It has also been purified by distillation from CaH_2 into Linde 4A molecular sieves which had been activated at 350° for 24 hours [Jaeger et al. *J Am Chem Soc* **101** 717 *1979*]. [*Beilstein* **1** IV 1609.]
Rapid purification: Dry *tert*-butanol over CaH_2 (5% w/v), distil and store it over 3A molecular sieves.

***n*-Butylamine** *[109-73-9]* **M 73.1, b 77.8°, d_4^{20} 0.740, n_D^{20} 1.4009, n^{25} 1.399, pK^{25} 10.66.** Dry it with solid KOH, K_2CO_3, $LiAlH_4$, CaH_2 or $MgSO_4$, then reflux it with, and fractionally distil it from P_2O_5, CaH_2, CaO or BaO. Further purification is by precipitation as the *hydrochloride,* **m** 213-213.5°, from ethereal solution by bubbling HCl gas into it. This is re-precipitated three times from EtOH by adding ether, followed by liberation of the free amine using excess strong base. The amine is extracted into ether, which is separated, dried with solid KOH, the ether is removed by evaporation and then the amine is distilled. It is stored in a desiccator over solid NaOH [Bunnett & Davis *J Am Chem Soc* **82** 665 *1960*, Lycan et al. *Org Synth* Coll Vol **II** 319 *1943*]. [*Beilstein* **4** IV 540.] **SKIN IRRITANT.**

R*-(-)-*sec*-Butylamine** *[13250-12-9]* **M 73.1, b 61-63°/atm, 62.5°/atm, d_4^{20} 0.731, n_D^{20} 1.393, $[\alpha]_D^{20}$ –7.5° (neat), pK^{25} 10.56.** Dry it over solid NaOH overnight and fractionate it through a short helices packed column. The L-*hydrogen tartrate salt* has **m** 139-140° (from H_2O), the *1H_2O* has **m** 96° $[\alpha]_D^{21}$ +18.1° (c 11, H_2O), the *hydrochloride* has **m** 152° $[\alpha]_D^{21}$ –1.1° (c 13, H_2O) and the *benzoyl* derivative crystallises from EtOH as needles with **m** 97°, $[\alpha]_D^{21}$–34.9° (c 11, H_2O). [Bruck et al. *J Chem Soc* 921 *1956*, Kjaer & Hansen *Acta Chem Scand* **11** 898 *1957*.] [*Beilstein* **4** H 161, **4** I 372, **4** III 308, **4** IV 617.] The ***S*-(+)-*enantiomer has has same properties except for the optical rotation which has the opposite sign.

***tert*-Butylamine** *[75-64-9]* **M 73.1, b 42°, d_4^{20} 0.696, pK^{25} 10.68.** Dry it with KOH or $LiAlH_4$, and/or distil it from CaH_2 or BaO. [*Beilstein* **4** IV 657.]

***tert*-Butylammonium bromide** *[60469-70-7]* **M 154.1, m >250°(dec).** Recrystallise the salt several times from absolute EtOH and thoroughly dry it at 105° *in vacuo*. [*Beilstein* **4** IV 657.]

***n*-Butyl bromide** *[109-65-9]* **M 137.0, b 101-102°, d^{25} 1.2678, n_D^{20} 1.4399, n^{25} 1.4374.** Wash the bromide with conc H_2SO_4, water, 10% Na_2CO_3 and again with water. Dry it over $CaCl_2$, $CaSO_4$ or K_2CO_3, and distil it. Redistil it after drying with P_2O_5, or pass it through two columns containing 5:1 silica gel/Celite mixture and store it with freshly activated alumina. [*Beilstein* **1** IV 258.]

***tert*-Butyl bromoacetate** *[5292-43-3]* **M 195.1, b 52°/10mm, 74-76°/25mm, d_4^{20} 1.324, n_D^{25} 1.4162.** Dissolve the ester in Et_2O, wash it well with ice cold 10% aqueous K_2CO_3, dry it over $CaCl_2$, filter and evaporate the Et_2O, then fractionate it through a Vigreux column in a vacuum. **LACHRYMATORY.** [Abramovitch et al. *J Am Chem Soc* **64** 2274 *1942*, Abramovitch & Hauser *J Am Chem Soc* **65** 986 *1943*, *Beilstein* **2** III 482.]

***tert*-Butyl carbazate** *[870-46-2]* **M 132.2, m 41-42°, b 64°/0.01mm, 55-57°/0.4mm.** Distil it in a Claisen flask with a water or oil bath at *ca* 80°. After a couple of drops have distilled, the carbazate is collected as an oil which solidifies to a snow white solid. It can be crystallised with 90% recovery from a 1:1 mixture of petroleum ether (b 30-60°) and petroleum ether (b 60-70°). [Carpino et al. *Org Synth* Coll Vol **V** 166 *1973*, Caprino et al. *Org Synth* **44** 20 *1964*, *Beilstein* **3** IV 175.]

***n*-Butyl chloride** *[109-69-3]* **M 92.6, b 78°, d_4^{20} 0.886, n_D^{25} 1.4021.** Shake it repeatedly with conc H_2SO_4 (until no further colour develops in the acid layer), then wash it with water, aqueous $NaHCO_3$ or Na_2CO_3, and more water. Dry it with $CaCl_2$, or $MgSO_4$ (then with P_2O_5 if desired), decant and fractionally distil it. *Alternatively*, a stream of oxygen continuing *ca* three times as long as is necessary to obtain the first coloration of starch iodide paper by the exit gas. After washing with $NaHCO_3$ solution to hydrolyse ozonides and to remove the resulting organic acid, the liquid is dried and distilled [Chien & Willard *J Am Chem Soc* **75** 6160 *1953*]. [*Beilstein* **1** IV 246.]

***tert*-Butyl chloride** *[507-20-0]* **M 92.6, f –24.6°, b 50.4°, d_4^{20} 0.851, n_D^{25} 1.38564.** Purification methods commonly used for other alkyl halides lead to decomposition. Some impurities can be removed by photochlorination with a small amount of chlorine prior to use. The liquid is washed with ice water, dried with $CaCl_2$ or $CaCl_2$ + CaO and fractionally distilled. It has been further purified by repeated fractional crystallisation by partial freezing. [*Beilstein* **1** IV 288.]

***tert*-Butyl chloroacetate** *[107-59-5]* **M 150.6, b 48-49°/11mm, 60.2°/15mm, 155°/atm (dec), d_4^{25} 1.4204, n_D^{20} 1.4259.** Check the NMR spectrum; if satisfactory then distil in a vacuum; if not then dissolve in Et_2O, wash with H_2O, 10% H_2SO_4 until the acid extract does not become cloudy when made alkaline with NaOH. Wash the organic layer again with H_2O, then saturated aqueous $NaHCO_3$, dry over Na_2SO_4, evaporate and fractionate it through a carborundum-packed column or a 6-inch Widmer column (*see tert-butyl ethyl malonate for precautions to avoid decomposition during disillation*). [Johnson et al. *J Am Chem Soc* **75** 4995 *1953*, Baker *Org Synth* Coll Vol **III** 144 *1944*, *Beilstein* **2** III 444.]

***tert*-Butyl cyanide (trimethylacetonitrile, pivalonitrile)** *[630-18-2]* **M 83.1, m 16-18°, d_4^{20} 0.765, b 104-106°.** Purify it by a two-stage vacuum distillation and de-gas by the freeze-pump-thaw technique. Store it under vacuum at 0°. **TOXIC,** use an efficient fume hood. [*Beilstein* **2** IV 875.]

***tert*-Butyl cyanoacetate** *[1116-98-9]* **M 141.2, b 40-42°/0.1mm, 54-56°/0.3mm, 90°/10mm, 107-108°/23mm, d_4^{20} 0.989, n_D^{20} 1.4198**. The IR spectrum of a film should have bands at 1742 (ester CO) and 2273 (C≡N), but no band at *ca* 3500 broad (OH) cm^{-1}. If it does not have the last-named band, then fractionally distil; otherwise dissolve in Et_2O, wash with saturated aqueous $NaHCO_3$, dry over K_2CO_3, evaporate Et_2O, and distil the residue under a vacuum (*see tert-butyl ethyl malonate for precautions to avoid decomposition during distillation*). [Beech & Piggott *J Chem Soc* 423 *1955*, Dahn & Hauth *Helv Chim Acta* **42** 1214 *1959*, *Beilstein* **2** I 255.]

***tert*-Butyl diazoacetate** *[3505950-8]* **M 142.2, b 51-53°/12mm, d_4^{25} 1.026, n_D^{20} 1.443.** It is a poisonous orange-yellow liquid which is explosive, and the necessary precautions should be strictly adhered to (i.e. efficient fume cupboard, and face and body protection; see reference below). Check the purity by TLC on Merck Kieselgel F_{254} or Eastman Kodak Silica Gel without indicator using $CHCl_3$ as eluent (R_F 0.72). If the

ester is suspect, then dissolve it in Et_2O, wash it with brine, H_2O, dry the organic layer (Na_2SO_4), and filter. Remove most of the Et_2O at 30°/water pump vacuum (rotovap), the remaing ether during distillation under lower pressure (<12mm), and the residual oil then distils as a coloured liquid using a water bath at ~50° (no higher as heat source). [Regitz et al. *Org Synth* Coll Vol **V** 179 *1972*.]

***n*-Butyl disulfide** *[629-45-8]* **M 178.4, b 110-113°/15mm, d_4^{20} 0.938, n^{22} 1.494.** Shake it with lead peroxide, filter and distil it in a vacuum under N_2. [*Beilstein* **1** IV 1560.]

***n*-Butyl ether (di-*n*-butyl ether)** *[142-96-1]* **M 130.2, b 52-53°/26mm, 142.0°/760mm, d_4^{20} 0.764, n_D^{20} 1.39925, n^{25} 1.39685, pK^{25} –5.40 (aqueous H_2SO_4).** Peroxides (detected by the liberation of iodine from weakly acid HCl solutions of 2% KI) can be removed by shaking 1L of ether with 5-10ml of a solution comprising of ferrous sulfate (6.0g) in conc H_2SO_4 (6ml) of water (110ml), with aqueous Na_2SO_3, or with acidified NaI, water, then aqueous $Na_2S_2O_3$. After washing with dilute NaOH, KOH, or Na_2CO_3, then water, the ether is dried with $CaCl_2$ and distilled. It can be further dried by distillation from CaH_2 or Na (after drying with P_2O_5), and stored in the dark with Na or NaH. The ether can also be purified by treating with CS_2 and NaOH, expelling the excess sulfide by heating. The ether is then washed with water, dried with NaOH and distilled [Kusama & Koike *J Chem Soc Jpn, Pure Chem Sect* **72** 229 *1951*]. Other purification procedures include passage through an activated alumina column to remove peroxides, or through a column of silica gel, and distillation after adding about 3% (v/v) of a 1M solution of MeMgI in *n*-butyl ether. [*Beilstein* **1** IV 1520.]

***n*-Butyl ethyl ether** *[628-81-9]* **M 102.2, b 92.7°, d_4^{20} 0.751, n_D^{20} 1.38175, n^{25} 1.3800.** Purify by drying with $CaSO_4$, by passage through a column of activated alumina (to remove peroxides), followed by prolonged refluxing with Na and then fractional distillation. [*Beilstein* **4** IV 1518.]

***tert*-Butyl ethyl ether** *[637-92-3]* **M 102.2, b 71-72°, d_4^{20} 0.741.** Dry the ether with $CaSO_4$, pass it through an alumina column, and fractionally distil it. [*Beilstein* **1** IV 1618.]

***tert*-Butyl ethyl malonate** *[32864-38-3]* **M 188.2, b 83-85°/8mm, 93-95°/17mm, 107-109°/24mm, d_4^{25} 0.994, n_D^{24} 1.4150.** A likely impurity is monoethyl malonate; check IR for OH bands at 3330 br cm^{-1}. To *ca* 50g of ester add ice cold NaOH (50g in 200ml of H_2O and 200g of ice). Swirl a few times (filter off ice if necessary), place it in a separating funnel and extract with Et_2O (2 x 75ml). Dry the extract ($MgSO_4$) (since traces of acid decompose the *t*-Bu group of the ester, the distillation flask has to be washed with aqueous NaOH, rinsed with H_2O and allowed to dry). Addition of some K_2CO_3 or MgO before distilling is recommended to inhibit decomposition. Distil it under reduced pressure through a 10cm Vigreux column. *Decomposition is evidenced by severe foaming due to autocatalytic decomposition and cannot be prevented from accelerating except by stopping the distillation and rewashing the distillation flask with alkali again.* [Breslow et al. *J Am Chem Soc* **66** 1287 *1944*, Hauser et al. *J Am Chem Soc* **64** 2714 *1942*, Strube *Org Synth* Coll Vol **IV** 417 *1963*, Stube *Org Synth* **37** 35 *1957*, *Beilstein* **2** IV 1884.]

***n*-Butyl formate** *[592-84-7]* **M 102.1, b 106.6°, d_4^{20} 0.891, n_D^{20} 1.3890.** Wash the formate with saturated $NaHCO_3$ solution in the presence of saturated NaCl, until no further reaction occurs, then with saturated NaCl solution, dry ($MgSO_4$), filter and fractionally distil the filtrate. [*Beilstein* **2** IV 28.]

Butyl glycolate *[7397-62-8]* **M 132.2, b 191-192°/755mm, 187-190°/atm, d_4^{20} 1.019, n_D^{20} 1.4263.** Dissolve the ester in $CHCl_3$ (EtOH-free), wash with 5% $KHCO_3$ until effervescence ceases (if free acid is present), dry over $CaCl_2$, filter, evaporate and distil through a short column. [Bøhme & Opfer *Z Anal Chem* **139** 255 *1953*, Filachione et al. *J Am Chem Soc* **73** 5265 *1951*, *Beilstein* **3** IV 589.]

***tert*-Butyl hydroperoxide (TBHP)** *[75-91-2]* **M 90.1, f 5.4°, m 0.5-2.0°, b 38°/18mm, d_4^{20} 0.900, n_D^{20} 1.4013, pK^{20} 12.8.** *Care should be taken when handling this peroxide because of the possibility of* **EXPLOSION. It explodes when heated over an open flame. Work in an efficient fume cupboard, behind a thick plastic transparent shield, and with eye protection.** Alcoholic and volatile impurities can be removed by prolonged refluxing at 40° under reduced pressure, or by steam distillation. For example, Bartlett, Benzing and Pincock [*J Am Chem Soc* **82** 1762 *1960*] refluxed at 30mm pressure in an apparatus for azeotropic liquid separation until the

two phases no longer separated, and then distilled at 41°/23mm. Pure material is stored under N_2, in the dark at 0°. Crude commercial material has been added to 25% NaOH below 30°, and the crystals of the sodium salt have been collected, washed twice with *benzene and dissolved in distilled water. After the pH of the solution is adjusted to 7.5 by adding solid CO_2, the peroxide is extracted into petroleum ether, from which, after drying with K_2CO_3, TBHP is recovered by distilling off the solvent under reduced pressure at room temperature [O'Brien et al. *J Am Chem Soc* **79** 6238 *1957*]. **The temperatures should be kept below 75°**. It has also been distilled through a helices packed column (*ca* 15 plates) and the material with **b 34-35°/20mm** is collected. Similarly, a solution in petroleum ether has been extracted with cold aqueous NaOH, and the hydroperoxide has been regenerated by adding at 0°, $KHSO_4$ to a pH not higher than 4.5, then extracted into diethyl ether, dried with $MgSO_4$, filtered and the ether evaporated in a rotary evaporator under reduced pressure at as low a temperature as possible [Milac & Djokic *J Am Chem Soc* **84** 3098 *1962*].
A 3M solution of TBHP in CH_2Cl_2 is prepared by swirling of commercial TBHP (85ml, 0.61mol, 70% TBHP-30% H_2O, **d** 0.935 *ca* 7.2mmol/ml) with of CH_2Cl_2 (140ml) in a separating funnel. The milky mixture is allowed to stand until the phases separate (*ca* 30 minutes). The organic (lower) layer (*ca* 200ml) containing 0.60mole of TBHP is separated from the aqueous layer (*ca* 21ml) and used without further drying. TBHP is assayed by iodometric titration. With 90% grade TBHP (w/w, d 0.90, *ca* 9.0mmole/ml) no separation of layers occurs, i.e. when TBHP (66.67ml, 0.60mole) is added to CH_2Cl_2 (140ml) the resulting solution (*ca* 200ml) should be clear. [Walling & Buckler *J Am Chem Soc* **77** 6032 *1955*, Rogers & Campbell *J Am Chem Soc* **74** 4742 *1952*, Akashi et al. *J Org Chem* **43** 2063 *1978* state the quality of available grades, handling and compatibility for reactions, *Beilstein* **1** IV 1616.]

***n*-Butyl iodide (1-iodobutane)** *[542-69-8]* **M 184.0, b 130.4°, d $_4^{20}$ 1.616, n^{25} 1.44967.** Dry the iodide with $MgSO_4$ or P_2O_5, fractionally distil it through a column packed with glass helices, taking the middle fraction and storing over calcium or mercury in the dark. *Alternatively*, purify it by prior passage through activated alumina or by shaking with conc H_2SO_4 then washing with Na_2SO_3 solution. It has also been treated carefully with sodium to remove free HI and H_2O, before distilling through a column containing copper turnings at the top. Another purification procedure consisted of treatment with bromine, followed by extraction of free halogen with $Na_2S_2O_3$, washing with H_2O, drying and fractionally distilling. [*Beilstein* **1** IV 271.]

***tert*-Butyl iodide** *[558-17-8]* **M 184.0, b 100°(dec), d $_4^{20}$ 1.544.** Vacuum distillation has been used to obtain a distillate which remained colourless for several weeks at –5°. More extensive treatment has been used by Boggs, Thompson and Crain [*J Phys Chem* **61** 625 *1957*] who washed it with aqueous $NaHSO_3$ solution to remove free iodine, dried this for 1 hour over Na_2SO_3 at 0°, and purified it by four or five successive partial freezings of the liquid to obtain colourless material, and was stored at –78° with Ag wool. [*Beilstein* **1** IV 300.]

***tert*-Butyl isocyanate** *[1609-86-5]* **M 99.1, m 10.5-11.5°, b 30.5-32°/10mm, 64°/52mm, d $_{25}^{25}$ 0.9079, n $_D^{25}$ 1.470.** It is **LACHRYMATORY** and **TOXIC**, and should have IR with 2251 (C≡N) cm^{-1} but no OH bands. The NMR should have one band at 1.37 ppm from TMS. Purify it by fractional distillation under reduced pressure. [Greene & Bergmark *J Org Chem* **36** 3056 *1971*, Curtius *J Prakt Chem* **125** 152 *1930*, *Beilstein* **4** IV 669.]

***tert*-Butyl isocyanide** *[7188-38-7]* **M 83.1, b 91-92°/730mm, 90°/758mm, d $_4^{20}$ 0.735.** Dissolve it in petroleum ether (b 40-60°), wash it with H_2O, dry (Na_2SO_4), filter, remove petroleum ether under slight vacuum, and distil it using a vacuum-jacketed Vigreux column at atmospheric pressure, its IR has a band at 2134 cm^{-1}. [Ugi & Meyr *Chem Ber* **93** 239 *1960*, *Beilstein* **4** IV 661.] It has **toxic vapours**.

***tert*-butyl isocyanoacetate** *[2769-72-4]* **M 141.2, b 50°/0.1mm, 49-50°/10mm, 63-65°/15mm, d $_4^{20}$ 0.970, n $_D^{20}$ 1.420.** If it contains some free acid (OH bands in IR), then dissolve it in Et_2O, shake with 20% Na_2CO_3, dry over anhydrous K_2CO_3, evaporate and distil it. [Ugi et al. *Chem Ber* **94** 2814 *1961*, Schhöllkopf *Angew Chem* **89** 351 1977.]

***n*-Butyl methacrylate** *[97-88-1]* **M 142.2, b 49-52°/0.1mm, 163-165°/atm, d $_4^{20}$ 0.896, n $_D^{20}$ 1.424.** Purify it as for butyl acrylate. [*Beilstein* **2** IV 1525.]

***tert*-Butyl methacrylate** *[585-07-9]* **M 142.2, f –48°, b 135-136°/760mm, d $_4^{20}$ 0.878, n$_D^{20}$ 1.415.** Purify it as for butyl acrylate. [*Beilstein* **2** IV 1582.]

***n*-Butyl methyl ether** *[628-28-4]* **M 88.2, b 70°, d $_4^{20}$ 0.744, pK^{25} –3.50 (aqueous H_2SO_4).** Dry it with $CaSO_4$, pass it through an alumina column to remove peroxides, and fractionally distil it. [*Beilstein* **1** IV 1518.]

***tert*-Butyl methyl ether** (methyl *tert*-butyl ether, MTBE) *[1634-04-4]* **M 88.2, b 56°, n 1.369.** Purify it as for *n*-butyl methyl ether. [*Beilstein* **1** IV 1615.]

***tert*-Butyl methyl ketone (3,3-dimethyl-2-butanone, pinacolone)** *[75-97-8]* **M 100.2, b 105°/746mm, 106°/760mm, d $_4^{20}$ 0.814, n$_D^{20}$ 1.401.** Reflux the ketone with a little $KMnO_4$. Dry it with $CaSO_4$ and distil it. [*Beilstein* **1** IV 3310.]

***tert*-Butyl nitrite** *[540-80-7]* **M 103.1, b 34°/250mm, 61-63°/atm, d $_4^{20}$ 0.8671, n $_D^{25}$ 1.3660.** If it is free from OH bands (IR) then distil it through a 12inch helices packed column under reduced pressure, otherwise wash with aqueous 5% $NaHCO_3$ (**effervescence**), then H_2O, dry (Na_2SO_4) and fractionate it through a 10 theoretical plates column at *ca* 10mm pressure. [Allen *J Chem Soc* 1968 *1954*, Coe & Doumani *J Am Chem Soc* **70** 1516 *1948*, UV: Ungnade & Smiley *J Org Chem* **21** 993 *1956*, IR: Terte *Bull Soc Chim Belg* **60** 240 *1951*, *Beilstein* **1** IV 1622.]

***tert*-Butyl peracetate** *[107-71-1]* **M 132.2, b 23-24°/0.5mm, n^{25} 1.4030.** Wash the ester with $NaHCO_3$ from a *benzene solution, then redistil to remove *benzene [Kochi *J Am Chem Soc* **84** 774 *1962*]. *Handle with adequate protection due to possible* **EXPLOSIVE** *nature*. [*Beilstein* **2** IV 391.]

***tert*-Butylperoxy isobutyrate** *[109-13-7]* **M 160.2, f –45.6°.** After diluting the material (90ml) with petroleum ether (120ml), the mixture is cooled to 5° and shaken twice with 5% NaOH solution (90ml portions, also at 5°). The non-aqueous layer, after washing once with cold water, is dried at 0° with a mixture of anhydrous $MgSO_4$ and $MgCO_3$ containing *ca* 40% MgO. After filtering, this material is passed, twice, through a column of silica gel at 0° (to remove *tert*-butyl hydroperoxide). The solution is then evaporated at 0°/0.5-1mm to remove the solvent, and the residue is recrystallised several times from petroleum ether at –60°, then subjected to high vacuum to remove traces of solvent [Milos & Golubovic *J Am Chem Soc* **80** 5994 *1958*]. *Handle with adequate protection due to possible* **EXPLOSIVE** *nature.*

Butyl stearate *[123-95-5]* **M 340.6, m 26.3°, d $_4^{20}$ 0.861.** Acidic impurities are removed by shaking with 0.05M NaOH or a 2% $NaHCO_3$ solution, followed by several water washes, then purified by fractional freezing of the melt and fractional crystallisation from solvents with boiling points below 100°. [*Beilstein* **2** IV 1219.]

S-*tert*-Butyl thioacetate *[999-90-6]* **M 132.2, b 31-32°/11mm, 38°/14mm, 44-45°/28mm, 67°/54mm, 135.6-135.9°/773mm, d $_4^{25}$ 0.9207, n $_D^{20}$ 1.4532.** Dissolve it in $CHCl_3$ (EtOH-free), wash with H_2O, 10% H_2SO_4, saturated aqueous $NaHCO_3$ (care CO_2 liberated), H_2O again, dry over Drierite and anhydrous K_2CO_3, and fractionate under reduced pressure. [Rylander & Tarbell *J Am Chem Soc* **72** 3021 *1950*, *Beilstein* **2** IV 546.]

***N*-*tert*-Butyl urea** *[1118-12-3]* **M 116.2, m 182°, 185°(dec).** Possible impurity is *N,N′*-di-*tert*-butyl urea which is quite insoluble in H_2O. Recrystallise it from hot H_2O, filter off insoluble material, and cool from 0° to –5° with stirring. Dry in vacuum at room temperature over KOH or H_2SO_4. If dried at higher temperatures, it sublimes slowly. It can be recrystallised from EtOH as long white needles or from 95% aqueous EtOH as plates. During melting point determination the bath temperature has to be raised rapidly as the urea sublimes slowly above 100° at 760mm. [Smith & Emerson *Org Synth* Coll Vol **III** 151 *1955*, *Beilstein* **4** IV 665.]

***n*-Butyl vinyl ether** *[111-34-2]* **M 100.2, b 93.3°, d $_4^{20}$ 0.775.** After five washings with equal volumes of water to remove alcohols (made slightly alkaline with KOH), the ether is dried with sodium and distilled under vacuum, taking the middle fraction [Coombes & Eley *J Chem Soc* 3700 *1957*]. Store it over KOH. [*Beilstein* **1** IV 2052.]

2-Butyne *[503-17-3]* **M 54.1, b 0°/253mm, d $_4^{20}$ 0.693.** Keep it over Na wire for 24 hours, then fractionally distil it under reduced pressure into a cooled receiver. [*Beilstein* **1** IV 971.]

2-Butyne-1,4-diol *[110-65-6]* **M 86.1, m 54-57°, 56-58°, b 238°.** Crystallise the diol from EtOAc. [*Beilstein* **1** IV 2687.]

Butyramide *[514-35-5]* **M 87.1, m 115°, b 230°.** Crystallise it from acetone, *benzene, CCl_4/petroleum ether, 20% EtOH or water. Dry it under vacuum over P_2O_5, $CaCl_2$ or 99% H_2SO_4. [*Beilstein* **2** H 275, **2** I 122, **2** II, 251, **2** III 616, **2** IV 804.]

***n*-Butyric acid** *[107-92-6]* **M 88.1, f –5.3°, b 163.3°, d $_4^{20}$ 0.961, n^{25} 1.396, pK^{25} 2.82.** Distil the acid, them mix it with $KMnO_4$ (20g/L), and fractionally redistil, discarding the first third of the distillate [Vogel *J Chem Soc* 1814 *1948*]. [*Beilstein* **2** IV 779.]

***n*-Butyric anhydride** *[106-31-0]* **M 158.2, b 198°, d $_4^{20}$ 0.968.** Dry the anhydride by shaking it with P_2O_5, then distilling it. [*Beilstein* **2** IV 802.]

γ-Butyrolactone *[96-48-0]* **M 86.1, b 83.8°/12mm, d $_4^{20}$ 1.124.** Dry the lactone over anhydrous $CaSO_4$, then fractionally distil it. *Handle it in a fume cupboard due to its* **TOXICITY.** [*Beilstein* **17** V 7.]

Butyronitrile *[109-74-0]* **M 69.1, b 117.9°, d $_4^{20}$ 0.793, n $_D^{20}$ 1.3846, n^{30} 1.37954.** Treat it with conc HCl until the smell of the isonitrile had gone, then dry with K_2CO_3 and fractionally distil [Turner *J Chem Soc* 1681 *1956*]. *Alternatively*, it is twice heated at 75° and stirred for several hours with a mixture of Na_2CO_3 (7.7g) and $KMnO_4$ (11.5g) per L of butyronitrile. The mixture is cooled, then distilled. The middle fraction is dried over activated alumina. [Schoeller & Wiemann *J Am Chem Soc* **108** 22 *1986*, *Beilstein* **2** IV 806.]

Butyryl chloride (butanoyl chloride) *[141-75-3]* **M 106.6, f –89°, b 101-102°/atm, d $_4^{20}$ 1.026, n$_D^{20}$ 1.412.** Check IR to see if there is a significant peak at 3000-3500 cm^{-1} (br) for OH. If OH is present then reflux it with less than one mole equivalent of $SOCl_2$ for 1 hour and distil directly. The fraction boiling between 85-100° is then refractionated at atmospheric pressure. Keep all apparatus free from moisture and store the product in sealed glass ampoules under N_2. **LACHRYMATORY**; *handle in a good fume hood***.** [Hefferich & Schaeffer *Org Synth* Coll Vol **I** 147 *1941*, *Beilstein* **2** IV 803.]

Capric acid (decanoic acid) *[334-48-5]* **M 172.3, m 31.5°, b 148°/11mm, d $_4^{20}$ 0.886, n^{25} 1.424, pK$_{Est}$ ~4.9.** The acid is best purified by conversion into its *methyl ester*, **b** 114.0°/15mm (using excess MeOH, in the presence of H_2SO_4). The H_2SO_4 and MeOH are removed, the ester is distilled *in vacuo* through a 3ft column packed with glass helices. The acid is then obtained from the ester by saponification and vacuum distillation. [Trachtman & Miller *J Am Chem Soc* **84** 4828 *1962*, *Beilstein* **2** IV 1041.]

***n*-Caproamide (*n*-hexanamide)** *[628-02-4]* **M 115.2, m 100°, 100.5°.** Recrystallise the amide from hot water. [*Beilstein* **2** H 324, **2** I 141, **2** II 286, **2** III 732.]

Caproic acid (hexanoic acid) *[142-62-1]* **M 116.2, b 205.4°, d $_4^{20}$ 0.925, n $_D^{20}$ 1.417, pK^{25} 4.85.** Dry the acid with $MgSO_4$ and fractionally distil it from $CaSO_4$. [*Beilstein* **2** IV 917.]

Capronitrile (hexanenitrile) *[628-73-9]* **M 97.2, m –80°, b 163.7°, n $_D^{20}$ 1.4069, n^{25} 1.4048.** Wash the nitrile twice with half-volumes of conc HCl, then with saturated aqueous $NaHCO_3$, dry over $MgSO_4$, filter and distil it. [*Beilstein* **2** H 324, **2** I 141, **2** II 286, **2** III 733, **2** IV 930.]

Caprylonitrile (heptylcyanide) *[124-12-9]* **M 125.2, m –45°, b 198-200°/~760mm, d $_4^{20}$ 0.812, n $_D^{20}$ 1.420.** Wash the nitrile twice with half-volumes of conc HCl, then with saturated aqueous $NaHCO_3$, dry over $MgSO_4$, filter and distil it. [*Beilstein* **2** H 349, **2** I 148, **2** II 303, **2** III 798, **2** IV 993.]

Carbon Black *[1333-86-4]* **M 12.0, d 1.887/ml, bulk d 0.056g/ml, surface area >200m^2/g, av pore diameter 64Å.** Leach the carbon for 24 hours with 1:1 HCl to remove oil contamination, then wash it repeatedly with distilled water. Dry it in air, and elute for one day each with *benzene and acetone. Again dry it in air at room temperature, then heat it in a vacuum for 24 hours at 600^o to remove adsorbed gases. [Tamamushi & Tamaki *Trans Faraday Soc* **55** 1007 *1959*.]

Carbon disulfide See entry in "Inorganic Compounds", Chapter 5.

Carbon tetrabromide *[558-13-4]* **M 331.7, m 92.5^o.** Reactive bromide is removed from CBr_4 by refluxing with dilute aqueous Na_2CO_3, then steam distilling, crystallising from EtOH, and drying in the dark under vacuum. [Sharpe & Walker *J Chem Soc* 157 *1962*.] It can be sublimed at 70^o and low pressure. **It must not be dried with sodium.** [*Beilstein* **1** IV 85.]

Carbon tetrachloride *[56-23-5]* **M 153.8, b 76.8^o, d^{25} 1.5842.** For many purposes, careful fractional distillation gives adequate purification. Carbon disulfide, if present, can be removed by shaking vigorously for several hours with saturated KOH, separating, and washing with water: this treatment is repeated. The CCl_4 is shaken with conc H_2SO_4 until there is no further coloration, then washed with water, dried with $CaCl_2$ or $MgSO_4$ and distilled (from P_2O_5 if desired). **It must not be dried with sodium.** An initial refluxing with mercury for 2 hours removes sulfides. Other purification steps include passage of dry CCl_4 through activated alumina, and distillation from $KMnO_4$. Carbonyl containing impurities can be removed by percolation through a Celite column impregnated with 2,4-dinitrophenylhydrazine (DNPH), H_3PO_4 and water. (Prepared by dissolving 0.5g DNPH in 6ml of 85% H_3PO_4 by grinding together, then mixing with 4ml of distilled water and 10g Celite.) [Schwartz & Parks *Anal Chem* **33** 1396 *1961*]. Photochlorination of CCl_4 has also been used: CCl_4 to which a small amount of chlorine has been added is illuminated in a glass bottle (e.g. for 24 hours with a 200W tungsten lamp near it), and, after washing out the excess chlorine with 0.02M Na_2SO_3, the CCl_4 is washed with distilled water and distilled from P_2O_5. It can be dried by passing through 4A molecular sieves and distilled. Another purification procedure is to wash CCl_4 with aqueous NaOH, then repeatedly with water and N_2 gas is bubbled through the liquid for several hours. After drying over $CaCl_2$ it is percolated through silica gel and distilled under dry N_2 before use [Klassen & Ross *J Phys Chem* **91** 3664 *1987*]. [*Beilstein* **1** IV 56.]
Rapid purification: Distil, discarding the first 10% of distillate or until the distillate is clear. The distilled CCl_4 is then stored over 5A molecular sieves.

Carbon tetrafluoride *[75-73-0]* **M 88.0, b –15^o.** Purify CF_4 by repeated passage over activated charcoal at solid-CO_2 temperatures. Traces of air are removed by evacuating while alternately freezing and melting. *Alternatively*, liquefy CF_4 by cooling in liquid air and then fractionally distil it under vacuum. (The chief impurity originally present is probably CF_3Cl). Use brass equipment. It is non-flammable, but is TOXIC. [*Beilstein* **1** H 59, **1** I 8, **1** II 11, **1** III 35, **1** IV 26.]

Carbon tetraiodide *[507-25-5]* **M 519.6, m 168^o(dec).** Sublime CI_4 *in vacuo*. [*Beilstein* **1** H 74, **1** IV 98.]

Carbonyl sulfide See "Inorganic Compounds"in Chapter 5.

Cerulenin (helicocerin, 2*R*,3*S*-2,3-epoxy-4-oxo-7*E*,10*E*-dodecadienamide) *[17397-89-6]* **M 223.3, m 93-94^o, 93-95^o, b 120^o/10^{-8}mm, $[\alpha]_D^{16}$ +63^o (c 2, MeOH).** It forms white needles from *C_6H_6. It has also been purified by repeated chromatography through Florisil and silica gel. It is soluble in EtOH, MeOH, *C_6H_6, slightly soluble in H_2O and petroleum ether. The *dl*-form has **m** 40–42^o (from *C_6H_6/hexane), and the 2*R*,3*S*-*tetrahydrocerulenin* has **m** 86–87^o, $[\alpha]_D^{20}$ +44.4 (c 0.25, MeOH after 24 hours). [Ohrui & Emato *Tetrahedron Lett* 2095 *1978*, Sneda et al. *Tetrahedron Lett* 2039 *1979*, Broeckman & Thomas *J Am Chem Soc* **99** 2805 *1977*, Jakubowski et al. *J Org Chem* **47** 1221 *1982*, *Beilstein* **18/2** V 201.]

Cetyl acetate *[629-70-9]* **M 284.5, m 18.3^o, b 158^o/2mm, 204^o/18mm, d_4^{20} 0.861.** Distil the ester in a vacuum twice, then recrystallise it several times from diethyl ether/MeOH. [*Beilstein* **2** H 136, **2** II 146, **2** III 265, **2** IV 171.]

Cetyl alcohol (1-hexadecanol) *[36653-82-4]* **M 242.5, m 49.3°.** Crystallise the alcohol from aqueous EtOH or from cyclohexane. *Alternatively*, purify it by zone refining. The purity can be checked by gas chromatography. [*Beilstein* **1** H 429, **1** I 219, **1** II 466, **1** III 1815, **1** IV 1876.]

Cetylamide *[629-54-9]* **M 255.4, m 104-104.5°, 106-107°, b 235-236°/12mm.** Crystallise the amide from thiophene-free *benzene and dry it under vacuum over P_2O_5. It is slightly soluble in EtOH, Me_2CO, $CHCl_3$ and toluene but insoluble in H_2O. [*Beilstein* **2** H 374, **2** II 341, **2** III 975, **2** IV 1182.]

Cetylamine (1-hexadecylamine) *[143-27-1]* **M 241.5, m 48°, b 162-165°/5.2mm, pK^{25} 10.60.** Crystallise the base from thiophene-free *benzene and dry under vacuum over P_2O_5. Store away from CO_2 [*Beilstein* **4** IV 818.]

Cetylammonium chloride *[1602-97-7]* **M 278.0, m 178°.** Crystallise the salt from MeOH. [*Beilstein* **4** IV 818.]

Cetyl bromide (1-bromohexadecane) *[112-82-3]* **M 305.4, m 15°, 16-18°, b 144.8°/1mm, 171.5-172°/5mm, 190°/11mm, 193-196°/14mm, d^{25} 0.999, n_D^{20} 1.461.** It is prepared by boiling hexadecan-1-ol with 48% aqueous HBr and 25% H_2SO_4 for several hours, distilling and purifying by shaking the bromide with H_2SO_4, washing with H_2O, drying with K_2CO_3 and fractionally distilling it *in vacuo*. [Bezzi & Lanza *Gazzetta* **80** 180 *1950*, Vogel *J Chem Soc* **146** 637 *1943*, Heston et al. *J Am Chem Soc* **72** 2071 *1950*, *Beilstein* **1** H 17, **1** I 68, **1** II 138, **1** III 559, **1** IV 542.]

Cetyl ether (dihexadecyl ether) *[4113-12-6]* **M 466.9, m 54°.** Distil the ether in a vacuum then crystallise it several times from MeOH/*benzene. [*Beilstein* **1** H 430, **1** II 467, **1** III 1820, **1** IV 1878.]

Cetyltrimethylammonium bromide (cetrimonium bromide, CTAB) *[57-09-0]* **M 364.5, m 227-235°(dec).** Crystallise it from EtOH, EtOH/*benzene or from wet acetone after extracting twice with petroleum ether. Shake it with anhydrous diethyl ether, filter and dissolve it in a little hot MeOH. After cooling in the refrigerator, the precipitate is filtered off at room temperature and re-dissolved in MeOH. Anhydrous ether is added and, after warming to obtain a clear solution, it is cooled and the crystalline material is collected and dried *in vacuo*. [Dearden & Wooley *J Phys Chem* **91** 2404 *1987*, Hakemi et al. *J Am Chem Soc* **91** 120 *1987*, *Beilstein* **4** IV 819.]

Cetyltrimethylammonium chloride *[112-02-7]* **M 320.0.** Crystallise the chloride from acetone/ether mixture, EtOH/ether, or from MeOH. [Moss et al. *J Am Chem Soc* **109** 4363 *1987*, *Beilstein* **4** IV 819.]

Charcoal *[7440-44-0]* **M 12.0, m ~3550°.** Charcoal (50g) is added to 1L of 6M HCl and boiled for 45 minutes. The supernatant is discarded, and the charcoal is boiled with two more lots of HCl, then with distilled water until the supernatant no longer gives a test for chloride ion. The charcoal (now phosphate-free) is filtered onto a sintered-glass funnel and dried in air at 120° for 24 hours. [Lippin et al. *J Am Chem Soc* **76** 2871 *1954*.] The purification can be carried out using a Soxhlet extractor (without cartridge), allowing longer extraction times. Treatment with conc H_2SO_4 instead of HCl has been used to remove reducing substances.

Chimyl alcohol (1-*O*-*n*-hexadecylglycerol) *[(±) 506-03-6, 10550-58-0 (chimyl alcohol)]* **M 316.5, m 64°.** Recrystallise it from hexane. [*Beilstein* **1** III 2322.]

Chloral (trichloroacetaldehyde) *[75-87-6, 302-17-0 (hydrate)]* **M 147.4, b 26°/35mm, 98°/760mm. pK^{25} 10.04.** Distil chloral, then dry it by distilling through a heated column of $CaSO_4$. It readily forms a *hydrate* **m 57°**, an *alcoholate* **m 47.5°** [515-83-3] and an *ammonia adduct* **m 72-74°** [507-47-1]. It is a sedative and a hypnotic. [*Beilstein* **1** H 616, **1** I 328, **1** II 467, **1** III 2663, **1** IV 3142 for anhydr, **1** IV 3143 for hydrate.]

Chloralacetone chloroform (2,2,2-trichloro-1-[2,2,2-trichloro-1,1-dimethylethoxy]ethanol) *[512-47-0]* **M 324.9, m 65°.** Crystallise it from *benzene. It sublimes on careful heating and hydrolyses in cold H_2SO_4 to chloral acetone and chloroform. [*Beilstein* **1** H 622.]

Chloroacetaldehyde dimethyl acetal *[97-97-2]* **M 124.6, m –34.4°, b 64°/23mm, 71-72°/35mm, d_4^{20} 1.0172, n_D^{20} 1.4175.** Purify the acetal by fractional distillation, preferably in a vacuum. [Melhotra *J Indian Chem Soc* **36** 4405 *1959*, *Beilstein* **1** IV 3134.]

α-Chloroacetamide *[79-07-2]* **M 93.5, m 121°, b 224-225°/743mm.** Recrystallise the amide from acetone and dry it under vacuum over P_2O_5. [*Beilstein* **2** IV 490.]

Chloroacetic acid *[79-11-8]* **M 94.5, m 62.8°, b 189°, pK^{25} 2.87.** Crystallise the acid from $CHCl_3$, CCl_4, *benzene or water. Dry it over P_2O_5 or conc H_2SO_4 in a vacuum desiccator. Further purification is by distillation from $MgSO_4$, and by fractional crystallisation from the melt. Store it under vacuum or under dry N_2. [Bernasconi et al. *J Am Chem Soc* **107** 3621 *1985*, *Beilstein* **2** IV 474.]

Chloroacetic anhydride *[541-88-8]* **M 171.0, m 46°, b 122-123°/20mm, 203°/760mm, d_4^{20} 1.5494.** Crystallise it from *benzene. [Eglinton et al. *J Chem Soc* 1860 *1954*, *Beilstein* **2** IV 487.]

Chloroacetone *[78-95-5]* **M 92.5, b 61°/50mm, 119°/763mm, d_4^{20} 1.15.** Dissolve it in water and shake it repeatedly with small amounts of diethyl ether which extracts, preferentially, 1,1-dichloroacetone present as an impurity. The chloroacetone is then extracted from the aqueous phase using a large volume of diethyl ether, and distill at slightly reduced pressure. It is dried with $CaCl_2$ and stored at Dry-ice temperature. *Alternatively*, it is kept over $CaSO_4$ for several hours, distilled and stored over $CaSO_4$. It is steam volatile. The *2,4-dinitrophenylhydrazone* forms yellow needles from EtOH with **m** 120° or 124°. [*Beilstein* **1** IV 3215.] **LACHRYMATOR with toxic vapour.**

Chloroacetonitrile *[107-14-2]* **M 75.5, b 125°.** Reflux it with P_2O_5 for one day, then distil it through a helices-packed column. Also purified by gas chromatography. [*Beilstein* **2** IV 492.] **LACHRYMATORY AND HIGHLY TOXIC.**

2-Chlorobutane *[78-86-4]* **M 92.6, b 68.5°, d_4^{20} 0.873, n^{25} 1.3945.** Purify it in the same way as *n*-butyl chloride. [*Beilstein* **1** IV 248.]

***N*-Chlorocarbonyl isocyanate** *[27738-96-1]* **M 105.5, m –68°, b 63.6°/atm, d_4^{20} 1.310.** Fractionally distil it at 760mm using a 40cm column. **TOXIC** *vapour, use a good fume hood.* Store it dry, its IR (film) has ν_{max} at 2260 (NCO), 1818 (CO) and 1420 (NCO sym) cm^{-1}. [Jäckl & Sundmeyer *Chem Ber* **106** 1752 *1975*.]

2-Chloroethanol (ethylene chlorohydrin) *[107-07-3]* **M 80.5, b 51.0°/31mm, 128.6°/760mm, d_4^{20} 1.201, n^{15} 1.444.** Dry it with, then distil it from, $CaSO_4$ in the presence of a little Na_2CO_3 to remove traces of acid. [*Beilstein* **1** IV 1372.]

2-Chloroethyl bromide (1-bromo-2-chloroethane) *[107-04-0]* **M 143.4, b 106-108°, d_4^{20} 1.723, n_D^{20} 1.490.** Wash it with conc H_2SO_4, water, 10% Na_2CO_3 solution, and again with water, then dry with $CaCl_2$ and fractionally distil before use. [*Beilstein* **1** H 89, **1** I 28, **1** II 61, **1** III 179, **1** IV 155.]

2-Chloroethyl chloroformate *[627-11-2]* **M 143.0, b 52-54°/12mm, 153°/760mm, d_4^{18} 1.3760, n_D^{20} 1.446.** Purify it by fractional distillation, preferably in a vacuum, and store it in a dry atmosphere. [Jones *J Chem Soc* 2735 *1957*, *Beilstein* **3** IV 24.]

2-Chloroethyl vinyl ether *[110-75-8]* **M 106.6, b 109°/760mm, d_4^{20} 1.048, n_D^{20} 1.437.** Wash the ether repeatedly with equal volumes of water made slightly alkaline with KOH, dry with sodium, and distil it under a vacuum. Stabilise it with ~0.01% of triethanolamine. [*Beilstein* **1** IV 2051.] **TOXIC**.

Chlorofluoroacetonitrile (ClFCHCN) *[± 92484-61-2 and 359-05-7]* **M 93.4, b 66°/atm, d_4^{20} 1.267, n_D^{25} 1.3627.** It is prepared from ethyl chlorofluoroacetate (see below) by conversion to the amide (0.5mol, b 72-77°/1mm) which is added slowly to, P_2O_5 (0.25mol), and the nitrile (3.5g) is distilled off at 50-70°/atmospheric and redistilled (30g, 66°/atmospheric). It is slowly hydrolysed by H_2O but rapidly by aqueous alkali. [Young &

Tarrant *J Am Chem Soc* **71** 2432 *1949*, *Beilstein* **2** III 454]. Theoretical studies of the molecular dynamics of the enantiomers {(+)- [85196-70-9] and (–)- [85196-71-0]} have been made although they had not been separated [Roselli et al. *J Mol Liq* **28** 1 *1984*, Evans *Phys Rev* A **30** 2062 *1984*, Craig & Elsam *Chem Phys* **73** 349 *1982*]. Samarium (II) iodide [32248-43-4] promotes the reaction of chlorofluoroacetonitrile with aldehydes to form cyanofluorohydrins in the presence of HMPA [Asano et al. *Synthesis* 1309 *2007*].

Chloroform *[67-66-3]* **M 119.4, b 61.2°, d^{15} 1.49845, d^{10} 1.47060, n^{15} 1.44858.** It reacts slowly with oxygen, or oxidising agents, when exposed to air and light, giving, mainly, phosgene, Cl_2 and HCl. Commercial $CHCl_3$ is usually stabilised with up to 1% of EtOH or of dimethylaminoazobenzene. Simplest purifications involve washing with water to remove the EtOH, drying with K_2CO_3 or $CaCl_2$, refluxing with P_2O_5, $CaCl_2$, $CaSO_4$ or Na_2SO_4, and distilling. **It must not be dried with sodium.** The distilled $CHCl_3$ should be stored in the dark to avoid photochemical formation of phosgene. In an alternative purification, $CHCl_3$ (500ml) was shaken (mechanically) with several small portions of 12% H_2SO_4 for 1 hour, washed thoroughly with water, saturated $NaHCO_3$, washed again with water, and dried over $CaCl_2$ or K_2CO_3 (100g) for 1 hour before filtering and distilling. After further drying for a short time over P_2O_5, the $CHCl_3$ was redistilled and stored over Drierite in the dark [Reynolds & Evans *J Am Chem Soc* **60** 2559 *1938*].
EtOH can be removed from $CHCl_3$ by passage through a column of activated alumina, or through a column of silica gel 4-ft long by 1.75-in diameter at a flow rate of 3ml/minute. (The alumina column, which can hold about 8% of its weight of EtOH, is regenerated by air drying and then heating at 600° for 6 hours. It is pre-purified by washing with $CHCl_3$, then EtOH, leaving in conc H_2SO_4 for about 8 hours, washing with water until the washings are neutral, then air drying, followed by activation at 600° for 6 hours. Just before use it is reheated for 2 hours at 154°.) [McLaughlin et al. *Anal Chem* **30** 1517 *1958*.]
Carbonyl-containing impurities can be removed from $CHCl_3$ by percolation through a Celite column impregnated with 2,4-dinitrophenylhydrazine (DNPH), phosphoric acid and water. (Prepared by dissolving 0.5g DNPH in 6ml of 85% H_3PO_4 by grinding together, then mixing with 4ml of distilled water and 10g of Celite.) [Schwartz & Parks *Anal Chem* **33** 1396 *1961*]. Chloroform can be dried by distillation from powdered type 4A Linde molecular sieves. For use as a solvent in IR spectroscopy, chloroform is washed with water (to remove EtOH), then dried for several hours over anhydrous $CaCl_2$ and fractionally distilled. This treatment removes material absorbing near 1600 cm^{-1}. (Percolation through activated alumina increases this absorbing impurity). [Goodspeed & Millson *Chem Ind (London)* 1594 *1967*, *Beilstein* **1** IV 42.]
Rapid purification: Pass through a column of basic alumina (Grade I, 10g/ml of $CHCl_3$), and either dry by standing over 4A molecular sieves, or *alternatively*, distil from P_2O_5 (3% w/v). Store away from light (to avoid formation of phosgene which is tested by shaking with conc NH_3 forming urea) and use as soon as possible.

Chloromethyl methyl ether (MOMCl) *[107-30-2]* **M 80.5, b 55-57°, d_4^{20} 1.060, n_D^{20} 1.396.** If suspect (check IR), shake it with saturated aqueous $CaCl_2$ solution, dry over $CaCl_2$ and fractionally distil taking the middle fraction. *Alternatively*, it can be prepared afresh. While working in a fume cupboard, a rapid stream of HCl gas ([7647-73-6] from a cylinder, or generated from concentrated H_2SO_4 on NaCl) is bubbled through a solution of MeOH (438ml, 10.9moles) and technical formalin **(**900ml, 252g, 8.4moles, [50-00-0]) which is cooled with running water. After 2 hours two layers are formed, but HCl flow is continued for 2 to 3 hours further until saturation. The MOMCl layer is separated, the aqueous phase is saturated with $CaCl_2$, and the additional MOMCl that is salted out is combined with the first lot, dried over $CaCl_2$, filtered and fractionally distilled at atmospheric pressure. The fraction that distils at 55-60° is redistilled to give pure MOMCl (586-600g, 86-89%). [Marvel & Porter *Org Synth* Coll Vol **I** 377 *1941*, *Beilstein* **1** H 580, **1** I 304, **1** II 645, **1** III 2587, **1** IV 3046.] **VERY TOXIC VAPOUR** and **CARCINOGENIC**.

1-Chloro-2-nitroethane *[625-47-8]* **M 109.5, b 37-38°/20mm, 55°/60mm, 127.5°/atm, n_D^{20} 1.4224, n^{25} 1.4235.** Dissolve it in alkali, extract with ether (discard), then the aqueous phase is acidified with hydroxylamine hydrochloride, and the nitro compound is collected and fractionally distilled under reduced pressure. [Pearson & Dillon *J Am Chem Soc* **75** 2439 *1953*, *Beilstein* **1** H 101, **1** III 202, **1** IV 173.]

Chloropicrin (trichloronitromethane) *[76-06-2]* **M 164.5, b 112°.** Dry it over $MgSO_4$ and fractionally distil. [*Beilstein* **1** IV 106.] **EXTREMELY NEUROTOXIC, use appropriate precautions.**

***RS*-2-Chloropropionic acid** *[598-78-7]* **M 108.5, b 98°/3mm, d $_4^{20}$ 1.182, n $_D^{20}$ 1.453 pK^{25} 2.89.** Dry it with P_2O_5 and fractionally distil it under vacuum. [*Beilstein* **2** IV 745.]

***S*-(–)-2-Chloropropionic acid** *[29617-66-1]* **M 108.5, b 77°/10mm, 80.7°/10mm, 185-188°/atm, d $_4^{25}$ 1.2485, n $_D^{25}$ 1.436, [α] $_D^{25}$ –14.6° (neat).** Purify the acid by fractionating twice through a 115cm Podbielniak column (calculated 50 theoretical plates at atmospheric pressure) using a take-off ratio of 1:5. The *acid chloride* is prepared by dissolving the acid in $SOCl_2$, adding a few drops of PCl_3, refluxing and then distilling through a 30cm column, **b** 53°/100mm, [α] $_D^{25}$ –4.6° (neat), d $_4^{25}$ 1.2689, n $_D^{25}$ 1.4368. [Fu et al. *J Am Chem Soc* **76** 6954 *1954*, *Beilstein* **2** IV 745.]

3-Chloropropionic acid *[107-94-8]* **M 108.5, m 41°, pK^{25} 4.08.** Crystallise the acid from petroleum ether or *benzene. [*Beilstein* **2** IV 748.]

3-Chloropropyl bromide (1-bromo-3-chloropropane) *[109-70-6]* **M 157.5, b 142-145°, n^{25} 1.4732.** Wash it with conc H_2SO_4, water, 10% Na_2CO_3 solution, water again and then dry with $CaCl_2$ and fractionally distil it just before use [Akagi et al. *J Am Chem Soc* **78** 4034 *1956*]. [*Beilstein* **1** H 109, **1** IV 212.]

2-Chloro-1,1,1-triethoxyethane *[51076-95-0]* **M 196.7, b 75-80°/5mm, 91°/25mm, 147°/atm, d $_4^{25}$ 1.024, n $_D^{20}$ 1.422.** Distil the chloroethane in a vacuum; but if it is discoloured or suspect, then it is better to prepare it anew. To $(EtO)_3CH$ (ethyl orthoformate see [122-51-0]) in CCl_4 add a slight excess of *N*-chlorosuccinimide and heat to 60° while exposing to a sun lamp. An exothermic reaction occurs during 30 minutes; filter off the succinimide formed, evaporate and distil the residue *in vacuo.* [McElvain & Nelson *J Am Chem Soc* **64** 1825 *1942*, Mylari et al. *Synth Commun* **19** 2921 *1989*, Ueno et al. *J Med Chem* **34** 2468 *1991*, *Beilstein* **2** III 442, **2** IV 482.]

2-Chlorotriethylamine hydrochloride *[869-24-9]* **M 172.1, m 208-210°, pK$_{Est}$ ~8.6 (free base).** Crystallise the salt from absolute MeOH (to remove highly coloured impurities). [*Beilstein* **4** III 240.]

Chlorotrifluoroethylene (CTFE) *[79-38-9]* **M 116.5, b –26 to –24°.** Scrub it with 10% KOH solution, then 10% H_2SO_4 solution to remove inhibitors, dry and pass it through silica gel. It is stabilised with ~1% tributylamine. Use brass equipment. [*Beilstein* **1** III 646.] **TOXIC GAS.**

Chlorotrifluoromethane *[75-72-9]* **M 104.5, m –180°, b –81.5°.** Main impurities are CO_2, O_2, and N_2. The CO_2 is removed by passage through saturated aqueous KOH, followed by concentrated H_2SO_4. The O_2 is removed using a tower packed with activated copper on Kieselguhr at 200°, and the gas is dried over P_2O_5. [Miller & Smyth *J Am Chem Soc* **79** 20 *1957*, *Beilstein* **1** III 42, **1** IV 34.] **TOXIC GAS.**

Choline acetate ([2-hydroxyethyl]trimethylammonium acetate) *[16586-35-7]* **M 163.2, m varies with amount of H_2O.** Choline acetate is a *very hygroscopic* solid and should be kept in well stoppered containers, preferably under N_2 or Ar. [Sasaki & Kobayashi *J Agric Chem Soc* **23** 456 *1949*, *Chem Abstr* **47** 2696 *1953*.] It forms a *gold complex* $[HOCH_2CH_2N^+(Me)_3][AcO^-]$ $[AuCl_3]$ with **m** 263°. *Choline Reineckate* has **m** 267-270° (from aqueous Me_2CO, **m** 226-258° was also reported). *Choline picrate* has **m** 247-247.5° (from EtOH, **m's** of 237-238° and 242-245° were also reported) [Taylor & Kraus *J Am Chem Soc* **69** 1732 *1947*] and *choline picrolonate* has **m** 186° (from EtOH). [*Beilstein* **4** IV 1444.]

Choline chloride ([2-hydroxyethyl]trimethylammonium chloride) *[67-48-1]* **M 139.6, m 302-305°(dec).** *Extremely deliquescent*. Check purity by $AgNO_3$ titration or by titration of OH-base after passage through an anion-exchange column. Crystallise it from absolute EtOH, or EtOH/Et_2O, dry it under vacuum and store it in a vacuum desiccator over P_2O_5 or $Mg(ClO_4)_2$. [*Beilstein* **4** IV 1443.]

Citraconic acid (methylmaleic acid) *[498-23-7]* **M 130.1, m 91°, pK $_1^{25}$ 2.2, pK $_2^{25}$ 5.60 (cis).** Steam distil and crystallise it from EtOH/ligroin. [*Beilstein* **2** H 768, **2** I 309, **2** II 652, **2** III 1938, **2** IV 2230.]

Citraconic anhydride (methylmaleic anhydride) *[616-02-4]* **M 112.1, m 8-9°, b 109°/30mm, 132°/74mm, 213°/760mm, d $_4^{20}$ 1.245, n $_D^{20}$ 1.472.** Possible contamination is from the acid formed by hydrolysis. If the IR

has OH bands, then reflux with Ac_2O for 30 minutes, evaporate, and distil the residue in a vacuum; otherwise distil in a vacuum. Store it in a dry atmosphere. [Vaughan & Andersen *J Am Chem Soc* **77** 6702 *1955*, Vaughan & Andersen *J Org Chem* **21** 680 *1956*, *Beilstein* **17** H 440, **17** I 234, **17** II 448, **17** III/IV 5912, **17/11** V 65.]

Citric acid (H_2O) *[5949-29-1 (monohydrate); 77-92-9 (anhydrous)]* **M 210.1, m 156-157°, 153° (anhyd), pK_1^{25} 2.96, pK_2^{25} 4.38, pK_3^{25} 5.68.** Crystallise it from hot H_2O solution (w/w solubility is 54% at 10°, 71% at 50° and 84% at 100°). The *monohydrate* (softens at ~75° and melts at ~100°) dehydrates in air or when heated gently above 40°. The *triethylester* (*[77-93-0]* **M 276.3, b 127°/1mm, 294°/atm, d_4^{20} 1.137, n_D^{20} 1.4420**) is a bitter tasting oil. [*Beilstein* **3** H 556 and 568, **3** IV 1272.]

Citronellal (3,7-dimethyloctan-6-al) *[R(+) 2385-77-5, S(–) 5949-05-3]* **M 154.3, b 67°/4mm, 89°/14mm, 104-105°/21mm, 207°/760mm, $[\alpha]_{546}^{20}$ (+) and (–) 20°, $[\alpha]_D^{20}$ (+) and (–) 16.5° (neat).** Fractionally distil it. *Alternatively*, extract it with $NaHSO_3$ solution, wash it with Et_2O, then acidify it to decompose the bisulfite adduct and extract with Et_2O, dry (Na_2SO_4), evaporate and distil. Check for purity by hydroxylamine titration. The ORD in MeOH (c 0.167) has: $[\alpha]_{700}$ +9°, $[\alpha]_{589}$ +11°, $[\alpha]_{275}$ +12° and $[\alpha]_{260}$ +12°. The *semicarbazone* has **m** 85°, and the *2,4-dinitrophenylhydrazone* has **m** 79-80°. [(+)-compound: Tietze & Beifuss *Org Synth* **71** 167 *1993*, IR: Carroll et al. *J Chem Soc* 3457 *1950*, ORD: Djerassi & Krakower *J Am Chem Soc* **81** 237 *1959*, *Beilstein* **1** IV 3515.]

β–Citronellene (2,6-dimethylocta-2,7-diene) *[S-(+) 2436-90-0, R-(–) 10281-56-8]* **M 138.3, b 153-154°/730mm, 155°/atm, d_4^{22} 0.757, n_D^{22} 1.431, $[\alpha]_{546}^{20}$ (+) and (-) 13°, $[\alpha]_D^{20}$ (+) and (–) 10° (neat).** Purify it by distillation over Na (three times) and fractionation. [(–) Arigoni & Jeager *Helv Chim Acta* **37** 881 *1954*, (+) Eschenmoser & Schinz *Helv Chim Acta* **33** 171 *1950*, *Beilstein* **1** IV 1059-1060.]

β–Citronellol (3,7-dimethyloctan-6-ol) *[R-(+): 11171-61-9, S-(-): 106-22-9]* **M 156.3, b 47°/1mm, 102-104(110)°/10mm, 112-113°/12mm, 221-224°/atm, 225-226°/atm, d_4^{24} 0.8551, n_D^{24} 1.4562, $[\alpha]_{546}^{20}$ (+) and (-) 6.3°, $[\alpha]_D^{20}$ (+) and (-) 5.4° (neat).** Purify them by distillation through a cannon packed (Ni) column and the main cut collected at 84°/14mm and redistilled. Also purify *via* the benzoate. [IR: Eschenazi *J Org Chem* **26** 3072 *1961*, Naves *Bull Soc Chim Fr* 505 *1951*, *Beilstein* **1** IV 2188.]

Crotonaldehyde (2-butenal) *[123-73-9]* **M 70.1, b 104-105°, d_4^{20} 0.851, n_D^{20} 1.437.** Fractionally distil it under N_2, through a short Vigreux column. Stabilise it with 0.01% of 2,6-di-tert-butyl-*p*-cresol and store it in sealed ampoules. [*Beilstein* **1** IV 3447.]

***trans*-Crotonic acid (*trans*-2-butenoic acid)** *[107-93-7]* **M 86.1, m 72-72.5°, pK_1^{25} –6.17 (aqueous H_2SO_4), pK_2^{18} 4.71.** Distil the acid under reduced pressure and/or recrystallise it from petroleum ether (b 60-80°) or water, or by partial freezing of the melt. [*Beilstein* **2** IV 1498.]

***E*- and *Z*-Crotonitrile (mixture)** *[4786-20-3]* **M 67.1, b 120-121°, d_4^{20} 1.091, n_D^{20} 1.4595.** Separate the mixture by preparative GLC on a column using 5% FFAP on Chromosorb G. [Lewis et al. *J Am Chem Soc* **108** 2818 *1986*, *Beilstein* **2** IV 1507.]

***trans*-Crotonoyl chloride** *[625-35-4]* **M 104.5, b 42-45°/20mm, 124-125°/760mm, d_4^{20} 1.080, n_D^{20} 1.4570.** If the IR of a film has no OH bands, then fractionally distil it, taking the middle fraction and redistilling it. If OH bands are present then add excess of oxalyl chloride, reflux for 3 hours, then distil off the reagent and fractionally distil the crotonoyl chloride as before. Stabilise the distillate with 160ppm of hydroquinone. The *amide* forms needles **m** 158° from aqueous ammonia, and the *anilide* also forms needles from H_2O, but with **m** 115-118°. [*Beilstein* **2** H 411, **2** I 188, **2** II 392, **2** III 1265, **2** IV 1506.]

Crotyl bromide *[29576-14-5]* **M 135.0, b 103-105°/740mm, n^{25} 1.4792.** Dry the bromide with $MgSO_4/CaCO_3$ mixture and fractionally distil it through an all-glass Todd column. [*Beilstein* **1** IV 789.]

Cyanoacetamide *[107-91-5]* **M 84.1, m 119.4°.** Crystallise the amide from MeOH/dioxane (6:4), then water

and dry it over P_2O_5 under vacuum. [*Beilstein* **2** IV 1891.]

Cyanoacetic acid *[372-09-8]* **M 85.1, m 70.9-71.1°, pK^{25} 2.47.** Recrystallise the acid to constant melting point from *benzene/acetone (2:3), and dry it over silica gel. [*Beilstein* **2** H 583, **2** I 253, **2** II 530, **2** III 1626, **2** IV 1888.]

Cyanoacetic acid hydrazide *[140-87-4]* **M 99.1, m 114.5-115°.** Crystallise the hydrazide from EtOH. The *hydrochloride* has **m** 178-180° and the *benzylidene* derivative has **m** 178°. It is converted to *3-oxo-5-iminopyrazolidine* in hot 40% aqueous NaOH. [*Beilstein* **2** H 591, **2** I 256, **2** III 1636.] **IRRITANT.**

Cyanoguanidine (dicyanodiamide) *[461-58-5]* **M 84.1, m 209.5°, pK^{25} -0.4.** Recrystallise cyanoguanidine from water or EtOH. [*Beilstein* **3** IV 160.]

***n*-Decane** *[124-18-5]* **M 142.3, m –29.7°, b 57.6°/10mm, 174.1°, d $_4^{20}$ 0.7300, n $_D^{20}$ 1.4102, n^{25} 1.40967.** It can be purified by shaking with conc H_2SO_4, washing with water, aqueous $NaHCO_3$, and more water, then drying with $MgSO_4$, refluxing with Na and distilling. Also purify through a column of silica gel or alumina. It has been purified by azeotropic distillation with 2-butoxyethanol, the alcohol being washed out of the distillate using water, the decane is next dried and redistilled. It can be stored with NaH. Further purification can be achieved by preparative gas chromatography on a column packed with 30% SE-30 (General Electric methyl-silicone rubber) on 42/60 Chromosorb P at 150° and 40psig, using helium [Chu *J Chem Phys* **41** 226 *1964*]. It is soluble in EtOH and Et_2O. [*Beilstein* **1** IV 484.]

Decan-1,10-diol *[112-47-0]* **M 174.3, m 72.5-74°.** Crystallise the diol from dry ethylene dichloride. [*Beilstein* **1** IV 2613.]

***n*-Decanol (*n*-decyl alcohol)** *[112-30-1]* **M 158.3, f 6.0°, b 109°/8mm, 231°/atm, d $_4^{20}$ 0.823, n $_D^{20}$ 1.434.** Fractionally distil *n*-decanol in an all-glass unit at 10mm pressure (**b** 110°), then fractionally crystallise by partial freezing. Also purify by preparative GLC, and by passage through alumina before use. [*Beilstein* **1** IV 1815.]

***n*-Decyl bromide (1-bromodecane)** *[112-29-8]* **M 221.2, b 117-118°/15.5mm, d $_4^{20}$ 1.066.** Shake the it with H_2SO_4, wash with H_2O, dry with K_2CO_3, and fractionally distil it. [*Beilstein* **1** IV 470.]

Decyltrimethylammonium bromide *[2082-84-0]* **M 280.3, m 239-242°.** Crystallise the salt from 50% (v/v) EtOH/Et_2O, or from acetone and wash with ether. Dry it under vacuum at 60°. Also recrystallise it from EtOH and dry it over silica gel. [McDonnell & Kraus *J Am Chem Soc* **73** 2170 *1952*, Dearden & Wooley *J Phys Chem* **91** 2404 *1987*, *Beilstein* **4** IV 784.]

Diacetamide *[625-77-4]* **M 101.1, m 75.5-76.5°, b 222-223°.** Purify the amide by recrystallisation from MeOH [Arnett & Harrelson *J Am Chem Soc* **109** 809 *1987*]. [*Beilstein* **2** H 181.]

(+)-Di-*O*-acetyl-L-tartaric anhydride [(*R,R*)-2,3-diacetoxysuccinic anhydride] *[6283-74-5]* **M 216.2, m 129-132°, 133-134°, 135°, 137.5°, [α] $_D^{20}$ +97.2° (c 0.5, dry $CHCl_3$), [α] $_D^{20}$ +60° (c 6, Me_2CO).** If the IR is good, i.e. no OH bands, then keep it in a vacuum desiccator overnight (over P_2O_5/paraffin) before use. If OH bands are present then reflux 4g in Ac_2O (12.6ml) containing a few drops of conc H_2SO_4 for 10 minutes (use a relatively large flask), pour onto ice, collect the crystals, wash with dry *C_6H_6 (2 x 2ml), stir with 17ml of cold Et_2O, filter and dry in it a vacuum desiccator as above, or store it in dark evacuated ampoules under N_2 in small aliquots. It is not very stable in air, the melting point of the crystals drop one degree in the first four days then remains constant (132-134°). If placed in a stoppered bottle, it becomes gummy and the **m** falls 100° in three days. Recrystallisation leads to decomposition. If good quality anhydride is required it, should be prepared freshly from tartaric acid. It sublimes in a CO_2 atmosphere. [Shriner & Furrow *Org Synth* Coll Vol **IV** 242 *1963*, Bell *Aust J Chem* **34** 671 *1981*, *Beilstein* **18** III/IV 2296.]

Diallyl amine (*N*-2-propenyl-2-propen-1-amine) *[124-02-7]* **M 97.2, b 107-111°/760mm, 112°/760mm, d_4^{20} 0.789, n_D^{20} 1.440, pK^{20} 9.42.** Keep the amine over KOH pellets overnight, decant and distil it from a few pellets of KOH at atmospheric pressure (**b** 108-111°), then fractionate through a Vigreux column. [Vliet *J Am Chem Soc* **46** 1307 *1924*, *Org Synth* Coll Vol **1** 201 *1941*.] The *hydrochloride* has **m** 164-165° (from Me_2CO/EtOH). [Butler & Angels *J Am Chem Soc* **79** 3128 *1957*.]

(+)-*N,N'*-Diallyl tartardiamide (DATD) *[58477-85-3]* **M 228.3, m 184°, $[\alpha]_{546}$ +141° (c 3, MeOH).** Wash DATD with Et_2O containing 10% EtOH until the washings are clear and colourless, and dry *in vacuo*. [*FEBS Lett* **7** 293 *1970*, *Beilstein* **4** H 218.]

1,4-Diaminobutane dihydrochloride (putrescine 2HCl) *[333-93-7]* **M 161.1, m >290°, pK_1^{25} 9.63, pK_2^{25} 10.80.** Crystallise the salt from EtOH/H_2O. [*Beilstein* **4** IV 1284.]

2,2'-Diaminodiethylamine (diethylenetriamine) *[111-40-0]* **M 103.2, b 208°, d_4^{20} 0.95, n_D^{20} 1.483, pK_1^{25} 4.34, pK_2^{25} 9.13, pK_3^{25} 9.94.** Dry the amine with Na and distil, preferably under reduced pressure, or in a stream of N_2. [*Beilstein* **4** IV 1284.]
§ Polymer-bound diethylenetriamine is commercially available.

3,3'-Diaminodipropylamine (Norspermidine, bis-[3-aminopropyl]amine) *[56-18-8]* **M 131.2, b 152°/50mm, d_4^{20} 0.938, n_D^{20} 1.481, pK_1^{25} 7.72, pK_2^{25} 9,57, pK_3^{25} 10.65.** Dry the amine with Na and distil it under vacuum. [*Beilstein* **4** IV 1278.]

1,8-Diaminooctane *[373-44-4]* **M 144.3, m 50-52°, 51-52°, 52-53°, b 121°/18mm, 120°/24mm, pK_1^{20} 10.1, pK_2^{20} 11.0.** Distil the diamine under vacuum in an inert atmosphere (N_2 or Ar), cool and store the distillate in an inert atmosphere in the dark. The *dihydrochloride* has **m** 273-274°. [Nae & Le *Helv Chim Acta* **15** 55 *1955*, *Beilstein* **4** III 612.]

1,5-Diaminopentane *[462-94-2]* **M 102.2, m 14-16°, b 78-80°/12mm, 101-103°/35mm, 178-180°/750mm, d_4^{20} 0.869, n_D^{20} 1.458, pK_1^{20} 10.02, pK_2^{20} 10.96.** Purify the base by distillation, after standing over KOH pellets (at room temperature, i.e. liquid form). Its *dihydrochloride* has **m** 275° (sublimes in a vacuum), and its *tetraphenyl boronate* has **m** 164°. [Schwarzenbach et al. *Helv Chim Acta* **35** 2333 *1952*, *Beilstein* **4** IV 1310.]

1,3-Diaminopropane dihydrochloride *[10517-44-9]* **M 147.1, m 243°, pK_1^{25} 8.29, pK_2^{25} 10.30.** Crystallise the salt from EtOH/H_2O. [*Beilstein* **4** IV 1258 free base.]

1,3-Diaminopropan-2-ol *[616-29-5]* **M 90.1, m 38-40°, pK_1^{25} 7.94, pK_2^{25} 9.57.** Dissolve it in an equal amount of water, shake it with charcoal and distil it at 68°/0.1mm. The distillate solidifies. It is too viscous to be distilled through a packed column. [*Beilstein* **4** IV 1694.]

1,11-Diamino-3,6,9-trioxaundecane [2,2'-oxybis(ethyleneoxy)bisethylamine] *[929-75-9]* **M 192.3, b 115°/0-2mm, 138-153°/1mm, 145-150°/2mm, 135°/3mm, n_D^{20} 1.440.** Distil the diamine under vacuum, but if it is suspect then dissolve it in EtOH add 6N HCl boil for 1 hour, evaporate to dryness, and dry the residue in a vacuum. The solid di-hydrochloride residue is treated with 4N NaOH to release the free base which is extracted into CH_2Cl_2, the extract is dried over K_2CO_3, filtered, evaporated and then distilled in a vacuum. It is a hydrophilic linker in dendrimer formation or biotinylation. [Zhan et al. *J Am Chem Soc* **123** 8914 *2001*, Han et al. *Synth Commun* **21** 79 *1999*, Bogatiskii et al. *J Org Chem USSR* (English Transl) **16** 1124 *1980*, McReynolds et al. *Bioorg Med Chem* **10** 625 *2002*.]

Diazomethane [H_2CN_2] *[334-88-3]* **M 42.0, m –145°, b –23°.** Diazomethane is produced when *N*-methyl-*N*-nitroso-amides, e.g. *N*-methyl-*N*-nitrosourea, *N,N'*-dimethyl-*N,N'*-dinitrosooxamide, *bis*-(*N*-methyl-*N*-nitroso)terephthalamide or *p*-toluenesulfonyl-*N*-methyl-*N*-nitrosoamide (Diazald), are treated with strong solutions of NaOH or KOH. [Fieser and Fieser's *Reagents for Organic Synthesis* **1** 191 *1967*, see also **2** 102 *1969*.] It has been commonly prepared from Diazald as it is commercially available, although *N*-methyl-*N*-nitrosourea, which is readily prepared and stored below 5° [Arndt *Org Synth* Coll Vol **II** 461 *1943*], is also

frequently used. *Diazomethane is a sweet smelling, highly irritating yellow gas which is TOXIC when inhaled, causing severe irritation, pulmonary oedema, asthma, chest pains, headaches, weakness as well as producing hypersensitivity reactions and skin irritation. It is a carcinogen. Diazomethane and its precursors should be handled in an efficient fume cupboard; and because of its potentially explosive nature experiments should be carried out behind a safety screen with face and eye protection.*
Preparation: A distilling flask (100ml) containing KOH (5g) in H_2O (8ml) and diluted with 95% EtOH (25ml) is heated to ~65° using a water bath, and a solution of Diazald (21.4g, see [80-11-5]) in Et_2O (130ml) is added through a dropping funnel in ~25 minutes while the ether which is yellow in colour due to the diazomethane distils off, and the distillate is collected in a receivers immersed in ice. When addition of Diazald is complete, a further volume of Et_2O (20ml) is added dropwise and distillation is continued until the Et_2O distillate is colourless. The yield of diazomethane in the distillate is ~3g. [Note that if 95% EtOH is not added to the KOH solution no diazomethane is formed since the base does not dissolve into the Et_2O.] Do **NOT** redistil this ethereal solution as an explosion may result, particularly from the smaller volume left in the flask. [For alcohol-free diazomethane distillate, the distilling flask should contain diethyleneglycol monomethyl ether (35ml), Et_2O (10ml) and KOH (6g) in H_2O (10ml) to which is added the ethereal Diazald as before.] [deBoer & Backer *Org Synth* **34** 96 1954, *Org Synth* Coll Vol **VI** 943 *1963*, *Rec Trav Chim Pays Bas* **73** 229 *1954*.] By using ^{13}C, ^{14}C and/or ^{2}H or ^{3}H methyl labeled Diazald (some of these are also commercially available) appropriately labeled diazomethane can be prepared. The amount of diazomethane is determined by adding a measured volume of 0.2N pure benzoic acid in ether to an aliquot of the ethereal diazomethane solution which will discharge the yellow colour, meaning that all the diazomethane has been consumed. Water is added to this mixture and the excess of benzoic acid is then titrated with 0.1N aqueous NaOH. (See the safer Me_3SiCHN_2 [18107-18-1].)
For most purposes it is not necessary to distil the diazomethane in ether. In such cases it is better to use *N*-methyl-*N*-nitrosourea because the unwanted products of the reaction are soluble in water. To a mixture of 50% aqueous KOH (60ml) and pure Et_2O (200ml) at 0 to 5° is added solid nitrosomethylurea (20g) with shaking or stirring. The ethereal layer becomes deep yellow and is decanted or siphoned off; or separated if in a separating funnel. The aqueous layer can be extracted with Et_2O to get a further amount of diazomethane. The ethereal solutions can be dried over KOH pellets and can be used directly or kept at ~0° for 2-3 days. [Arndt *Org Synth* Coll Vol **II** 165 *1943*] Diazomethane is a very powerful methylating agent and, in so doing the yellow colour disappears and N_2 bubbles off. It is a versatile reagent in organic synthesis [Black *Aldrichim Acta* **16** 2 *1983*.]

Di-*O*-benzoyl-(*R* and *S*)-tartaric acid (H_2O) *[R-(+) 17026-42-5, S-(–) 2743-38-6 (anhydrous), 62708-56-9 (hydrate)]* **M 376.3, m 88-89° (hydrate), 173° (anhydrous), $[\alpha]_{546}^{20}$ (+) and (–) 136° (c 2, EtOH), $[\alpha]_{D}^{20}$ (+) and (–) 117° (c 5, EtOH), $pK_{Est(1)}$ ~2.9, $pK_{Est(2)}$ ~4.2.** Crystallise the acid from water (18g from 400 ml boiling H_2O) and stir vigorously while cooling in order to obtain crystals; otherwise an oil will separate which solidifies on cooling. Dry it in a vacuum desiccator over KOH/H_2SO_4 (yield 16.4g) as *monohydrate*, **m** 88-89°.
It crystallises from xylene as the *anhydrous acid*, **m** 173° (150-153°). It does not crystallise from $*C_6H_6$, toluene, $*C_6H_6$/petroleum ether (oil), or $CHCl_3$/petroleum ether. [Butler & Cretcher *J Am Chem Soc* **55** 2605 *1933*, Acs et al. *Tetrahedron* **41** 2465 *1985*, *R*(+) *Beilstein* **9** IV 557, *S*(–) *Beilstein* **9** III 870.]

***trans*-1,4-Dibromobut-2-ene** *[821-06-7]* **M 213.9, m 54°, b 85°/10mm.** Crystallise the dibromide from ligroin and/or distil it in a vacuum. [*Beilstein* **1** IV 79.]

Dibromodichloromethane *[594-18-3]* **M 242.7, m 21.8°, b 66°/81mm, d_4^{20} 2.433, n_D^{25} 1.5499.** Crystallise CBr_2Cl_2, repeatedly from its melt, after washing with aqueous $Na_2S_2O_3$ and drying with BaO. *Alternatively*, distil it in a vacuum. Store away from light. [*Beilstein* **1** H 68, **1** III 88, **1** IV 82.]

1,2-Dibromoethane *[106-93-4]* **M 187.9, f 10.0°, b 29.1°/10mm, 131.7°/760mm, d 2.179, n^{15} 1.54160.** Wash the dibromide with conc HCl or H_2SO_4, then water, aqueous $NaHCO_3$ or Na_2CO_3, more water, and dry it with $CaCl_2$. Fractionally distil it. *Alternatively*, keep in daylight with excess bromine for 2 hours, then extract with aqueous Na_2SO_3, wash with water, dry with $CaCl_2$, filter and distil. It can also be purified by fractional crystallisation by partial freezing. Store it in the dark. [*Beilstein* **1** H 90, **1** I 28, **1** II 61, **1** III 182, **1** IV 158.]

Dibromomaleic acid *[608-37-7]* **M 273.9, m 123.5°, 125°(dec), pK_1^{25} 1.45, pK_2^{25} 4.62.** It has been recrystallised from Et_2O or $Et_2O/CHCl_3$. It is soluble in AcOH, also slightly soluble in water, but insoluble in

*C_6H_6 and $CHCl_3$. [Salmony & Simonis *Chem Ber* **38** 2583 *1905*, Ruggli *Helv Chim Acta* **3** 566 *1929*, *Beilstein* **3** IV 2224.]

1,3-Dibromopropane *[109-64-8]* **M 201.9, f –34.4°, b 63-63.5°/26mm, 76-77°/40mm, 90°/80mm, 165°/atm, d_4^{20} 1.977, n 1.522.** Wash the dibromide with dilute aqueous Na_2CO_3, then water. Dry and fractionally distil it under reduced pressure. [*Beilstein* **1** IV 216.]

***meso*-2,3-Dibromosuccinic acid** *[608-36-6]* **M 275.9, m 288-290°(sealed tube, dec), pK_1^{20} 1.56, pK_2^{20} 2.71.** Crystallise the acid from distilled water, keeping the temperature below 70°. [*Beilstein* **2** IV 1930.]

1,2-Dibromotetrafluoroethane *[124-73-2]* **M 259.8, b 47.3°/760mm.** Wash it with water, then with weak alkali. Dry with $CaCl_2$ or H_2SO_4 and distil it. [Locke et al. *J Am Chem Soc* **56** 1726 *1934*.] Also purify it by gas chromatography on a silicone DC-200 column.

Di-*n*-butylamine *[111-92-2]* **M 129.3, b 159°, d_4^{20} 0.761, n_D^{20} 1.41766, pK^{25} 11.25.** Dry this strong base with $LiAlH_4$, CaH_2 or KOH pellets, filter and distil it from BaO or CaH_2. [*Beilstein* **4** IV 550.]

Di-*tert*-butylazodicarboxylate *[870-50-8]* **M 230.3, m 89-92°**, **90-92°.** The *tert*-butyl ester has the advantage over the ethyl ester (below) in being a solid and more acid labile. It crystallises from ligroin and is best purified by covering the dry solid (22g) with petroleum ether (b 30-60°, 35-40 ml) heating to boiling and adding ligroin (b 60-90°) until the solid dissolves. On cooling, large lemon yellow crystals of the ester separate (~ 20g), **m** 90.7-92°. Evaporation of the filtrate gives a further crop of crystals [Carpino & Crowley *Org Synth* **44** 18 *1964*]. This reagent is useful in the Mitsunobu reaction [Mitsunobu *Synthesis* 1 *1981*, Gennari et al. *J Am Chem Soc* **108** 6394 *1986*, Evans et al. *J Am Chem Soc* **108** 6394 *1986*, Hughes *Org React* **42** 335 *1992*, Dodge et al. *Org Synth* **73** 110 *1996*, Hughes *Org Prep Proc Int* **28** 127 *1996*, Ferguson & Marcelle *J Am Chem Soc* **128** 4576 *2006*, see also **DEAD** and **DIAD** below].

Dibutylcarbitol (di[ethyleneglycol]-dibutyl ether, bis[2-butoxethyl]-ether *[112-73-2]* **M 218.3, b 125-130°/0.1mm, d_4^{20} 0.883, n_D^{20} 1.424.** Dibutylcarbitol is freed from peroxides by slow passage through a column of activated alumina. The eluate is then shaken with Na_2CO_3 (to remove any remaining acidic impurities), washed with water, and stored with $CaCl_2$ in a dark bottle [Tuck *J Chem Soc* 3202 *1957*]. [*Beilstein* **1** IV 2395.]

Di-*tert*-butyl dicarbonate (di-*tert*-butyl pyrocarbonate, Boc anhydride) *[24424-99-5]* **M 218.3, m 23° (21-22°), b 55-56°/0.15mm, 62-65°/0.4mm, d_4^{20} 0.950, n_D^{20} 1.409.** Melt the ester by heating at ~35°, and distil it in a vacuum. If the IR and NMR (ν_{max}1810m and 1765 cm^{-1}, δ in CCl_4 1.50 singlet) suggest that it is very impure, then wash it with an equal volume of H_2O containing citric acid to make the aqueous layer slightly acidic, collect the organic layer, dry it over anhydrous $MgSO_4$ and distil it in a vacuum. Store it away from moisture at ~ 4°. If some moisture enters the container pressure may develop since it hydrolyses to *tert*-BuOH and CO_2. It is also available commercially as a 1.0 M solution in THF. It is **FLAMMABLE.** [Pope et al. *Org Synth* **57** 45 *1977*, Keller et al. *Org Synth* **63** 160 *1985*.] It is a useful reagent for easy introduction of the *N*-Boc protecting group in amines [Iwanowicz et al. *Synth Commun* **23** 1443 *1993*], amino acids, peptides and proteins [Keller et al. *Org Synth* **63** 160 *1985*], amides [Flynn et al. *J Org Chem* **48** 2424 *1983*, Grehn et al. *Angew Chem* **97** 519 *1985*], and *N*-Boc-ylation of sensitive compounds in non-aqueous media [Kemp & Carey *J Org Chem* **54** 3640 *1989*]. Boc protection of alcohols has been achieved *via* Lewis acid catalysis [Bartoli et al. *Synlett* 2104 *2006*], and Boc reacted with 4-carboxyphenylhydrazine to form the *N,N,N'-tris*-Boc protected acid which was converted to 4-Fmoc(9-fluorenylmethoxycarbonyl ester)phenyl-hydrazine which is used as a chromophoric reagent to quantify aldehydes attached to a solid-phase since the hydrazine NH_2 group forms a coloured Schiff's base with the aldehyde [Shannon & Barany *J Org Chem* **69** 4586 *2004*]. [See the many volumes of Fieser and Fieser *Reagents for Organic Synthesis*, J Wiley & Sons, for more applications.]

***N,N*-Dibutyl formamide** *[761-65-9]* **M 157.3, b 63°/0.1mm, 118-120°/15mm, 244-246°/760mm, d_4^{20} 0.878, n_D^{20} 1.445.** Purify the amide by fractional distillation [Mandel & Hill *J Am Chem Soc* **76** 3981 *1954*]. [*Beilstein* **4** IV 565.]

Di-*tert*-butyl peroxide (*tert*-butyl peroxide) *[110-05-4]* **M 146.2, d 0.794, n_D^{20} 1.389.** Wash the peroxide with aqueous $AgNO_3$ to remove olefinic impurities, water and dry ($MgSO_4$). Free it from *tert*-butyl hydroperoxide by passage through an alumina column [Jackson et al. *J Am Chem Soc* **107** 208 *1985*], and if necessary two high vacuum distillations from room temperature to a liquid-air trap [Offenbach & Tobolsky *J Am Chem Soc* **79** 278 *1957*]. [*Beilstein* **1** IV 1619.] *The necessary protection from* **EXPLOSION** *should be used.*

Di-*n*-butyl sulfide *[544-40-1]* **M 146.3, α-form b 182°, β-form b 190-230°(dec).** Wash the sulfide with aqueous 5% NaOH, then water. Dry with $CaCl_2$ and distil it from sodium. [*Beilstein* **1** IV 1559.]

Di-*n*-butyl sulfone *[598-04-9]* **M 162.3, m 43.5°.** Purify it by zone melting. It crystallises from petroleum ether (**m** 44-44.5°), $CHCl_3$ (**m** 44°), and EtOH (**m** 45°). [*Beilstein* **1** H 371, **1** II 400, **1** III 1524, **1** IV 1561.]

***N,N'*-Di-*tert*-butylthiourea** *[4041-95-6]* **M 188.3, m 174-175°(evacuated capillary).** Recrystallise it from H_2O [Bortnick et al. *J Am Chem Soc* **78** 4358 *1956*]. [*Beilstein* **4** IV 585 for *N*-butylthiourea.]

Dichloroacetic acid *[79-43-6]* **M 128.9, m 13.5°, b 95.0-95.5°/17-18mm, d_4^{20} 1.563, n_D^{20} 1.466, pK^{25} 1.35.** Crystallise this strong acid from *benzene or petroleum ether. Dry it with $MgSO_4$ and fractionally distil it. [Bernasconi et al. *J Am Chem Soc* **107** 3612 *1985*, *Beilstein* **2** IV 498.]

***sym*-Dichloroacetone (1,3-dichloropropan-2-one)** *[534-07-6]* **M 127.0, m 41-43°, 45°, b 86-88°/12mm, 75-77°/22mm, 172-172.5°/760mm, 170-175°/760mm, d_4^{20} 1.383.** Crystallise it from CCl_4, $CHCl_3$ or *benzene and/or distil it under vacuum [Conant & Quayle *Org Synth* Coll Vol **I** 211 *1941*, Hall & Sirel *J Am Chem Soc* **74** 836 *1952*]. It is dimorphic [Daasch & Kagarise *J Am Chem Soc* **77** 6156 *1955*]. The *oxime* has **m** 130-131°, **b** 106°/25mm [*Arzneimittel-Forsch* **8** 638 *1958*]. [*Beilstein* **1** IV 3219.]

Dichloroacetonitrile *[3018-12-0]* **M 110.0, b 110-112°, d_4^{20} 1.369, n_D^{20} 1.440.** Purify the nitrile by distillation or by gas chromatography. [*Beilstein* **2** IV 506.] **FLAMMABLE.**

2,5-Dichlorobenzoic acid *[50-79-3]* **M 191.0, m 154°, b 301°/760mm, pK^{25} 2.47.** Recrystallise the acid from water. [*Beilstein* **9** IV 1005.]

2,3-Dichloro-1,3-butadiene *[1653-19-6]* **M 123.0, b 41-43°/85mm, 98°/760mm.** Crystallise it from pentane to constant melting point of –40°. A mixture of *meso* and *d,l* forms is separated by gas chromatography on an 8m stainless steel column (8mm i.d.) with 20% DEGS (diethyleneglycolsilyl chloride) on Chromosorb W (60-80 mesh) at 60° and 80ml He/min. Distil it under vacuum. [Su & Ache *J Phys Chem* **80** 659 *1976*.]

1,2-Dichloro-1,2-difluoroethane *[431-06-1]* **M 134.9, b 59°, n_D^{20} 1.376.** Purify it by fractional distillation [Hazeldine *J Chem Soc* 4258 *1952*]. For purification of a diastereoisomeric mixture, with resolution into *meso* and *rac* forms, see Machulla and Stocklin [*J Phys Chem* **78** 658 *1974*].

Dichlorodifluoromethane (Freon 12) *[75-71-8]* **M 120.9, m –158°, b –29.8°/atm, 42.5°/10atm.** Pass the gas through saturated aqueous KOH then conc H_2SO_4, and a tower packed with activated copper on Kielselguhr at 200° to remove CO_2 and O_2. A trap cooled to –29° removes a trace of high boiling material. It is a non-flammable propellant.

1,1-Dichloroethane (ethylidene dichloride) *[75-34-3]* **M 99.0, b 57.3°, d^{15} 1.18350, d_4^{20} 1.177, n^{15} 1.41975.** Shake it with conc H_2SO_4 or aqueous $KMnO_4$, then wash it with water, saturated aqueous $NaHCO_3$, again with water, dry with K_2CO_3 and distil it from CaH_2 or $CaSO_4$. Store it over silica gel. [*Beilstein* **1** IV 130.]

1,2-Dichloroethane *[107-06-2]* **M 99.0, b 83.4°, d_4^{20} 1.256, n^{15} 1.44759.** It is usually prepared by chlorinating ethylene, so that likely impurities include higher chloro derivatives and other chloro compounds depending on the impurities originally present in the ethylene. It forms azeotropes with water, MeOH, EtOH, trichloroethylene, CCl_4 and isopropanol. Its azeotrope with water (containing 8.9% water, has **b** 77°) can be

used to remove gross amounts of water prior to final drying. As a preliminary purification step, it can be steam distilled, and the lower layer is treated as below.
Shake it with conc H_2SO_4 (to remove alcohol added as an oxidation inhibitor), wash with water, then dilute KOH or aqueous Na_2CO_3 and again with water. After an initial drying with $CaCl_2$, $MgSO_4$ or by distillation, it is refluxed with P_2O_5, $CaSO_4$ or CaH_2 and fractionally redistilled. Carbonyl-containing impurities can be removed as described for chloroform. [*Beilstein* **1** IV 131.]

1,2-Dichloroethylene *[cis + trans 540-59-0]* **M 96.9, b 60° (*cis*), d $_4^{20}$ 1.284, b 48° (*trans*), d $_4^{20}$ 1.257.** Shake it successively with conc H_2SO_4, water, aqueous $NaHCO_3$ and water. Dry it with $MgSO_4$ and fractionally distil it through an efficient column to separate the *cis*- and *trans*-isomers. [*Beilstein* **1** IV 707-709.]

***cis*-1,2-Dichloroethylene** *[156-59-2]* **M 96.9, b 60.4°, d $_4^{20}$ 1.2830, n^{15} 1.44903, n $_D^{20}$ 1.4495.** Purify it by careful fractional distillation, followed by passage through neutral activated alumina. Also by shaking with mercury, drying with K_2CO_3 and distilling from $CaSO_4$. Stabilise it with 0.02% of 2,6-di-*tert*-butyl-*p*-cresol. [*Beilstein* **1** IV 707.]

***trans*-1,2-Dichloroethylene** *[156-60-5]* **M 96.9, b 47.7°, n^{15} 1.45189, d $_4^{20}$ 1.2551, n $_D^{20}$ 1.4462.** Dry it with $MgSO_4$, and fractionally distil it under CO_2. Fractional crystallisation at low temperatures has also been used. [*Beilstein* **1** IV 709.]

2,3-Dichloromaleic anhydride *[1122-17-4]* **M 167.0, m 105-115°, 120°, 121-121.5°.** Purify the anhydride by sublimation *in vacuo* [Katakis et al. *J Chem Soc, Dalton Trans* 1491 *1986*]. It has also been purified by Soxhlet extraction with hexane, recrystallisation from $CHCl_3$ and by sublimation. [MS, Relles *J Org Chem* **37** 3630 *1972*]. [*Beilstein* **17/11** V 63.]

Dichloromethane (methylene dichloride) *[75-09-2]* **M 84.9, b 40.0°, d $_4^{20}$ 1.325, n $_D^{20}$ 1.42456, n^{25} 1.4201.** Shake it with portions of conc H_2SO_4 until the acid layer remains colourless, then wash with water, aqueous 5% Na_2CO_3, $NaHCO_3$ or NaOH, then water again. Pre-dry with $CaCl_2$, and distil it from $CaSO_4$, CaH_2 or P_2O_5. Store it away from bright light in a brown bottle with Linde type 4A molecular sieves, in an atmosphere of dry N_2. Other purification steps include washing with aqueous $Na_2S_2O_3$, passage through a column of silica gel, and removal of carbonyl-containing impurities as described under **Chloroform**. It has also been purified by treatment with basic alumina, distillation, and stored over molecular sieves under nitrogen [Puchot et al. *J Am Chem Soc* **108** 2353 *1986*].
Dichloromethane from Japanese sources contained MeOH as stabiliser which is not removed by distillation. It can, however, be removed by standing over activated 3A Molecular Sieves (note that 4A Sieves cause the development of pressure in bottles), passed through activated Al_2O_3 and distilled [Gao et al. *J Am Chem Soc* **109** 5771 *1987*]. It has been fractionated through a platinum spinning band column, degassed, and distilled onto degassed molecular sieves Linde 4A (heated under high vacuum at over 450° until the pressure readings reached the low values of 10^{-6} mm, ~1-2 hours). Stabilise it with 0.02% of 2,6-di-*tert*-butyl-*p*-cresol [Mohammad & Kosower *J Am Chem Soc* **93** 2713 *1971*]. [*Beilstein* **1** IV 35.]
Rapid purification: Reflux over CaH_2 (5% w/v) and distil it. Store it over 4A molecular sieves.

1,2-Dichloropropane *[78-87-5]* **M 113°, b 95.9-96.2°, d $_4^{20}$ 1.158, n $_D^{20}$ 1.439.** Distil the propane from CaH_2. It has a limited shelf life. [*Beilstein* **1** IV 195.]

2,2-Dichloropropane *[594-20-7]* **M 113.0, b 69.3°, d $_4^{20}$ 1.090, n $_D^{20}$ 1.415.** Wash it with aqueous Na_2CO_3 solution, then distilled water, dry it over $CaCl_2$ and fractionally distil it. [*Beilstein* **1** IV 196.]

Di-*n*-decylamine *[1120-49-6]* **M 297.6, m 34°. b 153°/1mm, 359°/760mm, pK_{Est} ~11.0.** Dissolve the amine in *benzene and precipitate it as its bisulfate salt by shaking with 4M H_2SO_4. Filter, wash with *benzene, separate by centrifugation, then the free base is obtained by treating with NaOH [McDowell & Allen *J Phys Chem* **65** 1358 *1961*]. It is a strong base; store away from CO_2. [*Beilstein* **4** IV 780.]

Didodecylamine *[3007-31-6]* **M 353.7, m 51.8°, b 263-265°/27mm, d $_4^{25}$ 0.806, pK^{25} 11.00.** Crystallise the

amine from EtOH/*C_6H_6 under N_2, and store away from CO_2. It provides two crystalline forms: an α-form with **m** 44.4° and a β-form with **m** 51.8°. The *hydrochloride* has **m** 207-208°(dec, from isoProOH), the *hydroiodide* has **m** 23.8-234°(dec, sealed capillary), and the *nitrate* has **m** 125.4-125.2°(dec. sealed capillary) when crystallised from MeOH/Me_2CO. [Hoerr et al. *J Am Chem Soc* **65** 328 1943, Hoerr & Harwood *J Org Chem* **16** 779 *1951*, *Beilstein* **4** III 412, **4** IV 801.]

Didodecyldimethylammonium bromide *[3282-73-3]* **M 463.6, m 157-162°.** Recrystallise the salt from acetone, acetone/ether mixture, then from ethyl acetate, wash with ether and dry it in a vacuum oven at 60° [Chen et al. *J Phys Chem* **88** 1631 *1984*, Rupert et al. *J Am Chem Soc* **107** 2628 *1985*, Halpern et al. *J Am Chem Soc* **108** 3920 *1986*, Allen et al. *J Phys Chem* **91** 2320 *1987*]. [*Beilstein* **4** IV 801.]

Diethanolamine (2,2'-iminodiethanol) *[111-42-2]* **M 105.1, m 28°, b 154-155°/10mm, 270°/760mm pK^{25} 8.88.** Fractionally distil the amine twice, then fractionally crystallise it from its melt. Its solubility in H_2O is 10% at 20°. It absorbs CO_2 and HO_2 from the atmosphere. [Perrin & Dempsey *Buffers for pH and Metal Ion Control* Chapman & Hall, London *1974*, *Beilstein* **4** H 283, **4** II 729, **4** III 689, **4** IV 1514.]

***N,N*-Diethylacetamide** *[685-91-6]* **M 157.2, b 86-88°, d_4^{20} 0.994, n_D^{20} 1.474.** Dissolve the amide in cyclohexane, shake with anhydrous BaO and then filter. The procedure is repeated three times, and the cyclohexane is distilled off at atmospheric pressure. The crude amide is also fractionally distilled three times from anhydrous BaO. [*Beilstein* **4** III 349.]

Diethyl acetamidomalonate *[1068-90-2]* **M 217.2, m 96°.** Crystallise the ester from *benzene/petroleum ether. [*Beilstein* **4** III 2993.]

Diethyl acetylenedicarboxylate *[762-21-0]* **M 170.2, b 60-62°/0.3mm, 107-110°/11mm, 118-120°/20mm, d_4^{20} 1.0735, n_D^{20} 1.4428.** Dissolve the ester in *C_6H_6, wash it with $NaHCO_3$, H_2O, dry over Na_2SO_4, filter, evaporate and distil it in a vacuum [IR: Walton & Hughes *J Am Chem Soc* **79** 3985 *1957*, Truce & Kruse *J Am Chem Soc* **81** 5372 *1959*]. [*Beilstein* **2** H 803.]

Diethylamine *[109-89-7]* **M 73.1, b 55.5°, d_4^{20} 0.707, n 1.38637, pK^{15} 11.38.** Dry diethylamine with $LiAlH_4$ or KOH pellets. Reflux it with, and distil it from, BaO or KOH. Convert it to the *p*-toluenesulfonamide and crystallise it to constant melting point from dry petroleum ether (b 90-120°), then hydrolyse it with HCl; excess NaOH is added, and the amine is passed through a column of activated alumina. Redistil the amine and dry it with activated alumina before use [Swift *J Am Chem Soc* **64** 115 *1942*]. [*Beilstein* **4** III 313.]
§ A polystyrene diethylaminomethyl supported version is commercially available.

Diethylamine hydrochloride *[660-68-4]* **M 109.6, m 223.5°, 226-229°.** Crystallise salt from absolute EtOH. Also recrystallise it from dichloroethane/MeOH. *Hygroscopic.* [*Beilstein* **4** III 113.]

Diethyl azodicarboxylate (DEAD) *[1972-28-7]* **M 174.2, b 104.5°/12mm, 211-213°/atm, d_4^{20} 1.110, n_D^{20} 1.420.** Dissolve DEAD in toluene, wash it with 10% $NaHCO_3$ till neutral (may require several washes if too much hydrolysis had occurred: check IR for OH bands), then it wash with H_2O (2x), dry it over Na_2SO_4, filter, evaporate the toluene and distil it through a short Vigreux column at as high a vacuum as possible. The main portion boils at 107-111°/15mm. *Since it is likely to explode, use an oil bath for heating the still and all operations should be carried out behind an adequate shield with head protection.* [Rabjohn *Org Synth* Coll Vol **III** 375 *1955*, see Kauer *Org Synth* Coll Vol **IV** 412 *1963*]. [*Beilstein* **3** III 233.] It is commercially available as a 40% solution in toluene. This reagent is useful in the Mitsunobu reaction [Mitsunobu *Synthesis* 1 *1981*, Gennari et al. *J Am Chem Soc* **108** 6394 *1986*, Evans et al. *J Am Chem Soc* **108** 6394 *1986*, Hughes *Org React* **42** 335 *1992*, Dodge et al. *Org Synth* **73** 110 *1996*, Hughes *Org Prep Proc Int* **28** 127 *1996*, Ferguson & Marcelle *J Am Chem Soc* **128** 4576 *2006*; see also di-*tert*-butyl azodicarboxylate above and **DIAD** below].
§ A polystyrene supported DEAD version is commercially available with a loading of ~1.2mmol/g.

Diethyl bromomalonate *[685-87-0]* **M 239.1, b 116-118°/10mm, 122-123°/20mm, d_4^{20} 1.420, n_D^{20} 1.4507.** Purify the ester by fractional distillation in a vacuum. Its IR (film) has ν_{max} 1800 and 1700cm^{-1} [Abramovitch

Can J Chem **37** 1146 *1959*, Bretschneider & Karpitschka *Monatsh Chem* **84** 1091 *1053*]. [*Beilstein* **2** IV 1904.]

Diethyl *tert*-butylmalonate *[759-24-0]* **M 216.3, b 40-42°/0.03, 102-104°/11mm, 109.5-110.5°/17mm, 205-210°/760mm, d_4^{20} 0.980, n_D^{20} 1.425.** Dissolve it in Et_2O, wash with aqueous $NaHCO_3$, H_2O, dry ($MgSO_4$), filter, evaporate and distil the residue. Identify by hydrolysis to the acid and determine the neutralisation equivalent (theor: 80.0). The *acid* has **m** 155-157° effervescence [Hauser et al. *J Am Chem Soc* **64** 2715 *1942*, Bush & Beauchamp *J Am Chem Soc* **75** 2949 *1953*]. [*Beilstein* **2** IV 2027.]

Diethyl carbonate *[105-58-8]* **M 118.1, b 124-125°, 126.8°, d_4^{20} 0.975, n^{25} 1.38287.** Wash the ester (100ml) with an aqueous 10% Na_2CO_3 (20ml) solution, saturated $CaCl_2$ (20ml), then water (30ml). After drying by standing over solid $CaCl_2$ for 1 hour (note that prolonged contact should be avoided because slow combination with $CaCl_2$ occurs), it should be fractionally distilled. Also dry it over $MgSO_4$ and distil it. [*Beilstein* **3** H 5, **3** I 4, **3** II 4, **3** III 5, **3** IV 5.]

Diethyl disulfide *[110-81-6]* **M 122.3, b 86.2°/87mm, 154-155°/atm, d_4^{20} 0.993, n_D^{20} 1.506.** Dry the disulfide over silica gel or $MgSO_4$ and distil it under reduced pressure (optionally from $CaCl_2$). [*Beilstein* **1** H 347, **1** I 173, **1** II 345, **1** III 1377, **1** IV 1379.]

Diethylene glycol *[111-46-6]* **M 106.1, f -10.5°, b 244.3°, d_4^{20} 1.118, n^{15} 1.4490, n_D^{20} 1.4475.** Fractionally distil it in a vacuum (**b** 133°/14mm, 2.5cm x 1.3m heli-grid column), then recrystallise it by partial freezing. [Feldman et al. *J Am Chem Soc* **73** 4341 *1951*, *Beilstein* **1** III 2090, **1** IV 2390.]

Diethylene glycol diethyl ether *[112-36-7]* **M 162.2, b 76°/32mm, 85-86°/10mm, 188.2-188.3°/751mm, d_4^{20} 0.910, n_D^{20} 1.412.** Dry the ether with $MgSO_4$, then CaH_2 or $LiAlH_4$, under N_2. If sodium is used, the ether should be redistilled alone to remove any products which may be formed by the action of sodium on the ether. As a preliminary purification, the crude ether (2L) can be refluxed for 12 hours with 25ml of conc HCl in 200ml of water, under reduced pressure, with slow passage of N_2 to remove aldehydes and other volatile substances. After cooling, add sufficient solid KOH pellets (slowly and with shaking until no more dissolves) to give two liquid phases. The upper of these is decanted, dried with fresh KOH pellets, decanted, then refluxed over, and distilled from sodium. It can be passed through (alkaline) alumina prior to purification. [*Beilstein* **1** IV 2394.]

Diethylene glycol ditosylate *[7460-82-4]* **M 414.5, m 86-87°, 87-88°, 88-89°**. Purify the ester by recrystallisation from Me_2CO and dry it in a vacuum. [*Beilstein* **11** III 225.]

Diethylene glycol mono-*n*-butyl ether (butyl carbitol) *[112-34-5]* **M 162.2, b 69-70°/0.3mm, 230.5°/760mm, d_4^{20} 0.967, n_D^{20} 1.4286.** Dry the ether with anhydrous K_2CO_3 or $CaSO_4$, filter and fractionally distil it. Peroxides can be removed by refluxing with stannous chloride or a mixture of $FeSO_4$ and $KHSO_4$ (or, less completely, by filtration under slight pressure through a column of activated alumina). [*Beilstein* **1** IV 2394.]

Diethylene glycol monoethyl ether *[111-90-0]* **M 134.2, b 201.9°, d_4^{20} 0.999, n_D^{20} 1.4273, n^{25} 1.4254.** Ethylene glycol can be removed by extracting 250g in 750ml of *benzene with 5ml portions of water, allowing for phase separation, until successive aqueous portions show the same volume increase. Dry, and free from peroxides, as described for diethylene glycol mono-*n*-butyl ether. [*Beilstein* **1** IV 2393.]

Diethylene glycol monomethyl ether *[111-77-3]* **M 120.2, b 194°, d_4^{20} 1.010, n_D^{20} 1.423.** Purify it as for diethylene glycol mono-*n*-butyl ether. [*Beilstein* **1** IV 2392.]

Diethylenetriaminepenta-acetic acid (DTPA, DEPTAPAC) *[67-43-6]* **M 393.4, m 219-220°, pK_1^{25} 1.79, pK_2^{25} 2.56, pK_3^{25} 4.42, pK_4^{25} 8.76, pK_5^{25} 10.42.** Crystallise DTPA from water. Dry it under vacuum or at 110°. [Bielski & Thomas *J Am Chem Soc* **109** 7761 *1987*, NMR: Wenzel et al. *Anal Chem* **54** 615 *1982*, *Beilstein* **4** IV 2454.]

Diethyl ether (ethyl ether) *[60-29-7]* **M 74.1, b 34.6°/760mm, d_4^{20} 0.714, n^{15} 1.3555, n_D^{20} 1.35272.** Usual

impurities are water, EtOH, diethyl peroxide (which is explosive when concentrated), and aldehydes. Peroxides [detected by liberation of iodine from weakly acid (HCl) solutions of KI, or by the blue colour in the ether layer when 1mg of $Na_2Cr_2O_7$ and 1 drop of dilute H_2SO_4 in 1ml of water is shaken with 10ml of ether] can be removed in several different ways. The simplest method is to pass dry ether through a column of activated alumina (80g Al_2O_3/700ml of ether). More commonly, 1L of ether is shaken repeatedly with 5-10ml of a solution comprising 6.0g of ferrous sulfate and 6ml of conc H_2SO_4 in 110ml of water. Aqueous 10% Na_2SO_3 or stannous chloride can also be used. The ether is then washed with water, dried for 24 hours with $CaCl_2$, filtered and dried further by adding sodium wire until it remains bright. The ether is stored in a dark cool place, until distilled from sodium before use. Peroxides can also be removed by wetting the ether with a little water, then adding excess $LiAlH_4$ or CaH_2 and leaving to stand for several hours. (This also dried the ether.)
Werner [*Analyst* **58** 335 *1933*] removed peroxides and aldehydes by adding 8g $AgNO_3$ in 60ml of water to 1L of ether, then 100ml of 4% NaOH and shaking for 6 minutes. Fierz-David [*Chimia* **1** 246 *1947*] shook 1L of ether with 10g of a zinc-copper couple. (This reagent is prepared by suspending zinc dust in 50ml of hot water, adding 5ml of 2M HCl and decanting after 20 seconds, washing twice with water, covering with 50ml of water and 5ml of 5% cuprous sulfate with swirling. The liquid is decanted and discarded, and the residue is washed three times with 20ml of ethanol and twice with 20ml of diethyl ether).
Aldehydes can be removed from diethyl ether by distillation from hydrazine hydrogen sulfate, phenylhydrazine or thiosemicarbazide. Peroxides and oxidisable impurities have also been removed by shaking with strongly alkaline saturated-$KMnO_4$ (with which the ether was left to stand in contact for 24 hours), followed by washing with water, conc H_2SO_4, water again, then drying ($CaCl_2$) and distillation from sodium, or sodium containing benzophenone to form the ketyl. Other purification procedures include distillation from sodium triphenylmethide or butyl magnesium bromide, and drying with solid NaOH or P_2O_5. [*Beilstein* **1** IV 1314.]
Rapid purification: Same as for 1,4-dioxane.

Diethyl ethoxymethylene malonate *[87-13-8]* **M 216.2, b 014°/0.2mm, 109°/0.5mm, 279-283°/atm, d $_4^{20}$ 1.079, n $_D^{20}$ 1.4623.** Likely impurity is diethyl diethoxymethylene malonate which is difficult to separate from diethyl ethoxymethylene malonate by distillation, and it is necessary to follow the course of the distillation by the change in refractive index instead of boiling point. After a low boiling fraction is collected, there is obtained an intermediate fraction (n $_D^{20}$ 1.414—1.458), the size of which depends on the amount of the diethoxymethylene compound. This fraction is fractionated through a 5inch Vigreux column at low pressure, and avoiding interruption in heating. Fraction **b** 108-110°/0.25mm is *ca* 10° lower than the submitters' fraction (**b** 97.2°/0.25mm, n $_D^{20}$ 1.4612—1.4623) [*Org Synth* Coll Vol **III** 395 *1955*, Fuson et al. *J Org Chem* **11** 197 *1946*, Duff & Kendal *J Chem Soc* 893 *1948*]. [*Beilstein* **3** IV 1192.]

***N,N′*-Dimethylethylenediamine [1,2-bis(methylamino)ethane]** *[110-70-3]* **M 88.2, b 110-112°/750mm, 119°/760mm, d $_4^{20}$ 0.819, n $_D^{20}$ 1.431, (pK^{25} 7.01 and 9.88).** This strong base has been prepared in various ways including hydrolysis of *N,N'-di(benzylsulfonyl)-N,N'-dimethylethylenediamine* (**m 217-219°**, from AcOH) and concentrated HCl (120-130°) [Johnson & Bailey *J Am Chem Soc* **38** 2135 *1916*], the reaction of 1,2-dibromoethane with 21-33% aqueous $MeNH_2$ in EtOH (reflux for 2 hours, 50% yield) [Kermack & Wight *J Chem Soc* 1421 *1935*, Woodburn & O'Gee *J Org Chem* **17** 1235 *1952*], hydrolysis of *N,N'-di(p-toluenesulfonyl)-N,N'-dimethylethylenediamine* (1mol, **m 164°**, from AcOH) with H_2SO_4 (8.2mol) and H_2O (9mol) at 140-145°/7 hours [Boon *J Chem Soc* 307 *1947*], LAH reduction in THF of *3-benzenesulfonyloxy-5,6-dihydrouracil* (**m 175-176°**, from iso-PrOH) and isolated as the *dibenzoyl derivative* (41%, **m 177-178°**, from $*C_6H_6$) [Bauer *J Am Chem Soc* **78** 1945 *1956*], and by catalytic hydrogenation of *N-benzyl-N,N'-dimethylethylenediamine* (**b 73-74°/0.1mm**) with 10% Pd/C [Jucker & Rissi *Helv Chim Acta* **45** 2383 *1962*]. General isolation and purification procedures involve steam distillation of the product diamine, acidifying the distillate with HCl, evaporating to dryness, treating the residual salt with 10% excess of cold 32% aqueous NaOH, collecting the organic layer (**care**: very caustic solution), drying it over solid KOH, and distilling from it. Final distillation of the dry base over Na has been reported (see also [107-15-3]). The diamine is a strong base and readily absorbs CO_2 and H_2O from the atmosphere—store it in a dark stoppered bottle, wax the stopper if it should be stored for long periods. The *dihydrochloride* [5752-40-9] has **m 235-236°(dec)**, and the *picrate* has **m 160°** (from EtOH and Me_2CO in rectangular plates). It forms complexes with Cu, Ni, and Pt among other metals. Its FT-IR (neat) has ν_{max} at

3285.5, 2788.2, 1447.2, 1346.5, 1251.0, 1106.5, 1040.5, 876.9, 763.7 cm^{-1}. [For pK and metal complexes see Gastafson & Martell *J Am Chem Soc* **81** 525 *1959*, *Beilstein* **4** H 250, **4** I 415, **4** II 689, **4** III 512, **4** IV 1171.]

***N,N'*-Diethylformamide** *[617-84-5]* **M 101.2, b 29°/0.5mm, 61-63°/10mm, 178.3-178.5°/760mm, d $_4^{20}$ 0.906, n $_D^{25}$ 1.4313.** Distil it under reduced pressure, then at atmospheric pressure [Wintcler et al. *Helv Chim Acta* **37** 2370 *1954*, NMR: Hoffmann *Z Anal Chem* **170** 177 *1959*]. [*Beilstein* **4** IV 346.]

Diethyl fumarate *[623-91-6]* **M 172.2, b 218°, d 1.052, n 1.441.** Wash the fumarate with aqueous 5% Na_2CO_3, then with saturated $CaCl_2$ solution, dry with $CaCl_2$ and distil it. [*Beilstein* **2** IV 2207.] Note that **dimethyl fumarate** *[624-49-7]* **M 144.1, m 102°, b 192-193°/atm** is a solid. [*Beilstein* **2** IV 2205.]

***N,N*-Diethyl-1,1,2,3,3,3-hexafluoropropylamine (Ishikawa's Reagent, perfluoropropyldiethylamine, PPDA)** *[309-88-6]* **M 223.2, b 56-57°/58mm d $_4^{25}$ 1.230, n $_D^{20}$ 1.3460.** When this reagent is prepared from diethylamine (11g, 0.15mol) in dry Et_2O (30ml) in a glass pressure bomb cooled to –70° (Me_2CO/Dry Ice), and liquefied *F*-propene (25.5g, 0.17mol, see[116-15-4]) is added, and the temperature of the sealed bomb is allowed to rise to ~25°, and stirred at this temperature overnight, the reaction is complete. Crystalline $Et_2NH.HF$ is removed by fitration, the solvent (Et_2O) is evaporated, and the residual oil is distilled in a vacuum to give a liquid (23.7g, ~72%) which boils at **56-57°/58mm**. This liquid is shown, by its ^{19}F NMR signal intensities, to be a 3:1 mixture of PPDA and exclusively (*E*)-*N,N*-**d**iethyl-**p**entafluoro-**p**ropenyl**a**mine (*trans*-dppa) with respectively δ_F [PPDA] at -3.0 (1-CF_3), 6.0 (3-CF_A), 11.0 (3-CF_B), 131.0 (2-CF), and δ_F [*trans*-dppa] at –12.0 (1–CF_3, $^{1,3}J$ = 14Hz, $^{1,4}J$ = 23.5Hz), 41.0 (3-CF, $^{1,4}J$ = 23.5Hz, $^{1,3}J_{trans}$ = 117Hz), 122 (2-CF, $^{1.3}J$ = 14Hz, $^{1,3}J_{trans}$ = 117Hz) upfield from external CF_3CO_2H with 3:1 relative intensities. The mixture is easy to handle, and is stable on storage at room temperature without discolouration or loss of activity for at least 6 months. It reacts with a variety of CHOH groups to form the respective CHF derivatives, with carboxylic acids to form the acid fluorides [Takaoka, Iwakiri and Ishikawa *Bull Chem Soc Jpn* **11** 3377 *1979*, Watanabe, Fujita, Ushi and Kitazume *J Fluorine Chem* **31** 247 *1986*, Watanabe, Fujita, Sakamoto, Kuramochi and Kitazume *J Fluorine Chem* **36** 361 *1987*], and allylic alcohols to form α-fluoro-α-(trifluoromethyl)-γ,δ-unsaturated amide precursors [Ogu, Akazome and Ogura *Tetrahedron Lett* **39** 305 *1998*]. The crude 3:1 reaction product has been used satisfactorily without distillation. The presence of 33% of *trans*-dppa is not a drawback because HF is liberated in these reaction of PPDA with OH, and the HF that is liberated adds on to the olefinic *trans*-dppa to give PPDA; so that as long as there is at least equal amounts of these two compounds the mixture behaves as if it were completely made up of DDPA.
When the above synthesis is carried out at ~5-10° while *F*-propene is bubbled through (completely absorbed within 2 hours), then stirred at ~25° overnight, an oil is obtained (89% yield) with **51-53°/58mm** which is a 1:1 mixture (by ^{19}F NMR) of PPDA and *trans*-dppa. If *n*-Bu_2NH, or piperidine, replace Et_2NH in the reaction at –70° in sealed bombs, (*n*-$Bu)_2N$-CF_2CHFCF_3 and (*E*)-(*n*-$Bu)_2N$-CF=$CFCF_3$ (**55-57°/5mm**, 2:1, 78% yield) or $C_5H_{10}N$-CF_2CHFCF_3 only (**49-50°/7mm**, 80% yield) respectively are obtained [Takaoka, Iwakiri and Ishikawa *Bull Chem Soc Jpn* **11** 3377 *1979*].

Diethyl ketone (3-pentanone) *[96-22-0]* **M 86.1, b 102.1°, d $_4^{20}$ 0.8099, n $_D^{20}$ 1.392.** The ketone is dried with anhydrous $CaSO_4$ or $CuSO_4$, and distil from P_2O_5 under N_2 or under reduced pressure. Further purification is by conversion to the semicarbazone (recrystallise to constant **m** 139°, from EtOH) which, after drying *in vacuo* over $CaCl_2$ and paraffin wax, is refluxed for 30 minutes with excess oxalic acid, then steam distilled and salted out with K_2CO_3. Dry with Na_2SO_4 and distil [Cowan et al. *J Chem Soc* 171 *1940*]. [*Beilstein* **1** IV 3279.]

Diethyl malonate *[105-53-3]* **M 160.2, b 92°/22mm, 198-199°/760mm, d $_4^{20}$ 1.056, d^{25} 1.0507, n $_D^{20}$ 1.413.** If too impure (IR, NMR) the ester (250g) is heated on a steam bath for 36 hours with absolute EtOH (125ml) and conc H_2SO_4 (75ml), then fractionally distilled under reduced pressure. Otherwise fractionally distil it under reduced pressure and collect the steady boiling middle fraction. [*Beilstein* **2** IV 1881.]

2,2-Diethyl-1,3-propanediol *[115-76-4]* **M 132.2, m 61.4-61.8°, b 130-133°/16mm, n $_D^{20}$ 1.4574.** Crystallise the diol from petroleum ether (b 65-70°). **IRRITANT.** [McKusick *J Am Chem. Soc* **70** 1982 *1948*, *Beilstein* **1**

III 2217, **1** IV 2589.]

Diethyl pyrocarbonate (DEP) *[1609-47-8]* **M 162.1, b 38-40°/12mm, 160-163°/atm, d $_4^{20}$1.119, n $_D^{20}$ 1.398.** Dissolve the ester in Et_2O, wash it with dilute HCl, H_2O, dry over Na_2SO_4, filter, evaporate and distil the residue first *in vacuo* then at atmospheric pressure. It is soluble in alcohols, esters, ketones and hydrocarbon solvents. A 50% w/w solution is usually prepared for general use. **Treat with great CAUTION as DEP irritates the eyes, mucous membranes and skin.** [Boehm & Mehta *Chem Ber* **71** 1797 *1938*, Thoma & Rinke *Justus Liebigs Ann Chem* **624** 30 *1959*, *Beilstein* **3** IV 18.]

Diethyl succinate *[123-25-1]* **M 174.2, b 105°/15mm, 218°/atm, d $_4^{20}$ 1.047, n $_D^{20}$ 1.4199.** Dry the succinate with $MgSO_4$, and distil it at 15mm pressure. [*Beilstein* **2** IV 1914.]

Diethyl sulfate *[64-67-5]* **M 154.2, b 96°/15mm, 118°/40mm, d $_4^{20}$ 1.177, n $_D^{20}$ 1.399.** Wash the ester with aqueous 3% Na_2CO_3 (to remove acidic material), then distilled water, dry ($CaCl_2$), filter and distil it in a vacuum. *It is an ethylating agent and blisters the skin.* [*Beilstein* **1** IV 1236.]

Diethyl sulfide *[352-93-2]* **M 90.2, m 0°/15mm, b 90.1°/760mm, d $_4^{20}$ 0.837, n $_D^{20}$ 1.443.** Wash the sulfide with aqueous 5% NaOH, then water, dry with $CaCl_2$ and distil it from sodium. It can also be dried with $MgSO_4$ or silica gel. *Alternative*, purification is *via* the Hg(II) chloride complex [$(Et)_2S.2HgCl_2$] (see dimethyl sulfide). [*Beilstein* **1** IV 1394.]

Diethyl (–)-D- (from the non-natural) *[13811-71-7]* **and (+)-L- (from the natural acid)** *[89-91-2]* **tartrate M 206.2, m 17°, b 80°/0.5mm, 162°/19mm, 278-282°/atm, d $_4^{20}$ 1.204, n $_D^{20}$ 1.4476, [α] $_D^{20}$ (+) and (+) 26.5° (c 1, H_2O) and (–) and (+) 8.5° (neat), [α] $_{546}^{20}$ (+) and (+) 30° (c 1, H_2O).** Distil the esters under high vacuum and store them under vacuum or in an inert atmosphere in a desiccator in round bottomed flasks equiped with a vacuum stopcock. They have also been distilled by Kügelrohr distillation and/or by 'wiped-film' molecular distillation. They are slightly soluble in H_2O but miscible with EtOH and Et_2O. [Gao et al. *J Am Chem Soc* **109** 5770 (5771) *1987*, IR: Pristera *Anal Chem* **25** 844 *1953*, *Beilstein* **3** III 1025 for D-(–), **3** IV 1232 for L(+).]

***sym*-Diethylthiourea** *[105-55-5]* **M 132.2, m 76-77°. 77-79°.** Crystallise it from *benzene. [*Beilstein* **4** H 118, **4** I 355, **4** II 610, **4** III 220, **4** IV 375.]

Difluoroacetic acid *[381-73-7]* **M 96.0, m –0.35°, b 67-70°/20mm, 134°/760mm, d $_4^{20}$ 1.530, n $_D^{20}$ 1.3428, pK^{25} 1.28.** Purify the acid by distilling over P_2O_5. The *acid chloride* is a fuming liquid **b** 25°/atm, the *amide* has **b** 108.6°/35mm, **m** 52° (from *C_6H_6), and the *anilide* has **b** 90°/1mm, 114°/5mm, **m** 58° [Henne & Pelley *J Am Chem Soc* **74** 1426 *1952*, Coffman et al. *J Org Chem* **14** 749 *1949*, NMR: Meyer et al. *J Am Chem Soc* **75** 4567 *1953*, pK: Wegscheider *Z Phys Chem* **69** 614 1909]. [*Beilstein* **2** IV 455.]

Diglycolic acid (2-oxapentane-1,5-dioic acid) *[110-99-6]* **M 134.1, m 148° (monohydrate), pK $_1^{25}$ 2.97, pK $_2^{25}$ 4.37.** Crystallise diglycolic acid from water. [*Beilstein* **3** IV 577.]

Diglyme [bis(2-methoxyethyl) ether, diethylene glycol dimethyl ether] *[111-96-6]* **M 134.2, b 62°/17mm, 75°/35mm, 160°/760mm, d $_4^{20}$ 0.917, n $_D^{20}$ 1.4087.** Dry diglyme with NaOH pellets or CaH_2, then reflux with, and distil it (under reduced pressure) from Na, CaH_2, $LiAlH_4$, $NaBH_4$ or NaH. These operations are carried out under N_2. The amine-like odour of diglyme has been removed by shaking with a weakly acidic ion-exchange resin (Amberlite IR-120) before drying and distilling. Addition of 0.01% $NaBH_4$ to the distillate inhibits peroxidation. Purify it also as for dioxane. It has been passed through a 12-in column of molecular sieves to remove water and peroxides. [*Beilstein* **1** IV 2393.]

Dihydroxyfumaric (1,2-dihydroxybut-1-ene-1,2-dioic) acid dihydrate *[133-38-0]* **M 184.1, m 155°(dec), pK $_1^{25}$ 1.57, pK $_2^{25}$ 3.36.** Crystallise the acid from water. [*Beilstein* **3** IV 1975.]

1,2-Diiodoethane *[624-73-7]* **M 281.9, m 81-84°, d 2.134.** Dissolve it in ether, wash it with saturated aqueous $Na_2S_2O_3$, dry it over $MgSO_4$, and evaporate the ether *in vacuo* then distil it. Store it in the dark.

[Molander et al. *J Am Chem Soc* **109** 453 *1987*]. [*Beilstein* **1** IV 169.]

Diiodomethane (methylene diiodide) *[75-11-6]* **M 267.8, m 6.1°, b 66-70°/11-12mm, d_4^{20} 3.325.** Fractionally distil it under reduced pressure, then fractionally crystallise it by partial freezing, and stabilise it with silver wool if necessary. It has also been purified by drying over $CaCl_2$ and fractionally distilling from Cu powder. Store it in the dark. [*Beilstein* **1** IV 97.]

Diisopropanolamine *[110-97-4]* **M 133.2, m 41-44°, d_4^{20} 1.004, pK_{Est} ~10.7.** Crystallise the amine repeatedly from dry diethyl ether. It is a strong base, store away from CO_2 and H_2O. [*Beilstein* **4** III 761.]

Diisopropylamine *[108-18-9]* **M 101.2, b 83.5°/760mm, d_4^{20} 0.720, n_D^{20} 1.39236, pK^{25} 11.20.** Distil the amine from NaOH, or reflux it three minutes over Na wire or NaH, and distil it into a dry receiver under N_2. It is a strong base, store away from CO_2 and H_2O. [*Beilstein* **4** H 154, **4** I 369, **4** II 630, **4** III 274, **4** IV 510.]
§ A polystyrene supported version of diisopropylamine is commercially available.

Diisopropylazodicarboxylate (DIAD) *[2446-83-5]* **M 202.2, b 75°/0.2mm, d^{25} 1.420, n_D^{20} 1.420.** Purify the azo compound by distillation at as high a vacuum as possible. Since it is likely to explode, use an oil bath for heating the still, and all operations should be carried out behind an adequate shield. [Kauer *Org Synth* Coll Vol **IV** 412 *1963*, *Beilstein* **3** III 233]. This reagent is useful in the Mitsunobu reaction [Mitsunobu *Synthesis* 1 *1981*, Gennari et al. *J Am Chem Soc* **108** 6394 *1986*, Evans et al. *J Am Chem Soc* **108** 6394 *1986*, Hughes *Org React* **42** 335 *1992*, Dodge et al. *Org Synth* **73** 110 *1996*, Hughes *Org Prep Proc Int* **28** 127 *1996*, Ferguson & Marcelle *J Am Chem Soc* **128** 4576 *2006*; see also di-*tert*-butyl azodicarboxylate and **DEAD** above].

Diisopropylethylamine (Hünig's base) *[7087-68-5]* **M 129.3, b 119°/731mm, 127°/760mm, d_4^{27} 1.440, n_D^{25} 1.4376, pK_{Est} ~10.9.** Distil the amine from ninhydrin, then from KOH [Dryland & Sheppard, *J Chem Soc, Faraday Trans 1* 125 *1986*]. It is a strong base and should be stored in the absence of carbon dioxide. [Hünig & Kiessel *Chem Ber* **91** 380, 387 *1958*, Wotiz et al. *J Org Chem* **24** 1202 *1959*, *Beilstein* **4** IV 551.]

Diisopropyl ketone (2,4-dimethyl-3-pentanone) *[565-80-0]* **M 114.2, b 124°, d 0.801, n 1.400.** Dry the ketone with $CaSO_4$, shake it with chromatographic alumina and fractionally distil it from P_2O_5 under N_2. [*Beilstein* **1** IV 3334.]

Diketene See 2-methylene-oxetan-2-one in "Heterocyclic Compounds", in this Chapter, and see ketene below.

2,3-Dimercapto-1-propanol (BAL, British Anti-Lewisite) *[59-52-9]* **M 124.2, b 82-84°/0.8mm, 120°/15mm, d_4^{20} 1.239, n_D^{20} 1.5732, pK_1^{25} 8.62, pK_2^{25} 10.75.** Precipitate BAL as the Hg mercaptide [see Björberg *Chem Ber* **75** 13 *1942*], regenerate with H_2S, and distil it under a vacuum [Rosenblatt & Jean *Anal Chem* 951 *1955*]. *It is an antidote for heavy metal (As, Hg, Au, etc.) poisoning*. [*Beilstein* **1** IV 2770.]

1,3-Dimercapto-2-propanol *[584-04-3]* **M 124.2, b 68-69°/0.8mm, 82°/1.5mm, 94°/12mm, n_D^{23} 1.5696.** Purify the dithiol as for 2,3-dimercapto-1-propanol above. [Johary & Owen *J Chem Soc* 1305 *1955*, *Beilstein* **1** IV 2773 or **2** IV 1102.]

***meso*-2,3-Dimercaptosuccinic acid** *[304-55-2]* **M 182.2, m 191-192°(dec), 210°(dec), 210-211° (dec), pK_1^{25} 2.71, pK_2^{25} 3.48, pK_3^{25} 8.89, pK_4^{25} 10.75.** Purify the acid by dissolving it in NaOH and precipitating with dilute HCl, drying and recrystallising from MeOH. IR has $\nu_{\square\square\square}$ at 2544 (SH) and 1689 (CO_2H) cm^{-1}. The *bis-S-acetyl* derivative has **m** 183-185° (from EtOAc or Me_2CO), and its *Me ester* has **m** 119-120° (from petroleum ether) [Gerecke et al. *Helv Chim Acta* **44** 957 *1961*, Owen & Sultanbawa *J Chem Soc* 3112 *1949*]. [*Beilstein* **3** III 1033.]

1,2-Dimethoxyethane (DME, glycol dimethyl ether, glyme) *[110-71-4]* **M 90.1, b 84°, d_4^{20} 0.867, n 1.380.** Traces of water and acidic materials have been removed from it by refluxing with Na, K or CaH_2, decanting and distilling from Na, K, CaH_2 or $LiAlH_4$. The reaction has been speeded up by using vigorous high-speed stirring with molten potassium. For virtually complete elimination of water, 1,2-dimethoxyethane has been dried with

Na-K alloy until a characteristic blue colour is formed in the solvent at Dry-ice/cellosolve temperatures: the solvent is kept with the alloy until distilled for use [Ward *J Am Chem Soc* **83** 1296 *1961*]. *Alternatively*, glyme, refluxed with benzophenone and Na-K, is dry enough if, on distillation, it gives a blue colour of the ketyl immediately on addition to benzophenone and sodium [Ayscough & Wilson *J Chem Soc* 5412 *1963*]. It has also been purified by distillation under N_2 from sodium benzophenone ketyl (see above). [*Beilstein* **1** IV 2376.]

***N,N*-Dimethylacetamide (DMAc)** *[127-19-5]* **M 87.1, b 58.0-58.5°/11.4mm, 66-67°/15mm, 85-87°/33mm, 96°/80mm, 163-165°/760mm, d_4^{20} 0.940, n_D^{20} 1.4373.** Shake the amide with BaO for several days, reflux it over BaO for 1 hour, then fractionally distil it under reduced pressure. Store it over molecular sieves. It is a useful organic solvent for reactions, as it is soluble in many organic solvents and in H_2O. Use it in a fume hood because over-exposure causes liver damage, jaundice, lethargy and can irritate skin. [*Beilstein* **4** IV 180.]

***β,β*-Dimethylacrylic acid (senecioic acid, 3-methyl-2-butenoic acid)** *[541-47-9]* **M 100.1, m 68°, pK^{25} –5.4 (aqueous H_2SO_4).** Crystallise the acid from hot water or petroleum ether (b 60-80°). [*Beilstein* **2** IV 1555.]

Dimethyl adipate *[627-93-0]* **M 174.2, m 9-11°, b 109°/10mm, 121-123°/20mm, 235°/760mm, d_4^{20} 1.0642, n_D^{20} 1.4292.** Dissolve it in Et_2O, wash with $NaHCO_3$, H_2O, dry over $MgSO_4$, filter, evaporate and distil it several times until the IR and NMR are consistent with the structure [Lorette & Brown *J Org Chem* **24** 261 *1959*, Hoffmann & Weiss *J Am Chem Soc* **79** 4759 *1957*]. [*Beilstein* **2** IV 1959.]

Dimethyl adipimidate dihydrochloride *[14620-72-5]* **M 245.1, m 218-220°, 222-224°**. If the salt smells of HCl, then wash it with MeOH and dry Et_2O (1:3) under N_2 until the free HCl is completely removed. Recrystallise it from MeOH/Et_2O (it is very important that the solvents are super dry) [Hartman & Wold *Biochemistry* **6** 2439 *1967*, McElvain & Shroeder *J Am Chem Soc* **71** 40 *1949*].

Dimethylamine *[124-40-3]* **M 45.1, f –92.2°, b 0°/563mm, 6.9°/760mm, pK^{25} 10.73.** Dry dimethylamine by passage through a KOH-filled tower, or by standing with sodium pellets at 0° during 18 hours. It is a strong base — *do not inhale its vapours*. [*Beilstein* **4** IV 128.]
§ A dimethylaminomethyl polystyrene supported version is commercially available.

Dimethylamine hydrochloride *[506-59-2]* **M 81.6, m 171°.** Crystallise the salt from hot $CHCl_3$ or absolute EtOH. It also recrystallises from MeOH/ether solution. Dry it in a vacuum desiccator over H_2SO_4, then P_2O_5. *Hygroscopic.* [*Beilstein* **4** IV 132.]

2-Dimethylaminoethanol *[108-01-0]* **M 89.1, b 134.5-135.5°, d_4^{20} 1.430, n_D^{20} 1.4362, pK^{25} 9.23.** Dry the amine with anhydrous K_2CO_3 or KOH, and fractionally distil it. [*Beilstein* **4** IV 1424.]

1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI, DEC, 1-ethyl-3-(3-dimethyl aminopropyl) carbodiimide hydrochloride) *[25952-53-8]* **M 191.7, m 113.5-114.5°, 114-116°, pK_{Est} ~ 10.3.** It is an excellent H_2O-soluble peptide coupling reagent. It is purified by dissolving (*ca* 1g) in CH_2Cl_2 (10ml) at room temperature and then add dry Et_2O (~110ml) dropwise and the crystals that separate are collected, washed with dry Et_2O, recrystallised from CH_2Cl_2/Et_2O and dried in a vacuum over P_2O_5. It is important to work in a dry atmosphere or work rapidly, and then dry the solid as soon as possible. The material is moderately *hygroscopic*, but once it becomes wet it reacts slowly with H_2O. Store it away from moisture at –20° to slow down the hydrolysis process. The *free base* has **b** 47-48°/0.27mm, 53-54°/0.6mm, n_D^{25} 1.4582. The *methiodide* is recrystallised from $CHCl_3$/EtOAc, the crystals are filtered off, washed with dry Et_2O, recrystallised from $CHCl_3$/Et_2O, and dried *in vacuo* over P_2O_5, **m** 93-95°, 94-95°. [Sheehan et al. *J Am Chem Soc* **87** 2492 *1965*, Sheehan & Cruickshank *Org Synth* Coll Vol **V** 555 *1973*.]
§ A polymer bound version is commercially available.

***N,N*-Dimethylbiuret** *[7710-35-2]* **M 131.1, m 178°.** Purify it by repeated crystallisation from the melt, or from H_2O. [Bredereck & Richter *Chem Ber* **99** 2461 *1968*, Dunning & Close *J Am Chem Soc* **75** 3615 *1953*.]

2,3-Dimethyl-1,3-butadiene *[513-81-5]* **M 82.2, m –69-70°, b 68-69°/760mm, d_4^{20} 0.727, n_D^{20} 1.4385.** Distil

it from $NaBH_4$, and purify it by zone melting. [*Beilstein* **1** IV 1023.]

1,3-Dimethylbutadiene sulfone (1,3-dimethylsulfolene, 2,4-dimethyl-2,5-dihydrothiophen-1,1-dioxide) *[10033-92-8]* **M 145.2, m 40.4-41.0°.** Crystallise the sulfone from diethyl ether (three times), or from CCl_4 (**m** 39.5-40°). [Grummitt et al. *J Am Chem Soc* **72** 5768 *1950*, *Beilstein* **17/1** V 97.]

2,2-Dimethylbutane *[75-83-2]* **M 86.2, b 49.7°, d_4^{20} 0.649, n^{25} 1.36595.** Distil it azeotropically with MeOH, then wash it with water, dry (Na_2SO_4) it, and distil it. [*Beilstein* **1** IV 367.]

2,3-Dimethylbutane *[79-29-8]* **M 86.2, b 58.0°, d_4^{20} 1.375, n^{25} 1.37231.** Distil it from sodium, pass it through a column of silica gel (activated by heating in nitrogen to 350° before use) to remove unsaturated impurities, and again distil it from sodium. Also distil it azeotropically with MeOH, then wash with water, dry (Na_2SO_4), filter and redistil it. [*Beilstein* **1** IV 371.]

2,3-Dimethylbut-2-ene *[563-79-1]* **M 84.2, b 72-73°/760mm, d_4^{20} 0.708, n_D^{20} 1.41153.** Purify it by GLC on a column of 20% squalene on chromosorb P at 50° [Flowers & Rabinovitch *J Phys Chem* **89** 563 *1985*]. Also wash it with 1M NaOH solution followed by H_2O. Dry it over Na_2SO_4, distil it over powdered KOH under nitrogen and pass it through activated alumina before use. [Woon et al. *J Am Chem Soc* **108** 7990 *1986*, Wong et al. *J Am Chem Soc* **109** 3428 *1987*, *Beilstein* **1** IV 853.]

Dimethylcarbamoyl chloride *[79-44-7]* **M 107.5, m –33°, b 34°/0.1mm, d_4^{20} 1.172, n_D^{20} 1.4511.** It must be distilled under high vacuum to avoid decomposition. It is moisture sensitive. [*Beilstein* **4** IV 224.]

Dimethyl carbonate *[616-38-6]* **M 90.1, m 2-4°, 4.65°, b 89.5°/755mm, 90.2°/atm, 90-91°/atm, d_4^{20} 1.079, n_D^{20} 1.3687.** If the reagent has broad intense bands at 3300cm^{-1} and above (i.e. OH stretching), then it should be purified further. It will contain small amounts of water and/or alcohol which form azeotropes with it. Wash it successively with 10% Na_2CO_3 solution, saturated $CaCl_2$, H_2O, and dry it by shaking mechanically for 1 hour with anhydrous $CaCl_2$, and fractionate. *Alternatively*, stand it for several days in contact with Linde type 4A molecular sieves, then fractionally distil it. The middle fraction is frozen slowly at 2°, several times, retaining 80% of the liquid at each cycle. [Bowden & Butler *J Chem Soc* 78 *1939,* Vogel *J Chem Soc* 1847 *1948*, *Beilstein* **3** IV 3.]

Dimethyl dicarbonate (dimethyl pyrocarbonate) *[4525-33-1]* **M 134.1, m 15.2°, b 45-46°/5mm, d_4^{20} 1.2585, n_D^{20} 1.3950.** If the reagent has broad intense bands at 3300cm^{-1} and above (i.e. OH stretching), then it should be purified further. Dissolve it in Et_2O, shake this with a small volume of 0.1N HCl, dry the Et_2O solution (Na_2SO_4), and distil it *in vacuo* at as low pressure as possible, but below 100°, to give a clear liquid. It decomposes to CO_2 and dimethyl carbonate on heating at 123-149°. It is readily hydrolysed by H_2O and is a yeast inhibitor. It is an **IRRITANT**. [Brysov et al. *J Org Chem USSR* **10** 2551 *1974*, Boehm & Mehta *Chem Ber* **71** 1797 *1938, Beilstein* **3** IV 17.]

1,5-Dimethyl-1,5-diazaundecamethylene polymethobromide (Hexadimethrene, Polybrene) *[28728-55-4]* **M 5000—10,000 polymer.** Purify it by chromatography on Dowex 50 and/or by filtration through alumina before use [Frank *Hoppe-Seyler's Z Physiol Chemie* **360** 997 *1979*]. It is hygroscopic, and its solubility in H_2O is 10%.

***N,N'*-Dimethylethylenediamine [1,2-bis(methylamino)ethane]** *[110-70-3]* **M 88.2, b 110-112°/750mm, 119°/760mm, d_4^{20} 0.819, n_D^{20} 1.431, (pK^{25} 7.01 and 9.88).** This strong base has been prepared in various ways including hydrolysis of *N,N'-di(benzylsulfonyl)-N,N'-dimethylethylenediamine* (**m 217-219°**, from AcOH) and concentrated HCl (120-130°) [Johnson & Bailey *J Am Chem Soc* **38** 2135 *1916*], the reaction of 1,2-dibromoethane with 21-33% aqueous $MeNH_2$ in EtOH (reflux for 2 hours, 50% yield) [Kermack & Wight *J Chem Soc* 1421 *1935*, Woodburn & O'Gee *J Org Chem* **17** 1235 *1952*], hydrolysis of *N,N'-di(p-toluenesulfonyl)*

N,N'-dimethylethylenediamine (1mol, **m 164°**, from AcOH) with H_2SO_4 (8.2mol) and H_2O (9mol) at 140-145°/7 hours [Boon *J Chem Soc* 307 *1947*], LAH reduction in THF of *3-benzenesulfonyloxy-5,6-dihydrouracil* (**m 175-176°**, from iso-PrOH) and isolated as the *dibenzoyl derivative* (41%, **m 177-178°**, from *C_6H_6) [Bauer *J Am Chem Soc* **78** 1945 *1956*], and by catalytic hydrogenation of *N-benzyl-N,N'-dimethylethylenediamine* (**b 73-74°/0.1mm**) with 10% Pd/C [Jucker & Rissi *Helv Chim Acta* **45** 2383 *1962*]. General isolation and purification procedures involve steam distillation of the product diamine, acidifying the distillate with HCl, evaporating to dryness, treating the residual salt with 10% excess of cold 32% aqueous NaOH, collecting the organic layer (**care**: very caustic solution), drying it over solid KOH, and distilling from it. Final distillation of the dry base over Na has been reported (see also [107-15-3]). The diamine is a strong base and readily absorbs CO_2 and H_2O from the atmosphere—store it in a dark stoppered bottle, wax the stopper if it should be stored for long periods. The *dihydrochloride* [5752-40-9] has **m 235-236° (dec)**, and the *picrate* has **m 160°** (from EtOH and Me_2CO in rectangular plates). It forms complexes with Cu, Ni, and Pt among other metals. Its FT-IR (neat) has ν_{max} at 3285.5, 2788.2, 1447.2, 1346.5, 1251.0, 1106.5, 1040.5, 876.9, 763.7 cm^{-1}. [For pK and metal complexes see Gastafson & Martell *J Am Chem Soc* **81** 525 *1959*, *Beilstein* **4** H 250, **4** I 415, **4** II 689, **4** III 512, **4** IV 1171.]

Dimethyl disulfide *[624-92-0]* **M 94.2, f –98°, b 40°/12mm, 110°/760mm, d_4^{20} 1.0605, n 1.5260.** Pass it through neutral alumina before use. [Trost *Chem Rev* **78** 363 *1978*, *Beilstein* **1** IV 1281.]

***N,N*-Dimethylformamide (DMF)** *[68-12-2]* **M 73.1, b 40°/10mm, 61°/30mm, 88°/100mm, 153°/760mm, d_4^{20} 0.948, n^{25} 1.4269, pK^{25} –0.3.** DMF decomposes slightly at its normal boiling point to give small amounts of dimethylamine and carbon monoxide. The decomposition is catalysed by acidic or basic materials, so that even at room temperature DMF is appreciably decomposed if allowed to stand for several hours with solid KOH, NaOH or CaH_2. If these reagents are used as dehydrating agents, therefore, they should not be refluxed with the DMF. Use of $CaSO_4$, $MgSO_4$, silica gel or Linde type 4A molecular sieves is preferable, followed by distillation under reduced pressure. This procedure is adequate for most laboratory purposes. Larger amounts of water can be removed by azeotropic distillation with *benzene (10% v/v, previously dried over CaH_2), at atmospheric pressure: water and *benzene distil below 80°. The liquid remaining in the distillation flask is further dried by adding $MgSO_4$ (previously ignited overnight at 300-400°) to give 25g/L. After shaking for one day, a further quantity of $MgSO_4$ is added, and the DMF is distillied at 15-20mm pressure through a 3-ft vacuum-jacketed column packed with steel helices. However, $MgSO_4$ is an inefficient drying agent, leaving about 0.01M water in the final DMF. More efficient drying (to around 0.001-0.007M water) is achieved by standing with powdered BaO, followed by decanting before distillation, then with alumina powder (50g/L, previously heated overnight to 500-600°), and distilling from more of the alumina, or by refluxing at 120-140° for 24 hours with triphenylchlorosilane (5-10g/L), then distilling at *ca* 5mm pressure [Thomas & Rochow *J Am Chem Soc* **79** 1843 *1957*]. Free amine in DMF can be detected by the colour reaction with 1-fluoro-2,4-dinitrobenzene. It has also been purified by drying overnight over KOH pellets and then distilling from BaO through a 10 cm Vigreux column [Jasiewicz et al. *Exp Cell Res* **100** 213 *1976*]. [For efficiency of desiccants in drying dimethylformamide see Burfield & Smithers *J Org Chem* **43** 3966 *1978*, and for a review on purification, tests of purity and physical properties, see Juillard *Pure Appl Chem* **49** 885 *1977*.]
It has been purified by distilling from K_2CO_3 under high vacuum and fractionated in an all-glass apparatus. The middle fraction is collected, degassed (seven or eight freeze-thaw cycles) and redistilled under as high a vacuum as possible [Mohammad & Kosower *J Am Chem Soc* **93** 2713 *1971*]. [*Beilstein* **4** IV 171.]
Rapid purification: Stir over CaH_2 (5% w/v) overnight, filter, then distil at 20 mmHg. Store the distilled DMF over 3A or 4A molecular sieves. For solid phase synthesis, the DMF used must be of high quality and free from amines.

***d,l*-2,4-Dimethylglutaric acid** *[2121-67-7]* **M 160.2, m 144-145° $pK_{Est(1)}$~4.4, $pK_{Est(2)}$ ~5.4.** Distil the acid in steam and recrystallise it from ether/petroleum ether. [*Beilstein* **2** H 681, **2** I 284, **2** II 590, **21** III 1755, **2** IV 2022.]

3,3-Dimethylglutaric acid *[4839-46-7]* **M 160.2, m 103-104°, b 89-90°/2mm, 126-127°/4.5mm, pK_1^{25} 3.85, pK_2^{25} 6.45.** Crystallise the acid from water, *benzene or ether/petroleum ether. Dry it in a vacuum. [*Beilstein*

21 H 391, **21** I 334, **21** II 309, **21** III/IV 4601, **21/9** V 592.]

Dimethylglyoxime *[95-45-4]* **M 116.1, m 240°, pK $_1^{25}$ 10.60, pK $_2^{25}$ 11.85.** Crystallise it from EtOH (10ml/g) or aqueous EtOH. [*Beilstein* **1** III 3105.] **TOXIC.**

2,5-Dimethyl-2,4-hexadiene *[764-13-6]* **M 110.2, f 14.5°, b 132-134°, d $_4^{20}$ 0.773, n $_D^{20}$ 1.4796.** Distil it, then repeatedly fractionally crystallise it by partial freezing. Immediately before use, the diene is passed through a column containing Woelm silica gel (activity I) and Woelm alumina (neutral) in separate layers. [*Beilstein* **1** IV 1043.]

2,2-Dimethylhexane *[590-73-8]* **M 114.2, m –121.2°, b 107°, d $_4^{20}$ 0.695.** Dry the hexane over type 4A molecular sieves and distil it. [*Beilstein* **1** IV 432.]

2,5-Dimethylhexane *[592-13-2]* **M 114.2, m –91.2°, b 109°, d $_4^{20}$ 0.694.** Dry the hexane over type 4A molecular sieves and distil it. [*Beilstein* **1** IV 434.]

2,5-Dimethylhexane-2,5-diol *[110-03-2]* **M 146.2, m 88-90°.** Purify the diol by fractional crystallisation. Then the diol is dissolved in hot acetone, treated with activated charcoal, and filtered while hot. The solution is cooled and the diol is filtered off and washed well with cold acetone. The crystallisation process is repeated several times, and the crystals are dried under a vacuum in a freeze-drying apparatus [Goates et al. *J Chem Soc, Faraday Trans 1* **78** 3045 *1982*]. [*Beilstein* **1** IV 2600.]

1,1-Dimethylhydrazine *[57-14-7]* **M 60.1, b 60.1°/702mm, d $_4^{20}$ 0.790, n $_D^{20}$ 1.408 pK^{30} 7.21.** Fractionally distil the hydrazine through a 4-ft column packed with glass helices. Precipitate it as its oxalate from diethyl ether solution. After crystallising from 95% EtOH, the salt is decomposed with aqueous saturated NaOH, and the free base is distilled, dried over BaO and redistilled [McBride & Kruse *J Am Chem Soc* **79** 572 *1957*]. Distillation and storage should be under nitrogen. [*Beilstein* **4** IV 3322.]

Dimethyl itaconate *[617-52-7]* **M 158.2, m 38°, b 208°, d 1.124.** Crystallise the ester from MeOH by cooling to –78°. [*Beilstein* **2** IV 2229.]

Dimethylmaleic anhydride *[766-39-2]* **M 126.1, m 96°, b 225°/760mm.** Distil the anhydride from *benzene/ligroin and sublime in a vacuum. [*Beilstein* **17/11** V 69.]

Dimethylmalonic acid *[595-46-0]* **M 132.1, m 192-193° pK $_1^{25}$ 3.03, pK $_2^{25}$ 5.73.** Crystallise the acid from *benzene/petroleum ether. It sublimes in a vacuum with slight decomposition. [*Beilstein* **2** IV 1955.]

Dimethylnitrosamine (*N*-nitrosodimethylamine) *[62-75-9]* **M 74.0, m –28°, b 149-150°/atm, 153°/774mm, d $_4^{20}$ 1.006, n $_D^{20}$ 1.4370.** Dry the nitrosamine over anhydrous K_2CO_3 or dissolve it in Et_2O, dry it over solid KOH, filter, evaporate Et_2O and distil the yellow oily residue through a 30cm fractionating column discarding the first fraction which may contain Me_2N. Also dry over $CaCl_2$ and distil it at atmospheric pressure. All operations should be done in an efficient fume cupboard as the vapors are **TOXIC** and **CARCINOGENIC**. [Fischer *Chem Ber* **8** 1588 *1875*, Romberg *Rec Trav Chim Pays Bas* **5** 248 *1886*, Hatt *Org Synth* Coll Vol **II** 211 *1961*, Krebs & Mandt *Chem Ber* **108** 1130 *1975*.]

2,6-Dimethyl-2,4,6-octatriene see *neo*-alloocimene below.

Dimethylolurea (di-[hydroxymethyl]urea) *[140-95-4]* **M 120.1, m 137-139°.** Crystallise it from aqueous 75% EtOH. [*Beilstein* **3** IV 107.]

Dimethyl oxalate *[553-90-2]* **M 118.1, m 54°, b 163-165°, d $_4^{20}$ 1.148.** Crystallise the ester repeatedly from EtOH. De-gas it under nitrogen at high vacuum and distil it. [*Beilstein* **2** IV 1847.]

2,4-Dimethylpentane *[108-08-7]* **M 100.2, b 80.5°, d_4^{20} 0.763, n_D^{20} 1.3814, n^{25} 1.37882.** Extract it repeatedly with conc H_2SO_4, wash with water, dry and distil it. *Alternatively*, percolated it through silica gel (previously heated in nitrogen to 350°). Purify it by azeotropic distillation with EtOH, followed by washing out the EtOH with water, drying and distilling. [*Beilstein* **1** IV 406.]

4,4-Dimethyl-1-pentene *[762-62-9]* **M 98.2, b 72.5°/760mm, d_4^{20} 0.6827, n_D^{20} 1.3918.** Purify it by passing through alumina before use [Traylor et al. *J Am Chem Soc* **109** 3625 *1987*]. [*Beilstein* **1** IV 869.]

Dimethyl peroxide *[690-02-8]* **M 62.1, b 13.5°/760mm, d_4^{20} 0.8677, n_D^{20} 1.3503.** Purify dimethyl peroxide by repeated trap-to-trap fractionation until no impurities could be detected by gas IR spectroscopy [Haas & Oberhammer *J Am Chem Soc* **106** 6146 *1984*]. *All necessary precautions should be taken in case of* **EXPLOSION.**

2,2-Dimethyl-1,3-propanediol (neopentyl glycol) *[126-30-7]* **M 104.2, m 128.4-129.4°, b 208°/760mm.** Crystallise the diol from *benzene or acetone/water (1:1). [*Beilstein* **1** IV 2551.]

2,2-Dimethyl-1-propanol (*neo*-pentyl alcohol) *[75-84-3]* **M 88.2, m 52°, b 113.1°/760mm.** It is difficult to distil because it is a solid at ambient temperatures. Purify it by fractional crystallisation and sublimation. [*Beilstein* **1** IV 1690.]

***N,N*-Dimethylpropionamide** *[758-96-3]* **M 101.2, b 175-178°, d_4^{20} 0.920, n_D^{20} 1.440.** Shake the amide over BaO for 1-2 days, then distil it under reduced pressure. [*Beilstein* **4** III 126.]

***meso*-α,β-Dimethylsuccinic acid** *[608-40-2]* **M 146.1, m 211°, pK_1^{25} 3.77, pK_2^{25} 5.36.** Crystallise the *meso*-acid from EtOH/ether or EtOH/chloroform.

2,2-Dimethylsuccinic acid *[597-43-3]* **M 146.1, m 141°, pK_1^{20} 4.15, pK_2^{20} 6.40.** Crystallise the acid from EtOH/ether or EtOH/chloroform. [*Beilstein* **2** IV 1996.]

(±)-2,3-Dimethylsuccinic acid *[13545-04-5]* **M 146.1, m 129°, pK_1^{25} 3.82, pK_2^{25} 5.98.** Crystallise the *racemic* acid from water. [*Beilstein* **2** IV 1998.]

Dimethyl sulfide *[75-18-3]* **M 62.1, f –98.27°, b 0°/172mm, 37.5-38°/760mm, d^{21} 0.8458, n^{25} 1.4319.** Purify dimethyl sulfide *via* the Hg(II) chloride complex by dissolving 1 mole of $Hg(II)Cl_2$ in 1250ml of EtOH and slowly adding the boiling alcoholic solution of Me_2S to give the right ratio for $2(CH_3)_2S.3HgCl_2$. After recrystallisation of the complex to constant melting point, 500g of complex is heated with 250ml conc HCl in 750ml of water. The sulfide is separated, washed with water, and dried with $CaCl_2$ and $CaSO_4$. Finally, it is distilled under reduced pressure from sodium. Precautions should be taken (*efficient fume hood*) because of its very **UNPLEASANT ODOUR** and **TOXICITY**. [*Beilstein* **1** IV 1275.]

2,4-Dimethylsulfolane *[1003-78-7]* **M 148.2, b 128°/77mm, d^{25} 1.1314, n_D^{20} 1.474.** Distil the sulfolane in a vacuum. [*Beilstein* **17/1** IV 97.]

Dimethyl sulfone *[67-71-0]* **M 94.1, m 109°.** Crystallise the sulfone from water. Dry it over P_2O_5. [*Beilstein* **1** IV 1279.]

Dimethyl sulfoxide (DMSO) *[67-68-5]* **M 78.1, m 18.0-18.5°, b 75.6-75.8°/12mm, 190°/760mm, d_4^{20} 1.100, n_D^{20} 1.479.** This colourless, odourless, very *hygroscopic* liquid, is synthesised from dimethyl sulfide. The main impurity is water, with a trace of dimethyl sulfone. The Karl-Fischer test is applicable. It is dried with Linde types 4A or 13X molecular sieves, by prolonged contact and passage through a column of the material, then distilled under reduced pressure. Other drying agents include CaH_2, CaO, BaO and $CaSO_4$. It can also be fractionally crystallised by partial freezing. More extensive purification is achieved by standing overnight with freshly heated and cooled chromatographic grade alumina. It is then refluxed for 4 hours over CaO, dried

over CaH_2, and fractionally distilled at low pressure. For efficiency of desiccants in drying dimethyl sulfoxide see Burfield and Smithers [*J Org Chem* **43** 3966 *1978*, Sato et al. *J Chem Soc, Dalton Trans* 1949 *1986*]. [Reddy *Pure Appl Chem* **25** 459 *1969*, *Beilstein* **1** IV 1277.]
Rapid purification: Stand over freshly activated alumina, BaO or $CaSO_4$ overnight. Filter and distil it over CaH_2 under reduced pressure (~12 mmHg). Store it over 4A molecular sieves.

***N,N*-Dimethylthiocarbamoyl chloride** *[16420-13-6]* **M 123.6, m 42-43°, b 64-65°/0.1mm.** Crystallise it twice from pentane and/or distil it at low pressure. [*Beilstein* **4** III 147.]

***sym*-Dimethylurea** *[96-31-1]* **M 88.1, m 106°.** Crystallise the urea from acetone/diethyl ether by cooling in an ice bath. Also crystallise it from EtOH and dry it at 50°/5mm for 24 hours [Bloemendahl & Somsen *J Am Chem Soc* **107** 3426 *1985*]. [*Beilstein* **4** IV 207.]

2,2-Dinitropropane *[595-49-3]* **M 162.1, m 53.5°.** Crystallise it from EtOH or MeOH. Dry it over $CaCl_2$ or *in vacuo* for 1 hour just above the melting point. [*Beilstein* **2** H 117, **2** II 79, **2** III 261, **2** IV 234.]

Dioctadecyldimethylammonium bromide *[3700-67-2]* **M 630.9, m 161-163°.** Crystallise the bromide from acetone, then MeOH [Lukac *J Am Chem Soc* **106** 4387 *1984*]. Also purify it by chromatography on alumina by washing with $*C_6H_6$ and eluting with Me_2CO, evaporating and crystallising from MeCN [Swain & Kreevoy *J Am Chem Soc* **77** 1126 *1955*]. [*Beilstein* **4** IV 829.]

***N,N*-Dioctadecyl methylamine (hydrogen ionophore III)** *[4088-22-6]* **M 536.0, m 40°, 44-46°, 48-49°, b 252-259°, pK_{Est} ~10.** It can be distilled at high vacuum, but dissolving in $*C_6H_6$, filtering and evaporating give a waxy solid suitable for electrode use. It recrystallises from Me_2CO or MeCN. [Hoerr et al. *J Org Chem* **9** 201 *1944*, Wu & Yu *Talanta* **34** 577 *1987*, *Beilstein* **4** III 435.]

Dipropylene glycol (octan-4,5-diol) *[110-98-5]* **M 134.2, b 109-110°/8mm, d_4^{20} 1.022, n_D^{20} 1.441.** Fractionally distil the diol below 15mm pressure, using a packed column and taking precautions to avoid absorption of water. [*Beilstein* **1** IV 2473.]

Di-*n*-propyl ketone (4-pentanone) *[123-19-3]* **M 114.2, b 143.5°, d_4^{20} 0.8143, n_D^{20} 1.40732.** Dry 4-pentanone with $CaSO_4$, then distil it from P_2O_5 under nitrogen. [*Beilstein* **1** IV 3323.]

Di-*n*-propyl sulfide *[111-47-7]* **M 118.2, b 141-142°, d_4^{20} 0.870, n_D^{20} 1.449.** Wash the sulfide with aqueous 5% NaOH, then water. Dry it with $CaCl_2$ and distil it from Na [Dunstan & Griffiths *J Chem Soc* 1344 *1962*]. [*Beilstein* **1** IV 1452.]

***S*-1,2-Distearin (*S*-glycerol-1,2-distearate)** *[S- 1429-59-0, RS- 51063-97-9, R- 1188-58-5]* **M 625.0, m 76-77°, $[\alpha]_D^{20}$ –2.8° (c 6.3, $CHCl_3$), $[\alpha]_{546}^{20}$ +1.4° (c 10, $CHCl_3$/MeOH, 9:1).** Crystallise the glyceride from chloroform/petroleum ether. [cf p 678, *Beilstein* **2** IV 1231.]

1,4-Dithioerythritol (DTE, *erythro*-2,3-dihydroxy-1,4-dithiobutane) *[6892-68-8]* **M 154.3, m 82-84°, pK_1 9.0, pK_2 9.9.** Crystallise DTE from ether/hexane and store it in the dark at 0°. [*Beilstein* **1** III 2360.]

Dithiooxamide (rubeanic acid) *[79-40-3]* **M 120.2, m >300°.** Crystallise dithiooxamide from EtOH and sublime it at high vacuum. [*Beilstein* **2** IV 1871.]

***RS*-1,4-Dithiothreitol (DTT, Cleland's reagent)** *[27565-41-9]* **M 154.3, m 42-43°, pK_1 8.3, pK_2 9.5.** Crystallise DTT from ether and sublime it at 37°/0.005mm. It should be stored at 0°. [*Beilstein* **1** III 2360.]

***All-cis*-4,7,10,13,16,19-Docosahexaenoic acid** *[6217-54-5]* **M 328.5, m –44.1°, n_D^{20} 1.5017, pK_{Est} ~4.6.** Its solubility in $CHCl_3$ is 5%. It has been purified from fish oil by GLC using Ar as mobile phase and EGA as stationary phase with an ionisation detector [UV: Stoffel & Ahrens *J Lipid Res* **1** 139 *1959*], and *via* the ester by evaporative "molecular" distillation using a 'continuous molecular still' at 10^{-4} mm with the highest temperature

being 110° and a total contact time with the hot surface being 60 seconds [Farmer & van den Heuvel *J Chem Soc* 427 *1938*]. The *methyl ester [2566-90-7]* has **b** 208-211°/2mm, d_4^{20} 0.9398, n_D^{20} 1.5035. With Br_2 it forms a *dodecabromide* **m** *ca* 240°(dec). Also, the acid was converted to the methyl ester and purified through a three-stage molecular still [as described by Sutton *Chem Ind (London)* 11383 *1953*] at 96°, and the rate was adjusted so that one-third of the material was removed each cycle of three distillations. The distillate (numbered 4) (13g) was dissolved in EtOH (100ml containing 8g of KOH) at −70° and set aside for 4 hours at 30° with occasional shaking under a vacuum. Water (100ml) was added and the solution was extracted with pentane, washed with HCl, dried ($MgSO_4$), filtered and evaporated to give a clear oil (11.5g) **m** –44.5° to –44.1°. In the catalytic hydrogenation of the oil six mols of H_2 are absorbed and *docosanoic acid (behenic acid)* is produced with **m** 79.0-79.3° undepressed with an authentic sample (see docosanoic acid below) [Whitcutt *Biochem J* **67** 60 *1957*]. [*Beilstein* **2** IV 1812.]

Docosane (C22) *[629-97-0]* **M 310.6, m 47°, b 224°/15mm.** Crystallise docosane from EtOH or ether. [*Beilstein* **1** IV 572.]

Docosanoic acid (behenic acid) *[112-85-6]* **M 340.6, m 81-82°, pK_{Est} ~4.9.** Crystallise the acid from ligroin. [Francis & Piper *J Am Chem Soc* **61** 577 *1939*, *Beilstein* **2** IV 1290.]

1-Docosanol (behenyl alcohol) *[661-19-8]* **M 182.3, m 70.8°.** Crystallise docosanol from ether or chloroform/ether. [*Beilstein* **1** IV 1906.]

***n*-Dodecane** *[112-40-3]* **M 170.3, b 97.5-99.5°/5mm, 216°/760mm, d_4^{20} 0.748, n_D^{20} 1.42156.** Pass it through a column of Linde type 13X molecular sieves. Store it in contact with, and distil it from sodium. Pass it through a column of activated silica gel. It has been crystallised from diethyl ether at –60°. Unsaturated dry material which remained after passage through silica gel has been removed by catalytic hydrogenation (Pt_2O) at 45lb/in^2 (3.06 atmospheres), followed by fractional distillation under reduced pressure [Zook & Goldey *J Am Chem Soc* **75** 3975 *1953*]. It has also purified by partial crystallisation from the melt. [*Beilstein* **1** IV 498.]

Dodecane-1,10-dioic acid (decane-1,10-dicarboxylic acid) *[693-23-2]* **M 230.3, m 129°, b 245°/10mm, pK_{Est} ~4.8.** Crystallise the dioic acid from water, 75% or 95% EtOH (solubility is 10%), or glacial acetic acid. [*Beilstein* **2** IV 2126.]

1-Dodecanol (dodecyl alcohol) *[112-53-8]* **M 186.3, m 24°, b 91°/1mm, 135°/10mm, 167°/40mm, 213°/200mm, 259°/760mm, d^{24} 0.8309 (liquid).** Crystallise dodecanol from aqueous EtOH, and distil it through a spinning-band column under vacuum. [Ford & Marvel *Org Synth* **10** 62 *1930*, *Beilstein* **1** IV 1844.]

1-Dodecanthiol *[112-55-0]* **M 202.4, b 111-112°/3mm, 153-155°/24mm, d_4^{20} 0.844, n_D^{20} 1.458, pK_{Est} ~10.8.** Dry it with CaO for several days, then distil it from CaO. [*Beilstein* **1** IV 1851.]

Dodecylamine *[124-22-1]* **M 185.4, m 28°, 27-29°, 120-121°/2mm, 134°/15mm, 156°/33mm, pK^{25} 10.63.** Fractionally distil the amine, preferably under N_2 and in a vacuum. Store it in the absence of CO_2. It can be recrystallised from *n*-hexane at low temperature. The *hydrochloride* crystallises from Me_2CO (**m** 182-183°) or $CHCl_3$/petroleum ether (**m** 185-187°). [Magnien & Baltzly *J Org Chem* **23** 2029 *1958*, *Beilstein* **4** H 200, III 406, **4** IV 794.]

Dodecylammonium butyrate *[17615-97-3]* **M 273.4, m 39-40°, 39-41°, pK^{25} 10.63 (for free base).** Recrystallise the salt from *n*-hexane. [*Beilstein* **4** III 409, **4** IV 791.]

Dodecylammonium propionate *[17448-65-6]* **M 259.4, m 55-56°.** Recrystallise the salt from hexanol/petroleum ether (b 60-80°). [*Beilstein* **4** III 409, **4** IV 797.]

Dodecyldimethylamine oxide *[1643-20-5]* **M 229.4, m 102°.** Crystallise the oxide from acetone or ethyl

acetate. [Bunton et al. *J Org Chem* **52** 3832 *1987*, *Beilstein* **4** III 410, **4** IV 798.]

Dodecyl ether (didodecyl ether) *[4542-57-8]* **M 354.6, m 32.5-33°, 33°, b 175°/0.15mm, d^{36} 0.8127, n^{39} 1.4393.** Distil the ether in a vacuum, then crystallise it from MeOH or MeOH/*benzene. [Mannich & Nadelmann *Chem Ber* **63** 799 *1930*, Butterworth & Hey *J Chem Soc* 390 *1940*, *Beilstein* **1** III 1785, **1** IV 1846.]

Dodecyl methacrylate (lauryl methacrylate) *[142-90-5]* **M 254.4, m –7°, b 142°/4mm, d^{25} 0.8717, n_D^{25} 1.4330.** Purify the ester by fractional distillation in a high vacuum. Add 0.05% of hydroquinone monomethyl ether as stabiliser. [Rehberg & Fischer *Ind Eng Chem* **40** 1430 *1948*, *Beilstein* **2** III 1290, **2** IV 1528.]

Dodecyltrimethylammonium bromide *[1119-94-4]* **M 308.4, m 246°(dec).** Purify the salt by repeated crystallisation from acetone. Wash it with diethyl ether and dry it in a vacuum oven at 60° [Dearden & Wooley *J Phys Chem* **91** 2404 *1987*]. [*Beilstein* **4** IV 798.]

Dodecyltrimethylammonium chloride *[112-00-5]* **M 263.9, m 246°(dec).** Dissolve the chloride in MeOH, treat with active charcoal, filter and dry it *in vacuo* [Waldenburg *J Phys Chem* **88** 1655 *1984*], or recrystallise it several times from 10% EtOH in acetone. It has also been repeatedly crystallised from EtOH/ether or MeOH. [Cella et al. *J Am Chem Soc* **74** 2062 *1952*, *Beilstein* **4** IV 79.]

Eicosane (C20) *[112-95-8]* **M 282.6, m 36-37°, b 205°/15mm, $d^{36.7}$ 0.7779, n^{40} 1.43453.** Crystallise eicosane from EtOH. [*Beilstein* **1** IV 563.]

Elaidic (*trans*-oleic) acid *[112-79-8]* **M 282.5, m 44.5°, pK^{25} 4.9.** Crystallise the acid from acetic acid, then EtOH. [*Beilstein* **2** IV 1647.]

***RS*-Epichlorohydrin (± 2-chloromethyloxirane)** *[106-89-8]* **M 92.5, b 115.5°, d_4^{20} 1.180, n_D^{20} 1.438,.** Distil epichlorohydrin under atmospheric pressure, heat it on a steam bath with one-quarter its weight of CaO, then decant and fractionally distil it. [*Beilstein* **17** V 20.]

1,2-Epoxybutane *[106-88-7]* **M 72.1, b 66.4-66.6°, d_4^{20} 0.837, n_D^{20} 1.3841.** Dry it with $CaSO_4$, and fractionally distil it through a long (126cm) glass helices-packed column. The first fraction contains a water azeotrope. [*Beilstein* **17** II 17.]

Erucic acid (*cis*-13-docosenoic acid) *[112-86-7]* **M 338.6, m 33.8°, b 358°/400mm, pK_{Est} ~4.9.** Crystallise erucic acid from MeOH. [*Beilstein* **2** IV 1676.]

Ethane *[74-84-0]* **M 30.1, f –172°, b –88°, d_4^0 1.0493 (air = 1).** Ethylene can be removed by passing the gas through a sintered-glass disc into fuming H_2SO_4 then slowly through a column of charcoal saturated with bromine. Bromine and HBr are removed by passage through firebrick coated with *N,N*-dimethyl-*p*-toluidine. The ethane is also passed over KOH pellets (to remove CO_2) and dried with $Mg(ClO_4)_2$. Further purification is by several distillations of liquified ethane, using a condensing temperature of –195°. Yang and Gant [*J Phys Chem* **65** 1861 *1961*] treated ethane by standing it for 24 hours at room temperature in a steel bomb with activated charcoal treated with bromine. They then immersed the bomb in a Dry-ice/acetone bath and transferred the ethane to an activated charcoal trap cooled in liquid nitrogen. (The charcoal had previously been degassed by pumping for 24 hours at 450°.) By allowing the trap to warm slowly, the ethane distils, and only the middle third fraction is kept. Removal of methane is achieved using Linde type 13X molecular sieves (previously degassed by pumping for 24 hours at 450°) in a trap which, after cooling in Dry-ice/acetone, is saturated with ethane. After pumping for 10 minutes, the ethane is recovered by warming the trap to 25°. (The final gas contains less than 10^{-4} mole % of either ethylene or methane). [*Beilstein* **1** IV 108.]

Ethanesulfonyl chloride *[594-44-5]* **M 128.6, b 55°/9mm, 62°/12mm, 74°/19mm, 76-79°/22mm, 95-98°/50mm, 177°/760mm, d_4^{20} 1.357, n_D^{20} 1.4539.** Purify the sulfonyl chloride by repeated distillation to remove HCl formed from hydrolysis. **It is a fuming, corrosive liquid, handle in a good fumehood.** It is

hydrolysed by aqueous N NaOH at room temperature and is best stored in aliquots in sealed ampules under N_2. [Davies & Dick *J Chem Soc* 484 *1932*, Klamann & Drahowzal *Monatsh Chem* **83** 463 *1952*, Saunders et al. *Biochem J* **36** 372 *1942*, *Beilstein* **4** IV 34.]

Ethanethiol (ethyl mercaptan) *[75-08-1]* **M 62.1, b 32.9°/704mm, d^{52} 0.83147, pK^{25} 10.61.** Dissolve the thiol in aqueous 20% NaOH, extract it with a small amount of *benzene and then steam distil until clear. After cooling, the alkaline solution is acidified slightly with 15% H_2SO_4 and the thiol is distilled off, dried with $CaSO_4$, $CaCl_2$ or 4A molecular sieves, and fractionally distilled under nitrogen [Ellis & Reid *J Am Chem Soc* **54** 1674 *1932*]. It has a foul odour, work in an efficient fume cupboard. [*Beilstein* **1** IV 1390.]

Ethanol *[64-17-5]* **M 46.1, b 78.3°, d^{15} 0.79360, d^{5} 0.78506, n_D^{20} 1.36139, pK^{25} 15.93.** Usual impurities of fermentation alcohol are fusel oils (mainly higher alcohols, especially pentanols), aldehydes, esters, ketones and water. With synthetic alcohol, likely impurities are water, aldehydes, aliphatic esters, acetone and diethyl ether. Traces of *benzene are present in ethanol that has been dehydrated by azeotropic distillation with *benzene. Anhydrous ethanol is very *hygroscopic*. Water (down to 0.05%) can be detected by formation of a voluminous precipitate when aluminium ethoxide in *benzene is added to a test portion. Rectified spirit (95% ethanol) is converted to *absolute* (99.5%) ethanol by refluxing with freshly ignited CaO (250g/L) for 6 hours, standing overnight and distilling with precautions to exclude moisture.
Numerous methods are available for further drying of *absolute* ethanol for making "Super dry ethanol". Lund and Bjerrum [*Chem Ber* **64** 210 *1931*] used reaction with magnesium ethoxide, prepared by placing 5g of clean dry magnesium turnings and 0.5g of iodine (or a few drops of CCl_4), to activate the Mg, in a 2L flask, followed by 50-75 ml of *absolute* ethanol, and warming the mixture until a vigorous reaction occurs. When this subsides, heating is continued until all the magnesium is converted to magnesium ethoxide. Up to 1L of ethanol is then added and, after refluxing for an hour, it is distilled off. The water content should be below 0.05%. Walden, Ulich and Laun [*Z Phys Chem* **114** 275 *1925*] used ***amalgamated aluminium*** chips, prepared by degreasing aluminium chips (by washing with Et_2O and drying in a vacuum to remove grease from machining the Al), treating with alkali until hydrogen evolved vigorously, washing with H_2O until the washings were weakly alkaline and then stirring with 1% $HgCl_2$ solution. After 2 minutes, the chips were washed quickly with H_2O, then alcohol, then ether, and dried with filter paper. (The amalgam became warm.) These chips were added to the ethanol, which was then gently warmed for several hours until evolution of hydrogen ceased. The alcohol was distilled and aspirated for some time with pure dry air. Smith [*J Chem Soc* 1288 *1927*] reacted 1L of *absolute* ethanol in a 2L flask with 7g of clean dry sodium, and added 25g of pure ethyl succinate (27g of pure ethyl phthalate was an alternative), and refluxed the mixture for 2 hours in a system protected from moisture, and then distilled the ethanol. A modification used 40g of ethyl formate instead, so that sodium formate separated out and, during reflux the excess of ethyl formate decomposed to CO and ethanol.
Drying agents suitable for use with ethanol include Linde type 4A molecular sieves, calcium metal, and CaH_2. The calcium hydride (2g) is crushed to a powder and dissolved in 100ml of *absolute* ethanol by gently boiling. About 70ml of the ethanol are distilled off to remove any dissolved gases before the remainder is poured into 1L of *ca* 99.9% ethanol in a still, where it is boiled under reflux for 20 hours, while a slow stream of pure, dry hydrogen (better use nitrogen or Ar) is passed through. It is then distilled [Rüber *Z Elektrochem* **29** 334 *1923*]. If calcium is used for drying, about ten times the theoretical amount should be used, and traces of ammonia (from some calcium nitride in the Ca metal) would be removed by passing dry air into the vapour during reflux. Ethanol can be freed from traces of basic materials by distillation from a little 2,4,6-trinitrobenzoic acid or sulfanilic acid. *Benzene can be removed by fractional distillation after adding a little water (the *benzene/water/ethanol azeotrope distils at 64.9°), the alcohol is then re-dried using one of the methods described above. *Alternatively*, careful fractional distillation can separate *benzene as the *benzene/ethanol azeotrope (**b** 68.2°). Aldehydes can be removed from ethanol by digesting with 8-10g of dissolved KOH and 5-10g of aluminium or zinc per L, followed by distillation. Another method is to heat under reflux with KOH (20g/L) and $AgNO_3$ (10g/L) or to add 2.5-3g of lead acetate in 5ml of water to 1L of ethanol, followed (slowly and without stirring) by 5g of KOH in 25ml of ethanol: after 1 hour the flask is shaken thoroughly, then set aside overnight before filtering and distilling. The residual water can be removed by standing the distillate over activated aluminium amalgam for 1 week, then filtering and distilling. Distillation of ethanol from Raney nickel

eliminates catalyst poisons.
Other purification procedures include pre-treatment with conc H_2SO_4 (3ml/L) to eliminate amines, and with $KMnO_4$ to oxidise aldehydes, followed by refluxing with KOH to resinify aldehydes, and distilling to remove traces of H_3PO_4 and other acidic impurities after passage through silica gel, and drying over $CaSO_4$. Water can be removed by azeotropic distillation with dichloromethane (azeotrope boils at 38.1° and contains 1.8% water) or 2,2,4-trimethylpentane. [*Beilstein* **1** IV 1289.]
Rapid purification: Place degreased Mg turnings (grease from machining the turnings is removed by washing with dry EtOH then Et_2O, and drying in a vacuum) (5g) in a dry 2L round bottomed flask fitted with a reflux condenser (protect from air with a drying tube filled with $CaCl_2$ or KOH pellets) and flushed with dry N_2. Then add iodine crystals (~0.5g) and gently warm the flask until iodine vapour is formed and coats the turnings. Cool, then add EtOH (50ml) and carefully heat to reflux until the iodine disappears. Cool again, then add more EtOH (to 1L) and reflux under N_2 for several hours. Distil and store over 3A molecular sieves (pre-heated at 300°–350° for several hours and cooled under dry N_2 or argon).

Ethoxycarbonyl isocyanate *[19617-43-7]* **M 115.1, b 51-55°/13mm, 56°/18mm, 115-116°/781mm, d_4^{20} 1.15.** Distil it twice from P_2O_5 (1-2g) through a small Vigreux column and then through a 20-plate column. All fractional distillations should be under a vacuum. [Lamon *J Heterocycl Chem* **5** 837 *1968*, *Beilstein* **3** H 36, **3** I 17.]

Ethoxycarbonyl isothiocyanate *[16182-04-0]* **M 131.5, b 43°/14mm, 51-55°/13mm, 56°/18mm, d_4^{20} 1.12.** Fractionally distil it through a short column. It also distils at 83°/30mm with some decomposition liberating CO_2 and sulfurous gases, best distil below 20mm vacuum. [Capp et al. *J Chem Soc* 1340, *1948*, Lamon *J Heterocycl Chem* **5** 837 *1968*, *Beilstein* **3** H 174, **3** I 71, **3** III 279, **3** IV 323.]

2-Ethoxyethanol *[110-80-5]* **M 90.1, b 134.8°, d_4^{20} 0.931, n_D^{20} 1.40751.** Dry it with $CaSO_4$ or K_2CO_3, filter and fractionally distil it. Peroxides can be removed by refluxing with anhydrous $SnCl_2$ or by filtration under slight pressure through a column of activated alumina. [*Beilstein* **1** IV 2377.]

2-Ethoxyethyl methacrylate *[2370-63-0]* **M 158.2, b 91-93°/35mm, d_4^{20} 0.965, n_D^{20} 1.429.** Purify the ester as described under methyl methacrylate below. [*Beilstein* **2** III 1291.]

Ethyl acetate *[141-78-6]* **M 88.1, b 77.1°, d_4^{20} 0.9003, n_D^{20} 1.37239, n^{25} 1.36979, pK^{25} –6.93 (aqueous H_2SO_4).** The most common impurities in EtOAc are water, EtOH and acetic acid. These can be removed by washing with aqueous 5% Na_2CO_3, then with saturated aqueous $CaCl_2$ or NaCl, and drying with K_2CO_3, $CaSO_4$ or $MgSO_4$. More efficient drying is achieved if the solvent is further dried with P_2O_5, CaH_2 or molecular sieves before distillation. CaO has also been used. *Alternatively*, ethanol can be converted to ethyl acetate by refluxing with acetic anhydride (*ca* 1ml per 10ml of ester), the liquid is then fractionally distilled, dried with K_2CO_3 and redistilled. [*Beilstein* **2** III 127.]
Rapid purification: Distil, dry over K_2CO_3, re-distil and store over 4A molecular sieves.

Ethyl acetimidate *[1000-84-6]* **M 87.1, b 92-95°/atm, 89.7-90°/765mm, d_4^{20} 0.8671, n_D^{20} 1.4025, pK_{Est} ~5.5.** It is best to prepare it freshly from the *hydrochloride* (see below). Dissolve the hydrochloride (123.5g) by adding it slowly to an ice-cold mixture of H_2O (500ml), K_2CO_3 (276g) and Et_2O (200ml) and stirring rapidly. The Et_2O layer is separated, the aqueous layer is extracted with Et_2O (100ml), the combined Et_2O layers are dried ($MgSO_4$), evaporated and the residual oil is distilled through a glass helices packed column (70x1.2cm). The yield is 19g (22%). [Glickman & Cope *J Am Chem Soc* **67** 1020 *1945*, Chaplin & Hunter *J Chem Soc* 1118 *1937*, Hunter & Ludwig *Methods Enzymol* **25** 585 *1972*.]

Ethyl acetimidate hydrochloride *[2208-07-3]* **M 123.6, m 98-100°(dec), 110-115°(dec), 112-113°(dec), m 112-114°(dec), pK_{Est} ~5.5.** Recrystallise the hydrochloride by dissolving it in the minimum volume of super dry EtOH and adding dry Et_2O or from dry Et_2O. Dry it in a vacuum and store it in a vacuum desiccator with P_2O_5. *Alternatively*, it could be crystallised from EtOH (containing a few of drops of ethanolic HCl) and adding dry Et_2O. Filter and dry it in a vacuum desiccator over H_2SO_4 and NaOH. [Pinner *Chem Ber* **16** 1654 *1883*,

Glickman & Cope *J Am Chem Soc* **67** 1020 *1945*, Chaplin & Hunter *J Chem Soc* 1118 *1937*, McElvain & Schroeder *J Am Chem Soc* **71** 40 *1949*, McElvain & Tate *J Am Chem Soc* **73** 2233 *1951*, *Methods Enzymol* **25** 585 *1972*, *Beilstein* **2** III 418.]

Ethyl acetoacetate *[141-97-9]* **M 130.1, b 71°/12mm, 100°/80mm, d_4^{20} 1.026, n_D^{20} 1.419, pK^{25} 10.68.** Shake the ester with small amounts of saturated aqueous $NaHCO_3$ (until no further effervescence), then with water. Dry it with $MgSO_4$ or $CaCl_2$ and distil it under reduced pressure. [*Beilstein* **3** IV 1528.]

Ethyl acrylate *[140-88-5]* **M 100.1, b 20°/40mm, 99.5°/atm, d_4^{20} 0.922, n_D^{20} 1.406.** Wash the ester repeatedly with aqueous NaOH until free from inhibitors such as hydroquinone, then wash it with saturated aqueous $CaCl_2$ and distil it under reduced pressure. Hydroquinone should be added if the ethyl acrylate is to be stored for extended periods. [*Beilstein* **2** IV 1460.] **LACHRYMATORY.**

Ethylamine *[75-04-7]* **M 45.1, b 16.6°/760mm, d_4^{20} 1.3663, pK^{20} 10.79.** Condense it in an all-glass apparatus cooled by circulating ice-water, and store it with KOH pellets below 0°. [*Beilstein* **4** IV 307.]

Ethylamine hydrochloride *[557-66-4]* **M 81.5, m 109-110°.** Crystallise the hydrochloride from absolute EtOH or MeOH/$CHCl_3$, wash it with dry ether and dry it in a vacuum. [*Beilstein* **4** IV 310.]

Ethyl bromide *[74-96-4]* **M 109.0, b 0°/165mm, 38°/745mm, d_4^{20} 1.460, n_D^{20} 1.4241.** The main impurities are usually EtOH and water, both of which form azeotropes with it. Ethanol and unsaturated compounds can be removed by washing with conc H_2SO_4 until no further coloration is produced. The ethyl bromide is then washed with water, aqueous Na_2CO_3, and water again, then dried with $CaCl_2$, $MgSO_4$ or CaH_2, and distilled from P_2O_5. Olefinic impurities can also be removed by storing the ethyl bromide in daylight with elemental bromine, later removing the free bromine by extraction with dilute aqueous Na_2SO_3, drying the ethyl bromide with $CaCl_2$ and fractionally distilling it. *Alternatively*, unsaturated compounds can be removed by bubbling oxygen containing *ca* 5% ozone through the liquid for an hour, then washing with aqueous Na_2SO_3 to hydrolyse ozonides and remove hydrolysis products, followed by drying and distillation. [*Beilstein* **1** IV 150.]

Ethyl bromoacetate *[105-36-2]* **M 167.0, b 158-158.5°/758mm, d_4^{20} 1.50, n_D^{20} 1.450.** Wash the ester with saturated aqueous Na_2CO_3 (three times), 50% aqueous $CaCl_2$ (three times) and saturated aqueous NaCl (twice). Dry with $MgSO_4$, $CaCl_2$ or $CaCO_3$, and distil it. [*Beilstein* **2** IV 527.] **LACHRYMATORY.**

Ethyl 6-bromohexanoate (ethyl 6-bromocaproate) *[25542-62-5]* **M 223.1, b 120-125°/14mm, 126-127°/20-21mm, 128-130°/16mm, 127-130°/19mm, d_{23}^{23} 1.241, d^{25} 1.254, n_D^{20} 1.458, n_D^{21} 1.4566.** 6-Bromohexanoic acid (250g) is esterified by refluxing with EtOH (600ml) containing H_2SO_4 (15ml) for 8 hours, evaporating *in vacuo*, the residue is taken up in Et_2O, washed with H_2O, then 5% of aqueous Na_2CO_3 (effervescence), the Et_2O layer is dried ($CaCl_2$), filtered, evaporated, and the residual oil is distilled to give the ester (178-218g). [Brown & Partridge *J Am Chem Soc* **66** 819 *1844*.] It has also been prepared from 6-hydroxyhexanoic acid by reaction with PBr_3 in pyridine, or HBr (*d* 1.5) and H_2SO_4 and then esterifying in the same way [Barger et al. *J Chem Soc* 718 *1937*]. [*Beilstein* **2** IV 940.]

Ethyl 2-(bromomethyl)acrylate *[17435-72-2]* **M 193.1, b 38°/0.8mm, d_4^{20} 1.398, n_D^{20} 1.479.** If it contains some free acid, add H_2O, cool, and neutralise with $NaHCO_3$ until evolution of CO_2 ceases. Extract the mixture with Et_2O (3x) and dry the combined extracts (Na_2SO_4, 3 hours). Evaporate Et_2O and distil the ester collecting fraction **b** 39-40°/0.9mm, and check spectra. [Preparation and NMR: Ramarajan et al. *Org Synth* Coll Vol **VII** 211 *1990*, *Beilstein* **2** IV 1541.]

Ethyl α-bromopropionate *[535-11-5]* **M 181.0, b 69-70°/25mm, d_4^{20} 1.39, n_D^{20} 1.447.** Wash the ester with saturated aqueous Na_2CO_3 (three times), 50% aqueous $CaCl_2$ (three times) and saturated aqueous NaCl (twice). Dry with $MgSO_4$, $CaCl_2$ or $CaCO_3$, and distil it. [*Beilstein* **2** IV 762.] **LACHRYMATORY.**

Ethyl bromopyruvate *[70-23-5]* **M 195.0, b 47°/0.5mm, 71-73°/5mm, 87°/9mm, 89-104°/14mm, d_4^{20} 1.561,**

n_D^{20} 1.464. The most likely impurity is free acid (bromopyruvic or bromoacetic acids). Dissolve the ester in dry Et_2O or dry $CHCl_3$, stir with $CaCO_3$ until effervescence ceases, filter (may wash with a little H_2O rapidly), dry ($MgSO_4$) and distil it at least twice. The *2,4-dinitrophenylhydrazone* has **m** 144-145°. [Burros & Holland *J Chem Soc* 672 *1947*, Letsinger & Laco *J Org Chem* **21** 764 *1956*, Kruse et al. *J Am Chem Soc* **76** 5796 *1954*, *Beilstein* **3** IV 1519.] **LACHRYMATORY.**

2-Ethyl-1-butanol *[97-95-0]* **M 102.2, b 146.3°, n^{15} 1.4243, n^{25} 1.4205.** Dry it with $CaSO_4$ for several days, filter and fractionally distil it. [*Beilstein* **1** IV 1725.]

2-Ethylbut-1-ene *[760-21-4]* **M 84.1, b 66.6°, d_4^{20} 0.833, n_D^{20} 1.423.** Wash it with 10N aqueous NaOH, then water. Dry the organic layer with $CaCl_2$, filter and fractionally distil it. [*Beilstein* **1** IV 850.]

Ethyl *n*-butyrate *[105-54-4]* **M 116.2, b 49°/50mm, 119-120°/760mm, d_4^{20} 0.880, n_D^{20} 1.393.** Dry the ester with anhydrous $CuSO_4$ and distil it under dry nitrogen. [*Beilstein* **2** IV 787.]

Ethyl carbamate see **urethane** below.

Ethyl carbazate (*N*-ethoxycarbonyl hydrazine) *[4114-31-2]* **M 104.1, m 44-48°, 51-52°, b 95.5°/10m, 92-95°/12mm, 100-102°/11mm.** Fractionate the carbazate using a Vigreux column until the distillate crystallises [Allen & Bell *Org Synth* Coll Vol **III** 404 *1955*, *Beilstein* **3** IV 174].

Ethyl chloride *[75-00-3]* **M 64.5, b 12.4°, d_4^{20} 0.8978, n_D^{20} 1.3676.** Pass ethyl chloride through absorption towers containing, successively, conc H_2SO_4, NaOH pellets, P_2O_5 on glass wool, or soda-lime, $CaCl_2$, P_2O_5. Condense it into a flask containing CaH_2 and fractionally distil it. It has also been purified by illumination in the presence of bromine at 0° using a 1000W lamp, followed by washing, drying and distilling. [*Beilstein* **1** IV 124.]

Ethyl chloroacetate *[105-39-5]* **M 122.6, b 143-143.2°, d_4^{20} 1.150, n^{25} 1.4192.** Shake the ester with satutated aqueous Na_2CO_3 (three times), aqueous 50% $CaCl_2$ (three times) and saturated aqueous NaCl (twice). Dry it with Na_2SO_4 or $MgSO_4$ and distil it. [*Beilstein* **2** IV 481.] **LACHRYMATORY.**

Ethyl chlorofluoroacetate ($ClFCHCCO_2Et$) *[± 401-56-9]* **M 140.5, b 128°/atm, 133°/atm, d_4^{25} 1.225, n_D^{25} 1.3926.** The ester is prepared from 2-chloro-1,1,2-trifluoroethyl ether (340g, 2.09mol at < 5°) while 96% H_2SO_4 (228ml, 420g, 4.1mol) is added dropwise to it with stirring, and allowing the liberated HF (HIGHLY TOXIC vapour which etches glass) to vacate in an efficient fume cupboard, at a rate such that the temperature is maintained at 5-15° (*ca* 30-45 minutes). The mixture is stirred further at 10° for 2 hours when all the HF is released, then it is poured carefully onto crushed ice (I Kg) and H_2O (500ml). The lower white oily layer is allowed to settle, separated, washed until free of acid with saturated aqueous $NaHCO_3$ (3 x 25ml, **CARE**: CO_2 may be liberated), H_2O (4 x 25ml) and dried over Drierite (10g) [Note that thorough washing is essential to avoid decomposition on distillation]. The crude dry ester is filtered, and fractionated through an efficient helix packed column (2 x 12cm) to give pure *ethyl chlorofluoroacetate* (190-100g, 65-68%) boiling at 129-130° and atmospheric pressure.
The *free acid* has **b** 162°/atm (160.5-161°/atm has also been reported), d_4^{25} 1.532, n_D^{25} 1.4085, is obtained by hydrolysis of the *methyl ester*, **b** 116°/atm, with 10% aqueous NaOH. The ethyl ester provides *chlorofluoroacetamide*, **b** 72-77°/1mm, d_4^{25} 1.510, n_D^{25} 1.4535, by reaction with ammonia [Young & Tarrant *J Am Chem Soc* **71** 2432 *1949*, Hazeldine *J Chem Soc* 4259 *1952*]. [*Beilstein* **2** III 453, **2** IV 493, Englund *Org Synth* Coll Vol **IV** 423 *1963*, cf also Young & Terrant *J Am Chem Soc* **71** 982 *1949*.]

Ethyl chloroformate *[541-41-3]* **M 108.5, m –81°, b 94-95°, d_4^{20} 1.135, n_D^{20} 1.3974.** Wash the ester several times with water, redistil it using an efficient fractionating column at atmospheric pressure and a $CaCl_2$ guard tube to keep free from moisture [Hamilton & Sly *J Am Chem Soc* **47** 435 *1925*, Saunders et al. *J Am Chem Soc* **73** 3796 *1951*]. [*Beilstein* **3** IV 23.] **LACHRYMATORY AND TOXIC.**

Ethyl *trans*-crotonate *[623-70-1]* **M 114.2, b 137°, d_4^{20} 0.917, n_D^{20} 1.425.** Wash it with aqueous 5% Na_2CO_3,

then with saturated aqueous $CaCl_2$, dry it with $CaCl_2$ and distil it. [*Beilstein* **2** IV 1500.]

Ethyl cyanoacetate *[105-56-6]* **M 113.1, b 206.0°, d_4^{20} 1.061, n_D^{20} 1.41751.** Shake the ester several times with aqueous 10% Na_2CO_3, wash it well with water, dry with Na_2SO_4 and fractionally distil it. [*Beilstein* **2** IV 1889.]

Ethyl cyanoformate *[623-49-4]* **M 99.1, b 113-114°/740mm, 116.5-116.8°/765.5mm, d_4^{20} 1.0112, n_D^{20} 1.3818.** Dissolve the cyanoformate in Et_2O, dry it over Na_2SO_4, filter, evaporate and distil it [Malachowsky et al. *Chem Ber* **70** 1016 *1937*, Adickes et al. *J Prakt Chem* [2] **133** 313 *1932*, Grundmann et al. *Justus Liebigs Ann Chem* **577** 77 *1952*]. [*Beilstein* **2** IV 1862.]

Ethyl diazoacetate *[623-73-4]* **M 114.1, m –22°, b 42°/5mm, 45°/12mm, 85-86°/88mm, 140-141°/720mm, 140-143°/atm, $d_4^{17.6}$ 1.0852, $n_D^{17.6}$ 1.4588.** It is a very volatile yellow oil with a strong pungent odour. **EXPLOSIVE [distillation even under reduced pressure is dangerous and may result in an explosion — TAKE ALL THE NECESSARY PRECAUTIONS IF DISTILLATION IS TO BE CARRIED OUT].** It explodes in contact with conc H_2SO_4-trace acid causes rapid decomposition. It is slightly soluble in H_2O, but is miscible with EtOH, *C_6H_6, petroleum ether and Et_2O. To purify, dissolve it in Et_2O [using CH_2Cl_2 instead of Et_2O, protects the ester from acid], wash it with 10% aqueous Na_2CO_3, dry ($MgSO_4$), filter and repeat as many times as possible until the Et_2O layer loses its yellow colour, then remove the solvent below 20° (vacuum). Note that prolonged heating may lead to rapid decomposition and low yields. It can also be purified by steam distillation under reduced pressure but with considerable loss in yield. Place the residual oil in a brown bottle, keep below 10°, and use as soon as possible without distilling. For preparing esters usually the ethereal solution is used directly without purification. [Womack & Nelson *Org Synth* Coll Vol **III** 392 *1955*, UV: Miller & White *J Am Chem Soc* **79** 5974 *1957*, Fieser **1** 367 *1967*, *Beilstein* **3** IV 1495.]

Ethyl dibromoacetate *[617-33-4]* **M 245.9, b 81-82°/14.5mm, 194°/atm, d^{22} 1.9081, n^{22} 1.4973.** Wash the ester briefly with conc aqueous $NaHCO_3$, then with aqueous $CaCl_2$. Dry it with $CaSO_4$ and distil it under reduced pressure. [Hornyak & Amis *J Am Chem Soc* **79** 2079 *1957*, *Beilstein* **2** H 219, **2** I 97, **2** III 484, **2** IV 533.]

Ethyl dichloroacetate *[535-15-9]* **M 157.0, b 54-55°/11mm, 131.0-131.5°/40mm, d_4^{20} 1.28, n_D^{20} 1.438.** Shake the ester with aqueous 3% $NaHCO_3$ to remove free acid, wash with distilled water, dry for 3 days with $CaSO_4$ and distil it under reduced pressure. [*Beilstein* **2** IV 501.]

Ethyl 3,3-diethoxypropionate *[10601-80-6]* **M 190.2, b 58.5°/1.5mm, 65°/2mm, 95-96°/12mm, d_4^{20} 0.78, n_D^{25} 1.4101.** Dissolve it in dry Et_2O, and dry with solid $NaHCO_3$, filter, distil and carefully fractionate it [Dyer & Johnson *J Am Chem Soc* **56** 223 *1934*]. [*Beilstein* **3** II 411.]

Ethylene (ethene) *[74-85-1]* **M 28.0, m –169.4°, b –102°/700mm.** Purify ethylene by passage through a series of towers containing molecular sieves, or anhydrous $CaSO_4$, or cuprous ammonium solution, then conc H_2SO_4, followed by KOH pellets. *Alternatively*, it has been condensed in liquid nitrogen, with melting, freezing and pumping to remove air before passage through an activated charcoal trap, followed by a further condensation in liquid air. A sputtered sodium trap was used to remove oxygen. [*Beilstein* **1** IV 677.]

Ethylenediamine (1,2-diaminoethane) *[107-15-3]* **M 60.1, f 11.0°, b 117.0°, d_4^{20} 0.897, n_D^{20} 1.45677, n^{30} 1.4513, pK_1^{25} 6.86, pK_2^{25} 9.92.** It forms a constant-boiling (**b** 118.5°, *monohydrate*, **m** 10°) mixture with water (23w/w%). [It is *hygroscopic* and miscible with water.] Recommended purification procedure [Asthana & Mukherjee in J.F .Coetzee (ed), *Purification of Solvents,* Pergamon Press, Oxford, 1982 cf p 53]: to 1L of ethylenediamine is added 70g of type 5A Linde molecular sieves and shaken for 12 hours. The liquid is decanted and shaken for a further 12 hours with a mixture of CaO (50g) and KOH (15g). The supernatant is fractionally distilled (at 20:1 reflux ratio) in contact with freshly activated molecular sieves. The fraction distilling at 117.2° /760mm is collected. Finally it is fractionally distilled from sodium metal. All distillations and storage of ethylenediamine should be carried out under nitrogen to prevent reaction with CO_2 and water. The material containing 30% water is dried with solid NaOH (600g/L) and heated on a water bath for 10 hours.

Above 60°, separation into two phases takes place. The hot ethylenediamine layer is decanted off, refluxed with 40g of sodium for 2 hours and distilled [Putnam & Kobe *Trans Electrochem Soc* **74** 609 *1938*]. Ethylenediamine is usually distilled under nitrogen. *Alternatively*, it is dried over type 5A Linde molecular sieves (70g/L), then a mixture of 50g of CaO and 15g of KOH/L, with further dehydration of the supernatant with molecular sieves followed by distillation *from* molecular sieves and, finally, from sodium metal. A spectroscopically improved material is obtained by shaking with freshly baked alumina (20g/L) before distillation. [*Beilstein* **4** IV 1166.]

***N,N′*-Ethylenediaminediacetic acid (EDDA)** *[5657-17-0]* **M 176.2, m 222-224°(dec), pK_1^{25} 6.48, pK_2^{25} 9.57 (for NH groups).** Crystallise EDDA from H_2O. [*Beilstein* **4** IV 2446.]

Ethylenediamine dihydrochloride *[333-18-6]* **M 133.0, m >300°, pK_1^{25} 6.86, pK_2^{25} 9.92.** Crystallise the salt from H_2O or H_2O/EtOH. Wash the crystals with EtOH and dry them *in vacuo*. It sublimes on heating. [*Beilstein* **4** IV 1168.]

Ethylenediaminetetraacetic acid (EDTA) *[60-00-4]* **M 292.3, m 253°(dec), pK_1^{25} 0.26 pK_2^{25} 0.96, pK_3^{25} 2.60, pK_4^{25} 2.67, pK_5^{25} 6.16, pK_6^{25} 10.26.** Dissolve EDTA in aqueous KOH or ammonium hydroxide, and precipitate it twice with dilute HCl or HNO_3. Boil it twice with distilled water to remove mineral acid, then recrystallise it from water or dimethylformamide. Dry it at 110°. It also recrystallises from boiling 1N HCl; wash the crystals with distilled H_2O and dry them *in vacuo*. [Ma & Ray *Biochemistry* **19** 751 *1980*, *Beilstein* **4** IV 2449.]

Ethylene dimethacrylate (ethylene glycol dimethacrylate) *[97-90-5]* **M 198.2, b 98-100°/5mm, d_4^{20} 1.053, n_D^{20} 1.456.** Distil it through a short Vigreux column (p 11) at about 1mm pressure, in the presence of 3% (w/w) of phenyl-ß-naphthylamine. [*Beilstein* **2** IV 1532.]

Ethylene dimyristate [1,2-bis(myristoyloxy)ethane] *[627-84-9]* **M 482.8, m 61.7°.** Crystallise the ester from *benzene/MeOH or diethyl ether/MeOH, and dry it in a vacuum desiccator. It forms an inclusion compound with 25.9 mols of urea. [McGreer et al. *J Am Chem Soc* **74** 3441 *1952*, *Beilstein* **2** H 366, **2** II 327, **2** III 924, **2** IV 1133.]

Ethylene dipalmitate [1,2-bis(palmitoyloxy)ethane] *[624-03-3]* **M 538.9, m 69.1°, 71.2°.** Crystallise the ester from *benzene/MeOH , diethyl ether/MeOH or Me_2CO and dry it in a vacuum desiccator. It forms an inclusion compound with 28.2 mols of urea. [McGreer et al. *J Am Chem Soc* **74** 3541 *1952*, *Beilstein* **2** H 373, **2** I 166, **2** II 338, **2** III 926, **2** IV 1169.]

Ethylene distearate [1,2-bis(stearoyloxy)ethane] *[627-83-8]* **M 595.0, m 74.4-75°, 75.3°, 77°.** Crystallise the ester from *benzene/MeOH, diethyl ether/MeOH or Me_2CO and dry it in a vacuum desiccator. It forms an inclusion compound with 31 mols of urea. [McGreer et al. *J Am Chem Soc* **74** 3541 *1952*, *Beilstein* **2** H 380, **2** II 354, **2** III 1021, **2** IV 1223.]

Ethylene glycol *[107-21-1]* **M 62.1, b 68°/4mm, 197.9°/760mm, d_4^{20} 1.0986, n^{15} 1.43312, n^{25} 1.43056, pK^{25} 10.6.** It is very *hygroscopic*, and also likely to contain higher diols. Dry it with CaO, $CaSO_4$, $MgSO_4$ or NaOH and distil it under vacuum. Dry further by reaction with a small amount of sodium under nitrogen (to remove moisture), reflux for several hours and distil. The distillate is then passed through a column of Linde type 4A molecular sieves and finally distil under nitrogen, from more molecular sieves. Then fractionally distil it. [*Beilstein* **1** IV 2369.]

Ethylene glycol bis(ß-aminoethylether)-*N,N′*-tetraacetic acid (EGTA) *[67-42-5]* **M 380.4, m >245°(dec), pK_1^{20} 1.15 (2.40), pK_2^{20} 2.40 (2.50), pK_3^{20} 8.40 (8.67), pK_4^{20} 8.94 (9.22).** Dissolve EGTA in aqueous NaOH, precipitate it by adding aqueous HCl, wash it with water and dry at 100° *in vacuo*. [*Beilstein* **4** IV 217.]

Ethylene glycol diacetate *[111-55-7]* **M 146.2, b 190.1°, 79-81°/11mm, d^{25} 1.4188, n_D^{20} 1.4150.** Dry the diacetate with $CaCl_2$, filter (excluding moisture) and fractionally distil it under reduced pressure. [*Beilstein* **2** IV

1541.]

Ethylene glycol dibutyl ether *[112-48-1]* **M 174.3, b 78-80°/16mm, 200-201°/760mm, d_4^{20} 1.105, n_D^{20} 1.42.** Shake the ether with aqueous 5% Na_2CO_3, dry with $MgSO_4$ and store it with chromatographic alumina to prevent peroxide formation. [*Beilstein* **1** III 2083, **1** IV 2382.]

Ethylene glycol diethyl ether (1,2-diethoxyethane) *[629-14-1]* **M 118.2, m –74°, b 121.5°, d_4^{20} 0.842, n_D^{20} 1.392.** After refluxing for 12 hours, a mixture of the ether (2L), conc HCl (27ml) and water (200ml) is added with slow passage of nitrogen. The solution is cooled, and KOH pellets are added slowly and with shaking until no more dissolves. The organic layer is decanted, treated with some KOH pellets and again decanted. It is then refluxed with, and distilled from sodium immediately before use. *Alternatively*, after removal of peroxides by treatment with activated alumina, the ether is refluxed in the presence of the blue ketyl formed by sodium-potassium alloy with benzophenone, then distilled. [*Beilstein* **1** H 468, **1** II 519, **1** III 2078, **1** IV 2379.]

Ethyl formate *[109-94-4]* **M 74.1, b 54.2°, d_4^{20} 0.921, d^{30} 0.909, n_D^{20} 1.35994, n^{25} 1.3565.** Free acid or alcohol is removed by standing the ester over anhydrous K_2CO_3, with occasional shaking, then decanting and distilling from P_2O_5. *Alternatively*, the ester can be kept over CaH_2 for several days, then distilled from fresh CaH_2. It cannot be dried with $CaCl_2$ because it reacts rapidly with the ester to form a crystalline compound. [*Beilstein* **2** IV 23.]

Ethyl iodide (iodoethane) *[75-03-6]* **M 156.0, b 72.4°, d_4^{20} 1.933, n^{15} 1.5682, n^{25} 1.5104.** Drying the iodide with P_2O_5 is unsatisfactory, and with $CaCl_2$ it is incomplete. It is probably best to dry it with sodium wire and distil [Hammond et al. *J Am Chem Soc* **82** 704 *1960*]. Exposure of ethyl iodide to light leads to rapid decomposition, with the liberation of iodine. Free iodine can be removed by shaking with several portions of dilute aqueous $Na_2S_2O_3$ (until the colour is discharged), followed by washing with water, drying (with $CaCl_2$, then sodium), and distilling. The distilled ethyl iodide is stored, over mercury, in a dark bottle away from direct sunlight. Other purification procedures include passage through a 60cm column of silica gel, followed by distillation, and treatment with elemental bromine, extraction of free halogen with $Na_2S_2O_3$ solution, followed by washing with water, drying and distilling. Free iodine and HI have also been removed by direct distillation through a LeBel-Henninger column containing copper turnings. Purification by shaking with alkaline solutions, and storage over silver, are reported to be unsatisfactory. [*Beilstein* **1** IV 163.]

Ethyl isobutyrate *[97-62-1]* **M 116.2, b 110°, d_4^{20} 0.867, n_D^{20} 1.388.** Wash the ester with aqueous 5% Na_2CO_3, then with saturated aqueous $CaCl_2$. Dry it over $CaSO_4$ and distil. [*Beilstein* **1** IV 846.]

Ethyl isocyanate *[109-90-0]* **M 71.1, b 559.8°/759mm, 59-61°/760mm, 60-63°/~760mm, d_4^{20} 0.9031, n_D^{20} 1.3808.** Fractionate the isocyanate through an efficient column preferably in an inert atmosphere and store it in aliquots in sealed tubes [Bieber *J Am Chem Soc* **74** 4700 *1952*, Slocombe et al. *J Am Chem Soc* **72** 1888 *1950*]. [*Beilstein* **4** IV 402.]

Ethyl isovalerate *[108-64-5]* **M 130.2, b 134.7°, d_4^{20} 0.8664, n_D^{20} 1.39621, n^{25} 1.3975.** Wash the ester with aqueous 5% Na_2CO_3, then saturated aqueous $CaCl_2$. Dry it over $CaSO_4$ and distil. [*Beilstein* **2** IV 898.]

Ethyl levulinate (4-oxopentanoic acid ethyl ester) *[539-88-8]* **M 144.2, m 37.2°, b 106-108°/2mm, 138.8°/8mm, 203-205°/atm, d_4^{20} 1.012, n_D^{20} 1.423.** Stir the ester with Na_2CO_3 and charcoal, filter and distil. It is freely soluble in H_2O and EtOH [IR, NMR: Sterk *Monatsh Chem* **99** 1770 *1968*, Thomas & Schuette *J Am Chem Soc* **53** 2328 *1931*, Cox & Dodds *J Am Chem Soc* **55** 3392 *1933*]. [*Beilstein* **3** IV 1562.]

Ethyl malonate monoamide *[7597-56-0]* **M 131.1, m 47-50°, 49.5-50°, 50°, b 130-135°/2mm.** The amide crystallises from Et_2O or by slow evaporation of an aqueous solution as colourless crystals [Snyder & Elston *J Am Chem Soc* **76** 3039 *1954*, McAlvain & Schroeder *J Am Chem Soc* **71** 45 *1949*, Rising et al. *J Biol Chem* **89** 20 *1930*]. [*Beilstein* **2** IV 1887.]

Ethyl methacrylate *[97-63-2]* **M 114.2, b 59°/100mm, d_4^{20} 0.915, n_D^{20} 1.515.** Wash the ester successively

with 5% aqueous $NaNO_2$, 5% $NaHSO_3$, 5% NaOH, then water. Dry it over $MgSO_4$, add 0.2% (w/w) of phenyl-ß-naphthylamine, and distil it through a short Vigreux column [Schultz *J Am Chem Soc* **80** 1854 *1958*]. [*Beilstein* **2** IV 1523.]

Ethyl methyl ether *[540-67-0]* **M 60.1, b 7°/760mm, d^{o} 0.725, n^{4} 1.3420.** Dry the ether with $CaSO_4$, pass it through an alumina column (to remove peroxides), then fractionally distil it while collecting fractions in receivers kept below 0°. [*Beilstein* **1** H 314, **1** I 158, **1** II 311, **1** III 1288, **1** IV 1314.]

3-Ethyl-2-methyl-2-pentene *[19780-67-7]* **M 112.2, b 109°/757mm, 114.5°/760mm, d_4^{20} 0.72468, n_D^{20} 1.4124.** Purify it by preparative GLC on a column of 20% squalene on Chromosorb P at 70°. *Alternatively*, fractionate it under an inert atmosphere. It forms an azeotrope with methoxyethanol. [*Beilstein* **1** H 222, **1** III 8471, **1** IV 890.]

Ethyl nitroacetate *[626-35-7]* **M 133.1, b 42-43°/0.2mm, 71-72°/3mm, 93-96°/9mm, 194-195°/atm, d_4^{20} 1.1953, n_D^{20} 1.4260, pK^{25} 5.82.** Purify the ester by repeated distillation. IR:ν_{max} 1748 (CO_2), 1570 and 1337 (NO_2), and 800cm^{-1} [Haszeldine *J Chem Soc* 2525 *1953*]. The *hydrazine salt* crystallises from 95% EtOH or MeOH as yellow crystals **m** 104-105° [Ungnade & Kissinger *J Org Chem* **22** 1661 *1957*, Emmons & Freeman *J Am Chem Soc* **77** 4391 *1955*]. [*Beilstein* **2** IV 537.]

Ethyl propionate *[105-37-3]* **M 102.1, b 99.1°, d_4^{20} 0.891, n^{15} 1.38643, n_D^{20} 1.38394.** Treat the ester with anhydrous $CuSO_4$ and distil it under nitrogen. [*Beilstein* **2** IV 205.]

Ethyl pyruvate *[617-35-6]* **M 116.1, m –50°, b 44-45°/10mm, 56°/20mm, 69-71°/42mm, 63°/23mm, 155.5°/760mm, d_4^{20} 1.047, n_D^{20} 1.4052.** Shake the ester with 10ml portions of saturated aqueous $CaCl_2$ solution (removes ethyl acetate) and the organic layer is removed by centrifugation, decantation and filtration, and is distilled under reduced pressure. Purification of small quantities is carried out *via* the bisulfite adduct: the ester (2.2ml) is shaken with saturated $NaHSO_3$ (3.6ml), chilled in a freezing mixture when crystals separate rapidly (particularly if seeded). After 5 minutes EtOH (10ml) is added and the crystals are filtered off, washed with EtOH and Et_2O and dried. Yield *ca* 3g of *bisulfite adduct*. Then treat the adduct (16g) with saturated aqueous $MgSO_4$ (32ml) and 40% formaldehyde (5ml) and shake, whereby the ester separates as an oil which is extracted with Et_2O. The extract is dried ($MgSO_4$), filtered, evaporated and the residue is distilled (**b** 56°/20mm), and then redistilled (**b** 147.5°/750mm) to give 5.5g of pure ester. [Cornforth *Org Synth* Coll Vol **IV** 467 *1963*, *Beilstein* **3** IV 1513.]

Ethyl stearate *[111-61-5]* **M 312.5, m 33°, b 213-215°/15mm.** The solid portion is separated from the partially solid starting material, then crystallised twice from EtOH, dried by azeotropic distillation with *benzene, and fractionally distilled through a spinning-band column at low pressure [Welsh *Trans Faraday Soc* **55** 52 *1959*]. [*Beilstein* **2** IV 1218.]

Ethyl thiocyanate (ethyl rhodanide) *[542-90-5]* **M 87.1, b 144-145°, d_4^{20} 1.011, n_D^{20} 1.462.** Fractionally distil the ester at atmospheric pressure. [*Beilstein* **2** IV 1218.] **(CARE LACHRYMATOR.)**

Ethyl thioglycolate (ethyl 2-mercaptoacetate) *[623-51-8]* **M 120.2, b 50-51°/10mm, 55°/17mm, 62.5-64°/22mm, 67-68°/24mm, 155-158°/atm, d_4^{20} 1.096, n_D^{20} 1.457.** Dissolve the thioglycolate in Et_2O, wash with H_2O, dry it over Na_2SO_4, filter, evaporate and distil the residue under reduced pressure [Bredereck et al. *Chem Ber* **90** 1837 *1957*]. The *Ni complex [Ni(SCH$_2$CO$_2$Et)$_2$]*, when recrystallised twice from EtOH, gives crystals which become black when dried in a vacuum over H_2SO_4, **m** 104-105° [Dranet & Cefola *J Am Chem Soc* **76** 1975 *1954*]. [*Beilstein* **3** H 255.]

***N*-Ethyl thiourea** *[625-53-6]* **M 104.2, m 110°.** Crystallise the thiourea from EtOH, MeOH or ether. [*Beilstein* **4** IV 374.]

Ethyl trichloroacetate *[515-84-4]* **M 191.4, b 100-100.5°/30mm, d_4^{20} 1.383.** Shake the ester with saturated aqueous Na_2CO_3 (three times), aqueous 50% $CaCl_2$ (three times), saturated aqueous NaCl (twice), then distil it

over $CaCl_2$, and redistil it under reduced pressure. [*Beilstein* **2** IV 514.]

Ethyl trifluoroacetate *[383-63-1]* **M 142.1, b 61.3°/750, 60-62°/atm, 62-64°/755mm, d_4^{20} 1.191, n_D^{20} 1.30738.** It has been prepared by treating sodium trifluoroacetate with Et_2SO_4, or the acid with excess of EtOH and a small amount of H_2SO_4, distilling the azeotropic mixture of ester and EtOH, removing the latter with $CaCl_2$, filtering and fractionally distilling [Henne et al *J Am Chem Soc* **69** 1819]. Fractionate it through a long Vigreux column. IR has ν_{max} at 1800 (CO_2) and 1000 (OCO) cm^1 [Fuson et al. *J Chem Phys* **20** 1627 *1952*, Bergman *J Org Chem* **23** 476 *1958*]. [*Beilstein* **2** II 186, **2** III 427, **2** IV 463.]

Ethyl 4,4,4-trifluoroacetoacetate (ethyl 3-oxo-4,4,4-trifluorobutyrate) *[372-31-6]* **M 184.1, b 47-49°/25mm, 129-130°/atm, 131.8°/atm, d_4^{25} 1.259, n_D^{20} 1.375.** The ester was prepared by the method of Swarts [*Bull Acad Roy Belg* **13** 175 *1927*] in which ethyl trifluoroacetate (1mol) was added slowly to a stirred suspension of NaOEt (1mol) in EtOH (exothermic reaction), followed EtOAc (1mol), and refluxed overnight. An improved purification was by treatment with a concentrated aqueous solution of $NaHSO_4$ (very small molar excess), followed by addition of a clear aqueous solution of $Cu(OAc)_2$**,** and the organic layer was distilled off. The Cu derivative was filtered off and recrystallised from EtOH, washed with Et_2O to give green crystals of the *copper chelate* **m 189°** [UV has λ_{max} at 220nm (ε 11,000) and 270nm (ε 21,000), 3.0mg % in EtOH]. The dry Cu chelate was suspended in Et_2O (some dissolved) and H_2S was bubbled through until precipitation of CuS was complete. The CuS was filtered off, and the filtrate was carefully fractionation (to avoid losses) to provide the *ester* in 54% overall yield. Its UV has λ_{max} at 238nm (ε 3000) and 288nm (ε 400), in cyclohexane [Breslow et al. *J Am Chem Soc* **68** 102, *1946*, Henne et al. *J Am Chem Soc* **69** 1819 *1947*, Haszeldine et al. *J Chem Soc* 609 *1951*, *Beilstein* **3** II 425, **3** III 1206, **3** IV 1548].

Ethyl trifluoromethanesulfonate *[425-75-2]* **M 178.1, b 115°/atm, 118-120°/atm, d_4^{20} 1.378, n_D^{20} 1.336.** The ester reacts slowly with H_2O and aqueous alkali. If its IR has no OH bands (~3000 cm^{-1}) then purify it by redistillation. If OH bands are present, then dilute with dry Et_2O and shake (carefully) with aqueous $NaHCO_3$ until effervescence ceases, then wash with H_2O and dry ($MgSO_4$), filter, evaporate and distil the residue under a slight vacuum then at atmospheric pressure in a N_2 atmosphere. **It is a powerful alkylating agent, and the fumes are very toxic — perform all operations in an efficient fume cupboard.** [Gramstad & Haszeldine *J Chem Soc* 173 *1956*, Howells & McCown *Chem Rev* **77** 69 *1977*, *Beilstein* **3** IV 34.]

S-Ethyl trifluorothioacetate *[383-64-2]* **M 158.1, b 88-90°/atm, 90.5°/760mm, d_4^{20} 1.255, n_D^{20} 1.372.** If IR is free of OH bands then fractionally distil it; otherwise dilute the thio-ester with dry Et_2O, wash with 5% KOH and H_2O, dry over $MgSO_4$ and fractionate it through an efficient column [Hauptschein et al. *J Am Chem Soc* **74** 4005 *1952*]. [*Beilstein* **2** IV 567.] *Powerful obnoxious odour.*

Ethyl vinyl ether *[109-92-2]* **M 72.1, b 35.5°, d_4^{20} 0.755.** It usually contains polymerisation inhibitors (usually amines, e.g. triethanolamine) which can be removed by fractional distillation. Redistil it from sodium. [*Beilstein* **1** IV 2049.] **LACHRYMATORY.**

Fluoroacetamide *[640-19-7]* M 77.1, m 108°.

Crystallise fluoroacetamide from chloroform and dry it in a vacuum. **TOXIC** [*Beilstein* **2** IV 454.]

Formaldehyde *[50-00-0]* **M 30.0, m -92°, b -79.6°/20mm, -19.5°/760mm, d_4^{20} 0.815, pK^{25} 13.27 (hydrate).** Technical aqueous formaldehyde (***formalin***) solution commonly contains added MeOH (8-10%) to inhibit oxidation to formic acid. As a rough guide the d_4^{18} ***vs* [*concentration in g of HCHO/100ml (100g) of aqueous solution*]** is as follows: 1.0054 [2.24 (2.23)], 1.0126 [4.66 (4.60)], 1.0311 [11.08 (10.74)], 1.0410 [14.15 (13.59)], 1.0568 [19.89 (18.82)], 1.0719 [25.44 (23.73)], 1.0853 [30.17 (27.80)], 1.1057 [37.72 (34.11)] and 1.1158 [41.87 (37.53)]; values in curved brackets are from alternative determinations. [Marvel & Porter *Org Synth* Coll Vol **I** 377 1941]. If pure formaldehyde is required, add KOH solution (1 mole KOH: 100 moles HCHO) to ~37% by weight of aqueous formaldehyde solution (*formalin*), or evaporate formalin to dryness, to

give ***paraformaldehyde polymer*** {$HO(CH_2O)_nH$, [30525-89-4] **m 120-170°** depending on ***n***} as a white solid which, after washing with water, is dried in a vacuum desiccator over P_2O_5 or H_2SO_4. Formaldehyde is regenerated by heating the paraformaldehyde to 120° under vacuum, or by decomposing it with barium peroxide. The *monomer*, a colourless flammable gas, is passed through a glass-wool filter cooled to –48° in a $CaCl_2$/ice mixture to remove particles of polymer, then dried by passage over P_2O_5 and either condensed in a bulb immersed in liquid nitrogen or absorbed in ice-cold conductivity water. The gas or aqueous solutions have *pungent suffocating odours***,** are LACHRYMATORY and SUSPECTED CARCINOGEN, handle carefully. Formalin is a disinfectant and a preservative of dead animal and plant tissues. [*Beilstein* **1** IV 3017.]

Formaldehyde dimethyl acetal (dimethoxymethane, methylal, formal) *[109-87-5]* **M 76.1, m –108°, b 41-42°/736mm, 41-43°/atm, 42-46°/atm, d_4^{20} 0.8608, n_D^{20} 1.35335.** It is a volatile flammable liquid which is soluble in three parts of H_2O, and is readily hydrolysed by acids. Purify it by shaking with an equal volume of 20% aqueous NaOH, stand for 20 minutes, dry over fused $CaCl_2$, filter and fractionally distil it through an efficient column. Store it over molecular sieves. [Buchler et al. *Org Synth* Coll Vol **III** 469 *1955*, Rambaud & Besserre *Bull Soc Chim Fr* 45 *1955*, IR: Wilmshurst *Can J Chem* **36** 285 *1958*, *Beilstein* **1** IV 3026.]

Formaldehyde dimethyl mercaptal (bis-[methylthio]methane) *[1618-26-4]* **M 108.2, b 44-47°/13mm, 45.5°/18mm, 148-149°/~760mm, d_4^{20} 1.0594, n_D^{20} 1.5322. Work in an efficient fume cupboard as the substance may contain traces (or more) of methylmercaptan which has a very bad odour.** Dissolve the mercaptal in Et_2O, shake it with aqueous alkalis then dry it over anhydrous K_2CO_3, filter and distil it over K_2CO_3 under a stream of N_2. If the odour is very strong, then allow all gas efluents to bubble through 5% aqueous NaOH solution which is then treated with dilute $KMnO_4$ in order to oxidise MeSH to odourless products. Its UV has λ_{max} at 238 nm (log ε 2.73) [Fehnel & Carmack *J Am Chem Soc* **71** 90 *1949*, Fehér & Vogelbruch *Chem Ber* **91** 996 *1958*, Bøhme & Marz *Chem Ber* **74** 1672 *1941*]. Oxidation with aqueous $KMnO_4$ yields *bis-(methylsulfonyl)methane* which has **m** 142-143° [Fiecchi et al. *Tetrahedron Lett* 1681 *1967*]. [*Beilstein* **1** IV 3088.]

Formamide *[75-12-7]* **M 45.0, f 2.6°, b 103°/9mm, 210.5°/760mm(dec), d_4^{20} 1.13, n_D^{20} 1.44754, n^{25} 1.44682.** Formamide is easily hydrolysed by acids and bases. It also reacts with peroxides, acid halides, acid anhydrides, esters and (on heating) alcohols, while strong dehydrating agents convert it to a nitrile. It is very *hygroscopic*. Commercial material often contains acids and ammonium formate. Vorhoek [*J Am Chem Soc* **58** 2577 *1956*] added some bromothymol blue to formamide and then neutralise it with NaOH before heating to 80-90° under reduced pressure to distil off ammonia and water. The amide is again neutralised and the process is repeated until the liquid remained neutral on heating. Sodium formate is added, and the formamide is concentrated under reduced pressure at 80-90°. The distillate is again neutralised and redistilled. It is then fractionally crystallised in the absence of CO_2 and water by partial freezing.
Formamide (specific conductance 2 x 10^{-7} ohm^{-1} cm^{-1}) of low water content is dried by passage through a column of 3A molecular sieves, then deionised by treatment with a mixed-bed ion-exchange resin loaded with H^+ and $HCONH^-$ ions (using sodium formamide in formamide) [Notley & Spiro *J Chem Soc (B)* 362 *1966*]. [*Beilstein* **2** IV 45.]

Formamidine acetate *[3473-63-0]* **M 104.1, m 159-161°(dec), 164°(dec), pK_{Est} ~12.** Unlike the hydrochloride, the acetate salt is not hygroscopic. It is recrystallised from a small volume of acetic acid, by addition of EtOH, and the crystals are washed with EtOH then Et_2O and dried in a vacuum. [Taylor et al. *Org Synth* **46** 39 *1966*, *Beilstein* **2** IV 82.]

Formamidine sulfinic acid (thiourea-S-dioxide) *[1758-73-2]* **M 108.1, m 124-126°(dec).** Dissolve it in five parts of aqueous 1:1% $NaHSO_3$ at 60-63° (charcoal), then allow it to crystallise slowly, with agitation, at 10°. Filter and dry it immediately at 60° [Koniecki & Linch *Anal Chem* **30** 1134 *1958*]. [*Beilstein* **3** I 36, **3** IV 145.]

Formic acid *[64-18-6]* **M 46.0 (anhydrous), f 8.3°, b 25°/40mm, 100.7°/760mm, d_4^{20} 1.22, n 1.37140, n^{25} 1.36938, pK^{25} 3.74.** Anhydrous formic acid can be obtained by direct fractional distillation under reduced pressure, the receiver being cooled in ice-water. The use of P_2O_5 or $CaCl_2$ as dehydrating agents is unsatisfactory. Reagent grade 88% formic acid can be dried satisfactorily by refluxing with phthalic anhydride

for 6 hours and then distilling it. *Alternatively*, if it is left in contact with freshly prepared anhydrous $CuSO_4$ for several days about one half of the water is removed from 88% formic acid; distillation then removes the remainder. Boric anhydride (prepared by melting boric acid in an oven at a high temperature, cooling in a desiccator, and powdering) is a suitable dehydrating agent for 98% formic acid; after prolonged stirring with the anhydride the formic acid is distilled under vacuum. Formic acid can be further purified by fractional crystallisation using partial freezing. [*Beilstein* **2** IV 3.]

***N*-Formyl *tert*-butylamine (*N-tert*-butylformamide)** *[2425-74-3]* **M 101.2, m 16°, b 48°/0.2mm, 78-83°/9mm, 135-136°/107mm, 202°/760mm, d_4^{25} 0.903, n_D^{20} 1.4330.** If the IR indicates some hydrolysis, then dissolve it in Et_2O, wash it with 20% aqueous Na_2CO_3, dry it ($MgSO_4$), filter and fractionate it. Collect the fraction that solidifies on cooling and recrystallise it from Et_2O at low temperature if necessary. [Emmons *J Am Chem Soc* **79** 5753 *1957*, *Beilstein* **4** III 324, **4** IV 661.]

***N*-Formyl ethylamine (*N*-ethylformamide)** *[627-45-2]* **M 73.1, b 29°/0.5mm, 176-179°/758mm, d_4^{20} 0.950, n_D^{20} 1.4346.** If the IR is good, then distil it and collect the middle fraction and redistil if necessary; otherwise proceed as for the previous amide. [Erickson *J Org Chem* **20** 1569 *1955*, *Beilstein* **4** H 109, **4** I 352, **4** II 601, **4** III 207, **4** IV 346.]

Formyl hydrazine (formic acid hydrazide) *[624-84-0]* **M 60.1, m 54°, 54-57°, pK_{est} ~2.5.** Recrystallise it from EtOH and dry it *in vacuo*. Store below 10°; it may disproportionate on storage to 1,2-diformyl hydrazine and hydrazine. It forms a blue $[Cu(CH_4N_2O)]SO_4$ salt with $CuSO_4$. [*Beilstein* **2** H 93, **2** III 127, **2** IV 85.]

Formyloxy acetonitrile (cyanomethyl formate) *[150760-95-5]* **M 85.1, b 62-64°/12mm, 172-173°/atm, d_4^{25} 0.903, n_D^{20} 1.4330.** Purify it by fractional distillation and redistilling the middle fraction. It is useful for the formylation of alcohols and amines. The ^{13}C NMR has δ ($CDCl_3$) at 47.87, 114.47 and 159.46 ppm. [Deutsch & Niclas *Synth Commun* **23** 1561 *1993*, Duczek et al. *Synthesis* 37 *1966*.]

Fumaraldehyde bis-(dimethyl acetal) (*trans*-1,1,4,4-tetramethoxybut-2-ene) *[6068-62-8]* **M 176.2, b 100-103°/15mm, 101-103°/25mm, d_4^{20} 1.011, n_D^{20} 1.425.** Dry it over fused $CaCl_2$ and distil it *in vacuo*. The maleic (*cis*) isomer has **b** 112°/11mm, and d^{23} 0.932 and n_D^{25}1.4243. [Zeik & Heusner *Chem Ber* **90** 1869 *1957*, Clauson-Kaas et al. *Acta Chem Scand* **9** 111 *1955,* Clauson-Kaas *Acta Chem Scand* **6** 569 *1952*, *Beilstein* **1** IV 3754.]

Fumaric (*trans*-but-2-ene-1,4-dioic) acid *[110-17-8]* **M 116.1, m 289.5-291.5° (sealed tube), pK_1^{25} 3.10, pK_2^{25} 4.60 (4.38).** Crystallise it from hot M HCl or water and dry it at 100°. [*Beilstein* **2** IV 2202.]

Geraniol (*trans*-3,7-dimethyl-2,6-octadien-8-ol) *[106-24-1]* **M 154.3, b 114-115°/11-12mm, 230°, d_4^{20} 0.879, n_D^{20} 1.4766.** Purify geraniol by ascending chromatography or by thin layer chromatography on plates of kieselguhr G with acetone/water/liquid paraffin (130:70:1) as solvent system. Hexane/ethyl acetate (1:4) is also suitable. Also purify it by GLC on a silicone-treated column of Carbowax 20M (10%) on Chromosorb W (60-80 mesh). [Porter *Pure Appl Chem* **20** 499 *1969*.] Store it in full, tightly sealed containers in the cool and protect from light. It has a pleasant odour. [cf p 681, *Beilstein* **1** IV 2277.]

Glutaraldehyde *[111-30-8]* **M 100.1, b 71°/10mm, as 50% aqueous solution.** Likely impurities are oxidation products-acids, semialdehydes and polymers. It can be purified by repeated washing with activated charcoal (Norit) followed by vacuum filtration, using 15-20g charcoal/100ml of glutaraldehyde solution. Distil it at 60-65°/15mm, discarding the first 5-10%, then dilute with an equal volume of freshly distilled water at 70-75°, using magnetic stirring under nitrogen. The solution is stored at low temperature (3-4°), in a tightly stoppered container, and protected from light. Standardise by titration with hydroxylamine. [Anderson *J Histochem Cytochem* **15** 652 *1967*, *Beilstein* **1** IV 3659.]

Glutaric acid *[110-94-1]* **M 132.1, m 97.5-98°, pK_1^{25} 4.35, pK_2^{25} 5.40.** Crystallise the acid from *benzene, $CHCl_3$, distilled water or *benzene containing 10% (w/w) of diethyl ether. Dry it under vacuum. [*Beilstein* **2**

IV 1934.]

***dl*-Glyceraldehyde** *[56-82-6]* **M 90.1, m 145°.** Crystallise it from EtOH/diethyl ether. The D(+)-*enantiomer* [453-17-8] is a syrup (70 + % H_2O) with $[\alpha]_D^{25}$ +14° (c 2, H_2O) and the *dimethyl acetal* has **b** 124-127 °/14mm and $[\alpha]_D^{15}$ +21° (c 18, H_2O). [*Beilstein* **1** H 845, **1** IV 4114.]

Glycerol *[56-81-5]* **M 92.1, m 18.2°, b 182°/20mm, 290°/760mm, d_4^{20} 1.261, n_D^{25} 1.47352, pK^{25} 14.4.** Glycerol is dissolved in an equal volume of *n*-butanol (or *n*-propanol, amyl alcohol or liquid ammonia) in a water-tight container, cooled and seeded while slowly revolving in an ice-water slurry. The crystals are collected by centrifugation, then washed with cold acetone or isopropyl ether. [Hass & Patterson *Ind Eng Chem (Anal Ed)* **33** 615 *1941*.] Coloured impurities can be removed from substantially dry glycerol by extraction with 2,2,4-trimethylpentane. *Alternatively*, glycerol can be decolorised and dried by treatment with activated charcoal and alumina, followed by filtering. Glycerol can be distilled at 15mm in a stream of dry nitrogen, and stored in a desiccator over P_2O_5. Crude glycerol can be purified by digestion with concentrated H_2SO_4 and then saponification with a lime paste, re-acidification with H_2SO_4, filteration, treatment with an anion exchange resin and fractional distillation under vacuum. [*Beilstein* **1** IV 2751.]

Glycolic (α-hydroxyacetic) acid *[79-14-1]* **M 76.1, m 81°, pK^{25} 3.62.** Crystallise it from diethyl ether. [*Beilstein* **3** IV 571.]

Guanidine *[113-00-8]* **M 59.1, m 47.5-48.5°, 48-49°, ~50°, pK^{25} 13.6.** Crystallise it from water/EtOH under nitrogen. It is very deliquescent and absorbs CO_2 from the air readily. [Jones *Trans Faraday Soc* **55** 524 *1959*, *Beilstein* **3** H 82, **3** I 39, **3** II 69, **3** III 154, **3** IV 148.]

Guanidine carbonate *[593-85-1]* **M 180.2, m 197°, 230°.** Crystallise it from MeOH. [*Beilstein* **3** H 86, **3** I 41, **3** II 72, **3** III 161, **3** IV 152.]

Guanidine hydrochloride *[50-01-1]* **M 95.5, m 181-183°.** Crystallise the hydrochloride from hot methanol by chilling to about –10°, with vigorous stirring. The fine crystals are filtered through fritted glass, washed with cold (–10°) methanol, dried at 50° under vacuum for 5 hours. (The product is purer than that obtained by crystallisation at room temperature from methanol by adding large amounts of diethyl ether.) [Kolthoff et al. *J Am Chem Soc* **79** 5102 *1957*, *Beilstein* **3** H 86, **3** II 71, **3** III 160, **3** IV 150.]

Heptadecanoic acid (margaric) *[506-12-7]* **M 270.5, m 60-61°, b 227°/100mm, pK_{Est} ~4.9.** Crystallise the acid from MeOH or petroleum ether. [*Beilstein* **2** IV 1193.]

1-Heptadecanol *[1454-85-9]* **M 256.5, m 54°.** Crystallise it from acetone. [*Beilstein* **1** IV 1884.]

Heptafluoro-2-iodopropane *[677-69-0]* **M 295.9, b 39°/735mm, 41°/760mm, d_4^0 2.1306, n_D^{20} 1.3281.** Purify it by gas chromatography on a triacetin (glyceryl triacetate) column, followed by bulb-to-bulb distillation at low temperature. Store it over Cu powder to stabilise it. UV has ν_{max} at 271nm (ε 240) in petroleum ether (b 60-80°). [Haszeldine *J Chem Soc* 1767, 3761 *1953*, *Beilstein* **1** III 255, **1** IV 225.]

***n*-Heptaldehyde** *[111-71-7]* **M 114.2, b 40.5°/12mm, 152.8°/760mm, d_4^{20} 0.819, n_D^{25} 1.4130.** Dry *n*-heptaldehyde with $CaSO_4$ or Na_2SO_4 and fractionally distil it under reduced pressure. More extensive purification is by precipitation as the bisulfite compound (formed by adding the aldehyde to saturated aqueous $NaHSO_3$) which is filtered off and recrystallised from hot H_2O. The crystals, after being filtered and washed well with H_2O, are hydrolysed by adding 700ml of aqueous Na_2CO_3 (12.5% w/w of anhydrous Na_2CO_3) per 100g of aldehyde. The aldehyde is then steam distilled off, separated, dried with $CuSO_4$ and distilled under reduced pressure in a slow stream of nitrogen. [McNesby & Davis *J Am Chem Soc* **76** 2148 *1954*, *Beilstein* **1** H 695, **1** I 357, **1** II 750, **1** III 2844, **1** IV 3314.]

***n*-Heptaldoxime** *[629-31-2]* **M 129.2, m 53-55°.** Separate the *cis*(Z) and *trans*(E) oximes by liquid chromatography through a silica gel column and eluting with petroleum ether (b 40-65°)/EtOAc (50:10) at a flow rate of 2-3.4 ml/sec where the *trans-isomer* comes through first and is a liquid with n_D^{22} 1.38512, followed by the *cis-isomer* which is a solid, and crystallises from 60% aqueous EtOH with **m** 55°. They are identified by TLC on 0.2mm silica gel G by eluting with *C_6H_6/EtOAc (50/10) and visualising with I_2 vapour: the *trans-isomer* has R_F 0.6 and the *cis-isomer* has R_F 0.5 [Pejkovic-Tadic et al. *J Chromatography* **21** 239 *1966*, Emmous & Pagano *J Am Chem Soc* **77** 4557 *1955*]. [*Beilstein* **1** H 698, **1** I 358, **1** II 752, **1** III 2850.]

***n*-Heptane** *[142-18-5]* **M 100.2, b 98.4°, d_4^{20} 0.684, n_D^{20} 1.38765, n_D^{25} 1.38512.** Pass it through a silica gel column which greatly reduces the ultraviolet absorption of *n*-heptane. (The silica gel is previously heated to 350° before use.) For more extensive purification, heptane is shaken with successive small portions of conc H_2SO_4 until the lower (acid) layer remains colourless. The heptane is then washed successively with water, aqueous 10% Na_2CO_3, water (twice), and dried with $CaSO_4$, $MgSO_4$ or $CaCl_2$. It is distilled from sodium. *n*-Heptane can be distilled azeotropically with methanol, then the methanol is washed out with water and, after drying, the heptane is redistilled. Other purification procedures include passage through activated basic Al_2O_3, drying with CaH_2, storage with sodium, and stirring with 0.5*N* $KMnO_4$ in 6N H_2SO_4 for 12 hours after treatment with conc H_2SO_4. Carbonyl-containing impurities have been removed by percolation through a column of impregnated Celite made by dissolving 0.5g of 2,4-dinitrophenylhydrazine in 6ml of 85% H_3PO_4 by grinding together, then adding 4ml of distilled water and 10g Celite. [Schwartz & Parks *Anal Chem* **33** 1396 *1961*, *Beilstein* **1** IV 376.]

Hept-1-ene *[592-76-7]* **M 98.2, b 93°/771mm, d_4^{20} 0.698, n_D^{20} 1.400.** Distil hept-1-ene from sodium, then carefully fractionally distilling it using an 18-in gauze-packed column. It can also be purified by azeotropic distillation with EtOH. It usually contains the 2- and 3-isomers as impurities. These can be removed by gas chromatography using a Carbowax column at 70°. [*Beilstein* **1** IV 857.]

***n*-Heptyl alcohol (1-heptanol)** *[111-70-6]* **M 116.2, b 175.6°, d 0.825, n_D^{20} 1.425.** Shake the alcohol with successive lots of alkaline $KMnO_4$ until the colour persists for 15 minutes, then dry it with K_2CO_3 or CaO, and fractionally distil it. [*Beilstein* **1** IV 1731.]

***n*-Heptylamine** *[111-68-2]* **M 115.2, b 155°, d_4^{20} 0.775, n_D^{20} 1.434, pK^{25} 10.66.** Dry it in over KOH pellets for 24 hours, then decant it and fractionally distil it. Store away from CO_2. [*Beilstein* **4** IV 734.]

***n*-Heptyl bromide** *[629-04-9]* **M 179.1, b 70.6°/19mm, 180°/760mm, d_4^{20} 1.140, n_D^{20} 1.45.** Shake it with conc H_2SO_4, wash with water, dry it with K_2CO_3, and fractionally distil. [*Beilstein* **1** IV 391.]

Hexachloro-1,3-butadiene (perchlorobutadiene) *[87-68-3]* **M 260.8, b 144.1°/100mm, 210-212°/760mm, d_4^{20} 1.683, n_D^{20} 1.5556.** Wash the diene with four or five 1/10th volumes of MeOH (or until the yellow colour has been extracted), then stir it for 2 hours with H_2SO_4, wash it with distilled water until neutral and filter it through a column of P_2O_5. Distil it under reduced pressure through a packed column. [Rytner & Bauer *J Am Chem Soc* **82** 298 *1960*, *Beilstein* **1** IV 998.]

Hexachloroethane *[67-72-1]* **M 236.7, m 187°.** Steam distil it, then crystallise it from 95% EtOH. Dry it in the dark under vacuum. [*Beilstein* **1** IV 148.]

Hexacosane (C-26) *[630-01-3]* **M 366.7, m 56.4°, b 169°/0.05mm, 205°/1mm, 262°/15mm.** Distil hexacosane under vacuum and recrystallise it from diethyl ether. [*Beilstein* **1** IV 583.]

Hexacosanoic acid (cerotinic acid) *[506-46-7]* **M 396.7, m 86-87°, 88-89°, pK_{Est} ~4.9.** Crystallise the acid from EtOH, aqueous EtOH and petroleum ether/Me_2CO. [*Beilstein* **2** IV 1310.]

***n*-Hexadecane (Cetane)** *[544-76-3]* **M 226.5, m 18.2°, b 105°/0.1mm, d_4^{20} 0.773, n_D^{20} 1.4345, n^{25} 1.4325.** Pass cetane through a column of silica gel and distil it under vacuum in a column packed with Pyrex helices. Store it over silica gel. It also crystallises from acetone, or is fractionally crystallised by partial freezing.

[*Beilstein* **1** IV 537.]

1,14-Hexadecanedioic acid (Thaspic acid) *[505-54-4]* **M 286.4, m 126°, $pK_{Est(1)}$ ~4.5, $pK_{Est(2)}$ ~5.5.** Recrystallise thaspic acid from EtOH, ethyl acetate or $*C_6H_6$. [*Beilstein* **2** IV 2162.]

Hexadecanoic acid (palmitic acid) *[57-10-3]* **M 256.4, m 62-63°, b 215°/15mm, pK^{25} 6.46 (50% aqueous EtOH), 5.0 (H_2O).** Purify palmitic acid by slow (overnight) recrystallisation from hexane. Some samples are also crystallised from acetone, EtOH or EtOAc. The crystals are kept in air to lose solvent, or are pumped dry of solvent on a vacuum line. [Iwahashi et al. *J Chem Soc, Faraday Trans 1* **81** 973 *1985*, pK: White *J Am Chem Soc* **72** 1858 *1950*, *Beilstein* **2** IV 1157.]

1,5-Hexadiene *[592-42-7]* **M 82.2, b 59.6°, d_4^{20} 0.694, n_D^{20} 1.4039.** Distil 1,5-hexadiene from $NaBH_4$. [*Beilstein* **1** IV 1013.]

Hexafluoroacetone *[684-16-2, 34202-69-2 ($3H_2O$)]* **M 166.1, m –129°, (trihydrate m 18-21°), b -28°.** Dehydrate hexafluoroacetone by passing the vapours over P_2O_5. Ethylene is removed by passing the dried vapours through a tube containing Pyrex glass wool moistened with conc H_2SO_4. Further purification is by low temperature distillation using Warde-Le Roy stills. Store it in the dark at –78°. [Holmes & Kutschke *Trans Faraday Soc* **58** 333 *1962*, *Beilstein* **1** IV 3215.]

Hexafluoroacetylacetone (1,1,1,5,5,5-hexafluoro-2,4-pentanedione, hfacac) *[1522-22-1]* **M 208.1, b 63-65°/atm, 68°/736mm, 70-70.2°/760mm, 68-71°/atm, d_4^{20} 1.490, n_D^{20} 1.333.** Hfacac has been prepared from a mixture of Na wire (0.34mole) covered with dry Et_2O and CF_3CO_2Et (0.27mole see [383-63-1]) at 0°, to which was added trifluoroacetone (0.27mol, see [421-50-1]) at –78°. The mixture was then set aside overnight at ~25°, and any trifluoroacetone which distilled out was made to condense back into the reaction mixture which was stirred at ~25° until all the Na dissolved [Haszeldine et al. *J Chem Soc* 609 *1951*, compare with Henne et al. *J Am Chem Soc* **69** 1819 *1947*]. The reddish-brown mixture was treated with an excess of 2N H_2SO_4 and extracted with ether. The organic layer was dried (Na_2SO_4), and distilled to give *hfacac* (20g, 37%). By using NaOEt instead of Na metal, Henne and coworkers obtained a 72% yield of *hfacac*, which gave the *copper chelate* as bright grass green crystals (see below) [Henne et al. *J Am Chem Soc* **69** 1819 *1947*]. Hfacac (100g) is purified by shaking twice with 98% H_2SO_4 (300ml, *use protective clothing*) until it is completely dispersed, and set aside overnight. The anhydrous facac is separated and distilled through a glass-helices packed column with fraction b 70.2-70.5°/atm (~20g, analytically pure) being retained for metal complex studies [Buckingham et al. *Aust J Chem* **20** 281 *1967*]. The oil readily forms a solid white stable *covalent dihydrate* [CF_3-$C(OH)_2$-CH_2-$C(OH)_2$-CF_3] which is caused by the strong electron-withdrawing effect of the fluorine atoms. The dihydrate has no UV absorption spectrum; compare with λ_{max} ($CHCl_3$) 273nm (ε 7,800) for the anhydrous diketone. The dihydrate decomposes at ~90°. The hydrate (10g) can also be dehydrated by heating with anhydrous $CaSO_4$ (Drierite, 30g) and distilling; the distillate is treated with more $CaSO_4$ and redistilled (see above). When the distillate is treated with aqueous NaOH and heated, the dihydrate crystallises on cooling. The *Cu (II) complex* is more easily prepared from the anhydrous than from the hydrated diketone which needs to be dehydrated in the reaction medium, and has **m 135°** (after sublimation or crystallisation from CCl_4). Store hfacac as the dihydrate; but the anhydrous diketone should be kept in an anhydrous atmosphere. [Gilman et al. *J Am Chem Soc* **78** 2790 *1956*, Belford et al. *J Inorg Nucl Chem* **2** 11 *1956*, *Beilstein* **1** III 3123, **1** IV 3681.]

Hexafluoroethane *[76-16-4]* **M 138.0, b –79°.** Purify it for pyrolysis studies by passing through a copper vessel containing CoF_3 at *ca* 270°, and held for 3 hours in a bottle with a heated (1300°) platinum wire. It is then fractionally distilled. [Steunenberg & Cady *J Am Chem Soc* **74** 4165 *1962*, *Beilstein* **1** IV 132.]

Hexafluoropropene (hexafluoropropylene, perfluoropropene, *F*-propene) *[116-15-4]* **M 150.0, m –153°, –156.2°, b –28°/atm, –29.4°/atm, d_4^{-40} 1.583.** *F*-Propene is a gas that is available commercially in brass cylinders and is very **corrosive**, **toxic**, attacks skin and tissue membranes. It is prepared by treating $CFCl_2CFClCF_3$ with Zn in boiling EtOH (3 days), but is faster under pressure at 100°. The gas is best handled

in a vacuum line and should be scrubbed over caustic alkali in a brass tube, as any HF present in it will attack glass. [Henne & Waalkes *J Am Chem Soc* **68** 496 *1946*, Henne & Hinkamp *J Am Chem Soc* **67** 1194 *1945*, *Beilstein* **1** III 697, **1** IV 735.]

1,1,1,3,3,3-Hexafluoropropan-2-ol (HFIP) *[920-66-1]* **M 168.1, m –4°, b 57-58°/760mm, d_4^{20} 1.4563, n^{22} 1.2750, pK^{25} 9.30.** Distil it from 3A molecular sieves, retaining the middle fraction. It has been prepared by reduction of *hexafluoroacetone* in tetrahydrofuran (THF). In this case hexafluoropropanol forms a stable 1:1 THF complex which distils at 99-100°/760mm (n_D^{25} 1.3283). The complex is decomposed by mixing with 20% oleum and distilling in a vacuum; the distillate is redistilled to give pure hexafluoropropan-2-ol with **b** 59°/760mm. The ^{1}H NMR shows a doublet at 4.52ppm ($J_{H,H}$ = 2Hz). The *benzoyl* derivative, [10315-85-2] M 272.1, has **m** 53.9° after crystalllisation from pentane at –50°, and its IR has ν_{max} at 1760cm^{-1}. [Middleton & Lindsey *J Am Chem Soc* **86** 4948 *1964*, Urry et al. *J Org Chem* **32** 347 *1967*.] It has very high peptide solubilising properties, alone or with CH_2Cl_2 [use as a solvent: Narita et al. *Bull Chem Soc Jpn* **61** 281 *1988*, *Biochemistry* **29** 2639 *1990*.] It is **CORROSIVE, causes severe eye irritation.**

Hexamethylenediamine (1,6-diaminohexane) *[124-09-4]* **M 116.2, m 42°, b 46-47°/1mm, 84.9°/9mm, 100°/20mm, 204-205°/760mm, pK_1^{25} 10.24, pK_2^{25} 11.02.** Crystallise it in a stream of nitrogen. It sublimes in a vacuum. [*Beilstein* **4** IV 1320.]

Hexamethylenediamine dihydrochloride *[6055-52-3]* **M 189.2, m 248°.** Crystallise the salt from water or EtOH. [*Beilstein* **4** IV 1320.]

Hexamethylene glycol (1,6-hexanediol) *[629-11-8]* **M 118.2, m 41.6°, 43-45°, b 134°/10mm, 250°, n_D^{20} 1.458.** Fractionally crystallise it from its melt or from water. Distil it *in vacuo*. [*Beilstein* **1** IV 2556.]

***n*-Hexane** *[110-54-3]* **M 86.2, b 68.7°, d_4^{20} 0.660, n 1.37486, n^{25} 1.37226.** Purify as for *n*-heptane. Modifications include the use of chlorosulfonic acid or 35% fuming H_2SO_4 instead of conc H_2SO_4 in washing the alkane, and final drying and distilling from sodium hydride. Unsaturated impurities can be removed by shaking the hexane with nitrating acid (58% H_2SO_4, 25% conc HNO_3, 17% water, or 50% HNO_3, 50% H_2SO_4), then washing the hydrocarbon layer with conc H_2SO_4, followed by H_2O, drying, and distilling over sodium or *n*-butyl lithium. It can also be purified by distillation under nitrogen from sodium benzophenone ketyl solubilised with tetraglyme. Also purify it by passage through a silica gel column followed by distillation [Kajii et al. *J Phys Chem* **91** 2791 *1987*]. It is a FLAMMABLE liquid and a possible nerve toxin. [*Beilstein* **1** IV 338.]
Rapid purification: Distil, discarding the first forerun and stored over 4A molecular sieves.

(±)-1,2-Hexanediol *[6920-22-5]* **M 118.2, b 96-98°/1mm, 118.4-118.5°/13mm, 214-215°/760mm, d_4^{20} 0.951, n_D^{20} 1.442.** Fractionally distil it, preferably in a vacuum. *Alternatively*, dissolve it in Et_2O, dry with K_2CO_3 then Na_2SO_4, filter, evaporate and distil it in a vacuum. The *bis-4-nitrobenzoyl* derivative has **m** 101.5-102.5°. [Rudloff *Can J Chem* **36** 486 *1958*, *Beilstein* **1** I 251, **1** III 2200, **1** IV 2554.]

1-Hexene *[592-41-6]* **M 84.2, b 63°, d 0.674, n_D^{20} 1.388.** Purify it by stirring over Na/K alloy for at least 6 hours, then fractionally distil it from sodium under nitrogen. [*Beilstein* **1** IV 828.]

***cis*-2-Hexene** *[7688-21-3]* **M 84.2, b 68-70°, d_4^{20} 0.699, n_D^{20} 1.399.** Purify it as for 1-hexene above. [*Beilstein* **1** IV 833.]

***trans*-2-Hexene** *[4050-45-7]* **M 84.2, b 65-67°, n_D^{20} 1.390.** Purify it as for 1-hexene above. [*Beilstein* **1** IV 834.]

***trans*-3-Hexene** *[13269-52-8]* **M 84.2, b 67-69°, d_4^{20} 0.678, n_D^{20} 1.393.** Purify it as for 1-hexene above. [*Beilstein* **1** IV 837.]

***n*-Hexyl alcohol (1-hexanol)** *[111-27-3]* **M 102.2, b 157.5°, d_4^{20} 0.818, n^{15} 1.4198, n^{25} 1.4158.** The commer-

cial material usually contains other alcohols which are difficult to remove. A suitable method is to esterify with hydroxybenzoic acid, recrystallise the ester and saponify. [Olivier *Rec Trav Chim Pays Bas* **55** 1027 *1936*.] Drying agents include K_2CO_3 and $CaSO_4$, followed by filtration and distillation. (Some decomposition to the olefin occurs when Al amalgam is used as drying agent at room temperature, even if the amalgam is removed prior to distillation.) If the alcohol is required anhydrous, the redistilled material can be refluxed with the appropriate alkyl phthalate or succinate, as described under *Ethanol*. [*Beilstein* **1** IV 1694.]

***n*-Hexylamine** *[111-26-2]* **M 101.2, b 131°, d_4^{20} 0.765, n_D^{20} 1.419, pK^{25} 10.64.** Dry with, and fractionally distil the hexylamine from, KOH or CaH_2. Store away from CO_2. [*Beilstein* **4** IV 709.]

***n*-Hexyl bromide** *[111-25-1]* **M 165.1, b 87-88°/90mm, 155°/743mm, d_4^{20} 1.176, n_D^{20} 1.448.** Shake the bromide with H_2SO_4, wash with water, dry (K_2CO_3) and fractionally distil. [*Beilstein* **1** IV 352.]

***n*-Hexyl methacrylate** *[142-09-6]* **M 154.2, b 65-66°/4mm,88-88.5°/14mm, d_4^{20} 0.8849, n_D^{20} 1.4320.** Purify it as for *methyl methacrylate*. [IR: Hughes & Walton *J Am Chem Soc* **79** 3985 *1957*, *Beilstein* **2** III 1288, **2** IV1527.]

Hexyltrimethylammonium bromide *[2650-53-5]* **M 224.3, m 186°.** Recrystallise it from acetone. It is extremely *hygroscopic*. [McDowell and Kraus *J Am Chem Soc* **73** 2170 *1951*, *Beilstein* **4** IV 710.]

1-Hexyne *[693-02-7]* **M 82.2, b 12.5°/75mm, 71°/760mm, d_4^{20} 0.7156, n_D^{20} 1.3989.** Distil it from $NaBH_4$ to remove peroxides. Stand over sodium for 24 hours, then fractionally distil it under reduced pressure. Also dry it by repeated vacuum transfer into freshly activated 4A molecular sieves, followed by vacuum transfer onto Na/K alloy, and stirring for 1 hour before fractionally distilling. [*Beilstein* **1** IV 1006.]

2-Hexyne *[764-35-2]* **M 82.2, b 83.8°/760mm, d_4^{20} 0.73146, n_D^{20} 1.41382.** Purify as for 1-hexyne above. [*Beilstein* **1** IV 1009.]

3-Hexyne *[928-49-4]* **M 82.2, b 81°/760mm, d_4^{20} 0.7231, n_D^{20} 1.4115.** Purify as for 1-hexyne above. [*Beilstein* **1** IV 1009.]

(±)-5-Hexyn-3-ol (4-hydroxy-1-hexyne) *[19780-84-8]* **M 98.1, b 58-59°/25mm, 73-76°/60mm, d_4^{20} 0.8918, n_D^{20} 1.4437.** Purify the hexynol by fractionation in a vacuum. The *carbamoyl* derivative (prepared by reaction with $COCl_2$/toluene followed by NH_3) is crystallised by dissolving in the minimum volume of toluene and adding excess of petroleum ether (b 40-60°), and has **m** 70-71°. [Länger et al. *Helv Chim Acta* **42** 2379 *1959*, *Beilstein* **1** IV 2235.]

Hydrazine *N,N′*-dicarboxylic acid diamide *[110-21-4]* **M 116.1, m 245-246°(dec), 248°.** Crystallise the diamide from water, wash the crystals with EtOH then Et_2O and dry in vacuum over P_2O_5. It does **not** decompose on drying at 110° /48 hours. Its solubility in H_2O is 1% at 0°. [Andrieth & Mohr *Inorg Synth* **IV** 26 *1953*, *Beilstein* **3** H 116, **3** I 56, **3** III 229.]

3-Hydroxy-2-butanone (acetoin) *[513-86-0]* **M 88.1, b 144-145°, [m 100-105° dimer].** Wash acetoin with EtOH until colourless, then with diethyl ether or acetone to remove biacetyl. Dry it in air by suction and dry further in a vacuum desiccator. [*Beilstein* **1** IV 3991.]

(±)-α-Hydroxy-γ-butyrolactone *[19444-84-9,* S(–)- *733-52-4]* **M 102.1, b 84°/0.2mm, 133°/10mm, d_4^{20} 1.310, n_D^{20} 1.4656.** It has been purified by repeated fractionation and forms a colourless liquid. It has to be distilled at high vacuum; otherwise it will dehydrate. The *acetoxy* derivative has **b** 94°/0.2mm. The *S-enantiomer* has d_4^{20} 1.24, n_D^{20} 1.464, $[\alpha]_D^{25}$ –82° (c 2, MeOH). [NMR: Daremon & Rambaud *Bull Soc Chim Fr* 294 *1971*, Schmitz et al. *Chem Ber* **108** 1010 *1975*, *Beilstein* **18/1** V 5.]

12-Hydroxydodecanoic acid *[505-95-3]* **M 216.3, m 86-88°, pK_{Est} ~4.8.** Crystallise the acid from toluene

[Sadowik et al. *J Am Chem Soc* **108** 7789 *1986*]. [*Beilstein* **3** III 658.]

***N*-[2-Hydroxyethyl]ethylenediamine [2-(2-aminoethylamino)ethanol]** *[111-41-1]* **M 104.1, b 91.2°/5mm, 238-240°/752mm, d_4^{20} 1.030, n_D^{20} 1.485, pK_1^{20} 3.75, pK_2^{20} 9.15.** Distil the amine twice through a Vigreux column. Redistil it from solid NaOH, then from CaH_2. *Alternatively*, it can be converted to the dihydrochloride and recrystallised from water. It is then dried, mixed with excess of solid NaOH and the free base is distilled from the mixture. It is finally redistilled from CaH_2. [Drinkard et al. *J Am Chem Soc* **82** 2992 *1960*, *Beilstein* **4** IV 1558.]

***N*-[2-Hydroxyethyl]ethylenediaminetriacetic acid (HEDTA)** *[150-39-0]* **M 278.3, m 212-214°(dec), pK_1^{20} 2.51, pK_2^{20} 5.31, pK_3^{20} 9.86.** Crystallise HEDTA from warm H_2O, after filtering, by addition of 95% EtOH and allowing to cool. The crystals, collected on a sintered-glass funnel, are washed three times with cold absolute EtOH, then again crystallised from H_2O. After leaching with cold H_2O, the crystals are dried at 100° under vacuum. [Spedding et al. *J Am Chem Soc* **78** 34 *1956*, *Beilstein* **4** IV 2449.]

***N*-Hydroxyethyliminodiacetic acid (HIMDA)** *[93-62-9]* **M 177.2, m 181°(dec), pK_1^{25} 2.16, pK_2^{25} 8.72, pK_3^{25} 13.7 (OH).** Crystallise HIMDA from water. [*Beilstein* **4** IV 2432.]

2-Hydroxyethylimino-tris(hydroxymethyl)methane (MONO-TRIS) *[7343-51-3]* **M 165.2, m 91°, pK_{Est} ~9.8.** Crystallise it twice from EtOH. Dry it under vacuum at 25°.

2-Hydroxyethyl methacrylate *[868-77-9]* **M 130.1, b 67°/3.5mm, d_4^{20} 1.071, n_D^{20} 1.452.** Dissolve the ester in water and extract with *n*-heptane to remove ethylene glycol dimethacrylate (checked by gas-liquid chromatography and by NMR) and distil it twice under reduced pressure [Strop et al. *J Phys Chem* **80** 694 *1976*]. [*Beilstein* **2** IV 1530.]

***dl*-2-Hydroxy-2-methylbutyric acid** *[3739-30-8]* **M 118.1, m 72-73°, pK^{25} 3.73.** Crystallise the acid from *benzene, and sublime it at 90°. [*Beilstein* **3** H 324.] **IRRITANT.**

***dl*-2-Hydroxy-3-methylbutyric (α-hydroxyisovaleric) acid** *[600-37-3]* **M 118.1, m 86°, pK_{Est} ~3.9.** Crystallise the acid from ether/pentane. [*Beilstein* **3** IV 618.] **IRRITANT.**

***R*-γ-Hydroxymethyl-γ-butyrolactone** *[52813-63-5]* **M 116.1, b 101-102°/0.048mm, d_4^{20} 1.2238, n_D^{20} 1.471, $[\alpha]_{546}^{20}$ –38°, $[\alpha]_D^{20}$–33° (c 3, EtOH), $[\alpha]_D^{30}$–53.5° (c 3, EtOH).** Purify it by column chromatography on Silica gel 60 (Merck 70-230 mesh) and elute with 7% EtOH/73% $CHCl_3$. Its IR (film) has ν_{max} at 3400 (OH), 1765 (C=O) and 1180 (COC) cm^{-1}. [Eguchi & Kakuta *Bull Chem Soc Jpn* **47** 1704 *1974*, IR and NMR: Ravid et al. *Tetrahedron* **34** 1449 *1978, Beilstein* **3** III 620.]

3-Hydroxy-3-methylglutaric acid (Meglutol) *[503-49-1]* **M 162.1, m 99-102°, 108-109°, 100°, $pK_{Est(1)}$ ~4.0, $pK_{Est(2)}$ ~5.0.** Recrystallise the acid from diethyl ether/hexane and dry it under a vacuum at 60° for 1 hour. [*Beilstein* **3** IV 1166.]

4-Hydroxy-4-methyl-2-pentanone *[123-42-2]* **M 116.2, b 166°, d_4^{20} 0.932, n_D^{20} 1.4235, n_D^{25} 1.4213.** The pentanone loses water when heated. It can be dried with $CaSO_4$, then fractionally distilled under reduced pressure. [*Beilstein* **1** IV 403.]

2-Hydroxy-2-methylpropionic acid (α-hydroxyisobutyric acid, 2-methyllactic acid)) *[594-61-6]* **M 104.1, m 79°, b 114°/12mm, 212°/760mm, pK^{25} 3.78.** Distil the acid in steam, crystallise it from Et_2O or *benzene, dry it under vacuum, or sublime it at 50°. [*Beilstein* **3, 7** IV 782.]

(±)-2-Hydroxyoctanoic acid (2-hydroxycaprylic acid) *[617-73-2]* **M 160.2, m 69.5°, b 160-165°/10mm, pK_{Est} ~3.7.** Crystallise the acid from EtOH/petroleum ether or ether/ligroin. [*Beilstein* **3** IV 873.]

***N*-Hydroxysuccinimide** *[6066-82-6]* **M 115.1, m 96-98°, pK^{25} 6.0.** Recrystallise the imide from EtOH/ethyl

acetate [Manesis & Goodmen *J Org Chem* **52** 5331 *1987*]. [*Beilstein* **21/9** V 498.]

(±)-2-Hydroxytetradecanoic acid (α-hydroxymyristic acid) *[2507-55-3]* **M 244.4, m 81-82°, pK_{Est} ~3.7.** Crystallise the acid from chloroform or twice from MeOH (**m** 85.8-86.6°) [Horn & Pretorious *J Chem Soc* 1463 *1954,* Chibnall et al. *Biochem J* **30** 1034 *1963*, *Beilstein* **3** H 361, **3** I 130, **3** II 246, **3** III 660, **3** IV 921].

***R*-2-Hydroxytetradecanoic acid** *[26632-17-7]* **M 244.4, m 88-2-88.5°, $[\alpha]_D^{20}$ –3.1° ($CHCl_3$).** Crystallise the acid from chloroform or first from Me_2CO, then hexane [Horn & Pretorious *J Chem Soc* 1463 *1954,* Horn et al. *J Chem Soc* 177 *1954*, *Beilstein* **3** III 660.]

Hydroxyurea See in "Inorganic Compounds", Chapter 5.

Iminodiacetic acid

[142-73-4] **M 133.1, m 225°(dec), pK_1^{25} 2.50, pK_2^{25} 9.40.** Recrystallise iminodiacetic acid from water and dry it in a vacuum over P_2O_5. [*Beilstein* **4** IV 2428.]

Iodoacetamide *[144-48-9]* **M 185.0, m** *ca* **143°(dec).** Crystallise it from water or CCl_4. It is used for tagging proteins. [Gurd *Methods Enzymol* **25** 424 1972, *Beilstein* **2** IV 536.]

Iodoacetic acid *[64-69-7]* **M 160.6, m 78°, pK^{25} 3.19.** Crystallise it from petroleum ether (b 60-80°) or $CHCl_3/CCl_4$. [*Beilstein* **2** IV 534.]

2-Iodobutane (*sec*-butyl iodide) *[513-48-4]* **M 184.0, b 120.0, d_4^{20} 1.50, n_D^{25} 1.4973.** Purify the iodide by shaking with conc H_2SO_4, then washing it with water, aqueous Na_2SO_3 and again with water. Dry ($MgSO_4$) and distil. *Alternatively*, pass it through a column of activated alumina before distillation, or treat with bromine, followed by extraction of the free halogen with aqueous $Na_2S_2O_3$, thoroughly washing with water, drying and distilling. It is stored over silver powder and distilled before use. [*Beilstein* **1** IV 272.]

Iodoform *[75-47-8]* **M 393.7, m 119°.** Crystallise it from MeOH, EtOH or EtOH/EtOAc. It is steam volatile. It is a disinfectant. [*Beilstein* **1** IV 97.]

***N*-Iodosuccinimide** *[516-12-1]* **M 225.0, m 200-201°.** Crystallise it from dioxane/CCl_4. It iodinates arenes in triflic acid. [Olah et al *J Org Chem* **58** 3194 *1993*, *Beilstein* **21/9** V 544.]

Isoamyl acetate (1-butyl-3-methyl acetate, isopentyl acetate) *[123-92-2]* **M 130.2, b 142.0°, d_4^{20} 0.871, n_D^{20} 1.40535.** Dry the acetate with finely divided K_2CO_3 and fractionally distil it. [*Beilstein* **2** IV 157.]

Isoamyl alcohol (3-methyl-1-butanol, 1-butyl-3-methyl alcohol) *[123-51-3]* **M 88.2, b 128°/750mm, 132°/760mm, d^{15} 0.8129, n^{15} 1.4085, n_D^{20} 1.4075.** Dry the alcohol by heating with CaO and fractionally distilling, then heating with BaO and redistilling. *Alternatively*, boil it with concentrated KOH solution, wash it with dilute H_3PO_4, and dry it with K_2CO_3, then anhydrous $CuSO_4$, before fractionally distilling it. If very dry alcohol is required, the distillate is refluxed with the appropriate alkyl phthalate or succinate as described for *ethanol.* It is separated from 2-methyl-1-butanol by fractional distillation, fractional crystallisation and preparative gas chromatography. [*Beilstein* **1** IV 1677.]

Isoamyl bromide (1-butyl-3-methyl bromide) *[107-82-4]* **M 151.1, f -112°, b 119.2°/ 737mm, d_4^{20} 1.208, n 1.444.** Shake the bromide with conc H_2SO_4, wash with water, dry with K_2CO_3 and fractionally distil it. [*Beilstein* **1** IV 378.]

Isoamyl chloride (1-butyl-3-methyl chloride) *[107-84-6]* **M 106.6, b 99°/734mm, d_4^{20} 0.8704, n_D^{20} 1.4084.** Shake the chloride vigorously with 95% H_2SO_4 until the acid layer no longer becomes coloured during 12 hours, then wash it with water, saturated aqueous Na_2CO_3, and more water. Dry it with $MgSO_4$, filter and fractionally distil it. *Alternatively*, a stream of oxygen containing 5% of ozone is passed through the chloride for a time, three times longer than is necessary to cause the first coloration of starch iodide paper by the exit gas.

Subsequent washing of the liquid with aqueous $NaHCO_3$ hydrolyses the ozonides and removes organic acids. After drying and filtering, the isoamyl chloride is distilled. [Chien & Willard *J Am Chem Soc* **75** 6160 *1953*, *Beilstein* **1** IV 287.]

Isoamyl ether [diisopentyl ether, di-(1-butyl-3-methyl) ether] *[544-01-4]* **M 158.3, b 173.4°, d_4^{20} 0.778, n_D^{20} 1.40850.** This is a mixture of 2- and 3-methylbutyl ether. It is purified by refluxing with sodium for 5 hours, then it is distilled under reduced pressure, to remove alcohols. Isoamyl ether can also be dried with $CaCl_2$ and fractionally distilled from P_2O_5. [*Beilstein* **1** IV 1682.]

Isobutane (2-methylpropane) *[75-28-5]* **M 58.1, b -10.2°, d_4^{20} 0.557.** Olefins and moisture can be removed by passage at 65° through a bed of silica-alumina catalyst which has previously been evacuated at about 400°. *Alternatively*, water and CO_2 can be removed by passage through P_2O_5, then asbestos impregnated with NaOH. Treatment with anhydrous $AlBr_3$ at 0° then removes traces of olefins. Inert gases can be separated by freezing the isobutane at –195° and evacuating out the system. [*Beilstein* **1** IV 282.]

Isobutene (2-methylpropene, isobutylene) *[115-11-7]* **M 56.1, b –6.6°/760mm.** Dry isobutene by passage through anhydrous $CaSO_4$ at 0°. Purify it further by freeze-pump-thaw cycles and trap-to-trap distillation. [*Beilstein* **1** IV 796.]

Isobutyl bromide (1-bromo-2-methylpropane) *[78-77-3]* **M 137.0, b 91.2°, d_4^{20} 1.260, n_D^{20} 1.437.** Partially hydrolyse it to remove any tertiary alkyl halide, then fractionally distil it, then wash it with conc H_2SO_4, water and aqueous K_2CO_3, then redistil it from dry K_2CO_3. [Dunbar & Hammett *J Am Chem Soc* **72** 109 *1950*, *Beilstein* **1** IV 294.]

Isobutyl chloride (1-chloro-2-methylpropane) *[513-36-0]* **M 92.6, m –131°, 68.8°/760mm, d_4^{20} 0.877, n_D^{20} 1.398.** Use the same methods as described under *isoamyl chloride*. [*Beilstein* **1** IV 287.]

Isobutyl chloroformate *[543-27-1]* **M 136.6, b 123-127°/atm, 128.8°/atm, d_4^{20} 1.053, n_D^{20} 1.4070.** It can be dried over $CaCl_2$ and fractionated at atmospheric pressure while keeping moisture out. Its purity can be checked by conversion to the *phenyl urethane* derivative with PhNCO [Saunders et al. *J Am Chem Soc* **73** 3796 *1951*.] Its IR (film) has ν_{max} at 1780cm^{-1}. [Thompson & Jameson *Spectrochim Acta* **13** 236 *1959*, Röse *Justus Liebigs Ann Chem* **205** 227 *1880*]. [*Beilstein* **3** IV 26.]

Isobutyl formate *[542-55-2]* **M 102.1, b 98.4°, d_4^{20} 0.885, n_D^{20} 1.38546.** Wash the formate with saturated aqueous $NaHCO_3$, in the presence of saturated aqeous NaCl solution until no further reaction occurs, then with saturated aqueous NaCl, dry ($MgSO_4$) and fractionally distil it. [*Beilstein* **2** H 21, **2** I 18, **2** II 30, **2** III 41, **2** IV 29.]

Isobutyl iodide (1-iodo-2-methylpropane) *[513-38-2]* **M 184.0, b 83°/250mm, 120°/760mm, d_4^{20} 1.60, n_D^{20} 1.495.** Shake the iodide with conc H_2SO_4, and wash it with water, aqueous Na_2SO_3, and water, dry with $MgSO_4$ and distil it. *Alternatively*, pass it through a column of activated alumina before distillation. Store it under nitrogen with mercury in a brown bottle or in the dark. [*Beilstein* **1** IV 299.]

Isobutyl vinyl ether *[109-53-5]* **M 100.2, b 108-110°, d_4^{20} 0.768, n_D^{20} 1.398.** Wash the ether three times with equal volumes of aqueous 1% NaOH, dry it with CaH_2, reflux it with sodium for several hours, then fractionally distil it from sodium. [*Beilstein* **1** IV 2054.]

Isobutyraldehyde *[78-84-2]* **M 72.1, b 62.0°, d_4^{20} 0.789, n_D^{20} 1.377.** Dry isobutyraldehyde with $CaSO_4$ and use it immediately after distillation under nitrogen because of the great difficulty in preventing oxidation. It can be purified through its acid bisulfite derivative. [*Beilstein* **1** IV 3262.]

Isobutyramide (2-methylpropionamide) *[563-83-7]* **M 87.1, m 128-129°, b 217-221°/760mm.** Crystallise the amide from acetone, *benzene, $CHCl_3$, EtOAc or water, then dry it under vacuum over P_2O_5 or 99% at H_2SO_4, or at 70°/3 hours in a desiccator. Sublime it under vacuum. [Kent & McAlvain *Org Synth* Coll Vol **III**

491 *1955*, *Beilstein* **2** H 293, **2** I 129, **2** II 262, **2** III 654, **2** IV 852.]

Isobutyric acid (2-methylpropionic acid) *[79-31-2]* **M 88.1, b 78°/34mm, 154-154.5°/760mm, d_4^{20} 0.949, n_D^{20} 1.393, pK^{25} 4.60.** Distil the acid from $KMnO_4$, then redistil it from P_2O_5. [*Beilstein* **2** H 288, **2** I 126, **2** II 257, **2** III 637, **2** IV 843.]

Isobutyronitrile (2-methylpropionitrile, isopropyl cyanide) *[78-82-0]* **M 69.1, b 103.6°/760mm, d^{25} 0.7650, n_D^{20} 1.378.** Shake the nitrile with conc HCl (to remove isonitriles), then with water and aqueous $NaHCO_3$. After a preliminary drying with silica gel or Linde type 4A molecular sieves, it is shaken or stirred with CaH_2 until hydrogen evolution ceases, then decanted and distilled from P_2O_5 (not more than 5g/L, to minimise gel formation) or Drierite (**b** 101-103°/760mm). Finally it is refluxed with, and slowly distilled from CaH_2 (5g/L), taking precautions to exclude moisture. [*Beilstein* **2** H 294, **2** I 129, **2** II 263, **2** III 655, **2** IV 853.]

Isonitrosoacetone (*anti*-pyruvic aldehyde-1-oxime) *[31915-82-9]* **M 87.1, m 65-67°, 69°, pK^{25} 8.3.** Crystallise isonitrosoacetone from $*C_6H_6$, ether/petroleum ether or CCl_4. It sublimes at 90-100° (water bath temperature)/0.05mm [Kahovec & Kohlrausch *Chem Ber* **75** 1547 *1942*]. It forms an iron and a Cu^{2+} salt (**m** 170° dec). [*Beilstein* **1** H 763, **1** I 396, **1** II 822, **1** III 3092, **1** IV 3632.]

(±)-Isononane (3,3,4-trimethylhexane) *[34464-40-9]* **M 128.3, b 142°/760mm, 142°/760mm, d_4^{20} 0.7454, n_D^{20} 1.4178.** Isononane is passed through columns of activated silica gel and basic alumina (activity 1) and distilled under high vacuum from Na/K alloy. [*Beilstein* **1** III 517, **1** IV 462.]

Isopentyl formate *[110-45-2]* **M 116.2, b 27°/10mm, 123-123.6°/760mm, 123-124°/atm, d_4^{20} 0.8713, n_D^{20} 1.391.** The colourless liquid ester is soluble in 300 volumes of H_2O and is soluble in common organic solvents. It is purified by repeated distillation using an efficient column at atmospheric pressure. [*Beilstein* **2** H 22, **2** I 18, **2** II 31, **2** III 43, **2** IV 30.]

Isoprene (2-methyl-1,3-butadiene) *[78-79-5]* **M 68.1, b 34.5-35°/762mm, d_4^{20} 0.681, n^{25} 1.4225.** Reflux it with sodium then distil it from sodium or $NaBH_4$ under nitrogen, and pass it through a column containing KOH, $CaSO_4$ and silica gel. *tert*-Butylcatechol (0.02% w/w) is added, and the isoprene is stored in this way until redistilled before use. The inhibitor (*tert*-butylcatechol) in isoprene can be removed by several washings with dilute NaOH and water. The isoprene is then dried over CaH_2, distilled under nitrogen at atmospheric pressure, and the fraction distilling at 32° is collected. Store it under nitrogen at –15°. [*Beilstein* **1** H 252, **1** IV 1001.]

Isopropenyl acetate (1-methylvinyl acetate, 2-acetoxypropene) *[108-22-5]* **M 100.1, b 96.7°/749mm, 97.2-97.4°/757mm, d_4^{25} 0.909, n_D^{20} 1.4010.** Prepared by reacting ketene with a mixture of Me_2CO and polyphosphoric acid [Wacher US Patent 2 867 653 *1957*], fractionally distilling through a 75cm packed column, and collecting the fraction with **b** 96.7°/749mm. It forms an azeotrope with H_2O. Its equivalent weight is determined by hydrolysis in 90% EtOH containing twice the required amount of NaOH and titrating the excess of alkali; which should give an equivalent weight of ~100.1. Its heat of hydrolysis has been determined [Sunner *Acta Chem Scand* **11** 1757 *1957*]. It is a good source the $=CMe_2$ group, as in the preparation of Meldrum's acid (see [2033-24-1]), because it is the activated enol ester of acetone. Its FT-IR (neat) has ν_{max} at 1757.3, 1673.0, 1431.4, 1372.5, 1253.1, 1198.2, 1027.9, 900.0 and 871.4 cm^{-1}; the ^1H NMR (60MHz, $CDCl_3$, TMS) has δ at 1.92 (s, 3H, ester Me), 2.13 (s, 3H, isoPr-Me) and 7.00 (d, J = ~6Hz, 2H, $=CH_2$); and the ^{13}C NMR (15MHz, $CDCl_3$, TMS) has δ at 19.54, 21.05, 102.05, 152.94 and 169.04. [*Beilstein* **2** III 278, **2** IV 179.]

Isopropanol (propan-2-ol) *[67-63-0]* **M 60.1, b 82.5°, d_4^{20} 0.783, $n^{25.8}$ 1.3739, pK^{25} 17.1.** Isopropyl alcohol is prepared commercially by dissolution of propene in H_2SO_4, followed by hydrolysis of the sulfate ester. Major impurities are water, lower alcohols and oxidation products such as aldehydes and ketones. Purification of isopropanol follows substantially the same procedure as for *n*-propyl alcohol.
Isopropanol forms a constant-boiling mixture, **b** 80.3°, with water. Most of the water can be removed from this 91% isopropanol by refluxing with CaO (200g/L) for several hours, then distilling. The distillate can be dried further with CaH_2, magnesium ribbon, BaO, $CaSO_4$, calcium, anhydrous $CuSO_4$ or Linde type 5A molecular

sieves. Distillation from sulfanilic acid removes ammonia and other basic impurities. Peroxides [indicated by liberation of iodine from weakly acid (HCl) solutions of 2% KI] can be removed by refluxing with solid stannous chloride or with $NaBH_4$ then the alcohol is fractionally distilled. To obtain isopropanol containing only 0.002M of water, sodium (8g/L) is dissolved in material dried by distillation from $CaSO_4$. Isopropyl benzoate (35ml) is then added and, after refluxing for 3 hours, the alcohol is distilled through a 50-cm Vigreux column [Hine & Tanabe *J Am Chem Soc* **80** 3002 *1958*]. Other purification steps for isopropanol include refluxing with solid aluminium isopropoxide, refluxing with $NaBH_4$ for 24 hours, and removing acetone by treatment with, and distillation from 2,4-dinitrophenylhydrazine. Peroxides re-form in isopropanol if it is kept for several days in contact with air. [*Beilstein* **1** IV 1461.]

Isopropyl acetate *[108-21-4]* **M 102.1, b 88.4°, d $_4^{20}$ 0.873, n $_D^{20}$ 1.3773.** Wash the acetate with 50% aqueous K_2CO_3 (to remove acid), then with saturated aqueous $CaCl_2$ (to remove any alcohol). Dry it with $CaCl_2$ and fractionally distil it. [*Beilstein* **2** IV 141.]

Isopropyl acrylamide *[2210-25-5]* **M 113.2, m 60-63°, b 89-92°/2mm, 110-115°/15mm.** Fractionate the amide under reduced pressure, and recrystallise the solid distillate from hexane (**m** 59°), *C_6H_6 (**m** 62°) or *C_6H_6/hexane (**m** 62-63°). Store it with 0.05% of 4-*tert*-butylcatechol. It is used for making water soluble swellable hydrogels. [*Beilstein* **4** IV 517.]

Isopropyl bromide (2-bromopropane) *[75-26-3]* **M 123.0, b 0°/69.2mm, 59.4°/760mm, d $_4^{20}$ 1.31, n^{15} 1.42847, n $_D^{20}$ 1.4251.** Wash the bromide with 95% H_2SO_4 (concentrated acid partially oxidised it) until a fresh portion of acid did not become coloured after several hours, then with water, aqueous $NaHSO_3$, aqueous 10% Na_2CO_3 and again with water. (The H_2SO_4 can be replaced by conc HCl.) Prior to this treatment, isopropyl bromide has been purified by bubbling a stream of oxygen containing 5% ozone through it for 1 hour, followed by shaking with 3% hydrogen peroxide solution, neutralising with aqueous Na_2CO_3, washing with distilled water and drying. *Alternatively*, it has been treated with elemental bromine and stored for 4 weeks, then extracted with aqueous $NaHSO_3$ and dried with $MgSO_4$. After the acid treatment, isopropyl bromide can be dried with Na_2SO_4, $MgSO_4$ or CaH_2, and fractionally distilled. [*Beilstein* **1** IV 208.]

Isopropyl chloride (2-chloropropane) *[75-29-6]* **M 78.5, b 34.8°, d $_4^{20}$ 0.864, n $_D^{20}$ 1.3779, n^{25} 1.3754.** Purify the chloride with 95% H_2SO_4 as described for *isopropyl bromide*, then dry with $MgSO_4$, P_2O_5 or CaH_2, and fractionally distil it from Na_2CO_3 or CaH_2. *Alternatively*, a stream of oxygen containing *ca* 5% ozone is passed through the chloride for about three times as long as is necessary to obtain the first coloration of starch iodide paper by the exit gas, and the liquid is then washed with $NaHCO_3$ solution to hydrolyse ozonides and remove organic acids before drying and distilling. [*Beilstein* **1** IV 191.]

Isopropyl ether (diisopropyl ether) *[108-20-3]* **M 102.2, b 68.3°, d $_4^{20}$ 0.719, n $_D^{20}$ 1.3688, n^{25} 1.36618.** Common impurities are water and peroxides [detected by the liberation of iodine from weakly acid (HCl) solutions of 2% KI]. Peroxides can be removed by shaking with aqueous Na_2SO_3 or with acidified ferrous sulfate (0.6g $FeSO_4$ and 6ml conc H_2SO_4 in 110ml of water, using 5-10g of solution per L of ether), or aqueous $NaBH_4$ solution. The ether is then washed with water, dried with $CaCl_2$ and distilled. *Alternatively*, refluxing with $LiAlH_4$ or CaH_2, or drying with $CaSO_4$, then passage through an activated alumina column, can be used to remove water and peroxides. Other dehydrating agents used with isopropyl ether include P_2O_5, sodium amalgam and sodium wire. (The ether is often stored in brown bottles, or in the dark, with sodium wire.) Bonner and Goishi (*J Am Chem Soc* **83** 85 *1961*) treated isopropyl ether with dilute sodium dichromate/sulfuric acid solution, followed by repeated shaking with a 1:1 mixture of 6M NaOH and saturated $KMnO_4$. The ether is washed several times with water, dilute aqueous HCl, and water, with a final washing with, and storage over, ferrous ammonium sulfate acidified with H_2SO_4. Blaustein and Gryder (*J Am Chem Soc* **79** 540 *1957*), after washing with alkaline $KMnO_4$, then water, treated the ether with ceric nitrate in nitric acid, and again washed it with water. Hydroquinone is added before drying with $CaCl_2$ and $MgSO_4$, and refluxing with sodium amalgam (108g Hg/100g Na) for 2 hours under nitrogen. The distillate (nitrogen atmosphere) is made 2 x10^{-5}M in hydroquinone to inhibit formation of peroxides (which is negligible if the ether is stored in the dark). Catechol (pyrocatechol) and resorcinol are alternative inhibitors. [*Beilstein* **1** IV 1471.]

Isopropyl iodide (2-iodopropane) *[75-30-9]* **M 170.0, b 88.9°, d_4^{20} 1.70, n_D^{20} 1.4987.** Treat the iodide with bromine, followed by extraction of free halogen with aqueous $Na_2S_2O_3$ or $NaHSO_3$, washing with water, drying ($MgSO_4$ or $CaCl_2$) and distilling. (The treatment with bromine is optional.) Other purification methods include passage through activated alumina, or shaking with copper powder or mercury to remove iodine, drying with P_2O_5 and distilling. Washing with conc H_2SO_4 or conc HCl (to remove any alcohol), water, aqueous Na_2SO_3, water and aqueous Na_2CO_3 has also been used. Treatment with silica gel causes some liberation of iodine. Distillations should be carried out at slightly reduced pressure. Purified isopropyl iodide is stored in the dark in the presence of a little mercury. [*Beilstein* **1** IV 223.]

Isopropyl methyl ether *[598-53-8]* **M 74.1, b 32.5°/777mm, d^{15} 0.724, n_D^{20} 1.3576.** Purify the ether by drying with $CaSO_4$, passing through a column of alumina (to remove peroxides) and fractional distillation. [*Beilstein* **1** H 362, **1** II 381, **1** III 1458, **1** IV 1471.]

Isovaleric acid (3-methylbutyric acid) *[502-74-2]* **M 102.1, b 176.5°/762mm, d_4^{20} 0.927, n^{15} 1.4064, n_D^{20} 1.40331, pK^{25} 4.77.** Dry the acid (Na_2SO_4), then fractionally distil. [*Beilstein* **2** IV 895.]

Itaconic acid (2-propen-1,2-dicarboxylic acid) *[97-65-4]* **M 130.1, m 165-166°, pK_1^{25} 3.63, pK_2^{25} 5.00.** Crystallise itaconic acid from EtOH, EtOH/water or EtOH/*benzene. [*Beilstein* **2** IV 2228.]

Itaconic anhydride (2-propen-1,2-dicarboxylic anhydride) *[2170-03-8]* **M 112.1, m 66-68°, 67-68°, 68°, b 139-140°/30mm.** Crystallise the anhydride from $CHCl_3$/petroleum ether. It can be distilled under reduced pressure. Distillation at atmospheric pressure, or prolonged distillation causes rearrangement to citraconic anhydride (2-methylmaleic anhydride). If the material (as seen in the IR spectrum) contains much free acid, then heat with acetyl chloride or $SOCl_2$, evaporate and distil at as high a vacuum as possible. The crude anhydride deposits crystals of itaconic acid on standing probably due to hydrolysis by H_2O — store it in sealed ampoules under dry N_2. [Skinner et al. *Org Synth* Coll Vol **II** 368 *1943*, IR: Nagai *Bull Chem Soc Jpn* **37** 369 *1964*, Kelly & Segura *J Am Chem Soc* **56** 2497 *1934*, *Beilstein* **17/11** V 66.]

Kerosene *[8008-20-6]* **(mixture of hydrocarbons) b ~175-225°, ~190-250°, d_4^{20} 0.75-0.82, n_D^{20} 1.443.** Stir it with conc H_2SO_4 until a fresh portion of acid remains colourless, then wash with water, dry with solid KOH and distil it in a Claisen flask. For more complete drying, the kerosene can be refluxed with Na, and distilled from Na.

Ketene *[463-51-4]* **M 42.0, b –56°, –41°, d_4^{20} 1.093, n_D^{20} 1.441.** Ketene is prepared by pyrolysis of acetic anhydride. Purify it by passing through a trap at –75° and collecting in a liquid-nitrogen-cooled trap. Ethylene is removed by evacuating the ethylene in an isopentane-liquid-nitrogen slush pack at –160°. Store it at room temperature in a suitable container in the dark or better at –80°, but do not store it under pressure as it may **EXPLODE**. It is a strong **IRRITANT** when inhaled and is as **POISONOUS** as phosgene. See diketene in "Heterocyclic Compounds", in this Chapter. [Hurd *Org Synth* Coll Vol **I** 330 *1941*, Andreades & Carlson *Org Synth* Coll Vol **V** 679 *1973*.]

L(+)-Lactic acid **(*S*(+)-2-hydroxypropionic acid)** *[79-33-4]* **M 90.1, m 52.8°, b 105°/0.1mm, $[\alpha]_D^{20}$ +3.82° (H_2O), pK^{31} 3.83.** Purify lactic acid by fractional distillation at 0.1mm pressure, followed by fractional crystallisation from diethyl ether/isopropyl ether (1:1, dried with sodium). [Borsook et al. *J Biol Chem* **102** 449 *1933*.] The solvent mixture, *benzene/diethyl ether (1:1) containing 5% petroleum ether (b 60-80°) has also been used. [Brin *Biochemical Preparations* **3** 61 *1953*, *Beilstein* **3** IV 633.]

Lanthanide shift reagents A variety of these reagents are available commercially, and they are generally quite stable and should not deteriorate on long storage in a dry state and in the absence of light. [See J.R. Campbell *Aldrichimica Acta* **4** 55 *1971*, G.R. Sullivan in *Top Stereochem* (Eliel & Allinger Eds) J Wiley & Sons Vol 10 287 *1978*, T.C. Morrill Ed. *Lanthanide Shift Reagents* Deerfield Beach Florida *1986*, ISBN 0895731193.]

Lauraldehyde (1-dodecanal) *[112-54-9]* **M 184.3, b 99.5-100°/3.5mm, $n^{24.7}$ 1.4328.** Convert lauraldehyde to the bisufite addition compound by shaking with saturated aqueous $NaHSO_3$ for 1 hour. The precipitate is filtered off, washed with ice cold water, EtOH and ether, then decomposed with aqueous Na_2CO_3. The aldehyde is extracted into diethyl ether which, after drying and evaporating, gives an oil which is fractionally distilled under vacuum. [*Beilstein* **1** IV 3380.]

Lauric acid (1-dodecanoic acid) *[143-07-7]* **M 200.3, m 44.1°, b 141-142°/0.6-0.7mm, 225°/100mm, pK^{20} 5.3.** Distil the acid in a vacuum. Also crystallise it from absolute EtOH, or from acetone at –25°. *Alternatively*, purify it *via* its *methyl ester* (**b** 140.0°/15mm), as described for *capric* acid (see [334-48-5]). It has also been purified by zone melting. [cf *Beilstein* **1** III 2913.]

Lauryl peroxide (di-dodecyl peroxide) *[105-74-8]* **M 398.6, m 53-54°.** Crystallise it from *n*-hexane or *benzene and store it below 0°. Potentially **EXPLOSIVE**. [cf *Beilstein* **2** IV 1102.]

***Z*-Maleamic acid (*cis*-maleic acid monoamide)** *[557-24-4]* **M 115.1, m 172°, 172-173°(dec), 178-180°, pK_{Est} ~2.65.** Crystallise it from EtOH. [*Beilstein* **2** H 752, **2** II 646, **2** III 1927, **2** IV 1927.] **IRRITANT**.

Maleic acid *[110-16-7]* **M 116.1, m 143.5°, pK_1^{25} 1.91, pK_2^{25} 6.33.** Crystallise the acid from acetone/petroleum ether (b 60-80°) or hot water. Dry it at 100°. [*Beilstein* **2** H 748, **2** I 303, **2** II 641, **2** III 1911, **2** IV 2199.]

Maleic anhydride See furan-2,5-dione in "Heterocyclic Compounds', in this Chapter.

Maleic hydrazide *[123-33-1]* **M 112.1, m 144°(dec), pK_1^{25} 5.67, pK_2^{25} 13.3.** Crystallise the hydrazide from water. Dry it at ~100° over P_2O_5. [*Beilstein* **24** III/IV 1186.]

Maleimide See pyrrol-2,5-dione in "Heterocyclic Compounds", in this Chapter.

Maleuric acid (Z-*N*-carbamoylmaleamic acid) *[105-61-3]* **M 158.1, m 167-168°(dec).** Crystallise the acid from hot water. Dry it at ~100° over H_2SO_4. [Batt et al. *J Am Chem Soc* **76** 3663 *1954*.]

***dl*-Malic acid** *[617-48-1 and 6915-15-7]* **M 134.1, m 128-129°.** Crystallise the acid from acetone, then from acetone/CCl_4, or from ethyl acetate by adding petroleum ether (b 60-70°). Dry it at 35° under 1mm pressure to avoid formation of the anhydride. [*Beilstein* **3** IV 1124.]

L-Malic acid (*S*(–)-2-hydroxysuccinic acid) *[97-67-6]* **M 134.1, m 104.5-106°, $[\alpha]_D^{20}$ –2.3° (c 8.5, H_2O), $[\alpha]_D^{20}$ –30° (c 5.5, pyridine), pK_1^{25} 3.46, pK_2^{25} 5.10.** Crystallise *S*-malic acid (charcoal) from ethyl acetate/petroleum ether (b 55-56°), keeping the temperature below 65°. Or dissolve it by refluxing in fifteen parts of anhydrous diethyl ether, decant, concentrate to one-third volume and crystallise it at 0°, repeatedly to constant melting point. [*Beilstein* **3** IV 1123.]

Malonamide *[108-13-4]* **M 102.1, m 170°.** Crystallise the amide from water. [*Beilstein* **2** IV 1887.]

Malonic acid *[141-82-2]* **M 104.1, m 136°, pK_1^{25} 2.58, pK_2^{25} 5.69.** Crystallise malonic acid from *benzene/diethyl ether (1:1) containing 5% of petroleum ether (b 60-80°), wash with diethyl ether, then recrystallise it from H_2O or acetone. Dry it under vacuum over conc H_2SO_4. [*Beilstein* **2** IV 1874.]

Malononitrile *[109-77-3]* **M 66.1, m 32-34°, b 109°/20mm, 113-118°/25mm, 220°/760mm.** Crystallise the nitrile from water, EtOH, *benzene or chloroform. Distil it in a vacuum from, and store over, P_2O_5. [Bernasconi et al. *J Am Chem Soc* **107** 7692 *1985*, Gratenhuis *J Am Chem Soc* **109** 8044 *1987*, *Beilstein* **2** IV 1892.]

Meprobamate [2,2-di(carbamoyloxymethyl)pentane] *[57-53-4]* **M 246.3, m 104-106°.** Crystallise it from hot water, aqueous EtOH (**m** 104-105.5°) or xylene (**m** 104.1-105.3°). It can be an addictive drug. [*Beilstein* **3** IV 73.]

2-Mercaptoethanol *[60-24-2]* **M 78.1, b 44°/4mm, 53.5°/10mm, 58°/12mm, 68°/20mm, 78.5°/40mm, 96-97° (92°)/100mm, 157°/748mm, d_4^{20} 1.114, n_D^{20} 1.500, pK^{25} 9.72 (9.43).** Purify it by distilling in a vacuum. Distilling at atmospheric pressure causes some oxidation and should be done in an inert atmosphere. [Woodward *J Chem Soc* 1892 *1948*.] **It has a foul odour, is irritating to the eyes, nose and skin — should be handled in an efficient fume cupboard.** It is miscible with H_2O, EtOH, Et_2O and $*C_6H_6$ and the UV has λ_{max} at 235nm. The *2,4-dinitrophenyl thioether* has **m** 101-102° (from EtOH or aqueous MeOH) [Grogen et al. *J Org Chem* **20** 50 *1955*]. [*Beilstein* **1** IV 2428.]

Mesaconic acid (methylfumaric acid) *[498-24-8]* **M 130.1, m 204-205°, pK^{18} 4.82.** Crystallise it from H_2O or EtOH [Katakis et al. *J Chem Soc, Dalton Trans* 1491 *1986*]. [*Beilstein* **2** IV 2231.]

Mesityl oxide (4-methyl-3-penten-2-one) *[141-79-7]* **M 98.2, b 57°/55mm, 128-129°/745mm, 112°/760mm, n^{24} 1.4412, d 0.854, pK^{20} –5.36 (H_o scale, aqueous H_2SO_4).** Purify it by distillation, preferably in a vacuum or *via* the *semicarbazone* (**m** 165°) which is decomposed to pure ketone. The *2,4-dinitrophenylhydrazone* (**m** 205-206°) crystallises from EtOH. [Johnson *J Am Chem Soc* **73** 5888 *1951*, Johnson *J Am Chem Soc* **75** 2720 *1953*, Erskine & Waight *J Chem Soc* 3425 *1960*, *Beilstein* **1** H 736, **1** I 382, **1** II 793, **1** III 2995, **1** IV 3471.]

α-Methacraldehyde (methacrolein) *[78-85-3]* **M 68.1, b 68.4°, d_4^{20} 0.849, n_D^{20} 1.416.** Fractionally distil it under nitrogen through a short Vigreux column. Store it in sealed ampoules. (Slight polymerisation may occur.) [*Beilstein* **1** IV 3455.]

Methacrylamide *[79-39-0]* **M 85.1, m 111-112°.** Crystallise the amide from *benzene or ethyl acetate and dry it under vacuum at room temperature. [*Beilstein* **2** IV 1538.]

Methacrylic acid *[79-41-4]* **M 86.1, b 72°/14mm, 160°/760mm, d_4^{20} 1.015, n_D^{20} 1.431, pK^{25} 4.65.** Aqueous methacrylic acid (90%) is saturated with NaCl (to remove the bulk of the water), then the organic phase is dried with $CaCl_2$ and distilled under vacuum. Polymerisation inhibitors should be added to the distillate and include 0.25% *p*-methoxyphenol, 0.1% hydroquinone, or 0.05% *N,N′*-diphenyl-*p*-phenylenediamine. [*Beilstein* **2** IV 1518.]

Methacrylic anhydride *[760-93-0]* **M 154.2, b 65°/2mm, d_4^{20} 1.040, n_D^{20} 1.454.** Distil the anhydride at 2mm pressure, immediately before use, in the presence of hydroquinone. [*Beilstein* **2** IV 1537.]

Methacrylonitrile *[126-98-7]* **M 67.1, b 90.3°, d_4^{20} 0.800, n_D^{20} 1.4007, n^{30} 1.3954.** Wash it with saturated aqueous $NaHSO_3$ (to remove inhibitors such as *p-tert*-butylcatechol), 1% NaOH in saturated NaCl and then with saturated NaCl. Dry it with $CaCl_2$ and fractionally distil it under nitrogen to separate it from impurities such as methacrolein and acetone. [*Beilstein* **2** IV 1539.]

Methacryloyl chloride *[920-46-7]* **M 104.5, m -60°, b 95-96°/760mm, 98.4°/772mm, d^{25} 1.076, n_D^{20} 1.4432.** Purify the ester by fractional distillation. If it contains the acid (OH bands in the IR) then add redistilled $SOCl_2$ (with cooling) and cuprous chloride (ca to 2%), reflux the mixture gently for 1 hour and fractionate it through a 1 metre column packed with glass helices. Redistillation then provides the acid chloride in high purity as a colourless liquid. It is necessary to keep the apparatus moisture free (use $CaCl_2$ tubes). Stabilise it with 0.05% of 2,6-di-*tert*-butyl-4-methylphenol. [Lal & Green *J Org Chem* **20** 1032 *1955*, *Beilstein* **2** IV 1537.]

Methane *[74-82-8]* **M 16.0, m –184°, b –164°/760mm, –130°/6.7atmospheres, d_4^0 0.554 (**cf **d_4^0 1.00 for air).** Dry methane by passing over $CaCl_2$ and P_2O_5, then through a Dry-ice trap and fractionally distil it from a liquid-nitrogen trap. Oxygen can be removed by prior passage in a stream of hydrogen over reduced copper oxide at 500°, and higher hydrocarbons can be removed by chlorinating about 10% of the sample: the hydrocarbons, chlorides and HCl are readily separated from the methane by condensing the sample in the liquid nitrogen trap

and fractionally distilling it. Methane has also been washed with conc H_2SO_4, then solid NaOH and then 30% NaOH solution. It is dried with $CaCl_2$, then P_2O_5, and condensed in a trap at liquid air temperature, then transferred to another trap cooled in liquid nitrogen. CO_2, O_2, N_2 and higher hydrocarbons can be removed from methane by adsorption on charcoal. [Eiseman & Potter *J Res Nat Bur Stand* **58** 213 *1957*, *Beilstein* **1** IV 3.] **HIGHLY FLAMMABLE.**

Methanesulfonic acid *[75-75-2]* **M 96.1, m 20°, b 134.5-135°/3mm, d_4^{20} 1.483, n_D^{20} 1.432, pK^{25} –1.86 (–1.2).** Dry the acid, either by azeotropic removal of water with *benzene or toluene, or by stirring 20g of P_2O_5 with 500ml of the acid at 100° for 0.5 hours. Then distil it under vacuum and fractionally crystallise it by partial freezing. Sulfuric acid, if present, can be removed by prior addition of $Ba(OH)_2$ to a dilute solution, filtering off the $BaSO_4$ and concentrating under reduced pressure; and is sufficiently pure for most applications. [*Beilstein* **4** IV 10.]

Methanesulfonothioic acid Na salt (sodium methanethiosulfonate, sodium methylthiosulfonate) *[1950-85-2]* **M 134.1, m 265°(dec).** Recrystallise the salt from H_2O (plates as *monohydrate*) or MeOH. The *potassium salt* crystallises from H_2O, EtOH or MeOH (thick plates) with **m** 201-202° [Foss *Acta Chem Scand* **10** 868 *1956*]. The *S-benzylisothiouronium salt* has **m** 141-142° (from EtOH) [Kurzer & Powell *J Chem Soc* 3733 *1952*]. [*Beilstein* **4** IV 31.] It is used for preparing unsymmetrical disulfides [Grayson et al. *J Org Chem* **70** 9740 *2005*, Kalai et al. *Synthesis* 439 *2006*].

Methanesulfonyl chloride *[124-63-0]* **M 114.5. b 55°/11mmm, d_4^{20} 1.474, n_D^{20} 1.452.** Distil the sulfonyl chloride from P_2O_5 under vacuum. It is a strong **IRRITANT**. [*Beilstein* **4** IV 27.]

Methanol *[67-56-1]* **M 32.0, b 64.5°, d^{15} 0.79609, d^{25} 1.32663, n^{15} 1.33057, n^{25} 1.32663, pK^{25} 15.5.** Almost all methanol is now obtained synthetically. Likely impurities are water, acetone, formaldehyde, ethanol, methyl formate and traces of dimethyl ether, methylal, methyl acetate, acetaldehyde, carbon dioxide and ammonia. Most of the water (down to about 0.01%) can be removed by fractional distillation. Drying with CaO is unnecessary and wasteful. Anhydrous methanol can be obtained from "absolute" material by passage through Linde type 4A molecular sieves, or by drying with CaH_2, $CaSO_4$, or with just a little more sodium than required to react with the water present, in all cases the methanol is then distilled. Two treatments with sodium reduces the water content to about 5 x 10^{-5}%. [Friedman et al. *J Am Chem Soc* **83** 4050 *1961*.] Lund and Bjerrum [*Chem Ber* **64** 210 *1931*] warmed clean dry magnesium turnings (5g) and iodine (0.5g) with 50-75ml of "absolute" methanol in a flask until the iodine disappeared and all the magnesium was converted to the methoxide. Up to 1L of methanol was added and, after refluxing for 2-3 hours, it was distilled off, excluding moisture from the system. Redistillation from tribromobenzoic acid removes basic impurities and traces of magnesium oxides, and leaves conductivity-quality material. The method of Hartley and Raikes [*J Chem Soc* **127** 524 *1925*] gives a slightly better product. This consists of an initial fractional distillation, followed by distillation from aluminium methoxide, and then ammonia and other volatile impurities are removed by refluxing for 6 hours with freshly dehydrated $CuSO_4$ (2g/L) while dry air is passed through: the methanol is finally distilled. (The aluminium methoxide is prepared by warming with aluminium amalgam (3g/L) until all the aluminium has reacted. The amalgam is obtained by warming pieces of sheet aluminium with a solution of $HgCl_2$ in dry methanol.) This treatment also removes aldehydes.
If acetone is present in the methanol, it is usually removed prior to drying. Bates, Mullaly and Hartley [*J Chem Soc* 401 *1923*] dissolved 25g of iodine in 1L of methanol and then poured the solution, with constant stirring, into 500ml of M NaOH. Addition of 150ml of water precipitated iodoform. The solution was allowed to stand overnight, filtered, then boiled under reflux until the odour of iodoform disappeared, and fractionally distilled. (This treatment also removes formaldehyde.) Morton and Mark [*Ind Eng Chem (Anal Edn)* **6** 151 *1934*] refluxed methanol (1L) with furfural (50ml) and 10% NaOH solution (120ml) for 6-12 hours, the refluxing resin carries down with it the acetone and other carbonyl-containing impurities. The alcohol was then fractionally distilled. Evers and Knox [*J Am Chem Soc* **73** 1739 *1951*], after refluxing 4.5L of methanol for 24 hours with 50g of magnesium, distilled off 4L of it, which they then refluxed with $AgNO_3$ for 24 hours in the absence of moisture or CO_2. The methanol was again distilled, shaken for 24 hours with activated alumina before being filtered through a glass sinter and distilled under nitrogen in an all-glass still. Material suitable for conductivity

work was obtained.
Variations of the above methods have also been used. For example, a sodium hydroxide solution containing iodine has been added to methanol and, after standing for 1 day, the solution has been poured slowly into about a quarter of its volume of 10% $AgNO_3$, shaken for several hours, then distilled. Sulfanilic acid has been used instead of tribromobenzoic acid in Lund and Bjerrum's method. A solution of 15g of magnesium in 500ml of methanol has been heated under reflux, under nitrogen, with hydroquinone (30g), before degassing and distilling the methanol, which was subsequently stored with magnesium (2g) and hydroquinone (4g per 100ml). Refluxing for about 12 hours removes the bulk of the formaldehyde from methanol: further purification has been obtained by subsequent distillation, refluxing for 12 hours with dinitrophenylhydrazine (5g) and H_2SO_4 (2g/L), and again fractionally distilling. [*Beilstein* **1** IV 1227.]
Rapid purification: Methanol purification is the same as for ethanol. Another simple purification procedure consists of adding 2g of $NaBH_4$ to 1.5L methanol, gently bubbling argon through it and refluxing for a day at 30°, then adding 2g of freshly cut sodium (washed with methanol) and refluxing for 1 day before distilling. The middle fraction is taken. [Jou & Freeman *J Phys Chem* **81** 909 *1977*.]

Methoxyacetic acid *[625-45-6]* **M 90.1, b 97°/13-14mm, d_4^{20} 1.175, n_D^{20} 1.417, pK^{25} 3.57.** Fractionally crystallise the acid by repeated partial freezing, then fractionally distil it under vacuum through a vacuum-jacketed Vigreux column ~20cm long. [*Beilstein* **3** IV 574.]

Methoxyamine hydrochloride *[593-56-6]* **M 83.5, m 151-152°, pK^{25} 4.60.** Crystallise the hydrochloride from absolute EtOH or EtOH by addition of diethyl ether. [Kovach et al. *J Am Chem Soc* **107** 7360 *1985*, *Beilstein* **1** IV 1252.]

2-Methoxyethanol (methylcellosolve) *[109-86-4]* **M 76.1, b 124.4°, d_4^{20} 0.964, n_D^{20} 1.4017, pK^{25} 14.8.** Peroxides can be removed by refluxing with stannous chloride or by filtration under slight pressure through a column of activated alumina. 2-Methoxyethanol can be dried with K_2CO_3, $CaSO_4$, $MgSO_4$ or silica gel, then distilled from sodium. Aliphatic ketones (and water) can be removed by making the solvent 0.1% in 2,4-dinitrophenylhydrazine and allowing to stand overnight with silica gel before fractionally distilling. [*Beilstein* **1** IV 2375.]

2-Methoxyethoxymethylchloride (MEMCl) *[3970-21-6]* **M 124.6, b 50-52°/13mm, 140-145°(dec)/atm, d_4^{20} 1.092, n_D^{20} 1.427.** Possible impurities are methoxyethanol (**b** 124°/atm), HCHO and HCl which can be removed below the boiling point of MEMCl. Purify MEMCl by fractional distillation in a vacuum. If too impure, prepare it from methoxyethanol (152g) and *s*-trioxane (66g) by bubbling a stream of dry HCl (with stirring) until a clear mixture is obtained. Dilute with pentane (900ml), dry (3 hours over 100g $MgSO_4$, at 5°), evaporate and the residue is distilled in a vacuum. It is MOISTURE SENSITIVE and **TOXIC.** The $MEM.NEt_3^+Cl^-$ salt, prepared by reaction with 1.3 equivalents of Et_3N (16 hours/25°) and dried in a vacuum, has **m** 58-61°, and is moisture sensitive. [Corey et al. *Tetrahedron Lett* 809 *1976*, Yoshimatsu et al. *J Org Chem* **59** 1011 *1994*, Greene & Wuts *Protective Groups in Organic Synthesis* 3rd edn, J Wiley & Sons NY *1991*.] **CARCINOGEN.**

2-Methoxyethylamine *[109-85-3]* **M 75.1, b 94°, d_4^{20} 0.874, n_D^{20} 1.407, pK^{25} 9.40.** An aqueous 70% solution of the amine is dehydrated by azeotropic distillation with *benzene or methylene chloride and the amine is distilled twice from zinc dust. Store it in a tight container as it absorbs CO_2 from the atmosphere. [*Beilstein* **4** IV 1411.]

8-Methoxypsoralen See xanthotoxin in "Miscellaneous Compounds", Chapter 7.

***N*-Methylacetamide** *[79-16-3]* **M 73.1, m 30°, b 70-71°/2.5-3mm, pK_1^{25} –3.70, pK_2^{25} –0.42.** Fractionally distil it under vacuum, then fractionally crystallise it twice from its melt. Likely impurities include acetic acid, methyl amine and H_2O. For a detailed purification procedure, see Knecht and Kolthoff, *Inorg Chem* **1** 195 *1962*. Although *N*-methylacetamide is commercially available it is often extensively contaminated with acetic acid, methylamine, water and an unidentified impurity. The recommended procedure is to synthesise it in the laboratory by direct reaction. The gaseous amine is passed into hot glacial acetic acid, to give a partially

aqueous solution of methylammonium acetate which is heated to *ca* 130° to expel water. Chemical methods of purification such as extraction by petroleum ether, treatment with H_2SO_4, K_2CO_3 or CaO can be used but are more laborious.
Tests for purity include the Karl Fischer titration for water; this can be applied directly. Acetic acid and methylamine can be detected polarographically.
In addition to the above, purification of *N*-methylacetamide can be achieved by fractional freezing, including zone melting, repeated many times, or by vacuum distillation under reduced pressures. For details of zone melting techniques, see Knecht in *Recommended Methods for Purification of Solvents and Tests for Impurities*, Coetzee Ed. Pergamon Press *1982*. [*Beilstein* **4** IV 176.]

Methyl acetate *[79-20-9]* **M 74.1, b 56.7-57.2°, d $_4^{20}$ 0.934. n $_D^{20}$ 1.36193, n $_D^{25}$ 1.3538, pK^{20} –7.28 (H_o scale, aqueous H_2SO_4).** Methanol in methyl acetate can be detected by measuring its solubility in water. At 20°, the solubility of methyl acetate in water is *ca* 35g per 100ml, but 1% MeOH confers complete miscibility. Methanol can be removed by conversion to methyl acetate, by refluxing for 6 hours with acetic anhydride (85ml/L), followed by fractional distillation. Acidic impurities can be removed by shaking with anhydrous K_2CO_3 and distilling. An alternative treatment is with acetyl chloride, followed by washing with concentrated NaCl and drying with CaO or $MgSO_4$. (Solid $CaCl_2$ cannot be used because it forms a crystalline addition compound.) Distillation from copper stearate destroys peroxides. Free alcohol or acid can be eliminated from methyl acetate by shaking with strong aqueous Na_2CO_3 or K_2CO_3 (three times), then with aqueous 50% $CaCl_2$ (three times), saturated aqueous NaCl (twice), drying with K_2CO_3 and distilling it from P_2O_5. [*Beilstein* **2** IV 122.]

Methyl acetimidate hydrochloride *[14777-27-6]* **M 109.6, m 93-95°, 105°(dec), pK_{Est} ~5.5.** Crystallise the imidate from methanol by adding dry ether to a ratio of 1:1 and cooling at 0°. Filter off the crystals in a cold room, wash them with methanol/ether (1:2), then dry in a vacuum. [Hunter & Ludwig *J Am Chem Soc* **84** 3491 *1962*.] The *free base* has **b** 90-91°/765mm, d $_4^{20}$ 0.867, n $_D^{20}$ 1.403. [Hunter & Ludwig *Methods Enzymol* **25** 585 *1973*, *Beilstein* **2** IV 181.]

Methyl acrylate *[96-33-3]* **M 86.1, b 80°, d $_4^{20}$ 0.9535, n $_D^{20}$ 1.4040.** Wash the ester repeatedly with aqueous NaOH until free from inhibitors (such as hydroquinone), then wash it with distilled water, dry ($CaCl_2$) and fractionally distil it under reduced pressure in an all-glass apparatus. Seal it under nitrogen and store it at 0° in the dark. [Bamford & Han *J Chem Soc, Faraday Trans 1* **78** 855 *1982*, *Beilstein* **2** IV 1457.]

Methylamine (gas) *[74-89-5]* **M 31.1, b –7.55°/719mm, pK^{25} 10.62.** Dry the amine with sodium or BaO. It is commercially available in metal cylinders. [*Beilstein* **4** IV 118.]

Methylamine hydrochloride *[593-51-1]* **M 67.5, m 231.8-233.4°, b 225-230°/15mm, pK^{25} 10.62.** Crystallise the salt from *n*-butanol, absolute EtOH or MeOH/$CHCl_3$. Wash it with $CHCl_3$ to remove traces of dimethylamine hydrochloride. Dry it under vacuum first with H_2SO_4 then P_2O_5. It is deliquescent; store it in a desiccator over P_2O_5. [*Beilstein* **4** IV 122.]

Methyl bromide *[74-83-9]* **M 94.9, b 3.6°.** Purify it by bubbling through conc H_2SO_4, followed by passage through a tube containing glass beads coated with P_2O_5. Also purify it by distillation from $AlBr_3$ at –80°, by passage through a tower of KOH pellets and by partial condensation. [*Beilstein* **1** IV 68.]

2-Methylbutane (isopentane) *[78-78-4]* **M 72.2, b 27.9°, d $_4^{20}$ 0.621, n $_D^{20}$ 1.35373, n $_D^{25}$ 1.35088.** Stir isopentane for several hours in the cold with conc H_2SO_4 (to remove olefinic impurities), then wash it with H_2O, aqueous Na_2CO_3 and H_2O again. Dry it with $MgSO_4$ and fractionally distil it using a Todd column packed with glass helices. Material transparent down to 180nm is obtained by distilling from sodium wire, and passing through a column of silica gel which had previously been dried in place at 350° for 12 hours before use. [Potts *J Phys Chem* **20** 809 *1952*, *Beilstein* **1** IV 320.]

2-Methyl-1-butanol *[137-32-6, RS(±) 34713-94-5, S(–) 1565-80-6]* **M 88.2, b 130°(*RS*), 128.6°(*S*), [α] $_D^{25}$ –5.8° (neat), d $_4^{20}$ 0.809, n^{52} 1.4082.** Reflux the butanol with CaO, distil, reflux with magnesium and again

fractionally distil it. A small sample of highly purified material is obtained by fractional crystallisation after conversion into a suitable ester such as the trinitrophthalate or the 3-nitrophthalate. The latter is converted to the cinchonine salt in acetone and recrystallised from $CHCl_3$ by adding pentane. The salt is saponified, extracted with ether, and fractionally distilled. [Terry et al. *J Chem Eng Data* **5** 403 *1960*, *Beilstein* **1** IV 1666.]

3-Methyl-2-butanol *[598-75-4]* **M 88.2, b 111.5°, d $_4^{20}$ 0.807, n $_D^{20}$ 1.4095, n $_D^{25}$ 1.4076.** Reflux it with magnesium, then fractionally distil it. [*Beilstein* **1** IV 1675.]

3-Methyl-2-butanone (methyl isopropyl ketone) *[563-80-4]* **M 86.1, b 93-94°/752mm, d $_4^{20}$ 0.818, n 1.410, pK^{25} –7.1 (aqueous H_2SO_4).** Reflux the ketone with a little $KMnO_4$. Fractionate it through a spinning-band column, dry with $CaSO_4$ and distil it. [*Beilstein* **1** IV 3287.]

2-Methyl-2-butene see **amylene** above.

2-Methyl-3-butyn-2-amine (1,1-dimethylpropargylamine, 3-amino-3-methyl-1-butyne) *[2978-58-7]* **M 83.1, b 79-80°/760mm, d $_4^{25}$ 0.790, n $_D^{25}$ 1.4183, pK$_{Est}$ ~8.0.** Dissolve the amine in Et_2O, dry over anhydrous K_2CO_3, filter, evaporate and distil (preferably under N_2). Store it away from CO_2. The *hydrochloride* [2978-59-8] has **m** 234° (from EtOH/Et_2O). The *benzoyl* derivative has **m** 152-153° (from EtOH). [Hennion & Teach *J Am Chem Soc* **75** 1653 *1953*, Hennion & DiGiovanna *J Org Chem* **30** 2645 *1965*.]

Methyl *n*-butyrate *[623-42-7]* **M 102.1, b 102.3°/760mm, d $_4^{20}$ 0.898, n $_D^{20}$ 1.389.** Treat the ester with anhydrous $CuSO_4$, then distil it under dry nitrogen. [*Beilstein* **2** IV 786.]

***S*-(+)-2-Methylbutyric acid** *[1730-91-2]* **M 102.1, b 64°/2mm, 78°/15mm, 90-94°/23mm, 174-175°/atm, d $_4^{20}$ 0.938, n $_D^{20}$ 1.406, [α] $_{546}^{20}$ +23°, [α] $_D^{20}$ +19.8° (neat), [α] $_D^{13}$ +18.3° (c 6, EtOH), pK^{25} 4.76 (for *RS*).** Purify the acid by distilling it *in vacuo* [Sax & Bergmann *J Am Chem Soc* **77** 1910 *1955*, Doering & Aschner *J Am Chem Soc* **75** 393 *1953*]. The *methyl ester* is formed by addition of diazomethane and has **b** 112-115°/760mm, [α] $_D^{27}$ +21.1° (c 1.7, MeOH). [*Beilstein* **2** IV 888.]

Methyl carbamate *[598-55-0]* **M 75.1, m 54.4-54.8°, 56-58°, b 176-177°/~760mm.** Crystallise the carbamate from *benzene or distil it. [*Beilstein* **3** H 21.]

Methyl chloride *[74-87-3]* **M 50.5, b –24.1°.** Bubble methyl chloride through a sintered-glass disc dipped into conc H_2SO_4, then wash it with water, condense it at low temperature and fractionally distil it. It has been distilled from $AlCl_3$ at –80°. *Alternatively*, pass it through towers containing $AlCl_3$, soda-lime and P_2O_5, then condense and fractionally distil it. Store it as a gas. [*Beilstein* **1** IV 28.]

Methyl chloroacetate *[96-34-4]* **M 108.5, b 129-130°, d $_4^{20}$ 1.230, n $_D^{20}$ 1.423.** Shake the ester with saturated aqueous Na_2CO_3 (three times), aqueous 50% $CaCl_2$ (three times), saturated aqueous NaCl (twice), dry (Na_2SO_4) and fractionally distil it. **Very toxic.** [*Beilstein* **2** IV 480.]

***R*-(+) Methyl 2-chloropropionate** *[77287-29-7]* **M 122.6, b 49-50°/35mm, 78-80°/120mm, 132-134°/760mm, d $_4^{20}$ 1.152, n $_D^{20}$ 1.417, [α] $_D^{20}$ +26° (19.0°) (neat).** Purify the ester by repeated distillation [Walker *J Chem Soc* **67** 916 *1895*, Walden *Chem Ber* **28** 1293 *1985*, see also Gless *Synth Commun* **16** 633 *1986*]. [*Beilstein* **2** H 248.]

Methyl cyanoacetate *[105-34-0]* **M 99.1, f –13°, b 115°/36mm, 200.4-200.9°/761mm, d $_4^{20}$ 1.128, n $_D^{20}$ 1.420.** Purify the ester by shaking with 10% Na_2CO_3 solution, wash well with water, dry with anhydrous Na_2SO_4, and distil it. [*Beilstein* **2** H 584, **2** I 253, **2** II 530, **2** III 1628, **2** IV 1889.]

Methyl cyanoformate *[17640-15-2]* **M 85.1, b 81°/47mm, 97°/751mm, 100-101°/760mm, d $_4^{20}$ 1.072, n $_D^{20}$ 1.37378.** Purify the ester by fractionation through a 45cm glass helices packed column or a 30cm spinning band column. [Sheppard *J Org Chem* **27** 3756 *1962*.] It has been distilled through a short Vigreux column, and further purified by recrystallisation from Et_2O at –40° as white crystals which melt at room temperature.

NMR: δ 4.0 (CH_3), and the IR has ν_{max} at 2250 (CN) and 1750 (CO) cm^{-1}. [Childes & Weber *J Org Chem* **41** 3486 *1976*, *Beilstein* **2** III 1587.]

Methyl decanoate (methyl caprate) *[110-42-9]* **M 186.3, b 114°/15mm, 224°/760mm, d_4^{20} 0.874, n_D^{20} 1.426.** Pass the ester through alumina before use and distil in a vacuum. [*Beilstein* **2** IV 1044.]

***N*-Methyldiethanolamine [MDEA, *N,N*-bis(hydroxyethyl)methylamine, 2,2′-methyliminodiethanol]** *[105-59-9]* **M 119.2, b 75-77°/0.5mm, 115°/5mm, 131°/10mm, 141-142°/18mm, 246-248°/atm, d_4^{25} 1.038, n_D^{20} 1.469, pK^{25} 8.57, pK^{35} 8.31, pK^{45} 8.13, pK^{60} 7.87.** Purify MDEA by fractional distillation preferably under vacuum in a stream of N_2, and store it under N_2. The colourless distillate darkens in air and absorbs CO_2 under pressure [Goodridge *Trans Farad Soc* **51** 1703 *1955*]. It is a tertiary base, hence it does not form an *N-carbamate salt* like primary and secondary amines, but **does** form a *carbonate salt* in the presence of carbonic acid (i.e. $CO_2 + H_2O = H_2CO_3$). It is soluble in H_2O and EtOH, but slightly soluble in Et_2O. The *hydrochloride* is very hygroscopic; the *O,O′-diacetyl ester* has **b 110°/4mm**, **133°/15mm**, **b 251°/atm**, the *O,O′-bis(4-nitrobenzoyl) ester* has **m 112-113°**, the *Reineckate salt* has **m 168°**, the *picrate* crystallises from EtOAc with **m 95-96°**, and with a strong aqueous solution of $AuCl_3$/HCl the *chloroaurate salt*, **m 101-102°**, is formed which crystallises from H_2O. With $PtCl_4$/HCl, the *chloroplatinate salt* is obtained, forming orange-yellow rhombic crystals upon recrystallisation from a concentrated aqueous solution which sinter at **145°** and decompose at **148-150°**. The IR spectrum in CCl_4 has C-H str at ν_{max} (ε $mole^{-1}$ $L.cm^{-1}$) 2779 (93), 2844 (81), 2877 (99) and 2948 (107) cm^{-1}. [Hanby & Rydon *J Chem Soc* 516 *1947*, Hill & Meakin *J Chem Soc* 760 *1958*, Knorr & Matthes *Chem Ber* **31** 1071 *1898*, *Beilsten* **4** H 284, **4** II 729, **4** III 692, **4** IV 1517.]

Methyl dodecanoate (methyl laurate) *[111-82-0]* **M 214.4, m 5°, b 141°/15mm, d_4^{20} 0.870, n^{50} 1.4199.** Pass the ester through alumina before use, and distil it in a vacuum. [*Beilstein* **2** IV 1090.]

***N*-Methyleneaminoacetonitrile (MAAN)** *[109-82-0]* **M 68.1, m 129°.** Crystallise MAAN from EtOH or acetone. It crystallises nicely from H_2O but with considerable loss of material. It is an inhibitor of bone growth. [Adams & Langley *Org Synth* Coll Vol **I** 355 *1941*.]

Methyl ether (dimethyl ether) *[115-10-6]* **M 46.1, m -141°, b –63.5°/96.5mm, –24°/~760mm, d^{25} 1.918/L (at 1 atmosphere relative to air as 1).** Dry methyl ether by passing over alumina and then BaO, or over CaH_2, followed by fractional distillation at low temperatures. Its solubility is 37ml per ml of H_2O at 18°, and it is very soluble in EtOH and Et_2O. [*Beilstein* **1** IV 1245.]

***N*-Methyl ethylamine hydrochloride** *[624-60-2]* **M 95.6, m 126-130°, pK^{25} 10.9 (free base).** Crystallise the hydrochloride from absolute EtOH or diethyl ether. Dry it *in vcuo*. [*Beilstein* **4** H 94.]

***N*-Methyl formamide** *[123-39-7]* **M 59.1, m –3.5°, b 100.5°/25mm, d_4^{20} 1.005., n^{52} 1.4306** Dry it over molecular sieves for 2 days, then distil it under reduced pressure through a column packed with glass helices. Fractionally crystallise it by partial freezing and the solid portion is distilled in a vacuum. [*Beilstein* **4** IV 170.]

Methyl formate *[107-31-3]* **M 60.1, b 31.5°, 34°, d_4^{20} 0.971, n^{15} 1.34648, n_D^{20} 1.34332.** Wash the formate with strong aqueous Na_2CO_3, dry it with solid Na_2CO_3 and distil it from P_2O_5. (Procedure removes free alcohol or acid.) [*Beilstein* **2** IV 20.]

2-Methylglutaric acid *[18069-17-5]* **M 146.1, m 79°, pK_1^{25} 4.36, pK_2^{25} 5.37.** Crystallise the acid from distilled water, then dry it under vacuum over conc H_2SO_4. [*Beilstein* **2** IV 1989.]

3-Methylglutaric acid *[626-51-7]* **M 146.1, m 87°, pK_1^{25} 4.35, pK_2^{25} 5.44.** Crystallise the acid from distilled water, then dry it under vacuum over conc H_2SO_4. [*Beilstein* **2** IV 1992.]

Methylglyoxal *[78-98-8]* **M 72.1, b *ca* 72°/760mm.** Commercial 30% (w/v) aqueous solution is diluted to about 10% and distilled twice, taking the fraction boiling below 50°/20mm Hg. (This treatment does not remove lactic acid). [*Beilstein* **1** IV 3631.]

2-Methylhexane *[591-76-4]* **M 100.2, b 90.1°, d_4^{20} 0.678, n_D^{20} 1.38485, n_D^{20} 1.38227.** Purify it by azeotropic distillation with MeOH, then wash it with water (to remove the MeOH), dry it over type 4A molecular sieves and distil it. [*Beilstein* **1** IV 397.]

3-Methylhexane *[589-34-4]* **M 100.2, b 91.9°, d_4^{20} 0.687, n_D^{20} 1.38864, n_D^{20} 1.38609.** Purify it as for 2-methylhexene. [*Beilstein* **1** IV 399.]

Methyl hexanoate (methyl caproate) *[106-70-7]* **M 130.2, b 52°/15mm, 150°/760mm, d_4^{20} 0.885, n_D^{20} 1.410.** Pass it through alumina and distil it before use. [*Beilstein* **2** IV 921.]

Methylhydrazine *[60-34-4]* **M 46.1, b 87°/745mm, d_4^{20} 0.876, n_D^{20} 1.436, pK^{30} 7.87.** Dry with BaO, then distil it in a vacuum. Store it under nitrogen. [*Beilstein* **4** IV 3322.]

Methyl hydrazinocarboxylate *[6294-89-9]* **M 90.1, m 70-73°, b 108°/12mm.** To remove impurities, the material is melted and pumped under vacuum until the vapours are spectroscopically pure [Caminati et al. *J Am Chem Soc* **108** 4364 *1986*]. Distil it in a vacuum. [*Beilstein* **3** I 46.]

Methyl iodide *[74-88-4]* **M 141.9, b 42.8°, d_4^{20} 2.281, n_D^{20} 1.5315.** Methyl iodide deteriorates rapidly with liberation of iodine if exposed to light. It is usually purified by shaking it with dilute aqueous $Na_2S_2O_3$ or $NaHSO_3$ until colourless, then washing with water, dilute aqueous Na_2CO_3, and more water, drying with $CaCl_2$ and distilling. It is stored in a brown bottle away from sunlight in contact with a small amount of mercury, powdered silver or copper. (Prolonged exposure of mercury to methyl iodide forms methylmercuric iodide.) Methyl iodide can be dried further using $CaSO_4$ or P_2O_5. An alternative purification is by percolation through a column of silica gel or activated alumina, then distillation. The solution can be degassed by using repeated freeze-pump-thaw cycles. [*Beilstein* **1** IV 87.]

***O*-Methylisourea hydrogen sulfate (2-methylpseudourea sulfate)** *[29427-58-5]* **M 172.2, m 114-118°, 119°.** Recrystallise the salt from MeOH/Et_2O (327g of salt dissolved in 1L of MeOH and 2.5L of Et_2O is added) [Fearing & Fox *J Am Chem Soc* **76** 4382 *1954*]. The *picrate* has **m** 192° [Odo et al. *J Org Chem* **23** 1319 *1958*]. [*Beilstein* **3** IV 143.]

***N*-Methyl maleimide** *[930-88-1]* **M 111.1, m 94-96°.** Crystallise the imide three times from diethyl ether. Dry it *in vacuo*. [*Beilstein* **21/10** V 5.]

Methylmalonic acid *[516-05-2]* **M 118.1, m 135°(dec), pK_1^{25} 3.05, pK_2^{25} 5.76.** The acid crystallises as the *hydrate* from water. [*Beilstein* **2** IV 1932.]

Methyl methacrylate *[80-62-6]* **M 100.1, f –50°, b 46°/100mm, 100°/~760mm, d_4^{20} 0.937, n_D^{20} 1.4144.** Wash the ester twice with aqueous 5% NaOH (to remove inhibitors such as hydroquinone) and twice with water. Dry it with $CaCl_2$, Na_2CO_3, Na_2SO_4 or $MgSO_4$, then with CaH_2 under nitrogen under reduced pressure. The distillate is stored at low temperatures and redistilled before use. Prior to distilling, inhibitors such as hydroquinone (0.004%), ß-naphthylamine (0.2%) or di-β-naphthol are sometimes added. Also purify it by boiling with aqueous H_3PO_4 solution and finally with saturated NaCl solution. It is dried for 24 hours over anhydrous $CaSO_4$, distilled at 0.1mm Hg at room temperature and stored at –30° [Albeck et al. *J Chem Soc, Faraday Trans 1* **1** 1488 *1978*]. [*Beilstein* **2** II 398, **2** III 1279, **2** IV 1519.]

Methyl methanesulfonate *[66-27-3]* **M 110.3, b 59°/0.6mm, 96-98°/19mm, d_4^{20} 1.300, n_D^{20} 1.4140.** Purify the ester by careful fractionation and collecting the middle fraction. Suspected **CARCINOGEN.** Note that $MeSO_3H$ has **b** 167-167.5°/10mm and methanesulfonic anhydride has **b** 138°/10mm) — both are possible impurities. [*Beilstein* **4** IV 11.]

Methyl methanethiolsulfonate *[2949-92-0]* **M 126.2, b 69-71°/0.4mm, 96-97°/4.5mm, 104-105°/10mm, 119°/16mm, d_4^{20} 1.226, n_D^{20} 1.515.** Purify it by fractional distillation under reduced pressure, the IR has ν_{max} at 1350, 750 cm^{-1}. [Applegate et al. *J Org Chem* **38** 943 *1973*, *Beilstein* **4** IV 31.]

Methyl nitrate *[598-58-3]* **M 77.0, b 5°/50mm, 65°/760mm, d^5 1.2322, d^{15} 1.2167, d^{25} 1.2032.** Wash $MeONO_2$ once with H_2O then again with H_2O containing a few drops of concentrated NaOH to keep it slightly alkaline (litmus). Dry the ester over anhydrous $CaCl_2$, decant it and use it directly. It is possible to distil it under a vacuum with slow and gentle heating, as a sudden rise in temperature can cause decomposition with copious release of nitrous fumes (use extreme precautions and protection). The middle fraction can then be subjected to several freeze-pump-thaw cycles. [Black & Bakers *Org Synth* Col Vol **II** 412 *1943*.] [*Beilstein* **1** H 284, **1** I 141, **1** II 273, **1** III 1201, **1** IV 1254.] The **VAPOUR CAN EXPLODE ON HEATING.**

Methyl nitrite *[624-91-9]* **M 61.0, b –18°, –17°, d^{15} (liquid) 0.991.** Condense MeONO in a liquid nitrogen trap. Distil the greenish liquid under vacuum (preferably in a vacuum line), into the first trap containing dry Na_2CO_3 to free it from acid impurities then into further Na_2CO_3 and fused $CaCl_2$ traps before collection at –78°. It has been distilled through columns that are surrounded by Et_2O/Dri-ice cooled to –30°. [Leermakers & Ramsperger *J Am Chem Soc* **54** 1838 *1932*, Thompson & Purkis *Trans Farad Soc* **32** 675 *1936*, *Beilstein* **1** H 284, **1** I 141, **1** II 273, **1** III 1201, **1** IV 1253.] **CARCINOGEN.**

2-Methyl-2-nitro-1,3-propanediol *[77-49-6]* **M 135.1, m 145°, 147-148°, 149-150°.** Crystallise it from *n*-butanol or Me_2CO (**m** 150.6°). It decomposes on attempted distillation at 10mm. Its solubility in H_2O is 80g/100ml at 20°. [*Beilstein* **1** H 489, **1** II 547, **1** III 2190, **1** IV 2537.]

2-Methyl-2-nitro-1-propanol *[76-39-1]* **M 119.1, m 87-88°, b 94-95°/10mm.** Distil it under vacuum and/or crystallise it from petroleum ether or MeOH. [Astle & Abbott *J Org Chem* **21** 1229 *1956*, Kambe & Yasuda *Bull Soc Chem Jpn* **41** 1444 *1968*, *Beilstein* **1** H 378, **1** III 1546, **1** IV 1604.]

***RS*(±)-2-Methyl-2,4-pentanediol (MPD, pinecon, hexylene glycol)** *[107-41-5]* **M 118.2, m -40°, b 97°/10mm, 107.5-108.5°/25mm, 135-136°/40mm, 197°/760mm, d_4^{20} 0.922, n_D^{25} 1.4265.** Dry the diol with Na_2SO_4, then CaH_2, and fractionally distil it under reduced pressure through a helices packed column, taking precautions to avoid absorption of water. It is soluble in H_2O, EtOH, Et_2O, pentane and hexane. The *diacetate* is a liquid with **b 95°/15mm. It has very harmful vapours; use efficient fume cupboard** as it irritates eyes, skin throat and lungs, causing headaches and nausea and is a CNS depressant. [*Beilstein* **1** IV 2565.]

3-Methyloctane *[2216-33-3]* **M 128.3, b 142-144°/760mm, d_4^{20} 0.719, n_D^{20} 1.407.** Take it through a silica gel column and distil it. [Klassen & Ross *J Phys Chem* **91** 3668 *1987*, *Beilstein* **1** IV 455]

Methyl octanoate (methyl caprylate) *[111-11-5]* **M 158.2, b 83°/15mm, 193-194°/760mm, d_4^{20} 0.877, n_D^{20} 1.419.** Pass the ester through alumina and distil it before use. [*Beilstein* **2** IV 986.]

Methyl oleate (methyl *cis*-9-octadecenoate) *[112-62-9]* **M 296.5, f –19.9°, b 217°/16mm, d_4^{20} 0.874, n_D^{20} 1.4522.** Purify the oleate by fractional distillation under reduced pressure, and by low temperature crystallisation from acetone. Store it in the dark under N_2. [*Beilstein* **2** IV 1649.]

Methylpentane (mixture of isomers). Pass the mixture through a long column of activated silica gel (or alumina) and collect material that is transparent down to 200nm in the UV.

2-Methylpentane *[107-83-5]* **M 86.2, b 60.3°, d_4^{20} 0.655, n_D^{20} 1.37145, n_D^{25} 1.36873.** Purify it by azeotropic distillation with MeOH, followed by washing out the MeOH with water, drying ($CaCl_2$, then sodium), and distilling it. [Forziati et al. *J Res Nat Bur Stand* **36** 129 *1946*.]

3-Methylpentane *[96-14-0]* **M 86.2, b 63.3°, d_4^{20} 0.664, n_D^{20} 1.37652, n_D^{25} 1.37384.** Purify it by azeotropic distillation with MeOH, as for 2-methylpentane. Purify it for ultraviolet spectroscopy by passing it through

columns of silica gel or alumina activated by heating for 8 hours at 210° under a stream of nitrogen. *Alternatively*, treat it with conc (or fuming) H_2SO_4, then wash it with water, aqueous 5% NaOH, water again, then dry ($CaCl_2$, then sodium), and distil it through a long, glass helices-packed, column. [*Beilstein* **1** IV 363.]

2-Methyl-2,4-pentanediol *[107-41-5]* **M 118.2, b 107.5-108.5°/25mm, d_4^{20} 0.922, n_D^{25} 1.4265.** Dry the diol with Na_2SO_4, then CaH_2 and fractionally distil it under reduced pressure through a packed column, taking precautions to avoid absorption of water. [*Beilstein* **1** IV 2565.]

2-Methyl-1-pentanol *[105-30-6]* **M 102.2, b 65-66°/60mm, 146-147°/760mm, d_4^{20} 0.827, n_D^{20} 1.420.** Dry the 1-pentanol with Na_2SO_4 and distil it. [*Beilstein* **1** IV 1713.]

4-Methyl-2-pentanol *[108-11-2]* **M 102.2, b 131-132°, d_4^{20} 0.810, n_D^{20} 1.413.** Wash the 2-pentanol with aqueous $NaHCO_3$, dry and distil it. Purify it further by converting it to the phthalate ester by adding 120ml of dry pyridine and 67g of phthalic anhydride per mole of alcohol, purifying the ester and steam distilling it in the presence of NaOH. The distillate is extracted with ether, and the extract is dried and fractionally distilled. [Levine & Walti *J Biol Chem* **94** 367 *1931*, *Beilstein* **1** IV 1717.]

3-Methyl-3-pentanol carbamate (Emylcamate) *[78-28-4]* **M 145.2, m 56-58.5°.** Crystallise the carbamate from 30% aqueous EtOH. [*Beilstein* **1** IV 1773.]

4-Methyl-2-pentanone (methyl isobutyl ketone) *[108-10-1]* **M 100.2, b 115.7°/~760mm d_4^{20} 0.801, n_D^{20} 1.3958, n_D^{25} 1.3938.** Reflux the ketone with a little $KMnO_4$, wash it with aqueous $NaHCO_3$, dry with $CaSO_4$ and distil it. Acidic impurities are removed by passage through a small column of activated alumina. [*Beilstein* **1** IV 3305.]

2-Methyl-1-pentene *[763-29-1]* **M 84.2, b 61.5-62°, d_4^{20} 0.680, n_D^{20} 1.395.** Water is removed, and formation of peroxides is prevented by several vacuum distillations of 2-methyl-1-pentene from sodium. It is stored with sodium-potassium alloy. [*Beilstein* **1** IV 841.]

***cis*-4-Methyl-2-pentene** *[691-38-3]* **M 84.2, m –134.4°, b 57.7-58.5°, d_4^{20} 0.672, n_D^{20} 1.388.** Dry the *cis*-pentene with CaH_2, and distil it. [*Beilstein* **1** IV 841.]

***trans*-4-Methyl-2-pentene** *[674-76-0]* **M 84.2, m –140.8°, b 58.5°, d_4^{20} 0.669, n_D^{20} 1.389.** Dry the *trans*-isomer with CaH_2, and distil it. [*Beilstein* **1** IV 844.]

2-Methylpropane-1,2-diamine (1,2-diamino-2-methylpropane) *[811-93-8]* **M 88.2, b 47-48°/17mm, pK_1^{25} 6.25 (6.18), pK_2^{25} 9.82 (9.42).** Dry the diamine with sodium for 2 days, then distil it from sodium under reduced pressure. [*Beilstein* **4** IV 1306.]

2-Methylpropane-1-thiol (isobutylmercaptan) *[513-44-0]* **M 90.2, b 41.2°/142mm, 88.5°/760mm, n_D^{25} 1.43582, pK_{Est} ~10.8.** Dissolve the thiol in EtOH, and add to 0.25M $Pb(OAc)_2$ in 50% aqueous EtOH. The precipitated lead mercaptide is filtered off, washed with a little EtOH, and impurities are removed from the molten salt by steam distillation. After cooling, dilute HCl is added dropwise to the residue, and the mercaptan is distilled directly from the flask. Water is separated from the distillate, and the mercaptan is dried (Na_2CO_3) and distilled under nitrogen. [Mathias *J Am Chem Soc* **72** 1897 *1950*, *Beilstein* **1** H 378, **1** I 191, **1** II 412, **1** III 1565, **1** IV 1605.]

2-Methylpropane-2-thiol (*tert*-butylmercaptan) *[75-66-1]* **M 90.2, b 61.6°/701mm, 66°/760mm, d_4^{25} 0.79426, n_D^{25} 1.41984, pK^{25} 11.22.** Dry the thiol for several days over CaO, then distil it from CaO. Purify it as for *2-methylpropane-1-thiol* above. [*Beilstein* **1** H 383, **1** II 416, **1** III 1589, **1** IV 1634.]

2-Methyl-1-propanol (isobutanol) *[78-83-1]* **M 74.1, b 107.9°760mm, d_4^{20} 0.804, n^{15} 1.39768, n_D^{25} 1.3939.** Isobutanol is dried by refluxing with CaO and BaO for several hours, followed by treatment with calcium or aluminium amalgam, then fractional distilling it from sulfanilic or tartaric acids. More exhaustive purifications

involve formation of phthalate or borate esters. Heating it with phthalic anhydride gives the *acid phthalate* which, after crystallisation to constant melting point (**m** 65°) from petroleum ether, is hydrolysed with aqueous 15% KOH. The alcohol is distilled off as the water azeotrope and dried (K_2CO_3, then anhydrous $CuSO_4$), and finally magnesium turnings, followed by fractional distillation. [Hückel & Ackermann *J Prakt Chem* **136** 15 *1933*.] The borate ester is formed by heating the dried alcohol for 6 hours in an autoclave at 160-175° with a quarter of its weight of boric acid. After fractional distillation under vacuum, the ester is hydrolysed by heating for a short time with aqueous alkali and the alcohol is dried with CaO and distilled. [Michael et al. *J Am Chem Soc* **38** 653 *1916*.] *Alternatively*, dry the alcohol with K_2CO_3, $CaSO_4$ or $CaCl_2$, filter and fractionally distil it. For further drying, the redistilled alcohol can be refluxed with the appropriate alkyl phthalate or succinate as described under *ethanol*. [*Beilstein* **1** IV 1588.]

Methyl propiolate *[922-67-8]* **M 84.1, b 100°/atm, 102°/atm, 103-105°/atm, d_4^{20} 0.945, n_D^{20} 1.4080.** Purify the propiolate by fractional distillation and collecting the middle fraction, note that propiolic acid has a higher boiling point [144°(dec)/760mm]. [*Beilstein* **2** IV 1688.] **LACHRYMATORY**.

***N*-Methylpropionamide** *[1187-58-2]* **M 87.1, f –30.9°, b 103°/12-13mm, d_4^{20} 0.934, n_D^{25} 1.4356.** The amide is a colourless, odourless, neutral liquid at room temperature with a high dielectric constant. The amount of water present can be determined directly by Karl Fischer titration, GLC and NMR have been used to detect unreacted propionic acid. Commercial material of high quality is available, probably from the condensation of anhydrous methylamine with 50% excess of propionic acid. Rapid heating to 120-140° with stirring favours the reaction by removing water either directly or as the ternary xylene azeotrope. The quality of the distillate improves during the distillation.
N-Methylpropionamide can be dried over CaO. Water and unreacted propionic acid are removed as their xylene azeotropes. It is then distilled in a vacuum. Material used as an electrolyte solvent (specific conductance less than 10^{-6} ohm^{-1} cm^{-1}) is obtained by fractional distillation under reduced pressure, and storage over BaO or molecular sieves because it readily absorbs moisture from the atmosphere on prolonged storage. [Hoover *Pure Appl Chem* **37** 581 *1974*, *Recommended Methods for Purification of Solvents and Tests for Impurities,* Coetzee Ed., Pergamon Press, *1982*, *Beilstein* **4** IV 183.]

Methyl propionate *[554-12-1]* **M 88.1, b 79.7°.** Wash the ester with saturated aqueous NaCl, then dry it with Na_2CO_3 and distil it from P_2O_5. (This removes any free acid and alcohol.) It has also been dried with anhydrous $CuSO_4$. [*Beilstein* **2** IV 104.]

Methyl *n*-propyl ether *[557-17-5]* **M 74.1, b 39°/743mm d_4^{20} 0.736, n^{14} 1.3602, pK^{25} –3.79 (aqueous H_2SO_4).** Dry it with $CaSO_4$, then pass the ether through a column of alumina (to remove peroxides) and fractionally distil it. [*Beilstein* **1** H 354, **1** I 178, **1** II 367, **1** III 1413, **1** IV 1421.]

Methyl *n*-propyl ketone (pentan-2-one) *[107-87-9]* **M 86.1, b 102.4°, d_4^{20} 0.807, n_D^{20} 1.3903.** Purify the ketone by refluxing it with a little $KMnO_4$, dry it with $CaSO_4$ and distil it. It can be converted to its bisulfite addition compound by shaking with excess saturated aqueous $NaHSO_3$ at room temperature, cooling to 0°, filtering, washing with diethyl ether and drying. Steam distillation of the adduct gives a distillate from which the ketone is recovered, washed with aqueous $NaHCO_3$ and distilled water, dried (K_2CO_3) and fractionally distilled. [Waring & Garik *J Am Chem Soc* **78** 5198 *1956*, *Beilstein* **1** IV 3271.]

(±)-3-Methyl-1-propyn-3-ol carbamate (Meparfynol carbamate) *[302-66-9]* **M 141.2, m 55.8-57°, 56-58°, 120-121°/16mm.** Crystallise it from $*C_6H_6$, hexane, ether/petroleum ether or cyclohexane. [*Beilstein* **1** IV 65.] It is a sedative.

Methyl stearate *[122-61-8]* **M 298.5, m 41-43°, b 181-182°/4mm.** Crystallise the ester from petroleum ether or distil it in a vacuum. [*Beilstein* **2** IV 1216.]

Methylsuccinic acid *[498-21-5]* **M 132.1, m 115.0°, pK_1^{25} 3.88, pK_2^{25} 5.35.** Crystallise the acid from water. [*Beilstein* **2** IV 1948.]

***N*-Methylthioacetamide** *[5310-10-1]* **M 89.1, m 59°.** Recrystallise the amide from *benzene or EtOH. [Todd et al. *Chem Ber* **69** 220 *1936*, *Beilstein* **4** I 329, **4** III 124.]

Methyl trifluoromethanesulfonate (methyl triflate) *[333-27-7]* **M 164.1, b 97-97.5°/736mm, 99°/~760mm, 100-102°/~760mm, d_4^{20} 1.496, n_D^{25} 1.3238.** It is a strong methylating agent but is corrosive and **POISONOUS**. Fractionate it carefully and collecting the middle fraction (use an efficient fume cupboard) and keep away from moisture. It is a **POWERFUL ALKYLATING AGENT** and a strong **IRRITANT.** [IR: Gramstad & Haszeldine *J Chem Soc* 173 *1956*, *J Chem Soc* 4069 *1957*.] *Trifluoromethanesulfonic acid* (triflic acid) *[1493-13-6]* **M** 151.1, boils higher (**b** 162°/atm), has a **pKa** of 3.10, and is **TOXIC** and hygroscopic. [Hansen *J Org Chem* **30** 4322 *1965*, Kurz & El-Nasr *J Am Chem Soc* **104** 5823 *1982*, *Beilstein* **3** IV 34.]

Methyl vinyl ketone (3-buten-2-one) *[78-94-4]* **M 70.1, b 62-68°/400mm, 79-80°/760mm, d_4^{20} 0.845, n_D^{20} 1.413.** It forms an 85% azeotrope with water. After drying with K_2CO_3 and $CaCl_2$ (with cooling), the ketone is distilled at low pressures. [*Beilstein* **1** IV 3444.]

Methyl vinyl sulfone *[3680-02-2]* **M 106.1, b 116-118°/20mm, d_4^{20} 1.215, n_D^{20} 1.461.** Pass the sulfone through a column of alumina, then de-gas, distil it in a vacuum line and store it at –190° until required. [*Beilstein* **1** III 1866.]

***N*-Monobutyl urea** *[592-31-4]* **M 116.2, m 96-98°, pK_{Est} ~0.2.** Crystallise the urea from EtOH/water, then dry it under vacuum at room temperature. [*Beilstein* **4** I 371, **4** IV 578.]

***N*-Monoethyl urea** *[625-52-5]* **M 88.1, m 92-95°, pK_{Est} ~0.2.** Crystallise the urea from EtOH/water, then dry it under vacuum at room temperature. [*Beilstein* **4** IV 369.]

***N*-Monomethyl urea** *[598-50-5]* **M 74.1, m 93-95°, pK_{Est} ~0.2.** Crystallise the urea from EtOH/water, then dry it under vacuum at room temperature. [*Beilstein* **4** IV 205.]

***N*-Monopropyl urea** *[627-06-5]* **M 102.1, m 107°, 110°, pK_{Est} ~0.2.** Crystallise the urea from EtOH or EtOH/Et_2O. [Biovin & Biovin *Can J Chem* **29** 479 *1951*, IR: Biovin & Biovin *Can J Chem* **32** 563 *1954*, *Beilstein* **4** H 142, **4** III 261, **4** IV 482.]

Mucochloric acid (2,3-dichloro-4-oxo-2-butenoic acid) *[87-56-9]* **M 169.0, m 124-126°, pK^{25} 4.20.** Crystallise the acid twice from water (charcoal). [*Beilstein* **3** IV 1720.]

***trans, trans*-Muconic acid (hexa-2,4-dienedioic acid)** *[3588-17-8]* **M 142.1, m 300°, pK^{25} 4.51, for *cis,cis* pK^{25} 4.49.** Crystallise the diacid from H_2O. [*Beilstein* **2** IV 2298.]

Myristic acid (tetradecanoic acid) *[544-63-8]* **M 228.4, m 58°, pK^{20} 6.3 (50% aqueous EtOH), pK_{Est} ~4.9 (H_2O).** Purify the acid *via* the *methyl ester* (**b** 153-154°/10mm, n^{25} 1.4350), as for capric acid. [Trachtman & Miller *J Am Chem Soc* **84** 4828 *1962*.] Also purify it by zone melting. It crystallises from petroleum ether, and is dried in a vacuum desiccator containing shredded wax. [*Beilstein* **2** IV 1126.]

Neopentane (2,2-dimethylpropane) *[463-82-1]* **M 72.2, flash point 79.3°, m –19.8°, b 9.5°/760mm, d_4^{20} 0.6737, n_D^{20} 1.38273.** It is freed from isobutene by passage over conc H_2SO_4 or P_2O_5, and through silica gel. [*Beilstein* **1** H 141, **1** I 50, **1** II 104, **1** 369, **1** IV 333.]

Nerolidol (3,7,11-trimethyl-1,6,10-dodecatrien-3-ol) M 222.4 *[cis/trans 7212-44-4]* **b 122°/3mm, d_4^{20} 0.73, n_D^{20} 1.477,** *[cis 3790-78-1]* **b 70°/0.1mm,** *[trans 40716-66-3]* **b 78°/0.2mm, 145-146°/2mm.** Purify it by TLC on plates of Kieselguhr G [McSweeney *J Chromatogr* **17** 183 *1965*] or silica gel impregnated with $AgNO_3$, using 1,2-CH_2Cl_2/$CHCl_3$/EtOAc/PrOH (10:10:1:1) as solvent system. Also by GLC on butanediol succinate (20%) on Chromosorb W. Stored it under N_2 at ~5° in the dark. [*Beilstein* **1** IV 2336.]

Nitrilotriacetic acid [tris(carboxymethyl)amine, NTA, Complexone 1] *[139-13-9]* **M 191.1, m 247°(dec), pK_1 0.8, pK_2 1.71, pK_3 2.47, pK_4 9.71.** Crystallise it from water and dry it at 110°. [*Beilstein* **4** IV 2441.]

Nitroethane *[79-24-3]* **M 75.1, b 115°, d_4^{20} 1.049, n_D^{20} 1.3920, n_D^{25} 1.39015, pK^{25} 8.60 (8.46, pH equilibrium requires *ca* 5 minutes).** Purify it as described for *nitromethane* below. A spectroscopic impurity can be removed by shaking it with activated alumina, decanting and distilling it rapidly. [*Beilstein* **1** IV 170.]

Nitroguanidine *[556-88-7]* **M 104.1, m 246-246.5°(dec), 257°, pK_1^{25} -0.55, pK_2^{25} 12.20.** Crystallise it from water (20ml/g). The *nitrate* has **m** 147°(dec)(prisms, H_2O). [*Beilstein* **3** H 126, **3** III 236.]

Nitromethane *[75-52-5]* **M 61.0, f –28.5°, b 101.3°, d_4^{20} 1.13749, d^{30} 1.12398, n_D^{20} 1.3819, n^{30} 1.37730, pK^{25} 10.21.** Nitromethane is generally manufactured by gas-phase nitration of methane. The usual impurities include aldehydes, nitroethane, water and small amounts of alcohols. Most of these can be removed by drying with $CaCl_2$ or by distillation to remove the water/nitromethane azeotrope, followed by drying with $CaSO_4$. Phosphorus pentoxide is not suitable as a drying agent. [Wright et al. *J Chem Soc* 199 *1936*.] The purified material should be stored by dark bottles, away from strong light, in a cool place. Purifications using extraction are commonly used. For example, Van Looy and Hammett [*J Am Chem Soc* **81** 3872 *1959*] mixed about 150ml of conc H_2SO_4 with 1L of nitromethane and allowed it to stand for 1 or 2 days. The solvent was washed with water, aqueous Na_2CO_3, and again with water, then dried for several days with $MgSO_4$, filtered again with $CaSO_4$. It was fractionally distilled before use. Smith, Fainberg and Winstein [*J Am Chem Soc* **83** 618 *1961*] washed it successively with aqueous $NaHCO_3$, aqueous $NaHSO_3$, water, 5% H_2SO_4, water and dilute $NaHCO_3$. The solvent was dried with $CaSO_4$, then percolated through a column of Linde type 4A molecular sieves, followed by distillation from some of this material (in powdered form). Buffagni and Dunn [*J Chem Soc* 5105 *1961*] refluxed it for 24 hours with activated charcoal while bubbling a stream of nitrogen through the liquid. The suspension was filtered, dried (Na_2SO_4) and distilled, then passed through an alumina column and re-distilled. It has also been refluxed over CaH_2, distilled and kept under argon over 4A molecular sieves.
It has been purified by zone melting at low temperature, or by distillation under vacuum at 0°, subjecting the middle fraction to several freeze-pump-thaw cycles. An impure sample containing higher nitroalkanes and traces of cyanoalkanes was purified (on the basis of its NMR spectrum) by crystallisation from diethyl ether at –60° (cooling in Dry-ice) [Parrett & Sun *J Chem Educ* **54** 448 *1977*].
Fractional crystallisation is more effective than fractional distillation from Drierite in purifying nitromethane for conductivity measurements. [Coetzee & Cunningham *J Am Chem Soc* **87** 2529 *1965*.] Specific conductivities around 5 x 10^{-9} $ohm^{-1}cm^{-1}$ were obtained. [*Beilstein* **1** IV 100.]

1-Nitropropane *[108-03-2]* **M 89.1, b 131.4°, d_4^{20} 1.004, n_D^{20} 1.40161, n_D^{25} 1.39936, pK^{25} 8.98.** Purify it as for *nitromethane.* [*Beilstein* **1** IV 229.]

2-Nitropropane *[79-46-9]* **M 89.1, b 120.3°, d_4^{20} 0.989, n_D^{20} 1.3949, n_D^{25} 1.39206, pK^{25} 7.68.** Purify it as for *nitromethane.* [*Beilstein* **1** IV 230.]

***N*-Nitrosodiethanolamine (NDELA)** *[1116-54-7]* **M 134.4, b 100°/2.6x10^{-5}mm, 125°/0.01mm, n_D^{20} 1.4849.** Purify NDELA by dissolving the amine (0.5g) in 1-propanol (10ml) and 5g of anhydrous Na_2SO_4 added with stirring. After standing for 1-2 hours, it is filtered and passed through a chromatographic column packed with 10ml of AG 50W x 8 (H^+form 50-100mesh, a strongly acidic cation exchanger). The eluent and washings (50 ml EtOH) are combined and evaporated to dryness at 35°. It has also been extracted with EtOH from the nitrosation mixture of ethanolamine, filtered and distilled under high vacuum. [Fukuda et al. *Anal Chem* **53** 2000 *1981*, Jones & Wilson *J Chem Soc* 550, *1949*, *Beilstein* **1** III 721, see Spiegelhalder et al. *N-Nitroso Compounds*: *Occurrence Biological Effects and Relevance in Human Cancer* (eds. O'Neill et al. IARC Scientific Publications No 57; IARC Lyon p943 *1984*.] *Possible* **CARCINOGEN.**

Nitrourea *[556-89-8]* **M 105.1, m 158.4-158.8°(dec).** Crystallise it from EtOH/petroleum ether. Dry it *in vacuo* ~50°. [Ingersoll & Arenendt *Org Synth* Coll Vol **I** 417 *1941*.]

***n*-Nonane** *[111-84-2]* **M 126.3, b 150.8°, d_4^{20} 0.719, n_D^{20} 1.40542, n_D^{25} 1.40311.** Fractionally distil *n*-nonane,

then stir it with successive volumes of conc H_2SO_4 for 12 hours each until no further coloration is observed in the acid layer. Then wash it with water, dry with $MgSO_4$ and fractionally distil it. *Alternatively*, it is purified by azeotropic distillation with 2-ethoxyethanol, followed by washing out the alcohol with water, drying and distilling it. [Forziati et al. *J Res Nat Bur Stand* **36** 129 *1946*, *Beilstein* **1** IV 447.]

Nylon powder. Pellets are purified by dissolving them in ethylene glycol under reflux, then precipitating nylon as a white powder by adding EtOH at 25°. This is washed with EtOH and dried at 100° under vacuum.

***n*-Octacosane** *[630-02-4]* **M 394.8, m 62.5°.** Purify it by forming its adduct with urea, washing it and crystallising it from acetone/water. [McCubbin *Trans Faraday Soc* **58** 2307 *1962*.] Crystallise it then from hot filtered isopropyl ether solution (10ml/g). [*Beilstein* **1** IV 588.]

***n*-Octacosanol (octacosyl alcohol)** *[557-61-9]* **M 410.8, m 83.4°, 84°.** Recrystallise it from large volumes of Me_2CO. Sublime it at 200-250°/1mm instead of distilling it. [*Beilstein* **2** IV 1318.]

***n*-Octadecane** *[593-45-3]* **M 254.5, m 28.1°, b 173.5°/10mm, 316.1°/760mm, d_4^{20} 0.7768, n_D^{20} 1.4390.** Crystallise it from acetone and distil it from sodium in a vacuum. [*Beilstein* **1** IV 553.]

Octadecyl acetate *[822-23-1]* **M 312.5, m 32.6°, b 166-168°/1mm, 172-174°/1.5mm.** Distil the ester under high vacuum, then crystallise it from Et_2O/MeOH, EtOH (**m** 32.8°) or Me_2CO (**m** 32.4°). Also recorded are **m** 30.2°; and 35.3° for an α form as well as 38-39° for a β form. [Phillips & Mumford *J Chem Soc* 1663 *1934*, *Beilstein* **2** H 136, **2** II 147, **2** III 266, **2** IV 171.]

***n*-Octadecyl alcohol (stearyl alcohol, octadecanol)** *[112-92-5]* **M 270.5, m 61°, b 153-154°/0.3mm.** Crystallise octadecanol from MeOH, or dry Et_2O and $*C_6H_6$, then fractionally distil it *in vacuo*. Also purify it by column chromatography. Free it from cetyl alcohol by zone refining. [*Beilstein* **1** IV 1888.]

***n*-Octadecylamine (1-aminooctadecane, stearylamine, ODA)** *[124-30-1]* **M 269.5, m 49-52°, 50-52°, 52-54°, b 183.0-183.1°/5mm, 232°/32mm, pK^{25} 10.60.** *n*-Octadecylamine can be prepared from nonadecanoic acid (*n*-nonadecylic acid, [646-30-0]) by Schmidt's hydrazoic acid method whereby the carboxylic acid (15.8g, 53mmol) in $*C_6H_6$ (500ml) is treated carefully with concentrated H_2SO_4 (30ml), stirred vigorously at 40° and hydrazoic acid (52ml of a 5.3% solution in $*C_6H_6$, 1.2 equivalents, i.e. 63.3mmol; see [7782-79-8], **POISONOUS** use efficient fumehood] is added slowly. After evolution of N_2 and CO_2 have ceased (~2 hours) the acid layer is poured into cold H_2O whereby octadecylamine sulfate precipitates (~96% yield decomposing at ~200°). [see Briggs et al *J Chem Soc* 61 *1942*.] The free base is obtained by shaking with 10% KOH solution, extracting into Et_2O, drying (K_2CO_3), evaporating and distilling the residue in a vacuum. Its FT-IR (film) has ν_{max} at 2923.9, 1466.3, 792.4, 720.9 cm^{-1}; its ^1H NMR (300MHz, $CDCl_3$, TMS) has δ at 0.89 (t, J = 7 Hz, 3H, CH_3), 1.01 (s), 1.25 (s, 10H), 1.43 (m, 2H), 2.67 (t, J = ~7 Hz, 2H, CH_2-N); and the ^{13}C NMR (75MHz, $CDCl_3$, $CHCl_3$ standard) has δ at 42.35, 33.99, 31.95, 29.72, 29.56, 29.39, 26.94, 22.71, 14.11. It has also been prepared by the Gabriel Synthesis whereby octadecanol is converted to octadecyl iodide, m 29-32° (by reaction with P_2O_5/KI), then with potassium phthalimide in DMF, to the *N*-*n*-octdecylphthalimide, m 80-81°, followed by hydrazinolysis with 85% $NH_2NH_2.H_2O$, and isolation as the *hydrochloride* [1838-08-0] **m 162-163°** after crystallisation from EtOH/Et_2O [Wood *J Chem Soc* 3327 *1953*]. Another method of prepartion include reduction of stearic amide with LAH in ~60% yield using a Soxhlet extractor with the amide in the thimble and LAH/Et_2O in the boiling flask [Murr & Lester *J Am Chem Soc* **77** 1684 *1955*]. The *N-acetyl derivative* has **m 84-85°** (EtOH/Et_2O), and the *N-methyl derivative* [2439-55-6] has **m 42-46°**, **b 155°/0.5mm**. [*Beilstein* **4** II 661, **4** III 431, **4** IV 825.] The base and its derivatives are **skin and eye irritants**, and release histamine.

Octadecyl ether (dioctadecyl ether) *[6297-03-6]* **M 523.0, m 59.4°, n_D^{60} 1.440.** Distil the ether in a vacuum, then crystallise it from MeOH/$*C_6H_6$, MeOH (**m** 58.5-59.5°) or Me_2CO (**m** 59.5°). It has an α form **m** 57.8° and a β form **m** 40°. [*Beilstein* **1** IV 1891.]

Octafluoropropane (profluorane) *[76-19-7]* **M 188.0, m –183°, b –38°.** Purify it for pyrolysis studies by passage through a copper vessel containing CoF_3 at about 270°, then fractionally distil it. [Steunenberg & Cady *J Am Chem Soc* **74** 4165 *1952*.] Also purify it by several trap-to-trap distillations at low temperatures [Simons & Block *J Am Chem Soc* **59** 1407 *1937*].

***n*-Octane** *[111-65-9]* **M 114.2, m –56.8°, b 19.2°/10mm, 125.6°/760mm, d_4^{20} 0.704, n_D^{20} 1.39743, n_D^{25} 1.39505.** Extract the octane repeatedly with conc H_2SO_4 or chlorosulfonic acid, then wash it with water, dry and distil it. *Alternatively*, purify it by azeotropic distillation with EtOH, followed by washing with water to remove the EtOH, drying and distilling it. For further details, see n-*heptane*. It is also purified by zone melting at low temperature. [*Beilstein* **1** H 159, **1** I 60, **1** II 122, **1** III 457, **1** IV 412.]

***RS*-(±)-Octane-1,2-diol** *[1117-86-8]* **M 146.2, m 30-30.5°, 36°, b 103-105°/0.5mm, 131-132°/10mm.** Distil the diol *in vacuo* and/or recrystallise it from petroleum ether. The *α-naphthylurethane* has **m** 112-114°. [*Beilstein* **1**III 2217, **1** IV 2590.] *S*-(–)-*Octane-1,2-diol* [87720-91-0] also crystallises from petroleum ether with **m** 35-37° and $[\alpha]_D^{17}$ –4.7° (c 35, EtOH) [Späth et al. *Chem Ber* **66** 598 *1933*]; *R*-(+)-*octane-1,2-diol* [87720-90-9] has similar properties but with a positive optical rotation.

Octane-1,8-diol (octamethylene glycol) *[629-41-4]* **M 146.2, m 59-61°, b 172°/20mm.** Recrystallise the diol from EtOH and distil it in a vacuum. [*Beilstein* **1** IV 2592.]

1-Octanethiol *[111-88-6]* **M 146.3, b 86°/15mm, 197-200°/760mm, d_4^{20} 0.8433, n_D^{20} 1.4540, pK^{25} 10.72(dilute *t*-BuOH).** Pass the thiol through a column of alumina and work under N_2, or Ar. Distil it under N_2 and a vacuum. Store it under N_2, or Ar in the dark. [Battacharyya et al. *J Chem Soc, Faraday Trans 1* **82** 135 *1986,* Fletcher *J Am Chem Soc* **68** 2727 *1946*]. [*Beilstein* **1** III 1710, **1** IV 1767.]

1-Octene *[111-66-0]* **M 112.2, b 121°/742mm, d_4^{20} 0.716, n_D^{20} 1.4087.** Distil 1-octene under nitrogen from sodium which removes water and peroxides. Peroxides can also be removed by percolation through dried, acid washed, alumina. Store it under N_2, or Ar in the dark. [Strukul & Michelin *J Am Chem Soc* **107** 7563 *1985*, *Beilstein* **1** H 221, **1** II 199, **1** IV 874.]

***trans*-2-Octene** *[13389-42-9]* **M 112.2, b 124-124.5°/760mm, d_4^{20} 0.722, n_D^{20} 1.4132.** Purify it as for 1-octene above. [*Beilstein* **1** IV 879.]

***n*-Octyl alcohol** *[111-87-5]* **M 130.2, b 98°/19mm, 195.3°/760mm, d_4^{20} 0.828, n_D^{20} 1.43018.** Fractionally distil it under reduced pressure. Dry it with sodium and again fractionally distil or reflux with boric anhydride and re-distilled (**b** 195-205°/5mm), the distillate being neutralised with NaOH and again fractionally distilled. Also purify it by distillation from Raney nickel and by preparative GLC. [*Beilstein* **1** IV 1756.]

***n*-Octylamine (1-aminooctane, caprylamine)** *[111-86-4]* **M 129.2, m –5-1°, b 62-64°/11mm 175-177°/745mm, 185-187°/atm, d_4^{20} 0.7819, d_4^{25} 0.728, n_D^{20} 1.4292, pK^{25} 10.57.** *n*-Octylamine has been prepared from nonanoic acid (pelargonic acid, see [112-05-0]) by Schmidt's hydrazoic acid method as described for octadecylamine above. [Adamson & Kenner *J Chem Soc* 383 *1943*.] The syntheses decribed below for octadecyl amine can be used for preparing octylamine. A more recent preparation involves formation of tri-*n*-octylborane from 1-octene and BH_3.THF *in situ*, then reaction with NaN_3/HCl to give a 79% yield of octylamine [Kabalka et al. *Organometallics* **6** 1369 *1987*]. The free base can be isolated from its salts or the picrate by treatment with strong aqueous alkaline solution, extraction into Et_2O or CH_2Cl_2, drying (K_2CO_3), evaporating and distilling the residue preferably in a vacuum. Solubility in H_2O is ~2%. It is a strong base which readily absorbs CO_2 in moist air and should be stored under N_2. Its FT-IR (film) has ν_{max} at 3371.9, 2924.6, 1617.3, 1467.0, 1378.3, 1072.7, 822.1, 722.9 cm^{-1}; its ^1H NMR (300MHz, $CDCl_3$, TMS) has δ at 0.89 (t, J = ~7 Hz, 3H, CH_3), 1.15 (s), 1.29 (s, $6CH_2$), 1.42 (t, J = ~7 Hz, NH_2), 2.69 (t, J = ~7 Hz, 2H, CH_2-N) ppm; and the ^{13}C NMR (300MHz, $CDCl_3$, $CHCl_3$ standard) has δ at 42.32, 33.96, 31.88, 29.51, 29.34, 26.94, 22.69, 14,10 ppm. The *picrate* [78498-55-2] crystallises as plates with **m 111.5-112.5°**, the *N-acetyl derivative* [7462-62-6] has **b 148-149°/3mm**, and the *N-methyl derivative* [2439-54-5] has **b 60-65°/3mm**, **75-78°/13mm**. [*Beilstein* **4** H 196, **4** I 386, **4** II 655, **4** III 379, **4** IV 751.] *n*-Octylamine is quite a strong primary base capable of forming a carbamate

salt of the type $RNHCO_2^-$ RNH_3^+ in the presence of CO_2 and H_2O (see storage above). The free base and its derivatives are **skin and eye irritants**.

***n*-Octylammonium hexadecanoate** *[88020-97-7]* **M 385.7, m 52-53°.** Purify it by several recrystallisations from *n*-hexane or ethyl acetate. The solid is then washed with cold anhydrous diethyl ether, and dried *in vacuo* over P_2O_5. [*Beilstein* **4** IV 751 for octylamine.]

***n*-Octylammonium octadecanoate** *[32580-92-0]* **M 413.7, m 56-57°.** Purify it as for the *hexadecanoate* above.

***n*-Octylammonium tetradecanoate** *[17463-35-3]* **M 358.6, m 46-48°.** Purify it as the *hexadecanoate* above.

***n*-Octyl bromide** *[111-83-1]* **M 193.1, b 201.5°, d_4^{20} 1.118, n^{25} 1.4503.** Shake the bromide with H_2SO_4, wash it with water, dry with K_2CO_3 and fractionally distil it. [*Beilstein* **1** IV 422.]

1-Octyne *[629-05-0]* **M 110.2, b 76-77°/150mm, 126.2°/760mm, d_4^{20} 0.717, n^{25} 1.4159.** Distil I-octyne from $NaBH_4$ to remove peroxides. Fractionate it through a 10inch Widmer column at 125-126°/759mm [Sletzinger & Dawson *J Org Chem* **14** 853 *1949*.] [*Beilstein* **1** III 1005, **1** IV 1034.]

Oleic acid (*cis*-9-octadecenoic acid, olainic acid) *[112-80-1]* **M 282.5, m 16°, b 145°/0.1mm, 194-195°/1.2mm, 228-229°/15mm, 360°(dec), d_4^{20} 0.891, n^{30} 1.4571, pK^{25} 6.42 (50% aqueous EtOH), pK_{Est} ~4.8 (H_2O).** Purify the acid by fractional crystallisation from its melt, followed by molecular distillation at 10^{-3}mm, or by conversion to its methyl ester, the free acid can be crystallised from acetone at –40° to –45° (12ml/g). For purification by the use of lead and lithium salts see Keffler and McLean [*J Soc Chem Ind (London)* **54** 176T *1935*]. Purification based on direct crystallisation from acetone is described by Brown and Shinowara [*J Am Chem Soc* **59** 6 *1937,* pK White *J Am Chem Soc* **72** 1857 *1950*]. [*Beilstein* **2** H 463, **2** I 198, **2** II 429, **2** III 1387, **2** IV 1641.]

Oleyl alcohol *[143-28-2]* **M 268.5, b 182-184°/1.5mm, d_4^{20} 0.847, $n^{27.5}$ 1.4582.** Purify it by fractional crystallisation at –40° from acetone, then distil it under vacuum. [*Beilstein* **2** IV 2204.]

Oxalic acid ($2H_2O$) *[6153-56-6]* **M 90.0, m 101.5°,** *[anhydrous 144-62-7]* **m 189.5°, pK_1^{25} 1.08 (1.37), pK_2^{25} 3.55 (3.80).** Crystallise oxalic acid from distilled water. Dry it in a vacuum over H_2SO_4. The anhydrous acid can be obtained by drying at 100° overnight. [*Beilstein* **2** IV 1819.]

Oxaloacetic acid *[328-42-7]* **M 132.1, m 160°(decarboxylates), pK_1^{25} 2.22, pK_2^{25} 3.89, pK_3^{25} 13.0.** Crystallise it from boiling EtOAc, or from hot Me_2CO/hot $*C_6H_6$. [*Beilstein* **3** IV 1808.]

2-Oxoglutaric acid (2-oxopentane-1,5-dioic, α-ketoglutaric acid) *[328-50-7]* **M 146.1, m 114°, 115-117°, (pK_{Est} see oxaloacetic acid above).** Crystallise the keto-acid repeatedly from Me_2CO/*benzene, EtOAc or ethyl propionate. Dry it *in vacuo*. [*Beilstein* **3** IV 1813.]

Oxamide *[471-46-5]* **M 88.1, m >320°(dec).** Crystallise oxamide from water, grind it and dry it in an oven at 150°. [*Beilstein* **2** IV 1860.]

Palmitic acid anhydride (hexadecanoic anhydride) *[623-65-4]* **M 494.9, m 63-64°, 64°, d^{82} 0.838, n^{68} 1.436.** It is moisture sensitive and hydrolyses in water. Purify it by refluxing with acetic anhydride for 1 hour, evaporating and freeing the residue of acetic acid and anhydride by drying the residue at high vacuum and recrystallising from petroleum ether at low temperature. [*Beilstein* **2** IV 1181.]

Paraffin (oil) *[8012-95-1]* **d_4^{20} 0.880, n_D^{20} 1.482.** Treat the oil with fuming H_2SO_4 (care), then wash it with water and dilute aqueous NaOH, then percolate it through activated silica gel.

Paraffin Wax. Melt the wax in the presence of NaOH, wash it with water until all of the base had been removed. The paraffin is allowed to solidify after each wash. Finally, 5g of paraffin is melted by heating it on a water-bath, then shaken for 20-30 minutes with 100ml of boiling water and and dry the melt under vacuum.

Pelargonic acid (nonanoic acid) *[112-05-0]* **M 158, m 15°, b 98.9°/1mm, 225°/760mm, pK^{25} 4.96.** Esterify the acid with ethylene glycol and distil the ester. (This removes dibasic acids as undistillable residues.) The acid is regenerated by hydrolysing the ester in the usual way and is distilled *in vacuo*. [*Beilstein* **2** IV 1018.]

Pelargononitrile (octyl cyanide) *[2243-27-8]* **M 139.2, m –34°, b 92°/10mm, 224°, d_4^{20} 0.818, n_D^{20} 1.4255.** Stir the nitrile with P_2O_5 (~5%), distil it from P_2O_5 and redistil it under a vacuum. IR should have CN but no OH bands. [*Beilstein* **2** IV 1204.]

Pelargonyl chloride (nonanoyl chloride) *[764-85-2]* **M 176.7, b 88°/12mm, d_4^{20} 0.941, n_D^{20} 1.436.** Reflux it with acetyl chloride (~ 3 volumes) for 1 hour, then distil off AcCl followed by the nonanoyl chloride at ~12mm. It is moisture sensitive and should be stored in sealed ampoules. [*Beilstein* **2** IV 1023.]

Pentabromoacetone *[79-49-2]* **M 452.6, m 76°, pK^{25} 8.0 (MeOH), pK_{Est} ~4.6 (H_2O).** Crystallise it from Et_2O, EtOH or aqueous EtOH (**m** 73.2°) and sublime it. Its solubility in H_2O is 0.01mg/100ml. [*Beilstein* **1** H 659, **1** I 345, **1** III 2753, **1** IV 3226.]

Pentachloroethane (pentalin) *[76-01-7]* **M 202.3, b 69°/37mm, 152.2°/64mm, 162.0°/~760mm, d_4^{20} 1.678, n^{15} 1.50542.** Usual impurities include trichloroethylene. It partially decomposes if it is distilled at atmospheric pressure. Drying it with CaO, KOH or sodium is unsatisfactory because of the elimination of the elements of HCl. It can be purified by steam distillation, or by washing with conc H_2SO_4, water, and then aqueous K_2CO_3, drying with solid K_2CO_3 or $CaSO_4$, and fractionally distilling under reduced pressure. [*Beilstein* **2** IV 147.]

Pentadecafluoro octanoic acid (perfluorocaprylic acid) *[335-67-1]* **M 414.1, m 54.9-55.6°, b 189°/736mm, pK_{Est} <0.** Crystallise the acid from CCl_4 and toluene, and distil it. It forms micelles in H_2O and the solubility is 1% in H_2O. The *acid chloride* has **b** 129-130°/744mm. The *amide* has **m** 138°. [Bernett & Zisman *J Phys Chem* **63** 1911 *1959*, Bro & Sperati *J Polym Sci* **38** 289 *1959*, *Beilstein* **2** IV 994.]

Pentadecanoic acid *[1002-84-2]* **M 242.4, m 51-53°, 80°, b 158°/1mm, 257°/760mm, d_4^{80} 0.8424, pK_{Est} ~5.0.** Crystallise the acid from Et_2O and distil it *in vacuo*. It is very hygroscopic. See the purification of palmitic acid. [*Beilstein* **2** IV 1147.]

Pentadecanolide (1-oxacyclohexadecan-2-one, pentadecanoic-ω-lactone, 15-hydroxypentadecanoic lactone, exaltolide, Tibetolide) *[106-02-5]* **M 240.4, m 34-36°, 37-37.5°, 37-38°, b 102-103°/0.03mm, 112-114°/0.2mm, 137°/2mm, 169°/10-11mm, d_4^{40} 0.9401.** It has been recrystallised from MeOH (4 parts) at –15°, and distilled under high vacuum. [Hundiecker & Erlbach *Chem Ber* **80** 135 *1947*, Galli & Mandolini *Org Synth* **58** 100 *1978*, Demole & Enggist *Helv Chim Acta* **11** 2318 *1978*, *Beilstein* **17/9** V 106.]

Penta-1,3-diene *[cis: 1574-41-0, trans: 2004-70-8]* **M 68.1, b 42°, d_4^{20} 0.680, n_D^{20} 1.4316.** Distil the diene from $NaBH_4$. Purify it also by preparative gas chromatography. [Reimann et al. *J Am Chem Soc* **108** 5527 *1986*, *Beilstein* **1** IV 994.]

Penta-1,4-diene *[591-93-5]* **M 68.1, b 25.8-26.2°/756mm, d_4^{20} 0.645, n_D^{20} 1.3890.** Distil it from $NaBH_4$. Purify it by preparative gas chromatography or distillation and stabilise it with 0.1% of 2,6-di-*tert*-butyl-*p*-cresol. [Reimann et al. *J Am Chem Soc* **108** 5527 *1986*, *Beilstein* **1** IV 998.]

Pentaethylenehexamine *[4067-16-7]* **M 232.4, d_4^{20} 0.950, n_D^{20} 1.510, pK_1 1.2, pK_2 2.7, pK_3 4.3, pK_4 7.8, pK_5 9.1, pK_6 9.9 (all estimated).** Fractionally distil it twice at 10-20mm, the fraction boiling at 220-250° being collected. It can be further purified *via* the *hydrochloride*. Its solution in MeOH (40ml of base in 250ml) is cooled in an ice-bath and conc HCl (~50ml) is added dropwise with stirring. The precipitated *hydrochloride* is

filtered off, washed with Me_2CO, and Et_2O, then dried in a vacuum desiccator. The free base is then obtained by basification, extraction into Et_2O, drying (NaOH), filtering, evaporating and distilling the residue as before. It forms a Cu complex $[Cu(C_{10}H_{28}N_6)]^{2+}$. [Jonassen et al. *J Am Chem Soc* **79** 4279 *1957*, *Beilstein* **4** IV 1245.]

2,2,3,3,3-Pentafluoropropan-1-ol *[422-05-9]* **M 150.1, b 80°/~760mm, d_4^{20} 1.507, n_D^{20} 1.288, pK^{25} 12.74.** Shake the alcohol with alumina for 24 hours, dry with anhydrous K_2CO_3, and distil it, collect the middle fraction (**b** 80-81°) and redistil it. [*Beilstein* **1** IV 1438.]

***n*-Pentane** *[109-66-0]* **M 72.2, b 36.1°, d_4^{20} 0.626, n_D^{25} 1.35472.** Stir the pentane with successive portions of conc H_2SO_4 until there is no further coloration during 12 hours, then with 0.5N $KMnO_4$ in 3M H_2SO_4 for 12 hours, wash with water and aqueous $NaHCO_3$. Dry it with $MgSO_4$ or Na_2SO_4, then P_2O_5 and fractionally distil it through a column packed with glass helices. It is also purified by passage through a column of silica gel, followed by distillation and storage with sodium hydride. An alternative purification is by azeotropic distillation with MeOH, which is subsequently washed out from the distillate (using water), followed by drying and re-distilling. For removal of carbonyl-containing impurities, see n-*heptane.* Also purify it by fractional freezing (*ca* 40%) on a copper coil through which cold air is passed, then wash with conc H_2SO_4 and fractionally distil it. [*Beilstein* **1** IV 303.]

Pentane-1-thiol *[110-66-7]* **M 104.2, m –76°, b 122.9°/697.5mm, d^{25} 0.8375, pK_{Est} ~10.1.** Dissolve the thiol in aqueous 20% NaOH, then extract with a small amount of diethyl ether. The aqueous solution is acidified slightly with 15% H_2SO_4, and the thiol is distilled out, dried with $CaSO_4$ or $CaCl_2$, and fractionally distilled under nitrogen. [Ellis & Reid *J Am Chem Soc* **54** 1674 *1932*, *Beilstein* **1** IV 1453.]

(±)-Pentan-2-ol *[6032-29-7]* **M 88.2, b 119.9°/~760mm, d_4^{20} 0.810, n_D^{20}1.41787, n_D^{25} 1.4052.** Reflux it with CaO, distil it, then reflux it with magnesium and again fractionally distil it. [*Beilstein* **1** IV 1655.]

Pentan-3-ol *[584-02-1]* **M 88.2, b 116.2°, d_4^{20} 0.819, n_D^{25} 1.4072.** Reflux the alcohol with CaO, distil, then reflux it with magnesium and again fractionally distil it. [*Beilstein* **1** IV 1662.]

Pentan-3-one see **diethyl ketone** above.

Pent-2-ene (mixed isomers) *[109-68-2]* **M 70.1, b 36.4°, d_4^{20} 0.650, n_D^{20} 1.38003, n_D^{25} 1.3839.** Reflux the mixture with sodium wire, then fractionally distil it twice through a Fenske (glass helices packing) column. [*Beilstein* **1** IV 815.]

***cis*-Pent-2-ene** *[627-20-3]* **M 70.1, b 37.1°, d_4^{20} 0.657, n_D^{25} 1.3798.** Dry it with sodium wire and fractionally distil it, or purify it by azeotropic distillation with MeOH, followed by washing out the MeOH with water, drying and distilling. Also purify it by chromatography through silica gel and alumina [Klassen & Ross *J Phys Chem* **91** 3668 *1987*]. [*Beilstein* **1** IV 814.]

***trans*-Pent-2-ene** *[646-04-8]* **M 70.1, b 36.5°, d_4^{20} 0.6482, n_D^{20} 1.3793.** It is treated as above and washed with water, dried over anhydrous Na_2CO_3, and fractionally distilled. The middle cut is purified by two passes of fractional melting. [*Beilstein* **1** IV 814.]

Pent-2-yne *[627-21-4]* **M 68.1, b 26°/2.4mm, 56.1°/760mm, d_4^{20} 0.710, n_D^{25} 1.4005.** It is stood with, then distilled at low pressure from sodium or $NaBH_4$. [*Beilstein* **1** III 958, **1** IV 992.]

Perfluorobutyric acid (heptafluorobutyric acid) *[375-22-4]* **M 214.0, m -17.5°, b 120°/735mm, d_4^{20} 1.651, n_D^{16} 1.295, pK^{25} -0.17.** Fractionally distil the acid twice in an Oldershaw column with an automatic vapour-dividing head, the first distillation being in the presence of conc H_2SO_4 as a drying agent. (Take care with the hot acid.) [*Beilstein* **2** IV 810.]

Perfluoroheptane (hexadecafluoroheptane) *[335-57-9]* **M 388.1, b 99-101°, d_4^{25} 1.7200.** Purify it as for *perfluorodimethylhexane*. Other procedures include shaking with H_2SO_4, washing with water, and drying with

P_2O_5 for 48 hours then fractionally distilling. *Alternatively*, it has been refluxed for 24 hours with saturated acid $KMnO_4$ (to oxidise and remove hydrocarbons), then neutralised, steam distilled, dried with P_2O_5, and passed slowly through a column of dry silica gel. It has been purified by fractional crystallisation using partial freezing. [*Beilstein* **1** IV 388.]

Perfluoro-*n*-hexane (tetradecafluorohexane) *[355-42-0]* **M 338.1, m –4°, b 58-60°, d_4^{20} 1.684.** Purify the fluorohexane by fractional freezing. The methods described for *perfluoroheptane* should be applicable here. [*Beilstein* **1** IV 348.]

Perfluorononane (eicosafluorononane) *[375-96-2]* **M 488.1, b 126-127°, d_4^{20} 1.80, n_D^{20} 1.275.** Purify as for *perfluorodimethylcyclohexane.* [*Beilstein* **1** III 505.]

Perfluoropropyl iodide (heptafluoro-1-iodopropane) *[754-34-7]* **M 295.9, b 41°, d_4^{20} 2.13, n_D^{20} 1.339.** Purify the fluoro-iodide by fractional distillation. Store it over Cu as stabiliser. [*Beilstein* **1** IV 225.]

Perfluorotributylamine (heptacosafluorotributylamine) *[311-89-7]* **M 671.1, b 177.6°/760mm, d_4^{20} 1.881, n_D^{20} 1.291, pK_{Est} ~5.0.** Purify it as for perfluorodimethylcyclohexane (see [335-27-3]); see also perfluorotripropylamine below [Haszeldine *J Chem Soc* 102 *1951*]. [*Beilstein* **2** IV 819.]

Perfluorotripropylamine (heneicosafluorotripropylamine) *[338-83-0]* **M 521.1, b 130°/atm, 129.5-130.5°/atm, d_4^{20} 1.822, n_D^{20} 1.279, pK_{Est} ~5.6.** Purify it as for *perfluorodimethylcyclohexane* (see [335-27-3]) [Haszeldine *J Chem Soc* 102 *1951,* for azeotropes see Simons & Linevsky *J Am Chem Soc* **74** 4750 *1972*.] **IRRITANT.**

Petroleum ether *[8032-32-4]* **b 35-60°, d_4^{20} 0.640, n_D^{20} 1.363.** Shake it several times with conc H_2SO_4, then 10% H_2SO_4 and concentrated $KMnO_4$ (to remove unsaturated, including aromatic, hydrocarbons) until the permanganate colour persists. Wash it with water, aqueous Na_2CO_3 and again with water. Dry it with $CaCl_2$ or Na_2SO_4, and distil it. It can be dried further using CaH_2 or sodium wire. Passage through a column of activated alumina, or treatment with CaH_2 or sodium, removes peroxides. For the elimination of carbonyl-containing impurities without using permanganate, see *n-heptane*. These procedures could be used for all fractions of petroleum ethers. See **skellysolve** below, p. 201.
Rapid purification: Pass it through an alumina column and fractionally distilling, collecting the desired boiling fraction.

Phorone (2,6-dimethylhepta-2,5-dien-4-one) *[504-20-1]* **M 138.2, m 28°, b 197°/743mm.** Crystallise phorone repeatedly from EtOH. [*Beilstein* **1** IV 3564.]

Pimelic acid (heptane-1,7-dioic acid) *[111-16-0]* **M 160.2, m 105-106°, pK_1^{25} 4.46, pK_2^{25} 5.58.** Crystallise the acid from water or from *benzene containing 5% diethyl ether. [*Beilstein* **1** IV 2003.]

Pinacol (hexahydrate) *[6091-58-3 ($6H_2O$), 76-09-5 (anhydrous)]* **M 194.3, m 46.5°, b 59°/4mm.** Distil pinacol, then crystallise it repeatedly from water. (See also below.) [*Beilstein* **1** IV 2575.]

Pinacol (anhydrous) *[76-09-5]* **M 118.1, m 41.1°, b 172°.** The hydrate is rendered anhydrous by azeotropic distillation of water with *benzene. Recrystallise it from *benzene or toluene/petroleum ether, absolute EtOH or dry diethyl ether. It recrystallises from water to give the *hexahydrate*. [*Beilstein* **1** IV 2575.]

Pinacolone see ***tert*-butyl methyl ketone.**

Pinacolone oxime *[2475-93-6]* **M 115.2, m 75.5-76°, 78°, 78.5-79.5°, 171.6°/748mm.** Crystallise the oxime from aqueous EtOH, EtOH (small needles) or petroleum ether (plates). [Markownikoff *Chem Ber* **32** 1448 *1899*, Smith & Atkins *J Am Chem Soc* **60** 660 *1938*, Whitmore et al. *J Am Chem Soc* **61** 684 *1939*, *Beilstein* **1** H 694, **1** II 750, **1** III 2842, **1** IV 3310.]

Pivalic acid (trimethylacetic acid) *[75-98-9]* **M 102.1, m 35.4°, b 71-73°/0.1mm, pK^{25} 5.03.** Fractionally distil the acid under reduced pressure, then fractionally crystallise it from its melt. Recrystallise it from *benzene. [*Beilstein* **2** IV 908.]

Pivaloyl chloride (trimethylacetyl chloride) *[3282-30-2]* **M 120.6, b 57.6°/150mm, 70.5-71/250mm, 104°/754mm, 104-105°/atm, 105-108°/atm, d $_4^{20}$ 1.003, n $_D^{20}$ 1.4142.** First check the IR to see if OH bands are present. If absent, or present in small amounts, then redistil it under a moderate vacuum. If present in large amounts then treat it with oxalyl chloride or thionyl chloride and reflux for 2-3 hours, evaporate and distil the residue. **Strongly LACHRYMATORY – work in a fume cupboard.** Store it in sealed ampoules under N_2. [Traynham & Battiste *J Org Chem* **22** 1551 *1957*, Grignard reactions: Whitmore et al. *J Am Chem Soc* **63** 647 *1941*, *Beilstein* **2** IV 912.]

Polyacrylonitrile *[25014-41-9]***.** Precipitate it from dimethylformamide by addition of MeOH.

Poly(diallyldimethylammonium) chloride *[26062-79-3]***.** Precipitate it from water with acetone, and dry the salt in a vacuum for 24 hours. [Hardy & Shriner *J Am Chem Soc* **107** 3822 *1985*.]

Polyethylene *[9002-88-4]*. Crystallise it from thiophen-free *benzene and dry it over P_2O_5 under vacuum.

Polymethyl acrylate *[9003-21-8]*. Precipitate it from a 2% solution in acetone by addition of water.

Polyvinyl acetate *[9003-20-7]*. Precipitate it from acetone by addition of *n*-hexane.

Polyvinyl chloride *[9002-81-2]*. Precipitate it from cyclohexanone by addition of MeOH.

Propane *[74-98-6]* **M 44.1, m -189.7, b -42.1°/760mm, d $_4^{20}$ 0.5005, n $_D^{20}$ 1.2898.** Purify propane by bromination of the olefinic contaminants. Propane is treated with bromine for 30 minutes at 0°. Unreacted bromine is quenched, and the propane is distilled through two -78° traps and collected at -196° [Skell et al. *J Am Chem Soc* **108** 6300 *1986*]. It autoignites at 450° and the flash point is -104°. It is highly **FLAMMABLE** and is available in metal cylinders. [*Beilstein* **1** H 103, **1** I 33, **1** II 71, **1** III 204, **1** IV 175.]

Propane-1,2-diamine (propylenediamine) *[78-90-0]* **M 74.1, b 120.5°/~760mm, d $_4^{20}$ 0.868, n $_D^{20}$ 1.446, pK $_1^{25}$ 6.61, pK $_2^{25}$ 9.82.** Purify the diamine by azeotropic distillation with toluene. Then distil it. Store it in a CO_2 free atmosphere. [Horton et al. *Anal Chem* **27** 269 *1955*, *Beilstein* **4** IV 1255.]

(±)-Propane-1,2-diol (propyleneglycol) *[57-55-6]* **M 76.1, m -60°, b 45.5°/1.0mm, 70.8°/5.0mm, 83.2°/10mm, 96.4°/20mm, 104°/32mm, 111.2°/40mm, 119.9°/60mm, 132.0°/100mm, 149.7°/200mm, 168.1°/400mm, 188.2°/atm, d $_4^{20}$ 1.040, n $_D^{20}$ 1.433.** Dry the diol over Na_2SO_4, decant and distil it under reduced pressure. It is soluble in H_2O, Me_2CO, $CHCl_3$, many oils, is used as an antifreeze in dairies and breweries; and is a substitute for glycerol or ethylene glycol. [*Beilstein* **1** IV 2468.]

***R*-(–)- and *S*-(+)- Propane-1,2-diol (*R*- and *S*- propylene glycol)** *[R(–) 4254-14-2: S(+) 4254-15-3]* **M 76.1, b 78.5°/10mm, 94-96°/14mm, 186-188°/765mm, d $_4^{20}$ 1.036, n $_D^{20}$ 1.432, [α] $_D^{25}$ (–) or (+) 17.5° (neat).** The laevo *R-enantiomer* can be obtained from reduction of hydroxyacetone by yeast [Levene & Walti *Org Synth* Coll Vol **II** 545 *1943*], and the dextro *S-enantiomer* is obtained by reduction of *S*-(+)-lactic acid. Thus (+)-lactic acid (33.4g, 370mmol) in dry THF (200ml) is added dropwise to a suspension of LAH (32.1g, 850mmol) in dry THF (500ml) at 0° during 2 hours, allowed to warm to 25°, refluxed for 2 hours, cooled, then quenched by careful addition of ice-cold H_2O (32ml), followed by 4N NaOH (32ml) and again H_2O (96ml). The white precipitate is coagulated by refluxing the mixture for 0.5 hours, filtered, washed with THF, the white cake is slurred with hot THF (4 x ~100ml), the combined THF layers are evaporated *in vacuo* (~40°), and the residual oil is distilled through a vacuum jacketed Vigreux column under vacuum to give the *S*-diol as a colourless liquid (23,9g, 85%). [Fryzuk & Bosnich *J Am Chem Soc* **100** 5491 *1978*.]

Propane-1,3-diol *[504-63-2]* **M 76.1, b 110-122°/12mm, d $_4^{20}$ 1.053, n$^{18.5}$ 1.4398.** Dry this diol with K_2CO_3

and distil it under reduced pressure. More extensive purification involves conversion with benzaldehyde to *2-phenyl-1,3-dioxane* (**m** 47-48°) which is subsequently decomposed by shaking with 0.5M HCl (3ml/g) for 15 minutes and standing overnight at room temperature. After neutralisation with K_2CO_3, the benzaldehyde is removed by steam distillation and the diol is recovered from the remaining aqueous solution by continuous extraction with $CHCl_3$ for 1 day. The extract is dried with K_2CO_3, the $CHCl_3$ is evaporated and the diol is distilled. [Foster et al. *Tetrahedron* **6** 177 *1961*, *Beilstein* **1** IV 2493.]

***S*-(-)-Propane-1,2-diol bis(*p*-toluenesulfonate)** *[60434-71-1]* **M 384.5, m 68-70° (62°), $[\alpha]_D^{20}$ –20° (c 1, $CHCl_3$)**, is prepared in much the same way as for *S,S*-butane-2,3-diol bis-tosylate (see above) from *S*-(+)-propane-1,2-diol (310mmol) in dry pyridine (30ml) and toluene-*p*-sulfonyl chloride (700mmol, recrystallised from hexane) in dry pyridine (135ml) at 0° during 0.5 hours, then at 25° for 17 hours. The crude ester is purified by dissolving in CH_2Cl_2 and cyclohexane is added to cloud point at 40°, then allowed to crystallise at 25° when more cyclohexane is added and set aside (5°/12 hours) to give the *bis-tosylate* as white feathery crystals which are dried over $CaCl_2$ *in vacuo* (114g, 95%). [Fryzuk & Bosnich *J Am Chem Soc* **100** 5491 *1978*.] This *S*-(–)-2,3-ditosylate provides the chiral ligand *R*-(+)- [cf 15629-92-2], which involves inversion of configuration at the chiral centre.

Propane-1-thiol *[107-03-9]* **M 76.1, b 65.3°/702mm, d_4^{25} 0.83598, n_D^{25} 1.43511, pK^{20} 10.82.** Purify the thiol by dissolving it in aqueous 20% NaOH, extracting with a small amount of *benzene and steam distilling until clear. After cooling, the solution is acidified slightly with 15% H_2SO_4, and the thiol is distilled out, dried with anhydrous $CaSO_4$ or $CaCl_2$, and fractionally distilled under nitrogen. [Mathias & Filho *J Phys Chem* **62** 1427 *1958*.] Also purify it by liberating the mercaptan by adding dilute HCl to the residue remaining after steam distilling. After direct distillation from the flask, and separation of the water, the mercaptan is dried (Na_2SO_4) and distilled under nitrogen. [*Beilstein* **1** IV 1449.]

Propane-2-thiol (Isopropyl mercaptan) *[75-33-2]* **M 76.1, b 49.8°/696mm, d_4^{25} 0.80895, n_D^{25} 1.42154, pK^{25} 10.86.** Purify it as for propane-1-thiol above. [*Beilstein* **1** IV 1498.]

Propargyl alcohol (2-propyn-1-ol) *[107-19-7]* **M 56.1, b 54°/57mm, 113.6°/760mm, d_4^{20} 0.947, n_D^{20} 1.432.** The commercial material contains a stabiliser. An aqueous solution of propargyl alcohol can be concentrated by azeotropic distillation with butanol or butyl acetate. Dry it with K_2CO_3 and distil it under reduced pressure, in the presence of about 1% succinic acid, through a glass helices-packed column. [*Beilstein* **1** IV 2214.]

Propargyl chloride (3-chloropropyne) *[624-65-7]* **M 74.5, b 58°/760mm, 65°/760mm, d_4^{20} 1.03, n_D^{20} 1.435.** Purify the chloride by fractional distillation at atmospheric pressure. Note that a possible impurity is propargyl alcohol which has **b** 114-115°/~760mm (see above). [Henry *Chem Ber* **8** 398 *1875*.] **HIGHLY TOXIC** and **FLAMMABLE**. [*Beilstein* **1** IV 960.]

Propene (propylene) *[115-07-1]* **M 42.1, m -185.2°, b -47.8°/750mm, d_4^{20} 0.519, n^{-71} 1.357.** Purify it by freeze-pump-thaw cycles and trap-to-trap distillation. [*Beilstein* **1** IV 725.]

β-Propiolactone see oxetan-2-one in "Heterocyclic Compounds", in this Chapter.

Propionaldehyde *[123-38-6]* **M 58.1, b 48.5-48.7°, d_4^{20} 0.804, n_D^{20} 1.3733, n_D^{25} 1.37115.** Dry the aldehyde with $CaSO_4$ or $CaCl_2$, and fractionally distil it under nitrogen or in the presence of a trace of hydroquinone (to retard oxidation). Blacet and Pitts [*J Am Chem Soc* **74** 3382 *1952*] repeatedly distilled the middle fraction in a vacuum until it no longer gave a solid polymer when cooled to -80°. It is stored with $CaSO_4$. [*Beilstein* **1** IV 3165.]

Propionamide *[79-05-0]* **M 73.1, m 79.8-80.8°, pK^{24} –0.9 (H_o scale, aqueous H_2SO_4).** Crystallise it from acetone, *benzene, $CHCl_3$, water or acetone/water, then dry it in a vacuum desiccator over P_2O_5 or conc H_2SO_4. [*Beilstein* **2** H 243, **2** I 108, **2** II 223, **2** III 542, **2** IV 725.]

Propionic acid *[79-09-4]* **M 74.1, b 141°, d_4^{20} 0.992, n_D^{20} 1.3865, n_D^{25} 1.3843, pK_1^{25} –6.8 (H_o scale, aqueous H_2SO_4), pK_2^{25} 4.88.** Dry the acid with Na_2SO_4 or by fractional distillation, then redistil after refluxing with a few crystals of $KMnO_4$. An alternative purification uses conversion to the ethyl ester, fractional distillation and hydrolysis. [Bradbury *J Am Chem Soc* **74** 2709 *1952*.] Propionic acid can also be heated for 0.5 hour with an amount of benzoic anhydride equivalent to the amount of water present (in the presence of CrO_3 as catalyst), followed by fractional distillation. [Cham & Israel *J Chem Soc* 196 *1960*, *Beilstein* **2** IV 695.]

Propionic anhydride *[123-62-6]* **M 130.2, b 67°/18mm, 168°/780mm, d_4^{20} 1.407, n_D^{20} 1.012.** Shake the anhydride with P_2O_5 for several minutes, then distil. [*Beilstein* **2** IV 722.]

Propionitrile *[107-12-0]* **M 55.1, b 97.2°, d_4^{20} 1.407, n^{15} 1.36812, n^{30} 1.36132.** Shake the nitrile with dilute HCl (20%), or with concentrated HCl until the odour of isonitrile has gone, then wash with water, and aqueous K_2CO_3. After a preliminary drying with silica gel or Linde type 4A molecular sieves, it is stirred with CaH_2 until hydrogen evolution ceases, then decant and distil from P_2O_5 (not more than 5g/L, to minimise gel formation). Finally, it is refluxed with, and slowly distilled from CaH_2 (5g/L), taking precautions to exclude moisture. [*Beilstein* **2** IV 728.]

***n*-Propyl acetate** *[109-60-4]* **M 102.1, b 101.5°, d_4^{20} 0.887, n_D^{20} 1.38442, pK^{25} –7.18 (H_o scale, aqueous H_2SO_4).** Wash the ester with saturated aqueous $NaHCO_3$ until neutral, then with saturated aqueous NaCl. Dry it with $MgSO_4$ and fractionally distil it. [*Beilstein* **2** IV 138.]

***n*-Propyl alcohol (1-propanol)** *[71-23-8]* **M 60.1, b 97.2°, d_4^{25} 0.79995, n_D^{20} 1.385, pK^{25} 16.1.** The main impurities in *n*-propyl alcohol are usually water and 2-propen-1-ol, reflecting the commercial production by hydration of propene. Water can be removed by azeotropic distillation either directly (azeotrope contains 28% water) or by using a ternary system, e.g. by also adding *benzene. *Alternatively*, for removal of gross amounts of water, reflux over CaO for several hours is desirable, followed by distillation and a further drying. To obtain more nearly anhydrous alcohol, suitable drying agents are firstly NaOH, $CaSO_4$ or K_2CO_3, then CaH_2, aluminium amalgam, magnesium activated with iodine, or a small amount of sodium. *Alternatively*, the alcohol can be refluxed with *n*-propylsuccinate or phthalate in a method similar to the one described under EtOH. Allyl alcohol is removed by adding bromine (15ml/L), and then fractionally distilling from a small amount of K_2CO_3. Propionaldehyde, also formed in the bromination, is removed as the 2,4-dinitrophenylhydrazone. *n*-Propyl alcohol can be dried down to 20 ppm of water by passage through a column of pre-dried molecular sieves (type 3 or 4A, heated for 3 hours at 300°) in a current of nitrogen. Distillation from sulfanilic or tartaric acids removes impurities.
Albrecht [*J Am Chem Soc* **82** 3813 *1960*] obtained spectroscopically pure material by heating with charcoal to 50-60°, filtering and adding 2,4-dinitrophenylhydrazine and a few drops of conc H_2SO_4. After standing for several hours, the mixture is cooled to 0°, filtered and distilled in a vacuum. Gold and Satchell [*J Chem Soc* 1938 *1963*] heated *n*-propyl alcohol with 3-nitrophthalic anhydride at 76-110° for 15 hours, then recrystallised the resulting ester from H_2O, *benzene/petroleum ether (b 100-120°)(3:1), and *benzene. The ester was hydrolysed under reflux with aqueous 7.5M NaOH for 45 minutes under nitrogen, followed by distillation (also under nitrogen). The fraction with **b** 87-92° is dried with K_2CO_3 and stirred under reduced pressure in the dark over 2,4-dinitrophenylhydrazine, then freshly distilled. Also purify it by adding 2g $NaBH_4$ to 1.5L of alcohol, gently flushing with argon and refluxing for 1 day at 50°. Then 2g of freshly cut sodium (washed with propanol) is added and refluxed for one day, and finally distilled, taking the middle fraction [Jou & Freeman *J Phys Chem* **81** 909 *1977*]. [*Beilstein* **1** IV 1413.]

***n*-Propylamine** *[107-10-8]* **M 59.1, b 48.5°, d_4^{20} 0.716, n_D^{20} 1.38815, pK^{25} 10.69.** Distil the amine from zinc dust, under reduced pressure, in an atmosphere of nitrogen. [*Beilstein* **4** IV 464.]

***n*-Propyl bromide.** *[106-94-5]* **M 123.0, b 71.0°, d_4^{20} 1.354, n^{15} 1.43695, n_D^{25} 1.43123.** Likely contaminants include *n*-propyl alcohol and isopropyl bromide. The simplest purification procedure uses drying with $MgSO_4$ or $CaCl_2$ (with or without a preliminary wash of the bromide with aqueous $NaHCO_3$, then water), followed by fractional distillation away from bright light. Chien and Willard [*J Am Chem Soc* **79** 4872 *1957*] bubbled a stream of oxygen containing 5% ozone through *n*-propyl bromide for 1 hour, then stirred it with 3% hydrogen

peroxide solution, neutralised it with aqueous Na_2CO_3, washed it with distilled water and dried it. This was followed by vigorous stirring with 95% H_2SO_4 until fresh acid did not discolour within 12 hours. The propyl bromide was separated, neutralised, washed, dried with $MgSO_4$ and fractionally distilled. The centre cut was stored in the dark. Instead of ozone, Schuler and McCauley [*J Am Chem Soc* **79** 821 *1957*] added bromine and stored it for 4 weeks, the bromine then being extracted with aqueous $NaHSO_3$ before the sulfuric acid treatment was applied and finally distilled. Further purification is by preparative gas chromatography on a column packed with 30% SE-30 (General Electric ethylsilicone rubber) on 42/60 Chromosorb P at 150° and 40psi, using helium as carrier gas. [Chu *J Phys Chem* **41** 226 *1964*, *Beilstein* **1** IV 205.]

***n*-Propyl chloride** *[540-54-5]* **M 78.5, b 46.6°, d_4^{20} 0.890, n_D^{20} 1.3880.** Dry the chloride with $MgSO_4$ and fractionally distil. It can be more extensively purified using extraction with H_2SO_4 as for *n*-propyl bromide. *Alternatively*, Chien and Willard [*J Am Chem Soc* **75** 6160 *1953*] passed a stream of oxygen containing about 5% ozone through the *n*-propyl chloride for three times as long as was needed to cause the first coloration of starch iodide paper by the exit gas. After washing with aqueous $NaHCO_3$ to hydrolyse ozonides and remove organic acids, the chloride was dried with $MgSO_4$ and fractionally distilled. [*Beilstein* **1** IV 189.]

Propylene glycol diacetate (1,2-diacetoxypropane, propylene diacetate) *[623-84-7]* **M 160.2, b 84-85°/12mm, 191°/760mm, d_4^{25} 1.050, n_D^{20} 1.414.** Wash the ester with aqueous $NaHCO_3$ in the presence of solid NaCl, dry it with $MgSO_4$ and fractionally distil it. [*Beilstein* **2** H 142, **2** II 156, **2** III 312, **2** IV 220.]

Propylene glycol 1-methylether (1-methoxy-2-propanol) *[RS(±) 107-98-2, R(+) 4984-22-9, S(–) 26550-55-0]* **M 90.1, b 119-120°/atm for *RS*, 131-132°/atm for *R* or *S*, d_4^{25} 0.922, n_D^{20} 1.403.** Wash the ethers with aqueous $NaHCO_3$ in the presence of solid NaCl, dry them with $MgSO_4$ and fractionally distil them. The *RS-acetate* [108-65-6] **M** 132.2 has **b** 145-146°/atm. The *R(+)* and *S(–) enantiomers* have $[\alpha]_D^{20}$ ±20.5° (c 10, H_2O). [*Beilstein* **1** II 536, **1** III 2146, **1** IV 2471.]

***n*-Propyl ether (dipropyl ether)** *[111-43-3]* **M 102.2, b 90.1°, d_4^{20} 0.740, n^{15} 1.38296, n_D^{20} 1.3803, pK^{25} –4.40 (aqueous H_2SO_4).** Purify the ether by drying with $CaSO_4$, by passage through an alumina column (to remove peroxides), and by fractional distillation. [*Beilstein* **1** III 2146, **1** IV 1422.]

Propyl formate *[110-74-7]* **M 88.1, b 81.3°, d_4^{20} 0.9058, n_D^{20} 1.3779.** Distil the formate, then wash it with saturated aqueous NaCl, and with saturated aqueous $NaHCO_3$ in the presence of solid NaCl, dry it with $MgSO_4$ and fractionally distil it. [*Beilstein* **2** IV 26.]

***n*-Propyl iodide (1-iodopropane)** *[107-08-4]* **M 170.0, b 38°/80mm, 102.5°/atm, d_4^{20} 1.745, n_D^{20} 1.5041.** It should be distilled first under reduced pressure to avoid decomposition. Dry the iodide with $MgSO_4$ or silica gel and fractionally distil it. Store it under nitrogen with mercury in a brown bottle. Prior to distillation, free iodine can be removed by shaking with copper powder or by washing with aqueous $Na_2S_2O_3$ and drying. *Alternatively*, the *n*-propyl iodide can be treated with bromine, then washed with aqueous $Na_2S_2O_3$, dried and distilled. See also *n-butyl iodide*. [*Beilstein* **1** IV 222.]

2-Propylpentanoic acid (Valproic acid, VPA, di-*n*-propylacetic acid) *[99-66-1]* **M 144.2, b 120-121°/14mm, 219.5°/760mm, 220°/atm, d_4^{20} 0.91, n_D^{25} 1.425, pK^{25} 4.61.** Purify it in the same way as for propionic acid using $KMnO_4$ (see [79-09-4]). It distils as a colourless oil with a characteristic smell and is soluble in most organic solvents. Its solubility in H_2O is 1.3mg/ml at room temperature. Its FT-IR (film) has ν_{max} at 3572.9, 2969.9, 2885.0, 1771.8, 1465.6, 1388.2, 1102.6, 738.5, 586.5 cm^{-1}; its ^1H NMR (300MHz, $CDCl_3$, TMS) has δ at 0.92 (t, *J* = 7Hz, 2 CH_3), 1.40 (m, 6H), 1.60 (m, 2H), 2.29 (m, 1H), 12.2 (brs, OH); and the ^{13}C NMR (75MHz, $CDCl_3$, $CHCl_3$ standard) has δ at 183.41, 45.20, 34.37, 20.59, 13.99. The ***ethyl ester*** [17022-31-0] M 172.2 has **b 183°/760mm**. It forms a ***1:1 Na salt (sodium valproate, Depakin among other trade names)*** [1069-66-5] M 166.2 as a white, crystalline, odourless, hygroscopic solid with the following solubilities in g/ml: 2.5 in H_2O, 0.66 in EtOH, 0.2 in MeOH, and is insoluble in organic solvents. It also forms a ***2:1 Na salt* [*sodium hydrogen bis(2-propylpentanoate), valproate semisodium*]** [76584-70-8] M 310.4, a ***Magnesium salt (Depamag)***, and the pro-drug amide, ***Valpromide (Depramide)*** [2430-27-5] M 143.2, **m 123°, 122-124°, 125-126°**, obtained as needles by heating the acid with NH_3 at 180°, is a bitter, crystalline white

powder [*Beilstein* **2** IV 695]. These are all commercially available drugs for the treatment of epilepsy, dipolar disorders and migraine. They are **toxic** at high concentrations. [Wiemann et al. *Bull Soc Chim Fr* 189 *1958*, Nau et al. *Pharmacol Toxicol* **69** 310 *1991*, Lscher *Prog Neurobiol* **58** 31 *1999*, *Beilstein* **2** H 350.]

***n*-Propyl propionate** *[106-36-5]* **M 120.2, b 122°, d $_4^{20}$ 0.881, n 1.393.** Treat the ester with anhydrous $CuSO_4$, then distil it under nitrogen. [*Beilstein* **2** IV 707.]

Propyne *[74-99-7]* **M 40.1, m -101.5°, b –23.2°/760mm, d^{-50} 0.7062, n^{-40} 1.3863.** Purify it by preparative gas chromatography. [*Beilstein* **1** H 246.]

Pyruvic acid *[127-17-3]* **M 88.1, m 13°, b 65°/10mm, pK^{25} 2.39 (2.60).** Distil it twice, then fractionally crystallise it by partial freezing. [*Beilstein* **3** IV 1505.]

Ricinoleic acid (*dl* 12-hydroxyoleic acid) *[141-22-0]* **M 298.5, m 7-8° (α-form), 5.0° (γ-form), n $_D^{20}$1.4717, pK$_{Est}$ ~4.5.** Purify it as the methyl acetylricinoleate [Rider *J Am Chem Soc* **53** 4130 *1931*], fractionally distilling it at 180-185°/0.3mm, then 87g of this ester is hydrolysed by refluxing with KOH (56g), water (25ml), and MeOH (250ml) for 10 minutes. The free acid is separated on acidification and extracted into Et_2O, dried (Na_2SO_4), filtered, evaporated and the residue is crystallised from acetone at –50°, and distilled in small batches, **b** 180°/0.005mm. The *R-enantiomer* has **m** +5.5°, **b** 245°/10mm and $[\alpha]_D^{26}$ +7.2° (c 5, Me_2CO). [Bailey et al. *J Chem Soc* 3027 *1957*, *Beilstein* **3** IV 1026, 1207.]

Sebacic acid (1,10-decanedioic acid) *[111-20-6]* **M 202.3, m 134.5°, pK$_1^{25}$ 4.58, pK$_2^{25}$ 5.54.** Purify sebacic acid *via* the disodium salt which, after crystallisation from boiling water (charcoal), is then converted to the free acid. The free acid is crystallised repeatedly from hot distilled water or from Me_2CO/petroleum ether and dried under vacuum. [*Beilstein* **2** IV 2078.]

Sebacic acid monomethyl ester *[818-88-2]* **M 216.3, m 42-43°, b 169-171°/4mm.** Recrystallise the ester from Me_2CO/petroleum ether or petroleum ether at low temperature and distil it in a vacuum. [*Beilstein* **2** IV 608.]

Sebaconitrile (decanedinitrile) *[1871-96-1]* **M 164.3, m 8°, b 199-200°.** Mix the nitrile with P_2O_5 (10% by wt) distil the dinitrile from it, then redistil it. [*Beilstein* **2** IV 2089.]

Semicarbazide hydrochloride (hydrazine carboxamide hydrochloride) *[563-41-7]* **M 111.5, m 173°(dec), 175°(dec), pK^{24} 3.66.** Crystallise the salt from aqueous 75% EtOH and dry it under vacuum over $CaSO_4$. *Alternatively*, crystallise it from a mixture of 3.6 mole % MeOH and 6.4 mole % of water. [Kovach et al. *J Am Chem Soc* **107** 7360 *1985*.] It IR has ν_{max} at 700, 3500 cm^{-1} [Ingersoll et al. *Org Synth* Coll Vol **I** 485 *1941*, Davison & Christie *J Chem Soc* 3389 *1955*, Thiele & Stange *Chem Ber* **27** 33 *1894*, pK: Bartlett *J Am Chem Soc* **54** 2853 *1923*]. The ***free base*** crystallises as prisms from absolute EtOH, **m** 96°. [Curtius & Heidenreich *Chem Ber* **27** 55 1894, *Beilstein* **3** IV 177.] **TOXIC ORALLY**, possible **CARCINOGEN** and **TERATOGEN**.

Senecialdehyde (3,3-dimethylacraldehyde, 3-methyl-2-butenal) *[107-86-8]* **M 84.1, b 78-80°/70mm, 133-135°/atm, d $_4^{20}$ 0.911, n $_D^{20}$ 1.428.** This flammable oil oxidises readily and should be fractionated under N_2. It should be stored under N_2 and/or vacuum. The UV has λ_{max} at 235.5nm. The *semicarbazone* has **m** 221-222° (from MeOH) and the *2,4-dinitrophenylhydrazone* has **m** 184-185° (from MeOH). [Forbes & Skilton *J Org Chem* **24** 436 *1959*, *Beilstein* **1** III 2990, **1** IV 3464.]

Skellysolve A is essentially *n*-pentane, **b** 28-30°,
Skellysolve B is essentially *n*-hexane, **b** 60-68°,
Skellysolve C is essentially *n*-heptane, **b** 90-100°,
Skellysolve D is mixed heptanes, **b** 75-115°,
Skellysolve E is mixed octanes, **b** 100-140°,

Skellysolve F is petroleum ether, **b** 30-60°,
Skellysolve G is petroleum ether, **b** 40-75°,
Skellysolve H is hexanes and heptanes, **b** 69-96°,
Skellysolve L is essentially octanes, **b** 95-127°. For methods of purification, see **petroleum ether**.

Solanone [*S*(+)-*trans*-2-methyl-5-isopropyl-1,3-nonan-8-one] *[1937-54-8]* **M 194.3, b 60°/1mm, n_D^{20}1.4755, $[\alpha]_D^{20}$ +14° (neat).** Purify solanone by high vacuum distillation and store it in sealed ampules [Kohda & Sato *J Chem Soc, Chem Commun* 951 *1981*]. It has UV (hexane) at λ_{max} 230nm (ε 11,800). The *semicarbazone* crystallises from aqueous EtOH or toluene with **m** 160.5-161.5°. [Johnson et al. *J Org Chem* **30** 2918 *1965*.]

Sorbic acid (2,4-hexadienoic acid) *[110-44-1]* **M 112.1, m 134°, pK^{25} 4.76.** Crystallise the acid from water. Dry it air or in a desiccator over P_2O_5. [*Beilstein* **2** IV 1701.]

Spermidine [*N*-(3-aminopropyl)-1,4-diaminobutane] *[124-20-9]* **M 145.3, m 23-25°, b 128-131°/15mm, d_4^{20} 0.918, n_D^{20} 1.482, pK_1^{25} 8.25, pK_2^{25} 9.64, pK_3^{25} 10.43.** It is a strong base with an alkylamine odour and absorbs CO_2 from the atmosphere. It is purified by shaking with solid K_2CO_3 or NaOH, decanting and distilling from K_2CO_3 in a vacuum. Store it in the dark under N_2. [*Beilstein* **4** IV 1300.]

Spermidine trihydrochloride *[334-50-9]* **M 245.3, m ~250°(dec), 256-258°, for pKa see *free base* above.** Recrystallise the salt from dry 3% HCl in ethanol and adding dry Et_2O if necessary. Filter it off rapidly and dry it in a vacuum desiccator. *Alternatively*, centrifuge the crystals off, wash them with dry Et_2O and dry them in a vacuum. [*Beilstein* **4** IV 1300.]

Spermine 4HCl (*N,N*-bis(3-aminopropyl)-1,4-butanediamine 4HCl) *[306-67-2]* **M 348.2, m 313-315°.** Its pK values are similar to those of spermidine above. Purify it as for spermidine trihydrochloride above. [*Beilstein* **4** IV 1301.]

Stearic acid (octadecanoic acid) *[57-11-4]* **M 284.5, m 71.4°, 72°, b 144-145°/27mm, 383°/760mm, d_4^{20} 0.911, n_D^{20} 1.428, pK_{Est} ~5.0.** Crystallise stearic acid from acetone, acetonitrile, EtOH (5 times), aqueous MeOH, ethyl methyl ketone or petroleum ether (b 60-90°), or by fractional precipitation by dissolving in hot 95% EtOH and pouring into distilled water, with stirring. The precipitate, after washing with distilled water, is dried under vacuum over P_2O_5. It has also been purified by zone melting and partial freezing. [Tamai et al. *J Phys Chem* **91** 541 *1987*, *Beilstein* **2** IV 1206.]

Suberic acid (hexane-1,6-dicarboxylic acid) *[505-48-6]* **M 174.2, m 141-142°, pK_1^{25} 4.12, pK_2^{25} 5.40.** Crystallise it from acetone. It sublimes at 300° without decomposition. [*Beilstein* **2** IV 2028.]

Succinamic acid (succinic acid amide) *[638-32-4]* **M 117.1, m 155°, 156-157°, pK^{25} 4.54.** Crystallise the amide from Me_2CO or H_2O and dry it in a vacuum. It is not very soluble in MeOH. It is converted to succinimide above 200°. [*Beilstein* **2** H 614.]

Succinamide *[110-14-5]* **M 116.1, m 262-265°(dec).** Crystallise it from water. [*Beilstein* **2** H 614.]

Succinic acid *[110-15-6]* **M 118.1, m 185-185.5°, pK_1^{25} 4.21, pK_2^{25} 5.72.** Wash it with diethyl ether. Crystallise it from acetone, distilled water, or *tert*-butanol. Dry it under vacuum over P_2O_5 or conc H_2SO_4. Also purify it by conversion to the disodium salt which, after crystallisation from boiling water (charcoal), is treated with mineral acid to regenerate the succinic acid. The acid is then recrystallised and dried in a vacuum. [*Beilstein* **2** H 606, **2** IV 1908.]

Succinic anhydride *[108-30-5]* **M 100.1, m 119-120°.** Crystallise the anhydride from redistilled acetic anhydride or $CHCl_3$, then filter, wash with diethyl ether and dry it in a vacuum. [*Beilstein* **17** H 606, **17** V 6.]

Succinimide *[123-56-8]* **M 99.1, m 124-125°, pK^{25} 9.62.** Crystallise the imide from EtOH (1ml/g) or water. [*Beilstein* **21** H 369, **21/9** V 438.]

Succinonitrile *[110-61-2]* **M 80.1, m 57.9°, b 108°/1mm, 267°/760mm.** Purify the nitrile by vacuum sublimation, and/or crystallisation from acetone. [*Beilstein* **2** H 615, **2** IV 1923.]

***D*(–)-Tartaric acid** *[147-71-7]* **M 150.1, m 169.5-170° (2*S*,3*S*-form, natural) [α] $^{20}_{546}$ –15° (c 10, H_2O), m 208° (2*RS*,3*RS*-form), pK $^{25}_{1}$ 3.03, pK $^{25}_{2}$ 4.46, pK $^{25}_{3}$ 14.4.** Crystallise the acid from distilled H_2O or *benzene/diethyl ether containing 5% of petroleum ether (b 60-80°) (1:1). Soxhlet extraction with diethyl ether has been used to remove an impurity absorbing at 265nm. It has also been crystallised from absolute EtOH/hexane and dried in a vacuum for 18 hours [Kornblum & Wade *J Org Chem* **52** 5301 *1987*]. [*Beilstein* **3** IV 1229.]

***meso*-Tartaric acid** *[147-73-9]* **M 150.1, m 139-141°, pK $^{25}_{1}$ 3.17, pK $^{25}_{2}$ 4.91.** Crystallise it from water, wash it with cold MeOH and dry it at 60° under vacuum. [*Beilstein* **3** IV 1218.]

Tetra-*n*-amylammonium bromide (tetra-*n*-pentylammonium bromide) *[866-97-7]* **M 378.5, m 100-101°.** Crystallise it from petroleum ether, *benzene or acetone/ether mixtures and dry in vacuum at 40-50° for 2 days. It is used in ion-paired chromatography (Sagara et al. *J Chromatogr* **328** 289 *1985*). [*Beilstein* **4** IV 677.]

Tetra-*n*-amylammonium iodide *[2498-20-6]* **M 425.5, m 135-137°.** Crystallise the iodide from EtOH and dry it at 35° under a vacuum. It has also been purified by dissolving in acetone and precipitating by adding diethyl ether, and drying at 50° for 2 days. [*Beilstein* **4** IV 677.]

1,1,2,2,-Tetrabromoethane *[79-27-6]* **M 345.7, f 0.0°, b 119°/15mm, 243.5°/atm, d $^{20}_{4}$ 2.965, n $^{20}_{D}$ 1.63533.** Wash it successively with conc H_2SO_4 (three times) and H_2O (three times), dry it with K_2CO_3 and $CaSO_4$ and distil it in a vacuum or at ~760mm. [*Beilstein* **1** IV 162.]

Tetra-*n*-butylammonium bromide *[1643-19-2]* **M 322.4, m 119.6°.** Recrystallise the salt from *benzene (5ml/g) at 80° by adding hot *n*-hexane (three volumes) and allowing to cool. Dry it over P_2O_5 or $Mg(ClO_4)_2$, under vacuum. The salt is *very* ***hygroscopic*.** It can also be crystallised from ethyl acetate or dry acetone by adding diethyl ether and dried *in vacuo* at 60° for 2 days. It has been crystallised from acetone by addition of diethyl ether. It is so *hygroscopic* that all manipulations should be carried out in a dry-box. It has been purified by precipitation from a saturated solution in dry CCl_4 on addition of cyclohexane or by recrystallisation from ethyl acetate, then heating in vacuum to 75° in the presence of P_2O_5. [Symons et al. *J Chem Soc, Faraday Trans 1* **76** 2251 *1908*.] It also recrystallises from CH_2Cl_2/diethyl ether and is dried in a vacuum desiccator over P_2O_5. [Blau & Espenson *J Am Chem Soc* **108** 1962 *1986*, *Beilstein* **4** IV 657.]

Tetra-*n*-butylammonium chloride *[1112-67-0]* **M 277.9, m 15.7°.** Crystallise the chloride from acetone by addition of diethyl ether. It is very **hygroscopic** and forms crystals with $34H_2O$. It is used in ion-paired chromatography (Sagara et al. *J Chromatogr* **328** 289 *1985*). [*Beilstein* **4** IV 557.]

Tetra-*n*-butylammonium hexafluorophosphate *[3109-63-5]* **M 387.5, m 239-241°.** Recrystallise it from saturated EtOH/water and dry it for 10 hours in a vacuum at 70°. Also recrystallise it three times from absolute EtOH and dry it for 2 days in a drying pistol under a vacuum at boiling toluene temperature [Bedard & Dahl *J Am Chem Soc* **108** 5933 *1986*]. It is a stable supporting electrolyte in organic solvents [Baiser in *Organic Electrochemistry* M. Dekker NY p228 *1973*.]

Tetra-*n*-butylammonium hydrogen sulfate *[32503-27-8]* **M 339.5, m 171-172°.** The sulfate crystallises from acetone. It has been used as a phase transfer catalyst.

Tetra-*n*-butylammonium iodide *[311-28-4]* **M 369.4, m 146°.** Crystallise the iodide from toluene/petroleum ether (see entry for the corresponding bromide), acetone, ethyl acetate, EtOH/diethyl ether, nitromethane, aqueous EtOH or water. Dry it at room temperature under a vacuum. It has also been dissolved in MeOH/acetone (1:3, 10ml/g), filtered and allowed to stand at room temperature to evaporate to *ca* half its original volume. Distilled water (1ml/g) is then added, and the precipitate is filtered off and dried. It can also

be dissolved in acetone, precipitated by adding ether and dried in a vacuum at 90° for 2 days. It has also been recrystallised from CH_2Cl_2/petroleum ether or hexane, or anhydrous methanol and stored in a vacuum desiccator over H_2SO_4. [Chau & Espenson *J Am Chem Soc* **108** 1962 *1986*, *Beilstein* **4** IV 558.]

Tetra-*n*-butylammonium nitrate *[1941-27-1]* **M 304.5, m 119°.** Crystallise it from *benzene (7ml/g), EtOH or EtOAc (**m** 121-122°); dry it in a vacuum over P_2O_5 at 60° for 2 days. [*Beilstein* **4** IV 558.]

Tetra-*n*-butylammonium perchlorate *[1923-70-2]* **M 341.9°, m 210°(dec).** Crystallise the perchlorate from EtOH, ethyl acetate, *n*-hexane or diethyl ether/acetone mixture, or hot CH_2Cl_2. Dry it in a vacuum at room temperature over P_2O_5 for 24 hours. [Anson et al. *J Am Chem Soc* **106** 4460 *1984*, Ohst & Kochi *J Am Chem Soc* **108** 2877 *1986,* Collman et al. *J Am Chem Soc* **108** 2916 *1986*, Blau & Espenson *J Am Chem Soc* **108** 1962 *1986*, Gustowski et al. *J Am Chem Soc* **108** *1986*, Ikezawa & Kutal *J Org Chem* **52** 3299 *1987*, *Beilstein* **4** IV 557.]

Tetra-*n*-butylammonium picrate *[914-45-4]* **M 490.6, m 106.5-107°.** Crystallise the picrate from EtOH. Dry it in a vacuum desiccator over P_2O_5. [*Beilstein* **6** II 271, **4** III 292.]

Tetra-*n*-butylammonium tetrabutylborate (Bu_4N^+ Bu_4B^-) *[23231-91-6]* **M 481.7, m 155°, 161.8°**. Dissolve it in MeOH or acetone, and crystallise by adding distilled water. It also crystallises from EtOH or EtOAc. Dry it in a vacuum at 70°. It has also been successively recrystallised from isopropyl ether, isopropyl ether/acetone (50:1) and isopropyl ether/EtOH (50:1) for 10 hours, then isopropyl ether/acetone for 1 hour, and dried at 65° under reduced pressure for 1 week. [Kondo et al. *J Chem Soc, Faraday Trans 1* **76** 812 *1980*, *Beilstein* **4** III 293, **4** III 558.]

Tetra-*n*-butylammonium tetrafluoroborate *[429-42-5]* **M 329.3, m 161.8°, 161-163°, pK^{25} –4.9 (for HBF_4)**. Recrystallise it from H_2O, aqueous EtOH or from EtOAc by cooling in Dry-ice. Also recrystallise it from ethyl acetate/pentane or dry acetonitrile. Dry it at 80° under vacuum. [Detty & Jones *J Am Chem Soc* **109** 5666 *1987*, Hartley & Faulkner *J Am Chem Soc* **107** 3436 *1985*.] The *acetate* has **m** 118±2° (from BuCl), the *bromide* has **m** 118° (from EtOAc), and the *nitrate* has **m** 120° (from $*C_6H_6$). [Witschonka & Kraus *J Am Chem Soc* **69** 2472 *1947*, Wheeler & Sandstedt *J Am Chem Soc* **77** 2024 *1955*, *Beilstein* **4** IV 558.]

1,1,2,2-Tetrachloro-1,2-difluoroethane *[72-12-0]* **M 203.8, f 26.0°, b 92.8°/760mm, d_4^{25} 1.6252, n_D^{25} 1.4130.** Purify it as for trichlorotrifluoroethane. [*Beilstein* **1** III 165, **1** III 146.]

***sym*-Tetrachloroethane** *[79-34-5]* **M 167.9, b 62°/100mm, 146.2°/atm, d_4^{20} 1.588, n_D^{15} 1.49678.** Stir the ethane, on a steam-bath, with conc H_2SO_4 until a fresh portion of acid remains colourless. The organic phase is then separated, distilled in steam, dried ($CaCl_2$ or K_2CO_3), and fractionally distilled in a vacuum. [*Beilstein* **1** IV 144.]

Tetrachloroethylene *[127-18-4]* **M 165.8, b 62°/80mm, 121.2°, d_4^{15} 1.63109, d_4^{20} 1.623, n_D^{15} 1.50759, n_D^{20} 1.50566.** It decomposes under similar conditions to $CHCl_3$, to give phosgene and trichloroacetic acid. Inhibitors of this reaction include EtOH, diethyl ether and thymol (effective at 2-5 ppm). Tetrachloroethylene should be distilled under a vacuum (to avoid formation of phosgene) and stored in the dark out of contact with air. It can be purified by washing with 2M HCl until the aqueous phase no longer becomes coloured, then with water, drying with Na_2CO_3, Na_2SO_4, $CaCl_2$ or P_2O_5, and fractionally distilling just before use. 1,1,2-Trichloroethane and 1,1,1,2-tetrachloroethane can be removed by counter-current extraction with EtOH/water. [*Beilstein* **1** IV 715.]

Tetracosane (C24) *[646-31-1]* **M 338.7, m 54°, b 243-244°/15mm.** Crystallise it from diethyl ether and/or distil it under high vacuum. [*Beilstein* **1** IV 578.]

Tetracosanoic (lignoceric) acid *[557-59-5]* **M 368.7, m 84°, 87.5-88°, pK_{Est} ~5.0.** Crystallise the acid from acetic acid, Me_2CO, toluene, petroleum ether/Me_2CO or$*C_6H_6$/Me_2CO. [*Beilstein* **2** IV 1301.]

Tetracyanoethylene *[670-54-2]* **M 128.1, m 199-200°(sealed tube).** Rerystallise it from chlorobenzene, dichloroethane, or dichloromethane [Hall et al. *J Org Chem* **52** 5528 *1987*]. Store it at 0° in a desiccator over NaOH pellets. (It slowly evolves HCN on exposure to moist air **CARE**.) It can also be sublimed at 120° under vacuum. Also purify it by repeated sublimation at 120-130°/0.5mm. [Frey et al. *J Am Chem Soc* **107** 748 *1985*, Traylor & Miksztal *J Am Chem Soc* **109** 2778 *1987*, Fatiadi *Synthesis* 249 *1986*, *Synthesis* 749 *1967*, *Beilstein* **2** IV 1245.]

Tetradecane (C14) *[629-59-4]* **M 198.4, m 6°, b 122°/10mm, 252-254°, d_4^{20} 0.763, n_D^{20} 1.429.** Wash it successively with 4M H_2SO_4 and water. Dry it over $MgSO_4$ and distil it several times under reduced pressure [Poë et al. *J Am Chem Soc* **108** 5459 *1986*]. It is used as a standard in gas chromatography. [*Beilstein* **1** H 171, **1** IV 520.]

1-Tetradecanol *[112-72-1]* **M 214.4, m 39-39.5°, b 160°/10mm, 170-173°/20mm.** Crystallise the alcohol from aqueous EtOH. It has also been purified by zone melting. [*Beilstein* **1** IV 1864.]

Tetradecyl ether (di-tetradecyl ether) *[5412-98-6]* **M 410.7, m 43.5°, d_4^{43} 0.8117.** Distil the ether under a vacuum and then crystallise it repeatedly from MeOH/*benzene. It also crystallises from MeOH alone (**m** 31.2°, 33°, and 44.4° also reported), or Me_2CO (**m** 43.5°). [Di Giacomo & Smyth *J Am Chem Soc* **78** 2027 *1956*, *Beilstein* **1** IV 1865.]

Tetradecyltrimethylammonium bromide (myristyl trimethylammonium bromide) *[1119-97-7]* **M 336.4, m 244-245°, 244-249°.** Crystallise the bromide from Me_2CO or a mixture of Me_2CO and >5% MeOH or Me_2CO and EtOH. Wash it with diethyl ether and dry it in a vacuum oven at 60°. It is a cationic detergent. Its solubility is 1g/5g H_2O. [Dearden & Wooley *J Phys Chem* **91** 2404 *1987*, Shelton et al. *J Am Chem Soc* **68** 754 *1946*, *Beilstein* **4** III 419, **4** IV 813.]

Tetraethoxymethane See tetraethyl orthocarbonate below.

Tetraethylammonium bromide *[71-91-0]* **M 210.2, m 269°(dec), 284°(dec).** Recrystallise the bromide from EtOH, $CHCl_3$ or diethyl ether, or, recrystallise it from acetonitrile and dry it over P_2O_5 under reduced pressure for several days. It also recrystallises from EtOH/diethyl ether (1:2), EtOAc, water or boiling MeOH/acetone (1:3) or by adding an equal volume of acetone and allowing to cool. Dry it at 100° *in vacuo* for 12 days, and store over P_2O_5. [*Beilstein* **4** IV 332.]

Tetraethylammonium chloride hydrate *[68696-18-4 (H_2O), 56-34-8 (anhydrous)]* **M 165.7, m dec >200°.** Crystallise the chloride from EtOH by adding diethyl ether, from warm water by adding EtOH and diethyl ether, from dimethylacetamide or from CH_2Cl_2 by addition of diethyl ether. Dry it over P_2O_5 in vacuum for several days. It also crystallises from acetone/CH_2Cl_2/hexane (2:2:1) [Blau & Espenson *J Am Chem Soc* **108** 1962 *1986*, White & Murray *J Am Chem Soc* **109** 2576 *1987*]. [*Beilstein* **4** IV 332.]

Tetraethylammonium hexafluorophosphate *[429-07-2]* **M 275.2, m >300°, 331°(dec), pK_1^{25} ~0.5, pK_2^{25} 5.12 (for fluorophosphoric acid H_2PO_3F).** Dissolve the salt (0.8g) in hot H_2O (3.3ml) and cool to crystallise. Yield of prisms is 0.5g. Its solubility in H_2O is 8.1g/L at 19° [Lange & Müller *Chem Ber* **63** 1067 *1930*]. [*Beilstein* **4** III 199.]

Tetraethylammonium iodide *[68-05-3]* **M 257.2, m 302°, >300°(dec).** Crystallise the iodide from acetone/MeOH, EtOH/water, dimethylacetamide or ethyl acetate/EtOH (19:1). Dry it under a vacuum at 50° and store it over P_2O_5. [*Beilstein* **4** IV 332.]

Tetraethylammonium perchlorate *[2567-83-1]* **M 229.7, m 345°(dec).** Crystallise the perchlorate repeatedly from water, aqueous MeOH, acetonitrile or acetone, and dry it at 70° under a vacuum for 24 hours. [Cox et al. *J Am Chem Soc* **106** 5965 *1984*, Liu et al. *J Am Chem Soc* **108** 1740 *1986*, White & Murray *J Am Chem Soc* **109** 2576 *1987*.] It has also been crystallised twice from ethyl acetate/95% EtOH (2:1) [Lexa et al. *J Am Chem Soc*

109 6464 *1987*]. [*Beilstein* **4** IV 332.]

Tetraethylammonium picrate *[741-03-7]* **M 342.1, m >300°(dec).** Purify it by successive crystallisations from water or 95% EtOH followed by drying in vacuum at 70°. [*Beilstein* **4** IV 332.]

Tetraethylammonium tetrafluoroborate *[429-06-1]* **M 217.1, m 235°, 356-367°, 275-277°, 289-291°, pK^{25} –4.9 (for HBF_4)**. Dissolve the salt in hot MeOH, filter and add Et_2O. It is soluble in ethylene chloride [Thompson & Kraus *J Am Chem Soc* **69** 1016 *1947*, Wheeler & Sandstadt **77** 2025 *1955*]. It has also been recrystallised three times from a mixture of ethyl acetate/hexane (5:1) or MeOH/petroleum ether, then stored at 95° for 48 hours under vacuum [Henry & Faulkner *J Am Chem Soc* **107 3436** *1985*, Huang et al. *Anal Chem* **58** 2889 *1986*]. It is used as a supporting electrolyte. [*Beilstein* **4** IV 333.]

Tetraethylammonium tetraphenylborate *[12099-10-4]* **M 449.4.** Recrystallise the borate from aqueous acetone. Dry it in a vacuum oven at 60° for several days. *Similarly for the propyl and butyl homologues.* [*Beilstein* **4** IV 333.]

Tetraethylene glycol dimethyl ether *[143-24-8]* **M 222.3, b 105°/1mm, d_4^{20} 1.010, n_D^{20} 1.435.** Stand the ether over CaH_2, $LiAlH_4$ or sodium, and distil it when required. [*Beilstein* **1** IV 2404.]

Tetraethylenepentamine *[112-57-2]* **M 189.3, b 169-171°/0.05mm, d_4^{20} 0.999, n_D^{20} 1.506, pK_1^{25} 2.98, pK_2^{25} 4.72, pK_3^{25} 8.08, pK_4^{25} 9.10, pK_5^{25} 9.68.** Distil the amine under vacuum. Also purify *via* its penta hydrochloride, nitrate or sulfate. Jonassen, Frey and Schaafsma [*J Phys Chem* **61** 504 *1957*] cooled a solution of 150g of the base in 300ml of 95% EtOH, and added dropwise 180ml of conc HCl, keeping the temperature below 20°. The white precipitate was filtered off, crystallised three times from EtOH/water, then washed with diethyl ether and dried by suction. Reilley & Holloway [*J Am Chem Soc* **80** 2917 *1958*], starting with a similar solution cooled to 0°, added slowly (keeping the temperature below 10°) a solution of 4.5g-moles of HNO_3 in 600ml of aqueous 50% EtOH (also cooled to 0°). The precipitate was filtered by suction, recrystallised five times from aqueous 5% HNO_3, then washed with acetone and absolute EtOH and dried at 50°. [For purification *via* the sulfate see Reilley and Vavoulis (*Anal Chem* **31** 243 *1959*), and for an additional purification step using the Schiff base with benzaldehyde see Jonassen et al. *J Am Chem Soc* **79** 4279 *1957*]. [*Beilstein* **4** IV 1244.]

Tetraethyl 1,1,2,2-ethanetetracarboxylate *[632-56-4]* **M 318.3, m 73-74°.** Recrystallise the ester twice from EtOH by cooling to 0°. [Mochizuki et al. *Bull Chem Soc Jpn* **64** 1750 *1991*, Weinges et al. *Angew Chem* **93** 1008 *1981*, *Beilstein* **2** IV 2415.]

Tetraethyl orthocarbonate (ethyl orthocarbonate, tetraethoxy ethane) *[78-09-1]* **M 192.3, b 59.6-60°/14mm, 158°/atm, 159°/atm, 160-161°/atm, d_4^{20} 0.9186, n_D^{20} 1.3932.** Likely impurities are hydrolysis products. Shake the orthocarbonate with brine (saturated NaCl, dilute with a little Et_2O if amount of material is small) and dry ($MgSO_4$). The organic layer is filtered off and evaporated, and the residue is distilled through a helices packed fractionating column with a total reflux partial take-off head. All distillations can be done at atmospheric pressure in an inert atmosphere (e.g. N_2). [Roberts & McMahon *Org Synth* Coll Vol **IV** 457 *1963*, Connolly & Dyson *J Chem Soc* 828 *1937*, Tieckelmann & Post *J Org Chem* **13** 266 *1948*, for review see Kantlehner et al. *Justus Liebigs Ann Chem* **507** 207 *1982*, *Beilstein* **3** IV 6.]

2,2,3,3-Tetrafluoropropan-1-ol *[76-37-9]* **M 132.1, b 106-106.5°/~760mm, pK^{25} 12.74.** Tetrafluoro-1-propanol (450ml) is added to a solution of $NaHSO_3$ (2.25g) in water (90ml), shaken vigorously and set aside for 24 hours. The fraction distilling at or above 99° is refluxed for 4 hours with 5-6g of KOH and rapidly distilled, followed by a final fractional distillation. [Kosower & Wu *J Am Chem Soc* **83** 3142 *1961*.] *Alternatively*, shake the alcohol with alumina for 24 hours, dry it overnight with anhydrous K_2CO_3 and distil it, taking the middle fraction (**b** 107-108°). [*Beilstein* **1** IV 2438.]

Tetra-*n*-heptylammonium bromide *[4368-51-8]* **M 490.7, m 88.9-89.1°.** Crystallise the bromide from *n*-hexane, then dry it in a vacuum oven at 70°. [Goodrich et al. *J Am Chem Soc* **72** 4412 *1950*, *Beilstein* **4** IV 736.]

Tetra-*n*-heptylammonium iodide *[3535-83-9]* **M 537.7, m 102-103°.** Recrystallise the iodide from EtOH or aqueous EtOH. [Eriksen et al. *J Org Chem* **25** 849 *1960*, *Beilstein* **4** IV 736 for triheptylamine.]

Tetra-*n*-hexylammonium bromide *[4328-13-6]* **M 434.6, m 99-100°.** Wash the bromide with ether, and dry it in a vacuum at room temperature for 3 days.

Tetra-*n*-hexylammonium chloride *[5922-92-9]* **M 390.1.** Crystallise the chloride from EtOH.

Tetra-*n*-hexylammonium iodide *[2138-24-1]* **M 481.6, m 99-101°, 102-103°.** Wash the iodide with diethyl ether and dry it at room temperature *in vacuo* for 3 days. It is soluble in CH_2Cl_2. [Eriksen et al. *J Org Chem* **25** 849 *1960*, *Beilstein* **4** IV 711 for trihexylamine.]

Tetrahexylammonium perchlorate *[4656-81-9]* **M 454.1, m 104-106°.** Crystallise the salt from acetone and dry it *in vacuo* at 80° for 24 hours.

Tetrakis(dimethylamino)ethylene *[996-70-3]* **M 300.2, b 60°/1mm, d_4^{20} 0.861, n_D^{20}1.4817, $pK_{Est(1)}$<0, $pK_{Est(2)}$<0, $pK_{Est(3)}$~1.5, $pK_{Est(4)}$ ~5.1.** Impurities include tetramethylurea, dimethylamine, tetramethylethane-diamine and tetramethyloxamide. It is washed with water while being flushed with nitrogen to remove dimethylamine, dried over molecular sieves, then passed through a silica gel column (previously activated at 400°) under nitrogen. De-gas it in a vacuum line by distillation from a trap at 50° to one at –70°. Finally, it is stirred over sodium-potassium alloy for several days. [Holroyd et al. *J Phys Chem* **89** 4244 *1985*, Wiberg *Angew Chem Int Ed Engl* **7** 766 *1968*, *Beilstein* **4** IV 167.]

Tetramethylammonium bromide *[64-20-0]* **M 154.1, sublimes with dec >230°.** Crystallise the bromide from EtOH, EtOH/diethyl ether, MeOH/acetone, water or from acetone/MeOH (4:1) by adding an equal volume of acetone. It is dried at 110° under reduced pressure or at 140° for 24 hours. [*Beilstein* **4** IV 145.]

Tetramethylammonium chloride *[75-57-0]* **M 109.6, m >230°(dec).** Crystallise the chloride from EtOH, EtOH/$CHCl_3$, EtOH/diethyl ether, acetone/EtOH (1:1), isopropanol or water. Traces of the free amine can be removed by washing with $CHCl_3$. [*Beilstein* **4** IV 145.]

Tetramethylammonium hydroxide ($5H_2O$) *[10424-65-4 ($5H_2O$), 75-59-2 (aqueous solution)]* **M 181.2, m 63°, 65-68°.** It is freed from chloride ions by passage through an ion-exchange column (e.g. Amberlite IRA-400, prepared in its OH^- form by passing 2M NaOH until the effluent is free from chloride ions, then washed with distilled H_2O until neutral). A modification, to obtain carbonate-free hydroxide, uses the method of Davies and Nancollas [*Nature* **165** 237 *1950*]. [*Beilstein* **4** IV 145.]

Tetramethylammonium hexafluorophosphate *[558-32-7]* **M 219.1, m >300°, d_4^{25} 1.617, pK_1^{25} ~0.5, pK_2^{25} 5.12 (for fluorophosphoric acid H_2PO_3F).** The salt (0.63g) is recrystallised from boiling H_2O (76ml), yielding pure (0.45) $Me_4N.PF_6$ after drying at 100°. It is a good supporting electrolyte. [Lange & Müller *Chem Ber* **63** 1067 *1930*, *Beilstein* **4** III 110.]

Tetramethylammonium iodide *[75-58-1]* **M 201.1, m >230°(dec).** Crystallise the iodide from water or 50% EtOH, EtOH/diethyl ether, ethyl acetate, or from acetone/MeOH (4:1) by adding an equal volume of acetone. Dry it in a vacuum desiccator. [*Beilstein* **4** IV 145.]

Tetramethylammonium nitrate *[1941-24-8]* **M 136.2, m >300°, 410°.** Recrystallise the nitrate from EtOH and dry at 110° in an air oven. [Coats & Taylor *J Chem Soc* 1498 *1936, Beilstein* **4** III 113, **4** IV 147.]

Tetramethylammonium perchlorate *[2537-36-2]* **M 123.6, m>300°, pK^{25} –2.4 to –3.1 (for $HClO_4$)**. Crystallise it twice from H_2O and dry it at 110° in an air oven. It is insoluble in most organic solvents. [Mead et al. *J Chem Soc* 1210 *1933*, Coats & Taylor *J Chem Soc* 1498 *1936*.]

Tetramethylammonium tetraphenylborate *[15525-13-0]* **M 393.3.** Recrystallise it from acetone, acetone/CCl_4 and from acetone/1,2-dichloroethane. Dry it over P_2O_5 in a vacuum, or in a vacuum oven at 60° for several days. [*Beilstein* **4** IV 145.]

***N,N,N′,N′*-Tetramethylethylenediamine (TMEDA, TMED)** *[110-18-9]* **M 116.2, m –55°, b 122°, d $_4^{20}$ 1.175, n $_D^{25}$ 1.4153, pK $_1^{25}$ 5.90, pK $_2^{25}$ 9.14.** Dry TMEDA partially with molecular sieves (Linde type 4A), then distil it in a vacuum from butyl lithium. This treatment removes all traces of primary and secondary amines and water. [Hay et al. *J Chem Soc, Faraday Trans 1* **68** 1 *1972*.] Or dry it with KOH pellets, reflux for 2 hours with one-sixth its weight of *n*-butyric anhydride (to remove primary and secondary amines) and fractionally distil it. Reflux it with fresh KOH, and distil it under nitrogen. [Cram & Wilson *J Am Chem Soc* **85** 1245 *1963*.] It was also distilled from Na. Store it sealed under N_2. The *dipicrate* has **m** 263°(dec). [*Beilstein* **4** H 250, **4** I 415, **4** II 690, **4** III 512, **4** IV 1172.]

Tetramethylethylenediamine dihydrochloride *[7677-21-8]* **M 198.2, m ~300°.** Crystallise the salt from 98% EtOH/conc HCl. It is *hygroscopic*. [Knorr *Chem Ber* **37** 3510 *1904*, *Beilstein* **4** IV 1172.]

1,1,3,3-Tetramethylguanidine *[80-70-6]* **M 115.2, b 159-160°, d $_4^{20}$ 0.917 n $_D^{20}$ 1.470, pK^{25} 13.6.** Reflux it over granulated BaO, then fractionally distil it. Protect it from CO_2. [*Beilstein* **4** IV 227.]

Tetramethyl orthocarbonate (methyl orthocarbonate, tetramethoxy methane) *[1850-14-2]* **M 136.2, m –5.6°, –5°, –2°, b 113.5°/760mm, 113.5-114°/755mm, 112-114°/atm, d $_4^{20}$ 1.0202, n $_D^{20}$ 1.3860.** Purify it in the same way as for tetraethyl orthocarbonate. [Smith *Acta Chem Scand* **10** 1006 *1956*, Tiekelmann & Post *J Org Chem* **13** 266 *1948*, Kantlehner et al. *Synthesis* 73 *1977*, *Beilstein* **3** IV 4.]

2,6,10,14-Tetramethylpentadecane (pristane, norphytane) *[1921-70-6]* **M 268.5, b 68° (bath temp)/0.004mm, 158°/10mm, 296°/atm, d $_4^{20}$ 0.7827, n $_D^{20}$ 1.4385.** Purify pristane by shaking it with conc H_2SO_4 (**care**, if amount of pristane is too small then it should be diluted with petroleum ether *not* Et_2O which is quite soluble in H_2SO_4), then H_2O (**care,** as it may heat up in contact with conc H_2SO_4), dry ($MgSO_4$), evaporate and distil it over Na. [Sörensen & Sörensen *Acta Chem Scand* **3** 939 *1949*, *Beilstein* **1** III 570.]

Tetramethylthiuram disulfide [bis-(dimethylthiocarbamyl)disulfide, Thiram] *[137-26-8]* **M 240.4, m 146-148°, 155-156°.** Crystallise thiram (three times) from boiling $CHCl_3$, then recrystallise it from boiling $CHCl_3$ by adding EtOH dropwise to initiate crystallisation, and allow it to cool. Finally, it is precipitated from cold $CHCl_3$ by adding EtOH (which retains the monosulfide in solution). [Ferington & Tobolsky *J Am Chem Soc* **77** 4510 *1955*, *Beilstein* **4** IV 242.]

1,1,3,3-Tetramethyl urea *[632-22-4]* **M 116.2, f –1.2°, b 175.2°/760mm, d $_4^{20}$ 0.969, n $_D^{20}$ 1.453.** Dry it over BaO and distil it under nitrogen. It denatures proteins in H_2O. [Elbaum & Herskovits *Biochemistry **13** 1268* 1974*,* Kane *Anal Biochem* **53** 350 *1973*, *Beilstein* **4** IV 225.]

Tetranitromethane *[509-14-8]* **M 196.0, m 14.2°, b 46°/36mm, 21-23°/23mm, 126°/760mm, d $_4^{20}$ 1.640, n $_D^{20}$ 1.438.** Shake tetranitromethane with dilute NaOH, wash (H_2O), steam distil, dry with Na_2SO_4 and fractionally crystallise it by partial freezing. The melted crystals are dried with $MgSO_4$ and fractionally distilled under reduced pressure. *Alternatively*, shake it with a large volume of dilute NaOH until no absorption attributable to the *aci*-nitro anion (from mono- di- and tri- nitromethanes) is observable in the water. Then wash it with distilled water, and distil it at room temperature by passing a stream of air or nitrogen through the liquid and condensing it in a trap at –80°. It can be dried with $MgSO_4$ or Na_2SO_4, fractionally crystallised from the melt, and fractionally distilled under reduced pressure. [Liang *Org Synth* Coll Vol **III** 803 *1955*, *Beilstein* **4** H 80, **4** I 21, **4** II 45, **4** III 116, **4** IV 107.] **Potentially explosive (when impure e.g. with toluene), toxic, carcinogenic.**

Tetra-*n*-propylammonium bromide *[1941-30-6]* **M 266.3, m >280°(dec).** Crystallise it from ethyl acetate/EtOH (9:1), acetone or MeOH. Dry it at 110° under reduced pressure. [*Beilstein* **4** IV 471.]

Tetra-*n*-propylammonium iodide *[631-40-3]* **M 313.3, m >280°(dec).** Purify the iodide by crystallising it from EtOH, EtOH/diethyl ether (1:1), EtOH/water or aqueous acetone. Dry it at 50° under a vacuum and store it over P_2O_5 in a vacuum desiccator. Keep it away from light. [*Beilstein* **4** IV 472.]

Tetra-*n*-propylammonium perchlorate *[15780-02-6]* **M 285.8, m 238-240°, 239-241°, pK^{25} –2.4 to –3.1 (for $HClO_4$).** Purify it by recrystallisation from H_2O or MeCN/H_2O (1:4.v/v), and dry it in an oven at 60° for several days, or in a vacuum over P_2O_5 at 100°. [Walden & Hilgert *Z Phys Chem* **165** 245 *1933*, Walden & Birr *Z Phys Chem* **144** 281 *1929*, Walden & Busch *Z Phys Chem* **140** 97 *1929*, *Beilstein* **4** II 628.]

Thioacetamide *[62-55-5]* **M 75.1, m 112-113°, pK^{25} 13.4.** Crystallise the amide from absolute diethyl ether or *benzene. Dry it at 70° in a vacuum and store it over P_2O_5 at 0° under nitrogen. (*It develops an obnoxious odour on storage*, and the absorption at 269nm decreases, hence it should be freshly recrystallised before use). [*Beilstein* **2** IV 565.]

Thiodiglycollic acid (2,2′-dithioacetic acid) *[123-93-3]* **M 150.2, m 129°, pK$_1^{25}$ 3.15 (3.24), pK$_2^{25}$ 4.13 (4.56).** Crystallise the acid from water. [*Beilstein* **3** IV 612.]

3,3'-Thiodipropionic acid (bis[2-carboxyethyl]sulfide) *[111-17-1]* **M 178.2, m 134°, pK$_1^{25}$ 3.84, pK$_2^{25}$ 4.66.** Crystallise the sulfide from water (very soluble at 100°, but 3.7% at 26°). Antioxidant. [*Beilstein* **3** IV 735.]

Thioformamide *[115-08-2]* **M 61.0, m 29°, 32.0-33.8°, pK$_{Est}$ ~12.4.** Crystallise thioformamide from EtOAc, Et_2O or ether/petroleum ether. The *monohydrate* is a yellow oil soluble in many organic solvents. Its UV has λ_{max} at 263nm (ε 2500) in MeOH. [Erlenmyer & Menzi *Helv Chim Acta* **31** 2071 *1948*.] *Alternatively*, dissolve it in Et_2O to separate it from any formanide and/or polymers, filter, evaporate and recrystallise the residue from EtOAc at Dry-ice temperature [Londergan et al. *J Am Chem Soc* **75** 4456 *1953*]. Store it in Et_2O solution over P_2O_5. [Cousineau & Secrist *J Org Chem* **44** 4351 *1979*, *Beilstein* **2** H 95, **2** I 39, **2** III 128, **2** IV 92.]

Thioglycollic acid *[68-11-1]* **M 92.1, b 95-96°/8mm, d$_4^{20}$ 1.326, n$_D^{20}$ 1.505, pK$_1^{25}$ 3.42, pK$_2^{25}$ 10.20.** Mix the acid with an equal volume of *benzene; the *benzene is then distilled off to dehydrate the acid. After heating to 100° to remove most of the *benzene, the residue is distilled under vacuum and stored in sealed ampoules at 3°. [Eshelman et al. *Anal Chem* **22** 844 *1960*, *Beilstein* **3** IV 1130.]

(±)-Thiomalic (mercaptosuccinic) acid *[70-49-5]* **M 150.2, m 153-154°, pK$_1^{25}$ 3.64 (3.17), pK$_2^{25}$ 4.64 (4.67), pK$_3^{25}$ 10.37 (10.52).** Dissolve the acid in water and extract it several times with diethyl ether to remove imprities. The aqueous solution gave the acid on freeze-drying. [*Beilstein* **3** IV 472.]

Thiosemicarbazide *[79-19-6]* **M 91.1, m 181-183°, pK$_1^{25}$ 1.88, pK$_2^{25}$ 12.81.** Crystallise thiosemicarbazide from H_2O (solubility is 20.3% w/w at 80°). The *hydrochloride* has **m** 190-191°(dec, 184° also reported). It forms salts with heavy metals. [*Beilstein* **3** H 195, **3** I 79, **3** II 134, **3** III 315, **3** IV 374.]

Thiourea *[62-56-6]* **M 76.1, m 179°, pK^{20} –1.19 (aqueous H_2SO_4).** Crystallise thiourea from absolute EtOH, MeOH, acetonitrile or water. Dry it under vacuum over H_2SO_4 at room temperature. [*Beilstein* **3** IV 342.]

Tiglic acid (*trans*-2,3-dimethylacrylic acid) *[80-59-1]* **M 100.1, m 63.5-64°, b 198.5°, 95°/11mm, pK^{18} 4.96**. Crystallise it from water. It is steam volatile and is soluble in organic solvents. [*Beilstein* **2** IV 1552.]

***trans*-Traumatic acid (2-dodecene-1,12-dioic acid)** *[6402-36-4]* **M 228.3, m 165-166°, 150-160°/0.001mm, pK$_{Est(1)}$~4.2, pK$_{Est(2)}$~4.6.** Crystallise the acid from EtOH, acetone or glyme. The *bis-4-phenylphenacyl ester* has **m** 144-145° (from EtOH). [*Beilstein* **2** III 1978, **2** IV 2279.]

1,2,3-Triaminopropane trihydrochloride ***[free base** 21291-99-6]* **M 198.7, m 250° (sintering at 100°), pK$_1^{20}$ 3.72, pK$_2^{20}$ 7.95, pK$_3^{20}$ 9.59.** Crystallise the trihydrochloride from EtOH or H_2O. The *free base*

decomposes at 190°/760mm, but has **b 92-93°/9mm** without decomposition. [*Beilstein* **4** H 274, **4** III 630.]

Tribromochloromethane *[594-15-0]* **M 287.2, m 55°, b 158-159.5°/~760mm, 160°/~760mm.** Melt it, wash it with aqueous $Na_2S_2O_3$, dry it with BaO and fractionally crystallise from its melt. It also crystallises from EtOH and distils at atmospheric pressure. [*Beilstein* **1** H 68, **1** II 35, **1** III 91, **1** IV 85.]

Tri-*n*-butylamine (TBA) *[102-82-9]* **M 185.4, b 68°/3mm, 120°/44mm, d_4^{20} 0.7788, n_D^{20} 1.4294, pK^{25} 9.93.** Purify the amine by fractional distillation from sodium under reduced pressure. Pegolotti and Young [*J Am Chem Soc* **83** 3251 *1961*] heated the amine overnight with an equal volume of acetic anhydride, in a steam bath. The amine layer was separated and heated with water for 2 hours on the steam bath (to hydrolyse any remaining acetic anhydride). The solution was cooled, solid K_2CO_3 was added to neutralise any acetic acid that had been formed, and the amine was separated, dried (K_2CO_3) and distilled at 44mm pressure. Davis and Nakshbendi [*J Am Chem Soc* **84** 2085 *1926*] treated the amine with one-eighth of its weight of benzenesulfonyl chloride in aqueous 15% NaOH at 0-5°. The mixture was shaken intermittently and allowed to warm to room temperature. After a day, the amine layer was washed with aqueous NaOH, then water and dried with KOH. (This treatment removes primary and secondary amines.) It was further dried with CaH_2 and distilled under vacuum. [*Beilstein* **4** IV 554.]

Tri-*n*-butylammonium hydrobromide *[37026-85-0]* **M 308.3, m 75.2-75.9°.** Crystallise the hydrobromide from ethyl acetate. [*Beilstein* **4** H 157, **4** III 292, **4** IV 555.]

Tri-*n*-butylammonium nitrate *[33850-87-2]* **M 304.5.** Crystallise the nitrate from mixtures of *n*-hexane and acetone (95:5). Dry it over P_2O_5 in a vacuum. [*Beilstein* **2** IV 554.]

Tri-*n*-butylammonium perchlorate *[14999-66-7]* **M 285.5.** Recrystallise the perchlorate from *n*-hexane. (Potentially explosive.) [*Beilstein* **2** IV 554.]

Tricarballylic acid (propane-1,2,3-tricarboxylic acid) *[99-14-9]* **M 176.1, m 166°, pK_1^{25} 3.47, pK_2^{25} 4.54, pK_3^{25} 5.89.** Crystallise the acid from diethyl ether. [*Beilstein* **2** IV 2366.]

Trichloroacetamide *[594-65-0]* **M 162.4, m 139-141°, b 238-240°.** Its solution in xylene is dried with P_2O_5, then fractionally distilled. [*Beilstein* **2** IV 520.]

Trichloroacetic acid *[76-03-9]* **M 163.4, m 59.4-59.8°, pK^{25} 0.51.** Purify this strong acid (care) by fractional crystallisation from its melt, then crystallise it repeatedly from dry *benzene and store it over conc H_2SO_4 in a vacuum desiccator. It can also be crystallised from $CHCl_3$ or cyclohexane, and dried over P_2O_5 or $Mg(ClO_4)_2$ in a vacuum desiccator. Trichloroacetic acid can be fractionally distilled under reduced pressure from $MgSO_4$. Layne, Jaffé and Zimmer [*J Am Chem Soc* **85** 435 *1963*] dried trichloroacetic acid in *benzene by distilling off the *benzene-water azeotrope, then crystallised the acid from the remaining *benzene solution. Manipulations should be carried out under N_2. [*Toxic vapours, use a well ventilated fume cupboard*.] [*Beilstein* **2** IV 508.]

Trichloroacetonitrile *[545-06-2]* **M 144.4, m –42°, –44°, b 84.6°/741mm, 85.8-86°/764mm, 85.7°/760mm, d_4^{20} 1.441, n_D^{25} 1.4409.** It is prepared by mixing trichloroacetamide (150g, obtained from ethyl trichloroacetate and ammonia) with an equal weight of P_2O_5 and heating at ~200° in an oil bath, and a further amount of P_2O_5 is added before distilling the nitrile off. The distillate is then carefully fractionated, and the fraction **b** 85.8-86°/764mm is collected (yield 70-75%), and should contain <0.02% of amide: *cf* IR (film) has a nitrile band at 2250 cm^{-1}, and is almost free from bands at ~1735 (CO) and >2502 (NH) cm^{-1}. The liquid shows no signs of change after several months, even with traces of moisture, provided that it is kept in away from light. [Davies & Jenkins *J Chem Soc* 2374 *1954*, and references therein, Carpenter *J Org Chem* **27** 2085 *1962*, *Beilstein* **2** H 212, **2** I 95, **2** II 201, **2** III 477, **2** IV 524]. **It is lachrymatory, a skin and eye irritant, and has been used as a fumigant.**
It is a useful reagent for selectively esterifying phosphoric acid, e.g. with benzyl alcohol in the presence of Et_2N it gives monobenzylphosphate with H_2PO_4 [Cramer & Baldauf *Chem Ber* **92**, 370 *1959*], and converts a monophosphoric ester into a symmetrical pyrophosphate in the presence of pyridine [Cramer et al. *Justus*

Liebigs Ann Chem **654** 180 *1962*]. It is readily converted into its trichloroacetimidate esters by reaction with allylic alcohols in CH_2Cl_2, in the presence of DBU at ~0° to ambient temperatures [Anderson & Overman *J Am Chem Soc* **125** 12412 *2003*, Kirsch et al. *Org Lett* **9** 911 *2007*]; similarly prepared trichloroacetimidates of allylic alcohols were shown to undergo ether-directed Pd(II)-catalysed aza-Claisen rearrangements [Jamieson & Sutherland *Tetrahedron* **63** 2132 *2007*], and bis-trichloroacetimidates from 2-aminopropane-1,3-diols yielded dihydrooxazines through an acid catalysed cyclisation [Rondot et al. *Org Lett* **9** 247 *2007*].

1,1,1-Trichloroethane *[71-55-6]* **M 133.4, f -32.7°, b 74.0°, d $_4^{20}$ 1.337, n $_D^{20}$ 1.4385.** Wash it successively with conc HCl (or conc H_2SO_4), aqueous 10% K_2CO_3 (Na_2CO_3), aqueous 10% NaCl, dry it with $CaCl_2$ or Na_2SO_4, and fractionally distil it. It can contain up to 3% dioxane as preservative. This is removed by washing successively with 10% aqueous HCl, 10% aqueous $NaHCO_3$ and 10% aqueous NaCl, and distilling over $CaCl_2$ before use. [*Beilstein* **1** IV 138.]

1,1,2-Trichloroethane *[79-00-5]* **M 133.4, f -36.3°, b 113.6°, d $_4^{20}$ 1.435, n $_D^{20}$ 1.472.** Purify the chloroethane as for 1,1,1-trichloroethane above. [*Beilstein* **1** IV 139.]

Trichloroethylene *[79-01-6]* **M 131.4, f -88°, b 87.2°, d $_4^{20}$ 1.463, n $_D^{21}$ 1.4767.** Tricloroethylene undergoes decomposition in a similar way as $CHCl_3$, giving HCl, CO, $COCl_2$ and organic products. It reacts with KOH, NaOH and 90% H_2SO_4, and forms azeotropes with water, MeOH, EtOH, and acetic acid. It is purified by washing successively with 2M HCl, water and 2M K_2CO_3, then dried with K_2CO_3 and $CaCl_2$, then fractionally distilled before use. It has also been steam distilled from 10% $Ca(OH)_2$ slurry, most of the water being removed from the distillate by cooling to –30 to –50° and filtering off the ice through chamois skin: the trichloroethylene is then fractionally distilled at 250mm pressure and collected in a blackened container. [Carlisle & Levine *Ind Eng Chem (Anal Ed)* **24** 1164 *1932*, *Beilstein* **1** IV 712.]

1,1,2-Trichloro-1,2,2-trifluoroethane *[76-13-1]* **M 187.4, b 47.6°/760mm, d $_4^{20}$ 1.576, n $_D^{20}$ 1.360.** Wash it with water, then with weak alkali. Dry it with $CaCl_2$ or H_2SO_4 and distil it. [Locke et al. *J Am Chem Soc* **56** 1726 *1934*, *Beilstein* **1** III 157, **1** IV 142.]

Tridecanoic acid *[638-53-9]* **M 214.4, m 41.8°, 44.5-45.5° (several forms), b 199-200°/24mm, pK$_{Est}$ ~5.0.** Recrystallise the acid from acetone. [*Beilstein* **2** IV 1117.]

7-Tridecanone (dihexyl ketone) *[462-18-0]* **M 198.4, m 33°, b 255°/766mm.** Crystallise the ketone from EtOH. [*Beilstein* **1** H 715.]

Tri-*n*-dodecylamine (Hydrogen ionophore I) *[102-87-4]* **M 522.0, m 15.7°, b 220-228°/0.03mm, d $_4^{20}$ 0.833, n $_D^{20}$ 1.4577, pK$_{Est}$ ~11.0.** Distil tridodecylamine under high vacuum and N_2, and store it in the absence of CO_2. It can be recrystallised from 95%EtOH/*C_6H_6 at low temperature under vacuum. The *hydrochloride* has **m 78-79°**. [Ra et al. *J Org Chem* **9** 259 *1944*, *Beilstein* **4** III 413, **4** IV 801.]

Tri-*n*-dodecylammonium nitrate *[2305-34-2]* **M 585.0.** Crystallise the salt from *n*-hexane/acetone (95:5) and keep it in a desiccator over P_2O_5 under vacuum. [*Beilstein* **4** IV 801 for tridodecylamine.]

Tri-*n*-dodecylammonium perchlorate *[5838-82-4]* **M 622.4.** Recrystallise the salt from *n*-hexane or acetone and keep it in a desiccator over P_2O_5. (**Potentially explosive.**)

Triethanolamine *[102-71-6]* **M 149.2, m 20-22°, b 190-103°/5mm, 206-207°/15mm, 335.4°/760mm, d $_4^{20}$ 1.124, n $_D^{20}$ 1.485, pK^{25} 7.92.** Shake the amine gently with Linde type 4A molecular sieves for 24 hours, filter and fractionate it under a vacuum, and preferably in the presence of N_2. Store it in dark stoppered bottles under N_2 as it is *hygroscopic*, and turns brown in air and light. It has a strong ammoniacal odour (like diethanolamine). It is miscible with H_2O, MeOH and Me_2CO and its solubilities at 25° in *n*-heptane, Et_2O and *C_6H_6 are 0.4%, 1.6% and 4.2%, respectively. [See **diethanolamine** above, *Beilstein* **4** IV 1524.]

Triethanolamine hydrochloride *[637-39-8]* **M 185.7, m 177°, pK^{25} 7.92 (free base).** Crystallise the salt

from EtOH. Dry it at 80°. [*Beilstein* **4** IV 1525.]

1,1,2-Triethoxyethane *[4819-77-6]* **M 162.2, b 74°/28mm, 164°/~760mm, 167.2°/760mm, d_4^{20} 0.897, n_D^{20} 1.401.** Dry it with Na_2SO_4, and distil it. [McElvain & Walters *J Am Chem Soc* **64** 1964 *1942*, *Beilstein* **1** H 818, **1** I 418, **1** III 3184, **1** IV 3958.]

Triethylamine *[121-44-8]* **M 101.2, b 89.4°, d_4^{20} 0.7280, n_D^{20} 1.4005, pK^{25} 10.82.** Dry triethylamine with $CaSO_4$, $LiAlH_4$, Linde type 4A molecular sieves, CaH_2, KOH, or K_2CO_3, then distil it, either alone or from BaO, sodium, P_2O_5 or CaH_2. It has also been distilled from zinc dust, under nitrogen. To remove traces of primary and secondary amines, triethylamine has been refluxed with acetic anhydride, benzoic anhydride, phthalic anhydride, then distilled, refluxed with CaH_2 (ammonia-free) or KOH (or dried with activated alumina), and again distilled. Another purification method involved refluxing for 2 hours with *p*-toluenesulfonyl chloride, then distilling. Grovenstein and Williams [*J Am Chem Soc* **83** 412 1961] treated triethylamine (500ml) with benzoyl chloride (30ml), filtered off the precipitate, and refluxed the liquid for 1 hour with a further volume of benzoyl chloride (30ml). After cooling, the liquid was filtered, distilled, and allowed to stand for several hours with KOH pellets. It was then refluxed with, and distilled from, stirred molten potassium. Triethylamine has been converted to its *hydrochloride* (see below), crystallised from EtOH (to **m** 254°), then liberated with storng aqueous NaOH, dried with solid KOH and distilled from sodium under N_2. It is a strong base and should not be inhaled. [*Beilstein* **4** H 99, **4** I 348, **4** II 593, **4** III 194, **4** IV 322.]

Triethylammonium hydrobromide *[636-70-4]* **M 229.1, m 248°.** Equimolar portions of triethylamine and aqueous solutions of HBr in acetone are mixed with cooling. The precipitated salt is washed with anhydrous acetone and dried in a vacuum for 1-2 hours. [Odinekov et al. *J Chem Soc, Faraday Trans 2* **80** 899 *1984*.] Recrystallise it from $CHCl_3$ or EtOH. [*Beilstein* **4** IV 322.]

Triethylammonium hydrochloride *[554-68-7]* **M 137.7, m 257-260°(dec).** Purify it like the bromide above. [*Beilstein* **4** IV 327.]

Triethylammonium hydroiodide *[4636-73-1]* **M 229.1, m 181°.** Purify it as for triethylammonium bromide, except the solution for precipitation should be precooled acetone at –10°, and the precipitate is twice recrystallised from a cooled acetone/hexane mixture at –10°. Store it in the dark. [*Beilstein* **4** IV 327.]

Triethylammonium trichloroacetate *[4113-06-8]* **M 263.6.** Equimolar solutions of triethylamine and trichloroacetic acid in *n*-hexane are mixed at 10°. The solid so obtained is recrystallised from $CHCl_3$/*benzene. [Hoigbné & Gäumann *Helv Chim Acta* **42** 444 *1959*, *Beilstein* **4** IV 330.]

Triethylammonium trifluoroacetate *[454-49-9]* **M 196.2.** Purify as for the corresponding trichloroacetate but in Et_2O. Evaporation of the Et_2O gives the salt as a colourless viscous liquid at ambient temperature. [Emmons et al. *J Am Chem Soc* **76** 3472 *1954*, *Beilstein* **4** IV 330.]

Triethylene glycol *[112-27-6]* **M 150.2, b 115-117°/0.1mm, 278°/760mm, d_4^{15} 1.1274, n_D^{15} 1.4578.** Dry the glycol with $CaSO_4$ for 1 week, then it is repeatedly and very slowly fractionally distilled under a vacuum. Store it in a vacuum desiccator over P_2O_5. It is very *hygroscopic*. [*Beilstein* **1** IV 2400.]

Triethylene glycol dimethyl ether (triglyme) *[112-49-2]* **M 178.2, b 225°, d_4^{20} 0.987, n_D^{20} 1.425.** Reflux it with, and distil it from sodium hydride or $LiAlH_4$. [*Beilstein* **1** IV 2401.]

Triethylenetetramine (TRIEN, TETA, trientine, $H_2NCH_2CH_2NHCH_2CH_2NHCH_2CH_2NHCH_2CH_2NH_2$) *[112-24-3]* **M 146.2, m 12°, b 157°/20mm, d_4^{20} 0.971, n_D^{20} 1.497, pK_1^{25} 3.32, pK_2^{25} 6.67, pK_3^{25} 9.20, pK_4^{25} 9.92.** Dry the amine with sodium, then distil it under a vacuum. Further purification has been *via* the nitrate or the chloride salts. For example, Jonassen and Strickland [*J Am Chem Soc* **80** 312 *1958*] separated TRIEN from admixture with TREN (38%) by solution in EtOH, cooling to approximately 5° in an ice-bath and adding conc HCl dropwise from a burette, keeping the temperature below 10°, until all of the white crystalline precipitate of TREN.HCl (see p 216) had formed and was removed. Further addition of HCl then precipitated thick, creamy

white TRIEN.HCl (see below) which was crystallised several times from hot water by adding an excess of cold EtOH. The crystals were finally washed with Me_2CO, then Et_2O and dried in a vacuum desiccator. [*Beilstein* **4** H 255, **4** II 695, **4** III 542, **4** IV 1242.]

Triethylenetetramine tetrahydrochloride (TRIEN HCl) *[4961-10-4]* **M 292.1, m 266-270°.** Crystallise the salt repeatedly from hot water by precipitation with cold EtOH or EtOH/HCl. Wash it with acetone and absolute EtOH and dry it in a vacuum oven at 80° (see TRIEN above). The *tetrabenzoyl* derivative has **m** 230° after recrystallisation from boiling EtOH. [Peacock *J Chem Soc* 1519 *1936*, *Beilstein* **4** H 255, **4** II 695, **4** III 543.]

Triethyl orthoformate (ethyl orthoformate, 1,1,1-triethoxymethane) *[122-51-0]* **M 148.2, m 30°, b 60°/30mm, 144-146°/760mm, d_4^{20} 0.891, n_D^{20} 1.392.** Fractionate it first at atmospheric pressure, then in a vacuum. If impure, then shake it with aqueous 2% NaOH, dry it with solid KOH and distil it from sodium through a 20cm Vigreux column. *Alternatively*, wash it with H_2O, dry it over anhydrous K_2CO_3, filter and fractionate it through a Widmer column. [Sah & Ma *J Am Chem Soc* **54** 2964 *1932*, Ohme & Schmitz *Justus Liebigs Ann Chem* **716** 207 *1968*, *Beilstein* **2** IV 25.] **IRRITANT** and **FLAMMABLE**.

Triethyloxonium fluoroborate *[368-39-8]* **M 190.0, m 92-93°(dec).** Crystallise it from diethyl ether. It is *very hygroscopic*, and must be handled in a dry box and stored at 0°. [Meerwein *Org Synth* Coll Vol **V** 1096 *1973*.] Pure material should give a clear and colourless solution in dichloromethane (1 in 50, w/v). [*Beilstein* **1** IV 1322.]

Trifluoroacetic acid *[76-05-1]* **M 114.0, f -15.5°, b 72.4°, d_4^{20} 1.494, n_D^{20} 1.2850, pK^{25} 0.52.** Although an improved preparation of the acid (in 87% yield) involving the oxidation of 2,3-dichloro-1,1,1,4,4,4-hexafluorobut-2-ene (b 65-66°/745mm, [303-04-8], steam volatile, **d_4^{25} 1.605, n_D^{20} 1.3458)** *via* oxidation with $KMnO_4$/KOH/95°/8-10 hours has been reported [Henne & Trott *J Am Chem Soc* **69** 1820 *1947*], the next purification procedure should be avoided. The purification of trifluoroacetic acid, reported in earlier editions of this work, by refluxing over $KMnO_4$ for 24 hours and slowly distilling has resulted in very **SERIOUS EXPLOSIONS** on various occasions, but not always. This apparently depends on the source and/or age of the acid. The method is **NOT RECOMMENDED**. It form an azeotropic mixture of acid and H_2O (80:20) which boils at 103-105°/745mm. Water can be removed by adding trifluoroacetic anhydride (0.05%, to diminish water content) and distilling. [Conway & Novak *J Phys Chem* **81** 1459 *1977*]. It can be refluxed and distilled from P_2O_5, but do not use an excess of P_2O_5 as it produces the anhydride (see below and Schmidt & Staub *Chem Ber* **87** 388 *1954*) which can be separated by fractional distillation because the anhydride distils about 30° lower at atmospheric pressure. It is further purified by fractional crystallisation by partial freezing and again distilled. It is a strong acid and attacks skin (wear gloves) and eyes (wear safety glasses). **Highly TOXIC vapour — do not inhale it. Work in an efficient fume hood.** [*Beilstein* **2** II 186, **2** III 426, **2** IV 458.]

Trifluoroacetic anhydride *[407-25-0]* **M 210.0, b 38-40°/760mm, d_4^{20} 1.508.** Purification by distilling over $KMnO_4$, as for the acid above, is **EXTREMELY DANGEROUS** due to the possiblility of **EXPLOSION** (see preceding acid). It is best purified by distilling from P_2O_5 slowly, and collecting the fraction boiling at 39.5°. Store it in a dry atmosphere. **Highly TOXIC vapour and attacks skin, work in an efficient fume hood — see previous entry. [**Tedder *Chem Rev* **55** 787, *Beilstein* **2** II 186, **2** III 427, **2** IV 469.]

1,1,1-Trifluoroacetone *[421-50-1]* **M 112.1, b 21°/atm, 22°/atm, d_4^{25} 1.252, n_D^{20} 1.3.** The ketone was obtained by refluxing ethyl 4,4,4-trifluoroacetoacetate (see [372-31-6]) for 2 hours with 10% aqueous H_2SO_4 and collecting the distillate into a receiver containing P_2O_5, and redistilling it from P_2O_5. The *2,4-dinitrophentlhydrazone* has **m 139°** [Henne et al. *J Am Chem Soc* **69** 1819 *1947*]. *Alternatively*, ethyl 4,4,4-trifluoro-sodio-acetoacetate, prepared from the ester with one equivalent of NaOEt was heated with hot (80-90°) dilute H_2SO_4 in an all-glass apparatus to give trifluoroacetone which was condensed in dry Et_2O at –78°. The ethereal solution was dried ($MgSO_4$ or $CaCl_2$), distilled, and the desired product condensed at –78° [Haszeldine et al. *J Chem Soc* 609 *1951*]. The vapours are very **TOXIC (work in an efficient fume cupboard)**. The *semicarbazone* has, **m 129-130°**, and the *2,4-dinitrophenylhydrazone* has **m 141-142°**. [McBee et al. *J Am Chem*

Soc **75** 4090 *1953*, *Beilstein* **1** II 717, **1** III 2745, **1** IV 3214.] Trifluoroacetone has been used to prepare trifluoromethylimines of chiral amines in order to prepare *R* or *S* enantiopure α-trifluoromethyl alanines, diamines and amino alcohols *via* a Strecker-type synthesis in a few steps [Huguenot & Brigaud *J Org Chem* **71** 7075 *2006*]. It has also been used to synthesise 2-trifluoromethyl-7-azaindoles from 2,6-dihalopyridines [Schirok et al. *Synthesis* 251 *2007*].

2,2,2-Trifluoroethanol *[75-89-8]* **M 100.0, m –44°, b 72.4°/738mm, 77-80°/atm, n_D^{20} 1.30, d_4^{20} 1.400, pK^{25} 12.8.** Dry it with $CaSO_4$ and a little $NaHCO_3$ (to remove traces of acid) and distil it. It is used as a calibration standard for NMR spectroscopy. **Highly TOXIC vapour.** [*Beilstein* **1** IV 1370.]

Trifluoromethanesulfonic anhydride (triflic anhydride) *[358-23-6]* **M 282.1, b 82-85°, 84°, d_4^{20} 1.71, n_D^{20} 1.322.** Distil it through a short Vigreux column. It can be freshly prepared from the anhydrous acid (11.5g) and P_2O_5 (11.5g, or half this weight) by setting aside at room temperature for 1 hour, distilling off volatile products then distil it through a short Vigreux column. It is readily hydrolysed by H_2O and decomposes appreciably after a few days to liberate SO_2 and produce a viscous liquid. Store it dry at low temperatures. [Burdon et al. *J Chem Soc* 2574 *1957*, Beard et al. *J Org Chem* **38** 373 *1973*, *Beilstein* **3** IV 35.] **Highly TOXIC vapour.**

1,1,1-Trifluoro-2,4-pentanedione (α,α,α-trifluoroacetlyacetone, tfacac or facac) *[367-57-7]* **M 154.1, b 105-107°/atm, 107°/760mm, d_4^{25} 1.27, n_D^{20} 1.3890.** The diketone was prepared from ethyl trifluoroacetate (74.5g) and Na wire (10g, or an equivalent of NaOEt) in Et_2O (5ml) at 0°, by adding Me_2CO (80ml) at a rate to maintain a steady reaction, kept at 0° for 2 hours, and then allowed to warm to room temperature. Ice-water (5ml) was added, the aqueous layer was acidified with AcOH, and the Cu complex was precipitated with a warm saturated solution of $Cu(OAc)_2$. The *copper trifluoroacetylacetone* crystallised in long blue needles from EtOH and had **m 189°**; its UV has λ_{max} at 240nm (ε 19,500) and 294nm (ε 31,000) in EtOH, and the effect of fluorine substitution on the complexing properties has been studied in detail by Calvin and coworkers [Belford et al. *J Inorg Nucl Chem* **2** 11 *1956*]. An ethereal mixture of the complex (partly dissolved) was shaken with 2N H_2SO_4, then H_2O, the organic layer was separated, dried (Na_2SO_4), filtered and distilled to give a 62% yield of *trifluoroacetylacetone*. *Alternatively*, the metal can be removed by bubbling H_2S through the ethereal mixture, the CuS was filtered off and the filtrate was distilled. [Reid & Calvin *J Am Chem Soc* **72** 2948 *1950*, Henne et al. *J Am Chem Soc* **69** 1819 *1947*, Haszeldine et al. *J Chem Soc* 609 *1951*, Belford et al. *J Inorg Nucl Chem* **2** 11 *1956*]. Its UV has λ_{max} at 284nm (ε 10,500) in $CHCl_3$; the FT-IR (film) has ν_{max} at 1604.7, 1422.3, 1369.5, 1282.2, 1154.7, 887.4, 857.4, 795.2, 726.4 cm^{-1}; and the ^1H NMR (300MHz, $CDCl_3$, TMS) has δ at 2.36 (s), 4.60 (s, 3H, CH_3), 8.30 (s, CH); and the ^{13}C NMR (75MHz, $CDCl_3$, TMS) has δ at 193.47, 176.71, 176.22, 175.74, 175.25, 127.75, 119.00, 115.25, 111.50, 96.37, 96.35, 24.83. It enolises in aqueous solution, and rates of enolisation were determined by Ried and Calvin (*vide infra*) in H_2O, 0.1N and 0.5N HCl, and in aqueous EtOH of varying concentrations; and are temperature dependent. Thus at equilibrium, at 0.08-0.09M solution of *tfacac* and 25°, 16% aqueous EtOH contains 2.5% of enol+enolate, whereas at 95% it contains 20.7% of enol+enolate. This enolisation should be taken into account when measuring spectra and other physical parameters. Complexation with Cu, Fe and Al can be used to extract the metals from aqueous medium (acetate buffered) by a 0.10M of the diketone in $CHCl_3$ [Scribner et al. *Anal Chem* **37** 1136 *1965*], and Be into organic solvents [Scribner et al. *Anal Chem* **38** 1779 1966]. The *oxime*, **m 86-87°**, crystallises from H_2O or aqueous EtOH. [*Beilstein* **1** III 3123, **1** IV 3680.]

Trimethylamine *[75-50-3]* **M 59.1, b 3.5°, pK^{25} 9.80.** Dry triethylamine by passing the gas through a tower filled with solid KOH. Water and impurities containing labile hydrogen were removed by treatment with freshly sublimed, ground, P_2O_5. It has been refluxed with acetic anhydride, and then distilled through a tube packed with HgO and BaO. [Comyns *J Chem Soc* 1557 *1955*.] For more extensive purification, trimethylamine is converted to the hydrochloride, crystallised (see below), and regenerated by treating the hydrochloride with excess aqueous 50% KOH; the gas is passed through a $CaSO_4$ column into a steel cylinder containing sodium ribbon. After 1-2 days, the cylinder is cooled to –78° and hydrogen and air are removed by pumping. [Day & Felsing *J Am Chem Soc* **72** 1698 *1950*.] Me_3N has been distilled from trap-to-trap methods and degassed by freeze-pump-thaw [Halpern et al. *J Am Chem Soc* **108** 3907 *1986*]. It is commercially available under pressure

in tin cylinders. [*Beilstein* **4** H 43, **4** I 322, **4** II 553, **4** III 99, **4** IV 134.]

Trimethylamine hydrochloride *[593-81-7]* **M 95.7, m >280°(dec).** The salt crystallises from $CHCl_3$, EtOH or *n*-propanol, and is dried under vacuum. It also crystallises from *benzene/MeOH, MeOH/diethyl ether and is dried under vacuum over paraffin wax and H_2SO_4. It is kept over P_2O_5 as it is *hygroscopic*. [*Beilstein* **4** H 262, **4** I 419, **4** IV 138.]

Trimethylamine hydroiodide *[20230-89-1]* **M 186.0, m 263°.** It crystallises from MeOH.

Trimethylolpropane (1,1,1-tris-hydroxymethylpropane, 2-ethyl-2-hydroxymethyl-1,3-propanediol) *[77-99-6]* **M 134.2, m 57-59°, 60-62°, b 159-161°/2mm.** Crystallise it from acetone and ether, and it distils at high vacuum. [*Beilstein* **1** III 2349.]

2,2,3-Trimethylpentane *[564-02-3]* **M 114.2, b 109.8°, d_4^{20} 0.7161, n_D^{20} 1.40295, n_D^{25} 1.40064.** Purify it by azeotropic distillation with 2-methoxyethanol, which is subsequently washed out with water. The trimethylpentane is then dried and fractionally distilled. [Forziati et al. *J Res Nat Bur Stand* **36** 129 *1946*, *Beilstein* **1** IV 439.]

2,2,4-Trimethylpentane (isooctane) *[540-84-1]* **M 114.2, m -107°, b 99.2°, d_4^{20} 0.693, n_D^{20} 1.39145, n_D^{25} 1.38898.** Distil isooctane from sodium, pass it through a column of silica gel or activated alumina (to remove traces of olefins), and again distilled from sodium. Extract it repeatedly with conc H_2SO_4, then agitate it with aqueous $KMnO_4$, wash it with water, dry ($CaSO_4$) and distil it. Purify it also by azeotropic distillation with EtOH, which is subsequently washed out with water, and the trimethylpentane is dried and fractionally distilled. [Forziati et al. *J Res Nat Bur Stand* **36** 126 *1946*.] [*Beilstein* **1** IV 439.]

2,4,4-Trimethylpent-2-ene (β-diisobutylene) *[107-40-4]* **M 112.2, m -106°, b 104°, d_4^{20} 0.720, n_D^{20}1.4160.** Fractionate it under N_2 as it is highly flammable. [*Beilstein* **1** III 848, **1** IV 891.]

Trimethylsulfonium iodide *[2181-42-2]* **M 204.1, m 211-212.5°(dec), 215-220°(dec).** Crystallise the iodide from EtOH. [Emeleus & Heal *J Chem Soc* 1126 *1946*, Swain & Kaiser *J Am Chem Soc* **80** 4089 *1958*, Borredon et al. *J Org Chem* **55** 501 *1990*, Bouda et al. *Synth Commun* **17** 503 *1987*.]

Trimyristin *[555-45-3]* **M 723.2, m 56.5°.** Crystallise it from diethyl ether. [*Beilstein* **2** IV 1135.]

Tri-*n*-octylamine *[1116-76-3]* **M 353.7, b 164-168°/0.7mm, 365-367°/760mm, d_4^{20} 0.813, n_D^{20} 1.450, pK^{25} 10.65.** It is converted to the amine hydrochloride etherate which is recrystallised four times from diethyl ether at –30° (see below). Neutralisation of this salt regenerates the free amine which distil under high vacuum. [Wilson & Wogman *J Phys Chem* **66** 1552 *1962*.] Distil the strong base amine at <1-2mm pressure. [*Beilstein* **4** H 196, **4** III 382, **4** IV 754.]

Tri-*n*-octylammonium chloride *[1188-95-0]* **M 384.2, m 78-79°, pK^{25} 8.35 (in 70% aqueous EtOH).** Crystallise it from Et_2O, then *n*-hexane (see above). [Burrows et al. *J Chem Soc* 200 *1947*, *Beilstein* **4** H 196.]

Tri-*n*-octylammonium perchlorate *[2861-99-6]* **M 454.2, m >300°(dec).** Crystallise the perchlorate from *n*-hexane. (Possibly explosive.) [*Beilstein* **4** IV 754.]

Tripalmitin *[555-44-2]* **M 807.4, m 66.4°.** Crystallise it from acetone, diethyl ether or EtOH. It exists in an α-form (**m** 56.0°), a β'-form (**m** 63.5°) and a β-form (**m** 65.5°). [*Beilstein* **2** H 373, **2** I 167, **2** II 340, **2** III 971.]

Tri-*n*-propylamine *[102-69-2]* **M 143.3, b 156.5°, d_4^{20} 0.757, n_D^{20} 1.419, pK^{25} 10.66.** Dry the amine with KOH and fractionally distil it. Also reflux it with toluene-*p*-sulfonyl chloride and with KOH, then fractionally distil it. The distillate, after additon of 2% phenyl isocyanate, was redistilled and the residue fractionally distilled from sodium. It is a strong base. [Takahashi et al. *J Org Chem* **52** 2666 *1987*, *Beilstein* **4** IV 470.]

Tris(2-aminoethyl)amine (TREN) *[4097-89-6]* **M 146.2, b 114°/15mm, 263°/744mm, d_4^{20} 0.977, n_D^{20} 1.498, pK_1^{25} 8.42, pK_2^{25} 9.44, pK_3^{25} 10.13.** For a separation from a mixture containing 62% TRIEN, see entry under triethylenetetramine [112-24-3] above. Also purify it by conversion to the hydrochloride (see below), recrystallise it and regenerate the free base [Xie & Hendrickson *J Am Chem Soc* **109** 6981 *1987*]. [*Beilstein* **4** H 256, **4** II 695, **4** III 545, **4** IV 1250.]

Tris(2-aminoethyl)amine trihydrochloride (TREN.HCl) *[14350-52-8]* **M 255.7, m 300°(dec).** Crystallise the salt several times by dissolving it in the minimum of hot water and precipitating it with excess of cold EtOH. The precipitate is washed with acetone, then diethyl ether and dried in a vacuum desiccator. [*Beilstein* **4** H 256, **4** II 695, **4** III 545, **4** IV 1250.]

Tris(dimethylamino)methane (*N,N,N′,N′,N″,N″*-hexamethylmethanetriamine) *[5762-56-1]* **M 145.3, b 42-43°/12mm, n_D^{20} 1.4349, pK_{Est} ~10.** Dry it over KOH and distil it through a Vigreux column at water pump vacuum. Store it in the absence of CO_2. [Bredereck et al. *Chem Ber* **101** 1885 *1968* and *Angew Chem, Int Ed Engl* **5** 132 *1966*.]

Tris(hydroxymethyl)methylamine (TRIS) *[77-86-1]* **M 121.1, m 172°, pK^{25} 8.07.** TRIS can ordinarily be obtained in highly pure form suitable sources for use as an acidimetric standard. If only impure material is available, it should be crystallised from 20% EtOH, aqueous MeOH (**m** 171.1°) or isopropanol (**m** 172-173°). Dry it in a vacuum desiccator over P_2O_5 or $CaCl_2$. *Alternatively*, it is dissolved in twice its weight of water at 55-60°, filtered, concentrated to half its volume and poured slowly, with stirring, into about twice its volume of EtOH. The crystals which separate on cooling to 3-4° are filtered off, washed with a little MeOH, air dried by suction, then finally ground and dried in a vacuum desiccator over P_2O_5. It has also been recrystallised from water, MeOH or aqueous MeOH, and vacuum dried at 80° for 2 days. [*Beilstein* **4** H 303, **4** III 857, **4** IV 1903.]

Tris(hydroxymethyl)methylammonium hydrochloride (TRIS-HCl) *[1185-53-1]* **M 157.6, m 149-150°(dec).** Crystallise the salt from 50% EtOH, then from 70% EtOH. TRIS-hydrochloride is also available commercially in a highly pure state. Otherwise, recrystallise it from 50% EtOH, then 70% EtOH, and dry it below 40° to avoid risk of decomposition. [*Beilstein* **4** H 304.]

1,1,1-Tris(hydroxymethyl)ethane (2-hydroxymethyl-2-methyl-1,3-propanediol) *[77-85-0]* **M 120.2, m 200°.** Dissolve it in hot tetrahydrofuran, filter and precipitate it with hexane. It has also been crystallised from acetone/water (1:1). Dry it in a vacuum. [*Beilstein* **1** H 520, **1** IV 2780.]

***N*-Tris(hydroxymethyl)methyl-2-aminomethanesulfonic acid (TES)** *[7365-44-8]* **M 229.3, m 224-226°(dec), pK^{20} 7.50.** Crystallise the acid from hot EtOH containing a little water.

Tris(hydroxymethyl)nitromethane [2-(hydroxymethyl)-2-nitro-1,3-propanediol] *[126-11-4]* **M 151.1, m 174-175°(dec, tech. grade), 214°(pure).** Crystallise it from $CHCl_3$/ethyl acetate or ethyl acetate/*benzene. It is an acid and a 0.1M solution in H_2O has pH 4.5. **IRRITANT.** [*Beilstein* **1** H 520.]

Tris[2-(methylamino)ethyl]amine *[65604-89-9]* **M 188.3, b 77-78°/0.1mm, d_4^{20} 0.896, $pK_{Est(1)}$ ~8.8, $pK_{Est(2)}$ ~9.4, $pK_{Est(3)}$ ~10.4.** If this strong base contains carbonate (check IR) it should be shaken with solid KOH, decanted and distilled at high vaccum to give a colourless oil with a strong amine odour. Store it in the dark under N_2 as it absorbs CO_2 in moist air. It is synthesised in two steps. Ethyl chloroformate (33.4g, 310mmol, lachrymatory, see [541-41-3] above) is added dropwise to a mixture of TREN (29.2g, 200mmol, see [4097-89-6] above) in $*C_6H_6$ (225ml) and H_2O (100ml), and cooled to 5°. Then a solution of KOH (36.4g, 650mmol) in H_2O (35ml) is added simultaneously with more ethyl chloroformate (33.4g, 310mmol), with stirring, while keeping the reaction mixture below 5° for 2 hours followed, still with stirring, by 8 hours at ~25°. The $*C_6H_6$ layer is separated, the aqueous layer is extracted with $CHCl_3$ (3 x 100ml), the combined organic layers are dried ($MgSO_4$), filtered and the filtrate is evaporated to leave *tris[2-(ethoxycarbonylamino)ethyl]amine* (~85%) as a thick oil which is used directly in the subsequent step. [The crude tri-ester has IR (film) bands with ν_{max} at

3300, 1720, 1530, and 1250 cm^{-1}; and the ^1H NMR (300MHz, $CDCl_3$, TMS) has δ at 1.27 (t, 9H, $^3J_{HH}$ = 7.1Hz), 2.60 (t, 6H, $^3J_{HH}$ = 5.7 Hz), 3.23 (br s, 6H), 4.10 (q, 6H, $^3J_{HH}$ = 7.1 Hz) and 5.50 (br s, 3H)].
In the second step the preceding crude tri-ester (61.3g, 170mmol) in THF (250ml) is added dropwise to a suspension of $LiAlH_4$ (30.0g, 790mmol) in THF (700ml), and the reaction mixture is refluxed overnight. Water (50ml), followed by a solution of KOH (50g) in H_2O (50ml) are very carefully added to it (cool if necessary), the solvent is decanted from the inorganic gel, evaporated *in vacuo*, and the residual yellow oil is fractionated in a vacuum to give the desired *amine* in 88% yield. It has ^1H NMR (300MHz, $CDCl_3$, TMS) with δ at 1.30 (br s, 3H, NH), 2.39 (s, 9H, CH_3), 2.48 (m, 6H, $^3J_{HH}$ = 6.1 Hz, $3CH_2$) and 2.52 (m, 6H, $^3J_{HH}$ = 6.1 Hz, $3CH_2$); the ^{13}C NMR (75MHz, $CDCl_3$, TMS) has δ at 54.1 (CH_2), 49.6 (CH_2) and 36.3 (CH_3); and HRMS has *m/z* 189.2082 (calc for M + H is 189.20793). [Schmidt et al. *Z Anorg Allg Chem* **578** 75 *1989*.]

Triuret (1,3-dicarbamoylurea) *[556-99-0]* **M 146.1, m 233°(dec).** It crystallises from aqueous ammonia or H_2O (plates **m** 232-234°). It gives mono and dipotassium salts. [*Beilstein* **3** H 72, **3** I 35, **3** II 60, **3** III 142.]

Undecan-1-ol *[112-42-5]* **M 172.3, m 16.5°, 146°/30mm, d^{25} 0.830, n_D^{20} 1.440.** Purify the alcohol by repeated fractional crystallisation from its melt or by distillation in a vacuum. [*Beilstein* **1** H 427, **1** IV 1835.]

Undecanoic acid (C11, undecylic acid)) *[112-78-8]* **M 186.3, m 28.5°, b 164°/18mm, 228°/160mm, 248-250°/~760mm, d_4^{20} 0.8907, n_D^{25} 1.4294, pK_{Est} ~5.0.** Purify the acid by repeated fractional crystallisation from its melt or by distillation in a vacuum. [*Beilstein* **2** H 358, **2** IV 1068.]

Undec-10-enoic acid *[112-38-9]* **M 184.3, m 25-25.5°, b 131°/1mm, 168°/15mm, d_4^{20} 0.912, n_D^{25} 1.447, pK_{Est} ~5.0.** Purify the acid by repeated fractional crystallisation from its melt or by distillation, preferably in a high vacuum. [*Beilstein* **2** IV 1612.]

Urea *[57-13-6]* **M 60.1, m 132.7-132.9°, pK^{25} 0.12.** Crystallise urea twice from conductivity water using centrifugal drainage and keeping the temperature below 60°. The crystals are dried under vacuum at 55° for 6 hours. Levy and Margouls [*J Am Chem Soc* **84** 1345 *1962*] prepared a 9M solution in conductivity water (keeping the temperature below 25°) and, after filtering through a medium-porosity glass sinter, added an equal volume of absolute EtOH. The mixture was set aside at –27° for 2-3 days and filtered cold. The precipitate was washed with a small amount of EtOH and dried in air. Crystallisation from 70% EtOH between 40° and –9° has also been used. Ionic impurities such as ammonium isocyanate have been removed by treating the concentrated aqueous solution at 50° with Amberlite MB-1 cation- and anion-exchange resin, and allowing it to crystallise on evaporation. [Benesch et al. *J Biol Chem* **216** 663 *1955*.] It can also be crystallised from MeOH or EtOH, and is dried under vacuum at room temperature. [*Beilstein* **3** H 42, **3** I 19, **3** II 35, **3** III 80.]

Urea nitrate *[124-47-0]* **M 123.1, m 152°(dec), 157-158°, 163°.** Crystallise it from dilute HNO_3 or EtOH (**m** 157-158°), and dry it in a vacuum over P_2O_5. [*Beilstein* **3** H 54, **3** I 25, **3** II 45, **3** III 105, **3** IV 94.]

Urethane (ethyl carbamate, ethyl urethane) *[51-79-6]* **M 89.1, m 48-50°, b 182-184°/~760mm, d_4^{20} 0.986, n_D^{25} 1.4144.** Urethane is best purified by fractional distillation, but it can be sublimed at ~103°/~50mm. It has also been recrystallised from *benzene. Its solubilitiy at room temperature is 2g/ml in H_2O, 1.25g/ml in EtOH, 1.1g/ml in $CHCl_3$, 0.67g/ml in Et_2O and 0.03g/ml in olive oil. It is a suspected **human carcinogen**. [*Beilstein* **3** H 22, **3** IV 40.]

***cis*-Vaccenic acid (octadec-11-enoic acid)** *[506-17-2]* **M 282.5, m 14-15°, b 158-163°/0.4mm, d_4^{20} 0.880, n_D^{25} 1.4598, pK_{Est} ~ 4.9.** Purify the acid by fractional distillation under high vacuum or crystallisation form its melt in an inert atmosphere away from light. [*Beilstein* **2** I 198, **2** III 1384, **2** IV 1639.]

***trans*-Vaccenic acid (octadec-11-enoic acid)** *[693-72-1]* **M 282.5, m 43-44°, n_D^{50} 1.4472, pK_{Est} ~ 4.9.** Crystallise the acid from acetone (**m** 45-45.5°) or aqueous MeOH (**m** 43.5-43.7°). The *methyl ester* has **b** 174-

175°/5mm. [Böeseken & Hoagland *Rec Trav Chim Pays Bas* **46** 632 *1927*, Ahmad et al. *J Am Chem Soc* **70** 3391 *1948*, IR: Rao & Daubert *J Am Chem Soc* **70** 1102 *1948*.]

***n*-Valeraldehyde (pentanal)** *[110-62-3]* **M 86.1, m –92°, b 103°, d $_4^{20}$ 0.811, n $_D^{25}$ 1.40233.** Purify pentanal *via* the bisulfite derivative (see **2-butanone** above for the preparation and decomposition of the bisulfite derivative). [Birrell & Trotman-Dickinson *J Chem Soc* 2059 *1960*, *Beilstein* **1** H 676, **1** IV 3268.] The *2,4-dinitrophenylhydrazone* [2057-84-3] **M** 266.3 has **m** 103-105° (from EtOH). [*Beilstein* **15** III/IV 429.]

***n*-Valeramide (pentanamide)** *[626-97-1]* **M 101.1, m 115-116°.** Crystallise the amide from EtOH. It sublimes at 80°. [Philbrook *J Org Chem* **19** 624 *1954*, *Beilstein* **2** H 301, 2 I 131, **2** II 266, **2** III 674, **2** IV 874.]

Valeric acid (*n*-pentanoic acid) *[109-52-4]* **M 102.1, b 95°/22mm, 186.4°/~760mm, d $_4^{20}$ 0.938, n $_D^{20}$ 1.4080, pK^{25} 4.81.** Water is removed from the acid by distillation using a Vigreux column, until the boiling point reaches 183°. A few crystals of $KMnO_4$ are added, and after refluxing, the distillation is continued. [Andrews & Keefer *J Am Chem Soc* **83** 3708 *1961*, *Beilstein* **2** H 299, 2 I 130, **2** II 263, **2** III 663, **2** IV 868.]

Valeronitrile *[110-59-8]* **M 83.1, b 142.3°/~760mm, d $_4^{20}$ 0.799, n $_D^{15}$ 1.39913, n $_D^{30}$ 1.39037.** Wash the nitrile with half its volume of concentrated HCl (twice), then with saturated aqueous $NaHCO_3$, dry it with $MgSO_4$ and fractionally distil it from P_2O_5. [*Beilstein* **2** H 301, **2** I 131, **2** II 267, **2** III 675, **2** IV 875.]

Vinyl acetate *[108-05-4]* **M 86.1, b 72.3°, d $_4^{20}$ 0.938, n $_D^{20}$ 1.396.** Inhibitors such as hydroquinone and other impurities are removed by drying with $CaCl_2$ and fractionally distilling under nitrogen, then refluxing briefly with a small amount of benzoyl peroxide and redistilling it under nitrogen. Store it in the dark at 0°. Add inhibitor (~0.004%) for storage. [*Beilstein* **2** IV 176.]

Vinyl butoxyethyl ether (ethylene glycol butyl vinyl ether) *[4223-11-4]* **M 144.2, b 70-72°/20mm, d $_4^{20}$ 0.866, n $_D^{20}$ 1.4220.** Wash the ether with aqueous 1% NaOH, dry with CaH_2, then reflux with, and distil it from sodium. Stabilise it with 0.5% of 2,6-di-*tert*-butyl-*p*-cresol for storage. [*Beilstein* **1** IV 2387.] **IRRITANT.**

Vinyl chloroformate *[5130-24-5]* **M 106.5, b 46.5°/80mm, 67-69°/atm, 109-110°/760mm, d $_4^{20}$ 1.136, n $_D^{21}$ 1.420**. It has been fractionated through a Todd column (Model A with ~60 plates) under atmospheric pressure and the purity can be checked by gas chromatography. Stabilise it with 0.5% of 2,6-di-*tert*-butyl-*p*-cresol. It has IR with ν_{max} at 3100 + 2870 (CH_2), 1780 (C=O), 1640 (C=C) and 940 (CH_2 out-of-plane) and 910 (CH_2 wagging) cm^{-1}. [IR: Lee *J Org Chem* **30** 3943 *1965*, Levaillant *Ann Chim (Paris)* **6** 504 *1936*.] It is used for protecting NH_2 groups in peptide synthesis [Olofson et al. *Tetrahedron Lett* 1563 *1977*]. [*Beilstein* **3** III 28.]

Vinyl stearate *[111-63-7]* **M 310.5, m 35°, b 166°/1.5mm, 187-188°/4.3mm, d $_4^{40}$ 0.8517, n $_D^{40}$ 1.4423.** Distil the ester in a vacuum under nitrogen, then crystallise it from acetone (3ml/g) or ethyl acetate at 0°. Store it under nitrogen in the dark. [Swern & Jordan *J Am Chem Soc* **70** 2338 *1948*, Swern & Jordan *Org Synth* **30** 108 *1950*, *Beilstein* **2** III 1019.]

ALICYCLIC COMPOUNDS

Abietic acid *[514-10-3]* **M 302.5**, **m 172-175°**, **$[\alpha]_D^{25}$ –116° (–106°)(c 1, EtOH), pK^{25} 5.27.** Crystallise it by dissolving 100g of acid in 95% EtOH (700ml), adding to H_2O (600ml) and cooling. Filter, dry it in a vacuum (over KOH or $CaSO_4$) and store it in an O_2-free atmosphere. It can also be purified *via* the anhydride, tritylabietate and the potassium, piperidine and brucine salts. λ_{max} : nm(log ε): 2343(4.3), 241(4.4), 2505(4.2), 235(4.34) and 240(4.36) in EtOH. [Harris & Sanderson *Org Synth* Coll Vol **IV** 1 *1963*, *J Am Chem Soc* **35** 3736 *1949*, Lambard & Frey *Bull Soc Chim Fr* 1194 *1948*, Buchbauer et al. *Monatsh Chem* **116** 1345 *1985*.] [*Beilstein* **9** IV 2175.]

***S*-Abscisic acid (Dormin)** *[21293-29-8]* **M 264.3, m 160-161°, 161-163° (sublimation), $[\alpha]_{287}$ +24,000°, $[\alpha]_{245}$ –69,000° (c 1-50µg/ml in acidified MeOH or EtOH), pK_{Est} ~3.9.** Crystallise the acid from CCl_4/petroleum ether, EtOH/hexane and sublime it at 120°. Also purify it by dissolving ~30g in 30ml of EtOAc, adding 100ml of hexane and allow to crystallise overnight (yield 8.4g), **m** 156-158°, 161-163°, $[\alpha]_D^{20}$ +426° (c 0.005M H_2SO_4 in MeOH). [Cornforth et al. *Nature (London)* **206** 715 *1965*, Soukemp et al. *Helv Chim Acta* **72** 361 *1989*.] The *RS-isomer* was purified on a Kieselgel F_{254} plate with toluene/EtOAc/AcOH (50:50:3) and has **m** 188-190° [Cornforth et al. *Aust J Chem* **45** 179 *1992*]. [*Beilstein* **17/3** V 13.]

Acetylcyclohexane (cyclohexyl methylketone) *[823-76-7]* **M 126.2, b 64°/11mm, 76.2-77°/25mm, d_4^{20} 0.9178, n_D^{20} 1.4519.** Dissolve acetylcyclohexane in Et_2O, shake it with H_2O, dry, evaporate and fractionate it under reduced pressure. [UV: Mariella & Raube *J Am Chem Soc* **74** 518 *1952*, enol content: Gero *J Org Chem* **19** 1960 *1954*.] The *semicarbazone* has **m** 174° and the *2,4-dinitrophenylhydrazone* has **m** 139-140° [Theus & Schinz *Helv Chim Acta* **39** 1290 *1956*].

2-Acetylcyclohexanone *[874-23-7]* **M 140.2, m –11°, b 62-64°/2.5mm, 95-98°/10mm, 111-112°/18mm, d_4^{20} 1.08, n_D^{20} 1.51.** Dissolve it in ligroin (b 30-60°), wash it with saturated aqueous $NaHCO_3$, dry over Drierite and fractionate in a vacuum. [Perfetti & Levine *J Am Chem Soc* **75** 626 *1953*, Manyik et al. *J Am Chem Soc* **75** 5030 *1953*, Eistert & Reiss *Chem Ber* **87** 108 *1954*.] It forms a *Cu salt* which crystallises in green leaflets from EtOH, **m** 162-163° [UV: McEntee & Pinder *J Chem Soc* 4419 *1957*].

2-Acetylcyclopentanone *[1670-46-8]* **M 126.2, b. 72-75°/8mm, 82-86°/12mm, 88°/18mm, d_4^{20} 1.043, n_D^{20} 1.490.** Dissolve the ketone in petroleum ether (b 30-60°), wash it with saturated aqueous $NaHCO_3$, dry over Drierite and fractionate in a vacuum. It gives a violet colour with ethanolic $FeCl_3$ and is only slowly hydrolysed by 10% aqueous KOH but rapidly on boiling to yield 6-oxoheptanoic acid. [Manyik et al. *J Am Chem Soc* **75** 5030 *1953*, Acheson *J Chem Soc* 4232 *1956*, UV: Martin & Frenelius *J Am Chem Soc* **81** 2342 *1959*.] It gives a gray green *Cu salt* from Et_2O/pentane, **m** 237-238° [House & Wasson *J Am Chem Soc* **79** 1488 *1957*].

2-Acetyl-5,5-dimethylcyclohexane-1,3-dione (2-acetyldimedone) *[1755-15-3]* **M 182.2, m 36°**, **36-40°**, **b 132-133°/20mm, 138°/23mm, pK ~4.5.** It can be purified by fractional distillation. *Alternatively*, convert it into the insoluble Cu salt in H_2O and recrystallise it from EtOH, **m ~260°**. The Cu salt is decomposed with N H_2SO_4, extracted into Et_2O, dried (Na_2SO_4), evaporated and distilled in a vacuum. The residual oil, which solidifies on cooling can be recrystallised from AcOH. It gives a red colour with Fe^{3+} ions. The *oxime* has **m 115°**(dec, from EtOH), and with concentrated NH_3 it forms the *mono-imide* which crystallises from H_2O in needles with **m 133°**. Its UV in EtOH has $\lambda_{max}(\varepsilon)$ 231(10,620) and 273(10,800)nm. It is used as a protecting group for primary amines. [Dieckmann & Stein *Chem Ber* **37** 3379 *1904*, Birch *J Chem Soc* 3026 *1951*, Crossley & Renouf *J Chem Soc* **101** 1529 *1912,* Nash et al. *Tetrahedron Lett* **37** 2625 *1996*, Kellam et al. *Tetrahedron Lett* **38** 4849 *1997*, *Beilstein* **7** H 860, **7** I 471, **7** IV 2756.]

4-Acetyl-1-methyl-1-cyclohexene *[6090-09-1]* **M 138.2, b 73-75°/7.5mm, 85-86°/13mm, 94-94.7°/20mm, 204.5-206°/747mm, d_4^{20} 1.0238, n_D^{20} 1.469.** Purify it by fractionation under reduced pressure *in vacuo*, and if it is almost pure it can be fractionated at atmospheric pressure, preferably in an inert atmosphere. It forms two *semicarbazones* one of which is more soluble in $*C_6H_6$, and both can be recrystallised from EtOH; the more

soluble has **m** 149º(151º), and the less soluble has **m** 172-175º(191º). The *4-nitrophenylhydrazone* has **m** 166-167º and the *2,4-dinitrophenylhydrazone* has **m** 114-115º. [Pfau & Plattner *Helv Chim Acta* **17** 129, 142 *1934*, Adler & Vogt *Justus Liebigs Ann Chem* **564** 109 *1949*.]

2-Acetyl-1-methyl-3,5-dioxo-1-methylcyclohexanecarboxylic acid (ADCC-linker) *[181486-37-3]* **M 212.2, m 95-99º**, **pK_{est} ~4.5.** It is prepared from 3,5-dioxo-1-methylcyclohexane-1-carboxylic acid methyl ester (obtained from 3,5-dimethoxybenzoic acid [119-52-8] *via* Birch reduction, methylation with MeI and treatment with aqueous HCl) by acetylation to 3-acetoxy-5-oxo-1-methylcyclohex-3,4-ene-1-carboxylic acid methyl ester, rearrangement (heating with DMAP) to 4-acetyl-3,5-dioxo-1-methylcyclohexane carboxylic acid methyl ester (93% yield) followed by hydrolysis (LiOH/THF/MeOH/H_2O) and H^+ ion-exchange purification to give the ADCC-linker as a crystalline solid. It should be stored at ~5º. After attaching to a solid support through the carboxy function (e.g. to amino-modified polystyrene beads), it is used for linking to primary amines (including α-amino-acid esters) *via* enamine formation of the 4-acetyl group for combinatorial synthesis. The linker is stable to acids such as CF_3CO_2H, bases such as piperidine or BTU, and uronium type coupling agents; and by treatment with 2% hydrazine in DMF, the primary amine is released quantitatively from the support. Its ^1H NMR (250MHz, Me_2SO) has δ at 1.25 (s, Me-C1(1)), 2.50 (s, MeCO-C(4)), 2.50-3.00 (m, 2H-C(3), 2H-C(5)), 17.80 (2H, enol OH and COOH). [Bannwarth et al. *Bioorg Med Chem Lett* **6** 1525 *1966*.]

Adamantane (tricyclo[3.3.1.$1^{3,7}$]-decane) *[281-23-2]* **M 136.2, m 269.6-270.8º (sublimes).** Crystallise adamantane from acetone or cyclohexane, and sublime it in a vacuum below its melting point [Butler et al. *J Chem Soc, Faraday Trans I* **82** 535 *1986*]. Adamantane is also purified by dissolving it in *n*-heptane (*ca* 10ml/g of adamantane) on a hot plate, adding activated charcoal (2g/100g of adamantane), and boiling for 30 minutes, filtering the hot solution through a filter paper, concentrating the filtrate until crystallisation just starts, adding one quarter of the original volume of *n*-heptane, and allowing to cool slowly over a period of hours. The supernatant is decanted off and the crystals are dried *in vacuo* at 25º. [Prelog & Seiwerth *Chem Ber* **74** 1769 *1941*, Schleyer et al. *Org Synth* Coll Vol **V** 16 *1973*, Walter et al. *J Am Chem Soc* **107** 793 *1985*.] [*Beilstein* **5** III 393, **5** IV 469.]

1-Adamantane acetic acid *[4942-47-6]* **M 194.3, m 136º, pK_{Est} ~4.8.** Dissolve the acid in hot N NaOH, treat with charcoal, filter and acidify. Collect the solid, wash it with H_2O, dry and recrystallise it from MeOH. [Stetter et al. *Chem Ber* **92** 1629 *1959*.] The *acid chloride* [2094-72-6] has **M** 168.7, **m** 51-54º, and **b** 135-136º/1mm. **LACHRYMATORY.**

1-Adamantane carboxylic acid *[828-51-3]* **M 180.3, m 175-176.5º, 177º, pK_{Est} ~4.9.** Possible impurities are trimethylacetic acid and C9 and C13 acids. Dissolve 15g of the acid in CCl_4 (300ml) and shake with 110ml of 15N aqueous NH_3 whereby the ammonium salt separates and is collected. Acid impurities form soluble ammonium salts. The salt is washed with cold Me_2CO (20ml) and suspended in H_2O (250mL). This is treated with 12N HCl and extracted with $CHCl_3$ (100ml). The dried (Na_2SO_4) extract is evaporated and the residue is recrystallised from a mixture of MeOH (30ml) and H_2O (*ca* 10ml) to give the pure acid (10-11g). [Koch & Haaf *Org Synth* Coll Vol **V** 20 *1973*.] It was also recrystallised from absolute EtOH and dried under vacuum at 100º.
Alternatively, the acid (5g) is refluxed for 2 hours with 15ml of MeOH and 2ml of 98% H_2SO_4 (cool when mixing this solution). Pour into 10 volumes of H_2O and extract with the minimum volume of $CHCl_3$ to give clear separation of phases. The extract is washed with H_2O, dried ($CaCl_2$) and distilled. The *methyl ester* is collected at 77-79º/1mm, **m** 38-39º. The ester is hydrolysed with the calculated amount of N KOH and refluxed until clear. Acidification with HCl provides the pure acid with 90% recovery. The *amide* crystallises from cyclohexane, **m** 189º. [Stetter et al. *Chem Ber* **92** 1629 *1959*.] [*Beilstein* **9** IV 253.]

1,3-Adamantane diamine dihydrochloride *[26562-81-2]* **M 239.2, m >310º, $pK_{Est(1)}$ ~8.1, $pK_{Est(2)}$ ~10.1.** Dissolve it in boiling conc HCl (400mg in 15ml) and evaporate to dryness. Dissolve it in absolute EtOH and add dry Et_2O to crystallise the *dihydrochloride*. [Stetter & Wulff *Chem Ber* **93** 1366 *1960*, *Beilstein* **13** III 27,]

1,3-Adamantane dicarboxylic acid *[39269-10-8]* **M 224.3, m 276º, 276-278º, 279º, $pK_{Est(1)}$ ~4.9. $pK_{Est(2)}$ 5.9.** Dissolve the acid in aqueous NaOH, treat with charcoal, filter and acidify with dilute HCl. It crystallises

from MeOH. [Stetter & Wulff *Chem Ber* **93** 1366 *1960*, *Beilstein* **9** III 4066, **9** IV 2997.]

1-Adamantane methylamine *[17768-41-1]* **M 165.3, b 83-85°/0.3mm, d $_4^{20}$ 0.93, pK$_{Est}$ ~10.2.** Dissolve the amine in Et_2O, dry over KOH and distil it. The *N-Tosyl* derivative has **m** 134-135° (from EtOH). [Stetter & Goebel *Chem Ber* **96** 550 *1963*.]

1-Adamantanol (1-hydroxyadamantane) *[768-95-6]* **M 152.4, m 288.5-290°.** If 2-adamantanol is a suspected impurity, then dissolve the substance (10g) in acetone (100ml) and add Jones's reagent [CrO_3 (10.3g) in H_2O (30ml)], then conc H_2SO_4 (8.7ml) is added dropwise (turns green in colour) until excess reagent is present (slight red colour). Stir overnight, decant the acetone solution from the Cr salts and adamantan-2-one, dry (Na_2SO_4) and evaporate to dryness. The residue (*ca* 7g) is chromatographed through Al_2O_3 (250g) and washed with 50% *benzene/petroleum ether (b 40-60°), then 100% Et_2O (to remove any adamantan-2-one present) and the 1-adamantanol is then eluted with 5% MeOH in Et_2O. The eluate is evaporated, and the residue is recrystallised from petroleum ether (b 30-60°) at –70°, **m** 287.2-288.5°. It also crystallises from MeOH and can be sublimed *in vacuo*. It has characteristic IR, with ν_{max} *at* 3640, 1114, 1086, 982 and 930 cm^{-1}. [Schleyer & Nicholas *J Am Chem Soc* **83** 182 *1961*.] [*Beilstein* **6** IV 391.]
Alternatively, if free from the 2-isomer, dissolve it in tetrahydrofuran, and dilute with H_2O to precipitate the alcohol. Collect, dry and sublime it in a vacuum at 130°. [Stetter et al. *Chem Ber* **92** 1629 *1959*.]

2-Adamantanol (2-hydroxyadamantane) *[700-57-2]* **M 152.4, m 296.2-297.7°.** It can be purified by chromatography as for the 1-isomer. It crystallises from cyclohexane and has characteristic IR with ν_{max} at 3600, 1053, 1029 and 992 cm^{-1} [Schleyer & Nicholas *J Am Chem Soc* **83** 182 *1961*].

2-Adamantanone *[700-58-3]* **M 150.2, m 256-258°(sublimes).** Purify 2-admantanone by repeated sublimation *in vacuo.* [Butler et al. *J Chem Soc, Faraday Trans II* **82** 535 *1986*.]

***N*-(1-Adamantyl)acetamide** *[880-52-4]* **M 193.3, m 149°.** Wash the amide well with H_2O, dry and recrystallise it from cyclohexane. *It is an* **irritant.** [Stetter et al. *Chem Ber* **92** 1629 *1959*.]

1-Adamantylamine (1-adamantanamine) *[768-94-5]* **M 151.2, m 160-190° (sealed tube), 180-192°, 208-210°, pK^{25} 10.58.** Dissolve the amine in Et_2O, dry it over KOH, evaporate and sublime it *in vacuo*. [Stetter et al. *Chem Ber* **93** 226 *1960*.]

1-Adamantylamine hydrochloride (Amantadine hydrochloride, Amazolone, Mantadan, Mantadix, Virofral) *[665-66-7]* **M 187.7, m >360° (dec), pK^{25} 10.58.** Dissolve the salt in dry EtOH, add a few drops of dry EtOH saturated with HCl gas, followed by dry Et_2O to crystallise the hydrochloride out. Dry the salt in a vacuum. Its solubility in H_2O is >5%; and it is soluble in EtOH but insoluble Et_2O. [Stetter et al. *Chem Ber* **93** 226 *1960*.] It is antiviral and anti-Parkinsonian agent [Kornhuber et al. *J Neural Transm* **46** (Suppl) 399 *1995*].

2-Adamantylamine hydrochloride *[10523-68-9]* **M 187.7, m >300°, pK$_{Est}$ ~10.4.** The *free amine* in Et_2O, liberated by the action of alkali in H_2O, is dried over KOH, filtered, evaporated and sublimed at 110°/12torr, **m** 230-236°. The base is dissolved in EtOH, sufficient ethanolic HCl is added dropwise and crystallised by the addition of Et_2O. Dry it *in vacuo*. [Stetter et al. *Justus Liebigs Ann Chem* **658** 151 *1962*].

1-Adamantyl bromide *[768-90-1]* **M 215.1, m 117-119°, 118°, 119.5-120°.** If coloured, dissolve it in CCl_4, wash with H_2O, treat with charcoal, dry ($CaCl_2$), filter and evaporate to dryness. Dissolve the residue in a small volume of MeOH and cool in a CO_2/trichloroethylene bath and collect the crystals. Sublime it at 90-100°/water pump vacuum. [Stetter et al. *Chem Ber* **92** 1629 *1959*, Schleyer & Nicholas *J Am Chem Soc* **83** 2700 *1961*, *Beilstein* **5** III 469.]

1-Adamantyl bromomethylketone *[5122-82-7]* **M 257.2, m 76-79°, 78-79°.** Dissolve the ketone in Et_2O, wash it with H_2O, dry ($MgSO_4$), evaporate and crystallise the residue from small volumes of MeOH. **LACHRYMATORY.** [Stetter & Rauscher *Chem Ber* **93** 2054 *1960*.]

1-Adamantyl chloride *[935-56-8]* **M 170.7, m 164.3-165.6°.** Crystallise the chloride from aqueous MeOH and sublime it at 100°/12torr. It also crystallises from MeOH at –70°. Do not keep in contact with MeOH for too long. [Stetter et al. *Chem Ber* **92** 1629 *1959*, Schleyer & Nicholas *J Am Chem Soc* **83** 2700 *1961*, *Beilstein* **5** IV 469.]

1-Adamantyl chloroformate *[5854-52-4]* **M 214.6, m 46-47°.** Crystallise it from petroleum ether (b 30-60°) at –20°. Also purify it as for 1-adamantyl fluoroformate below. Its IR has ν_{max} at 4.2, 5.6 and 8.4μ (2380, 1786 and 1190 cm^{-1}). [Haas et al. *J Am Chem Soc* **88** 1988 *1966*, *cf* Moroder et al. *Hoppe-Seyler's Z Physiol Chem* **357** 1647 *1976*.]

1-(1-Adamantyl)ethylamine hydrochloride (Rimantadine hydrochloride, Flumadine, Roflual) *[1501-84-4]* **M 215.8, m >300° , 373-375°(sealed tube), pK_{Est} ~10.4.** It is prepared by adding the oxime of 1-adamantyl methyl ketone (6 parts, see [1660-04-4] below) in dry THF (200 parts) to a cold suspension of excess of $LiAlH_4$ in Et_2O, refluxing for 1 hour, decomposing with cold brine, making strongly alkaline and extracting thoroughly with Et_2O. The dried (Na_2CO_3) extract, is filtered, concentrated, and saturated with dry HCl. The hydrochloride (~5.25 parts) is collected, dried and recrystallised as for 2-adamantylamine hydrochloride above. [US patent to du Pont de Nemours 1069563 (1969, Brit amended), *Chem Abstr* **75** 140372w *1971*.] It is an antiviral agent [Burkinskaya et al. *J Gen Virol* **60** 49 *1982*].

1-Adamantyl fluoride (1-fluoroadamantane) *[768-92-3]* **M 154.2, m 210-212°(dec, sealed tube), 259-260°(dec).** Dissolve it in Et_2O, dry over Na_2SO_4, evaporate to dryness and sublime the residue at 90-100°/12mm. Recrystallise the sublimate from MeOH, **m** 259-260°. To remove 1-hydroxyadamantane impurity, dissolve it in cyclohexane, cool for many hours, filter off the hydroxyadamantane, and evaporate to dryness, or by passage through an Al_2O_5 column in dry cyclohexane. Recrystallise the residue from petroleum ether at –77° and sublime it in vacuum, **m** 210-212°dec (sealed tube). [Bhandari & Pinock *Synthesis* 655 *1974*, NMR: Fort et al. *J Org Chem* **30** 789 *1965*.]

1-Adamantyl fluoroformate *[62087-82-5]* **M 198.2, m 31-32°.** Dissolve it in *n*-hexane (*ca* 10g in 150 ml) and keep at 0° for 24 hours. Any 1-adamantanol present will separate. Filter and evaporate to dryness. The crystalline residue has **m** 31-32° and is recrystallised from *n*-hexane (90g/500ml), (IR (KBr): ν_{max} 1242, 1824 and 2340 cm^{-1}). There should be no OH str band above 2500 cm^{-1}. [Moroder et al. *Hoppe-Seyler's Z Physiol Chem* **357** 1647 *1976*, *cf* Haas et al. *J Am Chem Soc* **88** 1988 *1966*.]

1-Adamantyl iodide (1-iodoadamantane) *[768-93-4]* **M 262.1, m 75.3-76.4°.** Dissolve the iodide in Et_2O, shake with aqueous $NaHSO_3$, aqueous K_2CO_3, and H_2O, dry (Na_2SO_4), evaporate and recrystallise it from MeOH at –70° (to avoid alcoholysis) to give white crystals. [Schleyer & Nicholas *J Am Chem Soc* **83** 2700 *1961*, lit **m** of 151-152.5° is incorrect.] Also purify by recrystallisation from petroleum ether (40-60°C) followed by rigorous drying and repeated sublimation. [*Beilstein* **5** IV 470.]

1-Adamantyl isocyanate *[4411-25-0]* **M 177.3, m 144-145°.** Recrystallise the isocyanate from *n*-hexane and sublime it. **Irritant.** [Stetter & Wulff *Chem Ber* **95** 2302 *1962*.]

1-Adamantyl isothiocyanate *[4411-26-1]* **M 193.3, m 168-169°.** Dissolve it in Et_2O, wash with H_2O, dry (Na_2SO_4), evaporate and sublime the residue in a vacuum at 140°, then recrystallise it from MeOH. **Irritant.** [Stetter & Wulff *Chem Ber* **95** 2302 *1962*.]

1-Adamantyl methyl ketone *[1660-04-4]* **M 178.3, m 53-55°, 54-55°.** The ketone is prepared by bubbling acetylene through a vigorously stirred solution of 1-adamantylbromide (1g, see [769-90-1]) in 96% H_2SO_4 (40ml) at 5° for 5 hours with evolution of HBr. The mixture is poured onto ice, extracted with Et_2O, the extract is dried (Na_2SO_4), filtered and evaporated to give an ~80% yield of ketone. This was purified *via* the *2,4-dinitrophenyl hydrazine derivative* (by passage of a solution through silica gel/*C_6H_6) which gave orange needles from AcOH/EtOH or EtOH with **m 221° (219-222°** and **220-222°** also reported). The *ketone* has an IR (KBr) peak at ν_{max} 1690 cm^{-1} (C=O); its ^{1}HNMR has τ at 7.96 (s, 3H), 7.90 and 8.30 (15H); and its MS has *m/z* at 178 (M^+). [Kell & McQuillin *J Chem Soc Perk I* 2100 *1972*, Sasaki et al. *Chem Commun* 780 *1968*.]

Alternatively, 1-(ethoxycarbonylmethylcarbonyl)adamantane [1-(EtOCOCH$_2$CO)-Ad), b 108-115°/0.06mm, prepared from 1-adamantylcarbonyl chloride and diethyl malonate] (~25g) was hydrolysed and decarboxylated by boiling in AcOH (50ml), H_2O (30ml) and concentrated H_2SO_4 (5.5ml) until evolution of CO_2 ceased, poured into ice-water (~300ml), the oily *ketone* solidified (94-96% yield), and was recrystallised from MeOH or aqueous MeOH. It sublimes at 40°/0.1mm. ***1-Adamantyl methyl ketone oxime***, **m 182-184°** (used for the preparation of *Rimantadine hydrochloride* see [1501-84-4] above) is obtained by shaking hydroxylamine hydrochloride (2.5g) and recrystallised NaOAc (4g) in H_2O (10ml) in a glass test tube, then warming to 40° and adding the *ketone* (2.5g), replacing the stopper and shaking vigorously for a few minutes. The crystalline oxime that soon separates is filtered off, washed with H_2O, and gives colourless plates in high yield upon recrystallising from aqueous dioxane. [Stetter & Rauscher *Chem Ber* **93** 2054 *1960*, see also Hála & Landa *Col Czech Chem Comm* **25** 2692 *1960*.]

***N*-(1-Adamantyl)urea** *[13072-69-0]* **M 194.2, m >250°(dec), 268-272°(dec).** Wash the urea with H_2O and dioxane and recrystallise it from EtOH. [Stetter & Wulff *Chem Ber* **95** 2302 *1962*.]

(–)-Alloaromadendrene *[25246-27-9]* **M 204.4, b 96°/2mm, 265-267°/atm, $[\alpha]_D^{25}$–22° (neat), d_4^{20} 0.923, n_D^{23} 1.501.** Fractionally distil it from Na. It has IR bands at 6.06 and 11.27μ due to C=CH$_2$. [Birch *J Chem Soc* 715 *1953*, *cf* Büchi et al. *J Am Chem Soc* **91** 6473 *1969*.]

***Cis*-(±)-(1-*RS*,2-*SR*-)-6-Amino-3-cyclohexene-1-carboxylic acid (*cis*-(±)-1,2,3,6-tetrahydroanthranilic acid)** *[54162-90-2]* **M 141.5, m 216-218°, $pK_{Est(1)}$ ~3.5, $pK_{Est(2)}$ ~10.2.** Purify the free amino-acid by dissolving it in H_2O and passing it through a Dowex 50W (acid form) column and eluting with 1M aqueous NH_4OH. The eluate is evaporated (*in vacuo*) and the residue is dissolved in H_2O. Me_2CO is added to turbidity, cooled at 0° and the colourless crystals of the amino-acid are collected and dried *in vacuo* [Bernáth et al. *Tetrahedron* **41** 1315 *1958*, *cf* Mazza & Crapetta *Gazzetta* **57** 297 *1927*]. In earlier work, it was recrystallised from aqueous EtOH and had reported melting points of 265-265° [Kricheldorf *Justus Liebigs Ann Chem* 1378 *1975*] and 269-271° [Marconi & Mazzochi *J Org Chem* **31** 1372 *1966*]. The *hydrochloride* [57266-56-5] M 177.6 has **m** 210-213° and the *methyl ester hydrochloride* [52766-61-2] has **m** 85-87° (from Et_2O). The *trans*-(±)-(1*RS*,2*RS*)-*amino-acid* [97945-19-2] crystallises from aqueous Me_2CO with **m** 267-269°. [*Beilstein* **14** II 203.]

α-Amyrin *[638-95-9]* **M 426.7, m 186°, 244°/0.8mm, $[\alpha]_D^{25}$ +85° (c 2, $CHCl_3$).** Purify it by acetylation to the acetate followed by hydrolysis and recrystallisation from aqueous MeOH or from EtOH. The *acetate* when crystallised from petroleum ether, *n*-heptane or $CHCl_3$/MeOH, and sublimed *in vacuo* has **m** 227° (225-226°) and $[\alpha]_D^{20}$ +76.4° (c 0.6, $CHCl_3$). [Bently et al. *J Chem Soc* 3672 *1953*, IR: Cole & Thornton *J Chem Soc* 1332 *1957*, Corey & Cantrall *J Am Chem Soc* **81** 1745 *1958*, *Beilstein* **6** III 2889, **6** IV 4191.]

ß-Amyrin *[508-04-3]* **M 426.7, m 197-197.5°, 204-205°, 260°/0.8mm, $[\alpha]_D^{23}$ +91° (c 0.9, $CHCl_3$).** Purify it through an Al_2O_3 column and elute with petroleum ether (40-60°) then Et_2O and recrystallise from petroleum ether or EtOH. The *acetate* crystallises from Ac_2O or petroleum ether and has **m** 242-143° and $[\alpha]_D^{20}$ +82.8° (c 0.81, $CHCl_3$) [Crow & Michael *Aust J Chem* **8** 133 *1955*, Barton et al. *J Chem Soc (C)* 1031 *1968*, *Beilstein* **6** III 1894, **6** IV 4195.]

1,1'-Azobis(cyclohexane carbonitrile) *[2094-98-6]* **M 244.3, m 114-114.5°, 114-115°, ε_{350nm} 16.0.** Purify the nitrile by dissolving it in boiling 95%EOH as rapidly as possible, cool overnight at 0°, filter, wash with a little EtOH and dry it in a vacuum desiccator over $CaCl_2$. Note that prolonged heating >80° causes decomposition. Recrystallise it from EtOH. It should be regarded as **potentially explosive**. It is a radical initiator. [Overberger et al. *Org Synth* Coll Vol **IV** 66 *1963*, *J Am Chem Soc* **71** 2661 *1949*, *Beilstein* **16** II 97.]

Bicyclohexyl *[92-51-3]* **M 166.3, b 238° (*cis-cis*), 217-219° (*trans-trans*).** Shake bicyclohexyl repeatedly with aqueous $KMnO_4$ and with conc H_2SO_4, wash it with water, dry, first with $CaCl_2$ then with sodium, and distil it. [Mackenzie *J Am Chem Soc* **77** 2214 *1955*, *Beilstein* **5** IV 334.]

Bicyclo[3.2.1]octane *[6221-55-2]* **M 110.2, m 141°.** Purify it by zone melting. It has been sublimed under N_2

at 70° and atmospheric pressure (closed vessel), and resublimed over P_2O_5 to give an analytically pure sample **m** 137.5-139.5°. [Von E Doering & Farber *J Am Chem Soc* **71** 1514 *1949*, Cope et al. *J Am Chem Soc* **82** 4299 *1960*, NMR: Stothers et al. *Can J Chem* **55** 841 *1977*.]

***1R*-2-*endo*-Borneol** *[464-43-7]* **M 154.3, m 204.5-205.5°, 208°, 212°/atm, $[\alpha]_D^{20}$ +37° (c 5, EtOH).** It can be steam distilled, the distillate is extracted into Et_2O, the extract dried with Drierite, filtered and evaporated. The residue is then recrystallised from boiling EtOH (charcoal) or petroleum ether. [Clark & Read *J Chem Soc* 1773 *1934*, *Beilstein* **6** III 295, **6** IV 281.]

(±)-Borneol *[6627-72-1]* **M 154.3, m 206-207°, 210-215°.** Crystallise borneol from petroleum ether (b 60-80°) and sublime it *in vacuo*. [*Beilstein* **6** II 81, **6** IV 281.]

3-Bromoadamantane-1-carboxylic acid *[21816-08-0]* **M 259.1, m 145-146°, 146.5°, 147-150°, pK^{25} 6.28 (50% aqueous EtOH).** Purify the acid by recrystallising it from cyclohexane and/or subliming at 130°/10mm. It can be converted to the *methyl ester* (diazomethane) with **m** 32° (from petroleum ether at –10°). [Stetter & Mayer *Chem Ber* **95** 667 *1962*, Stetter & Wulff *Chem Ber* **93** 1366 *1960*, Bayal & Lantvoev *J Org Chem USSR (Engl Trans)* **9** 291 *1973*.]

(+)-3-Bromocamphor-8-sulfonic acid *[5344-58-1]* **M 311.2, m 195-196°(anhydrous), $[\alpha]_D^{20}$ +88.3° (c 1, H_2O), pK ~0.** Crystallise the acid from water. The *ammonium salt* has **m** 268-207°, $[\alpha]_D^{20}$ +81.9° (c 2.2, H_2O). [Kauffman *J Prakt Chem* **33** 95 *1966*.]

***1R(endo, anti)*-3-Bromocamphor-8-sulfonic acid ammonium salt,** see entry [55870-50-3] on p. 504.

(+)-3-Bromocamphor-10-sulfonic acid hydrate *[67999-30-8]* **M 329.2, m 119-121°, $[\alpha]_D^{20}$ +98.3° (c 1, H_2O), pK ~0.** Crystallise the acid from water. [Boyle *Quart Rev Chem Soc* **25** 323 *1971*, UV: Lowry & Owen *J Chem Soc* 609 1926, *Beilstein* **11** II 181, **11** III 592.]

4-*tert*-Butyl-1-cyclohexanone *[98-53-3]* **M 154.3, m 49-50°, 52-52.5, b 90-92°/9mm.** Purify it *via* the *semicarbazone* (crystallised from EtOH with **m** 203-205°), hydrolyse this with dilute HCl and steam distil it. The distillate is extracted into Et_2O, dried, evaporated and the residue is recrystallised from pentane, aqueous EtOH or EtOH [Houlihan *J Org Chem* **27** 3860 *1962*]. The *oxime* recrystallises from 1,2-dichloropropane and has **m** 137.5-138.5°. [Harvill et al. *J Org Chem* **15** 58 1950, *Beilstein* **7** IV 82.]

(+)-Calarene [(+)-β-gurjunen, 1,3,3,11-tetramethyltricyclo[5.4.0.$0^{2,4}$]undecan-7-ene, (1a*R*)-1,1,7c,7ac-tetramethyl-1a,2,3,5,6,7,7a,7b-octahydro-1*H*-cyclopropa[α]naphthalene, new name 1(10)aristolene)] *[17334-55-3]* **M 204.35, b 45-47°/0.008-0.01mm, 255-258°/atm, d_4^{20} 0.9340, n_D^{20} 1.55051, $[\alpha]_D^{20}$ +73° (c 2, EtOH), +81.8° (neat).** Purify the sesquiterpene Calarene by gas chromatography (7% propylene glycol adipate on unglazed tile particles of size 0.2-0.3mm, 400 cm column length and 0.6 cm diameter, at 184°, with N_2 carrier gas at a flow rate of 0.54 ml/sec using a thermal detector). Also purify it by chromatography on alumina (200 times the weight of calarene) and elute with petroleum ether. Its UV has λ_{max} at 200 and 210 nm (ε 9560, 5480) in EtOH. [IR: Sorm *Col Czech Chem Comm* **18** 512 *1953*, **29** 795 *1964*, Buchi et al. *Tetrahedron Lett* **3** 827 *1962*, Vrkoc *Tetrahedron Lett* **4** 225 *1963*, *Beilstein* **5** III 1093.]

1*R*,4*S*-(–)-Camphanic acid *[13429-83-9]* **M 198.2, m 190-192°, 198-200°, $[\alpha]_{548}^{20}$ –22.5° (c 1, dioxane), -4.4° (c 8, EtOH), pK_{Est} ~3.8.** Dissolve it in CH_2Cl_2, dry ($MgSO_4$), filter, evaporate and the residue is sublimed at 120°/0.5mm or 140°/1mm. [Gerlach *Helv Chim Acta* **61** 2773 *1978*, *Beilstein* **18/8** V 101.]

1*R*,4*S*-(–)-Camphanic acid chloride *[39637-74-6]* **M 216.7, m 65-66.5°, 70.5-71°, $[\alpha]_{548}$ –23° (c 2, CCl_4), $[\alpha]_{364}^{20}$ –29.2°, $[\alpha]_{405}^{20}$ –18.0°, $[\alpha]_{436}^{20}$ –13.5°, $[\alpha]_{546}^{20}$ –7.8°, $[\alpha]_{578}^{20}$ –6.0°, (c 0.67, *C_6H_6).** It is soluble in toluene (50g/100ml at 0°) and crystallises from petroleum ether (b 40-60°). It sublimes at 70°/5mm. Store it dry at 0°, IR (CCl_4) has ν_{max} at 1805s and 1780m cm^{-1}. [Armarego et al. *J Chem Soc, Perkin Trans I* 2229 *1976*, Gerlach *Helv Chim Acta* **51** 1587 *1968*, Gerlach *Helv Chim Acta* **68** 1815 *1985*, *Beilstein* **18/8** V 101.]

***RS*-Camphene** *[565-00-4]* **M 136.2, m 51-52°, b 40-70°/10mm.** Crystallised it twice from EtOH, then repeatedly melted and frozen at 30mm pressure. [Williams & Smyth *J Am Chem Soc* **84** 1808 *1962*.] *Alternatively*, it is dissolved in Et_2O, dried over $CaCl_2$ and Na, filtered, evaporated and the residue is sublimed in a vacuum [NMR: Hana & Koch *Chem Ber* **111** 2527 *1978*].

(–)-Camphene (1*S*-2,2-dimethyl-3-methylene norbornane) *[5794-04-7]* **M 136.2, m 49.2-49.6°, 49-50°, b 79-80°/58mm, 91.5°/100mm, d_4^{54} 0.8412, n_D^{54} 1.4564, $[\alpha]_D^{21}$ -119.1° (c 2.3, *C_6H_6), -117.5° (c 19, toluene), –113.5° (c 9.7, Et_2O).** Purify the norbornane by fractionation through a Stedman column (see p. 11) at 100mm in a N_2 atmosphere, crystallise it from EtOH and sublime it in a vacuum below its melting point. It is characterised by its *camphenilone semicarbazone*, **m** 217-218.5°, or *camphor semicarbazone*, **m** 236-238°. [NMR: Hana & Koch *Chem Ber* **111** 2527 *1978*, Bartlett et al. *Justus Liebigs Ann Chem* **623** 217 *1959*, Bain et al. *J Am Chem Soc* **72** 3124 *1950*, *Beilstein* **5** IV 461.]

Camphor (1*R*-bornan-2-one) *[R-(+)- 464-49-3, S-(–)- 464-48-2]* **M 136.2, m 178.8°, 179.97° (open capillary), b 204°/atm, $[\alpha]_{546}^{35}$ (+) and (–) 59.6° (in EtOH), $[\alpha]_D^{20}$ (+) and (–) 44.3° (c 10, EtOH), $[\alpha]_{579}^{179}$ (+) and (–) 70.85°(melt).** Crystallise it from EtOH, 50% EtOH/water, MeOH, or petroleum ether or from glacial acetic acid by addition of water. It can be sublimed (50°/14mm) and also fractionally crystallised from its own melt. It is steam volatile. It should be stored in tight containers as it is appreciably volatile at room temperature. The solubility is 0.1% (H_2O), 100% (EtOH), 173% (Et_2O) and 300% ($CHCl_3$). The *R-oxime* (from Et_2O, $CHCl_3$, or aqueous EtOH) has **m** 119° $[\alpha]_D^{20}$ –42.4° (c 3, EtOH), the ± *oxime* has **m** 118-119°. It has a characteristic odour. [Asahina & Ishidate *Chem Ber* **67** 1432 *1934*, Allan & Rodgers *J Chem Soc (B)* 632 *1971*, UV, NMR: Fairley et al. *J Chem Soc, Perkin Trans 1* 2109 *1973*, White & Bishop *J Am Chem Soc* **62** 8 *1940*, *Beilstein* **7** IV 213.]

Camphoric acid (1,2,2-trimethylcyclopentan-1*r*,3*c*-dicarboxylic acid) *[1R,2S)-(+)- 124-83-4, 1S,2R)-(–)- 560-09-8]* **M 200.2, m 186-188°, 187°, 186.5-189°, $[\alpha]_{546}^{20}$ (+) and (–) 57° (c 1, EtOH), $[\alpha]_D^{20}$ (+) and (–) 47.7° (c 4, EtOH) , pK_1^{25} 4.71, pK_2^{25} 5.83 (for + isomer).** Purify the acid by re-precipitation from an alkaline solution by HCl, filter it off, and recrystallise it from water several times, rejecting the first crop. It forms leaflets from EtOH, Me_2CO and H_2O, and is insoluble in $CHCl_3$. Its solubility in H_2O is 0.8% at 25° and 10% at 100°, 50% in EtOH and 5% in ethylene glycol. The *(±)-acid* has **m** 202-203°. The *(+)-1-methyl ester* has **m** 86° (from petroleum ether) $[\alpha]_D^{20}$ +45° (c 4, EtOH), and the *(+)-3-methyl ester* has **m** 77° (from petroleum ether) $[\alpha]_D^{17.5}$ +53.9° (c 3, EtOH). [Rupe & Thommen *Helv Chim Acta* **30** 933 *1947*, Tiovonan et al. *Acta Chem Scand* **2** 597 *1948*, Howell & Fisher *J Am Chem Soc* **80** 6316 *1958*, *Beilstein* **9** IV 2851.]

(±)-Camphoric anhydride *[595-30-2, 76-32-4]* **M 182.2, transition temp. 135°, m 223.5°.** Crystallise the anhydride from EtOH. If it contains too much of the acid (check the IR), then reflux it in Ac_2O, concentrate and collect the crystals, wash them with petroleum ether and dry them *in vacuo*. [Bunton et al *J Chem Soc* 2918 *1963*, NMR: Baker & Davis *Tetrahedron* **24** 1663 *1968*, *Beilstein* **18** H 400, 401.]

Camphorquinone (borna-2,3-dione) *[1R-(–)- 10334-26-6, 1S-(+)- 2767-84-2]* **M 166.2, m 198.7°, 198-199°, 197-201°, $[\alpha]_D^{25}$ (–) and (+) 101.1° (c 2, EtOH).** It can be purified by steam distillation, recrystallisation (yellow prisms) from EtOH, *C_6H_6 or Et_2O/petoleum ether and it can be sublimed in a vacuum. The *(±)-quinone* forms needles from EtOH, **m** 197-198°, 203°. [Buxtorf & Flatt *Helv Chim Acta* **13** 1026 *1930*, Asahena et al. *Chem Ber* **67** 1432 *1934*, *Beiltein* **7** I 325.]

***RS*-Camphorquinone** *[10373-78-1]* **M 166.2, m 199-202°.** Purification is the same as for above enantiomers. [Huckel & Fichtig *Justus Liebigs Ann Chem* **628** 81 *1962*, Evans et al. *J Chem Soc* 137 *1939*, *Beilstein* **7** I 325.]

(*1R*)-(–)Camphor-10-sulfonic acid *[35963-20-3]* **M 232.3, m 197.4-198°(dec), 197-198°, $[\alpha]_D^{20}$ –20.7° (c 5.4, H_2O), pK_{Est} ~ –1.** It forms prisms from AcOH or EtOAc, and is deliquescent in moist air. Store it in tightly stoppered bottles. The *NH_4 salt* forms needles from H_2O $[\alpha]_D^{16}$ ±20.5° (c 5, H_2O)**.** [Burgess & Lowry *J Chem Soc* **127** 279 *1925*, Marsi et al. *J Am Chem Soc* **78** 3063 *1956*.] The *RS-acid* recrystallises from AcOH. [60g of (±)-acid in 60ml of AcOH at 105° gave 40g of crystals has **m** 202-203°]. [Bartlett & Knox *Org Synth* **45** 12 *1965*, *Beilstein* **11** IV 642.]

(*1S*)-(+)Camphor-10-sulfonic acid *[3144-16-9]* **M 232.3, m 193°(dec), 197-198°, $[\alpha]_{546}^{20}$ +27.5° (c 10, H_2O), $[\alpha]_D^{20}$ +43.5° (c 4.3, EtOH), pK_{Est} ~ –1.** Crystallise the acid from ethyl acetate and dry it under vacuum (deliquescent). [Loudon *J Chem Soc* 823 *1933*, Komppa *J Prakt Chem* **162** 19 *1943*, *Beilstein* **11** IV 642.] See above for *RS*-isomer.

Camphor-10-sulfonyl chloride *[1S-(+)- 21286-54-4, 1R-(–)- 39262-22-1]* **M 250.7, m 67-68°, 70°, $[\alpha]_D^{20}$ (+) and (–) 32.2° (c 3, $CHCl_3$).** If free from OH bands in the IR, then recrystallise it from Et_2O or petroleum ether; otherwise treat it with $SOCl_2$ at 50° for 30 minutes, evaporate, dry the residue over KOH in a vacuum and recrystallise it. The *(±)-acid chloride* has **m** 85° [Bartlett & Knox *Org Synth* **45** 14 *1965*]. It is characterised as the *amide* (prisms from EtOH) **m** 132°, $[\alpha]_D^{17}$ (+) and (–) 1.5° (EtOH). On repeated recrystallisation from EtOH the *anilide* has **m** 120.5-121°, $[\alpha]_D^{25}$ +76° (c 1, $CHCl_3$). [Read & Storey *J Chem Soc* 2761 *1930*, Sutherland & Shriner *J Am Chem Soc* **58** 62 *1936*, Halterman et al. *J Am Chem Soc* **109** 8105 *1987*, Bartlett & Knox *Org Synth* **45** 55 *1945*, *Beilstein* **11** IV 650.]

2,10-Camphorsultam *[1R-(+)- 108448-77-7, 1S-(–)- 94594-90-8]* **M 215.3, m 181-183°, 183-184 185-187°, $[\alpha]_D^{20}$ (+) and (–) 32° (c 5, $CHCl_3$).** The (–)-enantiomer is recrystallised from 95% EtOH and dried in a vacuum desiccator. It dissolves in dilute aqueous NaOH and can be precipitated without hydrolysis by acidifying. It forms the *N*-Na salt in EtOH (by addition of Na to the EtOH solution), and the salt can be methylated with MeI to give the (–)-*N-Me lactam* with **m** 80° after recrystallisation from hot H_2O, and has $[\alpha]_D^{25}$ –59.6° (c 5, $CHCl_3$) [Shriner et al. *J Am Chem Soc* **60** 2794 *1938*]. [Oppolzer et al. *Helv Chim Acta* **69** 1142 *1986*, Weismiller et al. *Org Synth* **69** 154 *1955*, *Beilstein* **27** III/IV 1007.]

4-Carboethoxy-3-methyl-2-cyclohexen-1-one (Hagemann's ester) *[487-51-4]* **M 182, b 79-80°/0.2mm, 121-123°/4mm, 142-144°/15mm, n_D^{20} 1.488, d_4^{20} 1.038.** Dissolve the ester in ether, shake with solid K_2CO_3, aqueous saturated $NaHCO_3$, brine, dry ($MgSO_4$) and distil it. The *semicarbazone* has **m** 165-167° (169°). [Smith & Rouault *J Am Chem Soc* **65** 631 *1943*, *Beilstein* **10** H 631, **10** I 300, **10** III 2899, **10** IV 2666.]

(–)-Caryophyllene oxide (1-*S*-5*c*-6*t*-epoxy-6*c*,10,10-trimethyl-2-methylene-1*r*,9*t*-bicyclo[7.2.0]undecane) *[1139-30-6]* **M 220.4, m 62-63°, 63.5-64°, 64°, b 114-117°/1.8mm, 141-142°/11mm, d_4^{20} 0.967, n_D^{20} 1.4956, $[\alpha]_D^{20}$ –79° (c 2, $CHCl_3$), $[\alpha]_D^{20}$ –68° (supercooled melt).** Purify the oxide by TLC on silica gel with EtOAc/petroleum ether (b 60-80°) (15:85), and recrystallise it from MeOH or $*C_6H_6$. [NMR: Warnhoff *Can J Chem* **42** 1664 *1964*, Ramage & Whitehead *J Chem Soc* 4336 *1954*, *Beilstein* **17** IV 392.]

(+)-Cedrol [octahydro-3,6,8,8-tetramethyl-1-3a,7-methanoazulen-6-ol, 8a*S*-6*c*-hydroxy-3*c*,6*t*,8,8-tetramethyl(8a*r*-*H*)-octahydro-3*H*,3a*t*,7*t*-methanoazulene], *[77-53-2]* **m 82-86°, 86-87°, $[\alpha]_D^{28}$ +10.5° (c 5, $CHCl_3$), $[\alpha]_D^{18}$ +13.1° (c 5.5, EtOH), $[\alpha]_D^{18}$ +14.3° (c 10, dioxane).** Purify cedrol by recrystallisation from aqueous MeOH. It is estimated colorimetrically with H_3PO_4 in EtOH followed by vanillin and HCl [Hayward & Seymour *Anal Chem* **20** 572 *1948*]. The *3,5-dinitrobenzoyl* derivative has **m** 92-93°. [Stork & Clarke *J Am Chem Soc* **83** 3114 *1961, Beilstein* **6** III 424.]

Chaulmoogric acid [(13-cyclopent-2-enylyl)tridecanoic acid] *[29106-32-9]* **M 280.4, m 68.5°, b 247-248°/20mm, $[\alpha]_D^{20}$ +60° (c 4, $CHCl_3$), pK_{Est} ~5.0.** Crystallise the acid from petroleum ether or EtOH. The *Me ester [24828-59-9]* has **m** 22°, **b** 227°/20mm and $[\alpha]_D^{15}$ +50° (c 5, $CHCl_3$). [Mislow & Steinberg *J Am Chem Soc* **77** 3807 *1955*.]

Chlorendic anhydride (1,4,5,6,7,7-hexachloro-5-norbornene-2,3-dicarboxylic anhydride) *[115-27-5]* **M 370.9, m 234-236°. 235-237°, 238°.** Steam distil the anhydride or recrystallise it from H_2O to yield pure diacid. The pure diacid yields the anhydride with Ac_2O. [Prill *J Am Chem Soc* **69** 62 *1947*.]

Chlorocyclohexane (cyclohexyl chloride) *[542-18-7]* **M 118.6, b 46-48°/26mm, 142.5°/atm, d_4^{20} 1.00, n_D^{25} 1.46265.** It has been prepared using the general procedure of Norris and coworkers by refluxing the alcohol with 5 volumes of "constant boiling HCl" for 2-4 hours [Norris et al. *J Am Chem Soc* **38** 1071 (1077) *1916*]. It has also been prepared in 76% yield by the "$CaCl_2$" procedure described for chlorocyclopentane (see below

[930-28-9]). Wash the chlorocyclohexane several times with dilute $NaHCO_3$, then repeatedly with distilled water. Dry it with $CaCl_2$ and fractionally distil it slowly at atmospheric pressure or better under vacuum. [Perlman et al. *J Org Chem* **1** 288 (294) *1936*, IR: Roberts & Chambers *J Am Chem Soc* **73** 5031 1951, *Beilstein* **5** H 21, **5** I 8, **5** II 11, **5** III 37, **5** IV 48.]

2-Chlorocyclohexanone *[822-87-7]* **M 132.6, m 23°, b 82-83°/10mm, 98-99°/14-15mm, d^{25} 1.161, n_D^{20} 1.484.** The chlorocyclohexanone is prepared in a well ventilated fume cupboard by bubbling chlorine (215g, ~3moles, use mercury traps) rapidly through a mixture of cyclohexanone (284g, 3moles) and H_2O (900ml) while being stirred in an ice bath at a reaction temperature between 20° and 50°. After about 45 minutes all the chlorocyclohexanone separates as a heavy oil which is combined with the Et_2O (3 x 150ml) extract of the upper aqueous layer, washed with H_2O (150ml), saturated aqueous NaCl (200ml), filtered (by gravity) through anhydrous Na_2SO_4, the solvent is evaporated, the residue is distilled in a Claisen flask, and the fraction boiling below 110° (300-340g, b 110°/13mm, 92°/4mm) is collected. This is then carefully fractionated through a heated 42-inch Vigreux column with a variable take-off head to give pure *2-chlorocyclohexanone* (240-265g, 61-66%, **b 90-91°/14-15mm**) with 5-13% recovery of cyclohexanone b 52°/14-15mm. [Newman et al. *Org Synth* Coll Vol **3** 188 *1855*, *Beilstein* **7** H 10, **7** I 8, **7** II 11, **7** III 36, **7** IV 32.]

Chlorocyclopentane (cyclopentyl chloride) *[930-28-9]* **M 104.6, b 113-115°/atm, 114°/atm, d_4^{20} 1.005, n_D^{20} 1.4512.** It is prepared by mixing cyclopentanol (43g) with concentrated HCl (125ml) and anhydrous $CaCl_2$ (50g), and stirring under reflux on a steam bath for 10 hours. [As HCl gas evolves continuously, the reaction should be carried out in an sufficient fume cupboard.] After cooling, the upper layer is collected, washed wih brine, saturated aqueous $NaHCO_3$ (CARE, as evolution of CO_2 will occur), brine again and dried over anhydrous $CaCl_2$ for at least 24 hours. Filter off the solid and fractionate through an efficient column at atmospheric pressure to obtain a ~ 58% yield of *cyclopentyl chloride* (30g). Bubbling dry HCl gas through the reaction mixture does not appear to increase the yield. See preparation and purification of chlorocyclohexane above. [*Beilstein* **5** IV 18.]

(–)-α-Copaene (*1R,2S,6S,7S,8S*-8-isopropyl-1,3-dimethyltricyclo[4.4.0.$0^{2,7}$]dec-3-ene) *[3856-25-5]* **M 204.4, b 119-120°/10mm, 246-251°, d_4^{20} 0.908, n_D^{20} 1.489, $[\alpha]_D^{20}$ –6.3° (c 1.2, $CHCl_3$).** Purify it by distillation, preferably under vacuum. [Heathcock *J Am Chem Soc* **88** 4110 *1966*, Heathcock et al. *J Am Chem Soc* **89** 4133 *1967*, Corey & Watt *J Am Chem Soc* **95** 2303 *1973*, *Beilstein* **5** IV 1189.]

Cyclobutane *[287-23-0]* **M 56.1, m -50°, –80°, b 13°/740mm, 12°/atm, d_4^{20} 0.721, n_D^{20} 1.426.** This easily liquefiable gas is dried over Na at melting ice temperature for 4 days and distilled at low temperature through a Podbielniak precision still. A dry sample has been prepared by passage through P_2O_5 and distilled repeatedly until all fractions had similar vapour pressures at 0°. [Cansson & Wat *J Org Chem* **14** 31 *1949*, Heisig *J Am Chem Soc* **63** 1698 *1941*, Stodola & Heisig *Org Synth* Coll Vol **III** 213 *1955*.]

Cyclobutane carboxylic acid *[3721-95-7]* **M 100.1, m 3-4°, –5.4°, b 84-84.5°/10mm, 110°/25mm, 135-138°/110mm, 194°/760mm, d_4^{20} 1.061, n_D^{20} 1.453, pK^{25} 4.79.** Dissolve the acid in aqueous HCO_3^- then acidify with HCl and extract it into Et_2O, wash with H_2O, dry (Na_2SO_4), concentrate to a small volume, then distil it through a glass helices packed column. The S-*benzylisothiuronium salt* has **m** 176° (from EtOH), the *anilide* has **m** 112.5-113°, and the *p-toluide* has **m** 123°. [Payne & Smith *J Org Chem* **22** 1680 *1957*, Kantaro & Gunning *J Am Chem Soc* **73** 480 *1951*, Stodola & Heisig *Org Synth* Coll Vol **III** 213 *1955*, *Beilstein* **9** H 5.]

(±)-*trans*-Cyclobutane-1,2-dicarboxylic acid *[1124-13-6]* **M 144.1, m 131°, pK_1^{25} 4.11 (pK_1^{20} 3.77), pK_2^{25} 5.15 (pK_2^{20} 5.63).** Crystallise the acid from $*C_6H_6$ or $*C_6H_6$/EtOAc. The *diphenacyl ester* has **m** 98° (from EtOH) and the *p-bromodiphenacyl ester* has **m** 158° (from EtOH). The *cis*-acid isomerises to the *trans*-acid on heating in conc HCl at 190°. [Reed *J Chem Soc* 685 *1951*, Fison et al. *J Am Chem Soc* **51** 1536 *1929*, Fison et al. *J Am Chem Soc* **56** 1774 *1934*, pK: Bode *Chem Ber* **67** 332 *1934*, *Beilstein* **9** IV 2788.]

***cis*-Cyclobutane-1,2-dicarboxylic acid** *[1461-94-5]* **M 144.1, m 139.5°, 139-140°, pK_1^{20} 4.20, pK_2^{20} 6.56.** Purify the acid by crystallisation from H_2O or ligroin, or by hydrolysis of the *anhydride* [**b** 120-150°/40mm, **m** 77-77.5° (from $*C_6H_6$, 74-75° from H_2O or ligroin)] with H_2O. The *diphenacyl ester* has **m** 113° (from EtOH)

and the *p-bromodiphenacyl ester* has **m** 153° (from EtOH/Me_2CO). [Vogel *Justus Liebigs Ann Chem* **615** 13 *1958*, Reed *J Chem Soc* 685 *1951*, Fison et al. *J Am Chem Soc* **56** 1774 *1934*, pK: Bode *Chem Ber* **67** 332 *1934*, *Beilstein* **9** IV 2788.]

Cyclobutanone *[1191-95-3]* **M 70.1, b 96-97°, 99-100°/atm, d_4^{20} 0.931, n_D^{20} 1.4210, n_D^{52} 1.4189.** Treat cyclobutanone with dilute aqueous $KMnO_4$, dry it with molecular sieves and fractionally distil it. Purify it *via* the semicarbazone, then regenerate the ketone, dry it ($CaSO_4$), and distil it in a stainless steel spinning-band (or Vigreux column. *Alternatively*, purify it by preparative gas chromatography using a Carbowax 20-M column at 80°. (This treatment also removes acetone). It has FT-IR (NaCl) with ν_{max} at 3543.3, 2970.3 (CH), 1783.2 (C=O), 1392.5 (OH enol ?), 1208.9, 1136.4, 1080.8, 724.9, and 461.4 cm^{-1}; ^1H NMR (60MHz, $CDCl_3$, TMS) with δ at 2.01 (q, 2H, C-3 methylene), 3.09 (t, 4H, C-2 and C-4 methylenes); ^{13}C NMR (15MHz, $CDCl_3$, TMS) with δ at 9.74 (C-3), 47.73 (C-2,4) and 208.90 (C-1). The *oxime* has **m** 84-85° (from petroleum ether) and the *semicarbazone* has **m** 212-212-5° (220-221° from MeOH or H_2O, Buchanan et al. *J Am Chem Soc* **64** 2701 *1942*). [Salaun *Org Synth* **57** 36 *1977*, Fitzer & Quabeck *Synthesis* 299 1987, *Beilstein* **7** IV 3.]

Cyclobutylamine *[2516-34-9]* **M 71.1, b 82-83°/atm, 83.2-84.2°/760mm, d_4^{20} 0.839, n_D^{20} 1.437, pK^{25} 10.04 (9.34 in 50% aqueous EtOH).** It has been purified by steam distillation. The aqueous distillate (e.g. 2L) is acidified with 3N HCl (90ml) and evaporated to dryness in a vacuum. The *hydrochloride* is treated with a few ml of H_2O, cooled in ice and a slush of KOH pellets ground in a little H_2O is added slowly in portions and keeping the solution very cold. The amine separates as an oil from the strongly alkaline solution. The oil is collected, dried over solid KOH and distilled using a vacuum jacketed Vigreux column and protected from CO_2 using a soda lime tube. The fraction boiling at 79-83° is collected, dried over solid KOH for 2 days and redistilled over a few pellets of KOH (**b** 80.5-81.5°). Best distil in a dry N_2 atmosphere. The purity can be checked by GLC using a polyethylene glycol on Teflon column at 72°, 15 psi, flow rate of 102 ml/min of He. The sample can appear homogeneous but because of tailing it is not possible to tell if H_2O is present. The NMR in CCl_4 should show no signals less than 1 ppm from TMS. The *hydrochloride* has a multiplet at *ca* 1.5-2.6ppm (H 2,2,4,3,3,4,4), a quintet at 3.8 ppm (H 1) and a singlet at 4.75 for NH_2 [Roberts & Chambers *J Am Chem Soc* **73** 2509 *1951*]. The *benzenesulfonamide* has **m** 85-86° (from aqueous MeOH) and the *benzoyl* derivative has **m** 120.6-121.6°. [Roberts & Mazur *J Am Chem Soc* **73** 2509 *1951*, Iffland et al. *J Am Chem Soc* **75** 4044 *1953*, Werner & Casanova Jr *Org* Synth Coll Vol **V** 273 *1973*, *Beilstein* **12** IV 3.]

Cyclodecanone *[1502-06-3]* **M 154.2, m 21-24°, b 100-102°/12mm.** Purify the ketone *via* the *semicarbazone* (**m** 205-207°, from EtOH) and distil it through an efficient column. It sublimes in a vacuum. The *oxime* has **m** 80°, from MeOH or by sublimation in a high vacuum. [Cope et al. *Org Synth* Coll Vol **IV** 218 *1963*, Prelog et al. *Helv Chim Acta* **30** 1746 *1947*, Ruzicka et al. *Helv Chim Acta* **11** 675 1930, *Beilstein* **7** III 134, **7** IV 76.]

***cis*-Cyclodecene** *[935-31-9]* **M 138.3, m –3°, –1°, b 73°/15mm, 90.3°/33mm, 194-195°/740mm, 197-199°/atm, d_4^{20} 0.8770, n_D^{20} 1.4854.** Purify it by fractional distillation. It forms an $AgNO_3$ complex which crystallises from MeOH, **m** 167-187° [Cope et al. *J Am Chem Soc* **77** 1628 *1955*, IR: Blomqvist et al. *J Am Chem Soc* **74** 3636 *1952*, Prelog et al. *Helv Chim Acta* **35** 1598 *1952*].

***cis-cis-trans*-1,5,9-Cyclododecatriene (cyclododec-1c,5c,9t-triene)** *[2765-29-9]* **M 162.3, m –9°, –8°, b 117.5°/2mm, 237-239°/atm, 244°/760mm, d_4^{20} 0.907, n_D^{20} 1.5129.** Purify the triene by fractional distillation, preferably in a vacuum under N_2, and it forms an insoluble $AgNO_3$ complex. [IR: Breil et al. *Makromol Chemie* **69** 28 *1963*, *Beilstein* **5** IV 1114.]

Cyclododecylamine *[1502-03-0]* **M 183.3, m 27-29°, b 140-150°/*ca* 18mm, 280°/atm, pK 9.62 (in 80% methyl cellosolve).** It can be purified *via* the *HCl salt* **m** 274-275° (from EtOH) or the *picrate* **m** 232-234°, and the free base is distilled preferably at water-pump vacuum. It is a strong base and should be stored away from moisture and CO_2. [Prelog et al. *Helv Chim Acta* **33** 365 *1950*].

1,3-Cycloheptadiene *[4054-38-0]* **M 94.2, b 55°/75mm, 71.5°/150mm, 120-121°/atm, d_4^{20} 0.868, n_D^{20} 1.4972.** Purify the diene by dissolving it in Et_2O, washing with 5% HCl, H_2O, drying ($MgSO_4$), evaporating, and the residue is distilled under dry N_2 through a semi-micro column (some foaming occurs) [Cope et al. *J Am*

Chem Soc **79** 6287 *1957,* UV: Pesch & Friess *J Am Chem Soc* **72** 5756 *1950*]. [*Beilstein* **5** H 115, **5** III 317, **5** IV 390.]

Cycloheptane *[291-64-5]* **M 98.2, m ~12°, ~13°, b 114.4°, 118°/atm d_4^{20} 0.812, n_D^{20} 1.4588.** Distil it from sodium using a Vigreux column, under nitrogen. It is highly flammable. [Bocian & Strauss *J Am Chem Soc* **99** 2866 *1977*, Ruzicka et al. *Helv Chim Acta* **28** 395 *1945*, *Beilstein* **5** H 92, **5** IV 92.]

Cycloheptanol *[502-41-0]* **M 114.2, m 2°, b 77-81°/11mm, 83-84/14mm, 185°/atm, d_4^{20} 0.955, n_D^{20} 1.471.** Purify it as described for cyclohexanol. The *2,4-dinitrobenzoyl* derivative has **m** 79° and the *allophanate* has **m** 184° (from EtOAc). [Ruzicka et al. *Helv Chim Acta* **28** 395 *1945*, *Beilstein* **6** H 10.]

Cycloheptanone (suberone) *[502-42-1]* **M 112.2, b 105°/80mm, 172.5°/760, d_4^{20} 0.949, n_D^{20} 1.461.** Shake suberone with aqueous $KMnO_4$ to remove material absorbing around 230-240nm, then dry it with Linde type 13X molecular sieves and fractionally distil it through a glass helix packed column. [Blicke et al. *J Am Chem Soc* **74** 2924 *1952*, Dauben et al. *Org Synth* Coll Vol **IV** 221, 229 *1963*, *Beilstein* **7** H 13, **7** I 9, **7** II 14, **7** III 46, **7** IV 39.]

Cycloheptatriene *[544-25-2]* **M 92.1, b 60.5°/122mm, 114-115°/atm, d_4^{20} 0.895, n_D^{20} 1.522.** Wash the triene with alkali, then fractionally distil it. Store it under N_2 or Ar as it resinifies in air. [Dryden *J Am Chem Soc* **76** 2814 1954, Kohler et al. *J Am Chem Soc* **61** 1057 *1939*, *Beilstein* **5** IV 280.]

Cycloheptylamine *[5452-35-7]* **M 113.2, b 50-52°/11mm, 60°/18mm, d_4^{20} 0.887, n_D^{20} 1.472, pK_{Est} ~10.5 (H_2O), pK^{24} 9.99 (in 50% aqueous methyl cellosolve).** It can be purified by conversion to the *hydrochloride* **m** 242-246°, and the free base is distilled under dry N_2 in a vacuum [Cope et al. *J Am Chem Soc* **75** 3212 *1953*, Prelog et al. *Helv Chim Acta* **33** 365 *1950*]. [*Beilstein* **12** IV 115.]

1,3-Cyclohexadiene *[592-57-4]* **M 80.1, m -89°, b 83-84°/atm, d_4^{20} 0.840, n_D^{20} 1.471.** Distil the diene from $NaBH_4$ or Na under N_2 and collect it in a trap cooled in Dry Ice. It is highly flammable. [Marvel & Martell, *J Am Chem Soc* **81** 450 *1959*, *Beilstein* **5** IV 382.]

1,4-Cyclohexadiene *[628-41-1]* **M 80.1, b 83-86°/714mm, 88.3°/741mm, 86-88°/atm, 88.7-89°/760mm, d_4^{20} 0.8573, n_D^{20} 1.4725.** Dry the diene over $CaCl_2$ and distil it in a vacuum under N_2. [Hückel & Wörffel *Chem Ber* **88** 338 *1955*, Giovannini & Wegmüller *Helv Chim Acta* **42** 1142 *1959*.] [*Beilstein* **5** IV 385.]

Cyclohexane *[110-82-7]* **M 84.2, f 6.6°, b 80.7°, d_4^{24} 0.77410, n_D^{20} 1.42623, n_D^{25} 1.42354.** It is best to purify it by washing with conc H_2SO_4 until the washings are colourless, followed by water, aqueous Na_2CO_3 or 5% NaOH, and again water until neutral. It is then dried with P_2O_5, Linde type 4A molecular sieves, $CaCl_2$, or $MgSO_4$, then Na and distilled. Cyclohexane has been refluxed with, and distilled from Na, CaH_2, $LiAlH_4$ (which also removes peroxides), sodium/potassium alloy, or P_2O_5. Traces of *benzene can be removed by passage through a column of silica gel that has been freshly heated: this gives material suitable for ultraviolet and infrared spectroscopy. If there is much *benzene in the cyclohexane, most of it can be removed by a preliminary treatment with nitrating acid (a cold mixture of 30ml conc HNO_3 and 70ml of conc H_2SO_4) which converts *benzene into nitrobenzene. The impure cyclohexane and the nitrating acid are placed in an ice bath and stirred vigorously for 15 minutes, after which the mixture is allowed to warm to 25° during 1 hour. The cyclohexane is decanted, washed several times with 25% NaOH, then water, dried with $CaCl_2$, and distilled from sodium. Carbonyl-containing impurities can be removed as described for chloroform. Other purification procedures include passage through columns of activated alumina and repeated crystallisation by partial freezing. Small quantities may be purified by chromatography on a Dowex 710-Chromosorb W gas-liquid chromatographic column. **Flammable liquid.** [Sabatier *Ind Eng* Chem **18** 1005 *1926*, Schefland & Jacobs *TheHandbook of Organic Solvents* (Van Nostrand) p592 *1953, Beilstein* **5** IV 27.]
Rapid purification: Distil, discarding the forerun. Stand distillate over Grade I alumina (5% w/v) or 4A molecular sieves.

Cyclohexane butyric acid *[4441-63-8]* **M 170.3, m 31°, 26.5-28.5°, b 136-139°/4mm. 169°/20mm,**

188.8°/46mm, pK^{25} 4.95. Distil the acid through a Vigreux column, and the crystalline distillate is recrystallised from petroleum ether at low temperatures. The S-*benzylisothiuronium salt* has **m** 154-155° (from EtOH) [Friediger & Pedersen *Acta Chem Scand* **9** 1425 *1955*, English & Dayan *J Am Chem Soc* **72** 4187 *1950*]. [*Beilstein* **9** II 15.]

Cyclohexane carboxylic acid (hexahydrobenzoic acid) *[98-89-5]* **M 172.2, m 31-32°, b 63-67°/~0.1mm, 110°/8mm, 232-233°/atm, d^{15} 1.480, n^{20} 1.460, pK^{25} 4.90.** Crystallise the acid from hot H_2O (solubility is 0.2% w/w at 15°), it is soluble in organic solvents. Also distil it at as high a vacuum as possible and warm the condenser as it solidifies on cooling. The *acid chloride [2719-27-9]* **M 146.6,** has **b 184°/atm, d^{25} 1.096**, the *methyl ester* has **b** 183°/atm, and the *S-benzylisothiuronium salt* has **m** 165-166° (from EtOH). [*Beilstein* **9** H 7, **9** I 5, **9** II 6, **9** III15, **9** IV 16.]

Cyclohexane-1,2-diaminetetraacetic acid H_2O, (CDTA) *[H_2O: 12333-90-4; xH_2O: 13291-61-7]* **M 364.4, m >210°(dec), pK_1 1.34, pK_2 3.20, pK_3 5.75 (6.12), pK_4 9.26 (12.35).** Dissolve CDTA in aqueous NaOH as its disodium salt, then precipitate it by adding HCl. The free acid is filtered off and boiled with distilled water to remove traces of HCl [Bond & Jones *Trans Faraday Soc* **55** 1310 *1959*]. Recrystallise it from water and dry it *in vacuo*. [*Beilstein* **13** III 10.]

***cis*-Cyclohexane-1,2-dicarboxylic acid (*cis*-hexahydrophthalic acid)** *[610-09-3]* **M 172.2, m 191-192°, 191-194°, pK_1^{25} 4.25, pK_2^{25} 6.74.** It is purified by recrystallisation from EtOH or H_2O. [Smith & Byrne *J Am Chem Soc* **72** 4406 *1950*, Abell *J Org Chem* **22** 769 *1957*, *Beilstein* **9** III 3812, **9** IV 2801.]

***trans*-Cyclohexane-1,2-dicarboxylic acid (*trans*-hexahydrophthalic acid)** *[2305-32-0]* **M 172.2, m 227.5-228°, 228-230.5°, pK_1^{25} 4.30, pK_2^{25} 6.06.** It is purified by recrystallisation from EtOH or H_2O. It is formed by hydrolysing the anhydride with water. The *dimethyl ester* has **m** 95-96° (from $*C_6H_6$/petroleum ether). [Abell *J Org Chem* **22** 769 *1957*, Smith & Byrne *J Am Chem Soc* **72** 4406 *1950*, Linstead et al. *J Am Chem Soc* **64** 2093 *1942*, *Beilstein* **9** III 3812, **9** IV 2801.] The *1R,2R-(-)-trans-cyclohexane-1,2-acid* [46022-05-3] has **m** 171-182° and $[\alpha]_D^{20}$ -20° (c 1, Me_2CO).

***cis*-Cyclohexane-1,2-dicarboxylic anhydride (*cis*-hexahydrophthalic anhydride)** *[85-42-7, 13149-00-3]* **M 154.2, m 32-34°, b 158°/17mm.** It has been obtained by heating the *trans-acid* or *anhydride* at 200°. Crystallise it from $*C_6H_6/Et_2O$ or distil it. [Kohler & Jansen *J Am Chem Soc* **60** 2145 *1938*, Abell *J Org Chem* **22** 769 *1957*, *Beilstein* **17** II 452, **17** III/IV 5931.]

***trans*-Cyclohexane-1,2-dicarboxylic anhydride (*trans*-hexahydrophthalic anhydride)** *[14166-21-3]* **M 154.2, m 140-142°, 145-146°.** Crystallise the anhydride from $*C_6H_6/Et_2O$. It has been obtained by heating the *cis- acid* or *anhydride* with HCl at 180° for 3 hours. It is formed from the acid by heating in Ac_2O. It sublimes at 125-135°/0.02mm. [Kohler & Jansen *J Am Chem Soc* **60** 2145 *1938*, Fichter & Simon *Helv Chim Acta* **17** 1218 *1934*, *Beilstein* **9** IV 2802.]

(±)-*trans*-1,2-Cyclohexanediol *[1460-57-7]* **M 116.2, m 104°, 105°, 120°/14mm**. Crystallise the diol from Me_2CO and dry it at 50° for several days. It can also be recrystallised from CCl_4 or EtOAc and it can be distilled. The *2,4-dinitrobenzoyl* derivative has **m** 179°. [Winstein & Buckles *J Am Chem Soc* **64** 2780 *1942*.] [*Beilstein* **6** IV 5194.]

***trans*-1,2-Cyclohexanediol** *[1R,2R-(–)- 1072-86-2, 1S,2S-(+)- 57794-08-8]* **M 116.2, m 107-109°, 109-110.5°, 111-112°, 113-114°, $[\alpha]_D^{22}$ (–) and (+) 46.5° (c 1, H_2O).** The enantiomers have been recrystallised from $*C_6H_6$ or EtOAc. The (±) diol has been resolved *via* the distrychnine salt of the hemisulfate [Hayward et al. *J Chem Soc Perkin Trans 1* 2413 *1976*], or the *1-menthoxy acetates.* {*l-trans*- diastereoisomeric salt has **m** 64°, $[\alpha]_D$ –91.7° (c 1.4, EtOH) from petroleum ether or aqueous EtOH and yields the (–)-*trans*-diol} and {*d-trans*-diastereoisomeric salt has **m 126-127°**, $[\alpha]_D$ -32.7° (c 0.8, EtOH) from petroleum ether or aqueous EtOH and yields the (+)-*trans* diol}. The bis-*4-nitrobenzoate* has **m 126.5°** $[\alpha]_D$ (–) and (+) 25.5° (c 1.1, $CHCl_3$), and the bis-*3,5-dinitrobenzoate* has **m 160°** $[\alpha]_D$ (–) and (+) 83.0° (c 1.8, $CHCl_3$) [Wilson & Read *J Chem Soc* 1269 *1935*].[*Beilstein* **6** III 4060.]

***cis*-1,3-Cyclohexanediol** *[823-18-7]* **M 116.2, m 86°, 87°, 137°/13mm.** Crystallise the *cis*-diol from ethyl acetate and acetone or distil it in a vacuum . The *dibenzoyl* derivative has **m** 65.5° (from MeOH or petroleum ether). [Rigby *J Chem Soc* 1586 *1949*, Furberg & Hassell *Acta Chem Scand* **4** 518 *1950*, *Beilstein* **6** III 4077, **6** IV 5208.]

***trans*-1,3-Cyclohexanediol** *[5515-64-0]* **M 116.2, m 117°, 118-118.5°, 135°/13mm.** Crystallise the *trans*-diol from ethyl acetate or Me_2CO. The *dibenzoyl* derivative has **m** 123.5° (from EtOH or petroleum ether). [Rigby *J Chem Soc* 1586 *1949*, *Beilstein* **6** III 4077, **6** IV 5208.]

***cis*-1,4-Cyclohexanediol** *[931-71-5]* **M 116.2, m 102.5°, 113-114°.** Crystallise the *cis*-diol from acetone (charcoal), then dry and sublime it under vacuum. It also crystallises from Me_2CO or $Me_2CO/*C_6H_6$. The *diacetate* has **m** 40.6-41.1° (from petroleum ether or 34-36° from EtOH). [Grob & Baumann *Helv Chim* Acta **38** 604 *1955*, Owen & Robins *J Chem* Soc 320 *1949*, *Beilstein* **6** III 4080, **6** IV 5209.]

***trans*-1,4-Cyclohexanediol** *[6995-79-5]* **M 116.2, m 142.6-143.1°.** Crystallise the *trans*-diol from MeOH or Me_2CO. The *diacetate* has **m** 104.5-105° (from petroleum ether or 102-103° from EtOH). [Grob & Baumann *Helv Chim Acta* **38** 604 *1955*, Owen & Robins *J Chem* Soc 320 *1949*, *Beilstein* **6** III 4080, **6** IV 5209.]

Cyclohexane-1,3-dione *[504-02-9]* **M 112.1, m 107-108°, pK_1^{25} 5.25.** Crystallise the dione from *benzene. Dissolve ~50g of the diol in 140ml of $*C_6H_6$ under N_2, cool, collect the solid and dry it in a vacuum desiccator overnight. It is unstable and should be stored under N_2 or Ar at ~0°. [Thompson *Org Synth* Coll Vol **III** 278 *1955*, *Beilstein* **7** IV 1985.]

Cyclohexane-1,4-dione *[637-88-7]* **M 112.1, m 76-77°, 78°, 79.5°, 79-80°, b 130-133°/20mm, d_4^{91} 1.0861, n_D^{102} 1.4576.** Crystallise the dione from water, then *benzene. It can also be recrystallised from $CHCl_3$/petroleum ether or Et_2O. It has been purified by distillation in a vacuum, and the pale yellow distillate which solidified is then recrystallised from CCl_4 (14.3 g/100 ml) and has **m** 77-79°. The *di-semicarbazone* has **m** 231°, the *dioxime HCl* has **m** 150° (from $MeOH/*C_6H_6$) and the *bis-2,4-dinitrophenylhydrazone* has **m** 240° (from $PhNO_2$). [Nielsen & Carpenter *Org Synth* Coll Vol **V** 288 *1973*, IR: LeFevre & LeFevre *J Chem Soc* 3549 *1956*.] [*Beilstein* **7** IV 1986.]

Cyclohexane-1,2-dione dioxime (Nioxime) *[492-99-9]* **M 142.2, m 189-190°, pK_1^{25} 10.68, pK_2^{25} 11.92.** Crystallise Nioxime from alcohol/water and dry it in a vacuum at 40°. Also 2.5g of oxime have been recrystallised from 550ml of H_2O using Fe free Norit. It forms complexes with Ni and Pd. [Hach et al. *Org Synth* **32** 35 *1952*.] [*Beilstein* **7** IV 1982.]

1,4-Cyclohexanedione monoethylene acetal (1,4-dioxa-spiro[4.5]decan-8-one) *[4746-97-8]* **M 156.2, m 70-73°, 73.5-74.5°.** Recrystallise it from petroleum ether. It sublimes slowly on attempted distillation. Also purify it by dissolving it in Et_2O and adding petroleum ether (b 60-80°) until turbid, and cooling. [Gardner et al. *J Am Chem Soc* **22** 1206 *1957*, Britten & Lockwood *J Chem Soc Perkin Trans 1* 1824 *1974*.] [*Beilstein* **19/4** V 93.]

***cis,cis*-1,3,5-Cyclohexane tricarboxylic acid** *[16526-68-4]* **M 216.2, m 216-218°, $pK_{Est(1)}$ ~4.1, $pK_{Est(2)}$ ~5.4, $pK_{Est(3)}$ ~6.8.** Purify the acid by recrystallisation from toluene/EtOH or H_2O. It forms a *1.5 hydrate* with **m** 216-218°, and a *dihydrate* **m** 110°. Purify it also by conversion to the *triethyl ester* **b** 217-218°/10mm, 151°/1mm, the distillate solidifies on cooling, **m** 36-37°, which is hydrolysed by boiling in aqueous HCl. The *trimethyl ester* can be distilled and recrystallised from Et_2O, **m** 48-49°. [Newman & Lawrie *J Am Chem Soc* **76** 4598 *1954*, Lukes &S Galik *Col Czech Chem Comm* **19** 712 *1954*, *Beilstein* **9** III 4749.]

Cyclohexanol *[108-93-0]* **M 100.2, m 25.2°, b 161.1°, d 0.946, n_D^{20} 1.466, n_D^{25} 1.437, n_D^{30} 1.462.** Reflux it with freshly ignited CaO, or dry it with Na_2CO_3, then fractionally distil it. Redistil it from a very small amount of sodium, about 0.5-2% depending on the amount of H_2O estimated to be present. It is further purified by fractional crystallisation from the melt in dry air. Peroxides and aldehydes can be removed by prior washing with ferrous sulfate and water, followed by distillation under nitrogen from 2,4-dinitrophenylhydrazine, using a short fractionating column: water distils as the azeotrope. Dry cyclohexanol is *very hygroscopic*, store in a dry

atmosphere. The *3,4-dinitrobenzoate* has **m** 111-112° (EtOH or aqueous EtOH). It has **TOXIC** vapours. [*Beilstein* **6** III 10, **6** IV 20.]

Cyclohexanone *[108-94-1]* **M 98.2, f -16.4°, b 155.7°, d_4^{20} 0.947, n_D^{15} 1.452. n_D^{20} 1.451, pK^{25} –6.8 (aqueous H_2SO_4), pK^{25} 11.3 (enol), 16.6 (keto).** Dry cyclohexanone over $MgSO_4$, $CaSO_4$, Na_2SO_4 or Linde type 13X molecular sieves, then distil it. Cyclohexanol and other oxidisable impurities can be removed by treatment with chromic acid or dilute $KMnO_4$. More thorough purification is possible by conversion to the bisulfite addition compound, or the semicarbazone, followed by decomposition with Na_2CO_3 and steam distillation. [For example, equal weights of the bisulfite adduct (crystallised from water) and Na_2CO_3 are dissolved in hot water and, after steam distillation, the distillate is saturated with NaCl and extracted with Et_2O which is then dried (anhydrous $MgSO_4$ or Na_2SO_4), filtered, and the solvent evaporated prior to further distillation.] **FLAMMABLE.** The *semicarbazone* has **m 167°**, the *4-nitrophenylhydrazone* has **m 147°**, the *2,4-dinitrophenylhydrazone* has **m 162°**, and the *benzal derivative* has **m 118°**. [*Beilstein* **7** III 14, **7** IV 15.]

Cyclohexanone-2-carboxylic acid (2-oxocyclohexane carboxylic acid) *[18709-01-8]* **M 142.1, decarboxylates at 81-82°.** A preparation which is reproducible on a large scale involves adding cyclohexanone (49g, 52ml, 0.5mole) to a stirred suspension of $NaNH_2$ in Et_2O [obtained by dissolving Na (14g, 0.61g atom) in liquid NH_3 (500ml), and then replacing the NH_3 by Et_2O (500ml) carefully]. The mixture is boiled for 30 minutes, kept at ~35° while dry CO_2 is bubbled through for 3 hours, then poured into a slurry of ice and excess of 2M aqueous HCl, extracted with Et_2O (5 x 300ml), and the Et_2O is extracted with excess of saturated aqueous Na_2CO_3. The ice cold Na_2CO_3 solution is acidified with 2M aqueous HCl and again extracted with Et_2O (5 x 300ml). The combined extracts are dried ($MgSO_4$), filtered and evaporated *in vacuo* to give the carboxylic acid (29g, 41%) which can be recrystallised from Et_2O to form colourless needles. [Christie & Reid *J Chem Soc, Perkin Trans I* 880 *1976*, Gardner et al. *J Chem Soc* 1910 *1764*, cf Chiba et al. *Chem Lett* 1387 *1978*.]

Cyclohexanone oxime *[100-64-1]* **M 113.2, m 91°, b 100-105°/10-12mm, 206-210°/atm.** Crystallise the oxime from water or petroleum ether (b 60-80°). [Bousquet *Org Synth* Coll Vol **II** 313 *1943*, *Beilstein* **7** III 32, **7** IV 21.]

Cyclohexanone phenylhydrazone *[946-82-7]* **M 173.3, m 77°, 81°.** Crystallise it from EtOH.

Cyclohexene *[110-83-8]* **M 82.2, M –104°, b 83°, d_4^{20} 0.810, n_D^{20} 1.4464, n_D^{25} 1.4437.** Free cyclohexene from peroxides by washing with successive portions of dilute acidified ferrous sulfate, or with $NaHSO_3$ solution, then with distilled water, drying with $CaCl_2$ or $CaSO_4$, and distilling under N_2. Alternative methods for removing peroxides include passage through a column of alumina, refluxing with sodium wire or cupric stearate (then distilling from sodium). The diene is removed by refluxing with maleic anhydride before distilling under vacuum. Treatment with 0.1moles of MeMgI in 40ml of diethyl ether removes traces of oxygenated impurities. Other purification procedures include washing with aqueous NaOH, drying and distilling under N_2 through a spinning band column, redistilling from CaH_2, storing under sodium wire, and passing through a column of alumina, under N_2, immediately before use. Store it at <0° under argon. [Coleman & Johnstone *Org Synth* Coll Vol **I** 83 *1955*, Carson & Ipatieff *Org Synth* Coll Vol **II** 152 *1943*, Woon et al. *J Am Chem Soc* **108** 7990 *1986*, Wong et al. *J Am Chem Soc* **109** 3428 *1987*.] [*Beilstein* **5** IV 218.]

(±)-2-Cyclohexen-1-ol (3-hydroxycyclohex-1-ene) *[822-67-3]* **M 242.2, b 63-65°/12mm, 65-66°/13mm, 67°/15mm, 74°/25mm, 85°/35mm, 166°/atm, d_4^{20} 0.9865, n_D^{20} 1.4720.** Purify 2-cyclohexen-1-ol by distillation through a short Vigreux column. The *2,4-dinitrobenzoyl* derivative has **m** 120.5°, and the *phenylurethane* has **m** 107°. [Pedersen et al. *Org Synth* **48** 18 *1968*, Cook *J Chem Soc* 1774 *1938*, Deiding & Hartman *J Am Chem Soc* **75** 3725 *1953*, *Beilstein* **6** IV 196.]

Cyclohexene oxide (7-oxabicyclo[4.1.0]heptane] *[286-20-4]* **M 98.2, b 131-133°/atm, d_4^{20} 0.971, n_D^{20} 1.452.**

Fractionate the oxide through an efficient column. The main impurity is probably H_2O. Dry the oxide over $MgSO_4$, filter it, and redistil it several times (**b 129-134°/760mm**). The residue can be hard to remove from the distilling flask. To avoid this difficulty, add a small amount of a mixture of ground NaCl and Celite (1:1) to help break up the residue particularly if hot H_2O is added. [Osterberg *Org Synth* Coll Vol **I** 185 *1948*, *Beilstein* **17** H 21, **17/1** V 203.]

Cycloheximide (actidione) *[68-81-9]* **M 281.4, m 119.5-121°, $[\alpha]_{546}^{20}$ +9.5° (c 2, H_2O), pK 11.2.** Crystallise it from water/MeOH (4:1), amyl acetate, isopropyl acetate/isopropyl ether or water. The *acetate* has **m** 150-152° (from aqueous EtOH), the *p-nitrobenzoate* has **m** 215-220°(dec) (from aqueous dioxane) and the *oxime* has **m** 203-204° (from MeOH). [Kornfeld et al. *J Am Chem Soc* **71** 155 *1949*, *Beilstein* **21** IV 6632.]

Cyclohexylamine *[108-91-8]* **M 99.2, b 134.5°, d_4^{20} 0.866, d_4^{25} 0.863, n_D^{20} 1.4593, n_D^{25} 1.456, pK^{25} 10.63.** Dry the amine with $CaCl_2$ or $LiAlH_4$, then distil it from BaO, KOH or Na, under N_2. Also purify it by conversion to the hydrochloride (which is crystallised several times from water), then liberation of the amine with alkali and fractional distillation under N_2. The *hydrochloride* has **m** 205-207° (dioxane/EtOH). [Lycan et al. *Org Synth* Coll Vol **II** 319 *1943*, *Beilstein* **12** III 10, **12** IV 8.]

Cyclohexyl bromide *[108-85-0]* **M 156.3, b 72°/29mm, d_4^{20} 0.902, n_D^{25} 1.4935.** Shake the bromide with 60% aqueous HBr to remove the free alcohol. After removing excess HBr, the sample is dried and fractionally distilled. [IR: Roberts & Chambers *J Am Chem Soc* **73** 5031 *1951*, *Beilstein* **5** III 48, **5** IV 67.]

1-Cyclohexylethylamine *[S-(+)- 17430-98-7, R-(–)- 5913-13-3]* **M 127.2, b 177-178°/atm, d_4^{20}0.866, n_D^{20} 1.446, $[\alpha]_D^{15}$ (–) and (+) 3.2° (neat), pK_{Est} ~10.6.** Purify it by conversion to the *bitartrate salt* (**m** 172°), then decomposing with strong alkali and extracting into Et_2O, drying (KOH), filtering, evaporating and distilling. The *hydrochloride salt* has **m** 242° (from EtOH/Et_2O), $[\alpha]_D^{15}$ –5.0° (c 10 H_2O, from (+) amine). The *oxalate salt* has **m** 132° (from H_2O). The *(±)-base* has **b** 176-178°/760mm, and its *hydrochloride* has **m** 237-238°. [Reihlen et al. *Justus Liebigs Ann Chem* **532** 247 *1938*, Leithe *Chem Ber* **65** 660 *1932*, *Beilstein* **12** III 95.]

Cyclohexylidene fulvene (6,6-pentamethylene fulvene) *[3141-04-6]* **M 134.2.** Purify the fulvene by column chromatography and eluting with *n*-hexane [Abboud et al. *J Am Chem Soc* **109** 1334 *1987*].

Cyclohexyl mercaptan (cyclohexane thiol) *[1569-69-3]* **M 116.2, b 38-39°/12mm, 57°/23mm, 90°/100mm, 157°/763mm, d_4^{20} 0.949, n_D^{20} 1.493, pK_{Est} ~10.8.** Possible impurities are the sulfide and the disulfide. Purify the thiol by conversion to the Na salt by dissolving it in 10% aqueous NaOH, extract the sulfide and disulfide with Et_2O, and then acidify the aqueous solution (with cooling and under N_2) with HCl, extract with Et_2O, dry over $MgSO_4$, evaporate and distil it in a vacuum (**b** 41°/12mm). The *sulfide* has **b** 74°/0.2mm, $n_D^{18.5}$ 1.5162 and the *disulfide* has **b** 110-112°/0.2mm, $n_D^{18.5}$ 1.5557. The *Hg-mercaptide* has **m** 77-78° (needles from EtOH). [Naylor *J Chem Soc* 1532 *1947*, *Beilstein* **6** H 8, **6** I 6, **6** II 14, **6** III 46, **6** IV 72.]

Cyclohexyl methacrylate *[101-43-9]* **M 168.2, b 81-86°/0.1mm, d_4^{20} 0.964, n_D^{20} 1.458.** Purify it as for methyl methacrylate (see [80-62-6]). [Tong & Kenyon *J Am Chem Soc* **68** 1355 *1946*, *Beilstein* **6** III 25, **6** IV 39.]

Cyclononanone *[3350-30-9]* **M 140.2, m 142.0-142.8°, b 220-222°, 100-101.5°/15mm.** Purify it *via* the *semicarbazone* (**m** 179.5-180.5° from 90% MeOH) and regenerate it by steam distilling a mixture of 13.1g of semicarbazone, 22g of phthalic anhydride and 45ml of H_2O. After collecting 300ml of distillate, the latter is extracted with Et_2O. The dried extract ($MgSO_4$) gives on evaporation 8.4g of ketone **b** 100-101.5°/15mm. The *oxime* has **m** 76.5-77.5° (79° from MeOH) and the *iso-oxime* has **m** 138-139°. [Ruzicka et al. *Helv Chim Acta* **32** 548 *1949*.] It has also been repeatedly sublimed at 0.05-0.1mm pressure. [Blomquist et al. *J Am Chem Soc* **74** 3639, 3645 *1952*, *Beilstein* **7** III 110, **7** IV 62.]

***cis,cis*-1,3-Cyclooctadiene** *[3806-59-5]* **M 108.2, m –5°, –49°, b 55°/34mm, 142-144°/760mm, d_4^{20} 0.8690, n_D^{20} 1.48921.** Purify the diene by GLC. Fractional distillation through a Widmer column gives a mobile liquid, and redistil it with a Claisen flask or through a semi-micro column [Gould, et al. *Anal Chem* **20** 361 *1948*]. **NB:** It has a strong characteristic disagreeable odour detectable at low concentrations and causes headaches on

prolonged exposure. *Do not breath it internally*. [IR: Cope & Estes *J Am Chem Soc* **72** 1128 *1950*, UV: Cope & Baumgardner *J Am Chem Soc* **78** 2812 *1956*.] [*Beilstein* **5** IV 401.]

***cis-cis*-1,5-cyclooctadiene (COD)** *[111-78-4, 1552-12-1]* **M 108.2, m –69.5°, –70°, b 51-52°/25mm, 97°/144mm, 150.8°/757mm, d_4^{20} 0.880, n_D^{20} 1.4935.** Purify it by GLC. It has been purified *via* the $AgNO_3$ salt. This is prepared by shaking with a solution of 50% aqueous $AgNO_3$ w/w several times (e.g. 3 x 50 ml and 4 x 50 ml) at 70° for *ca* 20 minutes to get a good separation of layers. The upper layers are combined and further extracted with $AgNO_3$ at 40° (2 x 20 ml). The upper layer (19 ml) of original hydrocarbon mixture gives colourless needles of the $AgNO_3$ complex on cooling. The adduct is recrystallised from MeOH (and cooling to 0°). The hydrocarbon is recovered by steam distilling the salt. The distillate is extracted with Et_2O, dried ($MgSO_4$), filtered, evaporated and distilled. [Jones *J Chem Soc* 312 *1954*, [*Beilstein* **5** H 116, **5** IV 403.]

Cyclooctanone *[502-49-8]* **M 126.2, m 42°, 43.8°, b 115-115.5°/60mm.** Purify the ketone by sublimation after drying an ethereal solution over Linde type 13X molecular sieves, filtering and evaporating. The *semicarbazone* has **m** 168-169° (from dioxane) [Kohler et al. *J Am Chem Soc* **61** 1060 *1939*]. The *oxime* has **m** 36-37° after subliming at high vacuum, or distillation, and has **b** 128-129° /14mm. The *iso-oxime* has **m** 72-73° [Ruzicka et al. *Helv Chim Acta* **32** 548 *1949*]. [*Beilstein* **7** III 77, **7** IV 49.]

1,3,5,7-Cyclooctatetraene *[629-20-9]* **M 104.2, m –5° to –3°, b 141-141.5°, d_4^{20} 1.537, n_D^{25} 1.5350.** Purify the triene by shaking 3ml with 20ml of 10% aqueous $AgNO_3$ for 15 minutes, then filtering off the $AgNO_3$ complex which precipitates. The precipitate is dissolved in water and added to cold concentrated ammonia to regenerate the cyclooctatetraene which is fractionally distilled under vacuum onto molecular sieves and stored at 0°. It is passed through a dry alumina column before use [Broadley et al. *J Chem Soc, Dalton Trans* 373 *1986*]. [*Beilstein* **5** I 228, **5** IV 1331.]

***cis*-Cyclooctene** *[931-87-3; 931-88-4]* **M 110.2, b 32-34°/12mm, 66.5-67°/60mm, 88°/141mm, 140°/170mm, 143°/760mm, d_4^{20} 0.84843, n_D^{20} 1.4702.** The *cis*-isomer is freed from the *trans*-isomer by fractional distillation through a spinning-band column, followed by preparative gas chromatography on a Dowex 710-Chromosorb W GLC column. It is passed through a short alumina column immediately before use [Collman et al. *J Am Chem Soc* **108** 2588 *1986*]. It has also been distilled in a dry N_2 glove box from powdered fused NaOH through a Vigreux column, then passed through activated neutral alumina before use [Wong et al. *J Am Chem Soc* **109** 4328 *1987*]. *Alternatively*, it can be purified *via* the $AgNO_3$ salt. This salt is obtained from crude cyclooctene (40 ml) by shaking at 70-80° with 50% w/w $AgNO_3$ (2 x 15 ml) to remove cyclooctadienes (aqueous layer). Extraction is repeated at 40° (4 x 20 ml, of 50% $AgNO_3$). Three layers are formed each time. The middle layer contains the $AgNO_3$ adduct of cyclooctene which crystallises on cooling the layer to room temperature. The adduct (complex 2:1) is highly soluble in MeOH (at least 1g/ml) from which it crystallises in large flat needles when cooled at 0°. It is dried under slight vacuum for 1 week in the presence of $CaCl_2$ and paraffin wax soaked in cyclooctene. It has **m** 51° and loses hydrocarbon on exposure to air. *cis*-Cyclooctene can be recovered by steam distillation of the salt, collected, dried ($CaCl_2$) and distilled in a vacuum. [Braude et al. *J Chem Soc* 4711 *1957*, $AgNO_3$: Jones *J Chem Soc* 1808 *1954*, Cope & Estes *J Am Chem Soc* **72** 1128 *1950*, *Beilstein* **5** I 35, **5** IV 263.] **FLAMMABLE LIQUID.**

***cis*-Cyclooctene oxide {(1r, 8c)-9-oxabicyclo[6.1.0]nonane}** *[286-62-4]* **M 126.7, m 56-57°, 57.5-57.8°, 50-60°, b 85-88°/17mm, 82.5°/22mm, 90-93°/37mm, 189-190°/atm.** It can be distilled in a vacuum, and the solidified distillate can be sublimed in a vacuum below 50°. It has a characteristic odour. [IR: Cope et al. *J Am Chem Soc* **74** 5884 *1952*, *cf trans-isomer*: Cope et al. *J Am Chem Soc* **79** 3905 *1957*, Reppe et al. *Justus Liebigs Ann Chem* **560** 1 *1948*].

Cyclopentadecanone (Exaltone) *[502-72-7]* **M 224.4, m 63°, 65°, 65-66°, b 155-157°/5mm.** Subliming Exaltone is better than crystallising it from aqueous EtOH for purification. The *semicarbazone* has **m** 186-187°. [Stevens & Erickson *J Am Chem Soc* **64** 146 1942, Mathur et al. *J Chem Soc* 3505 *1963*, Biens & Hess *Helv Chim Acta* **71** 1704 *1988*, *Beilstein* **7** III 203, **7** IV 118.]

Cyclopentadiene *[542-92-7]* **M 66.1, b 41-42°, pK^{25} 15.** Dry the diene with $Mg(ClO_4)_2$ and distil it rapidly

as it dimerises readily at room temperature. It should be used immediately or stored in a Dry Ice or an ice-salt bath. **HIGHLY FLAMMABLE.** [Moffett *Org Synth* Coll Vol **IV** 238 *1963*.] *Cyclopentadiene Dimer (4,7-methano-3a,4,7,7a-tetrahydroindene)* has [77-73-6], **M** 132.3, **m** 33°, **b** 170°/atm, and $\mathbf{d^{25}}$ 0.986; add ~0.05% of 2,6-di-*tert*-butyl-4-methylphenol as stabiliser. Cyclopentadiene is prepared when required by de-polymerising the technical grade dimer by heating (and distilling) it carefully under a fractionating column [Wilkinson *Org Synth* Coll Vol **IV** 467 *1963*], as described by Moffett (above reference), or by adding the dimer at a steady rate onto mineral oil heated at 240-270° when it distils off. [Korach et al. *Org Synth* **42** 50 *1962*]. [*Beilstein* **5** II 391.]

Cyclopentane *[287-92-3]* **M 70.1, b 49.3°, $\mathbf{d_4^{20}}$ 0.745, $\mathbf{n_D^{20}}$ 1.40645, $\mathbf{n_D^{25}}$ 1.4340.** Free it from cyclopentene by two passages through a column of dried and degassed activated silica gel. It occurs in petroleum and is **HIGHLY FLAMMABLE.** [NMR: Christl *Chem Ber* **108** 2781 *1975*, Whitesides et al. **41** 2882 *1976*, *Beilstein* **5** III 10, **5** IV 4.]

Cyclopentane carbonitrile *[4254-02-8]* **M 95.2, m -75.2°, -76°, b 43-44°/7mm, 50-62°/10mm, 67-68°/14mm, 74.5-75°/30mm, $\mathbf{d_4^{20}}$ 0.912, $\mathbf{n_D^{20}}$ 1.441.** Dissolve the nitrile in Et_2O, wash it thoroughly with saturated aqueous K_2CO_3, dry ($MgSO_4$) and distil it through a 10 cm Vigreux column. [McElvain & Stern *J Am Chem Soc* **77** 457 *1955*, Bailey & Daly *J Am Chem Soc* **81** 5397 *1959*, *Beilstein* **9** IV 14.]

Cyclopentanecarboxaldehyde *[872-53-7]* **M 98.1, b 36°/12mm, 74-78°/100mm, 140-141°/atm, $\mathbf{d^{25}}$ 0.919, $\mathbf{n_D^{20}}$ 1.4420-1.4428.** Several preparations of this aldehyde have been described but only two will be briefly mentioned here, and both start from cyclohexene. The ***first*** requires decomposition of the mercuric sulfate complex where, under N_2, concentrated H_2SO_4 (43.5ml, 80.0g, 0.82mole) in H_2O (3L) and $HgSO_4$ (740.0g, 2.49moles, CARE **POISONOUS**) are stirred to form the deep-yellow basic salt. To this stirred mixture, under N_2 at 55°, is added all at once cyclohexene (101ml, 82.0g, 1mole, freshly distilled b 82-84°/atm [110-83-8]), and the temperature kept at 55-65° for 1 hour (optimal conditions for decomposition of complex). The colour of the mixture turns from deep-yellow to cream. The equipment is altered for distillation at the end of the hour, and the temperature is raised, stirring and the N_2 flow are continued as the crude *aldehyde* and H_2O distil during *ca* 2 hours. The layers are separated, the H_2O layer is extracted with Et_2O (3 x 50ml) which is combined with the product, dried (Na_2SO_4), filtered, and distilled rapidly (b 74-78°/100mm) to give the *aldehyde* (46-52g, 46-53%), which if not used immediately should be stored in a brown bottle at 0° for under N_2, after 0.1g of hydroquinone is added as stabiliser. The *aldehyde* readily forms a *trimer*, and does so on prolonged storage. [Grummit et al. *Org Synth* Coll Vol **5** 320 *1973*, English et al. *J Am Chem Soc* **73** 615 *1951*.] When the distillation residue is cooled a solid may be formed which can be distilled above 78°/100mm to give a clear liquid that solidifies, and can be recrystallised from 95% EtOH to give a white solid **m 122-124°**, identical with ***cyclopentanecarboxaldehyde trimer*** obtained from the *aldehyde* and 85% H_3PO_4 [Brook & Wright *Can J Chem* **29** 308 *1951*].
In the ***second*** procedure, $Tl(III)(NO_3)_3\ 3H_2O$ (4.4g, 10mmol, TTN [13453-38-8]) is dissolved in MeOH (50ml), cyclohexene (10mmol) is added, and the mixture is stirred at room temperature or heated until a starch-iodide paper indicates complete reduction of Tl(III) to Tl(I) (usually within a few minutes). The mixture is filtered, and an alcoholic solution containing 10mmol of 2,4-dinitrophenylhydrazine is added. This is evaporated to 1/3 its volume and after addition of H_2O (10ml) the mixture is heated on a steam bath for 10 minutes. On cooling to 0°, the ***2,4-dinitrophenylhydrazone*** *[20956-07-4]* crystallises out and is recrystallised from EtOH to **m 195.5-196°** (85% yield). Hydrolysis of the hydrazone in the usual way provides the free *aldehyde*. On a preparative scale the precipitated $Tl(I)(NO_3)$ salt is filtered off, the filtrate is evaporated to a small volume, the mixture of aldehyde and its methyl acetal formed is heated on a steam bath with excess of 5% H_2SO_4 for 30 minutes, and *cyclopentanecarboxaldehyde* is isolated by ether extraction followed by distillation as in the first preparation above. [Taylor et al. *J Am Chem Soc* **95** 3635 *1973*.] It should be stabilised with 0.1% of hydroquinone as before.

Cyclopentane carboxylic acid *[3400-45-1]* **M 114.1, m 3-5°, b 87-89°/2-3mm, 106.5-107°/10mm, 120-123°/27mm, 216°/atm, $\mathbf{d^{25}}$ 1.053, $\mathbf{n_D^{20}}$ 1.4530, $\mathbf{n_D^{25}}$ 1.4522, $\mathbf{pK^{25}}$ 4.98.** If it is discoloured, shake it with saturated aqueous NaCl, extract it with Et_2O, dry the extract ($MgSO_4$), filter, evaporate and distil the residue preferably under a vacuum. The **lachrymatory** *acid chloride [4524-93-0]* has **M** 132.6, **m** 4° and **b** 161-162°/

atm, **d** $_4^{20}$ 1.091, **n** $_D^{20}$ 1.4622. [*Beilstein* **9** H 6, **9** IV 11.] The *amide [3217-94-5]* has **m** 179°. Like the methyl ester below, the acid can also be prepared *via* a Favorskii reaction, but by using a little over 2 moles of alkoxide (1mol provides the ester). Thus, to sodium (83g, 3.61mol) in absolute EtOH (2.3L) is added dropwise 2-chlorocyclohexanone (240.5g, 1.82mol, [822-87-7]) during several hours, left overnight, the EtOH is distilled off, replaced by an equal volume of H_2O, acidified to pH 3, and the oily acid that separates is extracted with Et_2O. The extract is washed with H_2O, dried (Na_2SO_4), filtered, and distilled to give the pure *acid* (110g, 53%). [Jackman et al. *J Am Chem Soc* **70** 497 *1948*, Mourisson et al. *Bull Soc Chim Fr* 767 *1952*.] [*Beilstein* **6** H 6, **6** I 4, **6** II 6, **6** III 11, **6** IV 9.]

Methyl cyclopentanecarboxylate, *[4630-80-2]* **M 128.1, b 70-73°/48mm, 38-39°/7mm, 158.2°/760mm, n** $_D^{25}$ **1.4341**, can be obtained by reacting the acid chloride with MeOH and distilling; but it can also be obtained in ~55% yield directly from 2-chlorocyclohexanone and NaOMe (1mol) in dry Et_2O, *via* a Favorskii reaction, and purified by fractional distillation, using a Podbielniak column filled with tantalium wire spirals and a partial reflux head, under reduced pressure [Goheen & Vaughan *Org Synth* Coll Vol **4** 594 *1963*]. The *methyl ester* has also been prepared in 98% yield by direct esterification of cyclopentane carboxylic acid with MeOH in CH_2Cl_2 in the presence of H_2SO_4. The acid has FTIR (CCl_4) with ν_{max} at 2952(s), 2873 (m), 1734 (s), 1436 (w), 1165 (s) and 1140 (s) cm^{-1}; ^1H NMR (75MHz, $CDCl_3$, TMS) with δ at 1.5-2.0 (m, 8H, 4-methylenes), 2.7 (pentet, 1H, *J* = 9.0Hz), 3.7 (s, 3H, Me); ^{13}C NMR (300MHz, $CDCl_3$, TMS) with δ at 25.7, 29.9, 43.6, 51.5, 177.2, and the GCMS has *m/z* at 128 (M^+) [Davis et al. *J Org Chem* **58** 6843 *1993*].

1,1-Cyclopentanediacetic acid (3.3-tetramethyleneglutaric acid) *[16713-66-9]* **M 186.2, m 176-177°, 180-181°, pK** $_1^{25}$ **3.80, pK** $_2^{25}$ **6.77.** Purify it by recrystallisation from H_2O and dry it in air, *in vacuo* or over $CaCl_2$. However, if it is suspect it is better to convert the acid to the anhydride (8-oxaspiro[4.5]decane-7,8-dione, [5662-95-3], **m 64-66° (68°** also reported), **b 186°/15mm**) by refluxing it for 7 hours in excess of Ac_2O, evaporating to dryness, and distilling the residue in a vacuum or recrystallising it from light petroleum. [Kon & Thorpe *J Chem Soc* **115** 701 *1919*.] The anhydride (e.g. 30g) is then hydrolysed by refluxing it for 2.5 hours (i.e. until it dissolves) in aqueous KOH (35g, 3mols in 55ml of H_2O), then acidified with concentrated HCl, extracted with Et_2O (3 x 50ml) after saturating the aqueous solution with $(NH_4)_2SO_4$, drying the extract (Na_2SO_4), filtering, evaporating the Et_2O and recrystallising the *diacid* from hot H_2O. [Vogel *J Chem Soc* 1761 *1934*.] The *dimethyl ester [70179-60-3]* has **b 141°/17mm** [Vogel *J Chem Soc* 1761 *1934*, Dickins et al. *J Chem Soc* 1503 *1922*], and the *diethyl ester* has **b 153°/14mm** [Kon *J Chem Soc* 525 *1922*]. [*Beilstein* **9** I 319, and anhydride *Beilstein* **17/11** V 80.]

Cyclopentane-1,1-dicarboxylic acid *[5802-65-3]* **M 158.1, m 183°, 184°, (176-178°), pK$_1$ 3.23, pK$_2$ 4.08.** The dicarboxylic acid can be prepared in 71% yield by using the nickel(0) catalyst *2-{2-[2-(dicyclohexyl-phosphino)ethyl]pyridine}-4-oxo-2-nickela-3-oxa-cis-bicyclo[3.3.0]octane* which promotes the di-carbonylation of cyclopentene (1.16g, 2.44mmol) in THF (30ml)/pyridine (30ml), in the presence of BeCl (0.2g, 2.50mmol), by CO_2 (10 bar pressure) in an autoclave, and stirring at 60° for 24 hours. The solvent is evaporated off *in vacuo*, the residue is treated with Et_2O/HCl and the solid is collected, dried and recrystallised from pentane/Et_2O (10:1), or H_2O. The pure *dicarboxylic acid* melts at 183° with decarboxylation to *cyclopentanecarboxylic acid* (see preceding acid), and has FTIR (KBr) with ν_{max} at 3200-2500 (CO**OH**) and 1700 (C=O) cm^{-1}; ^1H NMR (200MHz, THF-d_8/TMS) with δ at 1.6 (m, 4H, 2-methylenes), 2.1 (m, 4H, 2-methylenes), 9.6 (br, 2H, 2-COO***H***) ppm; ^{13}C NMR (50MHz, THF-d_8/TMS) with δ at 26.3 (t), 35.2 (t), 60.6 (s), 174.2 ppm; and the MS (70 eV) has *m/z* at 158 (M^+). [Hoberg et al. *Synthesis* 395 *1991*]. ***Dimethyl 1,1-cyclopentanedicarboxylate*** *[74090-15-6]* **M 186.2, b 102°/10mm,** can be prepared in 76% yield from the preceding *methyl cyclopentanecarboxylate* (40mmol, [*4630-80-2*]) in THF (60ml), with (^{i}Pr)$_2$NH (60mmol) and *n*-BuLi (60mmol) followed by MeOCOCl (60mmol), and finally distilling. The *dimethyl ester* has FTIR (CCl_4) with ν_{max} at 2953(s), 2928 (w), 2876 (w), 1736 (s), 1434 (w), 1266 (s), 1165 (s) and 1159 (m) cm^{-1}; ^1H NMR (300MHz, $CDCl_3$, TMS) with δ at 1.7 (m, 4H, 2-methylenes), 2.1 (m, 4H, 2-methylenes), 3.7 (s, 6H, 2-Me) ppm; ^{13}C NMR (75MHz, $CDCl_3$, TMS) with δ at 25.3, 34.5, 52.4, 60.2, 173.0 ppm, and the GCMS has *m/z* at 187 (M^++1) [Davis et al. *J Org Chem* **58** 6843 *1993*].

***1RS,2SR*-(meso)-*cis*-1,2-Cyclopentanedicarboxylic acid** *[1461-96-7]* **M 158.2, m 139°, 140°, 141°, pK** $_1^{20}$ **4.42, p K** $_2^{20}$ **6.57.** The *cis*-acid has been prepared by hydrogenation of cyclopent-1-ene-1,2-dicarboxylic acid with Pt as catalyst [Peters *J Chem Soc* 1757 *1959*], heating diethyl 1-cyanocyclopentane-1,2-dicarboxylate (b

135-136°/3.5mm) with aqueous HCl and isolating the anhydride [Fuson & Cole *J Am Chem Soc* **60** 1237 *1938*, Dutta *J Indian Chem Soc* **17** 611, 617 *1940*], but is best prepared by boiling the *trans*-acid with excess of acetic anhydride for at least 2 hours (which provides the *cis-anhydride*), dissolving this in boiling H_2O or aqueous KOH with cooling (**care**, may be exothermic), and acidifying to pH ~2 in order to precipitate the *cis*-acid. The *cis*-acid crystallises from hot H_2O as colourless needles melting at 140°, and is rapidly converted to the *cis-anhydride* at 150-160°. The *cis*-acid is also obtained from the *trans*-acid by heating at 300 ° [Perkin Jnr *J Chem Soc* **51** 247 *1887*, Perkin Jnr *J Chem Soc* **65** 527 *1894*]. It is more soluble in H_2O than the (±)-*trans*-acid. It had not been possible to prepare *trans*-cyclopentane-1,2-dicarboxylic anhydride because all attempts gave the ***cis-anhydride*** (*cis*-**tetrahydro-*1H*-cyclopent[*c*]furan-1,3(*3aH*)-dione**, **m 73.5-74°, b 100-102°/1.5mm,** *[5763-49-5]*). [Perkin Jnr *J Chem Soc* **65** 588 *1894*, cf Fuson & Cole *J Am Chem Soc* **60** 1237 *1938*, Goldsworthy & Perkin Jnr *J Chem Soc* **105** 2639 *1914*.]. The nickel(0) catalyst *2-{2-[2-(dicyclohexylphosphino)ethyl]pyridine}-4-oxo-2-nickela-3-oxa-cis-bicyclo[3.3.0]octane* promotes the carbonylation of cyclopentene in THF by CO at 1bar pressure and –40°, then at ~25°/10 hours followed by treatment with 2N H_2SO_4 and recrystallisation from pentane/Et_2O (10:1), which provides cyclopentane-1,2-dicarboxylic acid (78% yield) presumed to be mainly the *cis-isomer*. However, its melting point of 124-125° suggests that it must be contaminated with some of the *trans*-isomer [Hoberg et al. *Synthesis* 395 *1991*]. Its FT-IR (KBr) has ν_{max} at 3300-2500 (CO**OH**) and 1710 (C=O) cm^{-1}; its ^1H NMR (200MHz, THF-*d*8/TMS) has δ_H at 10.4 (br s, 2H, OH), 2.9 (m, 2H, 2CH), 1.51-2.1 (m, 6H, $3CH_2$), 1.69 (m, 4H); its ^{13}C NMR (200MHz, THF-*d*8/TMS) has δ_C at 176.10 (s, carboxylic C), 47.5 (d, C1 and C2), 29.4 (t, C-3 and C-5) and 24.4 (t, C-4); and its MS (70 eV) has *m/z* = 158 (M^+), see GC-MS [below, Lu et al. *J Org Chem* **55** 2503, 2507 *1990*]. **Dimethyl *cis-cyclopentane-1,2-dicarboxylate*, b 129°/20mm, n_D^{21} 1.4528,** *[4841-91-2]*, is obtained by treating the acid with diazomethane in Et_2O, evaporating and distilling the residue [Owen & Peto *J Chem Soc* 2383, 2386 *1955*]. The ***cis-imide*** (*cis*-**tetrahydrocyclopent[*c*]pyrrole-1,3(*2H*,*3aH*)-dione**, *[5763-44-0]*) has **m 85-87° (**also **90°** reported**)** after recrystallisation from H_2O or petroleum ether (b 40-60°) [Menon & Simonsen *J Chem Soc* 302 *1929*, Rice et al. *J Org Chem* **24** 7 *1959*], and *cis-**cyclopentane-1,2-dicarboxylic acid dihydrazide***, prepared from the dimethyl ester and NH_2NH_2. H_2O in EtOH and recrsystallised from MeOH/Et_2O, has **m 125-126°** [Müller et al. *J Am Chem Soc* **73** 2489 *1951*]. [*Beilstein* **9** H 728, **9** III 3807, **9** IV 3793.]

1RS,2RS*-(±)-*trans*-1,2-Cyclopentanedicarboxylic acid** *[1461-97-8]* **M 158.2, m 160-161°, 161.5°, 162°, 162-163°, 163°, 163-165°, 164-165°, pK_1^{20} 4.14, pK_2^{20} 5.99.** Several syntheses of the (±)-*trans*-acid have been described. The first preparation involved tetraethyl cyclopentane-1,2,3,4-tetracarboxylate [b 185-190°/1mm, from trimethylene-1,3-dibromide (96g), Na (22g) and diethyl malonate (150g) in absolute EtOH (300ml)] which was refluxed with 2-3 volumes of AcOH, 1 volume of concentrated H_2SO_4 and 1 volume of H_2O for 2 days, and the AcOH and H_2O were distilled off to give *trans*-cyclopentane-1,2-dicarboxylic acid [Perkin Jnr *J Chem Soc* **65** 587 *1894*, Perkin Jnr *J Chem Soc* **51** 224 *1887*, Wassermann *Helv Chim Acta* **13** 207 *1930*, Perkin Jnr & Prentice *J Chem Soc* **59** 828 *1891*]. Other preparations include heating the *cis*-acid with concentrated HCl at 180° [Perkin Jnr *J Chem Soc* **65** 577, 590 *1894*], refluxing diethyl 1-cyanocyclopentane-1,2-dicarboxylate with concentrated aqueous HCl for 4 days which provided a 92% yield of the *trans*-acid [Fuson et al. *J Org Chem* **10** 121, 126 *1945*, Fuson & Cole *J Am Chem Soc* **60** 1237 *1938*], and electrochemical coupling between 1,3-dibromopropane and dimethyl maleate which gave a 10/1 ratio of *trans*/*cis* dimethyl esters in 42% yield [Lu et al. *J Org Chem* **55** 2503, 2507 *1990*]. Invariably the crude *trans*-diesters formed are contaminated with some *cis*-isomer and it was found that hydrolysing the ester mixture by refluxing the acidic solution for 4 to 5 days provided only the *trans*-acid in ~95% yields. The *trans*-acid crystallises (charcoal) from hot H_2O, and it is easily soluble in AcOH, and EtOH, but very soluble in Et_2O, $CHCl_3$, $*C_6H_6$ and petroleum ether. Its FT-IR (Nujol)) has ν_{max} at 3008.3, 2653.8, 1692.6, 1419.2, 1311.1, 1253.5, 1199.3, 935.7 and 689.4 cm^{-1}; its ^1H NMR (60MHz, $CDCl_3$) has δ_H at 12.2 (br s, 2H, OH), 2.96 (m, 2H, C1 and C2 methines), 1.99 (m, 2H,), 1.69 (m, 4H); its ^{13}C NMR (75MHz, $CDCl_3$) has δ_C at 176.10 (s, carboxylic C), 46.77 (s, C1 and C2), 30.03 (s, C3 and C5) and 25.01 (s, C-4); and its GC-MS has *m/z* (relative intensity) *trans*-isomer: 157(37, M^+ -2), 155(15), 126(67), 113(29), and 67(100), and *cis*-isomer: 157(6, M^+-2), 155(40), 126(32), 113(56), and 67(100) [Lu et al. *J Org Chem* **55** 2503, 2507 *1990*]. ***Dimethyl** trans-**cyclopentane-1,2-dicarboxylate*, b 118.5-119°/17mm, n_D^{20} 1.4491,** *[941-75-3]*, is obtained by treating the acid with diazomethane in Et_2O, evaporating and distilling the residue [Owen & Peto *J Chem Soc* 2383, 2386 *1955*]. *trans-**cyclopentane-1,2-dicarbonyl dichloride, has **b 98-100°/2mm** [Aspinall & Baker *J Chem Soc* 743, 747 *1950*], and *trans-**cyclopentane-1,2-dicarboxylic acid***

dihydrazide, prepared from the dimethyl ester and NH_2NH_2. H_2O in EtOH, and recrystallised from EtOH, has **m 224-225°** [Müller et al. *J Am Chem Soc* **73** 2489 *1951*]. [*Beilstein* **9** H 728, **9** I 316, **9** III 3807, **9** IV 2793.]

1S,2S*-(+)-*trans*-1,2-Cyclopentanedicarboxylic acid** *[21917-20-4]* **M 158.2, m 181°, $[\alpha]_D$ +87.6° (c 0.88, H_2O)** and ***1R,2R*-(–)-*trans*-1,2-cyclopentanedicarboxylic acid** *[17224-73-6]* **m 180-181°, $[\alpha]_D$ –85.9° (c 1.2, H_2O).** Optical resolution of the (±)-acid (above) is readily achieved *via* separation of the diastereoisomeric brucine salts (the base being *l*-brucine). Thus pure (±)-acid (15g, ~0.1mole) is dissolved in hot H_2O, and while stirring, the finely powdered brucine tetrahydrate (90g, 0.2 moles, [5892-11-5], care **POISONOUS**) that is added gradually dissolves. At the end of the addition, the mixture is stirred for ~10 minutes and filtered hot from a small amount of undissolved brucine. The brucine is washed well with hot H_2O, and the combined filtrate and washings are concentrated on a boiling water bath until crystals commence to form on the surface. When the liquid is cooled and vigorously stirred, copious crystals of the *d*-acid (*l*-base)$_2$ separate, and the whole mixture sets into a mass of crystals. These are filtered off and recrystallised from hot H_2O to constant specific rotation. An analytical sample of the *d*-acid (*l*-base)$_2$ is obtained by dissolving it in hot H_2O and allowing it to crystallise slowly in a desiccator over concentrated H_2SO_4. The decahydrate is obtained on drying the crystalline plates in air but they effloresce in a vacuum desiccator or on heating at 125° for 1 hour to give *anhydrous* ***d*-acid (*l*-base)$_2$** that has **$[\alpha]_D$ –19.9° (c 1.3, H_2O).** The *d*-acid (*l*-base)$_2$ is then decomposed by dissolving it in hot H_2O, adding aqueous ammonia, filtering off the solid brucine, washing it well with aqueous ammonia, and the combined hot filtrate and washings are cooled and acidified with hydrochloric acid. On cooling the **(+)-*acid (m 178-180°) separates and recrystallises from hot H_2O as plates with m 180°. ***Diethyl 1S,2S-(+)-trans-1,2-cyclopentanedicarboxylate*** **b 170°/100mm, $[\alpha]_D$ +70.3° (c 1.3, Me_2CO)**, is prepared by boiling the (+)-acid with 5 times its weight of 10% ethanolic H_2SO_4 for 6 hours, cooling, adding H_2O, the ester is extracted into Et_2O which is washed with dilute Na_2CO_3, dried (Na_2SO_4), filtered, evaporated and the residue is distilled in a vacuum. The ***1S,2S-(+)-trans-dianilide*****, m 245-247°, $[\alpha]_D$ +110.1° (c 0.85, Me_2CO)** is prepared by heating the (+)-acid with $SOCl_2$ in a sealed tube at 100° for 1 hour, evaporating, the di-acid chloride formed is then dissolved in $*C_6H_6$, treated with excess of aniline, evaporated again, the residue is stirred with dilute aqueous HCl, the precipitate is collected and recrystallised twice from large volumes of MeOH.
1R,2R-(–)-trans-1,2-cyclopentanedicarboxylic acid is obtained by concentrating the mother liquors from the first crystallisation of the *d*-acid (*l*-base)$_2$ above, which provides copious crystals of the more soluble ***diastereoisomeric l*-acid (*l*-base)$_2$**. Treatment of this salt with aqueous ammonia as above followed by recrystallisation from H_2O gives the pure ***(–)-acid*** with m 180-181°. ***Diethyl 1R,2R-(-)-trans-1,2-cyclopentanedicarboxylate*****,** prepared in the same way as its enantiomer above has similar properties except for the optical rotation which is **$[\alpha]_D$ -69.8° (c 1.7, Me_2CO)**. [Goldsworthy & Perkin Jnr *J Chem Soc* **105** 2639 *1914*]. [*Beilstein* **9** I 316] The absolute configuration of the ***(-)-acid*** was determined as ***1R,2R*** by comparing the ORD spectra of the respective 1,2-bis(N-methylthionamide) [1,2-(CSNHMe)$_2$] with those of the corresponding 1,2-disubstituted cyclopropane, cyclobutane and cyclohexane homologues [Inoue et al. *Tetrahedron* **23** 3237 *1967*]. [*Beilstein* **9** III 3807.]

***1RS,2SR-cis*-1,2-Cyclopentanediol (*meso-cis*-cyclopentane-1,2-diol)** *[5057-98-7]* **M 102.1, m 24-28°, 30°, b 88-92°/2mm, 108-109°/20mm, 123.5°/29mm, n_D^{21} 1.4770.** The *cis*-diol can be obtained by treating cyclopentene (21.8g, [142-29-0]) in EtOH (600ml) at –40° with a solution of $KMnO_4$ (40g) and anhydrous $MgSO_4$ (30g) in H_2O (800ml) dropwise, with vigorous stirring, during 2 hours. The MnO_2 is filtered off, washed with hot H_2O, the combined aqueous filtrates are evaporated *in vacuo* to 100ml and continuously extracted with Et_2O (liquid-liquid extractor) for 48 hours. The dried ($MgSO_4$) Et_2O extract is evaporated and the residual oil is distilled to give the *cis*-diol (11.1g, 34%). The cis-*di-p-nitrobenzoate* has **m 117° (117-118°)** (from EtOH) the cis-*di-methanesulfonate* has **m 82°** (needles from MeOH), and the cis-*di-toluene-p-sulfonate* has **m 92°** (prisms from EtOH) are obtained in the usual way in pyridine. The *cis-monoacetate* has **b 104-106°/20mm, n_D^{17} 1.4576**, the *cis-monoacetate-mono-p-nitrobenzoate* has **m 93-94°** (nodules from EtOH), and the *cis-diacetate* has **m –5°, b 80°/2mm**. The *cis-dibenzoate* has **m 47°**. [Owen & Smith *J Chem Soc* 4026 *1952*, *Beilstein* **6** I 369, **6** II 742, **6** III 4053, **6** IV 5187.]

***1RS,2RS*-(±)-*trans*-1,2-Cyclopentanediol [*trans*-(±)-cyclopentane-1,2-diol]** *[5057-99-8, (±) 86703-52-8]* **M 102.1, m 50°, 55°, b 93°/2mm, 122°/10mm, 136°/22mm.** The *cis*-diol can been prepared in a seven step synthesis from *racemic* diethyl tartrate [Cunningham & Kündig *J Org Chem* **53** 1823 *1988*], from *trans*-2-tri-

methylsilylcyclopentan-1-ol and MeOH [Kono & Ngai *Org Prep Proced Int* **6** 19 *1974*], and by performate oxidation of cyclopentene which is described herein. A mixture of 30% aqueous H_2O_2 (13g) and formic acid (105g) is added to cyclopentene (6.6g, b 44-45°/atm [142-29-0]) under a reflux condenser, when much heat is generated, the temperature is allowed to fall to 40° and is so maintained for 4 hours. The solvent is removed *in vacuo*, the residue is dissolved in 10% aqueous NaOH (50ml), boiled under reflux for 45 minutes, the solvent is distilled off, and the residue is twice distilled under reduced pressure to give pure *trans*-pentane-1,2-diol (6g, 60%) which solidified in the distillate. The *trans-dibenzoate* has **m 63°**, and the *trans-(±)-di-p-nitrobenzoate* **(m 145°**, from EtOH), the *trans-(±)-di-methanesulfonate* **(m 82°,** small needles from EtOH), and the *trans-(±)-di-p-toluenesulfonate* **(m 109°**, colourless plates from MeOH) are prepared in the usual way in pyridine. [Owen & Smith *J Chem Soc* 4026 *1952*, Englund *J Prakt Chem* **129** 1, 10 *1931*, *Beilstein* **6** H 739, **6** I 369, **6** II 743, **6** III 4053, **6** IV 5187.]

1R,2R*-(–)-*trans*-1,2-Cyclopentanediol [*trans-(-)*-cyclopentane-1,2-diol]** *[(–) 930-46-1, (-)86703-52-8]* **M 102.1, m 48-48.5°, $[\alpha]_D^{20}$ –24.88° (c 6, EtOH)** and ***1S,2S-trans*-1,2-cyclopentanediol [*trans*-(+)-cyclopentane-1,2-diol]** *[(+)107492-82-0], m 47-48°, $[\alpha]_D^{20}$ +24.54° (c 5.4, EtOH).** The *1R,2R-enantiomer* is obtained optically pure in a seven step synthesis from diethyl D(-)tartrate by benzylation (TlOEt/$PhCH_2Br$, 81%), reduction (LAH/Et_2O, 94%) to *2R,3R-(–)-2,3-bis(benzyloxy)-1,4-butanediol*, ditosylation (TsCl/py, 87%), dibromination (with LiBr/DMSO, 94%) to *2R,3R-(–)-2,3-bis(benzyloxy)-1,4-butanedibromide*, formation of the cyclopentane ring ($PhSO_2CH_2SO_2Ph/K_2CO_3$/DMF, 92%) to give *1R,2R-(–)-1,2-bis(benzyloxy)-4,4-bis(phenylsulfonyl)cyclopentane*. Removal of the bis-sulfonyl groups (Mg/MeOH, 82%) provide *1R,2R-(–)-1,2-bis(benzyloxy)cyclopentane*, and finally debenzylation (H_2/10% Pd/C, 99%) provides pure 1*R*,2*R*-(-)-cyclopentane-1,2-diol in 47% overall yield. The final step only is detailed here. The mixture of *trans-(–)*-1,2-bisbenzyloxycyclopentane (5.11g, 18.1mmol) in EtOH (35ml) containing 10% Pd/C (1.35g) is degassed three times, H_2 gas is introduced into the flask at a pressure of 6 atmospheres for 5 hours, the catalyst is filtered off, and the filtrate is evaporated to provide the 1*R*,2*R*-*trans*-(–)-diol (8.2g, 99%) as a white hygroscopic solid m 47-48° which should be stored under dry N_2 in a sealed vessel. The enantiomeric 1*S*,2*S*-*trans*-(–)-diol can be prepared in 40% overall yield from diethyl L(+)-tartrate *via* the same high yielding steps. Its IR (CH_2Cl_2) has ν_{max} at 3600, 3390br, 2920, 1450, 1280, 1075, 1040 and 970 cm^{-1}; and its ^1H NMR (200MHz, $CDCl_3$, TMS) with δ at 3.93-4.06 (m, 2H), 2.24 (s, 2H, exchanges with D_2O), 1.86-2.12 (m, 2H), 1.63-1.80 (m, 2H) and 1.42-1.62 (m, 2H). The enantiomers are >96% enantiomerically pure. The **1*R*,2*R*-*(–) [113350-86-0]*** and **1*S*,2*S*-*(+) [113303-27-8]* 1,2-bis(dimethoxyphosphinoxy)cyclopentane** derivatives, prepared from the respective diols ($2NEt_3/2(MeO)_2PCl$, in 80% and 73% yields respectively), are yellow oils with **b 120°/0.1mm** and **$[\alpha]_D^{20}$ –41.39°** and **+41.78° (c 4.8, CH_2Cl_2)**. The **1*R*,2*R*-*(–) [113303-35-8]*** and **1*S*,2*S*-*(+) [113303-28-9]* 1,2-bis(difluorophosphinoxy)cyclopentane** derivatives, prepared from the respective diols (PCl_3 in CH_2Cl_2/SbF_3 in pentane, 49% and 48% respectively) are mobile oils with **b 58°/80mm** and **$[\alpha]_D^{20}$ –12.22°** and **+12.96° (c 4.8, CH_2Cl_2)**. [Cunningham & Kündig *J Org Chem* **53** 1823 *1988*].

1,2-Cyclopentanedione *[3008-40-0]* **M 98.1, m 55-56°, 56°, b 67-69°/1.4mm, 87-88°/16mm, 97°/20mm, 105°/20mm, pK^{20} 9.14 (H_2O).** The dione has a weak amine-like odour and is soluble in H_2O, EtOH, and Et_2O, but poorly soluble in petroleum ether and CS_2, and is steam volatile. It has been prepared by various routes from cyclopentanone *via* oxidation by SeO_2 (23%) [Goto et al. *Bull Chem Soc, Jpn* **52** 2589 *1952*], conversion to the α-methylthio ether then oxidation with $CuCl_2$/CuO (42%) [Gregoire et al. *J Org Chem* 51 1419 1986], and autooxidation with O_2/*t*-BuOK/DME-*t*-BuOH (35.7%). Only the first is described because of its simplicity. *The following procedure should be carried out in a well-ventilated fume cupboard as selenium compounds have foul odours.* To cyclopentanone (1.5L) warmed at 30° is added dropwise, with stirring, a solution of selenium dioxide (361g, 3.25ml) in dioxane (420ml) and H_2O (155ml) during 24 hours, and stirring is continued for a further 18 hours at 35°. The red selenium that is formed is filtered off (Buchner) and extracted with EtOH (500ml) by boiling for 3 hours. The liquids are combined and distilled through a 60cm Vigreaux column at 20mm, the lower boiling portion (b 35-90°) is removed, and the remainder is distilled at 10mm until a thick brown residue is left in the distilling flask. This distillate is redistilled, and the fraction with b 86-88°/16mm is collected to give pure *1,2-dione* (74g, 23% based on SeO_2 used) which solidifies (m 56-58°). It should be stored at –30° under N_2, in the dark. Cyclopentane-1,2-dione has IR (NaCl) with ν_{max} at 1650 (C=C), 1700 (C=O), 3300 (OH enol) cm^{-1}; ^1H NMR (400MHz, CCl_4, TMS) with δ at 2.20-2.67 (m, 4H, 2-methylenes), 6.47-6.62 (m, 1H, C=C*H*), 6.93-7.36 (m, 1H, C=CO*H*); ^{13}C NMR (100MHz, $CDCl_3$, TMS) with δ 22.01, 32.58, 131.36, 153.62, 187.53.

In ethanolic solution the '*dione*' is almost entirely in the ***mono-enol***-form which slowly tautomerises to a mixture containing ~9% of the ***diketo-***form after 36 hours at 50°. The UV in hexane has λ_{max} (log ε) at 246nm (4.003) and 300nm (1.900) due mostly to the ***diketo***–form, whereas in 0.05N aqueous NaOH it has λ_{max} (log ε) at 288nm (3.383) due to the ***enol***-form [Hesse & Krebbiel *Justus Liebigs Ann Chem* **563** 35 *1934*].
Cyclopentane-1,2-dione dioxime (see above [6635-29-6]) decomposes at ~210° after recrystallisation from H_2O, and a 0.01M aqueous solution of it is used for the gravimetric determination of Ni. [Voter et al. *Anal Chem* **21** 1320 *1949*.] The *bis-phenylhydrazone* has **m 146°**.

1,3-Cyclopentanedione *[3859-41-4]* **M 98.1, m 149-150°, 151-152.5°, 151-154°, 151-153°, pKa 4.5.** Purify the dione by Soxhlet extraction with $CHCl_3$. The $CHCl_3$ is evaporated and the residue is recrystallised from EtOAc and/or sublimed at 120°/4mm. [IR: Boothe et al. *J Am Chem Soc* **75** 1732 *1953*, DePuy & Zaweski *J Am Chem Soc* **81** 4920 *1959*, *Beilstein* **7** IV 1981.]

Cyclopentanol *[96-41-3]* **M 86.1, m –20°, –19.5°, b 53°/10mm, 56.9-57.4°/34mm, 139.5°/752mm, 140.85°/760mm, d_4^{20} 0.9478, n_D^{20} 1.4531.** Cyclopentanol has been prepared by hydration of cyclopentene, or from cyclopentanone (see next entry) by catalytic reduction with H_2 (Ni/MeOH, Ra-Ni/EtOH, PtO_2, Pt-black in EtOH or AcOH, Cu-chromite), $Al(isoPrO)_3$/NaOH, LAH/Et_2O or $NaBH_4$ in MeOH or H_2O. The last named has many advantages in ease of use and efficiency. Thus cyclohexanone in H_2O (solubility is 15% at 10°, 8.7% at 20°, 5% 30°) is stirred with excess of $NaBH_4$ (theoretically 0.25 mol/mol ketone) at room temperature until the reaction is complete (addition of a drop of dilute HCl causes effervescence). The pH of the solution is adjusted to ~3-4, NaCl is added to almost saturation and the alcohol is extracted several times with Et_2O, dried (K_2CO_3), filtered, and the filtrate is distilled to give cyclopentanol in ~90% yield. [Chaikin & Brown *J Am Chem Soc* **71** 122 *1949*]. Its FT-IR (neat) has ν_{max} at 3334.9 (br OH), 2959.6 (CH), 1437.2 (OH ?), 1341.3, 1282.9, 1174.3, 1073.7, 994.3, and 837.1 cm^{-1}; the ^1H NMR (60MHz, $CDCl_3$, TMS) has δ at 1.55 (m, 4H, C-3 and C-4 -methylenes), 1.75 (m, 4H, C-2 and C-5 -methylenes), 2.30 (s, 1H, H-1) and 4.30 (brs, 1H, OH); and its ^{13}C NMR (15MHz, $CDCl_3$, TMS) has δ at 23.32 (C-3,4), 35.51 (C-2,5) and 73.86 (C-1). At atmospheric pressure cyclopentanol forms azeotropes with H_2O (96.3°, 42%), tetrachloroethylene (118.8°, 8%), chlorobenzene, *m*-xylene (132.8°, 40%), *p*-xylene (132.8°, 38%), *n*-Bu_2O (139.0°, 75%), among other solvents. It can be characterised as the *4-nitrobenzoate* (**m 56°**), *3,5-dinitrobenzoate* (**m 123°**), and *phenylcarbamate* (**m 137-138°**). [*Beilstein* **6** H 5, **6** I 3, **6** II 3, **6** III 4, **6** IV 5.]

Cyclopentanone (dumasine, adipic ketone) *[keto-form 120-92-3, enol-form 59557-02-7]* **M 84.1, m –58°, b 130°/atm, d_4^{20} 0.947, n_D^{20} 1.4366, n_D^{25} 1.4340. pK^{25} 16.7.** This is a flammable liquid (flash point 26-31°) with a pleasant odour, but which is a strong **SKIN** and **EYE IRRITANT**, and should be used in a well ventilated fume cupboard. It is sparingly soluble in H_2O, and forms explosive mixtures with HNO_3 and H_2O_2. It is volatile with Et_2O and care should be taken that careful fractionation is require when it is extracted with Et_2O. It is prepared by heating, in a distilling flask, a powdered mixture of adipic acid (200g, 1.34moles) and ground $Ba(OH)_2$ (10g) in a metal bath (e.g. Wood's metal) to 285-295° during 1-1.5 hours. [The temperature is best controlled with the thermometer within 5mm above the bottom of the flask and the temperature held as near as 290° as possible to minimising the amount of adipic acid which distils off.] During the heating period, the *cyclopentanone* distils slowly with small quantities of adipic acid, and after a further 2 hours of heating a very small amount of dry residue remains in the flask. The distillate is separated from some H_2O and adipic acid by salting out with K_2CO_3, washed with H_2O, dried over $CaCl_2$ or anhydrous K_2CO_3, filtered and fractionated through an efficient column; fraction with b 128-131°/atm of the pure *ketone* (86-92g, 75-80%) is collected. [Thorpe & Kon *Org Synth* Coll Vol **1** 192 *1932*.] If cyclopentanone has been standing for a while, it can be purified by shaking it with aqueous $KMnO_4$ to remove materials absorbing around 230 to 240nm. Dry it over Linde-type 13X molecular sieves and fractionally distil it. It has also been purified by conversion to the $NaHSO_3$ adduct which, after crystallising four times from EtOH/water (4:1), is decomposed by adding to an equal weight of Na_2CO_3 in hot H_2O. The free cyclopentanone is steam distilled from the solution. The distillate is saturated with NaCl and extracted with *benzene (do not use H_2O, see above) which is then dried (anhydrous K_2CO_3), filtered and evaporated. The residue is then distilled [Allen, et al. *J Chem Soc* 1909 *1960*]. Its FT-IR (NaCl) has ν_{max} at 2966 (CH), 1746.4 (C=O), 1407.6 (OH enol ?), 1278.2, 1153.0, 959.2, 834.2,

582.2 and 471.7 cm^{-1}; the ^1H NMR (15MHz, $CDCl_3$, TMS) has δ at 1.97 (t, 4H, C-3 and C-4 -methylenes), 2.17 (t, 4H, C-2 and C-5 -methylenes); and its ^{13}C NMR (60MHz, $CDCl_3$, TMS) has δ at 23.24 (C-3,4), 38.30 (C-2,5) and 220.16 (C-1).
The *oxime* [1192-28-5] forms prisms with **m 56.5°, b 120-121°/45mm**, **196°/atm**, the *semicarbazone* [5459-00-7] has **m 224°**, the *2,4-dinitrophenylhydrazone* [2057-87-6] has **m 145.5, 146.5°**, and the *ethylene ketal (1,4-dioxaspiro[4.4]nonane* [176-32-9] has **m 153°**. The ***enol***-form is present to the extent of 2.5 x 10^{-7}% in the gas phase.

Cyclopentyl methyl ether (CPME) *[5614-37-9]* **M 100.2, fp –134.8°, b 105.44°/760mm 105-106.5°/760mm 106°/760mm, d_4^{20} 0.8627, n_D^{20} 1.4206.** This ether has the advantage of having a high resistance to hydroperoxide formation. It is an "environmentally friendly" solvent and is an alternative to ether solvents like THF, Et_2O and methyl *tert*-butyl ether. Two methods after Williamson's synthesis have been reported. In the *first* Na (370g, 16g. atoms) is dissolved in MeOH (2370g, 74moles) and excess of MeOH is distilled off until NaOMe starts to separate. The solution is cooled to 60° and cyclopentyl chloride (1254g, 12moles, b 114°/atm [930-28-9]) is added slowly and kept at 60° for 100 hours. The mixture is then fractionated to give recovered cyclopentyl chloride (21%), cyclopentyl methyl ether (278g, 29% based on reacted cyclopentyl chloride) and cyclopentene (31% which distils as an azeotrope with MeOH (b 37-38°/atm). [Olson et al. *J Am Chem Soc* **69** 2451 *1947*.] In the *second*, Na (15g) is dispersed under hot xylene, cooled, the xylene is replaced with anhydrous Et_2O (150ml), and a solution of cyclopentanol (57g, b 141-142°/769mm, see [96-41-3]) in dry Et_2O (~100ml) is added with stirring during 3 hours and allowed to stand for 12 hours. Methyl iodide (103g) is then added during 2 hours to the preceding sodio compound as the Et_2O boils gently, allowed to stand overnight, the Et_2O is distilled off, the crude CPME is then distilled out and redistilled under N_2 at 105°/763mm to give pure *cyclopentyl methyl ether* (21g, 32%). It can be stabilised with 50ppm of BHT. [Vogel *J Chem Soc* 1809 *1948*, *Beilstein* **6** III 5, **6** IV 6.]

Cyclotetradecane *[295-17-0]* **M 192.3, m 56°.** Recrystallise it twice from aqueous EtOH, then sublime it *in vacuo* [Dretloff et al. *J Am Chem Soc* **109** 7797 *1987*].

Cyclotetradecanone *[3603-99-4]* **M 206.3, m 25°, b 145°/10mm, d_4^{20} 0.926, n_D^{20} 1.480.** It is converted to the semicarbazone which is recrystallised from EtOH and re-converted to the free cyclotetradecanone by hydrolysis [Dretloff et al. *J Am Chem Soc* **109** 7797 *1987*]. Fractionate it in a vacuum.

Decahydronaphthalene (decalin, mixed isomers) *[91-17-8]* **M 138.2, b 191.7°/760mm, d_4^{20} 0.886, n_D^{20} 1.476.** Stir decalin with conc H_2SO_4 for several hours. Then the organic phase is separated, washed with water, saturated aqueous Na_2CO_3, again with water, dried with $CaSO_4$ or CaH_2 (and perhaps dried further with Na), filtered and distilled under reduced pressure (**b** 63-70°/10mm). It has also been purified by repeated passage through long columns of silica gel previously activated at 200-250°, followed by distillation from $LiAlH_4$ and storage under N_2. Type 4A molecular sieves can be used as drying agent. Storage over silica gel removes water and other polar substances. [For the separation of *cis* and *trans* isomers see Seyer & Walker *J Am Chem Soc* **60** 2125 *1938*, and Baker & Schuetz *J Am Chem Soc* **69** 1250 *1949*.]

***cis*-Decahydronaphthalene** *[493-01-6]* **M 138.2, f –43.2°, b 195.7°, 81-83°/19mm, d_4^{20} 0.897, n_D^{20} 1.48113.** Purification methods described for the mixed isomers are applicable here. The individual isomers can be separated by very efficient fractional distillation, followed by fractional crystallisation by partial freezing. The *cis*-isomer reacts preferentially with $AlCl_3$ and can be removed from the *trans*-isomer by stirring the mixture with a limited amount of $AlCl_3$ for 48 hours at room temperature, filtering and distilling. [Seyer & Walker *J Am Chem Soc* **60** 2125 *1938*, Baker & Schuetz *J Am Chem Soc* **69** 1250 *1949*.] A very pure authentic sample is best obtained by synthesis from *cis*-1,2-bis-chloroethylcyclohexane [Whitesides & Gutowski *J Org Chem* **41** 2882 *1976*, *Beilstein* **5** IV 310.]

***trans*-Decahydronaphthalene** *[493-02-7]* **M 138.2, f –30.6°, b 187.3°, d_4^{20} 0.870, n_D^{20} 1.46968.** See purification of *cis*-isomer above. [Seyer & Walker *J Am Chem Soc* **60** 2125 *1938*, Baker & Schuetz *J Am Chem Soc* **69** 1250 *1949*, *Beilstein* **5** IV 311.]

(+)-Dehydroabietylamine (abieta-8,11,13-triene-18-ylamine) *[1446-61-3]* **M 285.5, m 41°, 42.5-45°, b 192-193°/1mm, 250°/12mm, n_D^{40} 1.546, $[\alpha]_{546}^{20}$ +51° (c 1, EtOH), pK_{Est} ~10.3.** The crude base is purified by converting 2g of base in toluene (3.3ml) into the *acetate salt* by heating at 65-70° with 0.46g of AcOH, and the crystals are collected and dried (0.96g from two crops, **m** 141-143°). The acetate salt is then dissolved in warm H_2O, basified with aqueous NaOH and extracted with $*C_6H_6$. The dried extract ($MgSO_4$) is evaporated in vacuum leaving a viscous oil which crystallises and can be distilled. [Gottstein & Cheney *J Org Chem* **30** 2072 *1965*.] The *picrate* has **m** 234-236° (from aqueous MeOH), and the *formate* has **m** 147-148° (from heptane). [*Beilstein* **12** IV 3005.]

Diamantane (congressane) *[2292-79-7]* **M 188.3, m 234-235°, 243-245°.** Purify diamantane by repeated crystallisation from MeOH or pentane. *Alternatively*, purify it by dissolving it in CH_2Cl_2, washing with 5% aqueous NaOH and water, and drying ($MgSO_4$). The solution is filtered, concentrated to a small volume, an equal weight of alumina is added, and the solvent evaporated. The residue is placed on an activated alumina column (*ca* 4 x weight of diamantane) and eluted with petroleum ether (b 40-60°). Eight sublimations and twenty zone refining experiments gave material **m** 251° of 99.99% purity by differential analysis [Gund et al. *Tetrahedron Lett* 3877 *1970*, Courtney et al. *J Chem Soc Perkin Trans I* 2691 *1972*]. [For spectra see Cupas et al. *J Am Chem Soc* **87** 919 *1965*.]

1.3-Diaminoadamantane *[10303-95-4]* **M 164.3, m 52°, $pK_{Est(1)}$ ~8.6, $pK_{Est(2)}$ ~10.6.** Purify it by zone refining. The *dibenzoyl* derivative has **m** 248°, and the *dihydrochloride salt* has **m** 310° (360°) after recrystallisation from aqueous EtOH or EtOH/Et_2O. [Prelog & Seiwerth *Chem Ber* **74** 1769 *1941*, Stetter & Wulff *Chem Ber* **93** 1366 *1960*.]

cis*-1,2-Diaminocyclohexane (*meso*-chxn)** *[1436-59-5]* **M 114.2, b 92-93°/8mm, 170°/atm, d_4^{25} 0.952, n_D^{20}1.493, pK_1^{20} 6.13 (6.41), pK_2^{20} 9.93(9.91).** It is prepared by reduction of the cis-1,2-dioxime with boiling Na/EtOH, or from *cis*-1,2-dihydrazinocarbonylcyclohexane with $NaNO_2$/HCl [Jaeger & Blumendal *Z Anorg Chem* **175** 165 *1928*]. Dry the diamine over solid KOH and distil it in a vacuum. It is a strong base, keep it away from CO_2, and store it in the dark under N_2. The *dihydrochloride* has **m 307-310°**, and the *dipicrate* **(**from H_2O) has **m 260°(dec)**. This cis-diamine is a ***meso form because its mirror image is identical to it, and is superimposable over it (see below) [*Beilstein* **13** II 3, **13** IV 5.]

(±)-*trans*-1,2-Diaminocyclohexane [(±)-chxn)] *[1121-22-8]* **M 114.2, m 14-15°, b 78-81°/15mm, 85-88°/25mm, d_4^{25} 0.951, n_D^{20} 1.489, pK_1^{20} 6.47(6.72), pK_2^{20} 9.94(9.86).** Purify this ***racemic base***, and store it as for the *cis*-isomer above since it is a strong base, and becomes yellow on storage. [*Beilstein* **13** H 1, **13** III 8, **13** IV 5.]

***cis/trans*-1,2-Diaminocyclohexane *resolution.* [*Note that the* trans- *isomer is a racemic mixture, whereas the* cis- *isomer has a* meso *configuration and its mirror image is identical and superimposable over it.*]** A solution of L(+)-tartaric acid (150g, 0.99mol) in distilled H_2O (400ml) in a 1L beaker is stirred until clear, and a mixture of *cis*- and *trans*- 1,2-diaminocylohexane (240ml, 1.94mol, of ~60/40 *trans*/*cis* mixture which is commercially available and is cheaper than the pure *trans* compound for which the same procedure applies) is added at a rate whereby the temperature rises to 70°. Glacial acetic acid (100ml, 1.75mol) is then added at such a rate that the temperature rises to 90°. A white precipitate immediately separates as the acid is added, and the slurry is stirred vigorously until the temperature cools slowly to 25°(~2 hours), and then is cooled further to ~5° in an ice bath for 2 hours, and is collected by filtration. The filter cake is washed with H_2O (100ml at ~5°), then EtOH (5 x 100ml), and dried by sucking air through it for 1 hour and analysed for enantiomeric purity *via* the bis-*m*-toluoyl amide*. The salt is then dried *in vacuo* at ~40° to give *R,R*-1,2-diamoniumcyclohexane mono-(+)-tartrate as a white solid (160g, 99%) in ≥99% enantiomeric excess (ee). If the optical purity is not as expected then recrystallise the salt in two crops from Me_2CO (1:20 w/v with ~60-70% recovery). The *S,S*-diastereomeric tartrate salt is obtained by using D(–)-tartaric acid. If the 'ee' is <99%, or if the difference between the top and the bottom of the cake is >0.2%, then the cake should be washed with more MeOH. If product of ≥99% 'ee' is required then recrystallisation of the tartrate salt by dissolving it in H_2O (≈ 1:10 w/v) with heating to 90°, followed by cooling to 5° overnight, gives ~60-70% recovery.

* The diammonium salt (25mg) is mixed with 4N NaOH (0.5ml), CH_2Cl_2 (1.5ml) and *m*-toluoyl chloride (50µl)

with vigorous mixing. The lower (organic layer) is diluted with 10µl of *iso*-propanol, and 10µl of this is analysed by HPLC using *iso*-propanol/hexane (1:9) mixture at 1ml/minute flow rate. [Larrow et al. *J Org Chem* **59** 1939 *1994*, Gasbøl et al. *Acad Chem Scand* **26** 3605 *1972*.]

***1R,2R*(–)-*trans*-1,2-Diaminocyclohexane [(–)-chxn)]** *[20439-47-8]* **M 114.2, m 41-45°, [α] $^{20}_{D}$ –25.5° (c 5 M HCl). m 14-15°.** Distil or recrystallise the diamine from petroleum ether under N_2 or Ar. It has a plain-negative ORD curve [Gillard *Tetrahedron* **21** 503 *1965*, O'Brien & Toole *J Am Chem Soc* **77** 1368 *1955*]. Store it as above. The *1R,2R-base L-tartrate salt* has *[39961-95-0]*, **M 264.3, m 273°** and **[α] $^{25}_{D}$ +12.5° (c 4, H_2O)**, and can be used to purify and/or optically enrich the free base. [*Beilstein* **13** III 6, and references below.]

***1S,2S*(+)-*trans*-1,2-Diaminocyclohexane [(+)-chxn)]** *[21436-03-3]* **M 114.2, m 42-45°, b 104-110°/40mm, [α] $^{20}_{D}$ +25.5° (c 5 M HCl).** Distil or recrystallise the diamine from petroleum ether under N_2 or Ar. Store it as above. It has a plain-positive ORD curve [Gillard *Tetrahedron* **21** 503 *1965*, O'Brien & Toole *J Am Chem Soc* **77** 1368 *1955*]. The *1S,2S-base D-tartrate salt* has *[67333-70-4]*, **M 264.3, m 180-184°(dec)** and **[α] $^{25}_{D}$ –12.5° (c 4, H_2O)** from which the free base can be purified or optically enriched. It is a useful chiral synthon. [Fjii et al. *J Chem Soc, Chem Commun* 45 *1985,* Takahashi et al. *Tetrahedron Lett* **30** 7095 *1989*, Hanassian et al. *J Org Chem* **58** 1991 *1993*, for absolute configuration see Gillard *Tetrahedron* **21** 503 *1965*, *Beilstein* **13** III 7.]

***trans*-1,4-Diaminocyclohexane** *[2615-25-0]* **M 114.2, m 69-72°, b 197°/760mm, $pK_{est(1)}$ ~9.4, $pK_{est(2)}$ 10.8.** Recrystallise the diamine from petroleum ether under N_2 or Ar as it should be an even stronger base than the above 1,2-diamine isomers. It distils under N_2. Store it in the dark under N_2. [*Beistein* **13** I 3, **13** III 11.]

(1*RS*,2S*R*)-*cis*-1,2-Diaminocyclopentane (1*RS*,2S*R*-*cis*-1,2-cyclopentanediamine, *meso*-1,2-cyclo-pentane-diamine, (*meso*)-cptn) *[40535-45-3; no configuration 41330-23-8]* **M 100.1, b 62-65°/13.5mm, 99°/60mm.** Whereas reduction of ***anti***-*cyclopentane-1,2-dione dioxime* (see below, and from reaction of cyclopentane-1,2-dione and NH_2OH) with Na/EtOH yields predominantly *trans-(±)-diamine,* the reaction of *cyclopentane-1,2-dione monooxime* [31597-37-0] with NH_2OH gives a 2:1 mixture of *anti*- and *amphi*- dioximes which provide the less water soluble red bis-*anti*-dioximatoNi(II) complex and the more water soluble yellow-brown bis-*amphi*-dioximatoNi(II) complex respectively. When this mixture of Ni(II) complexes, or the *amphi*-complex, is reduced with KBH_4 in "diglyme", the base finally isolated is pure *cis-1,2-cyclopentanediamine*.
Thus, ***bis(amphi-cyclopentane-1,2-dione dioximato)nickel(II)*** (79g, 90.5mol, dried over H_2SO_4 *in vacuo*) is added to a solution of KBH_4 (30g) dissolved in dry diglyme [600ml, bis(2-methoxyethyl) ether, [111-96-6]) in 2L flask. N_2 is bubbled through the solution, then during 1 hour anhydrous $AlCl_3$ (25g) in dry diglyme (100ml) is added dropwise carefully as vigorous evolution of H_2 ensues; the temperature being kept below 35° by cooling in ice-water. When evolution of H_2 ceases, the mixture is heated at 70° for 18 hours. Then a solution of KOH (100g) in H_2O (150ml) is added carefully, and the ***cis-diamine*** is steam distilled off; 6L of distillate are collected, acidified with 12M HCl (to pH 3), and the dry ***cis-1,2-cyclopentanediamine dihydrochloride*** (23g, 27% based on the Ni complex) is isolated as for the *trans-(±)-isomer* below. The free base, ***cis-1,2-cyclopentanediamine*** **b 62-65°/13.5mm (**83%, based on the dihydrochloride) is stored under N_2 at –20°. [Toftlund & Pedersen *Acta Chim Scand* **26** 4019 *1972*]. This *cis-diamine* has been fractionated through a vacuum-jacketed distillation column as described by Ray et al. *Rev Sci Instr* **28** 200 *1957*, and the fraction with **b 99°/60mm** contained pure *cis*-isomer [Phillips & Royer *Inorg Chem* **4** 616 *1965*].
The ^1H NMR in D_2O (TMS as external standard) can be used to distinguish between *trans-(±)-1,2-diamine* and and the preceding *cis-(meso)-1,2-diamine* because the triplets from carbon atoms 1 + 2 occur at δ 2.72 and δ 2.77 respectively [Phillips & Royer *Inorg Chem* **4** 616 *1965*].
Distinct bis- and tris- *cis*-cptn complexes such as $[Ni(cis\text{-cptn})_2](ClO_4)_2.6H_2O$, $[Ni(cis\text{-cptn})_3](ClO_4)_2$ and $[Co(cis\text{-cptn})_3]Br_2.3H_2O$ are readily formed [Toftlund & Pedersen *Acta Chim Scand* **26** 4019 *1972*]. [*Beilstein* **4** II 3.]

(1*RS*,2*RS*)-(±)-*trans*-1,2-Diaminocyclopentane [(1*RS*,2*RS*)-*trans*-1,2-cyclopentanediamine, (±)-*trans*-1,2-cyclopentanediamine, (±)-cptn] *[3145-88-8]* **M 100.1, b 65-67°/13.5mm, 103°/60mm, 170°/atm, $pK_{Est\ 1}$ ~7.0 , $pK_{Est\ 2}$ ~10.0.** This diamine is a strong base and is best kept as its salts which are not greatly affected by moisture and CO_2. It is prepared by reduction of anti-*cyclopentan-1,2-dione dioxime [6635-29-6]* **M 128.1, m 210° (215° dec; 210-225° dec, darkening at 192-205°** also reported for an analytically pure sample) which is

obtained by adding *2-ethoxycarbonylcyclopentanone* (31.2g, b 102-104°/12mm, [611-10-9]) to a solution of NaOH (8.8g) in H_2O (160ml) whereby a heavy white precipitate separates. A solution of $NaNO_2$ (13.8g) in H_2O (32ml) is then added to it and the mixture, under N_2, is shaken mechanically for 44 hours at ~25°. The resulting clear yellow solution is cooled to 0°, and at this temperature 6N H_2SO_4 is added carefully while CO_2, and oxides of nitrogen evolve. The solution is extracted with Et_2O (in a continuous liquid-liquid extractor) for 5.5 hours, the extract is evaporated under N_2 and reduced pressure to a small volume of ~20ml. This suspension of crude cyclopentane-1,2-dione monooximes is treated with a solution of hydroxylamine hydrochloride (13.9g) and NaOH (8.0g) in H_2O (50ml) when heat is evolved and a precipitate separates immediately. The mixture is allowed to stand overnight at 5°, the light tan crude ***anti**-cyclopentane-1,2-dione dioxime* (16.8g, 66%, decomposes at 230-240°) is filtered off and is dried *in vacuo*, leaving the more soluble ***amphi**-cyclopentane-1,2-dione dioxime* in the filtrate. The analytically pure *anti-dioxime* (dec at 210-225° without melting, 83% recovery, [6635-29-6]) can be obtained by dissolving the crude material (1g) in 2% aqueous NaOH (25ml) at ~25° (slightly turbid), stirring with Norit, filtering, neutralising the filtrate with 1 N HCl (to phenolphthalein), filtering off the solid, washing it twice with H_2O, once with Me_2CO and it drying *in vacuo*. [Cope et al. *J Am Chem Soc* **73** 1199 *1951*, Lloyd & Marshall *J Chem Soc* 2597 *1956*.]

Alternatively, to a stirred mixture of granulated Na (38g) and *C_6H_6 (900ml, dried over Na) is added diethyl adipate (225ml, 1.11mole, [141-28-6]) rapidly followed by absolute EtOH (5ml), and is boiled under reflux with stirring for 18 hours then cooled to 0°. The white solid that separated is filtered off, washed with a little *C_6H_6 and dried *in vacuo* over shredded paraffin wax to give ***sodium cyclopentanone-2-carboxylate*** (180g**)**. This salt (1mol) is partly dissolved in ice-water (600ml), N_2 is bubbled through for 15 minutes to remove O_2; and a mixture of a solution of NaOH (4g, 0.1mol) and $NaNO_2$ (70g, 1.03mol) in H_2O (160ml) is added dropwise to it. The mixture is then heated under N_2 with vigorous stirring at 40° for 30 hours. After cooling to 0°, 6M H_2SO_4 (200ml, 1.2mol) is added in one hour; and when evolution of CO_2 has ceased the solution is neutralised with 12M ammonia. A solution of NH_2OH HCl (70g, 1.0mol) in H_2O (160ml), neutralised with K_2CO_3 (70g, 0.5mol), is immediately added. After 1 hour, the precipitation of crude *anti-**cyclopentane-1,2-dione dioxime*** as light tanned needle-like crystals is complete; it is filtered off, washed with a little H_2O and dried *in vacuo* over H_2SO_4 for 48 hours (yield 90g, 62% calculated on diethyl adipate used). The filtrate contains the ***amphi-cyclopentane-1,2-dione dioxime*** which is isolated as the yellow-brown ***bis(**amphi**-cyclopentane-1,2-dione dioximato)nickel(II) complex*** (30g) by slowly adding Ni(II)SO_4 7H_2O (20g) in H_2O (60ml) to this filtrate, and washing the complex with H_2O and drying in air. [Toftlund & Pedersen *Acta Chim Scand* **26** 4019 *1972*.]

Bis(**amphi**-cyclopentane-1,2-dione dioximato)nickel(II) complex is obtained analytically pure, as a red precipitate in 70% yield, from ***anti-**cyclopentane-1,2-dione dioxime* (12.8g, 0.1mol) in 4M ammonia (15ml), by adding slowly Ni(II)Cl_2 6H_2O (12g, 0.05mol) in H_2O (40ml) to it, filtering off the solid, washing it with H_2O and drying it in air. [Toftlund & Pedersen *Acta Chim Scand* **26** 4019 *1972*.]

Reduction to (±)-diamine*:** The ***anti**-cyclopentane-1,2-dione dioxime* (10g) in absolute EtOH (2L) is reduced by addition of freshly cut small pieces of Na metal (180g) over a period of several hours. The solution is refluxed until all the metal has dissolved. The EtOH is distilled off *in vacuo*, the residue is basified strongly with 10N NaOH, and the base is steam distilled. The distillate is made strongly alkaline with aqueous NaOH, extracted with trichloroethylene, the solvent is evaporated and ***trans-1,2-cyclopenanediamine then distils at **65°/13.5mm, n_D^{25} 1.4850-1.4858** in 29% yield. When the fractional distillation is carried out using a column (90 x 1 cm) packed with glass helices and the reflux ratio is kept at >40:1, the first 25% of distillate contains a significant amount of lower boiling *cis-diamine*, **99°/60mm**; the remaining 75% of material then boils at a constant temperature, **103°/60mm**, and is the ***trans-(±)-diamine***. *Alternatively*, the steam distillate is acidified with concentrated HCl, the solution is evaporated to dryness *in vacuo*, and the residue is recrystallised from EtOH/Et_2O to provide ***trans-(±)-1,2-cyclopentanediamine dihydrochloride*** in 77% yield, which **decomposes at 287-290°** (darkening gradually >230°), and forms a ***dihydrate*** on exposure to air. The ***trans-(±)-dipicrate*** has **m 233-233.5° (dec)** after recrystallisation from aqueous EtOH or H_2O, and the ***trans-(±)-diacetyl derivative*** has **m 226.5-227.5° (dec)** after recrystallisation from EtOH by addition of Et_2O. [Cope et al. *J Am Chem Soc* **73** 1199 *1951*, Phillips & Royer *Inorg Chem* **4** 616 *1965*, Lloyd & Marshall *J Chem Soc* 2599 *1956*, Jaeger & Blumendal *Z Anorg Allgem Chem* **175** 161 *1928*.]

***Alternative reduction to (±)-diamine*:** The ***anti**-cyclopentane-1,2-dione dioxime* (20g, 156mmol) in absolute EtOH (1.5L) is reduced by heating to 40° (internal temperature), and stirring under a reflux condenser, with Mg powder (8g) and Hg(II)Cl_2 (0.1g) while Na metal (150g, 6.5mol, in 5g pieces) is added *via* the top of the condenser and keeping the temperature below 50° (internal temperature). The mixture is finally heated to boil-

ing in order to dissolve all the Na. The *(±)-diamine* is isolated by steam distillation (external heating being necessary so as to maintain a small volume in the flask) until the pH of the distillate is below 8 (*ca* 4L). This is acidified (pH 3) with 12M HCl, evaporated almost to dryness *in vacuo* (at ~25°), excess HCl is removed by washing with EtOH/Et_2O (2:1v/v, 20ml), and the hygroscopic salt is dried over KOH in a desiccator to give the ***(±)-diamine dihydrochloride*** (5g, 18% based on dioxime). The free base is obtained by adding the dihydrochloride (5g, 29mmol) in small portions with stirring to a 1:1v/v mixture of MeOH/Et_2O (50ml) into which is dissolved Na (1.7g, 74mmol, cooling). After stirring for 1 hour, the precipitated NaCl is filtered off, extracted with MeOH/Et_2O (1:1v/v, 5ml), the combined extract and filtrate are evaporated to ~3ml and this residue is distilled in a N_2 atmosphere to give **(±)-*trans*-cyclopentane-1,2-diamine**, **b 65-67°/13.5mm** (2.5g, 89%, based on the dihydrochloride) which is stored under N_2 at –20°. Distinct *trans*-(±)-cptn complexes of Ni, Co, Rh and Pt have been prepared; some are enantiomorphic and others are structural isomers [Phillips & Royer *Inorg Chem* **4** 616 *1965*, Jaeger & Blumendal *Z Anorg Allgem Chem* **175** 161 *1928*, Toftlund & Pedersen *Acta Chim Scand* **26** 4019 *1972*].
The ^1H NMR in D_2O (TMS as external standard) can be used to distinguish between *trans-(±)-1,2-diamine* and and the preceding *cis-(meso)-1,2-diamine* because the triplets from carbon atoms 1 + 2 occur at δ 2.72 and δ 2.77 respectively [Phillips & Royer *Inorg Chem* **4** 616 *1965*].

(1*R*,2*R*)-(–)-*trans*-1,2-Diaminocyclopentane dihydrochloride [(–)-cptn HCl] *[1030390-38-5]* **M 173.1, m dec, $[\alpha]_D^{25}$ –23.5° (c 2, 1M HCl)** and **(1*S*,2*S*)-(+)-*trans*-1,2-Diaminocyclopentane dihydrochloride [(+)-cptn HCl]** *[477873-22-6]* **M 173.1, m dec, $[\alpha]_D^{25}$ +23° (c 2, 1M HCl).** ***Optical resolution*:** (±)-Cptn (2g, 20mmol) is resolved by adding it to a solution of D-(+)-tartaric acid (7g, 47mmol) in MeOH (1ml) and H_2O (7ml), and at 40° MeOH (12ml) is added dropwise. The mixture is then kept at 3° for 18 hours, the crystalline solid is filtered off, washed with MeOH (10ml) to give the less soluble hydrogen tartrate salt [5.2g, 65% based on (±)-cptn]. After two recrystallisations, the **(–)-cptn-(+)-tartrate salt** [2.5g, 31.4% based on (±)–cptn] has **m 134-135°** (143-144° also reported), **$[\alpha]_D^{25}$ +10.1° (c 2,** H_2O**)**. When this salt (2.4g, 6mmol) in H_2O (8ml) is treated with a solution of KCl (0.9g, 12mmol) in H_2O (4ml), the highly insoluble potassium hydrogen tartrate separates and is filtered off after standing for 1 hour. Addition of solid KOH (8g, with cooling) allowed solid (–)-cptn hydrate to separate, but the mixture is extracted thoroughly with Et_2O (5 x 10ml), the extract is dried (KOH or $MgSO_4$), filtered, and evaporated to give **(–)-*trans*-cptn** (0.55g, 92% based on tartrate salt). When carried out on a larger scale the ***(–)-base*** can be distilled, **b 166°/atm, d^{25} 0.9463**, and has **$[\alpha]_D$ -54.7° (neat)**, **$[\alpha]_D$ -42° (*C_6H_6)**, **$[\alpha]_D$ –39° (H_2O)**, and a plain-negative ORD curve. **(–)-*trans*-Cptn sulfate** has **$[\alpha]_D$ -12° (H_2O)**. [Toftlund & Pedersen *Acta Chim Scand* **26** 4019 *1972*, Jaeger & Blumendal *Z Anorg Allgem Chem* **175** 161 *1928*, Phillips & Royer *Inorg Chem* **4** 616 *1965*]. **(+)-Cptn-(+)-tartrate** can be obtained from the mother liquors of the above resolution in order to isolate the (+)-base; but it is advisable to collect all the mother liquors, liberate the free base with KOH, isolate it and repeat the process using L-(–)-tartaric acid to form the less soluble diasterioisomeric **(+)-cptn-(–)-tartrate salt.** Pure **(+)-*trans*-cptn** can then be isolated as above and will have the same physical properties except for the optical rotations that will be of opposite sign and has a plain-positive ORD curve [Dunlop et al. *J Chem Soc* 3160 *1964*, Gillard *Tetrahedron* **21** 503 *1965*, O'Brien & Toole *J Am Chem Soc* **77** 1368 *1955*]. [*Beilstein* **4** II 3, **4** III 5]
Complexes of optically active cptn with Rh, Co, Ni and Pt have been prepared, and in some cases enantiomeric and geometrical isomers have been identified. One has been used to obtain pure enantiomeric diamine, for example, the complex **$[Co_2(\pm\text{-cptn})_7\ (H_2O)_2]^{6+}$** has been resolved into three bands on Amberlite CG-50 carboxylic acid resin 400-400 by elution with aqueous HCl (pH 2, flow rate 5ml/hour) and collecting 40ml fractions. Bands I, II and III are probably geometrical isomers because when the isolated complexes are decomposed with concentrated aqueous NaOH, extracted with *C_6H_6, the extract dried and evaporated, the free base ***(+)-cptn*** with **$[\alpha]_D$ –42° ±1° (*C_6H_6)** is obtained (compare with above) [Phillips & Royer *Inorg Chem* **4** 616 *1965*].
The optical properties (ORD, CD) of several cptn-transition metal complexes have been thoroughly investigated and used to determine and confirm the absolute configuration of cptn [Dunlop et al. *J Chem Soc* 3160 *1964*, Gillard *Tetrahedron* **21** 503 *1965*]. The crystal structure of **$(-)_{587}$-$[Co(+trans\text{-cptn})_3]Cl_3.4H_2O$** confirms the *1S,2S-configuration* for the dextro-enantiomer [Ito et al. *Acta Cryst* **B 27** 2187 *1971*].

trans*-1,2-Dibromocyclopentane** ***[*10230-26-9]* **M 227.9, b 72.5°/15mm, 74°/17mm, d_4^{20} 1.857, n_D^{25} 1.5460.** It is prepared by addition of bromine to cyclopentene at –20° followed by fractional distillation. The ^1H NMR

(60MHz, CCl_4) has a complex multiplet centered at ~2.5 ppm (3 x CH_2), and two triplets centered at 4.58ppm (J = 7.4Hz, for 2 x CHBr) from TMS. [Altona et al. *Rec Trav Chim, Pays Bas* **85** 983 *1966*, cf Abell et al. *J Am Chem Soc* **82** 3610 *1960*.]

***cis*-3,4-Dichlorocyclobutene** *[2957-95-1]* **M 123.0, b 70-71°/55mm, 74-76°/55mm, d $_4^{20}$ 1.297, n $_D^{20}$ 1.499.** Distil the cyclobutene at 55mm through a 36-in platinum spinning band column, a fore-run b 58-62°/55mm is mainly 1,4-dichlorobutadiene. When the temperature reaches 70° the reflux ratio is reduced to 10:1 and the product is collected quickly. It is usually necessary to apply heat frequently with a sun lamp to prevent any dichlorobutadiene from clogging the exit in the early part of the distillation [Pettit & Henery *Org Synth* **50** 36 *1970*].

Dicyclohexylamine (Cy_2NH_2) *[101-83-7]* **M 181.3, m 20°, b 83°/1mm, 99.3°/4mm, 113.5°/9mm, 117-120°/10mm, 135.4°/30mm, 154.3°/50mm, 199°/200mm, 255.8°/atm, d $_4^{20}$ 0.912, n $_D^{20}$ 1.4845, pK^{25} 11.25.** It is a strong base, has a fishy odour, is soluble in H_2O, and organic solvents and forms adducts with some of them. It can be purified by fractional distillation at atmospheric pressure, but if the distillate is coloured (e.g. green) then distillation under reduced pressure gives a clear colourless liquid [Vogel *J Chem Soc* 1828 *1928*]. The *hydrochloride [4693-92-9]* crystallises from H_2O or EtOH and has **m 334-335°** (sealed tube), and the *acetyl derivative [1563-91-3]* has **m 103°** (from Et_2O). [Diwoky & Adkins *J Am Chem Soc* **53** 1870 *1931*, *Beilstein* **12** H 6, **12** I 114, **12** II 7, **12** III 19, **12** IV 22.] **SKIN and EYE IRRITANT**.

1,3-Dicyclohexylcarbodimide (DCC) *[538-75-0]* **M 206.3, m 34-35°, b 95-97°/0.2mm, 120-121°/0.6mm, 155°/11mm.** It is sampled as a liquid after melting in warm H_2O. It is sensitive to air, and *it is a potent* ***skin irritant.*** It can be distilled in a vacuum, and is best stored in a tightly stoppered bottle in a freezer. It dissolves readily in CH_2Cl_2 and pyridine where the reaction product with H_2O, after condensation, is dicyclohexyl urea which is insoluble and can be filtered off. *Alternatively*, dissolve it in CH_2Cl_2, add powdered anhydrous $MgSO_4$, shake for 4 hours, filter, evaporate and distil the residue at 0.6mm pressure and oil bath temperature of 145°. [Bodansky et al. *Biochemical Preparations* **10**, 122 *1963*, Schmidt & Seefelder *Justus Liebigs Ann Chem* **571** 83 *1951*, Schmidt et al. *Justus Liebigs Ann Chem* **612** 11 *1958*, *Beilstein* **12** IV 72.]

***N,N*-Dicyclohexylmethylamine (Cy_2NMe, *N*-methyldicyclohexylamine)** *[7560-83-0]* **M 195.3, b 131-133°/13mm, 135-137°/15mm, 150°/50mm, 265°/atm, d $_4^{25}$ 0.912, n $_D^{25}$ 1.4900, pK 8.2.** When dicyclohexylamine (90.5g, 0.5mol, see 101-83-7) and 55% aqueous formic acid (121.1ml, 2.5mol) are heated at ~100° and 35% aqueous formaldehyde (97.5g, 11.25mol) is added dropwise over an hour, CO_2 evolution occurs. After gas evolution is complete, ~15 hours, concentrated HCl (1mol) is added and the mixture is evaporated *in vacuo*. The free base is liberated from the residue with strong aqueous NaOH and the oil is extracted with Et_2O, dried (solid KOH), filtered, the filtrate is evaporated *in vacuo* and the residue is fractionally distilled to give Cy_2NMe in 51% yield. It was also obtained by alkylating Cy_2NH with dimethylsulfate. [Hünig & Kiessel *J Prakt Chem* **5** 224 *1958*.] The *hydrochloride* has **m 154-154°** (from EtOAc), and the *methiodide* has m **228-229°** (from EtOH/Et_2O). [*Beilstein* **12** I 115, **12** II 8, **12** III 21, **12** IV 23.]

3,4-Diethoxy-3-cyclobutene-1,2-dione (diethyl squarate) *[5321-87-8]* **M 170.2, b 89-91°/0.4mm, 88-92°/0.4mm, d $_4^{20}$ 1.162, n $_D^{25}$ 1.5000.** Dissolve the ester in Et_2O, wash it with Na_2CO_3, H_2O and dry (Na_2SO_4) it, filter, evaporate and distil it using a Kügelrohr, or purify it by chromatography. Use a Kieselgel column and elute with 20% Et_2O/petroleum ether (b 40-60°), then with Et_2O/petroleum ether (1:1), evaporate and distil the residue *in vacuo*. [Dehmlow & Schell *Chem Ber* **113** 1 *1980*, Perri & Moore *J Am Chem Soc* **112** 1897 *1990*, IR: Cohen & Cohen *J Am Chem Soc* **88** 1533 *1966*] **It can cause severe dermatitis.** [Foland et al. *J Am Chem Soc* **111** 975 *1989*, Perri et al. *Org Synth* **69** 220 *1990*].

***N,N*-Diethylcyclohexylamine** *[91-65-6]* **M 155.3, b 85-87°/15mm, 193°/760mm, d $_{25}^{25}$ 0.850, n $_D^{25}$ 1.4562, pK^{25} 10.72.** Dry the amine with BaO and fractionally distil it. It is a strong base, store away from CO_2. The *picrate* has **m** 98-99° (from aqueous EtOH) and the *methiodide* has **m** 224° (from Me_2CO/petroleum ether) [Cadogan *J Chem Soc* 1081 *1957*.] [Bain & Pollard *J Am Chem Soc* **61** 2704 1939, *Beilstein* **12** H 6, **12** III 14, **12** IV 19.]

Diethyl cyclopropane-1,1-dicarboxylate *[1559-02-0]* **M 186.2, b 94-96°/10mm, d_4^{25} 1.055, n_D^{20} 1.433.** If it is free from OH bands in the IR, then fractionally distil the ester and redistil the middle fraction. Otherwise shake it with aqueous $NaHCO_3$, dry it ($MgSO_4$), filter and distil as before or re-esterify it. [As synthon see Danishefsky *Acc Chem Res* **12** 66 *1979*, *Beilstein* **9** I 314, **9** II 512, **9** III 3595, **9** IV 2786.]

Dimedone (5,5-dimethylcyclohexane-1,3-dione) *[126-81-8]* **M 140.2, m 148-149°, pK^{25} 5.27.** Crystallise dimedone from acetone (*ca* 8ml/g), water or aqueous EtOH. Dry it in air. [Schneider & Todd *Org Synth* Coll Vol **II** 200 *1943*, *Beilstein* **7** H 559, **7** IV 1999.]

***cis- and trans*-1,4-Dimethylcyclohexane** *[589-90-2]* **M 112.2, b 120°, d_4^{20} 0.788, n_D^{25} 1.427.** Free it from olefins by shaking with conc H_2SO_4, washing with water, drying and fractionally distilling it. [Haggis & Owen *J Chem Soc* 411 *1953*, *Beilstein* **5** III 102, **5** IV 122.]

1,2-Dimethylcyclohexene *[1674-10-8]* **M 110.2, b 135-136°/760mm, d_4^{25} 0.826, n_D^{25} 1.4587.** Pass it through a column of basic alumina and distil it. If removal of 2-methylmethylenecyclohexane or 2,3-dimethylcyclohexene is required, then fractionation through a centre-rod column operating at ~50 theoretical plates is required. [Hammond & Nevitt *J Am Chem Soc* **76** 4121 *1954*, *Beilstein* **5** III 213, **5** IV 268.]

Ethyl chrysanthemumate (ethyl ±2,2-dimethyl-3{c and t}-[2-methylpropenyl]cyclopropane carboxylate) *[97-41-6]* **M 196.3, b 98-102°/11mm, 117-121°/20mm.** Purify the ester by vacuum distillation. The free *trans-acid* has **m** 54° (from EtOAc), and the free *cis-acid* has **m** 113-116° (from EtOAc). The *4-nitrophenyl ester* has **m** 44-45° (from petroleum ether) [Campbell & Harper *J Chem Soc* 283 *1945*, IR: Allen et al. *J Org Chem* **22** 1291 *1957*]. [*Beilstein* **9** II 45.]

Ethylcyclohexane *[1678-91-7]* **M 112.2, b 131.2°/742mm, d_4^{20} 0.7839, n_D^{20} 1.43304, n_D^{25} 1.43073.** Purify it by azeotropic distillation with 2-ethoxyethanol; then the alcohol is washed out with water and, after drying, the ethylcyclohexane is redistilled. The dried material has been repeatedly fractionated over Na. [Baker & Groves *J Chem Soc* 1148 *1939, Beilstein* **5** H 35, **5** III 90, **5** IV 115.]

Ethyl cyclohexanecarboxylate *[3289-28-9]* **M 156.2, b 76-77°/10mm, 92-93°/34mm, 196-196.2°/760mm, d_4^{20} 0.955, n_D^{20} 1.441.** Wash the ester with N sodium hydroxide solution, then water, dry with Na_2SO_4 and distil it. The *amide* has **m** 185-186°. [Adkins & Cramer *J Am Chem Soc* **52** 4355 *1930*, Newman & Walborsky *J Am Chem Soc* **72** 4296 *1950*, *Beilstein* **9** III 17, **9** IV 18.]

Ethyl 2-oxocyclohexanecarboxylate (2-ethoxycarbonylcyclohexanone, 2-carbethoxycyclohexanone, ethyl 2-ketohexahydrobenzoate) *[1655-07-8]* **M 170.2, b 86-88°/3.2mm, 106°/11mm, d^{25} 1.064, n_D^{20} 1.47940, pK^{25} 10.94 (12.87).** The ester is obtained by the decarbonylation of *ethyl 2-ketocyclohexylglyoxalate* (which in turn is prepared from cyclohexanone and diethyl oxalate in the presence of NaOEt). The *ethyl glyoxalate* (~250-265g, boiling at 105° to 165°/10-15mm) is mixed with Fe powder (1-3mg) and finely ground soft glass 0.5-1.0g) in a Claisen flask (~500ml), and heated in a 40mm vacuum (bath temperature at 165-175°, not higher, to avoid unreacted ester from distilling) while CO [TOXIC] evolves and decarbonylated ester distils between 125-140°, requiring 1.5 to 2 hours for pyrolysis. The desired ester obtained (200-210g, 85.8%) has n_D^{25} 1.476 to 1.479. [Snyder et al. *Org Synth* Coll Vol **II** 531 *1943*.]
The ester has FT-IR (neat) with ν_{max} at 2939.5 (CH), 1716.2 (C=O), 1658.3 (C=O ester), 1442.5 (OH enol ?), 1365.2, 1299.3, 1219.0, 1082.9 and 832.9 cm^{-1}; ^1H NMR (60MHz, $CDCl_2$, TMS) with δ at 1.30 (t, 3H, ester C*H*$_3$), 1.65 (m, ~4H, 2-methylenes), 2.25 (m, 4H 2-methylenes), 3.35 (t, 1H, partly enolised), 4.20 (q, 2H, ester C*H*$_2$) and ~12.0 (s, enolic O*H*); and ^{13}C NMR (15MHz, $CDCl_3$, TMS) with δ at 14.17, 14.33, 21.97, 22.42, 23.31, 27.13, 29.10, 29.98, 41.55, 57.22, 60.12, 61.04, 97.72, 169.93, 171.93, 172.71, 206.19. [*Beilstein* **10** IV 2606.]
The *enol* content of *ethyl 2-oxocyclohexanecarboxylate* is higher than that of the *ethyl 2-oxocyclopentanecarboxylate* below ([611-10-9]) and varies with polarity of solvent, *viz*: 67% aqueous MeOH (22.2%), MeOH (45.1%), EtOH (61.7%), $CHCl_3$ (54.5%), $*C_6H_6$ (74.8%) [Kabachnik et al. *Tetrahedron* **1** 317

1957, Gero *J Org Chem* **19** 1960 *1954*, see also Schreck *J Am Chem Soc* **71** 1881 *1949*, Buu-Hoi & Cagniant *Bull Soc Chim Fr* **10 [5]** 251 *1943*, Lewin *Izv Akad S.S.S.R Ser fiz* **11** 413 *1947*, *Chem Abstr* **42** 3261 *1948*]. [*Beilstein* **10** H 601, **10** II 420, **10** III 2813, **10** IV 2606.]

Ethyl 2-oxocyclopentanecarboxylate (2-ethoxycarbonylcyclopentanone, 2-carbethoxycyclopentanone, Dieckmann Ester) *[611-10-9, ± 53229-92-8]* **M 156.1, b 79-81°/3mm**, **86-87°/6mm**, **102°/11mm, 108-111°/15mm**. The ester is prepared in a dry N_2 atmosphere by adding ethyl adipate (202g, 1mole), during 2 hours, to a stirred (important to use a Hershberg stirrer, Hershberg *Ind Eng Chem, Anal Ed* **8** 313 *1936*) suspension of Na metal (23g, 1g.atom) in dry toluene (250ml). The reaction starts immediately and the temperature is maintained at 100-115° (oil bath) during the 2 hours and for 5 hours longer, while dry toluene is added (~750ml to 1L) so as to keep the mixture fluid and efficiently stirred, and to avoid 'caking'. The mixture is cooled to 0° and slowly added with stirring to 10% aqueous KOH (below 1°), cold H_2O being added to keep the potassium salt in solution; the toluene layer is separated, washed with cold H_2O (2 x 150ml), cold 10% aqueous KOH (adding cold H_2O to dissolve separated potassium salt), the yellow toluene solution is finally washed with cold H_2O (2 x 150ml). The combined aqueous layers, after extraction with Et_2O (250ml), are run slowly, with stirring at 0°, into cold 10% AcOH. The oily ester which separates is extracted into Et_2O (400ml), the aqueous layer is extracted with Et_2O (4 x 250ml). The combined Et_2O extracts are washed with 7% aqueous Na_2CO_3, dried (Na_2SO_4), filtered, evaporated and the residue is distilled (**b 79-81°/4mm**) to give the *keto-ester* (100-115g, 64-74%) free from ethyl adipate. An alternative synthesis in $*C_6H_6$ with slight modification provided 79-82% yield of ester. [Pinkney *Org Synth* Coll Vol **II** 116 *1943*, Cornubert & Borrel *Bull Soc Chim Fr* **47** 301 *1930*.]

The *enol* content of *ethyl 2-oxocyclopentanecarboxylate* is low and varies little with polarity of solvent, *viz*: MeOH (4.0%), EtOH (3.9%), $CHCl_3$ (3.7%), $*C_6H_6$ (8.2%) [Kabachnik et al. *Tetrahedron* **1** 317 *1957*, Lewin *Izv Akad S.S.S.R Ser fiz* **11** 413 *1947*, *Chem Abstr* **42** 3261 *1948*]. The ester has FT-IR (neat) with ν_{max} at 2979.9 (CH), 1725.6 (C=O), 1678.8 (C=O ester), 1454.5 (OH enol ?), 1370.0, 1255.0, 1190.7, 1111.9 and 1026.3 cm^{-1}; ^1H NMR (60MHz, $CDCl_3$, TMS) with δ at 1.29 (t, J = ~7Hz, 3H, ester Me), 1.89 (m, 1H, C-3 H_{eq}), 2.24 (m, 1H, C-3 H_{ax}), 2.31 (m, 4H, C-4,5 methylenes), 3.15 (t, 1H, J = ~8Hz, C-1 H), 4.20 (q, J = ~7Hz, ester CH_2); ^{13}C NMR (15MHz, $CDCl_3$, TMS) with δ at 14.18, 20.98, 27.43, 38.04, 54.77, 61.26, 169.37 and 212.25.

N-Phenyl 2-oxocyclopentanecarboxamide *[4874-65-1]* **M 203.2, m 104°** is obtained by boiling aniline (25mmol) with ethyl 2-oxocyclopentanecarboxylate (100mmol) and pyridine (0.5ml) for 2 minutes, cooling and the solid that separates is filtered off, washed with cold EtOH, then with 4% aqueous NaOH to free it from any anil formed. The solution is filtered and acidified with dilute AcOH, the precipitate is filtered off, dried and the *anilide* is recrystallised from EtOH. [Barany & Pianka *J Chem Soc* 1420 *1947*.] It is soluble hot EtOH and in Me_2CO. A 0.3% solution of the anilide in EtOH is used for the gravimetric determination of Be, Hg V and U [Chaudhuri & Das *Anal Chim Acta* **57** 193 *1971*].

1-Ethynyl-1-cyclohexanol *[78-27-3]* **M 124.2, m 30-33°, 32-33°, b 74°/12mm, 76-78°/17mm, 171-172°/694mm, 180°/atm, d_4^{25} 0.9734, n_D^{25} 1.4801.** Dissolve it in Et_2O, wash it with H_2O, dilute $NaHCO_3$, H_2O again, dry (Na_2SO_4), filter, evaporate and distil the residue. The IR (CCl_4) has ν_{max} at 3448 (OH), 2941 (CH), 1449-1123 and 956 cm^{-1}, and the ^1H NMR (CCl_4) has δ at 3.2 (OH), 2.5 (≡ CH), 1.70 (m 10H, CH_2) [Hasbrouck & Kiessling *J Org Chem* **38** 2103 *1972*]. [*Beilstein* **6** II 100.] **TOXIC.**

Eucaliptol (1,8-cineol, 1,8-epoxy-*p*-menthane, 1,3,3-trimethyl-2-oxabicyclo[2.2.2]-octane) *[470-82-6]* **M 154.2, m 1.3°, 1.5°, b 39-39.3°/4mm, 176-176.4°/760mm, d_4^{20} 0.9232, n_D^{20} 1.4575.** Purify 1,8-cineol by dilution with an equal volume of petroleum ether, then saturate it with dry HBr. The precipitate is filtered off, washed with small volumes of petroleum ether, then cineole is regenerated by stirring the crystals with H_2O. It can also be purified *via* its *o*-cresol or resorcinol addition compounds. Store it over Na until required. Purify it also by fractional distillation. It is insoluble in H_2O but soluble in organic solvents. [IR: Kome et al. *Nippon Kagaku Zasshi* [*J Chem Soc Japan* (Pure Chem Sect)] **80** 66 *1959*, *Chem Abstr* 603 *1961*, *Beilstein* **17** II 32, **17/1** V 273.]

(+)-α-Fenchol (1*R*-1,3,3-trimethylnorbornan-2-ol) *[1632-73-1]* **M 154.3, m 40-43°, 47-47.5°, b 201-**

202°, $[\alpha]_D^{20}$ +12.5° (c 10, EtOH). It is prepared by reduction of (–)-fenchone and is purified by recrystallisation from $*C_6H_6$/petroleum ether, or distillation, or both. The *2-carboxybenzoyl (monophthalate) derivative* has **m** 146.5-147.5° $[\alpha]_D^{20}$ -20.4° (EtOH), and the *2-phenylurethane* has **m** 81°. [Beckmann & Metzger *Chem Ber* **89** 2738 *1956*]. [*Beilstein* **6** III 288, **6** IV 278.]

(+)- Fenchone (1*S*-1,3,3-trimethylnorbornan-2-one) *[4695-62-9]* **M 152.2, m 5-7°, 6.1°, b 63-65°/13mm, 66°/15mm, 122°/10mm, d_4^{20} 0.9434, n_D^{20} 1.4636, $[\alpha]_D^{20}$ +66.9° (neat, or in c 1.5, EtOH), $[\alpha]_{546}^{20}$ +60.4° (neat).** The oily liquid is purified by distillation in a vacuum and is very soluble in EtOH and Et_2O. [Boyle et al. *J Chem Soc, Chem Commun* 395 *1971,* Hückel *Justus Liebigs Ann Chem* **549** 186 *1941*, (±)-isomer: Braun & Jacob *Chem Ber* **66** 1461 *1933*.] It forms two *oximes*, the *cis-oxime* has **m** 167° (crystallises from petroleum ether) $[\alpha]_D^{20}$ +46.5° (c 2, EtOH), the *O-benzoyloxime* has **m** 81°, $[\alpha]_D^{18}$ +49° (EtOH), and the *oxime-HCl* has **m** 136°(dec). The *trans-oxime* has **m** 123° (from petroleum ether) $[\alpha]_D^{18}$ +148° (c 2, EtOH) and the *O-benzoyloxime* has **m** 125° $[\alpha]_D^{20}$ +128.5° (c 2, EtOH) [Hückel *Justus Liebigs Ann Chem* **549** 186 *1941*, Hückel & Sachs *Justus Liebigs Ann Chem* **498** 166 *1932*]. [*Beilstein* **7** III 212, **7** IV 212.]

(–)-Fenchone (1*R*-1,3,3-trimethylnorbornan-2-one) *[7787-20-4]* **M 152.2, m 5.2°, b 67.2°/10mm, 191-195°/atm, d_4^{20} 0.9484, n_D^{20} 1.4630, $[\alpha]_D^{20}$ –66.8° (neat).** Purification is as for the (+)-enantiomer above and should have the same physical properties except for opposite optical rotations. UV has λ_{max} 285nm (ε 12.29). [Braun & Jacob *Chem Ber* **66** 1461 *1933*, UV: Ohloff et al. *Chem Ber* **90** 106 *1957*.] [*Beilstein* **7** III 392, **7** IV 212.]

Gibberillic acid A_3 (gibberillin A_3) *[77-06-5]* **M 346.4, m 233-235°(dec), $[\alpha]_{546}^{20}$ +92° (c 1, MeOH), $[\alpha]_D^{20}$ +93° (c 0.5, MeOH), pK 4.0.** It crystallises from EtOAc, EtOAc/petroleum ether, MeOH/petroleum ether or Me_2CO/petroleum ether. [Cross *J Chem Soc* 3022 *1960*, *Beilstein* **18** III/IV 6533.]

1,2,3,4,5,6-Hexachlorocyclohexane *[α–319-84-6, γ–58–89–9]* **M 290.8, m 158° (α□), 312° (ß-), 112.5° (γ-isomer).** Crystallise it from EtOH. Purify it also by zone melting. **Possible CANCER AGENT, TOXIC.** [α: *Beilstein* **1** H **23,** γ: *Beilstein* **5** I 8, many isomers : *Beilstein* **5** III 41, **5** IV 55.]

1,2,3,4,5,5-Hexachlorocyclopenta-1,3-diene *[77-47-4]* **M 272.8, b 80°/1mm, 83-84°/3mm, 234°/atm, d_4^{25} 1.702, n_D^{25} 1.5628.** Dry the diene with $MgSO_4$, filter, and distil it under vacuum in a nitrogen atmosphere. **Irritates skin and eyes, HIGHLY TOXIC.** [McBee et al. *J Am Chem Soc* **77** 4378 *1955*, UV spectra: Idol et al. *J Org Chem* **20** 1746 *1955*, *Beilstein* **5** III 308, **5** IV 381.]

Hexahydromandelic acid *[R-(-)- 53585-93-6, S-(+)- 61475-31-8]* **M 158.2, m 127-129°, 128-129°, 129.7°, $[\alpha]_D^{20}$ (–) and (+) 25.5° (c 1, AcOH) and $[\alpha]_D^{20}$ (–) and (+) 13.6° (c 7.6, EtOH).** It forms hexagonal clusters on recrystallisation from CCl_4 or Et_2O. [Wood & Comley *J Chem Soc* 2638 *1924*, Lettré et al. *Chem Ber* **69** 1594 *1936*]. The *racemate* has **m** 137.2-137.6° (134-135°) [Smith et al. *J Am Chem Soc* **71** 3772 *1949*]. [*Beilstein R-* **10** II 5; *S-* **10** II 6.]

Hexamethyl(Dewar)benzene (HMDB, 1,2,3,4,5,6-hexamethyl-bicyclo[2.2.0]hexa-2,5-diene) *[7641-77-2]* **M 162.3, m 7.5°, b 60°/20mm, ~152°/760mm, d_4^{20} 0.8125, n_D^{20} 1.4480.** HMDB is obtained in ~80% yield when 2-butyne (dimethylacetylene, flammable gas b 27°/atm, [503-17-3]) in $*C_6H_6$ or CH_2Cl_2 containing anhydrous $AlCl_3$ is stirred at 35° for 5-7 hours. The brown reaction mixture is poured onto crushed ice, washed with dilute aqueous NaOH, and HMDB is isolated from the organic phase by fractional vacuum distillation. Hexamethylbenzene (m 165-166°, [87-85-4]) is a by-product (~12-18%) together with a mixture (~2%) of *syn-* (m 127°) and *anti-* (m 196°) octamethyltricyclo[4.2.0.$0^{2,5}$]octa-3,7-diene, and octamethylcyclooctatetraene (m 113°). Although longer reaction times increase the conversion of 2-butyne, they lower the yields of HMDB in favour of the other by-products. It is fairly thermally stable with half-life time conversions to hexamethylbenzene with 105 hours/120°, 5.5 hours/140°, and 2.1 hours/150°. It is best to store it at low temperature and away from light as radiation from a low pressure UV lamp converts it mainly to hexamethylbenzene with ~20-25% of the valence isomer hexamethylprismane (m 91°). The UV spectrum

exhibits tail end absorption from 220 to 250nm; the FT-IR (neat) has ν_{max} at 2950.0, 1683.5, 1439.5, 1368.8, 1275.4, 1222.2, 1064.8, 736.2 and 490.7 cm^{-1}; the ^1H NMR (60MHz, $CDCl_3$, TMS) has δ at 1.08 (s, 6H, 1,4-$(CH_3)_2$) and 1.69 (s, 12H, 2,3,5,6-$(CH_3)_4$), and the ^{13}C NMR (15MHz, $CDCl_3$, TMS) has δ at 10.06 (1,4-Me carbons) and 11.22 (2,3,5,6-Me carbons), 55.68 (2 saturated carbons) and 144.09 (4 olefinic carbons). [Schäfer & Hellmann *Angew Chem Internat Edn* **6** 518 *1967*.] Purify it also by passing it neat through alumina or in $*C_6H_6$ or CH_2Cl_2 solution. [Traylor & Miksztal *J Am Chem Soc* **109** 2770 *1987*].

Humulon *[26472-41-3]* **M 362.5, m 65-66.5°, $[\alpha]_D^{26}$ –212° (95% EtOH).** Crystallise humulon from Et_2O. It dissolves slightly in hot H_2O but precipitates on cooling. It has λ_{max} nm (ε) at 237 (13,760) and 282 (8,330) in EtOH. [Wollmer *Chem Ber* **49** 780 *1916*, Carson *J Am Chem Soc* **73** 4652 *1951*, *Beilstein* **8** II 537, **8** III 4034, **8** IV 3410.]

1-Hydroxymethyladamantane *[770-71-8]* **M 166.3, m 115°.** Dissolve the adamantane in Et_2O, wash it with aqueous 0.1N NaOH and H_2O, dry over $CaCl_2$, evaporate and recrystallise the residue from aqueous MeOH. [Stetter et al. *Chem Ber* **92** 1629 *1959*, *Beilstein* **6** IV 400.]

***N*-Hydroxy-5-norbornene-2,3-dicarboxylic acid imide** *[21715-90-2]* **M 179.2, m 165-166°, 166-169°, pK_{Est}~6**. Dissolve the imide in $CHCl_3$, filter, evaporate and recrystallise from EtOAc. The IR (nujol) has ν_{max} 1695, 1710 and 1770 (C=O), and 3100 (OH) cm^{-1}. The *O-acetyl* derivative has **m** 113-114° (from EtOH) with IR bands at ν_{max} 1730, 1770 and 1815 cm^{-1} only, and the *O-benzoyl* derivative has **m** 143-144° (from propan-2-ol or $*C_6H_6$). [Bauer & Miarka *J Org Chem* **24** 1293 *1959*, Fujino et al. *Chem Pharm Bull Jpn* **22** 1857 *1974*]. [*Beilstein* **21/10** V 188.]

i-Inositol (*myo*) See in "Miscellaneous", Chapter 7.

α-Ionone (*trans*-+) *[127-41-3]* **M 192.3, b 86-87°/1.9mm, 131°/13mm, d_4^{20} 0.929, n_D^{20} 1.5497, $[\alpha]_D^{20}$ +401° (neat) +415° (EtOH).** Purify α-ionone through a spinning band fractionating column. The *semicarbazone* has **m** 157-157.5° (from EtOH) and $[\alpha]_D^{20}$ +433° (c 4, $*C_6H_6$). [Naves *Helv Chim Acta* **30** 769 *1947*, CD: Ohloff et al. *Helv Chim Acta* **56** 1874 *1973*, Buchacker et al. *Helv Chim Acta* **56** 2548 *1973*, *Beilstein* **7** H 168, **7** III 640, **7** IV 363.]

β-Ionone *[79-77-6]* **M 192.3, b 150-151°/24mm, d_4^{20} 0.945, n_D^{20} 1.5211, ε_{296nm} 10,700.** Convert β-ionone to the *semicarbazone* (**m** 149°) by adding semicarbazide hydrochloride (50g) and potassium acetate (44g) in water (150ml) to a solution of ß-ionone (85g) in EtOH. (More EtOH is added to redissolve any ß-ionone that precipitates.) The semicarbazone crystallises on cooling in an ice-bath and is recrystallised from EtOH or 75% MeOH to constant **m** (148-149°). The semicarbazone (5g) is shaken at room temperature for several days with petroleum ether (20ml) and M H_2SO_4 (48ml); then the petroleum ether layer is washed with water and dilute aqueous $NaHCO_3$, dried and the solvent is evaporated. The ß-ionone is distilled under vacuum. (The customary steam distillation of ß-ionone semicarbazone did not increase the purity.) [Young et al. *J Am Chem Soc* **66** 855 *1944*]. [*Beilstein* **7** H 167, **7** I 109, **7** II 140, **7** III 634, **7** IV 361.]

(±)-Irone (6-methylionone, ±-*trans*-(α)-4*t*-[2,5,6,6-tetramethylcyclohex-2-yl]but-3*t*-en-2-one) *[79-69-6]* **M 206.3, b 85-86°/0.05mm, 109°/0.7mm, d_4^{20} 0.9340, n_D^{20} 1.4998.** If large amounts are available, then fractionate through a Podbielniak column or an efficient spinning band column, but small amounts are distilled using a Kügelrohr apparatus. The *4-phenylsemicarbazone* has **m** 174-175° (165-165.5°). [IR: Seidel & Ruzicka *Helv Chim Acta* **35** 1826 *1952*, Naves *Helv Chim Acta* **31** 1280 *1948*, Lecomte & Naves *J Chim Phys* **53** 462 *1956*, *Beilstein* **7** IV 378.]

***dl*-Isoborneol** *[124-76-5]* **M 154.3, m 212° (sealed tube).** Crystallise isoborneol from EtOH or petroleum ether (b 60-80°). It sublimes in a vacuum. The *4-nitrobenzoyl* derivative has **m** 153°. [Yager & Morgan *J Am Chem Soc* **57** 2081 1935, *Beilstein* **6** II 80, **6** III 299, **6** IV 281.]

(–)-γ-Isocaryophyllene (*1R,9S*-8-methylene-4,11,11-trimethylbicyclo[7.2.0]undec-4-ene) *[118-65-0]* **M 204.4, b 122-124°/12mm, 131-133°/16mm, 130-131°/24mm, 271-273°/atm, d_4^{20} 0.8959, n_D^{20} 1.496, $[\alpha]_{546}^{20}$**

–31°, [α] $^{20}_{D}$ –27° (neat). Purify it by vacuum distillation or GLC using a nitrile-silicone column [Corey et al. *J Am Chem Soc* **86** 485 *1964*, Ramage & Simonsen *J Chem Soc* 741 *1936*, Kumar et al. *Synthesis* 461 *1976*]. [*Beilstein* **5** III 1085.]

(–)-β-Isolongifolene (1-*R-(–)*-2,2,7,7-tetramethyltricyclo[6.2.1.0^{1,6}]undec-5-ene) *[1135-66-6]* **M 204.4, b 82-83°/0.4mm, 144-146°/30mm, 255-256°/atm, d $^{20}_{4}$ 0.930, n $^{20}_{D}$ 1.4992, [α] $^{20}_{546}$ –166°, [α] $^{20}_{D}$ –38° (c 1, EtOH).** Reflux it over, and distil it from Na. [Zeiss & Arakawa *J Am Chem Soc* **76** 1653 *1954*, IR: Reinaecker & Graafe *Angew Chem, Int Ed Engl* **97** 348 *1985*, UV and NMR: Ranganathan et al. *Tetrahedron* **26** 621 *1970*, *Beilstein* **5** IV 1191.]

Isophorone *[78-59-1]* **M 138.2, b 94°/16mm, d $^{20}_{4}$ 0.921, n $^{20}_{D}$ 1.4778.** Wash isophorone with aqueous 5% Na_2CO_3 and then distil it under reduced pressure immediately before use. *Alternatively*, it can be purified *via* the semicarbazone. [Erskine & Waight *J Chem Soc* 3425 *1960*, *Beilstein* **7** IV 165.]

Isopinocampheol (pinan-3-ol, 2,6,6-trimethylbicyclo[3.1.1]heptan-3-ol) *[1S,2S,3S,5R-(+)- 27779-29-9, 1R,2R,3R,5S-(–)- 25465-65-0]* **M 154.25, m 52-55°, 55-56°, 55-57°, b 103°/11mm, n $^{20}_{D}$ 1.4832, [α] $^{20}_{546}$ (+) and (–) 43°, [α] $^{20}_{D}$ (+) and (–) 36° (c 20, EtOH).** Dissolve it in Et_2O, dry it over $MgSO_4$, filter, evaporate, then recrystallise it from petroleum ether. Also recrystallise it from aqueous EtOH and distil it in a vacuum. [Kergomard & Geneix *Bull Soc Chim Fr* 394 *1958*, Zweifel & Brown *J Am Chem Soc* **86** 393 *1964*.] The *3,4-dinitrobenzoyl* derivative has **m** 100-101°, the *phenylcarbamoyl* derivative has **m** 137-138° and the *acid-phthalate* has **m** 125-126°. [*Beilstein* **6** III 282, 283.]

Isopropenylcyclobutane *[3019-22-5]* **M 98.1, b 98.7°/760mm, d $^{20}_{4}$ 0.7743, n $^{20}_{D}$ 1.438.** Purify the cyclobutane by preparative chromatography (silicon oil column), or fractional distillation. Dry it over molecular sieves. Its IR (film) has ν_{max} at 1640 (C=C), 887 and 1773 (C-H) cm^{-1}. [Chiurdohlu & Van Walle *Bull Soc Chim Belg* **66** 612 *1957*, *Beilstein* **5** IV 255.]

(1*S*,2*S*,4*R*)-(+)-Limonene-1,2-diol [1*S*,2*S*,4*R*)-(+)-4-isopropenyl-1-methylcyclohexan-1,2-diol, (1*S*,2*S*,4*R*)-(+)-*p*-menth-8-en-1,2-diol, (+)-1-hydroxyneodihydrocarveol, neolimonene glycol] *[38630-75-0]* **M 170.3, m 68-72°, 70-70.5°, 72-73°, [α] $^{25}_{D}$ +55° (c 1, Me_2CO, also +45° and +53.7° were reported).** It has been prepared from commercial grade (+)-limonene 1,2-oxide (500g, [α] $^{27}_{D}$ +63.3° (neat) by stirring at 0° with 6% H_2SO_4 (2.5L) for 5 hours, the solution is filtered, and the crude *diol hydrate* is dissolved in hot $CHCl_3$ separated from H_2O, concentrated, and crystallised from $CHCl_3$ or petroleum ether to give the *anhydrous diol* (375g, 67%) **m 70-70.5°**. The *tri-hydrate* crystallises from H_2O in plates with **m 60°**. On hydrogenation in EtOAc over Pt_2O, it provides ***(+)-1-hydroxyneocarvomenthol*, m 88°, [α] $^{25}_{D}$ +48° (Me_2CO)** after recrystallisation from *C_6H_6-petroleum ether (b 70-110°). [Royals & Leffingwell *J Am Chem Soc* **31** 1937 *1966*, Newhall *J Org Chem* **29** 185 *1964*, *Beilstein* **6** H 753, **6** II 758, **6** III 4137, **6** IV 5294.]

Lupulon (β-lupulic acid, bitter acid) *[468-28-0]* **M 414.6, m 92-94°, $pK_{Est(1)}$ ~4.2, $pK_{Est(2)}$ ~9.7.** Recrystallise Lupulon from 90% MeOH, hexane or petroleum ether at low temperature. It has been purified by chromatography through Kieselgel. [Wieland et al. *Chem Ber* **102** 2012 *1925*, Riedl *Chem Ber* **85** 692 *1952*, *Beilstein* **7** II 856, **7** III 4752, **7** IV 2866.]

***l*-(–)-Menthone (2*S*,5*R*-2-isopropyl-5-methylcyclohexan-1-one)** *[14073-97-3]* **M 154.3, b 98-100°/14mm, 205-208°/atm, 207-210°/760mm, d^{25} 0.8930, n $^{20}_{D}$ 1.4505, [α] $^{20}_{D}$ –28° (neat).** It is obtained by adding pure *l*-(–)-menthol (4.5g, see [2216-51-5]) in four portions to chromic acid [prepared from $Na_2Cr_2O_7$. $2H_2O$ (60g, CARE CARCINOGENIC) in H_2O (300ml) and concentrated H_2SO_4 (27ml) with cooling) when the temperature rises, but should be kept at 55° (warm if necessary). A black spongy mass is first formed which becomes soft and melts to a dark brown oil on the surface as the temperature rises. The temperature drops when the oxidation is complete, the mixture is cooled and extracted with Et_2O (100ml), the extract is separated, washed with 5% aqueous NaOH (100ml, CARE) several times (~ x 3) until the colour is light yellow, then H_2O and dried (Na_2SO_4 or Mg_2SO_4). The ethereal solution is evaporated and the residual oil is redistilled at

atmospheric pressure or in a vacuum through a short column to give pure *l-menthone* (38g, 91%). [Brown & Garg *J Am Chem Soc* **83** 2952 *1961*, Hussey & Baker *J Org Chem* **25** 1434 *1960*.] This menthone is the most frequently naturally occurring of the four optically active isomers. It has been used for the optical resolution of diols *via* acetalisation [Harada & Oku *Synlett* 95 *1994*], and the menthone spirocylic 1,3-dioxane-4,6-diones have been used for asymmetric [2 + 2]cycloaddition and Diels-Alder reactions [Sato et al. *Tetrahedron* **47** 7271 *1991*]. The *oxime* has **m 59°** (from petroleum ether), the *semicarbazone* has **m 189-191°** (from MeOH, EtOH or aqueous EtOH), the *phenylhydrazone* has **m 53°** (from aqueous EtOH), and the *2,4-dinitrophenylhydrazone* has **m 146°** (from EtOH, aqueous EtOH or EtOH/EtOAc). [*Beilstein* **7** H 38, **7** I 34, **7** II 39, **7** III 152, **7** IV 87.] It is used in flavourings and perfume.

1*R*-(−)-Menthyl chloride (1*S*,2*R*,4*R*-2-chloro-1-isopropyl-4-methylcyclohexane) *[16052-42-9]* **M 174.7, m −20.1° to −16.5°, b 88.5°/12.5mm, 101-105°/21mm, d_4^{20} 0.936, n_D^{20} 1.463, $[\alpha]_D^{20}$ −52.4° (neat).** Dissolve menthyl chloride in petroleum ether (b 40-60°), wash it with H_2O, conc H_2SO_4 until no discoloration of the organic layer occurs (care with conc H_2SO_4 during shaking in a separating funnel), again with H_2O and dry it ($MgSO_4$). Evaporate, and distil the residual oil through a Claisen head with a Vigreux neck of *ca* 40 cm length. [Smith & Wright *J Org Chem* **17** 1116 *1952*, Barton et al. *J Chem Soc* 453 *1952*, *Beilstein* **5** III 134, **5** IV 152.]

1-Methyladamantane *[768-91-2]* **M 150.2, m 103°, 104°.** Purify it by zone melting, chromatography through an Al_2O_3 column and eluting with pentane, and sublime it repeatedly at 90-95°/12mm. [Stetter et al. *Chem Ber* **92** 1629 *1959*, Schleyer & Nicholas *Tetrahedron Lett* **9** 305 *1961*, *Beilstein* **5** IV 479.]

2-Methyladamantane *[700-56-1]* **M 150.2, 144-146°.** Purify it by zone melting, chromatography through an Al_2O_3 column and eluting with pentane. Recrystallise it from EtOH and sublime it repeatedly at 90-95°/12mm. [Schleyer & Nicholas *J Am Chem Soc* **83** 182 *1961*, Molle et al. *Can J Chem* **65** 2428 *1987*.]

Methylcyclohexane *[108-87-2]* **M 98.2, b 100.9°, d_4^{25} 0.7650, n_D^{20} 1.4231, n_D^{25} 1.42058.** Passage through a column of activated silica gel gives material transparent down to 220nm. It can also be purified by passage through a column of activated basic alumina, or by azeotropic distillation with MeOH, followed by washing out the MeOH with H_2O, drying and distilling. Methylcyclohexane can be dried with $CaSO_4$, CaH_2 or sodium. It has also been purified by shaking with a mixture of conc H_2SO_4 and HNO_3 in the cold, washing with H_2O, drying with $CaSO_4$ and fractionally distilling it from potassium. Percolation through a column of Celite impregnated with 2,4-dinitrophenylhydrazine (DNPH), phosphoric acid and H_2O (prepared by grinding 0.5g DNPH with 6ml 85% H_3PO_4, then mixing with 4ml of distilled H_2O and 10g of Celite) removes carbonyl-containing impurities. [Cowan et al. *J Chem Soc* 1865 *1939, Beilstein* **5** III 65, **5** IV 94.]

***cis*- and *trans*- 2-Methylcyclohexanol** *[583-59-5]* **M 114.2, b 65°/20mm, 167.6°/760mm, d_4^{20} 0.922, n_D^{20} 1.46085.** Dry 2-methylcyclohexanol with Na_2SO_4 and fractionate it under vacuum. Note: The *cis-isomer* has **b** 165°/760mm, and the *trans-isomer* has **b** 166.5°/760mm. [Eliel & Haber *J Org Chem* **23** 2041 *1958*, *Beilstein* **6** III 61, **6** IV 100.]

***cis*- and *trans*-3-Methylcyclohexanol** *[591-23-1]* **M 114.2, b 69°/16mm, 172°/760mm, d_4^{20} 0.930, n_D^{20} 1.45757, $n_D^{25.5}$ 1.45444.** Dry 3-methylcyclohexanol with Na_2SO_4 and fractionate it under vacuum. Note: The *cis-isomer* has **b** 173°/760mm, and the *trans-isomer* has **b** 168-169°/760mm. [Eliel & Haber *J Org Chem* **23** 2041 *1958*, *Beilstein* **6** IV 102.]

4-Methylcyclohexanone *[589-92-4]* **M 112.2, m –40.6°, b 68°/23mm, 165.5°/743mm, d_4^{20} 0.914, n_D^{20} 1.44506.** Dry the ketone with $CaSO_4$, then fractionally distil it. The *semicarbazone* has **m** 197°, 203.5°(dec) (from MeOH or EtOH). [White & Bishop *J Am Chem Soc* **62** 8 1945, Vogel & Oommen *J Chem Soc* 774 *1930*, *Beilstein* **7** III 63, **7** IV 44.]

1-Methylcyclohexene *[591-49-1]* **M 96.2, m –120.4°, b 107.4-108°/atm, 110-111°/760mm, d_4^{20} 0.813, n_D^{20} 1.451.** Free it from hydroperoxides by passing through a column containing basic alumina or refluxing with cupric stearate, filter and fractionally distil it from sodium. [Vogel *J Chem Soc* 1332 *1938*, Cope et al. *J Am*

Chem Soc **79** 4729 *1957*, *Beilstein* **5** III 197, **5** VI 245.]

Methylcyclopentane *[96-37-7]* **M 84.2, b 64.32°/400mm, 71.8°/atm, d_4^{20} 0.749, n_D^{20} 1.40970, n_D^{25} 1.40700.** Purification procedures include passage through columns of silica gel (prepared by heating in nitrogen to 350° prior to use) and activated basic alumina, distillation from sodium-potassium alloy, and azeotropic distillation with MeOH, followed by washing out the methanol with water, drying and distilling. It can be stored with CaH_2 or sodium. [Vogel *J Chem Soc* 1331 *1938*, *Beilstein* **5** III 55, **5** IV 84.]

Methylnorbornene-2,3-dicarboxylic anhydride (5-methylnorborn-5-ene-2-endo-3-endo-dicarboxylic anhydride) *[25134-21-8]* **M 178.2, m 88.5-89°.** Purify the anhydride by thin layer chromatography on Al_2O_3 (previously boiled in EtOAc) and eluted with hexane/$*C_6H_6$ (1:2), then recrystallise it from $*C_6H_6$/hexane. The *free acid* has **m** 118.5-119.5°. [Miranov et al. *Tetrahedron* **19** 1939 *1963*, *Beilstein* **17/11** V 199.]

2,5-Norbornadiene (bicyclo[2.2.1]hepta-2,5-diene, NBD) *[121-46-0]* **M 92.1, b 89°, d_4^{20} 0.854, n_D^{20} 1.4707.** Purify the diene by distillation from activated alumina [Landis & Halpern *J Am Chem Soc* **109** 1746 *1987*]. [*Beilstein* **5** IV 879.]

***cis-endo*-5-Norbornene-2,3-dicarboxylic anhydride (carbic anhydride, 3aα,4,7,7,αα-tetrahydro-4α,7α-methanoisobenzofuran-1,3-dione)** *[129-64-6]* **M 164.2, m 164.1°, 164-165°, 165-167°, d_4^{20} 1.417.** It forms crystals from petroleum ether, hexane or cyclohexane. It is hydrolysed by H_2O to form the acid [Diels & Alder *Justus Liebigs Ann Chem* **460** 98 *1928*, Maitte *Bull Soc Chim Fr* 499 *1959*]. The *exo-exo-isomer* has **m** 142-143° (from $*C_6H_6$/petroleum ether) [Alder & Stein *Justus Liebigs Ann Chem* **504** 216 *1933*]. [*Beilstein* **17** II 461.]

(±)-*endo*-2-Norbornylamine hydrochloride (± *endo*[2.2.1]hept-2-ylamine HCl) *[14370-45-7]* **M 147.7, m ~295°(dec), pK_{Est} ~ 9.0(free base).** Recrystallise the salt from MeOH/EtOAc or EtOH/ Et_2O. The *free base* has **m** 75-80°, **b** 156-157°/atm and the *picrate* has **m** 179-180° (from aqueous MeOH). [*Beilstein* **12** III 160.]

Norbornylene (bicyclo[2.2.1]hept-2-ene) *[498-66-8]* **M 94.2, m 44-46°, b 96°.** Reflux it over Na, and distil it [Gilliom & Grubbs *J Am Chem Soc* **108** 733 *1986*]. It has also been purified by sublimation *in vacuo* onto an ice-cold finger. [Woon et al. *J Am Chem Soc* **108** 7990 *1986*, *Beilstein* **5** IV 394.]

(±)-*exo*-2-Norbornylformate *[41498-71-9]* **M 140.2, b 65-67°/16mm, 80-81°/25mm, d_4^{20} 1.048, n_D^{20} 1.4620.** Shake with $NaHCO_3$ and distil it *in vacuo* (*exo*-borneol has **m** 124-126°). *Alternatively*, mix the ester with formic acetic anhydride overnight and fractionate. [*Beilstein* **6** III 219.]

Norcamphor (bicyclo[2.2.1]heptan-2-one, ± norbornan-2-one) *[497-38-1]* **M 110.2, m 94-95°, 95.5-96.5°, b 89-94°/60mm.** Crystallise it from water and sublime it *in vacuo*. It has λ_{max} at 287nm (EtOH). The *semicarbazone* has **m** 196-196.5° (from EtOH/H_2O). The *2,4-dinitrophenylhydrazone* has **m** 137-138° (from EtOH). [Wildman & Hemminger *J Org Chem* **17** 1641 *1952*, Wood & Roberts *J Org Chem* **23** 1124 *1957*, Bixter & Niemann *J Org Chem* **23** 742 *1958, Beilstein* **7** III 243, **7** IV 139.]

1,2,3,4,5-Pentamethylcyclopentadiene (Cp') *[4045-44-7]* **M 136.2, b 55-60°/13mm, 58°/13mm, 58.3°/13.5mm**, **d^{25} 0.870, n_D^{20} 1.4740.** Of the many syntheses of this useful ligand, the following is the most economical on materials and can be scaled up. Strictly anhydrous and anaerobic conditions should be used and reagents should be dried appropriately, degassed, and precaution against fire should be exercised. Three steps are involved:
Step 1: Under argon, lithium (58g, 8.36moles, with 0.02%Na, of ~3.2mm diameter cut into the flask in ~5mm lengths) is covered with Et_2O (1600ml, freshly distilled from ~3:1w/w K/Na benzophenone), and 2-bromo-2-butene (120g, 0.88mole, 90.4ml of a molecular sieves 4Å dried commercial *cis*- and *trans*- mixture or prepared according to Bordwell & Landis *J Am Chem Soc* **79** 1593 *1957*) is added slowly with stirring (10ml aliquots slowly at first until the reaction begins; with evolution of bubbles and cloudiness due to separation of LiBr), and

at such a rate as to maintain gentle reflux of the Et_2O.
Step 2: After addition is complete (~1.5 hours), still under argon, a mixture of ethyl acetate (166g, 1.88mole, 184ml, dried over molecular sieves 4Å) and 2-bromo-2-butene (430g, 3.18mole, 324ml as above) are then added dropwise with stirring, while carefully maintaining gentle reflux over a period of 4-5 hours. When this addition is completed, a further volume of dry EtOAc (50g, 55.4ml) and a further portion of 2-bromo-2-butene (~10-20g, 7.5-15ml) are added, while stirring is continued, until refluxing of Et_2O ceases. The mixture is allowed to cool over 4 hours, saturated aqueous NH_4Cl solution is added dropwise to hydrolyse unreacted Li, the Et_2O layer is collected, the aqueous layer is extracted with Et_2O (3 x 200ml), and the combined Et_2O solutions are evaporated to ~350ml.
Step 3: The Et_2O concentrate is added, with stirring, to a slurry of *p*-toluenesulfonic acid monohydrate (26g) in Et_2O (500ml) under a reflux condenser, at such a rate the the solvent refluxes gently. The mixture is then stirred for 5 minutes after refluxing ceases, and poured into saturated aqueous $NaHCO_3$ (1200ml) containing Na_2CO_3 (19g). The yellow aqueous phase is removed, extracted with Et_2O (3 x 200ml), and the combined Et_2O solutions are dried (Na_2SO_4), filtered, evaporated to 250-300ml (rotavap), then trap-to-trap distilled *in vacuo* (bath temperature at 35-40°) to give a yellow liquid (85% pure by GC) which is fractionally distilled in a vacuum under N_2 using a 50cm vigreux column. The fraction with b 65-70°/20mm collected (142g, 53% yield based on EtOAc used) as pale-yellow liquid is *1,2,3,4,5-pentamethylcyclopentadiene* (92% pure by GC). An additional fraction (15g, 5%) with b 70-75°/20mm is 85% pure by GC. The liquids are colourless to pale-yellow in colour with a sweet olefinic odour, and are pure enough for use as ligands. They should be stored in a freezer under N_2 or argon. In comparison with the unsubstituted *cyclopentadiene* it is a stronger donor of electron density, exerting considerably enhanced thermal stability, and the metal complexes that it forms are generally more soluble and easier to crystallise.
The *pentamethylpentadiene* has FT-IR (neat) with ν_{max} at 2960 (vs), 2915 (vs), 2855 (vs), 2735 (w), 1660 (m), 1640 (w), 1390 (s), 1355 (m), 1150 (w), 1105 (mw), 1048 (w), 840 (mw) and 668 (w) cm^{-1}; ^1H NMR (60MHz, CCl_4, TMS) with δ at 2.4 (m, 1H), 1.75 (br s, 13H, 2,3,4,5-Me), 0.95 (d, $^3J_{H\text{-}H}$ = 8Hz, 3H, 1-Me); ^{13}C NMR (15MHz, $CDCl_3$, TMS) with δ at 14.18, 20.98, 27.43, 38.04, 54.77, 61.26, 169.37 and 212.25. [Manriquez et al. *Inorg Synth* **XXI** 181 *1982*, Feilter et al. *Inorg Chem* **15** 466 *1976*, Threlkel et al. *Org Synth* **65** 42 *1987*.]

Perfluorocyclobutane (octafluorocyclobutane) *[115-25-3]* **M 200.0, m −40°, b −5°, d^{-20} 1.654, d^{o} 1.72.** Purify octafluorocyclobutane by trap-to-trap distillation, retaining the middle portion. [Danus *Ind Eng Chem* **47** 144 *1955*, Claasen *J Chem Phys* **18** 543 *1950*, *Beilstein* **5** III 8, **5** IV 8.]

Perfluorocyclohexane (dodecafluorocyclohexane) *[355-68-0]* **M 300.1, m 51° (sublimes), sublimes on melting at 52°, m 58.2° (sealed tube), d_4^{25} 1.720, n_D^{30} 1.269.** Extract it repeatedly with MeOH, then pass it through a column of silica gel (previously activated by heating at 250°). [Haszeldine & Smith *J Chem Soc* 2691 *1950*, IR: Thompson & Temple *J Chem Soc* 1432 *1948*, *Beilstein* **5** III 37, **5** IV 48.]

Perfluoro-1,3-dimethylcyclohexane *[335-27-3]* **M 400.1, b 101°, d_4^{20} 1.829, n_D^{20} 1.300.** Fractionally distil it, then 35ml are sealed with about 7g KOH pellets in a borosilicate glass ampoule and heated at 135° for 48 hours. The ampoule is cooled, opened, and the liquid is resealed with fresh KOH in another ampoule and heated as before. This process is repeated until no further decomposition is observed. The substance is then washed with distilled water, dried ($CaSO_4$) and distilled. [Grafstein *Anal Chem* **26** 523 *1954*, *Beilstein* **5** III 378.] **IRRITANT.**

Perfluoro(methylcyclohexane) *[355-02-2]* **M 350.1, b 76.3°, d^{25} 1.7878.** Reflux it for 24 hours with saturated acid $KMnO_4$ (to oxidise and remove hydrocarbons), then neutralise, steam distil, dry with P_2O_5 and pass slowly through a column of dry silica gel. [Glew & Reeves *J Phys Chem* **60** 615 *1956*.] It can also be purified by percolation through a 1 metre neutral activated alumina column, and the impurities are checked by ^1H NMR. [*Beilstein* **5** IV 102.] **IRRITANT.**

***R*(−)-α-Phellandrene (*p*-menta-1,5-diene)** *[4221-98-1]* **M 136.2, b 61°/11mm, 175-176°/760mm, d_4^{20} 0.838, n_D^{20} 1.471, $[\alpha]_D^{20}$ −230° (c 10, Et_2O), −153° to −183° (neat).** Purify it by gas chromatography with an Apiezon column. Also purify it by steam distillation (with 0.5% hydroquinone), then re-distil it through a 50

plate bubble cap column and collecting the fraction with **b** 72-72.5°/22mm [Pines & Eschinazi *J Am Chem Soc* **77** 6318 *1955*]. UV: λ_{max} 263nm (ε 3,345) in octane. [Read & Storey *J Chem Soc* 2770 1930, *Beilstein* **5** III 341, **5** IV 436.]

Picrotoxin (cocculin) *[124-87-8]* **M 602.6, m 203°, $[\alpha]_{546}^{20}$ −40° (c 1, EtOH), $[\alpha]_{D}^{16}$ −29.3° (c 4, EtOH).** It is the toxic principle in the seeds of *Anamirta cocculus*. Crystallise picrotoxin from H_2O or Me_2CO/H_2O. The *monoacetate* has **m** 244-245° (*C_6H_6). [Meyer & Bruger *Chem Ber* **31** 2958 *1898*, Johns et al. *J Chem Soc* 4717 *1956*, *Beilstein* **19** III/IV 5245.] HIGHLY TOXIC, stimulates the CNS and respiration.

***1R,5S*-α-Pinene** *[7785-70-8]* **M 136.2, b 61°/30mm, 156.2°/760mm, d_4^{20} 0.858, n_D^{15} 1.4634, n_D^{20} 1.4658, $[\alpha]_D^{20}$ +51° (neat).** It is isomerised by heat, acids and certain solvents. It should be distilled under reduced pressure under N_2 and stored in the dark. It has been purified *via* the nitrosochloride [Waterman et al. *Recl Trav Chim, Pays Bas* **48** 1191 *1929*]. For purification of optically active forms see Lynn [*J Am Chem Soc* **91** 361 *1919*].
Small quantities (0.5ml) have been purified by GLC using helium as carrier gas and a column at 90° packed with 20 wt% of polypropylene sebacate on a Chromosorb support. Larger quantities are fractionally distilled under reduced pressure through a column packed with stainless steel gauze spirals. The material can be dried over CaH_2 or sodium, and stored in a refrigerator: $CaSO_4$ and silica gel are not satisfactory because they induce spontaneous isomerisation. [Bates et al. *J Chem Soc* 1521 *1962*, *Beilstein* **5** III 366, **5** IV 452.]

***1S,5S*–α-Pinene** *[7785-26-4]* **M 136.2, b 155-156°/760mm, d_4^{20} 0.858, n_D^{20} 1.4634, $[\alpha]_D^{20}$ −47.2°.** Purify as for *1R,5S*-α-Pinene above. [*Beilstein* **5** III 366, **5** IV 455.]

***R*(+)-Pulegone** *[89-82-7]* **M 152.2, b 69.5°/5mm, d_4^{20} 0.936, n_D^{20} 1.4866, $[\alpha]_{546}^{20}$ +23.5°(neat), $[\alpha]_D^{20}$ +24.2°(neat).** Purify pulegone *via* the *semicarbazone* which has **m** 174° (from MeOH) and $[\alpha]_D^{20}$ +68.2° (c 1, $CHCl_3$). Fractionally distil it *in vacuo*. [Short & Read *J Chem Soc* 1309 *1939*]. [Erskine & Waight *J Chem Soc* 3425 *1960*, *cf* Ort *Org Synth* **65** 203 *1987*, *Beilstein* **7** III 334, **7** IV 188.]

1*R*,3*R*,4*R*,5*R*-Quinic acid (1,3,4,5-tetrahydroxycyclohexane carboxylic acid) *[77-95-2]* **M 192.3, m 172°(dec), $[\alpha]_{546}^{20}$ −51° (c 20, H_2O), $[\alpha]_D^{23}$ −45° (c 5, H_2O), pK^{25} 3.58.** Quinic acid crystallises from H_2O with **m** 174°, and from EtOH with **m** 168-169°. [McComsey & Maryanoff *J Am Chem Soc* **59** 2652 *1994*, pK: Timberlake *J Chem Soc* 2795 *1959*, Anet & Reynolds *Aust J Chem* **8** 282 *1955*, *Beilstein* **10** III 2407, **10** IV 2257.]

Reductic acid (1,2-dihydroxycyclopent-1,2-en-3-one) *[80-72-8]* **M 114.1, m 213°, pK_1^{20} 4.80, pK_2^{20} 12.9**. Crystallise reductic acid from EtOH, EtOAc (**m** 213-213.5°) or EtOH/EtOAc. It has been sublimed at 0.5mm. The *osazone* has **m** 245°(dec) (from BuOH). [Hess et al. *Justus Liebigs Ann Chem* **563** 31 *1939*, **592** 137 *1955*, **736** 134 *1970*, *Beilstein* **8** III 1942, **8** IV 1714.]

Squaric acid (3,4-dihydroxy-3-cyclobutene-1,2-dione) *[2892-51-5]* **M 114.1, m 293°(dec), 294°(dec), >300°, pK_1^{20} 1.50, pK_2^{20} 2.93**. Purify squaric acid by recrystallisation from H_2O — this is quite simple because the acid is ~7% soluble in boiling H_2O and only 2% at room temperature. It is not soluble in Me_2CO or Et_2O; hence it can be rinsed with these solvents and dried in air or a vacuum. It is not hygroscopic and gives an intense purple colour with $FeCl_3$. It has IR with ν_{max} at 1820 (C=O) and 1640 (C=C) cm^{-1}, and UV with λ_{max} at 269.5nm (ε 37K $M^{-1}cm^{-1}$). [Cohn et al. *J Am Chem Soc* **81** 3480 *1959*, Park et al. *J Am Chem Soc* **84** 2919 *1962*.] See also **pKa** values of 0.59 ±0.09 and 3.48 ±0.023 [Scwartz & Howard *J Phys Chem* **74** 4374 *1970*]. [Schmidt & Reid *Synthesis* 869 *1978*, *Beilstein* **8** IV 2701.]

Terpin hydrate *[2451-01-6 cis-hydrate, 565-50-4 and 565-48-0 stereoisomers]* **M 190.3, m 105.5° (*cis anhydrous*), 116-117° (*cis hydrate*), 156-158°, 157.5°(*trans*).** Crystallise terpin from H_2O or EtOH. The

anhydrous *cis-isomer* distils at 258°/760mm, but hydrates on exposure to moist air. *Anhydrous* terpin is also obtained by recrystallisation from absolute EtOH. [Sword *J Chem Soc* **127** 1632 *1925*, Lombard & Ambrose *Bull Soc Chim Fr* 230 *1961*, *Beilstein* **5** IV 435.]

1,1,2,2-Tetrafluorocyclobutane *[374-12-9]* **M 128.1, b 50-50.7°, d_4^{20} 1.275, n_D^{20} 1.3046.** Purify 1,1,2,2-tetrafluorocyclobutane by distillation or by preparative gas chromatography using a 2m x 6mm(i.d.) column packed with ß,ß'-oxydipropionitrile on Chromosorb P at 33°. [Conlin & Fey *J Chem Soc, Faraday Trans 1* **76** 322 *1980*, Coffmann et al. *J Am Chem Soc* **71** 490 *1949*, *Beilstein* **5** III 8, **5** IV 8.]

2,2,4,4-Tetramethylcyclobutan-1,3-dione *[933-52-8]* **M 140.2, m 114.5-114.9°.** Crystallise the dione from $*C_6H_6$ and dry it *in vacuo* over P_2O_5 in an Abderhalden pistol. [*Beilstein* **7** III 3234, **7** IV 2004.]

3,3,5,5-Tetramethylcyclohexanone *[14376-79-5]* **M 154.3, m 11-12°, 13.2°, b 59-61°/5mm, 80-82°/13mm, 196°/760mm, 203.8-204.8°/760mm, d_4^{20} 0.8954, n_D^{20} 1.4515.** Purify the ketone first through a 24 inch column packed with Raschig rings, then a 40cm Vigreux column under reduced pressure (**b** 69-69.3°/7mm). The *oxime* has **m** 144-145° (from 60% EtOH), and the *semicarbazone* has **m** 196-197°, 197-198° (214.5°, 217-218°) [Karasch & Tawney *J Am Chem Soc* **63** 2308 *1941*, UV: Sandris & Ourisson *Bull Soc Chim Fr* 958 *1956*]. [*Beilstein* **7** III 163, **7** IV 89.]

(1*R*)-(−)-Thiocamphor (1*R*-bornane-2-thione, 1*R*-(−)-1,7,7-trimethylbicyclo[2.2.1]heptane-2-thione) *[53402-10-1]* **M 168.3, m 136-138°, 146°, $[\alpha]_D^{22}$ −22° (c 3, EtOAc).** It forms red prisms from EtOH and sublimes under vacuum. It possesses a sulfurous odour and is volatile like camphor. [Sen *J Indian Chem Soc* **12** 647 *1935*, Sen *J Indian Chem Soc* **18** 76 *1941*.] The *racemate* crystallises from $*C_6H_6$ and has **m** 145° [138.6-139°, White & Bishop *J Am Chem Soc* **62** 10 *1940*]. [*Beilstein* **7** III 419.]

1*r*,2*t*,4*t*-Trimethylcyclohexane *[2234-75-7]* **M 126.2, b 145.7-146.7°/760mm, d_4^{20} 0.786, n_D^{20} 1.4330.** Wash the trimethylcyclohexane with conc H_2SO_4 (removes aromatic hydrocarbons), then with H_2O, dry it (type 4A molecular sieves), and fractionally distil it through a glass helices packed column with partial take-off and reflux ratio between 50 and 75. **Flammable liquid.** [cf. Henne et al. *J Am Chem Soc* **63** 3475 *1941*, Rossini *Anal Chem* **20** 112 *1948*, *Beilstein* **5** H 42, **5** I 17, **5** II 24, **5** III 121.]

***R*-(−)-2,2,6-Trimethyl-1,4-cyclohexanedione** *[60046-49-3]* **M 154.2, m 88-90°, 91-92°, $[\alpha]_D^{20}$ −270° (c 0.4%, MeOH), $[\alpha]_D^{20}$ −275° (c 1, $CHCl_3$).** It is obtained from fermentation and is purified by recrystallisation from diisopropyl ether. [ORD: Leuenberger et al. *Helv Chim Acta* **59** 1832 *1976*.] The *racemate* has **m** 65-67°, and the *4-(4-phenyl)semicarbazone* has **m 218-220°** (from CH_2Cl_2/MeOH) [Isler et al. *Helv Chim Acta* **39** 2041 *1956*, *Beilstein* **7** IV 2032.]

***cis,cis*-1α,3α,5α-Trimethylcyclohexane-1,3,5-tricarboxylic acid (Kemp's acid)** *[79410-20-1]* **M 258.3, m 241-243°, pK_1 3.30, pK_2 5.85, pK_3 7.3 (H_2O); pK_1 4.7, pK_2 7.6, pK_3 8.8 (50% H_2O/MeOH).** Recrystallise the tricarboxylic acid from Me_2CO after re-precipitating it several times with mineral acid from aqueous alkaline soltion. The *trimethyl ester* has **m 78-81°**. [See Kemp *J Org Chem* **46** 5140 *1981*, Jeong et al. *J AmChem Soc* **113** 201 *1991*, Stack et al. *J Am Chem Soc* **114** 7007 *1992*.]

(±)-2,2,6-Trimethylcyclohexanone *[2408-37-9]* **M 140.2, b 69-71.5°/20mm, 177-178.5°/758mm d_4^{20} 0.904, n_D^{20} 1.4470.** Purify it *via* the *semicarbazone* (**m 218°**, from MeOH or EtOH), decompose this in the usual way (cf p 75 and 77, or MEK, p 123) and fractionally distil the liquid ketone through a Vigreux column at ~760mm. [Chakravarti *J Chem Soc* 1567 *1947*, Milas et al. *J Am Chem Soc* **70** 1831 *1948*, *Beilstein* **7** I 24, **7** II 32, **7** III 7.]

Xanthatin (3-methylene-7-methyl-6-[3-oxo-1-buten-1-yl]cyclohept-5-ene-[10,11-*b*]furan-2-one, (−)-2-[(*1R*)-7*t*-hydroxy-5*c*-methyl-4-(3-oxobut-1-en-ξ-yl)cyclohept-3-en-*r*-yl)-acrylic acid lactone *[26791-73-1]* **M 246.3, m 114.5-115°, $[\alpha]_D^{20}$ −20° (c 2, $CHCl_3$).** Crystallise xanthatin from MeOH, aqueous MeOH, EtOH

or aqueous EtOH. Its UV has $\lambda_{max}(\varepsilon)$ at 213 (22800) and 275nm (7300). The *2,4-dinitrophenylhydrazone* has **m** 240°(dec) (twice recrystallise from $CHCl_3$/MeOH). [Geissman et al. *J Am Chem Soc* **76** 685 *1954*, Deuel & Geissman *J Am Chem Soc* **79** 3778 *1957*, *Beilstein* **17** III/IV 6221, **17/1** V 305.]

AROMATIC COMPOUNDS

Acenaphthene *[83-32-9]* **M 154.2, m 94.0°.** Crystallise acenaphthene from EtOH. It has also been purified by chromatography from CCl_4 on alumina with *benzene as eluent [McLaughlin & Zainal *J Chem Soc* 2485 *1960*]. [*Beilstein* **5** IV 1834.]

Acenaphthenequinone *[82-86-0]* **M 182.2, m 260-261°.** Extract it with, then recrystallise it twice from *C_6H_6. Dry it *in vacuo.* [LeFevre et al. *J Chem Soc* 974 *1963*, *Beilstein* **7** IV 2498.]

RS*-Acenaphthenol** *[6306-07-6]* **M 170.2, m 144.5-145.5°, 146°, 148°**. If highly coloured (yellow), dissolve it in boiling *benzene (14g in 200ml), add charcoal (0.5g), filter it through a heated funnel, concentrate to 100ml and cool to give almost colourless needles. **Benzene vapour is* **TOXIC**; *use an efficient fume cupboard.* The *acetate* has **b** 166-168°/5mm (bath temperature 180-185°). [Cason *Org Synth* Coll Vol **III** 3 *1955*.] It can also be recrystallised from *C_6H_6 or EtOH [Fieser & Cason *J Am Chem Soc* **62** 432 *1940*]. It forms a brick-red crystalline ***complex with 2,4,5,7-tetranitrofluoren-9-one which is recrystallised from AcOH and is dried in a vacuum over KOH and P_2O_5 at room temperature, **m** 170-172° [Newman & Lutz *J Am Chem Soc* **78** 2469 *1956*]. [*Beilstein* **6** IV 4623.]

Acenaphthylene *[208-96-8]* **M 152.2, m 92-93°, b 280°/~760mm.** Dissolve acenaphthylene in warm redistilled MeOH, filter through a sintered glass funnel and cool to –78° to precipitate the material as yellow plates [Dainton et al. *Trans Faraday Soc* **56** 1784 *1960*]. *Alternatively* it can be sublimed *in vacuo*. [*Beilstein* **5** H 625, **5** IV 2138.]

4-Acetamidobenzaldehyde *[122-85-0]* **M 163.2, m 155°, 156°, 160°.** Recrystallise it from water. The *4-nitrophenylhydrazone*, **m** 264-265°, crystallises as orange needles from EtOH [Hodgson & Beard *J Chem Soc* 21 *1927, Beilstein* **14** H 38, **14** II 25, **14** III 75, **14** IV 71.]

***p*-Acetamidobenzenesulfonyl chloride (*N*-acetylsulfanilyl chloride)** *[121-60-8]* **M 233.7, m 149°(dec).** Crystallise the chloride from toluene, $CHCl_3$, or ethylene dichloride. [*Beilstein* **14** IV 2703.]

α-Acetamidocinnamic acid *[5469-45-4]* **M 205.2, m 185-186° ($2H_2O$), 190-191°(anhydrous), 193-195°, pK_{Est} ~3.2.** It crystallises from H_2O as the *dihydrate,* and on drying at 100° it forms the *anhydrous* compound which is *hygroscopic*. Alkaline hydrolysis yields NH_3 and phenylpyruvic acid. [Erlenmeyer & Früstück *Justus Liebigs Ann Chem* **284** 47 *1895*, *Beilstein* **14** IV 1769.]

2-Acetamidofluorene (*N*-[2-fluorenyl)acetamide) *[53-96-3]* **M 223.3, m 194°, 196-198°**. Recrystallise it from toluene (1.3mg in 100ml). Its solubility in H_2O is 1.3mg/l at 25°, its UV has λ_{max} at nm(log ε) : 288(4.43), 313(4.13). [Sawicki *J Org Chem* **21** 271 *1956*.] It can also be recrystallised from 50% AcOH. [Diels et al. *Chem Ber* **35** 3285 *1902*]. 9-^{14}C and ω-^{14}C 2-acetamidofluorene were recrystallised from aqueous EtOH and had **m** 194-195° and 194° respectively. *Potent* **CARCINOGEN.** [Miller et al. *Cancer Res* **9** 504 *1949*, **10** 616 *1950*, Sadin et al. *J Am Chem Soc* **74** 5073 *1952*, *Beilstein* **12** H 3287, **12** IV 3373.]

2-Acetamidophenol *[614-80-2]* **M 151.2, m. 209°, pK_{Est} ~9.4.** Recrystallise it from water, EtOH or aqueous EtOH. [*Beilstein* **13** H 370, **13** I 113, **13** II 171, **13** III 778.]

3-Acetamidophenol (Metacetamol) *[621-42-1]* **M 151.2, m 148-149°, pK^{25} ~9.59.** Recrystallise the phenol from water. The *3,5-dinitrobenzamide complex* gives orange-yellow crystals from hot H_2O and has **m** 212°. [*Beilstein* **13** H 415, **13** I 132, **13** II 213, **13** III 950, **13** IV 977.]

4-Acetamidophenol (Paracetamol, acetaminophen, 4'-hydroxyacetanilide) *[103-90-2]* **M 151.2, m 169-170.5°, pK_{Est} ~10.0.** Recrystallise Paracetamol from water or EtOH. The *3,5-dinitrobenzamide complex* gives orange crystals from hot H_2O and has **m** 171.5°. [*Beilstein* **13** H 460, **13** I 159, **13** II 243, **13** III 1056, **13** IV

1091.]

***p*-Acetamidophenylacetic acid (Actarit)** *[18699-02-0]* **M 193.2, m 167°, 168-170°, 174-175°, pK^{25} 3.49.** Crystallise the acid from MeOH/Me_2CO, aqueous EtOH or H_2O. The *amide* has **m** 231° (from 50% aqueous EtOH). [Gabriel *Chem Ber* **15** 841 *1882*, Cerecedo et al. *J Biol Chem* **42** 238 *1924*, Tramontano et al. *J Am Chem Soc* **110** 2282 *1988*, *Beilstein* **14** II 281.]

Acetanilide *[103-84-4]* **M 135.2, m 114°, pK^{25} 0.5.** Recrystallise acetanilide from water, aqueous EtOH, *benzene or toluene. [*Beilstein* **12** IV 373.]

Acetoacetanilide *[102-01-2]* **M 177.2, m 86°, pK^{25} 10.68.** Crystallise the anilide from H_2O, aqueous EtOH or petroleum ether (b 60-80°). [Williams & Krynitsky *Org Synth* Coll Vol **III** 10 *1955*.]

4-Acetophenetidide (phenacetin, *p*-methoxyacetanilide) *[62-44-2]* **M 179.2, m 136°.** Crystallise it from H_2O or EtOH, and its solubility in H_2O is 0.08% (at ~10°) and 1.2% (at ~100°), and in EtOH it is 6.7% (at ~10°) and 36% (at ~100°). *Alternatively*, it can be purified by solution in cold dilute alkali and re-precipitating by addition of acid to neutralisation point. Dry it in air. [*Beilstein* **13** H 461, **13** IV 1092.]

Acetophenone *[98-86-2]* **M 120.2, m 19.6°, b 54°/2.5mm, 202°/760mm, d_4^{25} 1.0238, n_D^{25} 1.5322, pK^{26} –7.6(basic), pK^{25} 19.2(acidic).** Dry it by fractional distillation or by standing with anhydrous $CaSO_4$ or $CaCl_2$ for several days, followed by fractional distillation under reduced pressure (from P_2O_5, optional), and careful, slow and repeated partial crystallisations from the liquid at 0° excluding light and moisture. It can also be crystallised at low temperatures from isopentane. Distillation can be followed by purification using gas-liquid chromatography [Earls & Jones *J Chem Soc, Faraday Trans 1* **71** 2186 *1975*.] [*Beilstein* **7** H 271, **7** I 146, **7** II 208, **7** III 936, **7** IV 619.]
§ A commercial polystyrene supported version is available — scavenger resin (for diol substrates).

Aceto-*o*-toluidide (2-methylacetanilide) *[120-66-1]* **M 149.2, m 110°, 112°, b 176°/14mm, 296°/760mm.** Crystallise the toluidide from hot H_2O (solubility 1g/210ml), EtOH or aqueous EtOH. Its UV has λ_{max} at 230 and 280nm (EtOH). [*Beilstein* **12** H 792, **12** I 376, **12** II 439, **12** III 1853, **12** IV 1755.]

Aceto-*m*-toluidide (3-methylacetanilide) *[537-92-8]* **M 149.2, m 65.5°, b 182-183°/14mm, 303°/760mm.** Crystallise the toluidide from H_2O, EtOH, aqueous EtOH or Et_2O/petroleum ether (**m** 66°). Its UV has λ_{max} at 245nm (EtOH). [*Beilstein* **12** H 860, **12** I 400, **12** II 468, **12** III 1962, **12** IV 1823.]

Aceto-*p*-toluidide (4-methylacetanilide) *[103-89-9]* **M 149.2, m 146°, b 307°/760mm.** Crystallise it from aqueous EtOH. [*Beilstein* **12** H 920, **12** I 420, **12** II 501, **12** III 2051, **12** IV 1902.]

***R*-(–)-α-Acetoxyphenylacetic (acetyl mandelic) acid** *[51019-43-3]* **M 194.2, m 96-98°, $[\alpha]_D^{20}$ -153.7° (c 2.06, Me_2CO), $[\alpha]_{546}^{20}$ -194° (c 2.4, Me_2CO), pK_{Est} ~2.9.** It crystallises from H_2O with 1mol of solvent which is removed on drying, or from other solvents as for the *S*-isomer below. [Angus & Owen *J Chem Soc* 227 *1943*, Parker *Chem Rev* **91** 1441 *1991*, *Beilstein* **10** III 453.]

***S*-(+)-α-Acetoxyphenylacetic (acetyl mandelic) acid** *[7322-88-5]* **M 194.2, m 80-81°, 95-97.5°, $[\alpha]_D^{27}$ +158° (c 1.78, Me_2CO), $[\alpha]_{546}^{20}$ +186° (c 2, Me_2CO).** Recrystallise it from *benzene/hexane or toluene, and it has characteristic NMR and IR spectra. [Pracejus *Justus Liebigs Ann Chem* **622** 10 *1959*, Breitholle & Stammer *J Org Chem* **39** 1311 *1974*, *Beilstein* **10** IV 567.]

9-Acetylanthracene *[784-04-3]* **M 220.3, m 75-76°.** Crystallise 9-acetylanthracene from EtOH. [Masnori et al. *J Am Chem Soc* **108** 1126 *1986*, *Beilstein* **7** II 450.]

***N*-Acetylanthranilic acid** *[89-52-1]* **M 179.1, m 182-184°, 185-186°, 190°(dec), pK^{20} 3.61.** Wash the acid with distilled H_2O and recrystallise it from aqueous AcOH, dry it and recrystallise again from EtOAc. Also recrystallise it from water or EtOH. Its UV has λ_{max} at 221, 252 and 305nm (EtOH). The *amide* crystallises

from aqueous EtOH and has **m** 186-187° and λ_{max} 218, 252 and 301nm. [Chattaway *J Chem Soc* 2495 *1931*, Walker *J Am Chem Soc* **77** 6698 *1955*, *Beilstein* **14** H 337, **14** I 540, **14** II 219, **14** III 922.]

2-Acetylbenzoic acid *[577-56-0]* **M 164.2, m 115-116°, 116-118°**, **pK^{20} 4.14, pK^{25} 4.10.** It crystallises from *C_6H_6 and H_2O (15g/100ml). The *oxime* has **m** 156-157°, and the *2,4-dinitrophenylhydrazone* has **m** 185-186°(needles from EtOH). [Yale *J Am Chem Soc* **69** 1547 *1947*, Panetta & Miller *Synthesis* 43 *1977*, *Beilstein* **10** H 690, **10** I 330, **10** II 479, **10** III 3025, **10** IV2766.]

4-Acetylbenzoic acid *[586-89-0]* **M 164.2, m 207.5-209.5°, 208.6-209.4°, pK^{25} 3.70, 5.21, 5.10 (EtOH).** Dissolve the acid in 5% aqueous NaOH, extract it with Et_2O, and acidify the aqueous solution. Collect the precipitate, and recrystallise it from boiling H_2O (100 parts) using decolorising charcoal [Pearson et al. *J Org Chem* **24** 504 *1959*, Pearson et al. *J Chem Soc* 265 *1957*, Detweiler & Amstutz *J Am Chem Soc* **72** 2882 *1950*, Bordwell & Cooper *J Am Chem Soc* **74** 1058 *1952*]. [*Beilstein* **10** IV 2769.]

4-Acetylbenzonitrile *[1443-80-7]* **M 145.2, m 57-58°.** Recrystallise the nitrile from EtOH [Wagner et al. *J Am Chem Soc* **108** 7727 *1986*]. [*Beilstein* **10** H 695, **10** III 3030.]

Acetyl-5-bromosalicylic acid *[1503-53-3]* **M 259.1, m (156°), 168°, 168-169°, pK_{Est} ~3.0.** Crystallise the acid from EtOH. [Robertson *J Chem Soc* **81** 1482 *1902*, *Beilstein* **10** H 108, **10** II 64.]

2-Acetylfluorene *[781-73-7]* **M 208.3, m 130-131°, 132°.** Crystallise acetylfluorene from EtOH (solubility is 60g/800ml) or Me_2CO (solubility is 60g/400ml). The *oxime* [110827-07-1] has **m** 192-193.5° and the *2,4-dinitrophenylhydrazone* [109682-26-0] has **m** 261-262°. [Ray & Rieveschl *Org Synth* Coll Vol **III** 23 *1973*.]

5(3)-Acetyl-2(6)-methoxybenzaldehyde *[531-99-7]* **M 166.2, m 144°.** Extract a solution of the aldehyde in *C_6H_6 with 20% aqueous sodium bisulfite, and the bisulfite adduct in the aqueous solution is decomposed by acidifying and heating whereby the aldehyde separates. It is collected, washed with H_2O, dried in a vacuum. It is recrystallised from EtOH (**m** 140-141°) and then from Et_2O (**m** 143-144°). [Gray & Bonner *J Am Chem Soc* **70** *1249 1948, Angyal* et al. *J Chem Soc* 2142 *1950*, *Beilstein* **8** IV 1984.]

4-Acetyl-*N*-methylaniline ([4-methylamino]acetophenone) *[17687-47-7]* **M 149.2, m 102-106°, 103-107°.** This herbicide crystallises from H_2O. The *4-acetyl-N,N-dimethylaniline* derivative forms colourless plates also from H_2O with **m** 58-59°. [Klingel *Chem Ber* **18** 2694 *1885*, Staudinger & Kon *Justus Liebigs Ann Chem* **384** 111 *1911*, *Beilstein* **14** H 47, **14** I 366.]

1-Acetylnaphthalene (1-acetonaphthenone) *[941-98-0]* **M 170.1, m 10.5°, b 93-95°/0.1mm, 167°/12mm, 302°/760mm, d_4^{20} 1.12, pK^{25} –6.22 (H_o scale, aqueous H_2SO_4).** If the NMR spectrum indicates the presence of impurities, probably 2-acetylnaphthalene, convert the substance to its *picrate* by dissolving in *benzene or EtOH and adding excess of saturated picric acid in these solvents until separation of picrates is complete. Recrystallise the picrate till the melting point is 118°. Decompose the picrate with dilute NaOH and extract with Et_2O. Dry the extract (Na_2SO_4), filter, evaporate and distil the residue. The *2,4-dinitrophenylhydrazone* crystallises from EtOH and has **m** 259°. [Stobbe & Lenzer *Justus Liebigs Ann Chem* **380** 95 *1911*, Williams & Osborne *J Am Chem Soc* **61** 3438 *1939*, *Beilstein* **7** IV 1292.]

2-Acetylnaphthalene (2-acetonaphthenone, ß-acetonaphthone, 2-acetonaphthalene, methyl-2-naphthylketone) *[93-08-3]* **M 170.2, m 52-53°, 55°, 55.8°, b 164-166°/8mm, 171-173°/17mm, 301-303°/760mm, pK^{25} -6.16 (H_o scale, aqueous H_2SO_4).** Separate it from the 1-isomer by fractional crystallisation of the *picrate* in EtOH (see entry for the 1-isomer above) to **m** 82°. Decomposition of the picrate with dilute NaOH and extraction with Et_2O, then evaporation, give purer 2-acetylnaphthalene. If this residue solidifies, it can be recrystallised from petroleum ether, EtOH or acetic acid; otherwise it should be distilled in a vacuum and the solid distillate is recrystallised [Gorman & Rodgers *J Am Chem Soc* **108** 5074 *1986*, Levanon et al. *J Phys Chem* **91** 14 *1987*]. Purity should be checked by high field NMR spectroscopy. Its *oxime* has **m** 145°(dec), and the *semicarbazone* has **m** 235°. [Stobbe & Lenzer *Justus Liebigs Ann Chem* **380** 95 *1911*, Raffauf *J Am Chem Soc* **72** 753 *1950,* Hunsberger *J Am Chem Soc* **72** 5626 *1950*, Immediata & Day *J Org Chem* **5** 512 *1940*,

Beilstein **7** IV 1294.]

1-Acetyl-2-phenylhydrazine *[114-83-0]* **M 150.2, m 128.5°, pK^{25} 1.3.** Crystallise the hydrazine from aqueous EtOH. [*Beilstein* **15** H 241.]

Acetylsalicylic acid (Aspirin) *[50-78-2]* **M 180.2, m 133.5-135° (and various), pK^{25} 3.38, (pK^{17} 3.56).** Crystallise aspirin twice from toluene, wash it with cyclohexane and dry it at 60° under vacuum for several hours [Davis & Hetzer *J Res Nat Bur Stand* **60** 569 *1958*]. It has been recrystallised from isopropanol and from diethyl ether/petroleum ether (b 40-60°). It crystallises from EtOH (**m** 143-144°), *C_6H_6 (**m** 143°), hexane (**m** 115° and 128°), octane (**m** 121°), and has **m** 110° after sublimation. It has pK^{26} 3.69(H_2O), 4.15(20% aqueous EtOH), 4.47(30% aqueous EtOH) and 4.94(40% aqueous EtOH). It is an analgesic. [*Beilstein* **10** H 67, **10** II 41, **10** III 102, **10** IV 138.]

***O*-Acetylsalicyloyl chloride** *[5538-51-2]* **M 198.6, m 45°, 46-49°, 48-52°, b 107-110°/0.1mm, 115°/5mm, 135°/12mm, n_D^{20} 1.536.** Check first the IR to see if an OH frequency is present. If so, some free acid is present. Then reflux with acetyl chloride for 2-3 hours and fractionate at high vacuum. The distillate should crystallise. It can be recrystallised from hexane or *C_6H_6 (**m** 60°, sintering at 52°). [Riegel & Wittcoff *J Am Chem Soc* **64** 486 *1942*, *Beilstein* **10** H 86, **10** I 43, **10** II 55, **10** III 151, **10** IV 169.]

***O*-Acetylsalicylsalicylic acid (Salsalate acetate)** *[530-75-6]* **M 300.3, m 159°.** Crystallise the analgesic from dilute AcOH or EtOH (**m** 161-162°), MeOH (**m** 165-168°), and *C_6H_6/EtOH (**m** 163-165°). Its solubilities in boiling Et_2O, *C_6H_6 and EtOH are 1.4%, 2.2% and 33%, respectively. [Baker et al. *J Chem Soc* 201 *1951*, Garrett et al. *J Am Pharm Soc* **48** 684 *1959*, *Beilstein* **10** I 41, **10** II 54, **10** IV 165.]

***N*-(4)-Acetylsulfanilamide (sulfacetamide)** *[144-80-9]* **M 214.2, m 216°.** Crystallise the amide from aqueous EtOH. [*Beilstein* **14** IV 2662.]

Acetyl *p*-toluenesulfonate *[26908-82-7]* **M 214.2, m 54-56°, b 186-188°/20mm.** The most likely impurity is *p*-toluenesulfonic acid (could be up to 10%). This can be removed by dissolving it in dry Et_2O and cooling until the anhydride crystallises out. It decomposes on heating; below ~130° it gives the disulfonic anhydride and above ~130° polymers are formed, but it can be distilled in a vacuum if it is free of acid. It is used for cleaving ethers [Prep, IR, NMR: Karger & Mazur *J Org Chem* **36** 528, Karger & Mazur *J Org Chem* **36** 532 *1971*]. [*Beilstein* **11** III 255.]

Allyl phenyl sulfide *[5296-64-0]* **M 150.2, b 59-60°/1.5mm, 79-80°/3mm, 114-114.3°/23.5mm, 225-226°/740mm, 215-218°/750mm, d_4^{20} 1.0275, n_D^{20} 1.5760.** Dissolve the sulfide in Et_2O, wash with alkali, H_2O, dry over $CaCl_2$, evaporate and fractionally distil it, preferably under vacuum. It should not give a precipitate with an alcoholic solution of $Pb(OAc)_2$. [Hurd & Greengard *J Am Chem Soc* **52** 3356 *1930*, Tarbell & McCall *J Am Chem Soc* **74** 48 *1952*, *Beilstein* **6** IV 1479.]

Amberlite IRA-904 Anion exchange resin (Rohm and Haas) *[9050-98-0]***.** Wash with 1M HCl, CH_3OH (1:10) and then rinse it with distilled water until the washings are neutral to litmus paper. Finally extract successively for 24 hours in a Soxhlet apparatus with MeOH, *benzene and cyclohexane [Shue & Yan *Anal Chem* **53** 2081 *1981*]. It is a strong basic resin also used for base catalysis [Fieser & Fieser *Reagents for Org Synth* **1** 511, Wiley *1967*].

***p*-Aminoacetanilide** *[122-80-5]* **M 150.2, m 162-163°, 163°, 165-167°, 166-167°, pK^{15} 4.46, pK^{40} 3.94.** Crystallise the anilide from water. It has an unstable crystalline form with **m** 141°. It has IR has ν_{max} (CCl_4) at 1681cm^{-1}. [*Beilstein* **13** H 94, **13** I 28, **13** II 50, **13** III 166, **13** IV 137.]

ω-Aminoacetophenone hydrochloride (phenacylamine hydrochloride, 2-aminoacetophenone HCl) *[5468-37-1]* **M 171.6, m 188°(dec), 194°(dec), pK^{25} 5.34.** Crystallise the salt from Me_2CO /EtOH, EtOH/ Et_2O, 2-propanol or 2-propanol and a little HCl (slowly after a few days). The *oxime* of the free base has **m** 140°, and

the *picrate* of the free base has **m** 182° (from EtOH). [Castro *J Am Chem Soc* **108** 4179 *1986*, Baumgarten & Petersen *Org Synth* Coll Vol **V** 909 *1973*, cf *Beilstein* **14** H 49, **14** III 105.]

***m*-Aminoacetophenone** *[99-03-6]* **M 135.2, m 98-99°, b 189-290°/760mm, pK^{25} 3.56.** Recrystallise it from EtOH or aqueous EtOH (**m** 99.5°). The *thiosemicarbazone* has **m** 202-204° (from EtOH). [*Beilstein* **14** H 45, **14** IV 96.]

***p*-Aminoacetophenone** *[99-92-3]* **M 135.2, m 104-106°, 105-107°, b 293°/atm, pK^{25} 2.19.** Recrystallise it from $CHCl_3$, *C_6H_6 or H_2O. It is soluble in hot H_2O. Its UV (EtOH) has λ_{max} at 403nm (log ε 4.42) [Johnson *J Am Chem Soc* **75** 2720 *1953*]. [Vandenbelt *Anal Chem* **26** 726 *1954*.] The *2,4-dinitrophenylhydrazone* has **m** 266-267° (from $CHCl_3$ or EtOH) with λ_{max} at 403nm (logε 4.42), and the *semicarbazone* has **m** 193-194°(dec)(from MeOH). The *hydrochloride* has **m** 98°(dec)(from H_2O). [*Beilstein* **14** IV 100.]

1-Aminoanthraquinone-2-carboxylic acid *[82-24-6]* **M 276.2, m 295-296°.** Crystallise the acid from nitrobenzene. It is used for the detection of Al, Mg Cd, Zn, Mn, Cu, Hg, Fe, Co, Ni and Pb. The *methyl ester* gives red needles from AcOH, **m** 228°. The *ethyl ester*, **m** 198°, crystallises also as red needles from AcOH. [Locher & Fietz *Helv Chim Acta* **10** 667 *1927*, *Beilstein* **14** II 419, **14** III 168.]

***p*-Aminoazobenzene (*p*-phenylazoaniline)** *[60-09-3]* **M 197.2, CI 11000, m 126°, pK^{25} ~2.82.** Crystallise this dye from EtOH, CCl_4, petroleum ether/*C_6H_6, or a MeOH/H_2O mixture. [*Beilstein* **16** IV 445.]

***o*-Aminoazotoluene (Fast Garnet GBC base, 4'-amino-2,3'dimethylazobenzene, Solvent yellow 3)** *[97-56-3]* **M 225.3, m 101.4-102.6°, CI 11160, pK^{26} 2.29 (50% aqueous EtOH).** Recrystallise the dye twice from EtOH, once from *benzene, then dry it in an Abderhalden drying apparatus. [Cilento *J Am Chem Soc* **74** 968 *1952*, Sawicki *J Org Chem* **21** 605 *1956*, *Beilstein* **16** H 334, **16** I 322, **16** II 178, **16** III 386, **16** IV 525.] **CARCINOGENIC**.

2-Aminobenzaldehyde *[529-23-7]* **M 121.1, m 39-40°, 80-82°/2mm, pK^{20} 1.36.** Distil it in steam and recrystallise it from H_2O or EtOH/ Et_2O. The *semicarbazone* has **m** 247°. [*Beilstein* **14** H 21, **14** I 356, **14** II 14, **14** III 47, **14** IV 42.]

2-Aminobenzaldehyde phenylhydrazone (Nitrin) *[63363-93-9]* **M 211.3, m 227-229°.** Crystallise it from acetone. [Knöpfer *Monatsh Chem* **31** 97 *1910*, *Beilstein* **14** H 21, **14** II 14, **14** III 47.]

3-Aminobenzaldehyde *[29159-23-7]* **M 121.1, m 28-30°, pK_{Est} ~2.0.** The aldehyde crystallises as light yellow plates from ethyl acetate. The UV has λ_{max} at 227 and 327.5nm in cyclohexane. The *acetyl* derivative has **m** 122° (from EtOH) and the *oxime* has **m** 195° (yellow-brown plates from EtOH). [*Beilstein* **14** H 28, **14** I 359, **14** II 21, **14** III 53, **14** IV 46.]

4-Aminobenzamide hydrochloride *[59855-11-7]* **M 199.6, m 284-285°, pK_{Est} ~1.7.** Recrystallise the salt from EtOH. The *free base* [2835-68-9] **M** 136.2, has **m** 182.9° and crystallises with $0.25H_2O$ (**m** 178-179°). [Rupe & Vogler *Helv Chim Acta* **8** 835 *1925*, *Beilstein* **14** H 425, **14** III 1061.]

***p*-Aminobenzeneazodimethylaniline** *[539-17-3]* **M 240.3, m 182-183°.** Crystallise the azo-dye from aqueous EtOH. [*Beilstein* **14** IV 1004.]

***o*-Aminobenzoic acid (anthranilic acid)** *[118-92-3]* **M 137.1, m 145°, pK_1^{25} 2.94, pK_2^{25} 4.72.** Crystallise anthranilic acid from water (charcoal). It has also been recrystallised from 50% aqueous acetic acid. It sublimes in a vacuum. [*Beilstein* **14** IV 1004.]

***m*-Aminobenzoic acid** *[99-05-8]* **M 137.1, m 174°, pK_1^{25} 3.29, pK_2^{25} 5.10.** Crystallise the acid from water. [*Beilstein* **14** IV 1092.]

***p*-Aminobenzoic acid** *[150-13-0]* **M 137.1, m 187-188°, pK_1^{25} 2.45, pK_2^{25} 4.85.** Purify *p*-aminobenzoic acid

by dissolving it in 4-5% aqueous HCl at 50-60°, decolorising with charcoal and carefully precipitating it with 30% Na_2CO_3 to pH 3.5-4 in the presence of ascorbic acid. It can be recrystallised from water, EtOH or EtOH/water mixtures. [*Beilstein* **14** IV 1126.]

p-**Aminobenzonitrile (*p*-cyanoaniline)** *[873-74-5]* **M 118.1, m 86-86.5°, 85-87°, pK^{25} 1.74.** It crystallises from water, 5% aqueous EtOH or EtOH and is dried over P_2O_5, or dried *in vacuo* for 6 hours at 40°. [Moore et al. *J Am Chem Soc* **108** 2257 *1986*, Edidin et al. *J Am Chem Soc* **109** 3945 *1987*, *Beilstein* **14** IV 1158.]

4-Aminobenzophenone *[1137-41-3]* **M 197.2, m 123-124°, pK^{25} 2.17.** Dissolve it in aqueous acetic acid, filter and precipitate it with ammonia. This process is repeated several times, then the amine is recrystallised from aqueous EtOH. [*Beilstein* **14** IV 248.]

2-Aminobiphenyl (*o*-**aminobiphenyl)** *[90-41-5]* **M 169.2, m 47-48°, 49°, 49.3°, 47-50°, b 114°/2mm, 135°/5.5mm, 160°/11mm, 166-168°/16mm, 182°/30mm, 299.0°/atm, pK^{18} 3.85, pK^{20} 3.39, pK^{20} 3.03, 3.34 (50% aqueous EtOH).** It is prepared by reduction of 2-nitrobiphenyl [see 86-00-0] with Fe/HCl [Morgan and Walls *J Soc Chem Ind* **49** 15T *1930*], or catalytically in batches of 150g by H_2 at 75 atmospheres pressure in the presence of Raney Ni, which begins at ~80° and is not allowed to rise above 100°, in 90% yield [Cookson & Mann *J Chem Soc* 2891 *1949*]. It crystallises from aqueous EtOH (charcoal). The *picrate* has **m 164-165°** (from EtOH or H_2O), the *N-acetyl derivative* has **m 118°** (from EtOH), the *N-phenylsulfonate dervative* has **m 292°** (from MeOH), and the *N-tosylate* has **m 194.1-195.6°** (from MeOH). [*Beilstein* **12** H 1317, **12** I 546, **12** II 747, **12** III 3124, **12** IV 3223.]

p-**Aminobiphenyl** *[92-67-1]* **M 169.2, m 53°, b 191°/16mm, pK^{18} 4.38.** Crystallise it from water or EtOH. [*Beilstein* **12** IV 3241.] **CARCINOGENIC.**

5-Amino-2-bromobenzoic acid *[2840-02-0]* **M 216.0, m 178°, 180°, pK$_{Est(1)}$ ~1.7, pK$_{Est(2)}$ ~4.4.** Crystallise the acid from H_2O or *C_6H_6 (**m** 128°). The *acetyl* derivative crystallises from H_2O (as *monohydrate*) or absolute EtOH with **m** 196-197° (*anhydrous*). [Koopal *Rec Trav Chim Pays Bas* **34** 148 *1915*, Bamberger *Chem Ber* **57** 2090 *1924*, *Beilstein* **14** H 413, **14** II 245.]

2-Amino-5-bromotoluene (4-bromo-2-methylaniline) *[583-75-5]* **M 186.1, m 59°, 59.5°, 240°/760mm, pK^{25} 3.58.** Steam distil the aniline and recrystallise it from EtOH. It has UV with λ_{max} at 292.5nm (H_2O). [*Beilstein* **12** H 838, **12** I 389, **12** II 456, **12** IV 1804.]

2-Amino-5-chlorobenzoic acid *[635-21-1]* **M 171.6, m 100°, pK$_1^{25}$ 1.69, pK$_2^{25}$ 4.35.** Crystallise the acid from water, EtOH or chloroform. [*Beilstein* **14** IV 1075.]

3-Amino-4-chlorobenzoic acid *[2840-28-0]* **M 171.6, m 216-217°, pK$_{Est(1)}$ ~2.7, pK$_{Est(2)}$ ~2.9.** Crystallise the acid from water. [*Beilstein* **14** IV 1115.]

4-Amino-4'-chlorobiphenyl *[135-68-2]* **M 203.5, m 132-133°, 134°, pK$_{Est}$ ~4.0.** Crystallise the amine from petroleum ether, EtOH or aqueous EtOH. The *acetyl* derivative has **m** 245° from EtOH. [Dewar & James *J Chem Soc* 4270 *1958*, Gelmo *Chem Ber* **39** 4176 *1906, Beilstein* **12** H 1319, **12** II 757, **12** IV 3269.]

2-Amino-4,6-dichlorophenol *[527-62-8]* **M 175.0, m 95-96°, pK$_{Est(1)}$ ~3.1, pK$_{Est(2)}$ ~6.8.** Crystallise the phenol from CS_2 or *benzene. It sublimes at 0.06mm. The *hydrochloride* has **m** 280-285° from EtOH. [Meyer *Helv Chim Acta* **41** 1890 *1958*, *Beilstein* **13** II 185, **13** III 856, **13** IV 889.]

4-Amino-*N,N*-diethylaniline hydrochloride *[16713-15-8]* **M 200.7, m 233.5°, pK^{22} 6.61.** Crystallise the salt from EtOH. The *free base* [93-05-0] M **164.2** distils at **260-262°/~760mm**. [*Beilstein* **14** IV 109.]

4-Amino-3,5-diiodobenzoic acid *[2122-61-4]* **M 388.9, m ~350°, pK$_{Est(1)}$ 0.4, pK$_{Est(2)}$ ~1.6.** Purify the iodo-acid by dissolving it in dilute NaOH and precipitating with dilute HCl. *Alternatively*, dissolve it in aqueous NH_3 and acidify it with AcOH. Dry it in air. The solubility of the *Na salt* in H_2O is 2.56% at 25°. [Klemme &

Hunter *J Org Chem* **5** 510 *1940*, *Beilstein* **14** H 439, **14** III 1161, **14** IV 1284.]

2-Aminodiphenylamine *[534-85-0]* **M 184.2, m 79-80°, $pK_{Est(1)}$ ~3.8 (NH_2), $pK_{Est(2)}$ <~0.** Crystallise the amine from H_2O. [*Beilstein* **13** IV 43.]

4-Aminodiphenylamine *[101-54-2]* **M 184.2, b 155°/0.026mm, pK^{25} 5.20.** It crystallises from EtOH with **m** 66°, and from ligroin with **m** 75°. It can be distilled at high vacuum. [*Beilstein* **13** IV 113.]

2-Amino-1,2-diphenylethanol *[530-36-9]* **M 213.3, m 165°, $pK_{Est(1)}$ ~7.5.** Recrystallise the ethanol from EtOH. The *1R,2S-(–)-* [23190-16-1] and the *1S,2R(+)- enantiomers* also crystallise from EtOH and have **m 142-145°, $[\alpha]_D^{20}$ (+) and (–) 7° (c 0.6, EtOH)**. [Masters et al. *J Org Chem* **56** 5666 1991, Masters & Hegedus *J Org Chem* **58** 4547 *1993*, *Beilstein* **13** IV 2150.]

2-Aminodiphenylmethane (2-benzylaniline) *[28059-64-5]* **M 183.3, m 52°, 51-54°, b 172°/12mm and 190°/22mm, $pK_{Est(1)}$ ~4.2.** Crystallise 2-benzylaniline from ether and distil it in a vacuum. [*Beilstein* **12** IV 3279.]

2-Aminofluorene (2-fluorenamine) *[153-78-6]* **M 181.2, m 127.8-128.8°, 132-133°, pK^{25} 4.64.** Wash the amine well with H_2O and recrystallise it from Et_2O or 50% aqueous EtOH (25g with 400ml), and dry it in a vacuum. Store it in the dark. [Bavin *Org Synth* Coll Vol **V** 30 *1973*, *Beilstein* **12** H 1331, **12** IV 337.]

9-Aminofluorene (9-fluorenamine) *[525-03-1]* **M 181.2, m 64-65°, pK_{Est} ~3.5.** Purify it by converting it to the hydrochloride with HCl, then basify it with NH_3 and recrystallise it from petroleum ether (**m** 62-63°) or from hexane. The *hydrochloride* [5978-75-6] **M** 217.7, has **m** ~255°(dec, from EtOH). [Ingold et al. *J Chem Soc* 1493 *1933*, Mathieu *Bull Soc Chim Fr* 1526 *1971*, *Beilstein* **12** H 1331, **12** I 553, **12** II 780, **12** III 3297, **12** IV 3390.]

1-Amino-4-hydroxyanthraquinone *[116-85-8]* **M 293.2, m 207-208°, $pK_{Est(1)}$ ~2.6 (NH_2), $pK_{Est(2)}$ ~9.0 (OH).** Purify it by TLC on SiO_2 gel plates (0.75mm thick) using toluene/acetone (9:1) as eluent. The main band is scraped off and extracted with MeOH. The solvent is evaporated, and the dye is dried in a drying pistol [Land et al. *J Chem Soc, Faraday Trans 1* **72** 2091 *1976*]. It has also been recrystallised from aqueous EtOH. [*Beilstein* **14** H 268, **14** I 503, **14** II 168, **14** III 652, **14** IV 891.]

3-Amino-4-hydroxytoluene (2-amino-*p*-cresol) *[95-84-1]* **M 123.2, m 135°, 137-138°, $pK_{Est(1)}$ ~4.7(NH_2), $pK_{Est(2)}$ ~9.6 (OH).** Recrystallise the cresol from H_2O, Et_2O or toluene. It sublimes *in vacuo* as plates or needles. The *hydrochloride* has **m** 222-224° (dec, from aqueous EtOH). [*Beilstein* **13** H 601, **13** I 227, **13** II 338, **13** III 1576.]

4-Amino-3(5)-hydroxytoluene (2-amino-*m*-cresol) *[2835-98-5]* **M 123.2, m 159°, 159-162°, $pK_{Est(1)}$ ~5.4 (NH_2), $pK_{Est(2)}$ ~10.2 (OH).** Crystallise it from H_2O, 50% EtOH, or toluene. [*Beilstein* **13** H 590, **13** III 1552.]

2-Amino-5-hydroxytoluene *[2835-99-6]* **M 123.2, m 162°(dec), 177-179°(dec), $pK_{Est(1)}$ ~5.4 (NH_2), $pK_{Est(2)}$ ~10.4 (OH).** Crystallise it from 50% EtOH. [*Beilstein* **13** H 593, **13** IV 1698.]

5-Aminoindane *[24425-40-9]* **M 133.2, m 37-38°, b 131°/15mm, 146-147°/25mm, 247-249°/745mm, pK^{16} 5.31.** Distil the indane, and then crystallise it from petroleum ether. [*Beilstein* **12** I 511, **12** III 2798.]

1*RS*,2*SR*-(±)-*cis*-1-Amino-2-hydroxyindane (*cis*-1-amino-2-indanol) *[7480-35-5]* **M 149.2, m 132-133°, 134-135°, pK_{Est} ~8.5.** It is obtained by hydrolysis of (±)-*cis*-indano[1,2-*d*]-2-oxazolidone [in turn formed by solvolysis of ethyl *N*-(*trans*-2-iodo-1-indan)carbamate, m 159.5-160° in 87% yield by refluxing in dry diglyme for 14 hours]. The *cis*-2-oxazolidone (360mg) is dissolved in 0.85N methanolic KOH (20ml), diluted with H_2O (5ml) and refluxed under N_2 for 18 hours, evaporated to dryness *in vacuo*, the residue is extracted with Et_2O, filtered, dried (Mg_2SO_4), concentrated to a small volume and cooled to –12°, and the *2-indanol* is collected as white plates (2 crops, m 134-135° and 133-134°) in 79% yield. [Hassner et al. *J Org Chem* **32** 540 *1967*.]

Similarly hydrolysis of *2-phenyl-3a,8a-dihydro-8H-indeno[1,2-d]oxazole* with diluted H_2SO_4 (16 hours reflux), cool, basify with 10N NaOH, extract with $CHCl_3$, dry (Mg_2SO_4), and evaporation gives an 88% yield of the *(±)-amino-alcohol* (m 132-133°). It can also be prepared from (±)-hydrindan-1,2-epoxide as described in the following entry. Its ^{1}HNMR (400MHz, $CDCl_3$, TMS) has δ at 2.0-2.5 (br s, 3H), 2.95 (dd, *J* = 3 and 15Hz, 1H), 3.1 (dd, *J* = 7 and 15Hz, 1H), 4.28 (d, *J* = 7Hz, 1H), 4.4 (m, 1H), 7.2-7.35 (m, 4H). [Thompson et al. *J Med Chem* **35** 1685 *1992*.] Large scale preparations of the (±)-*cis*-1-amino-2-indanol from indene *via* the (±)*trans*-acylamido-indanol by hydrolysis with strong acids (HCl, H_2SO_4 or $MeSO_3H$) which invert the OH stereochemistry have been patented [Gao et al. USP appl 5,599,985 *1997*; *Chem Abstr* **123** 55421b *1995*, Gao et al. USP 5,616,808 *1997*, *Chem Abstr* **126** 250997h *1997*]. [*Beilstein* **13** II 398a, 399d, **13** III 1841, **13** IV 2033.]

1*S*,2*R*-(–)-*cis*-1-Amino-2-hydroxyindane [(-)-*cis*-1-amino-2-indanol)] *[126456-43-7]* **M 149.2, m 117-117.5°, 118-121°, $[\alpha]_D^{20}$ -61° (c 0.5, $CHCl_3$), $[\alpha]_D^{25}$ -62° (c 1.0, MeOH).** This enantiomer has been prepared in several ways in high state of optical purity. Oxidation of indene [95-13-6] using Jaconsen's salen catalyst *R,R*-MnCl/NaOCl/CH_2Cl_2 gave *1R,2S-indane-1,2-epoxide* in 84%ee, which on treatment with NH_3/MeOH then PhCOCl/NaOH followed by 80% H_2SO_4 provided *2-phenyl-3aS,8aR-dihydro-8H-indeno[1,2-d]oxazole* [see (±) above] by a C-1 chirality transfer process which gave the desired 1*S*,2*R*-(–)-aminoindanol on hydrolysis. *Alternatively*, oxidation of indene using Jacobsen's salen catalyst *S,S*-MnCl/PhCl/NaOCl and P_3NO (see [34122-28-6]) gave the enantiomeric 1*S,*2*R*-indane-1,2-epoxide which was reacted with Oleum/MeCN then hydrolysed with H_2O (by C-2 chirality transfer *via* a Ritter reaction) to give the same desired 1*S*,2*R*-(–)-aminoindanol 78-80% yield with high optical purity. [Senanayake *Aldrichimica Acta* **31** 3 *1998*, Senanayake et al. *Tetrahedron Lett* **36** 3993 *1995*, Senanayake et al. *Tetrahedron Lett* **37** 3271 *1996*.] In a different approach *N*-(L-phenylalanyl)-(±)-amino-2-indanol was prepared [84% yield, from (±)-aminoindanol and BOC-L-phenylalanine *via* the 1-hydroxybenzotriazole/dimethyl 3-{3-(dimethylamino)-propyl}carbodiimide procedure], and the diastereoisomeric mixture was separated by low pressure chromatography on silica gel, eluting with 8% MeOH in $CHCl_3$ to give the faster moving L-Phe—1*S,*2*R*-1-aminoindan-2-ol diastereoisomer (40% yield). A mixture of this diastereomer (30g, 0.1mol), EtOH (1L)and 20% aqueous NaOH (265ml) was refluxed for 16 hours, concentrated to remove EtOH, diluted with H_2O (100ml) and brine (100ml), extracted with $CHCl_3$ (3 x 600ml), the combined extracts were dried (Mg_2SO_4), filtered and evaporated to give 1*S,*2*R*-1-aminoindan-2-ol (14g, 93%) as a white solid m 114-115°. Recrystallisation from Et_2O/hexanes gave analytically pure white rods m 117-117.5°, with little loss of material, and with $[\alpha]_D^{25}$ -62° (c 1.0, MeOH), with ^{1}HNMR (400MHz, $CDCl_3$, TMS) which had δ at 2.0-2.5 (br s, 3H), 2.95 (dd, *J* = 3 and 15Hz, 1H), 3.1 (dd, *J* = 7 and 15Hz, 1H), 4.28 (d, *J* = 7Hz, 1H), 4.4 (m, 1H), 7.2-7.35 (m, 4H), same as the racemate. [Thompson et al. *J Med Chem* **35** 1685 *1992*.] Both enantiomers of this *cis*-aminoalcohol have also been obtained *via* enzymatic transfomations [Didier et al. *Tetrahedron* **47** 4941 *1991*]. The oxazolines, oxazolidin-2-ones and the 2-*N*-tosylamides derived from the two enantiomers have been explored extensively as *chiral auxiliaries* [Senanayake *Aldrichimica Acta* **31** 3 *1998*]. For the preparation of CBS-oxazaboroline catalysis (**C**orey-**B**akshi-**S**hibata) see Chapter 6, Catalysis-Part 1. **NOTE:** Both enantiomers are commercially available from Sepracore in gram to hundred kilogram quantities [Hong et al. *Tetrahedron Lett* **35** 6631 *1994*, see also Stinson *Chemical and Engineering News* May 16 p.6 *1994*.] [*Beilstein* **13** II 398a, 399d, **13** III 1841, **13** IV 2033.]

1*R*,2*S*-(+)-*cis*-1-Amino-2-hydroxyindane [(+)-*cis*-1-amino-2-indanol)] *[136030-00-7]* **M 149.2, m 118-121°, $[\alpha]_D^{20}$ +63° (c 0.2, $CHCl_3$).** This compound was prepared using the same syntheses as for its enantiomer (preceding entry) and purified in the same way. It can be also obtained from the slower moving chromatographic band of the L-phenylalaninyl diastereoisomer (see preceding entry).

2-Amino-5-iodotoluene *[13194-68-8]* **M 233.0, m 87°, pK_{Est} ~3.6.** Crystallise it from 50% EtOH. [*Beilstein* **12** IV 1807.]

1-Amino-4-methylaminoanthraquinone *[1220-94-6]* **M 252.3, $pK_{Est(1)}$ ~1, $pK_{Est(2)}$ <~4.** Purify the quinone by TLC on silica gel plates using toluene/acetone (3:1) as eluent. The main band is scraped off and extracted with MeOH. The solvent is evaporated, and the residue is dried in a drying pistol [Land et al. *J Chem Soc, Faraday Trans 1* **72** 2091 *1976*]. [*Beilstein* **14** H 198, **14** I 462, **14** III 440, **14** IV 458.]

4-Aminomethylbenzenesulfonamide hydrochloride (Mafenide HCl) *[138-37-4]* **M 222.3, m 265-267°, pK_1^{20}**

8.18 (NH_2), pK_2^{20} 10.23 ($SONH_2$). Crystallise the salt from dilute HCl or 95% EtOH and dry it in a vacuum at 100°. It is an antibacterial. [Miller et al. *J Am Chem Soc* **62** 2099 *1940*, Bergeim & Barker *J Am Chem Soc* **66** 1459 *1944*.] The *sulfate salt* has **m** 254-255° (from aqueous EtOH). [*Beilstein* **14** III 2223, **14** IV 2799.]

4-Amino-2-methyl-1-naphthol See **Vitamin K_5** in "Miscellaneous Compounds", Chapter 7.

3-Amino-2-naphthoic acid *[5959-52-4]* **M 187.2, m 214°(dec), $pK_{Est(1)}$ ~1.5 $pK_{Est(2)}$ ~4.0.** Crystallise the naphthoic acid from aqueous EtOH. [*Beilstein* **14** III 1341.]

4-Amino-5-naphthol-2,7-disulfonic acid *[90-20-0]* **M 320.3, pK_1^{20} 3.54, pK_2^{20} 8.55; pK_1^{25} 3.63, pK_2^{25} 8.83.** A slightly alkaline solution of Na_2CO_3 (*ca* 22g) in water (litmus) is added to a solution of 100g of the dry acid in 750ml of hot distilled water, followed by 5g of activated charcoal and 5g of Celite. The suspension is stirred for 10 minutes and filtered by suction. The acid is then precipitated by adding *ca* 40ml of conc HCl (solution is blue to Congo Red), then filter it by suction through a shark skin filter circular sheet (or hardened filter paper) and wash it with 100ml of distilled water. The purification process is repeated. The acid is dried overnight in an oven at 60° and stored in a dark bottle The *diethylamine salt* has **m** 306-307°(dec, from aqueous EtOH). [Post & Moore *Anal Chem* **31** 1872 *1959*]. [*Beilstein* **14** H 840, **14** I 758, **14** II 502, **14** III 2292, **14** IV 2824.]

1-Amino-2-naphthol hydrochloride *[1198-27-2]* **M 195.7, m 250°(dec), $pK_{Est(1)}$ ~3.7 (NH_2), $pK_{Est(2)}$ ~9.9 (OH).** Crystallise the salt from the minimum volume of hot water containing a few drops of stannous chloride in an equal weight of hydrochloric acid (to reduce atmospheric oxidation). Filter the solution and add half its volume of conc HCl and set aside. The salt crystallises almost quantitatively. Dry it in a vacuum in the dark (**m** 260°). The salt is more stable than the *free base* which has **m** 150° (darkening at 130°) and its *O-methyl ether* has **m** 49° and **b** 159-159°/9mm. [Desai et al. *J Chem Soc* 324 *1938, Beilstein* **13** H 666, **13** I 268, **13** II 408, **13** III 1875, **13** IV 2080.]

1-Amino-2-naphthol-4-sulfonic acid *[116-63-2]* **M 239.3, m 295°(dec), $pK_{Est(1)}$ <0 , $pK_{Est(2)}$ ~2.8 (NH_2), $pK_{Est(2)}$ ~8.8.** Purify it by warming 15g of the acid, 150g of $NaHSO_3$ and 5g of Na_2SO_3 (anhydrous) with 1L of water to *ca* 90°, shaking until most of the solid had dissolved, then filtering hot. The precipitate obtained by adding 10ml of conc HCl to the cooled filtrate is collected, washed with 95% EtOH until the washings are colourless, and is dried under vacuum over $CaCl_2$. It is stored in a dark-coloured bottle, in the cold [Chanley et al. *J Am Chem Soc* **74** 4347 *1952*]. [*Beilstein* **14** IV 2825.]

2-Amino-4-nitrobenzoic acid (4-nitroanthranilic acid) *[619-17-0]* **M 182.1, m 269°(dec), pK_1^{25} 0.65, pK_2^{25} 3.70.** Crystallise the acid from water, EtOH (**m** 271°) or aqueous EtOH (**m** 269°). The *acetyl* derivative has **m** 217° (from EtOH), **m** 222° (from aqueous EtOH). [Chapman & Stephen *J Chem Soc* 1796 *1925*, *Beilstein* **14** II 234, **14** III 975, **14** IV 1087.]

5-Amino-2-nitrobenzoic acid *[13280-60-9]* **M 182.1, m 235°(dec), $pK_{Est(1)}$ ~1.1, $pK_{Est(2)}$ ~1.2.** Crystallise the acid from water. [*Beilstein* **14** III 1021.]

1-Amino-4-nitronaphthalene *[776-34-1]* **M 188.2, m 195°, 196-197°, pK^{20} 0.54.** It crystallises from EtOH, ethyl acetate or aqueous NH_3 as light yellow crystals. The *acetyl* derivative also forms yellow crystals, **m** 192.5-193.5°, from Me_2CO. [*Beilstein* **12** H 1259, **12** I 530, **12** II 704, **12** III 2971, **12** IV 3114.]

2-Amino-4-nitrophenol *[99-57-0]* **M 154.1, m 80-90° (hydrate), 142-143° (anhydrous), $pK_{Est(1)}$ ~3.9 (NH_2), $pK_{Est(2)}$ ~9.2.** Crystallise the phenol from water. [*Beilstein* **13** IV 896.]

2-Amino-5-nitrophenol *[121-88-0]* **M 154.1, m 207-208°, $pK_{Est(1)}$ ~3.8, $pK_{Est(2)}$ ~9.3.** Crystallise the phenol from water. [*Beilstein* **13** IV 803.]

***RS*-(±)-3-Amino-3-(4-nitrophenyl)propionic acid** *[35005-61-9]* **M 210.2, m 220-226°(dec), 226°(dec, browning at 215°), $pK_{Est(1)}$ ~3.0, $pK_{Est(2)}$ ~9.5.** The acid crystallises from 50% aqueous EtOH. The *hydrochloride* has **m** 218-220°(dec). The *N-benzoyl derivative* has **m** 204-205° (from MeOH) and the *N-*

benzoyl-hydrazide has **m** 226-227° (from MeOH or EtOH). [Posner *Justus Liebigs Ann Chem* **389** 44 *1912*, *Beilstein* **14** I 603, **14** IV 1548.]

2-Aminophenol *[95-55-6]* **M 109.1, m 175-176°, pK_1^{25} 4.65, pK_2^{25} 9.75.** Purify it by dissolving it in hot water, decolorising with activated charcoal, filtering and cooling to induce crystallisation. Maintain an atmosphere of N_2 over the hot phenol solution to prevent its oxidation [Charles & Freiser *J Am Chem Soc* **74** 1385 *1952*]. It can also be crystallised from EtOH using the same precautions. [*Beilstein* **13** IV 805.]

3-Aminophenol *[591-27-5]* **M 109.1, m 122-123°, pK_1^{25} 4.25, pK_2^{25} 9.90.** Crystallise it from hot water or toluene. [*Beilstein* **13** IV 952.]

4-Aminophenol *[123-30-8]* **M 109.1, m 190° (under N_2), pK_1^{25} 5.38, pK_2^{25} 10.4.** Crystallise it from EtOH, then water, excluding oxygen. It sublimes at 110°/0.3mm. It has been purified by chromatography on alumina with a 1:4 (v/v) mixture of absolute EtOH/*benzene as eluent. [*Beilstein* **13** IV 1014.]

4-Aminophenol hydrochloride *[51-78-5]* **M 145.6, m 306°(dec).** Purify the salt by treating an aqueous solution with saturated $Na_2S_2O_3$, filtering under N_2, then recrystallising it from 50% EtOH twice and once from absolute EtOH [Livingston & Ke *J Am Chem Soc* **72** 909 *1950*]. [*Beilstein* **13** III 993.]

4-Aminophenylacetic acid *[1197-55-3]* **M 151.2, m 199-200°(dec), pK_1^{20} 3.60, pK_2^{20} 5.26.** Crystallise the acid from hot water (60-70ml/g). [*Beilstein* **14** III 1182.]

***1RS,2RS-2*-Amino-1-phenylbutan-1-ol [α-(α-aminopropyl)benzyl alcohol]** *[(±)-threo 5897-76-7]* **M 165.1, m 79-80°, pK_{Est} ~9.7.** Crystallise the *free base* of the *threo* isomer from *benzene/petroleum ether which has **m** 79-80°. The *threo-hydrochloride*, **m** 204-205°, crystallised from EtOH [Abrams & Kipping *J Chem Soc* 1480 *1936*, Rebstock et al. *J Am Chem Soc* **73** 3666 *1951*]. The *1RS,2RS-erythro* isomer has **m** 80.5-81° and its *hydrochloride* has **m** 242° [Harturg et al. *J Am Chem Soc* **52** 3317 *1930*. [*Beilstein* **13** II 390, **13** III 1791, **13** IV 1952.]

***N*-Aminophthalimide** *[1875-48-5]* **M 162.2, m 200-202°, pK_{Est} ~0.** The imide has been recrystallised from 96% EtOH (solubility is ~2% at boiling temperature) to form a yellow solution. It sublimes *in vacuo* at *ca* 150°. It solidifies after melting, and remelts at 338-341° (see phthalhydrazide "Heterocyclic Compounds" in this Chapter). [*Beilstein* **22/11** V 122.]

4-Aminopropiophenone *[70-69-9]* **M 163.1, m 140°, b 180°/10mm, pK_{Est} ~2.2.** Crystallise it from water or aqueous EtOH. The *hydrochloride* has **m** 188-189° (aqueous EtOH/HCl drops), and the *semicarbazone* has **m** 139-140° (from EtOH/H_2O). [Derrick & Bornemann *J Am chem. Soc* **35** 1283 *1913*, *Beilstein* **14** H 59, **14** I 375, **14** III 146, **14** IV 139.]

4-(2-Aminopropyl)phenol (hydroxyamphetamine) *[103-86-6]* **M 151.2, m 125-126°, $pK_{Est(1)}$ ~9.4 (OH), $pK_{Est(2)}$ ~9.7(NH_2), pK^{25} 9.31.** Crystallise the phenol from *benzene. The *R-(–)-enantiomer* crystallises from EtOH or *C_6H_6 with **m** 110.5-111.5° and $[\alpha]_D^{17}$ -52.0° (c 1, EtOH). The *(±)-hydrochloride* has **m** 171-172° (EtOH/Et_2O), and the *2,4-dinitrophenylhydrazone* has **m** 190-192° (EtOH). [*Beilstein* **13** I 251, **13** III 1709, **13** IV 1871.]

1-Aminopyrene *[1606-67-3]* **M 217.3, m 117-118°, pK_1^{25} 2.91 (50% aqueous EtOH), pK_2^{25} 2.77 (50% aqueous EtOH).** Crystallise it from hexane. [*Beilstein* **12** IV 3460.]

4-Aminosalicylic acid *[65-49-6]* **M 153.1, m 150-151°(dec), pK_1^{25} 1.78 (CO_2H), pK_2^{25} 3.63 (NH_2), pK^{25} 13.74 (OH).** Crystallise the acid from EtOH. [*Beilstein* **14** IV 1967.]

5-Aminosalicylic acid (5-amino-2-hydroxybenzoic acid) *[89-57-6]* **M 153.1, m 276-280°, 283°(dec), pK_1^{25} 2.74 (CO_2H), pK_2^{25} 5.84 (NH_2).** It crystallises as needles from H_2O containing a little $NaHSO_3$ to avoid aerial oxidation to the quinone-imine. The *Me ester* gives needles from *C_6H_6, **m** 96°, and the *hydrazide* has **m** 180-

182° (from H_2O). [Fallab et al. *Helv Chim Acta* **34** 26 *1951*, Shavel *J Amer Pharm Assoc* **42** 402 *1953*, *Beilstein* **14** IV 2058.]

2-Amino-5-sulfanilylthiazole (thiazolsulfone) *[473-30-3]* **M 238.3, m 219-221°(dec), pK_{Est} ~4.5 (OH).** Crystallise the thiazole from EtOH. It is antibacterial. [Bambas *J Am Chem soc* **67** 671 *1945*.]

4-Amino-2-sulfobenzoic acid *[527-76-4]* **M 217.1.** Crystallise the sulfobenzoic acid from H_2O (solubility is 0.3% at 25°. [KasHe *J Am Chem Soc* **44** *490 1910*, *Beilstein* **19** I 356, **19** III/IV 1641 for 4-NO_2.]

9-Aminotriptycene *[793-41-9]* **M 269.3, m 223.5-224.5°.** Recrystallise aminotriptycene from ligroin [Imashiro et al. *J Am Chem Soc* **109** 729 *1987*].

***p-tert*-Amylphenol (*p*-2,2-dimethylpropylphenol)** *[80-46-6]* **M 146.3, m 93.5-94.2°, 94-96°, b 138°/15mm, 262°/760mm, pK_{Est} ~10.2.** Purify *via* its benzoate, as for phenol. After evaporating the solvent from its solution in ether, the material is recrystallised (from the melt) to a constant melting point. The *benzoyl* derivative has **m** 60° (from EtOH). [Berliner et al. *J Am Chem Soc* **76** 507 *1954*, Huston et al. *J Am Chem Soc* **67** 899 *1945*, *Beilstein* **6** H 548, **6** I 269, **6** II 506, **6** III 1965, **6** IV 3383.]

Aniline *[62-53-3]* **M 93.1, f -6.0°, b 68.3/10mm, 184.4°/760mm, d_4^{20} 1.0220, n_D^{20} 1.585, n_D^{25} 1.5832, pK^{25} 4.60.** Aniline is *hygroscopic*. It can be dried with KOH or CaH_2, and distilled under reduced pressure. Treatment with stannous chloride removes sulfur-containing impurities, reducing the tendency to become coloured by aerial oxidation. It can be crystallised from Et_2O at low temperatures. More extensive purifications involve preparation of derivatives, such as the double salt of aniline hydrochloride and cuprous chloride or zinc chloride, or *N*-acetylaniline (**m** 114°) which can be recrystallised from water.
Redistilled aniline is dropped slowly into a strong aqueous solution of recrystallised oxalic acid. Aniline oxalate (**m** 174-175°) is filtered off, washed several times with water and recrystallised three times from 95% EtOH. Treatment with saturated Na_2CO_3 solution regenerated aniline which was distilled from the solution, dried and redistilled under reduced pressure [Knowles *Ind Eng Chem* **12** 881 *1920*].
After refluxing with 10% acetone for 10 hours, aniline is acidified with HCl (Congo Red as indicator) and extracted with Et_2O until colourless. The hydrochloride is purified by repeated crystallisation before aniline is liberated by addition of alkali, then dried with solid KOH, and distilled. The product is sulfur-free and remains colourless in air [Hantzsch & Freese *Chem Ber* **27** 2529, 2966 *1894*].
Non-basic materials, including nitro compounds, are removed from aniline in 40% H_2SO_4 by passing steam through the solution for 1 hour. Pellets of KOH are then added to liberate the aniline which is steam distilled, dried with KOH, distilled twice from zinc dust at 20mm, dried with freshly prepared BaO, and finally distilled from BaO in an all-glass apparatus [Few & Smith *J Chem Soc* 753 *1949*]. Aniline is absorbed through skin and is **TOXIC**. [*Beilstein* **12** IV 223.]

Aniline hydrobromide *[542-11-0]* **M 174.0, m 286°.** Crystallise the hydrobromide from water or EtOH and dry it at 5mm over P_2O_5. Also recrystallise it four times from MeOH containing a few drops of conc HBr by addition of petroleum ether (b 60-70°), then dry it to constant weight over paraffin chips *in vacuo* [Gutbezahl & Grunwald *J Am Chem Soc* **75** 559 *1953*]. It precipitates from EtOH solution on addition of Et_2O, and the filtered solid is recrystallised from EtOH and dried *in vacuo*. [Buchanan et al. *J Am Chem Soc* **108** 1537 *1986*, *Beilstein* **12** III 232.]

Aniline hydrochloride *[142-04-1]* **M 129.6, m 200.5-201°.** Purification is as for aniline HBr above. [*Beilstein* **12** IV 232.]

Aniline hydroiodide *[45497-73-2]* **M 220.0, it decomposes on heating.** Purification is as for aniline HBr; store it in the dark. [*Beilstein* **12** III 232.]

***m*-Anisaldehyde (3-methoxybenzaldehyde)** *[591-31-1]* **M 136.2, b 143°/50mm, d_4^{20} 1.119.** Wash it with saturated aqueous $NaHCO_3$, then H_2O, dry it with anhydrous $MgSO_4$ and distil it under reduced pressure under N_2. Store it under N_2 in sealed glass ampoules. [*Beilstein* **8** IV 241.]

***p*-Anisaldehyde (4-methoxybenzaldehyde)** *[123-11-5]* **M 136.2, m -1°, b 249°/atm, 89-90°/2mm, d_4^{20} 1.119, n_D^{20} 1.576.** Wash the aldehyde with saturated aqueous $NaHCO_3$, then H_2O, steam distil, extract the distillate with Et_2O, dry ($MgSO_4$) the extract, filter and distil this under a vacuum and N_2. Store it in glass ampules under N_2 in the dark. [*Beilstein* **8** IV 252.]

***o*-Anisidine (2-methoxyaniline)** *[90-04-0]* **M 123.2, m ~5°, b 109°/17mm, 119°/21mm, 225°/atm, d_4^{20} 1.096, n_D^{20} 1.575, pK^{25} 4.52.** It is separated from the *m*- and *p*- isomers by steam distillation. It is also separated from its usual synthetic precursor *o*-nitroanisole by dissolving it in dilute HCl (pH <2.0) extracting the nitro impurity with Et_2O, adjusting the pH to ~8.0 with NaOH, extracting the amine into Et_2O or steam distilling. Extract the distillate with Et_2O, dry the extract (Na_2SO_4), filter, evaporate and fractionate the residual oil. Protect the almost colourless oil from light which turns it yellow in color. [Biggs & Robinson *J Chem Soc* 388*1961*, Nodzu et al. *Yakugaku Zasshi (J Pharm Soc Japan)* **71** 713, 715 *1951*, *Beilstein* **13** IV 806.]

***m*-Anisidine (3-methoxyaniline)** *[536-90-3]* **M 123.2, m ~5°, b 79°/1mm, 128°/17mm, 251°/atm, d_4^{20} 1.101, n_D^{20} 1.583, pK^{25} 4.20.** *o*-Isomer impurity can be removed by steam distillation. Another possible impurity is the precursor 3-nitroanisole which can be removed as for the preceding *o*-isomer and fractionating using an efficient column. It is a yellow liquid. [Gilman & Kyle *J Am Chem Soc* **74** 3027 *1952*, Bryson *J Am Chem Soc* **82** 4858 *1960*, Kadaba & Massie *J Org Chem* **22** 333 *1957*, *Beilstein* **13** IV 953.]

***p*-Anisidine (4-methoxyaniline])** *[104-94-9]* **M 123.2, m 57°, pK^{25} 5.31.** Crystallise *p*-anisidine from H_2O or aqueous EtOH. Dry it in a vacuum oven at 35° for 6 hours and store it in a dry box. [More et al. *J Am Chem Soc* **108** 2257 *1986*.] Purify it also by vacuum sublimation [Guarr et al. *J Am Chem Soc* **107** 5104 *1985*]. [*Beilstein* **13** IV 1015.]

Anisole *[100-66-3]* **M 108.1, f -37.5°, b 43°/11mm, 153.8°/760mm, d^{15} 0.9988, n_D^{20} 1.5143, pK^0 -6.61 (aqueous H_2SO_4).** Shake anisole with half its volume of 2M NaOH, and the emulsion is allowed to separate. Repeat three times, then wash twice with water, dry over $CaCl_2$, filter, dry over sodium wire and finally distil it from fresh sodium under N_2 using a Dean-Stark trap (samples in the trap being rejected until free from turbidity) [Caldin et al. *J Chem Soc, Faraday Trans 1* **72** 1856 *1976*]. *Alternatively*, dry it with $CaSO_4$ or $CaCl_2$, or by refluxing with sodium or BaO with crystalline $FeSO_4$ or by passage through an alumina column. Traces of phenols are removed by prior shaking with 2M NaOH, followed by washing with water. It has been be purified by zone refining. [*Beilstein* **6** IV 548.]

2-*p*-Anisyl-1,3-indanone (anisindione) *[117-37-3]* **M 252.3, m 156-157°, pK^{20} 4.09.** Crystallise anisidinone from acetic acid or EtOH. [Horeau & Jacqius *Bull Soc Chim Fr* 53 *1948*, Koelsch *J Am Chem. Soc* **58** 1331 *1936, Beilstein* **8** III 2931.]

Anthracene *[120-12-7]* **M 178.2, m 215-216°, 218°, b 342°/760mm, pK^{25} -7.4 (aqueous H_2SO_4).** Likely impurities are anthraquinone, anthrone, carbazole, fluorene, 9,10-dihydroanthracene, tetracene and bianthryl. Carbazole is removed by continuous-adsorption chromatography [see Sangster & Irvine *J Phys Chem* **24** 670 *1956*] using a neutral alumina column and eluting with *n*-hexane. [Sherwood in *Purification of Inorganic and Organic Materials*, Zief (ed), Marcel Dekker, New York, 1969.] The solvent is evaporated, and anthracene is sublimed under vacuum, then purified by zone refining, under N_2 in darkness or non-actinic light.
It has also been purified by co-distillation with ethylene glycol (boils at 197.5°), from which it can be recovered by addition of water, followed by crystallisation from 95% EtOH, *benzene, toluene, a mixture of *benzene/xylene (4:1), or Et_2O. It has also been chromatographed on alumina with petroleum ether in a dark room (to avoid photo-oxidation of adsorbed anthracene to anthraquinone). Other purification methods include sublimation in a N_2 atmosphere (in some cases after refluxing with sodium), and recrystallisation from toluene [Gorman et al. *J Am Chem Soc* **107** 4404 *1985*].
Anthracene has been crystallised from EtOH, chromatographed through alumina in hot *benzene (*fume hood)* and then sublimed in a vacuum in a pyrex tube that has been cleaned and baked at 100°. (For further details see Craig & Rajikan *J Chem Soc, Faraday Trans 1* **74** 292 *1978*, and Williams & Zboinski *J Chem Soc, Faraday Trans 1* **74** 611 *1978*.) It has been chromatographed on alumina, recrystallised from *n*-hexane and sublimed under reduced pressure. [Saltiel *J Am Chem Soc* **108** 2674 *1986*, Masnori et al. *J Am Chem Soc* **108** 1126 *1986*.]

Alternatively, recrystallise it from cyclohexane, chromatograph it on alumina with *n*-hexane as eluent, and recrystallise two more times [Saltiel et al. *J Am Chem Soc* **109** 1209 *1987*]. Anthracene is fluorescent and forms a *picrate complex*, **m** 139°, on mixing the components in $CHCl_3$ or $*C_6H_6$, but decomposes on attempted crystallisation. [*Beilstein* **5** IV 228.]

Anthracene-9-carboxylic acid (anthroic acid) *[723-62-6]* **M 222.2, m 214°(dec), pK^{20} 3.65.** Crystallise the acid from EtOH. It is fluorescent in EtOH. [*Beilstein* **9** IV 2671.]

9-Anthraldehyde *[642-31-9]* **M 206.2, m 104-105°.** Crystallise the aldehyde from acetic acid or EtOH. [Masnori et al. *J Am Chem Soc* **108** 1126 *1986*, *Beilstein* **7** IV 1738.]

Anthranol (enol tautomer of anthone, see below) *[529-86-2]* **M 196.2, m 120°(rapid heating), 160-170°(dec. but sainters >100°), pK^{25} -5.5 (aqueous H_2SO_4).** Crystallise anthrol from glacial acetic acid or aqueous EtOH. It is the less stable of two tautomers and is obtained by heating anthrone in aqueous NaOH (but not in cold NaOH) whereby it dissolves to form the sodium salt of anthrol. On cautious acidification anthrol precipitates as a yellowish-brown solid. It changes into anthrone on keeping, as it does on melting (120° in a preheated bath). The melting point depends on the initial bath temperature, and recrystallisation may cause it to tautomerise to *anthrone* (see below). The *acetate* (**m** 134°) crystallises from petroleum ether (**m** 134°) or EtOH (**m** 135.5-137°). [Meyer *Justus Liebigs Ann Chem* **379** 56 *1911*, Barnett et al. *J Chem Soc* 885 *1928*, for tautomerism see Almdal et al. *Acta Chem Scand* Series B **40** 230 *1986*.]

Anthranthrone *[641-13-4]* **M 306.3, m 300°, 415°, pK^{25} -7.9 (aqueous H_2SO_4).** Crystallise it from chlorobenzene, nitrobenzene or $CHCl_3$ (**m** 340°). [*Beilstein* **7** I 451, **7** II 783, **7** III 4406, **7** IV 2694.]

Anthraquinone *[84-65-1]* **M 208.2, m 286°, pK^{25} -8.27 (aqueous H_2SO_4).** Crystallise anthraquinone from $CHCl_3$ (38ml/g), *benzene, or boiling acetic acid, wash it with a little EtOH and dry it under vacuum over P_2O_5. [*Beilstein* **7** IV 2556.]

Anthrarufin (1,5-dihydroxy-9,10-anthraquinone) *[117-12-4]* **M 240.1, m 280°(dec), pK_1^{25} 9.90, pK_2^{25} 11.05.** Purify anthrarufin by column chromatography on silica gel with $CHCl_3/Et_2O$ as eluent, followed by recrystallisation from acetone. *Alternatively*, recrystallise it from glacial acetic acid [Flom & Barbara *J Phys Chem* **89** 4489 *1985*]. [*Beilstein* **7** III 2359, **8** IV 3268.]

1,8,9-Anthratriol *[480-22-8]* **M 226.2, m 176-181°, pK_{Est} ~9.5.** Crystallise it from petroleum ether and dry it *in vacuo*. [*Beilstein* **6** IV 7602.]

Anthrimide (1,1'-imino-bis-anthraquinone) *[82-22-4]* **M 429.4, m >250°(dec).** Crystallise anthrimide from chlorobenzene (red needles) or nitrobenzene (red rhombs). It is poorly soluble in organic solvents. [Eckert & Steiner *Monatsh Chem* **35** 1129 *1914*.]

Anthrone *[90-44-8]* **M 194.2, m 155°, pK^{25} -5.5 (aqueous H_2SO_4).** This stable keto tautomer of 9-anthranol (above) provides yellow crystals from a 3:1 mixture of $*C_6H_6$/petroleum ether (b 60-80°) (10-12ml/g), or successively from $*C_6H_6$ then EtOH. Dry it *in vacuo*. [Meyer *Org Synth* Coll Vol **I** 60 *1941*, *Beilstein* **6** IV 4930.]

(±)-Atrolactic acid ($0.5H_2O$) (2-hydroxy-2-phenylpropionic acid) *[515-30-0]* **M 166.2, m 94.5-95°(anhydrous), 88-91° ($0.5H_2O$), pK^{18} 3.53.** Crystallise the acid from water (4g/20ml boiling H_2O with charcoal, filter and cool overnight at 0-5°) and dry it at 55°/0.5mm [Eliel & Freeman *Org Synth* Coll Vol **IV** 58 *1963*]. The *(±)-ethyl ester* [76496-51-0] has **b 250°/~760mm, 129-130°/13mm**, and the *(±)-amide* [5908-94-1] has **m 101-102°**. [*Beilstein* **10** H 259, **10** I 113, **10** II 157, **10** III 560, **10** IV 467.]

***R*-(-) and *S*-(+) Atrolactic acid** *[R 3966-30-1 and S 13113-71-8]* **M 166.2, m 115-116°, 116-117°, *R* $[\alpha]_D^{14.6}$ -37.7° (c 3.3 EtOH) and $[\alpha]_D^{14.6}$ –51.1° (c 2.2, H_2O], *S* $[\alpha]_D^{14.6}$ +37.7° (c 3.5 EtOH).** Recrystallise them from $*C_6H_6$ or $*C_6H_6$/petroleum ether and dry them in a vacuum. [McKenzie & Clough *J Chem Soc* 1019 *1910*,

Meyers & Slade *Synth Commun* **6** 601*1972*, *Beilstein* **10** II 157, **10** III 560, **10** IV 657.]

Auramine O (4,4'-bis-dimethylaminobenzophenone imine hydrochloride) *[2465-27-2]* **M 321.9, m >250°(dec), pK^{25} 10.71 (free base), 9.78 (carbinolamine).** It crystallises from EtOH as the hydrochloride and is very slightly soluble in $CHCl_3$, its UV has λ_{max} at 434nm (ε 370). The *free base* (carbinolamine) has **m** 136° (from *C_6H_6). [Goldacre & Phillips *J Chem Soc* 1724 *1949*, Conrad et al. *Biochemistry* **9** 1540 *1970*, *Beilstein* **14** IV 256.]

Aurin tricarboxylic acid *[4431-00-9]* **M 422.4, m 300°.** The acid is dissolved in aqueous NaOH, $NaHSO_3$ solution is added until the colour is discharged and then the tricarboxylic acid is precipitated with HCl. [Heisig & Lauer *Org Synth* Coll Vol **I** 54 *1941*, *Beilstein* **10** IV 4161]. Do not extract the acid with hot water because it softens, forming a viscous mass. Make a solution in aqueous NH_3. **Aluminon** is the NH_4 salt.

Azobenzene *[103-33-3]* **M 182.2, m 68°, b 293°/atm, pK^{25} 2.48.** Ordinary azobenzene is nearly all in the *trans*-form. It is partly converted into the *cis*-form on exposure to light [for isolation see Hartley *J Chem Soc* 633 *1938*, and for spectra of *cis*- and *trans*-azobenzenes, see Winkel & Siebert *Chem Ber* **74B** 670*1941*]. *trans*-Azobenzene is obtained by chromatography on alumina using 1:4 *C_6H_6/heptane or petroleum ether, and it crystallises from EtOH (after refluxing for several hours) or hexane. All operations should be carried out in diffuse red light or in the dark. [*Beilstein* **16** IV 8.]

4-Azidoaniline hydrochloride *[91159-79-4]* **M 170.6, m 165°(dec).** Purify it in EtOAc with dry HCl gas followed by cold dry Et_2O. The *free base* has **m** 66°(dec) (MeOH) and the *picrate* has **m** 64-65°(dec) (MeOH). The IR has ν_{max} at (Nujol) at 2110cm^{-1} (N_3). [Escher et al. *Helv Chim Acta* **62** 1217 *1979*, Maffei & Rivolta *Gazetta Chim Ital* **84** 750 *1954*, *Beilstein* **12** H 772, **12** IV 1741.]

Azolitmin B *[1395-18-2]* **M ~3300, m >250°(dec)**. It crystallises from water as dark violet scales, or as a red powder on precipitation from H_2O by addtition of EtOH. It is an indicator which is red at pH 4.5 and blue at pH 8.3. [cf Kolthopff & Rosenblum *Acid-Base Indicators*, Macmillan, NY pp160-162, 365-366 *1937*.]

p,p'-**Azoxyanisole (4,4'-dimethoxyazoxybenzene)** *[1562-94-3]* **M 258.3, transition temperatures: 118.1-118.8°, 135.6-136.0°, pK^{25} -5.23 (20% aqueous EtOH + 80% aqueous H_2SO_4).** Crystallise the dye from absolute or 95% EtOH, or acetone, and dry it by heating under vacuum or sublime it in a vacuum onto a cold finger. [*Beilstein* **16** II 326.]

Azoxybenzene (Fenazox) *[495-48-7]* **M 198.2, m 36°, pK^{25} -6.16 (20% aqueous EtOH + 80% aqueous H_2SO_4).** Crystallise azobenzene from EtOH or MeOH, and dry it for 4 hours at 25°/10^{-3}mm. Sublime it before use. [Bigelow & Palm *Org Synth* Coll Vol **II** 57 *1943*, *Beilstein* **16** II 326.]

p,p-**Azoxyphenetole** *[4792-83-0]* **M 286.3, m 137-138° (turbid liquid clarifies at 167°).** Crystallise the dye from toluene or EtOH. [*Beilstein* **16** II 326.]

Azulene *[275-51-4]* **M 128.2, m 98.5-99°, pK^{25} -1.65 (aqueous H_2SO_4).** Crystallise azulene from EtOH. It has UV with λ_{max} at 270nm (logε 4.72) in hexane. [Platner & Magyar *Helv Chim Acta* **25** 581 *1942*, *Beilstein* **5** IV 1636.]

Benzalacetone (*trans*-**4-phenyl-3-buten-2-one)** *[122-57-6]* **M 146.2, m 42°.** Crystallise it from petroleum ether (b 40-60°), or distil it (**b** 137-142° /16mm). [*Beilstein* **7** IV 1003.]

Benzalacetophenone (Chalcone) *[94-41-7]* **M 208.3, m 56-58°, b 208°/25mm, pK^{25} -5.73 (aqueous H_2SO_4).** Crystallise it from EtOH by warming to 50° (about 5ml/g), iso-octane, or toluene/petroleum ether, or recrystallise it from MeOH, and then twice from hexane. SKIN IRRITANT. [*Beilstein* **7** IV 1658.]

Benzaldehyde *[100-52-7]* **M 106.1, f -26°, b 62° 58°/10mm, 179.0°/760mm, d_4^{20} 1.044, n_D^{20} 1.5455, pK^{25} -7.1**

(aqueous H_2SO_4). To diminish its rate of oxidation, benzaldehyde usually contains additives such as hydroquinone or catechol. It can be purified *via* its bisulfite addition compound but usually distillation (under nitrogen at reduced pressure) is sufficient. Prior to distillation it is washed with NaOH or 10% Na_2CO_3 (until no more CO_2 is evolved), then with saturated Na_2SO_3 and H_2O, followed by drying with $CaSO_4$, $MgSO_4$ or $CaCl_2$. [*Beilstein* **7** IV 505.]

***anti*-Benzaldoxime** *[932-90-1]* **M 121.1, m 33-34°.** Crystallise the oxime from diethyl ether by adding petroleum ether (b 60-80°). The *syn*-isomer [622-32-2] has **b** 121-124°/12mm, **m** 34-36°. [*Beilstein* **7** H 218, **7** IV 527.]

Benzamide *[55-21-0]* **M 121.1, m 129.5°, pK^{25} -2.16 (aqueous H_2SO_4).** Crystallise it from hot water (about 5ml/g), EtOH or 1,2-dichloroethane, and dry it in air. It has also been crystallised from dilute aqueous NH_3, H_2O, Me_2CO, then *C_6H_6 using a Soxhlet extractor. Dry it in an oven at 110° for 8 hours and store in a desiccator over 99% H_2SO_4. [Bates & Hobbs *J Am Chem Soc* **73** 2151 *1951*, *Beilstein* **9** IV 725.]

Benzamidine *[618-39-3]* **M 120.2, m 64-66°, pK^{20} 11.6.** It is liberated from its hydrochloride chloride (below) by treatment with 5M NaOH, extracted into diethyl ether, dried (Na_2SO_4) and sublimed *in vacuo*. [*Beilstein* 9 H 280, 9 I 123, 9 II 199, **9** 1264, 9 IV 898.]

Benzamidine hydrochloride hydrate *[206752-36-5]* **M 156.6 (anhydrous), m 86-88°, pK^{20} 11.6 (see free base above).** Recrystallise it from dilute HCl (crystals contain xH_2O) or EtOH/few drops HCl; dry it in a vacuum. It is a proteolytic inhibitor [Jeffcoate & White *J Clin Endocrinol Metab* **38** 155 *1974*, *Beilstein* **9** IV 898.]

Benzanilide *[93-98-1]* **M 197.2, m 164°, pK^{55} 1.26.** Crystallise benzanilide from petroleum ether (b 70-90°) using a Soxhlet extractor, and dry it overnight at 120°. Also crystallise it from EtOH. [*Beilstein* **12** IV 417.]

Benz[a]anthracene (1,2-benzanthracene, tetraphene) *[56-55-3]* **M 228.3, m 159-160°.** Crystallise 1,2-benzanthracene from MeOH, EtOH or *benzene (charcoal), then chromatograph it on alumina from sodium-dried *benzene (twice), using vacuum distillation to remove *benzene. Final purification is by vacuum sublimation. [*Beilstein* **5** IV 2549.]

Benz[a]anthracene-7,12-dione *[2498-66-0]* **M 258.3, m 169.5-170.5°**, **169-171°**. Crystallise the dione from MeOH (charcoal). toluene, toluene/hexane, Me_2CO, or AcOH. *Alternatively* purify it by sublimation *in vacuo*, or by zone refining. [*Beilstein* **7** H 826, **7** I 440, **7** II 760, **7** III 4278, **7** IV 2644.]

Benzanthrone *[82-05-3]* **M 230.3, m 170°, pK^{25} -3.2 (aqueous H_2SO_4).** Crystallise benzanthrone from EtOH or xylene. [*Beilstein* **7** IV 1819.]

***Benzene** *[71-43-2]* **M 78.1, f 5.5°, b 80.1°, d_4^{20} 0.874, n_D^{20} 1.50110, n_D^{25} 1.49790.** For most purposes, *benzene can be purified sufficiently by shaking with conc H_2SO_4 until free from thiophene, then with H_2O, dilute NaOH and water, followed by drying (with P_2O_5, sodium, $LiAlH_4$, CaH_2, 4X Linde molecular sieve, or $CaSO_4$, or by passage through a column of silica gel, and for a preliminary drying, $CaCl_2$ is suitable), and distillation. A further purification step to remove thiophene, acetic acid and propionic acid, is crystallisation by partial freezing. The usual contaminants in dry thiophene-free *benzene are non-benzenoid hydrocarbons such as cyclohexane, methylcyclohexane, and heptanes, together with naphthenic hydrocarbons and traces of toluene. Carbonyl-containing impurities can be removed by percolation through a *Celite column impregnated with 2,4-dinitrophenylhydrazine, phosphoric acid and H_2O*. (Prepared by dissolving 0.5g DNPH in 6ml of 85% H_3PO_4 by grinding together, then adding and mixing 4ml of distilled H_2O and 10g Celite.) [Schwartz & Parker *Anal Chem* **33** 1396 *1961*.] *Benzene has been freed from thiophene by refluxing with 10% (w/v) of Raney nickel for 15 minutes, after which the nickel is removed by filtration or centrifugation.
Dry *benzene is obtained by doubly distilling high purity *benzene from a solution containing the blue ketyl formed by the reaction of sodium-potassium alloy with a small amount of benzophenone.
Thiophene has been removed from *benzene (absence of a bluish-green coloration when 3ml of *benzene is

shaken with a solution of 10mg of isatin in 10ml of conc H_2SO_4) by refluxing the *benzene (1.25L) for several hours with 40g HgO (freshly precipitated) dissolved in 40ml glacial acetic acid and 300ml of water. The precipitate is filtered off, the aqueous phase is removed and the *benzene is washed twice with H_2O, dried and distilled. *Alternatively*, *benzene dried with $CaCl_2$ has been shaken vigorously for 0.5 hour with anhydrous $AlCl_3$ (12g/L) at 25-35°, then decanted, washed with 10% NaOH, and water, dried and distilled. The process is repeated, giving thiophene-free *benzene. [Holmes & Beeman *Ind Eng Chem* **26** 172 *1934*.]
After shaking successively for about an hour with conc H_2SO_4, distilled water (twice), 6M NaOH, and distilled water (twice), *benzene is distilled through a 3-ft glass column to remove most of the water. Absolute EtOH is added and the *benzene-alcohol azeotrope is distilled. (This low-boiling distillation leaves any non-azeotrope-forming impurities behind.) The middle fraction is shaken with distilled water to remove EtOH, and again redistilled. Final slow and very careful fractional distillation from sodium, then $LiAlH_4$ under N_2, removed traces of water and peroxides. [Peebles et al. *J Am Chem Soc* **82** 2780 *1960*.] ***Benzene liquid and vapour are very* TOXIC, CARCINOGENIC** *and* **HIGHLY FLAMMABLE**, *and all operations should be carried out in an efficient fume cupboard and in the absence of naked flames in the vicinity.* [*Beilstein* **5** H 175, **5** I 95, **5** II 119, **5** III 469.]
Rapid purification: To dry benzene, alumina, CaH_2 or 4A molecular sieves (3% w/v) may be used (dry for 6 hours). Then benzene is distilled, discarding the first 5% of distillate, and stored over molecular sieves (3A, 4A) or Na wire.

[$^2H_6$]*Benzene (benzene-d_6*) *[1076-43-3]* M 84.2, b 80°/773.6mm, 70°/562mm, 60°/399mm, 40°/186.3mm, 20°/77.1mm, 10°/49.9mm, 0°/27.5mm, d_4^{20} 0.9488, d_4^{40} 0.9257, n_D^{20} 1.4991, n^{40} 1.4865.** Hexadeuteriobenzene of 99.5% purity is refluxed over and distilled from CaH_2 onto Linde type 5A sieves under N_2. [*Beilstein* **5** III 518, **5** IV 630.]

Benzeneazodiphenylamine (4-phenylazodiphenylamine) *[28110-26-1; 101-75-7]* **M 273.3, m 82°, 86°, 87-91°, pK^{22} 0.48.** Purify the dye by chromatography on neutral alumina using dry *C_6H_6 with 1% of dry MeOH. The major component, which gave a stationary band, is cut out and eluted with EtOH or MeOH. [Högfeldt & Bigeleisen *J Am Chem Soc* **82** 15 *1960*.] It crystallises from petroleum ether, EtOH or aqueous EtOH, and has λ_{max} at 420nm (ε 28,000) (aqueous EtOH) and 540nm (aqueous EtOH/H_2SO_4) [Badger et al. *J Chem Soc* 1888 *1954*, *Beilstein* **16** H 314, **16** III 343, **16** IV 457.]

1-Benzeneazo-2-naphthol (Sudan I) *[842-07-9]* **M 248.3, m 106°, 120,5°, 132° (polymorphism) 134°, 135°, pK_{Est} ~9.5 (OH).** Crystallise the dye from EtOH. It forms Cu and Ni salts. [*Beilstein* **16** H 162, **16** I 254, **16** II 70, **16** III 129, **16** IV 228.]

1-Benzeneazo-2-naphthylamine (1-phenylazo-2-naphthylamine, Yellow AB) *[85-84-7]* **M 247.3, m 102-104°, 103-104°, pK_{Est} ~4.1.** Crystallise the dye from glacial acetic acid, acetic acid/water or ethanol. It forms Cu, Co and Ni salts. [*Beilstein* **16** H 369, **16** I 328, **16** II 193, **16** III 417, **16** IV 551.]

1,2-Benzenedimethanol (1,2-bishydroxymethylbenzene, phthalyl alcohol) *[612-14-6]* **M 138.2, m 61-64°, 63-64°, 64-65°, 65-66.5°, b 145°/3mm.** Recrystallise it from *C_6H_6, H_2O, petroleum ether or pentane. It has been extracted in a Soxhlet with Et_2O, evaporated and recrystallised from hot petroleum ether. It is also purified by dissolving in Et_2O, allowing to evaporate till crystals are formed, filtering off and washing the colourless crystals with warm petroleum ether or pentane. The *diacetate* has **m** 35°, 35-36°. [Nystrom & Brown *J Am Chem Soc* **69** 1197 *1947*, IR and UV: Entel et al. *J Am Chem Soc* **74** 441 *1952*, *Beilstein* **6** IV 5953.]

***m*-Benzenedisulfonic acid** *[98-48-6]* **M 238.2, pK_{Est} <0.** Free it from H_2SO_4 by conversion to the calcium or barium salts (using $Ca(OH)_2$ or $Ba(OH)_2$, and filtering). The calcium salt is then converted to the potassium salt, using K_2CO_3. Both the potassium and the barium salts are recrystallised from H_2O, and the acid is regenerated by passing through the H^+ form of a strong cation exchange resin. The acid is recrystallised twice from conductivity water and dried over $CaCl_2$ at 25°. [Atkinson et al. *J Am Chem Soc* **83** 1570 *1961*.] It has also been crystallised from Et_2O and dried in a vacuum oven. The *S-benzylisothiuronium salt* has **m** 214.3° (from EtOH/H_2O). [*Beilstein* **11** IV 553.] It is best kept as the *disodium salt* [831-59-4] which decomposes on heating [*Beilstein* **11** H 199, **11** I 48, **11** II 213, **11** III 453.]

***m*-Benzenedisulfonyl chloride** *[585-47-7]* **M 275.1, m 63°.** Crystallise it from $CHCl_3$ (EtOH free, by passing through an alumina column) or $*C_6H_6$/petroleum ether and dry it at 20mm pressure. [*Beilstein* **11** IV 553.]

Benzene-1,2-dithiol *[17534-15-5]* **M 142.2, m 24-25°, 27-28°, b 110-112°, $pK_{Est(1)}$ ~6.0, $pK_{Est(2)}$ ~9.4.** Likely impurities are the oxidation products, the disulfides which could be polymeric. Dissolve it in aqueous NaOH until the solution is alkaline. Extract with Et_2O and discard the extract. Acidify with cold HCl (diluted 1:1 by volume with H_2O) to Congo Red paper under N_2 and extract it three times with Et_2O. Dry the Et_2O with Na_2SO_4, filter, evaporate and distil the residue under reduced pressure in an atmosphere of N_2. The distillate solidifies on cooling. [UV: Dewar et al. *J Chem Soc* 3076 *1958*, Grunwald & Berkowitz *J Am Chem Soc* **81** 4939 *1951*, Ferretti *Org Synth* Coll Vol **V** 419 *1973*, *Beilstein* **6 IV** 5651.]

Benzenesulfinic acid *[618-41-7]* **M 142.2, m 84°, pK^{25} 2.16(2.74).** The acid is purified by dissolving the Na salt in H_2O, acidifying to Congo Red paper with HCl and adding a concentrated solution of $FeCl_3$ whereby Fe sulfinate precipitates. Collect the salt, wash it with a little H_2O, drain, suspend it in H_2O and add a slight excess of 1.5M aqueous NaOH. The $Fe(OH)_3$ precipitates, it is filtered off, the sulfinic acid in the aqueous solution is extracted with Et_2O, the extract is dried (Na_2SO_4) and evaporated to give colourless crystals of benzenesulfinic acid **m** 84° which are stored under N_2 in the dark, as it slowly oxidises in air to the sulfonic acid. [*Beilstein* **11** H 2, **11** I 3, **11** II 3, **11** III 3, **11** IV 3.]

Benzenesulfonic acid *[98-11-3]* **M 158.2, m 43-44°, 50-55°(anhydrous), 65-66°, pK^{25} -2.7, 0.70, (2.53?)** Purify benzenesulfonic acid by dissolving it in a small volume of distilled H_2O and stirring with slightly less than the theoretical amount of $BaCO_3$. When effervescence is complete and the solution is still acidic, filter off the insoluble barium benzenesulfonate. The salt is collected and dried to constant weight *in vacuo*, then suspended in H_2O and stirred with a little less than the equivalent (half mol.) of sulfuric acid. The insoluble $BaSO_4$ (containing a little barium benzenesulfonate) is filtered off and the filtrate containing the free acid is evaporated in a high vacuum. The oily residue will eventually crystallise when completely anhydrous. A 32% commercial acid is allowed to fractionally crystallise at room temperature over P_2O_5 in a vacuum desiccator giving finally colourless deliquescent plates **m** 52.5°. The anhydrous crystalline acid is deliquescent and should be stored over anhydrous Na_2SO_4 in the dark, and should be used in subdued sunlight as it darkens under sunlight. The main impurity is Fe which readily separates as the Fe salt in the early fractions [Taylor & Vincent *J Chem Soc* 3218 *1952*]. The *S-benzylisothiuronium salt* has **m** 148° (from EtOH/H_2O). It is a strong acid, and an IRRITANT to the skin and eyes. [See Adams & Marvel *Org Synth* Coll Vol **I** 84 *1941*, Michael & Adair *Chem Ber* **10** 585 *1877*, *Beilstein* **11** IV 27.]

Benzenesulfonic anhydride *[512-35-6]* **M 298.3, m 88-91°.** Crystallise the anhydride from Et_2O **(m** 88.5-91.5°), $CHCl_3$ or chlorobenzene **(m** 90-92°). Store it dry. [Field *J Am Chem Soc* **74** 394 *1952*, *Beilstein* **11** H 3, **11** I 11, **11** II 23, **11** III 50, **11** IV 50.]

Benzenesulfonyl chloride *[98-09-9]* **M 176.6, m 14.5°, b 120°/10mm, 251.2°/760mm(dec), d_4^{20} 1.384.** Distil the sulfonyl chloride, preferably under a vacuum, then treat it with 3mole % each of toluene and $AlCl_3$, and allow it to stand overnight. The sulfonyl chloride is distilled off at 1mm pressure and then carefully fractionally distilled at 10mm in an all-glass column. [Adams & Marvel *Org Synth* Coll Vol **I** 84 *1941*, Jensen & Brown *J Am Chem Soc* **80** 4042 *1958*, *Beilstein* **11** IV 49.] It is **TOXIC.**

Benzene-1,2,4,5-tetracarboxylic (pyromellitic acid) *[89-05-4]* **M 254.2, m 276°, 281-284°, pK_1^{25} 1.87, pK_2^{25} 2.72, pK_3^{25} 4.30, pK_4^{25} 5.52.** Dissolve it in 5.7 parts of hot dimethylformamide, decolorise, filter and cool. The precipitate is collected and dried in air. The solvent is removed by heating in an oven at 150-170° for several hours. It also crystallises from water. [*Beilstein* **9** H 997, **9** IV 3804.]

Benzene-1,2,4,5-tetracarboxylic dianhydride (pyromellitic dianhydride) *[89-32-7]* **M 218.1, m 286°, b 397-400°/760mm.** Crystallise the dianhydride from ethyl methyl ketone or dioxane. Dry, and sublime it *in vacuo*. [*Beilstein* **19** H 196, **19/5** V 407.]

Benzene-1,2,3-tricarboxylic (hemimellitic) acid (H_2O) *[36362-97-7]* **M 210.1, m 190°(dec), pK_1^{25} 2.62, pK_2^{25}**

3.82, pK_3^{25} 5.51. Crystallise the acid from water. [*Beilstein* **9** H 976, **9** IV 3745.]

Benzene-1,3,5-tricarboxylic (trimesic or trimellitic) acid *[554-95-0]* **M 210.1, m 360°(dec), pK_1^{25} 2.64, pK_2^{25} 3.71, pK_3^{25} 5.01.** Crystallise the acid from water. The *trimethyl ester* has **m** 144° (from MeOH or MeOH/H_2O). [*Beilstein* **9** H 978, **9** IV 3747.]

1,2,4-Benzenetriol *[533-73-3]* **M 126.1, m 140.5-141°(sintering at 139°), pK_1^{20} 9.08, pK_2^{20} 11.82.** Crystallise the triol from Et_2O or Et_2O/EtOH, and dry it in a vacuum. The *picrate* forms orange-red needles **m** 96°. [*Beilstein* **6** H 1087, **6** I 541, **6** II 1071, **6** III 6276.]

Benzethonium chloride (Hyamine 1622, [diisobutylphenoxyethoxyethyl]dimethylbenzyl-ammonium chloride, (*N,N*-dimethyl-*N*-[2-[2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]-ethoxy]-ethyl]-benzenemethan-ammonium chloride) *[121-54-0]* **M 448.1, m 164-166° (sinters at 120°, monohydrate).** Crystallise it from boiling acetone after filtering or from $CHCl_3$/petroleum ether. The precipitate is filtered off, washed with diethyl ether and dried for 24 hours in a vacuum desiccator. It is a cationic antiseptic surfactant which forms crystals also from a 1:9 MeOH/Et_2O mixture. It foams in water. [*Beilstein* **12** IV 2187.]

Benzhydrol (diphenylmethanol) *[91-01-0]* **M 184.2, m 69°, b 297°/748mm, 180°/20mm.** Crystallise benzhydrol from hot H_2O or petroleum ether (b 60-70°), petroleum ether containing a little *benzene, from CCl_4, or EtOH (1ml/g). An additional purification step includes passage of a *benzene solution through an activated alumina column. It sublimes in a vacuum. Also recrystallise it three times from MeOH/H_2O [Naguib *J Am Chem Soc* **108** 128 *1986*]. [*Beilstein* **6** IV 4648.]
§ A commercial polystyrene supported version is available.

Benzidine (4,4'-diaminobiphenyl) *[92-87-5]* **M 184.2, m 128-129°, pK_1^{20} 3.85, pK_2^{20} 4.95.** Its solution in *benzene is decolorised by percolating through two 2-cm columns of activated alumina, then concentrated until benzidine crystallises on cooling. Recrystallise alternately from EtOH and *benzene to constant absorption spectrum [Carlin et al. *J Am Chem Soc* **73** 1002 *1951*]. It has also been crystallised from hot water (charcoal) and from diethyl ether. Dry it under vacuum in an Abderhalden pistol. Store it in the dark in a stoppered container. **CARCINOGENIC. [***Beilstein* **13** IV 364.]

Benzidine dihydrochloride *[531-85-1]* **M 257.2, m >250°(dec).** Crystallise the salt by dissolving in hot H_2O, and adding conc HCl to the slightly cooled solution. **CARCINOGENIC**. [*Beilstein* **13** IV 365.]

Benzil *[134-81-6]* **M 210.2, m 96-96.5°.** Crystallise benzil from *benzene after washing with alkali. (Crystallisation from EtOH did not free benzil from material reacting with alkali.) [Hine & Howarth *J Am Chem Soc* **80** 2274 *1958*.] It has also been crystallised from CCl_4, diethyl ether or EtOH [Inoue et al. *J Chem Soc, Faraday Trans 1* **82** 523 *1986*]. [*Beilstein* **7** IV 2502.]

Benzilic acid (diphenylglycollic acid) *[76-93-7]* **M 228.3, m 150°, pK^{18} 3.06.** Crystallise benzilic acid from *benzene (*ca* 6ml/g), or hot H_2O. [*Beilstein* **10** IV 1256.]

Benzil monohydrazone *[5433-88-7]* **M 224.3, m 151°(dec).** Crystallise it from EtOH. The *monoacetyl hydrazone* has **m** 91° (from EtOH). [Metze & Meyer *Chem Ber* **90** 483 *1959*, *Beilstein* **7** I 394.]

α-Benzil monoxime *[14090-77-8]*, *[E 574-15-2]*, *[Z 574-16-3]* **M 105.1, m 140°.** The *trans-isomer* crystallises from *C_6H_6 (must not use animal charcoal) and has **m** 140°. The *cis-isomer* also crystallises from *C_6H_6 but crystals have 0.5*C_6H_6 (**m** 62-63°), and the solvent free compound has **m** 112°. [*Beilstein* **7** III 3812, **7** IV 2504.]

Benzo[*a*]biphenylene *[252-47-1]* **M 202.2, m 72-73° (compare with β-isomer).** It forms yellow needles from MeOH and sublimes *in vacuo* (**m** 72.0-72.8°). The *2,4,7-trinitrofluorenone complex* crystallises as black needles **m** 201.5-202.5°. [Cava & Stucker *J Am Chem Soc* **77** 6022 *1955*, Barton et al. *J Chem Soc(C)* 1276

1967, *Beilstein* **5** IV 2462.]

Benzo[*b*]biphenylene *[259-56-3]* **M 202.2, 242.6-243.6°.** It forms yellow crystals from *C_6H_6/cyclohexane **m** 234-245° (sublimation). The *2,4,7-trinitrofluorenone complex* crystallises as red needles from *C_6H_6/MeOH **m** 214-216°. It has been sublimed *in vacuo*. [Jensen & Coleman *Tetrahedron Lett* **No 20** 7 *1959*, Barton et al. *J Chem Soc Perkin Trans 1* 967 *1986*, *Beilstein* **5** IV 2462.]

Benzoic acid *[65-85-0]* **M 122.1, m 122.6-123.1°, pK^{25} 4.12.** For use as a volumetric standard, analytical reagent grade benzoic acid should be carefully fused to *ca* 130° (to dry it) in a platinum crucible, and then powdered in an agate mortar. Benzoic acid has been crystallised from boiling water (charcoal), aqueous acetic acid, glacial acetic acid, *C_6H_6, aqueous EtOH, petroleum ether (b 60-80°), and from EtOH solution by adding water. It is readily purified by fractional crystallisation from its melt and by sublimation in a vacuum at 80°. The *S-benzylisothiuronium salt* has **m** 167° (from EtOH/H_2O). [*Beilstein* **9** IV 273.]

Benzoic anhydride *[93-97-0]* **M 226.2, m 42°.** Free it from benzoic acid by washing with $NaHCO_3$, then water, and drying. Crystallise it from *benzene (0.5ml/g) by adding just enough petroleum ether (b 40-60°) to cause cloudiness, then cool in ice. It can be distilled at 210-220°/20mm. [*Beilstein* **19** IV 550.]

(±)-Benzoin (2-hydroxy-2-phenylacetophenone) *[119-53-9]* **M 212.3, m 137°.** Crystallise benzoin from CCl_4, hot EtOH (8ml/g), or 50% acetic acid. Also crystallise it from high purity *benzene, then twice from high purity MeOH, to remove fluorescent impurities [Elliott & Radley *Anal Chem* **33** 1623 *1961*]. It can be sublimed. [*Beilstein* **8** IV 1279.]

(±)-α-Benzoinoxime *[441-38-3]* **M 227.3, m 151°.** Crystallise the oxime from diethyl ether. It is used for the spectroscopic determination of Cu^{2+}, Pd^{2+}, Pt^{4+}, Rh^{3+} and V^{5+} [Singh et al. *Talanta* **26** 425 *1979*, *Beilstein* **8** IV 1282.]

Benzonitrile *[100-47-0]* **M 103.1, f -12.9°, b 191.1°, d_4^{20} 1.010, n_D^{20} 1.528.** Dry benzonitrile with $CaSO_4$, $CaCl_2$, $MgSO_4$ or K_2CO_3, and distil it from P_2O_5 in an all-glass apparatus, under reduced pressure (**b** 69°/10mm), collecting the middle fraction. Distillation from CaH_2 causes some decomposition of benzonitrile. Isonitriles can be removed by preliminary treatment with conc HCl until the odour of isonitrile (carbylamine) has gone, followed by preliminary drying with K_2CO_3. (This treatment also removes amines.) Steam distil (to remove small quantities of carbylamine). The distillate is extracted into ether, washed with dilute Na_2CO_3, dried overnight with $CaCl_2$, and the ether is removed by evaporation. The residue is distilled at 40mm (**b** 96°) [Kice et al. *J Am Chem Soc* **82** 834 *1960*].
Conductivity grade benzonitrile (specific conductance 2 x 10^{-8} mho) is obtained by treatment with anhydrous $AlCl_3$, followed by rapid distillation at 40-50° under vacuum. After washing with alkali and drying with $CaCl_2$, the distillate is redistilled in a vacuum several times at 35° before fractionally crystallising several times by partial freezing. It is dried over finely divided activated alumina from which it is withdrawn when required [Van Dyke & Harrison *J Am Chem Soc* **73** 402 *1951*]. [*Beilstein* **9** IV 892.]

Benzo[ghi]perylene (1,12-benzoperylene) *[191-24-2]* **M 276.3, m 273°, 277-278.5°, 278-280°.** It forms light green crystals on recrystallisation from *C_6H_6 or xylene and sublimes at 320-340°/0.05mm [UV: Hopff & Schweizer *Helv Chim Acta* **42** 2315 *1959*, Clar *Chem Ber* **65** 846 *1932*, Fluoresc. Spectrum: Bowen & Brocklehurst *J Chem Soc* 3875 *1954*]. It also recrystallises from propan-1-ol [Altman & Ginsburg *J Chem Soc* 466 *1959*]. The *1,3,5-trinitrobenzene complex* has **m** 310-313° (deep red crystals from *C_6H_6), the *picrate* has **m** 267-270° (dark red crystals from *C_6H_6), and the *styphnate (2,4,6-trinitroresorcinol complex)* has **m** 234° (wine red crystals from *C_6H_6). [*Beilstein* **5** IV 2766.]

3,4-Benzophenanthrene (benzo[c]phenanthrene) *[195-19-7]* **M 228.3, m 68°.** Crystallise benzo[c]phenanthrene from EtOH, petroleum ether, or EtOH/Me_2CO. [*Beilstein* **5** III 2378, **5** IV 2552.]

Benzophenone *[119-61-9]* **M 182.2, m 48.5-49°, pK^{25} -6.0(-8.4) (aqueous H_2SO_4).** Crystallise it from MeOH, EtOH, cyclohexane, *benzene or petroleum ether, then dry in a current of warm air and store it over BaO

or P_2O_5. It is also purified by zone melting and by sublimation [Itoh *J Phys Chem* **89** 3949 *1985*, Naguib et al. *J Am Chem Soc* **108** 128 *1986*, Gorman & Rodgers *J Am Chem Soc* **108** 5074 *1986*, Ohamoto & Teranishi *J Am Chem Soc* **108** 6378 *1986*, Naguib et al. *J Phys Chem* **91** 3033 *1987*]. [*Beilstein* **7** III 2048, **7** IV 1357.]

Benzophenone oxime *[574-66-3]* **M 197.2, m 142°, 143-144°, pK^{25} 11.18.** Crystallise the oxime from MeOH (4ml/g). [*Beilstein* **7** II 355, **7** III 2063 1370.]

Benzophenone-3,3',4,4'-tetracarboxylic dianhydride (BTDA) *[2421-28-5]* **M 322.2, m 218.5-219.5°, 225.5°.** The main impurity is the free acid formed by hydrolysis (check for OH bands in the IR). This can be converted to the dianhydride by treating with Ac_2O (molar ratio of 4 to 1 of acid), heating at 110-120° for 1.5 to 2 hours, cooling to 0—5° and collecting the dianhydride. This is then dissolved in hot dioxane or Me_2CO, filtered and cooled to 10—15°. The moisture sensitive solid is collected and dried at 120—130° *in vacuo*. It has been sublimed at high vacuum. [Faberov et al. *J Org Chem USSR* **4** 153 (English translation) *1968*.]

Benzopinacol *[464-72-2]* **M 366.5, m 170-180° (depends on heating rate), 171-173°.** Crystallise benzopinacol from EtOH. [*Beilstein* **6** IV 7053.]

Benzo[a]pyrene (3,4-benzpyrene, benzo[dcf]chrysene) *[50-32-8]* **M 252.3, m 177.5-178°, 179.0-179.5°.** A solution of 250mg of benzo[a]pyrene in 100ml of *benzene is diluted with an equal volume of hexane, then passed through a column of alumina, $Ca(OH)_2$ and Celite (3:1:1). The adsorbed material is developed with a 2:3 *benzene/hexane mixture. (It showed as an intensely fluorescent zone.) The main zone is eluted with 3:1 acetone/EtOH, and is transferred into 1:1 *benzene-hexane by adding H_2O. The solution is washed, dried with Na_2SO_4, evaporated and crystallised from *benzene by the addition of MeOH [Lijinsky & Zechmeister *J Am Chem Soc* **75** 5495 *1953*]. *Alternatively*, it can be chromatographed on activated alumina, eluted with a cyclohexane/*benzene mixture containing up to 8% *benzene, and the solvent is evaporated under reduced pressure [Cahnmann *Anal Chem* **27** 1235 *1955*], and crystallised from EtOH [Nithipatikom & McGown *Anal Chem* **58** 3145 *1986*]. [*Beilstein* **5** III 2517, **5** IV 2687.] **CARCINOGENIC.**

Benzo[e]pyrene (1,2-benzpyrene) *[192-97-2]* **M 252.3, m 178-179°, 178-180°.** Purify it by passage through an Al_2O_3 column (Woelm, basic, activity I) and elute with $*C_6H_6$ and recrystallise from 2 volumes of EtOH/$*C_6H_6$ (4:1). It forms colourless or light yellow prisms or needles. [Campbell *J Chem Soc* 3659 *1954*, Buchta & Kröger *Justus Liebigs Ann Chem* **705** 190 *1967*.] The *1,3,5-trinitrobenzene complex* has **m** 253-254° (orange needles from EtOH), the *picrate* prepared by mixing 20mg in 1ml of $*C_6H_6$ with 20mg of picric acid in 2ml $*C_6H_6$, collecting the deep red crystals, and recrystallising from $*C_6H_6$ has **m** 228-229° [NMR: Cobb & Memory *J Chem Phys* **47** 2020 *1967*]. [*Beilstein* **5** III 2520, **5** IV 2689.] **CARCINOGEN.**

***p*-Benzoquinone** *[106-51-4]* **M 108.1, m 115.7°.** Purify *p*-benzoquinone in one or more of the following ways: steam distillation followed by filtration and drying (e.g. in a desiccator over $CaCl_2$), crystallisation from petroleum ether (b 80-100°), *benzene (with, then without, charcoal), water or 95% EtOH, sublimation under vacuum (e.g. from room temperature to liquid N_2). It slowly decomposes and should be stored, refrigerated, in an evacuated or sealed glass vessel in the dark. It should be resublimed before use. [Wolfenden et al. *J Am Chem Soc* **109** 463 *1987*, *Beilstein* **7** IV 2065.]

1-Benzosuberone (6,7,8,9-tetrahydrobenzocyclohepten-5-one) *[826-73-3]* **M 160.2, b 80-85°/0.5mm, 90-93°/1mm, 138-139°/12mm, 154°/15mm, 175-175°/40mm, d_4^{20} 1.086, n_D^{20} 1.5638.** Purify it by dissolving in toluene, washing with aqueous 5% NaOH, then brine, drying ($MgSO_4$), and distilling. The *2,4-dinitrophenylhydrazone* has **m** 210.5°, 207-208° (from $CHCl_3$/MeOH). The *Z-O-picryloxime* has **m** 156-157° (from Me_2CO/MeOH), the *E-O-picryloxime* has **m** 107°. The *oxime* has **m** 106.5-107.5°. [UV: Gilmore & Horton *J Am Chem Soc* **73** 1411 *1951*, Hedden & Brown *J Am Chem Soc* **75** 3744 *1953*, Huisgen et al. *Chem Ber* **90** 1844 *1957*, *Beilstein* **7** IV 1029.]

Benzoylacetone (1-phenyl-1,3-butanedione) *[93-91-4]* **M 162.2, m 58.5-59.0°.** Crystallise benzoylacetone from Et_2O or MeOH and dry it under vacuum at 40°. [*Beilstein* **7** IV 2151.]

2-Benzoylbenzoic acid *[85-52-9]* **M 226.2, m 126-129°, 129.2, 130°, pK^{25} 3.54.** Recrystallise the acid from *C_6H_6 or cyclohexane, but it is best recrystallised by dissolving in a small volume of hot toluene and then adding just enough petroleum ether to cause turbidity, and cool. Dry it in a low vacuum at 80°. It can be sublimed at 230-240°/0.3mm [Bray et al. *J Chem Soc* 265 *1957*]. The *S-benzylisothiuronium salt* has **m** 177-178° (from EtOH). [Lewenz & Serijan *J Am Chem Soc* **75** 4087 *1953*, *Beilstein* **10** H 747, **10** IV 2977.]

3-Benzoylbenzoic acid *[579-18-0]* **M 226.2, m 164-166°, 165°, pK$_{Est}$~3.5.** Crystallise the acid from EtOH and sublime it at 160°/1mm. [*Beilstein* **10** H 752, **10** III 3304, **10** IV 2982.]

4-Benzoylbenzoic acid *[611-95-0]* **M 226.2, m 196.5-198°**, **197-200°, pK$_{Est}$ ~3.7.** Dissolve the acid in hot H_2O by adding enough aqueous KOH solution till distinctly alkaline, filter and then acidify with drops of conc HCl. Filter off, wash the solid with cold H_2O, dry it at 100°, and recrystallise it from EtOH. [Wertheim *J Am Chem Soc* **55** 2540 *1933*, *Beilstein* **10** H 753, **10** IV 3305.]

Benzoyl chloride *[98-88-4]* **M 140.6, b 56°/4mm, 196.8°/745mm, d$_4^{20}$ 1.2120, n$_D^{10}$ 1.5537.** A solution of benzoyl chloride (300ml) in *C_6H_6 (200ml) is washed with two 100ml portions of cold 5% $NaHCO_3$ solution, separated, dried with $CaCl_2$ and distilled [Oakwood & Weisgerber *Org Synth* **III** 113 *1955*]. Repeated fractional distillation at 4mm Hg through a glass helices-packed column (avoiding porous porcelain or silicon-carbide boiling chips, and hydrocarbon or silicon greases on the ground joints) gave benzoyl chloride that did not darken on addition of $AlCl_3$. Further purification is achieved by adding 3 mole% each of $AlCl_3$ and toluene, standing overnight, and distilling off the benzoyl chloride at 1-2mm [Brown & Jenzen *J Am Chem Soc* **80** 2291 *1958*]. Refluxing for 2 hours with an equal weight of thionyl chloride before distillation has also been used. [*Beilstein* **9** IV 721.] *Strong* **IRRITANT**. *Use in a fume cupboard.*

Benzoyl disulfide (dibenzoyl disulfide) *[644-32-6]* **M 174.4, m 131.2-132.3°.** About 300ml of solvent is blown off from a filtered solution of dibenzoyl disulfide (25g) in acetone (350ml). The remaining acetone is decanted from the solid which is recrystallised first from 300ml of 1:1 (v/v) EtOH/ethyl acetate, then from 300ml of EtOH, and finally from 240ml of 1:1 (v/v) EtOH/ethyl acetate. The yield is about 40% [Pryor & Pickering *J Am Chem Soc* **84** 2705 *1962*]. [*Beilstein* **9** H 424, **9** II 289, **9** III 1977.] *Handle in a fume cupboard because of* **TOXICITY** *and obnoxious odour.*

Benzoylformic acid (phenylglyoxylic acid) *[611-73-4]* **M 150.14, m 62-65°, 64.5-65.5°, 67°, b 84°/0.1mm, 163-167°/15mm, pK^{25} 1.39 (1.79).** If the sample is oily, then it may contain H_2O. In this case dry it in a vacuum desiccator over P_2O_5 or KOH until crisp. For further purification dissolve 5.5g in hot CCl_4 (750ml), add charcoal (2g, this is necessary otherwise the acid may separate as an oil), filter, cool in ice-water until crystallisation is complete. Filter the acid off, and the solvent on the crystals is removed by keeping the acid (4.5g) in a vacuum desiccator for 2 days. Slightly yellow crystals are obtained. It can be recrystallised also from *C_6H_6/petroleum ether, and can be distilled in a vacuum. The acid is estimated by titration with standard NaOH. The *phenylhydrazone* is recrystallised from EtOH, **m** 163-164°, and the *semicarbazone acid* has **m** 259°(dec) (from EtOH). The *methyl ester* distils at **137°/14mm, 110-111°/2mm, n$_D^{20}$ 1.5850**. [Baert & Kates *J Am Chem Soc* **67** 1482 *1945*, Schaffer & Corey *J Org Chem* **24** 1825 *1959*, *Beilstein* **10** H 654, **10** IV 2737.]

Benzoyl isothiocyanate *[532-55-8]* **M 163.2, m 25.5-26°**, **b 72.5-73°/6mm, 88-91°/20mm, 94-96°/21mm, 202.5-204°/724mm, 250-255°/atm, d$_4^{20}$ 1.213, n$_D^{20}$ 1.637.** Distil the isothiocyanate over a small amount of P_2O_5, whereby the distillate crystallises in prisms. It is readily hydrolysed by H_2O to give benzamide and benzoylurea, but with NH_3 it gives *benzoylurea* **m** 210° which can be recrystallised from EtOH. [Hill & Degnan *J Am Chem Soc* **62** 1595 *1940,* Terss & McEwen *J Am Chem Soc* **76** 580 *1954*, Frank & Smith *Org Synth* Coll Vol **III** 735 *1955*, *Beilstein* **9** IV 777.]

Benzoyl peroxide *[94-36-0]* **M 242.2, m 95°(dec).** Dissolve benzoyl peroxide in $CHCl_3$ at room temperature and precipitate it by adding an equal volume of MeOH or petroleum ether. Similarly, it is precipitated from acetone by adding two volumes of distilled water. It has also been crystallised from 50% MeOH and from diethyl ether. Dry it under vacuum at room temperature for 24 hours. Store it in a desiccator in the dark at 0°. When purifying in the absence of water it can be **EXPLOSIVE**, and operations should be done on a very small

scale with adequate protection. Large amounts should be kept moist with water and stored in a refrigerator. [Kim et al. *J Org Chem* **52** 3691 *1987*, *Beilstein* **9** IV 777.]

***p*-Benzoylphenol (4-hydroxybenzophenone)** *[1137-42-4]* **M 198.2, m 133.4-134.8°, pK^{25} 7.95.** Dissolve *p*-benzoylphenol in hot EtOH (charcoal), filter and cool. *Alternatively*, crystallise it once from EtOH/H_2O and twice from *benzene [Grunwald *J Am Chem Soc* **73** 4934 *1951*, Dryland & Sheppard *J Chem Soc Perkin Trans 1* 125 *1986*]. [*Beilstein* **8** IV 1263.]

***N*-Benzoyl-*N*-phenylhydroxylamine** *[304-88-1]* **M 213.2, m 121-122°.** Recrystallise it from hot water, *benzene Et_2O/hexane or acetic acid. It complexes with metals. [*Beilstein* **15** III 8, **15** IV 7.]

***N*-Benzoyl-*o*-tolylhydroxylamine** *[1143-74-4]* **M 227.3, m 104°.** Recrystallise the hydroxylamine from aqueous EtOH. [*Beilstein* **15** III 8, **15** IV 7.]

Benzyl acetate *[140-11-4]* **M 150.2, m -51°, b 92-93°/10mm, 134°/102mm, 214.9°/760mm, d $^{20}_{4}$ 1.0562, n $^{25}_{D}$ 1.4994.** Purify the acetate by fractional distillation, preferably in a good vacuum. Values of n^{25} of 1.5232-1.5242 are too high and should be nearer to 1.4994. [Merker & Scott *J Org Chem* **26** 5180 *1961*, *Beilstein* **6** IV 2262.]

Benzyl acetoacetate *[5396-89-4]* **M 192.2, b 130°/2mm, 156-157°/10mm, 162-167°/15mm, 275-277°/atm, d $^{20}_{4}$ 1.114, n $^{20}_{D}$ 1.514.** Fractionate the ester and collect fractions with the expected physical properties. Otherwise add *ca* 10% by weight of benzyl alcohol and heat in an oil bath (160-170°, open vessel) for 30 minutes during which time excess of benzyl alcohol will have distilled off, then fractionate. [Baker et al. *J Org Chem* **17** 77 *1952*, *Beilstein* **6** IV 2480.]

4'-Benzylacetophenone *[782-92-3]* **M 210.3, m 37°, 38°, 39°, b 197-198°/9mm, 209-210°/15mm.** Distil it in a vacuum, then recrystallise it from EtOH (*ca* 1ml/g). The *oxime* has **m** 99.5° (from 60% aqueous EtOH). [*Beilstein* **7** H 449, **7** III 2176.]

Benzyl alcohol *[100-51-6]* **M 108.1, f -15.3°, b 205.5°, 93°/10mm, 205.5°/atm, d $^{20}_{4}$ 0.981, n $^{20}_{D}$ 1.54033, pK^{25} 15.4.** It is usually purified by careful fractional distillation under reduced pressure in the absence of air. Benzaldehyde, if present, can be detected by UV absorption at 283nm. It has also been purified by shaking with aqueous KOH and extracting with peroxide-free diethyl ether. After washing with water, the extract is treated with saturated NaHS solution, filtered, washed, dried with CaO and distilled under reduced pressure [Mathews *J Am Chem Soc* **48** 562 *1926*]. Peroxy compounds can be removed by shaking with a solution of Fe^{2+} followed by washing the alcohol layer with distilled water and fractionally distilling it. [*Beilstein* **6** IV 2222.]

Benzylamine *[100-46-9]* **M 107.2, b 178°/742mm, 185°/768mm, d $^{20}_{4}$ 0.981, n $^{20}_{D}$ 1.5392, pK^{25} 9.33.** Dry it with NaOH or KOH, then distil it under N_2, through a column packed with glass helices, taking the middle fraction. Also distil it from zinc dust under reduced pressure. The *picrate* has **m** 196° (from EtOH), and the *p-toluenesulfonamide* has **m** 116° (from MeOH). [*Beilstein* **12** IV 2155.]

Benzylamine hydrochloride *[3287-99-8]* **M 143.6, m 248° (rapid heating).** Crystallise the salt from water. [*Beilstein* **12** IV 2155.]

***N*-Benzylaniline (*N*-phenylbenzylamine)** *[103-32-2]* **M 183.4, m 36°, b 306-307°, d $^{20}_{4}$ 1.061, pK^{25} 4.04.** Crystallise the amine from petroleum ether (b 60-80°) (*ca* 0.5ml/g). The *picrate* has **m** 113° (from Et_2O). [*Beilstein* **12** H 1023, **12** I 449, **12** II 548, **12** III 2215, **12** IV 2172.]

Benzyl bromide *[100-39-0]* **M 171.0, m -4°, b 85°/12mm, 192°/760mm, d $^{20}_{4}$ 1.438, n $^{20}_{D}$ 1.575.** Wash benzyl chloride with conc H_2SO_4 (CARE), water, 10% Na_2CO_3 or $NaHCO_3$ solution, and again with water. Dry it with $CaCl_2$, Na_2CO_3 or $MgSO_4$ and fractionally distil it in the dark, under reduced pressure. It has also been thoroughly degassed at 10^{-6} mm and redistilled in the dark. This gives material with λ_{max} at (MeCN): 226nm (ε 8200) [Mohammed & Kosower *J Am Chem Soc* **93** 2709 *1971*]. [*Beilstein* **5** IV 829.] *Handle in a fume cup-*

board, extremely **LACHRYMATORY.**

Benzyl bromoacetate *[5437-45-6]* **M 229.1, b 96-98°/0.1mm, 146°/12mm, 166-170°/22mm, d_4^{20} 1.444, n_D^{25} 1.5412.** Dilute the ester with Et_2O, wash it with 10% aqueous $NaHCO_3$, H_2O, dry ($MgSO_4$) and fractionate it using a Fenske (glass helices packing) column. [Bergmann & Szinai *J Chem Soc* 1521 *1956*, *Beilstein* **6** IV 2265.] **LACHRYMATORY.**

***N*-Benzyl-*tert*-butylamine (*N-tert*-butylbenzylamine)** *[3378-72-1]* **M 163.3, b 91°/12mm, 109-110°/25mm, 218-220°/atm, d_4^{20} 0.899, n_D^{25} 1.4942, pK^{25} 10.19.** Dissolve the amine in Et_2O, dry it over KOH pellets, filter and fractionate it in a N_2 atmosphere to avoid reaction with CO_2 from the air. The *hydrochloride* has **m** 245-246°(dec) (from MeOH/Me_2CO) and the *perchlorate* has **m** 200-201°. [Freidfelder et al. *J Am Chem Soc* **80** 4320 *1958*, *Beilstein* **12** IV 2166.]

Benzyl carbamate *[621-84-1]* **M 151.2, m 86°, 86-88°, 90-91°.** If it smells of NH_3, then dry it in a vacuum desiccator and recrystallise it from 2 volumes of toluene and dry it in a vacuum desiccator again. It forms glistening plates from toluene, and can be recrystallised from H_2O [Martell & Herbst *J Org Chem* **6** 878 *1941*, Carter et al. *Org Synth* Coll Vol **III** 168 *1955*]. [*Beilstein* **6** IV 2278.]

Benzyl chloride *[100-44-7]* **M 126.6, m 139°, b 63°/8mm, d_4^{20} 1.100, n_4^{20} 1.538.** Dry it with $MgSO_4$ or $CaSO_4$, or reflux it with fresh Ca turnings, then fractionally distil it under reduced pressure, collecting the middle fraction and storing it over CaH_2 or P_2O_5. It has also been purified by passage through a column of alumina. *Alternatively*, it is dried over $MgSO_4$ and distilled in a vacuum. The middle fraction is degassed by several freeze-thaw cycles and then fractionated in an 'isolated fractionating column' (which has been evacuated and sealed off at ~10^{-6} mm) over a steam bath. The middle fraction is retained. The final samples are distilled in a vacuum from this sample and again retaining the middle fraction. The purity is >99.9% (no other peaks are visible by GLC, and the NMR spectrum is consistent with the structure. [Mohammed & Kosower *J Am Chem Soc* **93** 1709 *1971*, *Beilstein* **5** IV 809.] **IRRITANT** and s*trongly* **LACHRYMATORY.**

***N*-Benzyl-ß-chloropropionamide** *[24752-66-7]* **M 197.7, m 94°, 96°.** Crystallise the amide from MeOH. [**12** III 2257, **12** IV 2234.]

Benzyl cinnamate *[103-41-3]* **M 238.3, m 34-35°, 39°, b 154-157°/0.5mm, 228-230°/22mm.** Recrystallise the ester to a constant melting point from 95% EtOH. It has the odour of balsam. *Alternatively*, dissolve it in Et_2O, wash it with 10% aqueous Na_2CO_3, H_2O, dry (Na_2SO_4), evaporate and fractionate it under reduced pressure using a short Vigreux column. It decomposes when boiled at atmospheric pressure. [Eliel & Anderson *J Am Chem Soc* **74** 547 *1952*, Bender & Zerner *J Am Chem Soc* **84** 2550 *1962*, *Beilstein* **9** IV 2012.]

Benzyl cyanide *[140-29-4]* **M 117.1, b 100°/8mm, 233.5°/760mm, d_4^{20} 1.015, n_4^{20} 1.523.** Any benzyl isocyanide impurity can be removed by shaking vigorously with an equal volume of 50% H_2SO_4 at 60°, washing with saturated aqueous $NaHCO_3$, then half-saturated NaCl solution, drying and fractionally distilling under reduced pressure. Distillation from CaH_2 causes some decomposition of this compound: it is better to use P_2O_5. Other purification procedures include passage through a column of highly activated alumina, and distillation from Raney nickel. *Precautions should be taken because of possible formation of free* **TOXIC** *cyanide, use an efficient fume cupboard*. [*Beilstein* **9** IV 1663.]

***N*-Benzyl dimethylamine** *[103-83-3]* **M 135.2, b 66-67°/15mm, 83-84°/30mm, 98-99°/24mm, 181°/760mm, d_4^{20} 0.898, n_D^{20} 1.516, pK^{25} 8.91.** Dry the amine over KOH pellets and fractionate it over Zn dust in a CO_2—free atmosphere. It has a pKa^{25} of 8.25 in 45% aqueous EtOH. Store it under N_2 or in a vacuum. The *picrate* has **m** 94-95°, and the *picrolonate* has **m** 151° (from EtOH). [Skita & Keil *Chem Ber* **63** 34 *1930*, Coleman *J Am Chem Soc* **55** 3001 *1933*, Devereux et al. *J Chem Soc* 2845 *1957*.] The *tetraphenyl borate salt* has **m** 182-185°. [Crane *Anal Chem* **28** 1794 *1956*, *Beilstein* **12** IV 2161.]

Benzyldimethyloctadecylammonium chloride *[122-19-0]* **M 442.2, m 150-158° (sinters at 120°.** Crystallise the salt from acetone, EtOAc or EtOAc/ Et_2O. [Sumiki et al. *J Agric Chem Soc Jpn* **26** 325 *1952*,

Chem Abstr 3505 *1953*, *Beilstein* **12** III 2212, **12** IV 2168.]

Benzyl ether (dibenzyl ether) *[103-50-4]* **M 198.3, b 298°, 158-160°/0.1mm, d_4^{20} 1.043, n_4^{20} 1.54057.** Reflux the ether over sodium, then distil it under reduced pressure. It been purified by fractional freezing. [*Beilstein* **6** IV 2240.]

***N*-Benzyl-*N*-ethylaniline** *[92-59-1]* **M 221.3, b 212-222°/54mm, 285-286°/710mm, 312-313°/atm (dec), d_4^{20} 1.029, n_4^{20} 1.595, pK_{Est} ~4.6.** Dry the amine over KOH pellets and fractionate it. The *picrate* crystallises from *C_6H_6 as lemon yellow crystals **m** 126-128° (softening at 120°). [Forrest et al. *J Chem Soc* 303 *1951*, IR: Hill & Meakins *J Chem Soc* 760 *1958*, *Beilstein* **12** H 1026, **12** IV 2176.]

Benzyl ethyl ether *[539-30-0]* **M 136.2, b 186°, 65°/10mm, d_4^{20} 0.949, n_D^{20} 14955.** Dry the ether with $CaCl_2$ or NaOH, then fractionally distil it. [Letzinger & Pollart *J Am Chem Soc* **78** 6079 *1956*, *Beilstein* **6** III 1454, **6** IV 2229.]

Benzyl ethyl ketone (1-phenylbutan-2-one) *[1007-32-5]* **M 148.2, b 49-49.5°/0.01mm, 66-69°/1mm, 83-85°/5mm, 101-102°/10mm, 229-233°/atm, d_4^{20} 0.989, n_D^{25} 1.5015.** Purify the ketone by fractionation using an efficient column. It can be converted into the *oxime* which is distilled, **b** 117-118°/2mm, 145-146°/15mm, d_{25}^{25} 1.036, n_D^{25} 1.5363; decompose the oxime, and the ketone is redistilled. It can also be purified *via* the *semicarbazone* which has **m** 154-155°. [Meyers et al. *J Am Chem Soc* **77** 5655 *1955*, Hass et al. *J Org Chem* **15** 8 *1950*, *Beilstein* **7** IV 712.]

***O*-Benzylhydroxylamine hydrochloride** *[2687-43-6]* **M 159.6, m 234-238°(sublimes), pK_{Est} ~5.9.** Recrystallise the hydrochloride from H_2O or EtOH. [*Beilstein* **6** IV 2562.]

***N*-Benzylideneaniline** *[538-51-2]* **M 181.2, m 48° (54°), 56°, b 310°/760mm.** It is steam volatile and crystallises from *benzene or 85% EtOH. The *picrate* has **m** 159°. [*Beilstein* **12** H 195, **12** I 169, **12** II 113, **12** III 319, **12** IV 311.]

Benzylidene malononitrile *[2700-22-3]* **M 154.2, m 83-84°, 87°.** Recrystallise the nitrile from EtOH [Bernasconi et al. *J Am Chem Soc* **107** 3612 *1985*]. It has λ_{max} at 307nm (EtOH). [*Beilstein* **9** H 895, **9** II 640, **9** III 4380, **9** IV 3462.]

Benzyl isocyanate *[3173-56-6]* **M 133.2, b 82-84°/10mm, 87°/14mm, 95°/17mm, 101-104°/33mm, d_4^{20} 1.08, n_D^{20} 1.524.** Purify the isocyanate by fractionation through a two-plate column. It is a viscous liquid and is **TOXIC**. [Howarth et al. *J Chem Soc* 182 *1947*, Ferstandig & Scherrer *J Am Chem Soc* **81** 4838 *1959*, IR: Derkosch et al. *Monatsh Chem* **88** 35 *1957*, *Beilstein* **12** IV 2276.]

Benzyl isothiocyanate *[622-78-6]* **M 149.2, b 123-124°/1mm, 138-140°/20mm, 255-260°/atm, d_4^{20} 1.1234, n_D^{20} 1.6039.** Dissolve benzyl isothiocyanate in Et_2O, filter, if there is any solid, and distil it through an efficient column at 11mm with a bath temperature at *ca* 150°. Characterise it by reacting (0.5ml) in EtOH (1ml) with 50% $NH_2NH_2.H_2O$ (2 ml) to give *4-benzylthiosemicarbazide* as colourless needles which are recrystallised from EtOH, **m** 130°. [Hoggarth & Young *J Chem Soc* 1582 *1950*, Schmidt et al. *Justus Liebigs Ann Chem* **612** 11 *1958*, IR and UV: Svátek et al. *Acta Chem Scand* **13** 442 *1959*, *Beilstein* **12** IV 2276.]

S-Benzylisothiuronium chloride *[538-28-3]* **M 202.7, two forms, m 150° and 175°, pK_{Est} ~9.8 (free base).** Crystallise the chloride from 0.2M HCl (2ml/g) or EtOH and it dry in air. [*Beilstein* **6** III 1600.]

Benzylmalonic acid *[616-75-1]* **M 194.2, m 121°, pK_1^{25} 2.91, pK_2^{25} 5.87.** Crystallise the acid from *C_6H_6. [*Beilstein* **9** IV 3357.]

Benzyl mercaptan *[100-53-8]* **M 124.2, b 70.5-70.7°/9.5mm, d_4^{20} 1.058, n_D^{20} 1.5761, pK^{25} 9.43.** Purify benzyl mercaptan *via* the mercury salt [see Kern *J Am Chem Soc* **75** 1865 *1953*], which crystallises from *benzene as needles (**m** 121°), and then dissolve it in $CHCl_3$. Pass H_2S gas through the solution to regenerate

the mercaptan. The HgS that precipitates is filtered off and washed thoroughly with $CHCl_3$. The filtrate and washings are evaporated to remove $CHCl_3$; then the residue is fractionally distilled under reduced pressure [Mackle & McClean, *Trans Faraday Soc* **58** 895 *1962*]. [*Beilstein* **6** IV 2632.]

(-)-*N*-Benzyl-*N*-methylephedrinium bromide [benzyl(2-hydroxy-1-methyl-2-phenethyl) dimethyl-ammonium bromide] *[58648-09-2]* **M 350.3, m 209-211°, 212-214°, $[\alpha]_D^{25}$ -3.8° (c 1.45, MeOH), $[\alpha]_D^{20}$ -5.3° (c 1.45, MeOH).** Recrystallise the bromide from MeOH/Et_2O. [Horner & Brich *Justus Liebigs Ann Chem* 710 *1978*.] The *chloride* is recrystallised from EtOAc/*n*-hexane, **m** 198-199° $[\alpha]_D^{25}$ -8.67° (c 1.45, MeOH). [Julia et al. *J Chem Soc, Perkin Trans 1* 574 *1981*, *Beilstein* **13** IV 1890.]

Benzyl 4-nitrophenyl carbonate *[13795-24-9]* **M 273.2, m 78-80°.** Dissolve the carbonate in Et_2O, wash with H_2O (3x) and saturated aqueous NaCl, dry ($MgSO_4$), evaporate this in a vacuum and recrystallise the residue from a small volume of MeOH, **m** 78-79°. *Alternatively*, dissolve it in Et_2O, wash it with N HCl (2x), 0.5N $NaHCO_3$ (4x) then H_2O, dry (Na_2SO_4), evaporate the Et_2O and recrystallise the residue from *C_6H_6/petroleum ether, **m** 79-80°. The *2-nitro-isomer* has **m** 27-28°, **b** 151°/11mm. [Khosla et al. *Indian J Chem* **5** 279 *1967*, Wolman et al. *J Chem Soc (C)* 596 *1976*, *Beilstein* **6** IV 2277.]

Benzyloxyacetyl chloride *[19810-31-2]* **M 184.6, b 81°/0.2mm, 84-87°/0.4mm, 105-107°/5mm, d_4^{20} 1.19, n_D^{20} 1.523.** Check the IR to see if there are OH bands. If so, then it may be contaminated with free acid formed by hydrolysis. Add oxalyl chloride (amount depends on contamination and needs to be judged, *ca* 3mols), heat at 50° in the absence of moisture for 1 hour and fractionate twice, **b** 81°/0.2mm (with bath temperature at 81°). Excessive heating results in decomposition to give benzyl chloride. The *anilide* is formed by adding aniline in $CHCl_3$ solution and has **m** 49°. [Fischer & Gohlke *Helv Chim Acta* **16** 1130 *1933*, *Beilstein* **6** IV 2470.]

3-Benzyloxybenzoic acid *[69026-14-8]* **M 228.2, m 133-137°, 135.5-136°, pK_{Est} ~4.1.** Recrystallise the acid from acetic acid (**m** 137-138°) [Kipping & Wren *J Chem Soc* 3246 *1957*, *Beilstein* **10** III 247, **10** IV 316.]

Benzyloxybutan-2-one *[6278-91-7]* **M 178.2, b 90-92°/0.1mm, 88-91°/0.5mm, 121-126°/5mm, d_4^{20} 1.0275, n_D^{20} 1.5040.** Dissolve the ketone in $CHCl_3$, wash with H_2O, aqueous saturated $NaHCO_3$, H_2O, dry ($MgSO_4$), evaporate the $CHCl_3$, and fractionate it. [Hoffman et al. *J Am Chem Soc* **79** 2316 *1957*, *Beilstein* **6** IV 2255.]

Benzyloxycarbonyl chloride (Cbz-Cl, BOC-Cl, benzyl chloroformate) *[501-53-1]* **M 170.6, b 103°/20mm, d_4^{20} 1.195, n_D^{20} 1.5190.** The commercial material is usually better than 95% pure and may contain some toluene, benzyl alcohol, benzyl chloride and HCl. After long storage, e.g. two years at 4°, Greenstein and Winitz [*The Chemistry of the Amino Acids* **Vol 2** p. 890, J Wiley and Sons NY, *1961*] recommended that the liquid should be flushed with a stream of dry air, filtered and stored over sodium sulfate to remove CO_2 and HCl which are formed by decomposition. It may further be distilled from an oil bath at a temperature below 85° because Thiel and Dent [*Annalen* **301** 257 *1898*] stated that benzyloxycarbonyl chloride decarboxylates to benzyl chloride slowly at 100° and vigorously at 155°. Redistillation at higher vacuum below 85° yields material which shows no other peaks than those of benzyloxycarbonyl chloride by NMR spectroscopy. [*Beilstein* **6** IV 2278.] **LACHRYMATORY** and **TOXIC**.

***p*-(Benzyloxy)phenol** *[103-16-2]* **M 200.2, m 122.5°, pK_{Est} ~10.1.** Crystallise it from EtOH or H_2O, and dry (P_2O_5) under vacuum. [Walter et al. *J Am Chem Soc* **108** 5210 *1986*, *Beilstein* **6** IV 5778.]

***S*-(-)-3-Benzyloxypropan-1,2-diol** *[17325-85-8]* **M 182.2, m 24-26°, b 117-118°/10^{-4}mm, 115-116°/0.02mm, 121-123°/0.2mm, d_4^{20} 1.1437, n_D^{22} 1.5295, $[\alpha]_D^{25}$ -5.9° (neat).** Purify the diol by repeated fractional distillation. [Baer et al. *J Biol Chem* **230** 447 *1958*, Gigg & Gigg *J Chem Soc C* 1865 *1967*, *Beilstein* **6** IV 2247.]

2-Benzylphenol *[28994-41-4]* **M 184.2, m 54.5°, b 312°/760mm, 175°/18mm, pK_{Est} ~10.0.** Distil 2-benzylphenol in a vacuum and recrystallise it from EtOH. It has a stable form with **m** ~52° and an unstable form with **m** 21°. [*Beilstein* **6** H 675, **6** IV 4628.]

4-Benzylphenol (α-phenyl-*p*-cresol) *[101-53-1]* **M 184.2, m 84°, pK_{Est} ~10.2.** Crystallise 4-benzylphenol

from water. [*Beilstein* **6** H 675, **6** IV 4628.]

4-*N*-Benzylsulfanilamide (Septazen) *[1709-54-2]* **M 262.3, m 175°, 178°.** Crystallise Septazen from dioxane/H_2O, EtOH/H_2O or Me_2CO (**m** 174.5-175.8°). Its solubility in H_2O at 37° is 0.03-0.43mg/100ml. [*Beilstein* **14** III 2026.]

Benzylthiocyanate *[3012-37-1]* **M 149.2, m 43°, b 256°(dec).** Crystallise the thiocyanate from EtOH or aqueous EtOH. [*Beilstein* **6** H 460, **6** IV 2680.]

Benzyl toluene-*p*-sulfonate *[1024-41-5]* **M 162.3, m 58°, 58.5-58.8°.** Crystallise the ester from petroleum ether (b 40-60°), $CHCl_3$/hexane or Et_2O/*C_6H_6. Dry it *in vacuo* but NOT in a desiccator over $CaCl_2$ as it causes hydrolysis of the ester. [Emmons & Ferris *J Am Chem Soc* **75** 2257 *1953*, *Beilstein* **11** II 48, **11** III 207, **11** IV 273.]

Benzyltributylammonium bromide *[25316-59-0]* **M 356.4, m 169-171°, 174-175°.** Recrystallise the bromide from EtOAc/EtOH and EtOH/Et_2O. [Kantor & Hauser *J Am Chem Soc* **73** 4122 *1951*, Petersen et al. *J Am Chem Soc* **81** 3264 *1959*, *Beilstein* **12** IV 2166.]

Benzyl 2,2,2-trichloroacetimidate *[81927-55-1]* **M 252.5, b 106°/0.5mm, m 3°, d_4^{20} 1.349, n_D^{20} 1.545.** Purify the imidate by distillation to remove up to 1% of $PhCH_2OH$ as stabiliser. A solution in hexane can be stored for up to 2 months without decomposition. It is *hygroscopic* and has to be stored dry. [Wessel et al. *J Chem Soc, Perkin Trans 1* 2247 *1985*, *Beilstein* **6** IV 2265.]

Benzyltrimethylammonium chloride *[56-93-9]* **M 185.7, m 238-239°(dec).** A 60% aqueous solution of the salt is evaporated to dryness under a vacuum on a steam bath, and then left in a vacuum desiccator containing a suitable drying agent. The solid residue is dissolved in a small volume of boiling absolute EtOH and precipitated by adding an equal volume of diethyl ether with cooling. After washing, the precipitate is dried under a vacuum [Karusch *J Am Chem Soc* **73** 1246 *1951*]. [*Beilstein* **12** IV 2162.]

Benzyltrimethylammonium hydroxide (Triton B) *[100-85-6]* **M 167.3, d 0.91.** A 38% solution (as supplied) is decolorised (charcoal), then evaporated under reduced pressure to a syrup, with final drying at 75°/1mm pressure. The *anhydrous* base is obtained by prolonged drying over P_2O_5 in a vacuum desiccator. [*Beilstein* **12** IV 2162.]

Bibenzyl (1,2-diphenylethane, dibenzyl) *[103-29-7]* **M 182.3, m 50-53°, 52.0-52.5°, 52.5-53.5°.** Crystallise bibenzyl from hexane, MeOH, or 95% EtOH. It has also been sublimed under vacuum, and further purified by percolation through columns of silica gel and activated alumina. It is prepared by reduction of benzoin or benzyl [Clemmensen *Chem Ber* **47** 688 *1914*], but is best obtained by catalytic reduction of stilbene. Thus a mixture of stilbene (5g, see [103-30-0]) in dioxane (200ml) and Raney Ni (22g) is refluxed with strring for 24 hours. The catalyst is filtered off, the filtrate is evaporated *in vacuo*, and the residue is recrystallised from MeOH to give an 80% yield of bibenzyl m 52.0-52.5°. Its FT-IR (melt) has ν_{max} at 3062.6, 1601.7, 1494.9, 1030.2, 906.0, 752.1, 696.9, 580.2 and 519.3 cm^{-1}; its ^1H NMR (300MHz, $CDCl_3$, TMS) has δ at 7.27 (t, 4H, arom-H), 7.18 (t, 6H, arom-H) and 2.90 (s, 4H, benzylic-H); and its ^{13}C NMR (15MHz, $CDCl_3$, $CDCl_3$ as internal standard with δ at ~77.0) has δ at 141.7, 128.36, 128.24, 125.83 and 37.89. [Kleiderer & Kornfeld *J Org Chem* **13** 455 *1948*.] [*Beilstein* **5** IV 1868.]

(±)-1,1'-Bi-(2-naphthol) [1,1'-di-(2-naphthol), BINOL] *[602-09-5, 41024-90-2]* **M 286.3, m 215-217°, 218°, $pK_{Est(1)}$ ~7.1, $pK_{Est(2)}$ ~11.2.** Crystallise the binaphthol from toluene or *benzene (10ml/g). When crystallised from chlorobenzene it has **m** 238°. Its solubility in dioxane is 5%. [*Beilstein* **6** IV 7020.]

1,1'-Bi-(2-naphthol) [1,1'-di-(2-naphthol)] *[R-(+)- 18531-94-7], [S-(–)- 18531-99-2]* **M 286.3, m 207.5-208.5°, 209-211°, $[\alpha]_D^{20}$ (+) and (-) 37.4.0° (c 0.5, THF), $[\alpha]_{546}^{25}$ (+) and (-) 51° (c 0.1, THF), pK as above.** Dissolve it in cold 2.5N NaOH, extract with CH_2Cl_2, and acidify with 5% HCl. Collect the white precipitate and

recrystallise it from aqueous EtOH and dry it in a vacuum [Akimoto & Yamada *Tetrahedron* **27** 5999 *1971*]. It is optically stable in dioxane-water (100°/24 hours). *Racemisation*: 72% in 1.2N HCl at 100°/24 hours and 68% in 0.67M KOH in BuOH at 118°/23 hours [Kyba et al. *J Am Chem Soc* **95** 2693 *1973*]. It has also been crystallised from $*C_6H_6$ (solubility is 1%) using Norite or aqueous EtOH after chromatography through silica gel, eluting with $Me_2CO/*C_6H_6$. [Kyba et al. *J Org Chem* **42** 4173 *1977*; see also Brussee & Jansen *Tetrahedron Lett* **24** 3261 *1983*, Akimoto & Yamada *Tetrahedron* **27** 5999 *1971*, *Beilstein* **6** IV 7020.]

1,1'-Binaphthyl *[(±)- 32507-32-7* and *604-53-5*, *R(–)- 24161-30-6*, *S(+)- 734-77-0]* **M 254.3, m 145°, 159°, b ~240°/13mm, (±, 2 forms), 153-154°, 154°, (+ and -), $[\alpha]_D^{20}$ (-) and (+) ~220° ($*C_6H_6$).** Purify 1,1'-binaphthyl through a silica gel column with $Me_2CO/*C_6H_6$ [or Al_2O_3 with 10% $*C_6H_6$/petroleum ether (b 30-60°)] and recrystallise it from EtOH, pentane, or slow evaporation of $*C_6H_6$, Me_2CO or Et_2O solutions. Half life ~10 hours at 25° in various solvents. [Wilson & Pincock *J Am Chem Soc* ***97*** 1474 *1975*, Akimoto & Yamada *Tetrahedron* **27** 5999 *1971*, *Beilstein* **5** I 358, **5** II 642, **5** III 2465, **5** IV 2634.]

2,2'-Binaphthyl (β, β'-binaphthyl) *[61-78-2]* **M 254.3, m 188°.** Crystallise the 2,2'-binaphthyl from $*C_6H_6$, or $Et_2O/*C_6H_6$ (**m** 187-189°). The *2,4,7-trinitrofluorenone complex* forms orange-red needles from $EtOH/*C_6H_6$ (**m** 170.6-171°). [*Beilstein* **5** H 727, **5** I 359, **5** II 643, **5** III 2467, **5** IV 2636.]

Biphenyl *[92-52-4]* **M 154.2, m 68-75°, 70-71°, b 112°/7mm, 255°/760mm, d_4^{20} 0.992.** Crystallise biphenyl from EtOH, MeOH, aqueous MeOH, petroleum ether (b 40-60°) or glacial acetic acid. Free it from polar impurities by passage through an alumina column in *benzene, followed by evaporation. The residue has been purified by distillation in a vacuum and by zone refining. Treatment with maleic anhydride removes anthracene-like impurities. It has been recrystallised from EtOH followed by repeated vacuum sublimation and passage through a zone refiner. [Taliani & Bree *J Phys Chem* **88** 2351 *1984*, *Beilstein* **5** H 576, 5 I 271, **5** II 479, **5** III 1726, **5** IV 1807.]

4-Biphenylcarbonyl chloride *[14002-51-8]* **M 216.7, m 114-115°.** Dissolve the carbonyl chloride in a large volume of petroleum ether (10 x, b 50-70°), filter it through a short column of neutral alumina, evaporate to dryness *in vacuo* and recrystallise it from petroleum ether (b 60-80°). [*Beilstein* **9** IV 2480.] **LACHRYMATORY.**

Biphenyl-2-carboxylic (2-phenylbenzoic) acid *[947-84-2]* **M 198.2, m 114°, b 343-344°, pK^{25} 3.46.** Crystallise the acid from $*C_6H_6$/petroleum ether or aqueous EtOH. [*Beilstein* **9** IV 2472.]

Biphenyl-4-carboxylic (4-phenylbenzoic) acid *[92-92-2]* **M 198.2, m 228°, pK^{25} 5.66 (in 50% 2-butoxyethanol)**. Crystallise the acid from $*C_6H_6$/petroleum ether or aqueous EtOH. [*Beilstein* **9** IV 2479.]

2,4'-Biphenyldiamine *[492-17-1]* **M 184.2, m 45°, b 363°/760mm, $pK_{Est(1)}$ ~4.8, $pK_{Est(2)}$ ~3.9.** Crystallise the diamine from aqueous EtOH or petroleum ether (**m** 54-54.5°). [*Beilstein* **9** III 416, **9** IV 360.]

Biphenyl-4,4'-dicarboxylic acid *[787-70-2]* **M 242.2, m >300°, $pK_{Est(1)}$ ~3.5, $pK_{Est(2)}$ ~4.3.** The dicarboxylic acid is a white amorphous or microcrystalline substance which does not melt or sublime. It is best purified by precipitation of an aqueous alkaline solution with mineral acid, washing well with H_2O and drying *in vacuo* at 100°. It is characterised by conversion to *diphenyl-4,4'-dicarbonyl chloride* (with PCl_5) [Work *J Chem Soc* 1317 1940], or by phase transfer catalysis with $SOCl_2$ + $BuEt_3N^+Cl^-$ in 1,2-dichloroethane [Burdett *Synthesis* 441 *1991*]) which crystallises from $*C_6H_6$ with **m** 184°. The di-acid chloride gives the *dimethyl ester* with MeOH, and has **m** 215-217° (plates from MeOH, **m's** of 214° and 224° were also reported)**.** The *diethyl ester* is similarly prepared with EtOH and has **m** 122° (from EtOH). [*Beilstein* **9** II 665, **9** III 4519, **9** IV 3563.]

Biphenylene *[259-79-0]* **M 152.2, m 111°.** Biphenylene forms yellow crystals from cyclohexane, MeOH (**m** 110-111°) or EtOH (**m** 111-112°). It sublimes *in vacuo*. The *2,4,7-trinitrofluorenone complex* has **m** 154° and the *picrate* gives red needles **m** 122° from EtOH. [*Beilstein* **5** I 298, **5** II 530, **5** III 1935, **5** IV 2137.]

(±)–α-(4-Biphenylyl)butyric acid *[959-10-4]* **M 240.3, m 124-125°, pK_{Est} ~4.5.** Crystallise the acid from

MeOH, petroleum ether or AcOH (**m** 123-125°). [*Beilstein* **9** III 3370, **9** IV 2558.]

γ-(4-Biphenylyl)butyric acid *[6057-60-9]* **M 240.3, m 118°, 120-121°, pK_{Est} ~4.8.** Crystallise the acid from MeOH (**m** 118°) or *C_6H_6 (**m** 118-119°). [*Beilstein* **9** I 290, **9** III 3370, **9** IV 2558.]

Bis-(*p*-bromophenyl) ether *[53563-56-7]* **M 328.0, m 60.1-61.7°.** Crystallise the ether twice from EtOH, petroleum ether, once from *benzene and dry it *in vacuo* [Purcell & Smith *J Am Chem Soc* **83** 1063 *1961*]. [*Beilstein* **6** III 745, **9** IV 1048.]

2*R*,3*R*-(+)-1,4-Bis-(4-chlorobenzyloxy)-2,3-butanediol *[85362-86-3]* **and 2*S*,3*S*-(-)-1,4-Bis-(4-chlorobenzyloxy)-2,3-butanediol** *[85362-85-2]* **M 371.3, m 76-77°, $[\alpha]_D^{20}$ (+) and (-) 6.4° (c 3.11 $CHCl_3$).** Recrystallise the diol from toluene-hexane. [Tamoto & Sugimori *Tetrahedron Lett* **23** 4107 1982, Tamoto *Tetrahedron* **40** 4617 *1984*.]

***N*,*N*-Bis-(2-chloroethyl) 2-naphthylamine (chlornaphthazine)** *[494-03-1]* **M 268.3, m 54-56°, b 210°/5mm, pK_{Est} ~5.3.** Crystallise it from petroleum ether. At 15° it is soluble in EtOH (3.2%), Et_2O (50%), Me_2CO (84%) and *C_6H_6 (80%). [*Beilstein* **12** III 2996, **12** IV 3126.] **CARCINOGENIC.**

1,4-Bis-(chloromethyl)durene (1,4-bischloromethyl-2,3,5,6-tetramethylbenzene) *[3022-16-0]* **M 231.2, m 197-198°.** Crystallise it three times from *C_6H_6 (**m** 193-194°) or petroleum ether (**m** 195-196°), then dry it *in vacuo* in a drying pistol. [Fuson et al. *J Am Chem Soc* **75** 5952 *1953*, *Beilstein* **5** IV 1140.]

2,2-Bis-(*p*-chlorophenyl)-1,1-dichloroethane (*p,p'*-DDD) *[72-54-8]* **M 320.1, m 109-111°, 111-112°.** Crystallise DDD from EtOH and dry it *in vacuo*. The purity is checked by TLC. [*Beilstein* **5** III 1830.] **TOXIC INSECTICIDE.**

2,2-Bis-(*p*-chlorophenyl)-1,1-dichloroethylene (*p,p'*-DDE) *[72-55-9]* **M 318.0, m 89-91°.** Crystallise DDE from MeOH or EtOH and dry it *in vacuo*. The purity is checked by TLC. [Gätzi & Stammbach *Helv Chim Acta* **28** 569 *1946, Beilstein* **5** H 639, **5** III1891.] **POSSIBLE CARCINOGEN.**

2,2-Bis-(4-chlorophenyl)-1,1,1-trichloroethane (*p,p'*-DDT, 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane) *[50-29-3]* **M 354.5, m 108.5-109°, 108°.** Crystallise DDT from *n*-propyl alcohol (5ml/g), then dry it in air or an air oven at 50-60°. *Alternatively*, crystallise it from 95% EtOH, and the purity is checked by TLC. [*Beilstein* **5** III 1833.] **TOXIC INSECTICIDE.**

4,4'-Bis-(diethylamino)benzophenone *[90-93-7]* **M 324.5, m 93-95°, 95-96°, b ~300°/10mm, $pK_{Est(1)}$ ~1.8, $pK_{Est(2)}$ ~3.3.** Crystallise the phenone from EtOH (25ml/g) and dry it under vacuum. Its *picrate* forms yellow needles from EtOH with **m** 178.5°. [*Beilstein* **14** II 59.]

Bis-(4-dimethylaminobenzylidene)benzidine *[6001-51-0]* **M 454.5, m 318°, pK_{Est} ~0.** Crystallise the benzidine from nitrobenzene. [*Beilstein* **14** H 35.]

Bis-(4-fluoro-3-nitrophenyl) sulfone *[312-30-1]* **M 344.3, m 193-194°.** Recrystallise the sulfone from Me_2CO and H_2O (5:1). It should give a yellow colour in aqueous base. [Zahn & Zuber *Chem Ber* **86** 172 *1953*, *Beilstein* **6** IV 172.]

3,4-Bis-(4-hydroxyphenyl)hexane (Hexesterol) *[5635-50-7 (no configuration), 84-16-2 (meso-3RS,4-SR)]* **M 270.4, m 185-186°, 187°.** Free it from diethylstilboestrol by zone refining. Crystallise *meso*-Hexesterol from *benzene or aqueous EtOH (**m 185-188°**). The *meso-dibenzoyl* derivative has **m 236-237°.** The ***3RS,4RS(±)-racemate*** [5776-72-7] crystallises from petroleum ether, *C_6H_6/petroleum ether, Et_2O/petroleum ether, or MeOH/H_2O and has **m 128-129°**. The *(±)-dibenzoyl* derivative has **m 123-124°**. The ***3R,4R(+)-isomer*** [26614-21-1] and ***3S,4S(–)-isomer*** [26614-22-2] crystallise from Et_2O/petroleum ether with **m 80-80.5°** and have $[\alpha]_D^{17}$ (+) and (–) 17.7° (c 5, EtOH). Their *dibenzoyl* derivatives have **m 116.5°**. [*Beilstein* **6** III 5503, **6** IV 6761.] They have estrogenic activity where optically active forms are more potent, and they have antineoplastic activity.

[Aboul-Enein et al. *Anal Profiles Drug Subst* **11** 347 *1982, J Am Chem Soc* **65** 491*1941*.]

4,4-Bis(4-hydroxyphenyl)valeric acid [diphenolic acid] *[126-00-1]* **M 286.3, m 168-171°, 171-172°, $pK_{Est(1)}$~ 4.8 (CO_2H), $pK_{Est(2)}$~ 7.55 (OH), $pK_{Est(3)}$~9.0 (OH)**. When recrystallised from *C_6H_6, the crystals have 0.5 mol of *C_6H_6 (**m** 120-122°), and when recrystallised from toluene, the crystals have 0.5 mol of toluene. Purify the acid by recrystallisation from hot H_2O. It is soluble in Me_2CO, AcOH, EtOH, propan-2-ol, methyl ethyl ketone. It can also be recrystallised from AcOH, heptane/Et_2O or Me_2CO/*C_6H_6. It has λ_{max} at 225 and 279nm in EtOH. The *methyl ester* has **m** 87-89° (aqueous MeOH to give the *trihydrate*). [Bader & Kantowicz *J Am Chem Soc* **76** 4465 *1954*, *Beilstein* **10** IV 1890.]

1,4-Bismethylaminoanthraquinone (Disperse Blue 14) *[2475-44-7]* **M 266.3, m 220-222°, C.I. 61500, λmax 640 (594)nm.** Purify the anthraquinone by thin-layer chromatography on silica gel plates, using toluene/acetone (3:1) as eluent. The main band is scraped off and extracted with MeOH. The solvent is evaporated and the dye is dried in a drying pistol [Land et al. *J Chem Soc, Faraday Trans 1* **72** 2091 *1976*]. It crystallises from *n*-butanol with **m** 221-222° and has λ_{max} at 539 and 644nm (EtOH). [*Beilstein* **14** H 198, **14** III 440, **14** IV 459.]

Bis-(1-naphthylmethyl)amine *[5798-49-2]* **M 329.4, m 62°, 63-64°, pK_{Est} ~8.4.** Crystallise the amine from petroleum ether, Et_2O (**m** 73-74°) or *C_6H_6 (**m** 62°). The *hydrochloride* crystallises from H_2O as needles **m** 239°, and the picrate has **m** 206°(202°). [*Beilstein* **12** II 741, **12** IV 3195.]

Bis-(4-nitrophenyl) carbonate *[5070-13-3]* **M 304.3, m 142-143°**. Dissolve the carbonate in $CHCl_3$, wash it with 2N NaOH (3 x) and once with conc HCl, dry (Na_2SO_4), evaporate and crystallise the residue from toluene (authors say prisms from 15 volumes of *benzene). [Glatthard & Matter *Helv Chim Acta* **46** 795 *1963*, *Beilstein* **6** III 820.]

Bis-(2-nitrophenyl) disulfide *[1155-00-6]* **M 308.3, m 192-195°, 195°, 194-197°, 198-199°.** Purify the disulfide by recrystallisation from glacial AcOH or from *C_6H_6 and the yellow needles are dried in an oven at 100° until the odour of the solvent is absent. It is sparingly soluble in EtOH and Me_2CO. [Bogert & Stull *Org Synth* Coll Vol **I** 220 *1941*, Bauer & Cymerman *J Chem Soc* 3434 *1949*, *Beilstein* **6** IV 1672.]

Bis-(4-nitrophenyl) ether *[101-63-3]* **M 260.2, m 142-143°, 144.4-144.7°, 147-148°.** Crystallise the ether twice from *C_6H_6 or petroleum ether and dry it *in vacuo*. [*Beilstein* **6** II 822, **6** IV 1290.]

Bis-(4-nitrophenyl) methane *[1817-74-9]* **M 258.2, m 183°, 184°, 187°.** Crystallise the methane twice from *C_6H_6, petroleum ether or AcOH (**m** 188.6-189.6°), and dry it *in vacuo*. [*Beilstein* **5** III 1797, **5** IV 1853.]

Bis-(trifluoroacetoxy)iodobenzene (BTI) *[2712-78-9]* **M 430.0, m 112-114°(dec), 120-121°, 124-126°.** Crystallise the iodo compound from warm trifluoroacetic acid and dry it over NaOH pellets. Recrystallise it also from Me_2CO/petroleum ether. Its melting point depends on the heating rate. [Spyroudis & Varvoglis *Synthesis* 445 *1975*, application: Almond et al. *Org Synth* **66** 132 *1988*.]

***N*-BOC-1,2-phenylenediamine ([2-aminophenyl]carbamic acid, *tert*-butyl ester)** *[146651-75-4]* **M 208.3, m 109-114°.** Purify the ester by crystallisation from $CHCl_3$/hexane (1:1, v/v) and dry it *in vacuo*. [Seto et al. *J Am Chem Soc* **115** 1321 *1993*, Seto et al. *J Am Chem Soc* **127** 11442 *2005*.]

Brilliant Green (4-dimethylaminotriphenyl carbinol) *[633-03-4]* **M 482.7, m 209-211°(dec), pK^{25} 4.75.** Purify the dye by precipitating the *perchlorate* from aqueous solution (0.3%) after filtering, heating to 75° and adjusting to pH 1-2. Recrystallise it from EtOH/water (1:4) [Kerr & Gregory *Analyst (London)* **94** 1036 *1969*]. [*Beilstein* **13** IV 2281.]

4-Bromoacetanilide *[103-88-8]* **M 214.1, m 167°.** Crystallise the anilide from aqueous MeOH or EtOH. Purify it by zone refining. [*Beilstein* **12** IV 1504.]

4-Bromoacetophenone *[99-90-1]* **M 199.1, m 54°.** Crystallise it from EtOH, MeOH or from petroleum ether (b 80-100°). [Tanner *J Org Chem* **52** 2142 *1987*, *Beilstein* **7** IV 647.]

ω–Bromoacetophenone (phenacyl bromide) *[70-11-1]* **M 199.1, m 57-58°.** Crystallise the bromide from EtOH, MeOH or petroleum ether (b 80-100°). [Tanner *J Org Chem* **52** 2142 *1987*, *Beilstein* **7** IV 649.]

4-Bromoaniline *[106-40-1]* **M 172.0, m 66°, pK^{25} 3.86.** Crystallise the aniline (with appreciable loss) from aqueous EtOH. The *benzoyl* derivative has **m** 204° (from EtOH). [*Beilstein* **12** IV 1497.]

2-Bromoanisole *[578-57-4]* **M 187.0, f 2.5°, b 124°/40mm, d$_4^{20}$ 1.513, n$_D^{25}$ 1.5717.** Crystallise the anisole by repeated partial freezing, then distil it under reduced pressure. [*Beilstein* **6** IV 1037.]

4-Bromoanisole *[104-92-7]* **M 187.0, f 13.4°, b 99-100°/18mm, 124°/40mm, d$_4^{20}$ 1.495, n$_D^{25}$ 1.5617.** Crystallise the anisole by repeated partial freezing, then distil it under reduced pressure. [*Beilstein* **6** III 741, **6** IV 1044.]

9-Bromoanthracene *[1564-64-3]* **M 257.1, m 98-100°.** Crystallise 9-bromoanthracene from MeOH or EtOH followed by sublimation *in vacuo*. [Masnori et al. *J Am Chem Soc* **108** 126 *1986*, *Beilstein* **5** IV 2295.]

4-Bromobenzal diacetate *[55605-27-1]* **M 287.1, m 95°.** Crystallise the diacetate from hot EtOH (3ml/g). [Liebermann & Connor *Org Synth* Coll Vol **II** 442 *1948*, *Beilstein* **7** II 182, **7** IV 579.]

Bromobenzene *[108-86-1]* **M 157.0, b 155.9°, d$_4^{20}$ 1.495, n$_D^{20}$ 1.5588, n$_D^{15}$ 1.56252.** Wash bromobenzene vigorously with conc H_2SO_4, then 10% NaOH or $NaHCO_3$ solutions, and H_2O. Dry it with $CaCl_2$ or Na_2SO_4, or pass it through activated alumina, before refluxing with, and distilling from, CaH_2, using a glass helix-packed column. [*Beilstein* **5** IV 670.]

4-Bromobenzene diazonium tetrafluoroborate *[673-40-5]* **M 270.8, m 133°(dec), 135-140° (dec), 135°(dec).** Wash the salt with Et_2O until the wash is colourless and allow it to dry by blowing N_2 over it. Store it at 0-4° in the dark. [Schiemann & Pillarsky *Chem Ber* **64** 1340 *1931*, *Beilstein* **16** III 517.]

4-Bromobenzenesulfonyl chloride *[98-58-8]* **M 255.5, m 73-75°, 74.3-75.1, 75-76°, 77°, b 153°/15mm, 150.6°/13mm**. Wash the sulfonyl chloride with cold water, dry and recrystallise it from petroleum ether, or from ethyl ether cooled in powdered Dry-ice after the ether solution had been washed with 10% NaOH until colourless, then dry it with anhydrous Na_2SO_4. *Alternatively*, dissolve it in $CHCl_3$, wash it with H_2O, dry (Na_2SO_4), evaporate and recrystallise it. [Huntress & Carten *J Am Chem Soc* **62** 511 *1940*.] Test for the SO_2Cl group by dissolving it in EtOH and boiling with NH_4CNS whereby a yellow amorphous precipitate forms on cooling. [*Beilstein* **11** IV 162.]

2-Bromobenzonitrile *[2042-37-7]* **M 182.0, m 52-54°, 55.8°, 56°, 53-57°, b 251-253°/754mm.** The nitrile is prepared from 2-bromobenzoic acid by treatment with $SOCl_2$ (23 hours boiling) and distilling to give *2-bromobenzoyl chloride*, **b 120-126°/15mm, n$_D^{20}$ 1.5925,** which on treatment with 12 equivalents of NH_3 gives a 98% yield of *2-bromobenzamide* **m 159.5-161.5°** [4001-73-4]. By boiling this amide with excess of $SOCl_2$ for 17 hours followed by evaporation and steam distillation gives an 84% yield of the nitrile that forms needles when crystallised from H_2O. [Lutz et al. *J Org Chem* **12** 666 *1947*.] It has also been prepared by the method of Miller [*Org Synth* Coll Vol **3** 646, 648 *1955*] in which the amide is treated with a large excess of $POCl_3$ in the presence of sodium metabisulfite ($Na_2S_2O_5$) to give the nitrile (**m 55-55.5°)** [Herbst & Wilson *J Org Chem* **22** 1142 *1957*]. [*Beilstein* **9** H 348, **9** II 232, **9** III 1387, **9** IV 1013.]

2-Bromobenzoic acid (*o*-bromobenzoic acid) *[88-65-3]* **M 201.0, m 148.9°, 150°, pK^{20} 2.88.** Crystallise the acid from *C_6H_6 or MeOH. The *anilide* has **m** 141° (from EtOH/H_2O). [*Beilstein* **9** IV 1011.]

3-Bromobenzoic acid (*m*-bromobenzoic acid) *[585-76-2]* **M 201.0, m 155°, pK^{25} 3.81.** Crystallise the acid from acetone/water, MeOH or acetic acid. The *anilide* has **m** 137° (from EtOH/H_2O). [*Beilstein* **9** IV 1013.]

4-Bromobenzoic acid (*p*-bromobenzoic acid) *[586-76-5]* **M 201.0, m 251-252°, 254-256°, 257-258°, pK^{25} 3.96.** Crystallise the acid from MeOH, or MeOH/water mixture, 90% EtOH and Et_2O. The *methyl ester* has **m** 81° from Et_2O or dilute MeOH. The *anilide* has **m** 197° (from EtOH). [Male & Thorp *J Am Chem Soc* **35** 269 *1913*, Lamneck *J Am Chem Soc* **76** 406 *1954*, Vandenbelt et al. *Anal Chem* **26** 926 *1954*, *Beilstein* **9** IV 1017.]

p-**Bromobenzophenone** *[90-90-4]* **M 261.1, m 81°, 81-82°.** Crystallise the phenone from EtOH. The *2,4-dinitrophenylhydrazone* forms orange-red leaflets from dioxane/EtOH with **m** 207-209°. [Allen & Van Allan *J Am Chem Soc* **66** 7 *1944*, *Beilstein* **7** H 422, **7** III 2079, **7** IV 1378.]

4-Bromobenzoyl acetonitrile *[4592-94-3]* **M 224.1, m 160-164°, 162.4-163.4°.** The nitrile is purified by dissolving in slightly alkaline H_2O (charcoal), filtering and acidifying with HCl to give colourless needles (**m** 162-163°). It recrystallises from EtOH. With Me_2SO_4/KOH at 130° it gives *4-bromo–β-methoxy-cinnamylnitrile* **m** 58.5-59.5° (from high boiling petroleum ether) [Fuson & Wolf *J Am Chem Soc* **61** 1940 *1939*, Grathaus & Dains *J Am Chem Soc* **58** 1334 *1936*]. [*Beilstein* **10** III 2998.]

p-**Bromobenzoyl chloride** *[586-75-4]* **M 219.5, m 36-39°, 39.8°, 41°, b 62°/0.1mm, 104.5°/6mm, 126.4-127.2°/14mm.** Check IR of a film to see if OH bands are present. If absent then recrystallise from petroleum ether and dry it *in vacuo*. If OH bands are weak, then distil it *in vacuo* and recrystallise if necessary. If OH bands are very strong, then treat with an equal volume of redistilled $SOCl_2$ reflux for 2 hours, then evaporate excess of $SOCl_2$ and distil the residual oil or low melting solid. Store it in the dark away from moisture. **LACHRYMATORY**. [Martin & Partington *J Chem Soc* 1175 *1936*, *Beilstein* **9** IV 1023.]

p-**Bromobenzyl bromide** *[589-15-1]* **M 249.9, m 60-61°.** Crystallise the bromide from EtOH. [*Beilstein* **5** IV 836.] **LACHRYMATORY.**

p-**Bromobenzyl chloride** *[589-17-3]* **M 205.5, m 40-41°, b 105-115°/12mm.** Crystallise the chloride from EtOH and distil it in a vacuum. [*Beilstein* **5** IV 832.] **LACHRYMATORY.**

2-Bromobiphenyl *[2052-07-5]* **M 233.1, m 1.5-2.0°, b 140°/11mm, 148-150°/10mm, 297-298°/atm, d$_4^{25}$ 1.352, n$_D^{20}$ 1.6248.** 2-Bromobiphenyl is prepared from 2-aminobiphenyl (12g) in hot constant-boiling aqueous HBr (21g, 3-equivalents) by diazotisation at 5° with a solution of $NaNO_2$ (6g) in H_2O (10ml), then excess of HNO_2 is removed at the end of the reaction by addition of urea with stirring for 20 minutes. This solution is added dropwise into a solution of CuBr (from 15g of $CuSO_4$) in constant-boiling aqueous HBr (20ml) with stirring, set aside for 20 minutes, after which the brown complex is decomposed by heating on a steam bath for 2 hours. The dark oil is extracted into Et_2O, the extract is filtered through glass wool, washed with H_2O, dilute NaOH, H_2O again, dried ($CaCl_2$), filtered, evaporated and the residual oil is distilled to give a pale yellow oil (7g, b 146-152°/12mm). Further purification can be achieved by it dissolving in $*C_6H_6$, passing through an alumina column and eluting with $*C_6H_6$, evaporating to dryness and distilling the residual oil (b 148-150°/10mm) to yield pure colourless 2-bromobiphenyl. This has been recrystallised from pentane at -40° to give a liquid with a freezing point of 1.5-2.0°. [de la Mare & Hassan *J Chem Soc* 3004 *1957*, Augood et al. *J Chem Soc* 3412 *1953*, NMR: Brownstein *J Am Chem Soc* **80** 2300 *1958*, *Beilstein* **5** H 580, **5** II 485, **5** III 1742, **5** IV 1818.] It is used for the preparation of John-Phos and related catalytic ligands (see Chapter 7, Catalysis—Part 2).

3-Bromobiphenyl *[2113-57-7]* **M 233.1, b 103-104°/0.2mm, 110°/1mm, 158-167°/11mm, 169-173°/17mm, d$_4^{25}$ 1.3976, n$_D^{20}$ 1.6380.** 3-Bromobiphenyl can be prepared by bromination of 2-acetamidobiphenyl (m 118-119° from aqueous AcOH) with one molecular equivalent of Br_2 in AcOH; the monobromo derivative (m 127-127.5° from EtOH) is hydrolysed with 95% EtOH/conc HCl (1.4:1, 4 hours reflux) poured into excess of H_2O, basified and filtered off to give 2-amino-5-bromobiphenyl (m 53-56°). The base is subsequently diazotised and the diazonium salt is deaminated by warming with Cu bronze or with hypophosphorous acid [*cf* Kornblum in *Organic Reactions* J. Wiley & Sons NY, **II** 294 *1944*] to yield crude 3-bromobiphenyl which is isolated by steam distillation, extraction of the distillate with $*C_6H_6$, washing the extract successively with, dilute NaOH,

H_2O, conc H_2SO_4, H_2O, drying (K_2CO_3), evaporating and distilling. This can be purified further by passing a solution of it in *C_6H_6 through an Al_2O_3 column, eluting with *C_6H_6, and the combined eluates are distilled. The distillate is dissolved in petroleum ether (b 40-60°), washed several times with concentrated H_2SO_4, H_2O again, aqueous $NaHCO_3$, H_2O again, dried ($CaCl_2$), filtered, the solvent is evaporated off and the residue is fractionally distilled to give pure *3-bromobiphenyl*. [de la Mare & Hassan *J Chem Soc* 3004 1957, Lichtin & Leftin *J Am Chem Soc* **74** 4207 *1952*, Huber et al. *J Am Chem Soc* **46** 1111 *1946*]. It has also been prepared in low yield (13%) from diazotized *m*-bromoaniline and *C_6H_6 according to Gomberg and purified as above [Marvel et al. *J Am Chem Soc* **61** 77 *1939*, also see 4-bromobiphenyl below]. [*Beilstein* **5** II 485, **5** III 1742, **5** IV 1818.]

4-Bromobiphenyl *[92-66-0]* **M 233.1, m 82-86°, 88.8-89.2°, 89.5°, 90°, b 170-175°/8mm, 310°/atm.** This biphenyl is prepared by the method of Gomberg & Bachmann [*Org Synth* **1** 113 *1944*] from diazotised 4-bromoaniline and benzene, then extract into Et_2O, wash with base, acid, brine, dry (Na_2SO_4), filter, evaporate and recrystallise to constant melting point from absolute EtOH (89.7°, after drying *in vacuo*). [Hey et al. *J Chem Soc* 1284 *1940*; Augood et al. *J Chem Soc* 3412 *1953*, *Beilstein* **5** H 580, **5 I 275, 5** II 485, **5** III 1742, **5** IV 1819.]

1-Bromo-2-chlorobenzene *[694-80-4]* **M 191.5, m -12°, b 79-82°/14mm, 200-202°/atm, 204°/atm, d_4^{25} 1.638, n_D^{20} 1.582.** *o*-Chlorobromobenzene has been prepared in at least three different ways. It is obtained in 54% yield by carrying out a Sandmeyer reaction from *o*-chloroaniline *via* diazotisation (using $NaNO_2$/HBr) and decomposing it with CuBr in 48% aqueous HBr. Steam distil off the product, basify the distillate with 20% aqueous NaOH (extract it into Et_2O if quantities are small), dry the organic layer (Na_2SO_4), filter and distil [Fry & Grote *J Am Chem Soc* **48** 710, *1926*]. The second procedure involves adding Br (32g) in CCl_4 (50ml) during 20 minutes to refluxing silver 2-chlorobenzoate in CCl_4 (250ml), boil for a further 30 minutes to complete the decarboxylation, filter off the AgBr, wash the filtrate with aqueous Na_2SO_3 (until red colour of Br is discharged), aqueous 0.5M Na_2CO_3 (2 x 25ml), evaporate the solvent and distil bromochlorobenzene (38-48% yield) [Dauben & Tilles *J Am Chem Soc* **72** 3185 *1950*, Barnes & Prochaska *J Am Chem Soc* **72** 3188 *1950*]. The third procedure involves a phase transfer catalytic radical bromination. *o*-Chlorobenzene free radical is generated from the corresponding *o*-benzenediazonium tetrafluoroborate with KOAc in tetrahydrofuran and a catalytic amount of 18-crown-6 using $CBrCl_3$ as brominating agent to produce *o*-bromochlorobenzene in 70% yield, a great improvement on the Sandmeyer method [Korzeniowski & Gokel *Tetrahedron Lett* 3519 *1977*]. [*Beilstein* **5** H 209, **5** I 115, **5** II 161, **5** III 562, **5** IV 680.]

4-Bromo-4'-chlorobenzophenone *[27428-57-5]* **M 295.6, m 150°.** Crystallise the phenone from EtOH or *C_6H_6 and further purify it by zone refining (100 passes) [Grove & Turner *J Chem Soc* 509 *1929*, Lin & Hanson *J Phys Chem* **91** 2279 *1987*]. [*Beilstein* **7** II 360, **7** III 2081.]

Bromocresol Green (3',3",5',5"-tetrabromo-*m*-cresolsulfonephthalein) *[76-60-8]* **M 698.0, m 218-219°(dec), 225°(dec), pK^{25} 4.51.** Crystallise the dye from glacial acetic acid or dissolve it in aqueous 5% $NaHCO_3$ solution and precipitate it from the hot solution by dropwise addition of aqueous HCl. Repeat this until the UV/VIS-extinction did not increase at λ_{max} 423nm. It is an indicator: at pH 3.81 (yellow) and pH 5.4 (blue-green). [*Beilstein* **19/3** V 460.]

Bromocresol Purple (5',5"-dibromo-*o*-cresolsulfonephthalein) *[115-40-2]* **M 540.2, m 241-242°(dec), pK_1 -2.15, pK_2 6.3.** Dissolve the dye in aqueous 5% $NaHCO_3$ solution and precipitate it from a hot solution by dropwise addition of aqueous HCl. Repeat this until the UV/VIS-extinction did not increase at λ_{max} 419nm. It can also be recrystallised from *benzene. It is an indicator: at pH 5.2 (yellow) and pH 6.8 (purple). [*Beilstein* **19/3** V 460.]

2'-Bromo-2,6-dimethoxybiphenyl *[755017-61-9]* **M 293.2, m 141-142°, 143-146°.** This intermediate, which is used for the preparation of the ligand S-Phos, is synthesised by adding *n*-BuLi (9.60ml, 1.6M solution in hexanes, 15.4mmol, 1.2 equivalents) *via* a syringe over 5 minutes to a cold (0°) solution of 1,3-dimethoxybenzene (2.00ml, 15.3mmol, 1.2 equivalents, [151-10-0]) in dry THF (30ml), allowing the tempera-

ture to rise to ~25°, then it is stirred for 5 hours. The mixture is re-cooled (0°) and 2-bromochlorobenzene (1.50ml, 12.8mmol, 1.0 equivalents, [694-80-4]) is added dropwise *via* a syringe over 15 minutes while stirring vigorously; and the burgundy coloured solution is stirred for a further 15 minutes at 0°. MeOH (0.25ml) is added *via* syringe to decompose excess BuLi, the whole is evaporated to dryness *in vacuo*, the residue is then stirred with Et_2O (50ml) and H_2O (50ml), the layers are separated, the aqueous phase is extracted with Et_2O (2 x 25ml), the combined Et_2O solutions are dried ($MgSO_4$), filtered and evaporated *in vacuo*. The yellow residue is recrystallised from MeOH to provide the analytically pure biphenyl (3.03g, 81%) as pale yellow crystals. The IR (film) has ν_{max} at 2964, 1584, 1472, 1432, 1248, 1108, 1025, 783 cm^{-1}; the ^1H NMR [100MHz, $CDCl_3$] has δ at 7.69 (dd, *J* = 6.9, 1.1Hz, 1H), 7.34-7.40 (m, 2H), 7.20-7.28 (m, 2H), 6.68 (d, *J* = 8.5Hz, 2H), 3.76 (s, 6H) from TMS; the ^{13}C NMR [75MHz, ^1H decoupled, $CDCl_3$] has δ at 157.8, 136.25, 132.52, 132.47, 129.6, 128.8, 127.1, 125.4, 119.0, 104.2, 56.2 from TMS. [Barder et al. *J Am Chem Soc* **127** 4685 *2005*.]

***p*-Bromo-*N*,*N*-dimethylaniline** *[586-77-6]* **M 200.1, m 55°, b 264°, pK 19.2 (acidic), pK^{25} 4.23.** Reflux the aniline for 3 hours with two equivalents of acetic anhydride, then fractionally distil it under reduced pressure. [*Beilstein* **12** IV 1499.]

1-Bromo-2,4-dinitrobenzene *[584-48-5]* **M 247.0, m 72.5-73°, 75°.** Crystallise it from ethyl ether, isopropyl ether, 80% EtOH or absolute EtOH. [*Beilstein* **5** III 640, **5** IV 749.]

***N*-(2-Bromoethyl)phthalimide** *[574-98-1]* **M 254.1, m 81-83°, 82.5-83.5°.** The following is to be carried out in an efficient **FUME HOOD**. Dissolve the compound (180g) in CS_2 (500 ml) by refluxing for 15 minutes (to cause the separation of the most likely impurity, 1,2-diphthalimidoethane), filter and evaporate under reduced pressure. The product forms light tan crystals (**m** 78-80°). Recrystallise it from EtOH (charcoal) [the compound (50g) is dissolved in hot 75% EtOH (200ml), boiled for *ca* 10 minutes, carbon is added (5g, Norite), filter and cool to 0°], to give white crystals (40g) which can be recrystallised (**m** 80-81°); and further recrystallisation gives **m** 82-83°. [Salzberg & Supniewski *Org Synth* Coll Vol **I** 119 *1932*, Landini & Rolla *Synthesis* 389 *1976*, *Beilstein* **21/10** V 275.]

3-Bromo-5-hydroxybenzoic acid *[140472-69-1]* **M 217.0, m 233.5°, 237-241°, $pK_{Est(1)}$ ~2.3, $pK_{Est(2)}$ ~13.0.** The acid crystallises from H_2O (**m** 238-239°), and with Me_2SO_4 it yields the *3-methoxy* derivative with **m** 190-191° (from EtOH). [Baddar et al. *J Chem Soc* 469 *1955*, *Beilstein* **10** IV 333.]

2-Bromomethylanthraquinone *[7598-10-9]* **M 301.1, m 200-202°.** Recrystallise the quinone from AcOH, wash the crystals with a little Et_2O, dry it in air and then in a vacuum at 100°. It is prepared by bromination of 2-methylanthraquinone with Br_2/$PhNO_2$ at 145-150°, or *N*-bromosuccinimide in CCl_4 containing a trace of $(PhCOO)_2$. [*Beilstein* **7** IV 2576.]

2-(Bromomethyl)benzonitrile *[22115-41-9]* **M 195.1, m 72-73°, 79°, b 152-155°/15mm.** Purify the nitrile by steam distillation. Extract the distillate with Et_2O, dry the extract (Na_2SO_4), evaporate and distil the residue. The solidified distillate can be recrystallised from petroleum ether or cyclohexane. ^1H NMR ($CDCl_3$) with δ at 7.8-7.2 (m 4H), 4.62 (s, 2H); the IR has ν 2238 cm^{-1}. [Drory *Chem Ber* **24** 2570 *1891*, Borsche et al. *Chem Ber* **74** 685 *1934*, Buckley et al. *Aust J Chem* **22** 594 *1969*, *Beilstein* **9** III 2312.] **LACHRYMATORY.**

4-Bromo-α-methylbenzyl alcohol *[(±) 5391-88-8, 25675-29-0, R-(+) 76155-78-7, S-(–) 100760-04-1]* **M 201.1.** The (±)-racemate is purified by distillation in a vacuum (**b** 90°/1mm, 119-121°/7mm, **d** 1.46) and it solidifies on cooling (**m** 36-37°) [Overberger et al. *Org Synth* Coll Vol **III** 200 *1955*]. The *(±)-tosyl* derivative [114200-15-6] has **m** 56-57°. The *R-(+)-enantiomer* is also purified by distillation in a vacuum (**b** 110°/3mm, d_4^{25} 1.322, n_D^{20} 1.569) and has $[\alpha]_D^{20}$ +39° (c 1, $CHCl_3$), +32.9° (c 1.39, MeOH). The *S-(–)-enantiomer* is similarly purified. [Stein et al. *Can J Chem* **63** 3442 *1985*, Crevinka et al. *Col Czech Chem Commun* **51** 401 *1986*, *Beilstein* **6** II 447.]

2-(Bromomethyl)-naphthalene *[939-26-4]* **M 221.1, m 52-54°, 56°, 56-57°, b 133-136°/0.8mm, 214°/100mm.** Dissolve the bromo compound in toluene, wash it with saturated aqueous $NaHCO_3$, dry (Mg

SO_4), evaporate, fractionally distil the residue and recrystallise the solidified distillate from EtOH. [Chapman & Williams *J Chem Soc* 5044, *1952*, Bergmann & Szmuszkovicz *Bull Soc Chim Fr* **20** 566 *1953*, *Beilstein* **5** IV 1698.]

1-Bromonaphthalene *[90-11-9]* **M 207.1, b 118°/6mm, d_D^{20} 1.489.** Purify 1-bromonaphthalene by passage through activated alumina, and three vacuum distillations. [*Beilstein* **5** H 547, **5** IV 1665.]

2-Bromonaphthalene *[580-13-2]* **M 207.1, m 59°.** Purify 2-bromonaphthalene by fractional elution from a chromatographic column of activated alumina. Crystallise it from EtOH. [*Beilstein* **5** IV 1667.]

1-Bromo-2-naphthol *[573-97-7]* **M 223.1, m 76-78°, 83°, 84°, pK_{Est} ~8.0.** Distil the naphthol at 10mm then recrystallise it from *C_6H_6/petroleum ether (b 30-60°) **m** 80-81°. The *benzoyl* derivative has **m** 98.5-99.5° (from MeOH). [Hazlet *J Am Cherm Soc* **62** 2156 *1940*, *Beilstein* **6** H 650, **6** II 604, **6** III 2994.]

6-Bromo-2-naphthol *[15231-91-1]* **M 223.1, m 122-126°, pK_{Est} ~9.1.** Crystallise the naphthol from EtOH or *C_6H_6/petroleum ether (**m** 128°). The *benzoyl* derivative has **m** 122°, (from EtOH). [Ruggli & Michels *Helv Chim Acta* **14** 779 *1931*, *Beilstein* **6** H 651, **6** II 605, **6** III 2996.]

ω-Bromo-4-nitroacetophenone *[99-81-0]* **M 244.1, m 98°.** Crystallise it from *C_6H_6/petroleum ether. [*Beilstein* **7** IV 661.]

o-**Bromonitrobenzene (2-bromo-1-nitrobenzene)** *[577-19-5]* **M 202.1, m 43°.** Crystallise it twice from petroleum ether, using charcoal before the first crystallisation. [*Beilstein* **5** III 618, **5** IV 728.]

m-**Bromonitrobenzene (3-bromo-1-nitrobenzene)** *[585-79-5]* **M 202.1, m 55-56°.** Crystallise it twice from petroleum ether, using charcoal before the first crystallisation. [*Beilstein* **5** III 618, **5** IV 729.]

p-**Bromonitrobenzene (4-bromo-1-nitrobenzene)** *[586-78-7]* **M 202.1, m 127°.** Crystallise it twice from petroleum ether, using charcoal before the first crystallisation. [*Beilstein* **5** III 619, **5** IV 729.]

p-**Bromophenacyl bromide** *[99-73-0]* **M 277.9, m 110-111°.** Crystallise the bromide from EtOH (*ca* 8ml/g). [*Beilstein* **7** IV 652.]

o-**Bromophenol** *[95-56-7]* **M 173.0, b 194°, d_D^{20} 1.490, pK^{25} 8.45.** Purify the phenol by at least two passes through a chromatographic column and distil it. [*Beilstein* **6** IV 1037.]

p-**Bromophenol** *[106-41-2]* **M 173.0, m 64°, pK^{25} 9.36.** Crystallise the phenol from $CHCl_3$, CCl_4, petroleum ether (b 40-60°), or water and dry it at 70° under vacuum for 2 hours. [*Beilstein* **6** IV 1043.]

Bromophenol Blue (3,3',5,5'-tetrabromophenolsulfonephthalein) *[115-39-9]* **M 670.0, m 270-271°(dec), 273°(dec), λ_{max} 422nm, pK^{25} 3.62 (acidic).** Crystallise the dye from *C_6H_6 or Me_2CO/AcOH, and dry it in air. It is an indicator: at pH 3.0 it is yellow and it is purple at pH 4.6. [*Beilstein* **19/3** V 458.]

(4-Bromophenoxy)acetic acid *[1878-91-7]* **M 231.1, m 157°, 158°, pK^{25} 3.13.** Crystallise the acid from EtOH or H_2O (**m** 161.4-161.8°). [Hayes & Branch *J Am Chem Soc* **65** 1555 *1943*, *Beilstein* **6** III 747, **6** IV 1052.]

3-(4-Bromophenoxy)propionic acid *[93670-18-9]* **M 247.1, m 146°, pK_{Est} ~4.2.** Crystallise the acid from EtOH, MeOH or *C_6H_6/hexane (**m** 144-145°). [*Beilstein* **6** III 748, **6** IV 1052.]

4-Bromophenylacetic acid *[1878-68-8]* **M 215.1, m 112-113°, 113-115°, 114°, pK^{25} 4.19.** The acid crystallises from H_2O as needles. The *acid chloride* has **b** 238°/760mm, **m** 50°, and the *anilide* has **m** 174-175°. [Dippy & Williams *J Chem Soc* 161 *1934,* 1251 *1948*, Schwenk & Pala *J Org Chem* **11** 798 *1946*, *Beilstein* **9** III 2275.]

4-Bromophenylhydrazine *[589-21-9]* **M 187.1, m 108-109°, pK^{20} -5.6 (aqueous H_2SO_4), pK^{25} 5.05.** Crystallise the hydrazine from H_2O. The *hydrochloride* crystallises from EtOH/H_2O with **m** 213-214°, and the *tosylate* has **m** 212° (from EtOH). [*Beilstein* **15** H 434, **15** I 117, **15** II 160, **15** III 289, **15** IV 282.]

4-Bromophenyl isocyanate *[2492-02-9]* **M 189.0, m 41-42°, b 158°/14mm.** Crystallise the isocyanate from petroleum ether (b 30-40°). It has a pungent odour. [*Beilstein* **12** H 647, **12** I 321.]

4-Bromophenyl isothiocyanate *[1985-12-2]* **M 214.1, m 56-58°.** Recrystallise the isothiocyanate from boiling *n*-hexane. Any insoluble material is most probably the corresponding urea. It is also purified by steam distillation, cool the receiver, add NaCl and extract in Et_2O, wash the extract with N H_2SO_4, dry ($MgSO_4$), evaporate and recrystallise the residual solid. [Cymerman-Craig et al. *Org Synth* Coll Vol **IV** 700 *1963*, cf Dains et al. *Org Synth* Coll Vol **I** 447 *1941*, *Beilstein* **6** IV 1051, **12** II 354, **12** III 1463p, **12** IV 1519.]

***N*-(3-Bromopropyl)phthalimide** *[5460-29-7]* **M 268.1, m 72-74°, 74°.** Place it in a Soxhlet and extract it with Et_2O, whereby the bis-phthalimido impurity is not extracted. Evaporate the Et_2O and recrystallise the residue from EtOH, aqueous EtOH or petroleum ether. [Gabriel & Weiner *Chem Ber* **21** 2669 1888, Gaudry *Can J Chem* **31** 1060 *1953*, *Beilstein* **21/10** V 1277.]

Bromopyrogallol Red (5,5'-dibromopyrogallolsulfonephthalein) *[16574-43-9]* **M 576.2, m 300°, λ_{max} 538nm (ε 54,500 H_2O pH 5.6-7.5), pK_1 2.9, pK_2 4.39, pK_3 9.15, pK_4 11.72.** Crystallise the dye from 50% EtOH, or aqueous alkaline solution followed by acidification. It is a metal chromic indicator. [Suk *Col Czech Chem Commun* **31** 3127 *1966*, *Beilstein* **19/10** V 226].

5-Bromosalicyl hydroxamic acid *[5798-94-7]* **M 210.1, m 232°(dec), $pK_{Est(1)}$~ 1.5, $pK_{Est(2)}$~ 7.0, $pK_{Est(3)}$~ 8.7.** Crystallise the hydroxamic acid from H_2O (**m** 249°) or from EtOH (**m** 232° dec). It sublimes at **m** 235°. It complexes with metals. [*Beilstein* **10** IV 221.]

4-Bromostyrene *[2039-82-9]* **M 183.1, b 49.5-50°/2.5mm, 87-88°/12mm, 102-104°/20mm, d_4^{20} 1.3984, n_D^{20} 1.5925**. It polymerises above 75° in the presence of benzoyl peroxide. To purify, if it has not gone to a solid resin, dissolve it in Et_2O, dry ($MgSO_4$) and add *ca* 0.1g of 4-*tert*butylcatechol (polymerisation inhibitor) per 100g of bromostyrene. Filter, evaporate this under reduced pressure (use as high a vacuum as possible) and distil the residue. Store it in dark bottles in the presence of the inhibitor (at above concentration). [Overberger & Saunders *Org Synth* Coll Vol **III** 204 *1955*, *Beilstein* **5** IV 1349.]

Bromothymol Blue (3',3''-dibromothymolsulfonephthalein) *[76-59-5]* **M 624.4, m 201-203°, pK_1 -0.66, pK_2 6.99.** Dissolved the dye in aqueous 5% $NaHCO_3$ solution and precipitate it from the hot solution by dropwise addition of aqueous HCl. Repeat this until the extinction at λ_{max} 420 nm does not increase. It is an indicator: aqueous solutions are yellow at pH 6.0, and blue at pH 7.6. [*Beilstein* **19/3** V 461.]

***o*-Bromotoluene** *[95-46-5]* **M 171.0, m -27°, b 58-60°/10mm, 74°/19mm, 181.7°/760mm, d_4^{20} 1.422, n_D^{20} 1.556.** Fractionally distil it through an efficient column. It can be separated from its isomers by gas chromatography on a column of "Sil-o-cel" firebrick (30-40mesh, 80 parts) coated with 5% (20 parts) of ICI E301 con rubber with N_2 carrier gas at 170°/atm and 100ml/minute and using a conductivity cell detector. [Cowley et al. *J Chem Soc* 1801 *1959*, *Beilstein* **5** H 304, **5** I 153, **5** II 234 **5** III 704, **5** IV 825.]

***p*-Bromotoluene** *[106-38-7]* **M 171.0, m 28°, b 184°, d_4^{20} 1.390.** Crystallise it from EtOH [Taylor & Stewart *J Am Chem Soc* **108** 6977 *1986*]. [*Beilstein* **5** IV 827.]

α-Bromo-4-toluic acid *[6232-88-8]* **M 215.1, m 229-230°, pK_{Est} ~3.2.** Crystallise the acid from Me_2CO. [*Beilstein* **9** IV 1745.]

α-Bromo-*p*-xylene (*p*-methylbenzyl bromide) *[104-81-4]* **M 185.1, m 35°, b 218-220°/740mm.** Crystallise the bromide from EtOH or pentane. [*Beilstein* **5** H 385, **5** IV 969.]

2-*tert*-Butoxycarbonyloxyimino-2-phenylacetonitrile (BOC-ON) *[58632-95-4]* **M 246.3, m 87-89°.** Triturate the solid with 90% aqueous MeOH, filter, wash with 90% aqueous MeOH and dry it in a vacuum. Recrystallise it from MeOH (needles or plates), but use warm MeOH and cool to crystallise; *do not boil as it decomposes slowly.* Its IR has ν_{max} at 1785 (C=O) cm^{-1} and NMR ($CDCl_3$) usually shows two *tert*-butyl singlets for *syn* and *anti* isomers. Store it in a brown bottle (fridge). It evolves CO_2 at room temperature (stoppered bottle can explode!), but can be stored over silica gel which may extend its useful life to more than a year. [Itoh et al. *Org Synth* **59** 95 *1980*.]

4-Butoxyphenylacetic acid *[4547-57-3]* **M 208.3, m 86-87°, 88.5°, pK_{Est} ~4.4.** Recrystallise it from petroleum ether (b 40-60°). [McElvain & Carney *J Am Chem Soc* **68** 2592 *1946*, *Beilstein* **10** IV 545.]

***n*-Butyl *p*-aminobenzoate (Butamben)** *[94-25-7]* **M 193.2, m 57-59°, b 174°/8mm, pK_{Est} ~2.5.** Crystallise Butamben from EtOH. [*Beilstein* **14** IV 1130.]

***tert*-Butylammonium bromide** *[60469-70-7]* **M 154.1, m >250°(dec).** Recrystallise the salt several times from absolute EtOH or by dissolving in absolute EtOH and adding Et_2O slowly to crystallise the salt. Dry it thoroughly at 105°. [IR: Chenon & Sandorfy *Can J Chem* **36** 1181 *1958*, *Beilstein* **4** IV 659.]

2-*tert*-Butylanthracene *[13719-97-6]* **M 234.3, m 148-149°.** Recrystallise the anthracene from EtOH and finally purify it by TLC. [*Beilstein* **5** IV 2364.]

***n*-Butylbenzene** *[104-51-8]* **M 134.2, b 183.3°, d_4^{20} 0.860, n_D^{20} 1.4897, n_D^{25} 1.487.** Distil butylbenzene from sodium. Wash it with small portions of conc H_2SO_4 until the acid is no longer coloured, then with water and aqueous Na_2CO_3. Dry it ($MgSO_4$), and distil it twice from Na, collecting the middle fraction [Vogel *J Chem Soc* 607 *1948*]. [*Beilstein* **5** IV 1033.]

***tert*-Butylbenzene** *[98-06-6]* **M 134.2, b 169.1°, d_4^{20} 0.867, n_D^{20} 1.493, n_D^{25} 1.490.** Wash it with cold conc H_2SO_4 until a fresh portion of acid is no longer coloured, then with 10% aqueous NaOH (care-effervescence), followed by distilled water until neutral. Dry it ($CaSO_4$), and distil it in a glass helices-packed column, taking the middle fraction. [*Beilstein* **5** IV 1045.]

4-*tert*-Butyl benzoyl chloride *[1710-98-1]* **M 196.7, b 135°/10mm, 149.9-150.5°/14mm, 266-268°(dec), d_4^{20} 1.082, n_D^{20} 1.536.** Distil it in a vacuum. If IR shows OH group, then treat it with thionyl chloride or oxalyl chloride at *ca* 50° for 30 minutes, evaporate and fractionate it in a vacuum using a short column. Strongly **LACHRYMATORY**; use a good fume hood. [Fuson & Turnbull *J Am Chem Soc* **71** 2544 *1949*, Tsuno et al. *Bull Chem Soc Jpn* **32** 960 *1959*, Swain et al. *J Am Chem Soc* **72** 5433 *1950*, *Beilstein* **9** III 2526.]

4-*tert*-Butylcatechol *[98-29-3]* **M 166.22, m 47-48°, 55-56°, 75°, b 265°/atm, $pK_{Est(1)}$ ~9.5, $pK_{Est(2)}$ ~13.0.** Distil it in a vacuum, then recrystallise it from pentane or petroleum ether (or $*C_6H_6$). [*Beilstein* **6** IV 6014.]

6-*tert*-Butyl-1-chloro-2-naphthol *[525-27-9]* **M 232.7, m 76°, b 185°/15mm, pK_{Est} ~8.0.** Recrystallise the naphthol from petroleum ether. Its *methyl ether* has **m** 115° (from EtOH/petroleum ether). [Buu-Hoi et al. *J Org Chem* **15** 1064 *1950*, *Beilstein* **6** IV 4367.]

2-*tert*-Butyl-4,5-dimethylphenol *[1445-23-4]* **M 178.3, b 144-150°/20mm**, **pK_{Est} ~11.8.** It is obtained by placing 3,4-dimethylphenol (170g, 1.39mol, m ~65°, see [95-65-8]), concentrated H_2SO_4 (1.5ml) and a magnetic stirrer bar in a medium pressure vessel, then purging the closed vessel with isobutylene while heating and stiring vigorously at 70° (which keeps the phenol in a moten state) under an isobutylene pressure of 20 psi. The reaction is complete when the liquid stops expanding. The mixture is cooled, Et_2O is added and the mixture is washed with saturated aqueous $NaHCO_3$ (3 x 150ml), the combined organic layers are dried ($MgSO_4$), filtered, the solvent is evaporated and the residual oil is distilled to give *2-tert-butyl-4,5-dimethylphenol*, with and the ^1H NMR (400MHz, $CDCl_3$, TMS) has δ at 7.02 (s, 1H, aromatic C*H*), 6.49 (s, 1H, aromatic C*H*), 2.19 (s, 3H, CH_3), 2.17 (s, 3H, CH_3), 1.40 (s, 9H, $C(CH_3)_3$). *Note tert-butyl 3,4-dimethylphenyl ether is formed instead when lower*

temperatures and very small amounts of acid are used [Stevens *J Am Chem Soc* **20** 1232 *1955*.] [Alexander et al. *J Am Chem Soc* **120** 4041 *1998*, Albert *J Am Chem Soc* **76** 1983 *1954*; for *acetyl derivative* see Fischer & Teo *Can J Chem* **56** 258 *1978*.]

2-*tert*-Butyl hydroquinone *[1948-33-0]* **M 166.2, m 125-127°, 127-128°, 129°, $pK_{Est(1)}$ ~10.5. $pK_{Est(2)}$ ~11.6.** Recrystallise the hydroquinone from H_2O or MeOH and dry it in a vacuum at 70°. Store it in a dark container. [Stroh et al. *Angew Chem* **69** 699 *1957*, *Beilstein* **6** IV 6013.]

2-*tert*-Butyl-4-methoxyphenol (2-*tert*-butyl-4-hydroxyanisole) *[121-00-6]* **M 180.3, m 64.1°, pK_{Est} ~10.8.** Fractionally distil the phenol *in vacuo*, then pass it as a solution in $CHCl_3$ through alumina, and evaporate the eluate. Recrystallise the residue from petroleum ether. [*Beilstein* **6** IV 6013.]

p-***tert*-Butylnitrobenzene** *[3282-56-2]* **M 179.2, m 28.4°, b 135°/10mm, 140-142°/15mm, n_D^{20} 1.5230.** Recrystallise it three times by partially freezing a mixture of the mono-nitro isomers, then recrystallise it twice from MeOH and dry it *in vacuo* [Brown *J Am Chem Soc* **81** 3232 *1959*]. [*Beilstein* **5** H 418, **5** I 203, **5** II 321, **5** III 943, **5** IV 1052.]

***tert*-Butyl perphthalic acid (monoperoxyphthalic acid 1-*tert*-butyl ester)** *[15042-77-0]* **M 238.2, m 104-104.5° (dec), pK_{Est} ~6.2.** Crystallise the per acid-ester from Et_2O or Et_2O/petroleum ether and dry it over H_2SO_4. The ester was prepared from *tert*-butylhydroperoxide and phthalic anhydride [Davies et al. *J Chem Soc* 1545 *1953*]. *Possibly* **EXPLOSIVE**. [*Beilstein* **9** IV 3260.]

p-***tert*-Butylphenol** *[98-54-4]* **M 150.2, m 99°, pK^{25} 10.39.** Crystallise the phenol to constant melting point from petroleum ether (b 60-80°). It sublimes *in vacuo*. Also purify it *via* the benzoate, as for phenol. The *salicylate ester* [87-18-30] has **m** 63-64° (from aqueous EtOH, or EtOH). [*Beilstein* **6** IV 3296.]

p-***tert*-Butylphenoxyacetic acid** *[1798-04-5]* **M 208.3, m 86.5°, 88-89°, 94°, 96.5°, pK_{Est} ~2.9.** Crystallise the acid from petroleum ether or petroleum ether/*C_6H_6 mixture. [*Beilstein* **6** H 524, **6** III 1869.]

***tert*-Butyl phenyl carbonate** *[6627-89-0]* **M 194.2, b 74-78°/0.5mm, 83°/0.6mm, d_4^{20} 1.05, n_D^{20} 1.480.** If IR is free from OH, then purify it by redistillation; otherwise dissolve it in Et_2O, wash it with 5% HCl, then H_2O, dry it ($MgSO_4$), evaporate and distil it through a Claisen head under vacuum. Care should be taken as distillation of large quantities can lead to decomposition with liberation of CO_2 and isobutylene; **take the necessary precautions.** [Carpino *J Am Chem Soc* **79** 98 *1957*, *Beilstein* **6** IV 629.]

***n*-Butyl phenyl ether** *[1126-79-0]* **M 150.2, b 95°/17mm, 210.20°/760mm, d_4^{20} 0.935, n_D^{20} 1.4969.** Dissolve it in diethyl ether, washed first with 10% aqueous NaOH to remove traces of phenol, then repeatedly with distilled water, followed by evaporation of the solvent and distillation under reduced pressure [Arnett & Wu *J Am Chem Soc* **82** 5660 *1960*]. [*Beilstein* **6** H 143, **6** I 82, **6** II 145, **6** III 550, **6** IV 558.]

***N*-*tert*-Butyl α-phenyl nitrone (PBN)** *[3376-24-7]* **M 177.2, m 73-74°.** Crystallise PBN from hexane. It is a free radical trap. [*cf* Janzen *Methods Enzymology* **105** 188 *1984*, *Beilstein* **7** IV 519.]

p-***tert*-Butyltoluene** *[98-51-1]* **M 148.3, f -53.2°, b 91°/28mm, 189-192°/atm, d_4^{20} 0.854, n_D^{20} 1.4920.** A sample containing 5% of the *meta*-isomer is purified by selective mercuration. Fractional distillation of the solid arylmercuric acetate, after removal from the residual hydrocarbon, gives pure *p-tert*-butyltoluene [Stock & Brown *J Am Chem Soc* **81** 5615 *1959*]. [*Beilstein* **5** H 439, **5** III 1003, **5** IV 1079.]

***tert*-Butyl 2,4,5-trichlorophenyl carbonate** *[16965-08-5]* **M 297.6, m 64-66°, 67-68.5°.** Crystallise the carbonate from a mixture of MeOH (90ml) and water (6ml) using charcoal [Broadbent et al. *J Chem Soc (C)* 2632 *1967*, Fieser & Fieser *Reagents for Organic Synthesis* **2** 55 *1969*].

Caffeic acid (3,4-dihydroxycinnamic acid) *[331-39-5]* **M 180.2, m 195°, 223-225°, pK_1^{25} 4.62, pK_2^{25} 9.07.**

Recrystallise this antioxidant from water. [*Beilstein* **10** IV 1776.]

Calcon carboxylic acid [3-hydroxy-4-(2-hydroxy-4-sulfo-1-naphthylazo)naphthalene-2-carboxylic acid] *[3737-95-9]* **M 428.4, m 300°, λ_{max} 560nm, pK_1 1.2, pK_2 3.8, pK_3 9.26, pK_4 13.14.** Purify it *via* its *p*-toluidinium salt, *viz*: dissolve the dye in warm 20% aqueous MeOH, treat with an equivalent of *p*-toluidine and cool to precipitate the salt. Finally recrystallise the acid from hot water. [Itoh & Ueno *Analyst (London)* **95** 583 *1970*.] It is an indicator and complexes with Ca^{2+} in presence of Mg^{2+} and other metal ions [Patton & Reeder *Anal Chem* **28** 1026 *1956*, Prentoe & Prentoe *Analyst* **106** 227 *1981*].

Calmagite [1-(1-hydroxy-4-methyl-2-phenylazo)-2-hydroxynaphthalene-4-sulfonic acid] *[3147-14-6]* **M 358.4, m 300°, pK_1 8.1, pK_2 12.4.** A crude dye is extracted with anhydrous diethyl ether and forms red crystals from Me_2CO. It gives a red colour in H_2O at pH 7—9 and a blue colour at pH 9—11 which turns red on addition of Ca^{2+} or Mg^{2+} ions. [Lindstrom & Diehl *Anal Chem* **32** 1123 *1960*]. Complexes with Ca, Mg and Th.

Capsaicin (*E*-*N*-[(4-hydroxy-3-methoxyphenyl)-methyl]-8-methyl-6-nonenamide) *[404-86-4]* **M 305.4, m 64-66°, 65°, 66.1°, b 210-220°/0.01mm, ε 7000 (281nm, EtOH).** Recrystallise capcaicin from petroleum ether (b 40-60°), or petroleum ether/Et_2O (9:1). Also purify it by chromatography on neutral Al_2O_3 (grade V) and elute successively with *C_6H_6, *C_6H_6/EtOAc (17:3) then *C_6H_6/EtOAc (7:3), and distil it at 120°/10^{-5}mm, then repeatedly recrystallise the needles from isopropanol (charcoal). [Crombie et al. *J Chem Soc* 11025 *1955*, Bennett & Kirby *J Chem Soc(C)* 442 *1968*.] It **causes pain** and is **neurotoxic** [Bevan & Szolcsanyi *Trends in Pharmacol Sci* **11** 330 *1990*, *Beilstein* **13** IV 2588].

4-(Carbamoylmethoxy)acetanilide *[14260-41-4]* **M 208.2, m 208°.** Crystallise the anilide from water.

***N*-Carboethoxyphthalimide (*N*-ethoxycarbonylphthalimide)** *[22509-74-6]* **M 219.2, m 87-89°, 90-92°.** Crystallise the imide from toluene/petroleum ether (or *benzene/petroleum ether). It is partly soluble in Et_2O, *benzene and $CHCl_3$. [Heller & Jacobsohn *Chem Ber* **54** 1112 *1921*, *Beilstein* **21/10** V 428.]

3-Carboxybenzaldehyde (3-formylbenzoic acid, isophthalaldehydic acid) *[619-21-6]* **M 150.1, m 173°, 173-175°, pK^{25} 3.84.** The acid was prepared in several ways including the following two. *m*-Bromomethylbenzoic acid (3g) is allowed to react with hexamine (3.9g) in $CHCl_3$ (30ml) by refluxing for 3 hours, cooled, the hexamine quaternary salt (4.7g) is collected, dried *in vacuo*, and decomposed by boiling in 50% aqueous acetic acid for 2 hours. The solution is cooled, diluted with an equal volume of H_2O and chilled to give a crop of the desired acid as needles, which are washed with aqueous $NaHCO_3$ and dried. A further crop can be obtained by extracting the acidic filtrate with Et_2O to give total yield of 48%. [Dyer et al. *J Chem Soc* 4778, 4781 *1952*]. *Alternatively*, *m*-carboxycinnamic acid (m 268-270°, 8.6g) in 1N Na_2CO_3 (50ml) and H_2O (400ml) is treated slowly at 4-5° with 5% of aqueous $KMnO_4$ (80ml) with vigorous stirring. MnO_2 is removed by filtration, the filtrate is concentrated to 150ml, acidified with 5N HCl and the mixture of acids that separated, together with the solution, are extracted thoroughly with Et_2O, which on evaporation give 3-formylbenzoic acid (3.6g) which is purified by recrystallisation from H_2O. [Berner *Acta Chim Scand* **10** 1208 *1956*].
The *acid chloride* [75650-38-3] has **b 130°/20mm**, the *methyl ester* [52178-50-4] has **m 53°**, the *ethyl ester* [33745-47-0] has **d^{18} 1.093** and **b 278°/atm**, the *amide* has **m 190°(dec)**, the *oxime* has **m 188°**, the *semicarbazone* has **m 275°(dec)** (from aqueous EtOH), the *bis(2-hydroxyethyl)amine salt* has **m 167°** (yellow crystals from aqueous EtOH), and the *phenylhydrazone* has **m 164°**. [Irreverre et al. *J Biol Chem* **236** 1093 *1961*, Davies et al. *J Chem Soc* 2202 *1922*, Simonis *Chem Ber* **45** 1584 *1912*, *Beilstein* **10** H 671, **10** I 317, **10** II 465, **10** III 2990, **10** IV 2750.]

4-Carboxybenzaldehyde (4-formylbenzoic acid, terephthalaldehydic acid) *[619-66-9]* **M 150.1, m 247°, 248°(dec), ~250°, 248-250°, 256°, pK^{25} 3.77.** Of the many syntheses of this acid, the more convenient one is by refluxing a solution of the commercially available 4-bromomethylbenzoic acid (21.0g, 6232-88-8) with 10% $Cu(NO_2)_2$ (300ml) for 6 hours, cooling, filtering off the solid and recrystallising it from glacial AcOH (100ml)

to give fine plates, which on further recrystallisation from H_2O, provide pure *4-formylbenzoic acid* as fine needles (2.2g 56%). The *phenylhydrazone* has **m 221-222°** [Stewart & Walker *Can J Chem* **35** 1561 *1957*], the *2,4-dinitrophenylhydrazone* has **m 319.5-320.5°**, after crystallisation from pyridine then $PhNO_2$ [Bowen & Wilkinson *J Chem Soc* 750 *1950*], the *oxime* has **m 216-217°** [Wheeler et al. *J Org Chem* **22** 547 *1957*]. The acid is also obtained by hydrolysis of the *methyl ester*, **m 61-61°** (from petroleum ether), **b 135°/12mm**, by aqueous H_2SO_4; the ester having been prepared from methyl 4-cyanobenzoate by reaction with $ZnCl_2$/HCl [Slotta & Kethur *Chem Ber* **71** 335 *1938*]. The UV in hexane of the *formyl acid* has λ_{max} (ε) at 249 (17,500), 257 (15,500) [*B*-band], and 279 (1,650), 288 (1,950), 298 (1,600) [*C-band*] nm [Dearden & Forbes *Can J Chem* **36** 1362 *1958*]. [for pK see Humffray et al. *JCS, Chem Comm* 610 *1965*; *Beilstein* **10** H 671, **10** I 317, **10** II 465, **10** III 2989, **10** IV 2752.]

4-**Carboxyphenylacetonitrile** *[6627-91-4]* **M 161.2, m 114-115°.** Crystallise the nitrile (with considerable loss) from *benzene, glacial acetic acid or H_2O. The *methyl ester* has **m** 47-48° (from $*C_6H_6$). [Price & Rogers *Org Synth* Coll Vol **III** 174 *1955*, *Beilstein* **9** H 859, **9** II 618, **9** III 4267.]

Catechol (1,2-dihydroxybenzene, pyrocatechol) *[120-80-9]* **M 110.1, m 105°, pK_1^{25} 9.45, pK_2^{25} 12.8.** Crystallise catechol from *benzene or toluene and sublime it *in vacuo*. [Rozo et al. *Anal Chem* **58** 2988 *1986*, *Beilstein* **6** IV 5557.]

Cation exchange resin. The resin should be conditioned before use by successive washing with water, EtOH and water, and taken through two H^+-Na^+-H^+ cycles by successive treatment with M NaOH, water and M HCl then washed with water until neutral.

***p*-Chloranil (2,3,5,6-tetrachloro-1,4-benzoquinone)** *[118-75-2]* **M 245.9, m 290°, 294.2-294.6°(sealed tube).** Crystallise *p*-chloranil from acetic acid, acetone, *benzene, EtOH or toluene, dry it in a vacuum over P_2O_5, or from acetic acid and drying over NaOH in a vacuum desiccator. It can be sublimed under vacuum at 290°. A sample may contain significant amounts of the *o*-chloranil isomer as impurity. Purify it by triple sublimation under vacuum and recrystallise before use. **It is a skin and mucous membrane irritant**. [UV: Pummerer et al. *Chem Ber* **85** 545 *1952*, Brook *J Chem Soc* 5040 *1952*, *Beilstein* **7** IV 2083.]

Chloranilic acid (2,5-dichloro-3,6-dihydroxy-1,4-benzoquinone) *[87-88-7]* **M 209.0, m 283-284° pK_1^{25} 1.22, pK_2^{25} 3.01.** A solution of 8g of quinone in 1L of boiling water is filtered while hot, then extracted twice at about 50° with 200ml portions of *benzene. The aqueous phase is cooled in ice-water. The crystals are filtered off, washed with three 10ml portions of water, and dried at 115°. It can be sublimed *in* vacuo. [Weissbart & Rysselberghe *J Phys Chem* **61** 765 *1957*.] The *diacetate* has **m** 182-185° [Conant & Fieser *J Am Chem Soc* **46** 1866 *1924*, Thamer & Voight *J Phys Chem* **56** 225 *1952*]. [*Beilstein* **8** IV 2707.]

p-**Chloroacetanilide** *[539-03-7]* **M 169.6, m 179°.** Crystallise the anilide from EtOH or aqueous EtOH. [*Beilstein* **12** IV 1178.]

2-Chloroacetophenone *[532-27-4]* **M 154.6, m 54-56°.** Crystallise it from MeOH [Tanner *J Org Chem* **52** 2142 *1987*]. [*Beilstein* **7** IV 641.]

o-**Chloroaniline** *[95-51-2]* **M 127.6, m -1.9°, b 84.5°/10mm, 108.4°/30mm, 208.8°/760mm, d_4^{20} 1.213, n_D^{20} 1.588, pK^{25} 2.66.** Free it from small amounts of the *p*-isomer by dissolving in one equivalent of H_2SO_4 and steam distilling. The *p*-isomer remains behind as the sulfate. [Sidgwick & Rubie *J Chem Soc* 1013 *1921*.] An alternative method is to dissolve it in warm 10% HCl (11ml/g of amine) and on cooling, *o-chloroaniline hydrochloride* separates out. The latter can be recrystallised until the acetyl derivative has a constant melting point (**m** 90°). (In this way, yields are better than *via* the recrystallisation of the *picrate* from EtOH or of the acetyl derivative from petroleum ether.) [King & Orton *J Chem Soc* 1377 *1911*]. [*Beilstein* **12** III 1281, **12** IV 1115.]

p-**Chloroaniline** *[106-47-8]* **M 127.6, m 70-71°, b 106.8-107.3-.5°/12mm, 116°/17mm, d_4^{20} 1.175, pK^{25} 3.98.**

Crystallise the aniline from MeOH, petroleum ether (b 30-60°), or 50% aqueous EtOH, then *benzene/petroleum ether (b 60-70°), and then dry it in a vacuum desiccator. It can be distilled under vacuum (**b** 75-77°/3mm). It sublimes in a very high vacuum. The *acetate* crystallises from aqueous MeOH (**m** 178°, 180°) or EtOH or AcOH (**m** 173-174°) and has **b** 331.3°/760mm. [*Beilstein* **12** III 1325, **12** IV 1116.]

***p*-Chloroanisole** *[623-12-1]* **M 142.6, b 79°/11.5mm, 196.6°/760mm, d_4^{20} 1.164, $n_D^{25.5}$ 1.5326.** Wash the anisole with 10% (by volume) aqueous H_2SO_4 (three times), 10% aqueous KOH (three times), and then with water until neutral. Dry it ($MgSO_4$), and fractionally distil it from CaH_2 through a glass helices-packed column under reduced pressure. [*Beilstein* **16** IV 822.]

9-Chloroanthracene *[716-53-0]* **M 212.9, m 104-106°, 105-107°.** 9-Chloroanthracene crystallises from EtOH or petroleum ether (**b** 60-80°) as yellow needles. [Nonhebel *Org Synth* Coll Vol **V** 206 *1973*, Masnori *J Am Chem Soc* **108** 1126 *1986*, *Beilstein* **5** H 663, **5** III 2133, **5** IV 2292.]

10-Chloro-9-anthraldehyde *[10527-16-9]* **M 240.7, m 218°, 217-219°.** The aldehyde crystallises as yellow needles from EtOH, AcOH or toluene. [*Beilstein* **7** III 2529.]

2-Chlorobenzaldehyde *[89-98-5]* **M 140.6, m 11°, b 213-214°, d_4^{20} 1.248, n_D^{20} 1.566.** Wash it with 10% Na_2CO_3 solution, then fractionally distil it in the presence of a small amount of catechol as stabiliser. [*Beilstein* **7** H 233, **7** IV 561.]

3-Chlorobenzaldehyde *[587-04-2]* **M 140.6, m 18°, b 213-214°, d_4^{20} 1.241, n_D^{20} 1.564.** Purify it by low temperature crystallisation from petroleum ether (b 40-60°) and distillation. [*Beilstein* **7** H 234, **7** IV 566.]

4-Chlorobenzaldehyde *[104-88-1]* **M 140.6, m 47°.** Crystallise it from EtOH/water (3:1), then sublime it twice at ~50°/2mm. [*Beilstein* **7** H 235, **7** IV 568.]

Chlorobenzene *[108-90-7]* **M 112.6, b 131.7°, d_4^{20} 1.107, n_D^{20} 1.52480.** The main impurities are likely to be chlorinated impurities originally present in the *benzene used in the synthesis of chlorobenzene, and also unchlorinated hydrocarbons. A common purification procedure is to wash it several times with conc H_2SO_4 then with aqueous $NaHCO_3$ or Na_2CO_3, and water, followed by drying with $CaCl_2$, K_2CO_3 or $CaSO_4$, then with P_2O_5, and distilling. It can also be dried with Linde 4A molecular sieve. Passage through, and storage over, activated alumina has been used to obtain low conductance material. [Flaherty & Stern *J Am Chem Soc* **80** 1034 *1958*, *Beilstein* **5** H 199, **5** IV 640.]

4-Chlorobenzenesulfonyl chloride *[98-60-2]* **M 211.1, m 53°, b 141°/15mm.** Crystallise it from ether in powdered Dry-ice, after the solution has been washed with 10% NaOH until colourless and dried (Na_2SO_4). Distil it *in vacuo* and store it in the absence of H_2O. [*Beilstein* **11** IV 114.]

4-Chlorobenzhydrazide *[536-40-3]* **M 170.6, m 164°.** Crystallise it from H_2O. [*Beilstein* **9** III 1368.]

2-Chlorobenzoic acid *[118-91-2]* **M 156.6, m 139-140°, pK^{25} 2.91.** Crystallise the acid successively from glacial acetic acid, aqueous EtOH, and petroleum ether (b 60-80°). Other solvents include hot water or toluene (*ca* 4ml/g). The crude material can be initially purified by dissolving 30g in 100ml of hot water containing 10g of Na_2CO_3, boiling with 5g of charcoal for 15 minutes, then filtering and adding 31ml of 1:1 aqueous HCl. The precipitate is washed with a little water and dried at 100°. [*Beilstein* **9** IV 956.]

3-Chlorobenzoic acid *[535-80-8]* **M 156.6, m 154-156°, 158°, d_4^{25} 1.496, pK^{25} 3.82 (5.25 in 50% dimethylacetamide).** Crystallise the acid successively from glacial acetic acid, aqueous EtOH and petroleum ether (b 60-80°). It also recrystallises from *C_6H_6 or Et_2O/hexane, and sublimes at 55° in a vacuum. [*Anal Chem* **26** 726 *1954*] The *methyl ester* has **m** 21°, **b** 231°/760mm. The *S-benzylisothiouronium salt* has **m** 164-165° (from EtOH) [Friediger & Pedersen *Acta Chem Scand* **9** 1425 *1955*, Samuel *J Chem Soc* 1318 *1960*]. [*Beilstein* **9** IV 969.]

4-Chlorobenzoic acid *[74-11-3]* **M 156.6, m 238-239°, pK^{25} 3.99.** Purify it as for *m*-chlorobenzoic acid. It has also been crystallised from hot water, and from EtOH. [*Beilstein* **9** IV 973.]

2-Chlorobenzonitrile *[873-32-5]* **M 137.6, m 45-46°.** Crystallise the nitrile to a constant melting point from *benzene/petroleum ether (b 40-60°). [*Beilstein* **9** IV 965.]

4-Chlorobenzophenone *[134-85-0]* **M 216.7, m 75-76°.** Recrystallise it from EtOH. [Wagner et al. *J Am Chem Soc* **108** 7727 *1986*, *Beilstein* **7** H 419, **7** I 227, **7** II 359, **7** III 2072, **7** IV 1375.]

***o*-Chlorobenzotrifluoride (*o*-chlorotrifluoromethylbenene)** *[88-16-4]* **M 180.6, m –6.37°, b 19.6°/3mm, 152.3°/760mm, d$_4^{25}$ 1.364, n$_D^{25}$ 1.4533.** Dry the trifluoride over $CaSO_4$, and distil it at high reflux ratio through a silvered vacuum-jacketed glass column packed with one-eight inch glass helices [Potter & Saylor *J Am Chem Soc* **73** 90 *1951*]. [*Beilstein* **5** H 302, **5** III 692, **5** IV 814.]

***m*-Chlorobenzotrifluoride** *[98-15-7]* **M 180.6, m –56.49°, b 50°/31mm, 137.6°/760mm, d$_4^{20}$ 1.3345, n$_D^{20}$ 1.4432.** Purify it as for *o*-chlorobenzotrifluoride above. [*Beilstein* **5** III 692, **5** IV 814.]

***p*-Chlorobenzotrifluoride** *[98-56-6]* **M 180.6, m –33.18°, b 19.3°/5mm, 138.6°/760mm, d$_4^{30}$ 1.3278, n$_D^{30}$ 1.4430.** Purify it as for *o*-chlorobenzotrifluoride above. [*Beilstein* **5** IV 815.]

***p*-Chlorobenzyl chloride** *[104-83-6]* **M 161.0, m 28-29°, b 96°/15mm.** Dry it over $CaSO_4$, then fractionally distil it under reduced pressure. Crystallise it from heptane or dry diethyl ether at low temperature. [*Beilstein* **5** IV 816.] **LACHRYMATORY.**

***p*-Chlorobenzylisothiuronium chloride** *[544-47-8]* **M 237.1, m 177-178°, and 197°, 201-203°, pK$_{Est}$ ~9.6 (free base).** Crystallise the salt from conc HCl by addition of water. Dry it in a vacuum over P_2O_5. Also crystallise it from EtOH, wash the crystals with EtOH, then Et_2O to give the lower melting form **m** 177-178°. By evaporating the filtrate and washings to a quarter of the volume and adding an equal volume of Et_2O the higher melting form **m** 201-203° is obtained. [Harvey & Jensen *J Org Chem* **28** 470 *1963*, *Beilstein* **6** III 1639, **6** IV 2778.]

***trans*-4-Chlorocinnamic acid** *[1615-02-7]* **M 182.6, m 243°, 248-250°, 249-251°, pK^{25} 4.41.** Recrystallise the acid from EtOH or aqueous EtOH (charcoal). Its UV has λ_{max} at 275nm (EtOH). [Walling & Wolfstirn *J Am Chem Soc* **69** 852 *1947*, *Beilstein* **9** H 596, **9** II 395, **9** III 2727, **9** IV 2033.]

4-Chloro-3,5-dimethylphenol *[88-04-0]* **M 156.6, m 115.5°, pK^{25} 9.70.** Crystallise the phenol from *benzene or toluene. [*Beilstein* **6** IV 3152.]

1-Chloro-2,4-dinitrobenzene *[97-00-7]* **M 202.6, m 48-50°, 51°, 52-54°, 54°, b 315°/atm, d$_4^{22}$ 1.697.** Usually it is recrystallised from EtOH or MeOH. It has also been crystallised from Et_2O, *C_6H_6, *C_6H_6/petroleum ether or isopropyl alcohol. A preliminary purification step is to pass its solution in *benzene through an alumina column. It has also been purified by zone refining. It exists in three forms: one stable and two unstable. The stable form crystallises as yellow needles from Et_2O, **m** 51°, **b** 315°/760mm with some decomposition, and is soluble in EtOH. A labile form also crystallises from Et_2O, **m** 43°, and is more soluble in organic solvents. The second labile form has **m** 27°. [Hoffman & Dame, *J Am Chem Soc* **41** 1015 *1919*, Welsh *J Am Chem Soc* **63** 3276 *1941*, *J Chem Soc* 2476 *1957*, *Beilstein* **5** IV 744.]

4-Chloro-3,5-dinitrobenzoic acid *[118-97-8]* **M 246.6, m 159-161°, 163°, pK$_{Est}$ ~2.5.** Crystallise the acid from EtOH/H_2O, EtOH or *C_6H_6. The 1:1 *naphthalene complex* (by fusing various ratios of ingredients and recrystallising from EtOH) has **m** 122°. [*Beilstein* **9** H 416, **9** III 1953, **9** IV 1360.]

Chlorogenic [1-(3,4-dihydroxycinnamoyloxy)-D-quinic] acid *[327-97-9]* **M 354.3, m 208°, [α]$_D^{25}$ -36° (c 1, H_2O), pK$_1^{25}$ 3.59, pK$_2^{25}$ 8.59.** Crystallise the acid from water and dry it at 110°. [*Beilstein* **10** H 537, **10** I 271, **10** II 378, **10** III 2408, **10** IV 2259.]

Chlorohydroquinone (2-chloro-1,4-dihydroxybenzene) *[615-67-8]* **M 144.6, m 106°, b 263°, pK_1^{25} 8.81, pK_2^{25} 10.78.** Crystallise the hydroquinone from $CHCl_3$ or toluene. [*Beilstein* **6** IV 5767.]

4-Chloroiodobenzene *[637-87-6]* **M 238.5, m 53-54°, 56.2°, b 104.2°/16mm, d_4^{57} 1.886.** Distil it in a vacuum then recrystallise it from EtOH. [Sugden *J Chem Soc* 1173 *1924*, *Beilstein* **5** H 221, **5** III 579, **5** IV 695.]

5-Chloro-2-methoxyaniline (2-amino-4-chloroanisole) *[95-03-4]* **M 157.6, m 81-83°, 82-84°, 84°, pK^{25} 3.56.** Purify the aniline by steam distillation and recrystallisation from H_2O or 40% aqueous EtOH. The *N-acetate* forms needles from hot H_2O with **m** 104°, the *N-benzoyl* derivative forms needles from aqueous EtOH with **m** 77-78°, and the *picrate* has **m** 194°(dec). [Raiford & Colbert *J Am Chem Soc* **48** 2657 *1926*, *Beilstein* **13** IV 879.]

3-Chloro-4-methoxyphenethylamine *[7569-87-1]* **M 149.6, b 140°/0.6mm, d_4^{25} ~1.081, n_D^{20} ~1.553, pK^{25} ~9.8.** This strong base is prepared by reduction of *3-chloro-4-methoxyphenylacetonitrile* (176mmol, b 140-145°/0.1-0.1mm, m 55-56°, [7569-58-6]) in THF (100ml) with $LiAlH_4$ (8.0g, 210mmol) suspended in THF (250ml) under reflux for 5 hours. The greenish coloured solution is carefully decomposed with ice cold H_2O, the solids are filtered off, washed with Et_2O, the combined organic liquids are dried (Na_2SO_4), filtered, evaporated and the crude brown residual amine is distilled in as high a vacuum as possible to give a clear oil (11.4g, 35%). It absorbs CO_2 from air and is best stored in an inert atmosphere. Its ^1H NMR [60MHz, $CDCl_3$] has δ at 7.20 (d, 1H, Ar*H*2), 7.04 (q, 1H, Ar*H*6), 6.83 (d, 1H, Ar*H*5), 3.88 (s, 3H, OCH_3), 3.12-2.20 (m, 4H, $PhCH_2CH_2N$), 1.28 (s, 2H, NH_2) ppm from TMS [Charifson et al. *J Med Chem* **31** 1941 *1988*]. *Alternatively*, the amine is prepared from the respective phenethyl bromide and dry NH_3 in EtOH followed by dilution with Et_2O, washing with aqueous NaOH, and evaporation. The residue is dissolved in 5% aqueous HCl and evaporated to dryness to give ***3-chloro-4-methoxyphenethylamine hydrochloride*** [7569-60-0] **M 186.1, m 192-195°,** as an apparently amorphous white powder when crystallisation from EtOH/Et_2O is attempted [Fosdick et al. *J Am Chem Soc* **68** 840 *1946*]. The ***N-benzoyl*** derivative [115514-67-5] **m 137-140°** is a colourless solid which is insoluble in Et_2O. [*Beilstein* **13** III 1650.]

9-Chloromethyl anthracene *[24463-19-2]* **M 226.7, m 141-142°(dec), 141-142.5°.** If it is free from OH in the IR then recrystallisation from hexane/*C_6H_6 or *C_6H_6 (as needles). If OH is present, then some solvolysis has occurred. In this case treat 8.5g of it with $SOCl_2$ (4.8g) in dioxane (60ml) and reflux for 5 hours, then evaporate to dryness and wash the residue with cold *C_6H_6 and recrystallise it. With KI/Me_2CO it forms the *iodomethyl* derivative. [Fierens et al. *Helv Chim Acta* **38** 2009 *1955*, Hunter et al. *J Org Chem* **21** 1512 *1956*, *Beilstein* **5** III 3152, **5** IV 2313.]

4-Chloro-2-methylphenol *[1570-64-5]* **M 142.6, m 49°, b 112-114°/18mm, 225°/760mm, pK^{25} 9.71.** Purify the phenol by crystallisation from petroleum ether (**m** 51°) and by zone melting. [*Beilstein* **6** H 359, **6** I 174, **6** II 332, **6** III 1264, **6** IV 1987.]

4-Chloro-3-methylphenol *[59-50-7]* **M 142.6, m 66°, b 238°/760mm, pK^{25} 9.55.** Crystallise the phenol from petroleum ether or *C_6H_6. [*Beilstein* **6** H 381, **6** I 187, **6** II 355, **6** III 1315, **6** IV 2064.]

4-Chloro-2-methylphenoxyacetic acid (MCPA) *[94-74-6]* **M 200.6, m 113-117°, 120°, 122-123°, pK^{20} 3.62(3.05).** It is insoluble in H_2O (solubility is 0.55g/L at 20°) and recrystallises from *C_6H_6 or chlorobenzene as plates [Jönsson et al. *Acta Chem Scand* **6** 993 *1952*]. The *S-benzylisothiouronium salt* has **m** 164-165°, and the Cu^{2+} salt has **m** 247-249°(dec) [Armarego et al. *Nature* **183** 1176 *1959*, UV: Duvaux & Grabe *Acta Chem Scand* **4** 806 *1950*, IR: Jöberg *Acta Chem Scand* **4** 798 *1950*]. [*Beilstein* **6** IV 1991.] It is a plant growth substance and a herbicide.

2-Chloromethyl-2-phenylpropane (neophyl chloride, 1-chloro-2-methyl-2-phenylpropane, β-chloro-*tert*-butylbezene) *[515-40-2]* **M 168.7, b 53°/1.0mm, 95.1-95.2°/10mm, 97°/13.0mm, 104°/18.0mm, 120°/30mm, 111°/90.0mm, 222°/741mm (dec), d_4^{25} 1.5228, n_D^{20} 1.5250.** It is prepared by adding β-methalyl chloride (603g, 6.66 moles, CH_2=C(Me)-CH_2Cl, 3-chloro-2-methyl-1-propene, prepared by the chlorination of butylene, b 71.5-72.5°/760mm, d_4^{20} 0.9165, n_D^{20} 1.4274 [563-47-3], *Beilstein* **1** IV 803) into a vigorously stirred mixture of

*benzene (1404g, 18.5 moles, washed twice with conc H_2SO_4 and used as such) and concentrated H_2SO_4 (104g, 1 mole) at 20° which required 12 hours, and stirring is continued for a further 11 hours at room temperature. The organic layer is collected, excess of $*C_6H_6$ is distilled off and the residue is fractionated through an 8-plate column to give pure (99.1 ±0.3% by acetolysis) *neophyl chloride* (765.5g, 68%). It is less reactive than neopentyl chloride towards Na metal and less reactive still towards EtNa, and both are inert towards most basic reagents. [Whitmore et al. *J Am Chem Soc* **65** 1469 *1943*, Smith & Sellas *Org Synth* Coll Vol **IV** 702 *1963*, *Beilstein* **5** IV 1048.]
It readily forms the Grignard reagent ***neophyl magnesium chloride*** [35293-35-7] **M 193.0**, with Mg in Et_2O; and a 0.5M solution of this reagent in Et_2O is available commercially. It reacts with solid CO_2 to give an 82% yield of *β-phenylisovaleric acid* [1010-48-6] (**m 58-59.5°,** from petroleum ether b 60-90°); and oxidation provides a 72% yield of *2-methyl-2-phenylpropan-1-ol* [2173-69-5] (**b 131°/30mm, n_D^{20} 1.5261**) whose *phenylurethane* has **m 59.5-60.5°**, α-*naphthylurethane* has **m 91.5-92.5°**, and its *p-toluenesulfonate* has **m 74-75°**. [Whitmore et al. *J Am Chem Soc* **65** 1469 *1943*, Fainberg & Winstein *J Am Chem Soc* **78** 2763*1956*, Winstein et al. *J Am Chem Soc* **74** 1113 *1952*.]

Chloromethyl phenyl sulfide *[7205-91-6]* **M 158.7, b 63°/0.1mm, 98°/12mm, 113-115°/20mm, d_4^{20} 1.184, n_D^{20} 1.5950.** Dissolve the sulfide in CH_2Cl_2 or CCl_4 and dry it ($CaCl_2$), or pass it through a tube of $CaCl_2$ and distil it using a fractionating column. ***Harmful*** *vapours.* It gives the *sulfone* [7205-98-3] (**b** 130°/1mm and **m** 53° from EtOH) [*Beilstein* **6** IV 1507] on oxidation with permonophthalic acid. [Böhme et al. *Justus Liebigs Ann Chem* **563** 54 64 *1949*.] [*Beilstein* **6** III 1002.]

***N*-(Chloromethyl)phthalimide** *[17564-64-6]* **M 195.6, m 131-135°, 134-135°, 136.5°.** Purify the imide by recrystallisation from EtOAc or CCl_4 or *via* the 1:1 complex with pyridine [Sakellarios *J Am Chem Soc* **70** 2822 *1948*, Böhme et al. *Chem Ber* **92** 1258 *1959*]. [*Beilstein* **21/10** V 372.]

1-Chloronaphthalene *[90-13-1]* **M 162.6, f -2.3°, b 136-136.5°/20mm, 259.3°/760mm, d_4^{20} 1.194, n_D^{20} 1.6326.** Wash the chloronaphthalene with dilute $NaHCO_3$, then dry it with Na_2SO_4 and fractionally distil it *in vacuo*. *Alternatively*, before distillation, it is passed through a column of activated alumina, or dried with $CaCl_2$, then distilled from sodium. It can be further purified by fractional crystallisation by partial freezing or by crystallisation of its *picrate* to constant melting point (**m** 132-133°) from EtOH, and recovering it from the picrate. [*Beilstein* **5** H 541, **5** III 1570, **5** IV 1658.]

2-Chloronaphthalene *[91-58-7]* **M 162.6, m 59.5-60°, 61°, b 121-122°/12mm. 264-266°/760mm.** Distil 2-chloronaphthalene in a vacuum, then crystallise it from 25% EtOH/water, then dry it under vacuum (see also the 1-isomer above). [*Beilstein* **5** H 541, **5** I 262, **5** II 445, **5** III 1573, **5** IV 1660.]

1-Chloro-2-naphthol *[633-99-8]* **M 178.6, m 70°, 71°, pK_{Est} ~8.3.** Crystallise the naphthol from petroleum ether. The *acetate* has **m** 42-43°. [*Beilstein* **6** I 315, **6** II 603, **6** III 2990, **6** IV 4289.]

2-Chloro-1-naphthol *[606-40-6]* **M 178.6, m 64-65°, 65°, pK^{20} 9.9 (aqueous EtOH).** Crystallise the naphthol from petroleum ether. [*Beilstein* **6** I 308, **6** II 581, **6** III 2933, **6** IV 4230.]

4-Chloro-1-naphthol *[604-44-4]* **M 178.6, m 116-117°, 120-121°, pK^{25} 8.86, 10.7 (aqueous EtOH).** Crystallise the naphthol from EtOH or $CHCl_3$. [*Beilstein* **6** H 611, **6** II 582, **6** III 2933, **6** IV 4233.]

4-Chloro-2-nitroaniline *[89-63-4]* **M 172.6, m 114-115°, 116-116.5°, pK^{25} -0.99.** Crystallise the aniline from hot H_2O (**m** 115.8-116°), EtOH, EtOH/H_2O or $*C_6H_6$, and dry it for 10 hours at 60° *in vacuo*. It has **m** 115.5-116° after sublimation. [*Beilstein* **12** H 729, **12** I 355, **12** II 396, **12** III 1649, **12** IV 1669.]

2-Chloro-4-nitrobenzamide *[3011-89-0]* **M 200.6, m 170-171°, 172°.** Crystallise the amide from EtOH. [Jensen & Ploug *Acta Chem Acta* **3** 15 *1949*, *Beilstein* **9** H 404, **9** III 1768.]

2-Chloro-1-nitrobenzene *[88-73-3]* **M 157.6, m 32.8-33.2°.** Crystallise it from EtOH, MeOH or pentane (charcoal). [*Beilstein* **5** IV 721.]

3-Chloro-1-nitrobenzene *[121-73-3]* **M 157.6, m 45.3-45.8°.** Crystallise the nitrobenzene from MeOH or 95% EtOH (charcoal), then pentane. [*Beilstein* **5** IV 722.]

4-Chloro-1-nitrobenzene *[100-00-5]* **M 157.6, m 80-83°, 83.5-84°, b 113°/8mm, 242°/atm, d $_4^{100.5}$ 1.2914.** Crystallise the nitrobenzene from 95% EtOH (charcoal) and sublime it *in vacuo*. [Emmons *J Am Chem Soc* **76** 3470 *1954*, Newman & Forrest *J Am Chem Soc* **69** 1221 *1947*, *Beilstein* **5** IV 723.]

3-Chloroperbenzoic acid (MCPBA) *[937-14-4]* **M 172.6, m 92-94°(dec), pK^{25} 7.57.** Recrystallise MCPBA from CH_2Cl_2 [Traylor & Mikztal *J Am Chem Soc* **109** 2770 *1987*]. Peracid of 99+% purity can be obtained by washing commercial 85% material with phosphate buffer pH 7.5 and drying the residue under reduced pressure. *Alternatively*, the peracid can be freed from *m*-chlorobenzoic acid by dissolving 50g/L of *benzene and washing with an aqueous solution buffered at pH 7.4 (NaH_2PO_4/NaOH) (5 x 100ml). The organic layer is dried over $MgSO_4$ and carefully evaporated under vacuum. *Necessary care should be taken in case of* **EXPLOSION**. The solid is recrystallised twice from CH_2Cl_2/Et_2O and stored at 0° in a plastic container as glass catalyses the decomposition of the peracid. The acid is assayed iodometrically. [Schwartz & Blumbrgs *J Org Chem* **29** 1976 *1964*, Bortolini et al. *J Org Chem* **52** 5093 *1987*, McDonald et al. *Org Synth* Coll Vol **VI** 276 *1988*, *Beilstein* **9** IV 972.]

2-Chlorophenol *[95-57-8]* **M 128.6, m 8.8°, b 61-62°/10mm, 176°/760mm, pK^{25} 8.34.** Pass 2-chlorophenol at least twice through a gas chromatography column. It has also been purified by fractional distillation. [*Beilstein* **6** IV 782.]

3-Chlorophenol *[108-43-0]* **M 128.6, m 33°, b 44.2°/1mm, 214°/760mm, pK^{25} 9.13.** It could not be obtained solid by crystallisation from petroleum ether. It is best purified by distillation under reduced pressure. [*Beilstein* **6** IV 810.]

4-Chlorophenol *[106-48-9]* **M 128.6, m 43°, 100-101°/10mm, pK^{25} 9.38.** Distil the phenol, then crystallise it from petroleum ether (b 40-60°) or hexane, and dry it under vacuum over P_2O_5 at room temperature. [Bernasconi & Paschalis *J Am Chem Soc* **108** 2969 *1986*, *Beilstein* **6** IV 820.]

Chlorophenol Red (3,3'-dichlorophenolsulfonephthalein) *[4430-20-0]* **M 423.3, m dec on heating, λ_{max} 573nm, pK^{25} 5.96.** Crystallise the dye from glacial acetic acid. It is yellow at pH 4.8 and violet at pH 6.7. [*Beilstein* **19/3** V 458.]

4-Chlorophenoxyacetic acid *[122-88-3]* **M 186.6, m 157°, pK^{20} 3.00, 4.15 (50% aqueous EtOH).** Crystallise the acid from EtOH. It is a plant growth substance and a herbicide. [*Beilstein* **6** IV 845.]

(±)-α-4-Chlorophenoxypropionic acid *[3307-39-9]* **M 200.6, m 116°, pK$_{Est}$ ~3.2.** Crystallise the acid from EtOH or HCOOH (**m** 114.5-115.5°). It is a plant growth substance. The *R(+)*- and *S(–)-enantomers* have **m** 103-104° (from petroleum ether) and $[\alpha]_D^{25}$ ±41° (c 1, EtOH). [*Beilstein* **6** III 695, **6** IV 850.]

ß-4-Chlorophenoxypropionic acid *[3284-79-5]* **M 200.6, m 138°, pK$_{Est}$ ~4.2.** Crystallise the acid from EtOH. It is a plant growth substance. [*Beilstein* **6** III 696, **6** IV 851.]

3-Chlorophenylacetic acid *[1878-65-5]* **M 170.6, m 74°, pK^{25} 4.11.** Crystallise the acid from EtOH/water, or as needles from *C_6H_6 or H_2O (charcoal). The *acid chloride* (prepared by boiling with $SOCl_2$) has **b** 127-129°/15mm. [Dippy & Williams *J Chem Soc* 161 *1934*, Misra & Shukla *J Indian Chem Soc* **28** 480 *1951*, *Beilstein* **9** III 2263, **9** IV 1674.]

4-Chlorophenylacetic acid *[1878-66-6]* **M 170.6, m 105°, 106°, pK^{25} 4.12.** Purify it as for 3-chlorophenylacetic acid. [*Beilstein* **9** III 2263, **9** IV 1674.]

4-Chloro-1-phenylbutan-1-one *[939-52-6]* **M 182.7, m 19-20°, b 134-137°/5mm, d $_4^{20}$ 1.149, n $_D^{20}$ 1.55413.** Fractionate the ketone several times using a short column. It recrystallises from petroleum ether at -20° in

glistening white rosettes and is filtered at 0°, and dried in a vacuum desiccator over H_2SO_4. The *semicarbazone* has **m** 136-137°. [Conant et al. *J Am Chem Soc* **46** 1882 *1924*, Cloke *J Chem Soc* 1174 *1929,* Hart & Curtis *J Am Chem Soc* **79** 931 *1957*, *Beilstein* **7** IV 711.]

1-(2-Chlorophenyl)-1-(4-chlorophenyl)-2,2-dichloroethane (Mitotane, *o,p'*-DDD) *[53-19-0]* **M 320.1, m 75.8-76.8°, 76-78°.** Purify Mitotane by recrystallisation from pentane, MeOH or EtOH. It is soluble in isooctane and CCl_4. [Haller et al. *J Am Chem Soc* **67** 1600 *1945*, *Beilstein* **5** IV 1883.]

3-(4-Chlorophenyl)-1,1-dimethylurea (Monuron) *[150-68-5]* **M 198.7, m 171°.** Crystallise monuron from MeOH. [*Beilstein* **12** IV 1191.]

4-Chloro-1,2-phenylenediamine *[95-83-0]* **M 142.6, m 69-70°, pK_1^{25} -0.27 (aqueous H_2SO_4), pK_2^{25} 3.35 (3.67).** Recrystallise the diamine from petroleum ether. [*Beilstein* **13** IV 68.]

4-Chlorophenyl isocyanate *[104-12-1]* **M 153.6, m 28-31°, 31-32°, 32°, 32.5°, b 80.6-80.9°/9.5mm, 115-117°/45mm.** Purify the isocyanate by recrystallisation from petroleum ether (b 30-40°) or better by fractional distillation. **TOXIC irritant.** [*Beilstein* **12** H 616, **12** III 1376, **12** IV 1213.]

4-Chlorophenyl isothiocyanate *[2131-55-7]* **M 169.6, m 44°, 43-45°, 45°, 46°, 47°, b 110-115°/4mm, 135-136°/24mm.** Check the IR first to see if free from OH frequencies. Triturate it with petroleum ether (b 30-60°) and decant the solvent. Repeat this 5 times. The combined extracts are evaporated under reduced pressure to give almost pure compound as a readily crystallisable oil with a pleasant anise odour. It can be recrystallised from the minimum volume of EtOH at 50° (do not boil too long as it could react). It can be purified by vacuum distillation. [van der Kerk et al. *Org Synth* Coll Vol **V** 223 *1973*, *Beilstein* **12** IV 1214.] **It is an IRRITANT and causes dermatitis; use gloves.**

4-Chlorophenyl 2-nitrobenzyl ether *[109669-56-9]* **M 263.7, m 44.5°, b 154-156°/3mm, 208°/11mm.** Distil it under reduced pressure, and it crystallises from EtOH (**m** 44-45°) or MeOH (**m** 46°) as yellow needles. [*Beilstein* **6** II 210, **6** III 801, **6** IV 1253.]

4-Chlorophenyl 4-nitrobenzyl ether *[5442-44-4]* **M 263.7, m 77°, b 215°/12mm.** Distil it in a vacuum and crystallise it from EtOH, MeOH (**m** 75.5-76°) or petroleum ether (**m** 76°, 77°). Its UV has λ_{max} at 222 and 302nm (EtOH). [*Beilstein* **6** II 222, **6** III 821, **6** IV 1288.]

4-Chlororesorcinol *[95-88-5]* **M 144.6, m 105°, $pK_{Est(1)}$~9.2, $pK_{Est(2)}$~10.1.** Crystallise it from boiling CCl_4 (10g/L, charcoal) and dry it in air. [*Beilstein* **6** II 818.] **IRRITANT.**

5-Chlorosalicaldehyde *[635-93-8]* **M 156.6, m 98.5-99°, 99.5°, 101°, pK^{25} 7.4.** Steam distil it, then crystallise it from aqueous EtOH or $*C_6H_6$ (**m** 100°). It forms complexes with Cu^{2+} and Fe^{2+}. [*Beilstein* **8** H 53, **8** II 45, **8** III 181, **8** IV 224.]

4-Chlorothiophenol *[106-54-7]* **M 144.6, m 51-52°, 53.5-54°, pK^{25} 6.14.** Recrystallise the thiophenol from aqueous EtOH. The *SMe ether* has **m** 129° and the *SEt ether* has **m** 64°. [D'Sousa et al. *J Org Chem* **52** 1720 *1987*, *Beilstein* **6** H 326, **6** I 149, **6** III 1034.]

2-Chlorotoluene *[95-49-8]* **M 126.6, b 159°, d_4^{20} 1.083, n_D^{20} 1.5255.** Dry 2-chlorotoluene for several days with $CaCl_2$, then distil it from Na using a glass helices-packed column. [*Beilstein* **5** IV 805.]

3-Chlorotoluene *[108-41-8]* **M 126.6, m -48°, b 161-163°, d_4^{20} 1.072, n_D^{20} 1.522.** Purify it as for 2-chlorotoluene above. [*Beilstein* **5** IV 806.]

4-Chlorotoluene *[106-43-4]* **M 126.6, m 7.2°, b 162.4°, d_4^{20} 1.07, n_D^{20} 1.521.** Dry it with BaO, fractionally distil it, then fractionally crystallise it by partial freezing. [*Beilstein* **5** IV 806.]

Chrysene *[218-01-9]* **M 228.3, m 255-256°.** Purify chrysene by chromatography on alumina from petroleum ether in a darkened room. Its solution in $*C_6H_6$ is passed through a column of decolorising charcoal, then crystallised by concentrating the eluate. It has also been purified by crystallising from $*C_6H_6$ or $*C_6H_6$/petroleum ether, and by zone refining. [Gorman et al. *J Am Chem Soc* **107** 4404 *1985*]. It is freed from 5*H*-benzo[*b*]carbazole by dissolving it in *N,N*-dimethylformamide and successively adding small portions of alkali and iodomethane until the fluorescent colour of the carbazole anion no longer appears when alkali is added. The chrysene (and alkylated 5*H*-benzo[*b*]carbazole) separate on addition of water. Final purification is by crystallisation from ethylcyclohexane and/or from 2-methoxyethanol [Bender et al. *Anal Chem* **36** 1011 *1964*]. It can be sublimed in a vacuum. [*Beilstein* **5** IV 2554.]

Chrysoidine G (4-phenylazo-1,3-benzenediamine monohydrochloride, basic orange 2) *[532-82-1]* **M 248.7, m 118-118.5°, pK_1 3.32, pK_2 5.21.** It is a red-brown powder which is recrystallised from H_2O. It gives a yellow solution in conc H_2SO_4 which turns orange on dilution. Its solubility at 15° is 5.5% (H_2O), 4.75% (EtOH), 6.0% (cellosolve), 9.5% (ethylene glycol), 0.005% (xylene) and is insoluble in $*C_6H_6$. The *hydroiodide* has **m** 184° (from EtOH) and the *picrate* forms red needles with **m** 196°. [Muramatsu *Bull Chem Soc Jpn* **31** 864 *1958*, *Beilstein* **6** IV 561.]

***trans*-Cinnamaldehyde** *[14271-10-9]* **M 132.2, m -4°, -7.5°, -9°, b 80°/0.4mm, 85.8°/1.1mm, 125-128°/11mm, 152.2°/40mm, 163.7°/60mm, 199.3°/200mm, 246°/760mm (dec), d_4^{20} 1.0510, n_D^{20} 1.623.** Purify the aldehyde by steam distillation (solubility is 1 in 700 parts H_2O) followed by distillation *in vacuo*. The *cis*-isomer has **b** 67-69°/40mm and d_4^{20} 1.0436 and n_D^{20} 1.5937. The *trans-semicarbazone* has **m** 210°(dec) from $CHCl_3$/MeOH (*cis-semicarbazone* has **m** 196°), the *trans-phenylsemicarbazone* has **m** 177° from $CHCl_3$/MeOH (the *cis-phenylsemicarbazone* has **m** 146°), the *trans-2,4-dinitrophenylhydrazone* has **m** 250°(dec) from MeOH as the *cis*-isomer [Gamboni et al. *Helv Chim Acta* **38** 255 *1955*, Holum *J Org Chem* **26** 4814 *1961*]. [*Beilstein* **9** IV 984.]

***cis*-Cinnamic acid (*Z*-3-phenyl-2-propenoic acid)** *[102-94-3]* **M 148.2, m 68° (for *allo*-form), pK^{25} 3.93.** The *cis*-acid is prepared by catalytic reduction of phenylpropiolic acid and after distillation in a high vacuum at ~95° it gives the most stable *allo*-isomer **m** 68°. Recrystallisation from petroleum ether yields **Liebermann's *iso*-cinnamic acid m 58°**. When the *allo*-acid (**m** 68°) is heated at 20° above its melting point in a sealed capillary for 0.5 hours and allowed to cool slowly, **Erlenmyer's *iso*-cinnamic acid m 42°** is formed. This form can also be obtained in larger amounts by heating the *allo*-acid at 80° for 3 hours, and on cooling it remains liquid for several weeks but gives the **m** 42° acid on innoculation with the crystals from the capillary tube. This form is unchanged in 6 weeks when kept in a dark cupboard. All three forms have the same pK values and the same rate of bromination. There is also a very labile form with **m** 32°. [Liebermann, *Chem Ber* **26** 1572 *1893*, Claisen & Crismer *Justus Liebigs Ann Chem* **218** 135 *1883*, Robinson & James *J Chem Soc* 1453 *1933*, Berthoud & Urech *Helv Chim Acta* **13** 437 *1930*, McCoy & McCoy *J Org Chem* **33** 2354 *1968*, *Beilstein* **9** IV 2001.]

***trans*-Cinnamic (*E*-3-phenyl-2-propenoic) acid** *[140-10-3, 621-82-9 for E-Z mixture]* **M 148.2, m 134.5-135°, pK^{25} 4.42 (4.50).** Crystallise the acid from *benzene, CCl_4, hot water, water/EtOH (3:1), or 20% aqueous EtOH. Dry it at 60° *in vacuo*. It is steam volatile. [*Beilstein* **9** IV 2002.]

***trans*-Cinnamic anhydride** *[538-56-7]* **M 278.4, m 136°.** Crystallise the anhydride from $*C_6H_6$ or toluene/petroleum ether (b 60-80°) or EtOH (**m** 135-136°). [*Beilstein* **9** III 2703, **9** IV 2018.]

***trans*-Cinnamoyl chloride** *[102-92-1]* **M 166.6, m 35-37°, b 101°/2mm, 154°/25mm, 256-258°/atm, $d_4^{37.6}$ 1.6202, $n_D^{37.6}$ 1.1632.** Refractionate it in a vacuum until the distillate solidifies on cooling, and recrystallise it from petroleum ether. The *trans-amide* has **m** 145-150° (from H_2O) [*Beilstein* **9** III 2711]. [Adams & Ulich *J Am Chem Soc* **42** 605 *1920*, Bergmann et al. *J Chem Soc* 2524 *1952*, *Beilstein* **9** H 587, **9** I 233, **9** II 390, **9** III 2710, **9** IV 2020.]

***N*-Cinnamoyl-*N*-phenylhydroxylamine** *[7369-44-0]* **M 239.3, m 158-163°.** Recrystallise the hydroxylamine from EtOH.

Cinnamyl alcohol *[104-54-1]* **M 134.2, m 33°, b 143.5°/14mm, λ_{max} 251nm (ε 18,180 M^{-1} cm^{-1}).** Crystallise the alcohol from diethyl ether/pentane. [*Beilstein* **6** I 281.]

Congo Red (4B) (cotton red B) *[573-58-0]* **M 696.7,** m **>360°, λ_{max} 497nm, pK_2^{28} 4.19.** Crystallise the dye from aqueous EtOH (1:3). Dry it in air. [*Beilstein* **6** I 342.]

Coniferyl alcohol [4-hydroxy-3-methoxy-cinnamyl alcohol, 3-(4-hydroxy-3-methoxy-phenyl)-2-propen-1-ol] *[458-35-5]* **M 180.2, m 73-75°, b 163-165°/3mm, pK^{25} 9.54.** It is soluble in EtOH and insoluble in H_2O. It can, however, be recrystallised from EtOH and distilled in a vacuum. It polymerises in dilute acid. The *benzoyl* derivative has **m** 95-96° (from petroleum ether), and the *tosylate* has **m** 66°. [Derivatives: Freudenberg & Achtzehn *Chem Ber* **88** 10 *1955*, UV: Herzog & Hillmer *Chem Ber* **64** 1288 *1931*, *Beilstein* **6** II 1093.]

Coronene *[191-07-1]* **M 300.4, m 438-440°, 442°, b 525°, λ_{max} 345nm (log ε 4.07).** Crystallise coronene from *benzene or toluene, then sublime it in a vacuum. [*Beilstein* **5** III 2651.]

***o*-Cresol** *[95-48-7]* **M 108.1, m 30.9°, b 191°/760mm, n_D^{41} 1.536, n_D^{46} 1.534, pK^{25} 10.22.** It can be freed from *m*- and *p*-isomers by repeated fractional distillation, It crystallises from *benzene by addition of petroleum ether. It has been fractionallly crystallised by partial freezing of its melt. The *3,5-dinitrobenzoate* (prepared from 3,5-dinitrobenzoyl chloride in dry pyridine, and recrystallised from EtOH or aqueous Me_2CO) has **m** 138°. [*Beilstein* **6** IV 1940.]

***m*-Cresol** *[108-39-4]* **M 108.1, f 12.0°, b 202.7°, d_4^{20} 1.034, n_D^{20} 1.544, pK^{25} 0.09.** Separation of the *m*- and *p*-cresols requires chemical methods, such as conversion to their sulfonates [Brüchner *Anal Chem* **75** 289 *1928*]. An equal volume of H_2SO_4 is added to *m*-cresol, stirred with a glass rod until solution is complete. Heat for 3 hours at 103-105°. Dilute carefully with 1-1.5 volumes of water, heat to boiling point and steam distil until all unsulfonated cresol has been removed. Cool and extract the residue with ether. Evaporate the solution until the boiling point reaches 134° and steam distil off the *m*-cresol. Another purification method involves distillation, fractional crystallisation from the melt, then redistillation. Free from *p*-cresol by solution in glacial acetic acid and bromination by about half of an equivalent amount of bromine in glacial acetic acid. The acetic acid is distilled off, then fractional distillation of the residue under vacuum gives bromocresols from which 4-bromo-*m*-cresol is obtained by crystallisation from hexane. Addition of the bromocresol in glacial acetic acid slowly to a reaction mixture of HI and red phosphorus or (more smoothly) of HI and hypophosphorus acid, in glacial acetic acid, at reflux, removes the bromine. After an hour, the solution is distilled at atmospheric pressure until layers are formed. Then it is cooled and diluted with water. The cresol is extracted with ether, washed with water, $NaHCO_3$ solution and again with water, dried with a little $CaCl_2$ and distilled [Baltzly et al. *J Am Chem Soc* **77** 2522 *1955*]. The *3,5-dinitrobenzoate* (prepared from 3,5-dinitrobenzoyl chloride in dry pyridine, and recrystallised from EtOH or aqueous Me_2CO) has **m** 165°. [*Beilstein* **6** IV 2035.]

***p*-Cresol** *[106-44-5]* **M 108.1, m 34.8°, b 201.9°, n^{41} 1.531, n^{46} 1.529, pK^{25} 10.27.** It can be separated from *m*-cresol by fractional crystalisation of its melt. Purify it by distillation, by precipitation from *benzene solution with petroleum ether, and *via* its benzoate, as for phenol. Dry it under vacuum over P_2O_5. It has also been crystallised from petroleum ether (b 40-60°) and by conversion to sodium *p*-cresoxyacetate which, after crystallisation from water is decomposed by heating with HCl in an autoclave [Savard *Ann Chim (Paris)* **11** 287 *1929*]. The *3,5-dinitrobenzoate* (prepared from 3,5-dinitrobenzoyl chloride in dry pyridine, and recrystallised from EtOH or aqueous Me_2CO) has **m** 189°. [*Beilstein* **6** II 2093.]

***o*-Cresolphthalein complexon (Metalphthalein)** *[2411-89-4]* **M 636.6, m 186°(dec), λ_{max} 575nm, pK_1 2.2, pK_2 2.9, pK_3 7.0, pK_4 7.8, pK_5 11.4, pK_6 12.0.** *o*-Cresolphthalein (a complexon precursor without the two bis-carboxymethylamino groups) is a contaminant and is one of the starting materials. It can be removed by dissolving the reagent in H_2O and adding a 3-fold excess of sodium acetate and fractionally precipitating it by dropwise addition of HCl to the clear filtrate. Wash the precipitate with cold H_2O and dry the *monohydrate* at 30° in a vacuum. The pure material gives a single spot on paper chromatography (eluting solvent EtOH/water/phenol, 6:3:1, and developing with NaOH). [Anderegg et al. *Helv Chim Acta* **37** 113 *1954*.] It complexes with Ba, Ca, Cd, Mg and Sr. [*Beilstein* **18** III/IV 8141.]

***o*-Cresol Red** *[1733-12-6]* **M 382.4, m 290°(dec), pK^{25} 1.26.** Crystallise it from glacial acetic acid. Dry it in air. Dissolve it in aqueous 5% $NaHCO_3$ solution and precipitate it from a hot solution by dropwise addition of aqueous HCl. Repeat the procedure till the UV maximum does not increase. [*Beilstein* **19** IV 1133.]

***o*-Cresotic acid (3-methylsalicylic acid)** *[83-40-9]* **M 152.2, m 163-164°, 165°, pK_1^{25} 3.32.** Crystallise the acid from water. [*Beilstein* **10** H 220, **10** II 131, **10** III 505, **10** IV 601.]

***m*-Cresotic acid (4-methylsalicylic acid)** *[50-85-1]* **M 152.2, m 176°, 177°, (182-183°), pK_1^{25} 3.15, pK_2^{25} 13.35.** Crystallise the acid from water. It sublimes at 130°/11mm. [*Beilstein* **10** H 233, **10** II 137, **10** III 521, **10** IV 617.]

***p*-Cresotic acid (5-methylsalicylic acid)** *[89-56-5]* **M 152.2, m 151°, 152°, 151-154°, pK_1^{25} 3.40, pK_2^{25} 13.45.** Crystallise the acid from H_2O. [*Beilstein* **10** H 227, **10** II 134, **10** III 516, **10** IV 610.]

Crystal Violet Chloride {Gentian violet, *N*-4[bis[4-(dimethylaminophenyl)methylene]-2,5-cyclohexadien-1-ylidene]-*N*-methylmethaninium chloride} *[548-62-9]* **M 408.0, pK 9.36.** Crystallise the dye from water (20ml/g), the crystals being separated from the chilled solution by centrifugation, then wash them with chilled EtOH (solubility is 1g in 10 ml of hot EtOH) and diethyl ether and dry under vacuum. It is soluble in $CHCl_3$ but insoluble in Et_2O. The carbinol is precipitated from an aqueous solution of the dye-hydrochloride, using excess NaOH, then dissolve in HCl and recrystallise it from water as the chloride [UV and kinetics: Turgeon & La Mer *J Am Chem Soc* **74** 5988 *1952*]. The *carbinol base* has **m** 195° (needles from EtOH). The *diphthalate* (blue and turns red in H_2O) crystallises from H_2O, **m** 153-154°(dec at 185-187°)[Chamberlain & Dull *J Am Chem Soc* **50** 3089 *1928*]. [*Beilstein* **13** H 233, **13** IV 2284.]

Cumene (isopropyl benzene) *[98-82-8]* **M 120.2, b 69-70°/41mm, 152.4°/760mm, d_4^{20} 0.864, n_D^{20} 1.49146, n_D^{25} 1.48892.** Usual purification is by washing it with several small portions of conc H_2SO_4 (until the acid layer is no longer coloured), then with water, 10% aqueous Na_2CO_3, again with water, and drying with $MgSO_4$, $MgCO_3$ or Na_2SO_4, followed by fractional distillation. It can then be dried with, and distilled from, Na, NaH or CaH_2. Passage through columns of alumina or silica gel removes oxidation products. It has also been steam distilled from 3% NaOH, and azeotropically distilled with 2-ethoxyethanol (which is subsequently removed by washing out with water). [*Beilstein* **5** IV 985.]

Cumene hydroperoxide *[80-15-9]* **M 152.2, b 60°/0.2mm, d_4^{20} 1.028, n_D^{24} 1.5232.** Purify the hydroperoxide by adding 100ml of 70% material slowly and with agitation to 300ml of 25% NaOH in water, keeping the temperature below 30°. The resulting crystals of the sodium salt are filtered off, washed twice with 25 ml portions of *benzene, then stirred with 100ml of *benzene for 20 minutes. After filtering off the crystals and repeating the washing, they are suspended in 100ml of distilled water and the pH is adjusted to 7.5 by addition of 4M HCl. The free hydroperoxide is extracted into two 20ml portions of *n*-hexane, and the solvent is evaporated under vacuum at room temperature, the last traces being removed at 40-50°/1mm [Fordham & Williams *Canad J Res* **27B** 943 *1949*]. Petroleum ether, **but not diethyl ether**, can be used instead of *benzene, and powdered solid CO_2 can replace the 4M HCl. [*Beilstein* **6** IV 3221.] *The material is potentially* **EXPLOSIVE.**

Cuminaldehyde (4-isopropylbenzaldehyde) *[122-03-2]* **M 148.2, b 82-84°/3.5mm, 120°/23mm, 131-135°/35mm, 235-236°/760mm, d_4^{20} 0.978, n_D^{20} 1.5301.** A likely impurity is the benzoic acid. Check the IR for the presence of OH from CO_2H, and the CO frequencies. If the acid is present, then dissolve the aldehyde in Et_2O, wash it with 10% $NaHCO_3$ until effervescence ceases, then with brine, dry over $CaCl_2$, evaporate and distil the residual oil, preferably under vacuum. It is almost insoluble in H_2O, but soluble in EtOH and Et_2O. The *thiosemicarbazone* has **m** 147° after recrystallisation from aqueous EtOH, MeOH or *C_6H_6. [Crounse *J Am Chem Soc* **71** 1263 *1949*, Bernstein et al. *J Am Chem Soc* **73** *906* 1951, Gensler & Berman *J Am Chem Soc* **80** 4949 *1958*, *Beilstein* **7** H 318, **7** II 347, **7** III 1095, **7** IV 723.]

9-Cyanoanthracene (anthracene-9-carbonitrile) *[1210-12-4]* **M 203.2, m 134-137°, 173-177°.** Crystallise the nitrile from EtOH or toluene, and sublime it in a vacuum in the dark under N_2 [Ebied et al. *J Chem Soc, Faraday Trans 1* **76** 2170 *1980*, Kikuchi et al. *J Phys Chem* **91** 574 *1987*]. [*Beilstein* **9** I 304.]

9-Cyanoanthracene photodimer *[33998-38-8]* **M 406.4, dec to monomer above ~147°.** Purify the dimer by dissolving it in the minimum amount of $CHCl_3$ followed by addition of EtOH at 5° [Ebied et al. *J Chem Soc, Faraday Trans 1* **75** 1111 *1979*, Ebied et al. *J Chem Soc, Faraday Trans 1* **76** 2170 *1980*].

***p*-Cyanobenzoic acid** *[619-65-8]* **M 147.1, m 219°, 219-221° (dec), pK^{25} 3.55.** Crystallise the acid from water and dry it in a vacuum desiccator over Sicapent. [*Beilstein* **9** IV 3324.]

4-Cyanobenzoyl chloride *[6068-72-0]* **M 165.6, m 68-70°, 69-70°, 73-74°, b 132°/8mm, 150-151°/25mm.** If the IR shows the presence of OH, then treat it with $SOCl_2$ boil for 1 hour, evaporate and distil it in a vacuum. The distillate solidifies and can be recrystallised from petroleum ether. It is moisture sensitive and an **IRRITANT.** [Ashley et al. *J Chem Soc* 103 *1942*, Fison et al. *J Org Chem* **16** 648 *1951*, [*Beilstein* **9** III 4255, **14** IV 3327.]

p*-Cyanophenol** (p*-hydroxybenzonitrile)** *[767-00-0]* **M 119.1, m 113°, pK^{25} 7.97.** Crystallise the phenol from petroleum ether, *benzene or water and keep it under vacuum over P_2O_5. [Bernasconi & Paschelis *J Am Chem Soc* **108** 2969 *1986*.] [*Beilstein* **10** H 167, **10** IV 441.]

Cyclohexylbenzene (phenylcyclohexane) *[827-52-1]* **M 160.3, f 6.8°, b 237-239°, d_4^{20} 0.950, n_D^{20} 1.5258.** Purify it by fractional distillation, and by fractional freezing. [*Beilstein* **5** IV 1424.]

Cyclopropyldiphenylcarbinol (cyclopropyldiphenylmethanol) *[5785-66-0]* **M 224.3, m 86-87°.** Crystallise the carbinol from *n*-heptane or *C_6H_6/pentane (**m** 82-83°). It sublimes at 60°/0.001mm. The *2,4-dinitrobenzoate* has **m** 140°. [*Beilstein* **6** III 3517, **6** IV 4888.]

***p*-Cymene (4-isopropyltoluene)** *[99-87-6]* **M 134.2, b 177.1°/760mm, d_4^{20} 0.8569, n_D^{20} 1.4909, n_D^{25} 1.4885.** Wash *p*-cymene with cold, conc H_2SO_4 until there is no further colour change, then repeatedly with H_2O, 10% aqueous Na_2CO_3 and H_2O again. Dry it over Na_2SO_4, $CaCl_2$ or $MgSO_4$, and distil it. Further purification steps include steam distillation from 3% NaOH, percolation through silica gel or activated alumina, and a preliminary reflux for several days over powdered sulfur. Store it over CaH_2. [*Beilstein* **5** IV 1060.]

Deoxybenzoin *[451-40-1]* **M 196.3, m 60°, b 177°/12mm, 320°/760mm.** Crystallise deoxybenzoin from EtOH and/or distil it in a vacuum. [*Beilstein* **7** II 368, **7** III 2098, **7** IV 1393.]

(±)-Desyl bromide (α-bromo-desoxybenzoin, ω-bromo-ω–phenyl acetophenone) *[484-50-0]* **M 275.2, m 57.1-57.5°.** Crystallise it from 95% EtOH. [*Beilstein* **7** H 436, **7** II 370, **7** III 2122.]

(±)-Desyl chloride (α-chloro-desoxybenzoin, ω-chloro-ω–phenyl acetophenone) *[447-31-4]* **M 230.7, m 62-64°, 66-67°, 67.5°, 68°.** For the purification of small quantities recrystallise it from petroleum ether (b 40-60°), but use MeOH or EtOH for larger quantities. For the latter solvent, dissolve 12.5g of chloride in 45ml of boiling EtOH (95%), filter and the filtrate yields colourless crystals (7.5g) on cooling. A further crop (0.9g) can be obtained by cooling in an ice-salt bath. It turns brown on exposure to sunlight but it is stable in sealed dark containers. The *R(+)-enantiomer* has **m** 75-76° (from petroleum ether) and $[\alpha]_{546}$ +168.4° (c 0.6, Me_2CO) [Roger & Wood *J Chem Soc* 811 *1954*]. [Henley & Turner *J Chem Soc* 1182 *1931*, Ward *Org Synth* Coll Vol **II** 159 *1943*, *Beilstein* **7** H 436, **7** I 234, **7** II 369, **7** III 2106, **7** IV 1396.]

Diacetoxyiodobenzene (iodobenzenediacetate) *[3240-34-4]* **M 322.1, m 163-165°.** The purity of diacetoxyiodobenzene can be checked by treatment with H_2SO_4 then KI, and the liberated I_2 is estimated with standard thiosulfate. It has been recrystallised from 5M acetic acid and dried overnight in a vacuum desiccator over $CaCl_2$. The surface of the crystals may become slightly yellow but this does not affect its usefulness. [Sharefkin & Saltzman *Org Synth* Coll Vol **V** 600 *1973*, *Beilstein* **5** IV 693.]

1,2-Diacetyl benzene *[704-00-7]* **M 162.2, m 39-41°, 41-42°, b 110°/0.1mm, 148°/20mm.** Purify it by

distilling and by recrystallising from petroleum ether. The *bis-2,4-dinitrophenylhydrazone* has **m** 221° (dec). [Halford & Weissmann *J Org Chem* **17** 1646 *1952*, Riemschneider & Kassahn *Chem Ber* **92** 1705 *1959*, [*Beilstein* **7** III 3501, **7** IV 2155.]

1,4-Diacetyl benzene *[1009-61-6]* **M 162.2, m 113-5-114.2°, b 128-130°/3mm.** Crystallise it from EtOH (**m** 114°) or *benzene and dry it in a vacuum over $CaCl_2$. Also purify it by dissolving it in acetone, treating with Norit, evaporating and recrystallising from MeOH. The *dioxime* has **m** 248-259°. [Wagner et al. *J Am Chem Soc* **108** 7727 *1986*]. [*Beilstein* **7** H 686, **7** II 624, **7** III 3504, **7** IV 2156.]

1,4-Diaminoanthraquinone *[128-95-0]* **M 238.3, m 268°.** Purify the anthraquinone by thin-layer chromatography on silica gel using toluene/acetone (9:1) as eluent. The main band is scraped off and extracted with MeOH. The solvent is evaporated, and the quinone is dried in a drying pistol [Land et al. *J Chem Soc, Faraday Trans 1* **72** 2091 *1976*]. It crystallises from EtOH (**m** 269°) in dark violet crystals. Store it in sealed ampoules in the dark. [*Beilstein* **14** H 197, **14** II 113, **14** III 437, **14** IV 458.]

1,5-Diaminoanthraquinone *[129-44-2]* **M 238.3, m 319°.** Recrystallise it from aniline (**m** 313-314°), EtOH or acetic acid [Flom & Barbara *J Phys Chem* **89** 4481 *1985*]. [*Beilstein* **14** H 303, **14** I 467, **14** II 116, **14** III 466, **14** IV 479.]

2,6-Diaminoanthraquinone *[131-14-6]* **M 238.3, m 310-320°.** Crystallise it from pyridine or nitrobenzene (red needles). Column-chromatography on Al_2O_3/toluene is used to remove a fluorescent impurity, then it is recrystallised from EtOH. [*Beilstein* **14** H 215, **14** I 471, **14** II 120, **14** III 480, **14** IV 486.]

3,3'-Diaminobenzidine tetrahydrochloride ($2H_2O$) *[7411-49-6]* **M 396.1, m >300°(dec), $pK_{Est(1)}$ ~3.3, $pK_{Est(2)}$ ~4.7 (free base).** Dissolve the salt in water and precipitate it by adding conc HCl, then drying it over solid NaOH. [*Beilstein* **13** IV 530.]

3,4-Diaminobenzoic acid *[619-05-6]* **M 152.2, m 213°(dec), 228-229°, pK_1^{25} 2.57 (4-NH_2), pK_2^{25} 3.39 (3-NH_2), $pK_{Est(3)}$ ~5.1 (CO_2H).** Crystallise it from H_2O or toluene. [*Beilstein* **15** IV 1503.]

3,5-Diaminobenzoic acid *[535-87-5]* **M 152.2, m 235-240°(dec), pK^{25} 5.13 (CO_2H), pK^{25} 7.12 (in 80% aqueous 2-$MeOCH_2CH_2OH$).** Crystallise the acid from water. The *dihydrochloride* has **m** 226-228°(dec). [*Beilstein* **14** H 453, **14** III 1179, **14** IV 1304.]

3,4-Diaminobenzophenone *[39070-63-8]* **M 212.3, m 116-117°, $pK_{Est(1)}$ ~ <0, $pK_{Est(2)}$ ~2.5.** Crystallise it from *C_6H_6/petroleum ether and sublime it *in vacuo* [Ayyanger et al. *Org Prep Proced Int* **23** 627 *1991*].

4,4'-Diaminobenzophenone *[611-98-3]* **M 212.3, m 242-244°, 243-245°, 246.5-247.5° (after sublimation at 0.0006mm), pK_1^{25} 1.37, pK_2^{25} 2.92.** Purify the phenone by recrystallisation from EtOH and by sublimation in high vacuum. The *dihydrochloride* has **m** 260°(dec) (from EtOH), and the *thiosemicarbazone* has **m** 207-207.5°(dec) (from aqueous EtOH). [Kuhn et al. *Chem Ber* **75** 711 *1942*, *Beilstein* **14** IV 255.]

1,2-Diamino-4,5-dichlorobenzene *[5348-42-5]* **M 177.0, m 162°, 162-163°, 163°, $pK_{Est(1)}$~1.0, $pK_{Est(2)}$~2.9.** Reflux the amine with activated charcoal in CH_2Cl_2, followed by recrystallisation from Et_2O/petroleum ether or petroleum ether [Koolar & Kochi *J Org Chem* **52** 4545 *1987*]. *Alternatively*, recrystallise the diamine from hexane, *C_6H_6, petroleum ether or H_2O (Na_2SO_4), and sublime it at 150°/15mm. [*Beilstein* **13** IV 72.]

4,4'-Diamino-3,3'-dinitrobiphenyl *[6271-79-0]* **M 274.2, m 275°, pK_{Est} ~ -0.2.** Crystallise the biphenyl from aqueous EtOH or pyridine/EtOH. [*Beilstein* **13** H 236, **13** I 68, **13** II 108, **13** III 415, **13** IV 387.]

4,4'-Diaminodiphenylamine *[537-65-5]* **M 199.3, m 158°, pK_{Est} ~5.0.** Crystallise the amine from water (its solubility at 25° is 0.42%). [*Beilstein* **13** H 110, **13** I 36, **13** II 55, **13** III 256, **13** IV 203.]

4,4'-Diaminodiphenyl ether (4,4'-oxydianiline, DADPE) *[101-80-4]* **M 200.2, m 185°, 186-187°, 188-192°,**

pK^{25} 5.12 (50% EtOH). This base has been prepared by several syntheses including, condensation of *p*-nitrophenol with *p*-chloroaniline, nitration of diphenyl ether to 4,4'-dinitrodiphenyl ether and reduction with hydrazine and Raney Ni [Shamis & Dashevski *J Org Chem, USSR Engl Transl* **3** 1005 *1967*], a Friedel-Crafts reaction of diphenyl ether (AcCl, $AlCl_3$) to 4,4'-diacetyldiphenyl ether (m 99-100°), conversion to the dioxime (m 180-183°), and a bis-Beckman rearrangement (AcOH, Ac_2O, HCl gas) gives 4,4'-bis-acetamidodiphenyl ether (90%). This amide (46g) in H_2O (600ml) and concentrated HCl (60ml) is refluxed for 2 hours until it all dissolved, filtered (charcoal), the filtrate is basified with Na_2CO_3 solution, the precipitate is filtered off, washed with H_2O, and dried at 100-110° to give the *free base* (32g). It is purified by zone melting and/or by sublimation at high vacuum. In the UV it has λ_{max} at 248 and 300nm in EtOH. [Franovskii et al. *J Org Chem, USSR Engl Transl* **6** 2315 *1970*.] The *benzenesulfonate salt* crystallises from MeOH with **m 286-288°(dec)**. [*Beilstein* **13** H 441, **13** I 148, **13** III 106, **13** IV 1038.]

4,4'-Diaminodiphenylmethane *[101-77-9]* **M 198.3, m 91.6-92°, 92-93°, b 232°/9mm, pK$_{Est}$ ~4.9.** Crystallise the amine from water, 95% EtOH or *benzene. [*Beilstein* **13** IV 390.]

4,4-Diaminodiphenyl sulfide (4,4'-thioaniline) *[139-65-1]* **M 216.3, m 108-109°, pK^{20} 2.28 (1:1 EtOH/H_2O).** It separates as needles from EtOH and is a **possible mutagen**. The free base is used for the detection of NO_3^- ions. The *diacetate* crystallises from aqueous AcOH with **m** 182° and the *sulfoxide*, [119-59-5] **m** 184°, forms prisms from EtOH or H_2O. [Fuson & Melamed *J Org Chem* **13** 690 I1948*, Beilstein* **13** III 1246, **13**, IV 1246.]

2,7-Diaminofluorene *[524-64-4]* **M 196.3, m 165°, pK$_{Est}$ ~4.6.** Recrystallise it from H_2O. [*Beilstein* **13** IV 449.]

1,5-Diaminonaphthalene *[2243-62-1]* **M 158.2, m 190°, pK^{25} 4.12.** Recrystallise the amino-naphthalene from boiling H_2O, but this is wasteful due to poor solubility. Boil it in chlorobenzene (charcoal), filter hot and cool the filtrate (preferably under N_2). This gives colourless crystals. Dry it in a vacuum till free from chlorobenzene (odour), and store it in sealed ampoules under N_2 away from light. [*Beilstein* **13** IV 340.]

1,8-Diaminonaphthalene *[479-27-6]* **M 158.2, m 66.5°, b 205°/12mm, pK^{25} 4.44.** Crystallise 1,8-diaminonaphthalene from water or aqueous EtOH, and sublime it in a vacuum. The *N,N'-dimethyl* derivative [20734-56-9] has **m** 103-104° and **pK^{25}** 5.61, the *N,N,N'-trimethyl-* derivative [20734-57-0] has **m** 29-30° and **pK^{25}** 6.43. [Hodgson et al. *J Chem Soc* 202 *1945*, *Beilstein* **13** IV 344.]

2,3-Diaminonaphthalene *[771-97-1]* **M 158.2, m 199°, pK^{21} 3.54 (in 50% aqueous EtOH).** Crystallise the diamine from water, or dissolve it in 0.1M HCl, by heating to 50°. After cooling, the solution is extracted with decalin to remove fluorescent impurities and centrifuged. [*Beilstein* **13** IV 346.]

2,5-Di-*tert*-amylhydroquinone *[79-74-3]* **M 250.4, m 185.8-186.5°.** Crystallise the hydroquinone under N_2 from boiling AcOH (7ml/g) plus boiling water (2.5ml/g). [Stolow & Bonaventura *J Am Chem Soc* **85** 3636 *1963*]. Store it in sealed ampoules under N_2 away from light. [*Beilstein* **6 H 952,** 6 III 4748.]

Di-n-amyl phthalate (dipentyl phthalate) *[131-18-0]* **M 306.4, b 204-206°/11mm, d_4^{25} 1.023, n_D^{20} 1.489.** Wash the ester with aqueous Na_2CO_3, then distilled water. Dry it with $CaCl_2$ and distil it in a vaccum. Store it in a vacuum desiccator over P_2O_5. [*Beilstein* **9** IV 3178.]

Diazoaminobenzene (1,3-diphenyltriazene) *[136-36-6]* **M 197.2, m 99°, 100°.** Crystallise the triazene from petroleum ether (b 60-80°) (**m** 94-96°), 60% MeOH/water or 50% aqueous EtOH (charcoal) containing a small amount of KOH. Its solubility in petroleum ether (b 60-80°) is ~6%. Also purify it by chromatography on alumina/toluene and elute with toluene/petroleum ether. Store the pale yellow needles in the dark. [Hartman & Dickey *Org Synth* Coll Vol **II** 163 *1943*, *Beilstein* **16** H 687, **16** I 404, **16** II 351, **16** III 643, **16** IV 904.]

Dibenzalacetone [1,5-diphenyl-1,4-dien-3-one, 1,5-(bisphenyl)-penta-1*E*,4*E*-diene-3-one] *[538-58-9]* **M 234.3, m 107-113°, 112°, 120-122°.** Purify the ketone by flash chromatography (150 mesh Al_2O_3 deactivated with 6% v/w H_2O) using petroleum ether 40-60°/EtOAc (4/1, v/v), and the yellow solid is recrystallised by

layering a concentrated CH_2Cl_2 solution with hexane (i.e. CH_2Cl_2/hexane, 1:4, v/v). Also recrystallise the ketone from hot ethyl acetate (2.5ml/g) or EtOH. The IR (CH_2Cl_2) has ν_{max} at 1657m, 1651m (C=O), 1627vs (C=C), 1591w (C=C aromatic), 1574w (C=C aromatic), 983m (CH trans) cm^{-1}; and UV has λ_{max} (THF) at 233 (π-π*) and 321 (n- π*) nm; the ^1H NMR (400MHz, $CDCl_3$) has δ at 7.65-7.15 (m, 10 H, ArH), 4.4 (dd, J = 5.8, 10.0 Hz, 1 H, C3a-H), 3.45-3.30 (m, 1 H, C6-H), 3.15-3.00 (m, 1 H, C6-H), 1.90-1.55 (m, 3 H, C4-H, C5-H_2), 0.95-0.75 (m, 1 H, C4-H), 0.40 (s, 3 H, B-CH_3). [*Beilstein* **7** IV 1747.]

Dibenz[*a,h*]anthracene (1,2:5,6-dibenzanthracene) *[53-70-3]* **M 278.4, m 266-267°.** The yellow-green colour (due to other pentacyclic impurities) is removed from it by crystallising from *benzene or by selective oxidation with lead tetraacetate in acetic acid [Moriconi et al. *J Am Chem Soc* **82** 3441 *1960*]. [*Beilstein* **5** IV 2722.]

***trans*-1,2-Dibenzoylethylene (*trans*-1,4-diphenyl-2-butane-1,4-dione)** *[959-28-4]* **M 236.3, m 109-112°, 111°.** It crystallises from MeOH or EtOH as yellow needles [Koller et al. *Helv Chim Acta* **29** 512 *1946*]. The *dioxime* has **m** 210-211°(dec) from AcOH. [IR: Kuhn et al. *J Am Chem Soc* **72** 5058 *1950*, Yates *J Am Chem Soc* **74** 5375 *1952*, Erickson et al. *J Am Chem Soc* **73** 5301 *1951*, *Beilstein* **7** IV 2578.]

Dibenzoylmethane (1,3-diphenyl-1,3-propanedione) *[120-46-7]* **M 224.3, m 80°.** Crystallise dibenzoylmethane from petroleum ether or MeOH. [*Beilstein* **7** IV 2512.]

2,3,6,7-Dibenzphenanthrene (pentaphene) *[222-93-5]* **M 276.3, m 255-256°, 257°.** Purify pentaphene through Al_2O_3 with $^*C_6H_6$ or xylene as eluant. It crystallises from xylene as yellow plates and sublimes in high vacuum. The *dipicrate* forms orange needles **m** 184° from $^*C_6H_6$. (Clar & John *Ber* **64** 986 *1931*, Clar & Stewart *J Chem Soc* 3215 *1951*, *Tet Lett* 3023 *1965*, French & Zander *Ber* **99** 396 *1966*.]

Dibenzyl amine *[103-49-1]* **M 197.3, m -26°, b 113-114°/0.1mm, 174-175°/6mm, 270°/250mm, 300° (partial dec), d_4^{20} 1.027, n_D^{20} 1.576, pK^{25} 8.52.** Purify the amine by distillation in a vacuum. **It causes burns to the skin.** The *dihydrochloride* has **m** 265-266° (from MeOH/HCl), and the *tetraphenyl boronate* has **m** 129-133°. [Bradley & Maisey *J Chem Soc* 247 *1954*, Hall *J Phys Chem* **60** 63 *1956*, Donetti & Bellora *J Org Chem* **37** 3352 *1972*, *Beilstein* **12** IV 2179.]

Dibenzyl disulfide *[150-60-7]* **M 246.4, m 71-72°, 74-75°, b 142-148°/0.05-0.1mm, 210-216°/18mm.** Crystallise the disulfide from EtOH (**m** 77°), petroleum ether or CS_2 (**m** 72°) or distil it. The $AgNO_3$ complex has **m** 103°. [*Beilstein* **6** H 465, **6** I 229, **6** II 437, **6** III 1635, **6** IV 2760.]

Dibenzylethylenediamine (benzathine, DBED) *[140-28-3]* **M 240.4, m 26°, b 195°/4mm, d_4^{20} 1.02, n_D^{20} 1.563, $pK_{Est(1)}$~ 5.9, $pK_{Est(2)}$~ 8.9.** Dissolve DBED in acid, extract with toluene, basify, extract it with Et_2O, dry over solid KOH, evaporate and fractionate it *in vacuo*. The *diacetate* crystallises from H_2O by addition of EtOH and has **m** 111° (solubility in H_2O is ~25%). The *dihydrochloride* has **m** 306-308° (from H_2O) and the *dipicrate* has **m** 212°(dec) (from H_2O). [Frost et al., *J Am Chem Soc* **71** 3842 *1949*, *Beilstein* **12** H 1067, **12** III 2304.]

Dibenzyl ketone (1,3-diphenyl-2-propanone) *[102-04-5]* **M 210.3, m 34.0°.** Fractionally crystallise it from its melt, then crystallise it from petroleum ether. Store it in the dark. [*Beilstein* **7** IV 1420.]

Dibenzyl malonate *[15014-25-2]* **M 284.3, b 188-190°/0.2mm, 193-196°/1mm, d_4^{20} 1.158, n_D^{20} 1.5452.** Dissolve the ester in toluene, wash it with aqueous $NaHCO_3$, H_2O, dry over $MgSO_4$, filter, evaporate and distil it at high vacuum. [Ginsburg & Pappo *J Am Chem Soc* **75** 1094 *1953*, Baker et al. *J Org Chem* **17** 77 *1952*, *Beilstein* **6** IV 2270.]

Dibenzyl sulfide *[538-74-9]* **M 214.3, m 48.5°, 50°.** Crystallise the sulfide from EtOH/water (10:1), or repeatedly from Et_2O. It has also been purified by chromatography on Al_2O_3 (pentane as eluent), then recrystallised from EtOH [Kice & Bowers *J Am Chem Soc* **84** 2390 *1962*]. Dry it in a vacuum at 30° over P_2O_5, fused under nitrogen and re-dried. [*Beilstein* **6** IV 2649.]

2,4-Dibromoaniline *[615-57-6]* **M 250.9, m 79-80°, pK^{25} 1.87.** Crystallise the aniline from aqueous EtOH. The *picrate* has **m** 124°. [*Beilstein* **12** H 655, **12** I 326, **12** II 356, **12** III 1471, **12** IV 1532.]

9,10-Dibromoanthracene *[523-27-3]* **M 336.0, m 222-224°, 226°.** Recrystallise it from toluene, xylene or CCl_4 (yellow needles), and sublime it in a vacuum [Johnston et al. *J Am Chem Soc* **109** 1291 *1987*]. [Heilbron & Heaton *Org Synth* Coll Vol **I** 207 *1941*, *Beilstein* **5** H 665.]

***p*-Dibromobenzene** *[106-37-6]* **M 235.9, m 87.8°.** Steam distil the dibromobenzene, then crystallise it from EtOH or MeOH and dry it in the dark under vacuum. Purify it by zone melting. [*Beilstein* **5** IV 683.]

2,5-Dibromobenzoic acid *[610-71-9]* **M 279.9, m 157°, pK$_{Est}$ ~1.5.** Crystallise the acid from water or EtOH. [*Beilstein* **9** H 358, **9** I 147, **9** II 237, **9** III 1428, **9** IV 1027.]

4,4'-Dibromobiphenyl *[92-86-4]* **M 312.0, m 164°, b 355-360°/760mm.** Crystallise it from MeOH. [*Beilstein* **5** IV 1820.]

(±)-2,2'-Dibromo-1,1'-binaphthyl *[74866-28-7, (±) 76284-65-6]* **M 412.1, m 178-183°, 180.5-181°.** Purify the binaphthyl by chromatography through a silica gel column (70-230mesh) using hexane as eluent. It gives pale yellow crystals from EtOH with **m** 187.3-187.9°. The *R*-(+)-*enantiomer* [86688-08-6] crystallises from hexane with **m** 157-157.5° and $[\alpha]_D^{25}$ +32.9° (c 1, pyridine) [Brown et al. *J Org Chem* **50** 4345 *1985*]. [Okamoto et al. *J Am Chem Soc* **103** 6971*1981*, *Beilstein* **5** III 2465.]

α,α-Dibromodeoxybenzoin *[15023-99-1]* **M 354.0, m 111.8-112.7°.** Crystallise α,α-dibromo deoxybenzoin from acetic acid, 50% aqueous EtOH (prisms, **m** 109-112°) or Et_2O (**m** 112°). [Curtius & Lang *J Prakt Chem* **44** 547 *1891, Beilstein* **7** H 436, **7** III 2114.]

2,5-Dibromonitrobenzene *[3460-18-2]* **M 280.9, m 84°, 85-86°.** It crystallises from Me_2CO or EtOH. [*Beilstein* **5** H 250, **5** II 190, **5** III 621, **5** IV 732.]

2,6-Dibromo-4-nitrophenol *[99-28-5]* **M 280.9, m 143-144°, pK^{25} 3.39.** Crystallise the phenol from aqueous EtOH, 50% aqueous AcOH (**m** 144-145°, dec varies with rate of heating). Dry it in an oven at 40-60° or *in vacuo* over NaOH. [Hartman & Dickey *Org Synth* Coll Vol **II** 173 *1943*, *Beilstein* **6** H 246, **6** I 123, **6** II 234, **6** III 849, **6** IV 1366.]

2,4-Dibromophenol *[615-58-7]* **M 251.9, m 37°, 41-42°, b 154°/10mm, 239°/760mm, pK^{25} 7.79.** Crystallise the phenol from $CHCl_3$ at -40°, or distil it in a vacuum. [*Beilstein* **6** H 202, **6** I 106, **6** II 188, **6** III 753, **6** IV 1061.]

2,6-Dibromophenol *[608-33-3]* **M 251.9, m 56-57°, b 138°/10mm, 255-256°/740mm, pK^{25} 6.67.** Distil the phenol under vacuum (at 10mm), then crystallise it from cold $CHCl_3$ or from EtOH/water. [*Beilstein* **6** H 202, **6** I 106, **6** II 188, **6** III 755, **6** IV 1064.]

α,α'-Dibromo-*o*-xylene *[91-13-4]* **M 264.0, m 95°, 95-96°, 98-99°, b 129-130°/4.5mm.** Crystallise it from $CHCl_3$ or petroleum ether, and/or distil it under vacuum. [Wenner *Org Chem* **17** 527 *1952*, *Beilstein* **5** H 366, **5** I 180, **5** II 285, **5** III 819, **5** IV 929.]

α,α'-Dibromo-*m*-xylene *[626-15-3]* **M 264.0, m 77°, 78-79°, b 156-160°/12mm.** Crystallise it from acetone or *benzene, and fractionally distil it under vacuum. [Wenner *Org Chem* **17** 527 *1952*, *Beilstein* **5** H 374, **5** I 184, **5** II 294, **5** III 839, **5** IV 946.]

α,α'-Dibromo-*p*-xylene *[623-24-5]* **M 264.0, m 143.4°, 142-144°, 145-147°, b 155-158°/12-15mm, 245°/760mm.** Distil it under a vacuum and recrystallise it from EtOH, *benzene or chloroform. [Wenner *Org Chem* **17** 527 *1952*, *Beilstein* **5** H 385, **5** I 187, **5** II 301, **5** III 859, **5** IV 970.]

α-Dibutylamino-α-(*p*-methoxyphenyl)acetamide (Ambucetamide) *[519-88-0]* **M 292.4, m 134°.** Crystallise ambucetamide from EtOH containing 10% diethyl ether. [Janssen *J Am Chem Soc* **76** 6192 *1954*, *Beilstein* **14** IV 2101.]

2,5-Di-*tert*-butyl aniline *[21860-03-7]* **M 205.4, m 103-104°, 103-106°, pK^{25} 3.34 (50% aqueous MeOH), 3.58 (90% aqueous MeOH).** The aniline recrystallises from EtOH in fine needles after steam distillation. It has a pKa^{25} of 3.58 (50% aqueous EtOH). The *tosylate* has **m** 164° (from AcOH). [Bell & Wilson *J Chem Soc* 2340 *1956*, Carpenter et al. *J Org Chem* **16** 586 *1951*, Bartlett et al. *J Am Chem Soc* **76** 2349 *1954*, *Beilstein* **12** IV 2891.]

***p*-Di-*tert*-butylbenzene** *[1012-72-2]* **M 190.3, m 80°, 236°/760mm.** Crystallise it from Et_2O or EtOH and dry it under vacuum over P_2O_5 at 55°. [Tanner et al. *J Org Chem* **52** 2142 *1987*, *Beilstein* **5** II 344.]

2,6-Di-*tert*-butyl-1,4-benzoquinone *[719-22-2]* **M 220.3, m 66-67°.** It can be recrystallised from MeOH and sublimes in a vacuum. [*Beilstein* **7** IV 2116.]

3,5-Di-*tert*-butyl-*o*-benzoquinone *[3383-21-9]* **M 220.3, m 112-114°, 113-114°.** It can be recrystallised from MeOH or petroleum ether, and forms fine red plates or rhombs. [Flaig et al. *Justus Liebigs Ann Chem* **597** 196 *1955*, IR: Ley & Müller *Chem Ber* **89** 1402 *1956*, *Beilstein* **7** IV 2113.]

3,5-Di-*tert*-butyl catechol *[1020-31-1]* **M 222.3, m 99°, 99-100°, pK$_{Est(1)}$~11.0, pK$_{Est(2)}$~13.1.** Recrystallise the catechol from petroleum ether. [Ley & Müller *Chem Ber* **89** 1402 *1956*, UV Flaig et al. *Z Naturforschung* **10b** 668 *1955*.] Also purify it by crystallising three times from pentane [Funabiki et al. *J Am Chem Soc* **108** 2921 *1986*].

2,6-Di-*tert*-butyl-*p*-cresol (2,6-di-*tert*-butyl-4-methylphenol, butylatedhydroxytoluene, BHT or DBPC) *[128-37-0]* **M 230.4, m 71.5°, pK^{25} 12.23.** Dissolve BHT in *n*-hexane at room temperature, then cool with rapid stirring, to -60°. The precipitate is separated, redissolved in hexane, and the process is repeated until the mother liquor is no longer coloured. The final product is stored under N_2 at 0° [Blanchard *J Am Chem Soc* **82** 2014 *1960*]. It has also been recrystallised from EtOH, MeOH, *benzene, *n*-hexane, methylcyclohexane or petroleum ether (b 60-80°), and is dried in a vacuum. [*Beilstein* **6** IV 3511.]

2,6-Di-*tert*-butyl-4-dimethylaminomethylphenol *[88-27-7]* **M 263.4, m 93-94°, b 172°/30mm, pK$_{Est}$ ~12.0.** Crystallise it from *n*-hexane. [*Beilstein* **13** IV 2014.]

Di-*tert*-butyldiperphthalate *[2155-71-7]* **M 310.3, m (48°) 57-57.5°, decomposes at 108°.** Crystallise the perphthalate from Et_2O or petroleum ether and dry it over H_2SO_4. The IR has ν_{max} at 1772cm^{-1} in CCl_4. [Milas & Surgemor *J Am Chem Soc* 68 642 *1946*, Milas & Kelin *J Org Chem* **36** 2900 *1971*, *Beilstein* **9** III 4190, **9** IV 3260.] **CARE**, potentially **EXPLOSIVE**.

2,6-Di-*tert*-butyl-4-ethylphenol *[4130-42-1]* **M 234.4, m 42-44°, pK$_{Est}$ ~12.3.** Crystallise the phenol from aqueous EtOH or *n*-hexane. [*Beilstein* **6** IV 3529.]

2,5-Di-*tert*-butylhydroquinone *[88-58-4]* **M 222.3, m 222-223°.** Crystallise the hydroquinone from *C_6H_6 or AcOH. [*Beilstein* **6** III 4741.]

2,6-Di-*tert*-butyl-4-isopropylphenol *[5427-03-2]* **M 248.4, m 39-41°, 38-42°, b 105-106°/0.3mm, pK$_{Est}$ ~12.3.** Crystallise the phenol from *n*-hexane or aqueous EtOH. It is used for making the respective *phenoxyl radical*. [Cook & Norcross *J Am Chem Soc* **78** 3797 *1956*, *Beilstein* **6** III 3534.]

2,6-Di-*tert*-butylphenol *[128-39-2]* **M 206.3, m 37-38°, pK^{25} 11.70.** Crystallise the phenol from aqueous EtOH or *n*-hexane. [*Beilstein* **6** III 2061.]

Dibutyl phthalate (DBP, butyl phthalate) *[84-74-2]* **M 278.4, f -35°, b 44°/2.5x10^{-4}mm, 182°/5mm,**

206°/20mm, 340°/760mm, d_4^{20} 1.4929, d^5 1.0426, n_D^{25} 1.490. Wash DBP with H_2O (to free it from alcohol), then dilute NaOH (to remove any butyl hydrogen phthalate or acid), aqueous $NaHCO_3$ (charcoal), then distilled water. Dry it ($CaCl_2$), distil it at 10torr or less, and store it in a desiccator over P_2O_5. [*Beilstein* **9** II 586, **9** III 4102, **9** IV 3175.]

Dichloramine-T (*N,N*-dichloro-*p*-toluenesulfonamide) *[473-34-7]* **M 240.1, m 83°.** Crystallise it from petroleum ether (b 60-80°) or $CHCl_3$/petroleum ether. Dry it in air <55° and store in the dark. It is soluble in $CHCl_3$ (~1:1), *C_6H_6 (~1:1) and CCl_4 (~1:2.5). It is a germicide and antibacterial as it readily liberates chlorine, and it should not smell strongly of chlorine; otherwise it should be purified. *Alternatively*, dissolve ~15g of reagent in 75ml of hot acetic acid and precipitate it by addition of 37ml of N/10 bleaching powder solution (NaOCl), filter off, wash it with a dilute solution of the latter, dry it as above (**m** 78-84°) and recrystallise it. Excessive drying, "Sharp drying", will decompose it. [Orton & Bradfield *J Chem Soc* 993 *1927*, Krauss & Crede *J Am Chem Soc* **39** 2720 *1917*, Soper *J Chem Soc* 1899 *1924*; see also chloramine-T (monochloramine T Na salt) in "Compounds of As, B, P, S, Si.." in this Chapter.] [*Beilstein* **11** H I07, **11** I 27, **11** II 63, **11** III 301.]

2,4-Dichloroaniline *[554-00-7]* **M 162.0, m 63°, pK^{25} 2.02.** Crystallise the aniline from EtOH/water. It also crystallises from EtOH and is dried *in vacuo* for 6 hours at 40° [Moore et al. *J Am Chem Soc* **108** 2257 *1986*, Edidin et al. *J Am Chem Soc* **109** 3945 *1987*]. [*Beilstein* **12** IV 1241.]

3,4-Dichloroaniline *[95-76-1]* **M 162.0, m 71.5°, pK^{25} 2.97.** Crystallise the aniline from MeOH. [*Beilstein* **12** IV 1257.]

9,10-Dichloroanthracene *[605-48-1]* **M 247.1, m 214-215°.** Purify it by crystallising it from MeOH, EtOH, *C_6H_6 or Me_2CO (**m** 210-211°) followed by subliming *in vacuo*. [Masnori & Kochi *J Am Chem Soc* **107** 7880 *1985*, *Beilstein* **5** H 664, **5** I 324, **5** II 575, **5** III 2134, **5** IV 2293.]

2,4-Dichlorobenzaldehyde *[874-42-0]* **M 175.0, m 72°.** Crystallise the aldehyde from EtOH or ligroin. [*Beilstein* **7** IV 575.]

2,6-Dichlorobenzaldehyde *[83-38-5]* **M 175.0, m 70.5-71.5°.** Crystallise the aldehyde from EtOH/H_2O or petroleum ether (b 30-60°). [*Beilstein* **7** IV 576.]

***o*-Dichlorobenzene (ODCB)** *[95-50-1]* **M 147.0, b 81-82°/31-32mm, 180.5°/760mm, d_4^{20} 1.306, n_D^{20} 1.551, n^{25} 1.549.** Contaminants may include the *p*-isomer and trichlorobenzene [Suslick et al. *J Am Chem Soc* **106** 4522 *1984*]. It should be shaken with conc or fuming H_2SO_4, washed with water, dried with $CaCl_2$, and distilled from CaH_2 or sodium in a glass-packed column. Low conductivity material (*ca* 10^{-10} mhos) has been obtained by refluxing with P_2O_5, fractionally distilling and passing it through a column packed with silica gel or activated alumina: it is stored in a dry-box under N_2 or with activated alumina. [*Beilstein* **5** IV 654.]

***m*-Dichlorobenzene** *[541-73-1]* **M 147.0, b 173.0°/atm, d_4^{20} 1.289, n_D^{20} 1.54586, n_D^{25} 1.54337.** Wash it with aqueous 10% NaOH, then with water until neutral, dry and distil it. Conductivity material (*ca* 10^{-10} mhos) has been prepared by refluxing over P_2O_5 for 8 hours, then fractionally distilling, and storing with activated alumina. *m*-Dichlorobenzene dissolves rubber stoppers. [*Beilstein* **5** IV 657.]

***p*-Dichlorobenzene** *[106-46-7]* **M 147.0, m 53.0°, b 174.1°, d_4^{20} 1.241, n_D^{60} 1.52849.** *o*-Dichlorobenzene is a common impurity. The *p*-isomer has been purified by steam distillation, crystallisation from EtOH or boiling MeOH, air-dried and dried in the dark under vacuum. It has also been purified by zone refining. [*Beilstein* **5** IV 658.]

2,2'-Dichlorobenzidine *[84-68-4]* **M 253.1, m 165°, $pK_{Est(1)}$ ~3.0, $pK_{Est(2)}$ ~4.0.** Crystallise the benzidine from EtOH or H_2O. [*Beilstein* **13** H 234, **13** I 66, **13** II 106, **13** III 477, **13** IV 384.]

3,3'-Dichlorobenzidine *[91-94-1]* **M 253.1, m 132-133°, $pK_{Est(1)}$ ~4.8, $pK_{Est(2)}$ ~5.7.** Crystallise the benzidine from EtOH, petroleum ether (**m** 133°) or *benzene. [*Beilstein* **13** H 234, **13** I 67, **13** II 106, **13** III 477,

13 IV 384.] **CARCINOGEN.**

2,3-Dichlorobenzoic acid *[50-45-3]* **M 191.0, m 168.3°, 169-170°, pK^{25} 2.67.** Aromatic acid impurities (to <0.05%) can be removed *via* the (±)-α-methylbenzylamine salt as described for 2,4-dichlorobenzoic acid [Ley & Yates *Organic Process Research & Development* **12** 120 *2008*.] Crystallise the acid from H_2O, aqueous EtOH, or 30% aqueous AcOH and several times from *C_6H_6, then dry it *in vacuo* at 40° overnight. The *methyl ester* has **m 35-39°**. [Hope & Riley *J Chem Soc* **123** 2478 *1923*, Lock *Monatsh Chem* **90** 687 *1959*, Shorter & Mather *J Chem Soc* 4744 *1961*, *Beilstein* **9** II 228, **9** IV 998.]

2,4-Dichlorobenzoic acid *[50-84-0]* **M 191.0, m 163-164°, pK^{25} 2.68.** Crystallise the acid from aqueous EtOH (charcoal), then *benzene (charcoal). It can also be recrystallised from water. [*Beilstein* **9** IV 998.] It can be freed from isomeric acids (to <0.05%) *via* the (±)-α-methylbenzylamine salt as follows: dissolve the dichloro-acid (10g, 50.2mmol) in isopropanol (200ml), heat to 60° and add the (±)-benzylamine (5.49g, 45.3mmol), then stir it at 60° for 1 hour. Cool the mixture to room temperature, filter the slurry, wash it with isopropanol (25ml) and dry it *in vacuo* at 40° overnight to give 79% of the *salt* with **m** 185.2°. Dissolve the salt (5g) in H_2O (50ml) and MeOH (20ml), then heat to 60° and add concentrated HCl to pH <2.0. Cool the solution to room temperature add H_2O (12ml), filter it, wash it with H_2O (30ml) and dry it *in vacuo* at 40° overnight to give 94% of the *acid* with **m** 162.0°. [Ley & Yates *Organic Process Research & Development* **12** 120 *2008*.]

2,5-Dichlorobenzoic acid *[50-79-3]* **M 191.0, m 154°, b 301°/760mm, pK^{25} 2.47.** Crystallise the acid from water. [*Beilstein* **9** IV 1005.] Aromatic acid impurities (to <0.05%) can be removed *via* the (±)-α-methylbenzylamine salt as described for 2,4-dichlorobenzoic acid [Ley & Yates *Organic Process Research & Development* **12** 120 *2008*.]

2,6-Dichlorobenzoic acid *[50-30-6]* **M 191.0, m 141-142°, pK^{25} 1.59.** Crystallise the acid from EtOH and sublime it *in vacuo*. [*Beilstein* **9** IV 1005.] Aromatic acid impurities (to <0.05%) can be removed *via* the (±)-α-methylbenzylamine salt as described for 2,4-dichlorobenzoic acid [Ley & Yates *Organic Process Research & Development* **12** 120 *2008*.]

3,4-Dichlorobenzoic acid *[51-44-5]* **M 191.0, m 206-207°, pK^{25} 3.64.** Crystallise the acid from aqueous EtOH (charcoal) or acetic acid. [*Beilstein* **9** IV 1006.] Aromatic acid impurities (to <0.05%) can be removed *via* the (±)-α-methylbenzylamine salt as described for 2,4-dichlorobenzoic acid [Ley & Yates *Organic Process Research & Development* **12** 120 *2008*.]

3,5-Dichlorobenzoic acid *[51-36-5]* **M 191.0, m 188°, pK^{25} 3.54.** Crystallise the acid from EtOH and sublime it in a vacuum. [*Beilstein* **9** IV 1008.] Aromatic acid impurities (to <0.05%) can be removed *via* the (±)-α-methylbenzylamine salt as described for 2,4-dichlorobenzoic acid [Ley & Yates *Organic Process Research & Development* **12** 120 *2008*.]

2,6-Dichlorobenzonitrile *[1194-65-6]* **M 172.0, m 145°.** Crystallise the nitrile from acetone. [*Beilstein* **9** IV 1006.]

4,4'-Dichlorobenzophenone *[90-98-2]* **M 251.1, m 145-146°.** Recrystallise it from EtOH [Wagner et al. *J Am Chem Soc* **108** 7727 *1986*]. The *oxime* has **m** 135.2-136.9° (from MeOH, Sieger & Klein *J Org Chem* **22** 953 *1957*). The *semicarbazone* has **m** 192-193° (from H_2O). [*Beilstein* **7** H 420, **7** I 228, **7** II 359, **7** III 2076, **7** IV 1376.]

2,5-Dichloro-1,4-benzoquinone *[615-93-0]* **M 177.0, m 161-162°, 163°.** Recrystallise it twice from 95% EtOH to give yellow needles [Beck et al. *J Am Chem Soc* **108** 4018 *1986*]. The *dioxime* has **m** 278°(dec). [*Beilstein* **7** H 632, **7** I 346, **7** II 580, **7** III 3376, **7** IV 2081.]

2,6-Dichloro-1,4-benzoquinone *[697-91-6]* **M 177.0, m 122-124°.** Recrystallise the quinone from petroleum ether (b 60-70°). It sublimes at 41°/17.6μ. [Carlson & Miller *J Am Chem Soc* **107** 479 *1985*, *Beilstein* **7** II 580. **7** III 3376.]

2,6-Dichlorobenzoyl chloride *[4659-45-4]* **M 209.5, m 15-17, b 122-124°/15mm, d_4^{20} 1.464.** Reflux the acid chloride for 2 hours with excess of acetyl chloride (3 volumes), distil off AcCl followed by the benzoyl chloride. Store it away from moisture. It is an **IRRITANT**. [*Beilstein* **9** III 1377.]

3,4-Dichlorobenzyl alcohol *[1805-32-9]* **M 177.0, m 38-39°, 148-151°/760mm.** Crystallise the alcohol from EtOH (**m** 32-34°) or water (**m** 38°, needles). Its solubility at 20° is 1g in 1250ml of H_2O. [*Beilstein* **6** H 445, **6** III 1558, **6** IV 2598.]

2,3-Dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) *[84-58-2]* **M 227.0, m 203°(dec), 213-216°, (210-215°)(dec).** Crystallise DDQ from $CHCl_3$, $CHCl_3$/*benzene (4:1), or *benzene and store it at 0°. [Pataki & Harvey *J Org Chem* **52** 2226 *1987*, *Beilstein* **10** H 902, **10** II 635, **10** IV 3521.]

2,4-Dichloro-6-methylphenol (2,4-dichloro-*o*-cresol) *[1570-65-6]* **M 177.0, m 55°, b 111-113°/16mm, 129-132°/40mm, 231.6-231.9°/760mm, pK^{20} 8.14.** Crystallise the cresol from Et_2O (**m** 55°) or water; it has **m** 53-54° after sublimation. [*Beilstein* **6** H 359, **6** II 332, **6** III 1267, **6** IV 2001.]

2,4-Dichloro-1-naphthol *[2050-76-2]* **M 213.1, m 106-107°, pK_{Est} ~7.7.** Crystallise the naphthol from MeOH. The *1-methyl ether* has **m** 58° (from EtOH). [*Beilstein* **6** H 612, **6** I 308, **6** II 582, **6** III 2934, **6** IV 4233.]

2,3-Dichloro-1,4-naphthoquinone *[117-80-6]* **M 227.1, m 193°.** Crystallise the quinone from EtOH. [*Beilstein* **7** IV 2426.]

2,5-Dichloro-4-nitroaniline *[6627-34-5]* **M 207.0, m 153-154°, 157-158°, pK^{25} -0.74 (aqueous H_2SO_4).** Recrystallise it from EtOH, then sublime it *in vacuo*. [*Beilstein* **12** H 735, **12** II 400.]

2,6-Dichloro-4-nitroaniline (Dichloran) *[99-30-9]* **M 207.0, m 193°.** Crystallise Dichloran from aqueous EtOH or *benzene/EtOH. [*Beilstein* **12** IV 1681.]

2,5-Dichloro-1-nitrobenzene (1,4-dichloro-4-nitrobenzene) *[89-61-2]* **M 192.0, m 56°, 266-269°/atm.** Crystallise the nitrobenzene from absolute EtOH. [*Beilstein* **5** IV 726.]

3,4-Dichloro-1-nitrobenzene (1,2-dichloro-4-nitrobenzene) *[99-54-7]* **M 192.0, m 43°.** Crystallise it from absolute EtOH. [*Beilstein* **5** IV 726.]

2,4-Dichloro-6-nitrophenol *[609-89-2]* **M 208.0, m 122-123°, pK_{Est} ~5.0.** Crystallise the chloronitrophenol from AcOH. [*Beilstein* **6** IV 1358.]

2,6-Dichloro-4-nitrophenol *[618-80-4]* **M 208.0, m 125°(dec), pK^{25} 3.55.** Crystallise the chloronitrophenol from EtOH and dry it *in vacuo* over anhydrous $MgSO_4$. [*Beilstein* **6** IV 1361.]

Dichlorophen [2,2'-methylenebis(4-chlorophenol)] *[97-23-4]* **M 269.1, b 177-178°, pK_{Est} ~9.7.** Crystallise dichlorophen from toluene. [*Beilstein* **6** III 5406.]

2,3-Dichlorophenol *[576-24-9]* **M 163.0, m 57°, pK^{25} 7.70.** Crystallise it from ether. [*Beilstein* **6** IV 883.]

2,4-Dichlorophenol *[120-83-2]* **M 163.0, m 42-43°, pK^{25} 7.89.** Crystallise it from petroleum ether (b 30-40°). Purify it also by repeated zone melting, using a P_2O_5 guard tube to exclude moisture. It is very *hygroscopic* when dry. [*Beilstein* **6** IV 885.]

2,5-Dichlorophenol *[583-78-8]* **M 163.0, m 58°, b 211°/744mm, pK^{25} 7.51.** Crystallise it from ligroin and sublime it in a vacuum or distil it. [*Beilstein* **6** IV 942.]

3,4-Dichlorophenol *[95-77-2]* **M 163.0, m 68°, b 253.5°/767mm, pK^{25} 8.58.** Crystallise 3,4- dichlorophenol

from petroleum ether/*benzene mixture and/or distil it. [*Beilstein* **6** IV 952.]

3,5-Dichlorophenol *[591-35-5]* **M 163.0, m 68°, b 122-124°/8mm, 233-234°/760mm, pK^{25} 8.81.** Crystallise 3,5-dichlorophenol from petroleum ether/*benzene mixture and/or distil it. [*Beilstein* **6** IV 957.]

2,4-Dichlorophenoxyacetic acid (2,4-D) *[94-75-7]* **M 221.0, m 146°, pK^{25} 2.90.** Crystallise 2,4-D from MeOH. It is a plant growth substance, a herbicide and is **TOXIC.** [*Beilstein* **6** IV 908.]

(±)-α-(2,4-Dichlorophenoxy)propionic acid (2,4-DP, Dichloroprop) *[120-36-5]* **M 235.1, m 117°, pK^{20} 2.86.** Crystallise 2,4-DP from MeOH. It is a plant growth substance, a herbicide and is **TOXIC.** The *R(+)- and S(–)- enantiomers* have **m** 124° (from *C_6H_6) and $[\alpha]_D^{25}$ ±35.2° (c 1, Me_2CO). [*Beilstein* **6** H 189, **6** III 708, **6** IV 922-923.]

2,4-Dichlorophenylacetic acid *[19719-28-9]* **M 205.0, m 131°, 132-133°, pK$_{Est}$ ~4.0.** Crystallise the acid from aqueous EtOH. [*Beilstein* **9** III 2271.]

2,6-Dichlorophenylacetic acid *[6575-24-2]* **M 205.0, m 157-158°, pK$_{Est}$ ~3.8.** Crystallise the acid from aqueous EtOH. [*Beilstein* **9** III 2272.]

3-(3,4-Dichlorophenyl)-1,1-dimethyl urea (Diuron) *[330-54-1]* **M 233.1, m 153-154°, 155°.** Recrystallise it from 95% EtOH [Beck et al. *J Am Chem Soc* **108** 4018 *1986*]. [*Beilstein* **12** IV 1263.]

4,5-Dichlorophthalic acid *[56962-08-4]* **M 235.0, m 200° (dec to anhydride), pK$_{Est(1)}$ 2.2, pK$_{Est(2)}$~4.7.** Crystallise the acid from water. It has been purified by converting to the anhydride, reacting it with boiling EtOH to form the *monoethyl ester* (**m** 133-134°), and hydrolysing it back to the diacid (see next entry). [*Beilstein* **9** III 4205.]

3,6-Dichlorophthalic anhydride *[4466-59-5]* **M 189-191°, 191-191.5°, b 339°.** Boil the anhydride in xylene (allowing any vapours which would contain H_2O to be removed, e.g. Dean and Stark trap), which causes any acid present to dehydrate to the anhydride, and cool. Recrystallise it from xylene [Villiger *Chem Ber* **42** 3539 *1909*, Fedoorow *Izv Akad Nauk SSSR Otd Khim Nauk* 397 *1948*, *Chem Abstr* 1585 *1948*]. [*Beilstein* **17/11** V 260.]

2,6-Dichlorostyrene *[28469-92-3]* **M 173.0, m 8°, b 72-73°/2mm, d_4^{20} 1.4045, n_D^{20} 1.5798.** Purify the styrene by fractional crystallisation from the melt and by distillation *in vacuo*. [*Beilstein* **5** III 1174.]

2,4-Dichlorotoluene *[95-73-8]* **M 161.1, m -13.5°, b 61-62°/3mm, d_4^{20} 1.250, n_D^{20} 1.5513.** Recrystallise 2,4-dichlorotoluene from EtOH at low temperature or fractionally distil it. [*Beilstein* **5** IV 815.]

2,6-Dichlorotoluene *[118-69-4]* **M 161.1, b 199-200°/atm, d_4^{20} 1.254, n_D^{20} 1.548.** Fractionally distil it and collect the middle fraction. [*Beilstein* **5** IV 815.]

3,4-Dichlorotoluene *[95-75-0]* **M 161.1, m -16°, b 205°/atm, d_4^{20} 1.2541, n_D^{20} 1.549.** Recrystallise it from EtOH at very low temperature or fractionally distil it. [*Beilstein* **5** IV 815.]

α,α'-Dichloro-*p*-xylene *[623-25-6]* **M 175.1, m 100°, 254°/atm.** Crystallise the xylene from *benzene and dry it under vacuum. [*Beilstein* **5** IV 967.]

Dicinnamalacetone (1,9-diphenyl-1,3,6,8-nonatetraen-5-one) *[622-21-9]* **M 314.4, m 144°, 146°.** Crystallise the ketone from *benzene/isooctane (1:1). The *1,3,5-trinitrobenzene complex* (1:1) has **m** 113° (from EtOH), and the *1,3,5-trinitrobenzene complex* (1:2) has **m** 110° (from EtOH). [*Beilstein* **7** H 524, **7** I 293, **7** II 484, **7** III 2756, **7** IV 1834.] The *2,4-dinitrophenylhydrazone* has **m** 199-200°.

Dicumyl peroxide *[80-43-3]* **M 270.4, m 39-40°.** Crystallise the peroxide from 95% EtOH (charcoal). Store

it at 0°. *Potentially* **EXPLOSIVE.** [*Beilstein* **6** IV 3220.]

9,10-Dicyanoanthracene *[1217-45-4]* **M 228.3, m 340°.** Recrystallise the dinitrile twice from pyridine [Mattes & Farid *J Am Chem Soc* **108** 7356 *1986*]. [*Beilstein* **9** IV 3667.]

1,4-Dicyanobenzene (terephthalonitrile) *[623-26-7]* **M 128.1, m 222°.** Crystallise the dinitrile from EtOH or AcOH, and has **m** 221.5-222.5° after sublimation. [*Beilstein* **9** H 846, **9** I 376, **9** II 613, **9** III 4255, **9** IV 3328.]

1,4-Dicyanonaphthalene *[3029-30-9]* **M 178.2, m 206°.** Purify it by recrystallisation from EtOH (charcoal), **m** 208°, and sublime it *in vacuo*. [Bradbrook & Linstead *J Chem Soc* 1742 *1936*, *Beilstein* **9** H 917, **9** II 651, **9** III 464.]

***trans*-4-(Diethylamino)azobenzene** *[3588-91-8]* **M 320.5, m 171° pK^{26} 3.08 (50% aqueous EtOH).** Purify the azobenzene by column chromatography on alumina, elute with, and crystallise it from, toluene, [Albini et al. *J Chem Soc Perkin Trans 2* 1393 *1982*, Flamigni & Monti *J Phys Chem* **89** 3702 *1985*]. The *deoxycholate (1:4) complex* has **m** 194-194° (from EtOH). [*Beilstein* **16** H 341, **16** I 311, **16** III 342, 16 IV 455.]

***N,N*-Diethylaniline** *[91-66-7]* **M 149.2, b 216.5°/atm, d_4^{20} 0.938, n_D^{20} 1.5409 pK^{25} 6.57.** Reflux the base for 4 hours with half its weight of acetic anhydride, then fractionally distil it under reduced pressure (**b** 92°/10mm). [*Beilstein* **12** IV 252.]

Di-(2-ethylhexyl)phthalate ('di-iso-octyl' phthalate) *[117-81-7]* **M 390.6, b 384°, 256-257°/1mm, d_4^{20} 0.9803, n_D^{20} 1.4863.** Wash the ester with Na_2CO_3 solution, then shake it with water. After the resulting emulsion has been broken by adding ether, the ethereal solution is washed twice with water, dried ($CaCl_2$), and evaporated. The residual liquid is distilled several times under reduced pressure, then stored in a vacuum desiccator over P_2O_5 [French & Singer *J Chem Soc* 1424 *1956*]. [*Beilstein* **9** IV 3184.]

Diethyl phenyl orthoformate (diethoxy phenoxy ethane) *[14444-77-0]* **M 196.3, b 111°/11mm, 122°/13mm, d_4^{20} 1.0099, n_D^{20} 1.4799.** Fractionate the ortho-ester through an efficient column under vacuum [Smith *Acta Chem Scand* **10** 1006 *1956*].

Diethyl phthalate *[84-66-2]* **M 222.2. b 172°/12mm, b 295°/760mm, d_4^{25} 1.1160, n 1.5022.** Wash the ester with aqueous Na_2CO_3, then distilled water, dry ($CaCl_2$), and distil it under reduced pressure. Store it in a vacuum desiccator over P_2O_5. [*Beilstein* **9** IV 3172.]

Diethyl 2-phthalimidomalonate *[56680-61-5]* **M 305.3, m 72-74°, 73-74°, pK^{25} 9.17.** Dissolve it in xylene and when the temperature is 30° add petroleum ether (b 40-60°) and cool to 20° whereby the malonate separates as a pale brown powder [Booth et al. *J Chem Soc* 666 *1944*]. *Alternatively*, dissolve it in *C_6H_6, dry it over $CaCl_2$, filter, evaporate and the residual oil solidifies. Grind this with Et_2O, filter and wash it with Et_2O until white in colour, and dry it in a vacuum. It forms a yellow *sodium salt* **m** 280°(dec). The anion has λ_{max} at 254nm (ε 18.5K) [Clark & Murray *Org Synth* Coll Vol **I** 271 *1941*, UV of Na salt: Nnadi & Wang *J Am Chem Soc* **92** 4421 *1970*]. [*Beilstein* **21** H 487, **21** I 379, **21** III/IV 5264.]

Diethylstilboesterol [stilbesterol, stilboesterol, (*E*)-3,4-bis(4-hydroxyphenyl)-3-hexene] *[56-23-1]* **M 268.4, m 169-172°.** Crystallise stilbesterol from *benzene. [*Beilstein* **6** IV 6856.]

Diethyl terephthalate *[636-09-0]* **M 222.2, m 44°, 142°/2mm, 302°/760mm.** Crystallise the ester from toluene and distil it under reduced pressure. [*Beilstein* **9** H 8, **9** I 374, **9** III 4250, **9** IV 3304.]

4,4'-Di-*n*-heptyloxyazoxybenzene *[2635-26-9]* **M 426.6, m 75°, 95° (smectic ∅ nematic) and 127° (nematic ∅ liquid), pK_{Est} ~ -5.** Purify azoxybenzene by chromatography on Al_2O_3 (*benzene), recrystallise it from hexane or 95% EtOH and dry it by heating under vacuum. The liquid crystals can be sublimed *in vacuo*. [Mellifiori et al. *Spectrochim Acta Part A* **37(A)** 605 *1981*, Dewar & Schroeder *J Am Chem Soc* **86** 5235 *1964*, Weygand & Glaber *J Prakt Chem* **155** 332 *1940*, *Beilstein* **16** III 600, **16** IV 5264.]

9,10-Dihydroanthracene *[613-31-0]* **M 180.3, m 110-110.5°, b ~312°/atm, d_4^{20} 0.880.** Crystallise it from EtOH [Rabideau et al. *J Am Chem Soc* **108** 8130 *1986*]. [*Beilstein* **5** H 641, **5** IV 2182.]

Dihydrochloranil (tetrachloro-1,4-hydroquinone) *[87-87-6]* **M 247.9, m 240.5°.** Crystallise the quinone from EtOH or AcOH/EtOH. Sublime it at 77°/0.6x10^{-3}mm. The *dibenzoyl* derivative has **m** 233°. [Conant & Fieser *J Am Chem Soc* **45** 2207 *1923*, Rabideau et al. *J Am Chem Soc* **108** 8130 *1986*, *Beilstein* **6** H 851, **6** I 417, **6** II 846, **6** III 4436, **6** IV 5775.]

1,4-Dihydro-1,4-epoxynaphthalene *[573-57-9]* **M 144.2, m 53-54.5°, 53-56°, 55-56°.** Dissolve it in Et_2O, wash it with H_2O, dry it over K_2CO_3, filter, evaporate and dry the residue at 15mm, then recrystallise it from petroleum ether (b 40-60°), dry it at 25°/0.005mm and sublime it (sublimes slowly at room temperature)[Wittig & Pohmer *Chem Ber* **89** 1334 *1956*, Gilman & Gorsich *J Am Chem Soc* **79** 2625 *1957*]. [*Beilstein* **17** III/IV 548.]

1,8-Dihydroxyanthraquinone (Danthrone) *[117-10-2]* **M 240.1, m 193-197°, pK_1^{25} 8.30, pK_2^{25} 12.46.** Crystallise Danthrone from EtOH and sublime it in a vacuum. [*Beilstein* **8** IV 3217.]

2,4-Dihydroxyazobenzene (Sudan orange G) *[2051-85-6]* **M 214.2, m 143-146°, 228°, $pK_{Est(1)}$ <0, $pK_{Est(2)}$ ~7.3, $pK_{Est(3)}$ ~9.3.** Crystallise the dye from hot EtOH (charcoal). Has UV max at 350nm. [*Beilstein* **16** IV 264.]

2,3-Dihydroxybenzaldehyde *[24677-78-9]* **M 138.1, m 135-136°, pK_1^{20} 7.73, pK_2^{20} 10.91.** Crystallise the aldehyde from water. [*Beilstein* **8** III 1979.]

2,4-Dihydroxybenzoic acid (β-resorcylic acid) *[89-86-1]* **M 154.1, m 226-227°(dec), pK_1^{25} 3.30, pK_2^{25} 9.12, pK_3^{25} 15.6.** Crystallise the acid from water. [*Beilstein* **10** IV 1420.]

2,5-Dihydroxybenzoic acid (Gentisic acid, 5-hydroxysalicylic acid) *[490-79-9]* **M 154.1, m 204.5-205°, pK^{25} 2.95.** Crystallise gentisic acid from hot water or *benzene/acetone. Dry it in a vacuum desiccator over silica gel. [*Beilstein* **10** H 384, **10** IV 1441.]

2,6-Dihydroxybenzoic acid (γ-resorcylic acid) *[303-07-1]* **M 154.1, m 167°(dec), pK^{25} 1.05.** Dissolve the acid in aqueous $NaHCO_3$ and the solution is washed with ether to remove non-acidic material. The acid is precipitated by adding H_2SO_4, and recrystallised from water. Dry it under vacuum and store it in the dark [Lowe & Smith *J Chem Soc, Faraday Trans 1* **69** 1934 *1973*]. [*Beilstein* **10** IV 1456.]

2,4-Dihydroxybenzophenone *[131-56-6]* **M 214.2, m 145.5-147° $pK_{Est(1)}$ ~7.0, $pK_{Est(2)}$ ~12.0.** Recrystallise it from MeOH. [*Beilstein* **8** IV 2442.]

4,4'-Dihydroxybenzophenone *[611-99-4]* **M 214.2, m 210°, 213-214°, 213-215°, 216.6-217.1°, pK_{Est} ~7.0.** The benzophenone was prepared by a Friedel-Crafts reaction between 4-methoxybenzoyl chloride and anisole with anhydrous $AlCl_3$ in anhydrous CS_2, followed by demethylation with $AlCl_3$ in boiling toluene. It could also be made directly from 4-hydroxybenzoic acid and an equivalent of phenol by heating with three parts of freshly fused anhydrous $ZnCl_2$ at 125-140° for 45 minutes; the cooled mass is treated with dilute HCl, the solid is filtered off, washed thoroughly with aqueous $NaHCO_3$ solution, H_2O, dried *in vacuo* and recrystallised from H_2O, aqueous EtOH, or dilute HCl. [Russell & Butler *J Am Chem Soc* **71** 3663 *1949*.] The *oxime* has **m 266-267° (dec) [**Zigeuner & Ziegler *Monatsh für Chemie* **89** 359 *1949*], and the *2,4-dinitrophenylhydrazone* has **m 190-192°** (from EtOH). [*Beilstein* **8** H 316, **8** I 641, **8** II 355, **8** III 2648, **8** IV 2452.]

2,5-Dihydroxybenzyl alcohol (Gentisyl alcohol) *[495-08-9]* **M 140.1, m 47-48°, $pK_{Est(1)}$ ~9.3, $pK_{Est(2)}$ ~11.3.** Crystallise the alcohol from ligroin, $CHCl_3$, AcOH or H_2O. Sublime it at ~70° under high vacuum. [*Beilstein* **6** II 1084, **6** III 6326.]

2,2'-Dihydroxybiphenyl *[1806-29-7]* **M 186.2, m 108.5-109.5°, pK_1^{25} 7.56, pK_2^{25} 11.80.** Crystallise the biphenyl repeatedly from toluene, then sublime it at 60°/10^{-4}mm. [*Beilstein* **6** IV 6645.]

4.4'-Dihydroxybiphenyl (4,4'-biphenol) *[92-88-6]* **M 186.2, m 280.5°, 280-285°, $pK_{Est(1)}$ ~3.6, $pK_{Est(2)}$ ~11.8.** Recrystallise the biphenol from aqueous EtOH preferably under N_2 to avoid oxidation to the extended qiunone. It is characterized as the *dimethyl derivative (4,4'-dimethoxybiphenyl)* from which it is prepared by demethylation. The dimethoxy derivative has **m** 176.5-177° (from AcOH, EtOH, hexane or $*C_6H_6$) and sublimes *in vacuo*. [Williamson & Rodebush *J Am Chem Soc* **63** 3019 *1941*, *Beilstein* **6** I 485, **6** II 962, **6** III 6389, **6** IV 6651.]

1,8-Dihydroxy-3-methylanthraquinone (chrysophanic acid) *[481-74-3]* **M 245.3, m 196°, $pK_{Est(1)}$ ~8.2, $pK_{Est(2)}$ ~12.4.** Crystallise chrysophanic acid from EtOH or *benzene and has **m** 195.6-196.2°, after sublimation it in a vacuum. The yellow *mono-acetate* has **m** 188-190° (from MeOH or Me_2CO). It forms Ni^{2+}, Co^{2+} and Cu^{2+} complexes. [*Beilstein* **8** H 470, **8** I 725, **8** II 510, **8** III 3808, **8** IV 3277.]

1,5-Dihydroxynaphthalene (1,5-naphthalenediol) *[83-56-7]* **M 160.7, m 258°, 260°, 265°, $pK_{Est(1)}$ ~9.0, $pK_{Est(2)}$ ~11.0.** The diol (~30g) is purified by making into a thick paste with H_2O and suspending this in 3L of H_2O containing 200ml of EtOH, boiling under reflux for 3 hours, cooling to 30°, saturating with SO_2, digesting below the boiling point for 1 hour and filtering fast through a large hot filter paper. The hot filtrate is poured onto crushed ice whereby the diol (15-20g) separates as colourless needles (**m** 258°) [Wheeler & Ergle *J Am Chem Soc* **52** 4873 *1930*]. Recrystallise it from H_2O or nitromethane under N_2 to avoid oxidation. The *dibenzoyl* derivative has **m** 245° (from EtOH). The *5-methoxy-1-naphthol* derivative [prepared from the diol in MeOH/HCl (1:30 weight to volume ratio) and set aside at 25° for 9-10days] crystallised from petroleum ether (**m 135-136°**) or from CH_2Cl_2/hexane (needles **m 140°**) [Bell & McCaffrey *Aust J Chem* **46** 731 *1993*]. [*Beilstein* **6** I 477, **6** II 950, **6** III 5265, **6** IV 6554.]

1,6-Dihydroxynaphthalene *[575-44-0]* **M 160.2, m 138-139° (with previous softening), pK_{Est} ~9.4.** Crystallise it from *benzene or *benzene/EtOH after treatment with charcoal. [*Beilstein* **6** IV 6557.]

2,5-Dihydroxyphenylacetic acid (homogentisic acid) *[451-13-8]* **M 168.2, m 152°, 154-152°, pK^{20} 4.14 (COOH).** Crystallise homogentisic acid from EtOH/$CHCl_3$ or H_2O (solubility is 85% at 25°). [*Beilstein* **10** IV 1506.]

3,4-Dihydroxytoluene (4-methylcatechol) *[452-86-8]* **M 124.1, m 65-66°, 68°, b 112°/3mm, 241°/760mm, pK_1^{25} 9.44 (9.7), pK_2^{25} 10.90 (11.9).** Crystallise the catechol from $*C_6H_6$. The purity is checked by TLC. Crystallise it from high-boiling petroleum ether and distil it in a vacuum. [*Beilstein* **6** IV 5878.]

1,4-Diiodobenzene *[624-38-4]* **M 329.9, m 132-133°.** Crystallise it from EtOH or boiling MeOH, then dry it in air. [*Beilstein* **5** IV 700.]

***trans*-4,4'-Dimethoxyazobenzene** *[501-58-6]* **M 242.3, m 162.7-164.7°, 165-166°, pK_{Est} ~0.** Chromatograph it on basic alumina and elute with *benzene. Then crystallise the residue from 2:2:1 (v/v) methanol/ethanol/*benzene or Me_2CO. [*Beilstein* **16** H 112, **16** I 237, **16** II 43, **16** III 93, **16** IV 172.]

3,5-Dimethoxybenzaldehyde *[7331-34-4]* M 166.2, **m 45.5°, 46-47°, 45-48°, b 151°/16mm.** The aldehyde was prepared by reduction of the corresponding acid chloride with 5%Pd/$CaCO_3$ in xylene, and was purified by distillation in a vacuum and by recrystallisation from hexane (**m 48°**), ligroin, petroleum ether (**m 45-46°**) or 70% aqueous EtOH. The *oxime* (**m 115°**) crystallises from $*C_6H_6$, the *thiosemicarbazone* (**m 211-212°**) crystallises from aqueous EtOH, and the *2,4-dinitrophenylhydrazone* (**m 260-261°**) forms orange needles from aqueous EtOH. [Mongolusk et al. *J Chem Soc* 2231 *1957*, Lambooy *J Am Chem Soc* **76** 133 *1954*, *Beilstein* **8** II 291, **8** III 2073, **8** IV 1786.]

1,2-Dimethoxybenzene (veratrole) *[91-16-7]* **M 137.2, m 23°, b 208.5-208.7, d_4^{20} 1.085, n_D^{25} 1.53232.** Steam distil veratrole, then fractionally distil it from BaO, CaH_2 or Na. Crystallise it from *benzene or low-boiling petroleum ether at 0°. Fractionally crystallise it from its melt. Store it over anhydrous Na_2SO_4. [*Beilstein* **6** IV 5564.]

1,3-Dimethoxybenzene *[151-10-0]* **M 137.2, b 212-213°, d_4^{20} 1.056, n_D^{20} 1.5215.** Extract it with aqueous NaOH, and water, then dry it. Fractionally distil it from BaO or Na. [*Beilstein* **6** IV 5663.]

1,4-Dimethoxybenzene *[150-78-7]* **M 137.2, m 57.2-57.8°.** Steam distil 1,4-dimethoxybenzene, then crystallise it from hexane or *benzene, and from MeOH or EtOH, but these are wasteful due to high solubilities. Dry it under vacuum. It also sublimes under vacuum. [*Beilstein* **6** IV 5718.]

2,4-Dimethoxybenzoic acid *[91-52-1]* **M 182.2, m 107.3°, 109°, pK^{25} 4.36.** Crystallise the acid from water and dry it in a vacuum desiccator over H_2SO_4. The *S-benzylisothiuronium salt* has **m** 158-159° (from $CHCl_3$). [*Beilstein* **10** H 379, **10** I 177, **10** II 252, **10** III 1371, **10** IV 1422.] Aromatic acid impurities (to <0.05%) can be removed *via* the (±)-α-methylbenzylamine salt as described for 2,4-dichlorobenzoic acid [Ley & Yates *Organic Process Research & Development* **12** 120 *2008*.]

2,6-Dimethoxybenzoic acid *[1466-76-8]* **M 182.2, m 186-187°, 188-191°, pK^{25} 3.44.** Crystallise the acid from water or 1,1-dichloroethane (**m** 187.5-188.5°). [*Beilstein* **10** H 388, **10** I 185, **10** II 259, **10** III 1401, **10** IV 1456.]

3,4-Dimethoxybenzoic acid (veratric acid) *[93-07-2]* **M 182.2, m 181-182°, 185-186°, pK^{25} 4.43.** Crystallise the acid from Et_2O, H_2O or aqueous acetic acid. It has **m** 180-181° after sublimation at 80°/1mm. [*Beilstein* **10** H 393, **10** I 188, **10** II 261, **10** III 1404, **10** IV 1406.]

3,5-Dimethoxybenzoic acid *[1132-21-4]* **M 182.2, m 185-186°, pK^{25} 3.97.** Crystallise the acid from water, EtOH or aqueous acetic acid and dry it in a vacuum. [*Beilstein* **10** H 405, **10** I 195, **10** III 1446, **10** IV 1501.]

p,p'-**Dimethoxybenzophenone** *[90-96-0]* **M 242.3, m 144.5°.** Crystallise the ketone from absolute EtOH, aqueous EtOH or EtOH/AcOH. The *2,4-dinitrophenylhydrazone* has **m** 199-200°. [*Beilstein* **8** H 317, **8** I 641, **8** II 355, **8** III 2649, **8** IV 2453.]

2,6-Dimethoxy-1,4-benzoquinone *[530-55-2]* **M 168.1, m 255-256°, 256°(dec), 262-263°.** Crystallise the quinone from H_2O or acetic acid. It sublimes at 175-180°/1mm. It has UV with λ_{max} at 287 and 377nm ($CHCl_3$). [*Beilstein* **8** H 385, **8** I 683, **8** II 433, **8** III 3354, **8** IV 2710,]

5,6-Dimethoxy-1-indanone *[2107-69-9]* **M 192.2, m 118-120°.** Crystallise the indanone from MeOH, then sublime it in a vacuum. [*Beilstein* **8** IV 1985.]

1,4-Dimethoxynaphthalene *[10075-62-4]* **M 188.2, m 87-88°.** Crystallise the naphthalene from EtOH, MeOH (**m** 85-86°) or petroleum ether. [*Beilstein* **6** H 984, **6** III 5261, **6** IV 6546.]

1,5-Dimethoxynaphthalene *[10075-63-5]* **M 188.2, m 183-184°, b 179°/13mm.** Crystallise it from EtOH, AcOH (**m** 178-180°) or $*C_6H_6$. Also distil it in a vacuum. [*Beilstein* **6** III 5266, **6** IV 6554.]

3,4-Dimethoxy-6-nitrobenzaldehyde (6-nitroverataldehyde) *[20357-25-9]* **M 211.2, m 132°, 133.5-134.5°.** The aldehyde is purified by dissolving 9g in 200ml of boiling 95% EtOH, and set aside overnight to crystallise. It is then dried *in vacuo* at 50° and recrystallised from 110ml of 95% EtOH to give 6-7g of aldehyde with **m** 132-133°. Crystallisation from aqueous EtOH provides light yellow needles. It is light sensitive and should be stored in the dark [Fetscher *Org Synth* Coll Vol **4** 735 *1963*]. [*Beilstein* **8** H 262, **8** I 610, **8** II 290, **6** III 2065, **6** IV 1785.]

2,6-Dimethoxyphenol (pyrogallol-1,3-diethylether) *[91-10-1]* **M 154.2, m 54-56°, pK_{Est} ~9.6.** Purify the phenol by zone melting or sublimation in a vacuum. [*Beilstein* **6** IV 7329.]

3,5-dimethoxyphenol (phloroglucinol dimethylether) *[500-99-2]* **M 154.2, m 42-43°, b 115°/0.04mm, pK^{25} 9.35.** Purify the phenol by distillation followed by sublimation in a vacuum. [*Beilstein* **6** IV 7362.]

3,4-Dimethoxyphenyl acetic acid (homoveratric acid) *[93-40-3]* **M 196.2, m 97-99°, pK^{25} 4.33.** Crystallise homoveratric acid from H_2O or *C_6H_6/ligroin. The *amide* has **m** 142° (from H_2O). [*Beilstein* **10** H 409, **10** I 197, **10** II 268, **10** III 1459, **10** IV 1509.]

3,5-Dimethoxyphenylacetonitrile *[13388-75-5]* **M 177.1, m 53°.** Crystallise the nitrile from MeOH or petroleum ether (b 90-110°). [Adams et al. *J Am Chem Soc* **70** 664 *1948*, Sankaraman et al. *J Am Chem Soc* **109** 5235 *1987*, *Beilstein* **10** I 198, **10** II 269, **10** III 1470.]

4,4'-Dimethoxythiobenzophenone *[958-80-5]* **M 258.3, m 120°.** Recrystallise the thioketone from a mixture of cyclohexane/dichloromethane (4:1) or EtOH (**m** 119°). [Bergmann & Wagenberg *Chem Ber* **63** 2590 *1930*, *Beilstein* **8** H 319, **8** II 355, **8** III 2658, **8** IV 2457.]

2,6-Dimethoxytoluene *[5673-07-4]* **M 152.2, m 39-41°, b 97-99°/15mm, 219-220°/731mm.** Sublime 2,6-dimethoxytoluene *in vacuo*. Distil it (preferably under reduced pressure) and/or recrystallise it from pentane, EtOH or aqueous MeOH. [Sankaraman et al. *J Am Chem Soc* **109** 5235 *1987*]. [*Beilstein* **6** H 872, **6** III 4513, **6** IV 5877.]

4,4'-Dimethoxytrityl chloride (DMT) *[40615-36-9]* **M 338.8, m 114°.** DMT crystallises from cyclohexane/acetyl chloride as the hydrochloride. Dry it over KOH pellets in a desiccator. When dissolved in *C_6H_6 and air is blown through, HCl is removed. It crystallises from Et_2O. [Baeyer & Villiger *Chem Ber* **36** 2788 *1903*, Smith et al. *J Am Chem Soc* **84** 430 *1962*, Smith et al. *J Am Chem Soc* **85** 3821 *1963*.] If it has hydrolysed considerably (see OH in IR), then repeat the crystallisation from cyclohexane/acetyl chloride — excess of AcCl is removed in a vacuum over KOH, then recrystallise it from Et_2O. [*Beilstein* **6** IV 1042.]

***p*-Dimethylaminoazobenzene (Dimethyl Yellow)** *[60-11-7]* **M 225.3, m 118-119°(dec), pK$_1^{25}$ -5.34 (aqueous H_2SO_4), pK$_2^{25}$ 2.96.** Crystallise the dye from acetic acid or isooctane, or from 95% EtOH by adding hot water and cooling. Dry it over KOH under vacuum at 50°. [*Beilstein* **6** IV 448.] **CARCINOGEN.**

4-*N*,*N*′-Dimethylaminoazobenzene-4'-isothiocyanate {DABITC, 4-[(4-isocyanatophenyl)-azo]-*N*,*N*′-dimethylaniline} *[7612-98-8]* **M 282.4, m 170-171°, pK$_{Est}$~2.5.** Crystallise DABITC by dissolving 1g in 150ml of boiling Me_2CO, filtering hot and allowing to cool at -20° overnight, collecting the solid and drying it in a vacuum. Solutions in pyridine should be used immediately, otherwise it decomposes. It is moisture sensitive. [Chang *Methods Enzymol* **91** 79, 455 *1983*.]

***p*-Dimethylaminobenzaldehyde (Ehrlich's Reagent, DMAB)** *[100-10-7]* **M 149.2, m 74-75°, pK$_{Est}$ ~2.6.** Crystallise DMAB from water, hexane, or from EtOH (2ml/g), after charcoal treatment, by adding excess of water. *Alternatively*, dissolve it in aqueous acetic acid, filter, and precipitate it with ammonia. Finally recrystallise it from EtOH. It is used for the detection of pyrroles [Iyer et al. *J Org Chem* **59** 6038 *1994*]. [*Beilstein* **14** IV 51.]

***p*-Dimethylaminobenzoic acid** *[619-84-1]* **M 165.2, m 242.5-243.5°(dec), pK$_1$ 2.51, pK$_2$ 6.03.** Crystallise the acid from EtOH/water. [*Beilstein* **14** IV 1164.]

***p*-Dimethylaminobenzophenone** *[530-44-9]* **M 225.3, m 92-93°, pK$_{Est}$ ~2.7.** Crystallise the pale green *p*-dimethylaminobenzophenone from EtOH. Dissolve 100g in 600ml of boiling EtOH, add 5g of charcoal, cool, isolate the solid by centrifugation and similarly wash the pale crystals with ice-cold EtOH. When filtered by suction, EtOH solution remains on the crystals and turns deep green in air. Dry it in a vacuum and store it in the dark. The *hydrazone* has **m** 128-130° and forms a ketyl with potassium. [Hurd & Webb *Org Synth* Coll Vol **I** 217 *1941*, *Beilstein* **14** H 82, **14** I 288, **14** III 218, **14** IV 248.]

***N*,*N*-Dimethylamino-*p*-chlorobenzene (*p*-chloro-*N*,*N*-dimethylaniline)** *[698-69-1]* **M 155.6, m 32-33.5°, 35.5°, b 231°/atm.** Purify it by vacuum sublimation [Guarr et al. *J Am Chem Soc* **107** 5104 *1985*]. The *picrate* has **m** 126-128° (from methanol).

4-Dimethylamino cinnamaldehyde *[6203-18-5]* **M 175.2, m 141°.** The aldehyde crystallises from EtOH or ligroin and is dried *in vacuo*. The *oxime* has **m** 157° (from ligroin). The *phenylhydrazone* has **m** 169° (form MeOH). It is used as a reagent for amines (with NH_3, UV has λmax at 630nm). [König et al. *Chem Ber* **61** 2075 *2075,* Quareshi & Kahn *Anal Chim Acta* **86** 309 *1976*, *Beilstein* **14** III 184, **14** IV 197.]

4-Dimethylamino cinnamic acid *[1552-96-1]* **M 191.2, m 225° (effervesces), $pK_{Est(1)}$ ~2.2, $pK_{Est(2)}$ ~4.6.** Recrystallise the acid from EtOH. The *methyl ester* has **m** 134-135° (from Me_2CO), and the *ethyl ester* has **m** 77-78° (from aqueous EtOH). [Shoppee *J Chem Soc* 982 *1938*, Galat *J Am Chem Soc* **68** 376 *1946*, *Beilstein* **14** H 522, **14** II 318, **14** III 1306, **14** IV 1716.]

2*S*,3*R*-(+)-4-Dimethylamino-1,2-diphenyl-3-methyl-2-butanol *[38345-66-3]* **M 283.4, m 55-57°, $[\alpha]_{546}^{20}$+9.3° (c 9.6, EtOH), $[\alpha]_D^{20}$ +7.7° (c 9.6, EtOH), pK_{Est} ~10.0.** Purify the *hydrochloride* by dissolving 1.5g in 13.5 ml of 5N HCl, heat to boiling and evaporate in a vacuum. Recrystallise the *hydrochloride* three times from MeOH/EtOAc giving **m** 189-190°, $[\alpha]_D$ -33.7° (c 1, H_2O) {enantiomer has +34.2°}. The *hydrochloride* in the minimum volume of water is basified with aqueous 5N NaOH and extracted with Et_2O. The extract is dried (K_2CO_3) and evaporated, leaving a residue which is stored in a desiccator over solid KOH as a low melting solid. It can be recovered using these procedures from asymmetric reductions with LAH, and re-used. [Pohland & Sullivan *J Am Chem Soc* **77** 3400 *1955*, Sullivan et al. *J Org Chem* **28** 2483 *1963*, *Beilstein* **13** IV 2221.]

***N*,*N*-Dimethylaniline** *[121-69-7]* **M 121.2, f 2°, b 84°/15mm, 193°/760mm, d_4^{20} 0.956, n_D^{25} 1.5556, pK^{25} 5.07.** Primary and secondary amines (including aniline and monomethylaniline) can be removed by refluxing for 4-5 hours with excess acetic anhydride, and then fractionally distilling. Crocker and Jones (*J Chem Soc* 1808 *1959*) used four volumes of acetic anhydride, then distilled off the greater part of it, and dissolved the residue in ice-cold dilute HCl. Non-basic materials were removed by ether extraction, then the dimethylaniline was liberated with ammonia, extracted with ether, dried, and distilled under reduced pressure. Metzler and Tobolsky (*J Am Chem Soc* **76** 5178 *1954*) refluxed with only 10% (w/w) of acetic anhydride, then cooled and poured it into excess 20% HCl, which, after cooling, was extracted with diethyl ether. (The amine hydrochloride remains in the aqueous phase.) The HCl solution was cautiously made alkaline to phenolphthalein, and the amine layer was drawn off, dried over KOH and fractionally distilled under reduced pressure, under nitrogen. Suitable drying agents for dimethylaniline include NaOH, BaO, $CaSO_4$, and CaH_2.
Other purification procedures include the formation of the *picrate* (**m** 163° from Me_2CO or EtOH/H_2O), prepared in *benzene solution and crystallised to constant melting point, then decomposed with warm 10% NaOH and extracted into ether: the extract was washed with water and distilled under reduced pressure. The *oxalate* salt has also been used for purification. The base has been fractionally crystallised by partial freezing and also from aqueous 80% EtOH then from absolute EtOH. It has been distilled from zinc dust, under nitrogen. [*Beilstein* **12** H 141, **12** I 151, **12** II 2, **12** III 245, **12** IV 243.]

2,3-Dimethylaniline [2,3-xylidine (*vic, o*)] *[87-59-2]* **M 121.2, m 2°, b 106°/15mm, 223°/760mm, d_4^{20} 1.570, n_D^{20} 0.991, pK^{25} 4.70.** Purify *vic*-xylidine by conversion into a derivative (see below), recrystallise the derivative, decompose the derivative with aqueous NaOH and fractionally distil the liquid base. The *acetyl* derivative has **m** 135° (from EtOH), and the *formyl* derivative has **m** 102° (from EtOH). [*Beilstein* **12** H 1101, **12** III 2438, **12** IV 2497.]

2,4-Dimethylaniline [2,4-xylidine (*uns, m*)] *[95-68-1]* **M 121.2, m 11°, b 212°/736mm, 213-214°/760mm, d_4^{20} 0.974, n_D^{20} 1.5604, pK^{25} 4.89.** Convert *uns*-xylidine to a derivative (see below) which, after recrystallisation, is decomposed with alkali to give the free base. Dry it over KOH and fractionally distil. The *acetyl* derivative has **m** 130°, the *benzoyl* derivative has **m** 192°, and the *picrate* has **m** 209°. [*Beilstein* **12** H 1111, **12** IV 2545.]

2,5-Dimethylaniline [2,5-xylidine (*p*)] *[95-78-3]* **M 121.2, m 11°, 15.5°, b 104°/15mm, 215°/739mm, 218°/760mm, d_4^{20} 0.974, n_D^{20} 1.5604, pK^{25} 4.53.** Convert *p*-xylidine to a derivative (see below) which, after recrystallisation, is decomposed with alkali to give the free base. Dry over KOH and fractionally distil. The *acetyl* derivative has **m** 142° (from H_2O or toluene), and the *benzoyl* derivative has **m** 140° (from EtOH). [*Beilstein* **12** H 1135, **12** IV 2567.]

2,6-Dimethylaniline [2,6-xylidine (*vic, m*)] *[87-62-7]* **M 121.2, m 11°, b 98°/14mm, 210-211°/736mm, 215°/760mm, d_4^{20} 0.974, n_D^{20} 1.5604, pK^{25} 3.95.** Convert *vic*-xylidine to a derivative (see below) which, after recrystallisation, is decomposed with alkali to give the free base. Dry it over KOH and fractionally distil. The ***formyl derivative*** [*N*-(2,6-dimethylphenyl)formamide] **M 149.2,** [607-92-1] has **m** 168-170°, the *acetyl* derivative has **m** 177°, the *benzoyl* derivative has **m** 168°, and the *picrate* has **m** 180°. [*Beilstein* **12** H 1107, **12** I 482, **12** II 604, **12** III 2462, **12** IV 2521.]

3,4-Dimethylaniline [3,4-xylidine] *[95-64-7]* **M 121.2, m 51°, b 116-118°/25mm, b 226°/760mm, pK^{25} 5.17.** Crystallise it from ligroin and distil it under vacuum. [*Beilstein* **12** H 1103, **12** IV 2502.]

3,5-Dimethylaniline [3,5-xylidine (*sym, m*)] *[108-69-0]* **M 121.2, b 105-106°/15mm, 221-222°/atm, d_4^{20} 0.974, n_D^{20} 1.557, pK^{25} 4.91.** Convert *sym*-xylidine to a derivative (see below) which, after recrystallisation, is decomposed with alkali to give the free base. Dry it over KOH and fractionally distil it. The *acetyl* derivative has **m** 144°, the *benzoyl* derivative has **m** 136° and the *picrate* has **m** 209° (from H_2O, EtOH or 10% AcOH). [*Beilstein* **12** H 1131, **12** IV 2561.]

9,10-Dimethylanthracene *[781-43-1]* **M 206.3, m 180-181°.** Purify 9,10-dimethylanthracene by crystallising from EtOH, and by recrystallising from the melt. [*Beilstein* **5** IV 2329.]

7,12-Dimethylbenz[*a*]anthracene (DMBA) *[57-97-6]* **M 256.4, m 122-123°.** Purify DMBA by chromatography on alumina/toluene or *benzene. Crystallise it from acetone/EtOH. [*Beilstein* **5** IV 2587.]

2,3-Dimethylbenzoic acid *[603-79-2]* **M 150.2, m 146°, pK^{25} 3.72.** Crystallise the acid from EtOH. It is volatile in steam. The *amide* has **m** 156° (from H_2O). [*Beilstein* **9** H 531, **9** III 2434, **9** IV 1797.]

2,4-Dimethylbenzoic acid *[611-01-8]* **M 150.2, m 125-126°, 126-127°, b 267°/727mm, pK^{25} 4.22.** Crystallise the acid from EtOH or H_2O, and sublime it in a vacuum. [*Beilstein* **9** H 531, **9** III 2436, **9** IV 1801.]

2,5-Dimethylbenzoic acid *[610-72-0]* **M 150.2, m 134°, b 268°/760mm, pK^{25} 4.00.** Steam distil the acid, then crystallise it from EtOH or H_2O (**m** 134-134.5°). [*Beilstein* **9** H 534, **9** IV 1802.]

2,6-Dimethylbenzoic acid *[632-46-2]* **M 150.2, m 117°, b 118-119°/2.5mm, pK^{25} 3.35.** Steam distil the acid, and crystallise it from EtOH or H_2O (**m** 116.3-116.7°). The *N-dimethylamide* has **m** 62-63° (from Et_2O). [*Beilstein* **9** H 531, **9** IV 1798.]

3,4-Dimethylbenzoic acid *[619-04-5]* **M 150.2, m 166°, pK^{25} 4.50.** Crystallise it from EtOH or H_2O (**m** 168-168.5°), and sublime it *in vacuo*. The *phenyl ester* has **m** 68° (from EtOH or petroleum ether) and **b** 155-157°/2mm. [*Beilstein* **9** II 353, **9** III 2441, **9** IV 1803.]

3,5-Dimethylbenzoic acid *[499-06-9]* **M 150.2, m 170°, pK^{25} 4.30.** Distil the acid in steam, crystallise it from H_2O (**m** 171.2-171.7°) or EtOH, and sublime it *in vacuo*. [*Beilstein* **9** H 536, **9** III 244, **9** IV 1806.]

4,4'-Dimethylbenzophenone *[611-97-2]* **M 210.3, m 95°, b 150-152/2mm. 333-334°/725mm.** Purify the benzophenone by zone refining or distllation, preferably in a vacuum. [*Beilstein* **7** III 2181, **7** IV 1434.]

2,5-Dimethyl-1,4-benzoquinone *[137-18-8]* **M 136.1, m 124-125°, 126-127°.** Crystallise the quinone from EtOH. [*Beilstein* **7** IV 2090.]

2,6-Dimethyl-1,4-benzoquinone (Phloron) *[527-61-7]* **M 136.1, m 72° (sealed tube).** Crystallise the quinone from water/EtOH (8:1). [*Beilstein* **7** IV 657, **7** III 3402, **7** IV 2096.]

3,3'-Dimethylcarbanilide (*N,N'*-bis-[*m*-tolyl]urea) *[620-50-8]* **M 240.3, m 220°, 225°.** Crystallise urea from ethyl acetate. The UV has λ_{max} at 258nm (EtOH). The *hydrochloride* has **m** 162°. [*Beilstein* **12** III 1970, **12** IV 1829.]

1,1-Dimethyl-1*H*-indene *[18636-55-0]* **M 144.2, b 57°/4.8mm, 115°/20mm.** Purify the oily indene by gas chromatography or by fractional distillation. [Bosch & Brown *Can J Chem* **42** 1718 *1964*, cf. *Beilstein* **5** I 251, **5** III 1377.]

1,5-Dimethylnaphthalene *[571-61-9]* **M 156.2, m 81-82°, b 265-266°.** Crystallise it from 85% aqueous EtOH. [*Beilstein* **5** IV 1709.]

2,3-Dimethylnaphthalene *[581-40-8]* **M 156.2, m 104-104.5°.** Steam distil the naphthalene and crystallise it from EtOH. [*Beilstein* **5** IV 1713.]

2,6-Dimethylnaphthalene *[581-42-0]* **M 156.2, m 110-111°, b 122.5-123.5°/10mm**, **261-262°/760mm.** Distil it in steam and crystallise it from EtOH. [*Beilstein* **5** IV 1714.]

3,3'-Dimethylnaphthidine (4,4'-diamino-3,3'-dimethyl-1,1'-binaphthyl) *[13138-48-2]* **M 312.4, m 213°.** Recrystallise the naphthidine from EtOH or petroleum ether (b 60-80°). [*Beilstein* **13** IV 493.]

***N,N*-Dimethyl-*m*-nitroaniline** *[619-31-8]* **M 166.1, m 60°, 61°, pK^{25} 2.63.** Crystallise the aniline from EtOH. The *picrate* has **m** 119° (from EtOH). [*Beilstein* **12** H 701, **12** III 1544, **12** IV 1591.]

***N,N*-Dimethyl-*p*-nitroaniline** *[100-23-2]* **M 166.1, m 164.5-165.2°, pK^{25} 0.61 (0.92).** Crystallise the nitroaniline from aqueous EtOH, EtOH or MeOH (**m** 163.5-164°). Dry it *in vacuo*. The *N-methiodide* has **m** 161°(dec) (from H_2O). [*Beilstein* **12** H 714, **12** III 1584, **12** IV 1616.]

***N,N*-Dimethyl-*p*-nitrosoaniline (4-nitroso-*N,N*-dimethylaniline)** *[138-89-6]* **M 150.2, m 86-87°, 92.5-93.5°, b 191-192°/100mm, pK^{25} 4.54.** Recrystallise the nitroso-aniline from petroleum ether or $CHCl_3$/CCl_4 and dry it in air. *Alternatively*, suspend it in H_2O, heat to boiling and add HCl until it dissolves. Filter, cool and collect the *hydrochloride [42344-05-8]* with **m** 177° after recrystallisation from H_2O containing a small amount of HCl. The *hydrochloride* (e.g. 30g) is made into a paste with H_2O (100ml) in a separating funnel. Add cold aqueous 2.5 NaOH or Na_2CO_3 to a pH of ~8.0 (green color due to the free base) and extract with toluene, $CHCl_3$ or Et_2O. Dry the extract (K_2CO_3), filter, distil off the solvent, cool the residue and collect the crystalline free base. Recrystallise it as above and dry it in air. [*Beilstein* **12** IV 1558.]

***R*-(+)-*N,N'*-Dimethyl-1-phenethylamine** *[19342-01-9]* **and *S*-(-)-*N,N'*-Dimethyl-1-phenethyl-amine** *[17279-31-1]* **M 149.2, b 81°/16mm, [α] $^{20}_{D}$ (+) and (-) 50.2° (c 1, MeOH), d $^{20}_{4}$ 0.908, pK$_{Est}$ ~9.0 (for *RS*).** The amine is mixed with aqueous 10N NaOH and extracted with toluene. The extract is washed with saturated aqueous NaCl, dried over K_2CO_3, and transferred to fresh K_2CO_3 until the solution is clear, and is filtered. The filtrate is distilled. If a short column packed with glass helices is used, the yield is reduced but a purer product is obtained. [Ingersoll *Org Synth* **25** 89 *1945*, Snyder & Brewster *J Am Chem Soc* **71** 291 4165 *1949*, Cope et al. *J Am Chem Soc* **71** 3931 *1949*.] The (–)-*picrate* has **m** 140-141° (from EtOH). The *racemate [1126-71-2]* has **b** 88-89°/16mm, 92-94°/30mm, 194-195°/760mm, d $^{20}_{4}$ 0.908. [*Beilstein* **13** III 2392.]

2,3-Dimethylphenol *[526-75-0]* **M 122.2, m 75°, b 120°/20mm, 218°/760mm, pK^{25} 10.54.** Crystallise 2,3-xylenol from aqueous EtOH. [*Beilstein* **6** IV 3096.]

2,5-Dimethylphenol *[95-87-4]* **M 122.2, m 73°, b 211.5°/762mm, pK^{25} 10.41.** Crystallise 2,5-xylenol from EtOH/ether. [*Beilstein* **6** IV 3164.]

2,6-Dimethylphenol *[576-26-1]* **M 122.2, m 49°, b 203°/760mm, pK^{25} 10.61.** Fractionally distil 2,6-xylenol under nitrogen, crystallise it from *benzene or hexane, and sublime it at 38°/10mm. [*Beilstein* **6** IV 3122.]

3,4-Dimethylphenol *[95-65-8]* **M 122.2, m 62.5°, 65°, 65-68°, 67°, b 142°/50mm, 225°/757mm, pK^{25} 10.36.** Heat 3,4-xylenol with an equal weight of conc H_2SO_4 at 103-105° for 2-3 hours, then dilute it with four volumes of water, reflux it for 1 hour, and either steam distil or extract it repeatedly with diethyl ether after cooling to room temperature. The steam distillate is also extracted and evaporated to dryness. (The purification

process depends on the much slower sulfonation of 3,4-dimethylphenol than most of its likely contaminants.) It can also be crystallised from water, hexane or petroleum ether, and sublimed in a vacuum. [Kester *Ind Eng Chem (Anal Ed)* **24** 770 *1932*, Bernasconi & Paschalis *J Am Chem Soc* **108** 2969*1986*, *Beilstein* **6** IV 3099.]

3,5-Dimethylphenol *[108-68-9]* **M 122.2, m 68°, b 219°, pK^{25} 10.19.** Purify it as for 3,4-dimethylphenol. [*Beilstein* **6** IV 3141.]

2,6-Dimethylphenylisocyanide *[2769-71-3]* **M 131.2, m 72-76°, 72-75°.** Like most isocyanides (isonitriles, carbylamines), it reacts with transition metals to form aldimines [Malatesta & Bonati *Isonitrile Complexes of Metals* Wiley Interscience, NY *1969*, SBN 470 565551, Treichel in *Advances in Organometallic Chemistry* **Vol 11**, (Stone & West Eds) Academic Press NY *1973*], and because of the crowded area around the nitrogen atom it coordinates with the metal in metal catalysts to enhance their stereoselectivity. The isocyanide can function as a nucleophile, electrophile, carbene, radical acceptor or pseudohalogen [Ugi (ed.) *Isonitrile Chemistry Academic Press NY 1971*, Library of Congress No 73-84156]. Among the general methods for preparing isocyanides the one that uses the ***Vilsmeier reagent*** {(chloromethylene)dimethyliminium chloride, $[ClCH{=}NMe_2]^+$ Cl^-, **M 128.0, m 132°(dec)**, [3724-43-4]} has been commonly used, and in this case it is prepared *in situ*. Thus a solution of redistilled $SOCl_2$ (0.5mol) in DMF (150ml) is added slowly to a stirred solution of ***N-(2,6-dimethylphenyl) formamide** (0.5mol, see below) {**M 149.2, m 165°**, see [607-92-1]} under N_2 and the temperature is kept below -50°. On completion, the cooling bath is momentarily removed to allow the temperature to rise to -45°, then the cooling bath is replaced while anhydrous Na_2CO_3 (1mol) is added very carefully with rapid stirring till evolution of CO_2 ceases. Stirring is continued while the mixture is heated to 35°, then kept at ~25° for 1 hour, diluted with ice-water and extracted into pentane. The extract is separated, dried (Na_2SO_4), and evaporated to give *2,6-dimethylphenylisocyanide* as a crystalline colourless solid in 74% yield. It can be recrystallised from pentane, and should be stored under N_2 between 2° to 8°. It is **toxic**. [Periasamy and Walborsky *Org Prep Proc Int* **11** 295 *1979*.]
***N-(2,6-Dimethylphenyl)formamide**, *[607-92-1]* **M 149.2, m 164°** (**164-5°**, **168-170°** also reported, and **176-177°** on rapid heating) is prepared by heating 2,6-dimethylaniline (see [87-62-7]) with formic acid, pouring into H_2O, filtering, drying and recrystallising from EtOH. [Hodgkinson & Limpach *J Chem Soc* **77 65 (**67) *1900*, *Beilstein* **12** H 1109, **12** I 604.]

Dimethyl phthalate *[131-11-3]* **M 194.2, b 282°/760mm, d_4^{20} 1.190, d_4^{25} 1.1865, n_D^{20} 1.5149.** Wash the ester with aqueous Na_2CO_3, then distilled water, dry ($CaCl_2$) and distil it under reduced pressure (**b** 151-152°/0.1mm). [*Beilstein* **7** IV 3170.]

2,4-Dimethylresorcinol *[634-65-1]* **M 138.1, m 111°, 112°, $pK_{Est(1)}$ ~9.8, $pK_{Est(2)}$ ~11.7.** Crystallise the resorcinol from petroleum ether (b 60-80°), *C_6H_6/petroleum ether or toluene/BuOAc. It sublimes at 100-110°/1mm. [*Beilstein* **6** H 918, **6** II 891, **6** III 4588, **6** IV 5955.]

Dimethyl terephthalate *[120-61-6]* **M 194.2, m 141.5-141.8°**, **142°.** Purify it by recrystallisation from aqueous EtOH, MeOH or CCl_4; or by zone melting. [*Beilstein* **6** H 843, **6** III 4250, **6** IV 3303.]

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***N,N*-Dimethyl-*o*-toluidine** *[609-72-3]* **M 135.2, b 68°/10mm, 211-211.5°/760mm, d_4^{20} 0.937, n_D^{20} 1.53664, pK^{25} 6.11.** Isomers and other bases are removed by heating in a water bath for 100 hours with two equivalents of 20% HCl and two and a half volumes of 40% aqueous formaldehyde, then making the solution alkaline and separating the free base. After washing well with water, it is distilled at 10mm pressure and redistilled at ambient pressure [von Braun & Aust *Chem Ber* **47** 260 *1914*]. Other procedures include drying with NaOH, distilling from zinc in an atmosphere of nitrogen under reduced pressure, and refluxing with excess of acetic anhydride in the presence of conc H_2SO_4 as catalyst, followed by fractional distillation in a vacuum. The *picrate* has **m** 124-125°. [*Beilstein* **12** H 857, **12** III 1843, **12** IV 1747.]

***N,N*-Dimethyl-*m*-toluidine (*m*-methyl-*N,N*-dimethylaniline)** *[121-72-2]* **M 135.2, b 72-74°/5mm, 128°/57mm, 211.5-212.5°/760mm, d_4^{20} 0.93, n_D^{20} 1.5500, pK^{25} 5.34.** Reflux it for 3 hours with 2 molar equivalents of Ac_2O, then fractionally distil it under reduced pressure. *Alternatively*, dry over BaO, distil and store it over KOH. The *hydrochloride* has **m** 176° (from EtOH) and the *picrate* has **m** 131°. Methods described

for *N,N*-dimethylaniline are applicable. [*Beilstein* **12** H 857, **12** III 1953, **12** IV 1815.]

***N,N*-Dimethyl-*p*-toluidine (*p*-methyl-*N,N*-dimethylaniline)** *[99-97-8]* **M 135.2, b 76.5-77.5°/4mm, 93-94°/11mm, b 211°/760mm, d_4^{20} 0.937, n_D^{20} 1.5469, $pK^{21.5}$ 5.56, pK^{25} 5.63.** Reflux for 3 hours with 2 molar equivalents of Ac_2O, then fractionally distil it under reduced pressure. *Alternatively*, dry it over BaO, distil and store it over KOH. The *picrate* has **m** 128° (from EtOH). Methods described for *N,N*-dimethylaniline are applicable here. [*Beilstein* **12** H 902, **12** III 2026, **12** IV 1874.]

2,4-Dinitroaniline *[97-02-9]* **M 183.1, m 180°, ε_{348} 12,300 in dilute aqueous $HClO_4$, pK^{25} -4.27 (aqueous H_2SO_4).** Crystallise the nitroaniline from boiling EtOH by adding one-third volume of H_2O and cooling slowly. Dry it on a steam oven. The *N-acetyl* derivative has **m** 180°. [*Beilstein* **12** IV 1689.]

2,6-Dinitroaniline *[606-22-4]* **M 183.1, m 139-140°, pK^{25} -5.37 (aqueous H_2SO_4).** Purify the nitroaniline by chromatography on alumina, then crystallise it from *benzene or EtOH. The *N-acetyl* derivative has **m** 197° (from EtOH). [*Beilstein* **12** IV 1729.]

2,4-Dinitroanisole *[5327-44-6]* **M 198.1, m 87-88°(metastable), 94-95°. m 206-207°/12mm.** Crystallise the anisole from aqueous EtOH. The *naphthalene complex* has **m** 50° (from EtOH). [*Beilstein* **6** H 254, **6** III 858, **6** IV 1372.]

3,5-Dinitroanisole *[119-27-7]* **M 198.1, m 105-106°.** Purify the anisole by repeated crystallisation from EtOH, MeOH or H_2O and dry it in a vacuum desiccator over P_2O_5. The *naphthalene complex* has **m** 69° (from EtOH). [*Beilstein* **6** III 869, **6** IV 1385.

1,2-Dinitrobenzene *[528-29-0]* **M 168.1, m 116.5°.** Crystallise it from EtOH. [*Beilstein* **5** IV 738.]

1,3-Dinitrobenzene *[99-65-0]* **M 168.1, m 90.5-91°.** Crystallise 1,3-dinitrobenzene from alkaline EtOH solution (20g in 750ml 95% EtOH at 40°, plus 100ml of 2M NaOH) by cooling and adding 2.5L of H_2O. The precipitate, after filtering off, is washed with H_2O, sucked dry, and crystallised from 120ml, then 80ml of absolute EtOH [Callow et al. *Biochem J* **32** 1312 *1938*]. *Alternatively*, crystallise it from MeOH, CCl_4 or EtOAc. It can be sublimed in a vacuum. [Tanner *J Org Chem* **52** 2142 *1987*, *Beilstein* **5** IV 739.]

1,4-Dinitrobenzene *[100-25-4]* **M 168.1, m 173°.** Crystallise 1,4-dinitrobenzene from EtOH or EtOAc. Dry it under vacuum over P_2O_5. It can be sublimed in a vacuum. [*Beilstein* **5** IV 741.]

2,4-Dinitrobenzenesulfenyl chloride *[528-76-7]* **M 234.6, m 96°.** Crystallise the sulfenyl chloride from CCl_4. [*Beilstein* **6** II 316.]

2,4-Dinitrobenzenesulfonyl chloride *[1656-44-6]* **M 266.6, m 102°.** Crystallise the sulfonyl chloride from *benzene or *benzene/petroleum ether. [*Beilstein* **11** H 78, **11** IV 214.]

2,4-Dinitrobenzoic acid *[610-30-3]* **M 212.1, m 183°, pK^{25} 1.42.** Crystallise the acid from aqueous 20% EtOH (10ml/g) and let it dry at 100°. [*Beilstein* **9** II 279, **9** III 1776, **9** IV 1239.]

2,5-Dinitrobenzoic acid *[610-28-6]* **M 212.1, m 179.5-180°, pK^{25} 1.62.** Crystallise the acid from distilled H_2O. Dry it in a vacuum desiccator. [*Beilstein* **9** II 279, **9** III 1778, **9** IV 1241.]

2,6-Dinitrobenzoic acid *[603-12-3]* **M 212.1, m 202-203°, pK^{25} 1.14.** Crystallise the acid from water. [*Beilstein* **9** II 279, **9** III 1778, **9** IV 1242.]

3,4-Dinitrobenzoic acid *[528-45-0]* **M 212.1, m 166°, pK^{25} 2.81.** Crystallise the acid from EtOH by addition of water. [*Beilstein* **9** III 1778, **9** IV 1242.]

3,5-Dinitrobenzoic acid *[99-34-3]* **M 212.1, m 205°, pK^{25} 2.73 (2.79).** Crystallise the acid from distilled H_2O or 50% EtOH (4ml/g). Dry it in a vacuum desiccator or at 70° over BaO under a vacuum for 6 hours. [*Beilstein* **9** II 279, **9** III 1779, **9** IV 1242.]

4,4'-Dinitrobenzoic anhydride *[902-47-6]* **M 406.2, m 192°, 195-195.5°.** Crystallise the anhydride from Me_2CO, toluene, *C_6H_6/EtOAc or EtOAc. [*Beilstein* **9** H 393, **9** II 268, **9** III 1684.]

3,5-Dinitrobenzoyl chloride *[99-33-2]* **M 230.6, m 69.5°.** Crystallise it from CCl_4 or petroleum ether (b 40-60°). It reacts readily with H_2O and should be kept in sealed ampoules. [*Beilstein* **9** IV 1350.]

2,2'-Dinitrobiphenyl *[2436-96-6]* **M 244.2, m 123-124°, b 194°/4mm.** Crystallise the biphenyl from EtOH, AcOH (**m** 124.5°) or petroleum ether (**m** 125.5-126°). [*Beilstein* **5** H 538, **5** III 1759, **5** IV 1826.]

2,4'-Dinitrobiphenyl *[606-81-5]* **M 244.2, m 92.7-93.7°.** Crystallise the biphenyl from EtOH. [*Beilstein* **5** H 538, **5** I 274, **5** II 491, **5** III 1759, **5** IV 1827.]

4,4'-Dinitrobiphenyl *[1528-74-1]* **M 244.2, m 240.9-241.8°.** Crystallise the biphenyl from *C_6H_6, EtOH (charcoal) or Me_2CO. Dry it under vacuum over P_2O_5. It sublimes at ~138°/2.9×10^{-3}mm. [*Beilstein* **5** H 584, **5** III 1760, **5** IV 1827.]

2,6-Dinitro-*p*-cresol (2,6-dinitro-4-methylphenol) *[609-93-8]* **M 198.1, m 78-79°, 80.5°, 81-82°, 85°, pK$_{Est}$~3.7.** Recrystallise the cresol from EtOH. It is steam volatile. The *piperidine salt* has **m** 195°. [*Beilstein* **6** H 414, **6** II 391, **6** III 1390, **6** IV 2152.] **TOXIC IRRITANT.**

4,6-Dinitro-*o*-cresol (4,6-dinitro-2-methylphenol) *[534-52-1]* **M 198.1, m 85-86°, 86-87°, 87°, pK^{25} 4.70.** The cresol crystallises from aqueous EtOH. [*Beilstein* **6** H 369, **6** III 1276.]

2,4-Dinitrodiphenylamine *[961-68-2]* **M 259.2, m 157°, 160°, pK$_{Est}$ <0.** The amine forms red crystals from aqueous EtOH or $CHCl_3$/EtOH (**m** 158°). The UV has λ_{max} at 335nm (cyclohexane). [*Beilstein* **12** H 751, **12** III 1683, **12** IV 1692.]

4,4'-Dinitrodiphenylurea [1,3-bis-(4-nitrophenyl)urea] *[587-90-6]* **M 302.2, m 312°(dec).** Crystallise the urea from EtOH (**m** 364°, long heating), EtOH/Me_2CO (**m** 301-303°, 300-304° dec, 318-319°) or Me_2CO (**m** 289° dec). It sublimes *in vacuo*. [*Beilstein* **12** H 723, **12** II 393, **12** III 1619, **12** IV 1646.]

2,4-Dinitrofluorobenzene (Sanger's reagent) *[70-34-8]* **M 186.1, m 25-27°, b 133°/2mm, 140-141°/5mm, d$_4^{20}$ 1.483.** Crystallise the reagent from Et_2O or EtOH. Distil it in a vacuum through a Todd Column. If it is to be purified by distillation *in vacuo*, the distillation unit must be allowed to cool before air is allowed into the apparatus; otherwise the residue carbonises spontaneously and an **EXPLOSION** may occur. The material is a **skin irritant** and may cause serious dermatitis. [*Beilstein* **5** IV 742.]

1,8-Dinitronaphthalene *[602-38-0]* **M 218.2, m 170-171°, 171.3°.** Crystallise it from *benzene. [*Beilstein* **5** H 559, **5** II 455, **5** III 1608.]

2,4-Dinitro-1-naphthol (Martius Yellow) *[605-69-6]* **M 234.2, m 81-82°, pK$_{Est}$ ~3.7.** Crystallise the naphthol from *benzene or aqueous EtOH. [*Beilstein* **6** IV 4240.]

2,4-Dinitrophenetole *[610-54-8]* **M 240.2, m 85-86°, 210-211°/15mm.** Crystallise it from aqueous EtOH. The 1:1 *naphthalene complex* has **m** 41° and is obtained by fusing the compound with naphthalene in various ratios, then crystallising the solidified mix from a little EtOH (Dermer & Smith *J Am Chem Soc* **61** 748 *1939*). [*Beilstein* **6** H 254, **6** III 858, **6** IV 1373.]

2,4-Dinitrophenol *[51-28-5]* **M 184.1, m 114°, pK^{25} 4.12.** Crystallise it from *benzene, EtOH, EtOH/H_2O or H_2O acidified with dilute HCl, dry it, then recrystallise it from CCl_4. Dry it in an oven and store it in a vacuum

desiccator over $CaSO_4$. The *benzoate* has **m** 132° (from EtOH). [*Beilstein* **6** IV 1369.]

2,5-Dinitrophenol *[329-71-5]* **M 184.1, m 108°, pK^{25} 5.20.** Crystallise 2,5-dinitrophenol from H_2O with a little EtOH. [*Beilstein* **6** IV 1383.]

2,6-Dinitrophenol *[573-56-8]* **M 184.1, m 63.0-63.7°, pK^{25} 3.73.** Crystallise it from H_2O, aqueous EtOH, *C_6H_6/cyclohexane, or *C_6H_6/petroleum ether (b 60-80°, 1:1). [*Beilstein* **6** III 867, **6** IV 1383.]

3,4-Dinitrophenol *[577-71-9]* **M 184.1, m 138°, pK^{25} 5.42.** Steam distil and crystallise it from H_2O then dry it in air. **EXPLOSIVE** when dry, store it with 10% H_2O. [*Beilstein* **6** III 868, **6** IV 1384.]

3,5-Dinitrophenol *[586-11-8]* **M 184.1, m 126°, pK^{25} 6.68.** Crystallise it from *C_6H_6 or $CHCl_3$/petroleum ether. Store it with 10% water as it is **EXPLOSIVE** when dry. [*Beilstein* **6** III 869, **6** IV 1383.]

2,4-Dinitrophenylacetic acid *[643-43-6]* **M 226.2, m 179°(dec), pK^{25} 3.50.** Crystallise the acid from H_2O. [*Beilstein* **9** IV 1691.]

2,4-Dinitrophenylhydrazine (DNPH) *[119-26-6]* **M 198.1, m 200°(dec), pK$_{Est}$ ~2.0.** Crystallise DNPH from butan-1-ol, dioxane, EtOH, *C_6H_6 or EtOAc. The *hydrochloride* has **m** 186° (dec). [*Beilstein* **15** IV 380.]

2,4-Dinitroresorcinol *[519-44-8]* **M 200.1, m 212.5-214.5°, pK^{25} 3.05 (3.79).** Crystallise the resorcinol from aqueous EtOH. Its solubility at 25° is 0.25% in EtOH and 0.08g/L in H_2O. **EXPLOSIVE.** [*Beilstein* **6** II 824, **6** III 4352, **6** IV 5696.]

3,5-Dinitrosalicylic acid *[609-99-4]* **M 228.1, m 173-174°, pK$_1^{25}$ 0.70, pK$_2^{25}$ 7.40.** Crystallise the acid from H_2O. [*Beilstein* **10** IV 270.]

2,6-Dinitrothymol *[303-21-9]* **M 240.2, m 54.5-55°, 80-81°, 81°.** Crystallise 2,4-dinitrothymol from aqueous EtOH or petroleum ether. [Ganguly & LeFévre *J Chem Soc* 851 *1934*, *Beilstein* **6** H 543, **6** III 1911.]

2,3-Dinitrotoluene *[602-01-7]* **M 182.1, m 59.2°, 63°.** Distil the toluene in steam and crystallise it from H_2O or *benzene/petroleum ether. Store it with 10% H_2O as it could be **EXPLOSIVE** when dry. [*Beilstein* **5** H 339, **5** III 758, **5** IV 865.]

2,4-Dinitrotoluene *[121-14-2]* **M 182.1, m 70.5-71.0°, 71.8-72.2°.** Crystallise it from Me_2CO, isopropanol or MeOH. Dry it in a vacuum over H_2SO_4. It has also been purified by zone melting. Store it with 10% of H_2O. *It could be* **EXPLOSIVE** *when dry*. [*Beilstein* **5** H339, **5** IV 865, **5** III 759.]

2,5-Dinitrotoluene *[619-15-8]* **M 182.1, m 50.3°, 51.2°.** Crystallise it from *benzene. Store it with 10% of H_2O. **EXPLOSIVE** *when dry*. [*Beilstein* **5** III 760, **5** IV 866.]

2,6-Dinitrotoluene *[606-20-2]* **M 182.1, m 64.3°, 66.1°.** Crystallise it from acetone. Store it with 10% of H_2O. **EXPLOSIVE** *when dry*. [*Beilstein* **5** III 761, **5** IV 866.]

3,4-Dinitrotoluene *[610-39-9]* **M 182.1, m 58.5°, 60°, 61°.** Steam distil it and crystallise it from *C_6H_6/petroleum ether. Store it with 10% of H_2O to avoid **EXPLOSION. [***Beilstein* **5** H 341, **5** III 761, **5** IV 866.]

3,5-Dinitro-*o*-toluic acid *[28169-46-2]* **M 226.2, m 206°, 207.5-208°, pK$_{Est}$ ~3.0.** Crystallise the acid from H_2O or aqueous EtOH. The *ammonium salt* forms yellow crystals from EtOH with **m** 218-219°, and the *urea salt* has **m** 189-190° (prisms from EtOH). [*Beilstein* **9** H 474, **9** II 323, **9** III 2316.]

2,4-Dinitro-*m*-xylene *[603-02-1]* **M 196.2, m 83-84°.** Crystallise the yellow 2,4-dinitro-*m*-xylene from EtOH. [*Beilstein* **5** H 379, **5** II 295, **5** III 844.]

Dinonyl phthalate (mainly 3,5,5-trimethylhexyl phthalate isomer) *[14103-61-8, 28553-12-0, 84-76-4]* **M 418.6, m 26-29°, b 170°/2mm, d_4^{20} 0.9640, n_D^{20} 1.4825.** Wash the ester with aqueous Na_2CO_3 then shake it with water. Ether is added to break the emulsion, and the solution is washed twice with water, and dried ($CaCl_2$). After evaporating the ether, the residual liquid is distilled three times under reduced pressure. It is stored in a vacuum desiccator over P_2O_5. [*Beilstein* **9** IV 3183.]

4,4'-Di-*n*-pentyloxyazoxybenzene *[64242-26-8]* **M 370.5, m 124.5° (with phase change at 82°, becomes clear and remelts at 119°).** Crystallise it from Me_2CO, and dry it by heating under vacuum. [*Beilstein* **16** III 599, **16** IV 175.]

Diphenic acid (diphenyl-2,2'-dicarboxylic acid) *[482-05-3]* **M 242.2, m 228-229°, pK^{25} 3.46.** Crystallise diphenic acid from water. Hot Ac_2O provides the *anhydride* below. [*Beilstein* **9** H 922, **9** IV 3552.]

Diphenic anhydride (diphenyl-2,2'-dicarboxylic anhydride) *[6050-13-1]* **M 466.3, m 217°, 222-224°.** After removing free acid by extraction with cold aqueous Na_2CO_3, the residue is crystallised from acetic anhydride and dried at 100°. Acetic anhydride converts the acid to the anhydride. It also crystallises from *C_6H_6 (**m** 219°) or chlorobenzene (**m** 224.5-225.5°). [*Beilstein* **17** H 526, **17** II 495, **17** III/IV 6425.]

***N,N*-Diphenylacetamidine** *[621-09-0]* **M 210.3, m 131°.** Crystallise it from EtOH, then sublime it under vacuum at *ca* 96° onto a "finger" cooled in solid CO_2/MeOH, with continuous pumping to free it from occluded solvent. [*Beilstein* **12** H 248, **12** II 144, **12** III 471, **12** IV 384.]

Diphenylacetic acid *[117-34-0]* **M 212.3, m 147.4-148.4°, pK^{25} 3.94.** Crystallise the acid from *benzene, H_2O or aqueous 50% EtOH. [*Beilstein* **9** H 673, **9** IV 2492.]

Diphenylacetonitrile *[86-29-3]* **M 193.3, m 73-75°.** Crystallise the nitrile from EtOH or petroleum ether (b 90-100°). [*Beilstein* **9** H 674, **9** IV 2505.]

Diphenylacetylene (tolan) *[501-65-5]* **M 178.2, m 62.5°, b 90-97°/0.3mm.** Crystallise tolan from EtOH. [*Beilstein* **5** H 656, **5** IV 2276.]

Diphenylamine *[122-39-4]* **M 169.2, m 62.0-62.5°, pK^{25} 0.77 (aqueous H_2SO_4).** Crystallise diphenylamine from petroleum ether, MeOH, or EtOH/water. Dry it under vacuum. [*Beilstein* **12** H 174, **12** IV 271.]

Diphenylamine-2-carboxylic acid (*N*-phenylanthranilic acid) *[91-40-7]* **M 213.2, m 182-183°, 184°, pK_1^{25} -1.28 (aqueous H_2SO_4), pK_2^{25} 3.86(CO_2H).** Crystallise the acid from EtOH (5ml/g) or AcOH (2ml/g) by adding hot water (1ml/g). [*Beilstein* **14** IV 1019.]

Diphenylamine-2,2'-dicarboxylic acid (2,2'-iminodibenzoic acid) *[579-92-0]* **M 257.2, m 298°(dec), 302°(dec), 320°(dec, long heating), pK_1^{35} 6.05, pK_2^{35} 7.02 (in 50% aqueous dioxane).** Crystallise the acid from EtOH. It complexes with Cu^{2+}, Zn^{2+}, Cd^{2+}, Co^{2+} and Ni^{2+}. [*Beilstein* **14** H 354, **14** I 545, **14** III 942, **14** IV 1058.]

9,10-Diphenylanthracene *[1499-10-1]* **M 330.4, m 248-249°.** Crystallise the anthracene from acetic acid or xylene [Baumstark et al. *J Org Chem* **52** 3308 *1987*]. [*Beilstein* **5** IV 2807.]

***N,N'*-Diphenylbenzidine** *[531-91-9]* **M 336.4, m 245-247°, 251-252°, pK^{25} 0.30.** Crystallise the benzidine from toluene or ethyl acetate. Store it in the dark. [*Beilstein* **13** H 223, **13** IV 368.]

***trans-trans*-1,4-Diphenylbuta-1,3-diene** *[538-81-8]* **M 206.3, m 153-153.5°.** Its solution in petroleum ether (b 60-70°) is chromatographed on an alumina-Celite column (4:1), and the column is washed with the same solvent. The main zone is cut out, eluted with ethanol and transferred to petroleum ether, which is then dried and evaporated [Pinckard et al. *J Am Chem Soc* **70** 1938 *1948*]. Recrystallise it from hexane. [*Beilstein* **5** H 676, **9** IV 2319.]

***sym*-(1,5)-Diphenylcarbazide** *[140-22-7]* **M 242.3, m 172°.** A common impurity is phenyl-semicarbazide which can be removed by chromatography: ~8g in H_2O is placed on a column (polyamide 6 powder, Macherey-Nagel-GmbH-Germany, washed several times with MeOH), eluted with H_2O/MeOH/AcOH (1:3:0.04) at 7-8 drops/second, then eluted with the same solvent mixture but diluted 5 fold with H_2O. The purification is followed by UV light at 280nm. The effluent is evaporated to dryness *in vacuo* at ~28°. [chromatography, IR & UV: Willems et al. *Anal Chim Acta* **51** 544 *1970*]. Recrystallise it from EtOH by adding CCl_4 to induce crystallisation, or AcOH to give a white crystalline powder which turns pink in air. It is air and light sensitive and should be stored in the dark under N_2. [*Beilstein* **15** H 292, **15** IV 182.]

1,5-Diphenylcarbazone (phenyldiazinecarboxylic acid 2-phenylhydrazide) *[538-62-5]* **M 240.3, m 124-127°, 156-159°(dec).** It crystallises from EtOH (*ca* 5ml/g), and dry the orange-red needles at 50°. A commercial sample, nominally *sym*-diphenylcarbazone (**m** 154-156°) was a mixture of diphenylcarbazide and diphenylcarbazone. The former was removed by dissolving 5g of the crude material in 75ml of warm EtOH, then adding 25g Na_2CO_3 dissolved in 400ml of distilled water. The alkaline solution was cooled and extracted six times with 50ml portions of diethyl ether (discarded). Diphenylcarbazone was then precipitated by acidifying the alkaline solution with 3M HNO_3 or glacial acetic acid. It was filtered off, air dried, and stored in the dark [Gerlach & Frazier *Anal Chem* **30** 1142 *1958*]. Other impurities are phenylsemicarbazide and diphenylcarbodiazone. Impurities can be detected by chromatography [Willems et al. *Anal Chim Acta* **51** 544 *1970*]. It is used for detection and estimation of Hg, Zn, Cd, Cr, Cu, Fe and Mo [Cheng et al. *Handbook of Organic Analytical Reagents,* Boca Baton 277 *1982*, *Beilstein* **16** H 24, **16** IV 17.]

Diphenyl carbonate (phenyl carbonate) *[102-09-0]* **M 214.2, m 80°, 168°/15mm, 306°/760mm.** Purify it by distillation under reduced pressure, sublimation, or by gas chromatography with 20% Apiezon on Embacel, and crystallisation from EtOH. [*Beilstein* **6** H 158, **6** IV 629.]

Diphenylcyclopropenone (Diphencyprone) *[886-38-4]* **M 206.2, m 87-90°(hydrate), 119-121°(anhydrous).** Crystallise it from cyclohexane. Its UV (MeCN) has λ_{max} at 226, 282, 297nm. [*Beilstein* **17** IV 1736.]

Diphenyl disulfide (phenyl disulfide) *[882-33-7]* **M 218.3, m 60.5°.** Crystallise the disulfide from MeOH. [Alberti et al. *J Am Chem Soc* **108** 3024 *1986*]. Also crystallise it repeatedly from hot Et_2O, then dry it in a vacuum at 30° over P_2O_5, fuse it under N_2 and re-dry it; the whole procedure being repeated, with a final drying under a vacuum for 24 hours. *Alternatively*, recrystallise it from hexane/EtOH solution. [Burkey & Griller *J Am Chem Soc* **107** 246 *1985*, *Beilstein* **6** H 323, **6** IV 1560.]

1,1-Diphenylethanol *[599-67-7]* **M 198.3, m 80-81°, 81-81.5°, 87°, 90°, b 144-145°/12mm, 260°/760mm (dec), d^{15} 1.1057.** Crystallise 1,1-diphenylethanol from *n*-heptane and/or distil it under vacuum. The *benzoyl* derivative has **m** 115° and the *phenylurethane* has **m** 119°. [Bromberg et al. *J Am Chem Soc* **107** 83 *1985*, *Beilstein* **6** H 685, **6** I 330, **6** II 639, **6** III 3395, **6** IV 4713.]

1,1-Diphenylethylene *[530-48-3]* **M 180.3, m 6°, b 101°/2mm, 134°/10mm, 268-270°/760mm, d_4^{20} 1.024, n_D^{20} 1.6088.** Distil it under reduced pressure from KOH. Dry it with CaH_2 and redistil it. [*Beilstein* **5** H 639, **5** III 1975, **5** IV 2173.]

***N,N'*-Diphenylethylenediamine (Wanzlick's Reagent)** *[150-61-8]* **M 212.3, m 67.5°, b 178-182°/2mm $pK_{Est(1)}$ ~0.5, $pK_{Est(2)}$ ~3.8.** Crystallise the reagent from aqueous EtOH or MeOH. [*Beilstein* **12** H 543, **12** IV 986.]

***(1S,2S)*-1,2-diphenylethylenediamine bis-triflamide** *[121788-77-0]* **M 478.4, m 213-214°, $[\alpha]_D^{23}$ -6.6° (c 1.4, $CHCl_3$).** The bis-amide is obtained from (1*S*,2*S*)-(–)-1,2-diphenylethylenediamine (see [*cis*-1-aminoindan-2-ol -69-8]) by treatment with triflic anhydride (358-23-6), Et_3N and 4-dimethylaminopyridine (DMAP, see [1122-58-3]) in CH_2Cl_2; and purified by flash chromatography on silica gel (15% EtOAc-hexane, v/v). Its ^1H NMR (400MHz, $CDCl_3$, TMS) has δ_H at 4.81(s, 2H), 6.80 (br s, 2H), 7.25 (s, 6H), 7.0 (s, 4H); and its ^{13}C NMR (100MHz, $CDCl_3$) has δ at 63.7, 127.0, 129.1 (2C), 135.1. It is a useful reagent for enantioselective Diels-Alder and aldol reactions using a chiral controller system. [Corey et al. *J Am Chem Soc* **111** 5493 *1989*, Pikul &

Corey *OrgSynth* **71** 30 *1993* and references herein.]

***N,N′*-Diphenylformamidine** *[622-15-1]* **M 196.2, m 142°, 137°, 136-139°.** Crystallise it from absolute EtOH. The *hydrate* is obtained from aqueous EtOH. [*Beilstein* **12** H 236, **12** IV 372.]

1,3-Diphenylguanidine *[102-06-7]* **M 211.3, m 148°, pK^{25} 10.12.** Crystallise it from toluene, aqueous acetone or EtOH, and dry it in a vacuum. [*Beilstein* **12** H 369, **12** IV 769.]

1,6-Diphenyl-1,3,5-hexatriene *[1720-32-7]* **M 232.3, m 200-203°.** Crystallise the hexatriene from $CHCl_3$ or EtOH/$CHCl_3$ (1:1). [*Beilstein* **5** H 691, **5** IV 2425.]

1,1-Diphenylhydrazine *[530-50-7]* **M 184.2, m 34.5°, 44°, b 120°/1.1mm, 220°/40-50mm, pK$_{Est}$ ~9.1.** Purify it *via* the *hydrochloride* [530-47-2], which has **m** 165-170°(dec) after crystallisation from aqueous EtOH (plus a few drops of HCl) and recover the free base with aqueous NaOH, extract it into Et_2O, dry it (KOH), filter, evaporate and distil the residue under a vacuum. The distillate crystallises on cooling. The *benzoyl* derivative has **m** 194° (from Me_2CO), and the *4-nitrophenyl hydrazone* (with the aldehyde) has **m** 131-132°. [Koga & Anselme *J Org Chem* **33** 3963 *1968*, *Beilstein* **15** IV 55.]

1,2-Diphenylhydrazine (hydrazobenzene) *[122-66-7]* **M 184.2, m 124-126°, b 175°/10mm, 222°/40mm, pK$_{Est}$ ~1.7.** Crystallise hydrazobenzene from hot EtOH containing a little ammonium sulfide or H_2SO_3 (to prevent atmospheric oxidation), preferably under N_2. Dry it in a vacuum desiccator, and store it in the dark or under N_2. It has been distilled in a vacuum. *Alternatively*, crystallise it from petroleum ether (b 60-100°) to constant absorption spectrum. It is almost colourless but in air it turns yellow, then red with the formation of azobenzene. The *hydrochloride* crystallises from EtOH and has **m** 163-164°(dec); however, hydrazobenzene readily rearranges to *benzidine* in the presence of acid. The *picrate* crystallises from *C_6H_6 and has **m** 123°(dec). [*Beilstein* **15** H 123.]

Diphenylmethane *[101-81-5]* **M 168.2, m 25.4°, b 74°/0.4mm, 260.5°/764.5mm.** Sublime it under vacuum, or distil it at 72-75°/0.4mm. Recrystallise it from cold EtOH. It has also been purified by fractional crystallisation from the melt. [Armarego *Aust J Chem* **13** 95 *1960*, *Beilstein* **5** II 498, **5** IV 1841.]

1,1-Diphenylmethylamine (benzhydrylamine, aminodiphenylmethane) *[91-00-9]* **M 183.2, m 12°, 34°, b 166°/12mm, 295°/atm, d$_4^{25}$ 1.063, n$_D^{20}$ 1.596, pK$_{Est}$ ~9.1.** Crystallise the amine from H_2O. The *free base* absorbs CO_2 from the atmosphere; store it accordingly. The *hydrochloride* [5267-34-5] **M** 219.7 **m** 293-295°, crystallises from H_2O. [*Beilstein* **12** H 1323, **12** IV 3282.]
§A polymer bound *benzhydrylamine hydrochloride* is commercially available.

Diphenylmethyl chloride (benzhydryl chloride) *[90-99-3]* **M 202.7, m 17.0°, b 140°/3mm, 167°/17mm, n 1.5960.** Dry the chloride with Na_2SO_4 and fractionally distil it under reduced pressure. [*Beilstein* **5** H 590, **5** I 278, **5** II 500, **5** III 1790, **5** IV 1847.]

***all-trans*-1,8-Diphenyl-1,3,5,8-octatetraene** *[3029-40-1]* **M 258.4, m 235-237°.** Crystallise the octatetraene from EtOH. [*Beilstein* **5** H 709, **5** II 620, **5** III 2328, **5** IV 2508.]

***N,N′*-Diphenyl-*p*-phenylenediamine** *[74-31-7]* **M 260.3, m 148-149°, b 219-224°/0.7mm, pK$_{Est}$ <0.** Crystallise the diamine from EtOH, chlorobenzene/petroleum ether or *benzene. It has also been crystallised from aniline, then extracted three times with absolute EtOH. [*Beilstein* **13** H 80.]

1,1-Diphenyl-2-picrylhydrazine *[1707-75-1]* **M 395.3, m 174°(dec), 178-179.5°(dec).** Crystallise the hydrazine from $CHCl_3$, or *benzene/petroleum ether (1:1), then degas it at 100° and $<10^{-5}$mm Hg for *ca* 50 hours to decompose the 1:1 molar complex formed with *benzene. [*Beilstein* **15** II 221, **15** IV 1210.]

2,2-Diphenylpropionic acid *[5558-66-7]* **M 226.3, m 173-174°, pK$_{Est}$ ~3.8.** Crystallise the acid from EtOH. [*Beilstein* **9** II 474.]

3,3-Diphenylpropionic acid *[606-83-7]* **M 226.3, m 155°, pK_{Est} ~4.5.** Crystallise the acid from EtOH. [*Beilstein* **9** H 680.]

Diphenyl sulfide *[139-66-2]* **M 186.3, b 145°/8mm, d_4^{20} 1.114, n_D^{20} 1.633.** Wash the sulfide with aqueous 5% NaOH, then water. Dry it with $CaCl_2$, then with sodium. The sodium is filtered off, and the diphenyl sulfide is distiiled under reduced pressure. [*Beilstein* **2** H 299, **6** IV 1488.]

Diphenyl sulfone *[127-63-9]* **M 218.3, m 125°, b 378°(dec).** Crystallise the sulfone from diethyl ether. It has been purified by zone melting. [*Beilstein* **6** H 300, **6** IV 1490.]

***sym*-Diphenylthiourea (thiocarbanilide)** *[102-08-9]* **M 228.3, m 154°.** Crystallise the thiourea from boiling EtOH by adding hot water and allowing to cool. [*Beilstein* **12** H 394, **12** IV 810.]

1,1-Diphenylurea *[603-54-3]* **M 212.3, m 238-239°.** Crystallise 1,1-diphenylurea from MeOH. [*Beilstein* for 1,3 **12** IV 741.]

2,6-Di-*iso*-propylaniline *[24544-04-5]* **M 177.3, m -45°, b 120-122°/10mm, 257°/atm, d_4^{25} 0.9367, n_D^{20} 1.5330, pK_{Est} ~0.** Nitration of 1,3-di-*iso*-propylbenzene in AcOH/Ac_2O (2:1 v/v) with 96% HNO_3 (1.24-2.05 equivalents) below 45-50°/24 hours gave, on fractionation through a 2.5 x 180cm column at 5-10mm, a mixture of lower boiling 4-nitro- (74%) and the higher boiling 2-nitro-1,3-di-*iso*-propylbenzene (24%). Reduction of the later in *iso*-propanol with H_2 (~1200psi, <100°) catalysed by Raney Ni (5-10% by weight), followed by filtration, evaporation of the solvent and fractionation through a 180cm column at 10mm, with a reflux ratio of 20:1 and a rate of 0.33ml/minute gave *2,6-di-iso-propylaniline* as a colourless oil in 94.9% yield. The *benzoyl derivative* separated as an oil which solidifies and provides a white crystalline powder, **m 106.0-106.7°**, on recrystallisation form *iso*-octane. [Newton *J Am Chem Soc* **65** 2434 *1943*.] *Alternatively*, aniline (300g), $AlCl_3$ (18g), and Al powder (6g) are heated in a pressure vessel at 290°, and propylene is pumped into the vessel to a pressure of 250 atmospheres. From time to time more propylene is added to sustain the pressure. After *ca* 8 hours the pressure ceased to decrease, the vessel is opened and the product is shaken with dilute aqueous NaOH and fractionated under a vacuum. The three fractions that separate are *2,6-di-iso-propylaniline* (78%), 2-*iso*-propylaniline (15%), and a small amount of 2,4,6-tri-*iso*-propylaniline [Stroh et al. *Angew Chem* **69** 124 *1957*, also report **m 184.5-187°** for the *acetyl* derivative, and **m 254-256°** for the *benzoyl* derivative.] [*Beilstein* **12** III 2764.]
It is used for making NHCs for metal catalysed α-arylation of acyclic ketones, e.g. propiophenones, and amination of haloarenes [Matsubara et al. *J Org Chem* **72** 5069 *2007*]. It has been sulfonated for making sulfonated anilines, and consequently sulfonated NHCs, which provide water soluble Pd-NHCs used for Suzuki coupling of arylhalides with arylboronic acids in aqueous medium [Fleckenstein et al. *Chem Commun* 2870 *2007*].
N-*Trimethylsilyl 2,6-di-isopropylaniline* *[78923-65-6]*, prepared by reaction of Me_3SiCl and the Li salt of the aniline in Et_2O, is purified by distillation in vacuum. It is used in preparing the key intermediate for the Schrock-Hoveyda molybdenum catalyst (see [205815-80-1]), and sometimes it is prepared *in situ* without isolating it while using Et_3N instead of Li as base. [Schrock et al. *J Am Chem Soc* **112** 3875 *1990*, Alexander et al. *Organometallics* **19** 3700 *2000*].

***N,N*-Di-*n*-propylaniline** *[2217-07-4]* **M 177.3, b 127°/10mm, 238-241°/760mm, pK^{23} 5.68.** Reflux the aniline for 3 hours with acetic anhydride, then fractionally distil under reduced pressure.

Dithizone (diphenylthiocarbazone) *[60-10-6]* **M 256.3, m 168°(dec), ratio of $\varepsilon_{620nm}/\varepsilon_{450nm}$ should be ≥1.65, ε_{620} 3.4 x 10^4 ($CHCl_3$), pK_2 4.6.** The crude dithizone is dissolved in CCl_4 to give a concentrated solution. This is filtered through a sintered glass funnel and shaken with 0.8M aqueous ammonia to extract dithizonate ion. The aqueous layer is washed with several portions of CCl_4 to remove undesirable materials. The aqueous layer is acidified with dilute H_2SO_4 to precipitate pure dithizone. This is dried in a vacuum. When only small amounts of dithizone are required, purification by paper chromatography is convenient. [Cooper & Hibbits *J Am Chem Soc* **75** 5084 *1933*.] Instead of CCl_4, $CHCl_3$ can be used, and the final extract, after washing with water, can be evaporated in air at 40-50° and dried in a desiccator. It complexes with Cd, Hg, Ni and Zn.

[*Beilstein* **16** H 26, **16** IV 18.]

Di-*p*-tolyl carbonate *[621-02-3]* **M 242.3, m 115°.** Purify the carbonate by GLC with 20% Apiezon on Embacel followed by sublimation *in vacuo* and recrystallisation from EtOH (**m** 114°). [*Beilstein* **6** H 398, **6** I 201, **6** II 380, **6** III 1366.]

***N,N'*-Di-*o*-tolylguanidine** *[97-39-2]* **M 239.3, m 179° (175-176°), pK^{18} 9.62.** The guanidine crystallises from aqueous EtOH. The *sulfate* has **m** 253-254°(dec, H_2O). [*Beilstein* **12** H 803, **12** II 445, **12** III 1871, **16** IV 1764.]

Di-*p*-tolylphenylamine *[20440-95-3]* **M 273.4, m 108.5°, b 250°/20-40mm, pK$_{Est}$ ~ -5.0.** Crystallise the amine once from EtOAc, then twice from EtOH to give pale yellow needles. [Marsden *J Chem Soc* 627 *1937*, *Beilstein* **12** III 2033.]

Di-*p*-tolyl sulfone *[599-66-6]* **M 278.3, m 158-159°, 163.5°, b 405°/760mm.** Crystallise the sulfone repeatedly from Et_2O or EtOH. It has been purified by zone melting. [*Beilstein* **6** H 419, **6** II 395, **6** III 1405, **6** IV 2174.]

1,2-Divinylbenzene *[1321-74-0]* **M 130.2, b 53°/3mm, 79.2-79.6°/15mm, 195°//760mm, d^{20} 0.919, n$_D^{20}$ 1.573.** Purify divinylbenzene by dissolving in Et_2O, shaking with H_2O, drying over $CaCl_2$, filtering, evaporating and distilling *in vacuo*. It polymerises within 2-3days unless 4-*tert*butylcatechol (0.05%) is added as stabiliser. [Fries & Bestian *Chem Ber* **69** 715 *1936*, *Beilstein* **5** III 1366.]

Duroquinone (tetramethylbenzoquinone) *[527-17-3]* **M 164.2, m 110-111°, 111-112°.** Crystallise duraquinone from 95% EtOH. Dry it *in vacuo*. [*Beilstein* **7** H 669, **7** III 3417, **7** IV 2101.]

Ellagic acid (4,4',5,5',6,6'-hexahydroxydiphenic acid dilactone) *[476-66-4]* **M 338.2, m >360°, pK$_{Est(1)}$~8, pK$_{Est(2)}$~11.** This antioxidant crystallises from pyridine. It forms a dark green solution in aqueous *N* NaOH. The *tetraactetate dilactone* crystallises from Ac_2O, with **m** 340°. [*Beilstein* **19** H 261, **19** III/IV 3164, **19/7** V 108.]

Emodine (1,3,8-trihydroxy-6-methyl-9,10-anthracenedione, archin) *[518-82-1]* **M 270.2, m 253-257°, 255-256°, 256-257°, 262°, 264° (phenolic pKs 7—10).** Archin forms orange needles from EtOH, Et_2O, *C_6H_6, toluene or pyridine. It sublimes above 200° at 12mm. [Tutin & Clewer *J Chem Soc* **99** 946 *1911*, IR: Bloom et al. *J Chem Soc* 178 *1959*, UV: Birkinshaw *Biochem J* **59** 495 *1955*, Raistrick *Biochem J* **34** 159 *1940*.]

1*R*,2*S*-(-)Ephedrine see (–)-ephedrine (1*R*,2*S*-2-methylamino-1-phenylpropanol) in "Miscellaneous" in Chapter 7.

(±)-Epichlorohydrin *[106-89-8]* **M 92.5, b 115.5°/760mm d$_4^{25}$ 1.183, n$_D^{20}$ 1.438.** Distil epichlorohydrin at 760mm, heat it on a steam bath with one-quarter its weight of CaO, then decant and fractionally distil it. [*Beilstein* **17** H 6, **17** III/IV 20.]

***R*(-)Epinephrine** See adrenalin in "Miscellaneous" in Chapter 7.

3-Ethoxy-*N,N*-diethylaniline *[1846-92-2]* **M 193.3, b 145°/14mm, 268-270°/760mm, n$_D^{25}$ 1.5325, pK$_{Est}$ ~6.1.** Reflux it for 3 hours with Ac_2O, then fractionally distil it, preferably under reduced pressure. The *3-nitroso* derivative has **m** 72.5° (green crystals from petroleum ether/*C_6H_6). [Klaassens & Schoot *Rec Trav Chim Pays Bas* **48** 1272 *1929*.]

1-Ethoxynaphthalene *[5328-01-8]* **M 172.2, b 136-138°/14mm, 282°/760mm, d$_4^{20}$ 1.061, n$_D^{20}$ 1.604.** Fractionally distil it (twice) under a vacuum, then dry it with, and distil it under a vacuum from sodium. The *picrate* has **m** 118.5-119° (from EtOH). [*Beilstein* **6** H 606, **6** II 578, **6** III 2924, **6** IV 4212.]

2-Ethoxynaphthalene *[93-18-5]* **M 172.2, m 35.6-36.0°, b 142-143°/12mm, 280°/760mm.** Crystallise it from petroleum ether or EtOH (**m** 37-38°). Dry it *in vacuo*, or distil it in a vacuum. The *picrate* has **m** 104.5° (from EtOH or $CHCl_3$). [*Beilstein* **6** H 606, **6** II 578, **6** III 2972, **6** IV 4257.]

Ethyl *p*-aminobenzoate (Benzocaine) *[94-09-7]* **M 165.2, m 92°, pK^{25} 2.39.** Crystallise Benzocaine from EtOH/H_2O or EtOH (**m** 93-94°), and dry it in air. [*Beilstein* **14** H 422, **14** IV 1129.]

***p*-Ethylaniline** *[589-16-2]* **M 121.2, b 88°/8mm, d_4^{20} 0.975, n_D^{20} 1.554, pK^{25} 5.00.** Dissolve *p*-ethylaniline in *benzene, then acetylate it. Recrystallise the *acetyl* derivative (**m** 93-94°, Hickinbottom & Waine *J Chem Soc* 1565 *1930*) from *C_6H_6/petroleum ether or EOH, and hydrolyse it by refluxing 50g with 500ml of H_2O and 115ml of conc H_2SO_4 until the solution becomes clear. The amine sulfate is isolated, suspended in H_2O and solid KOH is added to generate the free base, which separates. Dry it (KOH), and distil it from zinc dust in a vacuum [Berliner & Berliner *J Am Chem Soc* **76** *6179 1954*]. The *picrate* has **m** 171-172° (from 1,2-dichloroethane). [*Beilstein* **12** H 1090, **12** III 2380, **12** IV 2419.]

***trans*-Ethyl cinnamate** *[103-36-6]* **M 176.2, f 6.7°, b 127°/6mm, 272.7°/768mm, d_4^{20} 1.040, n_D^{20} 1.55983.** Wash the ester with aqueous 10% Na_2CO_3, then water, dry ($MgSO_4$), and distil it. The purified ester is saponified with aqueous KOH, and, after acidifying the solution, cinnamic acid is isolated, washed and dried. The ester is reformed by refluxing for 15 hours the cinnamic acid (25g) with absolute EtOH (23g), conc H_2SO_4 (4g) and dry *benzene (100ml), after which it is isolated, washed, dried and distilled under reduced pressure [Jeffery & Vogel *J Chem Soc* 658 *1958*]. [*Beilstein* **9** IV 2006.]

(±)-Ethyl α,β-dibromo-β-phenylpropionate *[5464-70-0, erythro 30983-70-1]* **M 336.0, m 75°.** Crystallise the propionate from petroleum ether (b 60-80°), EtOH or aqueous EtOH (**m** 78°, and an unstable form **m** 65°). [*Beilstein* **9** H 512, **9** I 202, **9** III 2406, **9** IV 1772.]

Ethylene di(*p*-toluenesulfonate) (ethylene glycol ditosylate) *[6315-52-2]* **M 370.44, m 124-127°, m 126-127°, m 128°.** It is prepared from ethylene glycol (0.5mole) and *p*-toluenesulfonyl chloride (1.0mole) are stirred in Me_2CO (100ml) in the presence of 25% aqueous NaOH (175ml, 44g, 1.1mole) at 2-10° for ~4 hours. Excess of ice-water is added, the solid is filtered off, washed with large volumes of H_2O, dried *in vacuo* and recrystallised from dry *C_6H_6 (absolute EtOH has also been used) to give the *di-tosylate* (**m 128°**) in 76% yield [Drahowzal & Klamann *Monatsh* **82** 452 *1951*]. *Alternatively*, ethylene glycol (0.25mole), *p*-toluenesulfonyl chloride (0.52mole) in dry pyridine (80g, 1mole) are stirred gently at -10° to -4° for 2 hours then treated with excess of ice-water as above gave the *diester* in 87.3% yield [Drahowzal & Klamann *Monatsh* **82** 460 *1951*]. The latter method is superior as there is no H_2O in the reaction medium. Note that attempts to prepare the *mono-p-tosylate ester* using equimolar amounts of glycol and sulfonyl chloride always produced the *diester* which crystallised as white plates (**m 126°**) from hot EtOH [Butler et al. *J Am Chem Soc* **57** 575 *1935*]. [*Beilstein* **11** II 296, **11** III 225, **11** IV 290.]

S,S'-Ethylene di(*p*-toluenethiosulfonate) (ethylene dithiotosylate) *[2225-23-2]* **M 402.5, m 75-76°.** This reagent is the lower homologue of *1,3-trimethylene di(thiotosylate) [3866-79-3]*, and is made from potassium thiotosylate (45g, 0.20 mole, see below [28519-50-8]) and 1,2-dibromoethane (18.8g, 0.1 mole) in EtOH (200ml, containing 10-20mg of KI to activate the dibromide) by refluxing, with stirring in the dark under a N_2 atmosphere, for 8 hours. The solvent is evaporated *in vacuo*, and the white solid residue is washed, by decantation, with a mixture of EtOH (80ml) and H_2O (150ml), and then with H_2O (3 x 50ml), and recrystallised from EtOH (~150ml) to provide the crude thioester (28.7g) with m 72-75°. The pure thioester (24g, 60%), **m 75-76°**, is obtained as white crystals after three recrystallisations from EtOAc/EtOH; and its ^{1}H NMR ($CDCl_3$, TMS) has δ at 2.47 (s, 6H, 2C***H***$_3$), 3.31 (s, 4H, C***H***$_2$C***H***$_2$), 7.48 (d, *J* = 9Hz, 4H, Aromatic H) and 7.97 (d, *J* = 9Hz, 4H, Aromatic H). [Woodward et al. *Org Synth* Coll Vol **V** 1016 *1988*, *Org Synth* **54** 33 *1974*.]
Like the trimethylene homologue below it can form 1,3-dithiolanes with activated methylene groups and carbonyl compounds.

Ethyl gallate *[831-61-8]* **M 198.2, m 150-151°, 163-165°.** Recrystallise the gallate from 1,2-dichloroethane. Its UV has λ_{max} (neutral species) at 275nm (ε 10,000), (anion) at 235nm (ε 10,300), 279nm (ε 11,400) and

324nm (ε 8 500) [Campbell & Coppinger *J Am Chem Soc* **73** 2708 *1951*]. [*Beilstein* **10** IV 2002.]

Ethyl *p*-nitrobenzoate *[99-77-4]* **M 195.2, m 56°.** Dissolve it in Et_2O and wash it with aqueous alkali, then the ether is evaporated and the solid recrystallised from EtOH. [*Beilstein* **13** H 3787, **13** IV 1074.]

***o*-Ethylphenol** *[90-00-6]* **M 122.2, f 45.1°, b 210-212°, d_4^{20} 1.020, n_D^{20} 1.537, pK^{25} 10.20.** Purify as for *p*-ethylphenol below. [*Beilstein* **6** H 470, **6** IV 3011.]

***p*-Ethylphenol** *[123-07-9]* **M 122.2, m 47-48°, b 76°/1mm, 153°/100mm, 218.0°/762mm, n_D^{25} 1.5239, pK^{25} 10.21.** Non-acidic impurities are removed by passing steam through a boiling solution containing 1 mole of the phenol and 1.75 moles of NaOH (as an aqueous 10% solution). The residue is cooled and acidified with 30% (v/v) H_2SO_4, and the free phenol is extracted into diethyl ether. The extract is washed with water, dried with $CaSO_4$ and the ether is evaporated. The phenol is distilled at 100mm pressure through a Stedman gauze-packed column. It is further purified by fractional crystallisation by partial freezing, and by zone refining, under N_2 [Biddiscombe et al. *J Chem Soc* 5764 *1963*]. *Alternatively*, purify it *via* the benzoate, as for phenol. The *4-nitrophenylbenzoate* has **m** 80° (from EtOH). [*Beilstein* **6** H 470, **6** III 1663, **5** IV 3020.]

Ethyl phenylacetate *[101-97-3]* **M 164.2, b 99-99.3°/14mm, d_4^{20} 1.030, n_D^{20} 1.499.** Shake the ester with saturated aqueous Na_2CO_3 (three times), aqueous 50% $CaCl_2$ (twice) and saturated aqueous NaCl (twice). Dry with $CaCl_2$ and distil it under reduced pressure. [*Beilstein* **9** H 434, **9** IV 1618.]

Ethyl Red [2-(4-diethylaminophenylazo)benzoic acid] *[76058-33-8]* **M 297.4, m 135°, 150-152°, pK_1 2.5, pK_2 9.5.** Crystallise the acid dye from EtOH/diethyl ether or toluene. It is an indicator: pH 4.4 (red) and 6.2 (yellow). Its UV has λ_{max} at 447nm. [*Beilstein* **16** I 316.]

Ethynyl *p*-tolylsulfone *[13894-21-8]* **M 180.2, m 65-67°, 73-74°.** Recrystallise the sulfone from petroleum ether, *C_6H_6 or EtOH (**m** 66°), and dry it in a vacuum. [*Beilstein* **6** III 1397, **6** IV 2160.]

Eugenol (4-allyl-2-methoxyphenol) *[97-53-0]* **M 164.2, b 253°/760mm, 255°/760mm, d_4^{20} 1.066, n_D^{20} 1.540, pK^{25} 10.19.** Fractional distillation of eugenol gives a pale yellow liquid which darkens and thickens on exposure to air. It should be stored under N_2 at -20°. [Waterman & Priedster *Rec Trav Chim Pays Bas* **48** 1272 *1929*, *Beilstein* **6** H 961, **6** IV 6337.]

Eugenol methyl ether (4-allyl-1,2-dimethoxybenzene) *[93-15-2]* **M 178.2, m -4°, b 127-129°/11mm, 146°/30mm, 154.7°/760mm, d_4^{20} 1.0354, n_D^{20} 11.53411.** Recrystallise the ether from hexane at low temperature and redistil it (preferably *in vacuo*). [Hillmer & Schorning *Z Phys Chem* [A] **167** 407 *1934*, Briner & Fliszár *Helv Chim Acta* **42** 2063 *1959*, *Beilstein* **6** H 963, **6** IV 6337.]

Fluoranthene (benzo[*j,k*]fluorene) *[206-44-0]* **M 202.3, m 110-111°, b 384°/760mm.** Purify it by chromatography of CCl_4 solutions on alumina, with *benzene as eluent. Crystallise it from EtOH, MeOH or *benzene. Also purify it by zone melting. [Gorman et al. *J Am Chem Soc* **107** 4404 *1985*, *Beilstein* **5** I 344, **5** IV 2463.]

Fluorene *[86-73-7]* **M 166.2, m 114.7-115.1°, b 160°/15mm, 298°/atm.** Purify fluorene by chromatography of CCl_4 or petroleum ether (b 40-60°) solution on alumina, with *benzene as eluent. Crystallise it from 95% EtOH, 90% acetic acid and again from EtOH. Crystallisation using glacial acetic acid retains an impurity which is removed by partial mercuration and precipitation with LiBr [Brown et al. *J Am Chem Soc* **84** 1229 *1962*]. It has also been crystallised from hexane, or *benzene/EtOH, distilled under vacuum and purified by zone refining. [Gorman et al. *J Am Chem Soc* **107** 4404 *1985*, *Beilstein* **5** IV 2142.]

Fluorene-2,7-diamine *[525-64-4]* **M 196.3, m 165-166°.** Crystallise the diamine from hot H_2O or aqueous EtOH, dry it *in vacuo* and store it in the dark. [*Beilstein* **13** H 266, **13** II 123, **12** III 507, **13** IV 449.]

9-Fluorenone *[486-25-9]* **M 180.2, m 82.5-83.0°, 85-86°, b 341°/760mm.** Crystallise 9-fluorenone from absolute EtOH, MeOH or *benzene/pentane. [Ikezawa *J Am Chem Soc* **108** 1589 *1986*.] Also recrystallise it twice from toluene and sublime it in a vacuum [Saltiel *J Am Chem Soc* **108** 2674 *1986*]. It can be distilled under high vacuum. The *oxime* has **m 195°**, **198°** (yellow crystals from $*C_6H_6$ or xylene, Anet et al. *Can J Chem* **35** 180 *1957*, Wislicenus & Waldmuller *Chem Ber* **41** 3335 *1908*.) [*Beilstein* **7** H 465, **7** III 2330, **7** IV 1629.]

9-Fluorenylmethyl chloroformate (FMOC-Cl) *[28920-43-6]* **M 258.7, m 61-63°, 61.4-63°.** If the IR contains no OH bands (at ~3000 cm^{-1}) due to the hydrolysis product 9-fluorenylmethanol, then purify it by recrystallisation from dry Et_2O. Its IR ($CHCl_3$) has a band at 1770 cm^{-1} (C=O), and the ^1H NMR ($CDCl_3$) has δ at 4-4.6 (m 2H, C*H*CH_2) and 7.1-7.8 (m, 8 aromatic *H*). The *azide* (*FMOC-*N_3) has **m** 89-90° (from hexane) and IR ($CHCl_3$) at 2135 (N_3) and 1730 (C=O) cm^{-1}, and the *carbazate* (*FMOC-*$NHNH_2$) has **m** 171°(dec) (from nitromethane) with IR (KBr) at 3310, 3202 (NH) and 1686 (CONH) cm^{-1}. [Caprino & Han *J Org Chem* **37**, 3404 *1972*, *J Am Chem Soc* **92** 5748 *1970*, Koole et al. *J Org Chem* **59** 1657 *1989*, Fürst et al. *J Chromatogr* **499** 537 *1990*.]

9-Fluorenylmethyl succinimidyl carbonate *[82911-69-1]* **M 337.3, m 147-151°(dec), 151° (dec).** Recrystallise the carbonate from $CHCl_3/Et_2O$, or from petroleum ether (b 40-60°). [Pauet *Can J Chem* **60** 976 *1982*, Lapatsaris et al. *Synthesis* 671 *1983*.]

Fluorobenzene *[462-06-6]* **M 96.1, b 84.8°/760mm, d_4^{20} 1.025, n_D^{20} 1.46573, n_D^{30} 1.4610.** Dry fluorobenzene for several days with P_2O_5, then fractionally distil it. [*Beilstein* **5** H 198, **5** IV 632.]

o-**Fluorobenzoic acid** *[445-29-4]* **M 140.1, m 127°, d^{25} 1.460, pK^{25} 3.27.** Crystallise the acid from 50% aqueous EtOH, dilute HCl or $*C_6H_6$, then purify it by zone melting or vacuum sublimation at 130-140°. [*Beilstein* **9** H 333. **9** III 1324, **9** IV 950.]

m-**Fluorobenzoic acid** *[445-38-9]* **M 140.1, m 124°, 125°, d^{25} 1.474 pK^{25} 3.86.** Crystallise the acid from 50% aqueous EtOH or $*C_6H_6$, then sublime it *in vacuo* at 130-140°. [*Beilstein* **9** H 333, **9** IV 952.]

p-**Fluorobenzoic acid** *[456-22-4]* **M 140.1, m 182°, d^{25} 1.479, pK^{25} 4.15.** Crystallise the acid from 50% aqueous EtOH, then purify it by zone melting or vacuum sublimation at 130-140°. [*Beilstein* **9** H 333, **9** III 1327, **9** IV 953.]

3-Fluoro-4-hydroxyphenylacetic acid *[458-09-3]* **M 170.1, m 33°, $pK_{Est(1)}$ ~4.4, $pK_{Est(2)}$ ~9.4.** Crystallise the acid from water. [*Beilstein* **10** III 440.]

4-Fluoro-2-methylbenzaldehyde *[63082-45-1]* **M 138.1, d_4^{25} 1.144, n_D^{25} 1.526.** The aldehyde has been purified by gas chromatography and should be kept under N_2 as it readily oxidises in air [Burgess et al. *Aust J Chem* **30** 543 *1977*].

2-Fluoro-4-nitroaniline *[369-35-7]* **M 156.1, m 134-135°, 135-136°, pK^{25} -0.44 (aqueous $HClO_4$).** The aniline forms yellow crystals on recrystallisation from aqueous MeOH or EtOH. The *acetyl* derivative has **m** 203-204° (from EtOH). [Wepster & Verkade *Rec Trav Chim Pays Bas* **68** 86 *1949*, *Beilstein* **12** III 1647.]

1-Fluoro-4-nitrobenzene *[350-46-9]* **M 141.1, m 27°(stable form), 21.5°(unstable form), b 86.6°/14mm, 95-97.5°/22mm, 205.3°/735mm.** Crystallise it from EtOH or distil it in a vacuum. [*Beilstein* **5** H 241, **5** IV 719.]

1-Fluoro-4-nitronaphthalene *[341-92-4]* **M 191.2, m 80°.** It crystallises from EtOH as yellow needles [Bunce et al. *J Org Chem* **52** 4214 *1987*]. [*Beilstein* **5** III 1596, **5** IV 1675.]

4-Fluoro-3-nitrophenylazide *[28166-06-5]* **M 182.1, m 53-55°, 54-56°.** Dissolve the azide in Et_2O, dry it over $MgSO_4$, filter, evaporate and recrystallise the residue from petroleum ether (b 20-40°) to give orange needles. Store it in a stoppered container at ~0°. The ^1H NMR has δ at 7.75 (m 1H) and 7.35 (m 2H) in $CDCl_3$. [Hagedorn et al. *J Org Chem* **43** 2070 *1978*.]

***o*-Fluorophenol** *[367-12-4]* **M 112.1, m 16°, b 53°/14mm, 171-172°/714mm, d_4^{20} 1.257, n_D^{20} 1.514, pK^{25} 8.70.** Pass *o*-fluorophenol at least twice through a gas chromatographic column for small quantities; otherwise fractionally distil it under reduced pressure. [*Beilstein* **6** I 97, **6** IV 770.]

***p*-Fluorophenoxyacetic acid** *[405-79-8]* **M 170.1, m 104.2-104.6°, 106°, pK^{25} 3.13.** Crystallise the acid from EtOH or H_2O. [Hayes & Branch *J Am Chem Soc* **65** 1555 *1943*, *Beilstein* **6** III 971, **6** IV 776.]

4-Fluorophenylacetic acid *[405-50-5]* **M 154.1, m 86°, 94°, b 164°/2mm, pK^{25} 4.22.** Crystallise it from heptane, but it is best purified by distillation at high vacuum. [Bergmann et al. *J Am Chem Soc* **78** 6037 *1956*, *Beilstein* **9** III 2261, **9** IV 1672.]

4-Fluorophenyl isocyanate *[1195-45-5]* **M 137.1, b 55°/8mm, n_D^{20} 1.514.** Purify the isocyanate by repeated fractionation through an efficient column. If its IR indicates that there is too much urea (in the presence of moisture the symmetrical urea is formed), then dissolve it in dry EtOH-free $CHCl_3$, filter, evaporate and distil it. **It is a pungent LACHRYMATORY liquid, TOXIC.** [See Hardy *J Chem Soc* 2011 *1934*, and Hickinbottom *Reactions of Organic Compounds* Longmans p493 *1957*.]

4-Fluorophenyl isothiocyanate *[1544-68-9]* **M 153.2, m 24-26°, 26-27°, b 66°/2mm, 215°/atm, 228°/760mm, n_D^{20} 1.6116.** A likely impurity is the symmetrical thiourea. Dissolve the isothiocyanate in dry $CHCl_3$, filter and distil the residue in a vacuum. It can also be steam distilled, the oily layer is separated, dried over $CaCl_2$ and distilled *in vacuo*. *Bis-(4-fluorophenyl)thiourea* has **m** 145° (from aqueous EtOH). [Browne & Dyson *J Chem Soc* 3285 *1931*, Buu Hoi et al. *J Chem Soc* 1573 *1955*, Olander *Org Synth* Coll Vol **I** 448 *1941*].

***p*-Fluorophenyl-*o*-nitrobenzyl ether** *[448-37-3]* **M 247.2, m 62°.** Crystallise the ether from EtOH. [Jones *J Chem Soc* 1416 *1938*, *Beilstein* **6** III 1564, **6** IV 2608.]

***o*-Fluorotoluene** *[95-52-3]* **M 110.1, m -62°, b 114.4°/760mm, d_4^{20} 1.005, n_D^{20} 1.475.** Dry *o*-fluorotoluene with P_2O_5 or $CaSO_4$ and fractionally distil it through a silvered vacuum-jacketed glass column with 1/8th-in glass helices. A high reflux ratio is necessary because of the closeness of the boiling points of the *o*-, *m*- and *p*-isomers [Potter & Saylor *J Am Chem Soc* **37** 90 *1951*]. [*Beilstein* **5** H 290, **5** III 676, **5** IV 799.]

***m*-Fluorotoluene** *[352-70-5]* **M 110.1, m -87°, b 116.5°/760mm, d_4^{20} 1.00, n_D^{27} 1.46524.** Purify it as for *o*-fluorotoluene. [*Beilstein* **5** H 290, **5** III 676, **5** IV 799.]

***p*-Fluorotoluene** *[352-32-9]* **M 110.1, m -56°, 116.0°/760mm, d_4^{20} 1.00, n_D^{20} 1.46884.** Purify it as for *o*-fluorotoluene. [*Beilstein* **5** H 290, **5** III 677, **5** IV 799.]

Formanilide *[103-70-8]* **M 121.1, m 50°, b 166°/14mm, 216°/120mm, d_4^{20} 1.14.** Crystallise formanilide from Et_2O (**m** 45.3°), Et_2O/petroleum ether (**m** 46°), petroleum ether (**m** 47.6°), ligroin/xylene, or distil it preferably under reduced pressure. [*Beilstein* **12** H 230, **12** II 135, **12** III 453.]

Gallic acid (H_2O) (3,4,5-trihydroxybenzoic acid) *[5995-86-8 (H_2O), 149-91-7 (anhydrous)]* **M 188.1, m 253°(dec), pK_1^{25} 4.27, pK_2^{25} 8.68.** Crystallise gallic from water. The *tri-O-acetyl* derivative has **m** 172° (from MeOH), and the *anilide* has **m** 207°(from EtOH). [*Beilstein* **10** H 470, **10** IV 1993.]

Galvinoxyl [2,6-di-*tert*-butyl-α-(3,5-di-*tert*-butyl-4-oxo-2,5-cyclohexadiene-1-ylidene)-*p*-tolyloxy] *[2370-18-5]* **M 421.65, m 153.2-153.6°, 158-159°.** It is a stable free radical scavenger of short-lived free radicals with odd electrons on C or O. It is best prepared freshly by oxidation of 3,3',5,5'-tetra-*tert*-butyl-4,4'-dihydroxydiphenyl-methane [**m** 154°, 157.1-157.6°, obtained by gently heating for 10-15 minutes 2,6-di-*tert*-butylphenol, formaldehyde and NaOH in EtOH and recrystallised from EtOH (20g/100ml) as colourless plates, Karasch & Joshi *J Org Chem* **22** 1435 *1957*, Bartlett et al. *J Am Chem Soc* **82** 1756 *1960* and **84** 2596 *1962*]. Oxidation is carried out under N_2 with PbO_2 in Et_2O or isooctane [Galvin A. Coppinger *J Am Chem Soc* **79** 501 *1957*, Bartlett et al. above] or with alkaline potassium ferricyanide [Karasch & Joshi, above], whereby

Galvinoxyl separates as deep blue crystals and is recrystallised twice under N_2 from *C_6H_6 solution by suction evaporation at 30°. The VIS spectrum has λ_{max} at 407nm (ε 30,000), 431nm (ε 154,000) and weak absorption at 772.5nm, and IR has ν_{max} at 1577 and 2967cm^{-1}, and is estimated by iodometric titration. It is sensitive to O_2 in the presence of OH^- ions and traces of strong acid in hydroxylic or hydrocarbon solvents. At 62.5° in a 0.62mM solution in *C_6H_6 the radical decays with a first order $k = 4 \times 10^{-8}$ sec^{-1} (half life 1.7×10^{17} sec, ~200 days) as observed by the change in OD at 550nm [see Green & Adam *J Org Chem* **28** 3550 *1963*].

***R(–)*-Guaiaretic acid [guaiacic acid, 4,4'-(2,3-dimethyl-1-butene-(1,4-diyl)-bis-(2-methoxyphenol)]** *[500-40-3]* **M 328.4, m 99-100.5°, $[\alpha]_D^{16}$ -91° (c 1.1, EtOH), pK_{Est} ~10.0.** Crystallise the acid once from petroleum ether (b 60-80°), twice from 60% aqueous MeOH and finally from EtOH (**m** 100-101°). Its UV has λ_{max} at 207 and 260nm (logε 4.64 and 4.28). [King et al. *J Chem Soc* 4011 *1964*, Schrecker & Hartwell *J Org Chem* **21** 381 *1956*.]

Guaiacol (2-methoxyphenol) *[90-05-1]* **M 124.1, m 32°, b 106°/24mm, 205°/746mm, pK^{25} 9.90.** Crystallise guaiacol from *benzene/petroleum ether or distil it in a vacuum. [*Beilstein* **6** H 768, **6** IV 5563.]

Guaiacol carbonate *[553-17-3]* **M 274.3, m 88.1°, 89°.** Crystallise the carbonate from EtOH. It is estimated by bromination to the *monobromo guaiacol carbonate* **m** 178° (from EtOH) [Chernoff *J Am Chem Soc* **51** 3073 *1929*]. [*Beilstein* **6** H 776, **6** I 386, **6** II 784, **6** III 4233.]

Guaiazuline (1,4-dimethyl-7-isopropylazulene) *[489-84-9]* **M 198.3, m 31.5°, b 153°/7mm, d^{25} 0.976.** It forms blue-violet plates from EtOH. Also redistil it *in vacuo* until distillate solidifies. Its UV has λ_{max} at 284nm (log ε 4.6, heptane). The *picrate* has **m** 122°(EtOH). [*Beilstein* **5** III 1677, **5** IV 1751.]

Guanabenz (1-[2,6-dichlorobenzylideneamino]guanidine WY-8677) *[5051-62-7]* **M 231.1, m 227-229°(dec), pK_{Est} ~9.** Crystallise the guanidine from MeCN and store it in a CO_2-free atmosphere. The *monoHCl* [23256-5-0] has **m** 178°(dec) [solubility w% at 25° is 1.1(H_2O), 5(EtOH), 0.1(EtOAc), 0.06($CHCl_3$)]. It is an antihypertensive drug. [Holmes et al. *Drugs* **26** 212 *1983*.]

Hexachlorobenzene

[118-74-1] **M 284.8, m 230.2-231.0°, b 323-326°/atm.** Crystallise hexachlorobenzene repeatedly from *benzene. Dry it under vacuum over P_2O_5. [*Beilstein* **5** H 205, **5** IV 670.]

Hexachlorophene (2,2'-methylenebis[3,4,6-trichlorophenol]) *[70-30-4]* **M 406.9, m 166-167°, pK_1^{20} 5.41, pK_2^{20} (30% aqueous MeOH).** It forms needles from MeOH, $C_2H_4Cl_2$, or toluene. The *diacetate* has **m** 175-176° (EtOH). A disinfectant is also available in MeOH (5mg/l). [*Beilstein* **6** III 5407, **6** IV 6659.]

Hexadecyl 3-hydroxynaphthalene-2-carboxylate *[531-84-0]* **M 412.6, m 73-74°, d^{135} 0.824.** Recrystallise the ester from hot EtOH and sublime it in a vacuum. It is soluble in *C_6H_6, petroleum ether and AcOH. [Oshima & Hayashi *J Soc Chem Ind Jpn* **44** 821 *1941*, *Chem Abs* **42** 2108 *1948*, *Beilstein* **5** H 471, **5** I 227, **5** II 358, **5** III 1106, **5** IV 1208.]

Hexaethylbenzene *[604-88-6]* **M 246.3, m 128.7-129.5°.** Crystallise this hydrocarbon from *C_6H_6, or *C_6H_6/EtOH. The *1,3,5-trinitrobenzene complex (1:1)* has **m** 174°(EtOH). [*Beilstein* **5** III 3038, **5** IV 1137.]

Hexafluorobenzene *[392-56-3]* **M 186.1, m 5.1°, b 79-80°/760mm, d_4^{20} 1.61, n_D^{20} 1.378.** Main impurities are incompletely fluorinated benzenes. Purify it by standing in contact with oleum for 4 hours at room temperature, repeating until the oleum does not become coloured. Wash it several times with water, then dry it with P_2O_5. Finally purify it by repeated fractional crystallisation. [*Beilstein* **5** III 523, **5** IV 640.]

Hexamethylbenzene *[87-85-4]* **M 162.3, m 165-165.5°, 165.75°, b 264°/atm.** It is prepared, in an efficient fume cupboard, by passing a solution of phenol (100g, 1.06moles) in MeOH (1L) dropwise at a rate of 110ml/hour through a column (5.08cm diameter × 40.6cm long) packed with Al_2O_3 (300g, 4-8 or 8-14 mesh) as

catalyst held at 370-380°, and arranged so that effluent is connected to a receiver that allows the exit gasses (CO, CH_4 and H_2) into the fume cupboard. The yellow product (112-115g, 65-67%, m 134-145°) from the effluent which solidifies is washed with cold MeOH, and purified by recrystallisation from EtOH (50g/ 650ml) with 65-67% recovery, or from *C_6H_6 (50g/130ml) with 60% recovery to give pure colourless *hexamethylbenzene* **m 165-166°.** [Cullinane et al. *Org Synth* Coll Vol **IV** 520 *1963*.] It is also formed in >80% yields when *hexamethyl-Dewar benzene* [HMDB, 7641-77-2] comes into contact with anhydrous Al_2Cl_3 in hot *benzene (highly exothermic) [Schäfer & Hellmann *Angew Chem Internat Edn* **6** 518 *1967*]. It has been purified by sublimation, then recrystallisation from abolute EtOH, *benzene, EtOH/*benzene or EtOH/cyclohexane. It has also been purified by zone melting. Dry it in a low vacuum over P_2O_5. It forms 1:1 addition compounds with *2.4.7-trinitrofluorenone* (m 165-166.3°), *1,3,5-trinitrobenzene* (m 173°), *2,4,6-trinitrotoluene* (m 123°), *2-chloro-1,3,5-trinitrobenzene* (m 151°), and 1:1 complexes with Ag^+, $Cr(CO)_3$ and $W(CO)_3$. Its FT-IR (Nujol) has ν_{max} at 1300.8, 1249.1, 1180.6, 1129.2, 1057.1, 994.9, 943.5, 794.7 and 772.0 cm^{-1}; the ^1H NMR (60MHz, $CDCl_3$, TMS) has δ at 2.22 (s, 18H, Me_6); and the ^{13}C NMR (15MHz, $CDCl_3$, TMS) has δ at 17.72 (6-Me C) and 132.89 (6-aromatic C). [*Beilstein* **5** H 450, **5** I 213, **5** II 341, **5** III 1038, **5** IV 1137.]

Homophthalic acid *[89-51-0]* **M 180.2, m 180-181°, 182-183°, 189-190°, (depends on heating rate) $pK_{Est(1)}$ ~3.5, $pK_{Est(2)}$ ~4.3.** Crystallise the acid from boiling H_2O (25ml/g; 63ml/g at 20°), aqueous AcOH (**m** 180°) Dry it at 100°. The *S-benzylisothiuronium salt* has **m** 155-156° (from EtOH). [Price *Org Synth* **22** 61 *1942*, Grummitt et al. *Org Synth* Coll Vol **III** 449 *1955*, *Beilstein* **9** H 857, **9** II 617, **9** III 4266, **9** IV 3343.] The *anhydride* [703-59-3] **M** 162.1 has **m** 141-142°. [*Beilstein* **17/11** V 270.]

Homoveratronitrile (3,4-dimethoxybenzylnitrile) *[93-17-4]* **M 177.2, m 62-64°, 68°, b 184°/20mm, 195-196°/2mm, 208°/atm.** Its solubility is 10% in MeOH, and it has been recrystallised from EtOH or MeOH. Purify it also by distillation followed by recrystallisation. [Price & Rogers *Org Synth* Coll Vol **III** 174 *1955*, Niederl & Ziering *J Am Chem Soc* **64** 885 *1952*, Julian & Sturgis *J Am Chem Soc* **57** 1126 *1935*, *Beilstein* **10** I 198.]

Homoveratrylamine (2-[3,4-dimethoxyphenyl]ethylamine) *[120-20-7]* **M 181.2, b 99.3-101.3°/0.5mm, 168-170°/15mm, d_4^{20} 1.091, n_D^{20} 1.5460, pK_{Est} ~9.8.** Purify the amine by fractionation through an efficient column in an inert atmosphere as it is a relatively strong base. [Horner & Sturm *Justus Liebigs Ann Chem* **608** 12819 *1957*, Jung et al. *J Am Chem Soc* **75** 4664 *1953*.] The *hydrochloride* has **m** 152°, 154°, 156° (from EtOH, Me_2CO or EtOH/Et_2O), the *picrate* has **m** 165-167°(dec), and the *4-nitrobenzoyl* derivative has **m** 147° [Buck *J Am Chem Soc* **55** 2593 *1933*]. [*Beilstein* **13** H 800, **13** IV 2604.]

Hordenine {4-[(2-dimethylamino)ethyl]phenol} *[539-15-1]* **M 165.2, m 117-118°, b 173-174°/11mm, pK^{25} 9.46 (OH).** Crystallise Hordenine from EtOH or H_2O and sublime it at 105°/5mm. The *4,4'-dichlorodiphenyl disulfimide salt* has **m** 145-146° (from Me_2CO/H_2O) [Runge et al. *Chem Ber* **88** 50 *1955*]. [*Beilstein* **13** H 626, **13** I 236, **13** II 356, **13** III 1640, **13** IV 1790.]

4-Hydrazinobenzoic acid *[619-67-0]* **M 152.2, m 217° (dec), pK^{25} 4.13.** The acid crystallises from water. [*Beilstein* **15** H 631, **15** IV 1372.] The *hydrochloride* [24589-37-3] **M** 188.6, has **m** 253°(dec) [*Beilstein* **15** III 837].

Hydrobenzamide [1-phenyl-*N,N'*-bis(phenylmethylene)-methanediamine] *[92-29-5]* **M 298.4, m 101-102°, 107-108°.** Crystallise hydrobenzamide from absolute EtOH, petroleum ether (**m** 107-108°), *C_6H_6 (**m** 103°), or cyclohexane/*benzene. Dry it under vacuum over P_2O_5. [Pirrone *Gazz Chim Ital* ***67*** 534 *1937*, *Beilstein* **7** H 215, **7** I 120, **7** II 166, **7** III 838.]

***dl*-Hydrobenzoin (1,2-diphenyl-1,2-ethanediol, *iso*-hydrobenzoin)** *[492-70-6]* **M 214.3, m 120°.** Crystallise the diol from Et_2O/petroleum ether or H_2O (**m** 121-122°) [*Beilstein* **6** H 1004, **6** I 490, **6** II 969, **6** III 5431.] The *R,R-(+)-* and *S,S-(–)- enantiomers* have **m** 148.5-149.5°(dec), $[\alpha]_D^{20}$ + and -94.0° (c 2, EtOH) [Eisenlohr & Hill *Chem Ber* **70** 942 *1937*].

***meso*-Hydrobenzoin** *[579-43-1]* **M 214.3, m 139°, 139-140°.** Crystallise it from EtOH or water. [*Beilstein* **6**

H 1003, **6** I 490, **6** II 967. **6** III 5429, **6** IV 6682.]

Hydroquinone (1,4-dihydroxybenzene, quinol) *[123-31-9]* **M 110.1, m 175.4, 176.6°, pK_1^{20} 9.91, p K_2^{20} 11.56.** Crystallise quinol from acetone, *benzene, EtOH, EtOH/*benzene, water or acetonitrile (25g in 30ml), preferably under nitrogen. Dry it under vacuum. [Wolfenden et al. *J Am Chem Soc* **109** 463 *1987*, *Beilstein* **6** H 836, **6** IV 5712.]

p-**Hydroxyacetophenone** *[99-93-4]* **M 136.2, m 109°, 111°, 147-148°/3mm, pK^{25} 8.01.** Crystallise it from diethyl ether, aqueous EtOH or *benzene/petroleum ether. [*Beilstein* **8** H 87, **8** IV 339.]

3-Hydroxyanthranilic acid (2-amino-3-hydroxybenzoic acid) *[548-93-6]* **M 153.1, m >240°(dec), 245-265°(dec), 253-154°, 252-255°, λ_{max} 298nm, log ε 3000 (0.1M HCl), pK_1^{20} 2.7, pK_2^{20} 5.19, pK_3^{20} 10.12.** Crystallise the acid from H_2O or EtOH (**m** 254-255°). Sublime it at 170°/0.1mm. The *hydrochloride* has **m** 227° (from dilute HCl). [*Beilstein* **14** H 587, **14** III 1463, **14** IV 2071.] **Possible carcinogen.**

5-Hydroxyanthranilic acid (2-amino-5-hydroxybenzoic acid) *[394-31-0]* **M 153.1, m 233-234°, 235-236°, 248°(dec), pK_1^{25} 2.72, pK_2^{25} 5.37, pK_3^{20} 10.12.** Crystallise the acid from water. The *benzamide* has **m** 240-242° (from AcOH). It is a **hypoglycemic agent**. [*Beilstein* **14** H 591, **14** II 357, **14** III 1468, **14** IV 2080.]

m-**Hydroxybenzaldehyde** *[100-83-4]* **M 122.1, m 108° pK_1^{25} 8.98, pK_2^{25} 15.81.** Crystallise the aldehyde from water. [*Beilstein* **8** H 58, **8** IV 240.]

p-**Hydroxybenzaldehyde** *[123-08-0]* **M 122.1, m 115-116°, 117-119°, pK^{25} 7.61.** Crystallise it from water (containing some H_2SO_4). Dry it over P_2O_5 under vacuum. [*Beilstein* **8** H 64, **8** IV 251.]

m-**Hydroxybenzoic acid** *[99-06-9]* **M 138.1, m 200.8°, pK_1^{25} 4.08, pK_2^{25} 9.98.** Crystallise the hydroxyacid from absolute EtOH. [*Beilstein* **10** IV 315.]

p-**Hydroxybenzoic acid** *[99-96-7]* **M 138.1, m 213-214°, pK_1^{25} 4.50, pK_2^{25} 9.11.** Crystallise the hydroxyacid from water. [*Beilstein* **10** IV 345.]

2-Hydroxybenzyl alcohol (saligenine) *[90-01-7]* **M 124.1, m 86-87°, 87°, pK^{25} 9.92.** Crystallise saligenine from water or EtOH/*C_6H_6 (**m** 89°). [*Beilstein* **6** III 4537, **6** IV 5896.]

3-Hydroxybenzyl alcohol *[620-24-6]* **M 124.1, m 71°, pK^{25} 9.83.** Crystallise the alcohol from *C_6H_6 or $CHCl_3$. [*Beilstein* **6** III 4545, **6** IV 5907.]

4-Hydroxybenzyl alcohol *[623-05-2]* **M 124.1, m 122°, 127°, 132°, pK^{25} 9.82.** Crystallise the alcohol from H_2O, *C_6H_6 (**m** 124°), *C_6H_6/EtOH or $ClCH_2CH_2Cl$ (**m** 122°). [*Beilstein* **6** III 4546, **6** IV 5909.]

2-Hydroxybiphenyl *[90-43-7]* **M 170.2, m 56°, b 145°/14mm, 275°/760mm, pK^{20} 10.01.** Crystallise it from petoleum ether. [*Beilstein* **6** IV 4579.]

4-Hydroxybiphenyl (4-phenylphenol) *[92-69-3]* **M 170.2, m 164-165°, b 305-308°/760mm, pK^{23} 9.55.** Crystallise the phenol from aqueous EtOH, *C_6H_6, and dry it in a vacuum over $CaCl_2$ [Buchanan et al. *J Am Chem Soc* **108** 7703 *1986*]. [*Beilstein* **6** IV 4600.]

***trans*-4-Hydroxycinnamic acid (*p*-coumaric acid)** *[501-98-4]* **M 164.2, m 210-213°, 214-215°, 215°, pK_1^{25} 4.64, pK_2^{25} 9.45.** Crystallise *p*-coumaric acid from H_2O (charcoal). It forms needles from concentrated aqueous solutions as the *anhydrous acid*, but from hot dilute solutions the *monohydrate acid* separates on slow cooling. The acid (33g) has been crystallised from 2.5L of H_2O (1.5g charcoal) yielding 28.4g of recrystallised acid, **m** 207°. It is insoluble in *C_6H_6 or petroleum ether. The UV in 95% EtOH has λ_{max} at 223 and 286nm (ε 14,450 and 19000 $M^{-1}cm^{-1}$). [UV Wheeler & Covarrubias *J Org Chem* **28** 2015 *1963*, Corti *Helv Chim Acta* **32** 681 *1949*, *Beilstein* **10** IV 1005.]

3-(4-Hydroxy-3,5-dimethoxyphenyl)acrylic acid (sinapinic acid) *[530-59-6]* **M 234.1, m 204-205°(dec), $pK_{Est(1)}$ ~4.6, $pK_{Est(2)}$ ~9.3.** Crystallise it from water. [*Beilstein* **10** H 508, **10** IV 2104.]

4-Hydroxydiphenylamine *[122-37-2]* **M 185.2, m 72-73°, pK_{Est} ~10.0.** Crystallise the amine from chlorobenzene/petroleum ether, pentane (**m** 72°) or *C_6H_6/petroleum ether (**m** 70°). [*Beilstein* **13** III 1019, **13** IV 1052.]

2-Hydroxy-4-(*n*-dodecyloxy)benzophenone *[2985-59-3]* **M 382.5, m 50-52°, pK_{Est} ~7.1.** Recrystallise it from *n*-hexane and then 10% (v/v) EtOH in acetonitrile [Valenty et al. *J Am Chem Soc* **106** 6155 *1984*].

4-Hydroxyindane *[1641-41-1]* **M 134.2, m 49-50°, b 120°/12mm, pK^{25} 10.32.** Crystallise 4-hydroxyindane from petroleum ether, pentane (**m** 50-50.5°) or *C_6H_6 (**m** 39.5-40°). It has UV with λ_{max} at 277nm (cyclohexane). The *acetyl* derivative has **m** 30-32° (from EtOH), **b** 127°/14mm and the *3,5-dinitrobenzoyl* derivative has **m** 114°. [Dallacker et al. *Chem Ber* **105** 2568 *1972*, *Beilstein* **6** III 2427, **6** IV 3827.]

5-Hydroxyindane *[1470-94-6]* **M 134.2, m 55°, b 127°/14mm, 255°/760mm, pK^{23} 10.24.** Crystallise 5-hydroxyindane from petroleum ether (**m** 56°) or pentane (**m** 59-60°). It has UV with λ_{max} at 283.5nm (cyclohexane). The *3,5-dinitrobenzoyl* derivative has **m** 156°. [*Beilstein* **6** III 2428, **6** IV 3829.]

4-Hydroxy-3-methoxyacetophenone (apocynin) *[498-02-2]* **M 166.2, m 115°, pK_{Est} ~7.9.** Crystallise apocynin from water, or EtOH/petroleum ether. [*Beilstein* **8** IV 1814.]

***trans*-4-Hydroxy-3-methoxycinnamic acid (ferulic acid)** *[537-98-4; 1135-24-6]* **M 194.2, m 174°, pK_1^{25} 4.58, pK_2^{25} 9.39.** Crystallise ferulic acid from H_2O. [*Beilstein* **10** H 436, **10** IV 1776.]

4-Hydroxy-2-methylazobenzene (3-methyl-4-phenylazophenol) *[1435-88-7]* **M 212.2, m 100-101°, 112°, pK_{Est} ~9.5.** Crystallise the phenol from hexane. [*Beilstein* **16** II 61, **16** IV 195.]

4-Hydroxy-3-methylazobenzene (2-methyl-4-phenylazophenol) *[621-66-9]* **M 212.2, m 125-126°.** Crystallise the phenol from hexane or petroleum ether (**m** 130°). [*Beilstein* **16** II 59, **16** III 104, **16** IV 193.]

3-Hydroxy-4-methylbenzaldehyde *[57295-30-4]* **M 136.1, m 73°, pK_{Est} ~10.2.** Crystallise it from water or *C_6H_6 (**m** 71-71°). The *O-methyl ether* has **m** 45-46° (from Et_2O/hexane). [Sedgwick & Allott *J Chem Soc* 2820 1923, Flitsch et al. *Justus Liebigs Ann Chem* 1413 *1985*, *Beilstein* **8** H 100, **8** II 103, **8** IV 368.]

5-Hydroxy-2-methyl-1,4-naphthaquinone (plumbagin) *[481-42-5]* **M 188.2, m 78-79°, $pK_{Est(1)}$~9.5, $pK_{Est(2)}$~11.0.** It crystallises in yellow needles from aqueous EtOH. It is soluble in organic solvents, it is steam volatile and it sublimes on heating in a vacuum. [Fieser & Dunn *J Am Chem Soc* **58** 572 *1936*, *Beilstein* **8** III 2576, **8** IV 2376.]

6-Hydroxy-2-methyl-1,4-naphthaquinone *[633-71-6]* **M 188.2, pK_{Est} ~10.0.** Crystallise the naphthaquinone from aqueous EtOH and sublime it in a vacuum.

2-Hydroxy-1-naphthaldehyde *[708-06-5]* **M 172.2, m 82°, b 139-142°/4mm, 192°/27mm, pK^{25} 8.27 (50% aqueous EtOH).** Crystallise the aldehyde from EtOH (1.5ml/g), aqueous EtOH, aqueous AcOH (**m** 84°), EtOAc or H_2O. [Russell & Lockhart *Org Synth* Coll Vol **III** 463 *1955*, *Beilstein* **8** H 143, **8** I 564, **8** II 171, **8** III 1108, **8** IV 1160.]

2-Hydroxy-1-naphthaleneacetic acid *[10441-45-9]* **M 202.2, m 147-148°, $pK_{Est(1)}$ ~4.2, $pK_{Est(2)}$ ~8.3.** Crystallise the acid from EtOH/water (1:9, v/v, activated charcoal), H_2O (**m** 157°) or xylene (**m** 147°). Dry it under vacuum, over silica gel, in the dark. Store it in the dark at -20° [Gafni et al. *J Phys Chem* **80** 898 *1976*]. It forms a cyclic lactone (**m** 107°) readily. [*Beilstein* **10** II 218, **10** III 1102, **10** IV 1201.]

6-Hydroxy-2-naphthalenepropionic acid *[553-39-9]* **M 216.2, m 180-181°, $pK_{Est(1)}$ ~4.6, $pK_{Est(2)}$~9.0.** Crystallise the acid from aqueous EtOH or aqueous MeOH. [Ormancey & Horeau *Bull Soc Chim Fr* 962 *1955*, *Beilstein* **10** III 1113.]

3-Hydroxy-2-naphthalide (Naphthol AS) *[92-77-3]* **M 263.3, m 248.0-248.5°, CI 37505.** Crystallise it from xylene or AcOH which forms plates **m** 243-244° [Schnopper et al. *Anal Chem* **31** 1542 *1959*]. [*Beilstein* **12** H 505.]

3-Hydroxy-2-naphtho-4'-chloro-*o*-toluidide *[92-76-2]* **M 311.8, m 243.5-244.5°.** Crystallise it from xylene [Schnopper et al. *Anal Chem* **31** 1542 *1959*].

3-Hydroxy-2-naphthoic-1'-naphthylamide *[123-68-3]* **M 314.3, m 217-.5-218.0°.** Crystallise the amide from xylene [Schnopper et al. *Anal Chem* **31** 1542 *1959*].

3-Hydroxy-2-naphthoic-2'-naphthylamide *[136-64-8]* **M 305.3, m 243.5-244.5°, and other naphthol AS derivatives.** Crystallise it from xylene [Schnopper et al. *Anal Chem* **31** 1542 *1959*].

2-Hydroxy-1,4-naphthoquinone (Lawsone B, Neutral Orange 6, tautomeric with 4-hydroxy-1,2-naphthoquinone) *[83-72-7]* **M 174.2, m 192°(dec), CI 75480 pK_1^{25} -5.6 (C=O protonation), pK_2^{25} 2.38, pK_3^{25} 4.00 (phenolic OH).** Crystallise Lawsone B from *C_6H_6 or AcOH (**m** 192.5°, 195-196°). It sublimes in a vacuum (**m** 194°). It has UV with λ_{max} at 455nm (aqueous NaOH). [*Beilstein* **8** H 300, **8** I 635, **8** II 344, **8** III 2543, **8** IV 2360.]

5-Hydroxy-1,4-naphthoquinone (Juglone) *[481-39-0]* **M 174.2, m 155°, 164-165°, pK^{25} 8.7.** Crystallise Juglone from *benzene/petroleum ether or petetroleum ether. [*Beilstein* **8** III 2558, **8** IV 2368.]

6-Hydroxy-2-naphthyl disulfide *[6088-51-3]* **M 350.5, m 221-222°, 226-227°, pK_{Est} ~9.0.** It crystallises as leaflets from AcOH and is slightly soluble in EtOH, and AcOH, but is soluble in *C_6H_6 and in alkalis to give a yellow solution. [Zincke & Dereser *Chem Ber* **51** 352 *1918*.] The *acetoxy* derivative has **m** 198-200° (from AcOH or dioxane/MeOH), and the *diacetyl* derivative has **m** 167-168° (from AcOH). A small amount of impure disulfide can be purified by dissolving it in a small volume of Me_2CO and adding a large volume of toluene, filter rapidly and concentrate to one-third of its volume. The hot toluene solution is filtered rapidly from any tarry residue, and crystals separate on cooling. Recrystallisation from hot acetic acid gives crystals with **m** 220-223° [Barrett & Seligman *Science* **116** 323 *1952*]. [*Beilstein* **6** I 481.]

2-Hydroxy-5-nitrobenzyl bromide (Koshland's reagent) *[772-33-8]* **M 232.0, m 147°, pK_{Est} ~8.0.** Crystallise the bromide from *benzene or *benzene/ligroin. It is slightly soluble in EtOH, soluble in *C_6H_6 and AcOH, and very soluble in ligroin. [*Beilstein* **6** H 367.]

2-Hydroxyphenylacetic acid *[614-75-5]* **M 152.2, m 148-149°, 152-153°, b 240-243°/760mm, $pK_{Est(1)}$~4.3, $pK_{Est(2)}$~10.1.** Crystallise the acid from ether or chloroform (**m** 147°, m from latter solvent is always lower). [*Beilstein* **10** H 187, **10** I 81, **10** II 112, **10** III 422, **10** IV 536.]

3-Hydroxyphenylacetic acid *[621-37-4]* **M 152.2, m 137°, $pK_{Ext(1)}$~4.3, $pK_{Ext(2)}$~10.** Crystallise the acid from *C_6H_6/ligroin or EtOAc/cyclohexane (**m** 131-132°). [*Beilstein* **10** H 189, **10** I 82, **10** II 112, **10** III 428, **10** IV 541.]

4-Hydroxyphenylacetic acid *[156-38-7]* **M 152.2, m 150-151°, 152°, pK_1 4.28, pK_2 10.1.** Crystallise the acid from water or Et_2O/petroleum ether. The *p-bromophenacyl ester* has **m** 117° (from EtOH). [*Beilstein* **10** II 112, **10** III 430, **10** IV 543.]

***N*-(4-Hydroxyphenyl)-3-phenylsalicylamide** *[550-57-2]* **M 305.3, m 183-184°, pK_{Est} ~9.5.** Crystallise the amide from aqueous MeOH. [*Beilstein* **13** IV 224.]

L-2-Hydroxy-3-phenylpropionic acid (3-phenyl lactic acid) *[20312-36-1]* **M 166.2, m 125-126°, $[\alpha]_D^{12}$ -18.7° (EtOH), $[\alpha]_D^{20}$ -22° (c 1, H_2O), pK see below.** Crystallise the acid from water, MeOH, EtOH or *benzene. [*Beilstein* **10** IV 653.]

***dl*-2-Hydroxy-3-phenylpropionic acid** *[828-01-3]* **M 166.2, m 97-98°, b 148-150°/15mm, pK_{Est} ~3.7.** Crystallise the propionic acid from *benzene or chloroform. [*Beilstein* **10** IV 653.]

3-*p*-Hydroxyphenylpropionic acid (phloretic acid) *[501-97-3]* **M 166.2, m 129-130°, 131-133°, $pK_{Est(1)}$~4.7, $pK_{Est(2)}$~10.1.** Crystallise phloretic acid from ether or H_2O. [*Beilstein* **10** IV 631.]

p-**Hydroxyphenylpyruvic acid** *[156-39-8]* **M 180.2, m 220°(dec), pK_{Est} ~2.3.** Crystallise it three times from 0.1M HCl/EtOH (4:1, v/v) immediately before use [Rose & Powell *Biochem J* **87** 541 *1963*], or from Et_2O. The *3,4-dinitrophenylhydrazone* has **m** 178°. [*Beilstein* **10** IV 3630.]

***N*-Hydroxyphthalimide** *[524-38-9]* **M 163.1, m 230°, ~235°(dec), 237-240°, pK^{30} 7.0.** Dissolve the imide in H_2O by adding Et_3N to form the salt and while hot, acidify, cool and pour into a large volume of H_2O. Filter off the solid, wash it with H_2O and dry it over P_2O_5 in a vacuum. [Nefken & Teser *J Am Chem Soc* **83** 1263 *1961*, Fieser **1** 485 *1976,* Nefkens et al. *Rec Trav Chim Pays Bas* **81** 683 *1962*] The *O-acetyl* derivative has **m** 178-180° (from EtOH). [*Beilstein* **21/11** V 100.]

4'-Hydroxypropiophenone *[70-70-2]* **M 150.2, m 149°, b 140-145°/0.5mm, pK^{25} 8.05.** Crystallise the phenone from H_2O (**m** 149.8-150.2°) or EtOH (**m** 147°). The *benzoyl derivative* has **m** 117°, and the *semicarbazone* has **m** 183° (EtOH). [*Beilstein* **8** H 102, **8** II 104, **8** III 379.]

***trans*-4-Hydroxystilbene** *[6554-98-9]* **M 196.3, m 189°.** Crystallise it from *C_6H_6, MeOH (**m** 186-187°) or acetic acid. [*Beilstein* **6** H 693, **6** II 657, **6** III 3497, **6** 4855.]

Hydroxy(tosyloxy)iodobenzene [phenyl(hydroxyl)tosyloxyiodine, hydroxy(4-methylbenzenesulfonato-O)phenyliodine, Koser's reagent] *[27126-76-7]* **M 392.2, m 134-136°, 135-138°, 134-136°, 136-138.5°.** Possible impurities are tosic acid (removed by washing with Me_2CO) and acetic acid (removed by washing with Et_2O). It is purified by dissolving in the minimum volume of MeOH, adding Et_2O to cloud point and setting aside for the prisms to separate [Koser & Wettach *J Org Chem* **42** 1476 *1977*, NMR: Koser et al. *J Org Chem* **41** 3609 *1976*]. It has also been crystallised from CH_2Cl_2 (needles, **m** 140-142°) [Neiland & Karele *J Org Chem, USSR (Engl Transl)* **6** 889 *1970*].

9-Hydroxytriptycene *[73597-16-7]* **M 270.3, m 245-246.5°.** Crystallise it from *benzene/petroleum ether. Dried it at 100° in a vacuum [Bartlett & Greene *J Am Chem Soc* **76** 1088 *1954*, Imashiro et al. *J Am Chem Soc* **109** 729 *1987*].

Hypericin (hypericum, 4,5,7,4',5',7'-hexahydroxy-2',2'-dimethylnaphthodianthrone) *[548-04-9]* **M 504.4, m 320°(dec).** Crystallise hypericin from pyridine by addition of methanolic HCl. [*Beilstein* **8** IV 3761.]

Ibuprofen [*(S+)* and *(R-)* 4-*iso*butyl-α-methylphenylacetic acid, Brufen, Nurofen, Motrui] *[(S +) 51146-56-6, (R —) 51146-57-7]* **M 206.3, m 52-53°, $[\alpha]_D^{20}$ +59° (c 2, EtOH).** Crystallise the (+) and (–) acids from EtOH or aqueous EtOH. The *racemate,* which crystallises from petroleum ether with **m** 75-77°, is sparingly soluble in H_2O and has IR (film) with ν_{max} at 1705 (C=O), 2300—3700 (OH broad) cm^{-1}. It is used as a non-steroidal anti-inflammatory. [Shiori et al. *J Org Chem* **43** 2936 *1978,* Kaiser et al. *J Pharm Sci* **65** 269 *1976*, *J Pharm Sci* **81** 221 *1992*, Freer *Acta Cryst* (C) **49** 1378 *1993* for the *(S+)-enantiomer*.]

1,3-Indandione *[606-23-5]* **M 146.2, m 129-132°, pK^{18} 7.2 (1% aqueous EtOH).** Recrystallise it from EtOH or *C_6H_6. In dilute alkali it gives a deep yellow solution of the enol. [Bernasconi & Paschalis *J Am Chem Soc* **108** 2969 *1986*]. [*Beilstein* **7** IV 2344.]

Indane (indan, hydrindene, 1,2-trimethyenebenzene) *[496-11-7]* **M 118.1, f –51.4°, b 79°/29mm, 177-179.5°/760mm, d_4^{20} 0.960, n_D^{20} 1.536.** Shake indane with conc H_2SO_4, then water, dry (Na_2SO_4) and fractionally distil it. [*Beilstein* **5** H 486, **5** I 234, **5** II 376, **5** III 1200, **5** IV 1371.]

Indene *[95-13-6]* **M 116.2, f -1.5°, m -5° to -3°, b 114.5°/100mm, 181-182°/atm, d_4^{20} 0.994, n_D^{20} 1.5763.** Shake indene with 6M HCl for 24 hours (to remove basic nitrogenous material), then reflux it with 40% NaOH for 2 hours (to remove benzonitrile). Fractionally distil, then fractionally crystallise it by partial freezing. The higher-melting portion is converted to its sodium salt by adding a quarter of its weight of sodamide under nitrogen and stirring for 3 hours at 120°. Unreacted organic material is distilled off at 120°/1mm. The sodium salts are hydrolysed with water, and the organic fraction is separated by steam disillation, followed by fractional distillation. Before use, the distillate is passed, under nitrogen, through a column of activated silica gel. It turns yellow in air as it readily oxidises and polymerises. Store it in the presence of *tert*-butylcatechol (50-100ppm) as antioxidant. [Russell *J Am Chem Soc* **78** 1041 *1956*, *Beilstein* **5** IV 1532.]

2-Iodoaniline *[615-43-0]* **M 219.0, m 60-61°, pK^{25} 2.54.** Distil 2-iodoaniline with steam and crystallise it from *benzene/petroleum ether. The *N-acetyl* derivative has **m** 110°. [*Beilstein* **12** IV 1542.]

4-Iodoaniline *[540-37-4]* **M 219.0, m 62-63°, pK^{25} 3.81.** Crystallise it from petroleum ether (b 60-80°) by refluxing, then cool it in an ice-salt bath freezing mixture. Dry it in air. *Alternatively*, crystallise it from EtOH and dry it *in vacuo* for 6 hours at 40° [Edidin et al. *J Am Chem Soc* **109** 3945 *1987*]. The *N-acetyl* derivative has **m** 184° (from MeOH). [*Beilstein* **12** IV 1544.]

4-Iodoanisole *[696-62-8]* **M 234.0, m 51-52°, b 133-133.3°/25mm, 139°/35mm, 237°/726mm.** Crystallise 4-iodoanisole from aqueous EtOH and/or distil it under vacuum. [*Beilstein* **6** H 208, **6** I 109, **6** II 199, **6** III 744, **6** IV 1075.]

Iodobenzene *[591-50-4]* **M 204.0, b 63-65°/10mm, 188°/atm, d_4^{20} 1.829, n_D^{25} 1.6169.** Wash it with dilute aqueous $Na_2S_2O_3$, then water. Dry it with $CaCl_2$ or $CaSO_4$, decolourise with charcoal and distil it under reduced pressure then store it with mercury or silver powder to stabilise it. [*Beilstein* **5** IV 688.]

***o*-Iodobenzoic acid** *[88-67-5]* **M 248.4, m 161-162°, 161.6-162°, 162°, 162.7-163.5°, 164°, pK^{20} 2.93, pK^{25} 2.84 (H_2O), pK^{20} 2.93 (1% EtOH), pK –7.78 (H_2SO_4).** Crystallise the acid repeatedly from water (charcoal), EtOH, aqueous EtOH, aqueous Me_2CO, Me_2CO/Et_2O or $*C_6H_6$. Sublime it under vacuum at 100°. *o*-Iodobenzoic acid is prepared by the following procedure: anthranilic acid (31.9g, 233mmol, see [118-92-3]) is dissolved in dilute H_2SO_4 (50g, 27ml, 98% acid, 500mmol, in 250ml of H_2O), cooled to 0°; and while stirring $NaNO_2$ (20g, 290mmol) in H_2O (40ml) is added dropwise keeping the temperature below 10° (add crushed ice to the mixture if necessary). Diazotisation is complete when starch-iodide paper wetted with a drop of the mixture turns blue or brown due to the presence of excess of HNO_2. A solution of KI (60g, 360mmol) in H_2O (100ml) is gradually added with stirring, the mixture is set aside for 1 hour then heated at ~100° until effernescence (N_2 liberated) ceases. The mixture is cooled in ice, the brown iodo-acid (~92%) is filtered off, washed well with H_2O and dried *in vacuo.* The brown colour is not easily removed by recrystallisation so the acid is converted into the ethyl ester e.g. by Fischer and Speier's method [Fischer & Speier *Chem Ber* **28** 2250 *1895*]. Dry HCl gas is bubbled through EtOH (~200ml) cooled in ice-water until the increase in weight is ~4g. The crude iodobenzoic acid is added to it and the mixture is boiled under reflux for 2 hours, or until an aliquot poured into H_2O does not deposit a solid. The mixture is poured into cold H_2O, the heavy oil that separated is extracted into Et_2O, the extract is washed with H_2O, saturated aqueous $NaHCO_3$ (care-effervescence), brine, dried ($CaCl_2$), filtered, evaporated and the residual oil is distilled to give a 73% yield of pure *ethyl* o-*iodobenzoate* **M 276.0** [1829-28-3], **b 151-152°/12-13mm (163-165°/23mm, 275°/atm).** This ester is dissolved in 0.5 *N* alcoholic KOH (from 7g of KOH dissolved in 7ml of H_2O and diluted to 250ml with EtOH) in the ratio of 1g:25ml, and refluxed for 30 minutes (or until a drop added to H_2O dissolves completely), poured it into H_2O, and the clear solution of the potassium salt is acidified to pH <0 when pure iodobenzoic acid (theoretical yield) separates. It is collected, washed with cold H_2O, and dried *in vacuo*. [Baker et al. *J Chem Soc* 3721 *1965*, Cohen & Raper *J Chem Soc* 1271 *1904*.] The FT-IR (Nujol) has ν_{max} at 3061.7, 2646.1, 1683.9, 1582.4, 1405.0,

1269.8, 1015.8, 739.0 and 679.7 cm^{-1}; the ^1H NMR (DMSOd_6, TMS) has δ at 7.25 (t of d, 1H, J = 7 Hz and 1.5 Hz, H-5), 4.85 (t, 1H, J = 7 Hz, H-4), 7.72 (d of d, 1H, J = 7 and 1.5 Hz, H-6) and 8.01 (d, 1H, J = 7 Hz, H-3); and the ^{13}C NMR (DMSOd_6, TMS) has δ at 167.93, 140.32, 136.72, 132.25, 129.88 127.97 and 93.92.
The *acid chloride* has **M 266.4** [609-67-6], **m 35-40°, b 135°/19mm (159°/27mm)**, and the *amide* has **M 247.0** [3930-83-4], **m 183°** (needles from H_2O). The *4-bromobenzylisothiuronium salt* has **m 154°** (from EtOH), and the *4-chlorobenzylisothiuronium salt* has **m 162°** (from dioxane). [*Beilstein* **9** H 363, **9** I 148, **9** II 239, **9** III 1432, **9** IV 1030.]

m-**Iodobenzoic acid** *[618-51-9]* **M 248.4, m 185-186°, 186.6-186.8°, 189°, 189-189.2°, pK^{25} 3.85, pK^{50} 3.97, pK –7.64 (H_2SO_4).** Crystallise the acid repeatedly from water, EtOH, aqueous EtOH, Me_2CO or aqueous AcOH. Sublime it under vacuum at 100°. *Ethyl* m-*iodobenzoate* **M 276.0** [58313-23-8] has **b 150.5°/15mm (165-166°/24mm)**, the m-*acid chloride* has **M 266.4** [1711-10-0], **b 104-105°/1mm (159-150°/23mm)**, and the m-*amide* has **M 247.0** [10388-19-9], **m 186°** (needles from H_2O). The *4-bromobenzylisothiuronium salt* has **m 152°** (from EtOH), and the *4-chlorobenzylisothiuronium salt* has **m 154°** (from dioxane). [Fieser *Org Synth* Coll Vol **II** 353 *1948*, *Beilstein* **9** H 365, **9** I 148, **9** II 240, **9** III 1437, **9** IV 1033.]

p-**Iodobenzoic acid** *[619-58-9]* **M 248.4, m 269-270°, 271-272°, 272.5°, 273°, pK^{25} 4.00, pK –7.50 (H_2SO_4).** Crystallise the acid repeatedly from water, aqueous EtOH, aqueous Me_2CO, aqueous AcOH. Sublime it under vacuum at 200°/0.4mm. *Ethyl* p-*iodobenzoate* **M 276.0** [51934-41-9] has **b 154°/15mm**, the p-*acid chloride* has **M 266.4** [1711-02-0] has **m 83° (77-78°)** (needles from Et_2O)**, b 126°/9mm (163-164°/32mm)**, and the p-*amide* has **M 247.0** [3956-07-8], **m 217.6° (209°)** (needles from H_2O). The *4-bromobenzylisothiuronium salt* has **m 181°** (from EtOH), and the *4-chlorobenzylisothiuronium salt* has **m 177°** (from dioxane). [Whitmore & Woodward *Org Synth* Coll Vol **II** 325 *1948*, *Beilstein* **9** H 366, **9** I 149, **9** II 240, **9** III 1442, **9** IV 1035.]

4-Iodobiphenyl *[1591-31-7]* **M 280.1, m 113.7-114.3°, b 207°/28mm.** Crystallise 4-iodobiphenyl from EtOH/*C_6H_6, and dry it *in vacuo* over P_2O_5. [*Beilstein* **5** H 581, **5** I 273, **5** II 486, **5** III 1748, **5** IV 1821.]

1-Iodo-2,4-dinitrobenzene *[709-49-9]* **M 294.0, m 88°.** Crystallise it from EtOAc. [*Beilstein* **5** H 270.]

1-Iodo-4-nitrobenzene *[636-98-6]* **M 249.0, m 171-172°.** Precipitate it from acetone by addition of water, followed by recrystallisation from EtOH. [*Beilstein* **8** H 523, **8** H 523, **8** II 191, **8** III 623, **8** IV 743.]

o-**Iodophenol** *[533-58-4]* **M 280.1, m 43°, pK^{25} 8.51.** Crystallise 2-iodophenol from $CHCl_3$ or diethyl ether. The *acetate* has **m** 65-66° (from MeOH). [*Beilstein* **6** H 208, **6** II 198, **6** III 774, **6** IV 1074.]

p-**Iodophenol** *[540-38-5]* **M 280.1, m 94°, 138-140°/5mm, pK^{25} 9.30.** Crystallise 4-iodophenol from petroleum ether (b 80-100°) or distil it *in vacuo*. If the material has a brown or violet colour, then dissolve it in $CHCl_3$, shake it with 5% sodium thiosulfate solution until is colourless. Dry (Na_2SO_4) the orgnic layer, fikter, evaporate and disil the residue *in vacuo*. [Dains & Eberly *Org Synth* Coll Vol **II** 355 *1943*, *Beilstein* **6** IV 1074.]

5-Iodosalicylic acid (2-hydroxy-5-iodobenzoic acid) *[119-30-2]* **M 264.0, m 197° pK_1^{25} 2.65, pK_2^{25} 13.05.** Crystallise the acid from water. [*Beilstein* **10** H 112.]

o-**Iodosobenzoic acid** *[304-91-6]* **M 264.0, m >200°, pK_{Est} ~2.6.** Crystallise the acid from EtOH and dry it *in vacuo*. [*Beilstein* **9** H 363.]

p-**Iodotoluene** *[624-31-7]* **M 218.0, m 35°, b 211-212°.** Crystallise 4-iodotoluene from EtOH and.or distil it. [*Beilstein* **5** IV 840.]

Isonitrosoacetophenone (phenylglyoxaldoxime) *[532-54-7]* **M 149.2, m 126-128°.** Crystallise it from water. [*Beilstein* **7** IV 2132.]

Isophthalic acid (benzene-1,3-dicarboxylic acid) *[121-91-5]* **M 166.1, m 345-348°, pK_1^{25} 3.70, pK_2^{25} 4.60.**

Crystallise the acid from aqueous EtOH. [*Beilstein* **9** IV 3292.]

4,4'-Isopropylidenediphenol (Bisphenol A, 2,2-bis[4-hydroxyphenol]propane) *[80-05-7]* **M 228.3, m 158°, pK_{Est} ~10.3.** Crystallise bisphenol from acetic acid/water (1:1). It is used for making polycarbonate bottles and leaches out slowly on heating. It is a known "estrogenic chemical" shown to disrupt chemical signalling in the complex network of glands, hormones and cell receptors which make up the endocrine system. It causes low sperm count and damages the ecosystem by the feminisation of fish, reptiles and birds. [cf Chapter 1, p 3, *Beilstein* **6** IV 6717.]

***N*-Isopropylidene-*N′*-2-nitrobenzenesulfonyl hydrazine (IPNBSH, isopropylidenehydrazide *o*-nitrobenzenesulfonic acid** *[6655-27-2]* **M 257.3, m 132-135°, 139-140°.** IPNSBH is more stable than NBSH (*vide infra*) from which it is readily prepared by dissolving it (1.14g, 1 equivalent) in Me_2CO (8ml) at 0°, and after 30 minutes the solvent is removed *in vacuo*, the residue is re-dissolved in Me_2CO (4ml), and added slowly into 150ml of hexanes. The fine powder is filtered off, rinsed with hexanes (2 × 5ml) and dried *in vacuo* to give IPNBSH as a white solid (1.20g, 89%; TLC has R_F 0.7, 66% EtOAc in hexanes). Its FTIR (thin film) has ν_{max} at 1177s, 1347m, 1375s, 1551s, 3264s cm^{-1}; its ^1H NMR [400MHz, $CDCl_3$, 20°] has δ at 8.30-8.28 (m, 1H), 7.87-7.85 (m, 2H), 7.79-7.77 (m, 2H), 1.96 (s, 3H), 1.92 (s, 3H), and its ^{13}C NMR [500MHz, $CDCl_3$, 20°] has δ at 158.9, 134.2, 133.5, 132.9.2, 132.0, 125.4, 25.5, 17.2. IPNBSH promotes the same reactions as NBSH except that it is more stable. A solution of 0.02M IPNBSH in DMSO is undecomposed at 50° during 30 minutes, whereas NBSH is 60% decomposed, and at is stable at 75° or 100° for 30 minutes so it can be stored at room temperature for several months without deterioration; all the same, store it under argon (as it is possibly flammable), and use gloves due to its toxicity.
It is a reagent used for allylic transposition, de-bromination and reduction of alcohols in the presence of DEAD and Ph_3P. [Movassaghi et al. *Angew Chem. Int Ed Engl* **45** 5859 *2006*, Movassaghi & Ahmad *J. Org. Chem.* **72** 1838 *2007*].

Isopropyl *p*-nitrobenzoate *[13756-40-6]* **M 209.2, m 105-106°.** Dissolve it in Et_2O, wash it with aqueous alkali, then H_2O and dry it. Evaporate the ether and recrystallise it from EtOH to give pure material. It gives yellow crystals from petroleum ether (**m** 109°, 110°). [*Beilstein* **9** H 391, **9** II 258, **9** III 1543, **9** IV 1075.]

Isovanillin (3-hydroxy-4-methoxybenzaldehyde) *[621-59-0]* **M 152.2, m 117°, b 175°/14mm, pK^{25} 8.89.** Crystallise isovaniline from H_2O or $*C_6H_6$. The *oxime* has **m** 147°. [*Beilstein* **8** IV 1764.]

Isoviolanthrone *[128-64-3]* **M 456.5, m 510-511°(uncorrected).** Dissolve isoviolanthrone in 98% H_2SO_4 and precipitate it by adding water to reduce the acid concentration to about 90%. It sublimes *in vacuo* to give dark green-violet needles [Parkyns & Ubblehode *J Chem Soc* 4188 *1960*]. [*Beilstein* **7** I 465, **7** II 815, **7** III 4538, **7** IV 2747.]

Janus Red B {3-[(2-hydroxy-1-naphtholenyl)azo-2-methylphenylazo]*N,N,N*-trimethyl-benzenaminium chloride} *[2636-31-9]* **M 460.0.** Crystallise the dye from EtOH/H_2O (1:1 v/v) and dry in vacuum. Store it in a dark bottle. [*Beilstein* **16** II 149.]

Ketone moschus (4-*tert*-butyl-2,6-dimethyl-3,5-dinitroacetophenone, Musk ketone) *[81-14-1]* **M 294.3, m 134-137°, 137-138°.** Purify the ketone by recrystallisation from MeOH. It has a strong odour of musk and is used in perfumery. [Fuson et al. *J Org Chem* 12 587 *1947*, *Beilstein* **7** IV 808.]

Lapachol [2-hydroxy-3-(3-methyl-2-butenyl)-1,4-naphthalenedione, Neutral Yellow 16] *[84-79-7]* **M 242.3, CI 7549, m 140°.** Crystallise Lapachol from petroleum ether/EtOH, EtOH or Et_2O. [*Beilstein* **8** H 326, **8** I 644, **8** II 365, **8** III 2720.]

Leucomalachite Green *[129-73-7]* **M 330.5, m 92-93°, pK^{25} 6.90 (several pK's).** Crystallise it from 95% EtOH (10ml/g), then from *benzene/EtOH, and finally from petroleum ether. [*Beilstein* **13** H 275, **13** II 89, **13** II 135, **13** III 529, **13** 481.]

Malachite Green (carbinol) *[510-13-4]* **M 346.4, m 112-114°, CI 42000, pK^{24} 6.84.** The *oxalate* [2437-29-8] [*Beilstein* **8** H 326, **13** IV 2279.] is recrystallised from hot water and dried in air. The carbinol is precipitated from the oxalate (1g) in distilled water (100ml) by adding M NaOH (10ml). The precipitate is filtered off, recrystallised from 95% EtOH containing a little dissolved KOH, then washed with ether, and crystallised from petroleum ether. Dry it in a vacuum at 40°. An acid, almost colourless, solution (2×10^{-5}M in 6×10^{-5}M H_2SO_4) rapidly reverts to the coloured dye. [Swain & Hedberg *J Am Chem Soc* **72** 3373 *1950*, *Beilstein* **13** H 243, 744.]

Mandelic acid (α-hydroxyphenylacetic acid) *[S-(+)- 17199-29-0, R-(–)- 611-71-2]* **M 152.2, m 130-133°, 133°, 133.1° (evacuated capillary), 133-133.5°, [α] $^{20}_{546}$ (+) and (-) 188° (c 5, H_2O), [α] $^{20}_{D}$ (+) and (-) 155° (c 5, H_2O) and (+) and (-) 158° (c 5, Me_2CO), pK^{25} 3.41.** Purify the mandelic acids by recrystallisation from H_2O, *C_6H_6 or $CHCl_3$. [Roger *J Chem Soc* 2168 *1932*, Jamison & Turner *J Chem Soc* 611 *1942*.] They have solubilities in H_2O of *ca* 11% at 25°. [Banks & Davies *J Chem Soc* 73 *1938*.] The *S-benzylisothiuronium salts* has **m** 180° (from H_2O) and [α] $^{25}_{D}$ (+) and (–) 57° (c 20, EtOH) [El Masri et al. *Biochem J* **68** 199 *1958*]. [*Beilstein* **10** IV 564.]

***RS*-(±)-Mandelic acid** *[61-72-3]* **M 152.2, m 118°, 120-121°.** Purify mandelic acid by Soxhlet extraction with *C_6H_6 (about 6ml/g) and allow the extract to crystallise. It can also be recrystallised from $CHCl_3$. The *S-benzylisothiuronium salt* has **m** 169° (166°) (from H_2O). Dry it at room temperature under vacuum. [*Beilstein* **10** IV 565.]

Mescaline sulfate [2-(3,4,5-trimethoxyphenyl)ethylamine sulfate] *[5967-42-0]* **M 309.3, m 181-184°, 183-184°, 186-189°, pK$_{Est}$ ~9.7.** The salt crystallises from water with $2H_2O$ or from hot MeOH. The *acid sulfate* has **m** 158°. [Slomon & Bina *J Am Chem Soc* **68** 2403 *1946*, *Beilstein* **13** I 338, **13** II 521, **13** III 2375, **13** IV 2919.]

Mesitylene (1,3,5-trimethylbenzene) *[108-67-8]* **M 120.2, m -44.7°, b 99.0-99.8°/100mm, 166.5-167°/760mm, d $^{20}_{4}$ 0.865, n $^{25}_{D}$ 1.4967.** Dry it with $CaCl_2$ and distil it from Na in a glass helices-packed column. Treat it with silica gel and redistil it. *Alternative* purifications include vapour-phase chromatography, or fractional distillation followed by azeotropic distillation with 2-methoxyethanol (which is subsequently washed out with H_2O), drying and fractional distilling. More exhaustive purification uses sulfonation by dissolving in two volumes of conc H_2SO_4, precipitating with four volumes of conc HCl at 0°, washing with conc HCl and recrystallising from $CHCl_3$. The mesitylene sulfonic acid is hydrolysed with boiling 20% HCl and steam distilled. The separated mesitylene is dried ($MgSO_4$ or $CaSO_4$) and distilled. It can also be fractionally crystallised from the melt at low temperatures. [*Beilstein* **5** IV 1016.]

Metanilic acid (3-aminobenzenesulfonic acid) *[121-47-1]* **M 173.2, m <300°(dec), pK $^{25}_{1}$ <1, pK $^{25}_{2}$ 3.74.** Crystallise the acid from water (as the hydrate), under CO_2 in a semi-darkened room. The solution is photosensitive. Dry it over 90% H_2SO_4 in a vacuum desiccator. [*Beilstein* **14** H 688, **14** IV 2640.]

p-**Methoxyacetophenone** *[100-06-1]* **M 150.2, m 39°, b 139°/15mm, 264°/736mm.** Crystallise the ketone from diethyl ether/petroleum ether. The *oxime* has **m 86°, 87°** (from petroleum ether, v. Auwers et al. *Chem Ber* **58** 41 *1925*). [*Beilstein* **8** H 87, **8** I 536, **8** II 84, **8** III 277, **8** IV 340.]

p-**Methoxyazobenzene** *[2396-60-3]* **M 212.3, m 54-56°.** Crystallise 4-methoxyazobenzene from EtOH. [*Beilstein* **16** IV 162.]

3-Methoxybenzanthrone *[3688-79-7]* **M 274.3, m 173°.** Crystallise it from *benzene, EtOH or Me_2CO to give yellow needles. [*Beilstein* **8** II 239, **8** III 1629, **8** IV 1476.]

***m*-Methoxybenzoic acid (*m*-anisic acid)** *[586-38-9]* **M 152.2, m 110°, pK^{25} 4.09.** Crystallise *m*-anisic acid from H_2O (**m** 109°, 110.5°) or EtOH/water. The *S-benzylisothiuronium salt* has **m** 176° (from EtOH). [*Beilstein* **10** II 80, **10** III 244, **10** IV 316.]

***p*-Methoxybenzoic acid (*p*-anisic acid)** *[100-09-4]* **M 152.2, m 184.0-184.5°, pK^{25} 4.51.** Crystallise *p*-anisic acid from EtOH, water, EtOH/water or toluene. The *S-benzylisothiuronium salt* has **m** 189° (from EtOH). [*Beilstein* **10** II 91, **10** III 280, **10** IV 346.]

4-Methoxybenzyl chloride (anisyl chloride) *[824-94-2]* **M 156.6, m -1°, b 76°/0.1mm, 95°/5mm, 110°/10mm, 117-117/5°/14mm, 117°/18mm, d $^{20}_{4}$ 1.15491, n $^{20}_{D}$ 1.55478.** Purify 4-anisyl chloride by fractional distillation under vacuum, and the middle fraction is redistilled at 10^{-6} mm at room temperature by intermittent cooling of the receiver in liquid N_2, and the middle fraction is collected. [Mohammed & Kosower *J Am Chem Soc* **93** 2709 *1971*, *Beilstein* **6** IV 2137.]

"Methoxychlor", (1,1-bis[*p*-methoxyphenyl]-2,2,2-trichloroethane, DMDT) *[72-43-5]* **M 345.7, m 78-78.2°, or 86-88°.** Free the insecticide from 1,1-bis(*p*-chlorophenyl)-2,2,2-trichloroethane by crystallising from EtOH. It is dimorphic and also crystallises from Et_2O/EtOH (**m** 92°). [Fritsch & Feldmann *Justus Liebigs Ann Chem* **306** 77 *1899*, Smith et al. *Aust J Chem* **29** 743 *1976*, *Beilstein* **6** H 1007.]

***trans*-*p*-Methoxycinnamic acid** *[830-09-1, 943-89-5 (trans)]* **M 178.2, m 173.4-174.8°, pK^{25} 4.54.** Crystallise the acid from MeOH to constant melting point and UV spectrum. [*Beilstein* **10** IV 1005.]

6-Methoxy-1-indanone *[13623-25-1]* **M 162.2, m 151-153°.** Crystallise it from MeOH, then sublime it at high vacuum. [*Beilstein* **8** IV 894.]

1-Methoxy-4-nitronaphthalene *[4900-63-4]* **M 203.2, m 85°.** Purify it by chromatography on silica gel, then recrystallise it from MeOH or EtOH (yellow needles). [Hodgson & Habeshaw *J Chem Soc* 47 *1942*, Bunce et al. *J Org Chem* **52** 4214 *1987*, *Beilstein* **6** H 616, **6** III 2938.]

***p*-Methoxyphenol** *[150-76-5]* **M 124.1, m 54-55°, b 243°/atm, pK^{25} 10.21.** Crystallise 4-methoxyphenol from *benzene, petroleum ether or H_2O, and dry it under vacuum over P_2O_5 at room temperature. Sublime it *in vacuo*. [Wolfenden et al. *J Am Chem Soc* **109** 463 *1987*, *Beilstein* **6** IV 5717.]

α-Methoxyphenylacetic acid (*O*-methyl mandelic acid), *[R-(–)- 3966-32-3, S-(+)- 26164-26-1]* **M 166.2, m 62.9°, 62-65°, 65-66°, [α] $^{20}_{546}$ (-) and (+) 179° (169.8°), [α] $^{20}_{D}$ (-) and (+) 150.7° (148°) (c 0.5, EtOH), pK$_{Est}$ ~3.1.** Purify the acids by recrystallising from *C_6H_6/petroleum ether (**b** 80-100°). [Neilson & Peters *J Chem Soc* 1519 *1962*, Weizmann et al. *J Am Chem Soc* **70** 1153 *1948*, Pirie & Smith *J Chem Soc* 338 *1932*, NMR: Dale & Mosher *J Am Chem Soc* **95** 512 *1973*, for resolution: Roy & Deslongchamps *Can J Chem* **63** 651 *1985,* Trost et al. *J Am Chem Soc* **108** 4974 *1986*.] The *racemic mixture* has **m** 72°, **b** 121-122°/0.4mm, 165°/18mm (from petroleum ether) [Braun et al. *Chem Ber* **63** 2847 *1930*]. [*Beilstein* **10** IV 566.]

***o*-Methoxyphenylacetic acid** *[93-25-4]* **M 166.2, m 124-125°, pK$_{Est}$ ~4.4.** Crystallise the acid from H_2O, EtOH or aqueous EtOH, petroleum ether/Et_2O and dry it in a vacuum desiccator over Sicapent. The *amide* has **m** 131° (from EtOH). [*Beilstein* **10** H 188, **10** III 422, **10** IV 536.]

***m*-Methoxyphenylacetic acid** *[1798-09-0]* **M 166.2, m 66-67°, 68-69°, 71.0-71.2°, pK$_{Est}$ ~4.3.** Crystallise the acid from H_2O, or aqueous EtOH. The *S-benzylisothiuronium salt* has **m** 160-161° (from EtOH). [*Beilstein* **10** I 82, **10** III 428, **10** IV 541.]

***p*-Methoxyphenylacetic acid (homoanisic acid)** *[104-01-8]* **M 166.2, m 85-87°, b 138-140°/2-3mm, pK^{25} 4.36.** Crystallise the acid from EtOH/water, EtOAc/petroleum ether (**m** 87°) or *C_6H_6/petroleum ether (**m** 84-86°). [*Beilstein* **10** III 431, **10** IV 544.] The *acid chloride* [4693-91-8] has **M** 184.6, **b** 143°/10mm, **d** $^{25}_{4}$ **1.208.** [*Beilstein* **10** III 434.]

***N*-(*p*-Methoxyphenyl)-*p*-phenylenediamine** *[101-64-4]* **M 214.3, m 102°, b 200°/2mm, 238°/12mm, pK^{25} 6.6 (5.9).** Crystallise the diamine from ligroin or *C_6H_6/petroleum ether (**m** 99-100°). The *picrate* has **m** 164° (from EtOH). [*Beilstein* **13** III 1161, **13** IV 1243.]

α-Methoxy-α-trifluoromethylphenylacetic acid (MTPA, Mosher's acid) *[R-(+)- 20445-31-2, S-(–)- 17257-71-5]* **M 234.2, m 43-45°, 90°/0.1mm, 105-107°/1mm, $[\alpha]_{546}^{20}$ (+) and (-) 87°, $[\alpha]_{D}^{20}$ (+) and (-) 73° (c 2, MeOH), pK_{Est} ~2.5.** A likely impurity is phenylethylamine from the resolution. Dissolve the acid in Et_2O/*benzene (3:1), wash with 0.5N H_2SO_4, then water, dry over magnesium sulfate, filter, evaporate and distil it. [Dale et al. *J Org Chem* **34** 2543 *1969*, *J Am Chem Soc* **75** 512 *1973*.]

α-Methoxy-α-trifluoromethylphenylacetyl chloride *[R-(–)- 39637-99-5, S-(+)- 20445-33-4]* **M 252.6, b 54-56°/1mm, 213-214°/760mm, d_4^{20} 1.353, n_D^{20} 1.468, $[\alpha]_{546}^{20}$ (-) and (+) 167°, $[\alpha]_{D}^{20}$ (-) and (+) 137° (c 4, CCl_4), $[\alpha]_{D}^{24}$ (-) and (+) 10.0° (neat).** The most likely impurity is the free acid due to hydrolysis and should be checked by IR. If free from acid, then distil, taking care to keep moisture out of the apparatus. Otherwise add $SOCl_2$ and reflux for 5 hours and distil it. Note that shorter reflux times result in a higher boiling fraction (**b** 130-155°/1mm) which has been identified as the anhydride. [Dale et al. *J Org Chem* **34** 2543 *1969*, for enantiomeric purity see Dale & Mosher *J Am Chem Soc* **97** 512 *1973*.]

***N*-Methylacetanilide** *[579-10-2]* **M 149.2, m 102-104°, b 145-146°/30mm, 225°/760mm.** Crystallise the anilide from water, ether, petroleum ether (b 80-100°) or *C_6H_6 (**m** 105°). The *BF_3 salt* has **m** 114° (from Me_2CO/diisopropyl ether). [*Beilstein* **12** III 465, **12** IV 378.]

***p*-Methylacetophenone** *[122-00-9]* **M 134.2, m 22-24°, b 93.5°/7mm, 110°/14mm, d_4^{20} 1.000, n_D^{20} 1.5335.** Impurities, including the *o*- and *m*-isomers, are removed by forming the *semicarbazone* (**m** 212-213.5°) which, after repeated crystallisation, is hydrolysed to the ketone. [Brown & Marino *J Am Chem Soc* **84** 1236 *1962*.] It can also be purified by distillation under reduced pressure, followed by low temperature crystallisation from isopentane. The *oxime* has **m 87-88°** (from MeOH then cyclohexane Pearson & Ball *J Org Chem* **14** 125 *1949*). [*Beilstein* **7** H 307, **7** I 154, **7** II 238, **7** III 1060, **7** IV 701.]

1-Methylaminoanthraquinone *[82-38-2]* **M 237.3, m 166.5°, pK_{Est}~2.** Crystallise it to constant melting point from butan-1-ol, then from EtOH. It can be sublimed under vacuum. [*Beilstein* **7** IV 2574.]

***N*-Methyl-*o*-aminobenzoic acid (*N*-methylanthranilic acid)** *[119-68-6]* **M 151.2, m 178.5°, pK_1^{25} 1.97, pK_2^{25} 5.34.** Crystallise the acid from water, MeOH (**m** 177°) or EtOH. [Casulich & Smith *J Am Chem Soc* **70** 1923 *1948*, *Beilstein* **14** H 323, **14** III 895, **14** IV 1015.]

3-(Methylamino)benzoic acid *[51524-84-6]* **M 151.1, m 129°, pK_1^{25} 3.08, pK_2^{25} 5.10.** Crystallise the acid from H_2O (needles), petroleum ether (plates) or $CHCl_3$ (**m** 127°). The *hydrochloride* has **m** 244° (plates from EtOH). [*Beilstein* **14** H 391, **14** I 559.]

***p*-Methylaminophenol sulfate (Photol, Metol)** *[55-55-0]* **M 344.4, m 260°(dec), pK^{25} 5.9.** Crystallise this photographic developer from H_2O (needles **m** 250-260°) (its solubility is 5% at 20° and 17% at 100°) or MeOH. It is used for determining Ag. [Palit et al. *Indian J Chem, Sect B* **28** 64 *1989*.]

***N*-Methylaniline** *[100-61-8]* **M 107.2, b 57°/4mm, 81-82°/14mm, d_4^{20} 0.985, n_D^{20} 1.570, pK^{25} 4.56.** Dry it with KOH pellets and fractionally distil it under vacuum. Acetylate, and the *acetyl* derivative is recrystallised to constant melting point (**m** 101-102°), then hydrolysed with aqueous HCl and distilled from zinc dust under reduced pressure. [Hammond & Parks *J Am Chem Soc* **77** 340 *1955*, *Beilstein* **12** IV 241.]

***N*-Methylaniline hydrochloride** *[2739-12-0]* **M 143.7, m 123.0-123.1°.** Crystallise the salt from dry *benzene/$CHCl_3$ and dry under vacuum. [*Beilstein* **12** IV 241.]

Methyl *p*-anisate *[121-98-2]* **M 166.2, m 48°, b 123.8°/12mm, 24-245°/760mm.** Distil the ester and/or crystallise it from EtOH. [*Beilstein* **10** H 159, **10** III 297, **10** IV 360.]

4-Methyl anisole *[104-93-8]* **M 122.2, b 56.2°/9mm, 67°/20mm, 175-176°/760mm, d_{15}^{15} 0.9757, n_D^{20} 1.512.** Dissolve 4-methyl anisole in diethyl ether, wash it with M NaOH, water, dry (Na_2CO_3), evaporate and distil it under vacuum. The *picrate* has **m** 103° (from aqueous EtOH). [*Beilstein* **6** IV 2098.]

2-Methylanthracene *[613-12-7]* **M 192.3, m 204-206°.** Chromatograph it on silica gel with cyclohexane as eluent and then recrystallise it from EtOH [Werst *J Am Chem Soc* **109** 32 *1987*]. [*Beilstein* **5** IV 2311.]

4-Methylanthracene *[779-02-2]* **M 192.3, m 77-79°, b 196-197°/12mm, d_4^{20} 1.066.** Chromatograph it on silica gel with cyclohexane as eluent and recrystallise it from EtOH [Werst *J Am Chem Soc* **109** 32 *1987*]. [*Beilstein* **5** IV 2312.]

2-Methylanthraquinone *[84-54-8]* **M 222.3, m 176°, b 236-238°/10mm.** Crystallise the quinone from EtOH, then sublime it. It has λ_{max} at 257, 275 and 330nm (EtOH). [Hersbery & Fieser *J Am Chem Soc* **63** 2562 *1941*, *Beilstein* **7** H 809, **7** III 4104, **7** IV 2574.]

Methylarenes (see also pentamethyl- and hexamethyl-benzenes). Recrystallise them from EtOH and sublime them in a vacuum [Schlesener et al. *J Am Chem Soc* **106** 7472 *1984*].

Methyl benzoate *[93-58-3]* **M 136.2, b 104-105°/39mm, 199.5°/760mm, d_4^{20} 1.087, n^{15} 1.52049, n_D^{20} 1.51701, pK^{20} -8.11, -6.51 (H_0 scale, aqueous H_2SO_4).** Wash the ester with dilute aqueous $NaHCO_3$, then water, dry with Na_2SO_4 and fractionally distil it in a vacuum. [*Beilstein* **9** IV 283.]

p-**Methylbenzophenone** *[134-84-9]* **M 196.3, m 57°, b 154-155°/3mm, 183-184°/15mm, 277-281°/3mm, d^{20} 0.9926.** Crystallise the ketone from MeOH, Et_2O (**m** 58-59°) or petroleum ether. The *cis-oxime* has **m** 154°(153-156°) (from EtOH), and the *trans-oxime* has **m** 114-116° (from petroleum ether). [*Beilstein* **7** H 440, **7** III 2127, **7** IV 1403.]

Methyl-1,4-benzoquinone (*p*-toluoquinone) *[553-97-9]* **M 122.1, m 68-69°.** Crystallise *p*-toluoquinone from heptane or EtOH, dry rapidly (vacuum/P_2O_5) and stored in a vacuum. [*Beilstein* **7** IV 2088.]

Methyl benzoylformate (methyl phenylglyoxalate) *[15206-55-0]* **M 164.2, m 246-248°.** Purify the ester by radial chromatography (diethyl ether/hexane, 1:1), and dry it at 110-112°/6mm. [Meyers & Oppenlaender *J Am Chem Soc* **108** 1989 *1986*, *Beilstein* **10** IV 2738.]

2-Methyl-3,4-benzphenanthrene (2-methylbenzo[*c*]phenanthrene) *[652-04-0]* **M 242.3, m 70°, 80.6-81.4°, b 200°/0.4mm.** Crystallise it from EtOH (**m** 81-82.5°). The *picrate* has **m** 118-118.5° (yellow needles from MeOH). [*Beilstein* **5** III 2394, **5** IV 2570.]

***R*-(+)-α-Methylbenzylamine** *[R(+) 3886-69-9, RS(±) 618-36-0]* **M 121.2, b 187-188°/atm, $[\alpha]_{546}^{20}$ +35° (c 10, EtOH), $[\alpha]_D^{25}$ +39.7° (neat), pK 9.08 (for *RS*).** Dissolve the amine in toluene, dry over NaOH and distil; fraction boiling at 187-188°/atm is collected. Store it under N_2 to avoid forming the carbamate and urea. Similarly for the *S*-(–) *enantiomer [2627-86-3]*. [Ingersoll *Org Synth* Coll Vol **II** 503 *1943*, Robinson & Snyder *Org Synth* Coll Vol **III** 717 *1955*, *Beilstein* **12** IV 2424, 2425.]

p-**Methylbenzyl chloride** *[104-82-5]* **M 140.6, b 80°/2mm, 98-101°/27mm, d_4^{20} 1.085, n_D^{20} 1.543.** Dry the chloride with $CaSO_4$ and fractionally distil it under vacuum. [*Beilstein* **5** H 384, **5** III 854, **5** IV 966.]

Methyl *o*-bromobenzoate *[610-94-6]* **M 215.1, b 131.4-132°/16mm, 234-244°/760mm.** A solution of the ester in ether is washed with 10% aqueous Na_2CO_3, water, then dried and distilled. [*Beilstein* **9** H 348, **9** III 1385, **9** IV 1012.]

Methyl *p*-bromobenzoate *[619-42-1]* **M 215.1, m 79.5-80.5°.** Crystallise the ester from MeOH. EtOH (**m** 81°, also 80.5°, 79.5°) or *C_6H_6/petroleum ether (**m** 78-79°). [*Beilstein* **9** H 352, **9** III 1405, **9** IV 1017.]

(±)-3'-Methyl-1,2-cyclopentenophenanthrene (16,17-dihydro-17-methyl-15*H*-cyclopenta-[*a*]-phenanthrene *[549-38-2]* **M 232.3, m 126-127°.** Crystallise it from AcOH or EtOH (plates, **m** 125.5-126°). The *picrate* has **m** 130-131° (orange-red needles from EtOH). [Tatta & Bardhan *J Chem Soc (C)* 893 *1968*, *Beilstein* **5** IV 2433.]

Methyl 2,4-dichlorophenoxyacetate *[1928-38-7]* **M 235.1, m 43°, b 119°/11mm.** Crystallise the herbicide ester from MeOH. [Branch & Jones *J Chem Soc* 2924 *1955*, *Beilstein* **6** III 705, **6** IV 909.]

3,4-Methylenedioxyaniline *[14268-66-7]* **M 137.1, m 44.5-45.5°, 45-46°, b 108°/1mm, 144°/14mm, 156°/30mm, pK_{Est} ~3.8.** Crystallise the base from petroleum ether and/or distil it in a vacuum. The *hydrochloride* has **m** 198°(dec). [Sonn & Benirschke *Chem Ber* **54** 1734 *1921*, *Beilstein* **19** H 328, **19** II 341, **19** III/IV 4056.]

***trans*-3,4-Methylenedioxycinnamic acid** *[2373-80-0]* **M 192.2, m 243-244°(dec), pK_{Est} ~4.6.** Crystallise the acid from glacial AcOH, EtOH (**m** 247°) or aqueous EtOH (**m** 240-242°), and it has **m** 242° after sublimation. [*Beilstein* **19** H 278, **19** II 299, **19** III/IV 3548.]

5,5'-Methylenedisalicylic acid *[122-25-8; 27496-82-2]* **M 288.2, m 238°(dec).** Crystallise the acid from Me_2CO, *C_6H_6 or $CHCl_3$/MeOH (**m** 268-268°). It has λ_{max} at 312nm (ε 7530)in EtOH. [Cushman & Kanamathareddy *Tetrahedron* **46** 1406 *1990*.]

***N*-Methylephedrine (2-dimethylamino-1-phenylpropanol)** *[1*S*,2*R*-(+)- *42151-56-4*, 1*R*,2*S*-(–)- *552-79-4]* **M 179.3, m 85-86°, 87-87.5°, 90°, b 115°/2mm, $[\alpha]_{546}^{20}$ (+) and (-) 35°, $[\alpha]_{D}^{20}$ (+) and (-) 30° (c 4.5, MeOH), pK^{26} 9.22.** *N*-Methylephedrine has been recrystallised from Et_2O, petroleum ether, of aqueous EtOH or aqueous MeOH and has been distilled under reduced pressure. [Smith *J Chem Soc* 2056 *1927*, Tanaka & Sugawa *Yakugaku Zasshi (J Pharm Soc Japan) 72* 1548 *1952* (*Chem Abstr* **47** 8682 *1953*), Takamatsu *Yakugaku Zasshi (J Pharm Soc Japan)* **76** 1227 *1956*, *Chem Abstr* **51** 4304 *1957*.] The *hydrochloride* has **m** 192-193° and $[\alpha]_{D}^{20}$+30° (c 5,H_2O) [Prelog & Hüfliger *Helv Chim Acta* **33** 2021 *1950*]. [*Beilstein* **13** IV 1884.]

Methyl gallate *[99-24-1]* **M 184.2, m 202°.** Crystallise the gallate ester from MeOH. [*Beilstein* **10** IV 1998.]

Methyl Green *[82-94-0, 7114-03-6 ($ZnCl_2$ salt)]* **M 458.5, m >200°(dec).** Crystallise the dye from hot water. [*Beilstein* **13** IV 2286.]

Methyl 4-hydroxybenzoate *[99-76-3]* **M 152.2, m 127.5°, pK_{Est} ~9.3.** Fractionally crystallise the ester from its melt, and recrystallise it from *benzene, then from *benzene/MeOH and dry it over $CaCl_2$ in a vacuum desiccator. [*Beilstein* **10** IV 360.]

Methyl 3-hydroxy-2-naphthoate *[883-99-8]* **M 202.2, m 73-74°, pK_{Est} ~9.0.** Crystallise the ester from MeOH (charcoal) containing a little water. [*Beilstein* **10** IV 1186.]

3-Methylmercaptoaniline *[1783-81-9]* **M 139.2, b 101.5-102.5°/0.3mm, 163-165°/16mm, d_4^{20} 1.147, n_D^{20} 1.641, pK^{25} 4.05.** Purify the aniline by fractional distillation in an inert atmostphere. It has UV max at 226 and 300nm. [Bordwell & Cooper *J Am Chem Soc* **74** 1058 *1952*.] The *N-acetyl* derivative has **m** 78-78.5° (from aqueous EtOH). The *hydrochloride* has **m** 260-261° (aqueous EtOH/HCl) or **m** 225-227° (EtOH/Et_2O). [*Beilstein* **13** H 533, **13** III 1221, **13** IV 1289.]

4-Methylmercaptoaniline *[104-96-1]* **M 139.2, b 140°/15mm, 151°/25mm, 155°/23mm, d_4^{20} 1.137, n_D^{20} 1.639, pK^{25} 4.40.** Purify the aniline by fractional distillation in an inert atmosphere. The *hydrochloride* has **m** 242-246° (from aqueous EtOH/HCl). The *sulfone* has **m** 137° (from H_2O), pK^{25} 1.48, and the *sulfone hydrochloride* has **m** 260-261° (from aqueous EtOH/HCl). [Lumbroso & Passerini *Bull Soc Chim Fr* 311 *1957*, Mangini & Passerini *J Chem Soc* 4954 *1956*, *Beilstein* **13** H 533, **13** II 297, **13** IV 1221.]

1-Methylnaphthalene *[90-12-0]* **M 142.2, f -30°, b 244.6°, d_4^{20} 1.021, n_D^{20} 1.6108.** Dry 1-methylnaphthalene for several days with $CaCl_2$ or by prolonged refluxing with BaO. Fractionally distil it through a glass helices-

packed column from sodium. Purify it further by solution in MeOH and precipitation of its *picrate complex* by adding to a saturated solution of picric acid in MeOH. The picrate, after crystallisation to constant melting point (**m** 140-141°) from MeOH, is dissolved in *benzene and extracted with aqueous 10% LiOH until the extract is colourless. Evaporation of the *benzene solution under vacuum gives 1-methylnaphthalene [Kloetzel & Herzog *J Am Chem Soc* **72** 1991 *1950*]. However, neither the picrate nor the styphnate complexes satisfactorily separate 1- and 2-methylnaphthalenes. To achieve this, 2-methylnaphthalene (10.7g) in 95% EtOH (50ml) has been precipitated with 1,3,5-trinitrobenzene (7.8g) and this complex has been crystallised from MeOH to **m** 153-153.5° (**m** of the 2-methyl isomer is 124°). [*Alternatively*, 2,4,7-trinitrofluorenone in hot glacial acetic acid could be used, and the derivative (**m** 163-164°) is recrystallised from glacial acetic acid]. The 1-methylnaphthalene is regenerated by passing a solution of the complex in dry *benzene through a 15-in column of activated alumina and washing with *benzene/petroleum ether (b 35-60°) until the coloured band of the nitro compound had moved down near the end of the column. The complex can also be decomposed using tin and acetic-hydrochloric acids, followed by extraction with diethyl ether and *benzene; the extracts are washed successively with dilute HCl, strongly alkaline sodium hypophosphite, water, dilute HCl and water. [Soffer & Stewart *J Am Chem Soc* **74** 567 *1952*.] It can be freed from anthracene by zone melting [*Beilstein* **5** IV 1687.]

2-Methylnaphthalene *[91-57-6]* **M 142.2, m 34.7-34.9°, b 129-130°/25mm.** Fractionally crystallise repeatedly from its melt, then fractionally distil under reduced pressure. It has been crystallised from *benzene and dried under vacuum in an Abderhalden pistol. It can be purified *via* its *picrate* (**m** 114-115°) or better *via* the *1,3,5-trinitrobenzene complex* as for 1-methylnaphthalene (above). [*Beilstein* **5** IV 1693.]

6-Methyl-2-naphthol *[17579-79-2]* **M 158.2, m 128-129°, b 177.5-178°/15mm, pK_{Est} ~9.8.** Crystallise the naphthol from EtOH or ligroin. Sublime it *in vacuo*. [*Beilstein* **6** II 618, **6** III 3028.]

7-Methyl-2-naphthol *[26593-50-0]* **M 158.2, m 118°, pK_{Est} ~9.7.** Crystallise the naphthol from EtOH or ligroin. It has **m** 118° after sublimation *in vacuo*. [Halsall & Thomas *J Chem Soc* 2564 *1956*, *Beilstein* **6** IV 3029.]

Methyl 1-naphthyl ether (1-methoxynaphthalene) *[2216-69-5]* **M 158.2, b 90-91°/2mm, d_4^{20} 1.095, n_D^{26} 1.6210.** Steam distil the ether from alkaline solution. The distillate is extracted with Et_2O. After drying ($MgSO_4$) the extract and evaporating Et_2O, the methyl naphthyl ether is then fractionated under reduced pressure from CaH_2. The *picrate* has **m** 129.5-130.5° (from EtOH). [*Beilstein* **6** IV 4211.]

Methyl 2-naphthyl ether (2-methoxynaphthalene, Nerolin) *[93-04-9]* **M 158.2, m 73.0-73.6°, b 138°/10mm 273°/760mm.** Fractionally distil the ether under vacuum. Crystallise it from absolute EtOH, aqueous EtOH, *C_6H_6, petroleum ether or *n*-heptane, and dry it under vacuum in an Abderhalden pistol or distil it *in vacuo*. The *picrate* has **m** 118° (from EtOH or $CHCl_3$). [Kikuchi et al. *J Phys Chem* **91** 574 *1987*, *Beilstein* **6** III 2969, **6** IV 4257.]

2-Methyl-3-nitroaniline *[603-83-8]* **M 152.2 m 92°, b 305°/760mm, pK_{Est} ~ 2.3.** Crystallise the nitrotoluidine from EtOH or *C_6H_6. It is steam volatile. The *acetyl* derivative crystallises from aqueous EtOH and has **m** 164°. [*Beilstein* **12** I 395, **12** II 460, **12** III 1944, **2** IV 1811.]

***N*-Methyl-4-nitroaniline** *[100-15-2]* **M 152.2, m 152.2°, pK^{25} 0.55.** Crystallise the aniline from aqueous EtOH. [*Beilstein* **12** H 714.]

2-Methyl-4-nitroaniline *[99-52-5]* **M 152.2 m 129°, pK_{25} 0.93.** Crystallise the nitrotoluidine from EtOH. The *acetyl* and *benzoyl* derivatives have **m** 200° and 174° (EtOH) respectively. [*Beilstein* **12** IV 1809.]

2-Methyl-5-nitroaniline *[99-55-8]* **M 152.2, m 109°, pK^{25} 2.35.** Acetylate the aniline, and the acetyl derivative is crystallised to constant melting point; then hydrolyse it with 70% H_2SO_4 and the free base is regenerated by treatment with NH_3 [Bevan et al. *J Chem Soc* 4284 *1956*]. [*Beilstein* **12** H 844. **12** IV 1807.]

4-Methyl-3-nitroaniline *[119-32-4]* **M 152.2, m 81.5°, pK^{25} 3.02.** Crystallise the aniline from hot water

(charcoal), then ethanol and dry it in a vacuum desiccator. [*Beilstein* **12** H 966.]

2-Methyl-5-nitroanisole *[4837-88-1]* **M 176.2, m 54-56°.** 2-Methyl-5-nitroanisole crystallises from MeOH (yellow needles) and sublimes *in vacuo*. [Kuffner *Monatsh Chem* **91** 1152 *1960*, *Beilstein* **6** I 178.]

Methyl 3-nitrobenzoate *[618-95-1]* **M 181.2, m 78°.** Crystallise the benzoate from MeOH (1g/ml). [*Beilstein* **9** H 378, **9** I 153, **9** II 248, **9** III 1493, **9** IV 1056.]

Methyl 4-nitrobenzoate *[619-50-1]* **M 181.2, m 95-95.5°.** Dissolve the benzoate in diethyl ether, then wash it with aqueous alkali; the ether is evaporated and the ester is recrystallised from EtOH. [*Beilstein* **9** H 390, **9** IV 1074.]

3-Methyl-2-nitrobenzoic acid *[5437-38-7]* **M 181.2, m 220-222.5°, pK^{20} 2.91 (1% aqueous EtOH).** Recrystallise it from EtOH. The *methyl ester* has **m** 74° (from MeOH), and the *amide* [60310-07-8] **M** 180.1, has **m** 192° (needles from H_2O, prisms from EtOH). [*Beilstein* **9** H 480, **9** IV 1722.]

4-Methyl-3-nitrobenzoic acid (3-nitro-*p*-toluic acid) *[96-98-0]* **M 181.2, m 190-191°, pK^{20} 3.62 (1% aqueous EtOH).** Recrystallise the acid from EtOH. The *S-benzylisothiuronium salt* has **m** 167-168° (EtOH). The *acid chloride* [10397-30-5] has **m** 20-21°, **b** 185°/36mm, and the *methyl ester* [7356-11-8] crystallises as pale yellow needles from MeOH with **m** 51°. [*Beilstein* **9** H 502, **9** II 334, **9** III 2359.]

***N*-Methyl-4-nitrosoaniline** *[10595-51-4]* **M 136.2, m 114-115°, 118°, pK_{Est} ~1.0.** Crystallise it from *C_6H_6. The *picrate* has **m** 166°(dec) (from MeOH or $CHCl_3$). [*Beilstein* **7** III 3370, **12** IV 1228.]

***N*-Methyl-*N*-nitroso-*p*-toluenesulfonamide (Diazald)** *[80-11-5]* **M 214.2, m 62°.** Crystallise diazald from *benzene by addition of petroleum ether and store it in a refrigerator. It is soluble in most organic solvents including Et_2O, and liberates diazomethane on treatment with alkali. Store it in the cold. It remains active for many months if it is kept in a stoppered bottle in a cold room at >10°. [deBoer & Backer *Org Synth* **34** 96 1954, *Org Synth* Coll Vol **VI** 943 *1963*, *Beilstein* **11** I 29.]

4-Methylphenylacetic acid (*p*-tolylacetic acid) *[622-47-9]* **M 150.2, m 94°, pK^{25} 4.37.** Crystallise the acid from heptane or water. [*Beilstein* **9** IV 1795.]

1-Methyl-1-phenylhydrazine sulfate *[33008-18-3]* **M 218.2, pK^{25} 4.98 (free base).** Crystallise the sulfate from hot H_2O by addition of hot EtOH. [*Beilstein* **15** IV 53 for free base.]

***N*-Methylphthalimide** *[550-44-7]* **M 161.1, m 133.8°.** Recrystallise the imide from absolute EtOH or AcOH (**m** 134°). The IR has ν_{max} at 1780 and 1380cm^{-1}. [*Beilstein* **21** H 461, **21** III/IV 5030.]

Methyl Red (4-dimethylaminoazobenzene-2'-carboxylic acid) *[493-52-7]* **M 269.3, m 181-182°, CI 13020, pK_1^{25} 2.30, pK_2^{25} 4.82.** The acid is extracted with boiling toluene using a Soxhlet apparatus. The crystals which separate on slow cooling to room temperature are filtered off, washed with a little toluene and recrystallised from glacial acetic acid, *benzene or toluene followed by pyridine/water. *Alternatively*, dissolve it in aqueous 5% $NaHCO_3$ solution, and precipitate it from a hot solution by dropwise addition of aqueous HCl. Repeat this until the extinction coefficients do not increase. [*Beilstein* **16** IV 504.]

Methyl salicylate (methyl 2-hydroxybenzoate, oil of winter green) *[119-36-8]* **M 152.2, m -8.6°, b 79°/6mm, 104-105°/14mm, 223.3°/atm, d_4^{20} 1.1149, n_D^{20} 1.5380, pK^{25} 10.19.** Dilute the ester with Et_2O, wash with saturated $NaHCO_3$ (it may effervesce due to the presence of free acid), brine, dry $MgSO_4$, filter, evaporate and distil it. Its solubility is 1g/1.5L of H_2O. The *benzoyl* derivative has **m** 92° (**b** 270-280°/120mm), and the *3,5-dinitrobenzoate* has **m** 107.5°, and the *3,5-dinitrocarbamoyl* derivative has **m** 180-181°. [Hallas *J Chem Soc* 5770 *1965*, *Beilstein* **10** IV 143.]

α-Methylstyrene (monomer, 2-phenylpropene) *[98-83-9]* **M 118.2, b 57°/15mm, d_4^{20} 0.910, n_D^{20} 1.5368.**

Wash the monomer three times with aqueous 10% NaOH (to remove inhibitors such as quinol), then six times with distilled water, dry with $CaCl_2$ and distil it under vacuum. The distillate is kept under nitrogen, in the cold, and redistilled if kept for more than 48 hours before use. It can also be dried with CaH_2. Add stabiliser if it is to be stored for long periods. [*Beilstein* **5** IV 1364.]

***trans*-ß-Methylstyrene (1-phenylpropene)** *[873-66-5]* **M 118.2, b 64-65°/10mm, 176°/760mm, d_4^{20} 0.910, n_D^{20} 1.5496.** Distil it under N_2 from powdered NaOH through a Vigreux column, and pass it through activated neutral alumina before use [Wong et al. *J Am Chem Soc* **109** 3428 *1987*]. [*Beilstein* **5** III 1184, **5** IV 1359.]

4-Methylstyrene *[622-97-9]* **M 118.2, b 60°/12mm, 106°/10mm, d_4^{20} 0.9173, n_D^{20} 1.542.** Purify it as the above styrenes and add a small amount of antioxidant if it is to be stored. It has UV in EtOH at λ_{max} at 285nm (log ε 3.07), and in EtOH + HCl 295nm (log ε 2.84) and 252nm (log ε 4.23). [Schwartzman & Carson *J Am Chem Soc* **78** 322 *1956*, Joy & Orchin *J Am Chem Soc* **81** 305 *1959*, Buck et al. *J Chem Soc* 2377*1949*, *Beilstein* **5** IV 1369.]

Methyl 4-toluenesulfonate *[80-48-8]* **M 186.2, m 25-28°, 28°, b 144.6-145.2°/5mm, 168-170°/13mm, d_4^{20} 1.23, n_D^{20} 1.5172.** The ester is purified by distillation *in vacuo* and could be crystallised from petroleum ether or Et_2O/petroleum ether at low temperature. It is a powerful methylating agent, is **TOXIC** and is a **skin irritant**, so it is better to purify it by repeated distillation. [IR: Schreiber *Anal Chem* **21** 1168 *1949*, Buehler et al. *J Org Chem* **2** 167 *1937*, Roos et al. *Org Synth* Coll Vol **I** 145 *1941*, *Beilstein* **11** IV 247.]

Methyl Violet 2B [4,4'-bis-(diethylamino)-4"-methyliminotriphenylmethyl hydrochloride) *[8004-87-3]* **M 394.0, m 137°(dec), CI 42535, λ_{max} ~580nm.** Crystallise the dye from EtOH by precipitation with Et_2O during cooling in an ice-bath. Filter it off and dry it at 105°. [*Beilstein* **13** IV 2283.]

Michler's ketone [4,4'-bis(dimethylamino)benzophenone] *[90-94-8]* **M 268.4, m 179°, pK^{25} 9.84.** Dissolve the ketone in dilute HCl, filter and precipitate it by adding ammonia (to remove water-insoluble impurities such as benzophenone). Then crystallise it from EtOH or petroleum ether. [Suppan *J Chem Soc, Faraday Trans1* **71** 539 *1975*.] It is also purified by dissolving in *benzene, then washing with water until the aqueous phase is colourless. The *benzene is evaporated off, and the residue is recrystallised three times from *benzene and EtOH [Hoshino & Kogure *J Phys Chem* **72** 417 *1988*]. [*Beilstein* **14** IV 255.]

Naphthacene **(benz[b]anthracene, 2,3-benzanthracene, rubene)** *[92-24-0]* **M 228.3, m >300°, 341° (open capillary), 349°, 357°.** Naphthacene crystallises in orange needles from EtOH, $*C_6H_6$ or toluene. Dissolve it in sodium-dried *benzene and pass it through a column of alumina. The eluent is evaporated under vacuum, and the chromatography is repeated using fresh *benzene. Finally, the naphthacene is sublimed *in vacuo* at 186°. [Martin & Ubblehode *J Chem Soc* 4948 *1961*, UV: Clar *Chem Ber* **65** 517 *1932,* Clar *Chem Ber* **69** 607 *1936*, IR: Cannon & Sutherland *Spectrochim Acta* **4** 373 *1951*, *Beilstein* **5** H 718, **5** IV 2545.]

1-Naphthaldehyde *[66-77-3]* **M 156.2, m 2°, b 160-161°/15mm, pK^{20} -7.04 (aqueous H_2SO_4).** Distil 1-naphthaldehyde with steam, extract the distillate into Et_2O, dry (Na_2SO_4), filter, evaporate the filtrate and distil the residue in a vacuum. [*Beilstein* **7** IV 1286.]

2-Naphthaldehyde *[66-99-9]* **M 156.2, m 59°, b 260°/19mm, pK^{20} -7.04 (aqueous H_2SO_4).** Distil 2-naphthaldehyde with steam then crystallise it from water or EtOH. [*Beilstein* **7** IV 1288.]

Naphthalene *[91-20-3]* **M 128.2, m 80.3°, b 87.5°/10mm, 218.0°/atm, d_4^{20} 1.0253, d_4^{100} 0.9625, n^{85} 1.5590.** Crystallise naphthalene once or more times from the following solvents: EtOH, MeOH, CCl_4, $*C_6H_6$, glacial acetic acid, acetone or diethyl ether, followed by drying at 60° in an Abderhalden drying apparatus. It has also been purified by vacuum sublimation and by fractional crystallisation from its melt. Other purification procedures include refluxing in EtOH over Raney Ni and chromatography of a CCl_4 solution on alumina with *benzene as eluting solvent. Baly and Tuck [*J Chem Soc* 1902 *1908*] purified naphthalene for spectroscopy by

heating with conc H_2SO_4 and MnO_2, followed by steam distillation (repeating the process), and formation of the *picrate* which, after recrystallisation (**m** 150°) is decomposed with base and the naphthalene is steam distilled. It is then crystallised from dilute EtOH. It can be dried over P_2O_5 under vacuum (take care not to make it sublime). Also purify it by sublimation and subsequent crystallisation from cyclohexane. *Alternatively*, it has been washed at 85° with 10% NaOH to remove phenols, with 50% NaOH to remove nitriles, with 10% H_2SO_4 to remove organic bases, and with 0.8g $AlCl_3$ to remove thianaphthalenes and various alkyl derivatives. Then it is treated with 20% H_2SO_4, 15% Na_2CO_3 and finally distilled. [Gorman et al. *J Am Chem Soc* **107** 4404 *1985*.] Zone refining purified naphthalene from anthracene, 2,4-dinitrophenylhydrazine, methyl violet, benzoic acid, methyl red, chrysene, pentacene and indoline. [*Beilstein* **5** IV 1640.]

Naphthalene-1,4-disulfonic acid *[92-41-1]* **M 288.2, pK_{Est} <0.** Crystallise the acid from conc HCl. The *disulfonamide* has **m** 273° (from EtOH). [*Beilstein* **11** II 119, **11** III 463.]

Naphthalene-1-sulfonic acid *[85-47-2]* **M 208.2, m ($2H_2O$) 90°, (anhydrous) 139-140°, pK^{20} -0.17.** Crystallise the acid from conc HCl and twice from H_2O. The *S-benzylisothiuronium salt* has **m** 137° (from aqueous EtOH). [*Beilstein* **11** H 155, **11** III 383, **11** IV 521.]

Naphthalene-2-sulfonic acid *[120-18-3]* **M 208.2, m 91°, pK_{Est} <1.** Crystallise the acid from conc HCl. The *S-benzylisothiuronium salt* has **m** 192° (from aqueous EtOH). [Berger *Acta Chem Scand* **8** 432 *1954*, *Beilstein* **11** H 171, **11** IV 527.]

Naphthalene-1-sulfonyl chloride *[85-46-1]* **M 226.7, m 64-67°, 68°, b 147.5°/0.9mm, 147.5°/13mm.** If the IR indicates the presence of OH, then treat it with an equal weight of PCl_5 and heat it at *ca* 100° for 2 hours, cool and pour onto ice + H_2O, stir well and filter off the solid. Wash the solid with cold H_2O and dry the solid in a vacuum desiccator over P_2O_5 + solid KOH. Extract the solid with petroleum ether (b 40-60°), filter off any insoluble solid and cool. Collect the crystalline sulfonyl chloride and recrystallise it from dry Et_2O, petroleum ether or *C_6H_6/petroleum ether. If large quantities are available, then it can be distilled under high vacuum. [Fierz-Davaid & Weissenbach *Helv Chim Acta* **3** 2312 *1920*.] The *sulfonamide* crystallises from EtOH **(m** 150.5°) or H_2O **(m** 153°). [*Beilstein* **11** H 175, **11** II 93, **11** IV 383.]

Naphthalene-2-sulfonyl chloride *[93-11-8]* **M 226.7, m 74-76°, 78°, 79°, 83°, b 148°/0.6mm, 201°/13mm.** Distil the chloride in a vacuum and/or recrystallise it (twice) from *benzene/petroleum ether (1:1 v/v). Purify it as the 1-sulfonyl chloride above. [Fierz-Davaid & Weissenbach *Helv Chim Acta* **3** 2312 *1920*.] The *sulfonamide* has **m** 217° (from EtOH). [*Beilstein* **11** III 399, **11** IV 529.]

1,8-Naphthalic acid (naphthalene-1,8-dicarboxylic acid) *[518-05-8]* **M 216.9, m 270°, $pK_{Est(1)}$~ 2.1, $pK_{Est(2)}$~ 4.5.** Crystallise the acid from EtOH or aqueous EtOH. [Raecke & Schrip *Org Synth* **40** 71 *1960*, *Beilstein* **9** II 651, **9** III 4466.]

1,8-Naphthalic anhydride *[81-84-5]* **M 198.2, m 274°, 274-275°.** Extract it with cold aqueous Na_2CO_3 to remove free acid, then crystallise from acetic anhydride. [*Beilstein* **17** III/IV 6392, **17/11** V 492.]

2-Naphthamide (2-naphthoic acid amide) *[2243-82-5]* **M 171.2, m 195°, pK^{20} -2.30 (H_0 scale, aqueous H_2SO_4).** Crystallise it from EtOH (197°). [Clemo & Spence *J Chem Soc* 2818 *1928*, *Beilstein* **9** H 657, **9** II 45, **9** IV 2417.]

Naphthazarin (5,8-dihydroxy-1,4-naphthoquinone) *[475-38-7]* **M 190.2, m ~ 220-230°(dec), m 225-230°, pK_1^{20} 8.2, p K_2^{20} 10.2.** It crystallises in red-brown needles with a green shine from EtOH. It also crystallises from hexane and is further purified by sublimation at 2-10mm. [Huppert et al. *J Phys Chem* **89** 5811 *1985*.] It is sparingly soluble in H_2O but soluble in alkalis. The *diacetate* forms golden yellow prisms from $CHCl_3$, **m** 192-193° and the *5,8-dimethoxy* derivative has **m** 157° (155°) (from petroleum ether) [Bruce & Thompson *J Chem Soc* 1089 *1955*, IR: Schmand & Boldt *J Am Chem Soc* **97** 447 *1975*, NMR: Brockmann & Zeeck *Chem Ber* **101** 4221 *1968*]. The *monothiosemicarbazone* has **m** 168°(dec) from EtOH [Gardner et al. *J Am Chem Soc* 74 2106 *1952*]. [*Beilstein* **8** H 412, **8** III 3600.]

Naphthionic acid (4-aminonaphthalene-1-sulfonic acid) *[84-86-6]* **M 223.3, m > 300°(dec), pK^{25} 2.68.** It crystallises from H_2O as needles of the 0.5 hydrate. Salt solutions fluoresce strongly blue. The *S-benzylisothiuronium salt* has **m** 195° (from aqueous EtOH). [*Beilstein* **14** IV 2793.]

1-Naphthoic acid *[86-55-5]* **M 172.2, m 162.5-163.0°, pK^{25} 3.60.** Crystallise the acid from toluene (3ml/g) (charcoal), petroleum ether (b 80-100°), or aqueous 50% EtOH. The *amide* has **m** 202° (from EtOH). [*Beilstein* **9** IV 2402.]

2-Naphthoic acid *[93-09-4]* **M 172.2, m 184-185°, pK^{25} 4.14.** Crystallise the acid from EtOH (4ml/g), aqueous 50% EtOH or Me_2CO (**m** 185-186°). Dry it at 100°. The *acid chloride* has **m** 52-52° (from *C_6H_6/petroleum ether) and **b** 160-162°/11mm [Hersberg & Carson *Org Synth* Coll Vol **III** 629 *1955*], the *amide* has **m** 192° (from EtOH), and the *N-Methyl amide* has **m** 109-109.5° (form *C_6H_6). [*Beilstein* **9** H 656, **9** III 3174, **9** IV 2402.]

1–Naphthol *[90-15-3]* **M 144.2, m 95.5-96°, pK^{25} 9.34.** Sublime 1-naphthol, then crystallise it from aqueous MeOH (charcoal), aqueous 25% or 50% EtOH, *C_6H_6, cyclohexane, heptane, CCl_4 or H_2O. Dry it over P_2O_5 *in vacuo*. The *4-nitrobenzoate* has **m** 143° (from EtOH). [Shizuka et al. *J Am Chem Soc* **107** 7816 *1985*, *Beilstein* **8** H 596, **6** IV 4208.]

2-Naphthol *[135-19-3]* **M 144.2, m 122.5-123.5°, pK^{25} 9.57.** Crystallise 2-naphthol from aqueous 25% EtOH (charcoal), H_2O, *benzene, toluene or CCl_4. *Alternatively*, extract it repeatedly with small amounts of EtOH, followed by dissolution in a minimum volume of EtOH and precipitation with distilled water, then drying over P_2O_5 under vacuum. It has also been dissolved in aqueous NaOH and precipitated by adding acid (repeat several times), then precipitated from *benzene by addition of heptane. Final purification can be by zone melting or sublimation *in vacuo*. The *4-nitrobenzoate* has **m** 104° (from EtOH). [Bardez et al. *J Phys Chem* **89** 5031 *1985*, Kikuchi et al. *J Phys Chem* **91** 574 *1987*, *Beilstein* **6** IV 4253.]

Naphthol AS-D (3-hydroxy-2-naphthoic-*o*-toluide) *[135-61-5]* **M 277.3, m 196-198°.** Purify it by recrystallisation from xylene. This gives yellow-green fluorescent solutions at pH 8.2-9.5. [IR: Schnopper et al. *Anal Chem* **31** 1542 *1959*.] The *naphthol AS-D acetate* is obtained with AcCl, **m** 168-169°, and with chloroacetyl chloride *naphthol AS-D-chloroacetate* is obtained [Moloney et al. *J Histochem Cytochem* **8** 200 *1960*, Burstone *Arch Pathology* **63** 164 *1957*]. [*Beilstein* **12** H 505.]

α-Naphtholbenzein [bis-(α-{4-hydroxynaphth-1-yl})-benzyl alcohol] *[6948-88-5]* **M 392.5, m 122-125°, pK_{Est} ~ 9.3.** Crystallise the alcohol from EtOH, aqueous EtOH or glacial acetic acid. [*Beilstein* **6** H 1150.]

1-Naphthol-2-carboxylic acid (1-hydroxy-2-naphthoic acid) *[86-48-6]* **M 188.2, m 203-204°, $pK_{Est(1)}$~2.5, $pK_{Est(2)}$~12.** Successively crystallise the acid from EtOH/water, diethyl ether and acetonitrile, with filtration through a column of charcoal and Celite. [Tong & Glesmann *J Am Chem Soc* **79** 583 *1957*, *Beilstein* **10** H 331, **10** IV 1194.]

3-Naphthol-2-carboxylic acid (3-hydroxy-2-naphthoic acid) *[92-70-6]* **M 188.2, m 222-223°, pK_1^{25} 2.79, pK_2^{25} 12.84.** Crystallise it from water or acetic acid. The *S-benzyisothiuronium salt* has **m** 216-217° (from EtOH). It forms many metal complex salts. [*Beilstein* **10** H 333, **10** III 1084.]

1,2-Naphthoquinone *[524-42-5]* **M 158.2, m 140-142°(dec).** Crystallise the quinone from ether (red needles) or *benzene (orange leaflets). [*Beilstein* **7** IV 2417.]

1,4-Naphthoquinone *[130-15-4]* **M 158.2, m 125-125.5°.** Crystallise the quinone from diethyl ether (charcoal). It distils in steam. It also crystallises from *benzene or aqueous EtOH and sublimes in a vacuum. [*Beilstein* **7** IV 2422.]

β-Naphthoxyacetic acid *[120-23-0]* **M 202.2, m 156°, pK_{Est} ~3.0.** Crystallise the acid from hot water or *benzene. [*Beilstein* **6** IV 4274.]

β-Naphthoyltrifluoroacetone (4,4,4-trifluoro-2-naphthylbutan-1,3-dione) *[893-33-4]* **M 266.2, m 70-71°, 74-76°, pK^{20} 6.35.** Crystallise the dione from EtOH. The *mono oxime* crystallises from H_2O or aqueous EtOH and has **m** 137-138°. [Reid & Calvin *J Am Chem Soc* **72** 2948 *1950*, *Beilstein* **7** IV 2478.]

Naphthvalene (2,3-dihydro-1,2,3-metheno-1*H*-indene) *[34305-47-0]* **M 128.1, m dec at 175° to benzvalene.** Purify it by chromatography on alumina and eluting with pentane, also by reverse phase (ODS) HPLC using MeCN as solvent. It is stable at room temperature [Kjell et al. *J Am Chem Soc* **108** 4111 *1986*, Abelt et al. *J Am Chem Soc* **107** 4148 *1985*]. The ^{1}H NMR in CCl_4 has τ 3.18 (4H), 6.17 (t *J* 1.5Hz, 2H), 7.60 (t *J* 1.5Hz 2H).

1-Naphthyl acetate *[830-81-9]* **M 186.2, m 45-46°, 48-49°, b 114-115°/1mm.** Chromatograph the acetate on silica gel and crystallise as the 2-isomer below. The *2,4,7-trinitrofluoren-9-one complex* has **m** 120° (from EtOH). [*Beilstein* **6** H 608, **6** III 2928, **6** IV 4217.]

2-Naphthyl acetate *[1523-11-1]* **M 186.2, m 71°, 71-72°, b 133-134°/2mm.** Distil the acetate in a high vaccum and/or crystallise it from petroleum ether (b 60-80°) or dilute aqueous EtOH. The *picrate* has **m** 80° (from EtOH). [*Beilstein* **6** H 644, **6** I 313, **6** II 600, **5** III 2982, **6** IV 4267.]

1-Naphthylacetic acid *[86-87-3]* **M 186.2, m 132°, pK^{25} 4.23.** Crystallise the acid from EtOH or water. [*Beilstein* **9** H 666, **9** IV 2424.]

2-Naphthylacetic acid *[581-96-4]* **M 186.2, m 143.1-143.4°, pK^{25} 4.30.** Crystallise the acid from water or *benzene. [*Beilstein* **9** H 666, **9** IV 2431.]

1-Naphthylamine *[134-32-7]* **M 143.2, m 50.8-51.2°, b 160°, pK^{25} 3.94.** Sublime the amine at 120° in a stream of nitrogen, then crystallise it from petroleum ether (b 60-80°), or absolute EtOH then diethyl ether. Dry it *in vacuo* in an Abderhalden pistol. It has also been purified by crystallisation of its *hydrochloride* (see below) from water, followed by liberation of the free base and distillation; it is finally purified by zone melting. The *styphnate* has **m** 181-182° (from EtOH). [*Beilstein* **12** III 2846, **12** IV 3009.] **CARCINOGEN.**

1-Naphthylamine hydrochloride *[552-46-5]* **M 179.7, m 240-250° sublimes on heating.** Crystallise the salt from water (charcoal). [*Beilstein* **12** III 2849, **12** IV 3009.]

2-Naphthylamine *[91-59-8]* **M 143.2, m 113°, pK^{25} 4.20.** Sublime the amine at 180° in a stream of nitrogen. Crystallise it from hot water (charcoal) or *benzene. Dry it under vacuum in a drying pistol. The *styphnate* has **m** 194-195° (from EtOH). [*Beilstein* **12** H 1265, **12** III 2989, **12** IV 3122.] **CARCINOGEN**.

2-Naphthylamine-1-sulfonic acid *[81-16-3]* **M 223.3, m >200°(dec), pK$_1^{25}$ <1, pK$_2^{25}$ 2.35 (NH$_2$).** Crystallise the acid under nitrogen from boiling water and dry it in a steam oven [Bryson *Trans Faraday Soc* **47** 522, 527 *1951*]. [*Beilstein* **14** III 2240, **14** IV 2792.]

5-Naphthylamine-1-sulfonic acid *[84-89-9]* **M 223.3, m >200°(dec), pK$_{Est(1)}$<1, pK$_2^{25}$ 3.69 (NH$_2$).** Crystallise the acid under nitrogen from boiling water and dry it in a steam oven [Bryson *Trans Faraday Soc* **47** 522, 527 *1951*]. [*Beilstein* **14** IV 2800.]

2-Naphthylamine-6-sulfonic acid *[93-00-5]* **M 223.3, m >200°(dec), pK^{25} 3.74.** Crystallise the acid from a large volume of hot water. The *diethylamine salt* has **m** 190.5-192° (from EtOH/*iso*BuOH), and the *S-benzylisothiuronium salt* has **m** 330° (from *n*BuOH). [*Beilstein* **14** H 760, **14** II 463, **14** III 2249, **14** IV 2804.]

1-(1-Naphthyl) ethanol *[R-(+)- 42177-25-3, S-(–)- 15914-84-8]* **M 172.2, m 46°, 45-47.5°, 48°, [α]$_{546}^{20}$ (+) and (-) 94°, [α]$_D^{20}$ (+) and (-) 78° (c 1, MeOH).** Purify the alcohol by recrystallisation from Et_2O/petroleum ether, Et_2O, hexane [Balfe et al. *J Chem Soc* 797 *1946*, IR, NMR: Theisen & Heathcock *J Org Chem* 53 2374 *1988*, see also Fredga et al. *Acta Chem Scand* **11** 1609 *1957*]. The *RS-alcohol [57605-95-5]* has **m** 63-65°, 65-66° from hexane. [*Beilstein* **6** III 3034, **6** IV 4346.]

1-(1-Naphthyl)ethylamine *[R-(+)- 3886-70-2, S-(–)- 10420-89-0]* **M 171.2, b 153°/11mm, 178-181°/20mm, d_4^{20} 1.067, n_D^{20} 1.624, $[\alpha]_{546}^{20}$ (+) and (-) 65°, $[\alpha]_D^{20}$ (+) and (-) 55° (c 2, MeOH), $[\alpha]_D^{17}$ (+) and (-) 82.8° (neat), pK_{Est} ~9.3.** Purify the amine by distillation in a good vacuum. [Mori et al. *Tetrahedron* **37** 1343 *1981*, cf Wilson in *Topics Stereochem* (Allinger and Eliel eds) **vol 6** 135 *1971*, Fredga et al. *Acta Chem Scand* **11** 1609 *1957*.] The *hydrochlorides* crystallise from H_2O $[\alpha]_D^{18}$ ±3.9° (c 3, H_2O), and the *sulfates* recrystallise from H_2O as *tetrahydrates* **m** 230-232°. The *RS-amine* [42882-31-5] has **b** 153°/11mm, 156°/15mm, 183.5°/41mm [Blicke & Maxwell *J Am Chem Soc* **61** 1780 *1939*]. [*Beilstein* **12** III 3111.]

***N*-(α-Naphthyl)ethylenediamine dihydrochloride** *[1465-25-4]* **M 291.2, m 188-190°, $pK_{Est(1)}$~3.8, $pK_{Est(2)}$~9.4.** Crystallise the salt from water. [*Beilstein* **12** II 699.]

1-Naphthyl isocyanate *[86-84-0]* **M 169.2, m 3-5°, b 140-142°/12mm, 269-270°/760mm, d_4^{20} 1.1774.** Distil the isocyanate at atmospheric pressure or in a vacuum. It can be crystallised from petroleum ether (b 60-70°) at low temperature. *It has a pungent odour, is* **TOXIC** *and is absorbed through the skin.* [*Beilstein* **12** H 1244, **12** III 2948.]

1-Naphthyl isothiocyanate *[551-06-4]* **M 185.3, m 58-59°.** Crystallise the isothiocyanate from hexane (1g in 9 ml). It forms white needles and is soluble in most organic solvents but is insoluble in H_2O. *It is absorbed through the skin and may cause dermatitis.* [Cymmerman-Craig et al. *Org Synth* Coll Vol **IV** 700 *1963*, *Beilstein* **12** H 1244, **12** III 2948.]

2-(2-Naphthyloxy)ethanol *[93-20-9]* **M 188.2, m 72-74°, 76.7°.** Crystallise it from *benzene/petroleum ether. [Yoshino et al. *Bull Chem Soc Jpn* **46** 553 *1973*.]

***N*-1-Naphthylphthalamic acid (Naptalam)** *[132-66-1]* **M 291.3, m 189° (dec), 203°.** Crystallise the herbicide from EtOH (**m** 183-185°). The *Na salt* has **m** 185°. [*Beilstein* **12** H 1236, **12** I 525, **12** III 2876.]

2-Naphthyl salicylate (Betol) *[613-78-5]* **M 264.3, m 94.4°, 95°, pK_{Est} ~10.0.** Crystallise Betol from EtOH. It is *dimorphic* with **m**'s at ~55° and ~96°. [*Beilstein* **10** H 80, **10** II 53, **10** III 136, **10** IV 158.]

1-Naphthyl thiourea (ANTU) *[86-88-4]* **M 202.2, m 198°.** Crystallise ANTU from EtOH. [*Beilstein* **12** III 2941, **12** IV 3086.]

1-Naphthyl urea *[6950-84-1]* **M 186.2, m 215-220°.** Crystallise the urea from EtOH (**m** 213-214° also 215°). [*Beilstein* **12** H 1238, **12** IV 3076.]

2-Naphthyl urea *[13114-62-0]* **M 186.2, m 212°, 219-220°.** Crystallise the urea from EtOH. [*Beilstein* **12** H 1292, **12** III 3029, **12** IV 3149.]

Narcein {6-[6-(2-dimethylaminoethyl)]-2-methoxy-3,4-(methylenedioxy)phenylacetyl]-2,3-dimethoxybenzoic acid} *[131-28-2]* **M 445.4, m 176-177° (145° anhydrous), pK_1^{15} 3.5, pK_2^{15} 9.3.** Recrystallise Narcein from water (as trihydrate). The *styphnate* has **m** 185-189° (from EtOH), and the *picrate* has **m** 200° (from EtOH). [*Beilstein* **19** H 370, **19** I 797, **19** II 386, **19** IV 4382.]

Neostigmine [(3-dimethylcarbamoylphenyl)trimethylammonium] bromide *[114-80-7]* **M 303.2, m 176°(dec), 181°(dec).** Crystallise neostigmine bromide from EtOH/diethyl ether. Its solubility in H_2O is ~50%. [*Beilstein* **13** III 939.] (It is cholinergic and *highly* **TOXIC**.) The starting material **3-dimethylcarbamoyl-*N,N*-dimethylaniline** *[59-99-4]* has **b 195°/20mm** [*Beilstein* **13** III 936], and its *picrate* has **m** 138° (from EtOH).

Neostigmine methyl sulfate (Prostigmine B) *[51-60-5]* **M 334.4, m 142-145°.** Crystallise the sulfate from EtOH or Me_2CO (**m** 143-144°). Its solubility in H_2O is ~10%. [*Beilstein* **13** III 939.] (It is cholinergic and *highly* **TOXIC**.)

Ninhydrin (1,2,3-triketohydrindene hydrate) *[485-47-2]* **M 178.1, m 241-243°(dec), pK^{30} 8.82.** Crystallise ninhydrin from hot water (charcoal). Dry it under vacuum and store it in sealed brown containers. [*Beilstein* **7** IV 2786.]

2-Nitroacetanilide *[552-32-9]* **M 180.2, m 93-94°, pK_{Est} <0.** Crystallise the anilide from H_2O, aqueous EtOH (**m** 92-93°) or EtOH (**m** 92.5-93.5°). [*Beilstein* **12** II 371, **12** III 1523, **12** IV 1574.]

4-Nitroacetanilide *[104-04-1]* **M 180.2, m 217°, pK_{Est} <0.** Precipitate the anilide from 80% H_2SO_4 by adding ice, then wash with water, and crystallise from aqueous EtOH. Dry it in air. [*Beilstein* **12** IV 1632.]

3-Nitroacetophenone *[121-89-1]* **M 165.2, m 81°, b 167°/18mm, 202°/760mm.** Distil the ketone in steam and crystallise it from EtOH. [*Beilstein* **7** IV 656.]

4-Nitroacetophenone *[100-19-6]* **M 165.2, m 80-81°, b 145-152°/760mm.** Crystallise the ketone from EtOH or aqueous EtOH. [*Beilstein* **7** IV 657.]

3-Nitroalizarin (1,2-dihydroxy-3-nitro-9,10-anthraquinone, Alizarin Orange) *[568-93-4]* **M 285.2, m 244° (dec), $pK_{Est(1)}$ ~4.6, $pK_{Est(2)}$ ~9.6.** Crystallise the dye from AcOH (**m** 244-245°). It has λ_{max} at 494nm (H_2SO_4) and forms Cu salts. [*Beilstein* **8** H 447, **8** II 491, **8** III 3774, **8** IV 2359.]

o-**Nitroaniline** *[88-74-4]* **M 138.1, m 72.5-73.0°, pK^{25} -0.25 (-0.31).** Crystallise the aniline from hot water (charcoal), then from aqueous 50% EtOH, or EtOH, and dry it in a vacuum desiccator. It has also been chromatographed on alumina, then recrystallised from *benzene. [*Beilstein* **12** IV 1563.]

m-**Nitroaniline** *[99-09-2]* **M 138.1, m 114°, pK^{25} 2.46.** Purify it as for *o*-nitroaniline. **Warning: it is absorbed through the skin. [***Beilstein* **12** IV 1589.]

p-**Nitroaniline** *[100-01-6]* **M 138.1, m 148-148.5°, pK^{25} 1.02.** Purify it as for *o*-nitroaniline. It also crystallises from acetone. It is freed from *o*- and *m*-isomers by zone melting and sublimation. [*Beilstein* **12** IV 1613.]

o-**Nitroanisole (2-methoxynitrobenzene)** *[91-23-6]* **M 153.1, f 9.4°, b 265°/737mm, d_4^{20} 1.251, n_D^{20} 1.563.** Purify it by repeated vacuum distillation in the absence of oxygen. [*Beilstein* **6** IV 1249.]

p-**Nitroanisole (4-methoxynitrobenzene)** *[100-17-4]* **M 153.1, m 54°.** Crystallise it from petroleum ether or hexane and dry it *in vacuo*. [*Beilstein* **6** IV 1282.]

9-Nitroanthracene *[602-60-8]* **M 223.2, m 142-143°.** Purify it by recrystallisation from EtOH or MeOH. Further purify it also by sublimation or TLC. [*Beilstein* **5** H 666, **5** II 578, **5** III 2136, **5** IV 2296.]

o-**Nitrobenzaldehyde** *[552-89-6]* **M 151.1, m 44-45°, b 120-144°/3-6mm.** Crystallise the aldehyde from toluene (2-2.5ml/g) by addition of 7ml petroleum ether (b 40-60°) for 1ml of solution. It can also be distilled under reduced pressures. [*Beilstein* **7** IV 584.]

m-**Nitrobenzaldehyde** *[99-61-6]* **M 151.1, m 58°.** Crystallise the aldehyde from water or EtOH/water, then sublime it twice at 2mm pressure at a temperature slightly above its melting point. [*Beilstein* **7** IV 591.]

p-**Nitrobenzaldehyde** *[555-16-8]* **M 151.1, m 106°.** Purify it as for *m*-nitrobenzaldehyde above. [*Beilstein* **7** IV 589.]

Nitrobenzene *[98-95-3]* **M 123.1, f 5.8°, b 84-86.5°/6.5-8mm, 210.8°/760mm, d_4^{20} 1.206, n^{15} 1.55457, n_D^{20} 1.55257, pK^{18} -11.26 (aqueous H_2SO_4).** Common impurities include nitrotoluene, dinitrothiophene, dinitrobenzene and aniline. Most impurities can be removed by steam distillation in the presence of dilute H_2SO_4, followed by drying with $CaCl_2$, and shaking with, then distilling at low pressure from BaO, P_2O_5, $AlCl_3$

or activated alumina. It can also be purified by fractional crystallisation from absolute EtOH (by refrigeration). Another purification process includes extraction with aqueous 2M NaOH, then water, dilute HCl, and water, followed by drying ($CaCl_2$, $MgSO_4$ or $CaSO_4$) and fractional distillation under reduced pressure. The pure material is stored in a brown bottle, in contact with silica gel or CaH_2. It is very *hygroscopic*. [*Beilstein* **5** H 233, **5** I 124, **5** II 171, **5** III 591, **5** IV 708.]

4-Nitrobenzene-azo-resorcinol (magneson-I) *[74-39-5]* **M 259.2, m 185°(dec), 199-200°(dec).** Crystallise the dye from EtOH. [*Beilstein* **16** H 181, **16** IV 1266.]

4-**Nitrobenzenediazonium fluoroborate** *[456-27-9]* **M 236.9.** It crystallises from water. Drain it well and use it as soon as possible. Do NOT store it. [Whetsch et al. *J Am Chem Soc* **78** 3360 *1956*, *Beilstein* **16** IV 816.] **It can be EXPLOSIVE when dry.**

2-Nitrobenzenesulfenyl chloride (NPS-Cl) *[7669-54-7]* **M 189.6, m 73-74.5°, 74.5-75°, 74-76°.** Recrystallise it from CCl_4 (2ml/g), filter off the solution at 5° (recovery 75%). It has also been recrystallised from petroleum ether (b 40-60°), dried rapidly at 50° and stored in a brown glass bottle, sealed well and stored away from moisture. [Hubacher *Org Synth* Coll Vol **II** 455 *1943*, Ito et al. *Chem Pharm Bull Jpn* **26** 296 *1978*, *Beilstein* **6** I 157.]

o*-Nitrobenzenesulfonyl chloride** *[1694-92-4]* **M 221.6, m 63-67°, 68-69°, 69.5-69.7°.** It is prepared by the oxidation of di-*o*-nitrophenyldisulfide with Cl_2 [Wertheim *Org Synth* Coll Vol **II** 471 *1943*] or from *o*-nitrobenzenesulfonic acid and PCl_5, then pouring into H_2O, washing the solid with H_2O, drying it *in vacuo* and recrystallising it from petrol, Et_2O/petrol, petroleum ether/CCl_4 or petroleum ether. With ammonia it is converted to the ***sulfonamide [5455-59-4] **M 202.1, m 193°,** which forms needles from hot aqueous EtOH; and with phenol/pyridine or Na_2CO_3, the ***phenyl ester*****, m 57°,** is obtained which crystallises from EtOH. The ***sulfonylazide***, **m 71-73°**, separates as needles from petroleum ether [Leffler et al. *J Org Chem* **28** 902 *1963*]. [*Beilstein* **11** H 67, **11** I 20, **11** II 32, **11** III 114, **11** IV 174.]

m*-Nitrobenzenesulfonyl chloride** *[121-51-7]* **M 221.6, m 61-62°, 63.9-64.2°.** It can be prepared from *m*-nitrobenzenesulfonic acid and PCl_5 as for the isomer above and crystallised from petroleum ether/CCl_4 or petroleum ether in needles. With ammonia it is converted to the ***sulfonamide [121-52-8] **M 202.1, m 167-168°,** which forms needles from hot aqueous EtOH and is a moderately strong base with **pK^{20} 9.20**. With phenol/pyridine or Na_2CO_3, the ***phenyl ester*****, m 94°,** is obtained which crystallises from acetic acid. [Gilbert *Synthesis* 315 *1977*, *Beilstein* **11** H 69, **11** I 21, **11** II 33, **11** III 126, **11** IV 182.]

p*-Nitrobenzenesulfonyl chloride (Nosyl chloride)** *[98-74-8]* **M 221.6, m 66-70°, 78-80°, 80°, b 143-144°/1.5mm, 180-181°/17mm.** It is prepared in the same way as for the *m*-isomer above from *p*-nitrobenzenesulfonic acid, and is purified by vacuum distillation and/or by recrystallisation from petroleum ether or Et_2O/petroleum ether. With ammonia it is converted to the ***sulfonamide [6325-93-5] **M 202.1, m 179-180°,** which forms prisms from hot aqueous EtOH and is a moderately strong base with **pK^{20} 9.14**. [Prinsen et al. *Rec Trav Chim Pays Bas* **84** 24 *1965*, *Beilstein* **11** H 72, **11** I 21, **11** II 34, **11** III 136, **11** IV 192.]
It is highly efficient in solid phase peptide synthesis when using *N-nosyl-α-amino acids* [Leggio et al. *Tetrahedron* **63** 8164 *2007*.]

***o*-Nitrobenzenesulfonylhydrazine (NBSH)** *[606-26-8]* **M 217.2, m 100-101°, 101° (dec).** NBSH is unstable unless handled properly. If the material is suspect, it is preferable to prepare freshly thus: hydrazine monohydrate (12.1ml, 2.5 equivalents) is added to a solution of *o*-nitrobenzenesulfonyl chloride (22.2g, 1 equivalent) in dry THF (100ml) at -30° under argon whereby the solution became brown, white N_2H_4.HCl deposited and after 30 minutes TLC (2/1, EtOAc/hexanes) indicated that all the sulfonyl chloride was used up. EtOAc (200ml, at 23°) is added to the cold mixture and washed repeatedly with ice-cold 10% aqueous NaCl (5 × 150ml, contact time with each wash should not be >1 minute; the use of just distilled H_2O results in much lower yields). The organic layer is washed, dried (Na_2SO_4 at 0°), then added slowly to a stirred solution of hexanes (1.2L) at 23° during 5 minutes. The off-white NBSH that precipitates within 10 minutes is isolated by vacuum filtration, the solid is washed with hexanes (2 × 50ml, 23°) and dried at 23°/<1.5mm for 14 hours to provide pure

NBSH as an off-white powder (17.6g, 81%; TLC has R_F 0.19, EtOAc/hexanes 2/1). Store it at ~0-5° under argon, and use gloves due to its toxicity. Its IR (EtOAc) has ν_{max} at 1165, 1352, 1547, 3400—3100 cm^{-1} and its ^1H NMR [300MHz, CD_3CN] has δ: 8.17-8.03 (1H, m), 7.91-7.78 (3H, m), 5.97 (1H, bs), 3.90 (2H, bs); and its ^{13}C NMR [75MHz, CD_3CN] has δ: 149.4, 135.5, 133.4, 133.2, 130.8 and 125.8. [Meyers et al. *J Org Chem* **62** 7507 *1997*, Dunn & Davies *J Chem Soc* 1050 *1929*.]
NBSH is a versatile reagent for synthesising allenes from propargyl alcohols [Meyers & Zheng *J Am Chem Soc* **118** 4492 *1996*], reductive transposition of allylic alcohols [Meyers & Zheng *Tetrahedron Lett* **37** 4841 *1996*], and deoxygenation of unhindered alcohols; each of which proceeds by Mitsunobu displacement of an alcohol with NBSH followed by *in situ* elimination of *o*-nitrobenzoylsulfinic acid to produce mono-alkyl diazene intermediates under mild reaction conditions, i.e. neutral pH and less than 23°, particularly useful with substrates that have sensitive substituents. [Mitsunobu *Synthesis* 1 *1981*, Hughes *Org React* **42** 335 *1992*.] For the success of these reactions it is imperative that the reagent is as pure as possible. Solutions of NBSH in THF that are pale yellow are still suitable for these applications.

4-Nitrobenzhydrazide *[606-26-8]* **M 181.1, m 124°.** Crystallise the hydrazide from EtOH or EtOAc (**m** 120°). [*Beilstein* **9** H 375, **9** I 152, **9** II 246, **9** III 1481, **9** IV 1052.]

2-Nitrobenzoic acid *[552-16-9]* **M 167.1, m 146-148°, pK^{25} 2.21.** Crystallise the acid from *benzene (twice), *n*-butyl ether (twice), then water (twice). Dry and store it in a vacuum desiccator. [Le Noble & Wheland *J Am Chem Soc* **80** 5397 *1958*.] It has also been crystallised from EtOH/H_2O. The *amide* has **m** 176.5° (from H_2O). [*Beilstein* **9** III 1466, **9** IV 1046.]

3-Nitrobenzoic acid *[121-92-6]* **M 167.1, m 143-143.5°, pK^{25} 3.46.** Crystallise the acid from *benzene, H_2O, EtOH (charcoal), glacial acetic acid or MeOH/H_2O. Dry and store it in a vacuum desiccator. The *amide* has **m** 143° (from H_2O or $*C_6H_6$). [*Beilstein* **9** III 1489, **9** IV 1055.]

4-Nitrobenzoic acid *[62-23-7]* **M 167.1, m 241-242°, pK^{25} 3.43.** Purify it as for 3-nitrobenzoic acid above. The *amide* has **m** 201.6° (from H_2O). [*Beilstein* **9** III 1537, **9** IV 1072.]

4-Nitrobenzoyl chloride *[122-04-3]* **M 185.6, m 75°, b 155°/20mm.** Crystallise the acid chloride from dry petroleum ether (b 60-80°), $*C_6H_6$ or CCl_4. Distil it under vacuum. **Irritant**. [Adama & Jenkins *Org Synth* Coll Vol **I** 394 *1941*, *Beilstein* **9** III 1709, **9** IV 1191.]

4-Nitrobenzyl alcohol *[619-73-8]* **M 153.1, m 93°.** Crystallise the alcohol from EtOH and sublime it *in vacuo*. Purity should be at least 99.5%. Sublimed samples should be stored in the dark over anhydrous $CaSO_4$ (Drierite). If the IR contains OH bands, then the sample should be resublimed before use. [Mohammed & Kosower *J Am Chem Soc* **93** 2709 *1979*, *Beilstein* **6** IV 2611.]

4-Nitrobenzyl bromide *[100-11-8]* **M 216.0, m 98.5-99.0°.** Recrystallise the bromide four times from absolute EtOH, then twice from cyclohexane/hexane/*benzene (1:1:1), followed by sublimation at 0.1mm and final recrystallisation from the same solvent mixture. [Lichtin & Rao *J Am Chem Soc* **83** 2417 *1961*.] It has also been crystallised from petroleum ether (b 80-100°, 10ml/g, charcoal). It slowly decomposes even when stored in a desiccator in the dark. **IRRITANT. [***Beilstein* **5** IV 861.]

m-**Nitrobenzyl chloride** *[619-23-8]* **M 171.6, m 45°.** Crystallise the chloride from petroleum ether (b 90-120°). **IRRITANT**. [*Beilstein* **5** IV 855.]

p-**Nitrobenzyl chloride** *[100-14-1]* **M 171.6, m 72.5-73°.** Crystallise the chloride from CCl_4, dry diethyl ether, or *n*-heptane, and dry it under vacuum. **IRRITANT**. [*Beilstein* **5** IV 856.]

p-**Nitrobenzyl cyanide** *[555-21-5]* **M 162.2, m 117°.** Crystallise the nitrile from EtOH. **TOXIC**. [*Beilstein* **9** H 456, **9** I 183, **9** II 313, **9** III 2291.]

2-Nitrobiphenyl *[86-00-0]* **M 199.2, m 36.7°, 37°, b 185-195°/20-30mm.** *o*-Nitrobiphenyl has been prepared

by a Gomberg reaction between diazotised 2-nitroaniline and $*C_6H_6$ [Elks et al. *J Chem Soc* 1282 *1940*] or by the nitration of biphenyl [Morgan & Walls *J Soc Chem Ind* **49** 15T *1930*]. Although the respective yields are ~45% and ~25%, the latter method is by far more convenient to perform experimentally. Crystallise it from EtOH (seeding required) or petroleum ether (b 40-60°). Sublime it under vacuum. [*Beilstein* **5** H 582, **5** I 273, **5** II 487, **5** III 1750.]

3-Nitrocinnamic acid *[555-68-0]* **M 193.2, m 200-201°, pK^{25} 2.58 (*trans*).** Crystallise the acid from $*C_6H_6$ or EtOH. The *p-bromophenacyl ester* has **m** 178° (from AcOH). [*Beilstein* **9** III 271, **9** IV 2043.]

4-Nitrocinnamic acid *[882-06-4]* **M 193.2, m 143° (*cis*), 286°(*trans*), pK_{Est} ~2.6 (*trans*).** Crystallise the acid from H_2O. The *p-bromophenacyl ester* has **m** 191° (from AcOH). [*Beilstein* **9** H 606, **9** III 2744.]

4-Nitrodiphenylamine *[836-30-6]* **M 214.2, m 133-134°, pK^{25} -2.5.** Crystallise the amine from EtOH or aqueous EtOH (**m** 135-136°) and has **m** 131.5-132° after sublimation *in vacuo*. [*Beilstein* **12** H 715, **12** III 1586.]

2-Nitrodiphenyl ether *[2216-12-8]* **M 215.2, b 106-108°/0.01mm, 137-138°/0.5mm, 161-162°/4mm, 188-189°/12mm, 195-200°/25mm, d_4^{20} 1.241, n_D^{25} 1.600.** Purify the ether by fractional disillation. Its UV (EtOH) has λ_{max} at: 255, 315mm (ε 6200 and 2800), and the IR (CS_2) has bands at 1350 (NO_2) and 1245, 1265 (COC) cm^{-1} [UV, IR: Dahlgard & Brewster *J Am Chem Soc* **80** 5861 *1958*, Tomita & Takase *Yakugaku Zasshi (J Pharm Soc Japan)* **75** 1077 *1955*, Fox & Turner *J Chem Soc* 1115 *1930*, Henley *J Chem Soc* 1222 *1930*]. [*Beilstein* **6** H 218, **6** II 210, **6** III 801.]

Nitrodurene (1,2,4.5-tetramethyl-3-nitrobenzene) *[3463-36-3]* **M 179.2, m 113-114°, b 143-144°/10mm.** Distil nitrodurene in a vacuum and/or crystallise it from EtOH (yellow prisms, **m** 113-113.5°), MeOH, acetic acid, petroleum ether or chloroform. It has been crystallised by dissolving in hexane and kept at -20° for crystals to form (**m** 111-112°). Its UV has λ_{max} at 238 and 400nm (iso-octane). [Masnovi et al. *J Am Chem Soc* **111** 2263 *1989*, cf Powell & Johnson *Og Synth* Coll Vol **II** 449 *1943*, *Beilstein* **5** H 432, **5** III 982, **5** IV 1080.]

3-Nitrofluoranthene *[892-21-7]* **M 247.3, m 159-160°.** Recrystallise it from AcOH or EtOAc (yellow crystals) and/or sublime it at high vacuum. It is soluble in CH_2Cl_2, Me_2CO or $*C_6H_6$, soluble in warm EtOH and very soluble in Et_2O. [Kloetzel et al. *J Am Chem Soc* **78** 1165 *1956*, *Beilstein* **5** III 2279.]

2-Nitrofluorene *[607-57-8]* **M 211.2, m 156°.** Crystallise 2-nitrofluorene from aqueous acetic acid or Me_2CO (**m** 158-158.5°, also 160-160.5°). [*Beilstein* **5** H 628, **5** III 1948.]

Nitromesitylene (2-nitro-1,3,5-trimethylbenzene) *[603-71-4]* **M 165.2, m 44°, b 255°/760mm.** Crystallise it from EtOH, or a small volume of MeOH and cool in an ice-salt bath (**m** 43.5°). [Powell & Johnson *Org Synth* Coll Vol **II** 449 *1943*, *Beilstein* **5** H 410, **5** III 923, **5** IV 1028.]

Nitromethylphenylsulfone *[21272-85-5]* **M 201.2, m 78-79°.** Recrystallise the sulfone from $CHCl_3$, or 95% EtOH, then sublime it at 100-120°/0.1 Torr and recrystallise again. It is an acidic analogue of nitromethane used for the general synthesis of aliphatic acids and nitriles and in cycloaddition reactions with olefins to form heterocycles. [Wade et al. *J Org Chem* **46** 765 *1981*, **49** 4595 *1984*, *Beilstein* **6** II 292.]

1-Nitronaphthalene *[86-57-7]* **M 173.2, m 57.3-58.3°, b 30-40°/0.01mm.** Fractionally distil 1-nitronaphthalene under reduced pressure, then crystallise it from EtOH, aqueous EtOH or heptane. Chromatograph it on alumina with *benzene/petroleum ether as eluent. It sublimes *in vacuo*. The *1:1 picrate complex* has **m** 72° (from EtOH). [*Beilstein* **5** H 553, **5** III 1593, **5** IV 1673.]

2-Nitronaphthalene *[581-89-5]* **M 173.2, m 79°, b 165°/15mm.** Distil it in a vacuum and/or crystallise it from aqueous EtOH and sublime in a vacuum. The 1:1 *1,3,5-trinitrobenzene complex* has **m** 75.5° (from EtOH). [*Beilstein* **5** H 555, **5** III 1596, **5** IV 1675.]

1-Nitro-2-naphthol *[550-60-7]* **M 189.2, m 103°, b 115°/0.05mm, pK^{25} 5.93.** Distil it under high vacuum and/or crystallise the naphthol (repeatedly) from *benzene/petroleum ether (b 60-80°)(1:1). [*Beilstein* **6** H 653, **6** III 3002, **6** IV 4370.]

2-Nitro-1-naphthol *[607-24-9]* **M 189.2, m 127-128°, pK^{25} 5.89.** Crystallise the naphthol (repeatedly) from EtOH. [*Beilstein* **6** H 615, **6** III 2938, **6** IV 4236.]

2-Nitrophenol *[88-75-5]* **M 139.1, m 44.5-45.5°, b 214-215°/760mm, pK^{25} 7.23.** Crystallise 2-nitrophenol from EtOH/water, water, EtOH, *benzene or MeOH/petroleum ether (b 70-90°). It can be steam distilled. Petrucci and Weygandt [*Anal Chem* **33** 275 *1961*] crystallised it from hot water (twice), then EtOH (twice), followed by fractional crystallisation from the melt (twice), drying over $CaCl_2$ in a vacuum desiccator and then in a drying pistol. The *4-nitrobenzoate* had **m** 141° (from EtOH). [*Beilstein* **6** IV 1246.]

3-Nitrophenol *[554-84-7]* **M 139.1, m 96°, b 160-165°/12mm, pK^{25} 8.36.** Crystallise 3-nitrophenol from water, $CHCl_3$, CS_2, EtOH or petroleum ether (b 80-100°), and dry it under vacuum over P_2O_5 at room temperature. It can also be distilled at low pressure. The *4-nitrobenzoate* had **m** 174° (from EtOH). [*Beilstein* **6** IV 1269.]

4-Nitrophenol *[100-02-7]* **M 139.1, m 113-114°, pK^{25} 7.16.** Crystallise 4-nitrophenol from water (which may be acidified, e.g. with *N* H_2SO_4 or 0.5*N* HCl), EtOH, aqueous MeOH, $CHCl_3$, *benzene or petroleum ether, then dry it *in vacuo* over P_2O_5 at 25°. It can be sublimed at 60°/10^{-4}mm. The *4-nitrobenzoate* had **m** 159° (from EtOH). [*Beilstein* **6** IV 1279.]

2-Nitrophenoxyacetic acid *[1878-87-1]* **M 197.2, m 150-159°, 158.2-158.5°, pK^{25} 2.90.** Crystallise the acid from water, and dry it over P_2O_5 *in vacuo*. The *S-benzylisothiuronium salt* has **m** 155-156° (from EtOH). [Hayes & Brooch *J Am Chem Soc* **65** 1577 *1943*, *Beilstein* **6** H 220, **6** II 211, **6** III 804, **6** IV 1261.]

***p*-Nitrophenyl acetate** *[830-03-5]* **M 181.2, m 78-79°.** Recrystallise the ester from absolute EtOH [Moss et al. *J Am Chem Soc* **108** 5520 *1986*]. [*Beilstein* **6** IV 1298.]

2-Nitrophenylacetic acid *[3740-52-1]* **M 181.2, m 141-142.5°, pK^{25} 3.95.** The acid crystallises as yellow needles from EtOH, EtOH/water and dry it over P_2O_5 under vacuum. The *amide* has **m** 160-161° (from *C_6H_6 plates or EtOH, needles). [*Beilstein* **9** III 2282, **9** IV 1687.]

4-Nitrophenylacetic acid *[104-03-0]* **M 181.2, m 153.4-154.6°, pK^{25} 3.92.** Crystallise the acid from EtOH/water (1:1), then from sodium-dried diethyl ether and dry it over P_2O_5 *in vacuo*. The *styphnate* has **m** 196.5-197° (prisms from EtOH). The *amide* has **m** 191° (from EtOH). [*Beilstein* **9** III 2284, **9** IV 1698.]

4-Nitro-1,2-phenylenediamine *[99-56-9]* **M 153.1, m 201°, pK$_1^{25}$ 1.39 (1-NH_2), pK$_2^{25}$ 2.61 (2-NH_2).** Crystallise the diamine from water. [*Beilstein* **13** IV 75.]

1-(4-Nitrophenyl)ethylamine hydrochloride *[R-(+)- 57233-86-0, S-(–)- 132873-57-5]* **M 202.6, m 225°, 240-242°(dec), 243-245°(dec), 248-250°, [α] $_D^{20}$ (+) and (-) 72° (c 1, 0.05 M NaOH), (+) and (-) 0.3° (H_2O), pK$_{Est}$ ~8.6.** To ensure dryness, the hydrochloride (*ca* 175 g) is extracted with EtOH (3×100ml) and evaporated to dryness (any residual H_2O increases the solubility in EtOH and lowers the yield). The hydrochloride residue is triturated with absolute EtOH and dried *in vacuo*. The product is further purified by refluxing with absolute EtOH (200 ml for 83g) for 1 hour, and cool to 10° to give 76.6g of hydrochloride **m** 243-245°(dec). The *free base* is prepared by dissolving in N NaOH, extracting with CH_2Cl_2 (3 x 500ml), drying (Na_2CO_3), filtering, evaporating and distilling it. It has **m** 27°, **b** 119-120°/0.5mm (105-107°/0.5mm, 157-159°/9mm, d $_4^{20}$ 1.1764, n $_D^{20}$ 1.5688, [α] $_D^{24}$ ±17.7° (neat) [Perry et al. *Synthesis* 492 *1977*, ORD: Nerdel & Liebig *Justus Liebigs Ann Chem* **621** 142 *1959*]. [*Beilstein* **12** IV 2451.]

4-Nitrophenylhydrazine *[100-16-3]* **M 153.1, m 158°(dec), pK$_1^{25}$ -9.2 (aqueous H_2SO_4), pK$_2^{25}$ 3.70.** Crystallise the hydrazine from EtOH. The *hydrochloride* has **m** 212°(dec) (from EtOH, also **m** 202-203° dec).

[*Beilstein* **15** III 331, **15** IV 317.]

3-Nitrophenyl isocyanate *[3320-87-4]* **M 164.1, m 52-54°, b 130-131°/11mm.** Distil the isocyanate in a vacuum, and/or recrystallise it from petroleum ether (b 28-38°) or toluene/petroleum ether (**m** 52°). [*Beilstein* **12** H 708, **12** III 1573.]

4-Nitrophenyl isocyanate *[100-28-7]* **M 164.1, m 53°, b 137-138°/11mm, 162-164°/20mm.** Distil the isocyanate in a vacuum, and/or recrystallise it from petroleum ether (b 28-38°), *C_6H_6/petroleum ether (**m** 58°) or CCl_4 (**m** 56-57°). [*Beilstein* **12** H 725, **12** III 1630.]

2-Nitrophenylpropiolic acid *[530-85-8]* **M 191.1, m 157°(dec), 160.5-161°, 166-167°(dec), pK^{25} 2.83 (50% aqueous dioxane), 3.39 (50% aqueous EtOH).** Digest the acid with boiling $CHCl_3$, then crystallise it from H_2O. The *amide* has **m** 159° (plates, from H_2O). [Schofield & Simpson *J Chem Soc* 516 *1945*, *Beilstein* **9** H 636, **9** I 267, **9** II 438, **9** III 3067, **9** IV 2330.]

4-Nitrophenyl trifluoroacetate *[658-78-6]* **M 235.1, m 37-39°, b 120°/12mm.** Recrystallise the ester from $CHCl_3$/hexane [Margolis et al. *J Biol Chem* **253** 7891 *1978*]. It sublimes *in vacuo* (**m** 36-38°). It is *moisture sensitive*. [Sakakibara & Inukai *Bull Chem Soc Jpn* **37** 1231 *1964*.]

4-Nitrophenyl urea *[556-10-5]* **M 181.2, m 232°(dec), 238°, 242°.** Crystallise the urea from EtOH or hot water. Its UV has λ_{max} at 322nm (EtOH). [*Beilstein* **12** II 392, **12** III 1617, **12** IV 1645.]

3-Nitrophthalic acid *[603-11-2]* **M 211.1, m 216-218°, pK^{25} 3.93.** Crystallise 3-nitrophthalic acid from hot water (1.5ml/g). Dry it in air. The *amide* has **m** 201° (from EtOH). [*Beilstein* **9** H 823, **9** IV 3275.]

4-Nitrophthalic acid *[610-27-5]* **M 211.1, m 165°, pK^{25} 4.12.** Crystallise 4-nitrophthalic acid from Et_2O, EtOAc or *C_6H_6 (**m** 166°). The *amide* has **m** 200° (from EtOH). [*Beilstein* **9** H 828, **9** IV 4234.]

3-Nitrophthalic anhydride *[641-70-3]* **M 193.1, m 164°.** Crystallise it from *C_6H_6, *C_6H_6/petroleum ether, Me_2CO, AcOH, or Ac_2O (**m** 164-165°). Dry it at 100°. [*Beilstein* **17** III/IV 6149, **17/11** V 266.]

4-Nitrophthalic anhydride *[5466-84-2]* **M 193.1, m 120-121.5°, b 196-197°/8mm.** Distil the anhydride in a vacuum and/or recrystallise it from *C_6H_6 or Et_2O/petroleum ether. Dry it *in vacuo*. It forms addition compounds with anthracene (**m** 118°), and phenanthrene (**m** 96°). [*Beilstein* **17** III/IV 6150, **17/11** V 267.]

5-Nitro-2-*n*-propoxyaniline *[553-79-7]* **M 196.2, m 47.5-48.5°, 49°. pK$_{Est}$ ~2.32.** Crystallise the aniline from *n*-propyl alcohol/petroleum ether or H_2O (136mg/L at 20°). [*Beilstein* **13** III 878, **13** IV 897.]

2-Nitroresorcinol *[601-89-8]* **M 155.1, m 81-81°, pK$_1^{20}$ 6.37, pK$_2^{20}$ 9.46.** Recrystallise 2-nitroresorcinol from aqueous EtOH. [*Beilstein* **6** H 823.]

4-Nitrosalicylic acid *[619-19-1]* **M 183.1, m 235-238°(dec), pK^{25} 2.23.** Crystallise the acid from H_2O (**m** 236-238°) or aqueous EtOH (**m** 235-236° dec). [*Beilstein* **10** III 194, **10** IV 231.]

5-Nitrosalicylic acid *[96-97-9]* **M 183.1, m 233°, pK$_1^{25}$ 2.32, pK$_2^{25}$ 10.34.** Crystallise the acid from Me_2CO (charcoal), then twice more from Me_2CO alone, aqueous EtOH (**m** 234-236°) or H_2O (**m** 232-233°). [*Beilstein* **10** III 197, **10** IV 255.]

Nitrosobenzene *[586-96-9]* **M 107.1, m 67.5-68°, b 57-59°/18mm.** Steam distil nitrosobenzene, then crystallise it from a small volume of EtOH with cooling below 0°, dry it over $CaCl_2$ in a dessicator at atmospheric pressure, and store it under N_2 at 0°. *Alternatively*, it can be distilled onto a cold finger cooled with brine at ~–10° in a vacuum at 17mm (water pump), while heating in a water bath at 65-70° [Robertson & Vaughan *J Chem Educ* **27** 605 *1950*]. [*Beilstein* **5** IV 702.]

4-Nitrosodiphenylamine (tautomer of benzoquinone-1,4-phenylimine oxime) *[156-10-5]* **M 198.2, m 144-145°(dec), 145.4-146.6°, 144-148°.** The amine forms dark green crystals from EtOH or *C_6H_6 (**m** 143°). It has UV with λ_{max} at 421nm (EtOH), and it is used for detecting Pd and Rh. *It is highly toxic and a possible carcinogen*. [*Beilstein* **12** H 207, **12** II 122, **12** III 347, **12** IV 1860ß.]

1-Nitroso-2-naphthol *[131-91-9]* **M 173.2, m 110.4-110.8°, pK^{25} 7.63.** Crystallise the naphthol from petroleum ether (b 60-80°, 7.5ml/g). [*Beilstein* **7** H 712, **7** IV 2419.]

2-Nitroso-1-naphthol *[132-53-6]* **M 173.2, m 162-164°, pK^{25} 7.24.** Purify the naphthol by recrystallisation from petroleum ether (b 60-80°) or by dissolving it in hot EtOH, followed by successive addition of small volumes of water (**m** 158° dec). It also crystallises from *C_6H_6 or H_2O. Crystallisation from *C_6H_6/petroleum ether gives **m** (106-109 °, also 109.5°). It has λ_{max} at 274.5 and 382nm ($CHCl_3$). It complexes with metals. [*Beilstein* **7** H 712, **7** I 385, **7** II 647, **7** III 3688, **7** IV 2419.]

4-Nitroso-1-naphthol *[605-60-7]* **M 173.2, m 198°(dec), pK^{25} 8.18.** Crystallise the naphthol from *C_6H_6 or H_2O (**m** 197°, dec). and sublime it at 75-80°/0.2mm. It has λ_{max} at 336nm (EtOH). [*Beilstein* **7** H 715, **7** II 653, **7** III 3700, **7** IV 2424.]

2-Nitroso-1-naphthol-4-sulfonic acid ($3H_2O$) *[3682-32-4]* **M 316.3, m 142-146°(dec), pK_{Est} ~6.3 (OH).** Crystallise the acid from dilute HCl solution. The crystals are dried over $CaCl_2$ in a vacuum desiccator. It has also been purified by dissolution in aqueous alkali and precipitation by addition of water. It is a reagent for cobalt. [*Beilstein* **11** H 331, **11** II 189, **11** III 621, **11** IV 668.]

4-Nitrosophenol (benzoquinone mono oxime) *[104-91-6]* **M 123.1, m >124°(dec), pK^{25} 6.36.** 4-Nitrosophenol forms yellow crystals from xylene, *C_6H_6 (**m** ~144°) or Et_2O (**m** 128-129°, dec). [*Beilstein* **7** H 622, **7** II 574, **7** III 3367.]

***N*-Nitroso-*N*-phenylbenzylamine** *[612-98-6]* **M 212.2, m 58°.** Crystallise the amine from absolute EtOH (yellow needles) and dry it in air. It is slightly soluble in organic solvents. [*Beilstein* **12** H 1071, **12** II 335, **12** III 2335.]

***trans*-β-Nitrostyrene** *[5153-67-3]* **M 149.2, m 60°.** Crystallise the styrene from absolute EtOH, or three times from *benzene/petroleum ether (b 60-80°) (1:1). [*Beilstein* **5** III 1180, **5** IV 1352.]

4-Nitrostyrene *[100-13-0]* **M 149.2, m 20.5-21°.** Crystallise it from $CHCl_3$/hexane. Purify it by addition of MeOH to precipitate the polymer, then crystallise it at -40° from MeOH. It has also been crystallised from EtOH. [Bernasconi et al. *J Am Chem Soc* **108** 4541 *1986*, *Beilstein* **5** H 478, **5** III 1180, **5** IV 1351.]

2-Nitro-4-sulfobenzoic acid *[552-23-8]* **M 247.1, m 111°, pK_{Est} ~1.65.** Crystallise the acid from dilute HCl. It is *hygroscopic*. [*Beilstein* **11** H 391, **11** III 685.]

2-Nitrotoluene *[88-72-2]* **M 137.1, m -9.55° (α-form), -3.85° (β-form), b 118°/16mm, 222.3°/760mm, d_4^{20} 1.163, n_D^{20} 1.545.** Crystallise 2-nitrotoluene (repeatedly) from absolute EtOH by cooling in a Dry-ice/alcohol mixture. Further purify it by passing an alcoholic solution through a column of alumina. [*Beilstein* **5** IV 845.]

3-Nitrotoluene *[99-08-1]* **M 137.1, m 16°, b 113-114°/15mm, 232.6°, d_4^{20} 1.156, n_D^{20} 1.544.** Dry 3-nitrotoluene over P_2O_5 for 24 hours, then fractionally distil it under reduced pressure. [Clark & Taylor *Org. Synth* Coll Vol **I** 415 *1941*, *Beilstein* **5** IV 847.]

4-Nitrotoluene *[99-99-0]* **M 137.1, m 52°.** Crystallise 4-nitrotoluene from EtOH, MeOH/water, EtOH/water (1:1) or MeOH. Dry it in air, then dry it in a vacuum desiccator over H_2SO_4. [Wright & Grilliom *J Am Chem Soc* **108** 2340 *1986*, *Beilstein* **5** IV 848.]

5-Nitrovanillin (nitroveratric aldehyde) *[6635-20-7]* **M 197.2, m 172-175°, 176°, 178°.** It forms yellow

plates from AcOH and needles from EtOH [Slotta & Szyszke *Chem Ber* **68** 184 *1935*]. With diazomethane, 5-nitro-3,4-dimethoxyacetophenone is formed [Brady & Manjunath *J Chem Soc* **125** 1067 *1924*]. The *methyl ether* crystallises from EtOAc or AcOH, **m** 88°, 90-91°, and the *phenylhydrazone* has **m** 108-110° (from aqueous EtOH). [Finger & Schott *J Prakt Chem* [2] **115** 288 *1927*.] The *oxime* has **m** 216° (from EtOH or AcOH), and the *oxime acetate* has **m** 147° (from aqueous EtOH) [Vogel *Monatsh Chem* **20** 384 *1899*, Brady & Dunn *J Chem Soc* **107** 1861 *1915*]. [*Beilstein* **8** III 2064.]

Nordihydroguaiaretic [1,4-bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane] acid *[500-38-9]* **M 302.4, m 184-185°, $pK_{Est(1)}$ ~9.7, $pK_{Est(2)}$ ~12.** Crystallise the acid from dilute acetic acid. [*Beilstein* **6** IV 7771.]

1,2,3,4,6,7,8,9-Octahydroanthracene *[1079-71-6]* **M 186.3, m 73°, 73.5°, 78°, d_4^{80} 0.9703, n_D^{80} 1.5372.** Crystallise the octahydro compound from EtOH, then purify it by zone melting. [*Beilstein* **5** III 1400.]

***n*-Octylammonium 9-anthranilate** *[88020-99-9]* **M 351.5, m 134-135°, pK^{25} 10.65 (for octylamine).** Recrystallise the ester several times from ethyl acetate.

4-Octylbenzoic acid *[3575-31-3]* **M 234.3, m 99-100°, pK^{25} 6.5 (80% aqueous EtOH), pK_{Est} ~4.5 (H_2O).** When crystallised from EtOH it has **m** 139°, but when crystallised from aqueous EtOH it has **m** 99-100°. It forms liquid crystals. [*Beilstein* **9** H 571, **9** III 2611.]

4-(*tert*-Octyl)phenol *[140-66-9]* **M 206.3, m 85-86°, b 166°/20mm, pK_{Est} ~10.4.** Crystallise the phenol from *n*-hexane and/or distil it in a vacuum. [*Beilstein* **6** III 2051, **6** IV 3484.]

Opianic acid (2-formyl-4,5-dimethylbenzoic acid) *[519-05-1]* **M 210.2, m 150°, pK^{25} 3.07.** Crystallise the acid from water. [*Beilstein* **10** H 990, **10** I 484, **10** II 719, **10** III 4511, **10** IV 3863.]

Orcine monohydrate (orcinol hydrate, 3,5-dihydroxytoluene) *[6153-39-5]* **M 142.2, m 56°, 56-58°, 58°, b 147°/5 mm, pK_1^{20} 9.48 (9.26), pK_2^{20} 11.20 (11.66).** Purify orcine by recrystallisation from H_2O as the *monohydrate*. It sublimes *in vacuo*, and the *anhydrous* compound has **m** 106.5-108° (110°, 108°). It can be recrystallised from $CHCl_3$ (plates) or *C_6H_6 (needles or prisms). [UV: Kiss et al. *Bull Soc Chim Fr* 275 *1949*, Adams et al. *J Am Chem Soc* **62** 732 *1940*.]

Orcinol (5-methylresorcinol) *[504-15-4; 6153-39-5 H_2O]* **M 124.2, m 107.5°, m 59-61° (hydrate cf orcine), pK_1^{20} 9.36 (9.48), pK_2^{20} 11.6 (11.20).** Crystallise orcinol from $CHCl_3$/*benzene (2:3). See *hydrate* in previous entry. [*Beilstein* **6** H 882, **6** IV 5892.]

Orthanilic acid (2-aminobenzenesulfonic acid) *[88-21-1]* **M 173.2, m >300°(dec), pK^{25} 2.49.** Crystallise orthanilic acid from aqueous solution, containing 20ml of conc HCl per L, then crystallise it from distilled water, and dry it in a vacuum desiccator over Sicapent (**m** 315°). When an aqueous solution is chilled below 13.5°, the hydrated form of the acid is obtained. It is used for the determination of nitrite and nitrate. The *S-benzylisothiuronium salt* has **m** 137° (from H_2O). [Wertheim *Org Synth* Coll Vol **II** 471 *1943*, *Beilstein* **14** H 681, **14** I 714, **14** II 429, **14** III 1896, **14** IV 2638.]

[2.2]-Paracyclophane (tricyclo[8.2.2.2^{4,7}]hexadeca-4,6,10,12,13,15-hexaene) *[1633-22-3]* **M 208.3, m 284°, 285-287°, 286-288°, 288-290°.** Purify it by recrystallisation from AcOH. ^{1}H-NMR δ: 1.62 (Ar-H) and 1.71 (CH_2) [Waugh & Fessenden *J Am Chem Soc* **79** 846 *1957*, IR and UV: Cram et al. *J Am Chem Soc* **76** 6132 *1954*, Cram & Steinberg *J Am Chem Soc* **73** 5691 *1951*. It complexes with unsaturated compounds: Cram & Bauer *J Am Chem Soc* **81** 5971 *1959*, Syntheses: Brink *Synthesis* 807 *1975*, Givens et al. *J Org Chem* **44** 16087 *1979*, Kaplan et al. *Tetrahedron Lett* 3665 *1976*]. [*Beilstein* **5** IV 2223.]

Para Red (1-(4-nitrophenylazo]-2-naphthol) *[6410-10-2]* **M 293.3, m 250-251°, pK_{Est} ~9.3.** Crystallise this

dye from AcOH or xylene and dry it *in vacuo*. It has λ_{max} at 488nm. [*Beilstein* **16** II 70.]

Pargyline hydrochloride (Eutonyl, *N*-methyl-*n*-propargylbenzylamine hydrochloride) *[306-07-0]* **M 195.7, m 154-155°, 155°, pK^{25} 6.9.** Recrystallise the salt from EtOH/Et_2O and dry it *in vacuo*. It is very soluble in H_2O, in which it is unstable. The *free base* has **b** 101-103°/11mm. It is a glucuronyl transferase inducer and a monoamine oxidase inhibitor. [von Braun et al. *Justus Liebigs Ann Chem* **445** 205 *1928*, Yeh & Mitchell *Experientia* **28** 298 *1972*, Langstrom et al. *Science* **225** 1480 *1984*, *Beilstein* **12** II 548.]

Pavatrine hydrochloride [fluorine-9-carboxylic acid, 2-(diethylamino)ethyl ester hydrochloride] *[548-65-2]* **M 333.7, m 143-144°, pK$_{Est}$ ~9.0** Recrystallise the salt from isopropanol, EtOAc/isoPrOH and dry it over P_2O_5 *in vacuo*. The *metho-bromide* has **m** 111-117° (from butanone). [*Beilstein* **9** III 3412, **9** IV 2596.]

Pentabromophenol *[608-71-9]* **M 488.7, m 229-230°, pK$_{Est}$ ~4.5.** Purify it by crystallisation (charcoal) from toluene then from CCl_4. Dry it for 2 weeks at *ca* 75°. The *diethylammonium salt* has **m** 191-193° (from MeOH). [*Beilstein* **6** H 206, **6** I 108, **6** II 197, **6** III 766, **6** IV 1069.]

1-Pentacene *[135-48-8]* **M 278.4, m 300°.** It forms blue crystals from *benzene or nitrobenzene and sublimes in a vacuum. [Clar & John *Ber* **62** 940 *1929*, **64** 981 *1931*, *Beilstein* **5** IV 2721.]

Pentachloronitrobenzene *[82-68-8]* **M 295.3, m 144-145°, 146°.** Crystallise it from EtOH. [*Beilstein* **5** H 247, **5** II 188, **5** III 618.]

Pentachlorophenol *[87-86-5]* **M 266.3, m 190-191°, pK^{25} 4.8.** Crystallise it twice from toluene/EtOH. Sublime it *in vacuo*. [*Beilstein* **6** IV 1025.]

Pentachlorothiophenol *[133-49-3]* **M 282.4, m between 228° and 235° , pK$_{Est}$ ~1.1.** Crystallise from *benzene, toluene (**m** 243°) or AcOH (**m** 240° also 242-244°). [*Beilstein* **6** IV 1642.]

Pentafluorobenzene *[363-72-4]* **M 168.1, b 85°/atm, 85-86°/atm, 88-89°/atm, d_4^{20} 1.524, n_D^{20} 1.3931.** Purify it by distillation and by gas chromatography. Its IR (film) has bands at 1535 and 1512 cm^{-1} (*C_6H_6 ring). [Stephen & Tatlow *Chem Ind (London)* 821 *1957*, Nield et al. *J Chem Soc* 166 *1959*, *Beilstein* **5** IV 639.]

2,3,4,5,6-Pentafluorobenzoic acid *[602-94-8]* **M 212.1, m 101-103°, 104-105°, 106-107°, pK^{25} 1.75.** Dissolve the acid in Et_2O, treat it with charcoal, filter, dry ($CaSO_4$), filter again, evaporate and recrystallise the residue from petroleum ether (b 90-100°) after adding a little toluene, to give large colourless plates. Its UV (H_2O) has λ_{max} at 265nm (ε 761) (H_2O). The *S-benzylisothiuronium salt* has **m** 187° (from H_2O). [McBee & Rapkin *J Am Chem Soc* **73** 1366 *1951*, Nield et al. *J Chem Soc* 166 *1959*, *Beilstein* **9** IV 956.]

***O*-(2,3,4,5,6-Pentafluorobenzyl)hydroxylamine hydrochloride (PFBHA.HCl)** *[57981-02-9]* **M 249.6, m 215°, 215-216°, pK$_{Est}$ ~1.1.** Recrystallise the salt from EtOH to form colourless leaflets. Drying the compound at high vacuum and elevated temperature will result in losses by sublimation. [Youngdale *J Pharm Sci* **65** 625 *1976*, Wehner & Handke *J Chromatog* **177** 237 *1979*, Nambara et al. give incorrect **m** as 115-116° *J Chromatogr* **114** 81 *1975*.]

2,3,4,5,6-Pentafluorophenol *[771-61-9]* **M 184.1, m 33-35°, 38.5-39.5°, b 72-74°/48mm, 142-144°/atm, 143°/atm, n_D^{20} 1.4270 (liquid prep), pK^{25} 5.53.** It is a *hygroscopic* low melting solid not freely soluble in H_2O. Purify it by distillation, preferably in a vacuum [Forbes et al. *J Chem Soc* 2019 *1959*, IR and pKa: Birchall & Haszeldine *J Chem Soc* 13 *1959*]. IR of a film has ν_{max} 3600 (OH) and 1575 (fluoroaromatic breathing) cm^{-1}. The *benzoyl* derivative has **m** 74-75°, *3,4-dinitrobenzoyl* derivative has **m** 107°, the *tosylate* has **m** 64-65° (from EtOH) and the *K salt* crystallises from Me_2CO, **m** 242°(dec), with *1H_2O-salt* the **m** is 248°(dec) and the *2H_2O-salt* has **m** 245°(dec). [*Beilstein* **6** IV 782.]

1-(Pentafluorophenyl)ethanol *[R-(+)- 104371-21-3, S-(–)- 104371-20-2]* **M 212.1, m 41-42°, 42°, 42.5-43°, $[\alpha]_{546}^{20}$ (+) and (-) 9°, $[\alpha]_D^{20}$ (+) and (-) 7.5° (c 1, *n*-pentane).** Recrystallise the ethanol from *n*-pentane at -40°

and sublime it at 25°/0.3mm (use ice-cooled cold finger). It has also been purified by column chromatography through Kieselgel 60 (0.063-0.2mm mesh, Merck) and eluted with EtOAc/*n*-hexane (1:5), then recrystallised from *n*-pentane and sublimed in a vacuum. It has R_F on Kieselgel 60 F_{254} TLC foil and eluting with EtOAc/*n*-hexane (1:5). [Meese *Justus Liebigs Ann Chem* 2004 *1986*.]
The *racemate [75853-08-6]* has **m** 32-34°, **b** 77-79°/8mm, 80-82°/37mm, n_D^{20} 1.4426, and the *3,4-dinitrobenzoate* has **m** 83° [Nield et al. *J Chem Soc* 166 *1959*]. [*Beilstein* **6** IV 3044.]

Pentamethylbenzene *[700-12-9]* **M 148.3, m 53.5-55.1°.** Successively crystallise it from absolute EtOH, aqueous EtOH, MeOH, toluene *C_6H_6, and dry it under vacuum. [Rader & Smith *J Am Chem Soc* **84** 1443 *1962*.] It has also been sublimed. The *1,3,5-trinitrobenzene complex (1:1)* has **m** 121° (EtOH). Its FT-IR (neat) has ν_{max} at 2939.4, 2728.0, 1568.1, 1475.5, 1381.8, 1067.6, 1013.9, 860.7 and 524.6 cm^{-1}; [*Beilstein* **5** H 443, **5** III 1010, **5** IV 1109.]

Perbenzoic acid *[93-59-4]* **M 138.1, m 41-43°, b 97-110°/13-15mm, pK_{Est} ~7.7.** Crystallise the peracid from *benzene or petroleum ether. It sublimes readily and is steam volatile. It is soluble in $CHCl_3$, CCl_4 and Et_2O. [Braun *Org Synth* Coll Vol **I** 431 *1941*.] **EXPLOSIVE.**

Perylene *[198-55-0]* **M 252.3, m 273-274°.** Purify perylene by silica-gel chromatography of its recrystallised picrate. [Ware *J Am Chem Soc* **83** 4374 *1961*.] Crystallise it from *benzene, toluene or EtOH and sublime it at 142° in a flow of oxygen-free nitrogen. It forms a 1:1 **benzene-complex* (**m** 223-224.5° needles from *C_6H_6), and a 1:2 **benzene-complex* (**m** 154-155° from *C_6H_6 or H_2O). The *2,4,7-trinitrofluoren-9-one* has **m** 270-271° (from EtOH/*C_6H_6). [Gorman et al. *J Am Chem Soc* **107** 4404 *1985,* Johansson et al. *J Am Chem Soc* **109** 7374 *1987*, *Beilstein* **5** III 2521, **5** IV 2689.]

Phenanthrene *[85-01-8]* **M 178.2, m 98°, 98.7-99°, 99.15°, 100.8-101.3°, b 148-149°/1mm, d^{25} 1.175.** Likely contaminants include anthracene, carbazole, fluorene and other polycyclic hydrocarbons. Purify it by distillation from sodium under vacuum, boiling with maleic anhydride in xylene, crystallisation from acetic acid, sublimation and zone melting. It has also been recrystallised repeatedly from EtOH, *benzene or petroleum ether (b 60-70°), with subsequent drying under vacuum over P_2O_5 in an Abderhalden pistol. Feldman, Pantages and Orchin [*J Am Chem Soc* **73** 4341 *1951*] separated most of the anthracene impurity by refluxing phenanthrene (671g) with maleic anhydride (194g) in xylene (1.25L) under nitrogen for 22 hours, then filtered. The filtrate was extracted with aqueous 10% NaOH, the organic phase was separated, and the solvent was evaporated. The residue, after stirring for 2 hours with 7g of sodium, was distilled in a vacuum, then recrystallised twice from 30% *benzene in EtOH. It was then dissolved in hot acetic acid (2.2ml/g), and to it was slowly added an aqueous solution of CrO_3 (60g in 72ml H_2O plus 2.2L of acetic acid), followed by slow addition of conc H_2SO_4 (30ml). The mixture was refluxed for 15 minutes, diluted with an equal volume of water and cooled. The precipitate was filtered off, washed with water, dried and distilled, then recrystallised twice from EtOH. Further purification is possible by chromatography from a $CHCl_3$ solution on activated alumina, with *benzene as eluent, and by zone refining. The *picrate (1:1)* forms golden yellow needles with **m** 146°, and the *styphnate (1:1)* has **m** 138-139° (plates or needles from EtOH or EtOH/H_2O respectively). [Dornfeld et al. *Org Synth* Coll Vol **III** 134 *1955*, *Beilstein* **5** H 667, **5** I 327, **5** II 579, **5** III 2136, **5** IV 2297.]

Phenanthrene-9-aldehyde *[4707-71-5]* **M 206.3, m 102-103°, pK^{25} -6.39 (aqueous H_2SO_4).** Crystallise the aldehyde from EtOH and sublime it at 95-98°/0.07mm. The *2,4-dinitrophenylhydrazone* has **m** 272-273°. [*Beilstein* **7** III 2532, **7** IV 1740.]

9,10-Phenanthrenequinone *[84-11-7]* **M 208.2, m 208°, pK^{25} -7.1 (aqueous H_2SO_4).** Crystallise the quinone from dioxane or 95% EtOH and dry it under vacuum. [*Beilstein* **7** IV 2565.]

Phenethylamine *[64-04-0]* **M 121.2, b 87°/13mm, d_4^{20} 0.962, n_D^{20} 1.535, pK^{25} 9.88.** Distil the amine from CaH_2, under reduced pressure, just before use. [*Beilstein* **12** H 1096, **12** IV 2453.]

Phenethyl bromide *[103-63-9]* **M 185.1, b 92°/11mm, d_4^{20} 1.368, n_D^{20} 1.557.** Wash the bromide with conc H_2SO_4, water, aqueous 10% Na_2CO_3 and water again, then dry it with $CaCl_2$ and fractionally distil it just before

use. [*Beilstein* **5** IV 907.]

(±)-*N*-1-Phenethyl urea (*N*-α-phenethyl urea) *[60295-51-4]* **M 164.2, m 137°.** Crystallise the urea from H_2O, EtOAc or *C_6H_6. [Buck *J Am Chem Soc* **56** 1607 *1934*, *Beilstein* **12** I 1096, **12** IV 1440.]

(+)-*S*-*N*-1-Phenethyl urea (*R*-*N*-α-phenethyl urea) *[16849-91-5]* **M 164.2, m 121-122°, $[\alpha]_D^{25}$ +48.8° (c 2, EtOH), $[\alpha]_D^{25}$ +46.2° (c 4.0, EtOH).** Crystallise the (+)-urea from H_2O or EtOH (**m** 122-123°). [Marckwald & Meth *Chem Ber* **38** 808 *1905*, Cairns *J Am Chem Soc* **63** 871 *1941*, *Beilstein* **12** I 1092, **12** III 2398.]

(-)-*S*-*N*-1-Phenethyl urea (*S*-*N*-α-phenethyl urea) *[25144-64-3]* **M 164.2, m 121-122°, $[\alpha]_D^{25}$ -43.6° (c 14, EtOH), $[\alpha]_D^{25}$ -52.1° (c 3.6, EtOH).** Crystallise the (–)-urea from H_2O or EtOH. [Lovén *J Prakt Chem* [2] **72** 313 *1905*, *Beilstein* **12** I 1094, **12** III 2398.]

***N*-2-Phenethyl urea** *[2158-04-5]* **M 164.2, m 112°.** Crystallise the (±)-urea from H_2O (**m** 112-113°) or EtOH. The *picrate* has **m** 113-115° (from H_2O) [Spica *Gazzetta* **9** 567 *1879*, Shapiro et al. *J Am Chem Soc* **81** 2224 *1959*]. [*Beilstein* **12** 1099, **12** III 2423, **12** IV 2470.]

Phenetole *[103-73-1]* **M 122.2, b 60°/9mm, 77.5°/31mm, 170.0°/760mm, d_4^{20} 0.967, n_D^{20} 1.50735, n^{25} 1.50485.** Small quantities of phenol can be removed by shaking with NaOH, but this is not a very likely contaminant of commercial material. Fractional distillation from sodium, at low pressures, probably gives adequate purification. It can be dissolved in diethyl ether and washed with 10% NaOH (to remove phenols), then water. The ethereal solution is evaporated, and the phenetole is fractionally distilled under vacuum. [*Beilstein* **6** H 140, **6** I 80, **6** II 142, **6** III 545.]

Phenocoll hydrochloride (4-ethoxyaniline, *p*-phenetidine HCl) *[536-10-6]* **M 230.7, m 234°, pK^{28} 5.20.** Crystallise the salt from water then sublime it *in vacuo*. [*Beilstein* **13** IV 1017.]

Phenol *[108-95-2]* **M 94.1, m 40.9°, b 85.5-86.0°/20mm, 180.8°/760mm, d_4^{20} 1.06, n_D^{41} 1.54178, n_D^{46} 1.53957, pK^{25} 9.86 (10.02).** Steam is passed through a boiling solution containing 1mole of phenol and 1.5-2.0moles of NaOH in 5L of H_2O until all non-acidic material has distilled. The residue is cooled, acidified with 20% (v/v) H_2SO_4, and the phenol is separated, dried with $CaSO_4$ and fractionally distilled under reduced pressure. It is then fractionally crystallised several times from its melt [Andon et al. *J Chem Soc* 5246 *1960*]. Purification *via* the benzoate has been used by Berliner, Berliner and Nelidow [*J Am Chem Soc* **76** 507 *1954*]. The *benzoate*, (**m** 70°, **b** 314°/760mm), is crystallised from 95% EtOH, then hydrolysed to the free phenol by refluxing with two equivalents of KOH in aqueous EtOH until the solution becomes homogeneous. It is acidified with HCl and extracted with diethyl ether. The ether layer is freed from benzoic acid by thorough extraction with aqueous $NaHCO_3$, and, after drying and removing the ether, the phenol is distilled.
Phenol has also been crystallised from a 75% w/w solution in water by cooling to 11° and seeding with a crystal of the hydrate. The crystals are centrifuged off, rinsed with cold water (0-2°), saturated with phenol, and dried. It can be crystallised from petroleum ether [Berasconi & Paschalis *J Am Chem Soc* **108** 2969 *1986*].
Draper and Pollard [*Science* **109** 448 *1949*] added 12% water, 0.1% aluminium (can also use zinc) and 0.05% $NaHCO_3$ to phenol, and distilled it at atmospheric pressure until the azeotrope was removed, The phenol was then distilled at 25mm. Phenol has also been dried by distillation from the *benzene solution to remove the water/*benzene azeotrope and the excess *benzene, followed by distillation of the phenol at reduced pressure under nitrogen. Processes such as this are probably adequate for analytical grade phenol which has as its main impurity water. Phenol has also been crystallised from petroleum ether/*benzene or petroleum ether (b 40-60°). The purified material is stored in a vacuum desiccator over P_2O_5 or $CaSO_4$. [*Beilstein* **6** IV 531.]

Phenol-2,4-disulfonic acid *[96-77-5]* **M 254.2, pK_1 <1, pK_2 <1, pK_3 ~8.3.** Crystallise the acid from EtOH/diethyl ether. [*Beilstein* **11** H 250, **11** I 58, **11** II 139, **6** III 522.]

Phenolphthalein *[77-09-8]* **M 319.2, m 263°, $pK_{Est(1)}$~ 4.2, $pK_{Est(2)}$~ 9.8.** Dissolve it in EtOH (7ml/g), then dilute it with eight volumes of cold water, filter and heat on a water-bath to remove most of the alcohol and the phenolphthalein that precipitates is filtered off and dried *in vacuo*. [*Beilstein* **18** II 119, **18** III/1V 1945, **18/4** V

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Phenolphthalol *[81-92-5]* **M 306.3, m 201-202°, pK_{Est} ~ 9.8.** Crystallise it from aqueous EtOH. [*Beilstein* **6** H 1146, **6** II 1110, **6** IV 7623.]

Phenoxyacetic acid *[122-59-8]* **M 152.2, m 98-99°, pK^{25} 3.18.** Crystallise the acid from water or aqueous EtOH. [*Beilstein* **6** IV 634.]

Phenoxyacetyl chloride *[701-99-5]* **M 170.6, b 112°/10mm, 102°/16mm, 225-226°/atm, d_4^{20} 1.235, n_D^{20} 1.534.** If it has no OH band in the IR then distil it in a vacuum, taking precautions for the moisture-sensitive compound. If it contains free acid (due to hydrolysis, OH bands in the IR), then add an equal volume of redistilled $SOCl_2$, reflux for 2-3 hours, evaporate and distil the residue in a vacuum as before. The *amide* has **m** 101°. [McElvain & Carney *J Am Chem Soc* **68** 2592 *1946*, *Beilstein* **6** III 613.]

4-Phenoxyaniline *[139-59-3]* **M 185.2, m 95°, pK^{20} 4.44 (50% aqueous EtOH).** Crystallise 4-phenoxyaniline from water. [*Beilstein* **13** IV 1020.]

Phenoxybenzamine [*N*-(2-chloroethyl)-*N*-(1-methyl-2-phenoxyethyl)benzylamine] *[59-96-1]* **M 303.5, m 38-40°, hydrochloride** *[63-92-3]* **M 340.0, m 137.5-140°, pK_{Est} ~4.2.** The free base is crystallised from petroleum ether, and the *HCl* is crystallised from EtOH/diethyl ether. [*Beilstein* **12** IV 2204.]

2-Phenoxybenzoic acid *[2243-42-7]* **M 214.2, m 113°, b 355°/760mm, $pK^{15/25}$ 3.53.** Crystallise the acid from aqueous EtOH or H_2O (**m** 114°). [*Beilstein* **10** H 65, **10** I 28, **10** II 40, **10** III 99, **10** IV 132.]

3-Phenoxybenzoic acid *[3739-38-6]* **M 214.2, m 145°, pK^{25} 3.95.** Crystallise the acid from aqueous EtOH. [*Beilstein* **10** H 138, **10** III 247, **10** IV 316.]

Phenoxybutyric acid *[6303-58-8]* **M 180.2, m 64°, 65-66°, 82-83°, 99°, b 180-185°/12mm, pK 3.17.** It has been purified by recrystallisation from petroleum ether, $*C_6H_6$, Et_2O/petroleum ether, EtOH and from H_2O. It can be steam distilled or distilled in a good vacuum. [UV: Ramart-Lucas & Hoch *Bull Soc Chim Fr* [4] **51** 824 *1932*, Dann & Arndt *Justus Liebigs Ann Chem* **587** 38 *1954*.] The *acid chloride* has **b** 154-156°/20mm [Hamford & Adams *J Am Chem Soc* **57** 921 *1935*], and the *amide* crystallises from $*C_6H_6$ as needles with **m** 113°. [*Beilstein* **6** IV 645.]

2-Phenoxypropionic acid (lactic acid *O*-phenylether) *[940-31-8]* **M 166.2, m 115-116°, b 105-106°/5mm, 265-266°/758mm, pK^{25} 3.11.** Crystallise the acid from water. [*Beilstein* **6** H 163, **6** II 158, **6** III 614.]

Phensuximide (*N*-methyl-2-phenylsuccinimide) *[86-34-0]* **M 189.2, m 71-73°.** Crystallise phensuximide from hot 95% EtOH (**m** 72-73°). At 25° 1g of the imide dissolves in 1g of $*C_6H_6$, 18g of Et_2O, 9.5g of EtOH, 5.1g of MeOH and 235g of H_2O. [*Beilstein* **21** II 300, **21** III/IV 5465.]

Phenylacetamide *[103-81-1]* **M 135.2, m 158.5°.** Crystallise the acetamide repeatedly from absolute EtOH, EtOAc (**m** 160-161°) or H_2O (**m** 159-160°). Dry it *in vacuo* over P_2O_5. [*Beilstein* **9** H 347, **9** III 2193, **9** IV 1632.]

Phenyl acetate *[122-79-2]* **M 136.2, b 78°/10mm, d_4^{20} 1.079, n_D^{22} 1.5039.** Phenyl acetate acid is freed from phenol and acetic acid by washing (either directly or as a solution in pentane) with aqueous 5% Na_2CO_3, then with saturated aqueous $CaCl_2$, drying with $CaSO_4$ or Na_2SO_4, and fractionally distilling under reduced pressure. [*Beilstein* **6** II 153, **6** III 595, **6** IV 611.]

Phenylacetic acid *[103-82-2]* **M 136.2, m 76-77°, b 140-150°/20mm, pK_1 -7.59 (aqueous H_2SO_4), pK_2 4.31.** Crystallise the acid from petroleum ether (b 40-60°), isopropyl alcohol, 50% aqueous EtOH or hot water (**m** 77.8-78.2°). Dry it *in vacuo*. It can be distilled under a vacuum. [*Beilstein* **9** II 294, **9** III 2169.]

Phenylacetone (1-phenylpropan-2-one) *[103-79-9]* **M 134.2, b 69-71°/3mm, d_4^{20} 1.00, n_D^{20} 1.516.** Convert the ketone to the *semicarbazone* and crystallise it three times from EtOH (**m** 186-187°). The semicarbazone is then hydrolysed with 10% phosphoric acid, and the ketone is distilled. [Kumler et al. *J Am Chem Soc* **72** 1463 *1950*, *Beilstein* **7** H 303, **7** I 161, **7** II 223, **7** III 1037, **7** IV 687.]

4'-Phenylacetophenone *[92-91-1]* **M 196.3, m 120.3-121.2°, b 196-210°/18mm, 325-327°/760mm.** Crystallise it from EtOH or acetone. It can also be distilled under reduced or atmospheric pressure. The *semicarbazone* has **m** 131-132° (aqueous EtOH). [*Beilstein* **7** H 443, **7** III 2134, **7** IV 1407.]

Phenylacetylene *[536-74-3]* **M 102.1, b 75°/80mm, d_4^{20} 0.930, n_D^{25} 1.5463, pK ~19.** Distil phenylacetylene through a spinning band column. It should be filtered through a short column of alumina before use [Collman et al. *J Am Chem Soc* **108** 2988 *1986*; for pK see Brandsma *Preparative Acetylenic Chemistry,* 1st Edn Elsevier 1971, p. 15, ISBN 0444409475]. [*Beilstein* **5** IV 1525.]

Phenylalaninol (2-amino-3-phenylpropan-1-ol) *[R-(+)- 5267-64-1, S-(–)- 3182-95-4]* **M 151.2, m 91-92°, 91.5°, 92-94°, b 80°/11mm (Kügelrohr), $[\alpha]_{546}^{20}$ (+) and (-) 28°, $[\alpha]_D^{20-25}$ (+) and (-) 23-28.7° (c 1-5, EtOH), pK_{Est} ~9.3.** It can be recrystallised from Et_2O, *C_6H_6/petroleum ether (b 40-60°) or toluene and distilled in a vacuum. It has been purified by dissolving in Et_2O, drying over K_2CO_3, filtering, evaporating to a small volume, cooling in ice and collecting the plates. Store them in the presence of KOH (i.e. CO_2-free atm). [Karrer & Ehrhardt *Helv Chim Acta* **34** 3203 *1951*, Oeda *Bull Chem Soc Jpn* **13** 465 *1938*.] The *picrate* has **m** 141-141.5° (from EtOH/petroleum ether). The *hydrogen oxalate* has **m** 177°, 161-162° [Hunt & McHale *J Chem Soc* 2073 *1957*]. The *racemate* has **m** 87-88° from *C_6H_6/petroleum ether (75-77° from Et_2O), and the *hydrochloride* has **m** 139-141° [Fodor et al. *J Chem Soc* 1858 *1951*]. [*Beilstein* **13** IV 1920.]

3-Phenylallyl chloride (cinnamyl chloride) *[E: 18685-01-3, Z: 39199-93-4]* **M 152.6, *trans*: m 7-8°, b 92-93°/3mm, d_4^{25} 1.086, n_D^{25} 1.5802, *cis*: 85°/3mm, d_4^{25} 1.0891, n_D^{25} 1.5746.** Distil the chloride under vacuum three times from K_2CO_3. [Hatch & Alexander *J Am Chem Soc* **72** 643 *1950*, *Beilstein* **5** III 1186.]

Phenyl 4-aminosalicylate (Phenamisal) *[133-11-9]* **M 229.2, m 153°, $pK_{Est(1)}$~2.0 (NH_2), $pK_{Est(2)}$~9.7 (OH).** Crystallise the ester from EtOH (**m** 155°, also 149-150.5°), aqueous EtOH (**m** 147-149°), or isopropanol. It is **tuberculostatic**. [*Beilstein* **13** IV 1979.]

4-Phenylanisole (4-methoxybiphenyl) *[361-37-6]* **M 184.2, m 89.9-90.1°.** Crystallise the biphenyl from *benzene/petroleum ether. Dry it under vacuum in an Abderhalden pistol. It has λ_{max} at 259.5nm (hexane). [*Beilstein* **6** H 674, **6** II 625, **6** III 3321, **6** IV 4600.]

9-Phenylanthracene *[602-55-1]* **M 254.3, m 153-154°, 156°, b 417°/760mm.** Chromatograph it on alumina in *C_6H_6 and recrystallise it from AcOH or toluene. [*Beilstein* **5** H 725, **5** II 639, **5** III 2462.]

***p*-Phenylazobenzoyl chloride** *[104-24-5]* **M 244.7, m 93°.** Crystallise the acid chloride from petroleum ether (b 60-80°). [*Beilstein* **16** III 224.]

4-Phenylazo-1-naphthylamine *[131-22-6]* **M 247.3, m 125-125.5°.** Crystallise the dye from cyclohexane or aqueous EtOH. [Brode et al. *J Am Chem Soc* **74** 4641 *1952*, *Beilstein* **16** H 361, **16** III 406, **16** IV 546.]

4-Phenylazophenacyl bromide *[62625-24-5]* **M 317.3, m 103-104°.** Purify the bromide on a column silica gel, using petroleum ether/ Et_2O (9:1 v/v) as solvent. It forms orange yellow crystals from *C_6H_6 (**m** 113-114°) or petroleum ether/Et_2O (**m** 114.5-115°). [*Beilstein* **16** II 22, **16** III 53, **16** IV 79.]

4-Phenylazophenol (4-hydroxyazobenzene) *[1689-82-3]* **M 198.2, m 155°, pK_1^{25} -0.93, pK_2^{25} 8.2.** Crystallise the dye from *benzene or 95% EtOH. [*Beilstein* **16** II 38, **16** III 86, **16** IV 159.]

Phenyl benzenethiosulfonate (diphenyldisulfoxide) *[1212-08-4]* **M 250.3, m 36-37°, 45-46°, 45-47°.** Recrystallise the disulfoxide from EtOH or MeOH. It has also been purified from phenylsulfide impurities by

dissolving in $CHCl_3$, washing with aqueous saturated $NaHCO_3$, drying (Na_2SO_4), filtering, evaporating the filtrate, and the residual oil is passed through a silica gel column (600g) and eluted with hexane/*C_6H_6 (1L, 4:1, eluting PhSSPh) then *C_6H_6 (1L) which elutes $PhSSO_2Ph$. [Trost & Massiot *J Am Chem Soc* **99** 4405 *1977*, Knoevenagel & Römer *Chem Ber* **56** 215 *1923*, *Beilstein* **11** IV 220.]

Phenyl benzoate *[93-99-2]* **M 198.2, m 69.5°, b 198-199°.** Crystallise the ester from EtOH using *ca* twice the volume needed for complete dissolution at 69°. [*Beilstein* **9** IV 303.]

Phenyl-1,4-benzoquinone *[363-03-1]* **M 184.2, m 114-115°.** Crystallise the quinone from heptane, petroleum ether (b 60-70°), *C_6H_6 (**m** 113.5-114.5°) or EtOH (**m** 112-113°) and sublime it *in vacuo*. [Carlson & Miller *J Am Chem Soc* **107** 479 *1985*, *Beilstein* **7** H 740, **7** III 3764.]

1-Phenylbiguanide *[102-02-3]* **M 177.2, m 144-146°, pK_1^{32} 2.16, pK_2^{32} 10.74.** Crystallise the biguanide from water or toluene. [*Beilstein* **12** H 370, **12** I 236, **12** III 807.]

***N*-Phenyl-bis(trifluoromethanesulfonimide) [ditriflic phenylimide, *N,N*-bis(trifluoromethylsulfonyl) aniline]** *[37595-74-7]* **M 357.3, m 93-94°, 100-102°.** This ditriflic imide is a very stable triflating agent. If hydrolysis appears to have occurred; it would be better to prepare anew from purified aniline with 2 mols of redistilled trifluoroacetic anhydride in CH_2Cl_2 at -78°, with 2 mols of Et_3N in order to keep the aniline as the free base and to mop up the free acid formed. It is then evaporated *in vacuo* to give the crystalline reagent. [Murry & Scott *Tetrahedron Lett* **24** 979 *1983*, Crisp & Scott *Synthesis* 335 *1985*, Hendrickson & Bergeron *Tetrahedron Lett* 4607 *1973*, Mascarenas et al. *Tetrahedron* **47** 3485 *1991*.]

***S*-(-)-1-Phenylbutanol** *[22135-49-5]* **M 150.2, m 46-47°, 46-48°, 49°, b 90-92°/2mm. $[\alpha]_D^{18}$ -51.4° (c 5, $CHCl_3$), -44.7° (c 5.13, *C_6H_6).** Purify the alcohol by distillation, and the distllate crystallises on cooling. The *hydrochloride* has $[\alpha]_D^{20}$ +45.1° (c 4.8, *C_6H_6). The (–)-*hydroperoxide* has **b** 58°/0.005mm, n_D^{20} 1.5123, α_D^{18} -2.14°, (*l* = 0.5dcm, neat). [Holding & Ross *J Chem Soc* 145 *1954*, Davies & Feld *J Chem Soc* 4637 *1958*.] The (±)-*racemate* has **b** 73°/0.05mm, and its *4-nitrophenylhydrazone* has **m** 58°. [*Beilstein* **6** IV 3272.]

2-Phenylbutyramide *[90-26-6]* **M 163.2, m 86°, 87°.** Crystallise the amide from H_2O, EtOH, Et_2O/petroleum ether or *C_6H_6. [*Beilstein* **9** I 212, **9** II 356, **9** III 2466.]

2-Phenylbutyric acid *[R-(–)- 938-79-4, S-(+)- 4286-15-1]* **M 164.2, b 102-104°/760mm, d_4^{20} 1.056, n_D^{20} 1.521, $[\alpha]_D^{20}$ (+) and (-) 96° (c 2.5, *C_6H_6), $[\alpha]_D^{23}$ (-) and (+) 5.8° (neat), pK_{Est} ~4.3.** Purify the acids by distillation at atmospheric pressure using an efficient column. The *acid chlorides* have **b** 106-107°/20mm, $[\alpha]_D^{18}$ (–) and (+) 108° (c 2, *C_6H_6). [Levene et al. *J Biol Chem* **100** 589 *1933*, Gold & Aubert *Helv Chim Acta* **41** 1512 *1958*, ORD in heptane: Rothen & Levene *J Chem Phys* **7** 975 *1939*, *Beilstein* **9** III 2461.]

3-Phenylbutyric acid *[R-(–)- 772-14-5, S-(+)- 772-15-6]* **M 164.2, b 94-95°/3mm, 134°/4mm, d_4^{26} 1.066, n_D^{25} 1.5167, $[\alpha]_D^{20}$ (-) and (+) 57° (c 1, *C_6H_6), pK^{25} 4.40.** Purify the acids as the 2-isomer above, i.e. by distillation, but under a good vacuum. [Prelog & Scherrer *Helv Chim Acta* **42** 2227 *1959*, Levene & Marker *J Biol Chem* **93** 761 *1932,* **100** 685 *1933*, Cram *J Am Chem Soc* **74** 2137 *1952*.] The *R-amide* crystallises from H_2O, with **m** 101.5-102°, and $[\alpha]_D^{20}$ -16.5° (c 1.2, EtOH). The *racemic acid* has **m** 39-40°, **b** 134-136°/6mm, 158°/12mm [Marvel et al. *J Am Chem Soc* **62** 3499 *1940*]. [*Beilstein* **9** IV 1813.]

4-Phenylbutyric acid *[1821-12-1]* **M 164.2, m 50°, pK^{25} 4.76.** Crystallise the acid from petoleum ether (b 40-60°). [*Beilstein* **9** IV 1811.]

***O*-Phenyl chlorothionoformate** *[1005-56-7]* **M 172.6, b 81-83°/6mm, 91°/10mm, d_4^{20} 1.276, n_D^{20} 1.585.** Purify it by dissolving in $CHCl_3$, washing with H_2O, drying ($CaCl_2$), filtering, evaporating and distilling twice under a vacuum to give a clear yellow liquid. **It is reactive and POISONOUS—work in a fume cupboard.** Store it in sealed ampoules under N_2. A possible impurity is *O,O'-diphenyl thiocarbonate* which has **m** 106° and remains behind in the distilling flask. [Bögemann et al. in *Methoden Der Organischen Chemie (Houben-Weyl)* 4th edn (E. Müller Ed.) **Vol 9** *Schwefel-Selen-Tellur Verbindungen* pp. 807-808 *1955*, Rivier & Schalch *Helv*

Chim Acta **6** 612 *1923*, Kalson *Chem Ber* **20**, 2384 *1987*, Rivier & Richard *Helv Chim Acta* **8** 490 *1925*, Schönberg & Varga *Justus Liebigs Ann Chem* **483** 176 *1930*, Schönberg & Vargha *Chem Ber* **64** 1390 *1931*, *Beilstein* **6** III 609.]

Phenyl cinnamate *[2757-04-2]* **M 224.3, m 75-76°, b 205-207°/15mm.** Crystallise the cinnamate from EtOH (2ml/g). It can also be distilled under reduced pressure. [Womack & McWhirter *Org Synth* Coll Vol **III** 715 *1955*, *Beilstein* **9** H 583, **9** II 387, **9** III 2689, **9** IV 2011.]

α-Phenylcinnamic acid (2,3-diphenylprop-2-enoic acid) *[cis-E 91-48-5, trans-Z 91-47-4]* **M 224.3, m 174°(*cis*), m 138-139°(*trans*), pK^{25} 4.8 (60% aqueous EtOH).** Crystallise the acid from Et_2O/petroleum ether. Crystallise the *cis-isomer* from petroleum ether or EtOH (**m** 174°) and has a pK^{25} of 4.44, and the *cis-amide* from aqueous Me_2CO (**m** 174°). Crystallise the *trans-isomer* from Et_2O/petroleum ether or EtOH (**m** 140°), and the *trans-amide* from $CHCl_3$/petroleum ether (**m** 167-168°). [*Beilstein* **6** H 691, **9** III 3414.]

o-**Phenylenediamine** *[95-54-5]* **M 108.1, m 100-101°, pK_1^{25} 0.67 (aqueous H_2SO_4), pK_2^{25} 4.47 (4.85).** Crystallise the diamine from aqueous 1% sodium hydrosulfite (charcoal), wash it with ice-water and dry it in a vacuum desiccator, or sublime it *in vacuo*. It has been purified by recrystallisation from toluene and zone refined [Anson et al. *J Am Chem Soc* **108** 6593 *1986*]. Purification by refluxing a CH_2Cl_2 solution containing charcoal is also carried out followed by evaporation and recrystallisation [Koola & Kochi *J Org Chem* **52** 4545 *1987*], protect from light. The *acetate* has **m** 186°. [*Beilstein* **13** IV 38.]

m-**Phenylenediamine** *[108-45-2]* **M 108.1, m 61-63°, 62-63°, 62.5°, 63-64°, b 146°/22mm, 282-284°/760mm, 284-287°/atm, d_{10}^{10} 1.1422, $n_D^{57.7}$ 1.6340, pK_1^{25} 2.41, pK_2^{25} 4.98.** Purify the diamine by distillation under a vacuum followed by recrystallisation from EtOH (rhombs) and if necessary redistillation. It should be protected from light; otherwise it darkens rapidly. [Neilson et al. *J Chem Soc* 371 *1962*, IR: Katritzky & Jones *J Chem Soc* 3674, 2058 *1959*, UV: Forbes & Leckie *Can J Chem* **36** 1371 *1958*.] The *hydrochloride* has **m** 277-278°, and the *bis-4-chlorobenzenesulfonyl* derivative has **m** 220-221° from H_2O (214-215°, from MeOH/H_2O) [Runge & Pfeiffer *Chem Ber* **90** 1737 *1957*]. The *acetate* has **m** 191°. [*Beilstein* **13** IV 79.]

p-**Phenylenediamine** *[106-50-3]* **M 108.1, m 140°, pK_1^{25} 2.89, pK_2^{25} 6.16.** Crystallise the diamine from EtOH or *benzene, and sublime it *in vacuo*; protect it from light. The *acetate* has **m** 304°. [*Beilstein* **13** IV 104.]

o-**Phenylenediamine dihydrochloride** *[615-28-1]* **M 181.1, m 180°.** Crystallise the salt from dilute HCl (60ml conc HCl, 40ml water, with 2g stannous chloride), after treatment of the hot solution with charcoal by adding an equal volume of conc HCl and cooling in an ice-salt mixture. The crystals are washed with a small amount of conc HCl and dried in a vacuum desiccator over NaOH. [*Beilstein* **13** IV 38.]

1,4-Phenylene diisothiocyanate (bitoscanate) *[4044-65-9]* **M 192.3, m 129-131°, 130-131°, 132°.** Purify bitoscanate by recrystallisation from AcOH, petroleum ether (b 40-60°), Me_2CO or aqueous Me_2CO. [van der Kerk et al. *Rec Trav Chim Pays Bas* **74** 1262 *1955*, Leiber & Slutkin *J Org Chem* **27** 2214 *1962*, *Beilstein* **13** IV 174.]

1-Phenyl-1,2-ethanediol *[R-(–)- 16355-00-3, S-(+)- 25779-13-9]* **M 138.2, m 64-67°, 65-66°, $[\alpha]_D^{24}$ (-) and (+) 40.5° (c 2.8, H_2O), $[\alpha]_D^{20}$ (-) and (+) 39° (c 3, EtOH).** Purify the diol by recrystallisation from *C_6H_6/ligroin and sublime it at 1-2mm. [Arpesella et al. *Gazetta* **85** 1354 *1955,* Prelog et al. *Helv Chim Acta* **37** 221 *1954*, *Beilstein* **6** IV 5939.]

***dl*-1-Phenylethanol (*dl*-α-methylbenzyl alcohol)** *[98-85-1; 13323-81-4]* **M 122.2, b 60.5-61.0°/3mm, 106-107°/22-23mm, d_4^{20} 1.01, n_D^{25} 1.5254.** Purify the alcohol *via* its hydrogen phthalate. [See Houssa & Kenyon *J Chem Soc* 2260 *1930*.] Shake it with a solution of ferrous sulfate, and the alcohol layer is washed with distilled H_2O, dried ($MgSO_4$) and fractionally distilled. [*Beilstein* **6** II 444.]

2-Phenylethanol *[60-12-8]* **M 122.2, b 215-217°, d 1.020.** Purify the ethanol by shaking it with a solution of ferrous sulfate, and the alcohol layer is washed with distilled water and fractionally distilled. [*Beilstein* **6** IV

3067.]

Phenyl ether (diphenyl ether) *[101-84-8]* **M 170.2, m 27.0°, b 83-84°/1mm, 138°/21mm, 257°/760mm, d_4^{20} 1.074, $n_D^{30.7}$ 1.57596.** Crystallise the ether from 90% EtOH. Melt it, wash it with 3M NaOH and water, dry it with $CaCl_2$ and fractionally distil it under reduced pressure. Fractionally recrystallise it from its melt and store over P_2O_5. [*Beilstein* **6** IV 562.]

1-Phenylethyl isocyanate (α-methylphenyl isocyanate) *[R-(+)- 33375-06-3, S(–)- 14649-03-7]* **M 147.2, b 82-83°/12-14mm, d_4^{20} 1.045, n_D^{20} 1.513, $[\alpha]_D^{24}$ (+) and (-) 2° (c 3.5, *C_6H_6), (+) and (-) 10.5° (neat).** Purify the isocyanates by fractional distillation under a vacuum. With ammonia they give the *ureido* derivatives which crystallise from H_2O with **m** 121-122°, $[\alpha]_D^{25}$ (+) and (–) 48.8°. [Cairns *J Am Chem Soc* **63** 870 *1941*.] The *racemate* has **b** 90-94°/3mm, 96°/18mm [Seiftan *Justus Liebigs Ann Chem* **562** 75 *1949*]. [*Beilstein* **12** IV 2443.]

(±)-*p*-α-Phenylethylphenol *[1988-89-2]* **M 198.3, m 56.0-56.3°, 64°, b 126°/0.4mm, 165-170°/5mm, 315-316°/742.2mm, pK_{Est} ~10.3.** Crystallise the phenol from petroleum ether. *S-(+)-enantiomer* has $[\alpha]_D$ +10.3° (*C_6H_6). [Okamoto et al. *Bull Chem Soc Jpn* **39** 303 *1966*.]

5-(α-Phenylethyl)semioxamazide *[93-95-8]* **M 207.1, m 167-168° (*l*-), 157° (*dl*-).** Crystallise it from EtOH. The *l-enantiomer* has $[\alpha]_D^{25}$ -102.5° (c 1, $CHCl_3$). [Leonard & Boyer *J Org Chem* **15** 42 *1950*.]

9-Phenyl-3-fluorone (2,6,7-trihydroxy-9-phenylxanthen-3-one) *[975-17-7]* **M 320.3, m >300°(dec), 350°, λ_{max} 462nm (ε 4.06 x 10^4, in 1M HCl aqueous EtOH).** Recrystallise it from warm, acidified EtOH by addition of ammonia. The crude material (1g) can be extracted with EtOH (50ml) in a Soxhlet apparatus for 10 hours to remove impurities. Impurities can be detected by paper electrophoresis. The *triacetate* forms yellow needles from EtOH (**m** 230-233°). [Petrova et al. *Anal Lett* **5** 695 *1972*, *Beilstein* **18** H 199, **18** I 404, **18** III/IV 2824.]

Phenylhydrazine *[100-63-0]* **M 108.1, m 23°, b 71.8°/1mm, 137-138°/18mm, 241-242°/760mm, d_4^{20} 1.10, n_D^{20} 1.607, pK_1^{20} -5.2 (aqueous H_2SO_4), pK_2^{25} 5.27.** Purify phenylhydrazine by chromatography, then crystallise it from petroleum ether (b 60-80°)/*benzene. Store it in the dark under N_2 as it turns yellow, then red, on exposure to air. It is best stored as the *hydrochloride salt*; see below. [Coleman *Org Synth* Coll Vol **I** 442 *1941*, Shaw & Stratton *J Chem Soc* 5004 *1962*, *Beilstein* **15** IV 50.]

Phenylhydrazine hydrochloride *[59-88-1]* **M 144.5, m 244°, 250-254°(dec).** Dissolve 100g of phenylhydrazine hydrochloride in 200ml of warm H_2O (60-70°) during 1-3 hours, then add 1L of boiling EtOH. The solution is filtered, while still hot, through Whatman No 2 filter paper and cooled in a refrigerator. The precipitate is collected on a medium sintered-glass filter and recrystallised twice this way, then washed with cold EtOH, dried thoroughly and stored in a stoppered brown bottle. [Peterson et al. *Anal Chem* **29** 144 *1957*.] Hough, Powell and Woods [*J Chem Soc* 4799 *1956*] boiled the hydrochloride with three times its weight of water, filtered hot (charcoal), added one-third volume of concentrated HCl and cooled to 0°. The crystals were washed with acetone, and dried over P_2O_5 under vacuum. The salt has also been crystallised from 95% EtOH, and it can be sublimed. [Coleman *Org Synth* Coll Vol **I** 442 *1941*, *Beilstein* **15** III 71.]

Phenylhydroxylamine (*N*-hydroxyaniline) *[100-65-2]* **M 109.1, m 81°, 82°, 83-84°, pK^{25} 3.2.** Impure base deteriorates rapidly. Crystallise it from H_2O, *C_6H_6 or *C_6H_6/petroleum ether (40-60°). The *picrate* has **m** 186° (from EtOH), and the *benzenesulfonate salt* has **m** 70° (dec)(EtOH/*C_6H_6). [*Beilstein* **15** H 2, **15** I 3, **15**, II 4, **15** III 5. **15** IV 4.]

2-Phenyl-1,3-indandione *[83-12-5]* **M 222.2, m 149-151°, pK^{20} 4.12 (1% aqueous MeOH).** Crystallise the dione from EtOH (**m** 156°) or $CHCl_3$ (**m** 148-150°). [*Beilstein* **7** H 808, **7** III 4100, **7** IV 2570.]

Phenylisocyanate *[103-71-9]* **M 119.1, b 45-47°/10mm, d_4^{20} 1.093, n_D^{20} 1.536.** Distil phenylisocyanate under reduced pressure from P_2O_5. [*Beilstein* **12** IV 864.]

Phenylisothiocyanate (phenyl mustard oil) *[103-72-0]* **M 135.2, m -21°, b 95°/12mm, 117.1°/33mm, 221°/760mm, d_4^{25} 1.1288, $n_D^{23.4}$ 1.64918.** It is insoluble in H_2O, but soluble in Et_2O and EtOH. If impure (due to formation of thiourea), then steam distil it into a receiver containing 5-10ml of N H_2SO_4. Separate the oil, dry over $CaCl_2$ and distil it under vacuum. [Dains et al. *Org Synth* Coll Vol **I** 447 *1941*, *Beilstein* **12** IV 867.]

8-Phenylmenthol *[1R,2S,5R-(–)- 65253-04-5, 1S,2R,5S-(+)- 57707-91-2]* **M 232.4, $[\alpha]_D^{20}$ (–) and (+) 26° (c 2, EtOH).** Dissolve the menthol in toluene, dry (Na_2SO_4), evaporate and chromatograph it on a silica gel column and eluting with 5% Et_2O in petroleum ether to give an oil with the desired rotation. Its IR has ν_{max} at 3420cm^{-1} (OH) with consistent ^1H NMR [Corey & Ensley *J Org Chem* **43** 1610 *1978*, Whitesell et al. *Tetrahedron* **42** 2993 *1986*, Bednarski & Danishefsky *J Am Chem Soc* **108** 7060 *1986*].

Phenyl methanesulfonate *[16156-59-5]* **M 172.1, m 61-62°.** Crystallise the sulfonate from MeOH or from H_2O (**m** 61.5°). [*Beilstein* **6** H 176, **6** III 650, **6** IV 689.]

Phenyl methanesulfonyl fluoride (PMSF) *[329-98-6]* **M 174.2, m 90-91°, 92-93°.** Purify PMSF by recrystallisation from *C_6H_6, petroleum ether or $CHCl_3$/petroleum ether. [Davies & Dick *J Chem Soc* 483 *1932*, cf Tullock & Coffman *J Org Chem* **23** 2016 *1960*.] It is a general protease inhibitor (specific for trypsin and chymotrypsin) and is a good substitute for diisopropylphosphorofloridate [Fahrney & Gould *J Am Chem Soc* **85** 997 *1963*]. [*Beilstein* **11** III 331.]

2-Phenylnaphthalene *[612-94-2]* **M 204.3, m 102-103°, 103.5°, 103-104°, b 185-190°/5mm, 357-358°/760mm.** Chromatograph it on alumina in *benzene and crystallise it from aqueous EtOH or MeOH/EtOH. It has been sublimed. It has λ_{max} at 248 and 286nm (methylcyclohexane). The *2,4,7-trinitrofluoren-9-one* has **m** 169.5-170.5° (from EtOH/*C_6H_6). [*Beilstein* **5** H 687, **5** II 603, **5** III 2231, **5** IV 2412.]

***N*-Phenyl-1-naphthylamine** *[90-30-2]* **M 219.3, m 63.7-64.0°, pK_{Est} ~0.1.** Crystallise it from EtOH, petroleum ether or *C_6H_6/EtOH. Dry it under vacuum in an Abderhalden pistol. [*Beilstein* **12** H 1224.]

***N*-Phenyl-2-naphthylamine** *[135-88-6]* **M 219.3, m 107.5-108.5°, 110°, pK_{Est} ~0.5.** Crystallise it from EtOH, MeOH, glacial acetic acid or *benzene/hexane. [*Beilstein* **12** H 1275, **12** I 535, **12** II 716, **12** III 2991.]

4-Phenylphenacyl bromide *[135-73-9]* **M 275.2, m 126°.** Crystallise (charcoal) the bromide from EtOH (15ml/g), or ethyl acetate/petroleum ether (b 90-100°). [*Beilstein* **7** III 2137.]

2-Phenylpropanal *[93-53-8]* **M 134.2, b 206°/760mm, d_4^{20} 1.001, n_D^{20} 1.5183.** It may contain up to 15% of acetophenone. Purify it *via* the bisulfite addition compound [Lodge & Heathcock *J Am Chem Soc* **109** 3353 *1987*] and see Chapter 2 for preparation and decomposition of bisulfite adducts. [*Beilstein* **7** IV 695.]

Phenylpropiolic acid *[637-44-5]* **M 146.2, m 137.8-138.4°, pK^{25} 2.23.** Crystallise the acid from *benzene, CCl_4 (**m** 136°) or aqueous EtOH. The *S-benzylisothiuronium salt* has **m** 184-186° (from EtOH). [*Beilstein* **9** II 436, **9** III 3061, **9** IV 2327.]

***RS*-2-Phenylpropionic acid** *[492-37-5]* **M 150.2, m 16-16.5°, b 153-155°/20mm, 189°/48mm, 260-262°/760mm, d_4^{20} 1.10, n_D^{20} 1.522, pK^{25} 4.3.** Fractionally distil the acid, or recrystallise it from petroleum ether (b 40-60°) with strong cooling (see references below). [*Beilstein* **9** II 348.]

2-Phenylpropionic acid *[R-(–)- 7782-26-5, S-(+)- 7782-24-3]* **M 150.2, m 30.3-31°, 30-32°, b 115°/1-2mm, 142°/12mm, $[\alpha]_D^{20}$ (-) and (+) 99.7° (l = 1 dcm, neat), (-) and (+) 89.1° (c 1.7, EtOH), (-) and (+) 75° (c 1.6, $CHCl_3$).** Purify the acids by vacuum distillation and by recrystallisation from petroleum ether. The *S-anilide* has **m** 103-104° (from H_2O or $CHCl_3$/*C_6H_6), $[\alpha]_D^{25}$ +47° (c 9, Me_3CO) [Argus & Kenyon *J Chem Soc* 916 *1939*, Campbell & Kenyon *J Chem Soc* 25 *1946*, Levene et al. *J Biol Chem* **88** 27, 34 *1930*]. [*Beilstein* **9** III 2417, **9** IV 1779.]

3-Phenylpropionic acid (hydrocinnamic acid) *[501-52-0]* **M 150.2, m 48-48.5°, pK^{25} 4.56.** Crystallise the acid from *benzene, $CHCl_3$ or petroleum ether (b 40-60°). Dry it in a vacuum. [*Beilstein* **9** H 508.]

3-Phenylpropyl bromide *[637-59-2]* **M 199.1, b 110°/12mm, 128-129°/29mm, d $_4^{20}$ 1.31.** Wash the bromide successively with conc H_2SO_4, water, 10% aqueous Na_2CO_3 and again with water, then dry it with $CaCl_2$ and fractionally distil it just before use. [*Beilstein* **5** IV 982.]

Phenylpyruvic acid *[156-06-9]* **M 164.2, m 150-154°, 158-159°, pK$_{Est}$ ~2.1.** Recrystallise the acid from *C_6H_6. The *phenylhydrazone* has **m** 173° [Zeller *Helv Chim Acta* **26** 1614 *1943*, Hopkins & Chisholm *Can J Research* [B] **24** 89 *1946*]. The *2,4-dinitrophenylhydrazone* has **m** 162-164° (189°, 192-194°) [Fones *J Org Chem* **17** *1952*]. [*Beilstein* **10** IV 2760.]

Phenyl salicylate (Salol) *[118-55-8]* **M 214.2, m 41.8-42.6°, pK$_{Est}$ ~9.9.** Fractionally crystallise salol from its melt, then crystallise it from *benzene. [*Beilstein* **10** IV 154.]

3-Phenylsalicylic acid *[304-06-3]* **M 214.3, m 186-187.5°, pK$_{Est(1)}$~2.8 (CO_2H), pK$_{Est(2)}$~11.0 (OH).** Dissolve the acid in *ca* 1 equivalent of saturated aqueous Na_2CO_3, filter and precipitate it by adding 0.8 equivalents of M HCl. Crystallise it from ethylene dichloride (charcoal), and sublime it at 0.1mm. [Brooks et al. *J Chem Soc* 661 *1961*.]

1-Phenylsemicarbazide *[103-03-7]* **M 151.2, m 172°, 173.5°.** Crystallise it from water and dry it in a vacuum over KOH. [*Beilstein* **15** H 287, **15** II 106, **15** III 184, **15** IV 180.]

4-Phenylsemicarbazide *[537-47-3]* **M 151.2, m 122°.** Crystallise it from water and dry it in a vacuum over KOH. [*Beilstein* **12** II 221, **12** III 822.]

Phenylsuccinic acid *[R-(–)- 46292-93-7, S-(+)- 4036-30-1]* **M 194.2, m 173-176°, 178.5-179°, 179-180°, [α] $_D^{25}$ (-) and (+) 171° (c 2, Me_2CO), [α] $_D^{26-30}$ (-) and (+) 148° (c 0.27-5, EtOH), pK $_1^{25}$ 3.78, pK $_2^{25}$ 5.55.** Purify the acids by re-precipitation from alkali and recrystallisation from H_2O. [Naps & Johns *J Am Chem Soc* **62** 2450 *1940*, Fredga & Matell *Bull Soc Chim Belg* **62** 47 *1953*, Wren & Williams *J Chem Soc* **109** 572 *1916*.] The *racemate [635-51-8]* has **m** 166-168°, 168° after recrystallisation from H_2O or MeCN. Its *S-benzylisothiuronium salt* has **m** 164-165° (from EtOH) [Griediger & Pedersen *Acta Chem Scand* **9** 1425 *1955*]. [*Beilstein* **9** IV 3351.]

1-Phenylthiosemicarbazide *[645-48-7]* **M 167.2, m 200-201°(dec).** Crystallise it from EtOH. [*Beilstein* **15** IV 183.]

4-Phenylthiosemicarbazide *[5351-69-9]* **M 167.2, m 140°.** Crystallise it from EtOH. [*Beilstein* **12** IV 827.]

1-Phenyl-2-thiourea *[103-85-5]* **M 152.1, m 154°.** Crystallise the thiourea from water and dry it at 100° in air. [*Beilstein* **12** IV 804.]

Phenyltoloxamine [2-(2-dimethylaminoethoxy)-diphenylmethane] hydrochloride *[6152-43-8]* **M 291.8, m 119-120°, pK^{25} 9.3 (free base).** Crystallise the salt from isobutyl methyl ketone. The *free base* has **b 144°/1mm**. [*Beilstein* **6** III 3351, **6** IV 4630.]

Phenyl 4-toluenesulfonate *[640-60-8]* **M 248.2, m 94.5-95.5°, 95.8-97.8°.** Crystallise the ester from MeOH or glacial acetic acid. [*Beilstein* **11** H 99, **11** II 47, **11** III 200, **6** IV 271.]

Phenyl 4-tolylcarbonate *[13183-20-5]* **M 228.2, m 94°.** Purify the carbonate by preparative GLC with 20% Apiezon on Embacel, and sublime it *in vacuo*. [*Beilstein* **6** H 398.]

1-Phenyl-2,2,2-trifluoroethanol *[R-(–)- 10531-50-7, S-(+)- 340-06-7]* **M 176.1, b 74-76°/10mm, 125-127°/760mm, d $_4^{20}$ 1.301, n $_D^{20}$ 1.4632, [α] $_D^{20}$ (-) and (+) 31° (neat).** Purify the chiral alcohols by fractional

distillation preferably in a vacuum. [Morrison & Ridgeway *Tetrahedron Lett* 573 *1969*, NMR: Pirkle & Beare *J Am Chem Soc* **90** 6250 *1968*.] The *racemate [340-05-6]* has **b** 52-54°/2mm, 57-59°/2mm, 64-65°/5mm, d_4^{20} 1.293, n_D^{20} 1.457, and the *2-carbobenzoyl* derivative has **m** 137-138° [Mosher et al. *J Am Chem Soc* **78** 4374 *1956*]. [*Beilstein* **6** IV 3043.]

Phenylurea *[64-10-8]* **M 136.2, m 148°, pK^{25} -1.45 (aqueous H_2SO_4).** Crystallise the urea from boiling water (10ml/g) or amyl alcohol (**m** 149°). Dry it in a steam oven at 100°. The 1:1 *resorcinol complex* has **m** 115° (from EtOAc/*C_6H_6). [*Beilstein* **12** H 346, **12** II 204, **12** III 760, **12** IV 734.]

Phloroacetophenone ($2H_2O$) (2',4',6'-trihydroxyacetophenone) *[480-66-0]* **M 186.2, m 218-219°, $pK_{Est(1)}$~7.9, $pK_{Est(2)}$~12.0.** Crystallise the ketone from hot H_2O (35ml/g). [*Beilstein* **8** IV 2729.]

Phloretin [2',4',6'-trihydroxy-3-(*p*-hydroxyphenyl)propiophenone] *[60-82-2]* **M 274.3, m 264-271°(dec), $pK_{Est(1)}$~7.5, $pK_{Est(2)}$~8.0, $pK_{Est(3)}$~10, $pK_{Est(4)}$~12 (phenolic OH's).** Crystallise phloretin from aqueous EtOH. [Zemplen & Bognár *Chem Ber* **75** 1040 *1942*, Zemplén *Chem Ber* **76** 386 *1943*, *Beilstein* **8** IV 3518.]

Phloroglucinol ($2H_2O$) (benzene-1,3,5-triol) *[6099-90-7 ($2H_2O$), 108-73-6 (anhydrous)]* **M 126.1, m 217-219°, 117° (anhydrous), pK_1^{25} -7.74 ($HClO_4$), pK_2^{20} 7.97, pK_3^{20} 9.23.** Crystallise the triol from water, and store it in the dark under nitrogen. [*Beilstein* **6** IV 7361.]

o-**Phthalic acid** *[88-99-3]* **M 166.1, m 211-211.5°, pK_1^{25} 2.76 (3.05), pK_2^{25} 4.92 (4.73).** Crystallise phthalic acid from water. [*Beilstein* **9** IV 3167.]

Phthalic anhydride *[85-44-9]* **M 148.1, m 132°, b 295°.** Distil the anhydride under reduced pressure. Purify it from the acid by extracting with hot $CHCl_3$, filtering and evaporating. The residue is crystallised from $CHCl_3$, CCl_4 or *benzene, or sublimed. Fractionally crystallise it from its melt. Dry it under vacuum at 100°. [Saltiel *J Am Chem Soc* **108** 2674 *1986*, *Beilstein* **17/11** V 253.]

Phthalide *[87-41-2]* **M 134.1, m 72-73°, pK -7.98 (aqueous H_2SO_4).** Crystallise phthalide from water (75ml/g) and dry it in air on filter paper. [*Beilstein* **17/10** V 7.]

Phthalimide *[85-41-6]* **M 147.1, m 235°, 238°, pK 8.30.** Crystallise the imide from EtOH (20ml/g) (charcoal), or sublime it. For potassium phthalimide see entry in "Metal-organic Compounds", Chapter 5. [*Beilstein* **21/10** V 270.]

Phthalonitrile (1,2-dicyanobenzene) *[91-15-6]* **M 128.1, m 141°.** Crystallise the nitrile from EtOH, toluene or *benzene. It has also been distilled under high vacuum. It is steam volatile. [*Beilstein* **9** H 815, **9** II 602, **9** III 4199, **9** IV 3268.]

Phthalylsulfacetamide *[131-69-1]* **M 362.3, m 304°.** It is prepared by hydrolysis of N-acetamidosulfophenylpthalimide by boiling for 3 hours in 15% aqueous KOH followed by treatment with Norit, filtration and acidification with AcOH. Crystallise the phthalamide from hot H_2O or EtOH [Jain et al. *J Indian Chem Soc* **24** 174 *1947*]. It is **antibacterial**. [*Beilstein* **14** III 2073.]

Phthiocol (2-hydroxy-3-methylnaphtha-1,4-quinone) *[483-55-6]* **M 188.1, m 173-174°, pK_{Est} ~4.2.** Crystallise the quinone from diethyl ether/petroleum ether. [*Beilstein* **8** III 2568, **8** IV 2375.]

Physodic acid [4,4',6'-trihydroxy-6-(2-oxoheptyl)-2'-pentyl-2,3'-oxydibenzoic acid 1,5-lactone] *[84-24-2]* **M 470.5, m 205°, $pK_{Est(1)}$~3.0, $pK_{Est(2)}$~10, $pK_{Est(3)}$~13.** Crystallise the acid from MeOH. The *diacetate* has **m** 155-156° (from Me_2CO/CS_2). [*Beilstein* **19** II 329, **19** III/IV 3988.]

Picene *[213-14-3]* **M 278.3, m 364°, 366-367°, 367-369°.** Crystallise picene from isopropylbenzene/xylene. After sublimation at 300°/2mm followed by crystallisation from xylene (charcoal), it gives white glistening leaflets with **m** 366-366.5° [Newman *J Org Chem* **9** 524 *1944*]. The *2,4,7-trinitrofluoren-9-one* has **m** 257-

257.8° (from *C_6H_6). [*Beilstein* **5** H 735, **5** I 369, **5** III 2555, **5** IV 2724.]

Picric acid *[88-89-1]* **M 229.1, m 122-123°, pK^{25} 0.33 (0.37).** Crystallise the acid first from acetic acid, then acetone, toluene, $CHCl_3$, aqueous 30% EtOH, 95% EtOH, MeOH or H_2O. Dry it in a vacuum for 2 hours. *Alternatively*, dry it over $Mg(ClO_4)_2$ or fuse (CARE) and allow it to solidify under a vacuum three times. Because it is **EXPLOSIVE**, picric acid should be stored moistened with H_2O, and only small portions should be dried at any one time. The dry acid should **NOT** be heated. [*Beilstein* **6** IV 1388.]

Picryl chloride (2-chloro-1,3,7-trinitrobenzene) *[88-88-0]* **M 226.3, m 83°.** Crystallise the chloride from $CHCl_3$ or EtOH. The 2:1 **C_6H_6-complex* has **m** 39° (from *C_6H_6). [*Beilstein* **5** II 205, **5** III 645, **5** IV 757.]

Picryl iodide (2-iodo-1,3,7-trinitrobenzene) *[4436-27-5]* **M 340.0, m 164-165°.** Crystallise the iodide from *benzene. [*Beilstein* **5** III 647, **5** IV 758.]

Pinacyanol chloride (Quinaldine Blue] *[2768-90-3]* **M 388.9, m 270°(dec).** Crystallise the chloride from EtOH/diethyl ether. [*Beilstein* **23** I 90.]

Piperic acid [*trans,trans*-5-(3,4-methylenedioxyphenyl)-2,4-pentadieneoic acid] *[136-72-1]* **M 218.2, m 217°, pK_{Est} ~4.7.** Crystallise the acid from EtOH. It turns yellow in light. It sublimes with partial decomposition. It has UV with λ_{max} at 340nm (MeOH). [*Beilstein* **19** H 281, **19** II 30, **19** III/IV 3565.]

Piperonal *[120-57-0]* **M 150.1, m 37°, b 140°/15mm, 263°/760mm.** Crystallise piperonal from aqueous 70% EtOH or EtOH/water. [*Beilstein* **19/4** V 225.]

Piperonylic acid *[94-53-1]* **M 166.1, m 229°, pK^{25} 4.50.** Crystallise the acid from EtOH or water. [*Beilstein* **19/7** V 300.]

Polystyrene (PS) *[9003-53-6]***.** Precipitate polystyrene repeatedly from $CHCl_3$ or toluene solution by addition of MeOH. Dry it *in vacuo*. [Miyasaka et al. *J Phys Chem* **92** 249 *1988*.]

Procaine [4-(2-diethylaminomethoxycarbonyl)aniline] *[59-46-1]* **M 236.3, m 51° (dihydrate), 61° (anhydrous), pK_1^{15} 2.45, pK_2^{15} 8.91.** Procain crystallises as the *dihydrate* from aqueous EtOH and as the *anhydrous* material from petroleum ether or diethyl ether. The latter is *hygroscopic*. [*Beilstein* **14** IV 1138.]

***p*-(1-Propenyl)phenol** *[cis/trans 6380-21-8, 539-12-8]* **M 134.2, m 93-94°, pK_{Est} ~10.2.** Crystallise the phenol from water. [*Beilstein* **6** III 2394, **6** IV 3796.]

1-Propyl-3-(*p*-chlorobenzenesulfonyl) urea *[94-20-2]* **M 260.7, m 126-128°, 127-129°.** Crystallise the urea from aqueous EtOH. [*Beilstein* **11** IV 119.]

***n*-Propyl gallate** *[121-79-9]* **M 212.2, m 150°.** Crystallise the ester from aqueous EtOH or *C_6H_6 (**m** 146-146.5°). [*Beilstein* **10** III 2078, **10** IV 2003.]

Protocatechualdehyde (3,4-dihydroxybenzaldehyde) *[139-85-5]* **M 138.1, m 153°.** Crystallise the aldehyde from water or toluene and dry it in a vacuum desiccator over KOH pellets or shredded wax respectively. [*Beilstein* **8** IV 1762.]

***1S,2S*-Pseudoephedrine (1-hydroxy-1-phenyl-2-methylaminopropane)** *[90-82-4]* **M 165.2, m 118-119°, $[\alpha]_D^{20}$ +53.0° (EtOH), +40.0° (H_2O), pK^{25} 9.71.** Crystallise the amine from dry diethyl ether, or from water and dry it in a vacuum desiccator. [*Beilstein* **13** IV 1878.]

***1S,2S*-Pseudoephedrine hydrochloride** *[345-78-8]* **M 210.7, m 181-182°, 185-188°, $[\alpha]_D^{20}$ +61° (c 1 H_2O).** Crystallise the salt from EtOH. [*Beilstein* **13** IV 1878.]

Purpurin (1,2,4-trihydroxy-5,10-anthraquinone) *[81-54-9]* **M 256.2, m 253-256°, $pK_{Est(1)}$~7.0 (2-OH), $pK_{Est(2)}$~9.0 (4-OH), $pK_{Est(3)}$~11.1 (1-OH).** Crystallise purpurin from aqueous EtOH, dry it at 100°. [*Beilstein* **8** IV 3568.]

Pyrene (benzo[*def*]phenanthrene) *[129-00-0]* **M 202.3, m 149-150°.** Crystallise pyrene from EtOH, glacial acetic acid, *benzene or toluene. Purify it also by chromatography of CCl_4 solutions on alumina, with *benzene or *n*-hexane as eluent. [Backer & Whitten *J Phys Chem* **91** 865 *1987*.] It can also be zone refined and purified by sublimation. Marvel and Anderson [*J Am Chem Soc* **76** 5434 *1954*] refluxed pyrene (35g) in toluene (400ml) with maleic anhydride (5g) for 4 days, then added 150ml of aqueous 5% KOH and refluxed for 5 hours with occasional shaking. The toluene layer was separated, washed thoroughly with H_2O, concentrated to about 100ml and allowed to cool. Crystalline pyrene was filtered off and recrystallised three times from EtOH or acetonitrile. [Chu & Thomas *J Am Chem Soc* **108** 6270 *1986*, Russell et al. *Anal Chem* **50** 2961 *1986*.] The material is free from anthracene derivatives. Another purification step involves passage of pyrene in cyclohexane through a column of silica gel. It can be sublimed in a vacuum and zone refined. The *picrate* has **m** 224°. [Kano et al. *J Phys Chem* **89** 3748 *1985*, *Beilstein* **5** IV 2467.]

Pyrene-1-aldehyde *[3029-19-4]* **M 230.3, m 125-126°.** Recrystallise the aldehyde three times from aqueous EtOH. [*Beilstein* **7** IV 1821.]

1-Pyrenebutyric acid *[3443-45-6]* **M 288.4, m 184-186°, pK_{Est} ~4.1.** Crystallise the butyric acid from *benzene, EtOH, EtOH/water (7:3 v/v) or *C_6H_6/AcOH. Dry it over P_2O_5. [Chu & Thomas *J Am Chem Soc* **108** 6270 *1986*, *Beilstein* **9** IV 2731.]

1-Pyrenecarboxylic acid *[19694-02-1]* **M 230.3, m 274-274°, pK_{Est} ~3,2.** Crystallise the acid from *C_6H_6, chlorobenzene, nitrobenzene or 95% EtOH. [*Beilstein* **9** H 712, **9** III 3575.]

1-Pyrenesulfonic acid *[26651-23-0]* **M 202.2, m >350°, pK_{Est} <0.** Crystallise the sulfonic acid from EtOH/H_2O. The *sulfonyl chloride* has **m** 120°(dec). [Vollmann et al. *Justus Liebigs Ann Chem* **531** 32 *1937* and *Justus Liebigs Ann Chem* **540** 189 *1939*, *Beilstein* **11** H 198, **11** III 448.]

1,3,6,8-Pyrenetetrasulfonic acid *[6528-53-6]* **M 522.2, m >400°, pK_{Est} <0.** Crystallise the tetrasulfonic acid from water. The tetra-Na salt crystallises also from H_2O. [Tietz & Bayer *Justus Liebigs Ann Chem* **540** 189 *1939*, *Beilstein* **11** III 486.]

***p*-Quaterphenyl** *[135-70-6]* **M 306.4, m 312-314°, b 428°/18mm.** Recrystallise *p*-quaterphenyl from dimethyl sulfoxide at *ca* 50°. [*Beilstein* **5** II 669.]

Quinalizarin (1,2,5,8-tetrahydroxy-9,10-anthraquinone) *[81-61-8]* **M 272.2, m 275°, $pK_{Est(1)}$~7.1 (1-OH), $pK_{Est(2)}$~9.9 (8-OH), $pK_{Est(3)}$~11.1 (5-OH), $pK_{Est(4)}$~11.8 (2-OH).** Crystallise the quinone from acetic acid or nitrobenzene. It can be sublimed *in vacuo*. The Cu salt forms red crystals. [*Beilstein* **8** H 549, **8** I 755, **8** II 584.]

Quinhydrone (1:1 complex of hydroquinone and benzoquinone) *[106-34-3]* **M 218.2, m 168°, 167-172°.** Crystallise quinhydrone from H_2O at 65°**,** then dry it *in vacuo*. [*Beilstein* **7** H 617, **7** IV 2069.]

Quinizarin (1,4-dihydroxy-9,10-anthraquinone) *[81-64-1]* **M 240.2, m 200-202°, pK_1^{25} 9.90 (9.5), pK_2^{25} 11.18.** Crystallise quinizarin from glacial acetic acid. [*Beilstein* **8** H 450, **8** IV 3260.]

***p*-Quinquephenyl (*p*-pentaphenyl)** *[61537-20-0]* **M 382.5, m 388.5°.** Recrystallise *p*-pentaphenyl from boiling dimethyl sulfoxide (**b** 189°, lowered to 110°). The solid obtained on cooling is filtered off and washed repeatedly with toluene, then with conc HCl. The final material is washed repeatedly with hot EtOH. It is also recrystallised from pyridine, then sublimed *in vacuo*. [Campbell & McDonald *Org Synth* Coll Vol **V** 986 *1973*, *Beilstein* **5** II 709, **5** III 2680, **5** IV 2874.]

Resorcinol *[108-46-3]* **M 110.1, m 111.2-111.6°, pK_1^{25} 9.23, pK_2^{25} 13.05.** Crystallise resorcinol from *benzene, toluene or *benzene/diethyl ether. The *benzoate* has **m** 117°. [*Beilstein* **6** IV 2069.]

Retene (1-methyl-7-*iso*propylphenanthrene) *[483-65-8]* **M 234.3, m 89°, 90°, 99°, 100.5-101°, b 208°/10mm.** Crystallise retene from EtOH. The *picrate* has **m** 126° (from EtOH). The 1:1 *1,3,5-trinitrobenzene-complex* has **m** 144° (from EtOH). [*Beilstein* **5** H 683, **5** II 598, **5** III 2199.]

***Para*Rosaniline (4,4',4"-triaminotrityllium [triphenylmethane] carbonium ion, para-fuschin, paramagenta)** *[467-62-9]* **M 305.4, pK^{25} 7.57 and free base has pK >13.** Dissolve the dye in EtOH (1.16g in 30ml), filter and add aqueous NH_3 till neutral (colourless) and precipitate it by adding H_2O giving 0.8g, **m** 247°(dec, sintering at 230°). Dissolve it in EtOH, neutralise with NH_3 till colourless, add 0.1g of charcoal, filter, and repeat, then add H_2O (100ml) to precipitate the colourless *carbinol* (pseudo-base) and dry it *in vacuo*, **m** 257°(dec, also 205°, sintering at 232°). [Weissberger & Theile *J Chem Soc* 148 *1934*.] The *carbinol* is slightly soluble in H_2O but is soluble in acids (e.g. HCl to give the coloured *chloride* [569-61-9]) and EtOH [pK: Goldacre & Phillips *J Chem Soc* 172 *1949*]. The *perchlorate* (dark red with a green shine) has **m** 300° and explodes at 317° [Dilthey & Diaklage *J Prakt Chem* [2] 129 *1931*]. [*Beilstein* **13** IV 2283.]

Rosaniline HCl (Magenta I, Fuschin) *[632-99-5]* **M 337.9, m >200°(dec).** Purify the dye by dissolving it in EtOH, filtering and adding H_2O. Filter or centrifuge it and wash the precipitate with Et_2O and dry it in air. It has also been recrystallised from water and dried *in vacuo* at 40°. The crystals have a metallic green lustre. It has UV with λ_{max} in EtOH at 543nm (ε 93,000). Its solubility in H_2O is 0.26%. A carmine red colour is obtained in EtOH. It is paraRosaniline with a methyl group. [Scalan *J Am Chem Soc* **57** 887 *1937*.]

***p*-Rosolic acid (4-[bis-{4-hydroxyphenyl}methylene]-2,5-cyclohexadien-one, 4',4"-di-hydroxy-fuschson, aurin, corallin)** *[603-45-2]* **M 290.3, m 292°, 295-300° (dec with liberation of phenol), 308-310°(dec), pK_1 3.11, pK_2 8.62.** It forms green crystals with a metallic luster, but the colour depends on the solvent used. When recrystallised from brine (saturated aqueous NaCl) acidified with HCl, it forms red needles, but when recrystallised from EtO/AcOH, the crystals have a beetle iridescent green colour. It has been recrystallised from Me_2CO (although it dissolves slowly), methyl ethyl ketone, 80-95% AcOH and from AcOH/*C_6H_6. An aqueous KOH solution is golden yellow, and a 70% H_2SO_4 solution is deep red in colour. An *alternative* purification is to dissolve this triphenylmethane dye in 1.5% of aqueous NH_3, filter, and heat to 70-80°, then acidify with dilute AcOH by adding it slowly with vigorous stirring, whereby the aurin separates as a brick-red powder or as purplish crystals depending on the temperature and period of heating. Filter off the solid, wash it with H_2O and a little dilute AcOH, then H_2O again. Stir this solid with Et_2O to remove any ketones and allow it to stand overnight in the Et_2O, then filter and dry it in air then in a vacuum. [Gomberg & Snow *J Am Chem Soc* 47 202 *1925*, Baines & Driver *J Chem Soc* 123 1216 *1923*, UV: Burawoy *Chem Ber* **64** 462 *1941*, *Beilstein* **8** IV 2646.]

Salicylaldehyde (*o*-hydroxybenzaldehyde) *[90-02-8]* **M 122.1, b 93°/25mm, 195-197°/760mm, d_4^{20} 1.167, n 1.574, pK^{25} 8.37.** It is precipitated as the bisulfite addition compound by pouring the aldehyde slowly and with stirring into a 25% solution of $NaHSO_3$ in 30% EtOH, then standing for 30 minutes. The precipitate, after filtering at the pump, and washing with EtOH, is decomposed with aqueous 10% $NaHCO_3$, and the aldehyde is extracted into diethyl ether, dried with Na_2SO_4 or $MgSO_4$, and distilled, under reduced pressure. *Alternatively*, salicylaldehyde is precipitated as its Cu complex by adding it to warm, saturated aqueous $Cu(OAc)_2$, shaking and standing in ice. The precipitate is filtered off, washed with EtOH, then Et_2O, and decomposed with 10% H_2SO_4; the aldehyde is extracted into Et_2O, dried and vacuum distilled. It was also purified by dry column chromatography on Kieselgel G [Nishiya et al. *J Am Chem Soc* **108** 3880 *1986*]. The *acetyl* derivative has **m** 38-39° (from petroleum ether or EtOH) and **b** 142°/18mm, 253°/atm. The *oxime*, [94-67-7] **M 137.1**, crystallises $CHCl_3$/petroleum ether (b 40-60°) with m 57°. [*Beilstein* **8** IV 176, 203.]

Salicylamide *[65-45-2]* **M 137.1, m 142-144°, pK^{20} 8.37.** Crystallise the amide from water or repeatedly from $CHCl_3$ [Nishiya et al. *J Am Chem Soc* **108** 3880 *1986*]. [*Beilstein* **10** IV 169.] The *anilide* [87-17-2] **M 213.2**, **m** 135° crystallises from H_2O. [*Beilstein* **12** H 500, **12** I 268, **12** II 256, **12** 944.]

Salicylhydroxamic acid *[89-73-6]* **M 153.1, m 179-180°(dec), pK_1^{30} 2.15, pK_2^{30} 7.46, pK_3^{30} 9.72.** Crystallise the hydroxamic acid from acetic acid. [*Beilstein* **10** H 98.]

Salicylic acid (2-hydroxybenzoic acid) *[69-72-7]* **M 138.1, m 157-159°, 158-160°, 159.5°, 159-160°, 162°, b 211°/20mm, pK_1^{25} 3.01, pK_2^{25} 13.43 (13.01).** It has been purified by steam distillation, by recrystallisation from H_2O (solubility is 0.22% at room temperature and 6.7% at 100°), absolute MeOH, or cyclohexane and by sublimation in a vacuum at 76°. The *acid chloride* (needles) has **m** 19-19.5°, **b** 92°/15mm, the *amide* has **m** 133° (yellow needles from H_2O), the *O-acetyl* derivative has **m** 135° (rapid heating and the liquid resolidifies at 118°), and the *O-benzoyl* derivative has **m** 132° (aqueous EtOH). [IR: Hales et al. *J Chem Soc* 3145 *1954*, Bergmann et al. *J Chem Soc* 2351 *1950*]. [*Beilstein* **10** IV 125.]

Solochrome Violet R [4-hydroxy-3-(2-hydroxynaphthyl-1-ylazo)benzenesulfonic acid] *[2092-55-9]* **M 367.3, CI 15670, λ_{max} 501nm, pK_2^{25} 7.22 (OH), pK_3^{25} 13.39 (OH).** Convert the acid to the monosodium salt by precipitation with NaOAc/AcOH buffer of pH 4, then purify by precipitation of the free acid from aqueous solution with conc HCl, washing and extracting with EtOH in a Soxhlet extractor. The acid precipitates on evaporating the EtOH and is reconverted to the sodium salt as described for *Chlorazole Sky Blue FF*. Dry it at 110°. It is *hygroscopic*. [Coates & Rigg *Trans Faraday Soc* **57** 1088 *1961*, *Beilstein* **16** II 127.]

***cis*-Stilbene** *[645-49-8]* **M 180.3, b 145°/12mm.** Purify it by chromatography on alumina using hexane and distil it under vacuum. (The final product contains *ca* 0.1% of the *trans*-isomer.) [Lewis et al. *J Am Chem Soc* **107** 203 *1985*, Saltiel *J Phys Chem* **91** 2755 *1987*, *Beilstein* **5** H 630.]

***trans*-Stilbene (*trans*-1,2-diphenylethylene)** *[103-30-0]* **M 180.3, m 125.9°, b 305-307°/744mm, d_4^{20} 0.970.** Purify it by vacuum distillation. (The final product contains about 1% of the *cis* isomer.) Crystallise it from EtOH. It has also been purified by zone melting. The *styphnate* (see next entry) has **m** 142°. [Lewis et al. *J Am Chem Soc* **107** 203 *1985*, Bollucci et al. *J Am Chem Soc* **109** 515 *1987*, Saltiel *J Phys Chem* **91** 2755 *1987*, *Beilstein* **5** IV 2156.]

Styphnic acid (2,4,6-trinitroresorcinol) *[82-71-3]* **M 245.1, m 177-178°, 179-180°, pK_1^{25} 0.06 (1.74), pK_2^{25} 4.23 (4.86).** Crystallise the phenol from ethyl acetate or water containing HCl [**EXPLODES violently on rapid heating.]** Its solubility in H_2O is 0.7% at 20° and 3% at 100°. It forms *addition compounds* with aromatic hydrocarbons, e.g. naphthalene (**m** 168°), anthracene (**m** 180°), phenanthrene (**m** 142°), fluorene (**m** 134°) and retene (**m** 141°). [*Beilstein* **6** H 830, **6** III 4354, **6** IV 5699.]

Styrene (vinylbenzene) *[100-42-5]* **M 104.2, b 41-42°/18mm, 145.2°/760mm, d_4^{20} 0.907, n_D^{20} 1.5469, n_D^{25} 1.5441.** Styrene is difficult to purify and keep pure. Usually it contains added inhibitors (such as a trace of hydroquinone). Wash it with aqueous NaOH to remove inhibitors (e.g. *tert*-butanol), then with water, dry it for several hours with $MgSO_4$ and distil it at 25° under reduced pressure in the presence of an inhibitor (such as 0.005% *p-tert*-butylcatechol). It can be stored at -78°. It can also be stored and kept anhydrous with Linde type 5A molecular sieves, CaH_2, $CaSO_4$, BaO or sodium, being fractionally distilled, and distilled in a vacuum line just before use. *Alternatively*, styrene (and its deuterated derivative) are passed through a neutral alumina column before use [Woon et al. *J Am Chem Soc* **108** 7990 *1986*, Collman *J Am Chem Soc* **108** 2588 *1986*]. [*Beilstein* **5** IV 1334.]

(±)-Styrene glycol (±-1-phenyl-1,2-ethanediol) *[93-56-1]* **M 138.2, m 67-68°, 272-274°/755mm.** Crystallise the diol from petroleum ether, Et_2O, Et_2O/*C_6H_6 (**m** 69-70°) or *C_6H_6. The *dibenzoyl dervative* has **m** 96-97°. [*Beilstein* **6** H 907, **6** I 444, **6** II 887, **6** III 4572, **6** IV 5939.]

Styrene oxide *[96-09-3]* **M 120.2, b 84-86°/16.5mm, d_4^{20} 1.053, n_D^{25} 1.535.** Fractional distillation under reduced pressure does not remove phenylacetaldehyde. If this material is present, the styrene oxide is treated with hydrogen under 3 atmospheres pressure in the presence of platinum oxide. The aldehyde, but not the oxide, is reduced to ß-phenylethanol, and separation is now readily achieved by fractional distillation. [Schenck & Kaizermen *J Am Chem Soc* **75** 1636 *1953*, *Beilstein* **17/1** V 577.]

Sudan II (Sudan Blue, Solvent Blue 35, 1,4-bis-(butylamino)-9,10-anthraquinone) *[17354-14-2]* **M 350.5, m 122°, λ_{max} 604, 652nm, pK_{Est} ~9.5 (OH).** It is formed from quinizarin (2g see [81-64-1]), 33% EtOH/*n*-$BuNH_2$ (20ml) and $Na_2S_2O_4$ (2g) at 140°/8 hours, evaporate, extract with toluene, chromatograph (Al_2O_3), the intense blue band in toluene is evaporated, and the residue gave purple needles (Cu lustre) from petroleum ether (b 60-80°) (1.1g, 38%) [Peters & Walker *J Chem Soc* 1429 *1956*, *Beilstein* **14** IV 460]. It forms Cu and Ni salts.

Sudan III [Solvent Red 23, 1-(*p*-phenylazo-phenylazo)-2-naphthol] *[85-86-9]* **M 352.4, m 199°(dec), CI 26100, λ_{max} 354, 508 nm, pK_{Est} ~9.0.** Crystallise the dye from EtOH, EtOH/water or *benzene/absolute EtOH (1:1). [*Beilstein* **16** II 75, **16** III 148, **16** IV 248.]

Sudan IV [Solvent Red 24, 1-(4-*o*-tolylazo-*o*-tolylazo)-2-naphthol] *[85-83-6]* **M 380.5, m ~184°(dec), CI 26105, λ_{max} 520nm, pK_{Est} ~9.0.** Crystallise the dye from EtOH/water or acetone/water. [*Beilstein* **16** IV 249.]

Sulfaguanidine *[57-67-0]* **M 214.2, m 189-190°, pK_1 0.48, pK_2 2.75.** Crystallise the antibacterial from hot water (7ml/g). [*Beilstein* **14** III 1970, **14** IV 2668.]

Sulfanilic acid (4-aminobenzenesulfonic acid) *[121-57-3]* **M 173.2, pK_1^{25} <1, pK_2^{25} 3.23.** Crystallise the acid (as *dihydrate*) from boiling water. Dry it at 105° for 2-3 hours, then over 90% H_2SO_4 in a vacuum desiccator. The *S-benzylisothiuronium salt* has **m** 187° (from aqueous EtOH). [*Beilstein* **14** IV 2655.]

***o*-Sulfobenzoic acid (H_2O)** *[123333-68-6 (H_2O), 632-25-7]* **M 202.2, m 68-69°, $pK_{Est(1)}$<1, $pK_{Est(2)}$~3.1 (CO_2H).** Crystallise the acid from water. The *S-benzylisothiuronium salt* has **m** 205.5-206.5° (from aqueous EtOH). [*Beilstein* **1** II 215, **1** III 658.] The *monoammonium salt [6939-89-5]* **M 219.5**, crystallises from water.

5-Sulfosalicylic acid *[5965-83-3]* **M 254.2, m 108-110°, pK_1^{25} <0, pK_2^{25} 2.67, pK_3^{25} 11.67.** Crystallise the acid from H_2O. *Alternatively*, it is converted to the monosodium salt which is crystallised from H_2O and washed with a little H_2O, EtOH and then Et_2O. The acid is recovered by acidifying. The *S-4-chlorobenzylisothiuronium salt* has **m** 181° (from dioxane). [*Beilstein* **11** H 411, **11** II 232, **11** III 704.]

Syringaldehyde (3,5-dimethoxy-4-hydroxybenzaldehyde) *[134-96-3]* **M 182.2, m 113°, pK_{Est} ~8.** Crystallise syringaldehyde from petroleum ether. [*Beilstein* **8** H 391, **8** IV 2718.]

Syringic acid (3,5-dimethoxy-4-hydroxybenzoic acid) *[530-57-4]* **M 198.2, m 204-205°, 206.5°, 206-209°, 209-210°, pK_1^{25} 4.34, pK_2^{25} 9.49.** Recrystallise syringic acid from H_2O using charcoal [Bogert & Coyne *J Am Chem Soc* **51** 571 *1929*, Anderson & Nabenhauer *J Am Chem Soc* **48** 3001 *1926*.] The *methyl ester* has **m** 107° (from MeOH), the *4-acetyl* derivative has **m** 190° and the *4-benzoyl* derivative has **m** 229-232°. [Hahn & Wassmuth *Chem Ber* **67** 2050 *1934*, UV: Lemon *J Am Chem Soc* **69** 2998 *1947* and Pearl & Beyer *J Am Chem Soc* **72** 1743 *1950*, *Beilstein* **10** IV 1995.]

Terephthalaldehyde *[623-27-8]* **M 134.1, m 116°, b 245-248°/771mm.** Crystallise terephthalaldehyde from water. [*Beilstein* **7** IV 2140.]

Terephthalic acid (benzene-1,4-dicarboxylic acid) *[100-21-0]* **M 166.1, m sublimes >300° without melting, pK_1^{20} 3.4, pK_2^{20} 4.34.** Purify the acid *via* the sodium salt which, after crystallisation from water, is re-converted to the acid by acidification with mineral acid. Filter off the solid, wash it with H_2O and dry it in a vacuum. The *S-benzylisothiuronium salt* has **m** 204° (from aqueous EtOH). [*Beilstein* **9** IV 3301.]

Terephthaloyl chloride *[100-20-9]* **M 203.0, m 80-82°.** Crystallise the acid chloride from dry hexane. [*Beilstein* **9** IV 3318.]

***o*-Terphenyl** *[84-15-1]* **M 230.3, m 58-59°, b 337°/atm.** Crystallise *o*-terphenyl from EtOH. Also purify it by chromatography of CCl_4 solution on alumina, with petroleum ether as eluent, followed by crystallisation from petroleum ether (b 40-60°) or petroleum ether/*C_6H_6. It also distils under vacuum. [*Beilstein* **5** III 2292, **5** IV

2478.]

m-**Terphenyl** *[92-06-8]* **M 230.3, m 88-89°, b 379°/atm.** Purify it as for *o*-terphenyl above. [*Beilstein* **5** IV 2480.]

p-**Terphenyl (1,4-diphenylbenzene)** *[92-94-4]* **M 230.3, m 212.7°, b 389°/atm.** Crystallise *p*-terphenyl from nitrobenzene or trichlorobenzene. It is also purified by chromatography on alumina in a darkened room, using petroleum ether, and then crystallising from petroleum ether (b 40-60°) or petroleum ether/*benzene. It is a fluorophore for scintillation counting and has λ_{ex} 286nm : λ_{em} 343nm in DMF, and λ_{max} at 277nm (logε 4.50). [*Beilstein* **5** IV 2483.]

Terreic acid (2-hydroxy-3-methyl-1,4-benzoquinone-5,6-epoxide) *[121-40-4]* **M 154.1, m 127-127.5°, $[\alpha]_D^{22}$ +74° (pH 4, phosphate buffer), -17° ($CHCl_3$), pK^{25} 4.5.** Crystallise terreic acid from *C_6H_6, *C_6H_6/petroleum ether or hexane. Sublime it 80-100°/1mm. [*Beilstein* **17** IV 6698.]

3',3",5',5"-Tetrabromophenolphthalein ethyl ester *[1176-74-5]* **M 662.0, m 212-214°.** Crystallise the ester from *benzene, dry at 120° and keep it under vacuum. [*Beilstein* **10** III 4490.]

2,3,4,5-Tetrachloroaniline *[634-83-3]* **M 230.9, m 117-118°, 119-120°, pK_{Est} ~–0.26.** Crystallise it from EtOH. The *acetyl* derivative has **m** 165-166° (from EtOH). [*Beilstein* **12** H 630, **12** I 313, **12** II 340, **12** IV 1286.]

2,3,5,6-Tetrachloroaniline *[3481-20-7]* **M 230.9, m 107-108°, pK_{Est} ~–1.8.** Crystallise it from EtOH. The *acetyl* derivative has **m** 213-214° (from EtOH). [*Beilstein* **12** II 340, **12** III 1414, **12** IV 1287.]

1,2,3,4-Tetrachlorobenzene *[634-66-2]* **M 215.9, m 45-46°, 47.5°, b 254°/760mm.** Crystallise it from EtOH. [*Beilstein* **5** H 204, **5** II 156, **5** III 550, **5** IV 667.]

1,2,3,5-Tetrachlorobenzene *[634-90-2]* **M 215.9, m 50-51°, 51°, 54-55°, b 246°/760mm, d^{10} 1.7344.** Crystallise it from EtOH. [*Beilstein* **5** II 157, **5** III 551, **5** IV 668.]

1,2,4,5-Tetrachlorobenzene *[95-94-3]* **M 215.9, m 139.5-140.5°, b 240°/760mm.** Crystallise it from EtOH, ether, *benzene, *benzene/EtOH or carbon disulfide. [*Beilstein* **5** IV 668.]

3,4,5,6-Tetrachloro-1,2-benzoquinone (*o*-chloranil) *[2435-53-2]* **M 245.9, m 130°.** Crystallise *o*-chloranil from AcOH. Dry it in vacuum desiccator over KOH. [*Beilstein* **7** IV 2068.]

Tetrachloro-*N*-methylphthalimide *[14737-80-5]* **M 298.9, m 209.7°.** Crystallise the imide from absolute EtOH. [*Beilstein* **21** H 505, **17/11** V 260.]

2,3,4,6-Tetrachloronitrobenzene (1,2,3,5-tetrachloro-4-nitrobenzene) *[879-39-0]* **M 260.9, m 41-42°, 42°.** Crystallise it from aqueous EtOH. [*Beilstein* **5** II 187, **5** III 617, **5** IV 728.]

2,3,5,6-Tetrachloronitrobenzene (1,2,4,5-tetrachloro-3-nitrobenzene) *[117-18-0]* **M 260.9, m 99-100°.** Crystallise it from aqueous EtOH or H_2O. [*Beilstein* **5** III 617, **5** IV 728.]

2,3,4,5-Tetrachlorophenol *[4901-51-3]* **M 231.9, m 116-117°, pK^{25} 6.95.** Crystallise the phenol from petroleum ether. The *benzoate* has **m** 110° (from EtOH). [*Beilstein* **6** II 182, **6** III 729, **6** IV 1020.]

2,3,4,6-Tetrachlorophenol *[58-90-2]* **M 231.9, m 70°, b 150°/15mm, pK^{25} 5.38.** Crystallise the phenol from petroleum ether. The *benzoate* has **m** 116° (from EtOH). [*Beilstein* **6** H 193, **6** III 729, **6** IV 1021.]

2,3,5,6-Tetrachlorophenol *[935-95-5]* **M 231.9, m 115°, pK^{25} 5.48.** Crystallise the phenol from petroleum ethers. The *benzoate* has **m** 136° (from EtOH). [*Beilstein* **6** II 182, **6** III 730, **6** IV 1025.]

Tetrachlorophthalic anhydride *[117-08-8]* **M 285.9, m 255-257°.** Crystallise the anhydride from chloroform or *benzene, then sublime it in a vacuum. [*Beilstein* **17/11** V 260.]

1,2,4,5-Tetracyanobenzene *[712-74-3]* **M 178.1, m 270-272° (280°).** Crystallise the tetra-nitrile from EtOH and sublime *in vacuo*. [Lawton & McRitchie *J Org Chem* **24** 26 *1959*, Bailey et al. *Tetrahedron* **19** 161 *1963*, *Beilstein* **9** IV 3800.]

Tetrahydroxy-*p*-benzoquinone ($2H_2O$) *[5676-48-2; 123334-16-7 $2H_2O$]* **M 208.1, pK_1^{30} 4,80, pK_2^{30} 6.8.** Crystallise the quinone from water. [*Beilstein* **8** H 534, **8** II 572, **8** III 4204, **8** IV 3604.]

Tetralin (1,2,3,4-tetrahydronaphthalene) *[119-64-2]* **M 132.2, m –35.79° (from CF_2Cl_2), b 65-66°/5mm, 207.6°/760mm, d_4^{20} 0.968, n_D^{20} 1.5413.** Wash tetralin with successive portions of conc H_2SO_4 until the acid layer is no longer coloured, then wash it with aqueous 10% Na_2CO_3, and then distilled water. Dry ($CaSO_4$ or Na_2SO_4), filter, reflux and fractionally distil it under under reduced pressure from sodium or BaO. It can also be purified by repeated fractional freezing.
Bass [*J Chem Soc* 3498 *1964*] freed tetralin, purified as above, from naphthalene and other impurities by conversion to ammonium tetralin-6-sulfonate. Concentrated H_2SO_4 (150ml) is added slowly to stirred tetralin (272ml) which is then heated on a water bath for about 2 hours for complete solution. The warm mixture, when poured into aqueous NH_4Cl solution (120g in 400ml water), gives a white precipitate which, after filtering off, is crystallised from boiling water, washed with 50% aqueous EtOH and dried at 100°. Evaporation of its boiling aqueous solution on a steam bath removes traces of naphthalene. The pure salt (229g) is mixed with conc H_2SO_4 (266ml) and steam distilled from an oil bath at 165-170°. An ether extract of the distillate is washed with aqueous Na_2SO_4, and the ether is evaporated, prior to distilling the tetralin from sodium. Tetralin has also been purified *via* barium tetralin-6-sulfonate, conversion to the sodium salt and decomposed in 60% H_2SO_4 using superheated steam. [*Beilstein* **5** H 491, **5** III 1219, **5** IV 1388.]

Tetralin hydroperoxide *[771-29-9]* **M 164.2, m 55.7-56°, 56°.** Crystallise the tetralin hydroperoxide from hexane, toluene at -30° (**m** 54.0-54.5°). The oxygen content should be ~9.70%. [Knight & Swern *Org Synth* Coll Vol **1V** 895 *1963*.]

α-Tetralone (1,2,3,4-tetrahydro-1-oxonaphthalene) *[529-34-0]* **M 146.2, m 2-7°, 7.8-8.0°, b 75-85°/0.3mm, 89°/0.5mm, 94-95°/2mm, 132-134°/15mm, 143-145°/20mm, d_4^{20} 1.0695, n_D^{20} 1.5665.** Check the IR first. Purify α-tetralone by dissolving 20ml in Et_2O (200ml), washing with H_2O (100ml), 5% aqueous NaOH (100ml), H_2O (100ml), 3% aqueous AcOH (100ml), 5% $NaHCO_3$ (100ml) then H_2O (100ml) and dry the ethereal layer over $MgSO_4$. Filter, evaporate and fractionate the residue through a 6in Vigreux column under reduced pressure to give a colourless oil (~17g) with **b** 90-91°/0.5-0.7mm. [Snyder & Werber *Org Synth* Coll Vol **III** 798 *1955*.] It has also been fractionated through a 0.5metre packed column with a heated jacket under reflux using a partial take-off head. It has λ_{max} at 247.5 and 290nm (hexane). The *phenylhydrazone* has **m** 83°. The *2,4,6-trinitrophenylhydrazone* has **m** 247.5-248° (from EtOH). [Olson & Bader *Org Synth* Coll Vol **IV** 898 *1963*, *Beilstein* **7** H 370, **7** III 1416, **7** IV 1015.]

β-Tetralone (1,2,3,4-tetrahydro-2-oxonaphthalene) *[530-93-8]* **M 146.2, m 17-18°, ~18°, b 93-95°/2mm, 104-105°/4mm, 114-115°/4-5mm, 140°/18mm, d_4^{20} 1.1000, n_D^{20} 1.5598.** If reasonably pure, then fractionate it through an efficient column. Otherwise purify it *via* the *bisulfite adduct*. To a solution of $NaHSO_3$ (32.5g, 0.31mol) in H_2O (57ml) is added 95% EtOH (18ml) and set aside overnight. Any bisulfite-sulfate that separated is removed by filtration, and the filtrate is added to the tetralone (14.6g, 0.1mol) and shaken vigorously. The adduct separates in a few minutes as a white precipitate and is kept on ice for ~3.5 hours with occasional shaking. The precipitate is collected, washed with 95% EtOH (13ml), then with Et_2O (4 × 15ml, by stirring the suspension in the solvent, filtering and repeating the process). The colourless product is dried in air and stored in air tight containers in which it is stable for extended periods (yield is ~17g). This bisulfite (5g) is suspended in H_2O (25ml), and $Na_2CO_3.H_2O$ (7.5g) is added (pH of solution is ~10). The mixture is then extracted with Et_2O (5 × 10ml, i.e. until the aqueous phase does not test for tetralone — see below). Wash the combined extracts with 10% aqueous HCl (10ml), H_2O (10ml, i.e. until the washings are neutral), dry ($MgSO_4$), filter, evaporate and distil the residual oil using a Claisen flask under reduced pressure and in a N_2 atmosphere. The pure

tetralone is a colourless liquid **b** 70-71°/0.25mm (see also above). The yield is ~2g. **Tetralone test:** Dissolve a few drops of the tetralone solution (ethereal or aqueous) in 95% EtOH in a test tube and add 10 drops of 25% NaOH down the side of the tube. A deep blue colour develops at the interface with air. [Soffer et al. *Org Synth* Coll Vol **IV** 903 *1963*, Cornforth et al. *J Chem Soc* 689 *1942*, UV: Soffer et al. *J Am Chem Soc* 1556 *1952*.] The *phenylhydrazone* has **m** 108° [Crawley & Robinson *J Chem Soc* 2001 *1938*]. [*Beilstein* **7** H 370, **7** II 295, **7** III 1422, **7** IV 1018.]

1,2,3,4-Teteramethylbenzene (prehnitine) *[488-23-3]* **M 134.2, m -6.3°, b 79.4°/10mm, 204-205°/760mm, d_4^{20} 0.905, n_D^{20} 1.5203.** Dry it over sodium and distil under reduced pressure. The *picrate* has **m** 92-95° (EtOH). [*Beilstein* **5** H 430, **5** I 206. **5** II 329, **5** III 974, **5** IV 1072.]

1,2,3,5-Tetramethylbenzene (isodurene) *[527-53-7]* **M 134.2, m -23.7°, b 74.4°/10mm, 198°/760mm, d_4^{20} 0.890, n_D^{20} 1.5130.** Reflux isodurene over sodium and distil it under reduced pressure. [Smith *Org Synth* Coll Vol **II** 248 *1943*, *Beilstein* **5** H 430, **5** II 329, **5** III 976, **5** IV 1073.]

1,2,4,5-tetramethylbenzene (durene) *[95-93-2]* **M 134.2, m 79.5-80.5°, 191-192°/760mm.** Chromatograph durene on alumina, and recrystallise it from aqueous EtOH or *benzene. Zone-refining removes duroaldehydes. Dry it under vacuum. [Yamauchi et al. *J Phys Chem* **89** 4804 *1985*.] It has also been sublimed *in vacuo* [Johnston et al. *J Am Chem Soc* **109** 1291 *1987*]. [*Beilstein* **5** H 431, **5** I 207, **5** II 329, **5** III 979, **5** IV 1076.]

***N,N,N′,N′*-Tetramethylbenzidine** *[366-29-0]* **M 240.4, m 195.4-195.6°, $pK_{Est(1)}$~3.4, $pK_{Est(2)}$~4.5.** Crystallise the benzidine from EtOH or petroleum ether, then from petroleum ether/*benzene, and sublime it in a vacuum. [Guarr et al. *J Am Chem Soc* **107** 5104 *1985*.] Dry it *in vacuo* in a drying pistol, or a vacuum line. It has **m** 195-196° after sublimation. [*Beilstein* **13** H 221, **13** I 61, **13** II 97, **13** III 429, **13** IV 368.]

***p,p′*-Tetramethyldiaminodiphenylmethane [bis(*p*-dimethylaminophenyl)methane, Michler's base, (*p,p′*-methylene-bis-(*N,N*-dimethylaniline)]** *[101-61-1]* **M 254.4, m 89-90°, b 155-157°/0.1mm, $pK_{Est(1)}$~5.8, $pK_{Est(2)}$~5.1.** Crystallise the base from EtOH (2ml/g) or 95% EtOH (*ca* 12ml/g). It sublimes on heating. [*Beilstein* **13** IV 390.]

***N,N,N′,N′*-Tetramethyl-1,8-naphthalenediamine [Proton sponge, 1,8-bis-(dimethylamino)-naphthalene** *[20734-58-1]* **M 214.3, m 45-48°, 47-48°, b 144-145°/4mm, pK_1 -10.5 (from half protonation in 86% aqueous H_2SO_4, diprotonation), pK_2 12.34 (monoprotonation).** It is prepared by methylating 1,8-diaminonaphthalene, and likely impurities are methylated products. The tetramethyl compound is a stronger base than the unmethylated, di and trimethylated derivatives. The pKa values are: 1,8-$(NH_2)_2$ = 4.61, 1,8-$(NHMe)_2$ = 5.61, 1-NHMe-8-$NHMe_2$ = 6.43 and 1,8-$(NMe_2)_2$ = 12.34. The mixture is then treated with H_2O at pH 8 (where all but the required base are protonated) and extracted with Et_2O or $CHCl_3$. The dried extract (K_2CO_3) yields the tetramethyldiamine on evaporation which can be distilled. It is a strong base with weak nucleophilic properties, e.g. it could not be alkylated by refluxing with EtI in MeCN for 4 days; and on treatment with methyl fluorosulfonate only the fluorosulfonate salt of the base is obtained. [NMR: Adler et al. *J Chem Soc, Chem Commun* 723 *1968*, Brown & Letang *J Am Chem Soc* **63** 358 *1941*, Brzezinski et al. *J Chem Soc Perkin Trans 2* 857 *1991*.] *Alternatively*, crystallise proton sponge from EtOH and dry it in a vacuum oven. Store it in the dark in a CO_2-free atmosphere. [Benoit et al. *Can J Chem* **65** 996 *1987*, *Beilstein* **13** IV 344.]

***N,N,N′,N′*-Tetramethyl-1,4-phenylenediamine** *[100-22-1]* **M 164.3, m 51°, b 135°/14mm, 260°/760mm, pK_1^{20} 2.29, pK_2^{20} 6.35.** Crystallise the amine from petroleum ether or water. It can be sublimed or dried carefully in a vacuum line, and stored in the dark under nitrogen. It has been recrystallised from its melt. [*Beilstein* **13** H 74, **13** I 22, **13** II 40, **13** III 111, IV 107.]

***N,N,N′,N′*-Tetramethyl-1,4-phenylenediamine dihydrochloride (Wurster's Reagent)** *[637-01-4]* **M 237.2, m 222-224°.** Crystallise the salt from isopropyl or *n*-butyl alcohols, saturated with HCl. Treat it with aqueous NaOH to give the *free base* (see previous entry) which is filtered, dried and sublimed in a vacuum. [Guarr et al. *J Am Chem Soc* **107** 5104 *1985*, *Beilstein* **13** H 74.] Oxidase reagent (1% aqueous solution) used for testing cytochrome +ve aerobic microorganisms.

Tetra(*p*-nitrophenyl)ethylene *[47797-98-8]* **M 512.4, m 298-299°.** Crystallise it from dioxane or AcOH (**m** 292°, yellow needles), and dry it at 150°/0.1mm. [Gorvin *J Chem Soc* 678 *1959*, Schlenk *Justus Liebigs Ann Chem* **394** 214 *1913*, *Beilstein* **5** H 744, **5** IV 2780.]

Tetraphenylethylene *[632-51-9]* **M 332.4, m 223-224°, b 415-425°/760mm.** Crystallise the ethylene from dioxane or from EtOH/*C_6H_6. Sublime it under high vacuum. [*Beilstein* **5** H 743, **5** IV 2780.]

Tetraphenylhydrazine *[632-52-0]* **M 336.4, m 147°, pK_{Est} ~0.** Crystallise the hydrazine from 1:1 $CHCl_3$/toluene, 1:5 $CHCl_3$/EtOH (**m** 149°), *C_6H_6 or *C_6H_6/petroleum ether. Store it in a refrigerator, in the dark. [*Beilstein* **15** H 125, **15** I 29, **15** III 77, **15** IV 59.]

***trans*-1,1,4,4-Tetraphenyl-2-methylbutadiene** *[20411-57-8]* **M 372.5.** Crystallise it from EtOH.

5,6,11,12-Tetraphenylnaphthacene (Rubrene) *[517-51-1]* **M 532.7, m>315°, 322°, d_4^{20} 1.255.** Rubrene forms orange crystals on sublimation at 250-260°/3-4mm [UV Badger & Pearce *Spectrochim Acta* **4** 280 *1950*]. It has also been recrystallised from *benzene under red light because it is chemiluminescent and light sensitive. [*Beilstein* **5** IV 2968.]

1,2,3,4-Tetraphenylnaphthalene *[751-38-2]* **M 432.6, m 199-201°, 204-204.5°.** Crystallise the naphthalene from MeOH or EtOH. [Fieser & Haddadin *Org Synth* **46** 107 *1966*, *Beilstein* **5** IV 2918.]

Thioacetanilide *[677-53-6]* **M 151.2, m 75-76°, 76-79°, pK_{Est} ~13.1.** Crystallise thioacetanilide from H_2O and dry it *in vacuo*. [*Beilstein* **12** H 245, **12** I 193, **12** II 142, **12** III 464, **12** IV 378.]

Thiobenzanilide *[636-04-4]* **M 213.2, m 101.5-102°, pK_{Est} ~12.6.** Crystallise thiobenzanilide from MeOH at Dry-ice temperature.

Thio-Michler's Ketone [4,4'-bis(dimethylamino)thiobenzophenone] *[1226-46-6]* **M 284.4, m 102-106°, λ_{max} 457 nm (ε 2.92 × 10^4 in 30% aqueous *n*-propanol).** Purify the thioketone by recrystallisation from hot EtOH or by trituration with a small volume of $CHCl_3$, followed by filtration and washing with hot EtOH [Terbell & Wystrade *J Phys Chem* **68** 2110 *1964*]. Also it recrystallises from $CHCl_3$/ MeOH. [*Beilstein* **14** H 101, **14** I 395, **14** II 60.]

1-Thionaphthol *[529-36-2]* **M 160.2, b 106°/1.5mm, 208.5°/200mm, d_4^{20} 1.161, n_D^{20} 1.6802, pK^{25} 6.34.** It is steam volatile and is purified by distillation in the absence of O_2, as it oxidises to the disulfide. It is soluble in Et_2O and EtOH but very slightly soluble in H_2O and dilute alkalis. The *S-ethyl* derivative [17539-31-0] **M** 188.2, has **b** 175-176°/25mm, and **d°** 1.120. [*Beilstein* **6** III 2943, **6** IV 4241.]

2-Thionaphthol *[91-60-1]* **M 160.2, m 81.8-82.4°, 82°, b 153.5°/15mm, 286°/760mm, pK^{25} 6.47.** It is steam volatile. It has to be distilled under Ar or N_2, as it oxidises to the disulfide, and crystallises from EtOH. The *S-methyl* derivative has **m** 104-105° (from *C_6H_6/petroleum ether), and the *S-ethyl* derivative [32551-87-4] **M** 188.2, has m 16° and b 175-170.5°/15mm. The *S-acetate* [831-23-2] has **m** 53.5° and **b** 191°/15mm, and the *diethylamine salt* forms yellow needles **m** 107° from dioxane. [*Beilstein* **6** H 657, **6** I 316, **6** II 610, **6** III 3006, **6** IV 4312.]

Thiophenol (benzenethiol) *[108-98-5]* **M 110.2, f -14.9°, b 46.4°/10mm, 168.0°/760mm, d_4^{20} 1.073, n_D^{20} 1.5897, pK^{25} 6.62.** Dry thiophenol with $CaCl_2$ or $CaSO_4$, and distil it at 10mm pressure or at 100mm (**b** 103.5°) in a stream of nitrogen. The *2,4-dinitrophenyl thioether* has **m** 121° (from EtOH), and the *2,4-dinitrophenyl sulfone* has **m** 161° (from EtOH). [*Beilstein* **6** IV 1463.]

Thiosalicylic (2-mercaptobenzoic) acid *[147-93-3]* **M 154.2, m 164-165°, pK_1^{25} 3.54, pK_2^{25} 8.80.** Crystallise the thio acid from hot EtOH (4ml/g), after adding hot distilled water (8ml/g) and boiling with charcoal. The hot solution is filtered, cooled, the solid is collected and dried *in vacuo* (P_2O_5). Crystallise it from AcOH and sublime *in vacuo*. [*Beilstein* **10** IV 272.]

Thymol (2-isopropyl-5-methylphenol) *[89-83-8]* **M 150.2, m 49-51°, 51.5°, b 232°/atm, d^{25} 0.965, n_D^{25} 1.5204, pK^{20} 10.62.** It occurs in the volatile oils of *Thymus vulgaris* and *Moranda punctate* L. from which it was first isolated [Arppe *Justus Liebigs Ann Chem* **58** 41 *1846*]. It is quite volatile at 100°, and is steam volatile, separating as white crystals which have a characteristic pungent odour, with a caustic taste. It should be stored in the dark, preferably under N_2 as it oxidises slowly in air. It possesses antimould properties, is an internal and external antiseptic, and has nematode anthelmintic activity. The *acetate* [528-93-2] is a yellow irritating oil, **b 243.5-245.5°/atm, d^0 1.009**, with the odour of thymol, and is soluble in most organic solvents, but almost insoluble in H_2O. [*Beilstein* **6** IV 3334.]

Thymolphthalein complexone *[1913-93-5]* **M 720.8, m 190°(dec), $pK_1^{18.2}$ 7.35, $pK_2^{18.2}$ 12.25.** Purify it as for phthalein complexone except that it is synthesised from thymolphthalein instead of cresolphthalein. [*Beilstein* **18/4** V 194.]

o-**Tolidine (3,3'-dimethylbenzidine)** *[119-93-7]* **M 212.3, m 131-132°, pK^{25} 4.45.** Dissolve the tolidine in *benzene by percolation through a column of activated alumina and crystallise it from *benzene/petroleum ether. [*Beilstein* **13** IV 410.]

p-**Tolualdehyde** *[104-87-0]* **M 120.2, b 83-85°/0.1mm, 199-200°/760mm, d_4^{20} 1.018, n_D^{20} 1.548.** Steam distil the aldehyde, dry it with $CaSO_4$, then fractionally distil it. [*Beilstein* **7** IV 672.]

o-**Toluamide** *[527-85-5]* **M 135.2, m 141°, 144-145°.** Crystallise *o*-toluamide from hot water (10ml/g) and dry in air. [Noller *Org Synth* Coll Vol **II** 586 *1943*, *Beilstein* **9** H 465, **9** II 319, **9** III 2304.]

Toluene *[108-88-3]* **M 92.1, b 110.6°, d_4^{10} 0.87615, d_4^{25} 0.86231, n_D^{20} 1.49693, n_D^{25} 1.49413.** Dry toluene with $CaCl_2$, CaH_2 or $CaSO_4$, and dry further by standing with sodium, P_2O_5 or CaH_2. It can be fractionally distilled from sodium or P_2O_5. Unless specially purified, toluene is likely to be contaminated with methylthiophenes and other sulfur-containing impurities. These can be removed by shaking with conc H_2SO_4, but the temperature must be kept below 30° if sulfonation of toluene is to be avoided. A typical procedure consists of shaking toluene twice with cold conc H_2SO_4 (100ml of acid per L), once with water, once with aqueous 5% $NaHCO_3$ or NaOH, again with H_2O, then drying successively with $CaSO_4$ and P_2O_5, with final distillation from P_2O_5 or over $LiAlH_4$ after refluxing for 30 minutes. *Alternatively*, the treatment with $NaHCO_3$ can be replaced by boiling under reflux with 1% sodium amalgam. Sulfur compounds can also be removed by prolonged shaking of the toluene with mercury, or by two distillations from $AlCl_3$, the distillate then being washed with water, dried with K_2CO_3 and stored with sodium wire. Other purification procedures include refluxing and distillation of sodium dried toluene from diphenylpicrylhydrazyl, and from $SnCl_2$ (to ensure freedom from peroxides). It has also been co-distilled with 10% by volume of ethyl methyl ketone, and again fractionally distilled. [Brown & Pearsall *J Am Chem Soc* **74** 191 *1952*.] For removal of carbonyl impurities see **benzene*. Toluene has been purified by distillation under nitrogen in the presence of sodium benzophenone ketyl. Toluene has also been dried with $MgSO_4$, after the sulfur impurities have been removed, and then fractionally distilled from P_2O_5 and stored in the dark [Tabushi et al. *J Am Chem Soc* **107** 4465 *1985*]. Toluene can be purified by passage through a tightly packed column of Fuller's earth.
Rapid purification: Alumina, CaH_2 and 4A molecular sieves (3% w/v) may be used to dry toluene (6 hours stirring and standing). Then the toluene is distilled, discarding the first 5% of distillate, and is stored over molecular sieves (3A, 4A) or Na wire. [*Beilstein* **5** H 280, **5** I 144, **5** II 209, **5** III 651, **5** IV 766.]

Toluene-2,4-diamine (4-methyl-*m*-phenylenediamine) *[95-80-7]* **M 122.2, m 99°, b 148-150°/8mm, 292°/760mm, $pK_{Est(1)}$~2.5, $pK_{Est(2)}$~4.4.** Recrystallise the diamine from water containing a very small amount of sodium dithionite (to prevent air oxidation), and dry it under vacuum. It also crystallises from *benzene. [*Beilstein* **13** IV 235.]

o-**Toluenesulfonamide** *[88-19-7]* **M 171.2, m 155.5°.** Crystallise the amide from hot H_2O (**m** 153°), then from EtOH or Et_2O/petroleum ether. The *N*-o-*toluenesulfonylphthalimide* has **m** 182° (from EtOH). [Evans & Dehn *J Am Chem Soc* **51** 3652 *1929*, *Beilstein* **11** H 86, **11** I 23, **11** II 39, **11** III 167, **11** IV 229.]

p-**Toluenesulfonamide** *[70-55-3]* **M 171.2, m 137-137.5°, 138°.** Crystallise the amide from hot water, then from EtOH or Et_2O/petroleum ether. [*Beilstein* **11** H 104, **11** IV 376.]

p-**Toluenesulfonic acid** *[6192-52-5]* **M 190.2, m 38° (anhydrous), m 105-107° (monohydrate), pK^{25} 1.55.** Purify the acid by precipitation from a saturated solution at 0° by introducing HCl gas. It can also be crystallised from conc HCl, then crystallised from dilute HCl (charcoal) to remove benzenesulfonic acid. It has been crystallised from EtOH/water. Dry it in a vacuum desiccator over solid KOH and $CaCl_2$. *p*-Toluenesulfonic acid can be dehydrated by azeotropic distillation with *benzene or by heating at 100° for 4 hours under water-pump vacuum. The anhydrous acid can be crystallised from *benzene, $CHCl_3$, ethyl acetate, anhydrous MeOH, or from acetone by adding a large excess of *benzene. It can also be dried under vacuum at 50°. The *S-benzylisothiuronium salt* has **m** 182° (from aqueous EtOH). [*Beilstein* **11** IV 241.]

Toluenesulfonic acid hydrazide (tosylhydrazide) *[1576-35-8]* **M 186.2, m 108-110°, 109-110°.** Dissolve the hydrazide in hot MeOH (~1g/4ml), filter through Celite and precipitate the material by adding 2-2.5 volumes of distilled H_2O. Dry it in air or in a vacuum. [Fiedman et al. *Org Synth* Coll Vol **V** 1055 *1973*, *Beilstein* **11** II 66.]

p-**Toluenesulfonyl chloride (tosyl chloride)** *[98-59-9]* **M 190.7, m 66-69°, 67.5-68.5°, 69°, b 138-139°/9mm, 146°/15mm, 167°/36mm.** Material that has been standing for a long time contains tosic acid and HCl and has **m** *ca* 65-68°. It is purified by dissolving (10g) in the minimum volume of $CHCl_3$ (*ca* 25ml) filtered, and diluted with five volumes (i.e. 125ml) of petroleum ether (b 30-60°) to precipitate impurities. The solution is filtered, clarified with charcoal and concentrated to 40ml by evaporation. Further evaporation to a very small volume gives 7g of white crystals which are analytically pure, **m** 67.5-68.5°. (The insoluble material is largely tosic acid and has **m** 101-104°.) [Pelletier *Chem Ind (London)* 1034 *1953*.]
It also crystallises from toluene/petroleum ether in the cold, from petroleum ether (b 40-60°) or *benzene. Its solution in diethyl ether has been washed with aqueous 10% NaOH until colourless, then dried (Na_2SO_4) and crystallised by cooling in powdered Dry-ice. It has also been purified by dissolving in *benzene, washing with aqueous 5% NaOH , then dried with K_2CO_3 or $MgSO_4$, and distilled under reduced pressure and can be sublimed at high vacuum [Ebel *Chem Ber* **60** 2086*1927*]. [*Beilstein* **11** IV 375.]

p-**Toluenethiol (*p*-thiocresol)** *[106-45-6]* **M 124.2, m 43.5-44°, pK^{25} 6.82.** Crystallise the thiol from petroleum ether (b 40-70°). The *2,4-dinitrophenyl thioether* has **m** 103° (from EtOH), and the *2,4-dinitrophenyl sulfone* has **m** 190° (from EtOH). [*Beilstein* **6** IV 2153.]

***p*-Toluenethiosulfonic acid potassium salt (potassium *p*-toluenethiosulfonate)** *[28519-50-8]* **M 226.4, m 227-229°.** When a solution of KOH (64.9g, 86.5%, 1.0 mole) in H_2O (28ml) is cooled in an ice bath while it is saturated with H_2S (in an efficient **fume cupboard**) and excess of H_2S is flushed out with N_2 (important to remove excess of H_2S), a fresh solution of KHS is obtained. This is diluted with H_2O (117ml) and stirred, under N_2 at 55-60°, while ground *p*-toluenesulfonyl chloride (95.3g, 0.5mole, freed from any acid by dissolving in *C_6H_6, washing with 5% aqueous NaOH, drying with Na_2SO_4, evaporating and distilling at 146°/15mm) at such a rate as not to allow the temperature to rise above 60°. The deep yellow colour of the solution disappears after 90g is added and the chloride ceases to dissolve. The mixture is filtered rapidly with suction through a warmed funnel, and the filtrate is set aside at 0-5° for many hours. The solid is filtered off, dissolved in hot 80% EtOH (200ml), filtered to remove traces of S, cooled for many hours at 0-5°, and the white crystals of *potassium* p-*toluenethiosulfonate* (48-55g, 42-49%) are collected and air dried. [Woodward et al. *Org Synth* Coll Vol **V** 1016 *1988*, *Org Synth* **54** 33 *1974*, *Beilstein* **11** IV 482.]

Toluhydroquinone (2-methylbenzene-1,4-dione) *[95-71-6]* **M 124.1, m 128-129°, pK$_1^{20}$ 10.15, pK$_2^{20}$ 11.75.** Crystallise the quinone from EtOH. [*Beilstein* **6** IV 5866.]

o-**Toluic acid** *[118-90-1]* **M 136.2, m 102-103°, b 258-259°/760mm, pK^{25} 3.91.** Crystallise the acid from *benzene (2.5ml/g) and dry in air. The *S-benzylisothiuronium salt* has **m** 146° (from aqueous EtOH). [*Beilstein* **9** IV 1697.]

m-**Toluic acid** *[99-04-7]* **M 136.2, m 111-113°, b 263°/760mm, pK^{25} 4.27.** Crystallise the acid from water. [*Beilstein* **9** IV 1712.] Aromatic acid impurities (to <0.05%) can be removed *via* the (±)-α-methylbenzylamine salt as described for 2,4-dichlorobenzoic acid [Ley & Yates *Organic Process Research & Development* **12** 120 *2008*]. The *S-benzylisothiuronium salt* has **m** 140° (from aqueous EtOH).

p-**Toluic acid** *[99-94-5]* **M 136.2, m 178.5-179.5°, b 274-275°/760mm, pK^{25} 4.37.** Crystallise the acid from water, water/EtOH (1:1), MeOH/water or *benzene. [*Beilstein* **9** IV 1724.] Aromatic acid impurities (to <0.05%) can be removed *via* the (±)-α-methylbenzylamine salt as described for 2,4-dichlorobenzoic acid [Ley & Yates *Organic Process Research & Development* **12** 120 *2008*]. The *S-benzylisothiuronium salt* has **m** 164° (from aqueous EtOH).

o-**Toluidine (2-methylaniline)** *[95-53-4]* **M 107.2, f -16.3°, b 80.1°/10mm, 200.3°/760mm, d $_4^{20}$ 0.999, n $_D^{20}$ 1.57246, n $_D^{25}$ 1.56987, pK^{25} 4.45.** In general, methods similar to those for purifying aniline can be used, e.g. distillation from zinc dust, at reduced pressure, under nitrogen. Berliner and May [*J Am Chem Soc* **49** 1007 *1927*] purified it *via* the oxalate. Twice-distilled *o*-toluidine is dissolved in four times its volume of diethyl ether, and the equivalent amount of oxalic acid needed to form the dioxalate is added as its solution in diethyl ether. (If *p*-toluidine is present, its oxalate precipitates and can be removed by filtration.) Evaporation of the ethereal solution gives crystals of *o*-toluidine dioxalate [*Beilstein* **12** III 1494, **12** IV 1817]. These are filtered off, recrystallised five times from water containing a small amount of oxalic acid (to prevent hydrolysis), then treated with dilute aqueous Na_2CO_3 to liberate the amine which is separated, dried ($CaCl_2$) and distilled under reduced pressure. The *benzoyl* derivative has **m** 144° (from EtOH). [*Beilstein* **12** H 772, **12** I 372, **12** II 429, **12** III 1837, **12** IV 1744.]

m-**Toluidine (3-methylaniline)** *[108-44-1]* **M 107.2, f -30.4°, b 82.3°/10mm, 203.4°/ 760mm, d $_4^{20}$ 0.989, n $_D^{20}$ 1.56811, n $_D^{25}$ 1.56570, pK^{25} 4.71.** It can be purified as for aniline. Twice-distilled, *m*-toluidine is converted to the hydrochloride using a slight excess of HCl, and the salt is fractionally crystallised from 25% EtOH (five times), and from distilled water (twice), rejecting, in each case, the first material that crystallised out. The amine is regenerated and distilled as for *o*-toluidine. The *benzoyl* derivative has **m** 125° (from EtOH). [Berliner & May *J Am Chem Soc* **49** 1007 *1927*, *Beilstein* **12** H 853, **12** I 397, **12** II 463, **12** III 1949, **12** IV 1813.]

p-**Toluidine (4-methylaniline)** *[106-49-0]* **M 107.2, m 44.8°, b 79.6°/10mm, 200.5°/ 760mm, d $_4^{20}$ 0.962, n $_D^{20}$ 1.5636, n $_D^{59.1}$ 1.5534, pK^{25} 5.08.** In general, methods similar to those for purifying aniline can be used. It can be separated from the *o*- and *m*-isomers by fractional crystallisation from its melt. *p*-Toluidine has been crystallised from hot water (charcoal), EtOH, *benzene, petroleum ether or EtOH/water (1:4), and dried in a vacuum desiccator. It can also be sublimed at 30° under vacuum. For further purification, use has been made of the oxalate, the sulfate and acetylation. The oxalate, formed as described for *o*-toluidine, is filtered, washed and recrystallised three times from hot distilled water. The base is regenerated with aqueous Na_2CO_3 and recrystallised three times from distilled water. [Berliner & May *J Am Chem Soc* **49** 1007 *1927*.] *Alternatively*, *p*-toluidine is converted to its acetyl derivative which, after repeated crystallisation from EtOH, is hydrolysed by refluxing (50g) in a mixture of 500ml of water and 115ml of conc H_2SO_4 until a clear solution is obtained. The amine sulfate is isolated, suspended in water, and NaOH is added. The free base is distilled twice from zinc dust under vacuum. The *p*-toluidine is then recrystallised from petroleum ether and dried in a vacuum desiccator or in a vacuum for 6 hours at 40°. The *benzoyl* derivative has **m** 158° (from EtOH). [Berliner & Berliner *J Am Chem Soc* **76** 6179 *1954*, Moore et al. *J Am Chem Soc* **108** 2257 *1986*, *Beilstein* **12** H 880, **12** I 140, **12** II 482, **12** III 2017, **12** IV 1866.]

p-**Toluidine hydrochloride** *[540-23-8]* **M 143.6, m 245.9-246.1°.** Crystallise the salt from MeOH containing a few drops of conc HCl or aqueous EtOH. Dry it under vacuum over paraffin chips. [*Beilstein* **12** II 587, **12** III 2021, **12** IV 1869.]

2-*p*-Toluidinylnaphthalene-6-sulfonic acid *[7724-15-4]* **M 313.9, pK$_{Est}$ ~0.** Crystallise the acid twice from 2% aqueous KOH and dry it under high vacuum for 4 hours at room temperature. It also crystallises from H_2O. It is tested for purity by TLC on silica gel with isopropanol as solvent. The free acid is obtained by acidifying a saturated aqueous solution. [*Beilstein* **14** H 762.]

o-**Tolunitrile** *[529-19-1]* **M 117.2, b 205.2°, d $_4^{20}$ 0.992, n $_D^{20}$ 1.5279.** Fractionally distil the nitrile, wash it with conc HCl or 50% H_2SO_4 at 60° until the smell of isonitrile has gone (this also removes any amines), then wash it with saturated $NaHCO_3$ and dilute NaCl solutions, then dry it with K_2CO_3 and redistil it. [*Beilstein* **9** IV 1703.]

m-**Tolunitrile** *[620-22-4]* **M 117.2, b 209.5-210°/773mm, d $_4^{20}$ 0.986, n $_D^{20}$ 1.5250.** Dry the nitrile with $MgSO_4$, fractionally distil it, then wash it with aqueous acid to remove possible traces of amines, dry and redistil it. [*Beilstein* **9** H 477, **9** I 191, **9** II 325, **9** III 2324, **9** IV 1717.]

p-**Tolunitrile** *[104-85-8]* **M 117.2, m 29.5°, b 104-106°/20mm.** Melt the nitrile, dry it with $MgSO_4$, fractionally crystallise it from its melt, then fractionally distil it under reduced pressure in a 6-in spinning band column. [Brown *J Am Chem Soc* **81** 3232 *1959*.] It can also be crystallised from *benzene/petroleum ether (b 40-60°). [*Beilstein* **9** H 489, **9** I 194, **9** II 330, **9** III 2348, **9** IV 1738.]

4-Tolyl-2-benzoic acid (4'-methylbiphenyl-2-carboxylic acid) *[7148-03-0]* **M 212.2, m 138-139°, 146-148°, pK^{25} 3.64.** Crystallise the acid from toluene or *C_6H_6 (**m** 147-148°). [*Beilstein* **9** H 677, **9** IV 2523.]

p-**Tolyl carbinol (4-methylbenzyl alcohol)** *[589-18-4]* **M 122.2, m 59.5-60°, 61°, b 116-118°/20mm, 217°/760mm.** Crystallise the alcohol from petroleum ether (b 80-100°, 1g/ml), Et_2O, pentane or H_2O (**m** 61-62.1°). It can also be distilled in a vacuum. [*Beilstein* **6** H 498, **6** I 248, **6** II 469, **6** III 1779.]

p-**Tolyl disulfide** *[103-19-5]* **M 246.4, m 45-46°, 168°/45mm.** Purify it by chromatography on alumina using hexane as eluent, then crystallise it from MeOH, and/or distil it in a vacuum. [Kice & Bowers *J Am Chem Soc* **84** 2384 *1962*, *Beilstein* **6** H 245, **6** I 212, **6** II 400, **6** III 1432, **6** IV 3206.]

Tolylene-2,4-diisocyanate (toluene-2,4-diisocyanate) *[584-84-9]* **M 174.2, m 19.5-21.5°, 20-22°, 28°, b 126°/11mm, 124-126°/18mm, 250°/760mm.** It is purified by fractionation in a vacuum and should be stored in a dry atmosphere. It is soluble in organic solvents but reacts with H_2O, alcohols (slowly) and amines, all of which could cause explosive polymerisation. It darkens on exposure to light. It has a sharp pungent odour, is **TOXIC** and is **IRRITATING TO THE EYES.** [Siefken *Justus Liebigs Ann Chem* **562** 75, 96, 127 *1949*, Bayer *Angew Chem* **59** 257 *1947*.] It is a reagent for covalent crosslinking of proteins [Wold *Methods Enzymol* **25** 623 *1972*.] [*Beilstein* **13** IV 243.]

Tolylene-2,6-diisocyanate (2-methyl-*m*-phenylenediisocyanate) *[91-08-7]* **M 174.2, b 129-133°/18mm, d^{25} 1.225.** It is purified by fractional distillation in a vacuum. Store it under N_2 in sealed dark ampoules as it is water and light sensitive. Like the preceding 2,4-isomer, it has a sharp pungent odour, is **TOXIC** and is **IRRITATING TO THE EYES.** [*Beilstein* **13** IV 259.]

***p*-Tolylsulfonylmethyl isocyanide (tosylmethyl isocyanide, TOSMIC)** *[36635-61-7]* **M 195.2, m 114-115°(dec), 116-117°(dec).** Use an efficient fume cupboard. Purify TOSMIC by dissolving (50g) in CH_2Cl_2 (150ml) and passing it through a column (40×3cm) containing neutral alumina (100g) in CH_2Cl_2 and eluting with CH_2Cl_2. A nearly colourless solution (700ml) is collected, evaporated *in vacuo* and the residue (42-47g) of TOSMIC (**m** 113-114° dec) is recrystallised once from MeOH (**m** 116-117° dec). [Hoogenboom et al. *Org Synth* **57** 102 *1977*, Lensen *Tetrahedron Lett* 2367 *1972*.] It also crystallises from EtOH (charcoal) [Saito & Itano, *J Chem Soc, Perkin Trans 1* 1 *1986*].
If the reagent had deteriorated considerably it can be synthesised in two steps. *Firstly N-(p-tolylsulfonylmethyl)formamide* is prepared by adding a mixture of aqueous 34-37% formalin (378g, 350ml, ~4.4moles), H_2O (750ml), excess of formamide (680g, 600ml, 15.5moles) and formic acid (244g, 200ml, 5.3moles) to sodium *p*-toluenesulfinate (267g, 1.5moles), and stirring at 90° to form a clear solution; and then heating at 90-95° is continued for 2 hours (prolonged heating diminishes the yield). The mixture is cooled (ice-salt bath) with continuous stirring, and set aside at -20° overnight after seeding. The white solid is collected, washed by stirring with ice-H_2O (3×250ml) and drained well. To removed occluded H_2O, the solid is dissolved in CH_2Cl_2, H_2O is removed (separating funnel), the organic layer is dried ($MgSO_4$), filtered, evaporated, and the residue is dried (over P_2O_5 at 70°) *in vacuo*, to give crude product (134-150g, 42-47%, m 106-110°) which is used in the following step. Pure *N-(p-tolylsulfonylmethyl)formamide*, **m 108-110°,** can be obtained by

recrystallisation from *C_6H_6 or 95% aqueous EtOH.
In the *second step*, with exclusion of moisture, $POCl_3$ (84g, 50ml, 0.55mole) in 1,2-dimethoxyethane (60ml) is added dropwise to a stirred solution of the crude preceding formamide (107g, 0.50mole) in 1,2-dimethoxyethane (250ml), anhydrous Et_2O (100ml) and Et_3N (255g, 350ml, 2.52moles) cooled to -5° (ice-salt bath), at such a rate as to keep the temperature between -5° and 0° (requires ~1 hour). During the reaction, the formamide dissolves, white Et_3NH^+ salts separate, and at the end of the reaction the suspension turns brown in colour. If the mixture is not brownish in colour then more $POCl_3$ needs to be added. Finally the mixture is stirred for 30 minutes at 0° and ice-H_2O (1.5L) is added to give a clear brown solution before a fine brown crystalline solid separates. Stir the mixture for 30 minutes at 0°, collect the solid, wash it with cold H_2O (250ml), dissolve the solid in warm *C_6H_6 (400ml at 40-60°), separate the H_2O, dry the organic layer ($MgSO_4$), filter, add charcoal (2g), heat at 60° for 5 minutes, filter, and add petroleum ether (1L, b 40-60°) with swirling. After 30 minutes, the solid is filtered off, dried *in vacuo* to give crude TOSMIC (74-82g, 76-84%) m 111-114° (dec), which can be used for most purposes. Analytically pure product can be obtained by a *third* purification through neutral Al_2O_3 as stated above. It has IR (Nujol) with ν_{max} at 2150 (N=C), 1320 and 1155 (SO_2) cm^{-1}, and the ^1H NMR ($CDCl_3$) has δ at 7.7 (q, 4H, C_6H_4), 4.6 (s, 2H, CH_2) and 2.5 (s, 3H, CH_3). [Hoogenboom et al. *Org Synth* Coll Vol **VI** 987 *1988*.] It is a versatile reagent, provides a formaldehyde anion or dianion equivalent, is used for the synthesis of various keto compounds and under reducing conditions amino and methylamino compounds have been prepared from the same intermediates, and it has been used for the preparation of several classes of heterocyclic compounds [van Leusen *Lect Heterocycl Chem* **5** S111 *1980*, see also a supplementary issue of Vol **17** of *J Heterocycl Chem*].

p-**Tolyl urea** *[622-51-5]* **M 150.2, m 181°.** Crystallise the urea from H_2O (**m** 186°), EtOH/water (1:1) or aqueous AcOH (**m** 184°). [*Beilstein* **12** H 941, **12** I 425, **12** II 512, **12** III 2084, **12** IV 1923.]

Tribenzylamine *[620-40-6]* **M 287.4, m 93-94°, 230°/13mm, pK_{Est} <0.** Crystallise the amine from absolute EtOH or petroleum ether. Dry it in a vacuum over P_2O_5 at room temperature. The *hydrochloride* has **m** 226-228° (from EtOH) and the *picrate* has **m** 191° (from H_2O or aqueous EtOH). [*Beilstein* **12** IV 2183.]

2,4,6-Tribromoacetanilide *[607-93-2]* **M 451.8, m 232°, 238-240°, 240°.** Crystallise the anilide from EtOH. [*Beilstein* **12** II 359, **12** III 1478.]

2,4,6-Tribromoaniline *[147-82-0]* **M 329.8, m 120°, 122°, pK_{Est} ~-0.5 (aqueous H_2SO_4).** Crystallise the aniline from MeOH. The *benzenesulfonamide* derivative has **m** 198°. [*Beilstein* **12** H 663, **12** I 329, **12** II 358, **12** III 1477, **12** IV 1538.]

***sym*-Tribromobenzene (1,3,5-tribromobenzene)** *[626-39-1]* **M 314.8, m 122°.** Crystallise it from glacial acetic acid/water (4:1), then wash with chilled EtOH and dry in air. [*Beilstein* **5** H 213, **5** IV 685.]

2,4,6-Tribromophenol *[118-79-6]* **M 330.8, m 94°, pK^{25} 6.00.** Crystallise the phenol from EtOH or petroleum ether. Dry it under vacuum over P_2O_5 at room temperature. [*Beilstein* **6** IV 1067.]

***sym*-Tri-*tert*-butylbenzene** *[1460-02-2]* **M 246.4, m 73.4-73.9°.** Crystallise it from EtOH. [*Beilstein* **5** IV 1206.]

2,4,6-Tri-*tert*-butylphenol *[732-26-3]* **M 262.4, m 129-132°, 131-131.2°, b 131°/1mm, 147°/10mm, 278°/760mm, pK^{25} 12.19.** Distil the phenol under reduced pressure and/or recrystallise it from *n*-hexane or several times from 95% EtOH until the EtOH solution is colourless [Balasubramanian & Bruice *J Am Chem Soc* **108** 5495 *1986*]. It has also been purified by sublimation [Yuan & Bruice *J Am Chem Soc* **108** 1643 *1986*, Wong et al. *J Am Chem Soc* **109** 3428 *1987*]. Purification has also been achieved by passage through a silica gel column followed by recrystallisation from *n*-hexane [Kajii et al. *J Phys Chem* **91** 2791 *1987*]. [*Beilstein* **6** III 2094, **6** IV 3539.]

Trichloroacetanilide *[2563-97-5]* **M 238.5, m 93.5-94°, 95°.** Crystallise the anilide from *benzene or 90% EtOH (**m** 93.5-95.5°). [Sukornick *Org Synth* Coll Vol **V** 1074 *1973*, *Beilstein* **12** H 224, **12** I 193, **12** II 142, **12**

III 464, **12** IV 377.]

2,3,4-Trichloroaniline *[634-67-3]* **M 196.5, m 67.5°, b 292°/774mm, pK_{Est} ~1.3.** Crystallise the aniline from ligroin. The *acetanilide* has **m** 120-122° (from EtOH or *C_6H_6). [*Beilstein* **12** H 626.]

2,4,5-Trichloroaniline *[636-30-6]* **M 196.5, m 96.5°, b 270°/760mm, pK 1.09.** Crystallise the aniline from ligroin. [*Beilstein* **12** H 627, **12** IV 1277.]

2,4,6-Trichloroaniline *[634-93-5]* **M 196.5, m 78.5°, b 127°/14mm, 262°/746mm, pK^{25} 0.03.** Crystallise the aniline from ligroin. The *benzoyl* derivative has **m** 174° (from EtOH). [*Beilstein* **12** H 627, **12** IV 1281.]

1,2,3-Trichlorobenzene *[87-61-6]* **M 181.5, m 52.6°.** Crystallise it from EtOH. [*Beilstein* **5** IV 664.]

1,2,4-Trichlorobenzene *[120-82-1]* **M 181.5, m 17°, b 210°.** Separate it from a mixture of isomers by washing with fuming H_2SO_4, then water, drying with $CaSO_4$ and slowly fractionally distilling. [Jensen et al. *J Am Chem Soc* **81** 3303 *1959*, *Beilstein* **5** IV 664.]

1,3,5-Trichlorobenzene *[108-70-3]* **M 181.5, m 64-65°.** Recrystallise it from dry *benzene or toluene. [*Beilstein* **5** IV 666.]

3,4,5-Trichloro-*o*-cresol (3,4,5-trichloro-2-methylphenol) *[608-92-4]* **M 211.5, m 77°, pK_{Est} ~7.6.** Crystallise the cresol from petroleum ether.

2,3,5-Trichloro-*p*-cresol (2,3,,5-trichloro-4-methylphenol) *[608-91-3]* **M 211.5, m 66-67°, pK_{Est} ~6.9.** Crystallise the cresol from petroleum ether. [Datta & Mitter *J Am Chem Soc* **41** 2034 *1919*, *Beilstein* **6** I 204.]

2,4,5-Trichloro-1-nitrobenzene (1,2,4-trichloro-5-nitrobenzene) *[89-69-0]* **M 226.5, m 57°.** Crystallise it from EtOH. [*Beilstein* **5** IV 728.]

3,4,6-Trichloro-2-nitrophenol *[82-62-2]* **M 242.4, m 92-93°, pK_{Est} ~4.1.** Crystallise the nitro-phenol from petroleum ether or EtOH. [*Beilstein* **6** III 842.]

2,4,5-Trichlorophenol *[95-95-4]* **M 197.5, m 67°, b 72°/1mm, 248°/740mm, pK^{25} 7.0.** Crystallise the phenol from EtOH or petroleum ether. [*Beilstein* **6** IV 962.]

2,4,6-Trichlorophenol *[88-06-2]* **M 197.5, m 67-68°, b 246°/760mm, pK^{25} 6.23.** Crystallise the phenol from *benzene, EtOH or EtOH/water. [*Beilstein* **6** IV 1005.]

3,4,5-Trichlorophenol *[609-19-8]* **M 197.5, m 100°, pK^{25} 7.84.** Crystallise the phenol from petroleum ether/*benzene mixture. [*Beilstein* **6** III 729.]

2,4,5-Trichlorophenoxyacetic acid (2,4,5-T) *[93-76-5]* **M 255.5, m 153°, 155-158°, pK^{25} 2.83.** Crystallise this herbicide from *benzene. **[***Beilstein* **6** III 721.] **(CANCER SUSPECT)**

1,2,4-Triethylbenzene *[877-44-1]* **M 162.3, b 96.8-97.1°/12.8mm, d_4^{20} 0.8738, n_D^{20} 1.5015.** For separation from a commercial mixture see Dillingham and Reid [*J Am Chem Soc* **60** 2606 *1938*]. [*Beilstein* **5** IV 1133.]

1,3,5-Triethylbenzene *[102-25-0]* **M 162.3, b 102-102.5°, d_4^{20} 0.8631, n_D^{20} 1.4951.** For separation from a commercial mixture see Dillingham and Reid [*J Am Chem Soc* **60** 2606 *1938*]. [*Beilstein* **5** IV 133.]

4-(Trifluoromethyl)acetophenone *[709-63-7]* **M 188.2, m 31-33°, b 79-81°/9mm.** Purify the ketone by distillation or sublimation *in vacuo*. [*Beilstein* **7** IV 1404.]

3-Trifluoromethyl-4-nitrophenol *[88-30-2]* **M 162.1, m 81°, b 135-138°/0.01mm, pK_{Est} ~6.1.** Crystallise

the nitrophenol from *benzene or from petroleum ether/*benzene mixture. [*Beilstein* **6** III 1328.]

α,α,α-Trifluorotoluene (benzotrifluoride) *[98-08-8]* **M 144.1, b 102.5°, d_4^{20} 1.190, n^{30} 1.4100.** Purify benzotrifluoride by repeated treatment with boiling aqueous Na_2CO_3 (until no test for chloride ion is obtained), dry it with K_2CO_3, then with P_2O_5, and fractionally distil it. [*Beilstein* **5** IV 802.]

2,3,4-Trihydroxybenzoic acid *[610-02-6]* **M 170.1, m 207-208°, $pK_{Est(1)}$ ~3.4, $pK_{Est(2)}$ ~7.8, $pK_{Est(3)}$ >12.** Crystallise the acid from water. [*Beilstein* **10** IV 1971.]

2,4,6-Trihydroxybenzoic acid *[83-30-7]* **M 170.1, m 205-212°(dec), $pK_{Est(1)}$ ~1.5, $pK_{Est(2)}$ ~8.0, $pK_{Est(3)}$ >12.** Crystallise the acid from water. [*Beilstein* **10** IV 1987.]

3,4,5-Triiodobenzoic acid *[2338-20-7]* **M 499.8, m 289-290°, 293°, pK^{25} 0.65.** Crystallise the acid from aqueous EtOH or water. [*Beilstein* **9** H 367, 9 III 1475.]

3,4,5-Triiodobenzyl chloride *[52273-54-8]* **M 504.3, m 138°.** Crystallise the chloride from CCl_4/petroleum ether (charcoal).

Trimellitic (benzene-1,2,4-tricarboxylic) acid *[528-44-9]* **M 210.1, m 218-220°, pK_1^{25} 2.42, pK_2^{25} 3.71, pK_3^{25} 5.01.** Crystallise the acid from acetic acid or aqueous EtOH. [*Beilstein* **9** IV 3746.]

1,2,3-Trimethoxybenzene *[634-36-6]* **M 168.2, m 45-46°.** Sublime it under vacuum. [*Beilstein* **6** H 1081, **6** I 540, **6** II 1066, **6** III 6265, **6** IV 7329.]

1,3,5-Trimethoxybenzene *[621-23-8]* **M 168.2, m 53°.** Sublime it under vacuum. [*Beilstein* **6** III 635, **6** IV 7362.]

3,4,5-Trimethoxyphenol (Antiarol) *[642-71-7]* **M 184.2, m 146°, 145-149°, pK_{Est} ~9.4.** Recrystallise the phenol from 10 times its weight of H_2O (white needles, **m** 148°). The *acetyl* derivative crystallises as elongated prisms from EtOH with **m** 74°. [Chapman et al. *J Chem Soc* 3028 *1927*, Shriner et al. *J Am Chem Soc* **61** 2325 *1939*, *Beilstein* **6** H 1154, **6** II 1118, **6** III 6656.]

1,2,4-Trimethylbenzene (pseudocumene) *[95-63-6]* **M 120.2, m -43.8°, b 51.6°/10mm, 167-168°/760mm, d_4^{20} 0.889, n_D^{20} 1.5048.** Reflux pseudocumene over sodium and distil it under reduced pressure. [*Beilstein* **6** H 1088, **6** I 542, **6** II 1072, **6** III 6278, **6** IV 7339.]

2,4,6-Trimethylbenzoic acid (mesitoic acid) *[480-63-7]* **M 164.2, m 155°, pK^{25} 3.45.** Crystallise mesitoic acid from water, ligroin or carbon tetrachloride [Ohwada et al. *J Am Chem Soc* **108** 3029 *1986*]. [*Beilstein* **9** H 553, **9** I 214, **9** II 360, **9** III 2489, **9** IV 1854.]

Trimethyl-1,4-benzoquinone *[935-92-2]* **M 150.1, m 29-30°, 36°, b 98°/10mm, 108°/18mm.** Distil the quinone in a vacuum or sublime it *in vacuo* before use. [Smith et al. *J Am Chem Soc* **60** 318 *1939*, *Beilstein* **7** H 161, **7** III 3407, **7** IV 2098.]

1,3-S,S'-Trimethylene di(*p*-toluenethiosulfonate) [1,3-di(*p*-tosylthio)propane, 1,3-trimethylene di(thiotosylate)] *[3866-79-3]* **M 416.6, m 64-67°.** This reagent is prepared from potassium thiosulfonate (40g, 0.18 mole, see above [28519-50-8]) and 1,3-dibromopropane (20g, 0.1 mole) which are added to a solution of 95% EtOH (150ml) containing KI (10-20mg, to activate the dibromide), and the stirred mixture is boiled under reflux in the dark under N_2 for 8 hours. After cooling to ~25°, the mixture is diluted with an equal volume of cold H_2O and shaken. After the mixture settles, the supernatant is removed by decantation, the pale yellow residual oil is washed with cold H_2O (3 × 200ml), once with cold 95% EtOH (100ml) and once with cold absolute EtOH (100ml) also by decantation. The oil is then dissolved in Me_2CO (10ml), diluted with hot absolute EtOH (80ml), and stirred under N_2 at 0°. If some oil separates, it should be re-dissolved by adding enough Me_2CO (say ~5ml). The solution is seeded with crystals (a small portion of the oil stored at -30° for a few days crystallises and is

used as seed*), stirred under N_2 at 0° for 1 hour then for several hours at -30°. The microcrystals are collected (20.2g) and have **m 63.5-65.0°.** This can be used for reactions; but if purer material is required then it should be recrystallised three times from EtOH (180ml, 9 parts) to provide white needles (17.2g, 41%) with **m 66-67°**. The *thioester* always separates as an oil when solutions are cooled to room temperature.
*If it is difficult to crystallise the ester then seed crystals could be obtained by chromatography through a column of Woelm neutral alumina (Activity Grade I) and eluting with *C_6H_6. The centre fractions giving solid with m 67° are combined and recrystallised from EtOH (9parts) to give the pure *trimethylene dithiotosylate* with **m 67.5°**. On a Durapak-Carbowax 400/Poracil C column (Waters Associates, 3ft x 0.125in) with $CHCl_3$ as eluent it exhibits a single peak. It has IR ($CHCl_3$) with ν_{max} at 810 (m), 1015 (w), 1075 (s), 1140 (s), 1180 (w), 1300 (m), 1325 (s), 1410 (w), 1440 (w), 1490 (w), 1590 (w), 2930 (w), and 3030 (w) cm^{-1}; and the ^1H NMR ($CDCl_3$, TMS) has δ at 1.98 (quintet, *J* = 7Hz, 2H, $CH_2C\boldsymbol{H}_2CH_2$), 2.43 (s, 6H, $2C\boldsymbol{H}_3$), 2.97 (t, *J* = 7Hz, 4H, $C\boldsymbol{H}_2CH_2C\boldsymbol{H}_2$), 7.30 (d, *J* = 9Hz, 4H, Arom) and 7.75 (d, *J* = 9Hz, 4H, Arom). [Woodward et al. *Org Synth* Coll Vol **V** 1016 *1988*, *Org Synth* **54** 33 *1974*.]
This reagent is useful for the synthesis of 1,3-dithianes from carbonyl compounds and activated methylene groups. Thus a ketone (0.163mmol), reagent (0.218mmol) and dry NaOK (0.907mmol) in EtOH (6ml) are refluxed for 6 hours, dilute with CH_2Cl_2, wash with aqueous $NaHCO_3$, evaporate extract and purify the residue through a silica gel column by eluting with 1:2 EtOAc/hexane containing 2% of *N*-methylpyrrolidine to give the desired 1,3-dithiane [McMurray et al. *J Org Chem* **49** 3803 *1984*, see also Saksena & Ganguli *Tetrahedron Lett* **22** 5227 *1981*]. It also forms 1.3-dithianes, e.g. 2,2-(trimethylenedithio)cyclohexanone, from the respective enamine, i.e. 1-pyrrolidinecyclohex-1-ene [Woodward et al. *Org Synth* **54** 39 *1974*].

Trimethyl-1,4-hydroquinone (2,3,5-trimethylbenzene-1,4-diol) *[700-13-0]* **M 152.2, m 173-174°, $pK_{Est(1)}$~ 11.1, $pK_{Est(2)}$~ 12.7.** Recrystallise the hydroquinone from water, under anaerobic conditions. [*Beilstein* **6** H 931, **6** IV 5997.]

2,3,5-Trimethylphenol *[697-82-5]* **M 136.2, m 95-96°, b 233°/760mm, pK^{25} 10.67.** Crystallise the phenol from water or petroleum ether. [*Beilstein* **6** IV 3248.]

2,4,5-Trimethylphenol *[496-78-6]* **M 136.2, m 70.5-71.5°, pK^{25} 10.57.** Crystallise the phenol from water. [*Beilstein* **6** H 509, **6** I 255, **6** II 482, **6** III 1831, **6** IV 3247.]

2,4,6-Trimethylphenol *[527-60-6]* **M 136.2, m 69°, b 220°/760mm, pK^{25} 10.86.** Crystallise the phenol from water and sublime it *in vacuo.* [*Beilstein* **6** IV 3253.]

3,4,5-Trimethylphenol *[527-54-8]* **M 136.2, m 107°, b 248-249°/760mm, pK^{25} 10.25.** Crystallise the phenol from petroleum ether. [*Beilstein* **6** IV 3245.]

Trimethylphenylammonium benzenesulfonate *[16093-66-6]* **M 293.3.** Crystallise it repeatedly from MeOH (charcoal). [*Beilstein* **12** IV 249.]

2,4,6-Trinitroanisole *[606-35-9]* **M 243.1, m 68°.** Crystallise it from EtOH or MeOH. Dry it *in vacuo*. [*Beilstein* **6** H 288, **6** I 140, **6** II 280, **6** III 968, **6** IV 1456.]

1,3,6(1,2,4)-Trinitrobenzene *[99-35-4]* **M 213.1, m 122-123°.** Crystallise it from glacial acetic acid, $CHCl_3$, CCl_4, EtOH aqueous EtOH or EtOH/*benzene, after (optionally) heating with dilute HNO_3. Dry it in air. Fuse it and crystallise it under vacuum. [*Beilstein* **5** H 271, 5 I 140, **5** II 203, **5** III 643, **5** IV 754.]

2,4,6-Trinitrobenzenesulfonic acid hydrate (TNBS, picrylsulfonic acid) *[2508-19-2]* **M 293.2, m 180°, λ_{max} 240nm (ε 650 $M^{-1}cm^{-1}$), pK_{Est}~ <0.** It is also available as 0.1M and 5%w/v solutions in H_2O. Recrystallise TNBS from 1M HCl, or a mixture of EtOH (50ml), H_2O (30ml) and conc HCl (70ml) for 65g of acid, and dry it at 100°. The *diethanolamine salt* had **m** 182-183° [Golumbic *J Org Chem* **11** 518 *1946*]. [*Beilstein* **11** III 161.]

2,4,6-Trinitrobenzoic acid *[129-66-8]* **M 225.1, m 227-228°, pK^{25} 0.65.** Crystallise the acid from distilled H_2O. Dry in a vacuum desiccator. The *amide* has **m** 264° (from EtOH). [*Beilstein* **9** H 417, **9** I 168, **9** II 285, **9** III 1956, **9** IV 1362.]

2,4,6-Trinitro-*m*-cresol *[602-99-3]* **M 243.1, m 107.0-107.5°, pK^{25} 2.8.** Crystallise the cresol successively from H_2O, aqueous EtOH and *benzene/cyclohexane, then dry at 80° for 2 hours. [Davis & Paabo *J Res Nat Bur Stand* **64A** 533 *1960*, *Beilstein* **6** H 387, **6** I 194, **6** II 363, **6** III 1331, **6** IV 2079.]

2,4,7-Trinitro-9-fluorenone *[129-79-3]* **M 315.2, m 176°.** Crystallise it from nitric acid/water (3:1), wash it with water and dry it under vacuum over P_2O_5, or recrystallise it from dry *benzene. [*Beilstein* **7** II 410, **7** III 2348, **7** IV 1638.]

2,4,6-Trinitrotoluene (TNT) *[118-96-7]* **M 227.1, m 81.0-81.5°.** Crystallise TNT from *benzene and EtOH. Then fuse **(CARE)** and allow to crystallise under vacuum. Gey, Dalbey and Van Dolah [*J Am Chem Soc* **78** 1803 *1956*] dissolved TNT in acetone and added cold water (1:2:15), the precipitate was filtered off, washed free from solvent and stirred with five parts of aqueous 8% Na_2SO_3 at 50-60° for 10 minutes. This was filtered, washed with cold water until the effluent was colourless, and air dried. The product was dissolved in five parts of hot CCl_4, washed with warm water until the washings were colourless and TNT was recoverd by cooling and filtering. It was recrystallised from 95% EtOH and carefully dried over H_2SO_4. The dry solid should not be heated without taking precautions for a possible **EXPLOSION**. Work with small quantities. [*Beilstein* **5** H 347, **5** I 172, **5** II 268, **5** III 767, **5** IV 873.]

2,4,6-Trinitro-*m*-xylene *[632-92-8]* **M 241.2, m 182.2°.** Crystallise the xylene from ethyl methyl ketone. [*Beilstein* **5** H 381, **5** I 185, **5** II 295, **5** III 845, **5** IV 950.]

Triphenylamine *[603-34-9]* **M 245.3, m 127.3-127.9°, pK^{25} -5.0 (in fluorosulfuric acid).** Crystallise the amine from EtOH or from *benzene/absolute EtOH, diethyl ether and petroleum ether. It is sublimed under vacuum and carefully dried in a vacuum line. Store it in the dark under nitrogen. [*Beilstein* **12** IV 276.]

1,3,5-Triphenylbenzene *[612-71-5]* **M 306.4, m 171-172°, 173-175°, 176°, d $^{0}_{4}$ 1.205.** Purify it by chromatography on alumina using *benzene or petroleum ether as eluents. Crystallise the triphenylbenzene from EtOH (**m** 174°). [*Beilstein* **5** H 737, **5** I 370, **5** II 670, **5** III 2563, **5** IV 2732.]

Triphenylene *[217-59-4]* **M 228.3, m 198°, b 425°.** Purify triphenylene by zone refining or crystallisation from EtOH or $CHCl_3$ and sublime. [*Beilstein* **5** IV 2556.]

1,2,3-Triphenylguanidine *[101-01-9]* **M 287.3, m 144°, pK^{25} 9.10.** Crystallise the guanidine from EtOH or EtOH/water. Dry it *in vacuo*. [*Beilstein* **12** H 451, **12** I 261, **12** II 246, **12** III 907, **12** IV 866.]

Triphenylmethane *[519-73-3]* **M 244.3, m 92-93°.** Crystallise triphenylmethane from EtOH or *benzene (with one molecule of *benzene of crystallisation which is lost on exposure to air or by heating on a water bath). It can also be sublimed under vacuum. It has been given a preliminary purification by refluxing with tin and glacial acetic acid, then filtered hot through a glass sinter disc, and precipitated by addition of cold water. [*Beilstein* **5** H 698, **5** IV 2495.]

Triphenylmethanol (triphenylcarbinol) *[76-84-6]* **M 260.3, m 164°, b 360-380° (without dec), pK^{25} -6.63 (aqueous H_2SO_4).** Crystallise the carbinol from EtOH, MeOH, CCl_4 (4ml/g), *benzene, hexane or petroleum ether (b 60-70°). Dry it at 90°. [Ohwada et al. *J Am Chem Soc* **108** 3029 *1986*, *Beilstein* **6** IV 5014.]

Triphenylmethyl chloride (trityl chloride) *[76-83-5]* **M 278.9, m 111-112°, b 230-235°/20mm.** Crystallise trityl chloride from iso-octane. Also crystallise it from 5 parts of petroleum ether (b 90-100°) and 1 part of acetyl chloride using 1.8g of solvent per g of chloride. Dry it in a desiccator over soda lime and paraffin wax. [Bachman *Org Synth* Coll Vol **III** 841 *1955*, Thomas & Rochow *J Am Chem Soc* **79** 1843 *1957*, Moisel et al. *J Am Chem Soc* **108** 4706 *1986*, *Beilstein* **5** H 750, **5** I 346, **5** II 615, **5** III 2315, **5** IV 2497.] It is moisture

sensitive, store in a well sealed container. **LACHRYMATORY**.

***dl*-Tropic [(3-hydroxy-2-phenylpropionic) acid, Tropaic acid]** *[529-64-6]* **M 166.2, m 116-117°, 118°, pK^{25} 4.12.** Tropic acid crystallises from H_2O or $*C_6H_6$ in needles or plates. It is the (±)-acid component (*dl*-tropyl ester) of atropine [51-55-8]. It is best prepared from acetophenone cyanohydrin *via* atrolactic acid [515-30-0], atropic acid, *chlorohydratropic acid* followed by hydrolysis of the latter in boiling aqueous 1.73N Na_2CO_3 in high yielding steps. No racemisation occurred when chiral intermediates were used (see next entry). [McKenzie & Wood *J Chem Soc* **115** 828 *1919*, McKenzie & Strathern *J Chem Soc* **127** 86 *1925*.] [*Beilstein* **10** IV 664.]

***S*(−)-Tropic acid [(−)3-hydroxy-2-phenylpropionic acid]** *[16202-15-6]* **M 166.2, m 128-129°, $[\alpha]_D^{13}$ −72.5° (c 2.6, EtOH), $[\alpha]_D^{15}$ −79.0° (c 1.5, H_2O), $[\alpha]_D^{15}$ −83.3° (c 1.8, Me_2CO).** It is the (−)-acid component of ***l*-hyoscyamine** (i.e *l*-tropyl atropine, [101-31-5]). It has been prepared by optical resolution of (±)-tropic acid using the quinine diastereomeric salt for obtaining (+)-tropic acid, and then with the morphine diastereomeric salt for obtaining the natural (−)-tropic acid. The salts were hydrolysed with dilute H_2SO_4, extracted thoroughly into Et_2O, dried (Na_2SO_4), evaporated, and the residue was recrystallised from $*C_6H_6$ (in which it is sparingly soluble) to give lustrous needles m 128-129°. It also crystallises from H_2O in glassy needles and plates grouped in rosettes. The enantiomer, obtained in the same way, has identical properties except for opposite rotations. [McKenzie & Wood *J Chem Soc* **115** 828 *1919*, McKenzie & Strathern *J Chem Soc* **127** 86 *1925*]. The absolute configuration of the (−)-tropic acid was deduced as *S*- by conversion into (+)-alanine. [Fedor & Csepreghy *J Chem Soc* 3222 *1961*, for enzymic kinetic resolution see Klomp et al. *Tetrahedron Asymmetry* **16** 3892 *2005*.]

Tropolone (2-hydroxycyclohepta-2,4.6-trien-1-one) *[533-75-5]* **M 122.1, m 49-50°, b 81-84°/0.1mm, pK_1 -0.53 (protonation of CO, aqueous H_2SO_4), pK_2 6.67 (acidic OH).** Crystallise tropolone from hexane or petroleum ether and sublime it at 40°/4mm. Also distil it at high vacuum. [*Beilstein* **8** IV 159.]

Tyramine (4-hydroxybenzylamine) *[51-67-2]* **M 137.2, m 164-165°, b 171-181°/8mm, pK_1^{25} 9.74 (OH), pK_2^{25} 10.52 (NH_2).** Crystallise tyramine from *benzene or EtOH. [*Beilstein* **13** IV 1788.]

Tyramine hydrochloride *[60-19-5]* **M 173.6, m 274-276°.** Crystallise the hydrochloride from EtOH by addition of diethyl ether, or from conc HCl. [*Beilstein* **3** II 355.]

Vanillin (4-hydroxy-3-methoxybenzaldehyde) *[121-33-5]* **M 152.2, m 83°, b 170°/15mm, pK^{25} 7.40.** Crystallise vanillin from water or aqueous EtOH, or by distillation *in vacuo*. [*Beilstein* **8** IV 1763.]

Veratraldehyde (vanillin methyl ether) *[120-14-9]* **M 166.2, m 42-43°.** Crystallise the ether from diethyl ether, petroleum ether, CCl_4 or toluene. [*Beilstein* **8** IV 1765.]

Variamine Blue RT [4-(phenylamino)benzenediazonium sulfate (1:1)] *[4477-28-5]* **M 293.3, m 120°(dec), CI 37240, λ_{max} 377 nm.** Dissolve 10g of the dye in 100ml of hot water. Sodium dithionite (0.4g) is then added, followed by active carbon (1.5g) and is filtered hot. To the colourless or slightly yellow filtrate a solution of saturated NaCl is added, and the mixture is cooled. The needles are filtered off, washed with cold water, dried at room temperature, and stored in a dark bottle (light sensitive). [Anderson & Steedly *J Am Chem Soc* **76** 5144 *1954*, Erdey *Chem Analyst* **48** 106 *1959*, *Beilstein* **16** H 602, **16** I 371, **16** II 307, **16** III 575.]

9-Vinylanthracene *[2444-68-0]* **M 204.3, m 65-67°, b 61-66°/10mm.** Purify it by vacuum sublimation. It has also been purified by chromatography on silica gel with cyclohexane as eluent, and recrystallised from EtOH [Werst et al. *J Am Chem Soc* **109** 32 *1987*]. [*Beilstein* **5** IV 2415.]

4-Vinylbenzyl chloride (4-chloromethylstyrene) *[1592-20-7]* **M 152.6, b 58-62°/0.4mm, 75.5-79°/2mm, 229°/760mm, d^{25} 1.083, n_D^{20} 1.572.** Purify 4-vinylbenzyl chloride by dissolving it in Et_2O, washing it with 0.5% of aqueous NaOH, separating, drying the organic layer (Na_2SO_4), evaporating and distilling the residual oil under N_2 *in vacuo*. Add 0.05% of 4-*tert*-butylcatechol as stabiliser. It is **lachrymatory.** [Nishikubo et al. *Tetrahedron Lett* **22** 3872 *1981*, Tanimoto et al. *Synth Commun* **4** 193 *1974*, *Beilstein* **6** IV 3818.]

1-Vinylnaphthalene *[826-74-4]* **M 154.2, b 68-69°/0.4mm, 100-101°/3.7mm, 124-125°/15mm, d 1.040, n_D^{20} 1.653.** Commercial material can contain up to 2% of poly-1-vinylnaphthalene. Fractionally distil it under reduced pressure using a spinning-band column, dry it with CaH_2 and again distil it under vacuum. Store it in sealed ampoules in a freezer. It has λ_{max} (cyclohexane) at 210 and 320nm. The *picrate* has **m** 105-106°. [*Beilstein* **5** H 585, **5** III 1773, **5** IV 1833.] It is an **irritant**.

2-Vinylnaphthalene *[827-54-3]* **M 154.2, m 66°, 65-68°, b 76-81°/2.5mm, 135-137°/18mm.** Commercial material can contain up to 5% of MeOH. The flammable solid can be fractionally distilled under reduced pressure using a spinning-band column; dry it with CaH_2 and again distil it under vacuum. It crystallises from aqueous MeOH, EtOH (**m** 66°) or petroleum ether (**m** 66-66.5°). Store it in sealed ampoules in a freezer. The *picrate* has **m** 91-92° (from EtOH). [*Beilstein* **5** III 1775, **5** IV 1833.] It is an **irritant**.

Violanthrene (dibenzanthrene, 5,10-dihydroviolanthrene A) *[81-31-2]* **M 428.5.** Purify violanthrene by vacuum sublimation over Cu in a muffle furnace at 450°/25mm in a CO_2 atmosphere [Scholl & Meyer *Chem Ber* **67** 1229 *1934*]. [*Beilstein* **5** I 392.] *Violanthrene A* (anthro[9,1,2-*cde*]benzo[*rst*]pentaphene *[188-87-4]* **M** 426.5 has **m** 506°. [Clar *Chem Ber* **76** 458 *1943*, *Beilstein* **5** III 2778; *Violanthrene B (violanthrone) Beilstein* **7** I 466, **7** II 818, **7** III 4539.]

Xylene *[1330-20-7]* **M 106.1 (mixed isomers).** Usual impurities are ethylbenzene, paraffins, traces of sulfur compounds and water. With a very efficient still, *o*-xylene can be fractionally distilled from a mixture of isomers. Purify (and dry) by fractional distillation from $LiAlH_4$, P_2O_5, CaH_2 or sodium. This treatment can be preceded by shaking successively with conc H_2SO_4, water, aqueous 10% NaOH, water and mercury, and drying with $CaCl_2$ for several days. [*Beilstein* **5** H 360.]

***o*-Xylene** *[95-47-6]* **M 106.2, f -25.2°, b 84°/14mm, 144.4°/760mm, d_4^{20} 0.88020, d_4^{25} 0.87596, n_D^{20} 1.50543, n_D^{25} 1.50292.** The general purification methods listed under xylene are applicable [Clarke & Taylor *J Am Chem Soc* **45** 831 *1923*]. *o*-Xylene (4.4Kg) is sulfonated by stirring for 4 hours with 2.5L of conc H_2SO_4 at 95°. After cooling, and separating the unsulfonated material, the product is diluted with 3L of water and neutralised with 40% NaOH. On cooling, sodium *o*-xylene sulfonate separates and is recrystallised from half its weight of water. [A further crop of crystals is obtained by concentrating the mother liquor to one-third of its volume.] The salt is dissolved in the minimum amount of cold water, then mixed with the same amount of cold water, and with the same volume of conc H_2SO_4 and heated to 110°. *o*-Xylene is regenerated and steam distils. The distillate is saturated with NaCl, the organic layer is separated, dried and redistilled. [*Beilstein* **5** H 362, **5** I 179, **5** II 281, **5** III 807, **5** IV 917.]

***m*-Xylene** *[108-38-3]* **M 106, f -47.9°, b 139.1°/760mm, d_4^{20} 0.86417, d_4^{25} 0.85990, n_D^{20} 1.49721, n_D^{25} 1.49464.** The general purification methods listed under *xylene* are applicable. The *o*- and *p*-isomers can be removed by their selective oxidation when a *m*-xylene sample containing them is boiled with dilute HNO_3 (one part conc acid to three parts water). After washing with water and alkali, the product can be steam distilled, collected as for *o*-xylene, then distilled and purified further by sulfonation. [Clarke & Taylor *J Am Chem Soc* **45** 831 *1923*.] *m*-Xylene is selectively sulfonated when a mixture of xylenes is refluxed with the theoretical amount of 50-70% H_2SO_4 at 85-95° under reduced pressure. By using a still resembling a Dean and Stark apparatus, water in the condensate can be progressively withdrawn while the xylene is returned to the reaction vessel. After cooling, then adding water, unreacted xylenes are distilled off under reduced pressure. The *m*-xylene sulfonic acid is subsequently hydrolysed by steam distillation up to 140°, the free *m*-xylene is washed, dried with silica gel and again distilled. It is stored over molecular sieves Linde type 4A. [*Beilstein* **5** H 370, **5** I 182, **5** II 287, **5** III 823, **5** IV 932.]

***p*-Xylene** *[106-42-3]* **M 106.2, f 13.3, b 138.3°/760mm, d_4^{20} 0.86105, d_4^{25} 0.85669, n_D^{20} 1.49581, n_D^{25} 1.49325.** The general purification methods listed for *xylene* above are applicable. *p*-Xylene can readily be separated from its isomers by crystallisation from such solvents as MeOH, EtOH, isopropanol, acetone, butanone, toluene, pentane or pentene. It can be further purified by fractional crystallisation by partial freezing, and stored over sodium wire or molecular sieves Linde type 4A. [Stokes & French *J Chem Soc, Faraday Trans 1* **76** 537 *1980*, *Beilstein* **5** H 382, **5** I 185, **5** II 296, **5** III 845, **5** IV 951.]

HETEROCYCLIC COMPOUNDS

Acetaldehyde ammonia trimer (hexahydro-2,4,6-trimethyl-1,3,5-triazine trihydrate) *[76231-37-3]* **M 183.3, m 94-96°, 95-97°, 97°, b 110°(partly dec).** It crystallises from EtOH/Et_2O. When prepared, it separates as the *trihydrate* which can be dried in a vacuum over $CaCl_2$ at room temperature to give the *anhydrous* compound with the same melting point. The *dihydrate* melts at 25-28°, then resolidifies and melts again at 94-95°. *IT IRRITATES THE EYES AND MUCOUS MEMBRANES.* [Nielson et al. *J Org Chem* **38** 3288 *1973*, *Beilstein* **26** III/IV 25.]

2-Acetamido-5-nitrothiazole (Acinitrazole) *[140-40-9]* **M 187.2, m 264-265°.** Recrystallise acinitrazole from EtOH or AcOH. [Hurd & Wehrmeister *J Am Chem Soc* **71** 4007 *1949*, *Beilstein* **27** III/IV 4676.]

4-Acetamido-2,2,6,6-tetramethylpiperidine-1-oxyl (acetamidoTEMPO) *[14691-89-5]* **M 213.3, m 144-146°, 146-147°.** Dissolve the 1-oxyl in CH_2Cl_2, wash it with saturated K_2CO_3, then saturated aqueous NaCl, dry (Na_2SO_4), filter and evaporate. The red solid is recrystallised from aqueous MeOH, **m** 147.5°. [Ma & Bobbitt *J Org Chem* **56** 6110 *1991*, Rozantsev & Kokhanov *Bull Acad Sci USSR, Div Chem Sci* **15** 1422 *1966*, *Beilstein* **22/8** V 174.]

5-Acetamido-1,3,4-thiadiazole-2-sulfonamide (Acetazolamide) *[59-66-5]* **M 222.3, m 256-259° (dec).** It is recrystallised from water. [Roblin & Clapp *J Am Chem Soc* **72** 4890 *1950*, *Beilstein* **27** III/IV 8219.]

Acetoacetylpiperidide *[1128-87-6]* **M 169.2, b 88.9°/0.1mm, n_D^{52} 1.4983.** Dissolve it in *benzene, extract with 0.5M HCl to remove basic impurities, wash with water, dry, and distil it at 0.1mm [Wilson *J Org Chem* **28** 314 *1963*]. [*Beilstein* **20** IV 1121.]

4-Acetoxy-2-azetidinone *[28562-53-0]* **M 129.1, m 38-41°.** Dissolve it in $CHCl_3$, dry ($MgSO_4$), concentrate at 40°/70mm, or better at room temperature to avoid decomposition. Wash and stir the residual oil with hexane by decantation and discard the wash. Dry the oil at high vacuum when it should solidify, **m** 34°. It can be distilled at high vacuum, 80-82°/10^{-3}mm, but this results in extensive losses. The purity can be checked by TLC using Merck Silica Gel F_{254} and eluting with EtOAc. The azetidinone has R_F 0.38 (typical impurities have R_F 0.67). The spots can be detected by the **TDM spray**. This is prepared from (A) 2.5g of 4,4'-tetramethyldiaminodiphenylmethane (TDM) in 10ml AcOH and diluted with 50ml of H_2O, (B) 5g KI in 100ml of H_2O and (C) 0.3g ninhydrin in 10ml of AcOH and 90ml of H_2O. The spray is prepared by mixing (A) and (B) with 1.5ml of (C) and stored in a brown bottle. [Clauβ et al. *Justus Liebigs Ann Chem* 539 *1974*, Michel et al. *Org Synth* **65** 135 *1987*, *Beilstein* **21/12** V 4.]

3*R*,4*R*,1'*R*-4-Acetoxy-3-[1-(*tert*-butylmethylsilyloxy)ethyl]-2-azetinone. See in "Miscellaneous As, B, P, Si, S, Se and Te Compounds" in this Chapter.

***N*-Acetylcaprolactam (1-acetylazepan-2-one, 1-acetylhexahydro-2*H*-azepin-2-one)** *[1888-91-1]* **M 155.2, b 85-86°/0.05mm, 119.5-222° /11mm, 134-135° /26mm, d_4^{25} 1.094, n_D^{20} 1.489.** Distil the lactam in a vacuum, but if the IR has broad OH bands (*ca* ν_{max} at ~3300cm^{-1}), then add *ca* one half volume or more of Ac_2O, reflux for 2 hours and distil or dissolve it in toluene add MeCOCl heat at 100°/2 hours and distil in a vacuum. Its IR has ν_{max} at 1730cm^{-1} (film). [Stoll & Griehl *Helv Chim Acta* **48** 1805 *1965*, Bose et al. *Tetrahedron* **30** 3 *1974*, *Beilstein* **21** III/IV 3210, **21/6** V 460.]

3-Acetyl-2,5-dimethylthiophene *[2530-10-1]* **M 154.2, b 62°/0.25mm, 105-108°/15mm, 224°/atm, d_4^{25} 1.086, n_D^{20} 1.544.** Distil the thiophene in a vacuum, or dissolve it in *C_6H_6, shake this with 6M HCl, then wash with H_2O, dry the organic layer, evaporate, and distil the residue preferably in a vacuum. [Glaze et al. *J Chem Soc Perkin Trans 1* 957 *1985*, *Beilstein* **17** H 298.]

***N*-Acetylimidazole** *[2466-76-4]* **M 110.1, m 101.5-102.5°, pK^{25} 3.6.** It is recrystallised from isopropenyl acetate and dried in a vacuum over P_2O_5. [Riordan & Valee *Methods Enzymol* **25** 500 *1972*, *Beilstein* **23/4** V 218.]

1-Acetylindole *[576-15-8]* **M 159.2, b 123-125°/8mm, 148-150°/10mm, 152-153°/15mm, d $^{25}_{4}$ 1.387, n $^{20}_{D}$ 1.6100.** It has been prepared by phase transfer catalysis of a mixture of AcCl/NaOH and Indole [Illi *Synthesis* 387 *1979*]. Purify it by distillation in a vacuum, but if it is very discoloured, then distil it in steam, separate the layers, dry the organic layer (Na_2SO_4), filter it, and distil it in a vacuum. The *picrate* has **m 98-99°**. *1,3-Diacetylindole* is formed when indole is treated with Ac_2O at 180-200°, and distils with 1-acetylindole. The latter distils in steam, whereas the diacetylindole remains behind. It is hydrolysed by boiling alkali to yield indole, and can be acetylated further to *1,3-diacetylindole* **m 151°**. [For NMR see Elguero et al. *Org Mag Res* **7** 445 *1975*, Ciamecian & *Chem Ber* ***22*** 1977 *1889*, Zatti & Ferratini *Chem Ber* **23** 1357 *1890*, Plieninger & Werst *Chem Ber* **89** 2783, 2788 *1956*, *Beilstein* **20** H 309, **20** II 200, **20** III/IV 3182, **20/7** V 19.]

3-Acetylindole *[703-80-0]* **M 159.2, m 189°, 188-190°, 188-192°, 191-193°, 194°, pK^{25} 12.99 (acidic NH).** It is formed by reaction of indole-MgCl and AcCl, and also by hydrolysis of 1,3-diacetylindole (see above). It is purified by recrystallisation from MeOH, *C_6H_6 containing a little EtOH or *C_6H_6; and by sublimation *in vacuo*. The *phenylureido* derivative has **m** 154°. The *(E)-oxime* has **m 144-145°** (also **149°** reported) (from H_2O) [Kostyuchenko et al. *J Org Chem USSR (Engl Trans)* **8** 2471 *1972*], and the *(Z)-oxime* has **m 95°** [Kostyuchenko et al. *J Org Chem USSR (Engl Trans)* **8** 2469, 2473 *1972*]. The *(E)-O-methyloxime* crystallises from EtOH with **127-129°**. [Oddo & Sessa *Gazz Chim Ital* **41** 234 *1911*, Baker *J Chem Soc* 461 *1946*, *Beilstein* **21** H 316, **21** I 300, **21** II 264, **21** III/IV 3775, **21/8** V 297.]

4-Acetylmorpholine *[1696-20-4]* **M 129.2, m 13.8-14°, 14°, 14.5°, b 96-97°/6mm, 113-128°/22mm, 242-247°/760mm, d $^{20}_{4}$ 1.0963, n $^{20}_{D}$ 1.4830.** Distil it through an 8inch Fenske (glass helices packing) column with a manual take-off head. Purify it by fractional distillation. The *hydrobromide* has **m** 172-175°. [Brace *J Am Chem Soc* **75** 357 *1953*, deBenneville et al. *J Org Chem* **21** 1072 *1956*, *Beilstein* **27** III/IV 274.]

***N*-Acetyl-D-penicillamine (*N*-acetyl-3-mercapto-D-valine)** see in "Miscellaneous Compounds", Chapter 7.

1-Acetylpiperazine *[13889-98-0]* **M 128.2, m 32-34°, 52°, pK^{25} 7.94.** Purify 1-acetylpiperazine by recrystallisation from 40% aqueous EtOH or from EtOH/Et_2O. It is an **irritant**, and is *hygroscopic*. The *hydrochloride* has **m** 191° (from EtOH), and the *tosylate salt* has **m** 148-149° (from EtOH/EtOAc, 1:16). The free base, however, cannot be isolated by basifying the tosylate salt and extraction with CH_2Cl_2. [Jacobi *Chem Ber* **66** 113 *1933*, Mosher et al. *J Am Chem Soc* **75** 4949 *1953*, Hall *J Am Chem Soc* **78** 2570 *1956*, *Beilstein* **23** IV 1786.]

1-Acetyl-4-piperidone *[32161-06-1]* **M 141.2, b 124-128°/0.2mm, 218°/760mm, d $^{25}_{4}$ 1.1444, n $^{20}_{D}$ 1.5023.** Purify it by fractional distillaton through a short Vigreux column (15mm). The *2,4-dinitrophenylhydrazone* has **m** 212-213° (from EtOH). It is freely soluble in H_2O but insoluble in Et_2O. [McElvain & McMahon *J Am Chem Soc* **71** 901 *1949*, *Beilstein* **21/6** V 246.]

3-Acetylpyridine *[350-03-8]* **M 121.1, m 13-14°, b 65-66°/1mm, 92-95°/8-9mm, 105°(113°)/16mm, 219-221°/760mm, d $^{20}_{4}$ 1.1065, n $^{20}_{D}$ 1.1065, pK^{25} 3.18.** It is purified by dissolving in HCl, extracting with Et_2O to remove the possible impurity of nicotinic acid, basified with NaOH and extracted with Et_2O. The dried extract is filtered, evaporated and the residual oil is distilled. If the NMR spectrum indicates further impurities, then convert it to the *phenylhydrazone* (**m** 137°, yellow needles from EtOH). This is hydrolysed with HCl [Engler & Kiby *Chem Ber* **22** 597 *1889*], the phenylhydrazine HCl is removed by filtration, $NaNO_2$ is added, the solution is basified with aqueous NaOH and extracted with Et_2O as before and distilled at atmospheric pressure to give 3-acetylpyridine as a colourless oil. Purification can also be achieved by shaking with 50% aqueous KOH, extracting with Et_2O, drying the extract and distilling it at atmospheric pressure or *in vacuo*. [Kloetzel & Chubb *J Am Chem Soc* **79** 4226 *1957*.] The *hydrochloride* has **m** 180-181° (from MeOH/EtOH), the *picrate* has **m** 133.8-134.8° (from H_2O), and the *phenylhydrazone* has **m** 137° (129-130°)(needles, from EtOH) [Webb & Webb *J Am Chem Soc* **71** 2285 *1949*]. The *ketoxime* has **m** 112° (from EtOH or *C_6H_6). [Strong & McElvain

J Am Chem Soc **55** 816 *1933*, Kolloff & Hunter *J Am Chem Soc* **63** 490 *1941*, *Beilstein* **21/7** V 394.]

2-Acetylthiazole *[24295-03-2]* **M 127.2, b 89-91° (90-95°)/12mm, 95-105°/15mm, d_4^{20} 1.23, n_D^{20} 1.55.** Check NMR spectrum; if it is not too bad, distil it through an efficient column in a vacuum. Otherwise purify it *via* the oxime. The *oxime* sublimes at 140-145°, **m** 159°, and when crystallised from H_2O has **m** 163-165.5°. [Erlenmeyer et al. *Helv Chim Acta* **31** 1142 *1948*, Waisvisz et al. *J Am Chem Soc* **79** 4524 *1957*, Menasseé et al. *Helv Chim Acta* **40** 554 *1957*, *Beilstein* **27** IV 2617.]

2-Acetylthiophene (methyl 2-thienyl ketone) *[88-15-3]* **M 126.2, m 9.2-10.5°, 10.45°, 10-11°, b 77°/4mm, 89-91°/9mm, 94.5-96.5°/13mm, 213-214°/atm, d_4^{20} 1.17, n_D^{20} 1.5666.** Fractionally distil the thiophene through a 12-plate column, and fraction **b** 77°/4mm is collected. Also wet the acetylthiophene in order to remove and free thiophene which forms an azeotrope with H_2O, **b** 68°. Store it in a brown bottle, and the clear colourless liquid remains thus for extended periods. [Kosak & Hartough *Org Synth* Coll Vol **III** 14 *1955*, Hartough & Kosak *J Am Chem Soc* **69** 3093 *1947*.] The red *4-nitrophenylhydrazone* crystallises from EtOH with **m** 181-182°. [*Beilstein* **17/9** V 387.]

3-Acetylthiophene (methyl 3-thienyl ketone, acetothienone) *[1468-83-3]* **M 126.2, m 57°, 60-63°, b 106-107°/25mm, 208-210°/748mm.** Recrystallise the thiophene from petroleum ether (b 30-60°) or EtOH. The *2,4-dinitrophenylhydrazone* crystallises from $CHCl_3$, **m** 265°, and the *semicarbazone* crystallises from EtOH, **m** 174-175°. [Campaigne & Le Suer *J Am Chem Soc* **70** 1555 *1948*, *Beilstein* **17/9** V 399.]

Aconitine *[302-27-2]* **M 645.8, m 204°, $[\alpha]_{546}$ +20° (c 1, $CHCl_3$), pK^{15} 8.35.** Crystallise it from EtOH, $CHCl_3$ or toluene. [*Beilstein* **21/6** V 310.]

Aconitine hydrobromide *[6034-57-7]* **M 726.7, m 207°.** Crystallise the salt from water or EtOH/ether. [*Beilstein* **21/6** V 310.]

Acridine (2,3-benzoquinoline) *[260-94-6]* **M 179.2, m 111° (sublimes), b 346°, pK^{25} 5.58 (pK^{25} of excited state 10.65).** Acridine has been crystallised twice from *benzene/cyclohexane, or from aqueous EtOH, then sublimed, removing and discarding the first 25% of the sublimate. The remainder is again crystallised and sublimed, discarding the first 10-15% [Wolf & Anderson *J Am Chem Soc* **77** 1608 *1955*].
Acridine can also be purified by crystallisation from *n*-heptane and then from ethanol/water after pre-treatment with activated charcoal, or by chromatography on alumina with petroleum ether in a darkened room. *Alternatively*, acridine can be precipitated as the hydrochloride from *benzene solution by adding HCl, after which the base is regenerated, dried at 110°/50mm, and recrystallised to constant melting point from petroleum ether [Cumper et al. *J Chem Soc* 4518 *1962*]. The regenerated free base may be recrystallised, chromatographed on basic alumina, then vacuum-sublimed and zone-refined. [Williams & Clarke, *J Chem Soc, Faraday Trans 1* **73** 514 *1977*, Albert, *The Acridines* Arnold Press *1966*.] It can exist in five crystalline forms and is steam volatile. It is a strong IRRITANT to skin and mucous membranes and can become a chronic irritant— handle it with CARE. [*Beilstein* **20/8** V 199.]

Acridine Orange (3,6-bisdimethylaminoacridine) *[494-38-2]* **M 349.94, m 165°(dec), 181-182°, 184-186° (free base)**, **pK_1^{20} -3.3, pK_2^{20} 0.2, pK_3^{20} 10.1.** The double salt with $ZnCl_2$ (6g) is dissolved in water (200ml) and stirred with four successive portions (12g each) of Dowex-50 ion-exchange resin (K^+ form) to remove the zinc. The solution is then concentrated in vacuum to 20ml, and 100ml of ethanol is added to precipitate KCl which is removed. Ether (160ml) is added to the solution from which, on chilling, the dye crystallises as its chloride. It is separated by centrifugation, washed with chilled ethanol and ether, and dried under vacuum, before being recrystallised from ethanol (100ml) by adding ether (50ml), and chilling. Yield 1g. [Pal & Schubert *J Am Chem Soc* **84** 4384 *1962*].
It was recrystallised twice as the free base from ethanol or methanol/water by dropwise addition of NaOH (less than 0.1M). The precipitate was washed with water and dried under vacuum. It was dissolved in $CHCl_3$ and chromatographed on alumina: the main sharp band was collected, concentrated and cooled to -20°. The precipitate was filtered off, dried in air, then dried for 2 hours under vacuum at 70°. [Stone & Bradley *J Am*

Chem Soc **83** 3627 *1961*, Blauer & Linschitz *J Phys Chem* **66** 453 *1962*, Albert *J Chem Soc* 244 *1947, Beilstein* **22** III/IV 5490, **22/11** V 326.]

Acridine Yellow G (2,7-dimethylacridine-3,6-diamine hydrochloride) *[135-49-9]* **M 273.8, m 325° (free base), CI 46025, pK_1^{20} -3.0, pK_2^{20} 0.5, pK_3^{20} 8.9.** Note that the hydrochloride is normally called Acridine Yellow G and not the free base. The free base recrystallises from 1:1 *benzene/methanol, or from 800 parts of EtOH. It is converted to the sparingly soluble hydrochloride with dilute HCl, filtered off and dried. [Albert *J Chem Soc* 248 *1947*, *Beilstein* **22** III/IV 5499, **22/11** V 340.]

***N*-(9-Acridinyl)maleimide (NAM)** *[49759-20-8]* **M 274.3, m 248°, 255-258°.** Purify NAM by chromatography on silica gel using CH_2Cl_2 as eluant. Evaporation of pooled fractions that gave the correct NMR spectra gave a solid which was crystallised from Me_2CO as pale yellow prisms. Its IR(nujol) has ν_{max} at 1710 (imide); the UV (MeOH) has λ_{max} (nm) (ε $M^{-1}cm^{-1}$) at 251 (159 500), 343 shoulder (7,700), 360 (12,400) and 382 shoulder (47,000). [Mashida et al. *Chem Pharm Bull Jpn* **26** 596 *1978*, Schuldiner et al. *Eur J Biochem* **25** 64 *1972*,]

Acridone *[578-95-0]* **M 195.2, m >300°, pK_1 -0.32 (basic), pK_2 12.80 (14.0, acidic).** Dissolve ~1g in *ca* 1% NaOH (100ml), add 3M HCl to pH 4 when acridone separates as a pale yellow solid with **m** just above 350° (sharp). It can be recrystallised from large volumes of H_2O to give a few mg. It is soluble in 160 parts of boiling EtOH (540 parts at 22°) [Albert & Phillips *J Chem Soc* 1294 *1956*]. A few decigms are best crystallised as the *hydrochloride* from 400 parts of 10N HCl (90% recovery) from which the free base is obtained by washing the salt with H_2O. A small quantity can be recrystallised (as the neutral species) from boiling AcOH. Larger quantities are best recrystallised from a mixture of 5 parts of freshly distilled aniline and 12.5 parts of glacial acetic acid. Acridone distils unchanged at atmospheric pressure, but the boiling point was not recorded, and some sublimation occurs below 350°. It has UV with λ_{max} at 399nm. [see Albert, *The Acridines* Arnold Press pp 201, 372 *1966*; for pKa see Kalatzis *J Chem Soc (B)* 96 *1969*, *Beilstein* **23/9** V 7.]

Acriflavine *[8048-52-0]* **M 196.2, pK^{25} >12.** Treat acriflavin twice with freshly precipitated AgOH to remove proflavine, then recrystallise it from absolute methanol [Wen & Hsu *J Phys Chem* **66** 1353 *1962*]. [*Beilstein* **22** III/IV 218.]

Acriflavin Mixture (Euflavin, 3,6-diamino-10-methylacridinium chloride) *[8063-24-9]* **M 259.7, m 179-181°.** Purify it by dissolving in 50 parts of H_2O, shaking with a small excess of freshly precipitated and washed Ag_2O. The mixture is set aside overnight at 0° and filtered. The cake is not washed. The pH of the filtrate is adjusted to 7.0 with HCl and evaporated to dryness. The residue is then crystallised twice from MeOH, twice from H_2O and dried at 120°. Its UV spectrum has λ_{max} at 452nm and a logε value of 4.67. It is a red powder which readily absorbs H_2O. The solubility is increased in the presence of proflavin. The *dihydrochloride* is a deep red crystalline powder. It is available as a mixture of 3,6-diaminoacridinium chloride (35%) and its 10-metho-chloride (65%). [See Albert, *The Acridines* Arnold Press p 346 *1966*, Benda *Chem Ber* **45** 1787 *1912*]. [*Beilstein* **23** I 650.]

Adenine (6-aminopurine, vitamin B_4) *[73-24-5]* **M 135.1, m 360-365°(dec rapid heating), pK_1^{25} 4.12, pK_2^{25} 9.83.** Crystallise adenine from distilled water. [*Beilstein* **26** III/IV 3561.]

Adenosine *[58-61-7]* **M 267.3, m 235-236°, $[\alpha]_{546}$ -85° (c 2, 5% NaOH), $[\alpha]_D^{24}$ -61.2° (c 1, H_2O), pK_1^{25} 3.48, pK_2^{25} 12.5.** Crystallise adenosine from distilled water and dry it at 110°. It has been purified *via* the *picrate*, where ethanolic picric acid is added to adenosine and the *picrate* is filtered off and recrystallised from EtOH. It has **m** 180-185°(dec). Adenosine is recovered by dissolving 0.4g of the picrate in 80ml of hot H_2O, treated with a small quantity of Dowex 1 anion exchange resin in the chloride form, and the resin is filtered off. The filtrate is treated with more resin and filtered again. One equivalent of aqueous NaOH is added to the colourless filtrate which is evaporated to 4ml and cooled to give 0.176g of adenosine **m** 236°. [Davoll et al. *J Chem* Soc 967 *1948*, Davoll & Lowy *J Am Chem Soc* **73** 1650 *1951*, *Beilstein* **26** III/IV 3598.]

Adrenochrome (3-hydroxy-1-methyl-5,6-indoline-dione) *[54-06-8]* **M 179.2, m 125-130° (dec).** It was

crystallised from MeOH/formic acid, as red crystals of the *hemihydrate*, and stored in a vacuum desiccator. The *mono-semicarbazone (Carbazochrome)* [69-81-8] M 236.2, crystallises as orange-red crystals from dilute EtOH with **m** ~203°(dec) and is haemostatic. [Heacock *Chem Rev* **59** 181 *1959*, *Beilstein* **21** III/IV 6434.]

Aetioporphyrin I (2,4,6,8-tetraethyl-1,3,5,7-tetramethylporphyrin) *[448-71-5]* **M 478.7, m 360-363°, pK^{25} 18.** Purify it by chromatography on an Al_2O_3 column (300g/300mg of porphyrin) and elute with CH_2Cl_2, evaporate the eluate and crystallise the residue from CH_2Cl_2/MeOH, pyridine or $CHCl_3$/petroleum ether (purple prisms, **m** > 300°) [Smith *J Chem Soc Perkin Trans 1* 1471 *1972*]. The copper salt crystallises as red needles from pyridine/AcOH. It complexes with metals. The *dihydrobromide* [69150-58-9] **M** 640.5 separates from aetioporphyrin I in Et_2O on addition of 10% of aqueous HBr after 2 days [Fischer & Treibs *Justus Liebigs Ann Chem* **457** 241 *1927*, Treibs & Dieter *Justus Liebigs Ann Chem* **513** 88-91 *1934*]. [*Beilstein* **26** III/IV 1915.]

Agroclavin *[548-42-5]* **M 238.3, m 198-203°(dec), 205-206°, 210-212°, $[\alpha]_D^{20}$ -155° (c 1, $CHCl_3$), pK_{Est} ~8.0.** It crystallises from diethyl ether or Me_2CO. The *hydrochloride* crystallises from H_2O and has **m** 265-266°, $[\alpha]_D^{20}$ -110° ($CHCl_3$). [Plieninger et al. *Justus Liebigs Ann Chem* **743** 95 *1971*, *Beilstein* **23** III/IV 1623.]

Ajmalicine (δ-yohimbine, Raubacine) *[483-04-5]* **M 352.4, m 250-252°(dec), 257°(dec), 261-263°(dec), $[\alpha]_{546}$ -76° (c 0.5, $CHCl_3$), $[\alpha]_D^{20}$ -45° (c 0.5, pyridine), -39° (c 0.25, MeOH), pK^{25} 5.7(90% aqueous 2-methoxyethanol), 6.46(66% aqueous Me_2NCHO).** It crystallises from MeOH, EtOH or EtOAc. [*Beilstein* **27** III/IV 7927.]

Ajmalicine hydrochloride *[4373-34-6]* **M 388.9, m 290°(dec), 294-295°(dec), $[\alpha]_D$ –18.5° (c 0.5, MeOH).** This hydrochloride crystallises from MeOH or EtOH. Its solubility is 0.315g/100g of H_2O at 100°. [*Beilstein* **27** III/IV 7928.]

Ajmaline (γ-yohimbine) *[4360-12-7]* **M 326.4, m 160° (MeOH), 205-206° (anhyd), $[\alpha]_D^{20}$ +144° (c 0.8, $CHCl_3$), pK^{25} 8.15(80% aqueous 2-methoxyethanol), 8.4(60%aqueous Me_2NCHO).** Ajmaline crystallises from MeOH or EtOAc containing a little H_2O to give the *trihydrate* **m** 158-160°. This loses $1H_2O$ at 110° and all H_2O at 150°. [*Beilstein* **23** III/IV 3212.]

Ajmaline hydrochloride *[4410-48-4]* **M 388.9, m 140°.** It crystallises from water as the *dihydrate* **m** 140°, and the *anhydrous salt* has **m** 252-255°, and $[\alpha]_D^{40}$ +84.6° (c 1, H_2O). The *dihydrochloride* crystallises from EtOH/Et_2O with **m** 305-306°. [*Beilstein* **23** III/IV 3212.]

Alizarin (1,2-dihydroxyanthraquinone) *[72-48-0]* **M 240.2, m 290°, d_4^{20} 0.884, CI 58000, pK_1^{25} 7.45, pK_2^{25} 11.80.** Alizarin crystallises from glacial acetic acid or 95% EtOH. It can also be sublimed at 110°/2mm. It is an indicator with λ_{max} at 452nm (pH 5.8) and 520nm (pH 7.2). [*Beilstein* **8** IV 3256.]

Alizarin-3-methyliminodiacetic acid (Alizarin Complexone) ($2H_2O$) *[3952-78-1]* **M 421.4, m 189°(dec), $pK_{Est(1)}$~4.9, $pK_{Est(2)}$~7.5.** It is purified by suspending it in 0.1M NaOH (1g in 50ml), filtering the solution and extracting alizarin with 5 successive portions of CH_2Cl_2. Then add HCl dropwise to precipitate the reagent, stirring the solution in an ice bath. Filter the precipitate onto a glass filter, wash it with cold water and dry it in a vacuum desiccator over KOH [Ingman *Talanta* **20** 135 *1973*, *Beilstein* **14** IV 931].

Alizarin Yellow R [5-(4-nitrophenylazosalicylic acid), Mordant Orange I] *[2243-76-7]* **M 287.2, m 253-254°(dec), >300°, CI 14030, pK^{25} 11.17.** The free acid is precipitated by adding HCl to an aqueous solution of the Na salt. After 2 recrystallisations from aqueous AcOH, it has **m** 255°(dec); [**m** 253-254°(dec) was reported by Hewitt & Fox *J Chem Soc* **79** 49 *1901*]. The free acid recrystallises from dilute AcOH as orange brown needles. The Na salt changes colour from yellow to red when the pH is increased from 10.2 to 12.0. [Woodland et al. *J Am Chem Soc* **75** 5835 *1953*, *Beilstein* **16** IV 372.]

***RS*-Allantoin** *[97-59-6]* **M 158.1, m 238°(dec).** It crystallises from water or EtOH [Hartman et al. *Org Synth* Coll Vol **II** 21 *1943*]. [*Beilstein* **25** III/IV 4071.]

Alloxan [2,4,5,6(1*H*,3*H*]pyrimidine, tetrone] *[50-71-5]* **M 142.0, m ~170°(dec), pK^{25} 6.64.** Crystallisation from water gives the *tetrahydrate*. *Anhydrous* crystals are obtained by crystallisation from acetone, glacial acetic acid or by sublimation *in vacuo*. [See below and *Beilstein* **24** H 500, **24** I 428, **24** II 301, **24** III/IV 2137.]

Alloxan monohydrate *[2244-11-3]* **M 160.1, m 255°(dec), pK^{25} 6.64.** Recrystallisation from H_2O gave the *tetrahydrate* in large prisms or rhombs. On heating at 100°, or on exposure to air, this is converted to the *monohydrate*. Dissolve it in its own weight of boiling H_2O and cool it for several days below 0°; the *tetrahydrate* crystallises from solution much more slowly when free from HNO_3. It is less soluble in bicarbonate solutions than in H_2O. Drying the solid over H_2SO_4 yields the *monohydrate*. The *anhydrous* crystals can be obtained by recrystallisation from dry Me_2CO or AcOH followed by washing with dry Et_2O, or by sublimation in a vacuum. On heating it turns pink at 230° and decomposes at *ca* 256°. It is acidic to litmus. [Hartman & Sheppard *Org Synth* Coll Vol **III** 37 *1955*.] It forms a compound with urea which crystallises from H_2O in yellow needles that become red at 170° and decompose at 185-186°. [*Beilstein* **24** H 500, **24** I 428, **24** II 301, **24** III/IV 2137.]

Alloxantin *[76-24-4]* **M 286.2, m 253-255°(dec) (yellow at 225°).** Alloxantin crystallises from water or EtOH and is kept under nitrogen. It turns red in air. [*Beilstein* **26** III/IV 2782.]

1-Allyl-6-amino-3-ethyluracil (Aminometradine) *[642-44-4]* **M 195.2, m 143-144° (anhydrous).** It crystallises from water (as monohydrate). It is a diuretic. [*Beilstein* **24** III/IV 4133.]

1-*N*-Allyl-3-hydroxymorphinan (Levallorphan) *[152-02-3]* **M 283.4, m 180-182°, [α] $^{20}_{D}$ -89° (c 3, MeOH).** It crystallises from aqueous EtOH. It is a narcotic antagonist. [Schneider & Grüssner *Helv Chim Acta* **34** 2211 *1951*, Hellerbach *Helv Chim Acta* **39** 429 *1956*.]

5-Allyl-5-*iso*butylbarbituric acid *[77-26-9]* **M 224.3, m 139°, 139-140°, 140-142°, pK^{18} 12.36.** It can be recrystallised from H_2O or dilute EtOH, and sublimes at 100-120°/8-12mm. It is soluble in $*C_6H_6$, cyclohexane, tetralin and petroleum ether at 20°. [Butler et al. *J Am Chem Soc* **77** 1486 *1955*, *Beilstein* **24** III/IV 2006.]

9-Aminoacridine [9-acridineamine] *[90-45-9]* **M 194.2, m 241°, pK^{20} 9.95.** It crystallises from EtOH or acetone and sublimes at 170-180°/0.04mm [Albert & Ritchie *Org Synth* Coll Vol **III** 53 *1955*, for hydrochloride, see below]. [*Beilstein* **22** H 463, **21** II 280, **21** III/IV 4174.]

9-Aminoacridine hydrochloride monohydrate (Acramine yellow, Monacrin) *[52417-22-8]* **M 248.7, m >355°, pK $^{20}_{1}$ 4.7, pK $^{20}_{2}$ 9.99.** Recrystallise it from boiling H_2O (charcoal; 1g in 300 ml) to give pale yellow crystals with a neutral reaction. It is one of the most fluorescent substances known. At 1:1000 dilution in H_2O it is pale yellow with only a faint fluorescence, but at 1:100,000 dilution it is colourless with an intense blue fluorescence. [Albert & Ritchie *Org Synth* Coll Vol **III** 53 *1955*; Falk & Thomas *Pharm J* **153** 158 *1944*, *Beilstein* **22** H 463, **21** II 280, **21** III/IV 4174.] See previous entry for the free base.

2-Amino-4-anilino-*s*-triazine (Amanozine) *[537-17-7]* **M 168.2, m 235-236°, pK$_{Est}$ ~5.5.** It crystallises from dioxane or 50% aqueous EtOH. [*Beilstein* **26** III/IV 1195.]

4-Aminoantipyrine *[83-07-8]* **M 203.3, m 109°.** It crystallises from EtOH or EtOH/ether. [*Beilstein* **25** III/IV 3554.]

2-Aminobenzothiazole *[136-95-8]* **M 150.2, m 132°, pK^{20} 4.48.** The thiazole cystallises from H_2O, aqueous EtOH, $*C_6H_6$ or petroleum ether. The *hydrochloride* crystallises from dilute HCl and has **m** 240.5°. [*Beilstein* **27** H 182, **27** III/IV 4824.]

6-Aminobenzothiazole *[533-30-2]* **M 150.2, m 87°, pK$_{Est}$ ~3.** It crystallises from aqueous EtOH, petroleum ether or $*C_6H_6$/petroleum ether. The *hydrochloride* has **m** 305°(dec) from dilute HCl, and the *picrate* has **m** 185°(dec) from Me_2CO. [Boggust & Cocker *J Chem Soc* 360 *1949*, *Beilstein* **27** III/IV 4884.]

3-*o*-Aminobenzyl-4-methylthiazolium chloride hydrochloride *[534-94-1]* **M 277.4, m 213°(dec).** The *hydrochloride* crystallises from aqueous EtOH, and the *iodide hydroiodide* has **m** 273° (from aqueous HI). [*Beilstein* **27** III/IV 973.]

4-Amino-1-benzylpiperidine *[50541-93-0]* **M 190.3, b ~180°/20mm, d_4^{20} 0.933, n_D^{20} 1.543, $pK_{Est(1)}$ ~8.3 $pK_{Est(2)}$ ~10.4.** Purify it by distillation *in vacuo* and store it under N_2 because it absorbs CO_2. The *dihydrochloride salt* [1205-72-7] has **m** 270-273° (255°) after recrystallisation from MeOH/EtOAc or EtOH. [Brookes *J Chem Soc* 3165, 3172 *1957*.] The *4-methylamino-1-benzylpiperidine* derivative has **b** 168-172°/17mm, n_D^{20} 1.5367 [Reitsema & Hunter *J Am Chem Soc* **70** 4009 *1948*]. The *1-(1-benzyl-4-piperidinyl)-3-cyano-2-methylisothiourea* derivative has **m** 160° from $CHCl_3/Et_2O$ [Preparation, IR, NMR: Ried et al. *Chem Ber* **116** 1547 *1983*, *Beilstein* **22** III/IV 3752].

2-Amino-4-chloro-6-methylpyrimidine *[5600-21-5]* **M 143.6, m 184-186°, pK_{Est} ~1.0.** Recrystallise it from EtOH. [*Beilstein* **24** H 84.]

2-Amino-5-chloropyridine *[1072-98-6]* **M 128.6, m 135-136°, pK^{25} 4.38.** Recrystallise this base from petroleum ether. It sublimes at 50°/0.5mm. [*Beilstein* **22** II 332, **22/8** V 541.]

2-Amino-4-chloropyrimidine *[3993-78-0]* **M 129.55, m 168-169°, m 170°, pK_{Est} ~1.2.** The pyrimidine crystallises in glistening plates from EtOH (**m** 170°, sintering at 167°). It has also been purified by sublimation in a vacuum and recrystallisation from H_2O. [Hilbert & Johnson *J Am Chem Soc* **52** 1155 *1930*, *Beilstein* **24** H 80, **25** III/IV 2117.]

2-Amino-3,5-dibromopyridine *[35486-42-1]* **M 251.9, m 103-104°, pK_{Est} ~2.4.** Steam distil it and recrystallise it from aqueous EtOH or petroleum ether. [*Beilstein* **22** H 431, **22** II 333, **22** III/IV 4041.]

3-Amino-2,6-dichloropyridine *[62476-56-6]* **M 164.0, m 119°, b 110°/0.3mm, pK_{Est} ~2.0.** Recrystallise it from water. [*Beilstein* **22** III/IV 4093.]

2-Amino-4,6-dimethylpyridine *[5407-87-4]* **M 122.2, m 69-70.5°, pK^{25} 7.84.** Recrystallise this base from hexane, ether/petroleum ether or *benzene. Residual *benzene is removed over paraffin-wax chips in an evacuated desiccator. The *dipicrate* crystallises from EtOH and has **m** 205-207°(dec). [*Beilstein* **22** III/IV 4210.]

2-Amino-4,6-dimethylpyrimidine *[767-15-7]* **M 123.2, m 152-153°, pK^{25} 4.95.** Recrystallisation from water gives the pyrimidine with **m** 197°, but recrystallisation from acetone gives **m** 153°. [*Beilstein* **25** III/IV 2205.]

2-(Aminomethyl)piperidine *[22990-77-8]* **M 114.2, b 66-67°/12mm, 80-81°/18mm, d_4^{20} 0.9406, n_D^{20} 1.4854, pK_1^{20} 6.33, pK_2^{20} 9.70.** Dry (over Na_2SO_4) and distil the piperidine under vacuum from KOH. It has been purified *via* the *Reinekate salt* (**m** 173-174°) and its *dipicrate salt* (**m** 201°, from H_2O). [Norton et al. *J Am Chem Soc* **68** 1330 *1946*, Mortimer *Aust J Chem* **11** 84 *1958*, Augustine *J Am Chem Soc* **81** 4667 *1959*, *Beilstein* **22** III/IV 3765.]

4-Amino-3-hydrazino-5-mercapto-1,2,4-triazole (Purpald) *[1750-12-5]* **M 146.2, m 228-230°(dec), 234-235°(dec), $pK_{Est(1)}$ ~2, $pK_{Est(2)}$ ~3 (NH_2), $pK_{Est(3)}$ ~8 (SH).** Recrystallise Purpald from H_2O (0.6g in 300-400ml). The *benzylidene* derivative has **m** 245-246°(dec) from *i*-PrOH [Hoggarth *J Chem Soc* 4817 *1952*, Dickinson & Jacobson *J Chem Soc, Perkin Trans I* 975 *1975*. [*Beilstein* **26** III/IV 547.]

5-Amino-8-hydroxyquinoline hydrochloride *[3881-33-2]* **M 196.7, pK_1^{20} 5.67, pK_2^{20} 11.24.** Dissolve the hydrochloride in the minimum volume of MeOH, then add Et_2O to initiate crystallisation. The crystals are filtered off and dried [Lovell et al. *J Phys Chem* **88** 1885 *1984*]. The *dihydrochloride* [21302-43-2] has **M 233.1, m 279°(dec).** [*Beilstein* **22** III/IV 5866.]

4-Aminoimidazole-5-carboxamide hydrochloride (AICAR HCl) *[72-40-2]* **M 162.6, m 255-256°(dec), $pK_{Est(1)}$ ~3.5, $pK_{Est(2)}$ ~9.4.** Recrystallise the hydrochloride from EtOH. [Kuroda & Hakko *J Heterocycl Chem* **30** 593 *1993*, Alhede et al. *J Org Chem* **56** 2139 *1991*, Cheru et al. *Heterocycles* **24** 1133 *1992*, *Beilstein* **25** II 221, **25** III/IV 4329.]

6-Aminoindazole *[6967-12-0]* **M 133.2, m 210°, pK^{25} 3.99.** It is recrystallised from H_2O or EtOH and sublimes in a vacuum. [*Beilstein* **25** H 317.]

2-Amino-3-iodopyridine *[104830-06-0]* **M 220.1, m 78-91°, 90-91.5°, pK_{Est} ~4.9.** Purify this pyridine by recrystallisation from hexane. The *N-Me* derivative [113975-23-8] has **m 50°,** and distils at **b 129°/14mm**. [Sakamoto et al. *Chem Pharm Bull, Japan* **33** 4764 *1985*, Estel et al. *J Org Chem* **53** 2740 *1988*.]

2-Amino-4-iodopyridine *[552331-00-7]* **M 220.1, m 163-164°, pK_{Est} ~5.1.** Purify this pyridine by recrystallisation from H_2O. The *picrate* has **m 253-254°** (from H_2O), the *N-acetyl* derivative has **m 150°** (from H_2O), and the *N-benzoyl* derivative has **m 167-168°** (from aqueous EtOH). [Graf *Chem Ber* **64** 21 (25) *1931*.]

2-Amino-5-iodopyridine *[20511-12-0]* **M 220.1, m 128-131°, 129-130°, 130°, pK_{Est} ~4.5.** The pyridine can be purified by steam distillation. Separate the solid from the cooled distillate by filtration, acidify the filtrate, decolorise it with charcoal, concentrate it to ~200ml, make alkaline with KOH and cool. Filter the solid, add it to the original solid that was collected, and dry it *in vacuo*. It crystallises from *C_6H_6 in white needles. The *picrate* separates as yellow needles from hot EtOH or Me_2CO, **m 240°**. [Caldwell et al. *J Am Chem Soc* **66** 1479 *1944*.]

5-Amino-2-iodopyridine *[29958-06-0]* **M 220.1, m 132°, pK_{Est} ~2.6.** Purify it by recrystallisation from EtOH (white needles). [Caldwell et al. *J Am Chem Soc* **66** 1479 *1944*.]

3-Amino-5-mercapto-1,2,4-triazole *[16691-43-3]* **M 116.1, m 298°, $pK_{Est(1)}$~ 3.0, $pK_{Est(2)}$~ 9.** Recrystallise the triazole from H_2O and dry it *in vacuo*. The *acetyl* derivative has **m** 325° (dec) after recrystallisation from H_2O. [*Beilstein* **26** III/IV 1351.] It has also been recrystallised from EtOH/ H_2O (3:1, 1g in 50 ml, 50% recovery), **m** 300-302° (dec subject to heating rate), (λ_{max} 263nm, log ε 4.12). The *S-benzyl* derivative, when crystallised from *C_6H_6/EtOH (20:1), or $CHCl_3$/Et_2O has **m** 109-111° [Godfrey & Kruzer *J Chem Soc* 3437 *1960*, *Beilstein* **26** III/IV 1351.]

2-Amino-4-methoxy-6-methylpyrimidine *[7749-47-5]* **M 139.2, m 157-159°, 158-158.5°, 158-160°, pK_{Est} ~6.0.** Recrystallise it from H_2O. The *picrate* has **m** 220-221°(dec). [Baker et al. *J Am Chem Soc* **69** 3072, 3075 *1947*, Sirakawa et al. *Yakugaku Zasshi* **73** 598 *1953*, Backer & Grevenstuk *Rec Trav Chim Pays Bas* **61** 291 *1942*, *Beilstein* **25** III/IV 3385.]

8-Amino-6-methoxyquinoline *[90-52-8]* **M 174.2, m 41-42°, 51°, b 137-138°/1mm, $pK^{70.1}$ 3.38.** Distil it under N_2 and at high vacuum, then recrystallise it several times from MeOH (0.4ml/g). It remains colourless for several months when purified in this way [Elderfield & Rubin *J Am Chem Soc* **75** 2963 *1953*]. The *hydrobromide* [312693-53-1] **M** 255.1 has **m** 238°(dec). [*Beilstein* **22** III/IV 5934.]

7-Amino-4-methylcoumarin *[26093-31-2]* **M 175.2, m 224-229°(dec), pK_{Est} ~3.2.** Dissolve it in 5% HCl, filter and basify with 2M ammonia. The precipitate is dried in a vacuum and recrystallised from dilute EtOH. It yields a blue solution and is light sensitive. [Sigler *Synthesis* 614 *1980*, Kanaoka et al. *Chem Pharm Bull Jpn* **30** 1485 *1982*, *Beilstein* **18/11** V 445.]

2-Amino-3-methylpyridine (2-amino-3-picoline) *[1603-40-3]* **M 108.1, m 33.2°, b 221-222°, pK^{25} 7.24.** Recrystallise the picoline three times from *benzene, most of the residual *benzene being removed from the crystals by standing over paraffin wax chips in an evacuated desiccator. The amine is also transferred to a separating funnel under N_2, and left in contact with NaOH pellets for 3 hours with occasional shaking. It is then placed in a vacuum distilling flask where it is refluxed gently in a stream of dry N_2 before fractionally distilling it. [Mod et al. *J Phys Chem* **60** 1651 *1956*, *Beilstein* **22/9** V 212].

2-Amino-4-methylpyridine (2-amino-4-picoline) *[695-34-1]* **M 108.1, m 99.2°, b 230°, pK^{25} 7.48.** Crystallise it from EtOH or a 2:1 *benzene/acetone mixture, and dry it under vacuum as in the prevous entry. [*Beilstein* **22/9** V 325.]

2-Amino-5-methylpyridine (6-amino-3-picoline) *[1603-41-4]* **M 108.1, m 76.5°, b 227°, pK^{25} 7.22.** Crystallise it from acetone. [*Beilstein* **22/9** V 289.]

2-Amino-6-methylpyridine (6-amino-2-picoline) *[1824-81-3]* **M 108.1, m 44.2°, b 208-209°, pK^{25} 7.41.** Crystallise it three times from acetone and dry it under vacuum at *ca* 45°. *Alternatively*, keep it in contact with NaOH pellets for 3 hours, with occasional shaking, decant and fractionally distil it [Mod et al. *J Phys Chem* **60** 1651 *1956*]. It also recrystallises from CH_2Cl_2 on addition of petroleum ether. [Marzilli et al. *J Am Chem Soc* **108** 4830 *1986*, *Beilstein* **22/9** V 210.]

2-Amino-4-methylpyrimidine *[108-52-1]* **M 109.1, m 159-160°, 161°, pK^{20} 4.15.** Crystallise the pyrimidine from H_2O or EtOH and sublime it in a vacuum. The *picrate* crystallises from EtOH and has **m** 235-236°(dec). **[***Beilstein* **24** H 84, **25** III/IV 2152.]

2-Amino-5-methylpyrimidine *[50840-23-8]* **M 109.1, m 193.5°, pK_{Est} ~4.0.** Crystallise it from water or *benzene/petroleum ether and sublime it at 50°/0.5mm. [*Beilstein* **24** H 87.]

4-Amino-2-methylquinoline (4-aminoquinaldine) *[6628-04-2]* **M 158.2, m 168°, b 333°/760mm, pK^{20} 9.42.** Recrystallise it from *benzene/petroleum ether. [*Beilstein* **22/10** V 347.]

6-Aminonicotinic acid *[3167-49-5]* **M 138.1, m 312°(dec), $pK_{Est(1)}$~2.2 (CO_2H), $pK_{Est(2)}$ ~6.5.** Crystallise the acid from aqueous acetic acid. Dry it *in vacuo* at 70°. [*Beilstein* **22** III/IV 6726.]

6-Aminopenicillanic acid *[551-16-6]* **M 216.2, m 208-209°**, **$[\alpha]_{546}$ +327° (in 0.1M HCl), pK_1^{25} 2.30, pK_2^{25} 4.90.** This acid crystallises from water. [Kleppe & Stroninger *J Biol Chem* **254** 4856 *1979*, *Beilstein* **27** III/IV 2858.]

2-Aminoperimidine *[28832-64-6]* **M 183.1, m 239°, b 170-175°/1.5mm, pK_{Est} ~7.9 (free base).** It crystallises from EtOH/H_2O (1:1). It precipitates as the *hydrochloride* with dilute HCl which has **m** 282°. [Dasgupta et al. *Anal Chim Acta* **94** 205 *1977*, *Beilstein* **24** H 193, **25** III/IV 2677.]

2-Aminoperimidine hydrobromide *[40835-96-9]* **M 264.1, m 299°, pK_{Est} ~7.9 (free base).** Purify the hydrobromide by boiling a saturated aqueous solution with charcoal, filtering and leaving the salt to crystallise. Store this *dihydrate salt* in a cool, stoppered flask in the dark place. The *anhydrous salt* is obtained by heating at 80°/4 hours, and it is hygroscopic. The solubilities of the hydrobromide at 26° are 2.4% in EtOH, 0.6% in H_2O, 0.3% in Et_2O, 0.1% in Me_2CO and 0.003% in $*C_6H_6$. [Dasgupta et al. *Anal Chim Acta* **94** 205 *1977*, Dasgupta & West *Microchim Acta* **2** 505 *1978*, Dasgupta et al. *Anal Chem* **50** 1793 *1978, Beilstein* **24** H 193, **25** III/IV 2677.]

2-Aminopyridine *[504-29-0]* **M 94.1, m 58°, b 204-210°, pK_1^{25} -7.6, pK_2^{25} 6.71.** It crystallises from *benzene/petroleum ether (b 40-60°) or $CHCl_3$ /petroleum ether. [*Beilstein* **22/8** V 280.]

3-Aminopyridine *[462-08-8]* **M 94.1, m 64°, b 248°, pK_1^{25} -1.5, pK_2^{25} 6.03.** It crystallises from *benzene, $CHCl_3$/petroleum ether (b 60-70°), or *benzene/petroleum ether (4:1). [*Beilstein* **22/9** V 3.]

4-Aminopyridine *[504-24-5]* **M 94.1, m 160°, b 180°/12-13mm, pK_1^{25} -6.55, pK_2^{25} 9.11 (9.18).** Crystallise the aminopyridine from *benzene/EtOH, then recrystallise it twice from water, then crush and dry it for 4 hours at 105° [Bates & Hetzer *J Res Nat Bur Stand* **64A** 427 *1960*]. It has also been crystallised from EtOH, *benzene, *benzene/petroleum ether, toluene and sublimes in a vacuum. [*Beilstein* **22/9** V 106.]

2-Aminopyrimidine *[109-12-6]* **M 95.1, m 126-127.5°, pK^{20} 3.45.** Crystallise 2-aminopyrimidine from *C_6H_6, EtOH or H_2O. [*Beilstein* **25** III/IV 2071.]

4-Aminopyrimidine *[591-54-8]* **M 95.1, m 149-151°, 154-156°, pK^{25} 5.69.** Recrystallise 10.6g of aminopyrimidine from hot EtOAc (200ml) to give 7.4g colourless needles as first crop; evaporation to 25ml gives a second crop of 1.7g. The *hydroiodide* has **m** 180°. The *picrate* has **m** 225°. [Brown *J Soc Chem Ind* (London) **69** 353 *1950*, *Beilstein* **24** H 81, **24** III/IV 2130.]

5-Aminopyrimidine *[591-55-9]* **M 95.1, m 171-172° (with sublimation), pK^{25} 2.52.** It is purified by conversion to the $MgCl_2$ complex in a small volume of H_2O. The complex (~ 5g) is dissolved in the minimum volume of hot H_2O, passed through a column of activated Al_2O_3 (200g), and the column is washed with EtOH. Evaporation of the EtOH gives a colourless residue of the aminopyrimidine which is recrystallised from *C_6H_6 (toluene could also be used) which forms needles at first, then prisms. It melts with sublimation. Acetylation yields *5-acetamidopyrimidine* which crystallises from *C_6H_6, **m** 148-149°. [Whittaker *J Chem Soc* 1565 *1951*.]

Aminopyrine (4-dimethylaminoantipyrene) *[58-15-1]* **M 231.3, m 107-109°, 108°, pK$_1^{25}$ -2.22, pK$_2^{25}$ 4.94.** It crystallises from petroleum ether, sublimes between 80° and 90°, and forms metal complexes. [*Beilstein* **25** H 452, **25** III/IV 3555.]

3-Aminoquinoline *[580-17-6]* **M 144.2, m 93.5°, pK$_1^{20}$ -0.58, pK$_2^{20}$ 4.94.** It crystallises from *C_6H_6, toluene, hexane and aqueous EtOH. [*Beilstein* **22** III/IV 4605, **22/10** V 233.]

4-Aminoquinoline *[578-68-7]* **M 144.2, m 155-155.5°, 158°, pK$_1^{25}$ -7.11(5.99), pK$_2^{20}$ 9.13.** It has been purified by zone refining and recrystallisation from *C_6H_6, EtOH or H_2O. The *hydrochloride* has **m** 308° (from MeOH), and the *picrate* has **m** 277° (from EtOH). [Albert et al. *J Chem Soc* 2240 *1948*, *Beilstein* **22** III/IV 4611, **22/10** V 341.]

5-Aminoquinoline *[611-34-7]* **M 144.2, m 110°, b 184°/10mm, 310°/760mm, pK$_1^{20}$ 0.97(0.49), pK$_2^{20}$ 5.42.** It crystallises from pentane and from *benzene or EtOH. The *picrate* has **m** 209-210°(dec) (202° dec) (from aqueous EtOH). [*Beilstein* **22** III/IV 4669, **22/10** V 297.]

6-Aminoquinoline *[580-15-4]* **M 144.2, m 117-119°, 120°, b 146°/0.3mm, 192-195°/14mm, pK$_1^{20}$ 1.63, pK$_2^{20}$ 5.59.** It is purified by column chromatography on a SiO_2 column using $CHCl_3$/MeOH (4:1) as eluent. It crystallises from *C_6H_6 or *C_6H_6/petroleum ether and is an **irritant**. The *styphnate* has **m** 239-240° (from EtOH) and **m** 242-243° (from aqueous Me_2CO). [Barrett et al. *J Chem Soc* 50, 57 1953, *Beilstein* **22** III/IV 4681, **22/10** V 303.]

8-Aminoquinoline *[578-66-5]* **M 144.2, m 70°, b 140.5-141°/7mm, 123°/5mm, pK$_1^{20}$ -0.52, pK$_2^{20}$ 3.95.** 8-Aminoquinoline crystallises from EtOH, ligroin, octane or H_2O, and complexes with metals. [*Beilstein* **22** III/IV 4708, **22/10** V 316.]

2-Aminothiazole *[96-50-4]* **M 108.1, m 93°, b 140°/11mm, pK^{20} 5.36.** It crystallises from petroleum ether (b 100-120°), or EtOH. [*Beilstein* **27** III/IV 4574.]

1-Amino-1,2,4-triazole *[24994-60-3]* **M 84.1, m 91-93°, pK$_{Est}$ ~2.** The triazole crystallises from water. [Barszez et al. *J Chem Soc, Dalton Trans* 2025 *1986*, Temple & Montgomery *1,2,4-Triazoles —The Chemistry of Heterocyclic Compounds* Vol 37 (Weissberger & Taylor eds.). Wiley & Sons NY *1981*, ISBN 0-471-0656-6.]

3-Amino-1,2,4-triazole (Amitrol) *[61-82-5]* **M 84.1, m 159°, pK$_1^{20}$ 4.04, pK$_2^{20}$ 11.08.** It crystallises from EtOH (charcoal), then three times from dioxane [Williams et al. *J Phys Chem* **61** 261 *1957*]. [*Beilstein* **26** H 137.] **Possible carcinogen. [***Beilstein* **26** H 137, Temple & Montgomery *1,2,4-Triazoles —The Chemistry of Heterocyclic Compounds* Vol 37 (Weissberger & Taylor eds.). Wiley & Sons NY *1981*, ISBN 0-471-0656-6.]

4-Amino-1,2,4(4*H*)-triazole *[584-13-4]* **M 84.1, m 80-81°, pK^{25} 3.23.** It crystallises from EtOH/ Et_2O or H_2O. The *hydrochloride* has **m** 151-152° (from EtOH, 1g/10ml). [Allen & Bell *Org Synth* Coll Vol **III** 96 *1955*, Barszez et al. *J Chem Soc, Dalton Trans* 2025 *1986*, *Beilstein* **26** H 16, **26** II 7, **26** III/IV 40, Temple & Montgomery *1,2,4-Triazoles —The Chemistry of Heterocyclic Compounds* Vol 37 (Weissberger & Taylor eds.). Wiley & Sons NY *1981*, ISBN 0-471-0656-6.]

7-Amino-4-(trifluoromethyl)coumarin, *[53518-15-3]* **M 229.1, m 222°, pK$_{Est}$ ~3.1.** Purify the coumarin by column chromatography on a C18 column, elute with acetonitrile/0.01M H_2O/HCl (1:1), and recrystallise it from isopropanol. *Alternatively*, it is eluted from a silica gel column with CH_2Cl_2, or by extracting a CH_2Cl_2 solution (4g/L) with 1M aqueous NaOH (3 x 0.1L), followed by drying ($MgSO_4$), filtration and evaporation. [Bissell *J Org Chem* **45** 2283 *1980*, Zimmermann et al. *Anal Biochem* **70** 258 *1976*.]

4(6)-Aminouracil (4-amino-2,6-dihydroxypyrimidine) *[873-83-6]* **M 127.1, m >350°, pK$_1^{20}$ 0.00 (basic), pK$_2^{20}$ 8.69 (acidic), pK$_3^{20}$ 15.32 (acidic).** Purify the aminouracil by dissolving it in 3M aqueous NH_3, filtering hot, and adding 3M formic acid until precipitation is complete. Cool, filter off (or centrifuge), wash well with cold H_2O, then EtOH and dry it in air. Dry it further in a vacuum at ~80°. [Barlin & Pfeiderer *J Chem Soc (B)* 1424 *1971*, *Beilstein* **25** III/IV 4107.]

Amodiaquin [4-(3-dimethylaminomethyl-4-hydroxyanilino)-7-chloroquinoline] *[86-42-0]* **M 355.9, m 208°(dec).** Amodiaquin crystallises from 2-ethoxyethanol or EtOH. [Burckhalter et al. *J Am Chem Soc* **70** 1363 *1948*, *Beilstein* **22** III/IV 4647.]

2-*n*-Amylpyridine (2-*n*-pentylpyridine) *[2294-76-0]* **M 149.2, b 63.0°/2mm, 206.5-207°/~760mm, n$_D^{26}$ 1.4861, pK^{25} 6.00.** Dry it with NaOH for several days, then distil it from CaO under reduced pressure, taking the middle fraction and redistilling it. The *picrate* has **m** 72-72.8° (from EtOH). [*Beilstein* **20** III/IV 2835.] *3-n-Pentylpyridine*, purified as the 2-isomer, has **b** 110-112°/20mm, 224-226°/748mm, and the *picrate* has **m** 79.5-80°(from EtOH). [*Beilstein* **20** III/IV 2835.]

4-*n*-Amylpyridine *[2961-50-4]* **M 149.2, b 78.0°/2.5mm, 229-230°/~760mm, n$_D^{20}$ 1.4908, pK$_{Est}$ ~6.1.** It is dried with NaOH for several days, then distilled from CaO under reduced pressure, taking the middle fraction and redistilling it. The *picrate* has **m** 104° (from EtOH). [*Beilstein* **20** III/IV 2836.]

Antipyrine [2,3-dihydro-1,5-dimethyl-3-oxo-2-phenylpyrazole] *[60-80-0]* **M 188.2, m 114°, b 319°, pK^{25} 1.45.** Antipyrine crystallises from EtOH/water mixture, *benzene, *benzene/petroleum ether or hot water (charcoal), and the crystals are dried under a vacuum. [*Beilstein* **24** H 27, **24** III/IV 75.]

Aspergillic acid (2-hydroxy-3-isobutyl-6-[1-methylpropyl]pyrazine 1-oxide) *[490-02-8]* **M 224.3, m 97-99°, pK^{25} 5.5, [α]$_D^{20}$ +13.3° (c 4, EtOH).** It is recrystallised from MeOH and is sublimed at 80°/10^{-3}mm. [Dutcher *J Biol Chem* **171** 321 *1947*, *Beilstein* **24** III/IV 235.]

Atropine [tropine (±)-tropate] *[51-55-8]* **M 289.4, m 114-116°, pK$_1^{20}$ 4.35, pK^{18} 9.85.** It crystallises from acetone or hot water, and sublimes at ~100°/high vacuum. Its solubility is 0.22%(~20°) and 1.3%(100°) in H_2O, and 83%(60°). The *sulfate monohydrate* has **m 190-194°**. [*Beilstein* **21** IV 183, **21/1** V 235.] *Antispasmodic*.

8-Azaadenine *[1123-54-2]* **M 136.1, m 345°(dec), pK$_1^{20}$ 2.65, pK$_2^{20}$ 6.29.** 8-Azaadenine crystallises from H_2O. [*Beilstein* **25** III/IV 4157.]

2-Azacyclotridecanone (laurolactam) *[947-04-6]* **M 197.3, m 152°.** 2-Azacyclotridecanone crystallises from $CHCl_3$ and is stored over P_2O_5 in a vacuum desiccator. [*Beilstein* **26/1** V 566.]

8-Azaguanine *[134-58-7]* **M 152.1, m >300°, pK$_1^{20}$ 1.04, pK$_2^{20}$ 6.29.** Dissolve it in hot M NH_4OH, filter, and cool. Recrystallise it, and wash it with water, then dry it in a vacuum. [*Beilstein* **26** III/IV 4171.]

7-Azaindole (1*H*-pyrrolo[2,3b]pyridine) *[271-63-6]* **M 118.1, m 105-106°, pK^{20} 4.57.** Recrystallise it

repeatedly from EtOH, then sublime it in a vacuum [Tokumura et al. *J Am Chem Soc* **109** 1346 *1987*]. The *N-acetate* has **m** 65-66° (from $*C_6H_6$), and the *picrate* has **m** 232-233° (from Me_2CO) [Clemo & Swan *J Chem Soc* 603 *1945*, *Beilstein* **23** III/IV 1105.]

1-Azaindolizine (1,7a-diazaindene, imidazo[1,2-a]pyridine) *[274-76-0]* **M 118.1, b 72-73°/1mm, pK^{20} 1.43 (in aqueous HCl).** 1-Azaindolizine is purified by distillation or gas chromatography. [Bower & Ramage *J Chem Soc* 4506 *1957*, Armarego *J Chem Soc* 4226 *1964*, *Beilstein* **23** II 1554, **23** III/IV 1104.]

8-Azapurine (1*H*-1,2,3-triazolo[4,5-*d*]pyrimidine, 1,2,3,4,6[3*H*]penta-azaindene) *[273-40-5]* **M 121.1, m 174-175° (effervescence, m depends on heating rate), pK_1^{20} 2.05 (equilib with covalent hydrate), pK_2^{20} 4.84.** Sublime 8-azapurine at 120-130°/0.01mm and recrystallise it from 3 parts of EtOH. [Albert *J Chem Soc(B)* 427 *1966*, *Beilstein* **26** III/IV 4108.]

Azetidine (trimethyleneimine) *[503-29-7]* **M 57.1, b 19°/132.5mm, 61.3-61.5°/760mm, d_4^{20} 0.846, n 1.432, pK^{25} 11.29.** Azetidine is a flammable, hygroscopic liquid smelling of ammonia, which absorbs CO_2 from air and should be kept under Argon. Purify it by drying it over solid KOH and distilling it through a short Vigreux column (p 11) at atmospheric pressure (under Argon) and keeping the pot temperature below 210°. It is moisture sensitive. The *hydrochloride* [36520-39-5] **M 93.6** has **m** > 300° and the *hydroiodide* has **m** 146.5°(from EtOH). The *N-Me* derivative has **m** 112°(from $*C_6H_6$/petroleum ether), and the *N-phenylcarbamoyl* derivative has **m** 189-190°(from EtOH). [Searles et al. *J Am Chem Soc* **78** 4917 *1956*, *Beilstein* **20** H 2, **20** I 3, **20** II 3, **20** III/IV 53, **20/1** V 136.]

Aziridine (ethyleneimine) *[151-56-4]* **M 43.1, b 55-56°/756mm, 56°/760mm, d_4^{24} 0.8321, pK^{25} 8.00.** Redistil it in an Ar or N_2 atmosphere in a fume hood, and store it over KOH in sealed bottles in a refrigerator. Commercial aziridine has been dried over sodium and distilled from the metal through an efficient column before use [Jackson & Edwards *J Am Chem Soc* **83** 355 *1961*, Wenker *J Am Chem Soc* **57** 2328 *1935*]. It is a weaker base than Me_2NH (pK^{25} 10.87) but is caustic to the skin. It should not be inhaled, causes inflammation of the eyes, nose and throat, and one may become sensitised to it. It is soluble in H_2O, has an ammoniacal smell and reacts with CO_2. Pure aziridine is comparatively stable but polymerises in the presence of traces of H_2O and is occasionally explosive in the presence of acids. CO_2 is sufficiently acidic to cause polymerisation (forms linear polymers) which is not free radical promoted. It is stable in the presence of bases. The violet *2:1 Cu complex* crystallises from EtOH containing a few drops of aziridine and adding Et_2O, and has **m** 142°(dec). The *picrate* has **m** 142°. [O'Rourke et al. *J Am Chem Soc* **78** 2159 *1956*.] It has also been dried over BaO and has been distilled from sodium under nitrogen. [Allen et al. *Org Synth* Coll Vol **IV** 433 *1963*, *Beilstein* **20** III/IV 1.] **TOXIC.**

Azuleno(1,2-b)thiophene *[25043-00-9]* **M 184.2.** It is crystallised from cyclohexane, then sublimed *in vacuo*.

Azuleno(2,1-b)thiophene *[248-13-5]* **M 184.2.** It is crystallised from cyclohexane, then sublimed *in vacuo*.

Azure A (3-amino-7-dimethylaminophenazin-5-ium chloride) *[531-53-3]* **M 291.8, CI 52005, m > 290°(dec), λ_{max} 633nm, pK^{25} 7.2.** Azure A has been twice recrystallised from H_2O and dried at 100°/1 hour in an oven. [*Beilstein* **27** III/IV 5151.]

Azure B (3-dimethylamino-7-methylaminophenazin-5-ium chloride) *[531-55-5]* **M 305.8, CI 52010, m > 201°(dec), λ_{max} 648nm, pK^{25} 7.4.** Azure B has been twice recrystallised from H_2O and dried at 100°/1 hour in an oven. [*Beilstein* **27** III/IV 5151.]

Azure C (3-amino-7-methylaminophenazin-5-ium chloride) *[531-57-7]* **M 277.8, λ_{max} 616nm, pK^{25} 7.0.** Azure C has been twice recrystallised from H_2O, and dried at 100°/1 hour in an oven.

Barbituric acid [6-hydroxypyrimidin-2,4-dione] *[67-52-7]* **M 128.1, m 250°(dec), pK_1^{25} 3.99, pK_2^{25} 12.5.** Recrystallise it twice from H_2O, then dry it for 2 days at 100°. [*Beilstein* **24** III/IV 1873.]

Benzimidazole *[51-17-2]* **M 118.1, m 172-173°, pK_1^{25} 5.53, pK_2^{25} 11.70.** It crystallises from water or aqueous EtOH (charcoal) and is dried at 100° for 12 hours. [*Beilstein* **23** H 131, **23/6** V 196.]

2-Benzimidazolylacetonitrile *[4414-88-4]* **M 157.2, m 200-205°(dec), 209.7-210.7°(corrected), 210°.** It is recrystallised from aqueous EtOH. It has also been recrystallised from hot H_2O using charcoal, and finally from aqueous EtOH. [Copeland & Day *J Am Chem Soc* **65** 1072 *1943*, *Beilstein* **25** III/IV 820.]

Benzo-15-crown-5 *[14098-44-3]* **M 268.3, m 78-80°.** It is recrystallised from *n*-heptane. **IRRITANT.** [Vögtle ed, Host Guest Complex Chemistry in *Topics in Current Chemistry* p98 *1981*, *Beilstein* **19/10** V 618.]

Benzo-18-crown-6 *[14098-24-9]* **M 312.2, m 42-45°, 43-43.5°.** Purify it by passage through a DEAE cellulose column in cyclohexane. It recrystallises from *n*-hexane. Its *thiourea complex* has **m** 127° [5-6 mol of urea to ether, Pedersen *J Org Chem* ***36*** 1690 *1971*]. The stability constants of the Na^+, K^+, Rb^+, Cs^+, Tl^+ and Ba^{2+} complexes are described in Hofmanova et al. *Inorg Chim Acta* **28** 73 *1978*. [NMR: Live & Chan *J Am Chem Soc* **98** 3769 *1976*]. [*Beilstein* **19/12** V 618.] **IRRITANT.**

Benzo[3,4]cyclobuta[1,2-*b*]quinoxaline *[259-57-4]* **M 204.2, m dec >250°.** It is purified by sublimation under reduced pressure.

Benzofuran (coumarone) *[271-89-6]* **M 118.1, b 62-63°/15mm, 97.5-99.0°/80mm, 170-173°/atm, 173-175°(169)/760mm, d_4^{20} 1.0945, n_D^{20} 1.565.** Benzofuran is steam distilled, dissolved in Et_2O, washed with 5% aqueous NaOH, saturated NaCl, dried (Na_2SO_4), evaporated and redistilled. The UV has λ_{max} at 245, 275, 282nm (log ε 4.08, 3.45, 3.48). The *picrate* has **m** 102-103°. [Burgstahler & Worden *Org Synth* Coll Vol **V** 251 *1973*, NMR: Black & Heffernan *Aust J Chem* **18** 353 *1965*, *Beilstein* **17/2** V 3.]

2-Benzofurancarboxylic acid *[496-41-3]* **M 162.1, m 192-193°, pK_{Est} ~3.2.** The acid crystallises from water. [*Beilstein* **18/6** V 419.]

Benzofurazan *[273-09-6]* **M 120.1, m 55°.** Purify benzofurazan by steam distillation from a dilute alkaline solution, crystallisation from EtOH (long white needles) and by sublimation. [Green & Rowe *J Chem Soc* **101** 2456 *1912*, Green & Rowe *J Chem Soc* **111** 618 *1917*, Ghosh et al. *J Med Chem* **15** 255 *1972*, *Beilstein* **27** H 568, **27** I 573, **27** III/IV 7115.]

Benzofuroxan (benzofurazan-1-oxide, benz[1,2,5]oxadiazol-1-oxide) *[480-96-6]* **M 136.1, m 70-71°, 72-73°.** Purify the 1-oxide by dissolving 3.6g in 45ml of 95% EtOH + 15ml H_2O, boil, filter hot and cool to 25°. The yellow crystalline solid is steam volatile (but less so than benzofurazan, above) and has a peculiar pungent odour. Its UV has λ_{max} at 355nm (EtOH). It was used as a dehydrogenation oxidant (Pätzold et al. *Synth Commun* **22** 281 *1992*]. [Mallory *Org Synth* Coll Vol **IV** 74 *1963*, Boulton & Ghosh *Adv Heterocyclic Chem* **10** 1 *1969*, Bo et al. *J Am Chem Soc* **79** 1750 *1977*, *Beilstein* **27** I 622, **27** II 629, **27** III/IV 7115.]

5,6-Benzoquinoline (benzo[f]quinoline) *[85-02-9]* **M 179.0, m 93°, 94°, b 350°, pK^{20} 5.11.** Purify as 3,4-benzoquinoline above. The *picrate* has **m** 258.1-259° (from EtOH or H_2O). [Albert et al. *J Chem Soc* 2240 *1948*, *Beilstein* **20** III/IV 4009, **20/8** V 220.]

7,8-Benzoquinoline (benzo[h]quinoline) *[230-27-3]* **M 179.0, m 52.0-52.5°, pK^{20} 4.21.** Purify it as for 3,4-benzoquinoline above. The *picrate* has **m** 196°(from Me_2CO). [*Beilstein* **20** H 463, **20** III/IV 4003, **20/8** V 215.]

1,2,3-Benzothiadiazole *[273-77-8]* **M 136.2, m 35°, 36-37°, b 63°/0.5mm, pK_{Est} ~<0.** 1,2,3-Benzothiadiazole crystallises from petroleum ether, and has λ_{max} at 264 and 306nm in hexane. [Overberger et al. *J Org Soc* **24** 1407 *1959*, *Beilstein* **27** III/IV 7113.]

2,1,3(1,2,5)-Benzothiadiazole *[272-13-2]* **M 136.2, m 44°, b 206°/760mm, pK_{Est} <0.** 2,1,3-Benzothiadiazole crystallises from petroleum ether and has UV with λ_{max} at 221-222, 304 and 330nm in EtOH. [Sanvicki & Carr

J Org Soc **22** 503 *1959*, *Beilstein* **27** III/IV 7118.]

1-Benzothiophene (benzo[b]thiophene, thianaphthene) *[95-15-8]* **M 134.2, m 29-32°, 30°, 31-32°, 32°, b 100°/16mm, 103-105°/20mm, 221-222°/760mm, $d_4^{32.2}$ 1.1484, n_D^{39} 1.6306.** 1-Benzothiophene has the odour of naphthalene. If the IR spectrum is not very good, then suspend it in a faintly alkaline aqueous solution and steam distil it. Extract the distillate with Et_2O, dry the extract ($CaCl_2$), filter, evaporate the solvent and fractionate the residue. The distillate sets solid. The *sulfoxide* has **m** 142°, the *picrate* has **m** 148-149° (yellow crystals from EtOH) and the *styphnate* has **m** 136-137°. [Hansch & Lindwall *J Org Chem* **10**, 381 *1945*, Meyer & Meyer *Chem Ber* **52B** 1249 *1919*, Weisgerber & Kruber **53** 1551 *1920*, Iddon & Scrowston *Adv Heterocycl Chem* **11** 177 *1970*, *Beilstein* **17/2** V 6.]

1,2,3-Benzotriazole *[95-14-7]* **M 119.1, m 96-97°, 98.5°, 100°, b 159°/0.2mm, 204°/15mm, pK_1^{20} 1.6, pK_2^{20} 8.64.** 1,2,3-Benzotriazole crystallises from toluene, $CHCl_3$, Me_2NCHO or a saturated aqueous solution, and is dried at room temperature or in a vacuum oven at 65°. Losses are less if the material is distilled in a vacuum. **CAUTION: may EXPLODE during distillation; necessary precautions must be taken.** [Damschroder & Peterson *Org Synth* Coll Vol **III** 106 *1955*, *Beilstein* **26** III/IV 93.]

***O*-Benzotriazol-1-yl-*N,N,N′,N′*-tetramethyluronium hexafluorophosphate (HBTU)** *[94790-37-1]* **M 379.2, m 200° (dec), 250°, 254°(dec).** Wash the salt with H_2O (3x), CH_2Cl_2 (3x), dry and recrystallise it from MeCN. Dry it in a vacuum and store it cold in the dark [Dourtoglou et al. *Tetrahedron Lett* 1269 *1978*, NMR: Dourtoglou and Gross *Synthesis* 572 *1984*].

Benzoxazolinone (2-hydroxybenzoxazole) *[59-49-4]* **M 135.1, m 137-139°, 142-143°(corrected), b 121-213°/17mm, 335-337°/760mm.** Benzoxazolinone is purified by recrystallisation from aqueous Me_2CO followed by distillation at atmospheric pressure, then in a vacuum. The *methyl mercury salt* recrystallises from aqueous EtOH and has **m** 156-158°. [Bywater et al. *J Am Chem Soc* **67** 905 *1945*, *Beilstein* **27** III/IV 2677.]

***S*-(+) and *R*-(-) 1-Benzoyl-2-*tert*-butyl-3-methyl-4-imidazolinone** *[R- 101055-57-6] [S-101055-56-5]* **M 260.3, m 142-143°, 145.6-146.6°, 145-147°, $[\alpha]_{546}^{20}$ (+) and (-) 155°, $[\alpha]_D^{20}$ (+) and (-) 133° (c 1, $CHCl_3$).** Recrystallise these chiral imidazolinones from boiling EtOH (solubility is 1.43g/ml) or better by dissolving in CH_2Cl_2 and adding pentane, filtering and drying for at least 12 hours at 60°/0.1mm and sublime them at 135°/0.01mm. They have also been purified by flash column chromatography through Merck silica gel at 0.04-0.063mm and using Et_2O/petroleum ether/MeOH (60:35:5) as eluent. They are then recrystallised from EtOH/petroleum ether. [IR, NMR: Seebach et al. *Helv Chim Acta* **70** 237 *1987*, Fitzi & Seebach *Angew Chem, Int Ed Engl* **25** 345 *1986*.] The *racemate* is purified in a similar manner and has **m** 104-105° [NMR: Seebach et al. *Helv Chim Acta* **68** 949 *1985*].

2-Benzoylpyridine *[91-02-1]* **M 183.2, m 41-43°, 48-50°, 72°/0.02mm, 104-105°/0.01mm, n_D^{24} 1.6032, pK_{Est} ~2.4.** Dissolve 2-benzoylpyridine in Et_2O, shake it with aqueous $NaHCO_3$, H_2O, dry it over $MgSO_4$ and evaporate. The residue solidifies on cooling. The solid can be recrystallised from petroleum ether. Its *hydrochloride* crystallises from Me_2CO, **m** 126-127°, and the *2,4-dinitrophenylhydrazone* has **m** 193-195°. It distils at high vacuum. [Kinkerton & Thames *J Organomet Chem* **24** 623 *1970*, *Beilstein* **21/8** V 566.]

***N*^{6}-Benzyladenine** *[1214-39-7]* **M 225.3, m 231-232°, 232.5°(dec), $pK_{Est(1)}$~ 4.2, $pK_{Est(2)}$~ 10.1.** It is purified by recrystallisation from aqueous EtOH. It has λ_{max} at 207 and 270nm (H_2O), 268 nm (pH 6), 274nm (0.1 N HCl) and 275nm (0.1 N NaOH). [Daly *J Org Chem* **21** 1553 *1956*, Bullock et al. *J Am Chem Soc* **78** 3693 *1956*, *Beilstein* **26** III/IV 3575.]

1-Benzyl-1-aza-12-crown-4 (10-benzyl-1,4,7-trioxa-10-azacyclododecane) *[84227-47-4]* **M 265.4, 122-125°/0.03mm, 140-143°/0.05mm, d_4^{20} 1.09, n_D^{20} 1.52, pK_{Est} ~ 7.7.** Dissolve it in CH_2Cl_2 or CCl_4 (1g in 30ml), wash it with H_2O (30ml), brine (30ml), H_2O (30 ml) again, dry ($MgSO_4$ or Na_2SO_4), and evaporate. The residue in CH_2Cl_2 is chromatographed through Al_2O_3 (eluting with 10% EtOAc in hexane); evaporate, collect the correct fractions and distil (Kügelrohr) them. Log K_{Na} in dry MeOH at 25° for Na^+ complex is 2.08. [White et al. *Tetrahedron Lett* **26** 151 *1985*, Arnold et al. *J Org Chem* **53** 5652 *1988*.]

2-Benzyl-1,3-dioxolane *[101-49-5]* **M 164.2, b 98-99°/1mm, 110°/5mm, 137-138°/34mm, 240-242°/atm, d $_4^{20}$ 1.087, n $_D^{20}$ 1.532.** Dissolve 2-benzyl-1,3-dioxolane in CH_2Cl_2, wash well with 1M NaOH, dry over K_2CO_3, filter, evaporate and distil it through a short path still (Kügelrohr). It has also been purified by preparative gas chromatography. [Raber & Guida *Synthesis* 808 *1974*, Lloyd & Luberoff *J Org Chem* **34** 3949 *1969*, *Beilstein* **19** III/IV 220.]

***S-(+)-* and *R-(-)-* Benzyl glycidyl ether (1-benzyloxyoxirane)** *[S:14618-80-5] [R:16495-13-9]* **M 164.2, b 68°/10^{-4} mm, 105°/0.4mm, d $_4^{20}$ 1.072, n $_D^{20}$ 1.517, [α] $_{546}^{20}$ (+) and (-) 5.5°, [α] $_D^{20}$ (+) and (-) 5.1° (c 5, toluene), [α] $_D^{20}$ (+) and (-) 1.79° (c 5.02, $CHCl_3$), [α] $_D^{21}$ (+) and (-) 15.3° (neat).** This ether in EtOAc is dried (Na_2SO_4), then purified by flash chromatography using petroleum ether/EtOAc (5:1) as eluent. The ether distils through a short path distillation apparatus (Kügelrohr) as a colourless liquid. *Alternatively*, dissolve it in $CHCl_3$, wash it with H_2O, dry (Na_2SO_4), evaporate and purify by silica gel chromatography. [Anisuzzamen & Owen *J Chem Soc* 1021 *1967*, Takano et al. *Heterocycles* **16** 381 *1981*, Lipshutz et al. *Org Synth* **69** 82 *1990*, Takano et al. *Synthesis* 539 *1989*, Honda et al. *Chem Pharm Bull Jpn* **39** 1385 *1991*, *Beilstein* **12** IV 2277.]

3-Benzyl-5-(2-hydroxyethyl)-4-methylthiazolinium chloride *[4568-71-2]* **M 269.8, m 142-144°, 145-147°.** Purify the chloride by recrystallisation from EtOH or H_2O. If placed in a bath at 125° and heated at 2°/minute, the melting point is 140.5-141.4°. [Livermore & Sealock *J Biol Chem* **167** 699 *1947,* Maier & Metzler *J Am Chem Soc* **79** 4386 *1957*, *Beilstein* **27** III/IV 1758.]

5-Benzyloxyindole *[1215-59-4]* **M 223.3, m 96-97°; 100-103°, 104-106°, pK^{25} <0.** It is recrystallised from *C_6H_6/petroleum ether or petroleum ether. The *picrate* forms red crystals from *C_6H_6 and has **m** 142-143°. [Burton & Leong *Chem Ind (London)* 1035 *1953*, Ek & Witkop *J Am Chem Soc* **76** 5579 *1954*, fluorescence: Bridges & Williams *Biochem J* **107** 225 *1968*, *Beilstein* **27** III/IV 1758.]

1-Benzyl-4-piperidone *[3612-20-2]* **M 189.3, b 107-108°/0.2mm, 114-116°/0.3mm, 143-146°/5mm, 157-158°/11mm, d $_4^{20}$ 1.059, n $_D^{20}$ 1.538.** If the physical properties show contamination, then dissolve it in the minimum volume of H_2O, made strongly alkaline with aqueous KOH, extract it with toluene several times, dry the extract with K_2CO_3, filter, evaporate and distil the residue at high vacuum using a bath temperature of 160-190°, and redistil it. [Brookes & Walker *J Chem Soc* 3173 *1957*, Bolyard *J Am Chem Soc* **52** 1030 *1930*.] The *hydrochloride* has **m** 159-161° (from Me_2CO/Et_2O), and the *picrate* has **m** 174-182° (from Me_2CO/Et_2O). [Grob & Brenneisen *Helv Chim Acta* **41** 1184 *1958*, *Beilstein* **21/6** V 424.]

2-Benzylpyridine *[101-82-6]* **M 169.2, b 98.5°/4mm, d $_4^{20}$ 1.054, n $_D^{26}$ 1.5771, pK^{25} 5.13.** Dry it with NaOH for several days, then distil it from CaO under reduced pressure, and redistil the middle fraction. [*Beilstein* **20/7** V 556.]

4-Benzylpyridine *[2116-65-6]* **M 169.2, b 110.0°/6mm, d $_4^{20}$ 1.065, n $_D^{26}$ 1.5814, pK^{25} 5.59.** Dry it with NaOH for several days, then distil it from CaO under reduced pressure, and redistil the middle fraction. [*Beilstein* **20/7** V 561.]

Berbamine *[478-61-5]* **M 608.7, m 197-210°, [α] $_D^{20}$ +115° ($CHCl_3$), pK^{20} 7.33. (70% aqueous EtOH).** Crystallise berbamine from petroleum ether or *C_6H_6 (with 1*C_6H_6 **m** 129-134°). [Bick *Aust J Chem* **9** 111, 118 *1956*, *Beilstein* **27** II 891, **27** III/IV 8732.]

Berberine *[2086-83-1]* **M 336.4, m 145°, 147-148°, pK $_1^{20}$ 2.47, pK $_2^{20}$ 11.73 (pseudobase?).** Berberine crystallises from petroleum ether or ether as yellow needles or from H_2O. [*Beilstein* **27** II 567, **27** III/IV 6539.]

Berberine chloride ($2H_2O$) (Neutral Yellow 18) *[633-65-8 (anhydrous), 5956-60-5 ($2H_2O$)]* **M 407.9, m 204-206°(dec), CI 75160, pK^{20} 2.47.** Berberine chloride crystallises from water to give the *dihydrate*. The anhydrous salt may be obtained by recrystallisation from EtOH/Et_2O, wash the crystals with Et_2O and dry them in a vacuum. The *iodide* has **m** 250°(dec) (from EtOH). [Perkin *J Chem Soc* **113** 503 *1918*, Kametani et al. *J Chem Soc(C)* 2036 *1969*, *Beilstein* **27** I 515, **27** II 567.]

Bicuculline See entry in "Miscellaneous", Chapter 7.

Bilirubin *[635-65-4]* **M 584.7, m >360°, ε_{450nm} 55,600 in $CHCl_3$, pK_{Est} ~3.0.** An acyclic tetrapyrrole bile pigment with impurities which can be eliminated by successive Soxhlet extraction with diethyl ether and MeOH. It crystallises from $CHCl_3$ as deep red-brown rhombs, plates or orange-red prisms from chlorobenzene (**m** 330° dec) and is dried to constant weight at 80° under vacuum. [Gray et al. *J Chem Soc* 2264, 2276 *1961*, *Beilstein* **26** III/IV 3268.]

Biliverdine *[114-25-0]* **M 582.6, m >300°, pK^{25} 3.0.** This is the precursor of bilirubin (above) and forms dark green plates or prisms, with a violet reflection, from MeOH. The *dimethyl ester*, when crystallised from MeOH has **m** 215°(209°), and when crystallised from $CHCl_3$/petroleum ether gives blue-green crystals with **m** 202°. [Gray et al. *J Chem Soc* 2264 *1961*, Sheldrick *J Chem Soc, Perkin Trans 2* 1457 *1976*, *Beilstein* **26** III/V 3272.]

2-(4-Biphenylyl)-5-phenyl-1,3,4-oxadiazole (BPD) *[852-38-0]* **M 298.4, m 166-167°, 167-170°.** BPD is recrystallised from toluene. It is a good scintillation material [Brown et al. *Discussion Faraday Soc* **27** 43 *1959*]. [*Beilstein* **27** III/IV 7283.]

2,2'-Bipyridyl *[366-18-7]* **M 156.2, m 70.5°, b 273°, pK_1^{25} -0.52, pK_2^{25} 4.44.** 2,2'-Bipyridyl crystallises from hexane, or EtOH, or (after charcoal treatment of a $CHCl_3$ solution) from petroleum ether. Also, it precipitates from a concentrated solution in EtOH by addition of H_2O. Dry it in a vacuum over P_2O_5. It can be further purified by chromatography on Al_2O_3 or by sublimation. Its UV (EtOH) has λ_{max} at 280nm (logε 4.13). [Airoldi et al. *J Chem Soc, Dalton Trans* 1913 *1986*, *Beilstein* **23** H 199, **23/8** V 16.]

4,4'-Bipyridyl *[553-26-4]* **M 156.2, m 73°(hydrate)** *[123333-55-1]***, 114° (171-171°)(anhydrous), b 305°/760mm, 293°/743mm, pK_1^{20} 3.17, pK_2^{20} 4.82.** It crystallises from water, *benzene/petroleum ether, ethyl acetate and sublimes *in vacuo* at 70°. Also purify it by dissolving in 0.1M H_2SO_4 and twice precipitating by addition of 1M NaOH to pH 8. Then recrystallise it from EtOH. For the *dihydrochloride* see Viologen below. [Collman et al. *J Am Chem Soc* **109** 4606 *1987*, *Beilstein* **23** H 800, **23** III/IV 1371, **23/8** V 28.]

2,2'-Biquinolin-4,4'-dicarboxylic (2,2'-bicinchoninic) acid *[1245-13-2]* **M 344.3, m 367°, $pK_{Est(1)}$ ~1.5, $pK_{Est(2)}$ ~4.0.** Dissolve the acid in dilute NaOH and precipitate it with acetic acid, filter, wash swell with H_2O and dry it at 100° in a vacuum oven. Attempts to form a picrate failed. The *methyl ester* ($SOCl_2$-MeOH) has **m** 165.6-166°. [Lesesne & Henze *J Am Chem Soc* **64** 1897 *1942*, Brown et al. *J Am Chem Soc* **68** 2705 *1946*, *Beilstein* **25** III/IV 1148.] For the di-K salt see entry in "Metal-organic Compounds" in Chapter 5.

2,2'-Biquinolyl (α,α'-diquinolyl) *[119-91-5]* **M 256.3, m 196°, pK_{Est} ~4.2.** Decolourise 2,2'-biquinolyl in $CHCl_3$ solution (charcoal), then crystallise it to constant melting point from EtOH or petroleum ether [Cumper et al. *J Chem Soc* 1188 *1962*]. [*Beilstein* **23/10** V 8.]

2,5-Bis(4-aminophenyl)-1,3,4-oxadiazole (BAO) *[2425-95-8]* **M 252.3, m 252-255°, 254-255°.** BAO is recrystallised from EtOH using charcoal and under N_2 to avoid oxidation. It is a fluorescent stain for DNA [Yataghanas et al. *Exptl Cell Res* **56** 59 *1969*]. [*Beilstein* **27** III/IV 8158.]

2,5-Bis(2-benzothiazolyl)hydroquinone *[33450-09-8]* **M 440.3, m dec >200°.** Purify the hydroquinone by repeated crystallisation from dimethylformamide followed by sublimation in vacuum [Erusting et al. *J Phys Chem* **91** *1404 1987*].

2,5-Bis(4-biphenylyl)-1,3,4-oxadiazole (BBOD) *[2043-06-3]* **M 374.5, m 229-230°, 235-238°.** BBOD is recrystallised from heptane or toluene. It is a good scintillant. [Hayes et al. *J Am Chem Soc* **77** 1850 *1955*.]

3,3-Bis(chloromethyl)oxacyclobutane (3,3-bis-[chloromethyl]oxetane) *[78-71-7]* **M 155.0, m 18.9°, b 65°/5mm, 80°/10mm, 103°/30mm, 198°/atm, d_4^{20} 1.290, n_D^{20} 1.486**. Shake it with aqueous $NaHCO_3$ or $FeSO_4$ to remove peroxides, separate, dry with anhydrous Na_2SO_4, then distil it under reduced pressure from a little CaH_2 [Dainton et al. *Trans Faraday Soc* **56** 1784 *1960*, Farthing *J Chem Soc* 3648 *1955*]. The *3,3-bis-*

(phenoxymethyl) derivative is described below. [*Beilstein* **17** III/IV 68.] **Lachrymatory.**

***N,N'*-Bis(nicotinic acid) hydrazide** *[840-78-8]* **M 227-228°, m dec 200°, pK_{Est} ~3.3.** The hydrazide crystallises from water; it is also soluble in hot EtOH but insoluble in *C_6H_6, petroleum ether or $CHCl_3$. [Graf *J Prakt Chem* [2] **138** 290 *1933*, *Beilstein* **22** III/IV 455.]

3,3-Bis(phenoxymethyl)oxacyclobutane (**3,3-bis-[phenoxymethyl]oxetane)** *[1224-69-7]* **M 270.3, m 67.5-68°, b 143°/0.05mm.** Distil it under high vacuum, then crystallise the solidified distillate from MeOH. [Farthing *J Chem Soc* 3648 *1955*, *Beilstein* **17** III/IV 2010.]

Blue Tetrazolium (tetrazolium blue chloride) *[1871-22-3]* **M 727.7, m 254-255°(dec).** Crystallise the chloride from 95% EtOH/anhydrous diethyl ether to constant absorbance at 254nm. [*Beilstein* **26** III/IV 1789.]

1-*N*-Boc-piperidine (*N-tert*-butoxycarbonylpiperidine, 1-piperidincarboxylic acid 1,1-dimethylethyl ester) *[75844-69-8]* **M 185.3, b 79°/0.05mm, d_4^{25} 0.964, n_D^{20} 1.454.** It is purifed by bulb-to-bulb distillation at 65°/1mm. If it is discoloured then dissolve it in Et_2O, wash it with brine, separate, dry the Et_2O layer over K_2CO_3, filter, evaporate, and distil in a vacuum. Its IR has ν_{max} at 1695 (CO) cm^{-1} (film). [IR, NMR, MS: Dieter & Li *J Org Chem* **62** 7726 *1997*, Beak & Lee *J Org Chem* **58** 1109 *1993*].

1-*N*-Boc-2-piperidone (1-*N-tert*-butoxycarbonyl-2-piperidone) *[85908-96-9]* **M 199.3, m 30-33°, 32-34°, 33-35°, 36°, b 110°/0.1mm.** This useful synthetic starting material is prepared by using the same principles as for the 4-oxo isomer below. Thus to a solution of γ-valerolactam (2-piperidone, 6.0g, 60.5mmol, [675-20-7]), DMAP (1.85g, 15.1mmol, 0.2 equiv, [1122-58-3] and Boc_2O (26.6g, 121.0mmol, 2.0 equiv, [24074-26-8]) in CH_2Cl_2 (70ml) at ~25° is added Et_3N (17.8g, 127.7mmol, 2.1 equiv) and is stirred for 32 hours, then quenched with 1.2N HCl (10ml). The aqueous layer is extracted with CH_2Cl_2, the combined CH_2Cl_2 solutions are washed with saturated aqueous $NaHCO_3$ (20ml), brine (30ml), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product is purified by flash chromatography through Kieselgel 60 (230-240 mesh with cyclohexane/EtOAc 8:2 elution) to give *1-N-Boc-2-piperidone* (9.71g, 48.7mmol, 81%) as a colourless low melting solid **m 36°**. It has R_F 0.40 (TLC on Kieselgel $60F_{254}$, cyclohexane/EtOAc 7:3), and its IR (KBr) has ν_{max} at 1713, 1302, 1249, 1159 and 1138 cm^{-1}; the ^1H NMR (300MHz, $CDCl_3$, with residual $CHCl_3$ as internal standard at δ 7.27) has δ at 3.66 (m, 2H, H-6,6), 2.50 (m, 2H, H-3,3), 1.90-1.74 (4H, H-3,3,4,4) and 1.53 (s, 9H, *t*-Bu); the ^{13}C NMR (75MHz, $CDCl_3$, with residual $CDCl_3$ as internal standard at δ 77.1) has δ at 171.1 (s), 152.4 (s), 82.5 (s), 46.0 (t), 34.6 (t), 27.7 (q), 22.5 (t) and 20.2 (t); and the EI MS has *m/z* (relative intensity) at 199 (M^+ 0.3), 144 (52), 126 (21), 100 (38), 99 (31), 98 (31), 82 (24), 57 (100), 56 (38) and 55 (30). [Cossy et al. *New J Chem* **27** 475 *2003*.] This synthesis has also been carried out in MeCN/DMAP at ~25°/24 hours (74% yield) without further base [Moody & Taylor *J Chem Soc, Perkin Trans 1* 721 *1989*].
1-N-Boc-2-piperidone is hydrolysed at ambient temperature by LiOH (30 minutes, 90%), or undergoes methanolysis by MeONa/MeOH (15 minutes, 94%) to provide γ-$BocNH(CH_2)_4CO_2H$ (after acidification) or γ-$BocNH(CH_2)_4CO_2Me$ without losing the Boc protecting group, respectively [Flynn et al. *J Org Chem* **54** 2424 *1989*]

1-*N*-Boc-3-piperidone (1-*N-tert*-butoxycarbonyl-3-piperidone) *[98977-36-7]* **M 199.3, m 35-40°, b 104-105°/0.4mm.** 3-Piperidone used to prepare the Boc derivative was obtained by hydrogenolysis of *N*-benzyl-3-piperidone hydrochloride hydrate (4.2g, 18.6mmol, [50606-58-1]) catalysed by 10% Pd/C (0.8g) and H_2 at 55 psi while stirring for 16 hours in degassed MeOH (200ml). This was filtered (Celite) and evaporated *in vacuo*. The crude oily 3-piperidone was dissolved in THF (200ml), treated with Boc_2O (5.27g, 24.1mmol) and saturated aqueous Na_2CO_3 (50ml), stirred for 4 hours and evaporated *in vacuo.* The white solid was partitioned between EtOAc and 1N HCl, the organic layer was collected, washed with 1N NaOH and brine, dried ($MgSO_4$), filtered, and evaporated *in vacuo* to give an oil which was purified by flash chromatography (silica gel, hexane/EtOAc 3:1) to give *1-N-Boc-3-piperidone* (2.93g, ~100%) as a colourless oil. [Lucca et al. *J Med Chem* **48** 2195 *2005*.] Its ^1H NMR (300MHz, $CDCl_3$, TMS) has δ at 3.99 (s, 2H, 2,2-H), 3.58 (t, *J* = 6.3 Hz, 2H, 6,6-H), 2.46 (t, *J* = 6.3 Hz, 2H 4,4-H), 1.97 (t, *J* = 6.3 Hz, 2H, 5,5-H), and 1.45 (s, 9H, *t*-Bu); and the HRMS has

m/z 200.1285 and calculated for $C_{10}H_{18}NO_3$ (M + H) was 200.1287. *Alternatively*, and almost similar preparation, was carried out except that saturated aqueous Na_2CO_3 was replaced by Et_3N (3 equiv) to give an 81% yield of *1-N-Boc-3-piperidone* which was distilled at high vacuum undecomposed. [Brehm et al. *J Med Chem* **29** 224 *1986*.]
In a completely different synthesis, involving catalysed intramolecular cyclisation, *(5-oxo-6-dimethyl-sulfoxonium-hexyl)-carbamic acid tert-butyl ester* (250mg, 0.901mmol) in CH_2Cl_2 (8.0ml, purged with N_2 for 30 minutes) was added *via* a syringe pump over 18 hours to a solution of $[Ir(COD)Cl]_2$ (6.05mg, 9.01μmol, 0.01 equiv, [12112-67-3]) in degassed CH_2Cl_2 (4.0ml) at 70°. The mixture was then evaporated *in vacuo*, and the residue was purified through a silica gel column and eluting with hexanes/EtOAc (3:2) to afford *1-N-Boc-3-piperidone* (147mg, 82%) identical with the above. [Mangion et al. *Org Lett* **11** 3566 *2009*.]

1-*N*-Boc-4-piperidone (1-*N*-*tert*-butoxycarbonyl-4-piperidone) *[98977-36-7]* **M 199.3, m 68-69°, 70-72°, 72°, 73-75°, 74-75°, 74.4-75.2°.** It is prepared by dissolving 4-piperidone (1g, 6.5mmol [41661-47-6]) and EtN(*iso*-Pr)$_2$ (2.8ml, 16mmol, DIPEA [7087-68-5]) in dioxane/H_2O (4:1, 10ml), adding Boc_2O (2.2g, 9.8mmol, [24074-26-8]) slowly with stirring at ~25° for 24 hours. The solvent is removed *in vacuo*, the residue is dissolved in CH_2Cl_2, washed with H_2O (3 x), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The residue is triturated with Et_2O, the white residue is collected by filtration and recrystallised from hexane to give the *Boc-piperidone* (75%), **m 73.5°**. It also crystallises from petroleum ether**,** toluene or EtOAc and can be dried in a vacuum desiccator over shredded paraffin wax. It has R_F 0.74 (TLC on Kieselgel $60F_{254}$, hexane/EtOAc 4:6), and its IR (KBr) has ν_{max} at 1715 and 1680 cm^{-1}. Its ^1H NMR (300MHz, $CDCl_3$) has δ at 3.72 (t, *J* = 6.3 Hz, 4H, 3,5-H), 2.44 (t, *J* = 6.3 Hz, 4H 2,6-H) and 1.50 (s, 9H, *t*-Bu); and the ^1H NMR (300MHz, DMSOd_6) has δ at 3.6 (t, 4H, 3,5-H), 2.4 (t, 4H, 2,6-H) and 1.4 (s, 9H, *t*-Bu). It has been used extensively to introduce a piperidine ring for making drugs because the 4-oxo group can be functionalised in various ways and deprotection of the nitrogen allows bonding to this atom. [Houssin et al. *J Med Chem* **45** 533 *2002*, Ellis et al. *J Med Chem* **51** 2170 *2002*.]

Brazilin (6a*S*-*cis*-7,11b-dihydrobenzo[b]indeno[1,2-d]pyran-3,6a,9,10(6*H*)-tetraol) *[474-07-7]* **M 269.3, m 130°(dec), 250°, $pK_{Est(1)}$ ~9.3, $pK_{Est(2)}$ ~10.0, $pK_{Est(3)}$ ~12.5 (all phenolic), CI 75280.** Brazilin crystallises from EtOH as yellow crystals which become orange when exposed to light and air, and is yellow in dilute acid but crimson in dilute alkali. When crystallised from H_2O, it has **m** 247-248°. It forms coloured metal salts and is oxidised in air to *Brazilein*, the quinonoid form. The *(±)-form has been resolved, and the (+)-enantiomer* has $[\alpha]_D^{20}$ +121° (c 1, MeOH). [Craig et al. *J Org Chem* **30** 1573 *1965*, Morsingh & Robinson *Tetrahedron* **26** 281 *1970*, *Beilstein* **17** H 194, **17** II 244, **17** III/IV 2711.]

Brilliant Cresyl Blue (*NN*-diethyl-3-imino-8-methyl-3*H*-phenoxazin-7-amine hydrochloride) *[4712-70-3]* **M 332.8, pK^{25} 3.2.** Crystallise the dye from petroleum ether. It has λ_{max} at 625nm (H_2O) and 622nm (95% aqueous EtOH). [*Beilstein* **27** H 400, **27** II 454, **27** III/IV 5160.]

5-Bromocytosine *[2240-25-7]* **M 190.0, m 245-255°(dec), 250°(dec), pK_1^{25} 3.04, pK_2^{25} 10.33.** 5-Bromocytosine is recrystallised from H_2O or 50% aqueous EtOH. *Alternatively*, dissolve *ca* 3g in conc HCl (10ml) and evaporate to dryness. Dissolve the residual hydrochloride in the minimum volume of warm H_2O and make faintly alkaline with aqueous NH_3. Collect the crystals and dry them in a vacuum at 100°. [Hilbdert & Jensen *J Am Chem Soc* **56** 134 *1934*, *Beilstein* **25** III/IV 3689.]

2-(2-Bromoethyl)-1,3-dioxane *[33884-43-4]* **M 195.1, b 67-70°/2.8mm, 71-72°/4mm, 95°/15mm, d_4^{20} 1.44, n_D^{20} 1.4219**. Purify it by vacuum fractionation. Also dissolve it in Et_2O, wash with aqueous $NaHCO_3$, dry the extract (Na_2SO_4), filter and fractionate at high vacuum. Its ^{1}HNMR in CCl_4 has δ at 1.3 (m, 1H), 2.1 (m, 3H), 3.36 (t, 2H), 3.90 (m, 4H) and 4.57 (t, H). [Stowell *J Org Chem* **41** 560 *1976*, NMR, MS: Schwarz & Franke *Tetrahedron* **35** 1969 *1979*, Kriesat & Gisvold *J Pharm Sci* **60** 1250 *1971*, *Beilstein* **19/1** V 69.]

2-(2-Bromoethyl)-1,3-dioxolane *[18742-02-4]* **M 181.1, b 68-80°/8mm, 68-73°/10mm, 78-80°/20mm, d_4^{20}**

1.510, n_D^{20} 1.479. Dissolve it in pentane, wash with 5% aqueous $NaHCO_3$, dry (Na_2SO_4), and evaporate. Distil the residue. [NMR: Büchi & Wüest *J Org Chem* **34** 1122 *1969*, Kriesat & Gisvold *J Pharm Sci* **60** 1250 *1971*, *Beilstein* **19/1** V 69.]

6-Bromo-5-fluoro-1*H*-indole *[259860-08-7]* **M 214.0, m 83-84°, $pK_{Est(1)}$ ~ −4.05 (basic), $pK_{Est(2)}$ ~15.9 (acidic).** There are several preparations of this indole. In a patent (to Vernallis Research Ltd, US6380238, *2002*] *N,N*-dimethylformamide dimethylacetal (8.5ml, 60mmol) was added to a stirred solution of 4-bromo-5-fluoro-2-nitrotoluene (11.8g, 50mmol) in DMF (30ml) in one portion under argon at ~25°, then heated at 120° for 16 hours and evaporated *in vacuo*. The residual oil crystallised from MeOH/CH_2Cl_2 (4:1) to give a purple solid (4.5g) which was dissolved in MeOH/THF (1:1, 30ml), mixed with Raney Ni (1g), cooled to 0° and $N_2H_4.H_2O$ (0.8ml, 16mmol) was added all at once. After stirring for 90 minutes, more $N_2H_4.H_2O$ (0.8ml) was added and stirred at 0° for 30 minutes. The mixture was filtered through Celite and the filter cakes was washed with THF. The combined filtrates were evaporated *in vacuo*, and the residue was purified by chromatography [SiO_2 with heptane/CH_2Cl_2 (4:1) as eluent] to give the *indole* (1.7g, 16%) as an off-white solid. In a second patent [to M.P. Dillon et al. US2004/224973, *2004*, see also Batcho & Leimgruber *Org Synth* **63** 214 *1985*] crude [2-(4-bromo-5-fluoro-2-nitrophenyl)vinyl]-dimethylamine and Raney Ni in THF gave after flash chromatography through a silica gel column (eluting with 10% EtOAc in hexane) which gave the indole as a light green solid (61%). However, when the same enamine (1.89g, 4.38mmol) in EtOH (35ml) was treated with a mixture of Fe (4.42g, 79mmol) in AcOH (35ml) and stirred at 90° overnight, then filtered, evaporated and the residue purified by chromatography as above, pure *6-bromo-5-fluoro-1H-indole* (0.83g, 89%) was obtained as a yellow solid [Patent to the Board of Trustees of the University of Illinois; WO2008/77138 *2008*]. It had IR (nujol) with ν_{max} at 3395, 2925, 2855, 1570, 1469, 1451, 1408, 1314, 1145, 1105, 865, 763 and 505 cm^{-1}; and the ^1H NMR (400MHz, $CDCl_3$) had δ at 7.85 (br s, 1H), 7.55 (dd, 1H, *J* = 5.6 and 0.9 Hz), 7.34 (d, 1H, *J* = 9.0 Hz), 7.23 (t, 1H, *J* = 2.8 Hz) and 6.45-6.51 (m, 1H).
6-Bromo-5-fluoro-1-methylindole was obtained as a colourless solid in 99% yield by converting the indole to its *N-sodio*- derivative with NaH (1.5mol) in DMF at 0°/30 minutes, followed by MeI (1.2mol) for 1 hour at ~25°, then purified by column chromatography as above. Its ^1H NMR (400MHz, $CDCl_3$) had δ at 3.66 (s, 3H, *N*-Me), 6.43 (d, 1H, *J* = 2.7 Hz), 7.05 (d, 1H, *J* = 2.7 Hz), 7.34 (d, 1H, *J* = 9.3 Hz) and 7.44 (d, 1H, *J* = 5.4 Hz) [Patent to the Board of Trustees of the University of Illinois; WO2008/77138 *2008*].

3-Bromofuran *[22037-28-1]* **M 147.0, b 38.5°/40mm, 50°/110mm, 102.5-103°/atm, d_4^{20} 1.661, n_D^{20} 1.4970.** Purify 3-bromofuran by two steam distillations and dry it over fresh CaO. It can be dried over Na metal (no obvious reaction) and fractionated. It is not very soluble in H_2O but is soluble in organic solvents. When freshly distilled, it is a clear oil, but darkens on standing and eventually resinifies. It can be stored for long periods by covering the oil with an alkaline solution of hydroquinone and is redistilled when required. It forms a characteristic *maleic anhydride adduct*, **m** 131.5-132°. [Shepard et al. *J Am Chem Soc* **52** 2083 *1930*, Huhes & Johnson *J Am Chem Soc* **53** 737 *1931*, adduct: van Campen & Johnson *J Am Chem Soc* **55** 430 *1933*, *Beilstein* **17/1** V 295.]

5-Bromoindole *[10075-50-0]* **M 196.1, m 90.5-91°, 90-92°, pK^{25} 16.13 (NH).** Purify it by steam distillation from a faintly alkaline solution. Cool the aqueous distillate, collect the solid, dry it in a vacuum desiccator over P_2O_5 and recrystallise it from aqueous EtOH (35% EtOH) or petroleum ether/Et_2O. Its UV in MeOH has λ_{max} at 279, 287 and 296nm (logε 3.70, 3.69 and 3.53). The *picrate* has **m** 137-138°(dec) (from Et_2O/petroleum ether). [UV: Thesing et al. *Chem Ber* **95** 2205 *1962*, UV and NMR: Lallemand & Bernath *Bull Soc Chim Fr* 4091 *1970*, *Beilstein* **20/7** V 36.]

5-Bromoisatin *[87-48-9]* **M 226.0, m 245°(dec), 251-153°, 255-256°.** 5-Bromoisatin forms red prisms or needles from EtOH. The *N-acetate* crystallises as yellow prisms from $*C_6H_6$, **m** 170-172°, and the *N-methyl* derivative forms orange-red needles from MeOH, **m** 172-173°. [Heller *Chem Ber* **53** 1545 *1920*, Buu-Hoi *Rec Trav Chim Pays Bas* **73** 197 *1954*, Baker etal. *Tetrahedron Lett* 215 *1978*, *Beilstein* **21** H 453, **21** III/IV 5009.]

6-Bromoisatin *[6326-79-0]* **M 226.0, m 270°, pK^{25} 10.35.** 6-Bromoisatin recrystallises from AcOH (yellow needles). It is a plant growth substance. Its IR ($CHCl_3$) has ν_{max} at 1320 and 3440cm^{-1}. [Sadler *J Org Chem*

21 169 *1956*, *Beilstein* **21** III/IV 5012.]

2-Bromo-3-methylindole (2-bromoskatole) *[1484-28-2]* **M 210.1, m 102-104°, pK_{Est} <0.** Purify 2-bromoskatole by chromatography on silica gel in $CHCl_3$/petroleum ether (1:2) followed by crystallisation from aqueous EtOH. [Phillips & Cohen *J Am Chem Soc* **108** 2023 *1986*, cf *Beilstein* **20** III/IV 3205.]

4-(Bromomethyl)-7-methoxycoumarin *[35231-44-8]* **M 269.1, m 208-209°, 213-215°, 216-218°.** The coumarin is crystallised from boiling AcOH, the crystals are washed with AcOH, EtOH and dried in a vacuum; The ^{1}HNMR (TFA) has δ at 3.97s, 4.57s, 6.62s, 6.92-7.19m and 7.80d. [Secrist et al. *Biochem Biophys Res Commun* **45** 1262 *1971*, Dünges *Anal Chem* **49** 442 *1977*, *Beilstein* **18** III/IV 348.]

5-Bromonicotinic acid *[20826-04-4]* **M 202.0, m 178-182°, 189-190°, pK_{Est} ~4.4, pK^{25} 4.02 (50% aqueous EtOH).** The acid is recrystallised from H_2O and then from EtOH using charcoal. The *amide* has **m** 219-219.5° (from aqueous EtOH), and the *methyl ester*, prepared by addition of ethereal diazomethane, can be purified by sublimation in a vacuum and has **m** 98-99°. The *acid chloride* also can be sublimed in *vacuo* and has **m** 74-75° and gives the *methyl ester* in MeOH. [Graf *J Prakt Chem* **138** 244 *1933*, Bachman & Micucci *J Am Chem Soc* **70** 2381 *1948*, Garcia et al. *J Am Chem Soc* **82** 4430 *1960*, Misic-Vokovic et al. *J Chem Soc* 34 *1978*, *Beilstein* **22/2** V 181.]

2-Bromopyridine *[109-04-6]* **M 158.0, b 49.0°/2.7mm, d_4^{20} 1.660, n_D^{20} 1.5713, pK^{25} 0.90.** Dry 2-bromopyridine over KOH for several days, then distil it from CaO under reduced pressure, and taking the middle fraction. [*Beilstein* **20/5** V 422.]

8-Bromotheophylline (bromo-1,3-dimethyl-2,6(1*H*,3*H*)-purinedione) *[10381-75-6]* **M 259.1, m 309°, 315-320° (with browning and dec), $pK_{Est(1)}$ ~5.5, $pK_{Est(2)}$ ~9.2.** It is purified by dissolving in the minimum volume of dilute NaOH (charcoal), filtering and acidifying to pH *ca* 3.5-4. The solid that separates is collected, dried *in vacuo* at 100° and stored in a dark container. It has also been recrystallised from EtOH or AcOH. [Blitz & Beck *J Prakt Chem* [2] **118** 158 *1928*, Fischer & Ach *Chem Ber* **28** 3142 *1895*, *Beilstein* **26** H 476, **26** II 227, **26** III/IV 2447.]

5-Bromothiazole *[3034-55-7]* **M 164.0, b 62-63°/15mm, d_4^{20} 1.835, n_D^{20} 1.5955, n_D^{25} 1.5976, pK_{Est} ~2.0.** If bromothiazole is too coloured, then suspend it in dilute NaOH and steam distil it. Add NaCl to the aqueous distillate, extract it with Et_2O, dry it (Na_2SO_4), evaporate and fractionate the residue in a vacuum. The $HgCl_2$ *salt* crystallises from EtOH with **m** 148° (dec). [Beyerman et al. *Rec Trav Chim Pays Bas* **73** 330 *1954*, *Beilstein* **27** III/IV 962.]

2,3-Bromothiophene *[3140-93-0]* **M 241.9, m -17.5°, b 89-91°/13mm, 212-213°/atm, 218.6-219.6°/atm, d_4^{25} 2.137, n_D^{20} 1.632.** Purify the dibromothiophene by fractional distillation, preferably in a vacuum. Low temperature crystallisation from a small volume of petroleum ether (use Et_2O/CO_2 bath) removes the more soluble 2,4-dibromothiophene isomer. Nitration with Ac_2O/HNO_3 at 50-55° yields *2,3-dibromo-5-nitrothiophene* **m 75°** (from EtOH). [Steinkopf et al. *Justus Liebigs Ann Chem* **512** 149-151 *1934*, Gronowitz et al. *Acta Chem Scand* **46** 654 *1992*, NMR: Fujikara et al. *Bull Chem Soc Jpn* **32** 201 *1959*, *Beilstein* **17/1** III/IV 247, **17/1** V 308.]

Bufotenine hydrogen oxalate (3-[2-{dimethylamino}ethyl]-5-hydroxyindole hydrogen oxalate]) *[2963-79-3]* **M 294.3, m 96.5°, pK_1^{25} ~4.9(estimated), pK_2^{25} 9.8 (5-OH), pK_3^{25} 11.2 (NMe_2), pK_4^{25} ~18.2 (estimated acidic indole NH).** The hydrogen oxalate crystallises from Et_2O, EtOH/Et_2O (gave *monohydrate*) or MeOH/Et_2O. [Wieland et al. *Justus Liebigs Ann Chem* **513** 11 *1934*, *Beilstein* **22** III/IV 5672.]

4-*tert*-Butylcalix[4]arene *[60705-62-6]* **M 648.9, m >300°(dec), 380°(dec), 344-346°.** The calixarene recrystallises from $CHCl_3$ in large solvated prisms (**m** 380° dec); it effloresces on drying in air. Its *tetra-acetate* crystallises from Ac_2O in colourless prisms **m** 332-333°(dec). It crystallises from CCl_4 or chlorobenzene /EtOH (**m** >300°) and the *tetra-acetate* crystallises from $CHCl_3$/EtOH **m** >290°(dec). It also crystallises from toluene in white plates with toluene of crystallisation **m** 344-346° (330-332°); the *tetra-acetate* crystallises with 1AcOH of crystallisation **m** 383-386° (softening at 330-340°, also **m** 283-286°), but acetylation with

Ac_2O/NaOAc gives the *triacetate* which recrystallises from AcOH with 1AcOH of crystallisation **m** 278-281°. 4-*tert*-Butylcalix[4]arene (100mg) is unchanged after boiling for 4 hours with 10N KOH (0.04ml) in xylene (4ml). [*Br J Pharmacol* **10** 73 *1955*, Kämmerer et al. *Monatsh Chem* **109** 767 *1978*, Gutsche et al. *J Am Chem Soc* **103** 3782 *1981*; see also Kluawer in *Calixarenes*, Vicens & Böhner eds Academic Press *1991*, *Beilstein* **6** IV 7858.]

4-*tert*-Butylcalix[6]arene *[78092-53-2]* **M 972.3, m >300°, 380-381°.** It is recrystallised from $CHCl_3$ or $CHCl_3$/MeOH to give a white solid from the mother liquors of the calix[8]arene preparation. The *hexa-acetate* (Ac_2O/H_2SO_4) crystallises from $CHCl_3$/MeOH with **m** 360-362°(dec), and the *$(SiMe_3)_6$* derivative crystallises from $CHCl_3$/MeOH with **m** 410-412°. Its stability in KOH-xylene is the same as for the 4-*tert*-butylcalix[4]arene. [Gutsche et al.*J Am Chem Soc* **103** 3782 *1981*. See also Kluawer in *Calixarenes*, Vicens & Böhner eds Academic Press *1991*, *Beilstein* **6** IV 7858.]

4-*tert*-Butylcalix[8]arene *[68971-82-4]* **M 1297.8, m 411-412°.** The calixarene recrystallises from $CHCl_3$ in fine colourless, glistening needles. It melts sharply between 400-401° and 411-412° depending on the sample and is sensitive to traces of metal ions. On TLC with silica gel (250µm thick) and elution with $CHCl_3$/hexane (3:4) it has R_F 0.75. The *octa-acetate* is prepared from 8g in Ac_2O (50ml) and 2 drops of conc H_2SO_4 and refluxed for 2 hours. On cooling, a colourless precipitate separates and is recrystallised from Ac_2O (1.2g 48%) with **m** 353-354°. The *$(SiMe_3)_8$* is prepared from 4-*tert*-butylcalix[8]arene (0.65g) in pyridine (4ml) with excess of hexamethyldisilazane (1ml) and trimethylchlorosilane (0.5ml) and refluxed under N_2 for 2 hours. Cool, evaporate the pyridine, triturate the gummy residue with MeOH. Chromatograph on silica gel using hexane/CH_2Cl_2 gave 0.5g (61%) with one spot on TLC. Recrystallise it from hexane/Me_2CO to give colourless needles **m** 358-360°. [Gutsche et al. *J Am Chem Soc* **103** 3782 *1981*, Gutsche & MuthuKrishnan *J Org Chem* **43** 4905 *1978*, Gutsche & MuthuKrishnan *J Org Chem* **44** 3962 *1979*, Andretti et al. *J Chem Soc, Chem Commun* 533 *1981*; see Kluawer in *Calixarenes*, Vicens & Böhner eds Academic Press *1991*.]

8-*sec*-Butylmetrazole *[25717-83-3]* **M 194.3, m 70°.** Crystallise it from petroleum ether and dry it for 2 days under vacuum over P_2O_5. [*Beilstein* **26** II 213 for Metrazole.]

***N*-(*n*-Butyl)-5-nitro-2-furamide** *[14121-89-2]* **M 212.2, m 89-90°, b 190°/10mm.** Distil the amide in a vacuum and recrystallise it twice from EtOH/water mixture or petroleum ether. [Gliman & Yale *J Am Chem Soc* **72** 3593 *1950*, *Beilstein* **18** III/IV 3995.]

Butyloxirane (1-hexene oxide) *[1436-34-6]* **M 100.2, b 116-117°/atm, 116-119°/atm, d_4^{20} 0.833, n_D^{20} 1.44051.** Purify it by fractional distillation through a 2ft helices-packed column at atmospheric pressure in a N_2 atmosphere. [Pasto & Cumbo *J Org Chem* **30** 1271 *1965*, Howarth et al. *J Chem Soc* 2433 *1927*, ^{13}C NMR Davies & Witham *J Chem Soc Perkin Trans 2* 861 *1975*, *Beilstein* **17/1** V 103.]

4-*tert*-Butylpyridine *[3978-81-2]* **M 135.2, f -44.4°, b 194-197°atm, 197°/765mm, d_4^{20} 0.923, n_D^{20} 1.495, pK^{25} 5.82.** Dry 4-*tert*-butylpyridine over solid KOH and purify it by fractional distillation through an efficient column under dry N_2. Its *picrate* has **m** 153.9-154°, and the *hydrochloride* has **m** 151.7-154.8° (from Me_2CO). [Brown & Murphey *J Am Chem Soc* **73** 3308 *1951*, IR: Arnett & Chawla *J Am Chem Soc* **100** 214 *1978*, Kyle et al. *J Chem Soc* 4454 *1960*, *Beilstein* **20/6** V 123.]

Cacotheline **(2,3-dihydro-4-nitro-2,3-dioxo-9,10-*seco*strychnidin-10-oic acid)** *[561-20-6]* **M 508.4, $pK_{Est(1)}$ ~4.4 (CO_2H), $pK_{Est(2)}$ ~10.2 (N).** Cacotheline gives yellow crystals from H_2O. It is then dried over H_2SO_4 which gives the *dihydrate*, and in a vacuum over H_2SO_4 at 105° it forms the *anhydrous* compound. The *hydrochloride* separates as the *hydrate* (on heating in vacuum at 80°) in orange-yellow prisms or plates, **m** 250°(dec) and forms a *resorcinol complex* which gives brown crystals from EtOH, **m** 325°; and a *hydroquinone complex* as dark red crystals from EtOH, **m** 319°. [Leuchs & Leuchs *Chem Ber* **43** 1042 *1910*, Teuber *Chem Ber* **86** 232, (UV: 242) *1953*; complexes: Gallo *Gazz Chim Ital* **85** 1441 *1955*.] It is used in the titrimetric estimation of Sn^{2+} ions [Szrvas & Lantos *Talanta* **10** 477 *1963*]. [*Beilstein* **27** III/IV 8014.]

Caffeine (1,3,7-trimethylxanthine) *[58-08-2]* **M 194.2, m 237°, pK_1^{40} -0.10, pK_2^{55} 1.22.** Caffeine crystallises from water or absolute EtOH. [*Beilstein* **26** III/IV 2338.]

Cannabinol *[521-35-7]* **M 310.4, m 76-77°, b 185°/0.05mm, 225°, pK_{Est} ~10.5 (phenolic OH).** Cannabinol crystallises from petroleum ether and sublimes in a vacuum. [Meitzer et al. *Synthesis* 985 *1981*, *Beilstein* **17** II 151, **17** III/IV 1652.]

ε-Caprolactam (azepan-2-one, aza-2-cycloheptanone, 2-oxohexamethyleneimine) *[105-60-2]* **M 113.2, m 70°, 70.5-71.5°, 70-71°, 262.5°/760mm.** The lactam is distilled under reduced pressure, recrystallised from acetone or petroleum ether and redistilled. It can be purified by zone melting. It is very *hygroscopic* and discolours in contact with air unless small amounts (0.2g/L) of NaOH, Na_2CO_3 or $NaBO_2$ are present. It has been crystallised from a mixture of petroleum ether (185ml of **b** 70°) and 2-methyl-2-propanol (30ml), from acetone, or petroleum ether. It is then distilled under reduced pressure and stored under nitrogen. [Pellegata et al. *Synthesis* 614 *1978*, *Beilstein* **21/6** V 444.]

Caprylolactam (azanon-2-one, azacyclononan-2-one, 8-aminooctanoic acid lactam, cyclooctanone isooxime) *[935-30-8]* **M 141.2, m 72°, 73°, 74-76°, 75°, 76-77°, b 119-122°/0.7mm, 150-151°/7-8mm, 164°/14mm, d_4^{73} 1.009, n_D^{73} 1.489, pK^{25} 0.55 (AcOH).** Dissolve it in $CHCl_3$, decolorise it with charcoal, evaporate to dryness and recrystallise it from $CHCl_3$/hexane. Sublime it at high vacuum. The *oxime* has **m** 117° (from $*C_6H_6$ or petroleum ether). [Guggisberg *Helv Chim Acta* **61** 1050 *1978*, Olah et al. *Synthesis* 538 *1979*, Behringer & Meier *Justus Liebigs Ann Chem* **607** 67 *1957*, *Beilstein* **21** III/V 3260.]

***1S,2'S*-Captopril (*S*-1-[3-mercapto-2-methyl-1-oxopropyl]-L-proline)** *[62571-86-2]* **M 217.3, m 103-104°(polymorphic unstable form m 86°, melts at 87-88° solidifies and then melts again at 104-105°), $[\alpha]_D^{22}$ -131° (c 1.7, EtOH), pK_1 3.7, pK_2 9.8.** Purify it by recrystallisation from EtOAc/hexane. It is also purified by dissolving in EtOAc and chromatographed on a column of Wakogel C200 using a linear gradient of MeOH in EtOAc (0-100°) and fractions which give a positive nitroprusside test (for SH), are combined, evaporated and recrystallised from EtOAc/hexane (1:1), to give white crystals with $[\alpha]_D^{20}$ -128.2° (c 2.0, EtOH). [Nam *J Pharm Sci* **73** 1843 *1984*]. *Alternatively*, dissolve it in H_2O, apply to a column of AG-50Wx2 (BioRad) and elute with H_2O. The free acid is converted to the *dicyclohexylamine salt* in MeCN by addition of the amine until the pH is 8-9. The salt is converted to the free acid by shaking with EtOAc and 10% aqueous $KHSO_4$ or passage through an AG50Wx2 column. The EtOAc solution is dried ($MgSO_4$), evaporated to dryness and the residue is recrystallised as above from EtOAc/hexane [Cushman et al. *Biochemistry* **16** 5484 *1977*, NMR and IR: Horii & Watanabe *Yakugaku Zasshi (J Pharm Soc Japan)* **81** 1786 *1961*]. It is an antihypertensive because it is a potent competitive inhibitor of the angiotensive convertive enzyme (ACE-inhibitor) with a Ki value of 0.0017μM [Shimazaki et al. *Chem Pharm Bull Jpn* **30** 3139 *1982*].

Carbamazepine (5*H*-dibenzo[*b*,*f*]azepine-5-carboxamide) *[298-46-4]* **M 236.3, m 190-193°, 191-192°.** Recrystallise from EtOH/$*C_6H_6$, and dry *in vacuo*. It is soluble in Me_2CO EtOH and propylene glycol, but not in H_2O. Anticonvulant and Na channel inhibitor. [Stenger & Roulet *Med Exp* **11** 191 *1964*.]

Carbazole *[86-74-8]* **M 167.2, m 240-243°, pK^{25} <0.** Dissolve carbazole (60g) in conc H_2SO_4 (300ml), extract with three 200ml portions of *benzene, then stir this into 1600ml of an ice-water mixture. The precipitate is filtered off, washed with a little water, dried, recrystallised from *benzene and then from pyridine/*benzene [Feldman et al. *J Am Chem Soc* **73** 4341 *1951*]. It has also been recrystallised from EtOH or toluene, sublimed in vacuum, zone-refined, and purified by TLC. [UV: Armarego in *Physical Methods in Heterocyclic Chemistry* (Ed Katritzky, Academic Press) **Vol III** 158 *1971*, *Beilstein* **20/8** V 9.]

9-Carbazoleacetic acid *[524-80-1]* **M 225.2, m 215°, pK_{Est} ~3.5.** Crystallise the acid from ethyl acetate. [Fan et al. *Anal Chim Acta* **367** 1 *1998*, *Beilstein* **20** III/IV 3841.]

Carbazole-9-carbonyl chloride *[73500-82-0]* **M 300.0, m 100-103°, 103.5-104.5°.** Recrystallise the acid chloride from $*C_6H_6$. If it is not very pure (presence of OH or NH bands in the IR), dissolve it in pyridine, shake it with phosgene in toluene, evaporate and recrystallise the residue. Carry out this experiment in a good

fume cupboard as $COCl_2$ is very **TOXIC**, and store the product in the dark. It is moisture sensitive. The *amide* has **m** 246.5-247°, and the *dimethylaminoethylamide hydrochloride* has **m** 197-198°. [Weston et al. *J Am Chem Soc* **75** 4006 *1953*, *Beilstein* **20** III/IV 3841.]

1-Carbethoxy-4-methylpiperazine hydrochloride *[532-78-5]* **M 204.7, m 168.5-169°, pK^{25} 7.31.** Crystallise the hydrochloride from absolute EtOH. Its solubility is 280g/100g of H_2O at 25°. The *free base ester* has **b** 97-98°/8mm. [*Beilstein* **23** III/IV 223.]

γ-Carboline (9*H*-pyrido[3,4-b]indole) *[244-69-9]* **M 168.2, m 225°, 230-233°, pK^{25} ~0.** Crystallise it from water or EtOAc. [Robinson & Thornley *J Chem Soc* **12S** 2169 *1924*, Dalton et al. *Aust J Chem* **22** 185 *1969*, Staab & Wendel *Org Synth* **48** 44 *1968*, *Beilstein* **23** II 223, **23** III/IV 1572.]

***N,N'*-Carbonyldiimidazole** *[530-62-1]* **M 162.2, m 115.5-116°.** Crystallise it from *benzene or tetrahydrofuran in a dry-box and store it dry. [Hearn *Methods Enzymol* **135** 102 *1987*, *Beilstein* **23/4** V 245.]

1,1'-Carbonyldi(1,2,4-triazole) (CDT) *[41864-22-6]* **M 164.1, m 134-136°, 145-150°.** Dissolve CDT in tetrahydrofuran and evaporate at 10mm until it crystallises. Wash the crystals with cold tetrahydrofuran and dry them in a vacuum desiccator over P_2O_5 in which it can be stored for months. [Bergmann & van den Brink *Rec Trav Chim Pays Bas* **80** 1372 *1961*, Potts *J Org Chem* **27** 2631 *1962*, Staab *Justus Liebigs Ann Chem* **106** 75 *1957*.]

(±)-Catechin *[7295-85-4]* **M 272.3, m 177° (anhydrous).** Crystallise it from hot water and dry it at 100°. [*Beilstein* **17/8** V 448.]

Cetylpyridinium chloride (H_2O) (hexadecylpyridinium chloride) *[6004-24-6]* **M 358.0, m 80-83°.** Crystallise the chloride from MeOH or EtOH/diethyl ether and dry it *in vacuo*. [Moss et al. *J Am Chem Soc* **108** 788 *1986*, Lennox & McClelland *J Am Chem Soc* **108** 3771 *1986*, *Beilstein* **20** V 233.]

Chelerythrine (1,2-dimethoxy-12-methyl[1,3]benzodioxolo[5,6-*c*]phenanthridinium] *[34316-15-9]* **M 389.4, m 207°.** Chelerythrine crystallises from $CHCl_3$ on addition of MeOH [Manske *Can J Res* **21B** 140 *1943*, UV: Hruban et al. *Col Czech Chem Commun* **35** 3420 *1970*]. The *pseudo base* is colourless while the salts are yellow in aqueous solution and are fluorescent.

Chelidonic acid (4-oxopyran-2,6-dicarboxylic acid) *[99-32-1]* **M 184.1, m 262°, pK_2^{25} 2.36.** The acid crystallises from aqueous EtOH. Dry it first at 100°/2 hours, then at 160° to constant weight to remove water of crystallisation. It decarboxylates at 220-230° in a vacuum. [Riegel & Zwilgmeyer *Org Synth* Coll Vol **II** 126 *1943*, *Beilstein* **18** H 490**, 18/8** V 646.]

2-Chlorobenzothiazole *[615-20-3]* **M 169.6, m 21°, 90-91.4°/4mm, 135-136°/28mm, d_4^{20} 1.303, n_D^{20} 1.6398.** It is purified by fractional distillation *in vacuo*. The *2-chloro-3-methylbenzothiazolinium 2,4-dinitrobenzenesulfonate* crystallises from Ac_2O, **m** 162-163°(dec). [Young & Amstutz *J Am Chem Soc* **73** 4773 *1951*, Brower et al. *J Org Chem* **19** 1830 *1954*, Hunter & Jones *J Chem Soc* 2190 *1930*, *Beilstein* **27** H 44, **27** II 18, **27** III/IV 1072.]

***o*-Chlorobenzotrifluoride** *[88-16-4]* **M 180.6, b 152.3°, d_4^{20} 1.371, n_D^{20} 1.456.** Dry it over $CaSO_4$, and distil it at high reflux ratio. [*Beilstein* **5** III 692.]

2-Chlorobenzoxazole *[615-18-9]* **M 153.6, b 95-96°/20mm, 198-202°/atm, d_4^{20} 1.331, n_D^{20} 1.570.** Purify it by fractional distillation, preferably in a vacuum. [Siedel *J Prakt Chem* **42** 456 *1890*, Katz *J Am Chem Soc* **75** 712 *1953*, Meyer & Sigel *J Org Chem* **42** 2769 *1977*, *Beilstein* **27** H 43**, 27** II 17.]

2-(4-Chlorobutyl)-1,3-dioxolane *[118336-86-0]* **M 164.6, b 56-58°/0.1mm, d_4^{20} 1.106, n_D^{20} 1.457.** If the IR has no CHO band, then just distil it in a vacuum. If it is present, then dissolve it in Et_2O, wash it with H_2O, then saturated $NaHCO_3$, dry over $MgSO_4$, evaporate and distil it. [*cf* Kriesat & Gisvold *J Pharm Sci* **60** 1250

1971, Loftfield *J Am Chem Soc* **73** 1365 *1951*.]

4-Chloro-2,6-diaminopyrimidine (2,4-diamino-6-chloropyrimidine) *[156-83-2]* **M 144.6, m 198°, 199-202°, pK^{25} 3.57.** It recrystallises from boiling H_2O (charcoal) as needles; it also crystallises from Me_2CO. [Büttner *Chem Ber* **36** 2232 *1903*, Roth *J Am Chem Soc* **72** 1914 *1950*, UV: Brown & Jacobsen *J Chem Soc* 3172 *1962*, *Beilstein* **24** H 318**, 25** III/IV 2788.]

2-Chloro-4,6-dimethylpyrimidine *[4472-44-0]* **M 142.6, m 34-38°, 38°, b 223°/atm, pK^{20} -0.68.** The chloro-pyrimidine has been distilled at atmospheric pressure, and solidifies on cooling. Purify it by recrystallisation from petroleum ether (b 40-60°). The 2-chloro-substituent is readily subject to nucleophilic substitution, and the kinetics of reaction with morpholine and piperidine are reported in detail (cf Chapman & Rees). It is a very weak base and requires 2N HCl to form the cation species. The UV has λ_{max} (logε) at 255 (3.65) and 263 (infl 3.49) nm at pH 2.0 (neutral species); and 261nm (3.87) in ~2N HCl (H_o -3.0, cation). [Boarland & McOmie *J Chem Soc* 1218 *1952*, Boarland & McOmie 3722 *1952*, Chapman & Rees *J Chem Soc* 1190 *1954*, Brown & England *J Chem Soc, C* 1922 *1967*, Matsukawa & Ohta *J Pharm Soc, Jpn* **69** 491 *1949*, *Chem Abstr* **44** 3456 *1950*, Andrisano & Modena *Gazz Chem Ital* **81** 405 *1951*, Angerstein *Chem Ber* **34** 3956 *1901*, *Beilstein* **23** H 95, **23** IV 918.]

2-Chloro-3,5-dinitropyridine *[2578-45-2]* **M 203.5, m 62-65°, 63-65°, 64°, pK$_{Est}$ <–5.** Dissolve it in $CHCl_3$, shake it with saturated $NaHCO_3$, dry ($MgSO_4$), evaporate and apply to an Al_2O_3 column, elute with petroleum ether (b 60-80°), evaporate and recrystallise it from *C_6H_6 or petroleum ether. [Ochiai & Kaneko *Chem Pharm Bull Jpn* **8** 28 *1960*, Plazek *Rec Trav Chim Pays Bas* **72** 573 *1953*, *Beilstein* **20/5** V 458.]

1-(2-Chloroethyl)pyrrolidine hydrochloride *[7250-67-1]* **M 170.1, m 167-170°, 173.5-174°, pK$_{Est}$ ~8.5 (free base).** Purify the hydrochloride by recrystallisation from isopropanol/di-isopropyl ether (charcoal) and recrystallise it twice more. The *free base*, **b** 55-56°/11mm, 60-63°/23mm and 90°/56mm, is relatively unstable and should be converted to the hydrochloride immediately, by dissolving in isopropanol and bubbling dry HCl through the solution at 0°, filtering off the hydrochloride and recrystallising it. The *picrate* has **m** 107.3-107.8° (from EtOH) [Cason *J Org Chem* **24** 247 *1959*, Wright et al. *J Am Chem Soc* **70** 3098 *1948*]. [*Beilstein* **20** III/IV 66.]

5-Chloroindole *[17422-32-1]* **M 151.6, m 69-71°, 72-73°, b 120-130°/0.4mm, pK$_{Est}$ <0.** It is distilled at high vacuum and recrystallises from petroleum ether (b 40-60°) or (b 80-100°) as glistening plates. The *picrate* has **m** 147° (146.5-147.5°)(from *C_6H_6). [Rydon & Tweddle *J Chem Soc* 3499 *1955*, Sugasawa *J Org Chem* **44** 578 *1979*, *Beilstein* **20/4** V 34.]

2-Chloro-6-(methylamino)purine *[82499-02-3]* **M 183.6, m >220°, > m 300°, pK$_{Est(1)}$ ~3.0, pK $_{Est(2)}$ ~10.0.** Purify by recrystallisation from glacial acetic acid or *C_6H_6/$EtOCH_2CH_2OH$, and dry *in vacuo*. Its UV has λ_{max}(ε) at 267(14400) (0.1N HCl), 271(15000) (aqueous pH 7.0); and 226(15300) and 272(5340) (0.1N NaOH in EtOH) [Montgomery & Holum *J Am Chem Soc* **80** 404 *1958*]. [Kim et al. *J Med Chem* **43** 746 *2000*, *Beilstein* **26** III/IV 3724.]

2-Chloro-3-methylindole (2-chloroskatole) *[51206-73-6]* **M 165.6, m 114.5-115.5°, pK$_{Est}$ <0.** Purify 2-chloroskatole by chromatography on silica gel in CH_2Cl_2/petroleum ether (1:2), followed by recrystallisation from aqueous EtOH, aqueous AcOH or petroleum ether (**m** 113.5°). The *picrate* has **m** 121-122°(dec) (orange-red crystals from petroleum ether). [Phillips & Cohen *J Am Chem Soc* **108** 2023 *1986*, *Beilstein* **20** H 317, **20** III/IV 3212.]

4-(Chloromethyl)pyridine hydrochloride *[1822-51-1]* **M 164.0, m 170-175°, 172-173°, pK$_{Est}$ ~5.6.** Purify it by recrystallisation from EtOH or EtOH/dry Et_2O. It melts between 171° and 175°, and the clear melt resolidifies on further heating at 190° and turns red to black at 280° but does not melt again. The *picrate-hydrochloride* (prepared in EtOH) has **m** 146-147°. The *free base* is an oil. [Mosher & Tessieri *J Am Chem Soc* **73** 4925 *1951*, *Beilstein* **20** III/IV 2752.]

2-Chloro-1-methylpyridinium iodide *[14338-32-0]* **M 255.5, m 203-205°, 205-206°(dec), 207°.** Purify it by dissolving in EtOH and adding dry Et_2O. The solid is washed with Me_2CO and dried at 20°/0.35mm. Store it in the dark. Attempted recrystallisation from Me_2CO/EtOH/petroleum ether (b 40-60°) causes some exchange of the Cl substituent by I. The *picrate* has **m** 106-107°, and the *perchlorate* has **m** 212-213°. [Jones et al. *J Am Chem Soc* **111** 1157 *1989*, UV and solvolysis: Barlin & Benbow *J Chem Soc, Perkin Trans 2* 790 *1974*, *Beilstein* **20/5** V 405.]

6-Chloronicotinic acid *[5326-23-8]* **M 157.6, m 190-193°, 198-199°(dec), pK^{25} 4.22 (50% aqueous EtOH).** Purify it by recrystallisation from hot H_2O and sublime it in a vacuum. [Pechmann & Welsch *Chem Ber* **17** 2384 *1884*, Herz & Murty *J Org Chem* **26** 122 *1961*, *Beilstein* **22/2** V 177.]

4-Chloro-7-nitrobenzofurazane (7-chloro-4-nitrobenzoxadiazole, NBD-chloride) *[10199-89-0]* **M 199.6, m 96.5-97°, 97°, 99-100°.** Wash the solid with H_2O, and it recrystallises from aqueous EtOH (1:1) as pale yellow needles. It sublimes in a vacuum [Gosh & Whitehouse *Biochem J* **108** 155 *1968*, UV, NMR: Bolton et al. *J Chem Soc* 1004 *1966*].

2-Chloro-3-nitropyridine *[5470-18-8]* **M 158.5, m 100-103°, 101-102°, 103-104° (sublimes), pK^{20} -2.6.** It forms needles from H_2O. Purify it by continuous sublimation over a period of 2 weeks at 50-60°/0.1mm [Barlin *J Chem Soc* 2150 *1964*]. The *N-oxide* has **m** 100°(from CH_2Cl_2/Et_2O). [Taylor & Driscoll *J Org Chem* **25** 1716 *1960*, Ochiai & Kaneko *Chem Pharm Bull Jpn* **8** 28 *1960*, *Beilstein* **20/5** V 451.]

2-Chloro-5-nitropyridine *[4548-45-2]* **M 158.5, m 108°, pK_{Est} ~-2.6.** It crystallises from *benzene or *benzene/petroleum ether. [*Beilstein* **20/5** V 452.]

9-Chloro-9-phenylxanthene (Pixyl chloride) *[42506-03-6]* **M 292.8, m 105-106°.** A possible impurity is 9-hydroxy-9-phenylxanthene. If the material contains a lot of the hydroxy product, then boil 10g of it in $CHCl_3$ (50ml) with redistilled acetyl chloride (1ml) until liberation of HCl is complete. Evaporation leaves the chlorophenylxanthene as the hydrochloride which on heating with *benzene loses HCl; and on adding petroleum ether prisms of chlorophenylxanthene separate and contain 0.5mol of *benzene. The *benzene-free compound is obtained on drying, and it melts to a colourless liquid. [Gomberg & Cone *Justus Liebigs Ann Chem* **370** 142 *1909*.] The 9-phenylxanthyl group is called "pixyl" and is a good protecting group [Chattopadhyaya & Reese *J Chem Soc, Chem Commun* 639 *1978*, *Beilstein* **17** III/IV 1704.]

Chlorophylls *a* and *b* See entries in "Miscellaneous Compounds", Chapter 7.

6-Chloropurine *[87-42-3]* **M 154.6, m 179°(dec), pK_1^{20} 0.45, pK_2^{20} 7.88.** 6-Chloropurine crystallises from water. The UV in water at pH 1 has λ_{max} 264nm (logε 3.94). [*Beilstein* **26** III/IV 1742.]

2-Chloropyrazine *[14508-49-7]* **M 114.5, b 62-63°/31mm, 153-154°/atm, d_4^{20} 1.302, n_D^{24} 1.535, pK_{Est} <0.** Fractionally distil it through a short column packed with glass helices. It has a penetrating, mildly pungent odour with a high vapour pressure at room temperature. [Erickson & Spoerri *J Am Chem Soc* **68** 400 *1946*, Hetman & O.Donnell *J Org Chem* **28** 1682 *1963*, *Beilstein* **23/5** V 366.]

2-Chloropyridine *[109-09-1]* **M 113.6, b 49.0°/7mm, d_4^{20} 1.20, n_D^{20} 1.532, pK^{20} 0.49 (0.72).** Dry 2-chloropyridine with NaOH for several days, then distil it from CaO under reduced pressure. [*Beilstein* **20/5** V 402.]

3-Chloropyridine *[626-60-8]* **M 113.6, b 148°, d_4^{20} 1.194, n_D^{20} 1.533, pK^{20} 2.84.** Distil 3-chloropyridine from KOH pellets. [*Beilstein* **20/5** V 406.]

4-Chloropyridine *[626-61-9]* **M 113.6, b 85-86°/100mm, 147-148°/760mm, pK^{20} 3.84.** Pour 4-chloropyridine into distilled water, and excess of 6M NaOH is added to give pH 12. The organic phase is separated and extracted with four volumes of diethyl ether. The combined extracts are filtered through paper to

remove water, and the solvent is evaporated. The dark brown residual liquid is kept under high vacuum [Vaidya & Mathias *J Am Chem Soc* **108** 5514 *1986*]. It can be distilled, but readily darkens and is best kept as the *hydrochloride [7379-35-3]* **M** 150.1, **m** 163-165°(dec). [*Beilstein* **20/5** V 410.]

2-Chloropyrimidine *[1722-12-9]* **M 114.5, m 63-65°, 66°, b 91°/26mm, pK^{20} -1.90.** It has been recrystallised from *C_6H_6, petroleum ether or a mixture of both. It sublimes at 50°/18mm and can be distilled in a vacuum. [IR: Short & Thompson *J Chem Soc* 168 *1952*, Boarland & McOmie *J Chem Soc* 1218 *1951*, *Beilstein* **23/5** V 343.]

2-Chloroquinoline *[612-62-4]* **M 163.6, m 34°, b 147-148°/15mm, d_4^{35} 1.235, n_D^{25} 1.629, pK_{Est} ~0.3.** Purify it by crystallisation of its *picrate* to constant melting point (123-124°) from *benzene, regenerating the base and distilling it under vacuum [Cumper et al. *J Chem Soc* 1183 *1962*]. 2-Chloroquinoline can be crystallised from EtOH. Its *picrate* has **m** 123-124° (from EtOH). [*Beilstein* **20** H 359, **20/7** V 312.]

4-Chloroquinoline *[611-35-8]* **M 163.6, m 29-32°, 31°, b 130°/15mm, 261°/744mm, pK^{25} 3.72.** Possible impurities include the 2-isomer. It is best purified by converting to the *picrate* (**m** 212-213° dec) in EtOH and recrystallising it from EtOH (where the picrate of the 2-chloroquinoline remains in solution) or EtOAc. The picrate is decomposed with 5% aqueous NaOH, extracted in $CHCl_3$, washed with H_2O, dried ($MgSO_4$), evaporated and distilled in a vacuum. It can be steam distilled from slightly alkaline aqueous solutions, the aqueous distillate is extracted with Et_2O, evaporated and distilled. The distillate solidifies on cooling. [Bobránski *Chem Ber* **71** 578 *1938*, *Beilstein* **20/7** V 314.]

8-Chloroquinoline *[611-33-6]* **M 163.6, b 171-171.5°/24mm, d_4^{20} 1.278, n_D^{20} 1.644, pK^{20} 3.12.** Purify it by crystallisation of its $ZnCl_2$ complex (**m** 228°) from aqueous EtOH. [*Beilstein* **20** III/IV 3381, **20/7** V 315.]

5-Chloroquinolin-8-yl trifluoromethanesulfonate (5-chloro-8-quinoline triflate) *[157437-38-2]* **M 311.7, m 79-83°.** If it is discoloured dissolve it in CH_2Cl_2, wash it with N NaOH and half saturated K_2CO_3, dry the organic layer over solid K_2CO_3, filter, evaporate and dry the solid *in vacuo*, (cf 2-methyl-5-pyridine triflate). [Matthew et al. *Tetrahedron Lett* **35** 5177 *1994*, Tilley & Zawoiski *J Org Chem* **53** 386 *1988,* Ellingboe et al. *J Med Chem* **37** 542 *1994*.]

8-Chlorotheophylline (8-chloro-1,3-dimethyl-2,6(1*H*,3*H*)-purinedione) *[85-18-7]* **M 214.6, m 311°(dec), $pK_{Est(1)}$ ~5.4, $pK_{Est(2)}$ ~9.1.** It crystallises from H_2O or EtOH (**m** 304°, dec). The *choline salt* crystallises from H_2O with **m** 60-62° (2 H_2O) and **m** 97-99° (anhydrous). [*Beilstein* **26** H 473, II 276, **26** III/IV 2442.]

2-Chlorothiophene (2-thienyl chloride) *[96-43-5]* **M 118.6, b 126-128°, 128°/~760mm, d_4^{20} 1.285, n_D^{20} 1.551.** Purify it by fractional distillation at atmospheric pressure or by gas chromatography. [Conde et al. *Synthesis* 412 *1976*, *Beilstein* **17/1** V 303.]

5-Chlorouracil (5-chloro-2,4(6)-dihydroxypyrimidine) *[1820-81-1]* **M 146.5, m 314-418°(dec), 324-325°(dec), pK_1^{25} 7.95, pK_2^{25} >13.** It recrystallises from hot H_2O (4g/500ml) using charcoal. [McOmie et al. *J Chem Soc* 3478 *1955*, West & Barrett *J Am Chem Soc* **76** 3146 *1954*, *Beilstein* **24** III/IV 1231.]

4-Chromanone (2,3-dihydro-4*H*-1-benzopyran-4-one) *[491-37-2]* **M 148.2, m 35-37°, 39°, 41°, b 92-93°/3mm, 130-132°/15mm, 160°/50mm.** It has been recrystallised from petroleum ether, or purified by dissolving in *C_6H_6 washing with H_2O, drying ($MgSO_4$), evaporating and distilling in a vacuum, then recrystallising the residue. The liquid has a pleasant lemon-like odour. The *semicarbazone* has **m** 227°. [Loudon & Razdan *J Chem Soc* 4299 *1954*.] The *oxime* is prepared from 3g of chromanone, 3g $NH_2OH.HCl$ in EtOH (50ml), 6g K_2CO_3 and refluxed on a water bath for 6 hours. The solution is poured into H_2O, the solid is filtered off, dried and dissolved in hot *C_6H_6 which on addition of petroleum ether yields the *oxime* as glistening needles **m** 140°. Hydrolysis of this gives very pure chromanone. The *benzal derivative* is prepared from 3g of chromanone and 4g PhCHO in 50ml EtOH, heated to boiling, 10ml of conc HCl are added dropwise and set aside for several days. The derivative separates and is recrystallised from EtOH to give yellow needles, **m** 112° [Powell *J Am Chem Soc* **45** 2711 *1923*]. Reaction with $Pb(OAc)_4$ yields the *3-acetoxy derivative* **m** 74°

(from petroleum ether + trace of EtOAc) [Cavill et al. *J Chem Soc* 4573 *1954*, *Beilstein* **17/10**V 14].

Cinnoline *[253-66-7]* **M 130.2, m 38°, 40-41°, b 114°/0.35, pK^{20} 2.37.** It is distilled at high vacuum, then recrystallised from petroleum ether. Keep it under N_2 in sealed tubes in the dark at 0°. The *hydrochloride* [5949-24-6] **M** 166.6 crystallises from EtOH/Et_2O and has **m** 156-158° (yellow *monohydrate*), and dehydrates on sublimation at 110-115°/3mm. The *picrate* has **m** 196-196.5°. [*Beilstein* **23** H 173, **23** III.IV 1217.]

Citrazinic acid (2,6-dihydroxyisonicotinic acid) *[99-11-6]* **M 155.1, m >300°, pK$_1$ 3.0, pK$_2$ 4.76.** The acid is normally a yellow powder with a greenish shade, but is white when ultra pure and turns blue on long standing. It is insoluble in H_2O but slightly soluble in hot HCl and soluble in alkali or carbonate solutions. It is purified by precipitation from alkaline solutions with dilute HCl, and dried in a vacuum over P_2O_5. The *ethyl ester* has **m** 232° (evacuated tube) and a pKa of 4.81 in $MeOCH_2CH_2OH$ [IR: Pitha *Col Czech Chem Comm* **28** 1408 *1963*]. [*Beilstein* **22/7** V 24.]

Clioquinol (5-chloro-8-hydroxy-7-iodoquinoline *[130-26-7]* **M 305.5, m 181°, pK$_1^{25}$ 2.7, pK$_2^{25}$ 7.9.** It crystallises from AcOH or xylene and dry it at 70° *in vacuo*. [*Beilstein* **21** III/IV 1190**.]**

Clofazimine [2-(4-chloroanilino)-3-isopropylimino-5-(4-chlorophenyl)-3,4-dihydrophenazine] *[2030-63-9]* **M 473.5, m 210-212°, pK^{20} 8.37 (8.51).** Clofazimine recrystallises from acetone as dark red crystals. Its solubility in $CHCl_3$ and EtOH is 7% and 0.1%, respectively, at room temperature. It is insoluble in H_2O. It is antibacterial. [Barry et al. *J Chem Soc* 859 *1958*, *Beilstein* **25** III/IV 3033.]

Colforsin, see **Forskolin.**

Conessine *[546-06-5]* **M 356.6, m 125°, 127-128.5°, [α]$_D^{20}$ -1.9° (in $CHCl_3$) and +26° (c 3, EtOH), pK$_{Est(1)}$~10.4 , pK$_{Est(2)}$~10.7.** It crystallises from acetone, sublimes at 95°/0.01mm and boils at 0.1mm with bath temperature at 220°. The *dihydrochloride* has **m** >340° (browns at 235° and decomposes at 338-240°) and has [α]$_D^{20}$ +9.3° (c 2, H_2O). [Marshall & Johnson *J Am Chem Soc* **84** 1458 *1962*, *Beilstein* **22** III/IV 4382.]

Coproporphyrin I *[531-14-6]* **M 654.7, λ$_{max}$ 591, 548, 401nm in 10% HCl.** It crystallises from pyridine/glacial acetic acid. The *dihydrochloride [69477-27-6]* has M 727.7 and λ_{max} at 395nm in water. [*Beilstein* **26** III/IV 3094.]

Coumalic acid (2-pyrone-5-carboxylic acid) *[500-05-0]* **M 140.1, m 205-210°(dec), pK$_{Est}$ ~0.** The acid crystallises from MeOH. The *methyl ester* has **m** 73-74° (from petroleum ether) and **b** 178-180°/60 mm. [*Beilstein* **18/8** V 120.]

Coumarin *[91-64-5]* **M 146.2, m 68-69°, b 298°, pK^{25} -4.97 (aqueous H_2SO_4).** Coumarin crystallises from ethanol or water and sublimes *in vacuo* at 43° [Srinivasan & deLevie *J Phys Chem* **91** 2904 *1987*]. [*Beilstein* **17/10** V 143.]

Coumarin-3-carboxylic acid *[531-81-7]* **M 190.2, m 188°(dec), pK$_{Est}$ ~1.5.** The acid crystallises from water. [*Beilstein* **18/8** V 323.]

γ-Crotonolactone [2(5*H*)-furanone] *[497-23-4]* **M 84.1, m 3-4°, 76-77°/3.5mm, 90.5-91°/11.5mm, 92-93°/14mm, 107-109°/24mm, 212-214°/760mm, d$_4^{20}$ 1.197, n$_D^{20}$ 1.470.** Fractionally distil the lactone under reduced pressure. Its IR(CCl_4) has 1784 and 1742 cm^{-1}, UV no max above 205nm (ε 1160 cm^{-1} M^{-1}) and ^{1}HNMR (CCl_3) has τ at 2.15 (pair of triplets 1H), 3.85 (pair of triplets 1H) and 5.03 (triplet 2H). [Price & Judge *Org Synth* Coll Vol **V** 255 *1973*, Smith & Jones *Can J Chem* **37** 2007, 2092 *1959*, *Beilstein* **17/9** V 112.]

15-Crown-5 *[33100-27-5]* **M 220.3, b 93-96°/0.1mm, d$_4^{20}$ 1.113, n$_D^{20}$ 1.465.** Dry it over 3A molecular sieves and distil it in a high vacuum. [*Beilstein* **19/12** V 252.]

18-Crown-6 *[17455-13-9]* **M 264.3, m 37-39°.** Recrystallise it from acetonitrile and dry it in a vacuum.

Purify it also by precipitating the 18-crown-6/nitromethane 1:2 complex with Et_2O/nitromethane (10:1 mixture). The complex is decomposed in vacuum whereby 18-crown-6 distils off under the reduced pressure. [*Beilstein* **19/12** V 601.]

Cryptopine *[482-74-6]* **M 369.4, m 220-221°, 220-223°, pK^{25} 8.09.** It crystallises from *benzene, hot EtOH (0.25% cold, 1.2% at boiling), petroleum ether or methyl ethyl ketone. The *perchlorate* crystallises from aqueous MeOH with **m** 226-228°(dec). [Thomas et al. *Can J Chem* **33** 570 *1955*, Howarth & Perkin *J Chem Soc* 1769 *1926*, *Beilstein* **27** III/IV 6652.]

Cupreine (6'-hydroxycinchonidine) *[524-63-0]* **M 310.4, m 202°(anhydrous), [α] $^{17}_{D}$ -176° (c 0.5, MeOH), pK^{15} 7.63.** Cupreine crystallises from EtOH (*anhydrous* crystals) and wet Et_2O (as *dihydrate* crystals). It has K_b 2.7x10^{-7} [Kolthoff *Biochem Z* **162** 323]. The *sulfate* forms needles, **m** 257°(dec), from MeOH, amyl alcohol or H_2O, with [α] $^{20}_{D}$-197.9° (c 1.2, H_2O). [*Beilstein* **22** I 165, **22** II 416.]

5-Cyanoindole *[15861-24-2]* **M 142.2, m 106-108°, 107-108°, pK^{25} <0.** Dissolve the nitrile in 95% EtOH, boil it in the presence of charcoal, filter, evaporate to a small volume and add enough H_2O to cause crystallisation and cool. Recrystallise it directly from aqueous EtOH and dry it in a vacuum. Its UV has λ_{max} at 276 nm (log ε 3.6) in MeOH. [Lindwall & Mantell *J Org Chem* **18** 345 *1953*, **20** 1458 *1955*, Thesing at al. *Chem Ber* **95** 2205 *1962*, NMR: Lallemend & Bernath *Bull Soc Chim Fr* 4091 *1970*, *Beilstein* **22/3** V 45.]

3-Cyanopyridine *[100-54-9]* **M 104.1, m 50°, pK^{25} 1.38.** It is recrystallised to constant melting point from *o*-xylene/hexane. [*Beilstein* **22/2** V 115.]

4-Cyanopyridine *[100-48-1]* **M 104.1, m 76-79°, pK^{25} 1.86.** It crystallises from dichloromethane/diethyl ether mixture. [*Beilstein* **22/2** V 214.]

Cyanuric acid (2,4,6-trichloro-1,3,5-triazine) *[108-80-5]* **M 120.1, m >300°, pK^{25} 6.78.** It crystallises from water. Dry it at room temperature in a desiccator in a vacuum. [*Beilstein* **26** III/IV 632.]

Cyanuric chloride (TCT, 2,4,6-trichloro-1,3,5-triazine) *[108-77-0]* **M 184.4, m 146-149°, 154°, b 190°.** TCT crystallises from CCl_4 or petroleum ether (b 90-100°) and is dried under vacuum. It has also been recrystallised twice from anhydrous *benzene immediately before use [Abuchowski et al. *J Biol Chem* **252** 3582 *1977*]. [*Beilstein* **26** III/IV 66.]

Cycloheximide (Actidione) *[66-81-9]* **M 281.4, m 119.5-121°, [α] $^{20}_{546}$ +9.5° (c 2, H_2O).** It crystallises from H_2O /MeOH (4:1), amyl acetate, isopropyl acetate/isopropyl ether or H_2O. [*Beilstein* **21/13** V 434.]

1-Cyclohexyl-5-methyl-1*H*-tetrazole *[7707-57-5]* **M 166.2, m 124-124.5°.** Crystallise it from absolute EtOH or H_2O (heavy needles), then sublime it at 115°/3mm. [Harvill et al. *J Org Chem* **15** 662, 668 *1950*, Billuber Inc USP 2507337 *1946*, *Beilstein* **26** III/IV 1661.]

Cyclotrimethylenetrinitramine (RDX, Cyclonite, 1,3,5-trinitrohexahydro-1,3,5-triazine) *[121-82-4]* **M 222.2, m 203.8°(dec), 205-206°(dec).** RDX crystallises from acetone. [Bachmann & Sheehan *J Am Chem Soc* **71** 1842 *1949*, *Beilstein* **26** II 5, **26** III/IV 22.] **EXPLOSIVE.**

Cytisine (7*R*,9*S*-7,9,10,11,12,13-hexahydro-7,9-methano-12*H*-pyrido[1,2-*a*][1,5]diazocin-8-one, Laburnine, Ulexine) *[485-35-8]* **M 190.3, m 152-153°, 155°, b 218°/2mm, [α] $^{17}_{D}$ -120° (H_2O), [α] $^{25}_{D}$ -115° (c 1, H_2O), pK $^{15}_{1}$ 1.20, pK $^{15}_{2}$ 8.12 [also stated are pK$_1$ 6.11, pK$_2$ 13.08].** Crystallise cytisine from acetone and sublime it in a vacuum. Its solubilities are: 77% (H_2O), 7.7% (Me_2CO), 28.6% (EtOH), 3.3% (*C_6H_6), 50% ($CHCl_3$) but it is insoluble in petroleum ether. The *tartrate* has **m** 206-207° [α] $^{24}_{D}$ +45.9°, the *N-tosylate* has **m** 206-207°, and the *N-acetate* has **m** 208°. [Bohlmann et al. *Angew Chem* **67** 708 *1955*, van Tamelen & Baran *J Am Chem Soc* **77** 4944 *1955*, Isolation: Ing *J Chem Soc* 2200 *1931*, Govindachari et al. *J Chem Soc* 3839 *1957*, Abs config: Okuda et al. *Chem Ind (London)* 1751 *1961*, *Beilstein* **24** H 134, **24** I 244, **24** II 70, **24** III/IV 321.] **TOXIC.**

Cytosine (4-amino-2-hydroxypyrimidine) See entry in "Miscellaneous Compounds", Chapter 7.

***cis*-Decahydroisoquinoline** *[2744-08-3]* **M 139.2, b 97-98°/15mm, 208-209°/730mm, pK^{20} 11.32.** The free base is treated with saturated aqueous picric acid, allowed to stand for 12 hours, filtered, washed with MeOH to remove the more soluble *trans* isomer and recrystallised from MeOH to give pure cis-*picrate* **m** 149-150°. The picrate (~5g) is shaken with 5M aqueous NaOH (50ml) and Et_2O (150ml) while H_2O is added to the aqueous phase to dissolve insoluble Na picrate. The Et_2O extract is dried over solid NaOH and then shaken with Al_2O_3 (Merck for chromatography) until the yellow color of traces of picric acid disappears (this color cannot be removed by repeated shaking with 5-10 M aqueous NaOH). The extract is concentrated to 50ml and dry HCl is bubbled through until separation of the white crystals of the cis-*HCl* is complete. These are washed with Et_2O, dried at 100° and recrystallised from EtOH/EtOAc to yield pure cis-*hydrochloride* **m** 182-183° (dried in a vacuum desiccator over KOH) with IR (KBr) ν_{max} 2920, 2820, 1582, 1470, 1445, 1410, 1395, 1313, 1135, 1080, 990, 870 cm^{-1}. The pure *free base* is prepared by dissolving the *hydrochloride* in 10 M aqueous NaOH, extracted with Et_2O, dried over solid KOH, filtered and distilled in a vacuum. It has IR (film) ν_{max} 2920, 2820, 2720, 2560, 1584, 1470, 1445, 1415, 1395, 1315, 1300, 1135, 1080, 1020, 990, 873 cm^{-1}. The ^{1}HNMR in $CDCl_3$ is characteristically different from that of the *trans*-isomer. [Armarego *J Chem Soc (C)* 377 *1967*, Gray & Heitmeier *J Am Chem Soc* **80** 6274 *1958*, Witkop *J Am Chem Soc* **70** 2617 *1948*, Skita *Chem Ber* **57** 1982 *1924*, Helfer *Helv Chim Acta* **6** 799*1923*, *Beilstein* **20** II 73, **20** III/IV 2026.]

***trans*-Decahydroisoquinoline** *[2744-09-4]* **M 139.2, b 106°/15mm, pK^{20} 11.32.** This is purified as the *cis*-isomer above. The trans-*picrate* has **m** 175-176°, and the trans-*hydrochloride* has **m** 221-222° and has IR (KBr) has ν_{max} at 2930, 3800, 1589, 1450, 1400, 1070, 952, 837 cm^{-1}. The pure *free base* is prepared as above and had IR (film) with ν_{max} at 2920, 2820, 2720, 2560, 1584, 1470, 1445, 1415, 1395, 1315, 1300, 1135, 1080, 1020, 990, 873 cm^{-1}. The ^{1}HNMR in $CDCl_3$ is characteristically different from that of the *cis*-isomer. (references as above and Helfer *Helv Chim Acta* **9** 818 *1926*). [*Beilstein* **20** II 73, **20** III/IV 2026.]

***cis*-Decahydroquinoline** *[10343-99-4]* **M 139.2, b 207-208°/708mm, pK^{20} 11.29.** It is available as a *cis-trans*-mixture (**b** 70-73°/10mm, Aldrich, ~18% *cis*-isomer *[2051-28-7]*), but the isomers can be separated by fractionating in a spinning band column (1~1.5 metre, type E) at atmospheric pressure and collecting 2ml fractions with a distillation rate of 1 drop in 8-10 seconds. The lower boiling fraction solidifies and contains the *trans*-isomer (see below, **m** 48°). The higher boiling fraction **b** 207-208°/708mm remains liquid and is mostly pure *cis*-isomer. This is reacted with PhCOCl and M aqueous NaOH to yield the *N-benzoyl derivative* **m** 96° after recrystallisation from petroleum ether (b 80-100°). It is hydrolysed with 20% aqueous HCl by refluxing overnight. $PhCO_2H$ is filtered off, the filtrate is basified with 5M aqueous NaOH and extracted with Et_2O. The dried extract (Na_2SO_4) is saturated with dry HCl gas, and the *cis-decahydroquinoline hydrochloride* which separates has **m** 222-224° after washing with Et_2O and drying at 100°; and has IR (KBr) with ν_{max} at 2900, 2780, 2560, 1580, 1445, 1432, 1403, 1165, 1080, 1036, 990, 867 cm^{-1}. The *free base* is obtained by dissolving the *hydrochloride* salt in 5M aqueous NaOH, extracting with Et_2O and drying the extract (Na_2SO_4), evaporating and distilling the residue; it has IR (film) with ν_{max} at 2900, 2840, 2770, 1445, 1357, 1330, 1305, 1140, 1125, 1109, 1068, 844 cm^{-1}. The ^{1}H NMR in $CDCl_3$ is characteristically different from that of the *trans*-isomer. [Armarego *J Chem Soc (C)* 377 *1967*, Hückel & Stepf *Justus Liebigs Ann Chem* **453** 163 *1927*, Bailey & McElvain *J Am Chem Soc* **52** 4013 *1930*, *Beilstein* **20** H 157, **20** I 35, **20** II 72-73, **20** III/IV 2017.]

***trans*-Decahydroquinoline** *[767-92-0]* **M 139.2, m 48°, b 205-206°/708mm, pK^{20} 11.29.** The lower boiling fraction from the preceding spinning band column fractionation of the commercial *cis-trans*- mixture (~ 20:60; see the *cis*-isomer above) solidifies readily (**m** 48°), and the receiver has to be kept hot with warm water. It is further purified by conversion to the *hydrochloride* **m** 285-286° after recrystallisation from EtOH/AcOEt. This has IR (KBr) with ν_{max} at 2920, 2760, 2578, 2520, 1580, 1455, 1070, 1050, 975, 950, 833 cm^{-1}. The *free base* is prepared as for the *cis*-isomer above and distilled; and has IR (film, at ca 50°) with ν_{max} at 2905, 2840, 2780, 1447, 1335, 1305, 1240, 1177, 1125, 987, 900, 835 cm^{-1}. The ^{1}HNMR in $CDCl_3$ is characteristically different from that of the *cis*-isomer. [Armarego *J Chem Soc (C)* 377 *1967*, Hückel & Stepf *Justus Liebigs Ann Chem* **453** 163 *1927*, Bailey & McElvain *J Am Chem Soc* **52** 4013 *1930*, Prelog & Szpilfogel *Helv Chim Acta* **28** 1684 *1945*, *Beilstein* **20** H 157, **20** I 35, **20** II 72-73, **20** III/IV 2017.]

Delphinine *[561-07-9]* **M 559.7, m 197-199°, $[\alpha]_D^{20}$ +26° (c 1, EtOH).** It crystallises from EtOH with 198-200° uncorrected (187.5-188.5°) and from Et_2O or Me_2CO. Its solubility at ~25° in EtOH, $CHCl_3$ and Et_2O is 4, 5 and 10% respectively. In c 1, EtOH, it has $[\alpha]_D^{20}$ +22° changing to +19° in 4 hours. [Markwood *J Am Chem Soc* **16** 931 *1927*.] The *hydrochloride* has **m** 214°(dec) from MeOH or MeOH/Et_2O. [Weissner et al. *Can J Chem* **50** 1925 *1972*, Jacobs & Craig *J Biol Chem* **127** 363 *1939*, *Beilstein* **21** III/IV 2867.]

3,6-Diaminoacridine hydrochloride *[952-23-8]* **M 245.7, m 270°(dec), ε_{456} 4.3 x 10^4, pK_1^{20} 1.5, pK_2^{20} 9.60 (9.65 free base).** It is first purified by precipitation of the free base by adding aqueous NH_3 solution to an aqueous solution of the hydrochloride or hydrogen sulfate (see below), drying the precipitate and subliming at 0.01mm Hg [Müller & Crothers *Eur J Biochem,* **54** 267 *1975*]. [*Beilstein* **22** H 487.]

3,6-Diaminoacridine sulfate (proflavin sulfate) *[1811-28-5]* **M 516.6, m >300°(dec), λ_{max} 456nm.** An aqueous solution, after treatment with charcoal, is concentrated, chilled overnight, filtered and the precipitate is rinsed with a little diethyl ether. The precipitate is dried in air, then overnight in a vacuum oven at 70°. [*Beilstein* **22** I 650, **22/11** V 323.]

4,5-Diamino-2,6-dihydroxypyrimidine (diamino uracil) sulfate *[32014-70-3]* **M 382.3, m >300°, pK_1^{20} 1.7, pK_2^{20} 3.20, pK_3^{25} 4.56.** The salt is quite insoluble in H_2O but can be converted to the free base which is recrystallised from H_2O and converted to the sulfate by addition of the required amount of H_2SO_4. The *hydrochloride* has **m** 300-305°(dec) and can be used to prepare the sulfate by addition of H_2SO_4; it is more soluble than the sulfate. The *perchlorate* has **m** 252-254°. The free base has λ_{max} at 260nm (log ε 4.24) in 0.1M HCl. [Bogert & Davidson *J Am Chem Soc* **86** 1668 *1933*, Bredereck et al. *Chem Ber* **86** 850 *1953*, Sherman & Taylor *Org Synth* Coll Vol **IV** 247 *1963*, Barlin & Pfleiderer *J Chem Soc (B)* 1425 *1971*, *Beilstein* **25** II 382.]

5,6-Diamino-1,3-dimethyluracil hydrate (5,6-diamino-1,3-dimethyl-2-pyrimidine-2,4-dione hydrate) *[5440-00-6]* **M 188.2, m 205-208°(dec), 209°(dec), 210° (dec), pK_1 1.7, pK_2 4.6.** It recrystallises from EtOH. The *hydrochloride* has **m** 310° (from MeOH), and the *perchlorate* has **m** 246-248°. [UV: Bredereck et al. *Chem Ber* **92** 583 *1959*, Taylor et al. *J Am Chem Soc* **77** 2243 *1955*, *Beilstein* **25** III/IV 4133.]

6,9-Diamino-2-ethoxyacridine (Ethacridine) *[442-16-0]* **M 257.3, m 226°, pK^{20} 11.6.** It crystallises from 50% EtOH or EtOH as orange-yellow crystals. It also crystallises as a *monohydrate* **m** 116-118°. It has a pK^{20} of 11.04 in 50% aqueous EtOH. The *methiodide* is soluble in H_2O and has **m** 332-334° (dec) (from aqueous Me_2CO). [Albert & Gledhill *J Soc Chem Ind* **61** 159 *1942*, Foye et al. *J Pharm Sci* **57** 1795 *1968*, Albert & Goldacre *J Chem Soc* 708 *1946*, *Beilstein* **22** II 458, **22** III/IV 6679, **22/12** V 243.]

6,9-Diamino-2-ethoxyacridine *dl*-lactate moohydrate (Rivanol, Acrinol) *[6402-23-9]* **M 361.4, m 235° (dark at ~200°), pK^{20} 11.6.** It forms yellow crystals from 90% EtOH/Et_2O. Its solubility in H_2O is ~15% at 25° and ~9% at 100°, and its solutions have a yellow fluorescence which is stable on boiling. It is an antiseptic. See ethacridine above, *Beilstein* **22** II 458, **22** III/IV 6680, **22/12** V 243.]

2,4-Diamino-6-hydroxypyrimidine *[56-06-4]* **M 126.1, m 260-270°(dec), pK_1^{25} 1.34, pK_2^{25} 3.27, pK_3^{25} 10.83.** It recrystallises from H_2O. [*Beilstein* **25** III/IV 3642.]

4,5-Diamino-6-hydroxypyrimidine hemisulfate *[102783-18-6]* **M 350.3, m 268°, 270°, pK_1^{25} 1.34, pK_2^{25} 3.57, pK_3^{25} 9.86.** It recrystallises from H_2O. The *free base* also crystallises from H_2O (**m** 239°). [Mason *J Chem Soc* 2071 *1954*, Elion et al. *J Am Chem Soc* **74** 411 *1952*, *Beilstein* **25** III/IV 3645.]

2,4-Diamino-5-phenylthiazole (Amiphenazole) *[490-55-1]* **M 191.3, m 163-164°(dec).** The thiazole crystallises from aqueous EtOH or water. Store it in the dark under N_2. The *hydrochloride* has **m** 273-274°(dec) (from MeOH/EtOAc), and the *picrate* has **m** 189-191°(dec) (from H_2O). [Davies et al. *J Chem Soc* 3491 *1950*, Dodson & Turner *J Am Chem Soc* **73** 4517 *1951*, *Beilstein* **27** III/IV 5139.]

2,3-Diaminopyridine *[452-58-4]* **M 109.1, m 116°, pK_1^{25} -0.50, pK_2^{25} 6.92.** It crystallises from *benzene

and sublimes *in vacuo*. [*Beilstein* **22/11** V 241.]

2,6-Diaminopyridine *[141-86-6]* **M 109.1, m 121.5° $pK_{Est(1)}$ <-6.0, $pK_{Est(2)}$ ~7.3.** It crystallises from *benzene and sublimes *in vacuo*. [*Beilstein* **22** III/IV 255.]

3,4-Diaminopyridine *[54-96-6]* **M 109.1, m 218-219°, pK_1^{20} 0.49, pK_2^{20} 9.14.** It crystallises from *benzene and is stored under N_2 because it is *deliquescent* and absorbs CO_2. [*Beilstein* **22/11** V 266.]

3,5-Diamino-1,2,4-triazole (Guanazole) *[1455-77-2]* **M 99.1, m 206°, pK_1^{20} 4.43, pK_2^{20} 12.12.** The triazole crystallises from water or EtOH. [*Beilstein* **26** III/IV 1161.]

1,3-Diazaazulene (cycloheptimidazole) *[275-94-5]* **M 130.1, m 110-112°, 120°.** It is recrystallised repeatedly from de-aerated cyclohexane in the dark or from petroleum ether/*C_6H_6 and forms yellow needles. It is soluble in H_2O, EtOH and *C_6H_6, and forms a *monohydrate* which loses H_2O at 60°. The *picrate* has **m** 207°(dec). [Nozoe et al. *J Am Chem Soc* **76** 3352 *1954*, Nukai et al. *Bull Chem Soc Jpn* **40** 1967 *1967*, *Beilstein* **23** III/IV 1216.]

1,5-Diazabicyclo[4.3.0]non-5-ene (DBN, 2,3,4,,6,7,8-hexahydropyrrolo[1,2-*a*]-pyrimidine) *[3001-72-7]* **M 124.2, b 96-98°/11mm, 100-102°/12mm, 118-121°/32mm, d_4^{20} 1.040, n_D^{20} 1.520, pK^{25} >13.0.** Distil DBN from BaO. It forms a *hydroiodide* on addition of 47% HI; dry it and dissolve it in MeCN, evaporate and repeat; recrystallise from EtOH, dry at 25°/1mm for 5 hours, then at 80°/0.03mm for 12 hours and store and dispense it in a dry box, **m** 154-156° [Jaeger et al. *J Am Chem Soc* **101** 717 *1979*]. The *methiodide* is recrystallised from $CHCl_3$/Et_2O, **m** 248-250°, and *hydrogen fumarate* has **m** 159-160° and is crystallised from *iso*-PrOH [Rokach et al. *J Med Chem* **22** 237 *1979*, Oediger et al. *Chem Ber* **99** 2012 *1966*, Reppe et al. *Justus Liebigs Ann Chem* **596** 210 *1955*]. [*Beilstein* **23/5** V 239.]

1,4-Diazabicyclo[2.2.2]octane (DABCO, triethylenediamine, TED) *[280-57-9]* **M 112.2, m 156-157° (sealed tube), pK_1^{25} 2.97, pK_2^{25} 8.82.** DABCO crystallises from 95% EtOH, petroleum ether or MeOH/diethyl ether (1:1). Dry it under vacuum over $CaCl_2$ and BaO. It can be sublimed *in vacuo*, and readily at room temperature. It has also been purified by removal of water during azeotropic distillation of a *benzene solution. It is then recrystallised twice from anhydrous diethyl ether under argon, and stored under argon [Blackstock et al. *J Org Chem* **52** 1451 *1987*]. [*Beilstein* **23/3** V 487.]

1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 2,3,4,6,7,8,9,10-octahydropyrimidino[1,2-*a*]-azepine) *[6674-22-2]* **M 152.2, b 115°/11mm, d_4^{20} 1.023, n_D^{20} 1.522, pK_{Est} ~ >13.** Fractionally distil DBU under vacuum. Also purify it by chromatography on Kieselgel and eluting with $CHCl_3$/EtOH/25% aqueous NH_3 (15:5:2) and checking by IR and MS. [Oediger et al. *Chem Ber* **99** 2012 *1962*, *Angew Chem, Int Ed Engl* **6** 76 *1967*, Guggisberg et al. *Helv Chim Acta* **61** 1057 *1978*, *Beilstein* **23/5** V 271.]

1,8-Diazabiphenylene *[259-84-7]* **M 154.2, m 156-158.5°, pK_{Est} ~4.4.** Recrystallise it from cyclohexane, then sublime it in a vacuum. [Barton & Walker *Tetrahedron Lett* 569 *1975*, Deroski & Marhgraf *Can J Chem* **62** 2235 *1984*.]

2,7-Diazabiphenylene *[31857-42-8]* **M 154.2, m 192-192.5°, pK_{Est} ~4.5.** It forms yellow crystals from cyclohexane, and sublimes in a vacuum. [MacBride *J Chem Soc, Chem Commun* 359 *1974*, Kramer & Berry *J Am Chem Soc* **94** 8336 *1972*.]

1,8-Diazafluorenone (cyclopenta[1.2-*b*:4,3-*b'*]dipyridin-9-one) *[54078-29-4]* **M 182.2, m 205°, 229-231°, pK_{Est} ~2.6.** Recrystallise it from Me_2CO. The *oxime* has **m** 119-200°. [Druey & Schmid *Helv Chim Acta* **33** 1080 *1950*, *Beilstein* **24** III/IV 622.]

Dibenzo-18-crown-6 *[14187-32-7]* **M 360.4, m 163-164°.** Crystallise it from *benzene, *n*-heptane or toluene and dry it under vacuum at room temperature for several days. [Szezygiel *J Phys Chem* **91** 1252 *1987*, Vögtle ed. *Top Corr Chem* (Host Guest Complex Chemistry) **98** *1981*.]

Dibenzo-18-crown-8 *[14174-09-5]* **M 448.5, m 103-106°.** Recrystallise it from EtOH, and dry in a vacuum at 60° over P_2O_5 for 16 hours. [Delville et al. *J Am Chem Soc* **109** 7293 *1987*, Vögtle ed. *Top Corr Chem* (Host Guest Complex Chemistry) **98** *1981*.]

Dibenzofuran *[132-64-9]* **M 168.2, m 82.4°.** Dissolve dibenzofuran in diethyl ether, then shake it with two portions of aqueous NaOH (2M), wash it with water, separate and dry ($MgSO_4$) it. After evaporating the ether, dibenzofuran is crystallised from aqueous 80% EtOH and then dried under vacuum. [Cass et al. *J Chem Soc* 1406 *1958*.] High purity material is obtained by zone refining. [*Beilstein* **17** V 234.]

Dibenzothiophene *[132-65-0]* **M 184.3, m 99°.** Purify dibenzothiophene by chromatography on alumina with petroleum ether, in a darkened room. Recrystallise it from water or EtOH. [*Beilstein* **17** V 239.]

1,3-Dibromo-5,5-dimethylhydantoin *[77-48-5]* **M 285.9, m 190-192°(dec), 190-193°(dec).** Recrystallise it from H_2O. Its solubility in CCl_4 is 0.003 mol/L at 25° and 0.024 mol/L at 76.5°. [*Beilstein* **24** III/IV 1101.]

4',5'-Dibromofluorescein *[596-03-2]* **M 490.1, m 285°.** Crystallise it from aqueous 30% EtOH. [*Beilstein* **19/6** V 462.]

5,7-Dibromo-8-hydroxyquinoline *[521-74-4]* **M 303.0, m 196°, pK_1^{25} 5.84, pK_2^{25} 9.56.** Crystallise it from acetone/EtOH. It can be sublimed. [*Beilstein* **21/3** V 290.]

2,6-Dibromopyridine *[626-05-1]* **M 236.9, m 117-119°, 118.5-119°, b 249°/757.5mm, pK_{Est} <0.** Purify 2,6-dibromopyridine by steam distillation, then recrystallise it twice from EtOH. It does not form an $HgCl_2$ salt. [den Hertog & Wibaut *Rec Trav Chim Pays Bas* **51** 381 *1932*, *Beilstein* **20/5** V 435.]

3,4-Dibromothiophene *[3141-26-2]* **M 241.9, m 4-5°, b 94-95°/12mm, 212-213° (atm), 221-222°(atm), d_4^{25} 2.188, n_D^{20} 1.640.** Distil it in a vacuum, but if it is discoloured then dissolve it in Et_2O, wash it with 2M NaOH solution, separate the layers, filter, dry the Et_2O layer over $CaCl_2$, filter, evaporate, and distil the residual oil in a vacuum. Nitration with Ac_2O/HNO_3 at 60° yields *3,4-dibromo-2-nitrothiophene* **m 115-116°** (from EtOH). [Steinkopf et al. *Justus Liebigs Ann Chem* **512** 149-151 *1934*, *Beilstein* **17** III/IV 248, **17/1** V 308.]

2,6-Di-*tert*-butyl-4-methylpyridine *[38222-83-2]* **M 205.4, m 31-32°, 33-36°, b 148-153°/ 95mm, 223°/760mm, n_D^{20} 1.476, pK_{Est} ~5.7.** A possible impurity is 2,6-di-*tert*-butyl-4-neopentylpyridine. Attempts to remove coloured impurities directly by distillation, acid-base extraction or treatment with activated charcoal were unsuccessful. Pure material is obtained by dissolving 0.3mole of the alkylpyridine in pentane (150ml) and introducing it at the top of a cold water jacketed chromatographic column (40 x 4.5cm) (cooling is necessary because the base in pentane reacts exothermically with alumina) containing activated and acidic alumina (300g). The column is eluted with pentane using a 1L constant pressure funnel fitted at the top of the column to provide slight pressure. All the pyridine is obtained in the first two litres of eluent (the progress of elution is monitored by spotting a fluorescent TLC plate and examining under short wave UV light—a dark blue spot is evidence for the presence of the alkylpyridine). Elution is complete in 1 hour. Pentane is removed on a rotovap with 90-93% recovery yielding a liquid which solidifies on cooling, **m** 31-32°, and the base can be distilled. The *H_2PtCl_6 salt* has **m** 213-314°(dec), and the *CF_3SO_3H salt* has **m** 202.5-203.5° (from CH_2Cl_2). [Anderson & Stang *Org Synth* Coll Vol **VII** 144 *1981*, *Beilstein* **20/6** V 190.]

2,6-Di-*tert*-butylpyridine *[585-48-8]* **M 191.3, b 100-101°/23mm, d_4^{25} 0.852, n_D^{20} 1.473, pK^{25} 5.02.** Redistil it from KOH pellets. [*Beilstein* **20** III/IV 2868.]
§ Polystyrene supported version is commercially available [107054-29-5] 200-400 mesh, crosslinked with 1% divinyllbenzene containing ~1.8mmol N/g polymer.

3,5-Dicarbethoxy-1,4-dihydro-2,4,6-collidine *[632-93-9]* **M 267.3, m 131-132°.** Crystallise the ester from hot EtOH/water mixture. [*Beilstein* **22** H 147, **22** I 529, **22** II 100, **22** III/IV 1594.]

(+) and (-) (8,8-Dichlorocamphorylsulfonyl)oxaziridine *[127184-05-8]* **M 298.2, m 178-180°, 183-186°, $[\alpha]_D^{20}$ (+) and (-) 88.3° (c 1.3, $CHCl_3$), (+) and (-) 91° (c 5, $CHCl_3$).** Recrystallise the enantiomers from EtOH [Davis & Weismiller *J Org Chem* **55** 3715 *1990*].

1,3-Dichloro-5,5'-dimethylhydantoin *[118-52-5]* **M 197.0, m 132-134°, 136°.** Purify it by dissolving in conc H_2SO_4 and diluting with ice H_2O, collect the solid, dry it in a vacuum and recrystallise it from $CHCl_3$. It sublimes at 100° in a vacuum. It exhibits time-dependent hydrolysis at pH 9. [Petterson & Grzeskowiak *J Org Chem* **24** 1414 *1959*, *Beilstein* **24** III/IV 1100.]

4,5-Dichloro-3*H*-1,2-dithiol-3-one *[1192-52-5]* **M 187.1, m 52-56°, 61°, b 87°/0.5mm, 125°/11mm.** Dissolve it in CH_2Cl_2 (1g in 250ml), filter, wash it twice with H_2O, evaporate and distil the residue *in vacuo* and then recrystallise it from petroleum ether. Its IR has ν_{max} at 1650 cm^{-1}. [Boberg *Justus Liebigs Ann Chem* **679** 109 *1964*, Boberg *Justus Liebigs Ann Chem* **693** 212 *1966*, *Beilstein* **19/4** V 72.]

5,7-Dichloro-8-hydroxyquinoline *[773-76-2]* **M 214.1, m 180-181°, pK_1 1.89, pK_2 7.62.** Crystallise the dichloro-oxine from acetone/EtOH. [*Beilstein* **21** H 95.]

6,9-Dichloro-2-methoxyacridine (**3,9-Dichloro-7-methoxyacridine)** *[86-38-4]* **M 278.1, m 160-161°, 164°, 163-165°.** Crystallise it from *benzene or 1,2-dichloroethane (**m** 162-163°). [Hall & Turner *J Chem Soc* 697 *1945*, *Beilstein* **21** III/IV 1553.]

5,7-Dichloro-2-methyl-8-hydroxyquinoline (5,7-dichloro-8-hydroxyquinaldine) *[72-80-0]* **M 228.1, m 114-115°, $pK_{Est(1)}$ ~2.0, $pK_{Est(2)}$ ~8.4.** Crystallise it from EtOH. [*Beilstein* **21/3** V 346.]

4,6-Dichloro-5-nitropyrimidine *[4316-93-2]* **M 194.0, m 100-103°, 101-102°, pK_{Est} <0.** If too impure, then dissolve it in Et_2O, wash it with H_2O, dry it over $MgSO_4$, evaporate it to dryness and recrystallise it from petroleum ether (b 85-105°) to give a light tan solid. It is soluble in *ca* 8 parts of MeOH [Boon et al. *J Chem Soc* 96 *1951*, Montgomery et al. in *Synthetic Procedures in Nucleic Acid Chemistry* Zorbach & Tipson eds, Wiley & Sons, NY, p76 *1968*]. [*Beilstein* **23** III/IV 899.]

2,6-Dichloropurine *[5451-40-1]* **M 189.0, m 180-181.5°, 181°, 185-195°(dec), 188-189°, pK_1^{20} 1.16 (aqueous H_2SO_4), pK_2^{20} 7.06.** It can be recrystallised from 150 parts of boiling H_2O and dried at 100° to constant weight. It is soluble in EtOAc. The *$HgCl_2$* salt separates from EtOH solution. It has UV with λ_{max} at 275nm (ε 8.9K) at pH 1; and 280nm (ε 8.5K) at pH 11 [Elion & Hitchings *J Am Chem Soc* **78** 3508 *1956*, Schaeffer & Thomas *J Am Chem Soc* **80** 3738 *1958*, Beaman & Robins *J Appl Chem (London)* **12** 432 *1962*, Montgomery *J Am Chem Soc* **78** 1928 *1956*]. [*Beilstein* **26** III/IV 1747.]

2,6-Dichloropyridine *[2402-78-0]* **M 148.0, m 87-88°, pK^{25} -2.86 (aqueous H_2SO_4).** It crystallises from EtOH. [*Beilstein* **20/5** V 416.]

3,5-Dichloropyridine *[2457-47-8]* **M 148.0, m 64-65°, 66-67°, b 178-178°/~760mm, pK^{25} 0.67.** Crystallise 3,5-dichloropyridine from EtOH, or distil it. [den Hertog et al. *Rec Trav Chim Pays Bas* **69** 685 *1950*, *Beilstein* **20** H 23, **20** III/IV 2502, **20** V 417.]

2,6-Dichloropyridine-3-carboxylic acid (2,6-dichloronicotinic acid) *[38496-18-3]* **M 192.0, m 146-148°, 147°, $pK_{Est(1)}$ ~ -1.** Purify the acid by recrystallisation from H_2O or Et_2O/petroleum ether (colourless needles), and the IR(KBr) has ν_{max} at 1738 cm^{-1}, and λ_{max} (ε) at 228.5(4700) and 273.5(8300)nm. The *acid chloride* [58584-83-1] **M 210.4, b 72-74°/0.01mm, 117-118°/45mm, n_D^{20} 1.5944**, was obtained by treatment with $SOCl_2$/DMF/*C_6H_6 and converted into the *amide* [70445-62-4] **M 191.0, m 148-148.5°**, or the *hydrazide* **m 171-173°** which crystallised from a large volume of MeCN. [Muterer et al. *Helv Chim Acta* **59** 222 *1976*, Newcome et al. *J Org Chem* **44** 2693 *1979*, *Beilstein* **22** H 44.] A pharmaceutical research building block acid of 90% grade is also available.

2,6-Dichloropyridine-4-carboxylic acid (2,6-dichloroisonicotinic acid) *[5398-44-7]* **M 192.0, m 210°, 209-212°, $pK_{Est(1)}$ ~ -1.** Purify the acid by crystallisation from H_2O, and it forms needles or platelets from EtOH. The *methyl ester* crystallises from aqueous MeOH with **m 82°**, the *ethyl ester* from aqueous EtOH has **m 66°**, and the *amide* from H_2O has **m 207-208°**. [Meyer et al. *Monatsh Chem* **36** 731 *1915*, Levelt & Wibaut *Rec Trav Chim Pays Bas* **48** 469 *1929*.]

5,6-Dichloropyridine-3-carboxylic acid (5,6-dichloronicotinic acid) *[41667-95-2]* **M 192.0, m 160-161°, 164-168°, 168°, $pK_{Est(1)}$ ~ 0.5.** Recrystallisation of the acid from H_2O provides the *monohydrate* which becomes *anhydrous* (**m 161-162°**) on heating at 100°. The *acid chloride* distils at **125°/~24mm**, solidifies on cooling, and crystallises from petroleum ether with **m 48-49°**. The *methyl ester* has **m 67-68°** (from aqueous MeOH), and the *amide* forms colourless plates from aqueous EtOH with **m 218-220°**. [Räth & Schiffmann *Justus Liebigs Ann Chem* **487** 133 *1931*, Meyer & Graf *Chem Ber* **61** 2212 *1928*, *Beilstein* **22** H 44, **22** II 36, **22** III/IV 511, **22/2** V 80.]

4,7-Dichloroquinoline *[86-98-6]* **M 198.1, m 86.4-87.4°, b 148°/10mm, pK^{25} 2.80.** Crystallise the dichloroquinoline from MeOH or 95% EtOH. [*Beilstein* **20/7** V 316.]

2,3-Dichloroquinoxaline *[2213-63-0]* **M 199.0, m 152-153°, 152-154°, pK_{Est} <0.** Recrystallise it from *C_6H_6 and dry it in a vacuum [Cheeseman *J Chem Soc* 1804 *1955*, *Beilstein* **23/7** V 144].

***cis*-Dicyclohexyl-18-crown-6** *[16069-36-6]* **M 372.5, m 47-50°.** Purify it by chromatography on neutral alumina and elute with an ether/hexane mixture [see Izatt et al. *Inorg Chem* **14** 3132 *1975*]. Dissolve it in ether at *ca* 40°, and spectroscopic grade MeCN is added to the solution, which is then chilled. The crown ether precipitates and is filtered off. It is dried *in vacuo* at room temperature [Wallace *J Phys Chem* **89** 1357 *1985*]. [Vögtle ed. *Top Corr Chem* (Host Guest Complex Chemistry) **98** *1981*.] **SKIN IRRITANT.**

5,5-Diethylbarbituric acid (Barbital) *[57-44-3]* **M 184.2, m 188-192°, pK_1^{25} 8.02, pK_2^{25} 12.7.** Crystallise barbital from water or EtOH and dry it in a vacuum over P_2O_5. [*Beilstein* **24** III/IV 1901.]

1,1'-Diethyl-2,2'-cyanine iodide *[977-96-8]* **M 454.4, m 274°(dec).** It crystallises from EtOH and is dried in a vacuum oven at 80° for 4 hours. [*Beilstein* **23** II 267.]

2,3-Dihydrobenzofuran (coumaran) *[496-16-2]* **M 120.2, m -21.5°, 72-73°/12mm, 84°/17mm, 188° /atm, d_4^{20} 1.065, n_D^{20} 1.5524.** Suspend coumaran in aqueous NaOH and steam distil it. Saturate the distillate with NaCl and extract it with Et_2O, dry the extract ($MgSO_4$), filter, evaporate and distil the residue. It gives a strong violet colour with $FeCl_3$ + H_2SO_4 and forms a yellow *picrate*, **m** 76° (from EtOH or *C_6H_6) which loses coumaran in a desiccator [Bennett & Hafez *J Chem Soc* 287 *1941*, Baddeley et al. *J Chem Soc* 2455 *1956*]. [*Beilstein* **17/1** V 581.]

Dihydropyran (3,4-dihydro-2*H*-pyran) *[110-87-2]* **M 84.1, b 84.4°/742mm, 85.4-85.6°/760mm, d_4^{20} 0.9261, n_D^{20} 1.4423, pK_{Est} ~ 4.2.** Partially dry dihydropyran with Na_2CO_3, then fractionally distil it. The fraction **b** 84-85° is refluxed with Na until hydrogen no longer evolves when fresh Na is added. It is then dried, and distilled again through a 60 x 1.2cm column packed with glass rings [Brandon et al. *J Am Chem Soc* **72** 2120 *1950*, UV: Elington et al. *J Chem Soc* 2873 *1952*, NMR: Bushweller & O'Neil *Tetrahedron Lett* 4713 *1969*]. It has been characterised as the *2-(3,5-dinitrobenzoyloxy)tetrahydropyrane* derivative, **m** 103° [prepared by dissolving 3,4-dinitrobenzoic acid (3g) in 50% excess of dihydropyran with warming, cooling, adding Et_2O (5ml), whereby the derivative crystallises out quantitatively] which forms pale yellow crystals from 80% dihydropyran/Et_2O [Woods & Kramer *J Am Chem Soc* **69** 2246 *1947*]. [*Beilstein* **17/1** V 181.]

3,4-Dihydro-2*H*-pyrido[1,2*a*]-pyrimidin-2-one *[5439-14-5]* **M 148.2, m 185-187°, 187-188°, 191-191.5°.** Dissolve it in $CHCl_3$, filter, evaporate, then recrystallise the residue from EtOH/Me_2CO (needles) which can be washed with Et_2O and dried. It can also be recrystallised from $CHCl_3$/petroleum ether or $CHCl_3$/hexane. The *hydrochloride* has **m** 295-295° (dec, from EtOH or MeOH/Et_2O), the *hydrobromide* has **m** 299-300°(dec) (from

MeOH/Et_2O) and the *picrate* has **m** 224-226°(corr), **m** 219-220° from EtOH. [Adams & Pachter *J Am Chem Soc* **74** 4906 *1952*, Lappin *J Org Chem* **23** 1358 *1958*, Hurd & Hayao *J Am Chem Soc* **77** 115 *1955*, *Beilstein* **24** III/IV 299.]

7,8-Dihydroxycoumarin (Daphnetin) *[486-35-1]* **M 178.2, m 256°(dec), $pK_{Est(1)}$ ~8.5, $pK_{Est(2)}$ ~12.3.** Crystallise it from aqueous EtOH. It can be sublimed. [*Beilstein* **18/3** V 202.].

***trans*-2,3-Dihydroxy-1,4-dioxane** *[4845-50-5]* **M 120.1, m 91-95°, 100°.** Recrystallise it from Me_2CO. With phenylhydrazine it gives *glyoxal phenylhydrazone* **m** 175° (from Me_2CO/petroleum ether). The *diacetyl* derivative has **m** 105-106° [Head *J Chem Soc* 1036 *1955*, Raudnitz *Chem Ind (London)* 166 *1956*]. [*Beilstein* **1** IV 3627.]

2,5-Dihydroxy-1,4-dithiane *[40018-26-6]* **M 152.2, m (142-147°) 150-152°, 151°.** Recrystallise the dithiane from EtOH. *2,5-Diethoxy-dithiane* has **m** 91° (92-93°); it crystallises from petroleum ether and can be sublimed at 60°/0.001mm [Hormatka & Haber *Monatsh Chem* **85** 1088 *1954*, Thiel et al. *Justus Liebigs Ann Chem* **611** 121 *1958*, Hesse & Jøeder *Chem Ber* **85** 924 *1952*]. [*Beilstein* **1** IV 3966.]

***S(-)*-4',7-Dihydroxyflavanone (3,4'-dihydroxyisoflavone, Liquiritigenin)** *[578-86-9]* **M 256.3, m 203-205° $[\alpha]_D^{20}$ -225° (c 0.95, 95%EtOH).** It crystallises from aqueous 50% EtOH. [*Beilstein* **18** III/IV 1780, **18/4** V 82.]

5,7-Dihydroxy-4'-methoxyflavone (Acacetin) *[480-44-4]* **M 284.3, m 261°, 260-265°.** Acacetin crystallises from 95% EtOH or acetic acid as pale yellow needles (m 263°). It is an anti-inflammatory. [Zemplen & Bognar *Chem Ber* **76** 452 *1943*, Pillon *Bull Soc Chim* Fr 9 *1954,* UV: Gaydou & Bianchini *Bull Soc Chim Fr* Part II 43 *1978*, *Beilstein* **18** III/IV 2683, **18/4** V 575.]

(±)-7-(2,3-Dihydroxypropyl)theophylline (Diprophylline, Dyphylline) *[479-18-5]* **M 254.3, m 158°, 160-164°, 161°, 161-164°, pK_{Est} ~ 8.7.** Recrystallise it from EtOH or H_2O. Its solubility in H_2O is 33% at 25°, in EtOH it is 2% and in $CHCl_3$ it is 1%. Its UV has λ_{max} (H_2O) at 273nm (ε 8,855). [Roth *Arch Pharm* **292** 234 *1959*.] The *4-nitrobenzoyl* derivative has **m** 178° [Oshay *J Chem Soc* 3975 *1956*]. [*Beilstein* **26** III/IV 2370.]

1,3-Diiminoisoindoline *[3468-11-9]* **M 145.2, m 193-194°(dec), 196°(dec), pK^{25} 8.27.** It crystallises from H_2O, MeOH or MeOH/Et_2O (charcoal) in colourless prisms that become green on heating. [Elvidge & Linstead *J Chem Soc* 5000 *1952*]. Its IR (nujol) has bands at 3150 and 690 cm^{-1}, and the UV has λ_{max} at 251nm (ε 12,500), 256nm (ε 12,5000) and 303nm (ε 4,600) [Elvidge & Golden *J Chem Soc* 700 *1957*, Clark et al. *J Chem Soc* 3593 *1953*]. The *thiocyanate* has **m** 250-255° (dec), the *monohydrochloride* has **m** 300-301° (turns green), and the *dihydrochloride* has **m** 326-328° (turns green) and the *picrate* crystallises from EtOH with **m** 299° (dec). [*Beilstein* **22/13** V 5.]

5,7-Diiodo-8-hydroxyquinoline *[83-73-8]* **M 397.0, m 214-215°(dec) $pK_{Est(1)}$~3.2, $pK_{Est(2)}$ ~8.2.** It crystallises from xylene and is dried at 70° in a vacuum. [*Beilstein* **21** II 58.]

6-Dimethylaminopurine *[938-55-6]* **M 163.1, m 257.5-258.5°, 259-262°, 263-264°, pK_1^{25} 3.87, pK_2^{25} 10.5.** It is purified by recrystallisation from H_2O, EtOH (0.32g in 10ml) or $CHCl_3$. [Albert & Brown *J Chem Soc* 2060 *1954*, UV: Mason *J Chem Soc* 2071 *1954*.] The *monohydrochloride* crystallises from EtOH/Et_2O, **m** 253°(dec) [Elion et al. *J Am Chem Soc* **74** 411 *1952*], the *dihydrochloride* has **m** 225°(dec) and the *picrate* has **m** 245° (235-236.5°) [Fryth et al. *J Am Chem Soc* **80** 2736 *1958*]. [*Beilstein* **26** III/IV 3566.]

1,3-Dimethylbarbituric acid *[769-42-6]* **M 156.1, m 123°, pK^{25} 4.56.** Crystallise the acid from water and sublime it in a vacuum. Also purify it by dissolving 10g in 100ml of boiling CCl_4/$CHCl_3$ (8:2) (1g charcoal), filtering and cooling to 25°. Dry it *in vacuo* [Kohn et al. *Anal Chem* **58** 3184 *1986*]. [*Beilstein* **24** III/IV 1875.]

5,6-Dimethylbenzimidazole *[582-60-5]* **M 146.2, m 205-206°, pK_1^{25} 5.96, pK_2^{25} 12.52.** Crystallise 5,6-dimethylbenzimidazole from diethyl ether. It sublimes at 140°/3mm. [*Beilstein* **23/6** V 454.]

2,3-Dimethylbenzothiophene *[31317-17-6]* **M 212.3, m 69-70°, b 123-124°/10mm, n_D^{19} 1.6171.** Fractionate it through a 90cm Monel spiral column, or other efficient fractionating or spinning band column and collect the middle fraction. It has also been purified by chromatography on basic alumina using pentane as eluent. [Tedjanulia et al. *J Heterocycl Chem* **20** 1485 *1983*, *Beilstein* **17** III/IV 161.]

4,4'-Dimethyl-2,2'-bipyridine *[1134-35-6]* **M 184.2, m 175-176°, $pK_{Est(1)}$ ~0.2, $pK_{Est(2)}$ ~4.9.** Crystallise it from ethyl acetate. [Elliott et al. *J Am Chem Soc* **107** 4647 *1985*, *Beilstein* **23/8** V 79.]

1,1'-Dimethyl-4,4'-bipyridylium dichloride ($3H_2O$; Methyl Viologen Dichloride, paraquat dichloride) *[1910-42-5]* **M 311.2, m >300°(dec).** Recrystallise the dichloride from MeOH/acetone mixture. It has also been recrystallised three times from absolute EtOH [Bancroft et al. *Anal Chem* **53** 1390 *1981*]. Dry it at 80° in a vacuum. [*Beilstein* **23/8** V 30.]

1,3-Dimethylbutadiene sulfone (1,3-dimethylsulfolene, 2,5-dihydro-2,4-dimethylthiophene) *[10033-92-8]* **M 145.2, m 40.4-41.0°.** Crystallise it from Et_2O, Et_2O/pentane or CCl_4. [Grummitt et al. *J Am Chem Soc* **72** 5167 *1950*, Bartlett et al. *J Org Chem* **32** 1290 *1967*, *Beilstein* **17** III/IV 161.]

2,2-Dimethyl-1,3-dioxan-4,6-dione (Meldrum's Acid) *[2033-24-1]* **M 144.1, m 92-96°, 94-95°, pK^{25} 5.1, 7.32.** Crystallise the dione from Me_2CO/H_2O. It is a useful synthon for the C3 malonic acid moiety. [Arnette et al. *J Am Chem Soc* **106** 6759 *1984*, Bihlmayer et al. *Monatsh Chem* **98** 564 *1967*, Review: McNab *Chem Soc, Rev* **7** 345 *1978*, Chan & Huang *Synthesis* 452 *1982*, *Beilstein* **19/5** V 8.] It is synthesised by a modified procedure in which concentrated H_2SO_4 (1.5ml) is added to a stirred suspension of powdered malonic acid (52g, 0.5 mole) in acetic anhydride (60ml, 0.6 mole), whereby the malonic acid dissolves with spontaneous cooling. Acetone (40ml, 0.55 mole) is added to the mixture while keeping the temperature at 20-25°, then cooled in a refrigerator overnight, the crystals are filtered off, washed three times with ice-water (enough to cover the crystals) and air dried. The crude product (35g, 49%) is recrystallised without heating by dssolving it (10g) in Me_2CO (20ml), filtering, and adding H_2O (40ml), with ~70% recovery of material m **94-95°**. [Pihlaja & Seilo *Acta Chem Scand* **22** 3053 *1968*.]
Alternatively concentrated H_2SO_4 (0.5ml) is added dropwise to a stirred suspension of powdered malonic acid (52g, 0.5 mole) in redistilled isoprenyl acetate (62ml, 55g, [108-22-5]), when the temperature rose from 23° to 31° in 45 minutes and all the solid dissolved within 1 hour. Treatment of the reaction as above gave Meldrum's acid (37g, 50%). [Davidson & Bernhard *J Am Chem Soc* **70** 3426 *1948*]. Its ^1H NMR ($CDCl_3$, TMS) has δ at 1.73 (s, 2-Me_2) and 3.60 (s, 5-H) [Schuster & Schuster *Tetrahedron* **25** 199 *1969*].

3,6-Dimethyl-1,4-dioxan-2,5-dione (Lactide) *[cis-RS,RS-(±) 615-95-2, cis-R,R-(+) 95-96-5, cis-S,S-(-) 4511-42-6]* **M 144.1.** This is the cyclic dilactone of lactic acid. The **(±)-*cis-racemate*** has been distilled with **b 142°/8mm**; the distillate which solidifies gives yellow needles on recrystallisation from EtOH with **m 128°**, from Et_2O with **m 129°**, or $CHCl_3$ with **m 126°**, with IR ν_{max} at 1720-1740 cm^{-1}. It hydrolyses in cold H_2O. [Carothers et al. *J Am Chem Soc* **54** 772 *1932*]. A ***trans-form*** (probably *RS,SR*) has been reported which crystallises from Et_2O with **m 42-43°** [Hummel et al. *Acta Cryst (Sect B)* **38** 1679 *1982*]. The ***R,R-(+)-lactide*** has **b 150°/2mm** and crystallises from Et_2O with **m 95°**, or **m 96.5-97.5°** (from $CHCl_3$) or **m 97.7°** (from EtOAc) and **$[\alpha]_D^{22}$ +297° (c 1.2, *C_6H_6)**. The ***S,S-(-)-lactide*** has **b 150°/2.5mm** and crystallises from EtOAc with **m 98.7°**, or **m 95°** (from $CHCl_3$) or **m 96.5-97.5°** (from CCl_4) and **$[\alpha]_D^{22}$ -297° (c 1.2, *C_6H_6)**. [Toniolo et al. *J Org Chem* **35** 6 *1970*, *Beilstein* **19** H 154, **19** I 179, **19** II 176, **19** IV 1927, **19/5** V 10.]

2,9-Dimethyl-4,7-diphenyl-1,10-phenanthroline (Bathocuproine) *[4733-39-5]* **M 360.5, m >280°, pK_{Est} ~5.6.** Purify it by recrystallisation from *benzene. [Smith & Wilkins *Anal Chem* **25** 510 *1953*, *Beilstein* **23** III/IV 2160.]

2,2-Dimethylethyleneimine (2,2-dimethylaziridine) *[2658-24-4]* **M 71.1, b 70.5-71.0°, 72°, n_D^{20} 1.405, pK^{25} 8.64.** Dry the 2,2-dimethylaziridine over solid KOH, filter and freshly distil from sodium before use, and store it under dry nitrogen. The *N-phenylthiocarbamoyl* derivative crystallises from petroleum ether containing a trace of Me_2CO with **m** 92.5-93.5°. [Hassner et al. *J Am Chem Soc* **91** 5046 *1969*, Cairns *J Am Chem Soc* **63** 871 *1941*, Lamaty et al. *Justus Liebigs Ann Chem* **726** 77 *1969*, *Beilstein* **20** III/IV 280.]

5,5-Dimethylhydantoin *[77-71-4]* **M 128.1, m 177-178° pK^{24} 9.19.** Crystallise the hydantoin from EtOH and sublime it *in vacuo.* [*Beilstein* **24** III/IV 1097.]

4,6-Dimethyl-2-hydroxypyrimidine *[108-79-2]* **M 124.1, m 198-199°, 202-205°, pK$_1^{20}$ 3.77, pK$_2^{20}$ 10.50.** Crystallise the pyrimidine from absolute EtOH (charcoal). [*Beilstein* **24/2** V 138.]

1,2-Dimethyl-1*H*-imidazole *[1739-84-0]* **M 96.1, m 38-40°, b 206°/760mm, d$_4^{20}$ 1.084, pK$_{Est}$ ~8.1.** Crystallise the imidazole from *benzene, dry and store it at 0-4°. The *picrate* crystallises from H_2O or EtOH with **m** 181°. [Balaban & Pymann *J Chem Soc* **125** 1570 *1924*, Gorun et al. *J Am Chem Soc* **109** 4244 *1987*, *Beilstein* **23** H 66, **23** II 56, **23** III/IV 594.]

1,3-Dimethyl-2-imidazolinone (DMI, *N*,*N*'-dimethylethyleneurea, DMEU) *[80-73-9]* **M 114.2, m 8.2°, b 67-68°/2mm, 104°/5mm, 106-107°/17mm, 224-226°/atm, d$_4^{25}$ 1.056, n$_D^{20}$ 1.472**. After preparation by reaction of *N*,*N*'-dimethylethylenediamine in toluene with phosgene in toluene below 15°, excess phosgene is removed by blowing air through the mixture. The hydrochloride salt that separates is removed by filtration, and washed with $CHCl_3$. The combined filtrate and washings are evaporated off, and the residue is distilled (b 129°/39mm). The crude distillate is treated with H_2O; K_2CO_3 is added to saturate the solution, and extracted with $CHCl_3$, the extract is dried (K_2CO_3), filtered, and pure *1,3-dimethylimidazolin-2-one* distils at **b 104°/5mm**. It has been used as an alternative to HMPA [see 680-31-9] as a high dielectric solvent for reactions. [Boon *J Chem Soc* 307 *1947*, Lien & Kumler *J Med Chem* **11** 241 *1968*, Kohn et al. *J Org Chem* **42** 941 *1977*, *Beilstein* **24** III/IV 9.]

3,3-Dimethyloxetane *[6921-35-3]* **M 86.1, b 79.2-80.3°/760mm, d$_4^{20}$ 0.836, n$_D^{20}$ 1.399.** Purify 3,3-dimethyloxetane by gas chromatography using a 2m silicone oil column or distil it. Fractionate it at atmospheric pressure (preferably under N_2 or Ar. [*Beilstein* **17** II 21.]

2,9-Dimethyl-1,10-phenanthroline (neocuproine hemihydrate) *[484-11-7]* **M 208.3, 217.3 (hemihydrate), m 162-164°, pK^{25} 5.85.** Purifiy it as the *hemihydrate* by crystallisation from water and as the *anhydrous* base from *benzene. [*Beilstein* **23/8** V 527.]

4,4-Dimethyl-2,6-piperidinedione (4,4-dimethylglutarimide) *[1123-40-6]* **M 141.2, m 144-146°, pK$_{Est}$ ~11.5.** Recrystallise the imide from hot H_2O or EtOH [Arnett & Harrelson *J Am Chem Soc* **109** 809 *1987*]. [*Beilstein* **21** H 391, **21** I 331, **21** II 309, **21** III/IV 4601, **21/9** V 592.]

2,5-Dimethylpyrazine *[123-32-0]* **M 108.1, b 156°, d$_4^{20}$ 0.990, n$_D^{20}$ 1.502, pK$_1^{25}$ -4.6 (aqueous H_2SO_4), pK$_2^{25}$ 1.85.** Purify it *via* its *picrate* (**m** 150°) which is decomposed with a base (e,g, KOH) and distilled. [Wiggins and Wise *J Chem Soc* 4780 *1956*]. [*Beilstein* **23/5** V 403.]

3,5-Dimethylpyrazole *[67-51-6]* **M 96.1, m 107-108°, pK^{20} 4.16.** Crystallise it from cyclohexane or water. [Barszez et al. *J Chem Soc, Dalton Trans* 2025 *1986*, *Beilstein* **23/5** V 110.]

2,3-Dimethylquinoxaline *[2379-55-7]* **M 158.2, m 106°, pK^{25} -3.84 (aqueous H_2SO_4).** It has been purified by steam distillation with the base crystallising in the distillate. Recrystallise it from distilled water or aqueous EtOH. The *sulfate* crystallises from EtOH with **m** 151-152°(dec). [Gibson *J Chem Soc* 343 1927, *Beilstein* **23** H 191, **23** II 197, **23** III/IV 1277.]

2,4-Dimethylsulfolane *[1003-78-7]* **M 148.2, b 128°/77mm, d$_D^{25}$ 1.1314, n$_D^{20}$ 1.474.** Distil the 2,4-dimethylsulfolane in a vacuum. [*Beilstein* **17/1** V 82.]

1,3-Dimethyluracil *[874-14-6]* **M 140.1, m 121-122°, pK^{25} -3.25 (aqueous H_2SO_4).** Crystallise it from EtOH/ether. [*Beilstein* **24** III/IV 1196.]

9,9-Dimethylxanthene (4,4-dimethyl-2,3:5,6-dibenzopyran) *[19814-75-6]* **M 210.3, m 36-38°, b 114-115°/0.6mm, n$_D^{20}$ 1.5973.** It is prepared under argon (Schlenk equipment) by adding Me_3Al solution (2.0M in

toluene, 320ml, 0.64mmol), *via* a septum over 50 minutes, to an ice-water cooled stirred suspension of 9-xanthone (50.0g, 0.255mol) in toluene (300ml) (exothermic reaction, no gas evolved). The dark red solution is allowed to warm to ~25° over 3 hours, and stirred for a further 14 hours. (*Alternatively* it can be heated to 60°. for ~0.5 hours.) The mixture is transferred (*via* a cannula under argon pressure) to a stirred mixture of concentrated HCl (250ml) and ice (4 L). The organic phase is separated, dried ($MgSO_4$), filtered, the solvent is evaporated *in vacuo* to give a yellow oil (51.5g, 96%) which distils at 114-115°/0.6mm, and solidifies on cooling. The ^1H NMR ($CDCl_3$, TMS) has δ at 1.63 (s, 6H, CH_3), 7.0-7.6 (m, 8H, aromatic-H); MS has *m/z* at 210 (M^+), 195 (base peak, M^+-CH_3). [Nowick et al. *J Am Chem Soc* **112** 8904 *1990*, Meisters & Mole *Aust J Chem* **27** 1655 *1974*, *Beilstein* **17** II 287.]

1,3-Dioxolan-2-one (ethylene carbonate) *[96-49-1]* **M 88.1, m 37°, 39°, 40°, b 65-67°/1mm, 126°/17mm, 238°/760mm, d_4^{20} 1.321, n^{40} 1.4199.** Dry 1,3-dioxolan-2-one over P_2O_5, then fractionally distil it at low or atmospheric pressure. Recrystallise it from dry Et_2O (plates, **m** 36.5°, 38.5-40° was also reported). It is soluble in H_2O. [*Beilstein* 19 II 135,**19** III/IV 1556, **19/4** V 6.]

1,3-Dioxane *[505-22-6]* **M 88.1, b 104.5°/751mm, d_4^{20} 1.040, n_D^{20} 1.417.** Dry the dioxane with sodium and fractionally distil it. [*Beilstein* **19/1** V 11.]

1,4-Dioxane *[123-91-1]* **M 88.1, f 11.8°, b 101.3°, d_4^{25} 1.0292, n_D^{15} 1.4236, n_D^{25} 1.42025.** It is prepared commercially either by dehydration of ethylene glycol with H_2SO_4 and heating ethylene oxide or bis(ß-chloroethyl)ether with NaOH. The usual impurities are acetaldehyde, ethylene acetal, acetic acid, water and peroxides. Peroxides can be removed (and the aldehyde content decreased) by percolation through a column of activated alumina (80g per 100-200ml solvent), by refluxing with $NaBH_4$ or anhydrous stannous chloride and distilling, or by acidification with conc HCl, shaking with ferrous sulfate and leaving in contact with it for 24 hours before filtering and purifying further.
Hess and Frahm [*Chem Ber* **71** 2627 *1938*] refluxed 2L of dioxane with 27ml conc HCl and 200ml water for 12 hours with slow passage of nitrogen to remove acetaldehyde. After cooling the solution, KOH pellets were added slowly and with shaking until no more would dissolve and a second layer had separated. The dioxane was decanted, treated with fresh KOH pellets to remove any aqueous phase, then transferred to a clean flask where it was refluxed for 6-12 hours with sodium, then distilled from it. *Alternatively*, Kraus and Vingee [*J Am Chem Soc* **56** 511 *1934*] heated it on a steam bath with solid KOH until fresh addition of KOH gave no more resin (due to acetaldehyde). After filtering through paper, the dioxane was refluxed over sodium until the surface of the metal was not further discoloured during several hours. It was then distilled from sodium.
The acetal (**b** 82.5°) is removed during fractional distillation. Traces of *benzene, if present, can be removed as the *benzene/MeOH azeotrope by distillation in the presence of MeOH. Distillation from $LiAlH_4$ removes aldehydes, peroxides and water. Dioxane can be dried using Linde type 4X molecular sieves. Other purification procedures include distillation from excess C_2H_5MgBr, refluxing with PbO_2 to remove peroxides, fractional crystallisation by partial freezing and the addition of KI to dioxane acidified with aqueous HCl. Dioxane should be stored out of contact with air, preferably under N_2.
A detailed purification procedure is as follows: Dioxane is stood over ferrous sulfate for at least 2 days, under nitrogen. Then water (100ml) and conc HCl (14ml)/ litre of dioxane are added (giving a pale yellow colour). After refluxing for 8-12 hours with vigorous N_2 bubbling, pellets of KOH are added to the warm solution to form two layers and to discharge the colour. The solution is cooled rapidly with more KOH pellets being added (magnetic stirring) until no more dissolved in the cooled solution. After 4-12 hours, if the lower phase is not black, the upper phase is decanted rapidly into a clean flask containing sodium, and refluxed over sodium (until freshly added sodium remained bright) for 1 hour. The middle fraction is collected (and checked for minimum absorbency below 250nm). The distillate is fractionally frozen three times by cooling in a refrigerator, with occasional shaking or stirring. This material is stored in a refrigerator. Before use it is thawed, refluxed over sodium for 48 hours, and distilled into a container. All joints are clad with Teflon tape.
Coetzee and Chang [*Pure Appl Chem* **57** 633 *1985*] dried the solvent by passing it slowly through a column (20g/L) of 3A molecular sieves activated by heating at 250° for 24 hours. Impurities (including peroxides) are removed by passing the effluent slowly through a column packed with type NaX zeolite (pellets ground to

0.1mm size) activated by heating at 400° for 24 hours or chromatographic grade basic Al_2O_3 activated by heating at 250° for 24 hours. After removal of peroxides the effluent is refluxed for several hours over sodium wire, excluding moisture, distilled under nitrogen or argon and stored in the dark.
One of the best tests of purity of dioxane is the formation of the purple disodium benzophenone complex during reflux and its persistence on cooling. (Benzophenone is better than fluorenone for this purpose and for the storing of the solvent.) [Carter et al. *Trans Faraday Soc* **56** 343 *1960*, *Beilstein* **19** V 16.] **TOXIC.**
Rapid purification: Check for peroxides (see Chapter 1 and Chapter 2 for test under ethers). Pre-dry with $CaCl_2$ or better over Na wire. Then reflux the pre-dried solvent over Na (1% w/v) and benzophenone (0.2% w/v) under an inert atmosphere until the blue colour of the benzophenone ketyl radical anion persists. Distil, and store it over 4A molecular sieves in the dark.

1,3-Dioxolane *[646-06-0]* **M 74.1, b 75.0-75.2°, d $^{20}_{D}$ 1.0600, n^{21} 1.3997.** Dry it with solid NaOH, KOH or $CaSO_4$, and distil it from sodium or sodium amalgam. Barker et al. [*J Chem Soc* 802 *1959*] heated 34ml of dioxalane under reflux with 3g of PbO_2 for 2 hours, then cooled and filtered. After adding xylene (40ml) and PbO_2 (2g) to the filtrate, the mixture is fractionally distilled. Addition of xylene (20ml) and sodium wire to the main fraction (**b** 70-71°) led to a vigorous reaction, following which the mixture was again fractionally distilled. Xylene and sodium additions are made to the main fraction (**b** 73-74°) before it is finally distilled. [*Beilstein* **19/1** V 6.]

5,5-Diphenylhydantoin *[57-41-0]* **M 252.3, m 293-295°.** Crystallise the hydantoin from EtOH. [*Beilstein* **24** III/IV 1748.]

1,3-Diphenylisobenzofuran *[5471-63-6]* **M 270.3, m 129-130°.** Recrystallise it from EtOH or EtOH/$CHCl_3$ (1:1) under red light (as in photographic dark rooms) or from *benzene in the dark. [*Beilstein* **17/2** V 503.]

2,5-Diphenyl-1,3,4-oxadiazole (PPD) *[725-12-2]* **M 222.3, m 70° (hydrate), 139-140° (anhydrous), b 231°/13mm, 248°/16mm.** Its solubility in $CHCl_3$ is 10%. Crystallise it from EtOH and sublime it *in vacuo*. [*Beilstein* **27** III/IV 2712.]

2,5-Diphenyloxazole (PPO) *[92-71-7]* **M 221.3, m 74°, b 360°/760mm.** Distil it in steam and crystallise it from ligroin. [*Beilstein* **27** III/IV 1437.]

2*RS*,5*RS*-(±)-2,5-Diphenylpyrrolidine (± *trans* isomer) ***[****22147-84-8]* **M 223.3, b 136°/0.3mm, n $^{25}_{D}$ 1.5866, pK_{Est} ~8.0.** A mixture of *cis-(meso)* and *trans*-(±) pyrrolidines (b ~130-145°/0.15-0.2mm, ~138g, 0.6mol) in EtOH (210ml) and concentrated HCl (100ml) was treated dropwise, during ~2 hours, with a solution of $NaNO_2$ (61.5g, 0.9mol) in H_2O (100ml) at ~0° (ice-bath cooling). The mixture was poured into H_2O (1L) and the precipitate (~160g) was collected, washed with H_2O and fractionally recrystallised from Me_2CO to give the *trans-nitroso* derivative (**m 140-140.9°**, 51%) [22147-82-6], and the *cis-nitroso* derivative (**m 97-98°**, 20%) [22147-81-5]. This *trans*-nitroso-pyrrolidine was de-nitrosated (HCl gas in Et_2O) to the *trans-hydrochloride* **m 196.5-180°** which was recrystallised from EtOH/Et_2O. The *trans-free base* was obtained by basifying an aqueous solution to pH 9-10 and extracting with Et_2O (3 x 50ml), drying the extract (Mg_2SO_4), filtering, evaporating and distilling the residual oil (**b 136°/0.3mm)**. The IR (film) has ν_{max} at 1110-1025 (three peaks, one is for C-N) and 3330 (N-H) cm^{-1}. Similarly the *cis (meso) N-nitroso derivative* gave the *2RS,5SR-diphenylpyrrolidine meso-hydrochloride* which had **m 224.7-225.5°**, and the *meso-free base* [22147-83-7] had **b 121-123.4°/0.2mm, n $^{25}_{D}$ 1.5850**. The optically active *2R,5R-(+)-diphenylpyrrolidine* enantiomer [155155-73-0] had **m 49-53°, [α] $^{22}_{D}$ +118° (c 1.0, $CHCl_3$)**. [Overberger et al. *J Am Chem Soc* **91** 687 *1969*, Breuer & Melumed *J Org Chem* **37** 3949 *1972*.]

(±)-α, α-Diphenyl-2-pyrrolidinemethanol (α, α-diphenyl-DL-prolinol) *[63401-04-7, 112022-88-55]* **M253.3, m 82-83° (76° also reported), pK_{Est} ~9.5.** It is prepared as the *(±)-hydrochloride* [16226-54-3] **M 289.8**, **m 267-269° (dec, 262-263°** was also reported**)** by dissolving the amine in Et_2O, Et_2O/MeOH or CH_2Cl_2, and dry HCl gas is bubbled through (avoid excess HCl as it may dissolve precipitated NH_4Cl), filtering,

evaporating, and the residue is recrystallised from MeOH/Me_2CO; and from which the *free base* is obtained by treatment with aqueous NaOH and extraction with Et_2O. It has psychostimulating activity. [Enders et al. *Org Synth* **58** 113 *1978*, Enders et al. *Org Synth* Coll Vol **VI** 542 *1988*, Enders et al. *Synthesis* 548 *1976*, Likhosherstov et al. *Khim Farm Z* **1** 30 *1967*, *Chem Abstr* **67** 90642 *1967*. *Beilstein* **21** III/IV 1519.]

***R*-(+)-α, α-Diphenyl-2-pyrrolidinemethanol (α, α-Diphenyl-D-prolinol)** *[22348-32-9]* **M253.3, m 78-80°, $[\alpha]_D^{20}$ +69° (c 3, $CHCl_3$).** It is purified by recrystallisation from EtOH or hexane. It was also purified *via* the *(R)-hydrochloride* [172152-19-1] as above.

***S*-(–)-α, α-Diphenyl-2-pyrrolidinemethanol (α, α-diphenyl-L-prolinol)** *[112068-01-6]* **M253.3, m 79-9.5°, 83°, $[\alpha]_D^{20}$ -68.1° (c 3.2, $CHCl_3$), $[\alpha]_D^{20}$ -87.5° (c 1.16, CH_2Cl_2).** It is purified by recrystallisation from EtOH or hexane. The *S-(-)-hydrochloride* [148719-90-8] melts above 240°, and the *benzoyl* derivative **m 183°** crystallises from H_2O, MeOH or EtOH. [Enders et al. *Bull Soc Chem Belg* **97** 691 *1988*, Kerrick & Beak *J Am Chem Soc* **113** 9708 *1991*, Corey & Bakshi *Tetrahedron Lett* **31** 611 *1990*, Mathre *J Org Chem* **58** 2880 *1993*, *Beilstein* **21** III/IV 1519.]

Dipicolinic acid (pyridine-2,6-dicarboxylic acid) *[499-83-2]* **M 167.1, m 255°(dec), λ_{max} 270nm, pK_1^{20} 2.10, pK_2^{20} 4.68.** Crystallise the acid from water, and sublime it in a vacuum. [*Beilstein* **22/4** V 128.]

Di-(4-pyridoyl)hydrazine (*N,N′*-disionicolinoyl hydrazine) *[4329-75-3]* **M 246.2, m 254-255°, 259-260°.** Crystallise it from water, aqueous EtOH or propan-1-ol. [Albert & Rees *Biochem J* **61** 128 *1955*, *Beilstein* **22** III/IV 663.]

2,2'-Dipyridylamine *[1202-34-2]* **M 171.2, m 84° and remelts at 95° after solidifying, b 176-178°/13mm, 222°/50mm, 307-308°/760mm, pK^{25} 6.69 (in 20% aqueous EtOH).** Crystallise the amine from *benzene or toluene [Blakley & De Armond *J Am Chem Soc* **109** 4895 *1987*]. The amine is also recrystallised from Me_2CO (**m** 95.1°) or distilled in a vacuum. [*Beilstein* **22** I 630, **22** II 331, **22** III/IV 3961.]

2,2'-Dipyridyl disulfide (2,2'dithiopyridine, Aldrithiol-2) *[2127-03-9]* **M 220.3, m 53°, 57-58°, pK_1^{25} 0.35, pK_2^{25} 2.45.** Recrystallise the disulfide H_2O from *C_6H_6/petroleum ether (6:7), ligroin or *C_6H_6. The *picrate* has **m** 119° (from EtOH). [Walter et al. *Justus Liebigs Ann Chem* **695** 7785 *1966*, Marckwald et al. *Chem Ber* **33** 1556 *1900*, Brocklehurst & Little *Biochem J* **133** 67,78 *1973, Beilstein* **21** III/IV 48.] It has been used as a 1mM solution in EtOH for the spectrophotometric estimation of thiols. Essentially the thiol displaces half the disulfide molecule liberating the 2-mercaptopyridine anion, thereby shifting the λ_{max} from 340nm (of the disulfide) to 268nm (of the anion) at pH 9, or 278nm in H_2O. (Compare with 4,4'-dipyridyl disulfide (below) which has been used for the same purpose [Humphrey et al. *Anal Chem* **40** 698 *1970*].

4,4'-Dipyridyl disulfide (4,4'-dithiopyridine, Aldrithiol-4) *[2645-22-9]* **M 220.3, m 74-76°, $pK_{Est(1)}$ ~1.5, $pK_{Est(2)}$ ~4.5.** Recrystallise the disulfide from H_2O, EtOH, Me_2CO, *C_6H_6 or petroleum ether. It has been used as a 1mM solution in EtOH for the spectrophotometric estimation of thiols. Essentially the thiol displaces half the disulfide molecule liberating the 4-mercaptopyridine (4-pyridinethiol) anion, thereby shifting the λ_{max} from 324nm (of the disulfide) to 285nm (of the anion) at pH 9. (Compare with 2,2′ dipyridyl disulfide above which has been used for the same purpose.) [Humphrey et al. *Anal Chem* **40** 698 *1970*, Cheng & Ritchie *Aust J Chem* **26** 1785 *1973*.] [*Beilstein* **21** II 35, for review see Aldrich in *Aldrichimica Acta* **4** 33 *1971*.]

1,2-Di-(4-pyridyl)-ethane *[4916-57-8]* **M 184.2, m 110.9-111.2°, 114.5-116°, b 167-174°/3mm, $pK_{Est(1)}$ ~3.8, $pK_{Est(2)}$ ~5.4.** Crystallise the ethane from cyclohexane/*benzene (3:1, solubility is ~7.5g/100ml). The *dihydrochloride* crystallises from EtOH with **m** 329-330°(dec). [Bergmann et al. *J Am Chem Soc* **74** 5981 *1952,* Thayer & Carson *J Am Chem Soc* **70** 2331 *1948*, Jampolsky et al. *J Am Chem Soc* **74** 5222 *1952*, Chow & Fouss *J Am Chem Soc* **80** 1095 *1958*, *Beilstein* **23** III/IV 1389.]

***trans*-1,2-Di-(4-pyridyl)-ethylene** *[13362-78-2]* **M 182.2, m 153-154°, 155.5-156.5°, pK_1^{25} 3.65, pK_2^{25} 5.6.** Crystallise the ethylene from water (1.6g/100ml at 100°). The *di-hydrochloride* has **m** 347°, from EtOH.

[*Beilstein* **23/8** V 239.]

1,3-Di-(4-pyridyl)-propane *[17252-51-6]* **M 198.3, m 60.5-61.5°, 62-65°, $pK_{Est(1)}$ ~4.5, $pK_{Est(2)}$ ~5.5.** Crystallise the propane from *n*-hexane/*benzene (5:1) or Me_2CO. The *picrate* has **m** 185-185°. [Jampolsky et al. *J Am Chem Soc* **74** 5222 *1952*, Chow & Fouss *J Am Chem Soc* **80** 1095 *1958*, *Beilstein* **23** III/IV 1400.]

2,5-Distyrylpyrazine *[14990-02-4]* **M 284.3, m 219°.** Recrystallise it from xylene; chromatograph it on basic silica gel (60-80 mesh) using CH_2Cl_2 as eluent, then sublime it in a vacuum on to a cold surface at 10^{-3}torr [Ebied *J Chem Soc, Faraday Trans 1* **78** 3213 *1982*]. All operations should be carried out in the dark.

1,3-Dithiane *[505-23-7]* **M 120.2, m 54°.** Crystallise the 1,3-dithiane from 1.5 times its weight of MeOH at 0°, and sublime it at 40-50°/0.1mm. [Gröbel & Seebach *Synthesis* 357 *1977*, *Beilstein* **19/1** V 13.]

2,2′-Dithiobis(benzothiazole) *[120-78-8]* **M 332.2, m 180°, 182.5-183.5°.** Crystallise it from *benzene. [*Beilstein* **27** H 109, **27** III/IV 1862.]

4,4'-Dithiodimorpholine (S,S′-di-*N,N′*-dimorpholine, dimorpholine-*N,N′*-disulfide) *[103-34-4]* **M 236.2, m 124-125°.** Crystallise it from hot aqueous dimethylformamide or EtOH. It is a fungicide. [Blake *J Am Chem Soc* **65** 1267 *1943*.]

1-Dodecylpyridinium chloride *[104-74-5]* **M 301.9, m 68-70°.** Purify the chloride by repeated crystallisation from acetone (charcoal); then recrystallise it twice from EtOH [Chu & Thomas *J Am Chem Soc* **108** 6270 *1986*]. It is *hygroscopic* and should be stored with a desiccant. [*Beilstein* **20** III/IV 2314.]

Ellipticine (5,11-dimethylpyrido[4,3:*b*]carbazole) *[519-23-3]* **M 246.3, m 311-315°(dec), 312-314°(dec), pK^{25} 5.78 (80% aqueous methoxyethanol).** This DNA intercalator is purified by recrystallisation from $CHCl_3$ or MeOH and is dried *in vacuo*. The UV has λ_{max} values in aqueous EtOH/HCl at 241, 249, 307, 335 and 426nm. [Marini-Bettolo & Schmutz *Helv Chim Acta* **42** 2146 *1959*.] The *methiodide* has **m** 360°(dec), with UV λ_{max} (EtOH/KOH) at 223, 242, 251, 311, 362 and 432nm. [Goodwin et al. *J Am Chem Soc* **81** 1903 *1959*, *Beilstein* **23/9** V 417.]

Elymoclavine (8,9-didehydro-6-methylergoline-8-methanol) *[548-43-6]* **M 254.3, m 249-253°(dec), 250-252°(dec), $[\alpha]_D^{20}$-109° (c 0.4, EtOH).** It crystallises from MeOH, $CHCl_3$, Et_2O, Me_2CO or $*C_6H_6$. [*Beilstein* **23** III/IV 2716.]

Emetine hydrochloride hydrate *[316-42-7]* **M 553.6 + aq, m 235-240°, 235-250°, 240-250°, 248-250° (depending on H_2O content), $[\alpha]_D^{20}$ -49.2° (free base, c 4, $CHCl_3$), +18° (c 6, H_2O, dry salt), pK_1 5.77, pK_2 6.64.** It crystallises from MeOH/Et_2O, MeOH or Et_2O/EtOAc. The *free base* has **m** 104-105°, and the *(-)-phenylthiourea* derivative has **m** 220-221° (from EtOAc/petroleum ether, $[\alpha]_D^{25}$ - 29.3° ($CHCl_3$)). Its IR has ν_{max} at 3413 (OH) and 2611 (NH^+) cm^{-1}; and UV λ_{max} at 230nm (ε 16 200) and 282nm (ε 6 890) [Brossi et al. *Helv Chim Acta* **42** 1515 *1959*, Barash et al. *J Chem Soc* 3530 *1959*]. [*Beilstein* **23** III/IV 3419.]

Ergocornine *[564-36-3]* **M 561.7, m 182-184°, $[\alpha]_D^{20}$ -176° (c 0.5, $CHCl_3$).** It crystallises with solvent of crystallisation from MeOH. [Stadler et al. *Helv Chim Acta* **52** 1549 *1969*, *Beilstein* **25** III/IV 963, **27** II 860.]

Ergocristine *[511-08-0]* **M 573.7, m 165-170°, $[\alpha]_D^{20}$ -183° (c 0.5, $CHCl_3$).** It crystallises with 2 molecules of solvent of crystallisation from *benzene. [Stadler et al. *Helv Chim Acta* **52** 1549 *1969*, *Beilstein* **25** III/IV 966, **27** II 860.]

Ergocryptine *[511-09-1]* **M 575.7, m 212-214°, $[\alpha]_D^{20}$ -180° (c 0.5, $CHCl_3$).** It crystallises with solvent of crystallisation, from acetone, *benzene or methanol. [Stadler et al. *Helv Chim Acta* **52** 1549 *1969*, *Beilstein* **25** III/IV 964, **27** II 860.]

Ergotamine *[113-15-5]* **M 581.6, m 212-214°(dec), $[\alpha]_D^{20}$ -160° (c 0.5, $CHCl_3$), pK^{25} 6.40.** Crystallise it from *benzene, then dry it by prolonged heating in high vacuum. It is very *hygroscopic*. [*Beilstein* **25** III/IV 964.]

Ergotamine tartrate *[379-79-3]* **M 657.1, m 203°(dec).** It crystallises from MeOH. [*Beilstein* **25** III/IV 964.]

Ergotaminine *[639-81-6]* **M 581.7, m 241-243°, $[\alpha]_D^{20}$ +369° (c 0.5, $CHCl_3$).** It forms rhombic plates from MeOH which retain solvent unlike its isomer ergotamine (previous entry). It is less soluble than ergotamine, and its solubility is 0.1% in boiling ethanol and 0.07% in methanol. [Stoll *Helv Chim Acta* **28** 1299 and 1306 *1945*, *Beilstein* **25** II 860, 862, **25** III/IV 966.]

D-Erythronic acid (3*R*-3,4-dihydroxyfuran-2-one) *[15667-21-7]* **M 118.1, m 98-100°, 103-104°, 104-105°, 105°, $[\alpha]_D^{20}$ -73.2° (c 0.5, H_2O), $[\alpha]_{546}^{20}$ -87.6° (c 4, H_2O).** Recrystallise it from EtOAc (20 parts) or isoPrOH (3 parts). [Baker & MacDonald *J Am Chem Soc* **82** 230 *1960*, Glattfeld & Forbrich *J Am Chem Soc* **56** 1209 *1934*, Weidenhagen & Wegner *Chem Ber* **72** 2010 *1939*, Musich & Rapoport *J Am Chem Soc* **100** 4865 *1978*, *Beilstein* **18/2** V 457.]

Esculetin (cichorigenin, 6,7-dihydroxycoumarin) *[305-01-1]* **M 178.2, m 272-275° (dec), 274° (dec), pK^{25} 8.60 (70% aqueous EtOH), $pK_{Est(1)}$ ~8.7, $pK_{Est(2)}$ ~12.4.** It forms prisms from AcOH, aqueous EtOH or aqueous MeOH, and provides leaflets on sublimation in a vacuum. [Kagan *J Am Chem Soc* **88** 2617 *1966*, Marby et al. *Phytochemistry* **4** 492 *1965*.] *Esculin (the 6-glucoside)* has **m** 215°(dec), $[\alpha]_D^{20}$ -41° (c 5, pyridine). [*Beilstein* **18** III/IV 1322, **18/3** V 202.]

Eserine (Physostigmine, Physostol, [(3aS-*cis*)-1,2,3,3a,8,8a-hexahydro-1,3a,8-trimethyl-pyrrolo[2,3-b]indol-5-ol methylcarbamate ester] *[57-47-6]* **M 275.4, m 102-104°, 105-106°, $[\alpha]_D^{17}$ -67° (c 1.3, $CHCl_3$), $[\alpha]_D^{25}$ -120° (*C_6H_6), pK_1^{25} 1.96, pK_2^{25} 8.08.** Eserine crystallises from Et_2O or *C_6H_6 and forms an unstable low melting form **m** 86-87° [Harley-Mason & Jackson *J Chem Soc* 3651 *1954*, Wijnberg & Speckamp *Tetrahedron* **34** 2399 *1978*]. [*Beilstein* **23/11** V 401.]

2-Ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (EEDQ) *[16357-59-8]* **M 247.3, m 63.5-65°, 66-67°.** Dissolve EEDQ (~180g) in $CHCl_3$, evaporate to dryness in a vacuum. Add dry Et_2O (20ml) and a white solid separates on standing. Set aside for a few hours, collect the solid, wash it thoroughly with cold Et_2O and dry it in a vacuum (~140g, **m** 63.5-65°). A further crop of solid (~25g) is obtained from the filtrate on standing overnight. [Fieser & Fieser *Reagents for Organic Synthesis* **2** 191 *1969*, Belleau et al. *J Am Chem Soc* **90** 823 *1968* and **90** 1651 *1968*, *Beilstein* **21/3** V 28.]

Ethoxyquin (1,2-dihydro-6-ethoxy-2,2,4-trimethylquinoline) *[91-53-2]* **M 217.3, b 169°/12-13mm, d_4^{20} 1.000, pK_{Est} ~5.8.** Purify Ethoxyquin by fractional distillation *in vacuo* whereby the distillate solidifies to a glass. [Knoevenagel *Chem Ber* **54** 1723, 1730 *1921*.] The *methiodide* has **m** 179° (from EtOH), and the *1-phenylcarbamoyl* derivative has **m** 146-147° (from EtOH). [Beaver et al. *J Am Chem Soc* **79** 1236 *1957*, *Beilstein* **21** III/IV 95.]

2-Ethyl-1,2-benzisoxazolium tetrafluoroborate *[4611-62-5]* **M 235.0, m 107-109°, 109.5-110.2°.** Recrystallise it from MeCN/EtOAc to give magnificent crystals. It is not hygroscopic but on long exposure to moisture it etches glass. It is light-sensitive and should be stored in brown glass bottles and free from moisture. The UV (H_2O), has λ_{max} at 258nm (ε 13 100) and λ_{max} 297nm (ε 2 900); the IR (CH_2Cl_2) has ν_{max} at 1613 (C=N) and 1111-1000 (BF_4^+) [UV, IR, NMR: Kemp & Woodward *Tetrahedron* **21** 3019 *1965*].

***N*-Ethylcarbazole** *[86-28-2]* **M 195.3, m 69-70°, 69-71°, b 199-200°/15mm.** Recrystallise it from MeOH, EtOH, EtOH/water or isopropanol and dry it below 55°. [*Beilstein* **20** H 436, **20** II 282, **20** III/IV 3829.]

Ethyl 1,3-dithiane-2-carboxylate *[20462-00-4]* **M 192.3, b 75-77°/0.2mm, 96°/0.4mm, d_4^{20} 1.220, n_D^{25} 1.5379.** Dissolve the ester in $CHCl_3$, wash with aqueous K_2CO_3, twice with H_2O, dry over $MgSO_4$, filter,

evaporate and distil the residue. [Eliel & Hartman *J Org Chem* **37** 505 *1972*, Seebach *Synthesis* **1** 17 *1969*, *Beilstein* **19/7** V 227.]

Ethyl 1,3-dithiolane-2-carboxylate *[20461-99-8]* **M 178.3, b 85°/0.1mm, d_4^{20} 1.250, n_D^{20} 1.538.** Dissolve the ester in $CHCl_3$, wash it with aqueous K_2CO_3, twice with H_2O, dry it over $MgSO_4$, filter, evaporate and distil the residue *in vacuo*. [Hermann et al *Tetrahedron Lett* 2599 *1973*, Corey & Erickson *J Org Chem* **36** 3553 *1971*]. [*Beilstein* **19/7** V 225.]

Ethylene oxide (oxirane) *[75-21-8]* **M 44.0, b 13.5°/746mm, d_4^{10} 0.882, n_D^{7} 1.3597.** Dry oxirane with $CaSO_4$, then distil it from crushed NaOH. It has also been purified by passage, as a gas, through towers containing solid NaOH. [*Beilstein* **17/1** V 3.]

Ethylene thiourea (2-imidazolidinethione) *[96-45-7]* **M 102.2, m 203-204°.** Crystallise it from EtOH or amyl alcohol. [*Beilstein* **24** III/IV 22.]

Ethylene urea (2-imidazolidone) *[120-93-4]* **M 86.1, m 131°.** Crystallise it from MeOH (charcoal). [*Beilstein* **24** III/IV 6.]

(±)-2-Ethylethylenimine (2-ethylaziridine) *[2549-67-9]* **M 71.1, b 88.5-89°, pK^{25} 8.31 (K_b 5.70x10^{-7}).** Freshly distil the aziridine from sodium before use. The *picrate* has **m** 103-104°. **TOXIC.** [O'Rourke et al. *J Am Chem Soc* **78** 2159 *1956*, *Beilstein* **20** III/IV 280.]

Ethyl hydrocupreine hydrochloride (Optochin) *[3413-58-9]* **M 376.9, m 249-251°, pK_1^{25} 5.50, pK_2^{25} 9.95.** Recrystallise it from H_2O [UV: Heidt & Forbes *J Am Chem Soc* **55** 2701 *1933*]. [*Beilstein* **24** H 385, **24** III/IV 1446.]

2-Ethyl-isothionicotinamide (ethionamide, 3-ethyl 4-pyrdinecarbothioamide) *[536-33-4]* **M 166.2, m 163-164°, 164-166°(dec).** It crystallises from EtOH as lemon yellow needles. The *hydrochloride* crystallises from EtOH (+ few drops of HCl) as orange yellow needles with **m** 212-214°. [Kutscherowa et al. *J Gen Chem USSR* (English transl) **29** 915 *1959*, *Beilstein* **22** III/IV 737.] It causes peripheral and occular **neuropathy** and is **carcinogenic** and **teratogenic**.

(±)-3-Ethyl-5-phenylhydantoin (Ethotoin) *[86-35-1]* **M 204.2, m 94°.** Crystallise it from water. It is an anticonvulsant and is used in epilepsy. [Dudley et al. *J Heterocycl Chem* **10** 173 *1973*, Pinner *Chem Ber* **21** 2320 *1888*, *Beilstein* **25** III/IV 963, **27** II 860.]

***N*-Ethyl-5-phenylisoxazolinium-3'-sulfonate (Woodward's reagent K)** *[4156-16-5]* **M 253.3, m 220°(dec).** Crystallise the reagent from diethyl ether or ethyl acetate/petroleum ether. [Lamas et al. *J Am Chem Soc* **108** 5543 *1986*.] It is best purified by dissolving in excess of aqueous N HCl and precipitating with Me_2CO to give a white fluffy solid. [Woodward et al. *Tetrahedron* **22** *Suppl* **8** 321 *1966*, Fieser & Fieser *Reagents for Organic Synthesis* **1** 385, **2** 198.]

(±)-3-Ethyl-3-phenyl-2,6-piperidinedione (Glutethimide) *[77-21-4]* **M 217.3, m 84°.** Crystallise glutethimide from diethyl ether or ethyl acetate/petroleum ether. It has **m** 91-92° (from aqueous EtOH), 87-87.5° (from Et_2O/petroleum ether), 84-87° (from isopropanol), and 83-84° (from Et_2O). [Penprase & Biles *J Am Pharm Assoc* **47** 523 *1958*, Hofmann et al. *Helv Chim Acta* **40** 387, 393 *1957*, *Beilstein* **21** III/IV 5493.] The *R(+)-enantomer* crystallises from EtOAc/petroleum ether with **m** 103-104°, and $[\alpha]_D^{20}$+184° (c 1, EtOH). [Branchini *Ricerche Scientifiche* **29** 2435 *1959*, Finch et al. *Experientia* **31** 1002 *1975*.]

2-Ethylpyridine *[100-71-0]* **M 107.2, b 148.6°, d_4^{25} 0.942, pK^{25} 5.89.** Dry 2-ethylpyridine with BaO, and fractionally distil it. Purify it further by conversion to the *picrate*, recrystallisation of the picrate and regeneration of the free base followed by distillation. [*Beilstein* **20/6** V 3.]

4-Ethylpyridine *[536-75-4]* **M 107.2, b 168.2-168.3°, d_4^{25} 0.942, pK^{25} 6.02.** Dry 4-ethylpyridine with BaO, and fractionally distil it. Also purified by converting to the *picrate*, recrystalising and the free base is regenerated and distilled. [*Beilstein* **20/6** V 10.]

4-Ethylpyridine-1-oxide *[14906-55-9]* **M 123.1, m 109-110°, pK_{Est}~1.1.** Crystallise the oxide from acetone/ether. [*Beilstein* **20/6** V 10.]

Etioporphyrin I See aetioporphyrin I above.

Flavone (2-phenyl-4*H*-1-benzopyran-4-one) *[525-82-6]* **M 222.3, m 100°.** Crystallise flavone from petroleum ether. [*Beilstein* **17/10** V 552.]

Fluorescein [9-(*o*-carboxyphenyl-6-hydroxy-3*H*-xanthene-3-one] *[2321-07-5]* **M 320.0, ε_{495nm} 7.84 x 10^4 (in 10^{-3}M NaOH), pK_1 2.2, pK_2 4.4, pK_3 6.7.** Dissolve it in dilute aqueous NaOH, filter and precipitate it by adding dilute (1:1) HCl. The process is repeated twice more, and the fluorescein is dried at 100°. *Alternatively*, it has been crystallised from acetone by allowing the solution to evaporate at 37° in an open beaker. It has also been recrystallised from EtOH and dried in a vacuum oven. [*Beilstein* **19** I 721, **19** II 248, **19** III/IV 2904, **19/8** V 456.]

Fluoresceinamine (mixture of 5- and 6-aminofluorescein) *[27599-63-9]* **M 347.3, m 215-220°(dec, 5-amino) and m 314-316°(dec, 6-amino).** Dissolve it in EtOH, treat with charcoal, filter, evaporate and dry the residue in a vacuum at 100° overnight. Also recrystallise it from 6% HCl, then dissolve it in 0.5% aqueous NaOH and precipitate it by acidifying with acetic acid. The separate amines are made from the respective nitro compounds, which are best separated *via* their acetate salts. They have similar R_F of 0.26 on Silica Gel Merck F_{254} in 5 ml MeOH + 150 ml Et_2O saturated with H_2O. The IR (Me_2SO) has a band at ν_{max} 1690 cm^{-1} (CO_2^-) and sometimes a weak band at ν_{max} 1750 cm^{-1} due to the lactone. The UV (EtOH) of the 6-isomer has λ_{max} at 222nm (ε 60,000) and the 5-isomer at λ_{max} 222nm (ε 60,000) and 285nm (ε 20,600). [IR: McKinney & Churchill *J Chem Soc (C)* 654 *1970*, McKinney et al. *J Org Chem* **27** 3986 *1962*, UV: Verbiscar *J Org Chem* **29** 490 *1964*, *Beilstein* **19** III/IV 4337, **19/8** V 713.]

Fluorescein isothiocyanate isomer I (5-isothiocyanato isomer) *[3326-32-7*; *27072-45-3 **mixture of 5- and 6-isomers**]* **M 389.4, m >160°(slow dec).** It is made from the pure 5-amino isomer. Purify it by dissolving it in boiling Me_2CO, filtering and adding petroleum ether (b 60-70°) until it becomes turbid. If an oil separates, then decant it and add more petroleum ether to the supernatant and cool. Orange-yellow crystals separate, collect and dry them *in vacuo*. It should give one spot on TLC (silica gel) in EtOAc/pyridine/AcOH (50:1:1) and in $Me_2NCHO/CHCl_3$/28% NH_4OH (10:5:4). Its IR (Me_2SO) has ν_{max} at 2110 (NCS) and 1760 (C=O) cm^{-1}. The ^{1}HNMR spectra in Me_2CO-d_6 of the 5- and 6-isomers are distinctly different for the protons in the *benzene ring; the UV in phosphate buffer pH 8.0 shows a λ_{max} at ~490nm. [Sinsheimer et al. *Anal Biochem* **57** 227 *1974*, McKinney et al. *Anal Biochem* **7** 74 *1964*, *Beilstein* **19** III/IV 4337.]

3-Fluoro-4-iodopyridine *[22282-75-3]* **M 223.0, m 80-81°, 85-89°, pK_{Est} ~1.7.** Crystallise it from petroleum ether and/or sublime it *in vacuo* (**m** 87°). The *picrate* [22282-76-4] has **m** 140° (from EtOH). [Gribble & Saulnier *Tetrahedron Lett* 4137 *1980*.]

4-Fluoro-7-nitrobenzofurazan (4-fluoro-7-nitrobenzo-2-oxa-1,3-diazole) *[29270-56-2]* **M 183.1, m 52.5-53.5°, 53-56°, 53.5-54.5°.** Purify it by repeated recrystallisation from petroleum ether (b 40-60°). On treatment with MeONa in MeOH it gives *4-methoxy-7-nitrobenzo-2-oxa-1,3-diazole* **m** 115-116°. [Nunno et al. *J Chem Soc (C)* 1433 *1970*.] It is a very good fluorophore for amino acids [Imai & Watanabe *Analyt Chim Acta* **130** 377 *1981*], as it reacts with primary and secondary amines to form fluorescent adducts with λ_{ex} 470nm and λ_{em} 530nm. It gives a *glycine* derivative with **m** 185-187° [Miyano et al. *Anal Chim Acta* **170** 81 *1985*].

5-Fluorouracil (5-fluoropyrimidinedi-2,4-[1*H*,3*H*]-one, 5-FU) *[51-21-8]* **M 130.1, m 282-283° (dec),**

282-286°(dec), pK_1^{25} 8.04, pK_2^{25} 13.0. Recrystallise it from H_2O or MeOH/Et_2O and sublime it at 190-200°/0.1mm or 210-230°/0.5mm. UV: λ_{max} at 265-266nm (ε 7070). [Barton et al. *J Org Chem* **37** 329 *1972*, Duschinsky & Pleven *J Am Chem Soc* **79** 4559 *1957*, *Beilstein* **24** III/IV 1229.]

Fluram (Fluorescamine, 4-phenyl-spiro[furan-2(3*H*)-1-phthalan]-3,3'-dione) *[38183-12-9]* **M 278.3, m 153-155°, 154-155°.** Fluram is a non-fluorescent reagent that reacts with primary amines to form highly fluorescent compounds. Purify it by dissolving (~1g) in Et_2O/*C_6H_6 (1:1, 180 ml), washing with 1% aqueous $NaHCO_3$ (50ml), drying (Na_2SO_4), and evaporating in a vacuum. Dissolve the residue in warm CH_2Cl_2 (5ml), dilute with Et_2O (12ml) and refrigerate. Collect the solid and dry it in a vacuum. Its IR ($CHCl_3$) has ν_{max} at 1810, 1745, 1722, 1625 and 1600 cm^{-1}, and ^{1}HNMR ($CDCl_3$) with δ at 8.71 (s, -O**H**C=). [Weigele et al. *J Am Chem Soc* **94** 5927 *1972*, Weigele et al. *J Org Chem* **41** 388 *1976*, Lai *Methods Enzymol* **47** 236 *1977*.]

Forskolin (Colforsin, Coleonol, 5-[acetyloxy]-3-ethenyldodecahydro-6,10,10b-trihydroxy-3,4a,7,7, 10a-penta-methyl-[3*R*-{3α-4aβ, 5β, 6β, 6aα, 10α, 10 aβ, 10bα}-1*H*-naphtho[2,1-b]pyran-1-one) *[66575-29-9]* **M 410.5, m 230-232°, 228-233°, $[\alpha]_D^{25}$ -96.2° (c 1.7, $CHCl_3$).** Recrystallise it from *C_6H_6/petroleum ether, EtOAc/petroleum ether. It is an antihypertensive, a positive ionotropic, a platelet aggregation inhibitor, and it has adenylate cyclase activating properties [*Chem Abstr* **89** 244150 *1978*, de Souza et al. *Med Res Rev* **3** 201 *1983*, X-ray: Tandon et al. *Indian J Chem* **15B** 880 *1977*]. [*Beilstein* **18/5** V 55.]

Fumagillin {2,4,6,8-decatetraene-1,10-dioic acid mono[4-(1,2-epoxy-1,5-dimethyl-4-hexenyl)-5-methoxy-1-oxaspiro[2.5]oct-6-yl] ester} *[23110-15-8]* **M 458.5, m 194-195°, $[\alpha]_D^{20}$ -26.2° (in 95% EtOH), pK_{Est} ~4.5.** Forty grams of a commercial sample containing 42% fumagillin, 45% sucrose, 10% antifoam agent and 3% of other impurities are digested with 150ml of $CHCl_3$. The insoluble sucrose is filtered off and washed with $CHCl_3$. The combined $CHCl_3$ extracts are evaporated almost to dryness at room temperature under reduced pressure. The residue is triturated with 20ml of MeOH, and the fumagillin is filtered off by suction. It is crystallised twice from 500ml of hot MeOH by standing overnight in a refrigerator (yellow needles). (The long-chain fatty ester used as antifoam agent is still present, but is then removed by repeated digestion, on a steam bath, with 100ml of diethyl ether.) For further purification, the fumagillin (10g) is dissolved in 150ml of 0.2M ammonia, and the insoluble residue is filtered off. The ammonia solution (cooled in running cold water) is then brought to pH 4 by careful addition of M HCl with constant shaking in the presence of 150ml of $CHCl_3$. (Fumagillin is acid-labile and must be removed rapidly from the aqueous acid solution.) The $CHCl_3$ extract is washed several times with distilled water, dried (Na_2SO_4) and evaporated under reduced pressure. The solid residue is washed with 20ml of MeOH. The fumagillin is filtered off by suction, then crystallised from 200ml of hot MeOH. [Tarbell et al. *J Am Chem Soc* **77** 5610 *1955*.]
Alternatively, 10g of fumagillin in 100ml $CHCl_3$ is passed through a silica gel (5g) column to remove tarry material, and the $CHCl_3$ is evaporated to leave an oil which gives fumagillin on crystallisation from amyl acetate. It recrystallises from MeOH (charcoal) or Me_2CO/MeOH. The fumagillin is stored in dark bottles in the absence of oxygen and at low temperatures. [Schenk et al. *J Am Chem Soc* **77** 5606 *1955*, *Beilstein* **19** III/IV 1012.]

Furan *[110-00-9]* **M 68.1, b 31.3°, d_4^{20} 1.42, n_D^{20} 1.4214.** Shake it with aqueous 5% KOH, dry it with $CaSO_4$ or Na_2SO_4, then distil it under nitrogen, from KOH or sodium, immediately before use. A trace of hydroquinone could be added as an inhibitor of oxidation. [*Beilstein* **17** H 27, **17** I 16, **17** II 34, **17/1** V 291.]

Furan-2-carboxylic (2-furoic) acid *[88-14-2]* **M 112.1, m 133-134°, b 141-144°/20mm, 230-232°/760mm, pK_1^{25} -7.3 (O-protonation), pK_2^{25} 3.32.** Crystallise the acid from hot water (charcoal), dry it at 120° for 2 hours, then recrystallise it from $CHCl_3$, and again dry it at 120° for 2 hours. For use as a standard in volumetric analysis, good quality commercial acid should be crystallised from $CHCl_3$ and dried as above or sublimed at 130-140°/50-60mm or less. [*Beilstein* **18** I 438, **18** II 265, **18** III/IV 3914, **18/6** V 102.]

Furan-3-carboxylic (3-furoic) acid *[488-93-7]* **M 112.1, m 122-123°, 123°.5, pK^{25} 4.03.** Crystallise the acid from water or aqueous EtOH, and sublime it in a vacuum. [*Beilstein* **18** I 439, **18** III/IV 4052, **18/6** V 196.]

Furan-3,4-dicarboxylic acid *[3387-26-6]* **M 156.1, m 217-218°, 221.5-222.5°, pK_1^{25} 1.44, pK_2^{25} 7.84.**

Crystallise it from water or Et_2O/petroleum ether, and sublime it in a vacuum. [*Beilstein* **18** III/IV 4497.]

Furan-2,5-dione (maleic anhydride) *[108-31-6]* **M 98.1, m 54°, b 94-96°/20mm, 199°/760mm.** Crystallise it from *benzene, $CHCl_3$, CH_2Cl_2 or CCl_4. Sublime it under reduced pressure. [Skell et al. *J Am Chem Soc* **108** 6300 *1986*, *Beilstein* **17** III/IV 5897, **17/11** V 55.]

3-(2-Furanyl)acrylic acid *[539-47-9]* **M 138.1, (*cis*-isomer) m 106-108°, pK^{25} 3.5; (*trans*-isomer) m 141°, 143-144°, b 285°, pK^{25} 4.5 (H_2O), 5.76 (50% aqueous EtOH), 6.65 (ethoxyethanol/H_2O—80:20).** Crystallise the *cis*-isomer from *C_6H_6 and the *trans*-isomer from H_2O, *C_6H_6 or petroleum ether (b 80-100°)(charcoal). [*Beilstein* **18** H 301, **18** III/IV 4143, **18/6** V 306.]

Furfural (2-furfuraldehyde) *[98-01-1]* **M 96.1, b 54-56°/11mm, 59-60°/15mm, 67.8°/20mm, 90°/65mm, 161°/760mm, d_4^{20} 1.159, n_D^{20} 1.52608, pK^{25} -6.5 (O-protonation).** Furfural is unstable to air, light and acids. Impurities include formic acid, ß-formylacrylic acid and furan-2-carboxylic acid. Distil it in an oil bath from 7% (w/w) Na_2CO_3 (added to neutralise acids, especially pyromucic acid). Redistil it from 2% (w/w) Na_2CO_3, and then, finally fractionally distil it under vacuum. It is stored in the dark. [Evans & Aylesworth *Ind Eng Chem (Anal ed)* **18** 24 *1926*.]
Impurities resulting from storage can be removed by passage through chromatographic grade alumina. Furfural can be separated from impurities other than carbonyl compounds by the bisulfite addition compound. The aldehyde is steam volatile.
It has been purified by distillation (using a Claisen head) under reduced pressure. This is essential as is the use of an oil bath with temperatures of no higher than 130° which is highly recommended. When furfural is distilled at atmospheric pressure (in a stream of N_2), or under reduced pressure with a free flame (caution: because the aldehyde is flammable), an almost colourless oil is obtained. After a few days and sometimes a few hours, the oil gradually darkens and finally becomes black. This change is accelerated by light and occurs more slowly when it is kept in a brown bottle. However, when the aldehyde is distilled under vacuum and the bath temperature kept below 130° during the distillation, the oil develops only a slight colour when exposed to direct sunlight during several days. The distillation of very impure material should NOT be attempted at atmospheric pressure; otherwise the product darkens very rapidly. After one distillation under vacuum, a distillation at atmospheric pressure can be carried out without too much decomposition and darkening. The liquid **irritates mucous membranes.** Store it in dark containers under N_2, preferably in sealed ampoules. [Adams & Voorhees *Org Synth* Coll Vol **I** 280 *1941*, *Beilstein* **17/9** V 292.]

Furfuryl alcohol (2-furylmethanol) *[98-00-0]* **M 98.1, b 68-69°/20mm, 170.0°/750mm, d_4^{20} 1.132, n_D^{20} 1.4873, n_D^{30} 1.4801, pK^{25} 2.61.** Distil it under reduced pressure to remove tarry material, shake with aqueous $NaHCO_3$, dry it with Na_2SO_4 and fractionally distil it under reduced pressure from Na_2CO_3. It can be further dried by shaking with Linde 5A molecular sieves. [*Beilstein* **17/3** V 338.]

Furfurylamine (2-aminomethylfuran) *[617-89-0]* **M 97.1, b 54-56°/17mm, 142.5-143°/735mm, d_4^{20} 1.059, n_D^{20} 1.489, pK^{30} 8.89.** Distil it under nitrogen from KOH through a column packed with glass helices, preferably under vacuum. The *picrate* has **m** 184-184°(dec), the *hydrochloride* has **m** 147-149°, and the *oxalate* has **m** 145-147°. [*Beilstein* **18** H 584, **18** II 416, **18** III/IV 3068, **18/9** V 541.]

6-Furfurylaminopurine (Kinetin) *[525-79-1]* **M 215.2, m 266-267°, 269-271°, 270-272°, 272° (sealed capillary), pK_1 <1, pK_2 3.8, pK_3 10.** It forms platelets from EtOH and sublimes at 220°, but is best done at lower temperatures in a good vacuum. It has been extracted from neutral aqueous solutions with Et_2O. [Miller et al *J Am Chem Soc* **78** 1375 *1956*, Bullock et al. *J Am Chem Soc* **78** 3693 *1956*, *Beilstein* **26** III/IV 3586.]

Furil *[492-94-4]* **M 190.2, m 165-166°.** Furil crystallises from MeOH or *benzene (charcoal). [*Beilstein* **19** III/IV 2008.]

(±)-Furoin [1,2-di-(2-furyl)-2-hydroxyethanone] *[552-86-3]* **M 192.2, m 135-136°, 138-139°, 158-162°/9mm.** It crystallises from MeOH (charcoal) and distils in a vacuum. [Hartman & Dickey *J Am Chem Soc* **55** 1228 *1933*.] The *(-)-enantiomer* crystallises from toluene or EtOH with **m** 131-131°, and $[\alpha]_D^{20}$ -4.9°

(dioxane) [Neuberg et al. *Arch Biochem* **1** 393 *1943*, *Beilstein* **19** H 204, **19** I 710, **19** II 224, **19** III/IV 2543.]

Fusaric acid (5-*n*-butylpyridine-2-carboxylic acid) *[536-69-6]* **M 179.2, m 96-98°, 98°, 98-100°, 101-103°, pK_1 5.7, pK_2 6.16 (80% aqueous methoxyethanol).** Dissolve it in $CHCl_3$, dry (Na_2SO_4), filter, evaporate and recrystallise the residue from 50 parts of petroleum ether (b 40-60°), $CHCl_3$/petroleum ether or EtOAc, then sublime it *in vacuo*. The *amide* crystallises from MeOH with **m** 128.2-129.0°. The *copper salt* forms bluish violet crystals from H_2O and has **m** 258-259°. [Hardegger & Nikles *Helv Chim Acta* **39** 505 *1956*, Schreiber & Adam *Chem Ber* **93** 1848 *1960*, NMR and MS: Tschesche & Führer *Chem Ber* **111** 3500 *1978*, *Beilstein* **22** III/IV 764, **22/2** V 384.]

Fuschin (Magenta I) See rosaniline hydrochloride in "Aromatic Compounds" [632-99-2] in this Chapter.

Glycidol (oxirane-2-methanol) *[RS-(±)- 556-52-5; R-(+)- 57044-25-4; S-(-)- 60456-23-7]* **M 74.1, (*R,S*) b 61-62°/15mm, d_4^{20} 1.117, n_D^{20} 1.433, [*S(-)-isomer,* § also available on polymer support, has b 49-50°/7mm, 66-67°/19mm, $[\alpha]_D^{20}$ -15°(neat)], [*R(+)-isomer* has b 56-56.5°/11mm, d_4^{20} 1.117, n_D^{20} 1.429, $[\alpha]_D^{20}$ +15° (neat)].** Purify glycidol by fractional distillation. The *4-nitrobenzoates* have **m** 56° (±); **m** 60-62°, $[\alpha]_D^{20}$ -37.9° (c 3.38 $CHCl_3$) for *R-(-)*-isomer *[106268-95-5]*; **m** 60-62°, $[\alpha]_D^{20}$ +38° (c 1 $CHCl_3$) for the *S-(+)*-isomer *[115459-65-9]* and are recrystallised from Et_2O or Et_2O/petroleum ether (b 40-60°) [*S-isomer*: Burgos et al. *J Org Chem* **52** 4973 *1987*, Sowden & Fischer *J Am Chem Soc* **64** 1291 *1942*.] [*Beilstein* **17** I 50, **17** III/IV 985, **17/3** V 9.]

Gramine (3-dimethylaminoethylindole) *[87-52-5]* **M 174.3, m 134°, pK^{25} 16.00 (NH acidic), basic pK^{25} 9.2 (50% aqueous EtOH).** Crystallise gramine from diethyl ether, ethanol or acetone. It sublimes at 59°/0.001mm. The *hydrochloride* crystallises from EtOH/Et_2O with **m** 190.5-191.0°(dec). [Culvenor et al. *Aust J Chem* **17** 1301 *1964*, *Beilstein* **22** III/IV 4302**, 22/10** V 25.]

(2*S*,6'*R*)(+)-Griseofulvin *[126-07-8]* **M 352.8, m 220°, $[\alpha]_D^{22}$ +365° (c 1, acetone).** Crystallise it from *benzene or EtOH. Purify 2g of griseofulvin by chromatography on Alumina (40 x 1.5cm) and elute with *C_6H_6/MeOH (199:1) and follow the UV blue fluorescent band. [MacMillan *J Chem Soc* 1823 *1959*, *Beilstein* **18** III/IV 3160, **18/5** V 150.]

Guanosine (H_2O) *[118-00-3]* **M 283.2, m 237-237.5°(dec), 239°(dec), $[\alpha]_{546}^{20}$ -86° (c 1, 0.1M NaOH), pK_1^{25} 1.9, pK_2^{25} 9.24, pK_3^{25} 12.33.** It crystallises from water as a *dihydrate*. Dry it at 110°. [*Beilstein* **26/18** V 81.]

Guanylic acid (guanosine-5'-monophosphoric acid) *[85-32-5]* **M 363.2, m 208°(dec), pK_2^{25} 2.4, pK_3^{25} 6.66 (6.1), pK_4^{25} 9.4.** Crystallise it from water and dry it at 110°. [*Beilstein* **26** III/IV 3910.]

Harmaline (7-methoxy-1-methyl-4,9-dihydro-3*H*-β-carboline, 4,9-dihydro-7-methoxy-1-methyl-3*H*-pyrido[3,4-*b*]indole) *[304-21-2]* **M 214.3, m 229-230°, 229-231°, 235-237° (after distillation at 120-140°/10^{-3}), pK_1 4.2.** Recrystallise harmaline from MeOH and sublime it at high vacuum. It has UV in MeOH with λ_{max} at 218, 260 and 376nm (log ε 4.27, 3.90 and 4.02, respectively); IR (Nujol) with ν_{max} at 1620, 1600, 1570 and 1535cm^{-1} and in $CHCl_3$ ν_{max} at 1470 and 1629cm^{-1}. [Spenser *Can J Chem* **37** 1851 *1959*, Marion et al. *J Am Chem Soc* **73** 305 *1951*, UV Prukner & Witkop *Justus Liebigs Ann Chem* **554** 127 *1942*.] The *hydrochloride dihydrate* has **m** 234-236°(dec), the *picrate* has **m** 228-229° (sinters at 215°) from aqueous EtOH, and the *N-acetate* forms needles **m** 204-205°. [*Beilstein* **23** H 396, **23** I 119, **23** II 345, **23** III/IV 2666, **23/12** V 148.]

Harmane (2-methyl-β-carboline, 1-methyl-9*H*-pyrido[3,4-*b*]indole, Aribine) *[486-84-0]* **M 182.2**, **m 235-238°, 237-238°, pK_1 7.37 (basic, Pry N), pK_2 14.7 (acidic, NH).** Crystallise it from heptane/cyclohexane. It is insoluble in H_2O, but soluble in dilute HCl or H_2SO_4. Solutions show a blue fluorescence. Its UV (MeOH) has λ_{max} nm (log ε) at 234 (4.57), 287 (4.21) and 347 (3.66). The *hydrochloride* forms needles from EtOH/dil HCl which sublimes at **m** 120-130°. It is an imidazoline binding site agonist. [Wolfbeis *Monatsh Chem* **113** 509 *1982*, *Beilstein* **23/12** 237.]

Harmine (7-methoxy-1-methyl-9*H*-pyrido[3,4-*b*]indole) *[442-51-3]* **M 212.3, m 261°(dec), 265°, pK^{20} 7.61.** Crystallise harmine from MeOH and sublime it in a vacuum. Its UV (MeOH) has λ_{max} nm (log ε) at 241 (4.61), 301 (4.21) and 336 (3.69). It is a CNS stimulant. See *hydrochloride* below. [*Beilstein* **23** II 348, **23** III/IV 2702, **23/12** V 237.]

Harmine hydrochloride (hydrate) *[343-27-1]* **M 248.7, m 262°(dec, hydrate), 280°(dec).** The *hydrate* crystallises as fluorescent crystals from water. Freely soluble in hot water, but only 2.5% in cold water. The *anhydrous* salt has **m** 319°. [*Beilstein* **23/12** V 237.]

Hesperetin (3',5,7-trihydroxy-4'-methoxyflavanone) *[520-33-2]* **M 302.3, (*R*,S) m 227-228°, pK$_{Est}$ ~8.5-10.5 (phenolic).** Crystallise it from EtOAc or ethanol. The natural *S*(-) form crystallises from EtOH and has **m** 216-218° and $[\alpha]_D^{20}$ -37.6° (c 2, EtOH). Note that C2 is chiral. [*Beilstein* **18** II 204, **18** III/IV 3215, **18/5** V 214.]

Hesperidin (hesperetin 7-rhamnoside) *[520-26-3]* **M 610.6, m 258-262°, 261-263°(dec), $[\alpha]_{546}^{20}$ -82° (c 2, pyridine).** Dissolve hesperidine in dilute aqueous alkali and precipitate it by adjusting the pH to 6-7. [*Beilstein* **18** III/IV 3219, **18/5** V 218.]

Hexahydro-1*H*-azepine (hexamethyleneimine, Azepane) *[111-49-9]* **M 99.2, b 70-72°/30mm, 135-138°/atm, d $_4^{20}$ 0.879, n $_D^{20}$ 1.466, pK^{25} 11.10 (pK^0 9.71, pK^{75} 9.71).** Purify azepane by dissolving in Et_2O and adding ethanolic HCl until all the base separates as the white *hydrochloride*, filter, wash with Et_2O and dry it (**m** 236°). The salt is dissolved in the minimum volume of H_2O and basified to pH ~14 with 10N KOH. The solution is extracted with Et_2O, the extract is dried over KOH, evaporated and distilled. The free base is a **FLAMMABLE** and **TOXIC** liquid, and best kept as the salt. The *nitrate* has **m** 120-123°, the *picrate* has **m** 145-147°, and the *tosylate* has **m** 76.5° (ligroin). [Müller & Sauerwald *Monatsh Chem* **48** 727 *1027*, Hjelt & Agback *Acta Chem Scand* **18** 194 *1964*, *Beilstein* **20** II 1406, **20** III/IV 1406, **20/4** V 3.]

Hexamethylenetetramine (Urotropine, hexamine, HMTA) *[100-97-0]* **M 140.1, m 280° (subln), 290-292° (sealed tube, CARE), d $_4^{20}$ 1.331, pK^{25} 4.85 (6.30).** It is soluble in H_2O (67%), $CHCl_3$ (10%), EtOH (8%) and Et_2O (0.3%), and a 0.2M solution has a pH of 8.4. Dissolve it in hot absolute EtOH (reflux, Norit), filter using a heated funnel, cool at room temperature first, then in ice. Wash the crystals with cold Et_2O, dry them in air or under a vacuum. A further crop can be obtained by adding Et_2O to the filtrate. It sublimes above 260° without melting. The *picrate* has **m** 179°(dec). [pK^{20} 4.85: Reilley & Schmid *Anal Chem* **30** 947 *1958*, pK^{20} 6.30: Pummerer & Hofmann *Chem Ber* **56** 1255 *1923*.] [*Beilstein* **26** I 306, **26** II 200, **26** III/IV 1680.]

***R*-(+)-2-Hexyloxirane [*R*-(+)-1,2-epoxyoctane, *R*-(+)-octene oxide)** *[77495-66-0]* **M 128.2, b 51-54°/10mm, 60-62°/15mm, 157°/atm, d $_4^{25}$ 0.839, n $_D^{20}$ 1.418, $[\alpha]_D^{20}$ +14° (neat), the *S*-(-)- enantiomer has** *[50418-68-3]* **$[\alpha]_D^{20}$ -14.5° (c 2.5, EtOH), n $_D^{20}$ 1.412.** The enantiomeric oxiranes have been purified by passage through a silica gel column in pentane and eluted with pentane/Et_2O. The eluate is evaporated and subjected to bulb-to-bulb distillation in a vacuum. The enantiomeric purity is checked by HPLC. [White & Emmons *Tetrahedron* **17** 31 *1962*, Johnson & Rogers *J Org Chem* **38** 1793 *1973*, *Beilstein* **17** H 17, **17** I 11, **17** III/IV 111, **17/1** V 138.]

Histamine *[51-45-6]* **M 111.2, m 86° (sealed tube), b 167°/0.8mm, 209°/18mm, pK $_1^{25}$ 6.02, pK $_2^{25}$ 9.70.** It crystallises from *benzene or chloroform. [*Beilstein* **25** I 628, **25** II 302, **25** III/IV 2049.]

Histamine dihydrochloride *[56-92-8]* **M 184.1, m 249-252° (244-245°).** The dihydrochloride crystallises from aqueous EtOH. The *phosphate ($2H_3PO_4$)* [51-74-1] has **m** 132-133° (from H_2O). [*Beilstein* **25** III/IV 2049.]

Homopiperazine (1,4-diazepane) *[505-66-8]* **M 100.2, m 38-40°, 43°, b 60°/10mm, 92°/50mm, 169°/atm, pK_1^{20} 6.70, pK_2^{20} 10.41.** Purify it by fractionation through a column of 10 theoretical plates with a reflux ratio of 3:1. It boils at 169°, and the cool distillate crystallises in plates **m** 43°. [Poppelsdorf and Myerly *J Org Chem* **26** 131 *1961*.] Its pKa values are 6.67 and 10.09 at 29.7°, and 6.28 and 9.86 at 40° [Pagano et al. *J Phys Chem* **65** 1062 *1961*]. The *1,4-bis(4-bromobenzoyl)* derivative has **m** 194-198° (from EtOH); the *hydrochloride* has **m** 270-290° (from EtOH) and the *picrate* has **m** 265°(dec) [Lloyd et al. *J Chem Soc (C)* 780 *1966*]. [*Beilstein* **23** III/IV 388, **23/3** V 240.]

1-Hydrazinophthalazine (hydralazine) *[86-54-4]* **M 160.1, m 172-173°(dec), pK_1^{25} 2.90, pK_2^{25} 7.25 (NNH_2).** It crystallises from MeOH. Its UV has λ_{max} at 656nm at pH ~11. It complexes with Bi^{3+}, Zn^{2+}, Fe^{2+} and Co^{2+}. The *hydrochloride (hydralazine hydrochloride) [304-20-1]* **M 196.6,** also crystallises from MeOH and has **m** 172-173°(dec)**.** [Druey et al. *Helv Chim Acta* **34** 195 *1951*, *Beilstein* **25** III/IV 4552.] It is an **antihypertensive**.

2-Hydrazinopyridine *[4930-98-7]* **M 109.1, m 41-44°, 46-47°, 49-50°, b 105°/0.5mm, 128-135°/13mm.** Purify it by distillation under a vacuum and by recrystallisation from Et_2O/hexane. [Kauffmann et al. *Justus Liebigs Ann Chem* **656** 103 *1962*, Potts & Burton *J Org Chem* **31** 251 *1966*.] The *mono-hydrochloride* has **m** 183°(dec) from aqueous HCl, and the *di-hydrochloride* has **m** 214-215°. [*Beilstein* **22** II 487, **22** III/IV 7025, **22/14** V 486.]

4-Hydroxyacridine (4-acridinol, neo-oxine) *[18123-20-1]* **M 195.2, m 116.5°, 122-123°, pK_1^{15} 5.28, pK_2^{15} 9.75.** Crystallise neo-oxine from EtOH or aqueous EtOH. It complexes with Zn^{2+}, Cd^{2+}, Ga^{2+}, Pb^{2+}, Cr^{2+}, Mn^{2+}, Fe^{2+}, Co^{2+} and Ni^{2+}. The *hydrochloride* crystallises from EtOH with **m** 242°. [*Beilstein* **21** II 78, **21** III/IV 1562, **21/4** V 90.]

1-Hydroxy-1,2-benziodoxol-3(1*H*)-one (IBX, 2-iodoxybenzoic acid) *[61717-82-6]* **M 280.0, m 224-225°, 226-234°, 232-233°(dec), 233°(dec), pK <4.** IBX prepared by the Dess-Martin procedure ($KBrO_3/H_2SO_4$) [Dess & Martin *J Am Chem Soc* **113** 7277 *1991*] has been reported as being explosive and comparable to TNT [Hartman & Meyer *Chem Ber* **26** 1727 *1893*, Plumb & Harper *Chem Eng News* **(**July 16) 3 *1990*] when apparently the iodine content was below 43.5% (theoretical value is 45.32%). In an attempt to avoid this, IBX has been washed with H_2O and EtOH to render it non-explosive. Although deliberate attempts to detonate it on several occasions have been unsuccessful; operators should exercise CAUTION when working with IBX particularly with large scale preparations. This is among the substances for which it may be difficult to obtain permission to transport it, so detailed preparations are described here.

Dess-Martin method: To a vigorously stirred mixture of 2-iodobenzoic acid (85.2g, 340mmol, see [88-67-5]) and 0.73 M H_2SO_4 (730ml) in a bath at 55° is added $KBrO_3$ (76.0g, 450mmol) over 1 hour. The mixture is stirred further for 3.6 hours at 65°, cooled in an ice bath, and the solid is filtered off, washed with H_2O (1000ml) then EtOH (2 x 50ml) and dried *in vacuo* to give BTX (89.1g, 320mmol, 93%) of analytical purity. [Dess & Martin *J Am Chem Soc* **113** 7277 *1991*]

Santagostino et al.'s method: To oxone (181.0g, 290mmol, see [70693-62-8] $2KHSO_5$—$KHSO_4$—K_2SO_4 triple salt) in deionised H_2O (650ml, 450mmol) is added rapidly 2-iodobenzoic acid (50.0g, 200mmol), and kept at 70-73° for 20 minutes then stirred mechanically at 70-73° for 3 hours. Initially a thick slurry coating along the walls of the container is formed which gradually becomes finely dispersed and the now easily stirred suspension readily sediments if stirring is interrupted. The mixture is then stirred slowly at 5° for 1.5 hours, the white crystalline solid is collected onto a medium porosity sintered-glass funnel, washed with H_2O (6 x 100ml) and Me_2CO (2 x 100ml) then Et_2O, and left in dry air for 16 hours to give IBX (44,8-45.7g, ~80%). The filtrates are disposed of by treating with solid Na_2SO_3 (70g, 55mmol) and neutralising with M aqueous NaOH. Analysis indicated that the purity was ≥95% (judging by the ^1H NMR integrals of the triplets at 7.84 and 7.47 ppm, and elemental analysis), and it contained 2-iodosobenzoic acid (~4%) and 2-iodobenzoic acid (~0.5%). IBX of analytical purity (≥99%) is similarly obtained on a small scale by adding 2-iodobenzoic acid (5.0g, 20mmol) to a solution of oxone in deionised H_2O (37.2g, 61mmol, in 200ml), and the suspension is kept at 70° for 1 hour when it becomes clear. After 0.5 hours at 0-5° the white crystals that separate are collected, washed and dried as before to give analytically pure IBX (4.4g, 77%), m 233° (dec). This procedure is more environmentally friendly than the Dess-Martin procedure. [Frigerio et al. *J Org Chem* **64** 4537 *1999*.] It has IR

(film) with a ν_{max} at 1640 cm^{-1}; the ^1H NMR (DMSOd_6, TMS) has δ at 8.15 (d, 1H), 8.01 (d, 1H), 7.89 (t, 1H), and 7.84 (t, 1H); and the ^{13}C NMR (DMSOd_6, TMS) has δ at 167.49, 146.59, 133.39, 132.97, 131.36, 130.10 and 124.99 [Frigerio & Santagostino *Tetrahedron Lett* **43** 8019 *1994*].
SIBX is an even more stabilised, non-explosive formulation that has all the oxidative characteristics of IBX. It is prepared as follows: 2-iodobenzoic acid (200g) and isophthalic acid (133g, see [121-91-5]) are added into a solution of oxone (625g) in H_2O (2000ml) and kept at 70° for 3 hours, then sodium benzoate (128g) in H_2O (500ml) is added at 40°. The precipitate that is formed on cooling to 20° is filtered off, washed with H_2O (700ml) and dried in a ventilated oven at 60° to give *SBTX* (420g, 90%) containing 49% w/w of active IBX. [Ozanne et al. *Org Lett* **5** 2903 *2003*.]
SIBX and/or IBX are water tolerant, inexpensive to prepare and easy to use. They oxidise primary and secondary alcohols smoothly to aldehydes and ketones, and vicinal diols are oxidised to mono and/or dicarbonyl compounds without C-C cleavage [Frigerio & Santagostino *Tetrahedron Lett* **43** 8019 *1994*], as well as allylic and benzylic alcohols to respective aldehydes [Ozanne et al. *Org Lett* **5** 2903 *2003*.], amino alcohols to amino carbonyls without amino protection, and sensitive heterocyclic substituents are not affected [Frigeio et al. *J Org Chem* **60** 7272 *1995*]. The structure and kinetics of the reactive intermediates in the oxidation have been studied in detail [Munari et al. *J Org Chem* **61** 9272 *1961*]. The reagents are generally sparingly soluble in organic solvents such as EtOAc, THF, Me_2CO, MeCN, toluene, DMSO and *N*-methylpyrrolidine, but the reactions usually proceed in these solvents, or mixtures of them, with ease and in good to excellent yields either at room temperature or at as high as reflux temperatures.

2-Hydroxybenzothiazole (benzothiazol-2(3*H*)-one) *[934-34-9]* **M 183.1, m 140-141°.** Crystallise it from aqueous EtOH or water. [Hoggarth *J Chem Soc* 3314 *1949*, Hunter *J Chem Soc* 135 1930, *Beilstein* **27** H 182, **27** I 270, **27** II 225, **27** III/IV 2693.]

1-Hydroxybenzotriazole hydrate (HOBt) *[2592-95-2; 123333-53-9 (H_2O)]* **M 135.1, m 157°, 159-160°, pK^{20} 7.88.** Crystallise HOBt from hot aqueous EtOH or water (charcoal). It is prepared from *o*-nitrophenylhydrazine or its hydrochloride dissolved in a small volume of H_2O by treating with 25% of aqueous KOH or aqueous ammonia whereby the mixture warms up immediately and discolours. After the mixture cools to room temperature it is acidified with hydrochloric acid and the *hydroxybenzotriazole* separates as colourless needles. It is soluble in hot H_2O, EtOH and AcOH, but much less soluble in Et_2O, petroleum ether, $*C_6H_6$ and $CHCl_3$. It is an acid and forms metal salts such the ***Pb salt*** which crystallises from hot H_2O in glistening leaflets with **m 270°**. In aqueous solution it exists mainly as the zwitterionic N-oxide tautomer with H^+ on N-2. [Nietzki & Braunschweig *Chem Ber* **27** 3381 *1894*, Zincke & Schwartz *Justus Liebigs Ann Chem* **329** 329 *1900*, Boyle & Jones *J Chem Soc Perkin Trans II* 160 *1973*, Tomita & Ikawa *J Pharm Soc Jpn* **75** 449 *1955*, *Beilstein* **26** III/IV 95.] It is a useful reagent for peptide synthesis [Heusel et al. *Angew Chem Int Ed* **16** 642 *1977*].
§ A polystyrene supported version is available. For use in solid phase peptide synthesis, see Dryland & Sheppard *J Chem Soc Perkin Trans 1* 125 *1986*.

4-Hydroxycoumarin (4-hydroxy-1-benzopyran-2-one) *[1076-38-6]* **M 162.1, m 206°, 211-213°, pK_{Est} ~9.0.** Crystallise 4-hydroxycoumarin from water and dry it in a vacuum desiccator over Sicapent. [*Beilstein* **18/1** V 378.]

***N*-2-Hydroxyethylpiperazine-*N'*-2-ethanesulfonic acid (HEPES)** *[7365-45-9]* **M 238.3, pK^{20} 7.55.** Crystallise the acid from hot EtOH and water. It is a useful buffer. [*Beilstein* **23** V 376.]

3-Hydroxyflavone (Flavanol) *[577-85-5]* **M 238.2, m 169-170°, 171-172°.** Recrystallise it from MeOH (**m** 169.5-170°), EtOH, aqueous EtOH (**m** 167°) or hexane. It has also been purified by repeated sublimation under high vacuum, and dried at high vacuum pumping for at least one hour [Bruker & Kelly *J Phys Chem* **91** 2856 *1987*]. [*Beilstein* **17** H 527, **17** I 268, **17** II 498, **17** III/IV 6428.]

7-Hydroxy-4-methylcoumarin (4-methylumbelliferone(β) hydrate) *[90-33-5]* **M 194.2, m 185-186°, 188-188.5°, 194-195°, pK^{25} 7.80 (phenolic OH).** Purify it by recrystallisation from EtOH. It is very slightly soluble in cold H_2O (solubility at 37° is 0.22%), slightly soluble in Et_2O and $CHCl_3$, but soluble in MeOH and

AcOH. It has a blue fluorescence in aqueous EtOH and has UV with λ_{max} at 221, 251 and 322.5nm (MeOH). The IR has ν_{max} at 3077 br, 1667, 1592, 1385, 1267, 1156, 1130 and 1066 cm^{-1}. The *acetate* has **m** 153-154°. [Woods & Sapp *J Org Chem* **27** 3703 *1962*, *Beilstein* **18** III/IV 332, **18/1** V 439.]

2-Hydroxymethyl-12-crown-4 *[75507-26-5]* **M 206.2, b 115°/0.04mm, d_4^{20} 1.186, n_D^{20} 1.480.** Purify it by chromatography on Al_2O_3 with EtOAc as eluent to give a *hygroscopic* colourless oil, which is distilled under high vacuum and is distilled *in vacuo*. It has IR with ν_{max} at 3418 (OH) and 1103 (COC) cm^{-1}, and NMR: δ 3.70s. [Kimura et al. *J Chem Soc, Chem Commun* 492 *1983*, Pugia et al. *J Org Chem* **52** 2617 *1987*.]

***S*-(-)-5-Hydroxymethyl-2(5*H*)-furanone** *[78508-96-0]* **M 114.1, 39-42°, 40-44°, b 130°/0.3mm, $[\alpha]_{546}^{20}$ -180°, $[\alpha]_D^{20}$ -148° (c 1.4, H_2O).** It is purified by chromatography on Silica gel using hexane/EtOAc (1:1) to give a colourless oil which is distilled using a Kügelrohr apparatus, and the distillate crystallises on cooling. It has R_F 0.51 on Whatman No 1 paper using pentan-1-ol and 85% formic acid (1:1) and developing with ammoniacal $AgNO_3$. [Boll *Acta Chem Scand* **22** 3245 *1968*, NMR: Oppolzer et al. *Helv Chim Acta* **68** 2100 *1985*, *Beilstein* **18** III/IV 56, **18/1** V 54.]

5-(Hydroxymethyl)furfural *[67-47-0]* **M 126.1, m 33.5°, b 114-116°/1mm, d_{25}^{25} 1.2620, n_D^{25} 1.5533.** Crystallise it from diethyl ether/petroleum ether. [*Beilstein* **18** III/IV 100, **18/1** V 130.]

***dl*-3-Hydroxy-*N*-methylmorphinan** *[297-90-5]* **M 257.4, m 251-253°.** Crystallise it from MeOH or aqueous EtOH. The *hydrochloride* has **m** 176-177°. The *hydrobromide* has **m** 200-201° when recrystallised from EtOH/Et_2O. [Sneider & Hellerbach *Helv Chim Acta* **33** 1446 *1950*, *Beilstein* **21** III/IV 100.]

8-Hydroxy-2-methylquinoline *[826-81-3]* **M 159.2, m 74-75°, b 266-267°, pK_1^{25} 5.61, pK_2^{25} 10.16.** Crystallise the quinoline from EtOH or aqueous EtOH. Its solubility at 20° in H_2O is 0.366g/L, and in $CHCl_3$ it is 466g/L. It complexes with many metals. [*Beilstein* **21** H 106, **21** III/IV 2132.]

4-Hydroxy-2-*n*-nonylquinoline *N*-oxide *[316-66-5]* **M 287.4, m 148-149°, pK_{Est} ~6.0.** Crystallise the *N*-oxide from EtOH. Its UV has λ_{max} at 220-230nm in 0.001N NaOH. [Cornforth & James *Biochem J* **63** 124 *1956*, *Beilstein* **21** III/IV 3834.]

1-Hydroxyphenazine (Hemipyocyanine) *[528-71-2]* **M 196.2, m 157-158°, 165-166°, pK_1^{15} 1.61, pK_2^{15} 8.33 (10% aqueous MeOH).** Purify the hydroxyphenazine by chromatography on acidic alumina with *benzene/ether, and recrystallise it from aqueous EtOH, *benzene/heptane, then sublime it at 140°/1.5mm. [UV, IR: Badger et al. *J Chem Soc* 3204 *1951*, Hegedüs *Helv Chim Acta* **33** 746 *1950*, *Beilstein* **23** II 360, **23** III/IV 2753.]

2-(2-Hydroxyphenyl)benzothiazole *[3411-95-8]* **M 227.2, m 132-133°, b 173-179°/3mm.** Recrystallise it several times from aqueous EtOH or dilute AcOH and sublime it. [Itoh & Fujiwara *J Am Chem Soc* **107** 1561 *1985*, Bogert & Corbitt *J Am Chem Soc* **48** 786 *1926*, *Beilstein* **27** II 91.]

2-(2-Hydroxyphenyl)benzoxazole *[835-64-3]* **M 211.2, m 127°, b 338°/760mm.** Recrystallise it several times from aqueous EtOH or dilute AcOH and sublime it. An aqueous alkaline solution containing EtOH has a blue fluorescence. [Itoh & Fujiwara *J Am Chem Soc* **107** 1561 *1985*, *Beilstein* **27** II 91.]

3-Hydroxy-2-phenylcinchoninic acid (Oxycincophen) *[485-89-2]* **M 265.3, m 206-207°(dec).** It is precipitated from alkaline solution on acidification and crystallises from EtOH or AcOH in yellow crystals. [Marshall & Blanchard *J Pharmacol* **95** 186 *1949*, *Beilstein* **22** H 245, **22** II 183, **22** III/IV 2383.]

(±)-2-(α-Hydroxypropyl)piperidine [2-piperidinepropanol, *RS*-1-(*RS*-2-piperidyl)propan-1-ol, (±)-α-conhydrine] *[3238-62-8, 63401-12-7, 24448-89-3]* **M 143.2, m 99-100°, pK_{Est} ~10.2.** Crystallise it from ether. The [*RS-1-(SR-2)]*-isomer also crystallises from ether and has **m** 98-98.5°. The *methiodide* crystallises from Me_2CO/MeOH with **m** 127-130.5°. **POISONOUS** [Sicher & Tichy *Col Czech Chem Commun* **23** 2081 *1958*, Govindachari & Rajappa *J Chem Soc* 1306 *1958*, Stereochemistry: Hill *J Am Chem Soc* **80** 1609 *1958*,

Beilstein **21** II 21, **21** III/IV 122.]

(+)-2-(α-Hydroxypropyl)piperidine [2-piperidinepropanol, *R*-1-(*S*-2-piperidyl)propan-1-ol, (+)-α-conhydrine] *[495-20-5]* **M 143.2, m 121°, b 224-5°/720mm, $[\alpha]_D^{20}$ -9.8° (c 4, EtOH), pK_{Est} ~10.2.** This very **POISONOUS** alkaloid from hemlock crystallises in leaflets from ether. The *O,N-dibenzoyl* derivative has **m** 133-134° and $[\alpha]_D^{24}$ -13° (c 3, $CHCl_3$). [Sicher & Tichy *Col Czech Chem Commun* **23** 2081 *1958*, Stereochemistry: Hill *J Am Chem Soc* **80** 1609 *1958*, Absolute config & ORD: Fodor et al. *Canad J Chem* **47** 4393 *1969*, *Beilstein* **21** I 191, **21** II 21, **21** III/IV 122.]

(-)-2-(α-Hydroxypropyl)piperidine [2-piperidinepropanol, *R*-1-(*R*-2-piperidyl)propan-1-ol, (-)-α-conhydrine] *[495-20-5]* **M 143.2, m 121°, b 224-5°/720mm, $[\alpha]_D^{20}$ +10° (c 10, EtOH), pK_{Est} ~10.2.** Crystallise the piperidine from ether. **POISONOUS.** [Galinovsky & Mulley *Monatsh Chem* **79** 426 *1948*, *Beilstein* **21** I 191, **21** II 21, **21** III/IV 122.]

(±)-7-(2-Hydroxypropyl)theophylline (Proxyphylline, 1,3-dimethyl-3*H*,7*H*-purine-2,6-dione) *[603-00-9]* **M 238.2, m 135-136°.** Crystallise it from EtOH, aqueous MeOH or EtOAc. Roth *Archiv Pharmazie* **292** 234 *1959*, Zelnik et al. *Bull Soc Chim Fr* 1733 *1956*, *Beilstein* **26** III/IV 2366.]

6-Hydroxypurine (hypoxanthine) *[68-94-0]* **M 136.1, m 150°(dec), pK_1^{20} 1.98, pK_2^{20} 8.96, pK_3^{20} 12.18.** Crystallise it from hot water and dry it at 105°. [*Beilstein* **26** II 252, **26** III/IV 2081.]

2-Hydroxypyridine (2-pyridone) *[142-08-5]* **M 95.1, m 105-107°, b 181-185°/24mm, ε_{293nm} 5900 (H_2O) pK_1^{25} 1.25, pK_2^{25} 11.99.** Distil the pyridone under vacuum to remove coloured impurity, then recrystallise from *benzene, CCl_4, EtOH or $CHCl_3$/diethyl ether. It can be sublimed under high vacuum. [DePue et al. *J Am Chem Soc* **107** 2131 *1985*, *Beilstein* **21/7** V 106.]

3-Hydroxypyridine *[109-00-2]* **M 95.1, m 129°, 130°, pK_1^{25} 5.10, pK_2^{25} 8.6.** Crystallise 3-hydroxypyridine from *C_6H_6, water or EtOH. [*Beilstein* **21** III/IV 402, **21/2** V 68.]

4-Hydroxypyridine (4-pyridone) *[626-64-2]* **M 95.1, m 65°, 68° (hydrate), 148.5°, 151-152° (anhydr), b >350°/760mm, pK_1^{20} 3.20, pK_2^{20} 11.12.** Crystallise 4-pyridone from H_2O or wet $CHCl_3$ as the *monohydrate*. It loses H_2O on drying *in vacuo* over H_2SO_4. Store it over KOH because it is *hygroscopic*. [*Beilstein* **21** III/IV 446, **21/7** V 152.]

2(6)-Hydroxypyridine-5(3)-carboxylic acid (6-hydroxynicotinic acid) *[5006-66-6]* **M 139.1, m 304°(dec), pK_1^{20} 3.82 and pK_2^{20} 9.92.** It crystallises from water with **m** 303.4-303.7°(dec), or with **m** 325°(dec) from aqueous EtOH. The *methyl ester* crystallises from Me_2CO with **m** 166° and pK^{20} 9.92. [Albert *J Chem Soc* 1020 *1960*, *Beilstein* **22** III/IV 2147, **22/6** V 119.]

4-Hydroxypyridine-2,6-dicarboxylic acid (chelidamic acid) *[134.828-60-3]* **M 183.1, m 248°(dec, 1 H_2O), 254°(dec), 263°(dec), pK_1^{22} 1.9, pK_2^{22} 3.18, pK_3^{22} 10.85; pK_1 3.62, pK_2 4.82 (80% aqueous methoxyethanol).** It crystallises from water. The *dimethyl ester* crystallises from MeOH with **m** 167° (*monohydrate*, from H_2O), **m** 170-171° (*anhydrous*, from MeOH), and pK^{25} 6.25. [Bensaude et al. *J Am Chem Soc* **99** 4438 *1972*, *Beilstein* **22** III/IV 2583, **22/7** V 164.]

2-Hydroxypyrimidine *[557-01-7]* **M 96.1, m 179-180°, pK_1^{20} 2.24, pK_2^{20} 9.17.** It crystallises from EtOH or ethyl acetate. Its solubility in H_2O at 20° is 1g/2.2ml. [Albert *J Chem Soc* 4219 1952, *Beilstein* **24** III/IV 194.]. *2-Hydroxypyrimidine hydrochloride [38353-09-2]* M 132.5, has **m** 203-205.5°(dec) and crystallises from EtOH. [*Beilstein* **24** III/IV 173.] The *picrate* has **m** 199° and crystallises from EtOH. [Brown et al. *J Chem Soc* 211 1955.]

4-Hydroxypyrimidine *[4562-27-0]* **M 96.1, m 164-165°, pK_1^{20} 1.66, pK_2^{20} 8.63.** It crystallises from *benzene or ethyl acetate. The *picrate* has **m** 164-166° and crystallises from EtOH [Brown et al. *J Chem Soc* 4035 *1955*, *Beilstein* **24** III/IV 171.]

***R*-(+)-3-Hydroxypyrrolidine** *[(±) 2799-21-5 and 104706-47-0, R(+) 40499-83-0, S(-) 100243-39-8]* **M 87.1, b 215-216°/atm, d_4^{20} 1.078, n_D^{20} 1.490, $[\alpha]_D^{20}$ +6.5° (c 1.5, MeOH), pK_{Est} ~10.1.** The *(±)-isomer* is purified by repeated distillation (**b** 102-104°/12mm, 108-110°/18mm), and the *(±)-picrate* crystallises from EtOH with **m** 140-141°. The *R(+)-enantiomer* has **b** 70°/0.6mm and $[\alpha]_D^{20}$ +5.6° (c 3.63, MeOH). Its *hydrochloride* has a negative rotation and its *dimethiodide* has **m** 230° and $[\alpha]_D^{24}$ -8.02°. [Suyama & Kanno *Yakugaku Zasshi (J Pharm Soc Japan)* **85** 531 *1965*, Uno et al. *J Heterocycl Chem* **24** 1025 *1987*, Flanagan & Joullie *Heterocycles* **26** 2247 *1987, Beilstein* **21** III/IV 44.]

2-Hydroxyquinoline (carbostyril) *[59-31-4]* **M 145.2, m 199-200°, pK_1^{20} -0.31, pK_2^{20} 11.76.** Crystallise it from MeOH. It has **m** 200-201° after sublimation in a vacuum. The *picrate* has **m** 132° after crystallisation from Et_2O. [Gibson et al. *J Chem Soc* 4340 *1955*, *Beilstein* **21** III/IV 1057, **21/8** V 217.]

8-Hydroxyquinoline (oxine, 8-quinolinol) *[148-24-3]* **M 145.2, m 71-73°, 75-76°, 76°, b 122°/0.1mm, ~267°/atm, pK_1^{25} 4.91, pK_2^{25} 9.81.** Crystallise oxine from hot EtOH, acetone, petroleum ether (b 60-80°) or water. Crude oxine can be purified by precipitation of copper oxinate, followed by liberation of free oxine with H_2S or by steam distillation after acidification with H_2SO_4. Store it in the dark. It forms complexes with many metals. [Manske et al. *Can J Research* **27F** 359 *1949*, Phillips *Chem Rev* **56** 271 *1956*, *Beilstein* **21** III/IV 1135, **21/3** V 252.]

8-Hydroxyquinoline-5-sulfonic acid (H_2O) *[84-88-8]* **M 243.3, m 322-323°(sintering at ~305°), >310°, pK_1^{25} 4.09, pK_2^{25} 8.66.** Crystallise the acid from water (as the 1.5 *hydrate*, **m** 316-317°) or dilute HCl (*ca* 2% by weight). [*Beilstein* **22** I 620, **22** II 313, **22** III/IV 3493.]

4-Hydroxy-2,2,6,6-tetramethylpiperidine *[2403-88-5]* **M 157.3, m 130-131°, pK^{20} 10.05.** The piperidine crystallises from water as a *hydrate* and crystallises from dry ether or *C_6H_6 as the *anhydrous* base. The *hydrochloride* has **m** 282-284° (from EtOH/H_2O), and the *formate* has **m** 207°(dec, from EtOH/EtOAc). [Mailey & Day *J Org Chem* **22** 1061 *1957*, *Beilstein* **21** I 195, **21** III/IV 146, **21/1** V 159.]

4(6)-Hydroxy-2,5,6(2,4,5)-triaminopyrimidine sulfate *[35011-47-3]* **M 257.22, m >340°, pK_1 2.0, pK_2 5.1, pK_3 10.1.** This salt has very low solubility in H_2O. It is best purified by conversion into the dihydrochloride salt, which is then re-converted to the insoluble sulfate salt. The sulfate salt (2.57g, 10mmoles) is suspended in H_2O (20ml) containing $BaCl_2$ (10mmoles) and stirred in a boiling water bath for 15 minutes. After cooling, the insoluble $BaSO_4$ is filtered off and washed with boiling H_2O (10ml). The combined filtrate and washings are made acidic with HCl and evaporated to dryness. The residual hydrochloride salt is recrystallised from H_2O by adding conc HCl whereby the *dihydrochloride salt* separates as clusters which darken at 260° and dec > 300°[darkening > 360°]. [Baugh & Shaw *J Org Chem* **29** 3610 *1964*, King & Spengley *J Chem Soc* 2144 *1952*]. The hydrochloride is then dissolved in H_2O, and while hot an equivalent of H_2SO_4 is added when the sulfate separates as a white microcrystalline solid which is filtered off washed liberally with H_2O and dried in vacuum over P_2O_5. [Albert & Wood *J Appl Chem London* **3** 521 *1953*, UV: Cavalieri et al. *J Am Chem Soc* **70** 3875 *1948*; see also Pfleiderer *Chem Ber* **90** 2272 *1957*, Traube *Chem Ber* **33** 1371 *1900*.] The *hydrochloride* has **m** > 300°. [*Beilstein* **25** II 384, **25** III/IV 3648.]

3-Hydroxyxanthone *[3722-51-8]* **M 212.2, m 246°, 249-250°.** Purify the xanthone by chromatography on SiO_2 gel with petroleum ether/*benzene as eluent. Recrystallise it from *benzene or EtOH. The *acetate* has **m** 157-158°. [Itoh et al. *J Am Chem Soc* **107** 4819 *1985*, Davies et al. *J Org Chem* **23** 307 *1958*]. [*Beilstein* **18** H 46, **18** I 315, **18** II 29, **21** III/IV 601.]

Ibogaine (12-methoxybogamine) *[83-74-9]* **M 300.3, m 152-153°, $[\alpha]_D^{20}$ -54° (EtOH), pK^{25} 8.1 (80% aqueous $MeOCH_2CH_2OH$).** Crystallise this akaloid from EtOH or aqueous EtOH and sublime it at 150°/0.01mm. It is soluble in organic solvents but insoluble in H_2O. The *hydrochloride*, **m** 299-300°(dec), is soluble in H_2O and alcohols. [Büchi et al. *J Am Chem Soc* **88** 3099 *1866*, Rosenmund *Chem Ber* **108** 1871 *1975*, *Beilstein* **23** III/IV 2742.]

Imidazole (glyoxaline) *[288-32-4]* **M 68.1, m 89.5-91°, 89-90°, b 140-145°/15mm, 256°/atm, 262-264°/atm, pK_1^{25} 6.99, pK_2^{25} 14.44.** Crystallise imidazole from *benzene, CCl_4, CH_2Cl_2, EtOH, petroleum ether, acetone/petroleum ether and distilled de-ionized water. Dry it at 40° under vacuum over P_2O_5. Distil it at low pressure. It is also purified by sublimation or by zone melting. [Snyder et al. *Org Synth* Coll Vol **III** 471 *1955*, Bredereck et al. *Chem Ber* **97** 827 *1964*, Caswell & Spiro *J Am Chem Soc* **108** 6470 *1986*.] *^{15}N-imidazole* crystallises from *benzene [Scholes et al. *J Am Chem Soc* **108** 1660 *1986*]. [*Beilstein* **23** II 34, **23** III/IV 564, **23/4** V 191.]

1*H*-Indazole-3-carboxylic acid *[4498-67-3]* **M 162.2, m 265-265.5°, 268-268.5°, $pK_{Est(1)}$ ~4.5.** Purify the acid by recrystallisation from glacial acetic acid (charcoal), and dry the yellow crystals *in vacuo*. *Alternatively*, dissolve the acid in boiling H_2O, concentrate the solution to one third its volume, cool and collect the yellow powder. Its UV has λ_{max} (H_2O) at 295 (logε 3.88) nm. The *ethyl ester* (prepared *via* the acid chloride) has **m 139°** (from EtOH) and has λ_{max} (MeOH) at 393 nm, and the *N-methylamide* crystallises in tan needles from $MeNO_2$ with **m 191-191°** (**187-188.5°** was also reported). [Rousseau & Lindwall *J Am Chem Soc* **72** 3048 *1950*, Snyder et al. *J Am Chem Soc* **74** 2009 *1952*, *Beilstein* **25** H 129, **25** I 238, **25** II 128, **25** IV 808.]

1*H*, *2H*-Indazol-3-one (3-hydroxy-1*H*-indazole) *[7364-25-2]* **M 134.1, m 250-252°, 253-254°, $pK_{Est(1)}$ ~6.0.** Purify indazol-3-one by recrystallisation from $MeNO_2$ or aqueous MeOH, and sublimation at 220°/0.1mm. In the UV it has λ_{max} in MeOH at 215 and 306 nm, and it is in the 3-OH form in ethanolic solution. There appears to be some controversy regarding the tautomeric form in the solid state, but the IR peak at ν_{max} 1627 cm^{-1} (KBr) supports the keto form. [Ainsworth *J Am Chem Soc* **79** 524 *1957*, Elguero et al. *Adv Heterocycl Chem,* **Suppl 1** 354 *1976*, Chernokal'skii et al. *Khim Geterotsikl Soedin* 96 *1966*, *Beilstein* **24** H 111, **24** II 59, **24** III/IV 270.]

4′-(Imidazol-1-yl)acetophenone *[10041-06-2]* **M 186.2, m 104-107°, pK^{25} 4.54.** Recrystallise it twice from CH_2Cl_2/hexane [Collman et al. *J Am Chem Soc* **108** 2588 *1986*].

2-Iminothiolane hydrochloride (2-iminotetrahydrothiophene, Traut's reagent) *[4781-83-3]* **M 137.6, m 187-192°, 190-195°, 192-193°, 193-194°, 202-203°, pK^{25} <2 (free base).** Recrystallise the hydrochloride from MeOH/Et_2O (**m** 187-192°) or (MeOH/Me_2CO), but after sublimation at ~180°/0.2mm the melting point rises to 202-203°. It has ^{1}HNMR with δ 2.27 (2H, t), 3.25 (2H, t) and 3.52 (2H, t) in $(CD_3)_2SO$. [King et al. *Biochemistry* **17** 1499 *1978*.] The *free base* is purifed by vacuum distillation (**b** 71-72°/6mm), has IR (film) with ν_{max} at 1700 (C=N)cm^{-1} and ^{1}HNMR ($CDCl_3$) with δ at 3.58 (2H, t) and 2.10-2.8 (4H, m). The *free base* is stable on storage but slowly hydrolyses in aqueous solutions with half-lives at 25° of 390 hours at pH 9.1, 210 hours at pH 10 and 18 hours at pH 11. [Traut et al. *Biochemistry* **12** 3266 *1973*, *Biochemistry* **17** 399 *1978*, Alagon & King *Biochemistry* **19** 4343 *1980*, *Beilstein* **17/9** V 12.]

Indanthrene (*N*,*N*′-dihydro-1,2,1′,2′-anthraquinonazine) *[81-77-6]* **M 442.4, m 470-500°(dec).** Crystallise indanthrene repeatedly from 1,2,4-trichlorobenzene to give a blue powder. It is soluble in alkali and conc H_2SO_4. [Weinstein & Merritt *J Am Chem Soc* **81** 3759 *1959*, *Beilstein* **24** II 317, **24** III/IV 2193.]

Indazole *[271-44-3]* **M 118.1, m 147°, 150°, pK_1^{20} 1.32, pK_2^{20} 13.80 (acidic NH).** Crystallise indazole from water, sublime it *in vacuo*, then recrystallise it from petroleum ether (b 60-80°). The *picrate* crystallises from Et_2O with **m** 136°. [Ainsworth *Org Synth* Coll Vol **IV** 536 *1963*, *Beilstein* **23** III/IV 1055, **23/6** V 156.]

Indigo *[482-89-3]* **M 262.3, sublimes at ~300°, m 390°(dec), and halogen-substituted indigo dyes.** First reduce indigo in alkaline solution with sodium hydrosulfite, and filter. The filtrate is then oxidised by air, and the resulting precipitate is filtered off, dried at 65-70°, ground to a fine powder, and extracted with $CHCl_3$ in a Soxhlet extractor. Evaporation of the $CHCl_3$ extract gives the purified dye. [Brode et al. *J Am Chem Soc* **76** 1034 *1954*; spectral characteristics are listed, *Beilstein* **24** II 233, **24** III/IV 1791.]

Indole *[120-72-9]* **M 117.2, m 52°, 54.5°, b 124°/5mm, 253-254°/760mm, pK_1^{25} -2.47 (H_0 scale), pK_2^{25} 16.97 (acidic NH).** Crystallise indole from *benzene, hexane, petroleum ether, water or EtOH/water (1:10). It can be further purified by sublimation in a vacuum or by zone melting. The *picrate* forms orange crystals from

EtOH and has **m** 175°. [*Beilstein* **20** II 196, **20** III/IV 3176, **20/7** V 5.]

Indole-3-acetic acid (heteroauxin) *[87-51-4]* **M 175.2, m 167-169°(dec), pK_1^{25} -6.13 (aqueous H_2SO_4), pK_2^{25} 4.54 (CO_2H).** Recrystallise heteroauxin from EtOH/water [James & Ware *J Phys Chem* **89** 5450 *1985*]. [*Beilstein* **22** III/IV 65.] *Alternatively*, recrystallise 30g of the acid with 10g of charcoal in 1L of hot water, filter and cool when 22g of colourless acid separate. Dry it and store it in a dark bottle away from direct sunlight [Johnson & Jacoby *Org Synth* Coll Vol **V** 654 *1973*]. The *picrate* has **m** 178-180°. [*Beilstein* **22** H 66, **22** I 508, **22** II 50, **22** III/IV 1088.] It is a plant growth substance.

3-Indoleacetonitrile *[771-51-7]* **M 156.2, m 33-36°, 36-38°, b 157°/0.2mm, 158-160°/0.1mm, viscous oil n_D^{20} 1.6097.** Distil the nitrile at very high vacuum, and the viscous distillate crystallises on standing after a few days; the *picrate* has **m** 127-128° (from EtOH) [Coker et al. *J Org Chem* **27** 850 *1962*, Thesing & Schülde *Chem Ber* **85** 324 *1952*]. Store it away from light. The *N-acetate* has **m** 118° (from MeOH) and has R_F = 0.8, on Silica Gel F_{254} in $CHCl_2$/MeOH 19:1 [Buzas et al. *Synthesis* 129 *1977*]. [*Beilstein* **22** III/IV 1097, **22/3** V 74.] It is a plant growth substance.

Indole-2-carboxaldehyde *[19005-93-7]* **M 145.2, m 138°, 140-141°, 138-142°, pK_{Est} <1.** Recrystallise the indole from aqueous MeOH (**m** 141-142°), Et_2O (**m** 138°) or sublime it *in vacuo* (**m** 138°). The *N,N-dimethylhydrazone* [127280-17-5] has **m** 105-106° (from hexane/*C_6H_6). The *thiosemicarbazone* has **m** 229° (dec) (from 50% aqueous EtOH) [Doyle et al. *J Chem Soc* 2854 *1956*]. The *2,4-dinitrophenylhydrazone* has **m** 315-320° (dec) (from pyridine/MeOH). [Suzuki et al. *Chem Pharm Bull Jpn* **39** 2170 *1991*, *Beilstein* **21** III/IV 3754.]

Indole-3-propionic acid *[830-96-6]* **M 189.2, m 134-135°, pK^{25} 4.95.** Recrystallise it from EtOH/water [James & Ware *J Phys Chem* **89** 5450 *1985*]. The *picrate* has **m** 143-144°, and the *methyl ester* crystallises from *C_6H_6 or MeOH with **m** 81-83°. [*Beilstein* **22** III/IV 1113, **22/3** V 114.]

(±)-Indoline-2-carboxylic acid (2,3-dihydro-1*H*-indole-2-carboxylic acid) *[78348-24-0]* **M 163.2, m 168°(dec), $pK_{Est(1)}$ ~2.1, $pK_{Est(2)}$ ~3.8.** Dissolve the acid in hot EtOH, add excess of dry Et_2O and cool to yield colourless plates that decompose in the range of 120-150°. The *amide* **(m 208-209°)** crystallises as colourless plates which sublime at 150°/1.0mm and has ν_{max} at 1625cm^{-1} (paraffin mull) [Hudson & Robertson *Aust J Chem* **20** 1935 *1967*]. [*Beilstein* **22/2** V 421.] See Chapter 6, Catalysts-Part 1 for optical isomers

Indolizine [pyrrocoline, pyrrolo(1,2-*a*)pyridine] *[274-40-8]* **M 117, m 73-74°, 75°, pK^{20} 3.94 (C-protonation).** Purify indolizine through an alumina column in *C_6H_6 and elute with *C_6H_6 (toluene could be used instead). The eluate contained in the fluorescent band (using UV light λ 365mn) is collected, evaporated and the crystalline residue is sublimed twice at 40-50°/0.2-0.5mm. The colourless crystals have a *naphthalene* odour, darken on standing and should be stored in dark sealed containers. If the original sample is dark in color then it should be covered with water and steam distilled. The colourless crystals in the distillate are collected and dried between filter paper and sublimed. It protonates on C3 in aqueous acid. It should give one fluorescent spot on paper chromatography (Whatman 1) in 3% aqueous ammonia and in *n*-BuOH/AcOH/H_2O (4:1:1). The *picrate* has **m** 101° from EtOH. [Armarego *J Chem Soc* 226 *1964*, Armarego *J Chem Soc (B)* 191 *1966*, Scholtz *Chem Ber* **45** 734 *1912*, *Beilstein* **20** II 200, **20** III/IV 3195.]

***trans*-Indol-3-ylacrylic acid** *[1204-06-4]* **M 187.2, m 190-195°(dec), 195°(dec), 196°(dec), 195-196°(dec), pK_{Est} ~ 4.2.** Recrystallise the acid from AcOH, H_2O or EtOAc/cyclohexane. UV in MeOH has λ_{max} at 225, 274 and 325nm. [Shaw et al. *J Org Chem* **23** 1171 *1958*, constitution: Rappe *Acta Chem Scand* **18** 818 *1964*, Moffatt *J Chem Soc* 1442 *1957*, Kimming et al. *Hoppe Seyler's Z Physiol Chem* **371** 234 *1958*, *Beilstein* **22** V 249.]

3-Indolylbutyric acid *[133-32-4]* **M 203.2, m 120-123°, 123-125°, 124°, pK^{25} 4.84.** Recrystallise the acid from H_2O. It is soluble in EtOH, Et_2O and Me_2CO but insoluble in $CHCl_3$. [Bowman & Islip *Chem Ind London* 154 *1971*, Jackson & Manske *J Am Chem Soc* **52** 5029 *1930*, Albaum & Kaiser *Am J Bot* **24** 420 *1937*.] It has also been recrystallised from EtOH/water [James & Ware *J Phys Chem* **89** 5450 *1985*]. Its UV

has λ_{max} at 278 and 320nm in isoPrOH [Elvidge *Quart J Pharm Pharmacol* **13** 219 *1940*]. The *methyl ester* has **m** 73-74° (from *C_6H_6/petroleum ether) and **b** 230°/6mm [Bullock & Hand *J Am Chem Soc* **78** 5854 *1951*]. [*Beilstein* **22** III/IV 1128, **22/3** V 140.]

3-Indolylpyruvic acid *[392-12-1]* **M 203.2, m~210°(dec), 208-210°(dec), 219°(dec), pK_{Est} ~2.4.** Recrystallise the acid from Me_2CO/*C_6H_6, EtOAc/$CHCl_3$, Me_2CO/AcOH (crystals have 1 molecule of AcOH) and dioxane/*C_6H_6 (with 0.5 molecule of dioxane) [Shaw et al. *J Org Chem* **23** 1171 *1958*, Kaper & Veldstra *Biochim Biophys Acta* **30** 401 *1958*]. The *ethyl ester* has **m** 133° (from Et_2O), and its *2,4-dinitrophenylhydrazone* has **m** 255° (from Me_2CO). [Baker *J Chem Soc* 461 *1946*.] The *oxime* has **m** 157°(dec, from EtOAc/Et_2O) and pK^{20} 3.40 [Ahmad & Spenser *Canad J Chem* **39** 1340 *1961*]. [*Beilstein* **22** II 250, **22** III/IV 3080, **22/6** V 324.]

7-Iodoindole *[89976-15-8]* **M 243.0, m 52-56°, pK_{Est} <1.** Purify 7-iodoindole by chromatography through a silica gel column and eluting with CH_2Cl_2/hexane (1:3, v/v) followed by recrystallisation from hexane (colourless plates, **m** 55-56°). [Somei et al. *Chem Pharm Bull Jpn* **35** 3146 *1987*, Somei & Saida *Heterocycles* **23** 3114 *1985*.]

Iodinin (1,6-dihydroxyphenazine-5,10-dioxide) *[68-81-5]* **M 244.1, m 236°(dec), pK^{25} 12.5.** Purify iodinin through a column of silica gel and elute with Me_2CO/$CHCl_3$, then recrystallise it from $CHCl_3$ to give purple crystals with a copper-coloured luster. [Clemo & Dalgleish *J Chem Soc* 1481 *1950*, Gerber & Lechevalier *Biochemistry* **3** 598 *1964*, *Beilstein* **23** III/IV 3227,]

Iodonitrotetrazolium chloride (2[4-iodophenyl]-3-[4-nitrophenyl]-5-phenyl-2*H*-tetrazolium chloride) *[146-68-9]* **M 505.7, m 229°(dec), ~245°(dec).** Recrystallise the chloride from H_2O, aqueous EtOH or EtOH/Et_2O. *Alternatively*, dissolve it in the minimum volume of EtOH and add Et_2O; or dissolve it in hot H_2O (charcoal), filter and precipitate it by adding conc HCl. Filter the solid off and dry it at 100°. Its solubility in H_2O at 25° is 0.5%, and in hot MeOH/H_2O (1:1) it is 5%. [Fox & Atkinson *J Am Chem Soc* **72** 3629 *1950*, *Beilstein* **26** III/IV 1776.]

Iodonitrotetrazolium violet-Formazan *[7781-49-9]* **M 471.3, m 185-186°.** Dissolve it in boiling dioxane (20g in 300ml), add H_2O (100ml) slowly, cool, filter and dry it *in vacuo* at 100°. Its solubility in $CHCl_3$ is ~1%. [UV: Fox & Atkinson *J Am Chem Soc* **72** 3629 *1950*, *Beilstein* **26** III/IV 1776.]

Isatin (indole-2,3-dione) *[91-56-5]* **M 147.1, m 201-203°, 205°, pK^{25} >12 (acidic NH).** Crystallise isatin from amyl alcohol and sublime it at 180°/1mm. In aqueous NaOH the ring opens to yield sodium *o*-aminobenzoylformate. [*Beilstein* **21** II 327, 567, **21** III/IV 4981, **21/10** V 221.]

Isatoic anhydride (3,1-benzoxazin-2,4[1-*H*]-dione) *[118-48-9]* **M 163.1, m 235-240°, 240-243°, 243°, 243-245°.** Recrystallise it from EtOH or 95% EtOH (30ml/g) or dioxane (10ml/g) and dry it in a vacuum. [Wagner & Fegley *Org Synth* Coll Vol **III** 488 *1955*, Ben-Ishai & Katchalski *J Am Chem Soc* **74** 3688 *1952*, UV: Zentmyer & Wagner *J Org Chem* **14** 967 *1949*, *Beilstein* **27** II 299, **27**III/IV 3330.]

3-Isobutyl-1-methylxanthine (3-isobutyl-1-methylpurine-2,6-dione) *[28822-58-4]* **M 222.3, m 199-210°, 202-203°, pK_{Est} ~ 6.7 (acidic NH).** Recrystallise it from aqueous EtOH. [*Beilstein* **26** III/IV 2350.]

(+)-Isolysergic acid *[478-95-5]* **M 268.3, m 218°(dec), $[\alpha]_D^{20}$ +281° (c 1, pyridine) pK_1^{24} 3.33, pK_2^{24} 8.46.** It crystallises from water as the *dihydrate*. The *methyl ester* has **m** 172-174° (from MeOH or *C_6H_6) and $[\alpha]_D^{20}$ +179° (c 0.5 $CHCl_3$). [Smith & Timmis *J Chem Soc* 1440 *1936*, Craig et al. *J Biochem* **125** 289 *1938*, Stenlake *J Chem Soc* 1626 *1955*, Leemann & Fabbri *Helv Chim Acta* **4** 2696 *1959*, *Beilstein* **25** III/IV 935.]

Isonicotinamide *[1453-82-3]* **M 122.1, m 155.5-156°, pK_1^{20} -1.0 (protonation of $CONH_2$), pK_2^{20} 3.61, pK_3^{25} 11.47 (acidic $CONH_2$).** Recrystallise isonicotinamide from hot water or isopropanol (158.5-159°), and dry it in a vacuum at 100°. The *picrate* crystallises from aqueous EtOH or H_2O and has **m** 217-218° (214-215°). [*Beilstein* **22** III/IV 527, **22/2** V 195.]

Isonicotinic acid (pyridine-4-carboxylic acid) *[55-22-1]* **M 123.1, m 320°, 323-325°(dec), pK_1^{25} 1.70, pK_2^{25} 4.89.** Crystallise the acid repeatedly from water and dry it under vacuum at 110° or sublime it at 260°/15mm (**m** 319°). [*Beilstein* **22** III/IV 518, **22/2** V 188.]

Isonicotinic acid hydrazide (isoniazide) *[54-85-3]* **M 137.1, m 172°, pK_1 1.75 ($NHNH_2$), pK_2 3.57 (=N-), pK_3 10.75 (-NH).** Crystallise isoniazide from 95% EtOH and dry it in a vacuum. [*Beilstein* **22** III/IV 545, **22/2** V 219.]

1-Isonicotinyl-2-isopropylhydrazide (Iproniazid) *[54-92-2]* **M 179.2, m 112.5-113.5°, 114-115°, pK_{Est} ~3.5.** Crystallise it from *benzene or *benzene /petroleum ether and dry it in a vacuum. It is soluble in H_2O and EtOH. [Fox & Gibas *J Org Chem* **18** 994 *1953*.] The *dihydrochloride* has **m** 227-228° (from EtOH). [*Beilstein* **22** III/IV 551.] It is an antidepressant.

1-Isonicotinyl-2-isopropylhydrazide phosphate (Iproniazid phosphate, Marsilide) *[305-33-9]* **M 277.2, m 178-179°, 180-184°, pK_{Est} ~3.5 (free base).** Crystallise it from H_2O and Me_2CO. The *free base* (see above) has **m** 113-114° from $*C_6H_6$/petroleum ether and is soluble in H_2O and EtOH. [Fox & Gibas *J Org Chem* **18** 994 *1953*, *Beilstein* **22** III/IV 551.]

1-Isonicotinyl-2-salicylidenehydrazide *[495-84-1]* **M 241.2, m 232-233°.** Crystallise it from EtOH (**m** 265-266° or 244-245°), aqueous EtOH or MeOH (252-253°) and dry it in a vacuum at 100°. [*Beilstein* **22** III/IV 584.]

5-Isonitrosobarbituric acid (violuric acid) *[26851-19-9]* **M 175.1, m 221-223°, 245-250°, pK_1 4.41, pK_2 9.66 (10.1).** Crystallise violuric acid from water or EtOH. *1,1-Dimethylvioluric acid*, **m** 144-147° has pK^{25} 4.72 [Taylor & Robinson *Talanta* **8** 518 *1961*]. [*Beilstein* **24** III/IV 2142.]

***N*-Isopropylcarbazole** *[1484-09-9]* **M 209.3, m 120°.** Crystallise it from isopropanol. It sublimes under vacuum. It was also purified by zone refining. The *picrate* has **m** 143° after recrystallisation from EtOH. [*Beilstein* **20** I 164.]

Isoquinoline *[119-65-3]* **M 129.2, m 24°, 25.5-26°, b 120°/18mm, 243.25°/760mm, d_4^{20} 1.0986, n_D^{20} 1.6148, pK^{25} 5.40.** Dry isoquinoline with Linde type 5A molecular sieves or Na_2SO_4 and fractionally distil at reduced pressure. *Alternatively*, it can be refluxed with, and distilled from, BaO. It is also purified by fractional crystallisation from the melt and distilled from zinc dust. It forms a *phosphate* (**m** 135°) and a *picrate* (**m** 223°), which are purified by crystallisation, and the free base can be recovered and distilled. [Packer et al. *J Am Chem Soc* **80** 905 *1958*.] The procedure for purification *via* the picrate comprises the addition of quinoline to picric acid dissolved in the minimum volume of 95% EtOH to yield yellow crystals which are washed with EtOH and air dried before recrystallising from acetonitrile. The crystals are dissolved in dimethyl sulfoxide (previously dried over 4A molecular sieves) and passed through a basic alumina column, on which picric acid is adsorbed. The free base in the effluent is extracted with *n*-pentane and distilled under vacuum. Traces of solvent from small quantities are removed by vapour phase chromatography. The *hydrochloride* crystallises from EtOH with **m** 193°. [Mooman & Anton *J Phys Chem* **80** 2243 *1976*, *Beilstein* **20** II 236, **20** III/IV 3410, **20/7** V 333.]

Isoxanthopterin (2-amino-4,7-dihydroxypteridine) *[529-69-1]* **M 179.4, m>300°, pK_1^{20} -0.5 (basic), pK_2^{20} 7.34 (acidic), pK_3^{20} 10.06 (acidic).** Purify it by repeated precipitation from alkaline solution with acid (preferably AcOH or formic acid), filter, wash well with H_2O, then EtOH and dry at 100°. The purity is checked by paper chromatography [R_F 0.15 (*n*-BuOH/AcOH/H_2O, 4:1:1); 0.33 (3% aqueous NH_4OH). [Goto et al. *Arch Biochem Biophys* **111** 8 *1965*.] [For biochemistry see Blakley *Biochemistry of Folic Acid and Related Pteridines* North Holland Publ Co, Amsterdam 1969.] [*Beilstein* **26** III/IV 3999.]

Janus Green B (3-dimethylamino-7-[4-dimethylaminoazo]-5-phenylphenazonium chloride) *[2869-83-2]* **M 511.1, m >200°, CI 11050.** The dye dissolves in H_2O to give a bluish violet solution which becomes colourless when made 10M in NaOH. It dissolves in EtOH to give a blue-violet colour, filter from insoluble

material, then add dry Et_2O whereby the dye separates out leaving a small amount of blue colour in solution. Filter off the solid and dry it in a vacuum. Store it in a dark bottle. [Colour Index Vol 4, 3rd edn, 4015 *1971*.]

Jervine (3β,23β-17,23-epoxy-2-hydroxyvertraman-11-one, a steroidal alkaloid) *[469-59-0]* **M 425.6, m 243-245°, 247-248°, $[\alpha]_D^{20}$ -150° (in EtOH), pK_{Est}~9.4.** Crystallise Jervine from MeOH/H_2O or Me_2O. The *hydrochloride* has **m** 300-302° (from MeOH/Et_2O), and the *picrate* has **m** 262.5° (from aqueous MeOH). [Kutney et al. *Can J Chem* **53** 1796 *1975*, *Beilstein* **27** III/IV 3590.] It is **teratogenic**.

Julolidine (2,3,6,7-tetrahydro-1*H*,5*H*-benzo[*ij*]quinolizidine) *[479-59-4]* **M 173.3, m 34-36°, 40°, b 105-110°/1mm, 155-156°/17mm, 280°(dec), pK_{Est} ~7.0.** Purify julolidine by dissolving it in dilute HCl, steam is bubbled through the solution and the residual acidic solution is basified with 10N NaOH, extracted with Et_2O, washed with H_2O, dried (NaOH pellets), filtered, evaporated and distilled *in vacuo*. The distillate crystallises on cooling (**m** 39-40°). It develops a red colour on standing in contact with air for several days. The colour can be removed by distilling or dissolving in 2-3 parts of hexane, adding charcoal, filtering and cooling in an Me_2CO/Dry-ice bath when julolidine crystallises out (85-90% yield **m** 39-40°). The *hydrobromide [83646-41-7]* has **m** 218° (239-242°), the *picrate* has **m** 174°(165°) and the *methiodide* crystallises from MeOH, with **m** 186° [Glass & Weisberger *Org Synth* Coll Vol **III** 504 *1955*, Smith & Yu *J Org* Chem **17** 1285 *1952*, *Beilstein* **20** H 332, **20** I 133, **20** II 214, **20** III/IV 3281.] **Highly TOXIC.**

Kainic acid H_2O **(2*S*,3*S*,4*S*-2-carboxy-4-isoprenyl-3-pyrrolidine- acetic acid)** *[487-79-6]* **M 231.4, m 235-245°(dec), 251°(dec), $[\alpha]_D^{20}$ -14.6° (c 1.46, H_2O), pK_1 2.09, pK_2 4.58, pK_3 10.21.** Purify the acid by adsorbing on to a strongly acidic ion-exchange resin (Merck), elute the diacid with aqueous M NaOH, the eluate is evaporated, H_2O is added, and filtered through a weakly acidic ion-exchange resin (Merck). The filtrate is then evaporated and recrystallised from EtOH. Its solubility is 0.1g in 1ml of 0.5N HCl. (±)-α-Kainic acid is recrystallised from H_2O with **m** 230-260°. Its UV (MeOH) has λ_{max} at 219 (log ε 3.9); the ^{1}HNMR (CCl_4, 100MHz, Me_4Si standard) has δ at 1.64 (s 1H), 1.70 (s 3H), 3.24 (d *J* = 7.5, 2H), 3.3-4.2 (1H), 3.70 (s 3H), 3.83 (s 3H), 4.35 (dd *J* = 7.5, 14.5, 1H), 5.21 (t *J* = 7.5, 1H), 7.26 (*t J* = 7.5, 1H). [Oppolzer & Andres *Helv Chim Acta* **62** 2282 *1979*, *Beilstein* **22** III/IV 1523.]

Ketanserin [3(4-*p*-fluorobenzoylpiperidinyl-*N*-ethyl)quinazolin-2,4-dione] *[74050-98-9]* **M 395.4, m 227-235°, pK^{25} 7.5.** Its solubility is 0.001% in H_2O, 0.038% in EtOH and 2.34% in Me_2NCHO. It has been purified by recrystallisation from 4-methyl-3-pentanone [Peeters et al. *Cryst Structure Commun* **11** 375 *1982*, Kacprowicz et al. *J Chromatogr* **272** 417 *1983*, Davies et al. *J Chromatogr* **275** 232 *1983*]. It is an antihypertensive.

Khellin (4,9-dimethoxy-7-methyl-5-oxofuro[3,2-g]-1,2-chromene) *[82-02-0]* **M 260.3, m 154-155°, b 180-200°/0.05mm.** Crystallise khellin from H_2O, MeOH, petroleum ether or Et_2O. The *hydrochloride* has **m** 98°(dec) (from EtOH/HCl). [*Beilstein* **19** II 236, **19** III/IV 2816, **19/6** V 320.]

Kojic acid [(5-hydroxy-2-hydroxymethyl)-4*H*-pyran-4-one] *[501-30-4]* **M 142.1, m 152°, 154-155°, pK_1^{25} –1.38, pK_2^{25} 7.66.** Crystallise the acid from MeOH (charcoal) by adding Et_2O. It sublimes at 150-200°/0.1torr. [*Beilstein* **18** II 57, **18** III/IV 1145, **18/2** V 516.]

Kynurenic acid (4-hydroxyquinoline-2-carboxylic acid) *[492-27-3]* **M 189.1, m 282-283°, 285°, $pK_{Est(1)}$~2, $pK_{Est(2)}$~10.** Crystallise the acid from absolute EtOH. The *methyl ester* crystallises from MeOH with **m** 224-226°. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p2723 *1961*, *Beilstein* **22** II 174, **22** III/IV 2245, **22/6** V 280.]

L-Kynurenine *[343-65-7]* **M 208.2, m 190°(dec), 210°(dec), $[\alpha]_D^{20}$ -30° (c 0.4, H_2O), $pK_{Est(1)}$~2.3, $pK_{Est(2)}$~3.5, $pK_{Est(3)}$~9.2.** Crystallise it from H_2O or aqueous AcOH. The *picrate* has **m** 188.5-189°(dec) after crystallisation from H_2O. *(±)-Kynurenine* has **m** 218°. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p2726 *1961*, *Beilstein* **14** III 1657, **14** IV 2562.]

L-Kynurenine sulfate *[16055-80-4]* **M 306.3, m 194°, monohydrate m 178°, $[\alpha]_D^{25}$ +9.6° (H_2O).** Crystallise the sulfate from water by addition of EtOH. The *(±)-sulfate* has **m** 173°. [*Beilstein* **14** IV 2562.]

***dl- and l-*Laudanosine {1-[(3,4-dimethoxyphenyl)methyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-isoquinoline}** *[(±) 1699-51-0, (-) 2688-77-9]* **M 357.4, m 114-115°, 118°.** Crystallise these from EtOH. The *(±)-picrate* crystallises from EtOH with **m** 177-178°. The *(-)*-isomer has **m** 83-85° and $[\alpha]_D^{24}$ -110° (c 0.3, EtOH). The *hydrobromide tetrahydrate* [303136-74-5] **M** 436.3 has **m** 232-234°. [Frydman et al. *Tetrahedron* **4** 342 *1958*, Elliott *J Heterocycl Chem* **9** 853 *1972*, *Beilstein* **21** II 183, **21** III/IV 2704.]

Lumichrome (7,8-dimethylalloxazine) *[1086-80-2]* **M 242.2, m >290°, $pK_{Est(1)}$~-0.1 (basic), $pK_{Est(2)}$~9.9 (acidic).** Recrystallise lumichrome twice from glacial AcOH and dry it at 100° in a vacuum. [Cresswell & Wood *J Chem Soc* 4768 *1960*, *Beilstein* **26** III/IV 2538.]

Luminol (5-aminophthalazin-1,4-dione) *[521-31-3]* **M 177.2, m 329-332°, pK_1 3.37, pK_2 6.35.** Dissolve luminol in KOH solution, treat with Norit (charcoal), filter and precipitate it with conc HCl. [Hardy et al. *Talanta* **24** 297 *1977*.] Store it in the dark in an inert atmosphere, because its structure changes during its luminescence. It has been recrystallised from 0.1M KOH [Merenyi et al. *J Am Chem Soc* **108** 77716 *1986*]. [*Beilstein* **25** II 389, **25** III/IV 4192.]

***dl*-Lupinine (1-hydroxymethyloctahydroquinolizine, 1-hydroxymethylquinolizidine)** *[10248-30-3]* **M 169.3, m 57-58°, 59°, 107°/1mm, pK_{Est} ~7.0.** It crystallises from Me_2CO, pentane and petroleum ether (b. 40-60°) and can be sublimed or distilled in high vacuum. The *picrate* has **m** 127°(from Et_2O), the *picrolonate* has **m** 203-204°, and the *methiodide* has **m** 203°(dec, from EtOH). [Clemo et al. *J Chem Soc* 969 *1937*, Boekelheide & Lodge *J Am Chem Soc* **73** 3684 *1951*, *Beilstein* **21** II 28, **21** III/IV 291.]

Lutidine (mixture). For the preparation of pure 2,3-, 2,4- and 2,5-lutidine from commercial "2,4- and 2,5-lutidine" see Coulson et al. *J Chem Soc* 1934 *1959*, and Kyte, Jeffery and Vogel *J Chem Soc* 4454 *1960*.

2,3-Lutidine *[583-61-9]* **M 107.2, f -14.8°, b 160.6°, d_4^{20} 0.9464, n_D^{20} 1.50857, pK^{25} 6.57.** Steam distil it from a solution containing about 1.2 equivalents of 20% H_2SO_4, until *ca* 10% of the base has been carried over with the non-basic impurities. The acidic solution is then made alkaline, and the base is separated, dried over NaOH or BaO, and fractionally distilled. The distilled lutidine is converted to its urea complex by stirring 100g with 40g of urea in 75ml of H_2O, cooling to 5°, filtering at the pump, and washing with 75ml of H_2O. The complex, dissolved in 300ml of H_2O, is steam distilled until the distillate gives no turbidity with a little solid NaOH. The distillate is then treated with excess solid NaOH, and the upper layer is removed: the aqueous layer is then extracted with diethyl ether. The upper layer and the ether extract are combined, dried (K_2CO_3), and distilled through a short column. Final purification is by fractional crystallisation using partial freezing. The *picrate* crystallises from EtOH with **m** 187-188°. [Kyte et al. *J Chem Soc* 4454 *1960*, *Beilstein* **20** H 243, **20** II 159, **20** III/IV 2765, **20/6** V 15.]

2,4-Lutidine *[108-47-4]* **M 107.2, b 157.8°, d_4^{20} 0.9305, n_D^{20} 1.50087, n_D^{25} 1.4985, pK^{25} 6.77.** Dry it with Linde type 5A molecular sieves, BaO (***do not use Na, see picolines below***), and fractionally distil it. The distillate (200g) is heated with *benzene (500ml) and conc HCl (150ml) in a Dean and Stark apparatus on a water bath until water no longer separates, and the temperature just below the liquid reaches 80°. When cold, the supernatant *benzene is decanted, and the 2,4-lutidine hydrochloride, after washing with a little *benzene, is dissolved in water (350ml). After removing any *benzene by steam distillation, an aqueous solution of NaOH (80g) is added, and the free lutidine is steam distilled. It is isolated by saturating the distillate with solid NaOH and distilling it through a short column. The precipitation cycle is repeated, then the final distillate is partly frozen in an apparatus at -67.8-68.5° (cooled by acetone/CO_2). The crystals are collected, then melted and distilled. [Kyte et al. *J Chem Soc* 4454 *1960*.] *Alternative* purifications are *via* the *picrate* **m** 183-184° (from H_2O). [Clarke & Rothwell *J Chem Soc* 1885 *1960*], or the *hydrobromide* [Warnhoff *J Org Chem* **27** 4587 *1962*]. The latter is precipitated from a solution of lutidine in *benzene by passing dry HBr gas: the salt is recrystallised from $CHCl_3$/methyl ethyl ketone, then decomposed with NaOH, and the free base is extracted

into Et_2O, dried, evaporated and the residue is distilled. [*Beilstein* **20** II 180, **20** III/IV 2718, **20/6** V 19.]

2,5-Lutidine *[589-93-5]* **M 107.2, m -15.3°, b 156.7°/759mm, d_4^{20} 0.927, n_D^{25} 1.4982, pK^{25} 6.40.** Steam distil the lutidine from a solution containing 1-2 equivalents of 20% H_2SO_4 until about 10% of the base has been carried over with the non-basic impurities, then the acidic solution is made alkaline, and the base is separated, dried with NaOH and fractionally distilled twice. Dry the distillate with Na and fractionally distil it through a Todd column packed with glass helices. The *hydrochloride* has **m** 219°(dec), and the *picrate* has **m** 170.5° (from EtOH or H_2O). [*Beilstein* **20** H 244, **20** II 160, **20** III/IV 2774, **20/6** V 27.]

2,6-Lutidine *[108-48-5]* **M 107.2, m -59°, b 144.0°, d_4^{20} 0.92257, n_D^{20} 1.49779, pK^{25} 6.72.** Likely contaminants include 3- and 4-picoline (similar boiling points). However, they are removed by using BF_3, with which they react preferentially, by adding 4ml of BF_3 to 100ml of dry fractionally distilled 2,6-lutidine and redistilling. Distillation of commercial material from $AlCl_3$ (14g per 100ml) can also be used to remove picolines (and water). *Alternatively*, lutidine (100m) can be refluxed with ethyl benzenesulfonate (20g) or ethyl *p*-toluenesulfonate (20g) for 1 hour, then the upper layer is cooled, separated and distilled. The distillate is refluxed with BaO or CaH_2, then fractionally distilled through a glass helices-packed column.
2,6-Lutidine can be dried with KOH (do not use Na, see picolines below) or by refluxing with (and distilling from) BaO, prior to distillation. For purification *via* its *picrate*, 2,6-lutidine, dissolved in absolute EtOH, is treated with an excess of warm ethanolic picric acid. The precipitate is filtered off, recrystallised from acetone (to give **m** 163-164.5° (166-167°), and partitioned between ammonia and $CHCl_3$/diethyl ether. The organic layer, after washing with dilute aqueous KOH, is dried with Na_2SO_4 and fractionally distilled. [Warnhoff *J Org Chem* **27** 4587 *1962*.] *Alternatively*, 2,6-lutidine can be purified *via* its urea complex, as described under 2,3-lutidine. Other purification procedures include azeotropic distillation with phenol [Coulson et al. *J Appl Chem (London)* **2** 71 *1952*], fractional crystallisation by partial freezing, and vapour-phase chromatography using a 180-cm column of polyethylene glycol-400 (Shell, 5%) on Embacel (May and Baker) at 100°, with argon as carrier gas [Bamford & Block *J Chem Soc* 4989 *1961*]. The *hydrochloride* has **m** 235-237°, 239° (from EtOH). [*Beilstein* **20** II 160, **20** III/IV 2776, **20/6** V 32.]

3,5-Lutidine *[591-22-0]* **M 107.2, f -6.3°, b 172.0°/767mm, d_4^{20} 0.9419, n_D^{20} 1.50613, n_D^{25} 1.5035, pK^{25} 6.15.** Dry 3,5-lutidine with CaH_2 and fractionally distil it through a Todd column packed with glass helices. Dissolve (100ml) in dilute HCl (1:4) and steam distil this until 1L of distillate is collected. Excess conc NaOH is added to the residue which is again steam distilled. The base is extracted from the distillate, using diethyl ether. The extract is dried over K_2CO_3, and distilled. It is then fractionally crystallised by partial freezing. The *hydrochloride* has **m** 229°(sublimes at 190-231°), and the *picrate* has **m** 242-243°(dec, from H_2O), 249-250°(dec, from AcOH). [*Beilstein* **20** II 161, **20** III/IV 2788, **20/6** V 60.]

Lycorine *[476-28-8]* **M 552.9, m 275-280°(dec), b 175-185°/0.002mm. $[\alpha]_D^{20}$ -91° (c 0.16, EtOH), pK^{25} 6.9 (30% aqueous dimethylformamide).** It crystallises as orange crystals from MeOH (**m** 281-283°), $CHCl_3$/EtOH (**m** 272-274°), pyridine or from EtOH (**m** 277° dec). It has been distilled under high vacuum. The *hydrochloride* has **m** 288° (from MeOH/HCl), and the *picrate* has **m** 196-197°(from EtOH), [Cook et al. *J Chem Soc* 4176 *1954*, Martin & Tu *J Org Chem* **46** 3763 *1981*, *Beilstein* **27** II 547, **27** III/IV 6463.]

(+)-Lysergic acid *[82-58-6]* **M 268.3, m 240°(dec), $[\alpha]_D^{20}$ +40° (pyridine), pK_1^{25} 3.32, pK_2^{25} 8.66, pK^{20} 8.50, pK^{40} 8.27.** It crystallises from water as a *hydrate*. The *methyl ester* crystallises from $*C_6H_6$ and has **m** 168°; the *amide* [478-94-4] has **m** 242°(dec) (from MeOH) and $[\alpha]_{546}$ +15° (c 0.5, pyridine). The *(-)-hydrochloride* has **m** 208-210°(dec, from MeOH). [Kornfeld et al. *J Am Chem Soc* **76** 5256 *1954*, Kornfeld et al. *J Am Chem Soc* **78** 3087 *1956*, *Beilstein* **25** III/IV 934.]

Maltol (3-hydroxy-2-methyl-4-pyrone) *[118-71-8]* **M 126.1, m 161-162°, 162-162.5°.** It crystallises from $CHCl_3$, toluene, aqueous 50% EtOH or H_2O, and is volatile in steam. It can be readily sublimed in a vacuum. It forms a Cu^{2+} complex. [*Beilstein* **17** III/IV 5916, **18/1** V 114.]

Meconic acid (3-hydroxy-γ-pyrone-2,6-dicarboxylic acid) *[497-59-6]* **M 200.1, m 100° (loses H_2O), pK_1^{25}**

1.83, pK_2^{25} 2.3, pK_3^{20} 10.10. Crystallise the acid from water (0.25g/ml) and dry it at 100° for 20 minutes to dehydrate the *mono* or *dihydrate*. It decarboxylates above 120° or in boiling H_2O. It is soluble in MeOH (2%), EtOAc (2%) and Me_2CO (1%). The *picrate* has **m** 206.5-208.5°(dec, from H_2O). [Wibaut & Kleinpool *Rec Trav Chim Pays Bas* **66** 24 *1947*, *Beilstein* **18** H 409, **18** I 523, **18** II 367, **18** III/IV 6136.]

Melamine (2,4,6-triamino-1,3,5-triazine) *[108-78-1]* **M 126.1, m 353°, pK^{25} 5.00.** Crystallise Melamine from water or dilute aqueous NaOH. It sublimes at ~240° on prolonged heating. [*Beilstein* **26** I 74, **26** II 132, **26** III/IV 1253.]

(±)-Mellein [(±)-3,4-dihydro-8-hydroxy-3-methyl-2-benzopyran-1-one, 8-hydroxy-3-methylisochroman-1-one] *[1200-93-7]* **M 178.2, m 37-39°, 39°, pK_{Est} ~9.5.** Purify it by recrystallisation from H_2O or aqueous EtOH. It has UV with λ_{max} at 247 and 314nm. [Arakawa et al. *Justus Liebigs Ann Chem* **728** 152 *1969*, Blair & Newbold *Chem Ind (London)* 93 *1955*, *J Chem Soc* 2871 *1955*.] The *methyl ether* has **m** 66-67° and UV with λ_{max} at 242nm (ε 7,400) and 305nm (ε 4,600). *R*(-)-*Mellein* has **m** 56°(aqueous Me_2CO), $[\alpha]_D^{25}$ -102.5° (c 1, $CHCl_3$) and *R*(+)-*mellein* has **m** 56-57°(hexane), $[\alpha]_D^{25}$ +102° (c 1, $CHCl_3$) or $[\alpha]_D^{25}$ +88° (c 1, MeOH). [*Beilstein* **18** III/IV 188, **18/1** V 274.]

2-Mercaptobenzimidazole *[583-39-1]* **M 150.2, m 302-304°, 312°, pK^{20} 10.24.** Crystallise it from aqueous EtOH, AcOH or aqueous ammonia. It complexes with many metals. [Brown *J Chem Soc* 1976 *1958*, *Beilstein* **24** II 65, **24** III/IV 287.]

2-Mercaptobenzothiazole *[149-30-4]* **M 167.2, m 182°, pK^{25} 7.5 (50% aqueous AcOH).** Crystallise it repeatedly from 95% EtOH, or purify it by incomplete precipitation by dilute H_2SO_4 from a basic solution, followed by several crystallisations from acetone/H_2O or *benzene. It complexes with Ag, Au, Bi, Cd, Hg, Ir, Pt, and Tl. [*Beilstein* **27** II 233, **27** III/IV 2709.]

2-Mercaptoimidazole *[872-35-5]* **M 100.1, m 221-222°, 226-228°(monohydrate), pK_1^{20} -1.6, pK_2^{20} 11.6.** Crystallise 2-mercaptoimidazole from Me_2CO or H_2O. Its UV has λ_{max} at 208 and 252nm (H_2O). [Fox et al. *J Am Chem Soc* **67** 496 *1947*, *Beilstein* **24** II 7, **24** III/IV 61.]

2-Mercapto-1-methylimidazole *[60-56-0]* **M 114.2, m 145-147°, 146-148°, pK_1^{20} -2.0, pK_2^{20} 11.9.** Crystallise it from EtOH. Its UV has λ_{max} at 251nm (H_2O), 260nm (EtOH) and 267nm ($CHCl_3$). [Lawson & Morley *J Chem Soc* 1103 *1956*, *Beilstein* **24** H 17, **24** III/IV 61.]

6-Mercaptopurine monohydrate *[6112-76-1]* **M 170.2, m 314-315°(dec), ~315°(dec), 313-315°(dec), pK_1^{20} 0.5, pK_2^{20} 7.77, pK_3^{20} 10.84.** Crystallise 6-mercaptopurine from pyridine (30ml/g), wash it with pyridine, then triturate with water (25ml/g) and adjust to pH 5 by adding M HCl. Recrystallise it by heating, then cooling, the solution. Filter off the solid, wash it with water and dry it at 110°. It has also been crystallised from water (charcoal) as yellow crystals of the *monohydrate* which become *anhydrous* on drying at 140°. It has UV with λ_{max} at 230 and 312nm (ε 14,000 and 19,600) in 0.1N NaOH; 222 and 327nm (ε 9,2400 and 21,300), and 216 and 329nm (ε 8,740 and 19,300) in MeOH. It forms a 1:1 complex with Zn^{2+}, Pb^{2+}, Co^{2+}, and Ni^{2+} in aqueous dioxan. It is an antineoplastic. [Albert & Brown *J Chem Soc* 2060 *1954*, IR: Brown & Mason *J Chem Soc* 682 *1957*, UV: Fox et al. *J Am Chem Soc* **80** 1669 *1958*, UV: Mason *J Chem Soc* 2071 *1954*, *Beilstein* **26** III/IV 2097.]

8-Mercaptoquinoline ($2H_2O$, thioxine) *[491-33-8]* **M 197.3, m 58-59°, pK_1^{25} 2.0, pK_2^{25} 8.40.** Thioxine readily oxidises in air to give diquinolyl-8,8'-disulfide (which is stable). It is more convenient to make 8-mercaptoquinoline by reduction of the disulfide. [Nakamura & Sekido *Talanta* **17** 515 *1970*.] The *hydrochloride* (see thiooxine hydrochloride below) is more stable. [*Beilstein* **21** III/IV 1197, **21/3** V 30.]

3-Methoxycarbonyl-2,5-dihydrothiophen-1,1-dioxide (methyl 3-sulfolene-3-carboxylate) *[67488-50-0]* **M 176.1, m 57-58°, 60-62°.** If the IR shows OH bands, then dissolve the dioxide in $CHCl_2$, wash it with aqueous Na_2CO_3 and H_2O, dry it over $MgSO_4$, filter, evaporate and wash the residue with cold Et_2O and dry *in vacuo*. Its ^{1}HNMR ($CDCl_3$) has δ at 7.00 (m 1H), 3.98 (bs 4H) and 3.80 (s Me). [McIntoch & Sieber *J Org Chem* **43**

4431 *1978*, *Beilstein* **18/6** V 5.]

5-Methoxyindole *[1006-94-6]* **M 147.2, m 55°, 57°, b 176-178°/17mm, pK_{Est} ~0.** Crystallise 5-methoxyindole from cyclohexane petroleum ether or petroleum ether/Et_2O. [Saito & Kikugawa *J Heterocycl Chem* **16** 1325 *1979*, *Beilstein* **21** III/IV 765, **21/3** V 18.]

5-(*p*-Methoxyphenyl)-1,2-dithiole-3-thione *[42766-10-9]* **M 240.2, m 111°.** Crystallise the thione from EtOAc, BuOAc or EtOH. It sublimes at 90°/0.001mm and complexes with Sb^{3+}, Sb^{5+}, Bi^{3+}, Sn^{4+}, Ag^{+}, Au^{3+} and Hg^{2+}. [*Beilstein* **19** III/IV 2538.]

8-Methoxypsoralen (Methoxsalen) See xanthotoxin in "Miscellaneous Compounds" in Chapter 7.

6-Methylaminopurine *[443-72-1]* **M 149.2, m >300°, 312-314° (dec), pK_1^{20} <1, pK_2^{20} 4.15, pK_3^{20} 10.02.** The purine is best purified by recrystallising 2g from 50ml of H_2O and 1.2g of charcoal. [UV: Albert & Brown *J Chem Soc* 2060 *1954*; UV: Mason *J Chem Soc* 2071 *1954*; see also Elion et al. *J Am Chem Soc* **74** 411 *1952*.] The *picrate* has **m** 265°(257°) [Bredereck et al. *Chem Ber* **81** 307 *1948*]. [*Beilstein* **26** III/IV 3565.]

Methyl 3-aminopyrazine-2-carboxylate *[16298-03-6]* **M 153.1, m 169-172°, 172°.** The ester forms yellow needles from H_2O (100 parts using charcoal). If it contains the free acid (see IR), then dissolve it in CH_2Cl_2, wash it with saturated aqueous Na_2CO_3, brine, dry over $MgSO_4$ filter, evaporate and recrystallise the residue. The *free acid* has **m** 203-204° (dec) [UV: Brown & Mason *J Chem Soc* 3443 *1956*] with pK_1 <1 and pK_2 3.70. The *ammonium salt* has **m** 232°(dec) (from aqueous Me_2CO) and the *amide* has **m** 239.2° (from H_2O) [Ellingson et al. *J Am Chem Soc* **67** 1711 *1945*]. [*Beilstein* **25** III/IV 4412.]

9-Methylcarbazole (*N*-methylcarbazole) *[1484-12-4]* **M 181.2, m 87°, 89°.** Purify *N*-methylcarbazole by chromatography on silica gel and eluting with $CHCl_3/Me_2CO/Et_2O$ (100:5:1 v/v), or by flash chromatography using petroleum ether, or by zone melting followed by recrystallisation from petroleum ether or EtOH. [Flo & Pindus *Annalen* 509 *1987*, Kashima et al. *J Heterocycl Chem* **24** 913 *1987*, UV: Armarego *Physical Methods in Heterocyclic Chemistry* (Ed Katritzky, Academic Press) **Vol III** 158 *1971*, *Beilstein* **20** H 436.]

5-Methylcytosine [4-amino-5-methylpyrimidin-2(1*H*)-one] *[554-01-8]* **M 125.1, m 270°(dec), pK_1 4.6, pK_2 12.4.** Crystallise it from water (solubility is 3.4%). The *hydrochloride* has **m** 299-301° (sintering at 280°) (from aqueous HCl/Me_2CO). [Hitchings et al. *J Biol Chem* **177** 537 *1949*, Cohn *J Am Chem Soc* **73** 1539 *1951*, *Beilstein* **25** II 183, **25** III/IV 3727.]

2-Methyl-1,3-dithiane *[6007-26-7]* **M 134.3, b 53-54°/1.1mm, 66°/5mm, 79-80°/8-10mm, 85°/12mm, d_4^{20} 1.121, n_D^{20} 1.560.** Wash the dithiane with H_2O, 2.5 M aqueous NaOH, H_2O, brine, dry over K_2CO_3 (use toluene as solvent if the volume of reagent is small), filter, evaporate and distil the colourless residue. Its IR film has ν_{max} at 1455, 1371 and 1060 (all medium and CH_3), 1451m, 1422s, 1412m, 1275m, 1236m, 1190m, 1171w, 918m and 866w (all dithiane) cm^{-1} [Corey & Erickson *J Org Chem* **36** 3553 *1971*, Seebach & Corey *J Org Chem* **40** 231 *1975*]. [*Beilstein* **19** III/IV 49, **19/1** V 53.]

Methylene Blue [3,7-bis-(dimethylamino)phenothiazin-5-ium chloride *[61-73-4]* **M 319.9, CI 52015, ε_{654} 94,000 (EtOH), ε_{664} 81,000 (H_2O), pK^{25} 3.8.** Crystallise the chloride from 0.1M HCl (16ml/g), the crystals are separated by centrifugation, washed with chilled EtOH and diethyl ether, and dried under vacuum. Crystallise it from 50% aqueous EtOH, wash it with absolute EtOH, and dry it at 50-55° for 24 hours. It has also been crystallised from *benzene/MeOH (3:1). It has been salted out with NaCl from a commercial concentrated aqueous solution, then crystallised from water, and dried at 100° in an oven for 8-10 hours. [*Beilstein* **27** III/IV 5152.]

Methylene Green [3,7-bis-(dimethylamino)-4-nitrophenothiazin-5-ium chloride] *[2679-01-8]* **M 364.9, m >200°(dec), CI 52020, pK^{25} 3.2.** Crystallise the dye three times from water (18ml/g). [*Beilstein* **27** H 399.] The *$ZnCl_2$ double salt* [6722-15-2] **M** 866.0 has the same **CI**. [*Beilstein* **27** III/IV 5157.]

2-Methylene-oxetan-2-one (diketene) *[674-82-8]* **M 84.1, m -7°, b 41°/50.5mm, 66-68°/90mm, 127°/760mm, d_4^{20} 1.440, n_D^{20} 1.4376, n^{25} 1.4348.** Diketene polymerises violently in the presence of alkali. Distil it under reduced pressure, then fractionally crystallise it by partial freezing (using as a cooling bath made from a 1:1 solution of $Na_2S_2O_3$ in water, cool with Dry-ice until slushy, and store it in a Dewar flask). Freezing proceeds slowly, and takes about a day for half completion. The crystals are separated and stored in a refrigerator under N_2. [Miller & Carlson *J Am Chem Soc* **79** 3995 *1957*, Andreades & Carlson *Org Synth* Coll Vol **V** 679 *1973*, *Beilstein* **7** H 552, **7** I 309, **7** II 525, **1** III 2947, **17** III/IV 4297, **17/9** V 115.] See ketene [463-51-4] in "Aliphatic Compounds", in this Chapter.

2-Methylfuran (Silvan) *[534-22-5]* **M 82.1, f –90.19°, b 62.7-62.8°/731mm, d_4^{20} 0.917, n_D^{20} 1.436.** Wash it with acidified saturated ferrous sulfate solution (to remove peroxides), separate, dry with $CaSO_4$ or $CaCl_2$, and fractionally distil it from KOH immediately before use. To reduce the possibility of spontaneous polymerisation, addition of about one-third of its volume of heavy mineral oil to 2-methylfuran prior to distillation has been recommended. [*Beilstein* **17** H 36, **17** I 18, **17** II 39, **17** III/IV 265.]

1-Methylguanine *[938-85-2]* **M 165.2, m >300°(dec), pK_1^{20} ~0, pK_2^{20} 3.13, pK_3^{20} 10.54.** Crystallise it from H_2O or 50% aqueous acetic acid. [*Beilstein* **26** III/IV 3892.]

7-Methylguanine *[578-76-7]* **M 165.2, pK_1^{20} ~0, pK_2^{20} 3.50, pK_3^{20} 9.95.** Crystallise it from water. It has UV with λ_{max} at 280nm (pH 2.1). The *picrate* has **m** 267° (270-272° dec, also reported). [*Beilstein* **26** H 455, **26** I 134, **26** II 263, **26** III/IV 3890.]

***N*-Methylimidazole** *[616-47-7]* **M 82.1, b 81-84°/27mm, 197-198°/760mm, d_4^{20} 1.032, n_D^{20} 1.496, pK^{25} 7.25.** Dry it with sodium metal and then distil it. Store it at 0° under dry argon. The *picrate* has **m** 159.5-160.5° (from H_2O). [*Beilstein* **23** III/IV 568.]

2-Methylimidazole (2-methylglyoxaline) *[693-98-1]* **M 82.1, m 140-141°, 144.5-145.5°, b 267°/760mm, pK^{25} 7.86.** Recrystallise 2-methylimidazole from *benzene or petroleum ether. The *picrate* has **m** 215° (from H_2O). [*Beilstein* **23** III/IV 594, **23/5** V 35.]

4-Methylimidazole *[822-36-6]* **M 82.1, m 47-48°, b 263°/760mm, pK^{25} 7.61.** Recrystallise 4-methylimidazole from *benzene or petroleum ether. It has **m** 56° after sublimation. The *picrate* has **m** 162-163.5° (from EtOH). [*Beilstein* **23** II 60, **23** III/IV 597, **23/5** V 89.]

2-Methylindole *[95-20-5]* **M 131.2, m 61°, pK^{25} -0.28 (C-3 protonation, aqueous H_2SO_4).** Crystallise it from *benzene. It has also been purified by zone melting. The *picrate* has **m** 139° (from Et_2O or Et_2O/MeOH). [Cohen et al. *J Am Chem Soc* **82** 2184 *1960*, *Beilstein* **20** III/IV 3202, **20/7** V 59.]

3-Methylindole (skatole) *[83-34-1]* **M 131.2, m 95°, pK^{25} -4.55 (C-3-protonation, aqueous H_2SO_4).** Crystallise skatole from *benzene or petroleum ether (**m** 96.5°). It has also been purified by zone melting. The *picrate* has **m** 182° (from Et_2O or Et_2O/MeOH). [*Beilstein* **20** III/IV 3206, **20/7** V 69.]

***N*-Methylmorpholine (4-methylmorpholine)** *[109-02-4]* **M 101.2, b 116-117°/764mm, d_4^{20} 0.919, n_D^{20} 1.436, pK^{25} 7.41.** Dry it by refluxing with BaO or sodium, then fractionally distil it through a helices-packed column. The *picrate* has **m** 227°, the *thiocyanate salt* has **m** 103° (from butanone). [Hall *J Phys Chem* **60** 63 *1956*, *Beilstein* **27** I 203, **27** III/IV 22.]

4-Methylmorpholine-4-oxide monohydrate *[7529-22-8]* **M 135.2, m 71-73°.** When the oxide is dried for 2-3 hours at high vacuum, it dehydrates. Add MeOH to the oxide and distil off the solvent under vacuum until the temperature is *ca* 95°. Then add Me_2CO at reflux and cool to 20°. The crystals are filtered off, washed with Me_2CO and dried. The degree of hydration may vary and may be important for the desired reactions. [van Rheenan et al. *Tetrahedron Lett* 1973 1076, Schneider & Hanze *US Pat 2 769 823*; see also Sharpless et al. *Tetrahedron Lett* 2503 *1976*.]

3-Methyl-2-oxazolidone *[19836-78-3]* **M 101.1, m 15°, b 88-91°/1mm, d_4^{20} 1.172, n_D^{20} 1.455.** Purify the oxazolidone by successive fractional freezing, then dry it in a dry-box over 4A molecular sieves for 2 days. Distil it under high vacuum and store it dry as before. [*Beilstein* **27** III/IV 2517.]

3-Methyl-3-oxetanemethanol (3-hydroxymethyl-3-methyloxetane) *[3143-02-0]* **M 102.1, b 80°/4mm, 92-93°/12mm, d_4^{20} 1.033, n_D^{25} 1.4449.** Purify the oxetane by fractionation through a glass column [Pattison *J Am Chem Soc* **79** 3455 *1957*, Corey et al. *J Am Chem Soc* **106** 2736 *1984*]. [*Beilstein* **17** III/IV 1128.]

5-Methyl-1,10-phenanthroline *[3002-78-6]* **M 194.2, m 67°(monohydrate), 113°(anhydrous), pK^{25} 5.28.** Crystallise it from *benzene/petroleum ether or from H_2O as the monohydrate. It complexes with many metals. [*Beilstein* **23** III/IV 1714.]

5-Methylphenazinium methyl sulfate *[299-11-6]* **M 306.3, m 155-157° (198°dec by rapid heating), pK^{25} –3.5.** It forms yellow-brown prisms from EtOH (charcoal), or EtOH/Et_2O. Its solubility in H_2O at 20° is 10%. In the presence of aqueous KI it forms a *semiquinone* which crystallises as blue leaflets from EtOH. [Wieland & Roseen *Chem Ber* **48** 1117 *1913*, Voriskova *Col Czech Chem Commun 12* 607 *1947*, Bülow *Chem Ber* **57** 1431 *1924*, Campbell et al. *J Chem Soc* 404 1938, Morley *J Chem Soc* 4008 *1952*, *Beilstein* **23** I 59, **23** II 234, **23** III/IV 1658, **23/8** V 395.]

***N*-Methylphenothiazine (10-methylphenothiazine)** *[1207-72-3]* **M 213.2, α-form m 99.3°, 100-102°, and b 360-365°, β-form m 78-79°.** Recrystallise it (three times) from EtOH to give the α-form (prisms). Recrystallisation from EtOH/*benzene gives the β-form (needles). It has also been purified by vacuum sublimation and is carefully dried in a vacuum line. It has been crystallised from toluene or MeOH and stored in the dark [Guarr et al. *J Am Chem Soc* **107** 5104 *1985*, Olmsted et al. *J Am Chem Soc* **109** 3297 *1987*]. Its solubility in H_2O (pH 6.5) is 0.0544mg/100ml, and in hexane it is 2083mg/100ml. Its UV has λ_{max} at 255nm (logε 4.60) (pH 6.3) and 255nm in hexane. [Cymerman-Craig & Warburton *Aust J Chem* **9** 294 *1956*, *Beilstein* **27** II 33, **27** III/IV 1215.]

3-Methyl-1-phenyl-5-pyrazolone *[89-25-8]* **M 174.2, m 127°, 129°, pK^{25} 2.7.** Crystallise the pyrazolone from hot H_2O, EtOH or EtOH/water (1:1). It complexes with metals. [Veibel et al. *Acta Chim Scand* **6** 1066 *1952*, *Beilstein* **24** II 9, **24** III/IV 71.]

1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine hydrochloride (MPTP) *[23007-85-4]* **M 209.7, m 196-198°, pK_{Est} ~9.3, pK_a 8.07 (50% aqueous EtOH).** Purify MPTP by recrystallisation from Me_2CO/isoPrOH. The *free base* has **m** 40-42° (from heptane), **b** 99-100°/1.3mm, 128-132°/12mm, (137-142°/0.8mm), n_D^{25}1.5347. The *hydrochloride* has **m** 251-252° (from Me_2CO/isoPrOH) [Schmidle & Mansfield *J Am Chem Soc* **78** 425 *1956*, Defeudis *Drug Dev Res* **15** 1 *1988*, *Beilstein* **20** III/IV 3240, **20/7** V 121.]

(±)-2-Methylpiperazine *[109-07-9]* **M 100.2, m 61-62°, 66°, b 147-150°/739mm, pK_1^{25} 5.46, pK_2^{25} 9.90.** Purify it by zone melting and by distillation. It is *hygroscopic*. The *picrate* has **m** 275-276°. [*Beilstein* **23** II 16, **23** III/IV 393, **23/3** V 267.]

(±)-3-Methylpiperidine *[626-56-2]* **M 99.2, b 125°/763mm, d_4^{20} 0.846, n_D^{25} 1.4448, pK^{25} 10.92.** Purify it *via* the *hydrochloride* (**m** 172°). The *hydrobromide* has **m** 162-163° (from iso-PrOH). [Chapman et al. *J Chem Soc* 1925 *1959*, *Beilstein* **20** III/IV 1499, **20/4** V 100.]

4-Methylpiperidine *[626-58-4]* **M 99.2, b 124.4°/755mm, d_4^{20} 0.839, n_D^{25} 1.4430, pK^{25} 10.78.** Purify it *via* the *hydrochloride* (**m** 189°). It is freed from 3-methylpyridine by zone melting. The *hydrobromide* has **m** 173° (from butanone/*C_6H_6). [*Beilstein* **20** III/IV 1511, **20/4** V 116.]

1-Methyl-4-piperidone *[1445-73-4]* **M 113.2, b 53-56°/0.5mm, 54-56°/9mm, 68-71°/17mm, 85-87°/45mm, d_4^{20} 0.972, n_D^{25} 1.4588, pK^{25} 7.9.** It is best purified by fractional distillation The *hydrochloride* of the hydrate (4-diol) has **m** 94.7-95.5°, but the anhydrous *hydrochloride* which crystallises from $CHCl_3$/Et_2O has **m** 165-168° (164-167°), and can also be obtained by sublimation at 120°/2mm. The *oxime* has **m** 130-132° (from

Me_2CO). The *methiodide* crystallises from MeOH, the crystals with 1MeOH have **m** 189-190°, and the solvent-free *iodide* has **m** 202-204°(dec). [Lyle et al. *J Org Chem* **24** 342 *1959*, Bowden & Greeen *J Chem Soc* 1164 *1952*, Tomita *Yakugaku Zasshi (J Pharm Soc Japan)* **71** 1053 *1951*, *Beilstein* **21** IIII/IV 3183, **21/6** V 419.]

2-Methylpyrazine *[109-08-0]* **M 94.1, f –28.8°, b 136-137°, d $_4^{20}$ 1.025, n $_D^{20}$ 1.505, pK$_1^{25}$ -5.25 (aqueous H_2SO_4), pK$_2^{25}$ 1.47.** Purify it *via* the picrate and distil the *free base.* The *picrate* has **m** 133-134°(from EtOH). [Wiggins & Wise *J Chem Soc* 4780 *1956*, *Beilstein* **23** III/IV 911, **23/5** V 386.]

2-Methylpyridine (2-picoline) *[109-06-8]* **M 93.1, b 129.4°, d $_4^{20}$ 0.9444, n $_D^{20}$ 1.50102, pK^{25} 5.96.** Biddiscombe and Handley [*J Chem Soc* 1957 *1954*] steam distilled a boiling solution of the base in 1.2 equivalents of 20% H_2SO_4 until about 10% of the base had been carried over, along with non-basic impurities. Excess aqueous NaOH is then added to the residue, the free base is separated, dried with solid NaOH and fractionally distilled.
2-Methylpyridine can also be dried with BaO, CaO, CaH_2, $LiAlH_4$, or Linde type 5A molecular sieves. An alternative purification is *via* the $ZnCl_2$ adduct, which is formed by adding 2-methylpyridine (90ml) to a solution of anhydrous $ZnCl_2$ (168g) and 42ml conc HCl in absolute EtOH (200ml). Crystals of the complex are filtered off, recrystallised twice from absolute EtOH (to give **m** 118.5-119.5°), and the free base is liberated by addition of excess aqueous NaOH. It is steam distilled, and solid NaOH is added to the distillate to form two layers, the upper one of which is then dried with KOH pellets, stored for several days with BaO and fractionally distilled. Instead of $ZnCl_2$, $HgCl_2$ (430g in 2.4L of hot water) can be used. The complex, which separates on cooling, can be dried at 110° and recrystallised from 1% HCl (to **m** 156-157°). *The alkali metals, Na, Li or Cs should NOT be used for drying pyridine, and pyridine derivatives, as they form coloured pyridine radical anions leading to bipyridyls.* [see Schmulback et al. *J Am Chem Soc* **90** 6600 *1968*].
The *hydrochloride* has **m** 78-79°, and the *picrate* has **m** 165.5°(from EtOH) and 180°(from H_2O). [*Beilstein* **20** III/IV 2679, **20/5** V 464.]

3-Methylpyridine (3-picoline) *[108-99-6]* **M 93.1, m -18.5°, b 144°/767mm, d $_4^{20}$ 0.957, n $_D^{20}$ 1.5069, pK^{25} 5.70.** In general, the same methods of purification that are described for *2-methylpyridine* can be used. However, 3-methylpyridine often contains 4-methylpyridine and 2,6-lutidine, neither of which can be removed satisfactorily by drying and fractionation, or by using the $ZnCl_2$ complex. Biddiscombe and Handley [*J Chem Soc* 1957 *1954*], after steam distillation as for *2-methylpyridine*, treated the residue with urea to remove 2,6-lutidine, then azeotropically distilled with acetic acid (the azeotrope had **b** 114.5°/712mm), and recovered the base by adding excess of aqueous 30% NaOH, drying with solid NaOH and carefully fractionally distilling. The distillate is then fractionally crystallised by slow partial freezing. An alternative treatment [Reithoff et al. *Ind Eng Chem (Anal Edn)* **18** 458 *1946*] is to reflux the crude base (500ml) for 20-24 hours with a mixture of acetic anhydride (125g) and phthalic anhydride (125g) followed by distillation until phthalic anhydride begins to pass over. The distillate is treated with NaOH (250g in 1.5L of water) and then steam distilled. Addition of solid NaOH (250g) to this distillate (*ca* 2L) led to the separation of 3-methylpyridine which is removed, dried (K_2CO_3, then BaO) and fractionally distilled. (Subsequent fractional freezing would probably be advantageous.) *The alkali metals, Na, Li or Cs should NOT be used for drying pyridine, and pyridine derivatives, as they form coloured pyridine radical anions leading to bipyridyls.* [see Schmulback et al. *J Am Chem Soc* **90** 6600 *1968*]. The *hydrochloride* has **m** 85°, and the *picrate* has **m** 153°(from Me_2CO, EtOH or H_2O). [*Beilstein* **20** III/IV 2710, **20/5** V 506.]

4-Methylpyridine (4-picoline) *[108-89-4]* **M 93.1, m 4.25°, b 145.0°/765mm, d $_4^{20}$ 0.955, n $_D^{20}$ 1.5058, pK^{25} 4.99.** It can be purified as for *2-methylpyridine*. Biddescombe and Handley's method (above) for 3-methylpyridine is also applicable. Lidstone [*J Chem Soc* 242 *1940*] purified it *via* the *oxalate* (**m** 137-138°) by heating 100ml of 4-methylpyridine to 80° and adding slowly110g of anhydrous oxalic acid, followed by 150ml of boiling EtOH. After cooling and filtering, the precipitate is washed with a little EtOH, then recrystallised from EtOH, dissolved in the minimum quantity of water and distilled with excess 50% KOH. The distillate is dried with solid KOH and again distilled. Hydrocarbons can be removed from 4-methylpyridine by converting the latter to its hydrochloride, crystallising from EtOH/diethyl ether, regenerating the free base by adding alkali and distilling. As a final purification step, 4-methylpyridine can be fractionally crystallised by partial freezing

to effect a separation from 3-methylpyridine. Contamination with 2,6-lutidine is detected by its strong absorption at 270nm. *The alkali metals, Na, Li or Cs should NOT be used for drying pyridine, and pyridine derivatives, as they form coloured pyridine radical anions leading to bipyridyls.* [see Schmulback et al. *J Am Chem Soc* **90** 6600 *1968*]. The *hydrochloride* has **m** 161°, and the *picrate* has **m** 167°(from Me_2CO, EtOH or H_2O). [*Beilstein* **20** III/IV 2732, **20/5** V 543.]

2-Methylpyridin-5-yl trifluoromethanesulfonate (2-methyl-5-pyridine triflate) *[111770-91-3]* **M 241.2, b 80-82°/1.9mm, d_4^{25} 1.412, n_D^{20} 1.442.** Distil the triflate under vacuum, or if it is discoloured dissolve it in CH_2Cl_2, wash it with N NaOH and half saturated K_2CO_3, dry it over solid K_2CO_3, filter, evaporate, and distil by bulb-to-bulb distillation at 65-70°/0.1mm, then redistil *in vacuo*. Its ^{1}H NMR [$(CD_3)_2SO$] has δ at 2.50 (s, 3H, Me), 7.45 (d, *J* = 9.2 Hz, 1H), 7.90 (dd, *J* = 9.2, 2.3 Hz, 1H) and 8.60 (d, *J* = 2.3 Hz, 1H). [Tilley & Zawoiski *J Org Chem* **53** 386 *1988,* Ellingboe et al. *J Med Chem* **37** 542 *1994*.] When stirred with *m*-chloroperbenzoic acid in CH_2Cl_2 (16 hours, 25°), filtered, concentrated and purified by flash chromatography (2% MeOH/ CH_2Cl_2), the triflate gave colourless crystals of the *triflate N-oxide* **m 47-48°** with ^{1}H NMR [$(CD_3)_2SO$] with δ at 2.36 (s, 3H, Me), 7.56 (dd, *J* = 8.9, 2.3 Hz, 1H), 7.69 (d, *J* = 8.9 Hz, 1H) and 8.84 (d, *J* = 2.3 Hz, 1H)*,* Ellingboe et al. *J Med Chem* **37** 542 *1994*].

***N*-Methylpyrrole** *[96-54-8]* **M 81.1, b 115-116°/756mm, d_4^{20} 0.908, n_D^{20} 1.487, pK^{25} -3.4 (-2.90).** Dry *N*-methylpyrrole with $CaSO_4$, then fractionally distil it from KOH immediately before use. [*Beilstein* **20** III/IV 2080, **20/5** V 8.]

1-Methyl-2-pyrrolidinone (1-methyl-2-pyrrolidone) *[872-50-4]* **M 99.1, f -24.4, b 65-76°/1mm, 78-79°/12mm, 94-96°/20mm, 202°/760mm, d_4^{20} 1.0328, n_D^{20} 1.4678, pK^{25} -0.17 (also -0.92, and 0.2).** Dry the pyrrolidone by removing water as the *benzene azeotrope. Fractionally distil at 10 torr through a 100-cm column packed with glass helices. [Adelman *J Org Chem* **29** 1837 *1964*, McElvain & Vozza *J Am Chem Soc* **71** 896 *1949*.] The *hydrochloride* has **m** 86-88° (from EtOH or Me_2CO/EtOH) [Reppe et al. *Justus Liebigs Ann Chem* **596** 1 *1955*]. [*Beilstein* **21** II 213, **21** III/IV 3145, **21/6** V 321.]

2-Methylquinoline (quinaldine) *[91-63-4]* **M 143.2, b 86-87°/1mm, 155°/14mm, 246-247°/760mm, d_4^{20} 1.058, n_D^{20} 1.6126, pK^{25} 5.65.** Dry it with Na_2SO_4 or by refluxing with BaO, then fractionally distil it under reduced pressure and redistil it from zinc dust. Purify it further by conversion to its *phosphate* (**m** 220°) or *picrate* (**m** 192°) from which after recrystallisation, the free base is regenerated. [Packer et al. *J Am Chem Soc* **80** 905 *1958*.] Its $ZnCl_2$ complex can be used for the same purpose. [*Beilstein* **20** III/IV 3454, **20** V 375.]

4-Methylquinoline (lepidine) *[491-35-0]* **M 143.2, b 265.5°, d_4^{20} 1.084, n_D^{20} 1.61995, pK^{25} 5.59.** Reflux lepidine with BaO, then fractionally distil it. Further purify it *via* its recrystallised *dichromate salt* (**m** 138°) (from H_2O). [Cumper et al. *J Chem Soc* 1176 *1962*.] [*Beilstein* **20** III/IV 3477, **20/7** V 389.]

6-Methylquinoline *[91-62-3]* **M 143.2, b 258.6°, d_4^{20} 1.067, n_D^{20} 1.61606, pK^{25} 4.92.** Reflux it with BaO, then fractionally distil it. Further purified *via* its recrystallised *$ZnCl_2$ complex* (**m** 190°). [Cumper et al. *J Chem Soc* 1176 *1962*, *Beilstein* **20** III/IV 3498, **20/7** V 400.]

7-Methylquinoline *[612-60-2]* **M 143.2, m 38°, b 255-260°, d_4^{20} 1.052, n_D^{20} 1.61481, pK^{25} 5.29.** Purify it *via* its *dichromate complex* (**m** 149°, after five recrystallisations from water). [Cumper et al. *J Chem Soc* 1176 *1962*, *Beilstein* **20** III/IV 3497, **20/7** V 402.]

8-Methylquinoline *[611-32-5]* **M 143.2, b 122.5°/16mm, 247.8°/760mm, d_4^{20} 1.703, n_D^{20} 1.61631, pK^{25} 4.60.** Purify it as for 2-methylquinoline. The *phosphate* and *picrate* have **m** 158° and **m** 201°, respectively. [*Beilstein* **20** III/IV 3500, **20/7** V 405.]

(±)-3-Methylsulfolane (3-methyl-tetrahydrothiophene-1,1-dioxide) *[872-93-5]* **M 134.2, m 0.5°, b 101°/2mm, 125-130°/12mm, 278-282°/763.5mm, d_4^{20} 1.1885, n_D^{20} 1.4770.** Distil the sulfolane under vacuum and recrystallise it from Et_2O at -60° to -70°. An IR film has strong bands at 570 and 500 cm^{-1}. [Eigenberger *J Prakt Chem [2]* **131** 289 *1931*, Freaheller & Katon *Spectrochim Acta* **20** 1099 *1964*, Whitehead et al. *J Am*

Chem Soc **73** 3632 *1951*, *Beilstein* **17** I 8, **17** III/IV 64.]

(±)-2-Methyltetrahydrofuran *[96-47-9]* **M 86.1, b 80.0°, d_4^{20} 0.856, n_D^{20} 1.4053.** Likely impurities are 2-methylfuran, methyldihydrofurans and hydroquinone (stabiliser, which is removed by distillation under reduced pressures). It is washed with 10% aqueous NaOH, dried, vacuum distilled from CaH_2, passed through freshly activated alumina under nitrogen, and refluxed over sodium metal under vacuum. Store it over sodium. [Ling & Kevan *J Phys Chem* **80** 592 *1976*.] Distil it from sodium under vacuum, and store it with sodium-potassium alloy (this treatment removes water and prevents the formation of peroxides). *Alternatively*, it can be freed from peroxides by treatment with ferrous sulfate and sodium bisulfate, then solid KOH, followed by drying with, and distilling from, sodium, or type 4A molecular sieves under argon. It may be difficult to remove *benzene if it is present as an impurity (can be readily detected by its ultraviolet absorption in the 249-268nm region). [Ichikawa & Yoshida *J Phys Chem* **88** 3199 *1984*.] It has also been purifed by percolating through Al_2O_3 and fractionated collecting fraction **b** 79.5-80°. After degassing, the material is distilled onto degassed molecular sieves, then distilled onto anthracene and a sodium mirror. The solvent is then distilled from the green solution onto potassium mirror or sodium-potassium alloy, from which it is distilled again. [Mohammad & Kosower *J Am Chem Soc* **93** 2713 *1971*.] It should be stored in the presence of 0.1% of hydroquinone or 2,6-di-*tert*-butyl –*p*-cresol as stabiliser. The *R*(+)-*enantiomer* has **b** 78-80°/atm and $[\alpha]_D^{20}$ +27.5° (neat), and the *S*(-)-*enantiomer* has **b** 86°/atm and $[\alpha]_D^{20}$ -27.0° (neat) [Iffland & Davis *J Org Chem* **42** 4150 *1977*, Gagnaire & Butt *Bull Soc Chim Fr* 312 *1961*, *Beilstein* **17** III/IV 60, **17/1** V 78.] **HARMFUL VAPOURS.**

3-Methylthiophene *[616-44-4]* **M 98.2, b 60°/116mm, 111-113°/atm, 115.5°/atm, d_4^{20} 1.024, n_D^{20} 1.531.** Dry it with Na_2SO_4, then distil it from sodium. [*Beilstein* **17** III/IV 277, **17/1** V 331.]

6(4)-Methyl-2-thiouracil *[56-04-2]* **M 142.2, m 330°(dec), 299-303°(dec), 323-324°(dec), pK^{25} 8.1.** Crystallise the thiouracil from a large volume of H_2O. Purify it further by dissolving in base, adding charcoal, filtering and acidifying with AcOH. Suspend the wet solid (*ca* 100g) in boiling H_2O (1L), stir and add AcOH (20ml), stir and refrigerate. Collect the product, wash it with cold H_2O (4 x 200ml), drain it for several hours then place it in an oven at 70° to constant weight. [IR: Short & Thompson *J Chem Soc* 168 *1952*, Foster & Snyder *Org Synth* Coll Vol **IV** 638 *1063*, *Beilstein* **24** III/IV 1289.]

4-Methyl-1,2,4-triazoline-3,5-dione (MTAD) *[13274-43-6]* **M 113.1, m 103-104°, m 107-109°.** MTAD is obtained as pink needles by sublimation at 40-50°/0.1mm (see 4-phenyl-1,2,4-triazoline-3,5-dione, PTAD below). [Cookson et al. *Org Synth* **51** 121 *1971*, Cheng et al. *J Org Chem* **49** 2910 *1984*, *Beilstein* **26** III/IV 538.]

2-Methyltricycloquinazoline *[2642-52-6]* **M 334.4, m >300°.** Purify it by crystallisation from $^*C_6H_6$, toluene or xylene followed by vacuum sublimation. [*cf*: *Beilstein* **26** III/IV 1932.] **CARCINOGEN.**

5-Methyltryptamine hydrochloride (3-[2-aminoethyl]-5-methylindole hydrochloride) *[1010-95-3]* **M 210.7, m 289-291°(dec), 290-292°, $pK_{Est(1)}$~ –3 (protonation of ring NH), $pK_{Est(2)}$~ 9.0 (CH_2NH_2), $pK_{Est(3)}$~ 10.9 (acidic indole NH).** Recrystallise the hydrochloride from H_2O. The *free base* has **m** 96-98° (from $^*C_6H_6$/cyclohexane) or **m** 99-100° (from petroleum ether), and the *picrate* has **m** 243°(dec) (from EtOH). [Young *J Chem Soc* 3493 *1958*, Gaddum et al. *Quart J Exp Physiol* **40** 49 *1955*, Röhm *Hoppe Seyler's Z Physiol Chem* **297** 229 *1954*, *Beilstein* **22** III/IV 4364, **22/10** V 167.]

6-Methyluracil *[626-48-2]* **M 126.1, m 270-280°(dec), λ_{max} 260$_{nm}$ logε 3.97, pK_1 ~1.1, pK_2 9.8.** Crystallise 6-methyluracil from EtOH or acetic acid. [*Beilstein* **24** III/IV 1281.]

1-Methyluric acid *[708-79-2]* **M 182.1, m >350°, pK_1 5.75 (basic), pK_2 10.6 (acidic).** Recrystallise it from H_2O. Its solubility at 17.5° is 1g in 353ml of H_2O. [Bergmann & Dikstein *J Am Chem Soc* **77** 691 *1955*.] It has UV with λ_{max} at 231 and 283nm (pH 3), and 217.5 and 292.5nm (pH >12) [Johnson *Biochem J* **5** 133 *1952*]. [*Beilstein* **26** II 299, **26** III/IV 2621.]

3-Methyluric acid *[39717-48-1]* **M 182.1, m >350°, pK_1 5.75 (6.2), pK_2 >12.** Crystallise it from water. Its solubility at 17.5° is 1g in 19.7L of H_2O. It has UV with λ_{max} at 232 and 287 nm (pH 3), and 214 and 292.5nm (pH >12). [*Beilstein* **26** II 299, **26** III/IV 2621.]

7-Methyluric acid *[612-37-3; 30409-21-3]* **M 182.1, m >380°, pK_1 5.6, pK_2 10.3.** Crystallise it from water. It has UV with λ_{max} at 234 and 286nm (pH 3), 237 and 293nm (8.5), and 222 and 296.5nm (pH >12) [*Beilstein* **26** H 525, **26** II 299, **26** III/IV 2622.]

9-Methyluric acid *[30345-24-5]* **M 182.1, m 385-400°(dec), >400°.** Crystallise it from water. [*Beilstein* **26** II 299, **26** III/IV 2622.]

1-Methylxanthine (1-methyl-purin-2,6(3-*H*,7-*H*)-dione) *[6136-37-4]* **M 166.1, m >360° pK_1^{20} 1.3, pK_2^{20} 7.9, pK_3^{20} 11.8.** Crystallise it from water. It has UV with λ_{max} at 266nm (pH 2.08), 242.5 and 276nm (pH 9). [*Beilstein* **26** II 263, **26** III/IV 2329.]

3-Methylxanthine *[1076-22-8]* **M 166.1, m >360° pK_1^{20} 8.45, pK_2^{20} 11.92.** Crystallise it from water. [*Beilstein* **26** II 263, **26** III/IV 2329.]

7-Methylxanthine *[552-62-5]* **M 166.1, m >380°(dec) pK_1^{20} 8.42, pK_2^{20} >13.** Crystallise it from water. [*Beilstein* **26** II 263, **26** III/IV 2330.]

8-Methylxanthine *[17338-96-4]* **M 166.1, m 292-293°(dec).** Crystallise it from water. [*Beilstein* **26** III/IV 2330.]

9-Methylxanthine *[1198-33-0]* **M 166.1, m 384°(dec), pK_1^{20} 2.0, pK_2^{20} 6.12, pK_3^{20} 10.5 (>13).** Crystallise it from water. [*Beilstein* **26** II 263, **26** III/IV 2330.]

Metrazol (Cardiazol, Leptazol, 3a,4,5,6,7,8-hexahydro-1,2,3,3a-tetraaza-azulene, 1,5-pentamethylene-1,2,3,4-tetrazole) *[54-95-5]* **M 138.2, m 61°, b 194°/12mm, pK_{Est} ~<0.** Crystallise metrazol from diethyl ether and dry it under vacuum over P_2O_5, or distil it. [Schmidt *Chem Ber* **57** 704 *1924*, *Beilstein* **26** II 213.]

Morin (hydrate) (2',3,4',5,7-pentahydroxyflavone) *[480-16-0]* **M 302.2, m 289-292°, CI 75660, pK_1 5.3, pK_2 8.74.** Stir morin at room temperature with ten times its weight of absolute EtOH, then leave overnight to settle. Filter it off, and evaporate under a heat lamp to one-tenth its volume. An equal volume of water is added, and the precipitated morin is filtered off, dissolved in the minimum amount of EtOH and again precipitated with an equal volume of water. The precipitate is filtered off, washed with water and dried at 110° for 1 hour (yield *ca* 2.5%.). [Perkins & Kalkwarf *Anal Chem* **28** 1989 *1956*.] It complexes with W and Zr. [*Beilstein* **18** H 239, **18** III/IV 3468, **18/5** V 492.]

(-)-Morphine (H_2O) *[57-27-2]* **M 302.2, m 230°(dec), 254°(dec, rapid heating), 260°(Kofler block), $[\alpha]_D^{23}$ -130.9° (MeOH), pK_1 8.31, pK_2 9.51.** Crystallise the narcotic from MeOH or anisole. It dehydrates at 130°. Its solubility in H_2O is 0.2g/L at 20° and 0.9g/L at 100°, and in EtOH it is 5g/L at 20° and 10g/L on boiling. The *styphnate* has **m** 189° (from aqueous EtOH). [*Beilstein* **27** II 118, **27** III/IV 2223.]

Morpholine *[110-91-8]* **M 87.1, f -4.9°, b 128.9°, d_4^{20} 1.0007, n_D^{20} 1.4540, n_D^{25} 1.4533, pK^{25} 8.33.** Dry morpholine with KOH, fractionally distil it, then reflux it with Na, and again fractionally distil it. Dermer & Dermer [*J Am Chem Soc* **59** 1148 *1937*] precipitated it as the *oxalate* by adding slowly to slightly more than 1 molar equivalent of oxalic acid in EtOH. The precipitate is filtered off and recrystallised twice from 60% EtOH [1:1 salt has **m** 190-195°(dec)]. Addition of the oxalate to concentrated aqueous NaOH regenerated the base, which is separated and dried with solid KOH, then sodium, before being fractionally distilled. The *hydrochloride* has **m** 178-179° (from MeOH/Et_2O), and the *picrate* has **m** 151.6° (from aqueous EtOH). [*Beilstein* **27** II 3, **27** III/IV 15.]
§ A polystyrene supported morpholine is commercially available.

2-(*N*-Morpholino)ethanesulfonic acid (MES) *[4432-31-9]* **M 213.3, m >300°(dec), pK^{20} 6.15.** Crystallise MES from hot EtOH containing a little water. The *picrate* crystallises from EtOH and has **m** 178.8-182°. [Malkiel & Mason *J Org Chem* **8** 199 *1943*, *Beilstein* **27** III/IV 370.]

Murexide (ammonium purpurate) *[3051-09-0]* **M 284.2, m >300°, λ_{max} 520nm (ε 12,000), pK$_2$ 9.2, pK$_3$ 10.9.** The sample may be grossly contaminated with uramil, alloxanthine, etc., and may be difficult to purify. It is better to synthesise it from pure alloxanthine [Davidson *J Am Chem Soc* **58** 1821 *1936*]. Recrystallise it from water. [Kuhn & Lyman *Chem Ber* **69** 1547 *1936*, *Beilstein* **25** I 709, **25** III/IV 4236.]

α-Naphthoflavone (7,8-benzoflavone) *[604-59-1]* **M 272.3, m 153-155°, 155°, pK^{25} 8-9 (phenolic OH).** Recrystallise the flavone from EtOH or aqueous EtOH. [IR: Cramer & Windel *Chem Ber* **89** 354 *1956*, UV Pillon & Massicot *Bull Soc Chim Fr* 26 *1954*, Smith *J Chem Soc* 542 *1946*, Mahal & Venkataraman *J Chem Soc* 1767 *1934*.] It is a competitive inhibitor of human estrogen synthase. [Kellis & Vickery *Science* **225** 1032 *1984*, *Beilstein* **17** III/IV 5550.]

Naphthol AS-acetate (3-acetoxynaphthoic acid anilide) *[1163-67-3]* **M 305.3, m 152°, 160°.** Recrystallise it from hot MeOH and dry *in vacuo* over P_2O_5. It has **m** 252° after sublimation at 210-215°. It is slightly soluble in AcOH, EtOH, $CHCl_3$ or *C_6H_6. It is a fluorogenic substrate for albumin esterase activity. [Chen & Scott *Anal Lett* **17** 857 *1984*.] At λ_{ex} 320nm it has fluorescence at λ_{em} 500nm. [Brass & Sommer *Chem Ber* **61** 1000 *1928*, *Beilstein* **12** II 260, **12** III 960, **12** IV 923.]

1,5-Naphthyridine *[254-79-5]* **M 130.1, m 75°, b 112°/15mm, pK^{20} 2.84.** Purify 1,5-naphthyridine by repeated sublimation. The *picrate* crystallises from EtOH with **m** 200°(dec). [UV: Armarego *Physical Methods in Heterocyclic Chemistry* (Ed Katritzky, Academic Press) **Vol III** 133 *1971*, *Beilstein* **23** II 178, **23** III/IV 1235.]

1,8-Naphthyridine *[254-60-4]* **M 130.1, m 98-99°, pK^{20} 3.36.** Purify 1,8-naphthyridine through an Al_2O_3 column and elute with toluene and petroleum ether, evaporate the eluate, crystallise the residue from petroleum ether (b 60-80°), and sublime it at 80°/13mm. The *picrate* [15936-16-0] has **m** 207-208° (from EtOH), and the *methiodide* has **m** 180-181° (from EtOH). [Hawes & Wibberley *J Chem Soc (C)* 1564 *1967*, UV: Armarego *Physical Methods in Heterocyclic Chemistry* (Ed Katritzky, Academic Press) **Vol III** 134 *1971*, *Beilstein* **23** II 178, **23** III/IV 1237.]

(±)-Naringenin (4',5,7-trihydroxyflavanone) *[480-41-1]* **M 272.3, m 251° (phenolic pKs ~8-11).** Crystallise it from EtOH or aqueous EtOH. It has UV with λ_{max} at 290nm (EtOH). The *S*(-)-*enantiomer* (natural form) has **m** 255-256° (from EtOH) and $[\alpha]_D^{20}$ -28.0° (c 2, EtOH), $[\alpha]_D^{20}$ -35.2° (c 1, pyridine). [*Beilstein* **18** H 503, **18** II 164, **18** III/IV 2630.] **Genistein (4',5,7-trihydroxyisoflavone)** *[446-72-0]* **M 270.2** crystallises from 60% aqueous EtOH or water with **m 297-298°** and **$[\alpha]_D^{20}$ -28° (c 0.6, 20mM NaOH).** [*Beilstein* **18/4** V 594.]
For **Naringin (naringenin 7-rhamnoglucoside).** See "Carbohydrates" in Chapter 7.

Neutral Red (2-amino-8-dimethylamino-3-methylphenazine HCl, Basic Red 5, CI 50040) *[553-24-2]* **M 288.8, m 290°(dec), pK^{25} 6.5.** Crystallise the dye from *benzene/MeOH (1:1). In aqueous solution it is red at pH 6.8 and yellow at pH 8.0. [*Beilstein* **25** III/IV 3054.]

Nicotinaldehyde thiosemicarbazone *[3608-75-1]* **M 180.2, m 222-223°.** Crystallise the derivative from EtOH, BuOH or water. Its *hydrochloride* crystallises from aqueous EtOH with **m** 237-239° (dec). [*Beilstein* **21** III/IV 3542 **21/7** V 342.]

Nicotinamide (Niacin, Vitamin B3, vitamin PP) *[98-92-0]* **M 122.1, m 128-131°, b ~150-160°/high vac, pK $^{20}_{1}$ 0.5, pK $^{20}_{2}$ 3.33.** Crystallise niacin from *benzene. It has solubility in g/ml: H_2O (1), EtOH (0.7) and glycerol (0.1). [*Methods in Enzymology* **66** 23 *1980*, UV: Armarego *Physical Methods in Heterocyclic Chemistry* (Ed Katritzky, Academic Press) **Vol III** 83 *1971*, *Beilstein* **22** III/IV 389, **22/2** V 80.]

Nicotinic acid (Niacin *is also used for the acid***, pyridine-3-carboxylic acid)** *[59-67-6]* **M 123.1, m 232-234°, pK_1^{25} 2.00, pK_2^{25} 4.82.** Crystallise the acid from *benzene, EtOH or H_2O. It sublimes without decomposition. [McElvain *Org Synth* Coll Vol **I** 385 *1941*, *Beilstein* **22** III/IV 439, **22/2** V 57.]

Nicotinic acid hydrazide *[553-53-7]* **M 137.1, m 158-159°, pK_1^{25} 2.2, pK_2^{25} 3.63, pK_3^{25} 11.49(NH).** Crystallise it from aqueous EtOH or *benzene. [*Beilstein* **22** III/IV 439, **22/2** V 121.]

Nile Blue A (a benzophenoxazinium sulfate dye) *[3625-57-8]* **M 415.5, m >300°(dec), CI 51180, pK^{25} 2.4.** Crystallise the dye from aqueous AcOH. It has UV with λ_{max} at 630nm (96% aqueous EtOH) and 635nm (H_2O). The *betaine* has UV with λ_{max} at 513nm (EtOH). [Crossley et al. *J Am Chem Soc* **74** 57, 578 *1952*, Merill & Spencer *J Am Chem Soc* **70** 3683 *1948*, *Beilstein* **27** II 457, **27** III/IV 5166.]

5-Nitrobarbituric acid (dilituric acid) *[480-68-2]* **M 173.1, m 176°, 176-183°(dec), pK^{20} 10.25.** Crystallise diliuric acid from water as the *trihydrate* (**m** 180-181° (dec). Drying over 70% H_2SO_4 converts the trihydrate to the *dihydrate* [Loeffler & Moore *J Am Chem Soc* **70** 3650 *1948*]. [*Beilstein* **24** H 474, **24** II 273, **24** III/IV 1882.]

4'-Nitrobenzo-15-crown-5 *[60835-69-0]* **M 313.3, m 84-85°, 93-95°.** Recrystallise the crown ether from EtOH, MeOH or *C_6H_6/hexane as for the 18-crown-6 compound below. It complexes with Na^+, K^+, NH_4^+, Ca^{2+}, Mg^{2+} and Cd^{2+}. The ^{1}HNMR spectrum ($CDCl_3$) has δ (ppm) at 3.6-4.4 (m 16CH_2), 6.8 (d 1H arom), 7.65 (d 1H arom), 7.80 (dd 1H arom J_{ab} = 9Hz and J_{bc} = 3Hz) [Schmid et al. *J Am Chem Soc* **98** 5198 *1976*, Kikukawa et al. *Bull Chem Soc Jpn* **50** 2207 *1977*, Toke et al. *Justus Liebigs Ann Chem* **349** 349, 761 *1988*, Lindner et al. *Z Anal Chem* **322** 157 *1985*].

4'-Nitrobenzo-18-crown-6 *[53408-96-1]* **M 357.4, m 83-84°, 83-84°.** If impure and discoloured, then chromatograph it through Al_2O_3 and elute with *C_6H_6/hexane (1:1) containing 1% MeOH. The fractions are followed by TLC on Al_2O_3 (with Dragendorff's reagent for detection: R_F 0.6 in the above solvent system). Recrystallise the residues from the required fractions from *C_6H_6/hexane to give yellowish leaflets. It complexes with Na or K ions with $\log K_{Na}$ 3.95 and $\log K_K$ 4.71. [Petranek & Ryba *Col Chem Czech Chem Commun* **39** 2033 *1974*.]

4-(4-Nitrobenzyl)pyridine (PNBP) *[1083-48-3]* **M 214.2, m 70-71°, 74°, pK_{Est} ~5.0.** Crystallise PNBP from aqueous EtOH or cyclohexane. The *hydrochloride* has **m** 194-196°(dec, from EtOH), and the *picrate* has **m** 168°(dec, from EtOH/EtOAc). [*Beilstein* **20** II 272, **20/7** V 564.]

5-Nitroindole *[6146-52-7]* **M 162.1, m 141-142°, pK^{25} -7.4 (aqueous H_2SO_4).** Decolourise (charcoal) 5-nitroindole and recrystallise it twice from aqueous EtOH or recrystallise it from octane. It has UV has λ_{max} at 265 and 324nm (EtOH). [*Beilstein* **20** III/IV 3194, **20/7** V 41.]

Nitron [1,4-diphenyl-3-phenylamino-(1*H*)-1,2,4-triazolium (hydroxide) inner salt] *[2218-94-2]* **M 312.4, m 189°(dec).** Crystallise it from EtOH, chloroform or EtOH/*C_6H_6. [*Beilstein* **25** III/IV 1075.]

5-Nitro-1,10-phenanthroline *[4199-88-6]* **M 225.2, m 197-198°, pK^{25} 3.33.** Crystallise the phenanthroline from *benzene/petroleum ether, until anhydrous. It also crystallises from H_2O with **m** 202°, and EtOAc with **m** 203°. Its pK^{25} varies from 3.20 to 2.69 with varying MeOH/H_2O ratios from 0 to 0.95 moles/L, and from 3.20 to 1.95 in varying EtOH/H_2O ratios from 0 to 0.94 moles/L [Ram et al. *J Prakt Chem* **319** 719 *1977*]. It forms complexes with Cu^{2+}, Zn^{2+}, In^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}. [*Beilstein* **23** III/IV 1682, **23/8** V 425.]

3-Nitro-2-pyridinesulfenyl chloride *[68206-45-1]* **M 190.2, m 217-222°(dec).** The chloride crystallises as yellow needles from CH_2Cl_2. When pure, it is stable for several weeks at room temperature, and no decomposition was observed after 6 months at <0°. It is moisture sensitive. Its UV (MeCN) has λ_{max} at 231nm (ε 12,988), 264nm (ε 5,784) and 372nm (ε 3,117). [NMR and UV: Matsuda & Aiba *Chem Lett* 951 *1978*, Wagner et al. *Chem Ber* **75** 935 *1942*.]

5-Nitroquinoline *[607-34-1]* **M 174.2, m 70°, pK^{20} 2.69.** Crystallise 5-nitroquinoline from pentane, then from *benzene. The *hydrochloride* has **m** 224° and the *picrate* has **m** 206°, 214°(from MeOH). [*Beilstein* **20** H 371, **20** II 235, **20** III/IV 3397.]

8-Nitroquinoline *[706-35-2]* **M 174.2, m 88-89°, 91-92°, pK^{20} 2.55.** Crystallise 8-nitroquinoline from hot water, MeOH, EtOH or EtOH/diethyl ether (3:1). It sublimes at 70°/2mm. [*Beilstein* **20** H 373, **20** III/IV 3399.]

4-Nitroquinoline 1-oxide *[56-57-5]* **M 190.2, m 154-155°, 157°.** The *N*-oxide recrystallises from aqueous acetone as yellow needles or platelets. [Ochiai *J Org Chem* **18** 534 *1953*, Seki et al. *J Phys Chem* **91** 126 *1987*, *Beilstein* **20** III/IV 3396.]

5-Nitrouracil (2,4-dihydroxy-5-nitropyrimidine) *[611-08-5]* **M 157.1, m 280-285°, >300°, pK$_1^{20}$ 0.03, pK$_2^{20}$ 5.55, pK$_3^{20}$ 11.3.** The uracil recrystallises in prisms from boiling H_2O as the *monohydrate* and loses H_2O on drying *in vacuo*. [UV: Brown *J Chem Soc* 3647 *1959*, Brown *J Appl Chem* **2** 239 *1952*, Johnson *J Am Chem Soc* **63** 263 *1941*, *Beilstein* **24** I 313, **24** II 171, **24** III/IV 1236.]

4-Nonadecylpyridine (hydrogen ionophore II [ETH 1907] - Proton ionophore) *[70268-36-9]* **M 345.6, b 180°/0.07mm, pK$_{Est}$ ~6.0.** Dissolve the waxy ionophore (*ca* 60g) in $CHCl_3$ (200ml), wash it with H_2O (3 x 200ml), dry it and evaporate it to dryness, then distil it in a vacuum. A waxy solid is formed on cooling the distillate. Its UV has λ_{max} at 257nm (ε 1.86 x 10^3 $M^{-1}cm^{-1}$), 308nm (ε 1.7 x 10^2 $M^{-1}cm^{-1}$). [IR, NMR UV: Valenty et al. *Inorg Chem* **18** 2160 *1979*.]

Norcodeine *[467-15-2]* **M 285.3, m 185°, 186°, pK^{20} 9.10.** It crystallises from acetone or ethyl acetate. [Speyer & Walther *Chem Ber* **63** 822 *1930*.] The *hydrochloride* has **m** 309°(dec) when crystallised from H_2O. [*Beilstein* **18** III/IV 8091.]

Octadecyl isonicotinate (hydrogen ionophore IV ETH 1778) *[103225-02-1]* **M 375.6, m 57.5°, pK$_{Est}$~ 3.5**. Dissolve it in Et_2O and wash it 3 times with H_2O. Dry the extract ($MgSO_4$), evaporate, and recrystallise the residue from EtOAc/hexane (4:1). [Oesch et al. *Anal Chem* **58** 2285 *1986*.]

Orotic acid (H_2O) *[50887-69-9]* **M 174.1, m 334°(dec), 235-346°(dec), pK$_1^{25}$ 1.8, pK$_2^{25}$9.55.** It crystallises from water. The *anhydrous acid* [65-86-1] **M** 156.1 has **m** 245-246°(dec). [Nye & Mitchell *J Am Chem Soc* **69** 1382 *1947*, *Beilstein* **25** III/IV 1759.]

Orotic acid Li salt H_2O (1-carboxy-4,6-dihydroxypyrimidine Li salt H_2O) *[5266-20-6]* **M 180.0, m >300°, pK$_1$ 2.8 (CO_2H), pK$_2$ 9.4 (OH), pK$_3$ >13 (OH) (for free acid).** The salt is soluble in H_2O at 17° and 100°. Best to acidify an aqueous solution of the salt, isolate the *free acid* (see above) which is recrystallised from H_2O (as *monohydrate*) **m** 345-347° (345-346°), then dissolve it in EtOH, add an equivalent amount of LiOH in EtOH and evaporate. Its solubility in H_2O is 1.28% (17°) and 2.34% (100°). [Bachstez *Chem Ber* **63** 1000 *1930*, Johnson & Shroeder *J Am Chem Soc* **54** 2941 *1932*, UV: Shugar & Fox *Biochim Biophys Acta* **9** 199 *1952*, *Beilstein* **25** III/IV 1759.]

Oxalylindigo *[2533-00-8]* **M 316.3.** It crystallises twice from nitrobenzene as small yellow crystals and is dried by heating *in vacuo* for several hours. [Schanze et al. *J Am Chem Soc* **108** 2646 *1986*.]

2-Oxazolidinone (ethylene carbamate) *[497-25-6]* **M 87.1, m 88-90°, 89-90°, 91°, b 152°/0.4mm, 200°/12mm.** It is prepared by reaction of ethanolamine with phosgene or diethylcarbonate. It can be prepared from ethanolamine (2g) in $CHCl_3$ (200ml, EtOH free by passing through an Al_2O_3 column) by bubbling $COCl_2$ through the solution which is allowed to stand for 3 hours, the acid is neutralised with powdered $PbCO_3$, filtered, evaporated to dryness and the solid residue is recrystallised from $CHCl_3$. *Alternatively*, ethanolamine (61g), Et_2CO_3 (150ml) and NaOMe (0.5g) are heated in an oil bath; and after the EtOH (~112ml) has distilled off, the residue solidifies on cooling and is recrystallised from $CHCl_3$ (100ml) to give the *oxazolidinone* (57g,

65%), m 87-89°. Its IR (film) has ν_{max} at 3000, 2920 (CH), 1766 (carbamate, C=O), 1690 (amide, C=O), 1465, 1382 and 1357 (CH_2), 1298 (C-N), 1212, 1140 and 1030 (COC, C-O), 953 cm^{-1}; and ^1H NMR ($CDCl_3$) with δ at 6.68 (NH, br s, 1H), 4.47 (H_5, t, ^3J = 8Hz, 2H), 3.63 (H_4, t, ^3J = 8Hz, 2H); and ^{13}C NMR ($CDCl_3$) with δ at 161.2 (C_2), 65.1 (C_5), 40.8 (C_4); and ^{13}C NMR (D_2O) with δ at 165.1 (C_2), 68.8 (C_5), 43.1 (C_4). [Hammer et al. *J Org Chem* **46** 1521 *1981*.] [Homeyer US Pat 2,399,118 *1964*, *Chem Abs* **40** 4084 *1964*.] It can be recrystallised from *benzene, dichloroethane, $CHCl_3$ or EtOH. It is a cyclic urethane, and as such it is not very stable in aqueous solvents. The ***N-acetyl derivative*** [1432-43-5] **M 129.1, m 69-70°**, is obtained by boiling 2-oxazolidinone (3g) with Ac_2O (20ml) and NaOAc (1g) for 1.5 hours, and is recrystallised from $*C_6H_6/Et_2O$ or sublimed at 65° *in vacuo*. [Homeyer US Pat 2,399,118 *1964*, *Chem Abs* **40** 4084 *1964*.] The ***N-methyl derivative*** [19836-78-3] **M 101.1, b 120°/0.1mm**, is prepared from *N*-methyl ethanolamine with $COCl_2/CHCl_3/PbCO_3$ or as for the preparation of the parent compound [with $(EtO)_2CO$], and distilled in a vacuum. It is **TOXIC**. The yellow *picrolonate* has **m 137-138°**. [*cf*: Fränkel & Cornelius *Chem Ber* **51** 1662 *1918*, Ben-Ishai *J Am Chem Soc* **78** 4962 *1956*, *Beilstein* **27** H 135, **27** I 259, **27** III/IV 2516.]

Oxetane (1.3-trimethylene oxide) *[503-30-0]* **M 58.1, b 45-46°/736mm, 47-49°/atm, 48°/760mm, d_4^{20} 0.892, n_D^{20} 1.395.** Distil oxetane twice from sodium metal and then fractionate it through a small column at atmospheric pressure, **b** 47.0-47.2°. It can also be purified by preparative gas chromatography using a 2m silica gel column. *Alternatively*, add KOH pellets (50g for 100g of oxetane) and distil it through an efficient column or a column packed with 1/4in Berl Saddles with the main portion boiling at 45-50° being collected and redistilled over fused KOH. [Noller *Org Synth* Coll Vol **III** 835 *1955*, Dittmer et al. *J Am Chem Soc* **79** 4431 *1957*, *Beilstein* **17** H 6, **17** I 3, **17** II 12, **17** III/IV 13, **17/1** V 11.]

Oxetan-2-one (β-propiolactone, propan-3-olide) *[57-57-8]* **M 72.1, m -31.2°, -35°, b 51°/10mm, 83°/45mm, d_4^{20} 1.1460, n_D^{25} 1.4117.** Fractionally distil the lactone from sodium under reduced pressure. It gives an acidic solution in H_2O. It irritates the skin and is a possible **carcinogen**. [*Beilstein* **17** I 130, **17** III/IV 4157.]

Oxine Blue [3-(4-hydroxyphenyl)-3-(8-hydroxy-6-quinilinyl)-1(3*H*)-isobenzofuranone] *[3733-85-5]* **M 369.4, m 134-135°.** Recrystallise the dye from EtOH and dry it in a desiccator over H_2SO_4.

Oxolinic acid (5-ethyl-5,8-dihydro-8-oxo-1,3-dioxolo[4,5-*g*]quinoline-3-carboxylic acid) *[14698-29-4]* **M 261.2, m 313-314°(dec), 314-316°(dec), pK_{Est} ~ 2.3.** Purify the acid by recrystallisation from aqueous Me_2CO, 95% EtOH or dimethylformamide. It has UV with λ_{max} at 220, (255.5sh), 259.5, 268, (298sh, 311sh), 321 and 326nm [ε 14.8, (36.8sh), 38.4, 38.4, (6.4sh, 9.2sh), 10.8 and 11.2 x 10^3]. [Kaminsky & Mettzer *J Med Chem* **11** 160 *1968*, *Beilstein* **17** H 6, **17** I 3, **17** II 202, **17** III/IV 13, **17/1** V 11.]

Papaverine hydrochloride (6,7-dimethoxy-1-veratrylisoquinoline hydrochloride) *[61-25-6]* **M 375.9, m 215-220°, 222.5-223.5°(dec), 231°, pK^{25} 6.41.** Recrystallise it from H_2O. It sublimes at 140°/0.1mm. Its solubility in H_2O is 5%. [Saunders & Srivastava *J Pharm Pharmacol* **3** 78 *1951*, Biggs *Trans Faraday Soc* **50** 800 *1954*.] The *free base* has **m** 148-150°. The *picrate* has **m** 186-189°(dec, 186-186.5°(dec) [Bobbitt *J Org Chem* **22** 1729 *1957*]. [*Beilstein* **21** II 202, **21** III/IV 2788, **21/6** V 182.]

Paraldehyde (acetaldehyde trimer, 2r,4c,6c-trimethyl-1,3,5-trioxane, *all-cis*) *[123-63-7]* **M 132.2, m 12.5°, b 124°/751mm, d_4^{20} 0.995, n_D^{20} 1.407.** Wash paraldehyde with water and fractionally distil it. *Alternatively*, it is purified by drying with anhydrous Na_2SO_4, then cooled to 5°, and the frozen material is separated by decantation. The solid is distilled (**b** 121-124°/atm), the distillate is collected, stored over anhydrous Na_2SO_4 for several days and re-distilled at atmospheric pressure before use [Le Fevre et al. *J Chem Soc* 290 *1950*]. The *2r,4c,6t-trimethyl-1,3,5-trioxane* has **m** 14.5°, **b** 125°/760mm. [*Beilstein* **19** II 394, **19** III/IV 4715. **19/9** V 112.]

Patulin [4-hydroxy-4*H*-furo(3.2-*c*)pyran-2(6*H*)-one, Clavatin] *[149-29-1]* **M 154.1, m 110°, 111-112°.** Crystallise patulin from $*C_6H_6$, Et_2O, EtOH or chloroform. It sublimes at 90°/high vacuum [Bergel et al. *J Chem Soc* 415 *1944*]. [*Beilstein* **18** III/IV 1184, **18/3** V 5.] (*Highly* **TOXIC**).

Pentachloropyridine *[2176-62-7]* **M 251.3, m 122-124°, 123°, 124°, 124-125°, 125-126°, b 279-280°/atm, pK^{20} -6.02 (aqueous H_2SO_4).** Purify it by recrystallisation from EtOH or aqueous EtOH. It sublimes at 150°/3mm. [den Hertog et al. *Rec Trav Chim Pays Bas* **69** 673 *1950*, Schikh et al. *Chem Ber* **69** 2604 *1936*, *Beilstein* **20** I 81, **20** III/IV 2503, **20/5** V 422.]

Pentafluoropyridine *[700-16-3]* **M 169.1, m -41.5°, b 83.5°, 84°, 83-85°, d_4^{20} 1.609, n_D^{20} 1.3818, pK_{Est} ~<0.** Distil it through a concentric tube column; it has λ_{max} in cyclohexane at 256.8nm. [Chambers et al. *J Chem Soc* 3573 *1964*, ^{19}F NMR: Bell et al. *J Fluorine Chem* **1** 51 *1971*.] The *hexafluoroantimonate* has **m** 98-102°(dec) after crystallisation from liquid SO_2. [*Beilstein* **20/5** V 401.]

3,3,6,9,9-Pentamethyl-2,10-diazabicyclo[4.4.0]dec-1-ene (PMDBD, 1,2,3,4,4a,5,6,7-octahydro-2,2,4a,7,7-pentamethylnaphthyridine) *[69340-58-5]* **M 208.3, m 15°, b 65°/0.07mm, d_4^{20} 0.924, n_D^4 1.4840, pK >11 ($MeOCH_2CH_2OH/H_2O$, 1:1).** The pentamethylhydronaphthyridine is obtained by intramolecular cyclisation of 5-amidino-2,5,8-trimethylnona-2-7-diene [190.0g, 0.914mol, prepared from 2mols BuLi, one mol of propionitrile and 2mols of 3-methylbut-2-enyl bromide (isoprenehydrobromide) in THF at -78°, followed by $NaNH_2$ in boiling *C_6H_6] in CH_2Cl_2 (500ml) solution at 0°, by bubbling dry HCl gas through it until the pH is 4. The solution is evaporated *in vacuo* until free from HCl vapour to give a dark hygroscopic hydrochloride which is heated in a flask (protected from air with a $CaCl_2$ tube) at 200°, whereby excess of HCl is released after 30 minutes (cyclisation begins at *ca* 125°), and heating is continued for 18 hours. The dark brown residue is treated with H_2O (1.0L), acidified with 2N H_2SO_4 (500ml) and the aqueous phase is extracted with Et_2O (2 x 100ml), the aqueous phase is basified (cooling is necessary) with NaOH (*ca* 100g) to pH >10. The brown oil that separates is extracted with Et_2O (2 x 500ml), dried over K_2CO_3, filtered, and evaporated to give a viscous oil (190g) which is distilled through a Vigreux column at 0.05mm, and after a small fore run (3.8g), a colourless viscous oil of the *naphthyridine* distils (156.6g, 80% yield, b 60-67°). An analytical sample has m ~15° and b 65°/0.07mm. Store it in an inert dry atmosphere as it absorbs CO_2 in the presence of moisture to form a *bicarbonate* (see below). Its UV/VIS has λ_{max} (ε) at 219 (11,600) nm; the IR (7,5% in $CHCl_3$) has ν_{max} at 3660w, 3350w, 2970s, 2930s, 2860s, 2500w, 1630s, 1475m/sh, 1460m, 1415w, 1385s, 1375m, 1365m, 1360m, 1335m, 1325m, 1250m, 1235m, 1180m, 1150s, 1130m, 1065w, 1000w, 875w, 840w, 655m, 630w, with the immonium band of the hydrochloride in $CHCl_3$ at 2500 cm^{-1}; the ^{1}H NMR (CCl_4) of the free base has δ at 1.08-1.13 (2s, 12H, $4CH_3$), 1.19 (s, 3H, CH_3), 1.2-2.0 (m, 8H), 3.38 (s, NH); MS (200°) has *m/z* at 209 (4), 208 (M^+ 25), 194 (25), 193 (100).
The *hydrochloride*, when recrystallised twice from CH_2Cl_2/Et_2O (15 hours at 0°), has **m 195-196°**, and the ^{1}H NMR (CCl_4) has δ at 1.34-1.13 (2s, 9H, $3CH_3$), 1.42 (s, 6H, $2CH_3$), 1.6-2.3 (m, 8H), 9.78 (br s, 2H NH).
The *hydrogen carbonate salt* is formed from the free base and moist CO_2 in 2 minutes, then by extraction with CH_2Cl_2, drying (K_2CO_3) and evaporating gives a labile salt decomposing at **122-125°**, and the ^{1}H NMR has δ at 1.28 (s, 6H, $2CH_3$), 1.30 (s, 3H, CH_3), 1.36 (s, 6H, $2CH_3$), 1.4-2.2 (m, 8H), and **no** NH/OH signals except in $CHCl_3$ where an intense singlet appears at 7.25.
The *benzoate* crystallises from CH_2Cl_2 with **m 183-185°**, the *hydrogen sulfate* crystallises from CH_2Cl_2/hexane with **m 208-209°**, the *tosylate* has **m 114°**, and the *dihydrogen phosphate* crystallises from MeOH/Et_2O with **m 225-228°**. [Heinzer, Soukup and Eschenmoser *Helv Chim Acta* **61** 2851 *1978*, Sternbach et al. *Angew Chem* **91** 670 *1979*, *Beilstein* **23/5** V 302.] The strong basicity, proximity of the nitrogen atoms, and the steric hinderance from methyl groups around them, confer remarkable coordination properties to this amidine without the usual nucleophilic behaviour of nitrogen bases [Eschenmoser et al. *Angew Chem* **91** 670 *1979*, Boyle et al. *J Chem Soc, Chem Commun* 239 *1992*, Denmark *J Org Chem* **46** 3144 *1981*].

Pentaquine monophosphate (1,4-pentanediamine, *n*-[6-methoxy-8-quinolinyl)-*N*'-[1-methylethyl) (1:1) phosphate] *[5428-64-8]* **M 399.4, m 189-190°, pK^{70} 8.22.** Crystallise it from H_2O or 95% EtOH. The *free base* has **b** 165-170°/0.05mm, n_D^{25} 1.5785. The *picrate* crystallises from Me_2CO/EtOH with **m** 164.5-165.5°. [Drake et al. *J Am Chem Soc* **68** 1529 *1946*, *Beilstein* **22** III/IV 5814.]

(±)-Pentobarbital (5-ethyl-5-1'-methylbutyl barbituric acid, Nembutal is the Na salt) *[76-74-4]* **M 226.4, m ~127°(dec), $pK_{Est(1)}$~ 8.0, $pK_{Est(2)}$~12.7.** A solution of the sodium salt in 10% HCl is prepared, and the acid is extracted with ether. Evaporation of the extract gives a solid which is then purified by repeated crystallisation

from $CHCl_3$. It sublimes at 95-105°/10-12mm. [Bucket & Sandorfy *J Phys Chem* **88** 3274 *1984*.] The *(+)-* and *(-)-enantiomers* crystallise from 50% aqueous EtOH with **m** 120-121° and have $[\alpha]_D^{25}$ +4.73° to –4.93° (EtOH) [Kleiderer & Shonle *J Am Chem Soc* **56** 1772 *1934*]. [*Beilstein* **24** I 419, **24** II 287, **24** III/IV 1951.]

Pericyazine [10-{3-(4-hydroxy-1-piperidinyl)-propyl}-10*H*-phenothiazine-2-carbonitrile, Propericiazine] *[2622-26-6]* **M 365.4, m 116-117°.** It recrystallises from a saturated solution in cyclohexane. It is antipsychotic and is a sensitive reagent for Pd, Va, Ru, Rh and Au. [Gowda et al. *Anal Chem* **55** 1816 *1983*, *Anal Chim Acta* **154** 347 *1983*, *Beilstein* **27** III/IV 4110.]

Phenanthridine (benzo[c]quinoline, 3,4-benzoquinoline) *[229-87-8]* **M 179.2, m 106.5°, 108-109°, b 350°/760mm, pK^{20} 4.61 (4.48).** Purify it *via* the $HgCl_2$ addition compound formed when phenanthridine (20g) in 1:1 HCl (100ml) is added to aqueous $HgCl_2$ (60g in 3L), and the mixture is heated to boiling. The $HgCl_2$ complex separates as yellow red crystals with **m** 195-198° [Arcus & Mesley *J Chem Soc* 1780 *1953*]. Conc HCl is then added until all of the solid has dissolved. The compound separates on cooling and is decomposed with aqueous NaOH (*ca* 5M). Phenanthridine is extracted into Et_2O, evaporated, and the residue is crystallised from petroleum ether (b 80-100°) or EtOAc. [Cumper et al. *J Chem Soc* 45218 *1962*.] It is also purified by chromatography on activated alumina from *benzene solution, with diethyl ether as eluent. Evaporation of ether gives crystalline material which is freed from residual solvent under vacuum, then further purified by fractional crystallisation, under N_2, from its melt. It was purified by zone melting and sublimes in a vacuum. The *picrate* has **m** 218.5-219.5° (from *iso*-PrOH) (also reported are **m** 244-245° and 247-248°, from EtOH or H_2O). [Slough & Ubbelhode *J Chem Soc* 911 *1957*.] [*Beilstein* **20** H 466, **20** III/IV 4016, **20/8** V 223.]

1,10-Phenanthroline (*o*-phenanthroline) *[66-71-7 (anhydr); 5144-89-8 (H_2O)]* **M 198.2, m 98-101°, 108-110° (hydrate), 118° (anhydrous), b >300°, pK_1^{25} -0.7 (aqueous $HClO_4$), pK_2^{25} 4.86 (4.96).** Crystallise its *picrate* (**m** 191°) from EtOH; then the free base is liberated with aqueous alkali, dried at 78°/8mm over P_2O_5 and crystallised from petroleum ether (b 80-100°). [Cumper et al. *J Chem Soc* 1188 *1962*.] It can be purified by zone melting. It has also been crystallised from hexane, *benzene/petroleum ether (b 40-60°) or sodium-dried *benzene, dried and stored over H_2SO_4. The *monohydrate* is obtained by crystallisation from aqueous EtOH or ethyl acetate. It has been crystallised from H_2O (300 parts) to give the *monohydrate* **m** 102-103° which sublimes at 10^{-3}mm [Fielding & LeFevre *J Chem Soc* 1811 *1951*.] The *anhydrous* compound has **m** 118° (after drying at high vacuum at 80°) and is also obtained by recrystallisation from petroleum ether or $*C_6H_6$ (70 parts) and drying at 78°/8mm. [UV: Badger et al. *J Chem Soc* 3199 *1951*.] It has a pKa in H_2O of 4.857 (25°) or 5.02 (20°) and 4.27 in 50% aqueous EtOH (20°). [Albert et al. *J Chem Soc* 2240 *1948*]. [*Beilstein* **23** H 227, **23** II 235, **23/8** V 419.]

1,10-Phenanthroline hydrochloride (*o*-phenanthroline hydrochloride) *[3829-86-5]* **M 243.7, m 212-219°.** The hydrochloride crystallises from 95% EtOH, **m** 212-219° as the *monohydrate*; the *half hydrate* has **m** 217°. The *3HCl* has **m** 143-145° (sinters at 128°). [Thevenet et al. *Acta Cryst Sect B* **33** 2526 *1977*]. [*Beilstein* **23** II 235, **23/8** V 421.]

4,7-Phenanthroline-5,6-dione *[84-12-8]* **M 210.2, m 295°(dec).** The dione crystallises from MeOH. The *mono-oxime* forms yellow crystals from MeOH with **m** 250°(dec), the *di-oxime* forms yellow crystals from MeOH with **m** 300°(dec) and the *mono-semihydrazone* forms yellow crystals from MeOH with **m** 195°(dec). [Druey & Schmidt *Helv Chim Acta* **33** 1080 *1950*, *Beilstein* **24** III/IV 1741.]

Phenazine *[92-82-0]* **M 180.2, m 171°, pK_1^{20} -4.9 (aqueous H_2SO_4), pK_2^{20} 1.21.** Phenazine crystallises from EtOH, $CHCl_3$ or ethyl acetate, after pre-treatment with activated charcoal. It can be sublimed *in vacuo* and purified by zone refining. [*Beilstein* **23/8** V 389.]

Phenosafranine (3,7-diamino-5-phenylphenazinium chloride) *[81-93-6]* **M 322.8, m >300°, λ_{max} 530nm (H_2O).** Crystallise the chloride from dilute HCl. It has UV with λ_{max} at 530nm in H_2O. The *picrate* decomposes on heating and has a solubility of 0.0048% in H_2O at 18°. [*Beilstein* **23** H 395, *Beilstein* **25** H 394, **25** I 654, **25** II 338, **25** III/IV 3050.]

Phenothiazine *[92-84-2]* **M 199.3, m 184-185°.** Crystallise it from *benzene, toluene, hexane or Me_2CO (charcoal) after boiling for 10 minutes under reflux. Filter the crystals off and dry them in an oven at 100°, then in a vacuum desiccator over paraffin chips. Also recrystallise it twice from water and dry it in an oven at 100° for 8-10 hours. It sublimes at 130°/1mm and has UV with λ_{max} at 253nm in heptane. [*Beilstein* **27** I 225, **27** II 32, **27** III/IV 1214.]

Phenoxazine *[135-67-1]* **M 199.2, m 156°, 156-158°, 158-159°, b 215°/4mm.** Crystallise phenoxazine from EtOH and sublime it *in vacuo*. If too impure then extract it in a Soxhlet extractor using toluene. Evaporate the solvent and dissolve the residue (*ca* 100g) in $*C_6H_6$ (1L), **CARCINOGEN** (use an efficient fume cupboard) and chromatograph it through an Al_2O_3 column (50 x 450 mm) using $*C_6H_6$. The eluent (*ca* 3L) is evaporated to *ca* 150ml and cooled when *ca* 103g of phenoxazine **m** 149-153° are obtained. Sublimation yields platelets **m** 158-159°. It forms a green *picrate* **m** 141.5-142°. [Gilman & Moore *J Am Chem Soc* **79** 3485 *1957*, Müller et al. *J Org Chem* **24** 37 *1959*, *Beilstein* **27** I 223, **27** III/IV 1209.]

2-Phenyl-1-azaindolizine *[4105-21-9]* **M 194.2, m 140°, pK_{Est} ~1.9.** Crystallise the indolizine from EtOH, *benzene/petroleum ether, hexane (**m** 135-136°) or cyclohexane (**m** 136-137°). The *hydrochloride* $2H_2O$ has **m** 114-116° (from H_2O) and the *picrate* has **m** 228-229° (from AcOH) and 236-238° (from Me_2CO). [Adams & Dix *J Am Chem Soc* **80** 4618 *1958*, *Beilstein* **23** III/IV 1705.]

Phenylbutazone (4-butyl-1,2-diphenylpyrazolidin-3,5-dione) *[50-33-9]* **M 308.4, m 105°, 106-108°.** Crystallise the dione from EtOH. Its pK^{23} is 4.52 (in H_2O), 4.89 (in 50% aqueous EtOH) and 5.25 (80% 2-methoxyethanol). It complexes with Hg^{2+}, Cd^{2+} and Zn^{2+}. It has UV with λ_{max} at 239.5nm in MeOH+50% aqueous $HClO_4$ and 264nm in aqueous 0.1N NaOH. [*Beilstein* **24** III/IV 1123.]

2-Phenyl-1,3-diazahexahydroazulene *[2161-31-1]* **M 212.3.** Recrystallise the azulene three times from de-aerated cyclohexane in the dark.

2-Phenylindolizine *[25379-20-8]* **M 193.2, m 214°(dec), pK_{Est} ~4.4.** Crystallise 2-phenylindolizine from EtOH. The *0.25HCl* crystallises from MeCN with **m** 109°, and the *picrate* has **m** 161° when crystallised from EtOAc. [*Beilstein* **20** II 304, **20** III/IV 4033, **20/8** V 244.]

1-Phenyl-5-mercaptotetrazole *[86-93-1]* **M 178.2, m 150° (dec), 155° (dec), 157-158°, pK^{25} 3.65 (5% aqueous EtOH).** Purify the tetrazole by recrystallisation from EtOH or $CHCl_3$ (**m** 152°) [Tautomerism: Kauer & Sheppard *J Org Chem* **32** 3580 *1967*, UV: Leiber et al. *Can J Chem* **37** *563 1959*]. The *ammonium salt* crystallises from EtOH and decomposes at 176°. The *sodium salt* crystallises from EtOH/$*C_6H_6$, melts at 96° and decomposes at 145° [Stollé *J Prakt Chem* [2] **133** 60 *1932*]. It is used for the determination of Bi and Pd. [Fresenius *Z Anal Chem* **261** 151 *1972*, *Beilstein* **26** III/IV 2065.]

4-(3-Phenylpropyl)pyridine [1-phenyl-3(4-pyridyl)propane] *[2057-49-0]* **M 197.3, b 150-152°/5mm, 322°/atm, d_4^{25} 1.03, n_D^{20} 1.563, pK_{Est} ~6.0.** This is prepared from the potassium salt of 4-picoline [obtained by dissolving K metal (1 mol) and a few mg of ferric oxide as catalyst in liquid NH_3 until the blue colour is discharged, indicating the formation of KNH_2, to which is added 4-picoline (1 mol) rapidly forming a reddish-amber solution] and phenethyl bromide (1 mol, see [103-63-9]), allowing the NH_3 to evaporate (6-10 hours, in an efficient fume cupboard), adding H_2O, the mixture is extracted into Et_2O, evaporated to dryness and the residual oil is distilled, preferably under a vacuum to give the desired *phenylpropylpyridine*, **b 150-152°/5-6mm**, in 56% yield. The *hydrochloride*, obtained by evaporating a concentrated HCl solution of the base on a steam bath and the residual solid, recrystallised from EtOH/Et_2O, has **m 143.5°** and is hygroscopic. [Bergstrom et al. *J Org Chem* **10** 452 *1945*, *Beilstein* **20** III/IV 3687.]

4-Phenylpyridine-2-carbonitrile *[18714-16-4]* **M 180.1, m 97-101°, pK_{Est} <0.** Purify the nitrile by recrystallisation from petroleum ether (**m** 99-100°). [Case & Gasper *J Am Chem Soc* **78** 5842 *1956*, *Beilstein* **22** III/IV 1261.]

Phenyl 2-pyridyl ketoxime *[1826-28-4]* **M 198.2, m 151-152°, 154-156°, pK_1^{25} 3.84, pK_2^{25} 10.71 for *E*-isomer.** The *E-isomer* crystallises from EtOH (charcoal). It isomerises to the *Z-isomer* on melting or in boiling *o*-xylene, and crystallises from EtOH or cyclohexanol with **m** 166-168°. [*Beilstein* **21** H 330, **21** III/IV 4120, **21/8** V 568.]

6-Phenylquinoline *[612-95-3]* **M 205.3, m 110.5-111.5°, pK_{Est} ~5.2.** Crystallise 6-phenylquinoline from EtOH (charcoal). The *picrate* has **m** 105° (from Me_2CO). It has UV with λ_{max} at 253nm in aqueous EtOH and 263 and 325nm in aqueous HCl. [*Beilstein* **20** H 483, **20** III/IV 4151.]

2-Phenylquinoline-4-carboxylic acid (Cinchophen, Atophen) *[132-60-5]* **M 249.3, m 215°, $pK_{Est(1)}$~0.5 (CO_2H), $pK_{Est(2)}$~5.1 (N).** It crystallises from EtOH (*ca* 20ml/g), in several modifications with **m** 196° and 216°(subliming at 65°). [*Beilstein* **22** H 103, **22** II 518, **22** II 70, **22** III/IV 1358.]

1-Phenyl-5-sulfanilamidopyrazole *[526-08-9]* **M 314.3, m 177-178°, 178-179°.** Crystallise it from EtOH or aqueous EtOH. [Schmidt & Druey *Helv Chim Acta* **41** 309 *1958*, *Beilstein* **25** III/IV 2029.]

4-Phenyl-1,2,4-triazole-3,5-diol (4-phenylurazole) *[15988-11-1]* **M 175.2, m 207-209°.** Crystallise 4-phenylurazole from water or 95% EtOH. Dissolve 35g in 80ml of boiling 95% EtOH and on cooling 90-95% is recovered with **m** 209-210°. It has IR with ν_{max} at 1685 and 3120cm^{-1}. [Cookson et al. *Org Synth* **51** 121 *1971*, *Beilstein* **26** I 64, **26** III/IV 540.]

4-Phenyl-1,2,4-triazoline-3,5-dione (PTAD) *[4233-33-4]* **M 175.2, m 165-170°(dec), 170-177°(dec).** PTAD forms carmine red needles by sublimation (ice cold finger) at 100°/0.1mm, and/or by recrystallisation from EtOH. Its IR has ν_{max} at 1760 and 1780 cm^{-1}. [Cookson et al. *Org Synth* **51** 121 *1971*, Moore et al. *J Org Chem* **39** 3700 *1974*, *Beilstein* **26** I 57, **26** III/IV 540.]

9-Phenyl-9-xanthenol (hydroxypixyl) *[596-38-3]* **M 274.3, m 158-161°, 158.5-159°, 159°.** Dissolve hydroxypixyl in AcOH and add H_2O whereby it separates as colourless prisms. It is slightly soluble in $CHCl_3$, soluble in $*C_6H_6$ but insoluble in petroleum ether. It sublimes on heating. Its UV in H_2SO_4 has λ_{max} at 450nm (ε 5620) and 370nm (ε 24,900) and the *$HClO_4$* salt in $CHCl_3$ has λ_{max} at 450 (ε 404) and 375nm (ε 2420). [Sharp *J Chem Soc* 2558 *1958*, Bünzly & Decker *Chem Ber* **37** 2983 *1904*, Chattopadhyaya & Reece *J Chem Soc, Chem Commun* 639 *1978*, Gomberg & Cone *Justus Liebigs Ann Chem* **370** 142 *1909*, *Beilstein* **17** I 80, **17** II 161, **17** III/IV 1704, **17/4** V 675.]

"Phosphine" [dye CI 793, Chrysaniline mononitrate, 3-amino-9-(4-aminophenyl)-acridinium mononitrate) *[10181-37-0]* **M 348.4, m >250°(dec), pK^{20} 7.71 (50% aqueous EtOH).** Crystallise the dye from *benzene/EtOH. The *free base* crystallises from $*C_6H_6$ in yelow crystals **m** 229-230°. [Albert & Goldacre *J Chem Soc* 709 *1946*, *Beilstein* **22** H 91, **22** I 651, **22** II 403, **22** III/IV 5513.]

Phthalazine *[253-52-1]* **M 130.2, m 90-91°, b 190°/30mm, 175°/17mm, pK^{20} 3.47.** Phthalazine crystallises from diethyl ether or *benzene, and sublimes under a vacuum. The *hydrochloride* forms needles from EtOH with **m** 235-236°(dec) and the *picrate* has **m** 208-210°. [Armarego *J Appl Chem* **11** 70 *1961*, *Beilstein* **23** H 174, **23** III/IV 1233.]

Phthalazine-1,4-dione (phthalhydrazide) *[1445-69-8]* **M 162.2, m 330-333°, 336°, 346°, pK_1^{20} -3.29 pK_2^{20} -0.99, pK_3^{20} 5.67, pK_4^{20} 13.0.** Recrystallise it twice from 0.1M KOH [Merenyi et al. *J Am Chem Soc* **108** 7716 *1986*], EtOH or dimethylformamide and it sublimes >300°. [*Beilstein* **24** H 371, **24** II 194.]

Phthalazone (1-hydroxyphthalazine) *[119-39-1]* **M 146.2, m 183-184°, 186-188°, b 337°/760mm, pK_1^{20} -2.2, pK_2^{20} -1.4, pK_3^{20} 11.99.** Phthalazone crystallises from H_2O or EtOH and sublimes *in vacuo.* [*Beilstein* **24** H 142, **24 24** III/IV 400.]

2-Picoline-*N*-oxide (2-methylpyridine-1-oxide) *[931-19-1]* **M 109.1, m 41-45°, b 89-90°/0.8-0.9mm, 90-100°/1mm, 110°/4mm, 135°/5mm, 123°/9mm, 123-124°/15mm, 259-261°/atm, n_D^{25} 1.5854 (supercooled),**

pK^{25} 1.10. Purify the *N*-oxide by fractional distillation, and it can be recrystallised from *C_6H_6/hexane but is *hygroscopic*. [Bullitt & Maynard *J Am Chem Soc* **76** 1370 *1954*, Ross et al. *J Am Chem Soc* **78** 3625 *1956*, IR: Wiley & SlaymAker *J Am Chem Soc* **79** 2233 *1957*.] The *picrate* has **m** 125-126.5º (from EtOH) [Boekelheide & Linn *J Am Chem Soc* **76** 1286 *1954*]. The *phthalate* has **m** 115-116º (from EtOH) [den Hertog et al. *Rec Trav Chim Pays Bas* **70** 591 *1951*]. [*Beilstein* **20** III/IV 2689, **20/5** V 479.]

3-Picoline-*N*-oxide (3-methylpyridine-1-oxide) *[1003-73-2]* **M 109.1, m 37-39º, 37-38º (evacuated capillary), 84-85º/0.3mm, 101-103º/0.7-0.8mm, 114-115º/1.5mm, 118º/2mm, pK^{25} 1.08.** Purify the *N*-oxide by careful fractionation *in vacuo*. The distillate remains supercooled for several days before solidifying. It is a slightly *hygroscopic* solid which could melt in the hand. The *picrate* has **m** 149-151º (from EtOH). [Taylor & Corvetti *Org Synth* Coll Vol **IV** 654 *1963*, IR: Katritzky et al. *J Chem Soc* 3680 *1959*, Jaffé & Doak *J Am Chem Soc* **77** 4441, 4481 *1955*, Boekelheide & Linn *J Am Chem Soc* **76** 1286 *1954*]. [*Beilstein* **20** III/IV 2719, **20/5** V 517.]

4-Picoline-*N*-oxide (4-methylpyridine-1-oxide) *[1003-67-4]* **M 109.1, m 182-184º, 185-186º, 186-188º, pK^{25} 1.29.** Recrystallise the *N*-oxide from EtOH/EtOAc, Me_2CO/Et_2O or *C_6H_6. [Bullitt & Maynard *J Am Chem Soc* **76** 1370 *1954*, Boekelheide & Linn *J Am Chem Soc* **76** 1286 *1954*]. [*Beilstein* **20** III/IV 2741, **20/5** V 558.]

Picolinic acid (pyridine-2-carboxylic acid) *[98-98-6]* **M 123.1, m 138º, pK$_1^{25}$ 1.03 (1.36), pK$_2^{25}$ 5.30 (5.80).** Crystallise the acid from water or *benzene. The *picrate* has **m** 185-187º (from MeOH). [*Beilstein* **22** H 33, **22** I 502, **22** II 30, **22** III/IV 303, **22/2** V 3.]

α-Picolinium chloride *[14401-91-3]* **M 129.6, m 77-78º, 85º, b 229º/atm.** A 1:1 mixture of α-picoline and HCl is distilled at 275º, then sublimed in a vacuum at 91-91.5º. [*Beilstein* **20** H 236, **20** III/IV 2685, **20/5** V 474.]

***N*-4-Picolinoylbenzimidazole** *[100312-29-6]* **M 173.3, m 105-107º.** Recrystallise the imidazole three times from hexane [Fife & Przystas *J Am Chem Soc* **108** 4631 *1986*].

Picrolic acid [3-methyl-4-nitro-1-(4-nitrophenyl)-2-pyrazolin-5-one, picrolonic acid] *[550-74-3]* **M 264.2, m 120º(dec), 116.5º(dec at 125º) 125º.** Crystallise picrolic acid from water or EtOH (solubility is 0.123% at 15º and 1.203% at 100º in H_2O; and 1.107% at 0º and 11.68% at 81º in EtOH). It forms Ca, Cu Hg, Mg, Na, Sr, Pb and many other metal complexes [Maquestian et al *Bull Soc Chim Belg* **82** 233 *1973*, Isaki et al. *Chem Ber* **74** 1420 *1941*]. [*Beilstein* **24** H 51, **24** I 218, **24** II 25, **22** III/IV 105.]

Pinacyanol chloride (Quinaldine Blue) *[2768-90-3]* **M 388.9, CI 808, m 270º(dec).** Crystallise the dye from EtOH/diethyl ether. The *iodide* [605-91-4] crystallises from MeOH or EtOH with **m** 298-299º(dec). [*Beilstein* **23** H 320, 23 I 89, II 282, III/IV 2064, **23/10** V 129.]

***dl*-Pipecolinic acid (piperidine-2-carboxylic acid)** *[4043-87-2]* **M 129.1, m 264º, 280º(dec), pK$_1^{25}$ 2.29, pK$_2^{25}$ 10.77.** It crystallises from water. The (±)-picrate has **m** 158-159º (from EtOH or *C_6H_6). [*Beilstein* **22** H 7, **22** III/IV 97, **22/1** V 220.] The *R(+)-enantiomer* [1723-00-8] has **m** 277º(dec) and $[\alpha]_D^{20}$ +27º (c 4, H_2O), and the *S(-)-enantiomer* [3105-95-1] has **m** 277º(dec) and $[\alpha]_D^{20}$ -26º (c 4, H_2O). [cf p 603, *Beilstein* **22** III/IV 96, **22/1** V 220.]

Piperazine *[110-85-0]* **M 86.1, m 110-112º, 44º (hexahydrate** *142-63-2***) b 125-130º/760mm, pK$_1^{25}$ 5.33, pK$_2^{25}$ 9.73.** Piperazine crystallises from EtOH or anhydrous *benzene and is dried at 0.01mm. It can be sublimed under vacuum and purified by zone melting. The *hydrochloride* has **m** 172-174º (from EtOH), and the *dihydrochloride* crystallises from aqueous EtOH and has **m** 318-320º (dec, sublimes at 295-315º). The *picrate* has **m** ~200º, and the *picrolonate* crystallises from dimethylformamide (**m** 259-261º). [*Beilstein* **23** H 4, **23** I 4, **23** II 3, **23** III/IV 15, **23/1** V 30.]

§ Piperazine on polystyrene support is commercially available.

Piperazine-*N,N'*-bis(2-ethanesulfonic acid) (PIPES) *[5625-37-6]* **M 302.4, pK_1^{25} <3, pK_2^{25} 6.82 (7.82).** Purify PIPES from boiling water (maximum solubility is about 1g/L) or as described for ADA (see [*26239-55-4*] in "Aliphatic Compounds" in this Chapter). [Good et al. *Biochemistry* **5** 469 *1966*, *Beilstein* **23/12** V 380.]

Piperazine dihydrochloride (H_2O) *[142-64-3 (2HCl)*; *6094-40-2 (xHCl)]* **M 177.1, m 82.5-83.5°.** Crystallise the salt from aqueous EtOH and dry it at 110°. [*Beilstein* **23** III/IV 17, **23/1** V 30.]

Piperazine phosphate (H_2O) *[18534-18-4]* **M 197.6.** Crystallise it twice from water, air-dry and store for several days over Drierite. The salt dehydrates slowly if heated at 70°. [*Beilstein* **23** III/IV 18, **23/1** V 30.]

Piperidine *[110-89-4]* **M 85.2, f -9°, b 35.4°/40mm, 106°/760mm, d_4^{20} 0.862, n_D^{20} 1.4535, n_D^{25} 1.4500, pK^{25} 11.20 (basic).** Dry piperidine with BaO, KOH, CaH_2, or sodium, and fractionally distil (optionally from sodium, CaH_2, or P_2O_5). Purify from pyridine by zone melting. [*Beilstein* **22** H 6, **22** I 5, **22** II 3, **22** III/IV 287, **22/2** V 3.]
§ Piperidine on polystyrene support is commercially available.

Piperidine-2,6-dione (glutarimide) *[1121-89-7]* **M 113.1, m 163-165°, 155-157°, 154°, 152-154°, pK^{25} 11.43 (acidic).** Purify it by dissolving 75g in 200ml of H_2O, boil for 30 minutes with 2g of charcoal, filter, evaporate to dryness and recrystallise the residue from 125m L of 95% EtOH to give 70g of white crystals, **m** 152-154°. It also crystallises from Me_2CO (**m** 163-165°) or EtOH (**m** 153-154°). The *N-bromo* derivative (a brominating agent) crystallises from H_2O with **m** 180-185°. [Paris et al. *Org Synth* Coll Vol **IV** 496 *1963*, *Beilstein* **21** H 382, **21** I 331, **21** II 307, **21** III/IV 4582.]

Piperidinium chloride *[6091-44-7]* **M 121.6, m 244-245, 247-248°.** Crystallise the salt from EtOH/diethyl ether in the presence of a small amount of HCl. [*Beilstein* **20** H 6, **20** II 10, **20** III/IV 295, **20/2** V 13.]

Piperidinium nitrate *[6091-45-8]* **M 145.2, m 141°, (155-157° from EtOH).** The nitrate crystallises from acetone/ethyl acetate or EtOH. [*Beilstein* **20** H 12, **20** II 10, **20** III/IV 295, **20/2** V 14.]

4-Piperidone [piperidin-4(1*H*)-one, γ-] *[41661-47-6]* **M 99.1 (anhydrous), cannot be distilled, pK^{25} 8.6 (acidic).** It is a yellow irritating oil which is an alkaloid in the leaves and branches of *Dichilus* species (leguminosae), e.g. *D. strictus, D. gracilis, D. lebeckioides, D. pilosus* and *D. reflexus*. It decomposes on distillation and is purified and stored as the *monohydrate monohydrochloride* [*anhydrous* 41979-39-9; *hydrate* 40064-34-4], M 135.6 (*anhydrous salt*), which is in fact *4,4-dihydroxy-piperidinium chloride* that recrystallises from H_2O with **m 94-96°, 97-100°** (+ 1 H_2O), or from EtOH/Et_2O with **m 139-141°** (+ 1.5 EtOH); and the *anhydrous salt* has **m 147-149°**. See above for the *N*-acetyl, *N*-benzyl and *N*-methyl derivatives. The *N-benzoyl* derivative [24686-78-0], M 203.2, has **m 49-50°** and **b 158-160°/0.2mm**, and the *oxime* [79858-41-6], M 114.1, crystallises from dry *C_6H_6 in needles **m 117-118°** (anhydrous), and is hygroscopic. [*Beilstein* **21/6** V 419.]

Piperine (1-piperoylpiperidine) *[94-62-2]* **M 285.4, m 129-129.5°, pK^{15} 1.98.** Piperine crystallises as light yellow crystals from EtOH or EtOAc (**m** 132°), aqueous EtOH (**m** 128-129°), Et_2O (**m**129°), or *benzene/ligroin. [*Beilstein* **20** H 79, **20** I 23, **20** II 53, **20** III/IV 1341, **20/3** V 469.]

Poly(*N*-vinylcarbazole) *[25067-59-8]***.** Precipitate it seven times from tetrahydrofuran with MeOH, with final freeze-drying from *benzene. Dry it under vacuum.

Poly(4-vinylpyridine) *[25232-41-1]* **M $(105.1)_n$.** Purify it by repeated precipitation from solutions in EtOH and dioxane, and then EtOH and ethyl acetate. Finally, freeze-dry a *tert*-butanol solution.

Poly(*N*-vinylpyrrolidone) *[9003-39-8]* **M $(111.1)_n$, crosslinked** *[25249-54-1]* **m >300°.** Purify it by dialysis, and freeze-drying. Also by precipitation from $CHCl_3$ solution by pouring into ether. Dry it in a vacuum over P_2O_5. For the crosslinked polymer, purification is by boiling for 10 minutes in 10% HCl and then washing with glass-distilled water until free from Cl ions. Finally, Cl ions are removed more readily by neutralising with

KOH and continued washing.

(±)-Primaquine diphosphate (*RS*- 8-[4-amino-1-methylbutylamino]-6-methoxyquinoline di-phosphate) *[63-45-6]* **M 455.4, m 197-198°, 204-206°(dec), $pK_{Est(1)}$ ~3.38 (ring N^+), $pK_{Est(2)}$ ~10.8 NH_3^+).** It forms yellow crystals from 90% aqueous EtOH and is moderately soluble in H_2O. The *oxalate salt* has **m** 182.5-185° (from 80% aqueous EtOH), and the *free base* is a viscous liquid **b** 165-170°/0.002mm, 175-177°/2mm. [Elderfield et al. *J Am Chem Soc* **68** 1526 *1964*, Elderfield et al. *J Am Chem Soc* **77** 4817 *1955*, *Beilstein* **22** III/IV 5817.]

Proclavine (3,6-diaminoacridine) *[92-62-6]* **M 209.2, m 284-286°, pK_1^{25} -2.7, pK_2^{25} 0.55, pK_3^{25} 9.49.** It crystallises from aqueous MeOH. The *picrate* crystallises from aqueous pyridine with **m** ~185°. [*Beilstein* **22** H 487, **22** I 649, **22** II 397, **22** III/IV 5487, **22/11** V 322.] For proflavin see 3,6-diaminoacridine hydrochloride.

Propidium iodide (3,8-diamino-5-(3-diethylaminopropyl)-6-phenylphenantridinium iodide methiodide) *[25535-16-4]* **M 668.4, m 210-230°(dec), $pK_{Est(1)}$ ~4 (aniline NH_2), $pK_{Est(2)}$ ~8.5 (EtN_2).** It crystallises as red crystals from H_2O containing a little KI. It fluoresces strongly with nucleic acids. [Watkins *J Chem Soc* 3064 *1952*, *Beilstein* **22** III/IV 5519.] **TOXIC.**

(±)-Propylene carbonate (4-methyl-1,3-dioxalan-2-one) *[108-32-7]* **M 102.1, b 79-80°/0.08mm, 110°/0.5-1mm, 112-114°/2mm, 241°/760mm, d_4^{20} 1.204, n_D^{20} 1.423.** It is manufactured by reaction of 1,2-propylene oxide with CO_2 in the presence of a catalyst (quaternary ammonium halide). Contaminants include propylene oxide, carbon dioxide, 1,2- and 1,3-propanediols, allyl alcohol and ethylene carbonate. It can be purified by percolation through molecular sieves (Linde 5A, dried at 350° for 14 hours under a stream of argon), followed by distillation under a vacuum. [Jasinski & Kirkland *Anal Chem* **39** 163 *1967*.] It can be stored over molecular sieves under an inert gas atmosphere. When purified in this way it contains less than 2 ppm of water. Activated alumina and dried CaO have also been used as drying agents prior to fractional distillation under reduced pressure. It has been dried with 3A molecular sieves and distilled under nitrogen in the presence of *p*-toluenesulfonic acid, then redistilled and the middle fraction collected. [*Beilstein* **19** III/IV 1564, **19/4** V 21.]

***dl*-Propylene oxide** *[75-56-9]* **M 58.1, b 34.5°, d_4^{20} 0.829, n_D^{20} 1.3664.** Dry the oxide with Na_2SO_4 or CaH_2 and fractionally distil it through a packed column (glass helices), after refluxing with Na, CaH_2, or KOH pellets. [*Beilstein* **17** I 4, **17** II 131, **17** III/IV 17, **17/1** V 17.] The *R(+)enantiomer* [15448-47-2] and the *S(-)enantiomer* [16088-62-3] have **b** 33-34°/atm and $[\alpha]_D^{20}$ (+)14.6° and (-)14.6° (neat). [*Beilstein* **17/1** V 17.]

6-Propyl-2-thiouracil (propacil, propyail) *[51-52-5]* **M 170.2, m 218-220°, 218-220°, pK_1^{21} -6.54 (aqueous H_2SO_4), pK_2^{21} -4.22 (aqueous H_2SO_4), pK_3^{21} 8.25 (4% aqueous EtOH).** Purify propacil by recrystallisation from H_2O (soluble in 900 parts at 20°, and 100 parts at 100°). Its UV (MeOH) has λ_{max} at 277nm. [Anderson et al. *J Am Chem Soc* **67** 2197 *1945*, Vanderhaegue *Bull Soc Chim Belg* **59** 689 *1950*, *Beilstein* **24** III/IV 1333.]

Protopine [fumarine, macleyine, 4,6,7,14-tetrahydro-5-methyl-bis[1,3]-benzodioxolo[4,5-*c*:5',6'-*g*]azecine-13(5*H*)-one] *[130-86-9]* **M 353.4, m 208°, 209°, 211°, pK^{25} 5.99.** It crystallises from EtOH/$CHCl_3$. The *picrate* has **m** ~240°(dec). [*Beilstein* **27** H 558, **17** I 568, **17** II 620, **17** III/IV 6881.]

Pteridine *[91-18-9]* **M 132.2, m 139.5-140°, pK_1^{20} 4.05 (equilibrium, hydrate), pK_2^{20} 11,90 (OH of hydrate).** It crystallises from EtOH, *benzene, *n*-hexane, *n*-heptane or petroleum ether. It is best purified by sublimation at 120-130°/20mm. Store at 0°, in the dark. The yellow crystalline solid turns green in the presence of light and on long standing in the dark, and sublimation leaves the dark-coloured material behind. [Albert et al. *J Chem Soc* 474 *1951*; see Albert & Armarego *Adv Heterocycl Chem* **4** 1 *1965*, *Beilstein* **26** III/IV 1770.]

2,4-(1*H*,3*H*)-Pteridinedione H_2O (lumazine) *[487-21-8]* **M 182.1, m >350°, pK_1^{20} <1.0, pK_2^{20} 7.94.** Crystallise the dione from water. It has also been purified as for pterin [2236-60-4] below. [Dallacker & Steiner *Justus Liebigs Ann Chem* **660** 98 *1962*, *Beilstein* **26** III/IV 2489.]

Pterin (2-aminopteridin-4(3*H*)-one) *[2236-60-4]* **M 163.1, m >300°, pK_1^{20} 2.27 (basic), pK_2^{20} 7.96 (acidic).** It is dissolved in hot 1% aqueous ammonia, filtered, and an equal volume of hot 1M aqueous formic acid is added. The solution is allowed to cool at 0-2° overnight. The solid is collected and washed with distilled water several times by centrifugation and dried *in vacuo* over P_2O_5 overnight, and then at 100° overnight (any ammonium formate in the sample evaporates off). [*Beilstein* **26** III/IV 3936.]

Pterocarpin {(6a*R*-*cis*)-6a,12a-dihydro-3-methoxy-6*H*-[1,3]dioxolo[5,6]benzofuro[3,2*c*][1]-benzopyran} *[524-97-0]* **M 298.3, m 165°, 165-166°, $[\alpha]_{546}^{20}$ -215° (c 0.5, $CHCl_3$).** Crystallise it from EtOH, or petroleum ether. [Fukui & Nakayama *Bull Chem Soc Jpn* **42** 1408 *1969*, Packler & Underwood *Tetrtahedron* **23** 1817 *1967*, *Beilstein* **19** II 459, **19** III/IV 5789.]

Pteroic acid (2-amino-6-*p*-carboxyanilinomethylpteridin-4(3*H*)-one) *[119-24-4]* **M 312.3, m >300°(dec), $pK_{Est(1)}$~ 2.3 (basic, N1), $pK_{Est(2)}$~ 2.6 (basic, CH_2NH), $pK_{Est(3)}$~ 4.5 (COOH), $pK_{Est(4)}$ ~ 7.9 (acidic 4-OH).** Crystallise it from dilute HCl. Dry it *in vacuo*. Hygroscopic **IRRITANT.** [Nair et al. *J Org Chem* **46** 3152 *1981*, *Beilstein* **26** III/IV 3942.]

Purine *[120-73-0]* **M 120.1, m 216-217°, pK_1^{20} 2.30, pK_2^{20} 9.86.** It crystallises from toluene or EtOH, and sublimes at 100-150°/0.1mm or 160°/10^{-4}mm. The *picrate* has **m** 207-209° after crystallisation from 20 volumes of H_2O. [*Beilstein* **26** H 354, **26** III/IV 1736.]

Pyocyanine (1-hydroxy-5-methylphenazinium zwitterion) *[85-66-5]* **M 210.2, m 133° (sublimes and decomposes on further heating), pK^{25} –3.5.** It crystallises from H_2O as dark blue needles. The *picrate* has **m** 190° (dec). [*Beilstein* **23** H 395, **23** I 59, **23** II 234, **23/8** V 395.]

Pyrazine *[290-37-9]* **M 80.1, m 47°, 57°, b 115.5-115.8°, pK_1^{20} -6.25 (aqueous H_2SO_4), pK_2^{20} 1.1 (0.51 at 20°).** Distil pyrazine in steam and crystallise it from water. Purify also by zone melting. [*Beilstein* **23** H 91, **23** II 80, **23** III/IV 899, **23/5** V 351.]

Pyrazinecarboxamide *[98-96-4]* **M 123.1, m 189-191° (sublimes slowly at 159°), pK^{25} -0.5.** The amide crystallises from water, EtOH or 1:1 hexane/EtOH in four modifications *viz* α-form, β-form, δ-form and γ–form. [Rø & Sørum *Acta Cryst* **28B** 1677 *1972*, *Beilstein* **25** III/IV 772.]

Pyrazinecarboxylic acid *[98-97-5]* **M 124.1, m 225-229°(dec), pK_1^{25} -3.0, pK_2^{25} -0.7, pK_3^{25} 2.70.** It crystallises from water. The *methyl ester* has **m** 62° (from petroleum ether). [Sauville & Spoerri *J Am Chem Soc* **63** 3153 *1941*, *Beilstein* **25** III/IV 771.]

Pyrazine-2,3-dicarboxylic acid *[89-01-0]* **M 168.1, m 183-185°(dec), 187°(dec), pK_1 <–2.0, pK_2 0.9, pK_3 2.77 (2.20).** Crystallise the dicarboxylic acid from water and dry it at 100°. The *dimethyl ester* has **m** 62-63° (from Et_2O or Et_2O/petroleum ether). [*Beilstein* **25** H 168, **25** II 164, **25** III/IV 1064.]

Pyrazine-1,4-dioxide *[2423-65-6]* **M 112.1, m 285-286°, pK_{Est} <0.** If the sample contains pyrazine-1-oxide, then place it in a Soxhlet extractor and extract it with hot petroleum ether (b 60-68°) in which the mono-oxide is soluble. Collect the dioxide from the thimble and recrystallise it from MeOH. It is dried *in vacuo*. It has ν_{max} at 1270cm^{-1}. [Koelsch & Gumprecht *J Org Chem* **23** 1605 *1958*.]

Pyrazine-1-oxide *[2433-84-9]* **M 96.1, m 113-114°, pK_{Est} <0.** Recrystallise the oxide from *C_6H_6. It is soluble in hot petroleum ether (b 60-68°, see pyrazine-1,4-dioxide above). Dry it *in vacuo*. It has ν_{max} at 1305cm^{-1}. [Koelsch & Gumprecht *J Org Chem* **23** 1605 *1958*.]

Pyrazole *[288-13-1]* **M 68.1, m 70°, b 96°/16mm, pK^{25} 2.48.** Crystallise pyrazole from petroleum ether, cyclohexane, or water. Its solubility in H_2O at 9.6° is 2.7moles/L, and at 24.8° it is 19.4moles/L; in cyclohexane at 31.8° it is 0.577moles/L, and at 56.2° it is 5.86moles/L; and in benzene at 5.2° it is 0.31moles/L, and at 46.5° it is 16.8moles/1000ml. [Barszcz et al. *J Chem Soc, Dalton Trans* 2025 *1986*, *Beilstein* **23** H 39, **23** I 15, **23** II 33, **23** III/IV 550, **23/4** V 122.]

Pyrazole-*N*-1-carboximidine hydrochloride (Praxadine, 1-amidinopyrazole hydrochloride, 1*H*-pyrazole-1-carboxamidine hydrochloride) *[4023-02-3]* **M 146.6, m 165-166°, 167-168°, 167-168.5°, 167-170°, pK_{Est} ~8.5.** The white crystalline hydrochloride, which can be prepared from pyrazole and cyanamide in *p*-dioxane containing HCl, is purified by recrystallisation from dioxane/H_2O. It is a good guanylating agent for primary and secondary amines [Bernatowicz et al. *J Org Chem* **57** 2497 *1992*, Bernatowicz et al. *Tetrahedron Lett* **34** 3389 *1993*]. The *free base* can be obtained by suspending the hydrochloride in $CHCl_3$ and bubbling NH_3 gas through, whereby NH_4Cl separates and is filtered off. $CHCl_3$ is then distilled off and the residue is washed with a little EtOH and dried *in vacuo*. It crystallises from *C_6H_6 and has **m 93-96° (94-98.5°** and **97-101°** have also been reported). The *picrate* has **m 202-203° (208°** has also been reported). [Bredereck et al. *Chem Ber* **98** 3178 *1965*, Jones et al. *J Org Chem* **19** 1428 *1954*, 2497 *1992*, *Beilstein* **23/4** V131.]

1*H*-Pyrazole-3-carboxylic acid *[1621-91-6]* **M 112.1, m 208-210°, 210-214° (decarboxylates), pK^{25} 3.74, $pK_{Est(2)}$ ~12 (acidic NH).** Purify the acid by precipitation from an alkaline solution with mineral acid, and recrystallise it from H_2O. On heating, it decarboxylates (to pyrazole m 70°) more readily than the 4-carboxylic acid below. The *N-2-methyl derivative* has **m 222° (**from H_2O) and **pK^{25} 3.27**. [Habraken at al. *Rec Trav Chim Pays Bas* **85** 1194 *1966*, Jones et al. *J Org Chem* **19** 1428 *1954*, Allen & Shirley *J Am Chem Soc* **80** 6273 *1958*, Knorr *Justus Liebigs Ann Chem* **273** 231 *1893*, Knorr *Justus Liebigs Ann Chem* **279** 217 *1894*.]

1*H*-Pyrazole-4-carboxylic acid *[37718-11-9]* **M 112.1, m 282° (decarboxylates), $pK_{Est(1)}$ ~3.6, $pK_{Est(2)}$ ~12 (acidic NH).** This acid, also obtained by decarboxylating the more water soluble 3,4,5-tricarboxylic acid, crystallises in yellow prisms from H_2O. [Buchner & Fritsch *Justus Liebigs Ann Chem* **273** 253 *1893*, Knorr & Rothenburg *Chem Ber* **28** 693 *1895*, *Beilstein* **25** H 116.]

Pyrazole-3,5-dicarboxylic acid *[3112-31-0]* **M 174.1, m 287-289°(dec), 295-297°(dec), $pK_{Est(1)}$~1.2 (CO_2H), $pK_{Est(2)}$~3.7 (CO_2H), $pK_{Est(3)}$~12 (NH).** It crystallises from water as a *monohydrate*, or EtOH. Dry it in a vacuum at 100°. The *dimethyl ester* crystallises from *C_6H_6 with **m** 155°. [*Beilstein* **25** III/IV 1047.]

Pyridazine *N*-oxide (pyridazine 1-oxide) *[1457-42-7]* **M 96.1, m 38-39°, b 138-140°/4mm, pK_{Est} <1.** Purify the oxide by distillation in a vacuum and by sublimation *in vacuo*. When a solution of the oxide in MeOH is treated with an aqueous solution of $CuCl_2$, the $[C_4H_4N_2O]_2$—$CuCl_2$-$2H_2O$-*complex* (**m** 182-183°) is formed from which the oxide can be recovered . [Pollak et al. *J Org Chem* **35** 2478 *1970*, Klinge et al. *Rec Trav Chim Pays Bas* **95** 21 *1976*, Ohsawa et al. *Tetrahedron Lett* 1979 *1978*, Koelsch & Gumprecht *J Org Chem* **23** 1605 *1958*, *Beilstein* **23** III/IV 890.]

Pyridine *[110-86-1]* **M 79.1, f -41.8°, b 115.6°, d_4^{20} 0.9831, n_D^{20} 1.51021, pK^{25} 5.23.** Likely impurities are H_2O and amines such as the picolines and lutidines. Pyridine is *hygroscopic* and is miscible with H_2O and organic solvents. It can be dried with solid KOH, NaOH, CaO, or BaO, followed by fractional distillation. Other methods of drying include standing with Linde type 4A molecular sieves, CaH_2 or $LiAlH_4$, azeotropic distillation of the H_2O with toluene or *benzene, or treated with phenylmagnesium bromide in ether, followed by evaporation of the ether and distillation of the pyridine. A recommended [Lindauer & Mukherjee *Pure Appl Chem* **27** 267 *1971*] method dries pyridine over solid KOH (20g/Kg) for 2 weeks and fractionally distils the supernatant over Linde type 5A molecular sieves and solid KOH. The product is stored under CO_2-free nitrogen. Pyridine can be stored in contact with BaO, CaH_2 or molecular sieves. Non-basic materials can be removed by steam distilling a solution containing 1.2 equivalents of 20% H_2SO_4 or 17% HCl until about 10% of the base has been carried over along with the non-basic impurities. The residue is then made alkaline, and the base is separated, dried with NaOH and fractionally distilled. *The alkali metals, Na, Li or Cs should NOT be used for drying pyridine, and pyridine derivatives, as they form coloured pyridine radical anions leading to bipyridyls.* [see Schmulback et al. *J Am Chem Soc* **90** 6600 *1968*].
Alternatively, pyridine can be treated with oxidising agents. Thus pyridine (800ml) has been stirred for 24 hours with a mixture of ceric sulfate (20g) and anhydrous K_2CO_3 (15g), then filtered and fractionally distilled. Hurd and Simon [*J Am Chem Soc* **84** 4519 *1962*] stirred pyridine (135ml), water (2.5L) and $KMnO_4$ (90g) for 2 hours at 100°, then set aside for 15 hours before filtering off the precipitated manganese oxides. Addition of solid KOH (*ca* 500g) caused pyridine to separate. It was decanted, refluxed with CaO for 3 hours and distilled.

Separation of pyridine from some of its homologues can be achieved by crystallisation of the oxalates. Pyridine is precipitated as its *oxalate* by adding it to the stirred solution of oxalic acid in acetone. The precipitate is filtered, washed with cold acetone, and pyridine is regenerated and isolated. Other methods are based on complex formation with $ZnCl_2$ or $HgCl_2$. Heap, Jones and Speakman [*J Am Chem Soc* **43** 1936 *1921*] added crude pyridine (1L) to a solution of $ZnCl_2$ (848g) in 730ml of water, 346ml of conc HCl and 690ml of 95% EtOH. The crystalline precipitate of $ZnCl_2$.$(pyridine)_2$ was filtered off, recrystallised twice from absolute EtOH, then treated with a conc NaOH solution, using 26.7g of solid NaOH to 100g of the complex. The precipitate was filtered off, and the pyridine was dried with NaOH pellets and distilled. Similarly, Kyte, Jeffery and Vogel [*J Chem Soc* 4454 *1960*] added pyridine (60ml) in 300ml of 10% (v/v) HCl to a solution of $HgCl_2$ (405g) in hot water (2.3l). On cooling, crystals of pyridine-$HgCl_2$ (1:1) complex separated and were filtered off, crystallised from 1% HCl (to **m** 178.5-179°), washed with a little EtOH and dried at 110°. The free base was liberated by addition of excess aqueous NaOH and separated by steam distillation. The distillate was saturated with solid KOH, and the upper layer was removed, dried further with KOH, then BaO and distilled. Another possible purification step is fractional crystallisation by partial freezing.
Small amounts of pyridine have been purified by vapour-phase chromatography, using a 180-cm column of polyethyleneglycol-400 (Shell 5%) on Embacel at 100°, with argon as carrier gas. The Karl Fischer titration can be used for determining water content. A colour test for pyrrole as a contaminant is described by Biddiscombe et al. [*J Chem Soc* 1957 *1954*]. The *1:1-hydrochloride* crystallises from EtOH with **m** 144°, **b** 218-219°/760mm (see below) and is hygroscopic. The *1:2-hydrochloride* has **m** 46° [58888-58-7] and the *picrate* has **m** 165-166° [1152-90-5]. [*Beilstein* **20** H 181, **20** I 54, **20** II 96, **20** III/IV 2205, **20/5** V 160.]
§ Polystyrene-supported pyridine is commercially available.

Pyridine-2-aldehyde *[1121-60-4]* **M 107.1, b 81.5°/25mm, d_4^{20} 1.121, n_D^{20} 1.535, pK_1^{25} 3.84, pK_2^{25} 12.68.** Purification is achieved by bubbling sulfur dioxide into a solution of 50g of the aldehyde in 250ml of boiled water, under nitrogen, at 0°, until precipitation is complete. The bisulfite addition compound is filtered off rapidly and, after washing with a little water, is refluxed in 17% HCl (200ml) under nitrogen until a clear solution is obtained. Neutralisation with $NaHCO_3$ and extraction with ether separated the aldehyde which is recovered by drying the extract, then distilling twice, under nitrogen. [Kyte et al. *J Chem Soc* 4454 *1960*, *Beilstein* **21** I 287, **21** III/IV 3495, **21/7** V 293.]

Pyridine-3-aldehyde *[500-22-1]* **M 107.1, b 89.5°/14mm, d_4^{20} 1.141, n_D^{20} 1.549, pK_1^{20} 3.80, pK_2^{20} 13.10.** Purified as for pyridine-2-aldehyde. [*Beilstein* **21** I 288, **21** III/IV 3517, **21/7** V 334.]

Pyridine-4-aldehyde *[872-85-5]* **M 107.1, b 79.5°/12mm, d_4^{20} 1.137, n_D^{20} 1.544, pK_1^{20} 4,77, pK_2^{20} 12.20.** Purified as for pyridine-2-aldehyde. [*Beilstein* **21** III/IV 2529, **21/7** V 351.]

Pyridine-2-aldoxime (pyridine-2-carboxaldoxime) *[873-69-8]* **M 122.1, m 111-113°, 114°, pK_1^{25} 3.56, pK_2^{25} 10.17.** Recrystallise it from Et_2O/petroleum ether or H_2O. The *picrate* has **m** 169-171° (from aqueous EtOH). It is used in peptide synthesis. [UV: Grammaticakis *Bull Chem Soc Fr* 109, 116 *1956*, Ginsberg & Wilson *J Am Chem Soc* **79** 481 *1957*, Hanania & Irvine *Nature* **183** 40 *1959*, Green & Saville *J Chem Soc* 3887 *1956*, *Beilstein E-isomer* **21** I 288, **21** III/IV 3504, **21/7** V 305.]

Pyridine-3-aldoxime *[1193-92-6]* **M 122.1, m 150°, pK_1^{20} 4.07, pK_2^{20} 10.39.** Crystallise the oxime from water. [*Beilstein E-isomer* **21** III/IV 3521, **21/7** V 339.]

Pyridine-4-aldoxime *[696-54-8]* **M 122.1, m 129°, pK_1^{20} 4.73, pK_2^{20} 10.03.** Crystallise the oxime from water. [*Beilstein E-isomer* **21** III/IV 3533, **21/7** V 355.]

2,6-Pyridinedialdoxime *[2851-68-5]* **M 165.1, m 212°, 216°, $pK_{Est(1)}$~3.0, $pK_{Est(2)}$~10.** Crystallise it several times from water or EtOH to give colourless needles. [Lions & Martin *J Am Chem Soc* **79** 2738 *1957*, *Beilstein* **21** III/IV 4746.]

Pyridine-2,5-dicarboxylic acid (isocinchomeronic acid) *[100-26-5]* **M 167.1, m 254°, (267°, dec), pK_1^{25} 0.60, pK_2^{25} 2.49, pK_3^{25} 5.12.** Crystallise it from H_2O or dilute HCl. [Napoli *J Inorg Nucl Chem* **32** 1907 *1970*, *Beilstein* **22** H 153, **22** I 533, **22** II 105, **22** III/IV 1632, **22/4** V 124.]

Pyridine-3,4-dicarboxylic acid (cinchomeronic acid) *[490-11-9]* **M 167.1, m 253-255°, 256°, pK_1^{25} 1.50 (0.6), pK_2^{25} 2.43 (2.95), pK_3^{25} 4.78 (5.07).** Crystallise the acid from H_2O or dilute aqueous HCl. It has also been purified *via* the *dimethyl ester* which is distilled (**b** 95-100°/1.5mm) and hydrolysed with 3.5N HCl, evaporated and recrystallised. [Armarego & Evans *J Appl Chem* **12** 45 *1962*, Foye et al. *J Med Chem* **9** 61 *1966*, *Beilstein* **22** H 155, **22** I 534, **22** II 106, **22** III/IV 1641, **22/4** V 135.]

Pyridine hydrobromide perbromide (pyridinium bromide perbromide) *[39416-48-3]* **M 319.9, m 130° (dec), 132-134°(dec), 135°(dec).** It is a very good brominating agent-liberating one mol of Br_2. Purify it by recrystallisation from glacial acetic acid (33g from 100ml of AcOH) to give orange-red crystals. [Fieser & Fieser's *Reagents for Organic Chemistry* **1** 967 *1967*, Englert & McElvain *J Am Chem Soc* **51** 865 *1929*, *Beilstein* **20** II 103, **20/5** V 181.]

Pyridine hydrochloride *[628-13-7]* **M 115.6, m 144°, b 218°/760mm.** Crystallise the salt from $CHCl_3$/EtOAc and wash it with Et_2O. It is *hygroscopic*. [*Beilstein* **20** H 185, **20** I 57, **20** II 103, **20** III/IV 2230, **20/5** V 180.]

Pyridine *N*-oxide *[694-59-7]* **M 95.1, m 67°, 68-69°, pK^{24} 0.79.** Purify the *N-oxide* by crystallisation from Et_2O and by vacuum sublimation. The *picrolonate* has **m** 182-184°. [Katritzky *J Chem Soc* 2407 *1956*, *Beilstein* **20** III/IV 2305, **20/5** V 217.]

Pyridine 3-sulfonic acid *[636-73-7]* **M 159.2, m 365-366°(dec), 357°, pK^{25} 2.89 (12% aqueous EtOH), 3.22 (H_2O)(protonation on N).** Purify the acid by recrystallisation from H_2O or aqueous EtOH as needles or plates. [pKa: Evans & Brown *J Org Chem* **27** 3127 *1962*, IR: Arnett & Chawla *J Am Chem Soc* **100** 214 *1978*.] Its UV in 50% aqueous EtOH has λ_{max} at 208 and 262nm. The *ammonium salt* has **m** 243° (from H_2O), the *sulfonyl chloride* has **m** 133-134° (from petroleum ether), the *amide* has **m** 110-111° (from H_2O), the *hydrochloride* has **m** >300°(dec), and the *N-methyl betaine* has **m** 130° (from H_2O). [Gastel & Wibaut *Rec Trav Chim Pays Bas* **53** 1031 *1934*, McIlvain & Goese *J Am Chem Soc* **65** 2233 *1943*, Machek *Monatsh Chem* **72** 77 *1938*, *Beilstein* **22** I 616, **22** II 309, **22/7** V 552.]

2-Pyridinethiol (2-mercaptopyridine) *[2637-34-5; 73018-10-7]* **M 111.2, m 127.4°, 127-130°, 130-132°, pK_1^{20} -1.07, pK_2^{20} 9.97.** If impure, dissolve it in $CHCl_3$, wash it with dilute AcOH, H_2O, dry ($MgSO_4$), evaporate under reduced pressure and recrystallise the residue from $*C_6H_6$ or H_2O. *2-Methylmercaptopyridine* (**b** 100-104°/33mm, pK^{20} 3.59) was formed by treatment with MeI/NaOH. [Albert & Barlin *J Chem Soc* 2394 *1959*, Phillips & Shapiro *J Chem Soc* 584 *1942*, *Beilstein* **21** H 45, **21** III/IV 373, **21/7** V 147.]

4-Pyridinethiol (4-mercaptopyridine) *[4556-23-4]* **M 111.2, m 177°, 179-189°, 186°, pK_1^{20} 1.43, pK_2^{20} 8.86.** Purify the thiol by dissolving ~45g in boiling H_2O (100ml) (charcoal), filter and precipitate it by adding 50% aqueous NaOH (~80ml) to pH ~6. Dissolve the precipitate in EtOH, evaporate it to dryness, then crystallise it from boiling EtOH (~100ml, charcoal) to give yellow flat hexagonal plates (**m** 186°). It sublimes readily *in vacuo*. [King & Ware *J Chem Soc* 873 *1939*.] The *picrate* forms yellow needles from H_2O with **m** 222°(dec). The *4-methylmercaptopyridine* derivative crystallises from petroleum ether (**m 47°**, also **44-45°** was reported, with a **pK^{20}** of **5.97**) and was prepared by treatment with MeI/NaOH. Its *picrate* has **m 245°** (from H_2O, MeOH or EtOH). The *N-methyl-4-pyridinethiol* derivative has **m 168.5-170°** (from EtOH), a **pK^{20}** of **1.30** and is soluble in $CHCl_3$. [Albert & Barlin *J Chem Soc* 2384 *1959*, *Beilstein* **21** II 35, **22** III/IV 373, **22/7** V 147.]

Pyridoxal hydrochloride, pyridoxamine hydrochloride and pyridoxine hydrochloride (vitamin B_6). See entries in "Miscellaneous Compounds" in Chapter 7.

1-(2-Pyridylazo)-2-naphthol (PAN) *[85-85-8]* **M 249.3, m 140-142°, 142°, pK_1^{30-36} 2.9, pK_2^{30-36} 11.2.** Purify PAN by repeated crystallisation from EtOH or MeOH. It can also be purified by sublimation under vacuum. Purity can be checked by TLC using a mixed solvent (petroleum ether/Et_2O/EtOH; 10:10:1) on a silica gel plate. It has pK_1 1.9 and pK_2 12.2 in 20% aqueous ethoxyethanol. It chelates with copper [Pease & Williams *Anal Chem* **31** 1046 *1959*]. [*Beilstein* **22** I 694, **22** III/IV 7073, **22/4** V 618.]

4-(2-Pyridylazo)-resorcinol (PAR) *[1141-59-9]* **M 215.2, m >195°(dec), λ_{max} 415nm, ε 2.59 x 10^4 (pH 6-12), pK_1^{25} 2.69 (3.1), pK_2^{25} 5.50 (5.8), pK_3^{25} 12.5 (11.9).** Purify PAR as the sodium salt by recrystallisation from 1:1 EtOH/water. Purity can be checked by TLC using a silica gel plate and a mixed solvent (*n*-BuOH:EtOH:2M NH_3; 6:2:2). [*Beilstein* **22** I 694, **22** III/IV 7074, **22/14** V 619.]

3-(2-Pyridyl)-5,6-diphenyl-1,2,4-triazine *[1046-56-6]* **M 310.4, m 191-192°.** Purify it by repeated recrystallisation from EtOH/dimethylformamide. It is a reagent for estimating Fe(II) and Ru(II). [Chriswell & Schilt *Anal Chem* **46** 992 *1974*, Kamra & Ayers *Anal Chem* **78** 423 *1975*.]

1-(4-Pyridyl)ethanol *[R-(+) 27854-88-2; S-(-) 54656-96-1]* **M 123.2, m 63-65°, 67-69°, b 138-140°/30mm, 254°/760mm, $[\alpha]_D^{20}$ *R*(+) +49.8° and *S*(-) -49.8° (c 0.5, EtOH), pK_{Est} ~5.4.** Purify it by recrystallisation from petroleum ether. The **m** recorded after sublimation was 59.9-60.2°, and 55° after crystallisation from $*C_6H_6$/petroleum ether or petroleum ether/$*C_6H_6$. The (-)-*di-O-benzoyl tartrate salt* has **m** 146-148° (from EtOH). [UV, ORD: Harelli & Samori *J Chem Soc Perkin Trans 2* 1462 *1974*.] The *racemate* recrystallises from Et_2O with **m** 74-76°, **b** 90-94°/1mm. The *picrate* has **m** 125-126° (from $*C_6H_6$). [Ferles & Attia *Col Czech Chem Commun* **38** 611 *1973*, UV, NMR: Nielson et al. *J Org Chem* **29** 2898 *1964*, *Beilstein* **21** III/IV 522, **21/2** V 217.]

5-(3-Pyridyl)-4*H*-1,2,4-triazole-3-thiol [1,2-dihydro-5-(3-pyridinyl)-3*H*-1,2,4-triazole-3-thione] *[32362-88-2]* **M 178.2, , m 285-286°, 296-302°, $pK_{Est(1)}$ ~3.0 (py N), $pK_{Est(2)}$ ~9 (SH).** This thio-1,2,4-triazole was prepared by fusing nicotinoylhydrazide with thiourea at ~150° then at 160-165° (30 minutes), cooled, EtOH was added and the white solid was filtered off [Beyerman et al. *Rec Trav Chim Pays Bas* **73** 109 *1954*]; or by heating 1-nicotinoyl-3-thiosemicarbazide in 5% aqueous NaOH at 100° (4 hours), cooled, acidified with AcOH, and filtered off [Yale & Piala *J Med Chem* **9** 42 *1966*]. It was recrystallised from 95% EtOH, *n*-BuOH/H_2O, H_2O, and 0.5% aqueous HCl provides the *hydrochloride*, which is dried *in vacuo* [over P_2O_5 or H_2SO_4]. [Yoshida & Asai *J Pharm Soc Jpn* **74** 948 *1954*, *Chem Abstr* **49** 10937 *1955*, *Beilstein* **26** IV 2129].

5-(4-Pyridyl)-4*H*-1,2,4-triazole-3-thiol [1,2-Dihydro-5-(4-pyridinyl)-3*H*-1,2,4-triazole-3-thione] *[14910-06-6]* **M 178.2, , m 301-303° (dec), 305-308° (dec), 308-313°, 320-322° (dec), 321-322° (dec), $pK_{Est(1)}$ ~3.5 (py N), $pK_{Est(2)}$ ~9 (SH).** This thio-1,2,4-triazole was prepared and purified as for the 3-pyridyl-isomer above but by using isonicotinic acid derivatives. It has mild diuretic and natriuretic activity. [Blackman et al. *J Chem Soc C* 661 *1967*, Beyerman et al. *Rec Trav Chim Pays Bas* **73** 109 *1954*, Yale & Piala *J Med Chem* **9** 42 *1966*, Yoshida & Asai *J Pharm Soc Jpn* **74** 948 *1954*, *Chem Abstr* **49** 10937 *1955*, *Beilstein* **26** IV 2129]. ***5-(4-Pyridyl)-4H-1,2,4-triazole-3-sulfonic acid*** *hydrate* was obtained by oxidising the 3-thiol with saturated aqueous $KMnO_4$ 25° (1 hour), decomposed with EtOH, filtered, precipitated as the Ag salt, filtered off, and decomposed with 5% HCl, then evaporated, and the residue was recrystallised from H_2O. It decomposed on heating. [Blackman et al. *J Chem Soc C* 661 *1967*.]

α-Pyrone (2*H*-pyran-2-one, coumalin) *[504-31-4]* **M 96.1, m 5°, 8-9°, b 103-111°/19-22mm, 110°/26mm, 104°/ 30mm, 115-118°/37mm, 206-207°/atm, d_4^{20} 1.1972, n_D^{20} 1.5298, pK^{25} -1.14 (aqueous H_2SO_4).** Dissolve α-pyrone in Et_2O, wash it with brine, dry (Na_2SO_4), filter, evaporate, distil the residue under vacuum and redistil it. It is a colourless liquid. Its IR has ν_{max} at 1622 and 1752cm^{-1} ($CHCl_3$). [Zimmermann et al. *Org Synth* Coll Vol **V** 982 *1973*, Nakagawa & Saegusa *Org Synth* **56** 49 *1977*, Elderfield *J Org Chem* **6** 566 *1941*.] The *picrate* has **m** 106-107° (from EtOH). [*Beilstein* **17** H 271, **17** II 305, **17** III/IV 4399, **17/9** V 288.]

γ-Pyrone (4*H*-pyran-4-one) *[108-97-4]* **M 96.1, m 32.5-32.6°, 33°, 32-34°, b 88.5°/7mm, 91-91.5°/9mm, 95-97°/13mm, 105°/23mm, 215°/atm, pK^{25} 0.10.** Purify γ-pyrone by vacuum distillation; the distillate crystallises and is *hygroscopic*. It is non-steam volatile. The *hydrochoride* has **m** 139° (from EtOH), and the *picrate* has **m** 130.2-130.3° (from EtOH or H_2O). [Mayer *Chem Ber* **90** 2362 *1957*, IR: Jones et al. *Can J Chem* **37** 2007 *1959*, Neelakatan *J Org Chem* **22** 1584 *1957*, *Beilstein* **17** H 271, **17** I 145, **17** II 305, **17** III/IV 4399, **17/9** V 290.]

Pyronin G [3,6-bis(dimethylamino)xanthenylium chloride] *[92-32-0]* **M 302.8, m 250-260°, CI 45005, λmax 522nm, pK_{Est} ~7.6.** Commercial material may contain a large quantity of zinc. Purify it by dissolving 1g in 50ml of hot water containing 5g NaEDTA. Cool to 0°, filter, evaporate to dryness and the residue is extracted with EtOH. The solution is evaporated to 5-10ml, filtered, and the dye is precipitated by addition of excess of dry diethyl ether. It is centrifuged, and the crystals are washed with dry ether. The procedure is repeated, then the product is dissolved in $CHCl_3$, filtered and evaporated. The dye is stored in a vacuum. [*Beilstein* **18** H 596, **18** III/IV 7361, **18/10** V 181.]

Pyrrol-2,5-dione (maleimide) *[541-59-3]* **M 97.1, m 91-93°, 92.6-93°, $d_D^{105.5}$ 1.2493, $n_D^{110.7}$ 1.49256.** Purify it by sublimation in a vacuum. The UV has λ_{max} at 216 and 280nm in EtOH. [de Wolf & van de Straete *Bull Soc Chim Belg* **44** 288 *1935*, UV: Rondestvedt et al. *J Am Chem Soc* **78** 6115 *1956*, IR: Chiorboli & Mirone *Ann Chim (Rome)* **42** 681 *1952*, *Beilstein* **21/10** V 3.]

Pyrrole *[109-97-7]* **M 67.1, m 23.4°, b 66°/80mm, 129-130°/atm, d_4^{20} 0.966, n_D^{20} 1.5097, pK_1^{25} -4.4 (Protonation on carbon), pK_2^{25} 17.51 (aqueous KOH, H_- scale).** Dry pyrrole with NaOH, CaH_2 or $CaSO_4$. Fractionally distil it under reduced pressure from CaH_2. Store it under nitrogen as it turns brown in air. Redistil it immediately before use. The *picrate* forms orange-red crystals with **m** 69°(dec). [*Beilstein* **20** H 4, **20** I 3, **20** II 3, **20** III/IV 61, **20/5** V 3.]

1*H*-Pyrrole-1-propanoic acid (3-[pyrrol-1-yl]propionic acid) *[89059-06-3]* **M 139.2, m 59-64°, 62.5°, pK_{Est} ~4.5.** Recrystallise the acid from petroleum ether (b 80-100°) and dry it *in vacuo*. The *ethyl ester* has **b** 122°/23mm. The *amide* forms colourless needles from $*C_6H_6$ with **m** 81° and is soluble in cold H_2O. [Clemo & Ramage *J Chem Soc* 49 *1931*, Jefford & Johncock *Helv Chim Acta* **66** 2666 *1983*.]

Pyrrolidine *[123-75-1]* **M 71.1, b 87.5-88.5°, d_4^{20} 0.860, n_D^{20} 1.443, pK^{25} 11.31.** Dry pyrrolidine with BaO or sodium, then fractionally distil it, under N_2, through a Todd column packed with glass helices. [*Beilstein* **20** H 159, **20** I 36, **20** II 79, **20** III/IV 2072, **20/1** V 162.]

Pyrrolidine-1-carbodithioic acid ammonium salt *[5108-96-3]* **M 164.3, m 128-130°, pK^{25} 3.25 (free acid).** Purify the salt by recrystallising twice by dissolving in MeOH and adding Et_2O. It has also been purified by recrystallisation from EtOH. It is used for the precipitation of As, Bi, Cd, Co, Cu, Fe, Mn, Ni, Pb, Sb, Su, V and Zn from acidic solutions [Kinrade & van Loon *Anal Chem* **46** 1894 *1974*]. The *ethyl ester* has **b** 87-89°/0.01mm. [Synthesis and Polarography: Kitagawa & Taku *Bull Chem Soc Jpn* **64** 2151 *1973*, Malissa & Schöffmann *Mikrochim Acta* 187 *1955*, *Beilstein* **20** III/IV 195, **20/1** V 331.]

Quercetin ($2H_2O$) (3,3',4',5,6-pentahydroxyflavone) *[6151-25-3 ($2H_2O$); 117-39-3 (anhydrous)]* **M 338.3, m *ca* 315°(dec), 317.4-317.9°(dec), (phenolic pKs 7—10).** Crystallise the flavone from aqueous EtOH and dry at 100°. It also sublimes in a vacuum. Its IR has ν_{max} at 2.5μ and 16.7μ (KBr). It complexes with Cu^{2+}, Al^{3+}, Ca^{2+}, Ge^{4+}, Zn^{2+}, Ti^{4+}, Zr^{4+}, Th^{4+}, UO^{4+}. [*Beilstein* **18** H 242, **18** I 242, **18** II 236, **18** III/IV 3470, **18/5** V 494.]

(±)-Quinacrine [Atebrine, Mepacrine, 3-chloro-9(4-diethylamino-1-methyl)butylamino-7-methoxy)-acridine] dihydrochloride. *[69-05-6]* **M 472.9, m 248-250°(dec), pK_1^{30} -6.49 (aq H_2SO_4), pK_2^{30} 7.73 (ring NH^+), pK_3^{30} 10.18 (Et_2N).** It crystallises from H_2O (solubility is 2.8% at room temperature) as yellow crystals. It is slightly soluble in MeOH and EtOH. The *free base* crystallises from Me_2CO or petroleum ether with **m** 86-88°, or aqueous EtOH with 85-87.5°. The *bismethiodide* has **m** 224° (from MeOH/EtOAc/Et_3N), and the *picrate* has **m** 207-208°(dec) when crystallised from Me_2CO/EtOH. It is an antimalarial, antiprotozoal and intercalates DNA. [Wolfe *Antibiot* **3** (Springer-Verlag) 203 *1975*, *Beilstein* **22** III/IV 6247, **22/12** V 235.]

Quinaldic (quinoline-2-carboxylic) acid *[93-10-7]* **M 173.2, m 156-157°, pK_1^{25} 1.45, pK_2^{25} 2.49 (2.97).** Crystallise quinaldic acid from $*C_6H_6$ or AcOH. It is used for the estimation of many metals. The *methyl ester* has **m** 86-87° (from hexane) and pK^{25} 1.76. [Chauduri et al. *Frez Z Anal Chem* **281** 361 *1976, Beilstein* **22** H 71, **22** II 55, **22** III/IV 1149, **22/3** V 183.]

Quinazoline *[253-82-7]* **M 130.2, m 48.0-48.5°, b 120-121°/17-18mm, pK_1^{20} -4.51 (aqueous H_2SO_4, anhydrous dication), pK_2^{20} 2.01 (anhydrous monocation), pK_3^{20} 4.3 (equilibrium with 3,4-hydrated species), pK_4^{20} 12.1 (hydrated anion).** Purify quinazoline by passage through an activated alumina column in $*C_6H_6$ or petrolum ether (b 40-60°). Distil it under reduced pressure, sublime it under vacuum and crystallise it from petroleum ether. The *picrate* has **m** 188-189° (from MeOH). [Armarego *J Appl Chem* **11** 70 *1961*, Armarego *Quinazolines, Fused Pyrimidines Part I* Brown Ed, Wiley-Interscience *1967*, Brown *Quinazolines Supplement I* Taylor Ed, Wiley-Interscience *1996*, ISBN 0-471-14565-3; for covalent hydration see Albert & Armarego *Adv Heterocycl Chem* **4** 1 *1965*, *Beilstein* **23** H 175, **23** II 177, **23** III/IV 1221.]

***S*(+)-Quinidine** *[56-54-2]* **M 324.4, m 171°, $[\alpha]_{546}^{20}$ +301.1° ($CHCl_3$ containing 2.5% (v/v) EtOH), pK_1^{15} 4.13, pK_2^{15} 8.77.** Crystallise it from $*C_6H_6$ or dry $CHCl_3$/petroleum ether (b 40-60°), discarding the initial, oily crop of crystals. Dry it under vacuum at 100° over P_2O_5. It has been used as a chiral catalyst [Wynberg & Staring *J Am Chem Soc* **104** 166 *1982*, *J Org Chem* **50** 1977 *1985*]. [*Beilstein* **23** H 506, **23** I 164, **23** II 414, **23** III/IV 3261, **23/13** V 395.]

8*S*,9*R*-Quinine *[130-95-0]* **M 324.4, m 177°(dec), $[\alpha]_{546}^{20}$ -160° (c 1, $CHCl_3$), pK_1^{20} 4.13 (quinoline N), pK_2^{20} 8.52 (piperidine N).** Crystallise the quinine from absolute EtOH. It has been used as a chiral catalyst (see previous entry). [*Beilstein* **23** H 511, **23** I 166, **23** II 416, **23** III/IV 3265, **23/13** V 395.]

Quinine bisulfate *[6183-68-2 ($7H_2O$), 549-56-4 (anhydrous)]* **M 422.4, m 160° (anhydrous).** Crystallise the bisulfate from 0.1M H_2SO_4, and recrystallise it from water to give the *heptahydrate*. [*Beilstein* **23** III/IV 3270, **23/13** V 396.]

Quinine sulfate ($2H_2O$) *[6119-70-6 (H_2O), 804-63-7 (anhydrous)]* **M 783.0, m 205° (219°).** Crystallise it from water and dry it at 110°. [*Beilstein* **23** H 522, **23** I 168, **23** II 420, **23** III/IV 3269, **23** V 396.]

Quinoline *[91-22-5]* **M 129.2, m -20°, -16°, b 113-114°/17mm, 236°/758mm, d_4^{20} 1.0937, n_D^{20} 1.625, pK^{25} 4.80 (4.93).** Dry quinoline with Na_2SO_4 and distil it from zinc dust in a vacuum. It has also been dried by boiling with acetic anhydride, then fractionally distilled. Calvin and Wilmarth [*J Am Chem Soc* **78** 1301 *1956*] cooled redistilled quinoline in ice and added enough HCl to form its hydrochloride. Diazotization removed aniline, the diazo compound being broken down by warming the solution to 60°. Non-basic impurities were removed by ether extraction. Quinoline was then liberated by neutralising the hydrochloride with NaOH, then dried with KOH and fractionally distilled at low pressure. Addition of cuprous acetate (7g/L of quinoline) and shaking under hydrogen for 12 hours at 100° removed impurities due to the nitrous acid treatment. Finally the hydrogen was pumped off, and the quinoline was distilled. Other purification procedures depend on conversion to the *phosphate* (**m** 159°, precipitated from MeOH solution, filtered, washed with MeOH, then dried at 55°) or the *picrate* (**m** 201°) which, after recrystallisation, were reconverted to quinoline.
The method using the picrate [Packer et al. *J Am Chem Soc* **80** 905 *1958*] is as follows: quinoline is added to picric acid dissolved in the minimum volume of 95% EtOH, giving yellow crystals which are washed with EtOH, air-dried and crystallised from acetonitrile. These are dissolved in dimethyl sulfoxide (previously dried over 4A molecular sieves) and passed through a basic alumina column, onto which the picric acid is adsorbed. The free base in the effluent is extracted with *n*-pentane and distilled under vacuum. Traces of solvent can be removed by vapour-phase chromatography. [Moonaw & Anton *J Phys Chem* **80** 2243 *1976*.] The $ZnCl_2$ and dichromate complexes have also been used [Cumper et al. *J Chem Soc* 1176 *1962*]. [*Beilstein* **20** H 339, **20** I 134, **20** II 222, **20** III/IV 3334, **20/7** V 276.]

2-Quinolinealdehyde *[5470-96-2]* **M 157.2, m 71°, pK_{Est} ~3.3.** Distil it in steam and recrystallise it from H_2O. Protect it from light. The *semicarbazone* has **m** 254° (from aqueous EtOH), and the *picrate* has **m** 197-199°. [*Beilstein* **21** H 322, **21** III/IV 4034, **21/8** V 442.]

8-Quinolinecarboxylic acid *[86-59-9]* **M 173.2, m 186-187.5°, pK_1^{25} 1.82, pK_2^{25} 6.87.** Crystallise the acid from water, aqueous EtOH, EtOH or $*C_6H_6$. The *ethyl ester* has **m** 45° and **b** 194-197°/13mm. [*Beilstein* **22** H 81, **22** III/IV 1200, **22/3** V 217.]

Quinoline ethiodide (1-ethylquinolinium iodide) *[634-35-5]* **M 285.1, m 158-159°.** Crystallise it from aqueous EtOH or EtOH/peroxide free Et_2O. [*Beilstein* **20** H 352, **20** I 139, **20** II 231, **20** III/IV 3357, **20/7** V 276.]

Quinoxaline *[91-19-0]* **M 130.2, m 28° (anhydrous), 37°(H_2O), b 108-110°/0.1mm, 140°/40mm, pK_1^{20} -5.52 (-5.8, dication), pK_2^{20} 0.56 (c 0.5), 0.72 (c 1.0) (monocation).** Crystallise quinoxaline from petroleum ether. It crystallises as the *monohydrate* on addition of water to a petroleum ether solution. It has UV with λ_{max} at 242 and 331nm (H^o –2); 234 and 316nm (pH 7.1). The *picrate* has **m** 161-162°. [Albert & Phillips *J Chem Soc* 1294 1956, *Beilstein* **23** H 176, **23** II 177, **23** III/IV 1226, **23/7** V 135.]

Quinoxaline-2,3-dithiol *[1199-03-7]* **M 194.1, m 345°(dec), pK_1 6.9, pK_2 9.9.** Purify the dithiol by repeated dissolution in alkali and re-precipitation by acetic acid. It complexes with Ag^+, Cd^{2+}, Pb^{2+}, Bi^{3+} and Ni^{2+} in aqueous NH_3. [*Beilstein* **24** III/IV 1428.]

Quinuclidine (1-azabicyclo[2.2.2]octane) *[100-76-5]* **M 111.2, m 158°(sublimes), pK^{25} 10.95.** Crystallise it from diethyl ether. The *hydrochloride* has **m** 364-365°(dec) (from EtOH or n-BuOH), and the *picrate* has **m** 225° (from aqueous EtOH). [*Beilstein* **20** H 144, **20** II 71, **20** III/IV 1966, **20/4** V 335.]

Rescinnamine

(Anaprel, Apoterin, a β-carboline alkaloid) *[24815-24-5]* **M 634.7, m 238-239°(vacuum), 240°, $[\alpha]_D^{20}$ -97° (c 1, $CHCl_3$), $pK_{Est(1)}$~<0 (carbazole N), $pK_{Est(2)}$~7.0 (quinolizidine N), pK^{25} 6.4 (75% aqueous $HCONMe_2$).** Crystallise it from *benzene, MeOH or aqueous Me_2CO. The *hydrochloride* has **m** 232°(dec) (from MeOH) and $[\alpha]_D^{20}$ -74° (MeOH). It is an antihypertensive. [Klohs et al. *J Am Chem Soc* **77** 2241 *1955*, *Beilstein* **25** III/IV 1323.]

(-)-Reserpic acid *[83-60-3]* **M 400.5, m 241-243°, $[\alpha]_D^{24}$ -70° (c 1, H_2O), $pK_{Est(1)}$~<0 (carbazole N), $pK_{Est(2)}$~4.0 (CO_2H), $pK_{Est(3)}$~7.4 (quinolizidine N), pK_1 6.2, pK_2 8.2 (66% aqueous $HCONMe_2$).** Crystallise the acid from MeOH. It has UV with λ_{max} at 222, 268 and 294nm (EtOH). The *hydrochloride 0.5H_2O* has **m** 257-259° (from EtOH/Et_2O), $[\alpha]_D^{23}$-81° (H_2O). [Dorfman et al. *Helv Chim Acta* **77** 59 *1954*, *Beilstein* **25** III/IV 1305.]

Reserpine *[50-55-5]* **M 608.7, m 262-263°, $[\alpha]_{546}^{20}$ -148° (c 1, $CHCl_3$), $pK_{Est(1)}$~<0 (carbazole N), pK_2 6.6 (7.4)(quinolizidine N).** Crystallise reserpine from aqueous Me_2CO or Et_2O. [Woodward et al. *Tertrahedron* **2** 155 *1958*, *Beilstein* **25** III/IV 1319.]

Rhamnetin (3,3'-4',5-tetrahydroxy-7-methoxy flavone, 7-methyl quercitin) *[90-19-7]* **M 316.3, m >300°(dec), several phenolic pKs ~7-10.5.** Crystallise rhamnetin from EtOH (**m** 292-293°), aqueous EtOH (**m** 294-296°) or MeOH (**m** 290-294°), or Me_2CO/MeOH. [Kuhn & Low *Chem Ber* **77** 211 *1944*, Jurd *J Am Chem Soc* **80** 5531 *1958*.] The *tetra-acetate* has **m** 189-190° (from Me_2CO/MeOH). [*Beilstein* **18** H 245, **18** II 237, **18** III/IV 3474.]

Rhodamine 3B chloride [3,5-bis-(diethylamino)-9-(2-carboxyphenyl)xanthylium chloride] *[81-88-9]* **M 479.0, m 210-211°(dec), CI 45170, λ_{max} 543nm, {Free base** *[509-34-2]* **CI 749}, pK^{25} 5.53.** Major impurities are partially dealkylated compounds not removed by recrystallisation. Purify the dye by chromatography, using ethyl acetate/isopropanol/ammonia (conc)(9:7:4, R_F 0.75 on Kieselgel G). It has also been crystallised from a concentrated solution in MeOH by slow addition of dry diethyl ether; or from EtOH containing a drop of conc HCl by slow addition of ten volumes of dry diethyl ether. The solid is washed with ether and air dried. The dried material has also been extracted with *benzene to remove oil-soluble material prior to recrystallisation. Store it in the dark. [*Beilstein* **18** II 486, **18** III/IV 8246, **19/8** V 669.]

Rhodamine 6G [Basic Red 1, 3,5-bis-(ethylamino)-9-(2-ethoxycarbonylphenyl)-2,7-dimethylxanthylium chloride] *[989-38-8]* **M 479.3, CI 45160, λmax 524nm, pK^{25} 5.58.** Crystallise the dye from MeOH or EtOH, and dry it in a vacuum oven. [*Beilstein* **18** III/IV 8244, **18/12** V 283.]

Rhodanine (2-mercaptothiazolidin-4-one) *[141-84-4]* **M 133.2, m 168.5° (capillary), pK^{20} 5.18.** Crystallise rhodanine from glacial acetic acid or water. It is used to estimate Ag and gallic acid [Thies & Fischer *Microchimica Acta* 809 *1973*]. [*Beilstein* **27** H 242, **27** I 309, **27** II 288, **27** III/IV 3188.]

Riboflavin, riboflavin-5'-phosphate (Na salt, $2H_2O$). See entries in "Miscellaneous Compounds" and for **ribonucleic acids** see entry in "Proteins, Enzymes, DNA and RNA" in Chapter 7.

Saccharin (1,2-benzisothiazol-3(2*H*)-one 1,1-dioxide, *o*-benzoic acid sulfimide) *[81-07-2]* **M 183.2, m 227-229°, 229°, 228.8-229.7°, pK_1^{25} 1.31, pK_2^{25} 12.8.** Purify saccharin by recrystallisation from Me_2CO [solubility 7.14% at 0°, 14.4% at 50°], or aqueous isoPrOH to give a fluorescent solution. It sublimes *in vacuo*. It is an artificial sweetener and is 500 times sweeter than sucrose. [DeGarmo et al. *J Am Pharm Assoc (Sci Ed)* **41** 17 *1952*, *Beilstein* **27** H 168, 870, **27** I 266, **27** II 214, **27** III/IV 2649.]

Safranine O (Safranine T, 3,7-diamino-2,8-dimethyl-5-phenylphenazinium chloride) *[477-73-6]* **M 350.9, λ_{max} 530nm, pK^{25} 6.4.** Crystallise it from *benzene/MeOH (1:1) or water. Dry it *in vacuo* over H_2SO_4. It has UV: λ_{max} at 520nm (H_2O) and 530nm (EtOH). [*Beilstein* **25** H 403, **25** I 657, **25** III/IV 3056.]

Safrole (5-allyl-1,3-benzodioxole, 4-allyl-1,2-methylenedioxybenzene) *[94-59-7]* **M 162.1, m~ 11°, b 69-70°/1.5mm, 104-105°/6mm, 231.5-232°/atm, 235-237°/atm, d_4^{20} 1.0993, n_D^{20} 1.53738.** Safrole has been purified by fractional distillation, although it has also been recrystallised from low boiling petroleum ether at low temperatures. [IR: Briggs et al. *Anal Chem* **29** 904 *1957*, UV: Patterson & Hibbert *J Am Chem Soc* **65** 1962 *1943*.] The *maleic anhydride adduct* forms yellow crystals from toluene **m** 257° [Hickey *J Org Chem* **13** 443 *1948*], and the *picrate* forms orange-red crystals from $CHCl_3$ [Baril & Magrdichian *J Am Chem Soc* **58** 1415 *1936*]. [*Beilstein* **19** H 39, **19** I 617, **19** II 29, **19** III/IV 275, **19/1** V 553.]

Scopolamine (hyoscine, atroscine, 6β,7β-epoxy-3-α-tropanyl *S*-(–)-tropate) *[51-34-3]* **M 321.4, m 59°, $[\alpha]_D^{20}$ -18° (c 5, EtOH), -28° (c 2, H_2O), $[\alpha]_{546}^{20}$ -30° (c 5, $CHCl_3$), pK^{25} 7.55.** Crystallise it from *benzene/petroleum ether, EtOH or H_2O. It is polymorphic with **m** 165-166° and 190-191°. The *racemate* has **m** 56-57° (H_2O), 37-38° ($2H_2O$), syrup (anhydrous), *l* and *d* isomers can separate as syrups when anhydrous. [*Beilstein* **27** H 99, 102, **27** I 247-248, **27** II 43-44, 27 III/IV 1790.]

Scopoletin (7-hydroxy-6-methoxycoumarin) *[92-61-5]* **M 192.2, m 206°, 208-209°, pK^{25} 8.96 (70%aqueous EtOH).** Crystallise it from water, acetic acid or *C_6H_6/MeOH. It is dimorphic with a second **m** at 193-195°. It sublimes at 120-130°/12mm. [*Beilstein* **18** H 99, **18** I 348, **18** II 68, **18** III/IV 1323, **18/3** V 203.]

Secobarbital (5-allyl-5-1'-methylbutylbarbituric acid) *[76-73-3]* **M 260.3, m 100°, pK_1^{25} 8.08, pK_2^{25} 12.6.** It is purified by dissolving the *sodium salt* [309-43-3] in 10% HCl which precipitates the acid form that is extracted into Et_2O. The extract is dried (Na_2SO_4) and evaporated. The residue is then purified by repeated crystallisation from $CHCl_3$. [Buchet & Sandorfy *J Phys Chem* **88** 3274 *1984*, *Beilstein* **24** III/IV 2013.]

Serotonin creatinine sulfate (H_2O) *[971-74-4]* **M 405.4, m 220°(dec), pK_1 10.1, pK_2 11.1, pK_3 18.25 (NH) for serotonin, pK^{25} 4.9 for creatinine.** It crystallises as the monohydrate from water. [*Beilstein* **22** III/IV 5667, **22/12** V 18.]

Sinomenine hydrochloride (7,8-didehydro-4-hydroxy-3,7-dimethoxy-17-methyl-9α,13α,14α-morphan-6-one HCl) *[6080-33-7]* **M 365.9, m 231°, $[\alpha]_D^{17}$ -83° (c 4, H_2O), $pK_{Est(1)}$~10.0 (N), $pK_{Est(2)}$~10.4 (OH).** Crystallise the salt from water (1g/1.5ml) or EtOH. The *free base* [115-53-7] **M** 329.4, has **m** 161° (from EtOH) (and again at 182°) after crystallisation from *C_6H_6, and $[\alpha]_D^{20}$ -78.9° (c 1, EtOH). The *picrate* has **m** 159-162°(dec) (from H_2O). [*Beilstein* **21** II 470, **21** III/IV 6670.]

(-)-Sparteine sulfate pentahydrate *[6160-12-9]* **M 422.5, m loses H_2O at 100° and turns brown at 136° (dec), $[\alpha]_D^{20}$ -22° (c 5, H_2O), $[\alpha]_D^{21}$ -16° (c 10, EtOH for free base), pK_1^{20} 2.24, pK_2^{20} 9.46.** Recrystallise the

sulfate from aqueous EtOH or H_2O, although the solubility in the latter is high. The *free (-)-base* has **b** 173°/8mm and is steam volatile but resinifies in air. The *dipicrate* forms yellow needles from EtOH/Me_2CO, **m** 205-206° [Clemo et al. *J Chem Soc* 429 *1931*; see also Bolnmann & Schuman *The Alkaloids* (Ed Manske) Vol 9 175 *1967*]. The *free (±)-base* has **m** 71-72.5° [van Tamelen & Foltz *J Am Chem Soc* **82** 2400 *1960*]. [*Beilstein* **23** II 99, **23** III/IV 18.]

(-)-Strychnine *[57-24-9]* **M 334.4, m 268°, 278-279.5°, $[\alpha]_{546}^{20}$ -139° (c 1, $CHCl_3$), pK_1^{20} 2,50, pK_2^{20} 8.2, pK_1^{20} 7.37 [80% aqueous $MeO(CH_2)_2OH$].** It crystallises from $CHCl_3$/Et_2O and sublimes at 125°/0.01mm. It can also be purified by conversion to the *hydrochloride* [**m** 275-295° (dec), $[\alpha]_D^{20}$ -44° (0.03N HCl)] with aqueous HCl, then neutralisation with ammonia. [*Beilstein* **27** II 723, **27** III/IV 7530.] It is POISONOUS.

Sulfamethazine (Sulfadimidine, *N′*-[4,6-dimethyl-2-pyrimidinyl]sulfanilamide) *[57-68-1]* **M 278.3, m 178-179°, 198-200°, 205-207°, pK_1 2.65, pK_2 7.4.** Crystallise it from dioxane or aqueous dioxane. [Caldwell et al. *J Am Chem Soc* **63** 2188 *1941*, Roblin et al. *J Am Chem Soc* **64** 567 *1942*, *Beilstein* **25** III/IV 2215.]

Sulfapyridine *[144-83-2]* **M 349.2, m 193°, pK^{20} 8.64.** Crystallise sulfapyridine from 90% acetone and dry it at 90°. Its solubility in Me_2CO, EtOH and H_2O is 1.5%, 0.22% and 0.02%, respectively. [Winterbottom *J Am Chem Soc* **62** 160 *1940*, *Beilstein* **22** III/IV 3978.]

2-Sulfobenzoic cyclic anhydride (2,1-benzoxathiazol-3-one-1,1-dioxide) *[81-08-3]* **M 184.2, m 126-127°, 129.5°, 130°, b 184-186°/18mm.** The anhydride is purified by distillation in a vacuum and readily solidifies to a crystalline mass on cooling. [Heitman *J Am Chem Soc* **34** 1594 *1912*.] *Alternatively*, purify it by dissolving it in the minimum volume of toluene and refluxing for 2 hours using a Dean-Stark trap. Evaporate under reduced pressure and distil the anhydride at 18mm. It is then recrystallised three times from its own weight of dry $*C_6H_6$. It is sensitive to moisture and should be stored in the dark in a dry atmosphere. The *O-methyloxime* has **m** 110-112° [Levy *Tetrahedron Lett* 3289 *1972*]. If the sample has hydrolysed extensively (presence of OH band in the IR) then treat with an equal bulk of $SOCl_2$, reflux it for 3 hours ($CaCl_2$ tube), evaporate and distil the residue in a vacuum, then recrystallise it from $*C_6H_6$, Et_2O/$*C_6H_6$ or $CHCl_3$ (EtOH free by passing through Al_2O_3, or standing over $CaCl_2$). [Clarke & Dreger *Org Synth* Coll Vol **I** 495 *1941*.] It is used for modifying ζ-amino functions of lysyl residues in proteins [Bagree et al. *FEBS Lett* **120** 275 *1980*]. [*Beilstein* **19** I 659, **19** II 137, **19** III/IV 1641, **19/4** V 215.]

Sulfolane (tetramethylenesulfone) *[126-33-0]* **M 120.2, m 28.5°, b 153-154°/18mm, 285°/760mm, d_4^{20} 1.263, n_D^{30} 1.4820.** It is prepared commercially by a Diels-Alder reaction of between 1,3-butadiene and sulfur dioxide, followed by Raney nickel hydrogenation. The principal impurities are water, 3-sulfolene, 2-sulfolene and 2-isopropyl sulfolanyl ether. It is dried by passage through a column of molecular sieves. Distil it under reduced pressure through a column packed with stainless steel helices. Again dry it with molecular sieves and distil. [Cram et al. *J Am Chem Soc* **83** 3678 *1961*, Coetzee *Pure Appl Chem* **49** 211 *1977*.] *Alternatively*, it is stirred at 50°, and small portions of solid $KMnO_4$ are added until the colour persists during 1 hour. Dropwise addition of MeOH then destroys the excess $KMnO_4$; the solution is filtered, freed from potassium ions by passage through an ion-exchange column and dried under vacuum. It has also been distilled in a vacuum from KOH pellets. It is *hygroscopic*. [See Sacco et al. *J Phys Chem* **80** 749 *1976*, *J Chem Soc, Faraday Trans 1* **73** 1936 *1977*, **74** 2070 *1978*, *Trans Faraday Soc* **62** 2738 *1966*.] Coetzee has reviewed the methods of purification of sulfolane, and also the removal of impurities. [Coetzee in *Recommended Methods of Purification of Solvents and Tests for Impurities*, Coetzee Ed. Pergamon Press, 1982, *Beilstein* **17** I 5, **17** III/IV 37, **17/1** V 39.]

2,2′:6′,2″-Terpyridyl *[1148-79-4]* **M 233.3, m 91-92°, pK_1^{23} 2.64, pK_2^{23}4.33.** Crystallise it from diethyl ether, toluene or from petroleum ether, then aqueous MeOH, followed by sublimation in a vacuum at 90°. It is used for estimating Ag and Ru. [Kamra et al. *Anal Chim Acta* **81** 177 *1976*, *Beilstein* **26** III/IV 258.]

Terthiophene (2,5-di[thienyl]thiophene; α–terthienyl) *[1081-34-1]* **M 248.4, m 94-95.5°, 94-96°.** Possible impurities are bithienyl and polythienyls. Suspend it in H_2O and steam distil it to remove bithienyl.

The residue is cooled and extracted with $CHCl_3$, dried ($MgSO_4$), filtered, evaporated and the residue chromatographed on Al_2O_3 using petroleum ether/3% Me_2CO as eluent. The terphenyl zone is then eluted from the Al_2O_3 with Et_2O, the extract is evaporated and the residue is recrystallised from MeOH (40ml per g). The platelets are washed with cold MeOH and dried in air. [UV: Sease & Zechmeister *J Am Chem Soc* **69** 270 *1947*; Uhlenbroek & Bijloo *Rec Trav Chim Pays Bas* **79** 1181 *1960*.]
It has also been recrystallised from MeOH, $*C_6H_6$, petroleum ether or AcOH. [UV: Zechmeister & Sease *J Am Chem Soc* **69** 273 *1947*, Steinkopf et al. *Justus Liebigs Ann Chem* **546** 180 *1941*.] It is a phototoxic nematocide [Cooper & Nitsche *Bioorg Chem* **13** 36 *1985*, *Chan* et al. *Phytochem* **14** 2295 *1975*]. [*Beilstein* **19** III/IV 4763, **19/9** V 226.]

2,4,5,6-Tetraaminopyrimidine sulfate *[5392-28-9]* **M 238.2, m 255° (dec), >300°, >350° (dec), pK^{20} 6.82.** Purify the salt by recrystallisation from H_2O, 2N H_2SO_4 (20 parts, 67% recovery) or 0.1N H_2SO_4 (40 parts, 62% recovery), and dried in air. [UV: Konrad & Pfleiderer *Chem Ber* **103** 722 *1970*, Malletta et al. *J Am Chem Soc* **69** 1814 *1947*, Cavalieri et al. *J Am Chem Soc* **70** 3875 *1948*, *Beilstein* **25** H 423, **25** III/IV 3106.]

1,4,8,11-Tetraazacyclotetradecane (cyclam) *[295-37-4]* **M 200.33, m 173° (closed capillary and sublimes at 125°), 183-185°, 185°, $pK_{Est(1)}$ ~3.8, $pK_{Est(2)}$ ~6.0, $pK_{Est(3)}$ ~9.0, $pK_{Est(4)}$ ~9.6.** Purify cyclam by recrystallisation from dioxane (white needles), and it sublimes above 120°. It has been distilled, **b** 132-140°/4-8mm. It forms complexes with metals and gives a sparingly soluble *nitrate salt*, **m** 205°(dec), which crystallises from H_2O and is dried at 150°. [UV: Bosnich et al. *Inorg Chem* **4** 1102 *1963*, van Alphen *Rec Trav Chim Pays Bas* **56** 343 *1937*, *Beilstein* **26** III/IV 1647.]

Tetrabenazine (2-oxo-3-isobutyl-9,10-dimethoxy-1,2,3,4,6,7-hexahydro-11b*H*-benzo[a]-quinolizine) *[58-46-8]* **M 317.4, m 127-128°, pK_{Est} ~8.** Crystallise it from MeOH. The *hydrochloride* has **m** 208-210°, and the *oxime* has **m** 158° (from EtOH). [*Beilstein* **21** III/IV 6488.]

2,3,4,6-Tetrachloropyridine *[14121-36-9]* **M 216.9, m 74-75°, (? 37-38°), b 130-135°/16-20mm, 248.5-249.5°/760mm, pK_{Est} ~ –5.7.** Crystallise it from 50% EtOH and/or distil it. The *N-oxide* has **m** 210° (from EtOH/$CHCl_3$). [Chivers & Suschitzky *J Chem Soc* 2870 *1971*, *Beilstein* **20** III/IV 6488, **20/5** V 421.]

Tetrahydrofuran (oxalane, THF) *[109-99-9]* **M 72.1, b 25°/176mm, 66°/760mm, d_4^{20} 0.889, n_D^{20} 1.4070, pK^{25} -2.48 (aqueous H_2SO_4).** It is obtained commercially by catalytic hydrogenation of furan from pentosan-containing agricultural residues. It was purified by refluxing with, and distilling from $LiAlH_4$ which removes water, peroxides, inhibitors and other impurities [Jaeger et al. *J Am Chem Soc* **101** 717 *1979*]. Peroxides can also be removed by passage through a column of activated alumina, or by treatment with aqueous ferrous sulfate and sodium bisulfate, followed by solid KOH. In both cases, the solvent is then dried and fractionally distilled from sodium. Lithium wire or vigorously stirred molten potassium have also been used for this purpose. CaH_2 has also been used as a drying agent.
Several methods are available for obtaining the solvent almost anhydrous. Ware [*J Am Chem Soc* **83** 1296 *1961*] dried it vigorously with sodium-potassium alloy until a characteristic blue colour was evident in the solvent at Dry-ice/cellosolve temperatures. The solvent is kept in contact with the alloy until distilled for use. Worsfold and Bywater [*J Chem Soc* 5234 *1960*], after refluxing and distilling from P_2O_5 and KOH, in turn, refluxed the solvent with sodium-potassium alloy and fluorenone until the green colour of the disodium salt of fluorenone was well established. [*Alternatively*, instead of fluorenone, benzophenone, which forms a blue ketyl, can be used.] The tetrahydrofuran was then fractionally distilled, degassed and stored above CaH_2. *p*-Cresol or hydroquinone inhibit peroxide formation. The method described by Coetzee and Chang [*Pure Appl Chem* **57** 633 *1985*] for 1,4-dioxane also applies here. Distillations should always be done in the presence of a reducing agent, e.g. $FeSO_4$. [*Beilstein* **17** H 10, **17** I 5, **17** II 15, **17** III/IV 24, **17/1** V 27.] **It irritates the skin, eyes and mucous membranes, and the vapour should never be inhaled. It is HIGHLY FLAMMABLE, and the necessary precautions should be taken.**
Rapid purification: Purification as for diethyl ether.

***l*-Tetrahydropalmatine (2,3,9,10-tetramethoxy-6*H*-dibenzo[a,g]quinolizidine)** *[10097-84-4]* **M 355.4, m 148-149°, $[\alpha]_D^{20}$ -291° (EtOH).** Crystallise it from MeOH or EtOH by addition of water [see Kametani & Ihara

J Chem Soc (C) 530 *1967*, Bradsher & Dutta *J Org Chem* **26** 2231 *1961*]. When crystallised from Me_2CO/Et_2O, it has **m** 142°. The *hydrate* has **m** 115°(effervescence). The *picrate* has **m** 188°(dec) (from aqueous EtOH). [Bradsher & Datta *J Org Chem* **26** 2231 *1961*, *Beilstein* **21** II 196, **21** III/IV 2769.]

Tetrahydropyran (oxane, THP) *[142-68-7]* **M 86.1, b 88.0°, d $_4^{20}$ 0.885, n $_D^{20}$ 1.4202, pK^{25} -2.79 (aqueous H_2SO_4).** Dry oxane with CaH_2, then pass it through a column of silica gel to remove olefinic impurities and fractionally distil it. Free it from peroxides and moisture by refluxing with sodium, then distil it from $LiAlH_4$. *Alternatively*, peroxides can be removed by treatment with aqueous ferrous sulfate and sodium bisulfate, followed by solid KOH, and fractional distillation from sodium. [*Beilstein* **17** H 12, **17** I 6, **17** II 18, **17** III/IV 51, **17/1** V 64.]

Tetrahydro-4*H*-pyran-4-one *{29943-42-8]* **M 100.1, b 57-59°/11mm, 65-66°/15mm, 67-68°/18mm, 73°/20mm, 164.7°/atm, 166-166.5°/atm, d $_4^{20}$ 1.0844, n $_D^{20}$ 1.4551.** Purify the pyrone by repeated distillation, preferably in a vacuum. [Baker *J Chem Soc* 296 *1944*, IR: Olsen & Bredoch *Chem Ber* **91** 1589 *1958*.] The *oxime* has **m** 87-88° and **b** 110-111°/13mm [Cornubert et al. *Bull Soc Chim Fr* 36 *1950*]. The *4-nitrophenylhydrazone* forms orange-brown needles from EtOH, **m** 186° [Cawley & Plant *J Chem Soc* 1214 *1938*]. [*Beilstein* **17** I 131, **17** II 287, **17** III/IV 4171, **17/9** V 21.]

Tetrahydrothiophene (thiophane) *[110-01-0]* **M 88.2, m -96°, b 14.5°/10mm, 40.3°/39.7mm, 120.9°/760mm, d $_4^{20}$ 0.997, n $_D^{20}$ 1.5289.** The crude material is purified by crystallisation of the mercuric chloride complex to a constant melting point. It is then regenerated, washed, dried, and fractionally distilled. [Whitehead et al. *J Am Chem Soc* **73** 3632 *1951*.] It has been dried over Na_2SO_4 and distilled in a vacuum [Roberts & Friend *J Am Chem Soc* **108** 7204 *1986*]. [*Beilstein* **17** I 5, **17** II 15, **17** III/IV 34, **17/1** V 36.]

Tetrahydro-4*H*-thiopyran-4-one *[1072-72-6]* **M 116.2, m 60-62°, 61-62°, 64-65°, 65-67°.** Purify it by recrystallisation from diisopropyl ether or petroleum ether and dry it in air. If too impure, then dissolve it in Et_2O, wash with aqueous $NaHCO_3$, then H_2O, dry ($MgSO_4$), filter, evaporate and the residue is recrystallised as before. [Cardwell *J Chem Soc* 715 *1949*.] The *oxime* can be recrystallised from $CHCl_3$/petroleum ether (at -20°) and has **m** 84-85° [Barkenbus et al. *J Org Chem* **20** 871 *1955*]. The *2,4-dinitrophenylhydrazone* has **m** 186° (from EtOAc) [Barkenbus et al. *J Org Chem* **16** 232 *1951*]. The *S-dioxide* is recrystallised from AcOH, **m** 173-174° [Fehnel & Carmack *J Am Chem Soc* **70** 1813 *1948*, *Beilstein* **17** II 287, **17** III/IV 4172, **17/1** V 21].

Tetramethylene sulfoxide (tetrahydrothiophen 1-oxide) *[1600-44-8]* **M 104.2, b 235-237°, d $_4^{20}$ 1.175, n $_D^{20}$ 1.525.** Shake the oxide with BaO for 4 days, then distil it from CaH_2 under reduced pressure. [*Beilstein* **17** III/IV 36, **17/1** V 38.]

2,2,6,6-Tetramethylpiperidinyl-1-oxy (TEMPO) *[2564-83-2]* **M 156.3, m 36-38°.** Purify TEMPO by sublimation (33°, water aspirator) [Hay & Fincke *J Am Chem Soc* **109** 8012 *1987*, Keana *Chem Rev* **78** 37 *1978*].

2,2,6,6-Tetramethyl-4-piperidone hydrochloride (triacetoneamine) *[33973-59-0]* **M 191.7, m 190°(dec), 198-199°(dec), pK^{25} 7.90.** Purify the salt by recrystallisation from EtOH/Et_2O, MeCN or Me_2CO/MeOH. The *free base* has **m** 37-39° (after sublimation), **b** 102-105°/18mm, and the *hydrate* has **m** 56-58° (wet Et_2O); the *hydrobromide* has **m** 203° (from EtOH/Et_2O), and the *picrate* has **m** 196° (from aqueous EtOH). [Sandris & Ourisson *Bull Soc Chim Fr* 345 *1958*, *Beilstein* **21** H 246, **21** I 273, **21** II 222, **21** III/IV 3278, **21/6** V 538.]

1,3,7,9-Tetramethyl uric acid *[2309-49-1]* **M 224.2, m 225°, 228°, pK$_{Est}$<0.** Crystallise the uric acid from H_2O or MeOH. [*Beilstein* **26** H 532, **26** I 156, **26** II 302, **21** III/IV 2623.]

1,3,5,5-Tetranitrohexahydropyrimidine *[81360-42-1]* **M 270.1, m 153-154°.** Crystallise the nitropyrimidine from EtOH (5x) and sublime it (~65°/0.05mm) [Cichra & Adiolph *J Org Chem* **47** 2474 *1982*, *J Labelled Comp Radiopharm* **29** 1197 *1991*].

4,7,13,18-Tetraoxa-1,10-diazabicyclo[8.5.5]eicosane (Cryptand 211) *[31250-06-3]* **M 288.1, b 130°/0.002mm, d_4^{20} 1.097, n_D^{20} 1.505, pK_{Est} ~7.9.** Redistil Cryptand 211, dry it under high vacuum over 24 hours, and store it under nitrogen.

1,7,10,16-Tetraoxa-4,13-diazacyclooctadecane (4,13-diaza-18-crown-6) *[23978-55-4]* **M 262.3, m 118-116°, pK_{Est} ~8.8.** Twice recrystallise it from *benzene/*n*-heptane, and dry it for 24 hours under high vacuum [Weber & Vögtle *Top Curr Chem* (Springer Verlag, Berlin) **98** 1 *1981*, D'Aprano & Sesta *J Phys Chem* **91** 2415 *1987*].

5,10,15,20-Tetraphenylporphyrin (TPP) *[917-23-7]* **M 614.7, m 450° (sublimes >400°), λ_{max} 482nm.** Purify TPP by chromatography on neutral (Grade I) alumina, and recrystallisation from CH_2Cl_2/MeOH or $*C_6H_6$. It forms complexes with metals. [Yamashita et al. *J Phys Chem* **91** 3055 *1987*, *Beilstein* **26** III/IV 1958.]

5,10,15,20-Tetra-4'-pyridinylporphyrin *[16834-13-2]* **M 618.7, m >300°(dec).** Purify it by chromatography on alumina (neutral, Grade I), with $CHCl_3$/MeOH (80:20) followed by recrystallisation from CH_2Cl_2/MeOH [Yamashita et al. *J Phys Chem* **91** 3055 *1987*]. [Kalyanasundaram *Inorg Chem* **23** 2453 *1984*, Okuno et al. *Synthesis* 537 *1980*.]

Tetrathiafulvalene *[31366-25-3]* **M 204.4, m 122-124°.** Recrystallise it from cyclohexane/hexane under an argon atmosphere [Kauzlarich et al. *J Am Chem Soc* **109** 4561 *1987*]. [*Beilstein* **19/11** V 380.]

1,2,3,4-(1*H*)Tetrazole *[288-94-8]* **M 70.1, m 156°, 157.5-158°, pK^{25} 4.89 (acidic).** Crystallise the tetrazole from EtOH and sublime it under high vacuum at *ca* 120° (*care should be taken due to possible* **EXPLOSION**). [*Beilstein* **26** H 346, **26** I 108, **26** II 196, **26** III/IV 1652.]

Thebaine *[115-37-7]* **M 311.4, m 193°, $[\alpha]_D^{25}$ -219° (EtOH), pK^{20} 8.15.** Crystallise Thebaine from Et_2O or EtOH. Sublime it at 170-180°. The *hydrochloride* decomposes >182° (from MeOH/Et_2O). [*Beilstein* **27** II 177, **27** III/IV 2271.] It is a **NARCOTIC**.

2-Thenoyltrifluoroacetone [1-(2-thienyl)-4,4,4-trifluorobutan-1,3-dione] *[326-91-0]* **M 222.2, m 42-44°, b 96-98°/9mm, pK^{25} 6.4.** Crystallise the dione from hexane or *benzene. (An aqueous solutions slowly decomposes it). It has ν_{max} at 1638(C=O), 1657(C=C)cm^{-1}. The *oxime* crystallises from H_2O or aqueous EtOH. It is used for the determination of Actinides and Lanthanides. [Chaston et al. *Aust J Chem* **18** 673 *1956*, Jeffrey et al. In *Vogel's Textbook of Qunatitative Chemical Analysis* 5thedn J Wiley & Sons, p170 *1989*, *Beilstein* **17** III/IV 5989, **17/11** V 128.]

2-Thenylamine (2-thiophenemethylamine) *[27757-85-3]* **M 113.1, b 78.5°/15mm, d_4^{20} 1.137, n_D^{20} 1.5643, pK^{30} 8.92.** Distil the amine under reduced pressure (nitrogen), from BaO, through a column packed with glass helices. The *hydrochloride* has **m** 193-194° (from EtOH/Me_2CO) and the *picrate* has **m** 181-182°. [*Beilstein* **18** III/IV 7096.]

Theobromine (3,7-dimethyl-2,6-dioxopurine) *[83-67-0]* **M 180.2, m 337° (sublimes slowly at 290° and finally melts melts at ~351°), pK_1^{40} -0.16, pK_2^{25} 9.96.** It crystallises from H_2O. Its solubility in H_2O is 0.06% at 15° and 1.25% at 100°, and it is poorly soluble in organic solvents. It forms salts with heavy metals and is a diuretic, vasodilator and a cardiac stimulant. [Lister *Purines Part II, Fused Pyrimidines* Brown Ed, Wiley-Interscience pp254-225 *1971*, ISBN 0-471-38205-1, *Beilstein* **26** H 457, **26** I 135, **26** II 264, **26** III/IV 2336.]

Theophylline (1,3-dimethyl-2,6-dioxopurine, Theocin) *[58-55-9]* **M 180.2, m 272-274°, pK_1^{40} -0.24, pK_2^{40} 8.79, pK_3 11.5 (acidic).** It crystallises from H_2O as the *monohydrate* which becomes *anhydrous* above 100°. It is freely soluble in hot H_2O, but its solubility at 15° is 0.44%. It complexes with heavy metals. It is a diuretic, vasodilator and a cardiac stimulant. [Lister *Purines Part II, Fused Pyrimidines* Brown Ed, Wiley-Interscience pp253-254 *1971*, ISBN 0-471-38205-1, *Beilstein* **26** H 455, **26** I 134, **26** II 263, **26** III/IV 2331.]

Thianthrene *[92-85-3]* **M 216.3, m 158°.** Crystallise thianthrene from Me_2CO (charcoal), AcOH or EtOH. It sublimes in a vacuum. [*Beilstein* **19** H 45, **19** I 619, **19** II 34, **19** III/IV 347, **19/2** V 49.]

5-Thiazolecarboxaldehyde *[1003-32-3]* **M 113.1, b 92-94°/16mm, d_4^{20} 1.304, n_D^{20} 1.5874, pK_{Est} ~0.6.** Dry the aldehyde over Na_2SO_4 and fractionate it in a vacuum. The *2,4-dinitrophenylhydrazone* forms red crystals from MeOH with **m** 238-240°, and the *semicarbazone* has **m** 210-212° (from MeOH). [Erne et al. *Helv Chim Acta* **34** 148 *1951*, *Beilstein* **27** III/IV 2615.]

Thiazoline-2-thiol *[96-53-7]* **M 119.2, m 106-107°, 106-108°, pK_{Est} ~13.0.** Purify the thiol by dissolution in aqueous alkali, precipitation by addition of HCl and then recrystallisation from H_2O (as needles). [IR: Flett *J Chem Soc* 347 *1953* and Mecke et al. *Chem Ber* **90** 975 *1957*, Gabriel & Stelzner *Chem Ber* **28** 2931 *1895*, *Beilstein* **27** III/IV 2540.]

4-(2-Thiazolylazo)-resorcinol *[2246-46-0]* **M 221.2, m 200-202°(dec), 218-219°, λ_{max} 500 nm, pK_1^{25} 1.25, pK_2^{25} 6.53, pK_3^{25} 10.76.** Dissolve it in aqueous alkali, extract it with diethyl ether, and re-precipitate it with dilute HCl. The purity is checked by TLC on silica gel using petroleum ether/diethyl ether/EtOH (10:10:1) as the mobile phase. It complexes with Cu^{2+} (pH 3-4), Co^{2+} and Ni^{2+} (pH 7) and Zn^{2+}, and Cd^{2+} (pH 8.4). [*Beilstein* **27** III/IV 5988.]

Thiazolyl blue tetrazolium bromide (MTT, 3-[4,5-dimethyl-2-thiazolyl]-2,5-diphenyl-2*H*-tetrazolium bromide) *[298-93-1, 2348-71-2]* **M 414.3, m 171°.** It is recrystallised by dissolving in MeOH containing a few drops of HBr and then adding dry Et_2O to complete the crystallisation, wash the needles with Et_2O and dry them in a vacuum desiccator over KOH. [Beyer & Pyl *Chem Ber* **87** 1505 *1954*, *Beilstein* **27** III/IV 6045.]

Thietane (trimethylene sulfide) *[287-27-4]* **M 74.1, m -64°, -73.2°, b 93.8-94.2°/752mm, 95°/atm, d_4^{20} 1.0200, n_D^{20} 1.5020.** Purify thietane by preparative gas chromatography on a dinonyl phthalate column. It has also been purified by drying over anhydrous K_2CO_3, and distilling through a 25cm glass helices-packed column (for 14g of thietane), then drying over $CaSO_4$ before sealing it in a vacuum. [Haines et al. *J Phys Chem* **58** 270 *1954*.] It is characterised as the *dimethylsulfonium iodide* **m** 97-98° [Bennett & Hock *J Chem Soc* 2496 *1927*]. The *S-oxide* has **b** 102°/25mm, n_D^{21} 1.5075 [Tamres & Searles *J Am Chem Soc* **81** 2100 *1959*]. [*Beilstein* **17** I 3, **17** II 12, **17** III/IV 14, **17/1** V 14.]

2-Thiobarbituric acid *[504-17-6]* **M 144.2, m 235°(dec), pK_1^{25} 2.25, pK_2^{25} 10.72 (2% aqueous EtOH).** Crystallise it from water. [*Beilstein* **24** H 476, **24** I 414, **24** II 275, **24** III/IV 1884.]

1,1'-Thiocarbonyldiimidazole *[6160-65-2]* **M 178.1, m 100-102°, 105-106°.** It forms yellow crystals on recrystallisation from tetrahydrofuran or by sublimation at 10^{-3}torr (bath temperature 70-80°). It is hydrolysed by H_2O and should be stored dry. [Staab & Walther *Justus Liebigs Ann Chem* **657** 98 *1962*; Pullukat et al. *Tetrahedron Lett* 1953 *1967*, Hanessian et al. *Can J Chem* **65** 1859 *1987*, Rajanbabu et al. *J Am Chem Soc* **111** 1759 *1989*.]

Thiochrome {2,7-dimethyl-5*H*-thiachromine-8-ethanol; 3,8-dimethyl-2-hydroxyethyl-5*H*-thiazolo-[2,3:1',2']pyrimido[4',5'-*d*]pyrimidine} *[92-35-3]* **M 262.3, m 227-228°, pK_1^{20} 8.11, pK_2^{20} 12.6.** Crystallise thiochrome from chloroform. The *monohydrochloride* has **m** 235-236°(dec) (from EtOH) and the *dihydrochloride* has **m** 237°(dec). [*Beilstein* **27** III/IV 9599.]

2-Thiocytosine (4-amino-2-mercaptopyrimidine) *[333-49-3]* **M 127.2, m 236-237°(dec), 285-290°(dec), pK_1^{20} 3.90 (NH_2), pK_2^{20} 11.10 (SH).** It is recrystallised from hot H_2O and dried at 100° to constant weight. [Brown *J Appl Chem (London)* **9** 203 *1959*, Russell et al. *J Am Chem Soc* **71** 2279 *1949*.] It is used in transcription and translation studies [Rachwitz & Scheit *Eur J Biochem* **72** 191 *1977*].

Thioflavine T [2-(4-dimethylaminophenyl)-3,6-dimethylbenzothiazolium chloride] *[2390-54-7]* **M 318.9, pK^{25} 2.7.** Crystallise the chloride from *benzene/EtOH (1:1). [*Beilstein* **27** III/IV 5052.]

1-Thioflavone (2-phenylthiochromen-4-one) *[784-62-3]* **M 238.3, m 129-130°.** This yellow solid is purified by passage through a silica gel column, eluting with *C_6H_6/Me_6CO, evaporating and crystallising the residue from EtOH. The *sulfoxide* [65373-82-2] has **m** 133-135°, and the *sulfone* [22810-82-2] has **m** 136.5-137° (from EtOH). The *dimethylhydrazone* has **m** 111-113° (from BuOH). It forms easily hydrolysable salts. [Nakazumi et al. *J Heterocycl Chem* **21** 193 *1984*, Chen et al. *J Org Chem* **51** 3282 *1986*, Van Allen & Reynolds *J Heterocycl Chem* **8** 807 *1971*, *Beilstein* **17** I 204, **17** III/IV 5420, **17/10** V 560.]

6-Thioguanine *[154-42-7]* **M 167.2, m >300°, pK_1^{23} 8.2 (SH), pK_2^{23} 11.6 (acidic, 9-NH).** It crystallises from H_2O as needles. It has UV with λ_{max} at 258 and 347nm (H_2O, pH 1) and 242, 270 and 322nm (H_2O, pH 11). [Elion & Hitchings *J Am Chem Soc* **77** 1676 *1955*, Fox et al. *J Am Chem Soc* **80** 1669 *1958*.] It is an antineoplastic agent [Kataoka et al. *Cancer Res* **44** 519 *1984*]. [*Beilstein* **26** III/IV 3926.]

Thioindigo *[522-75-8]* **M 296.2, m >280°.** Adsorb it on silica gel from CCl_4/*benzene (3:1), elute with *benzene, evaporate, crystallise the residue from $CHCl_3$ and dry it at 60-65° [Wyman & Brode *J Am Chem Soc* **73** 1487 *1951*; this paper also gives details of purification of other thioindigo dyes]. [*Beilstein* **19** H 137, **19** I 690, **19** II 192, **19** III/IV 2091.]

Thiomorpholine (tetrahydro-*2H*-1,4-thiazine) *[123-90-0]* **M 103.2, b 110°/100mm, 169°/atm, d_4^{20} 1.026, n_D^{20} 1.540, pK^{25} 9.00.** Purify it by vacuum distillation. The *hydrochloride* has **m** 179° (from isoPrOH or EtOH/Et_2O/HCl). [Davies *J Chem Soc* 306 *1920*, *Beilstein* **27** II 4, **2** III/IV 636.]

Thionine (3,7-diaminophenothiazine, Lauth's violet) *[135-59-1, 581-64-6 (HCl), 78338-22-4 (acetate)]* **M 263.7, ε_{590} 6.2 x 10^4 M^{-1} cm^{-1}, pK^{15} 6.9.** The standard biological stain is usually highly pure. It can be crystallised from water or 50% EtOH, then chromatographed on alumina using $CHCl_3$ as eluent [Shepp et al. *J Phys Chem* **66** 2563 *1962*]. Dry it overnight at 100° and store it in a vacuum. The *hydrochloride* can be crystallised from 50% EtOH or dilute HCl and aqueous *n*-butanol. Purify it also by column chromatography and washed with $CHCl_3$ and acetone. Dry it *in vacuo* at room temperature. [*Beilstein* **27** H 391, **27** I 412, **27** II 447, **27** III/IV 5149.]

Thiooxine hydrochloride (8-mercaptoquinoline hydrochloride) *[34006-16-1]* **M 197.7, m 170-175° (dec), pK_1^{25} 2.16, pK_2^{25} 8.38.** It forms yellow crystals from EtOH. It has pKa^{20} values of 2.05 and 8.29 in H_2O. It is more stable than thiooxine. [UV: Albert & Barlin *J Chem Soc* 2384 *1959*.] [*Beilstein* **21** H 99, **21** III/IV 1197, **21/3** V 30.]

Thiophene *[110-02-1]* **M 84.1, f -38.5°, b 84.2°, d_4^{20} 1.525, n_D^{20} 1.52890, n_D^{30} 1.5223.** The simplest purification procedure is to dry thiophene with solid KOH, or reflux it with sodium, and fractionally distil it through a glass-helices-packed column. More extensive treatments include an initial wash with aqueous HCl, then water, drying with $CaSO_4$ or KOH, and passage through columns of activated silica gel or alumina. Fawcett and Rasmussen [*J Am Chem Soc* **67** 1705 *1945*] washed thiophene successively with 7M HCl, 4M NaOH, and distilled water, dried with $CaCl_2$ and fractionally distilled it. *Benzene was removed by fractional crystallisation by partial freezing, and the thiophene was degassed and sealed in Pyrex flasks. [Also a method is described for recovering the thiophene from the *benzene-enriched portion.] [*Beilstein* **17** H 29, **17** I 17, **17** II 35, **17** III/IV 234, **17/1** V 297.]

Thiophene-2-acetic acid *[1918-77-0]* **M 142.2, m 63-64°, 76°, b 160°/22mm, pK^{25} 3.89, pK^{25} 6.43 [$MeO(CH_2)_2OH$-H_2O/80:20].** Crystallise the acid from ligroin, hexane and/or distil it in a vacuum. The *amide* has **m** 148° (from H_2O or petroleum ether). [*Beilstein* **18** H 293, **18** III/IV 4062, **18/6** V 207.]

Thiophene-3-acetic acid *[6964-21-2]* **M 142.2, m 79-80°, pK_{Est} ~3.1.** Crystallise the acid from ligroin or H_2O. [*Beilstein* **18** III/IV 4066.]

2-Thiophenecarboxaldehyde *[98-03-3]* **M 112.2, b 75-77°/11mm, 106°/30mm, 198°/756mm, d_4^{20} 1.593, n_D^{20} 1.222.** Wash it with 50% HCl and distil it under reduced pressure just before use. It has UV with λ_{max} 234nm (hexane). The *Z-oxime* has **m** 144°, 136-138° and 142° (H_2O). [*Beilstein* **17** H 285, **17** I 148, **17** II 313, **17** III/IV 4477, **17/9** V 349.]

Thiophene-2-carboxylic acid *[527-72-0]* **M 128.2, m 129-130°, pK^{25} 3.59.** Crystallise the acid from water and dry it in a vacuum. The *amide* has **m** 181°(from H_2O) and pK^{25} 10.54 (50% aqueous dioxane). [*Beilstein* **18** H 289, **18** I 438, **18** II 269, **18** III/IV 4011, **18/6** V 158.]

Thiophene-3-carboxylic acid *[88-31-1]* **M 128.1, m 138-139°, pK^{25} 6.23(4.11).** Crystallise the acid from water and dry it in a vacuum. [*Beilstein* **18** H 292, **18** III/IV 4053, **18/6** V 199.] The *amide* has **m** 179-180° (from H_2O) [*Beilstein* **18** III/IV 4056].

Thiophene-2,5-dicarbonyl dichloride [2,5-bis(chlorocarbonyl)thiophene) *[3857-36-1]* **M 209.5, b 102-103°/2mm, 150-152°/11mm, m 43-47°, 45-46°.** Purify it by distillation in a vacuum; or if discoloured, then heat it with $SOCl_2$ or oxalyl chloride, and distil it in a vacuum. It solidifies on cooling, and can be recrystallised from *C_6H_6/heptane. It provides the *di-phenyl ester* (**m 136-137°**), when treated with phenol at 200° or phenol/pyridine at 100°, followed by adding to cold H_2O, filtering, drying, and recrystallising from EtOH. [Griffing & Salisbury *J Am Chem Soc* **70** 3416 *1968*, *Beilstein* **18** H 330, **18** III/IV 4496.]

Thiophene-2,5-dicarboxylic acid (2,5-dicarboxythiophene) *[4282-31-4]* **M 172.2, m 332-333°(sealed capillary), 358.5-359.5°(corrected, sealed tube), 360°, pK$_{Est(1)}$ ~3.3, pK $_{Est(2)}$ ~7.4.** It can be precipitated from alkaline solution with acid, filtered and recrystallised from H_2O, dried and sublimed at 0.0001 mm. Its *mono-methyl ester* crystallises from aqueous MeOH (**m 187-190°, pK$_{Est(1)}$ ~3.2)** or petroleum ether (**m 192°**), and sublimes in a vacuum unchanged. With diazomethane/Et_2O it provides the *di-methyl ester* (**m 148.5-149.5°**; **m's 146-147°** and **152°** were also reported) which crystallises from MeOH or 1:1 aqueous MeOH in flattened needles, and sublimes at 80-95° in high vacuum. This ester has λ_{max}(logε) at 275(4.27) in EtOH. [Hartough & Kosak *J Am Chem Soc* **68** 1012 *1947*, Birkinshaw & Chaplen *Biochem J* **60** 255 *1955*, Griffing & Salisbury *J Am Chem Soc* **70** 3416 *1968*, *Beilstein* **18** H 330, **18** III/IV 4496.]

Thiopyronine (2,7-dimethylaminothiaxanthene chloride hydrochloride) *[2412-14-8]* **M 318.9, λ_{max} 564nm (ε 78,500) H_2O, pK$_{Est}$ ~ 7.** Purify it as the hydrochloride by recrystallisation from hydrochloric acid forming needles **m** 245° (dec) and UV with λ_{max} at 564nm (ε 78,500, H_2O). [Fanghanel et al. *J Phys Chem* **91** 3700 *1987*, *Beilstein* **18** H 596, **18** III/IV 7291.]

Thiothienoyltrifluoroacetone [1-(2-thienyl)-4,4,4-trifluorobutan-3-one-1-thione] *[4552-64-1]* **M 228.2, m 61-62°, 64.5-65°, 73-74°, 74°.** It is easily oxidised and has to be purified before use. This is achieved by recrystallisation from *benzene or by dissolution in petroleum ether, extraction into 1M NaOH solution, acidification of the aqueous phase with 1-6M HCl solution, back extraction into petroleum ether and final evaporation of the solvent. The purity can be checked by TLC. It is stored in ampoules under nitrogen at 0° in the dark. It crystallises in red crystals from petroleum ether. Its IR has ν_{max} at 815m(C-S, C-H), 1260m(C-S), 1570sh(C=C) and 1612s(C=O)cm^{-1}. [Müller & Rother *Anal Chim Acta* **66** 49 *1973*, Chaston et al. *Aust J Chem* **18** 673 *1965*.]

2-Thiouracil *[141-90-2]* **M 128.2, m 240°(dec), 315°(dec), pK$_1^{25}$ 7.75, pK$_2^{25}$ 12.7.** Crystallise 2-thiouracil from water or EtOH. [*Beilstein* **24** H 323, **24** I 315, **24** II 171, **24** III/IV 1237.]

9*H*-Thioxanthene-9-one (thioxanthone, thionanthone) *[492-22-8]* **M 212.3, m 200-202°, 209°, 212-214°, b 371-373°/712mm.** It forms yellow needles from $CHCl_3$ or EtOH and sublimes *in vacuo*. It is soluble in CS_2, hot AcOH, and dissolves in conc H_2SO_4 to give a yellow colour with green fluorescence in VIS light. The *sulfone* has **m** 187° (from EtOH), and the *hydrazone* has **m** 115° (yellow leaflets from EtOH/*C_6H_6). The *oxime* has **m** 194-196° (from petroleum ether). [Szmant et al. *J Org Chem* **18** 745 *1953*, Ullmann et al. *Chem Ber* **49** 2509 *1916*, NMR: Sharpless et al. *Org Magn Res* **6** 115 *1974*, *Beilstein* **17** H 357, **17** I 191, **17** III/IV 5302, **17/10** V 437.]

β-Thymidine *[50-89-5]* **M 242.2, m 185°, 186-188°, $[\alpha]_D^{20}$ +19° (c 1, H_2O), pK_2^{25} 9.65.** Crystallise β-thymidine from ethyl acetate, MeOH/Et_2O (**m** 188°) or H_2O (as *2H_2O* **m** 189°). It is soluble in water and hot organic solvents. The *picrate* has **m** 230° (from EtOH). [*Beilstein* **24** III/IV 1297.]

Thymine (5-methylpyrimidin-2,4-dione) *[65-71-4]* **M 126.1, m 326°(dec), pK_1^{25} 9.90 (9.82) pK_2^{25} >13.0.** Crystallise thymine from EtOAc, 10% aqueous EtOH or water. It has **m** 318-320° after sublimation at 200°/12mm. Purify it by preparative (2mm thick) TLC plates of silica gel, eluting with ethyl acetate/isopropanol/water (75:16:9, v/v; R_F 0.75). The desired spot is located with a uv lamp, cut the band from the plate, place it in MeOH, shake and filter it through a millipore filter, then evaporate. [Infante et al. *J Chem Soc, Faraday Trans 1* **68** 1586 *1973*, *Beilstein* **24** H 353, **24** I 330, **24** II 183, **24** III/IV 1292.]

Tinuvin P (2-[2*H*-benzotriazol-2-yl]-*p*-cresol) *[50936-05-5]* **M 225.3, m 131-133°, $pK_{Est(1)}$~1.6 (N protonation), $pK_{Est(2)}$~ 8 (phenolic OH).** Recrystallise it from *n*-heptane or Me_2CO/pentane. [Woessner et al. *J Phys Chem* **81** 3629 *1985*.]

Toluidine Blue O *[93-31-9]* **M 305.8, CI 52040, λ_{max} 626nm, pK^{25} 7.5.** Crystallise the dye from hot water (18ml/g) by adding one and a half volume of alcohol and chilling on ice. Dry it at 100° in an oven for 8-10 hours. [Merrill & Spencer *J Am Chem Soc* **70** 3683 *1948*, *Beilstein* **27** I 417, **27** II 454, **27** III/IV 5161.]

1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD, 1,3,4,6,7,8-hexahydro-2*H*-pyrimido[1,2-a]-pyrimidine) *[5807-14-7]* **M 139.2, m 125-130°, pK^{25} ~16.** It crystallises from Et_2O but readily forms white crystals of the carbonate. It is a strong base (see pK, i.e. about 100 times more basic than tetramethylguanidine). The *picrate* has **m** 220.5-222° (from EtOH). It forms the *5-nitro* derivative **m** 145-160° that gives a *5-nitro nitrate* salt **m** 100-101° (from EtOH/Et_2O) and a *5-nitro picrate* **m** 144-145° (from H_2O) [McKay & Kreling *Can J Chem* **35** 1438 *1957*, Schwesinger *Chimia* **39** 369 *1985*, Hilpert et al. *J Chem Soc, Chem Commun* 1401 *1983*, Kamfen & Eschenmoser *Helv Chim Acta* **72** 185 *1989*]. [*Beilstein* **26** III/IV 60.]

1,2,4(1*H*)-Triazole *[288-88-0]* **M 69.1, m 121°, 260°, pK_1^{25} 2.27 (basic), pK_2^{25} 10.26 (acidic).** Crystallise 1,2,4-triazole from EtOH, H_2O, EtOAc (**m** 120.5-121°), or EtOH/*C_6H_6. The *hydrochloride* has **m** 170°, and the *picrate* has **m** 163-164° (from H_2O or $CHCl_3$). [Barszcz et al. *J Chem Soc, Dalton Trans* 2025 *1986*]. [*Beilstein* **26** H 13, **26** II 6, **26** III/IV 35.]

Tricycloquinazoline *[195-84-6]* **M 230.3, m 322-323°.** Crystallise it repeatedly from toluene, xylene or these solvents mixed with *C_6H_6. It can also be crystallised from $CHCl_3$ or cymene (**m** 308-310°), followed by sublimation at 210°/0.15-0.3 Torr in subdued light. [*Beilstein* **26** III/IV 1932.]

Trifluoperazine dihydrochloride (10-[3-{4-methyl-1-piperazinyl}propyl]-2-trifluoro-methyl-phenothiazine 2HCl) *[440-17-5]* **M 480.4, m 240-243°, 242-243°, pK_1 3.9, pK_2 8.1.** Recrystallise the salt from absolute EtOH, filter the crystals, dry them *in vacuo* and store them in tightly stoppered bottles because it is *hygroscopic*. It is soluble in H_2O but insoluble in *C_6H_6, Et_2O and alkaline aqueous solution. It has UV with λ_{max} at 258 and 307.5nm (log ε 4.50 and 3.50) in EtOH (neutral species). [Craig et al. *J Org Chem* **22** 709 *1957*.] It is a calmodulin inhibitor [Levene & Weiss *J Parmacol Exptl Ther* **208** 454 *1978*] and is a psychotropic agent [Fowler *Arzneim.-Forsch* **27** 866 *1977*]. [*Beilstein* **27** III/IV 1353.]

Trigonelline (1-methylnicotinic acid zwitterion) *[535-83-1]* **M 137.1, m 218°(dec), pK_1^{25} 2.10.** Crystallise trigonelline (as *monohydrate*) from aqueous EtOH, then dry it at 100°. It also crystallises from H_2O as the monohydrate with **m** 230-233°(dec). It has been crystallised from EtOH with **m** 214-215°(dec). The *hydrochloride* [6138-41-6] **M 173.6** has **m** 258-259°(dec) (from EtOH) [Smissman & Hite *J Am Chem Soc* **81** 1201 *1959*]. The *picrate* crystallises from EtOH with **m** 204-206°. [Green & Tong *J Am Chem Soc* **78** 4896 *1956*, Kosower & Patton *J Org Chem* **26** 1319 *1961*, *Beilstein* **22** I 504, **22** II 35, **22** III/IV 462, **22/2** V 143.]

4',5,7-Trihydroxyflavone (apigenin) *[520-36-5]* **M 270.2, m 296-298°, 300-305°, 345-350° (pK's 7—10, for phenolic OH).** Crystallise it from aqueous pyridine or aqueous EtOH. It dyes wool yellow when mixed with Cr ions. [*Beilstein* **18** H 181, **18** I 396, **18** II 178, **18** III/IV 2682, **18/4** V 574.]

2,2,5-Trimethyl-1,3-dioxane-4,6-dione (Methyl Meldrum's Acid, methylmalonic acid cyclic isopropylidene ester) *[3709-18-0]* **M 158.2, m 111-114°, 113-114°, 115°, pK^{25} 4.77.** This 'acid' is synthesised and purified in the same was as *Meldrum's acid* [2033-24-1], except that malonic acid is replaced by methylmalonic acid, in 58% yield. [Pihlaja & Seilo *Acta Chim Scand* **22** 3053 *1968*, Davidson & Bernhard *J Am Chem Soc* **70** 3426 *1948*]. Its ^{1}H NMR ($CDCl_3$, TMS) has δ at 1.77 (m, isopropylidene Me, *J* = 0.6Hz), 1.85 (m, isopropylidene Me, *J* = 0.6Hz), 1.52 (d, 5-Me, *J* = 7Hz) and 3.81 (q, 5-H, *J* = 7.0Hz) ppm [Schuster & Schuster *Tetrahedron* **25** 199 *1969*], and the proportion of *enol-form* is apparently not seriously altered by the polarity of the solvent, i.e. MeOH (55.7%), EtOH (1.2%), $CDCl_3$ (60.8%) and *C_6H_6 (58.9%) [Kabachnik et al. *Tetrahedron* **1** 317 *1967*]. The uncatalysed and acid-catalysed aqueous hydrolysis has been studied in detail with the 5,5-dimethyl-dione (not described here) hydrolysing slightly faster then the 5-methyl-4,6-dione (described here) and the unmethylated acid [Meldrum's acid, 2033-24-1] because, unlike the 5,5-dimethyl-4,6-dione, the latter two can enolise [Pihlaja & Seilo *Acta Chim Scand* **22** 3053 *1968*.] [*Beilstein* **18** I 480, **19** III/IV 1928, **19/5** V 11.]

2,2,6-Trimethyl-4*H*-1,3-dioxin-4-one (diketene acetone adduct) *[5394-63-8]* **M 142.2, m 12-13°, b 40°/0.03mm, 65-67°/2mm, 275°/atm, d $_4^{20}$ 1.0879, n $_D^{20}$ 1.4678.** The reactions of this dioxinone are very similar to those of diketene and it acts as a β-keto-ester synthon. Its purity can be easily assessed by ^{1}H NMR spectroscopy as it has only three characteristic peaks (see below). Purify it by fractional distillation, preferably under a vacuum. It is a pleasant smelling liquid that is quite stable in the **absence** of alkali. It is slightly soluble in H_2O that becomes faintly acidic, it gives a red colour with $FeCl_3$, and it rapidly reduces alkaline permanganate in alcoholic solution. It is readily prepared by refluxing a mixture of dry acetone (100ml), diketene (100ml, 109g, 1.3moles, see [674-82-8] **toxic**) and *p*-toluenesulfonic acid (0.5g, amount is critical) for 3 hours when the odour of diketene disappears. Excess of acetone is distilled off first followed by the *adduct* (168g, 1.18moles, 91% based on diketene). This procedure should be carried out in an efficient fume cupboard as diketene is **TOXIC**. [Carroll & Bader *J Am Chem Soc* **75** 5400 *1953*, Naylor (uses $ZnCl_2$ as catalyst) *J Chem Soc* 244 *1945*, Dehmlow & Shamout (using quaternary ammonium salts as catalysts) *Justus Liebigs Ann Chem* 1783 *1982*.] The structure of the adduct has been determined with certainty [Bader et al. *J Org Chem* **21** 821 *1956*]. Its FT-IR (film) has ν_{max} at 1738.7, 1640.0, 1392.8, 1272.6, 1205.3, 1031.5, 901.2, 805.1 and 548.3 cm^{-1}; the ^{1}H NMR ($CDCl_3$, TMS) has δ at 1.69 [s, 6H, gem $(CH_3)_2$], 2.00 (s, but d at very high resolution with *J* ~1 Hz, 3H, allyl CH_3) and 5.21 (s, but q at very high resolution with *J* ~1 Hz, 1H, vinyl H); and the ^{13}C NMR ($CDCl_3$) has δ at 168.65, 161.06, 106.32, 93.81, 25.02 and 19.92. Labelling experiments with $(CD_3)_2CO$ showed that isoprenyl acetoacetate may be the key intermediate in the synthesis [Hyatt *J Org Chem* **49** 5102 *1984*]. In addition to reacting as a diketene reagent, it has been functionalised, e.g. to 6-bromomethyl-2,2-dimethyl-4*H*-1,3-dioxin-4-one and 6-methylene-4-diethylphosphoryl-2,2-dimethyl-1,3-dioxinane, for the synthesis of natural products such as ikarugamycin and tirandamycin [Boeckman & Thomas *J Org Chem* **47** 2823 *1982*]. [*Beilstein* **19** IV 1604]

1',3',3'-Trimethyl-6-nitrospiro[2*H*-benzopyran-2,2'-indoline] *[1498-88-0]* **M 322.4, m 180°.** This photochromic dye crystallises from absolute EtOH [Hinnen et al. *Bull Soc Chim Fr* 2066 *1968*, Ramesh & Labes *J Am Chem Soc* **109** 3228 *1987*, Berman et al. *J Am Chem Soc* **81** 5607 *1959*]. [*Beilstein* **27** III/IV 1460.]

2,2,4-Trimethyl-6-phenyl-1,2-dihydroquinoline *[3562-69-4]* **M 249.3, m 102°.** It is the principal ingredient in Santoflex. Crystallise it three times from absolute EtOH. The *1-phenylcarbamoyl* derivative has **m** 148-149.6° (from EtOH). [Hively et al. *Anal Chem* **27** 100 *1955*, *Beilstein* **20** III/IV 4116.]

2,4,6-Trimethylpyridine (sym-collidine) *[108-75-8]* **M 121.2, m -46°, b 10°/2.7mm, 36-37°/2mm, 60.7°/13mm, 65°/31mm, 170.4°/760mm, 175-178°/atm, d $_4^{25}$ 0.9100, n $_D^{20}$ 1.4939, 1.4981, n $_D^{25}$ 1.4959, pK^{25} 6.69(7.45).** Commercial samples may be grossly impure. Likely contaminants include 3,5-dimethylpyridine, 2,3,6-trimethylpyridine and water. Brown, Johnson and Podall [*J Am Chem Soc* **76** 5556 *1954*] fractionally distilled 2,4,6-trimethylpyridine under reduced pressure through a 40cm Vigreux column and added to 430ml of the distillate slowly, with cooling to 0°, 45g of BF_3-diethyl etherate. The mixture was again distilled, and an equal volume of dry *benzene was added to the distillate. Dry HCl was passed into the solution, which was

kept cold in an ice-bath, and the hydrochloride was filtered off. It was recrystallised from absolute EtOH (1.5ml/g) to **m** 286-287°[**m** 256°(sealed tube), also **m** 293-294° subliming slowly]. The free base was regenerated by treatment with aqueous NaOH, then extracted with *benzene, dried ($MgSO_4$) and distilled under reduced pressure. Sisler et al. [*J Am Chem Soc* **75** 446 *1953*] precipitated trimethylpyridine as its phosphate salt from a solution of the base in MeOH by adding 85% H_3PO_4, shaking and cooling. The free base was then regenerated as above. Garrett and Smythe [*J Chem Soc* 763 *1903*] purified the trimethylpyridine *via* the $HgCl_2$ complex. It is more soluble in cold than hot H_2O [the solubility is 20.8% at 6°, 3.5% at 20°, 1.8% at 100°].
Alternatively, purify it by dissolving it in $CHCl_3$, adding solid K_2CO_3 and Drierite, filtering and fractionally distilling through an 8in helix-packed column. *The alkali metals, Na, Li or Cs should NOT be used for drying pyridine, and pyridine derivatives, as they form coloured pyridine radical anions leading to bipyridyls.* [see Schmulback et al. *J Am Chem Soc* **90** 6600 *1968*]. The *sulfate* has **m** 205°, and the *picrate* (from hot H_2O) has **m** 155-156°. [Frank & Meikle *J Am Chem Soc* **72** 4184 *1950*, *Beilstein* **20** H 250, **20** I 87, **20** II 164, **20** III/IV 2810, **20/6** V 93.]

1,3,7-Trimethyluric acid *[5415-44-1]* **M 210.2, m 345°(dec), pK^{25} 6.0.** Crystallise it from water and dry it at 100° in a vacuum. It has UV with λ_{max} at 289nm (pH 2.5). [*Beilstein* **26** III/IV 2623.]

1,3,9-Trimethyluric acid *[7464-93-9]* **M 210.2, m 340°(dec), 347°, pK^{20} 9.39.** Crystallise it from water and dry it at 100° in a vacuum. [*Beilstein* **26** H 530, **26** II 301, **26** III/IV 2623.]

1,7,9-Trimethyluric acid *[55441-82-2]* **M 210.2, m 316-318°, 345°, pK_{Est} ~9.0.** Crystallise the uric acid from water or EtOH, and sublime it *in vacuo*. [*Beilstein* **26** H 530, **26** II 302, **26** III/IV 2623.]

3,7,9-Trimethyluric acid *[55441-72-0]* **M 210.2, m 373-375°(dec), pK^{20} 9.39.** Crystallise the uric acid from water and dry it at 100° in a vacuum. It has UV with λ_{max} at 294nm (pH 2.5). [Bergmann & Dikstein *J Am Chem Soc***77** 691 *1955*, *Beilstein* **26** H 530, **26** I 156, **26** II 301, **26** III/IV 2623.]

1,3,5-Trioxane *[110-88-3]* **M 90.1, m 64°, b 114.5°/759mm.** Crystallise 1,3,4-trioxane from sodium-dried diethyl ether or water, and dry it over $CaCl_2$. It can also be purified by zone refining. [*Beilstein* **19** H 381, **19** II 392, **19** III/IV 4710, **19/9** V 103.]

Trioxsalen (2,5,9-trimethyl-7*H*-furo[3,2-*g*]benzopyran-7-one) *[3902-71-4]* **M 228.3, m 233-235°, 234.5-235°.** Purify trioxsalen by recrystallisation from $CHCl_3$. If too impure, it is fractionally crystallised from $CHCl_3$/petroleum ether (b 30-60°) using Norit, and finally crystallised from $CHCl_3$ alone to give colourless prisms, **m** 234.5-235°. It is a photosensitiser so it should be stored in the dark. [UV: Kaufmann *J Org Chem* **26** 117 *1961*, Baeme et al. *J Chem Soc* 2976 *1949*, *Beilstein* **19/4** V 472.]

2,3,5-Triphenyltetrazolium chloride (TTC, TTZ) *[298-96-4]* **M 334.8, m 243°(dec).** Crystallise TTZ from EtOH or $CHCl_3$, and dry it at 105°. [*Beilstein* **26** H 363, **26** II 216, **26** III/IV 1774.]

Tripyridyl triazine *[3682-35-7]* **M 312.3, m 245-248°, 248-250°.** Purify it by repeated crystallisation from aqueous EtOH. It is a reagent for the determination of Fe(II) and total Fe [Collins et al. *Anal Chem* **31** 1862 *1959*]. [*Beilstein* **26** III/IV 4192.]

1,1,1-Tris(acetyloxy)-1,1-dihydro-1,2-benzoiodoxol-3-(1*H*)-one (Dess-Martin periodinane, DMP) *[87413-09-0]* **M 424.1, m 130-133°, 133-134° (dec).** DMP is essentially the acetylated form of IBX (see above) that renders the latter more soluble in organic solvents. Unlike IBX, it is not explosive on melting or upon hard impact. However, it is subject to hydrolysis in the presence of moisture that may give rise to explosive impurities. It is important that it should be stored in a dry atmosphere and that care should be taken when using it. The original Dess-Martin preparation [Dess-Martin *J Am Chem Soc* **113** 7277 *1991*] has been improved and is reported here.
1-Hydroxy-1,2-benziodoxol-3(1*H*)-one (100g, 360mmol, see IBX [61717-82-6]) is added to Ac_2O (400ml, ~4mol) and $TsOH.H_2O$ (0.5g), and stirred under N_2 at 80° for 2 hours, then cooled in an ice-water bath. The

white solid that separates in the cold mixture is filtered off onto a fritted glass funnel, rinsed with anhydrous Et_2O (5 x 50ml), and the crystalline solid (138g, 91%, m 134°) is rapidly transferred to an argon filled amber-glass bottle and stored in a freezer. When exposed to light for several weeks some decomposition occurs so it should be kept away from light. [Ireland & Liu *J Org Chem* **58** 2899 1993.] Its IR (CH_2Cl_2) has ν_{max} at 1726.9 (s) and 1707.5 cm^{-1}; the ^1H NMR ($CDCl_3$, TMS) has δ at 2.01 (s, 6H, COC*H*$_3$), 2.33 (s, 3H, COC*H*$_3$), 7.80 (t, 1H, J_{HH} = 7.3 and 8.5 Hz) and 8.07 (t, 1H, J_{HH} = 7.3 and 8.5 Hz) (C-4 and C-5), 8.29 (d, 1H, J_{HH} = 8.5 Hz) and 8.31 (d, 1H, J_{HH} = 8.5 Hz) (C-3 and C-6); and the ^{13}C NMR ($CDCl_3$) has δ at 20.29 (2 CO*C*H$_3$), 20.43 (1 CO*C*H$_3$), 126.01 (C-2), 126.51, 131.79, 133.81, 135.76, 142.36 (C-1), 166.08 (endocyclic C=O), 173.96 (1 acetate C=O), 175.66 and (2 acetate C=O's). A 0.3M solution of DMP in CH_2Cl_2 is available commercially.
DMP is an extremely useful reagent for the oxidation of primary and secondary alcohols to aldehydes and ketones to completion, without further oxidation to the acids, within ~2 hours at 20°; allylic and benzylic alcohols require ~30 minutes. The reaction is increased rapidly on addition of an alcohol. Furan rings or sulfides and vinyl ethers are unreactive. Geraniol is oxidised to geranial without rearrangement to nerol, and it oxidises *N*-benzylbenzamide to benzaldehyde. The reagent is usually added in an appropriate anhydrous solvent (e.g. $CHCl_3$, CH_2Cl_2, MeCN, etc.) followed by the substrate. Workup can be by adding Et_2O followed by aqueous NaOH which decomposes the reagent to iodobenzoate, or for base-sensitive substrates $NaHCO_3$ and sodium thiosulfate ($Na_2S_2O_3$) are added, which also remove iodine. A pyridine buffer can be used to keep near-neutral conditions throughout the entire oxidation followed by a thiosulfate work up procedure. [see Dess-Martin *J Am Chem Soc* **113** 7277 *1991*, and papers cited in this reference.] In the peptide field, substances like *N*-Fmoc phenylglycinol are oxidised to *N*-Fmoc phenylglycinal almost quantitatively in water-saturated CH_2Cl_2 with this reagent [Myers et al. *Tetrahedron Lett* **41** 1359 *2000*].

1,3,5-Trithiane (trithioformaldehyde) *[291-21-4]* **M 138.3, m 216-218°(dec).** Crystallise it from AcOH or toluene, after Soxhlet extraction with toluene (30g/300ml) [*Beilstein* **19** III/IV 4711, **19/9** V 105.]

3-Tropanol (Tropine) *[120-29-6]* **M 141.2, m 63°, 64-66°, b 229°/760mm, pK^{15} 3.80.** Distil 3-tropanol in steam and crystallise it from Et_2O or toluene/petroleum ether. It is soluble in H_2O, EtOH, $CHCl_3$, and sublimes at 60°/0.1mm. *Hygroscopic*. A 0.05M solution in H_2O has a pH of 11.5. The *hydrochloride* has **m** 280° (from EtOH/Et_2O). [*Beilstein* **21** H 16, **21** I 197, **21** II 17, **21** III/IV 168, **21/1** V 219.]

Tryptamine [3-(2-aminoethyl)indole)] *[61-54-1]* **M 160.1, m 116°, pK_1^{25} -6.31 (aqueous H_2SO_4), diprotonation), $pK_{Est(2)}$~4.9, pK_3^{25} 16.60 (acidic indole NH).** Crystallise tryptamine from *benzene, Et_2O (**m** 114°) or petroleum ether (**m** 118°). It has UV with λ_{max} at 222, 276, 282 and 291nm (EtOH) and 226, 275, 281 and 290nm (HCl). [*Beilstein* **22** II 346, **22** III/IV 4319, **22/10** V 45.]

Tryptamine hydrochloride *[343-94-2]* **M 196.7, m 252-253°.** Crystallise the salt from EtOH/water or EtOH/Et_2O. See previous entry for UV. [*Beilstein* **22** II 347, **22** III/IV 4319, **22/10** V 46.]

Tryptophol [3-(2-hydroxyethyl)indole] *[526-55-6]* **M 161.2, m 59°, b 174°/2mm.** Crystallise it from diethyl ether/petroleum ether, *C_6H_6, *C_6H_6/petroleum ether. The *picrate* has **m** 100-101° (from *C_6H_6). [*Beilstein* **21** I 218, **21** II 49, **21** III/IV 788, **21/3** V 61.]

(+)-Tubocurarine chloride ($5H_2O$) *[57-94-3]* **M 771.7, m 274-275°(dec) (anhydrous), $[\alpha]_{546}^{20}$ +235° (c 0.5, H_2O), $pK_{Est(1)}$~8.5, $pK_{Est(2)}$~8.8.** Crystallise this chloride from water. It forms various hydrates. The *hydrochloride pentahydrate* has **m** 268-269° (from H_2O) and $[\alpha]_D^{21}$ +190° (0.5, H_2O). Its solubility in H_2O at 25° is 50mg/ml. [*Beilstein* **27** II 897, **27** III/IV 8727.]

Umbelliferone (7-hydroxycoumarin) *[93-35-6]* **M 162.2, m 225-228°, 230-233°, pK_{Est} ~8.0.** It crystallises from water (**m** 232-232.2°) or EtOH (**m** 232°). It sublimes at 160°/0.001mm. Fluorescence: Em $_{max}$ 452nm/Exc $_{max}$ 325nm in 50% EtOH. [*Beilstein* **18** H 27, **18** I 306, **18** II 16, **18** III/IV 294, **18/1** V 386.]

Uracil (pyrimidine-2,4(1*H*)-dione) *[66-22-8]* **M 122.1, m 335°(dec), pK_1^{25} 9.43, pK_2^{25} 13.3-14.2.** Uracil crystallises from water (**m** 339-341°) and **m** 338° after sublimation in high vacuum. Its solubility in H_2O at 20° is 1g/300ml. [*Beilstein* **24** H 312, **24** I 312, **24** II 169, **24** III/IV 1193.]

Uramil (5-aminobarbituric acid) *[118-78-5]* **M 143.1, m 310-312°, 320°, >400°(dec), $pK_{Est(1)}$~3.9, $pK_{Est(2)}$~8.0, $pK_{Est(3)}$~12.5.** It crystallises from water. It has also been purified by dissolving it in aqueous ammonia and precipitating it by dropwise addition of formic acid. The solid is collected and dried in a vacuum at 100°. [Hartman & Sheppard *Org Synth* Coll Vol **II** 617 *1943*, *Beilstein* **25** H 492, **25** I 704, **25** III/IV 4228.]

Uric acid *[69-93-2]* **M 168.1, m >300° (dec) pK_1 5.75, pK_2 10.3.** Crystallise uric acid from hot distilled H_2O (the solubility in H_2O is 1part/39,000parts at 18° and 1part/2,000parts at 100°). It is best purified by dissolving in an alkaline solution and acidifying with dilute HCl and drying it at 100° in a vacuum. [Bergmann & Dikstein *J Am Chem Soc* **77** 691 *1955*, Lister *Purines Part II, Fused Pyrimidines* Brown Ed, Wiley-Interscience pp256-257 *1971*, ISBN 0-471-38205-1, *Beilstein* **26** H 513, **26** I 151, **26** II 293, **26** III/IV 2619.]

β-Uridine *[58-96-8]* **M 244.2, m 165°, $[\alpha]_D^{20}$ +10.0° (c 1.6, H_2O), pK^{25} 9.51 (9.25).** Crystallise β-uridine from aqueous 75% MeOH or EtOH (**m** 165-166°). [*Beilstein* **24** III/IV 1202.]

Urocanic acid (4-imidazolylacrylic acid) *[104-98-3]* **M 138.1, m 225°, 226-228°, $pK_{Est(1)}$~2.5, $pK_{Est(2)}$~6, $pK_{Est(3)}$~11.** Crystallise the acid from water and dry it at 100°. The *trans-isomer* [3465-72-3] has **m** 225° (229-230°, 230-231° or 231°(dec, from H_2O) and pK_1 3.5 and pK_2 5.6, and the *picrate* has **m** 225°(dec, from H_2O). The *cis-isomer* [7699-35-6] has **m** 175-176° (178-179° or 180-184° dec, from H_2O) and pK_1 3.0 and pK_2 6.7, and the *picrate* has **m** 204° (from H_2O). [*Beilstein* **25** H 124, **25** I 536, **25** II 121, **25** III/IV 786.]

δ-Valerolactam (2-piperidone) *[675-20-7]* **M 99.1, m 38.5-39.5°, 39-40°, 40°, b 81-82°/0.1mm, 136-137°/15mm, pK^{25} 0.75 (in AcOH).** Purify it by repeated fractional distillation. [Cowley *J Org Chem* **23** 1330 *1958*, Reppe et al. *Justus Liebigs Ann Chem* **596** 198 *1955*, IR: Huisgen et al. *Chem Ber* **90** 1437 *1957*.] The *hydrochloride* [5174-67-4] has **m** 183-184° (from isoPrOH or EtOH/Et_2O) [Hurd et al. *J Org Chem* **17** 865 *1952*], and the *oxime* has **m** 122.5° (from petroleum ether) [Behringer & Meier *Justus Liebigs Ann Chem* **607** 67 *1957*]. The *N-benzoyl* derivative [4252-56-6] has **m** 115° (from $CHCl_3$/petroleum ether), the *N-methyl* derivative [931-20-4] is a water soluble hygroscopic liquid with **b** 115°/14mm, and the *N-methyl hydrochloride* [87243-73-0] crystallises from from EtOH/Et_2O with **m** 115°. The *picrate* has **m** 92-93°. [*Beilstein* **21** H 239, **21** III/IV 3170, **21/6** V 396.]

δ-Valerolactone (tetrahydro-2*H*-pyran-2-one) *[542-28-9]* **M 100.1, m -13°, -12°, b 88°/4mm, 97°/10mm, 124°/24mm, 145-146°/40mm, 229-229.5°/atm, d_4^{20} 1.1081, n_D^{20} 1.4568.** Purify the δ-lactone by repeated fractional distillation. Its IR has ν_{max} at 1750 (in CS_2), 1732 (in $CHCl_3$), 1748 (in CCl_4) and 1733 (in MeOH) cm^{-1} [Huisgen & Ott *Tetrahedron* **6** 253 *1959*, Linstead & Rydon *J Chem Soc* 580 *1933*, Jones et al. *Can J Chem* **37** 2007 *1959*]. [*Beilstein* **17** H 235, **17** II 287, **17** III/IV 4169, **17/9** V 17.]

γ-Valerolactone (± 4,5-dihydro-5-methyl-2(3*H*)-furanone) *[108-29-2]* **M 100.1, m -37°, 36°, b 82-85°/10mm, 102-103°/28mm, 125.3°/68mm, 136°/100mm, 205.75-206.25°/ 754mm, d_4^{20} 1.072, n_D^{20} 1.4322.** Purify the γ-lactone by repeated fractional distillation [Boorman & Linstead *J Chem Soc* 577, 580 *1933*]. Its IR has ν_{max} at 1790 (CS_2), 1775 ($CHCl_3$) cm^{-1} [Jones et al. *Can J Chem* **37** 2007 *1959*]. The *BF_3-complex* distils at 110-111°/20mm [Reppe et al. *Justus Liebigs Ann Chem* **596** 179 *1955*]. It is characterised by conversion to γ-hydroxy-*n*-valeramide on treatment with NH_3, which has **m** 51.5-52° (by slow evaporation of a $CHCl_3$ solution). [*Beilstein* **17** H 235, **17** I 131, **17** II 288, **17** III/IV 4176, **17/9** V 24.]

(±)-Vinclozolin [3-(3,5-dichlorophenyl)-5-methyl-5-vinyloxazolidine-2,4-dione] *[50471-44-8]* **M 286.1, m 108°.** Crystallise the fungicide from Me_2CO/H_2O. Its solubility at 20° (w/w%) is 44 (Me_2CO), 32 ($CHCl_3$), 25 (EtOAc) and 10 (H_2O). It irritates the eyes and skin. [**GP** 2,207,576 *1973*, *Chem Abstr* **79** 137120 *1973*.]

***N*-Vinylcaprolactam** *[2235-00-9]* **M 139.2, m 35-38°(polym), b 95-95.5°/4mm, 128°/21mm, d_4^{20} 1.0287, n_D^{20} 1.5133.** Distil it under vacuum and with 0.0015% of 4-*tert*-butylcatechol as stabilizer. [*Beilstein* **21** III/IV 3207.]

***N*-Vinylcarbazole** *[1484-13-5]* **M 193.3, m 66°.** Crystallise *N*-vinylcarbazole repeatedly from MeOH in amber glassware. It sublimes in a vacuum. [*Beilstein* **20** II 282, **20** III/IV 3830, **20/8** V 19.]

Vinylene carbonate (1,3-diaxol-2-one) *[872-36-6]* **M 86.1, m 22° , b 76-78°/37mm, 165°/~760mm.** Purify it by zone melting, or distillation, and stabilise it with 0.5% of 2,6-di-*tert*-butyl-*p*-cresol. [*Beilstein* **19** III/IV 1597, **19/4** V 72.]

2-Vinylpyridine monomer *[100-69-6]* **M 105.1, b 79-82°/29mm, d 0.974, n 1.550, pK^{25} 4.92(4.98).** Steam distil it, then dry it with $MgSO_4$ and distil it in a vacuum. [*Beilstein* **20** H 256, **20** III/IV 2884, **20/6** V 211.]

4-Vinylpyridine monomer *[100-43-6]* **M 105.1, b 40-41°/1.4mm, 54°/5mm, 58-61°/12mm, 68°/18mm, 79°/33mm, d_4^{20} 0.9836, n_D^{20} 1.5486, pK^{25} 5.62.** Purify the monomer by fractional distillation under a good vacuum and in a N_2 atmosphere; store it in sealed ampoules under N_2, and keep it in the dark at -20°. The *picrate* has **m** 175-176°. [UV: Coleman & Fuoss *J Am Chem Soc* **77** 5472 *1955*, Overberger et al. *J Polymer Sci* **27** 381 *1958*, Petro & Smyth *J Am Chem Soc* **79** 6142 *1957*.] It is used for alkylating SH groups in peptides [Anderson & Friedman *Can J Biochem* **49** 1042 *1971*, Cawins & Friedman *Anal Biochem* **35** 489 *1970*]. [*Beilstein* **20** II 170, **20** III/IV 2887, **20/6** V 213.]

Viologen (4,4'-dipyridyl dihydrochloride) *[27926-72-3]* **M 229.1, m 278° (also reported m 302-306°, >300°, with sublimation**), **pK_1^{20} 3.17, pK_2^{20} 4.82.** Purify viologen by precipitation on adding excess of acetone to a concentrated solution of it in aqueous MeOH. It has also been recrystallised several times from MeOH or *iso*-propanol and dried at 70° under vacuum for 24 hours [Prasad et al. *J Am Chem Soc* **108** 5135 *1986*], and recrystallised three times from MeOH/isopropanol [Stramel & Thomas *J Chem Soc, Faraday Trans* **82** 799 *1986*, Michaelis & Hill *J Am Chem Soc* **55** 1481 *1933*, Tilford et al. *J Am Chem Soc* **70** 4005 *1948*]. [*Beilstein* **23** I 49.]

Visnagin (4-methoxy-7-methyl-5*H*-furo[3,2-g][1]benzopyran-5-one) *[82-57-5]* **M 230.2, m 142-145°.** Crystallise visnagin from water. It is soluble in $CHCl_3$ but slightly soluble in EtOH. [Aneja et al. *Tetrahedron* **3** 230 *1958*, *Beilstein* **19** III/IV 2640.]

9*H*-Xanthene (dibenzopyran) *[92-83-1]* **M 182.2, m 100.5°, 101-102.5°, b 310-312°/760mm.** Crystallise dibenzopyran from *benzene, MeOH or EtOH. [*Beilstein* **17** H 73, **17** I 30, **17** II 72, **17** III/IV 614, **17/2** V 252.]

Xanthine (2,6-dihydroxypurine, purine-2,6(1*H*,3*H*)dione) *[69-89-6]* **M 152.1, pK_1 0.8 [protonation of imidazole 7(9)NH], pK_2 7.44 [monoanion 1(3)NH], pK_3 11.12 [dianion 1,3-N^{2-}].** The *monohydrate* separates in a microcrystalline form on slow acidification with acetic acid of a solution of xanthine in dilute NaOH. It is also precipitated by addition of conc NH_3 to its solution in hot 2N HCl (charcoal). After washing with H_2O and EtOH, it is dehydrated by heating above 125°. Its solubility in H_2O is 1 in 14,000 parts at 16° and 1 in 1,500 parts of boiling H_2O, and separates as plates. It has no **m**, but the *perchlorate* has **m** 262-264° [Lister *Purines Part II, Fused Pyrimidines* Brown Ed, Wiley-Interscience pp 252-253 *1971*, ISBN 0-471-38205-1]. [*Beilstein* **26** H 447, **26** I 131, **26** II 260, **26** III/IV 2327.]

9-Xanthone (9-xanthenone) *[90-47-1]* **M 196.2, m 175.6-175.4°.** Crystallise xanthone from EtOH (25ml/g) and dry it at 100°. It has also been recrystallised from *n*-hexane three times and sublimed *in vacuo*. [Saltiel *J Am Chem Soc* **108** 2674 *1986*]. [*Beilstein* **17** H 354, **17** I 190, **17** II 378, **17** III/IV 5292, **17/10** V 430.]

Xanthosine ($2H_2O$) [9-(β-D-ribosyl)purin-2,6(1*H*,3*H*)-dione] *[5968-90-1]* **M 320.3, $[\alpha]_D^{20}$ -53° (c 8, 0.3M NaOH), pK_1^{25} <2.5, pK_2^{25} 5.67, pK_3^{25} 12.85.** It crystallises from EtOH (anhydrous) or water (as dihydrate).

[Howard et al. *J Chem Soc* 232 *1949*, *Beilstein* **31** H 28, **26** III/IV 2428.]

Xanthurenic acid (5,8-dihydroxyquinoline-2-carboxylic acid) *[59-00-7]* **M 205.2, m 286°, 290-295°(dec), 297-29°(dec), $pK_{Est(1)}$~ 1.5, $pK_{Est(2)}$~ 4.9, $pK_{Est(3)}$~ 9.8.** It is precipitated by the addition of 2N formic acid to its solution in hot 2M ammonia (charcoal). The solid is filtered off, dried in a vacuum at ~80° in the dark. Its UV (H_2O) has λ_{max} nm (ε $M^{-1}cm^{-1}$) at 243 (30,000) and 342 (6,500). The *methyl ester* has **m** 262° (from MeOH). It forms Cu^{2+}, Zn^{2+}, Fe^{2+} and Fe^{3+} salts. [*Beilstein* **22** III/IV 2513.]

Xanthydrol *[90-46-0]* **M 198.2, m 122-123°, 123-124°, 124-126°.** Crystallise xanthydrol from EtOH and dry it at 40-50°. [*Beilstein* **17** H 129, **17** I 72, **17** II 146, **17** III/IV 1602, **17/4** V 502.]

Xylenol Orange {3*H*-2,1-benzoxathiol-3-ylidene-bis-[(6-hydroxy-5-methyl-*m*-phenylene)-methylnitrilo]-tetraacetic acid, S,S-dioxide} *[1611-35-4]* **M 672.6, m 210°(dec), ε_{578} 6.09 x 10^4 (pH 14), ε_{435} 2.62 x 10^4 (pH 3.1), pK_1 -1.74, pK_2 -1.09 (aqueous H_2SO_4-HNO_3), pK_3 2.58, pK_4 3.23, pK_5 6.46, pK_6 10.46, pK_7 12.28.** It is generally contaminated with starting material (cresol red) and semi-xylenol orange. Purify it by ion-exchange chromatography using DEAE-cellulose, eluting with 0.1M NaCl solution, which will give the sodium salt [3618-43-7] . Cresol Red, semi-xylenol orange and iminodiacetic acid bands elute first. This procedure will give the sodium salt of the dye.
To obtain the *free acid*, dissolve the salt in H_2O and acidify it with AcOH. Filter it off, wash it with H_2O and dry it first in air and then in a vacuum desiccator over P_2O_5 in the dark [Sato et al. *Anal Chim Acta* **94** 317 *1977*]. [*Beilstein* **19** II 111, **19** III/IV 1135, **19/3** V 461.]

α-Yohimbine (17α-Hydroxy-20α-yohimban-16α-carboxylic acid methyl ester, Rauwolscine) *[146-48-5]* **M 354.5, m 234°, 235-237°(dec), 278°(dec), $[\alpha]_D^{20}$ +55.6° (c 2, EtOH), +108° (pyridine), pK_1^{22} 3.0, pK_2^{22} 7.45.** Crystallise the *Rauwolfia* alkaloid from EtOH or dilute EtOH (needles), and dry it in a vacuum to remove EtOH of crystallisation. It is soluble in MeOH, $CHCl_3$, warm $*C_6H_6$, moderately soluble in Et_2O but difficultly soluble in H_2O. Its has UV (MeOH) with λ_{max} nm(logε) at 226(4.56), 280(3.88) and 291(380). The ***hydrochloride*** [45-19-0] crystallises in plates or prisms from EtOH with **m 302°(dec), $[\alpha]_D^{20}$ +105° (H_2O)**. Its solubility in H_2O is 83% (giving a neutral solution), and 0.25% in EtOH. [Van Tamelen et al. *J Am Chem Soc* **91** 7315 *1969*, Stork & Guthikonda *J Am Chem Soc* **94** 5109 *1972*, Wenkert et al. *J Am Chem Soc* **100** 4894 *1978* and *J Am Chem Soc* **101** 5370 *1982*, *Beilstein* **25** II 201, **25** III/IV 1234.], It is pharmacologically active being a 5□HT_{1A} serotonin receptor agonist and an α_2-adrenoceptor antagonist.
For δ-yohimbine and γ-yohimbine see ajmalicine [483-04-5] and ajmaline [4360-12-7] above.

MISCELLANEOUS As, B, P, Si, S, Se and Te COMPOUNDS.

This section contains miscellaneous organic compounds of As, B, P, Si, S, Se, Te, and ammonium and metal salts of their acids, and salts of their bases. See other sections and chapters for further entries of sulfur, phosphorous and silicon compounds; and for sulfur heterocyclic compounds see section on "Heterocyclic Compounds",

Acetonyltriphenylphosphonium chloride *[1235-21-8]* **M 354.8, m 237-238°, 244-246°(dec).** Recrystallise it from $CHCl_3$/*C_6H_6/petroleum ether (b 60-80°) or by dissolving it in $CHCl_3$ and pouring it into dry Et_2O. It has UV(EtOH) with λ_{max} nm(ε) at 255(3,600), 262(3,700), 268(4,000) and 275(3,100). The *iodide salt* crystallises from H_2O and has **m** 207-209°. [Ramirez & Dershowitz *J Org Chem* **22** 41 *1957*.] It is an **IRRITANT** and is *hygroscopic.* When shaken with a 10% aqueous solution of Na_2CO_3 (8 hours) it gives ***acetylmethylene triphenyl phosphorane*** which is recrystallised from MeOH/H_2O, and after drying at 70°/0.1mm has **m** 205-206°. It has UV with λ_{max} nm(ε) at 268 (6600), 275 (6500) and 288 (5700), and its IR has ν_{max} at 1529(s), 1470(m), 1425(s), 1374(m), 1105(s) and 978(s) (cm^{-1}). [Ramirez & Dershowitz *J Org Chem* **22** 41, 44 *1957*, *Beilstein* **16** H 761, **16** II 373.]

3*R*,4*R*,1'*R*-4-Acetoxy-3-[1-(*tert*-butylmethylsilyloxy)ethyl]-2-azetinone *[76855-69-1]* **M 287.4, m 107-108°, $[\alpha]_D^{20}$ +55° (c 0.5, toluene), $[\alpha]_D^{20}$ +53.7° (c 1.04, $CHCl_3$).** Purify it by chromatography on silica gel (3 x 14cm) for 50g of ester using 20% EtOAc in *n*-hexane. The eluate is evaporated, and the residue is recrystallised from hexane (white fluffy crystals). [Leanza et al. *Tetrahedron* **39** 2505 *1983*.]

***N*-Acetyl-4-hydroxy-*m*-arsanilic acid (Acetarsol, 3-acetamido-4-hydroxyphenylarsonic acid)** *[97-44-9]* **M 275.1, m 240-250°, pK_1 3.73, pK_2 7.9, pK_3 9.3.** It crystallises from water in colourless prisms. It decomposes slowly on prolonged boiling in H_2O or dilute alkalis. The *N-propionyl* derivative recrystallises from H_2O with **m** 228-229°(dec). [Raiziss & Fisher *J Am Chem Soc* **48** 1323 *1926*, Hewitt & King *J Chem Soc* 823 *1926*, *Beilstein* **16** I 491, **16** II 521, **16** III 1129.]

Alizarin Red S (3,4-dihydroxy-9,10-dioxo-2-anthracene sulfonic acid, Na salt. H_2O) *[130-22-3]* **M 360.4, pK_1^{25} <1, pK_2^{25} 5.49, pK_3^{25} 10.85 (11.01).** Commercial samples contain large amounts of sodium and potassium chlorides and sulfates. It is purified by passing through a Sephadex G-10 column (size exclusion column), followed by elution with water, then 50% aqueous EtOH [King & Pruden *Analyst (London)* **93** 601 *1968*]. Finally dissolve it in EtOH and precipitate it with Et_2O several times [Sacconi *J Phys Chem* ***54*** 829 *1950*, polarography: Furnam & Stone *J Am Chem Soc* **70** 3055 *1948*, *Beilstein* **11** IV 682.]

Allyl trimethylsilane (2-propenyltrimethylsilane) *[762-72-1]* **M 114.3, b 83.0-84.5°, 84-88°, 85.5-86.0°, d_4^{20} 0.713, n_D^{20} 1.405.** Fractionate it through an efficient column at atmospheric pressure. If impure, dissolve it in THF, shake it with H_2O (2x), dry (Na_2SO_4), filter and fractionate it. [Cudlin & Chvalovský *Col Czech Chem Commun* **27** 1658 *1962*, *Beilstein* **4** IV 3927.]

Ammonium dodecylsulfate (ammonium laurylsulfate) *[2235-54-3]* **M 283.4.** Recrystallise it first from 90% EtOH and then twice from absolute EtOH, and finally dry it in a vacuum. [*Beilstein* **1** III 1786.]

Ammonium tetraphenylborate *[14637-34-4]* **M 337.3, m *ca* 220°(dec).** Dissolve it in aqueous Me_2CO and allow crystallisation to proceed slowly; otherwise very small crystals are formed. No trace of Me_2CO is left in the crystals after drying at 120° [Davies & Staveley *Trans Faraday Soc* **53** 19 *1957*]. Also, the salt can be precipitated from a dilute AcOH solution of sodium tetraphenylborane in the presence of NH_4^+ ions. After standing for 5 minutes, the precipitate is filtered off onto a sintered porcelain crucible, washed with very dilute AcOH and dried at room temperature for at least 24 hours [Vendlandt *Anal Chem* **28** 1001 *1956*]. *Alternatively*, a solution of sodium tetraphenylborane (5% excess) in H_2O is added to NH_4Cl solution. After 5 minutes the precipitate is collected, washed several times with H_2O and recrystallised from aqueous Me_2CO. [Howick & Pflaum *Analyt Chim Acta* **19** 342 *1958*, *Beilstein* **16** IV 1625.]

9-Anthraceneboronic acid *[100622-34-2]* **M 222.0, m 203-250°.** Crystallise the boronic acid from dilute HCl (**m** 180-184°). The *disodium salt* has **m** 209-213°. [*Beilstein* **16** IV 1679.]

Anthraquinone Blue B (Acid Blue 45, 1,5-diamino-4,8-dihydroxy-9,10-anthraquinone-3,7-disulfonic acid di-Na salt) *[2861-02-1]* **M 474.3, m >300°, CI 63010, λ_{max} 595nm, $pK_{Est(1)}$~<0, $pK_{Est(2)}$~2, $pK_{Est(3)}$~9.** Purify it by salting out an aqueous solution three times with sodium acetate, followed by repeated extraction with EtOH [McGrew & Schneider *J Am Chem Soc* **72** 2547 *1950*, *Beilstein* **14** H 706, 725].

Anthraquinone Blue RXO *[4403-89-8]* **M 445.5.** Purify the dye by salting out an aqueous solution three times with sodium acetate, followed by repeated extraction with EtOH [McGrew & Schneider *J Am Chem Soc* **72** 2547 *1950*]. [*Beilstein* **14** H 706, 725.]

Anthraquinone Green G [Acid Green 25, Alizarin Cyanine Green F, 1,4-bis-(4-methyl-2-sulfophenyl-1-amino)-9,10-anthraquinone di-Na salt] *[4403-90-1]* **M 624.6, m 235-238°, CI 61570, λ_{max} 642nm, pK^{25} >0.** Purify it by salting out three times from an aqueous solution with sodium acetate, followed by repeated extraction with EtOH [McGrew & Schneider *J Am Chem Soc* **72** 2547 *1950*]. It is a green powder that is slightly soluble in Me_2CO, EtOH and pyridine. It is soluble in conc H_2SO_4 to give a blue solution that becomes turquoise in colour on dilution. [Allen et al. *J Org Chem* **7** 63 *1942*, *Beilstein* **14** H 725.]

9,10-Anthraquinone-2,6-disulfonic acid (disodium salt) *[853-68-9]* **M 412.3, m >325°, pK_{Est} ~<0 (for SO_3H).** Crystallise it three times from water, in the dark [Moore et al. *J Chem Soc. Faraday Trans 1* **82** 745 *1986*]. [*Beilstein* **11** IV 673.]

***o*-Arsanilic acid** *[2045-00-3]* **M 216.1, m 153°, pK_1^{22} 3.77 (AsO_3H_2), pK_2^{22} 8.66 (AsO_3H^-).** Crystallise it from water or ethanol/ether. **POISONOUS.** [*Beilstein* **16** I 463.]

***p*-Arsanilic acid** *[98-50-0]* **M 216.1, m 232°, pK_1^{22} 4.05 (AsO_3H_2), pK_2^{22} 8.66 (AsO_3H^-).** Crystallise it from water or ethanol/ether. **POISONOUS.** [*Beilstein* **16** I 466.]

Arsenazo I [3(2-arsonophenylazo)-4,5-dihydroxy-2,7-naphthalenedisulfonic acid di Na salt] *[66019-20-3]* **M 614.3, ε 2.6 x 10^4 at 500nm, pH 8.0, pK_1 0.6(0.8), pK_2 3.52, pK_3 2.97(AsO_3H_2), pK_4 8.20(AsO_3H^-), pK_5 9.98(OH), pK_6 15.0.** A saturated aqueous solution of the free acid is slowly added to an equal volume of conc HCl. The orange precipitate is filtered off, washed with acetonitrile and dried for 1-2 hours at 110° [Fritz & Bradford *Anal Chem* **30** 1021 *1958*]. It is then titrated with NaOH to form the di or tri Na salt as set out below.

Arsenazo III [3,6-bis(2-arsonophenylazo)-4,5-dihydroxy-2,7-naphthalenedisulfonic acid di Na salt] *[62337-00-2]* **M 776.4, pK_1 -2.7, pK_2 -2.7, pK_3 0.6, pK_4 0.8, pK_5 1.6, pK_6 3.4, pK_7 6.27, pK_8 9.05, pK_9 11.98, pK_{10} 15.1.** Contaminants include monoazo derivatives, starting materials for synthesis and by-products. It is partially purified by precipitation of the dye from aqueous alkali on addition of HCl. More thorough purification is achieved by taking a 2g sample in 15-25ml of 5% aqueous NH_3 and filter. Add 10ml HCl (1:1) to the filtrate to precipitate the dye. Repeat the procedure and dissolve the solid dye (0.5g) in 7ml of a 1:1:1 mixture of *n*-propanol/conc NH_3/water at 50°. After cooling, filter the solution and chromatograph the filtrate through a cellulose column using a 3:1:1 mixture of *n*-propanol/conc NH_3/water as eluent. Collect the blue band and evaporate it to 10-15ml below 80°, then add 10ml of conc HCl to precipitate pure Arsenazo III. Wash it with EtOH and dry it in air [Borak et al. *Talanta* **17** 215 *1970*]. The sodium salt is then obtained by dissolving it in the equivalent amount of dilute NaOH and freeze-drying. The purity of the dye can be checked by paper chromatography using M HCl as eluent. It is used for the estimation of Th, U, Zr, Cd and Zn [Michaylova & Yuroukova *Anal Chim Acta* **68** 73 *1974*.]

Benzaldehyde-2-sulfonic acid sodium salt *[1008-72-6]* **M 208.2, m decomposes on heating.** It forms prisms or plates by extracting with boiling EtOH, filtering, evaporating to dryness and recrystallising the Na salt from a small volume of H_2O. The *N-phenylhydrazone sodium salt* recrystallises from H_2O with **m** 174.5°. [Gnehm & Schüle *Justus Liebigs Ann Chem* **299** 363 *1898*, *Beilstein* **11** IV 652.]

Benzeneselenenyl bromide (phenylselenenyl bromide) *[34837-55-3]* **M 236.0, m 58-62°, 60°, 62°, b 107-108°/15mm, 134°/35mm.** Distil it in a vacuum, recrystallise it from petroleum ether, $CHCl_3$ (EtOH free), or Et_2O (cooling mixture) to give dark red or orange crystals. These sublime at 25°/0.001mm [Behaghel et al. *Chem Ber* **65** 815 *1932*, Pitteloud & Petrzilka *Helv Chim Acta* **62** 1319 *1979*]. [*Beilstein* **6** III 1111.] **HIGHLY TOXIC.**

Benzeneselenenyl chloride (benzeneselenyl chloride, phenylselenenyl chloride) *[5707-04-0]* **M 191.5, m 59-60°, 64-65°, b 92°/5mm, 120°/20mm.** Purify it by distillation in a vacuum, and recrystallisation (orange needles) from hexane [Foster *J Am Chem Soc* **55** 822 *1933*, Foster et al. *Rec Trav Chim Pays Bas* **53** 405, 408 *1934*, Behaghel & Seibert *Chem Ber* **66** 714 *1933*]. [*Beilstein* **6** III 1110.] **HIGHLY TOXIC.**

Benzeneseleninic acid *[6996-92-5]* **M 189.1, m 122-124°, pK^{25} 4.70.** Add 10% excess of 15M NH_3 to the solid acid and stir until the solid dissolves, filter, decolorise with charcoal (2x, Norite) and acidify by slow addition of 6M HCl, filter the solid off and wash it with H_2O. Dissolve the acid in the minimum volume of MeOH, and this solution is added dropwise to boiling H_2O until cloudiness appears. At this point add 25% more boiling H_2O, filter hot (decolorise if necessary) and cool rapidly, with scratching, to 0°. After 30 minutes the solid is filtered off and recrystallised as before but with very slow cooling. The colourless needles are filtered off and dried in a vacuum desiccator ($CaCl_2$) before the melting point is measured [McCullough & Gould *J Am Chem Soc* **71** 674 *1949*]. The *HNO_3 complex* has **m** 112°. [*Beilstein* **11** H 422, **11** I 110, **11** III 716.]

Benzeneseleninic anhydride *[17697-12-0]* **M 360.1, m 124-126°, 164-165°, 170-173°.** When the anhydride is recrystallised from *C_6H_6 it has **m** 124-126°, but when this is heated at 140°/1 hour in a vacuum or at 90°/2 hours it has **m** 164-165° and gives a solid **m** 124-126° when then recrystallised from *C_6H_6. Both depress the melting point of the acid $PhSeO_2H$. If the high melting anhydride is dissolved in *C_6H_6 and seeded with the high melting anhydride, the high melting anhydride crystallises out. It readily absorbs H_2O to form the acid ($PhSeO_2H$, **m** 122-124°). Because of this, the commercial anhydride could contain up to 30% of the acid. It is best purified by converting to the HNO_3 complex (**m** 112°) and heating this *in vacuo* at 120°/72 hours to give the anhydride as a white powder **m** 164-165°. *Alternatively*, heat the anhydride *in vacuo* at 120°/72 hours until the IR shows no OH band. [Ayvrey et al. *J Chem Soc* 2089 *1962*, Barton et al. *J Chem Soc, Perkin Trans 1* 567 *1977*, *Beilstein* **11** H 422, **11** I 110, **11** III 716, **11** IV 708.] **TOXIC** solid.

Benzeneselenol (phenylselenol, selenophenol) *[645-96-5]* **M 157.1, b 57-59°/8mm, 71-72°/18mm, 84-86°/25mm, d_4^{20} 1.480, n_D^{20} 1.616.** Dissolve it in aqueous N NaOH, acidify this with conc HCl and extract with Et_2O, dry over $CaCl_2$, filter, evaporate on a steam bath and distil the residue from a Claisen flask or through a short column collecting the middle fraction, and seal immediately in a glass vial, otherwise the colourless liquid becomes yellow. The alkali insoluble materials consist of diphenylselenide (**b** 167°/16mm) and diphenyldiselenide, **m** 63° (from EtOH). **TOXIC**, use rubber gloves. It has a foul odour. [Foster *Org Synth* Coll Vol **III** 771 *1955*, *Beilstein* **6** III 1104, 1110, **6** IV 1777.]

Benzeneselenonic acid (benzeneselenoic acid) *[39254-48-3]* **M 205.1, m 64°, pK^{25} 4.79.** Purify it by dissolving in H_2O and passing through a strong cation exchange resin (H^+ form). Evaporate the effluent under reduced pressure and dry the residue in a high vacuum to give colourless hygroscopic crystals [Dostal et al. *Z Chem* **6** 153 *1966* and IR: Dostál et al. *Chem Ber* **104** 2044 *1971*]. [*Beilstein* **11** H 422, **11** I 111.]

Benzenestibonic acid *[535-46-6]* **M 248.9, m >285°(dec).** It crystallises from acetic acid (needles), or from EtOH/$CHCl_3$ mixture on addition of water. [Schmidt *Justus Liebigs Ann Chem* **542** 288 *1939*, May *J Chem Soc* **101** 1033 *1912*.]

Benzopurpurin 4B {3,3'-[(3,3'-dimethyl[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[4-amino-1-naphthalene-

sulfonic acid] di-Na salt, Direct red 2} *[992-59-6]* **M 724.7, λ_{max} 500nm, CI 23500, pK^{25} <0**. It crystallises from H_2O. It is a biological stain that is violet at pH 1.2 and red at pH 4.0 and is used for detecting Al, Mg, Hg, Au and U. [*Beilstein* **16** H 411, **16** II 224, **16** III 474, **16** IV 601.]

Benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (BOP, Castro's Reagent) *[56602-33-6]* **M 442.29, m >130°(dec), 147-149°(dec).** Dissolve it in CH_2Cl_2, dry ($MgSO_4$), filter, concentrate it under a vacuum, then add dry Et_2O and filter off the first crop. Add CH_2Cl_2 to the filtrate and concentrate again to obtain a second crop. The solid is washed with dry Et_2O and dried in a vacuum. Also recrystallise it from dry Me_2CO/Et_2O and check the purity by NMR. Store it in the dark. [Castro et al. *Synthesis* 751 *1976*, Nguyen et al *J Chem Soc, Perkin Trans I* 1915 *1987*, Coste et al. *Tetrahedron Lett* **36** 4253 *1995*.]

Benzyl Orange [4-(4-benzylaminophenylazo)benzenesulfonic acid potassium salt] *[589-02-6]* **M 405.5, $pK_{Est(1)}$~<0, $pK_{Est(2)}$~3.8.** Crystallise it from H_2O.

Benzyltriphenylphosphonium chloride *[1100-88-5]* **M 388.9, m 280° (sintering), 287-288°.** Wash it with Et_2O and crystallise it from EtOH (six-sided plates). It is *hygroscopic* and forms crystals with one molecule of H_2O. [Michaelis & Soden *Justus Liebigs Ann Chem* **229** 320 *1885*, Kröhnke *Chem Ber* **83** 291 *1950*, *Beilstein* **16** IV 994.]

Biphenyl-2-yl diphenyl phosphate *[132-29-6]* **M 302.4, b 280-290°/9mm, d_{25}^{25} 1.184, n_D^{25} 1.5925.** Distil the ester in a vacuum, then percolate it through an alumina column. Pass the ester through a packed column maintained at 150° to remove residual traces of volatile materials by a counter-current stream of nitrogen at reduced pressure. [Dobry & Keller *J Phys Chem* **61** 1448 *1957*, *Beilstein* **6** III 3295, **6** IV 4585.]

Bis(*p-tert*-butylphenyl)phenyl phosphate *[115-87-7]* **M 438.5, b 281°/5.5mm, d_4^{25} 1.108, n_D^{25} 1.5412.** Purify as for biphenyl-2-yl diphenyl phosphate (above). [*Beilstein* **6** III 1871, **6** IV 3310.]

Bis(2-chlorophenyl) phenyl phosphate *[597-80-8]* **M 395, b 254°/4mm, n_D^{25} 1.5767.** Purify as for biphenyl-2-yl diphenyl phosphate above. [Fox et al. *J Phys Chem* **59** 1097 *1955*, *Beilstein* **6** III 680, **6** IV 807.]

Bis(2-ethylhexyl) 2-ethylhexyl phosphonate *[25103-23-5]* **M 434.6, n_D^{25} 1.4473.** Purify it by stirring a 0.4M solution in *benzene with an equal volume of 6M HCl at *ca* 60° for 8 hours. The *benzene layer is then shaken successively with equal volumes of water (twice), aqueous 5% Na_2CO_3 (three times), and water (eight times), followed by evaporation of the *benzene and distillation of the residue under reduced pressure at room temperature (using a rotating evacuated flask). It should be stored dry and in the dark [Peppard et al. *J Inorg Nucl Chem* **24** 1387 *1962*]. Distil it in a vacuum, then percolate it through an alumina column before finally passing it through a packed column maintained at 150° where residual traces of volatile materials are removed by a counter-current stream of N_2 under reduced pressure [Dobry & Keller *J Phys Chem* **61** 1448 *1957*].

Bis(2-ethylhexyl) phosphoric acid ('diisooctyl' phosphate) *[298-07-7, 27215-10-7]* **M 322.4, m -60°, b 209°/10mm, d_4^{20} 0.965, pK_{Est} ~1.7.** Contaminants of commercial samples include the monoester, polyphosphates, pyrophosphate, 2-ethylhexanol and metal impurities. Dissolve the acid in *n*-hexane to give an 0.8M solution. Wash this with an equal volume of M HNO_3, then with saturated $(NH_4)_2CO_3$ solution, with 3M HNO_3, and twice with water [Petrow & Allen *Anal Chem* **33** 1303 *1961*]. Similarly, the impure sodium salt, after scrubbing with petroleum ether, is acidified with HCl and the free organic acid is extracted into petroleum ether and purified as above [Peppard et al. *J Inorg Nucl Chem* **7** 231 *1958*], or as described by Stewart & Crandall [*J Am Chem Soc* **73** 1377 *1951*]. It can be purified *via* its copper salt [McDowell et al. *J Inorg Nucl Chem* **38** 2127 *1976*]. [*Beilstein* **1** IV 1796.]

2,4-Bis(methylthio)-1,3,2λ^5,4λ^5-dithiadiphosphetane-2,4-dithione (Davy's reagent methyl) *[82737-61-9]* **M 284.4, m 160°.** It crystallises from *C_6H_6 in yellow plates or from hot trichlorobenzene. The low melting point reported in the literature (112° with gradual softening at 68-102°) has been attributed to the presence of elemental sulfur in the crystals. It has a **foul odour** and is a *suspected carcinogen*. [Yousif et al. *Tetrahedron*

40 2663 *1984*, Scott et al. *J Org Chem* **22** 789 *1957*.]

Bismuthiol I (2,5-dimercapto-1,3,4-thiadiazole) potassium salt *[4628-94-8]* **M 226.4, m 275-276°(dec), ~294°(dec), $pK_{Est(1)}$~4.1.** Usually contaminated with disulfide. Purify it by recrystallisation from EtOH. It is a reagent for the detection of Bi, Cu, Pb and Sb. [Najumdar & Chacraborty *Anal Chim Acta* **19** 372 *1958*, Fries *Z Anal Chem* **165** 100, *1959*, *Beilstein* **27** IV 7725.]

Bis[4-(1,1,3,3-tetramethylbutyl)phenyl]phosphate calcium salt (Selectophore) *[40835-97-0]* **M 987.3.** The Ca diester salt is washed with H_2O (x3) and MeOH (x3) alternately and dried in a vacuum oven at 50°. If the Ca salt is contaminated with much Ca salt of the monoester, then it (10g) is converted to the free acid by adding 6N HCl (*ca* 10 volumes) and Et_2O (> 50 volumes) is added to it and stirred vigorously to form the free acids. When no white precipitate remains (*ca* 5 minutes), the Et_2O is separated, washed with H_2O (2 >50 ml) and dried by filtering through a bed of anhydrous Na_2SO_4 (11 x 5 cm) which is then washed with Et_2O (2 >50 ml). Evaporation gives an oil (TLC R_F 0.81 for diester and 0.50 for monoester). The oil is dissolved in *benzene (*ca* 25ml) and extracted with ethane-1,2-diol (25ml, 10x). After ten washings, a small sample of the *benzene layer is washed twice with H_2O to remove the diol and showed that it is pure *bis-[4-(1,1,3,3-tetramethylbutyl)-phenyl]phosphoric acid* by TLC, i.e. no monophosphate. To form the Ca salt, the oil is dissolved in MeOH and to it is added the equivalent amount of $CaCl_2$ together with aqueous NaOH to keep the pH >10. The resulting white precipitate is collected, washed alternately with 3 batches of H_2O and MeOH and dried in a vacuum oven at 50°. [Craggs et al. *J Inorg Nucl Chem* **40** 1483 *1978*, Morton & Chung *Anal Biochem* **157** 345 *1986*.]

2,4-Bis(*p*-tolylthio)-1,3,2λ^5,4λ^5-dithiadiphosphetane-2,4-dithione (Heimgartner's reagent or Davy's reagent *p*-tolyl) *[114234-09-2]* **M 436.6, m 175-176°.** Recrystallise it from toluene (light yellow solid), wash it with Et_2O and dry *in vacuo*. [Jennt & Heimgarter *Helv Chim Acta* **70** 1001 *1987*.]

***N,O*-Bis(trimethylsilyl)acetamide (BSA)** *[10416-59-8]* **M 203.4, b 71-73°/35mm, d_4^{20} 0.836, n_D^{20} 1.4150.** Fractionate it through a spinning band column and collect liquid **b** 71-73°/35mm, and not higher because the main impurity $MeCONHSiMe_3$ distils at **b** 105-107°/35mm. It is used for derivatising alcohols and sugars [Klebe et al. *J Am Chem Soc* **88** 3390 *1966*, see Matsuo et al. *Carbohydr Res* **241** 209 *1993*, Johnson *Carbohydr Res* **237** 313 *1992*]. It is **FLAMMABLE** and **TOXIC**.

Bis(trimethylsilyl)acetylene (BTMSA) *[14630-40-1]* **M 170.4, m 26°, b 134-136°/atm.** Dissolve it in petroleum ether and wash it with ice-cold dilute HCl. The petroleum ether extract is dried ($MgSO_4$), evaporated and fractionated at 760mm. [Walton & Waugh *J Organomet Chem* **37** 45 *1972*, *Beilstein* **4** IV 3950.]

Bis(trimethylsilyl) sulfide (hexamethyldisilathiane) *[3385-94-2]* **M 178.5, b 65-67°/16mm, 162.5-163.5°/750mm, 164°/760mm, d_4^{20} 0.85, n_D^{20} 1.4598.** Dissolve it in petroleum ether (b *ca* 40°), remove the solvent and distil it. Redistil it under atmospheric pressure of dry N_2. It is collected as a colourless liquid which solidifies to a white solid in Dry-ice. On standing for several days it turns yellow possibly due to liberation of sulfur. Store it below 4° under dry N_2. [Eaborn *J Chem Soc* 3077 *1950*, *Beilstein* **4** IV 4033.]

9-Borabicyclo[3.3.1]nonane (9BBN) ***[monomer** 280-64-8] [**dimer** 21205-91-4 or 70658-61-6] [**1:1 coordination compound with tetrahydrofuran** 76422-63-4]* **M 122.0 (monomer), 244.0 (dimer), m 141-143° (monomer), 150-152°, 154-155° (dimer), b 195°/12mm.** It is available as the solid dimer or in tetrahydrofuran solution. The solid is relatively stable and can be purified by distillation in a vacuum (as dimer) and by recrystallisation from tetrahydrofuran (solubility at room temperature is 9.5%, 0.78M), filter off the solid under N_2, wash it with dry pentane and dry it *in vacuo* at *ca* 100°. The solid is a dimer (IR 1567cm^{-1}), stable in air (for *ca* 2 months), and can be heated for 24 hours at 200° in an inert atmosphere without loss of hydride activity. It is a dimer in tetrahydrofuran solution also (IR 1567cm^{-1}). It is sensitive to H_2O and air (O_2) in solution. Its concentration in solution can be determined by reaction with MeOH and measuring the volume of H_2 liberated, or it can be oxidised to *cis*-cyclooctane-1,5-diol (**m** 73.5-74.5°). [IR: Knights & Brown *J Am Chem Soc* **90** 5280 *1968*, Brown et al. *J Am Chem Soc* **96** 7765 *1974*, Brown et al. *J Org Chem* **41** 1778 *1976*, Brown & Chen *J Org*

Chem **46** 3978 *1981*, Fieser & Fieser's *Reagents for Org Synth* **2** 31, **3** 24, **10** 48, **15** 43, **17**, 49.]

Borane pyridine complex *[110-51-0]* **M 92.9, m 8-10°, 10-11°, b 86°/7mm, 100-101°/12mm, d_4^{20} 0.785.** Dissolve it in Et_2O and wash it with H_2O in which it is insoluble. Evaporate the Et_2O and distil the residual oil to gives better than 99.8% purity. Its vapour pressure is less than 0.1mm at room temperature. [Taylor et al. *J Am Chem Soc* **77** 1506 *1955*, *Beilstein* **20** IV 2235.]

Borane triethylamine complex *[1722-26-5]* **M 115.0, b 76°/4mm, 8°/7mm, 100-101°/12mm, d_4^{20} 0.78.** Distil it in a vacuum using a 60cm glass helices-packed column. [Brown et al. *J Am Chem Soc* **64** 325 *1942*, Ashby & Foster *J Am Chem Soc* **84** 3407 *1962*, Matsuura & Tolcura *Tetrahedron Lett* 4703 *1968*, *Beilstein* **4** IV 329.]

Borane trimethylamine complex *[75-22-9]* **M 73.0, m 94-94.5°, b 171°/atm.** It is sublimed using equipment described in Burg and Schlesinger [*J Am Chem Soc* **59** 780 *1937I*]. Its vapour pressure is 86mm at 100°. It forms colourless hexagonal crystals varying from needles to short lumps, which are slightly soluble in H_2O (1.48% at 30°), EtOH (1%), hexane (0.74%), but very soluble in Et_2O, $*C_6H_6$ and AcOH. It is stable at 125°. [Burg & Schlesinger *J Am Chem Soc* **59** 780 *1937*, Brown et al. *J Am Chem Soc* **104** 325 *1942*, *Beilstein* **4** IV 140.]

2-Bromoallyltrimethylsilane *[81790-10-5]* **M 193.2, b 64-66°/10mm, 82-85°/58-60mm, d_4^{25} 1.13.** It is fractionally distilled through an efficient column. It is **flammable.** [Trost & Chan *J Am Chem Soc* **104** 3733 *1982*, Trost & Coppola *J Am Chem Soc* **104** 6879 *1982*.]

2-Bromo-1,3,2-benzodioxaborole *[51901-85-0]* **M 198.8, m 47°, 51-53°, b 76°/9mm.** Keep at 20°/15mm for some time and then fractionally distil. [Gerrard *J Chem Soc* 1529 *1959*, *Beilstein* **6** IV 5612.]

***1R(endo, anti)*-3-Bromocamphor-8-sulfonic acid ammonium salt** *[55870-50-3]* **M 328.2, m 284-285°(dec), $[\alpha]_D^{25}$ +84.8° (c 4, H_2O).** Pass a hot aqueous solution of it through an alumina column to remove water-soluble coloured impurities which remain on the column when the ammonium salt is eluted with hot water. The salt is crystallised from water and is dried over $CaCl_2$ in a desiccator [Craddock & Jones *J Am Chem Soc* **84** 1098 *1962*, Kauffmann *J Prakt Chem* **33** 295 *1966*]. [*Beilstein* **11** H 319, **11** I 77, **11,** II 183, **11** III 595.]

Bromopyrogallol Red. See in " Aromatic Compounds", in this Chapter.

Bromosulfalein (phenoltetrabromophthalein 3',3'-disulfonic acid disodium salt) *[71-67-0]* **M 838.0.** Purify it by TLC on silica Gel G (Merck 250µ particle size) in two solvent systems (BuOH/AcOH/H_2O 30:7.5:12.5 v/v, and BuOH/propionic acid/H_2O 30:20:7.5 v/v). When the solvent reaches a height of ~10cm, the plate is removed, dried in air and developed with NH_3 vapour giving blue-coloured spots. Also, the dye can be chromatographed on MN Silica Gel with *t*-BuOH/H_2O/*n*-BuOH (32:10:5 v/v) as eluent and visualised with a dilute KOH (or NaOH if the Na salt is required) spray. The product corresponding to bromosulfalein is scraped off and eluted with H_2O, filtered and evaporated to dryness in a vacuum. It is then dissolved in H_2O, filtered through Sephadex G-25 and evaporated to dryness. [UV and IR identification: Barbier & DeVeerdt *J Pharm Sci* **57** 819 *1968*, NMR: Kato et al. *Chem Pharm Bull Jpn* **20** 581 *1972*, McGuire *Anal Biochem* **83** 75 *1977*, *Beilstein* **18/9** V 461.]

Bromotrimethylsilane (trimethylbromosilane, trimethylsilyl bromide) *[2857-97-8]* **M 153.1, m -43.5° to -43.2°, b 40.5°/200mm, 77.3°/735mm, 79°/744mm, 79.8-79.9°/754mm, d_4^{20} 1.1805, n_D^{20} 1.422.** Purify it by repeated fractional distillation and store it in sealed ampoules in the dark. [McCusker & Reilly *J Am Chem Soc* **75** 1583 *1953*.] Also fractionate it through a 15-plate column (0.8 x 32cm packed with 1/16in single turn helices of Pt-Ir wire). [Gilliam et al. *J Am Chem Soc* **68** 1161 *1946*, Pray et al. *J Am Chem Soc* **70** 433 *1948*, *Beilstein* **4** IV 4008.]

But-3-enylboronic acid *[379669-72-4]* **M 99.9, m 84-90°, pK_{Est} 8.8.** Recrystallise the acid from toluene and dry it *in vacuo*. [*cf* Letsinger & Skoog *J Org Chem* **18** 895 *1953*.]

Butylboronic acid (1-butanedihydroxyborane) *[4426-47-5]* **M 101.9, m 90-92°, 94-96°, pK_{Est} ~8.8.** Purify the acid by recrystallisation from *C_6H_6/petroleum ether and dry it *in vacuo*. [Corey et al. *J Am Chem Soc* **116** 3151 *1994*, Quallich et al. *J Am Chem Soc* **116** 8515 *1994,* Seerden *Tetrahedron Lett* **35** 4419 *1994*, *Beilstein* **4** IV 4383.]

(±)-*sec*-Butylboronic acid ([*sec*-butyl]-dihydroxyborane) *[88496-88-2]* **M 101.9, m 86-89°, 87-88°, pK_{Est} ~8.8.** Purify the acid by recrystallisation from *C_6H_6/petroleum ether and dry *in vacuo*. [McCusker et al. *J Am Chem Soc* **79** 5179 *1957*, *Beilstein* **4** IV 4386.]

***tert*-Butyldicyclohexylphosphine (dicyclohexyl-*tert*-butylphosphine, Cy_2P^tBu)** *[93634-87-8]* **M 254.4, m ~22-25° , d_4^{25} 1.094, pK_{Est} ~8.7.** This phosphine was prepared by adding *t*-BuLi (18ml, 27.2mmol, 1.5M in pentane) dropwise to a solution of chloro-dicyclohexylphosphine (5.75g, 24.7mmol, [16523-54-9] see above) in THF (20ml) at -78° and the yellow suspension was allowed to warm to ~25° and stirred overnight. The mixture was evaporated to dryness, extracted with pentane (2 x 20ml), filtered through Celite, concentrated to 20ml, cooled to -78° and after 2 hours the *Cy_2P^tBu* crystallised in white crystals (5.6g, 89%) which were filtered off and washed with cold pentane under N_2 or Ar. It is highly air sensitive, flammable and should be stored under N_2 or Ar. It melts at room temperature. The ^{1}H NMR ($CDCl_3$) has peaks at δ: 1.90-1.05 (m, 22H, C_6H_{11}), 1.10 (d, 9H, $C(CH_3)_3$, $^3J_{H\text{-}P}$ = 10.8Hz); the ^{13}C NMR ($CDCl_3$) has peaks at δ: 33.11 (d, *C*Me_3, $^1J_{C\text{-}P}$ = 19.4Hz), 33.61 (d, C_1 C_6H_{11}, $^1J_{C\text{-}P}$ = 16.2Hz), 30.96, 27.82 (2d, C_2 C_6H_{11}, $^2J_{C\text{-}P}$ = 9.7Hz), 30.33 (d, $CH_3)_3$, $^2J_{C\text{-}P}$ = 13.2Hz), 27.69, 27.61 (2s, C_3 C_6H_{11}), 26.41 (s, C_4 C_6H_{11}); and ^{31}P NMR ($CDCl_3$) has a peak at δ 28.58. [Jan et al. *J Organomet Chem* **55** 606 *2000*.]

***tert*-Butyldimethylsilyl chloride (TBDMSCl)** *[18162-48-6]* **M 150.7, m 87-89°, 92.5°, b 125°/760mm.** Fractionally distil it at atmospheric pressure. [Sommer & Tyler *J Am Chem Soc* **76** 1030 *1954*, Corey & Venkateswarlu *J Am Chem Soc* **94** 6190 *1972*, *Beilstein* **4** IV 4076.]

***tert*-Butyldiphenylchlorosilane (TBDPSCl, *tert*-butylchlorodiphenylsilane)** *[58479-61-1]* **M 274.9, b 90°/0.015mm, d_4^{20} 1.057, n_D^{20} 1.568.** Purify it by repeated fractional distillation. It is soluble in DMF and pentane [Hanessian & Lavalee *Can J Chem* **53** 2975 *1975*, Robl et al. *J Med Chem* **34** 2804 *1991*]. [*Beilstein* **4** IV 4076 *for tert-butylchlorodimethylsilane*.]

***n*-Butylphenyl *n*-butylphosphonate** *[36411-99-1]* **M 270.3.** Crystallise it three times from hexane as its compound with uranyl nitrate. See *tri-n-butyl phosphate* below.

***p-tert*-Butylphenyl diphenyl phosphate** *[981-40-8]* **M 382.4, b 261°/6mm, n^{25} 1.5522.** Purify it by vacuum distillation, and percolation through an alumina column, followed by passage through a packed column maintained at 150° to remove residual traces of volatile materials in a counter-current stream of N_2 at reduced pressure [Dobry & Keller *J Phys Chem* **61** 1448 *1957*].

Cacodylic acid (dimethylarsinic acid) *[75-60-5]* **M 138.0, m 195-196°, pK_1^{25} 1.57, pK_2^{25} 6.27 [$Me_2As(O)OH$].** Recrystallise it from warm EtOH (3ml/g) by cooling and filtering. Dry it in a vacuum desiccator over $CaCl_2$. It has also been recrystallised twice from propan-2-ol. [Kilpatrick *J Am Chem Soc* **71** 2608 *1949*, Nichol *J Am Chem Soc* **72** 2367 *1950*, Koller & Hawkridge *J Am Chem Soc* **107** 7412 *1985*, *Beilstein* **4** H 610, **4** I 567, **4** II 993, **4** III 1818, **4** IV 3681.]

Cadion [1-(4-nitrophenyl)-3-(4-phenylazophenyl)-triazene] *[5392-67-6]* **M 346, m 189°(dec).** Commercial cadion is purified by recrystallisation from 95% EtOH and is dried *in vacuo*. It is stable in 0.2 N KOH (in 20% aqueous EtOH) at 25°. It is a sensitive reagent for Cd, and the Cd complex has λ_{max} (EtOH) 475nm. [Chavanne & Geronimi *Anal Chim Acta* **19** 377 *1958*, *Beilstein* **16** III 664.]

(4-Carbamylphenylarsylenedithio)diacetic acid *[531-72-6]* **M 345.1, pK_{Est}~3.5.** Recrystallise it from MeOH or EtOH.

Catecholborane (1,3,2-Benzodioxaborole) *[274-07-7]* **M 119.2, b 50°/50mm, 66°/80mm, 76-77°/100mm, 88°/165mm, d_4^{20} 1.125, n_D^{20} 1.507 (also available as a 1.0M solution in THF or toluene).** It is a moisture-sensitive flammable liquid which is purified by distillation in a vacuum under a N_2 atmosphere and stored under N_2 at 0-4°. It liberates H_2 when added to H_2O or MeOH. A solution in THF, after 25 hours at 25°, has residual hydride of 95% (under N_2) and 80% (under air) [Brown & Gupta *J Am Chem Soc* **97** 5249 *1975*].

Chloramine-T (*N*-chloro-*p*-toluenesulfonamide sodium salt) $3H_2O$ *[7080-50-4]* **M 281.7, m 168-170°(dec).** Recrystallise it from hot water (2ml/g). Dry it in a desiccator over $CaCl_2$ where it loses water. Protect it from sunlight. It is used for the detection of bromate and halogens, and Co, Cr, Fe, Hg, Mn, Ni and Sb ions. [Campbell & Johnson *Chem Rev* **78** 65 *1978*, Bremner *Synthetic Reagents* **6** 9 *1985*, Chattaway *J Chem Soc* **87** 145 I1905, Inglis *J Soc Chem Ind (Lond)* **37** 288 *1918*, *Beilstein* **11** H 107, **11** I 29, **11** II 62, **11** III 300, **2** IV 457.]

Chlorazol Sky Blue FF {6,6'-[(3,3'-dimethoxy[1,1'-biphenyl]-4,4'-diyl)bis(azo)bis(4-amino-5-hydroxy-1,3-naphthylenedisulfonic acid) tetra-Na salt *[2610-05-1]* **M 996.9, m >300°(dec).** Free it from other electrolytes by adding aqueous sodium acetate to a boiling solution of the dye in distilled water. After standing, the salted-out dye is filtered on a Büchner funnel, the process being repeated several times. Finally, the precipitated dye is boiled several times with absolute EtOH to wash out any sodium acetate, then dried (as the sodium salt) at 105°. [McGregor et al. *Trans Faraday Soc* **58** 1045 *1962*, *Beilstein* **16** II 259.]

Chlorodicyclohexylphosphine [Cy_2PCl] *[16523-54-9]* **M 232.7, b 132-138°/3mm, 165°/12mm, 173-174°/17mm, 182-183°/23mm, d_4^{25} 1.054, n_D^{20} 1.533.** Cy_2PCl can be obtained as a colourless oil from cyclohexyldichloro-phosphine and cyclohexylmagnesium chloride, also from dicyclohexyldiethylamino-phosphine and HCl in the presence of NH_4Cl in petroleum ether (b 70-90°) followed by fractional distillation. *Alternatively*, reaction of cyclohexylmagnesium chloride (from 12.6g of Mg and 62g of cyclohexyl chloride) in Et_2O (250ml) and PCl_3 (35g) in Et_2O (300ml) under N_2 followed by fractional distillation gives (22g, 37.2%) of Cy_2PCl. [Issleib & Seidel *Chem Ber* **92** 2681 *1959*, *Beilstein* **16** IV 968.]

Chlorodiphenylphosphine (diphenylphosphinous chloride) *[1079-66-9]* **M 220.6, m 15-16°, b 124-126°/0.6mm, 174°/5mm, 320°/atm, d_4^{20} 1.229, n_D^{20} 1.636.** This air-sensitive, pale yellow **lachrymatory** liquid is purified by careful fractional distillation and discarding the lower boiling fraction which contains the main impurity $PhPCl_2$ (**b** 48-51°/0.7mm), and checking for impurities by NMR. [Weinberg *J Org Chem* **40** 3586 *1975*, Honer et al. *Chem Ber* **94** 2122 *1961*, *Beilstein* **16** IV 969.]

Chlorodi(*o*-tolyl)phosphine *[36042-94-1]* **M 248.7, m 36-37°, b 120-122°/0.03mm, 146-147°/1.1mm.** It is purified by fractional distillation in a vacuum (**b** 179-183°/7mm, 253-257°/15mm) and the distillate solidifies (**m** 36°, also reported is **m** 37°). [Weinberg *J Org Chem.* **40** 3586 *1975*, McEwen et al. *J Am Chem Soc* **100** 7304 *1978*, *Beilstein* **16** H 769, **16** IV 970 *for chlorodi(p-tolyl)phosphine*.]

(Chloromethyl)dimethylvinylsilane *[16709-86-7]* **M 134.7, b 122-126°/atm, d_4^{25} 0.908, n_D^{20} 1.440.** Distil the silane in a vacuum, but if it is suspect then dissolve it in Et_2O, shake it with saturated aqueous NH_4Cl, dry the Et_2O layer (anhydrous Na_2SO_4), filter evaporate and fractionate in a vacuum. [Altamura et al. *J Org Chem* **60** 8403 *1995*.]

Chloromethylphosphonic acid dichloride *[1983-26-2]* **M 167.4, b 50°/0.5mm, 52-53(59)°/2mm, 63-65°/3mm, 78-79°/10mm, 87-88°/15mm, 102-103°/30mm, d_4^{20} 1.638, n_D^{20} 1.4971.** It is fractionally distilled using a short Claisen column and redistilled. The *aniline salt* has **m** 199-201°. The ^{31}P NMR has a single peak at -38±2 ppm from 85% H_3PO_4. [Kinnear & Perren *J Chem Soc* 3437 *1952*, NMR: van Wazer et al. *J Am Chem Soc* **78** 5715 *1956*, McConnell et al. *J Org Chem* **22** 462 *1957*, *Beilstein* **1** III 2593, **1** IV 3068.]

2-Chloro-2-oxo-1,3,2-dioxaphospholane *[6609-64-9]* **M 142.5, m 12-14°, b 89-91°/0.8mm, d_4^{20} 1.549, n_D^{20}**

1.448. It should be distilled under high vacuum as some polymerisation occurs at atmospheric pressure. It has IR bands at 3012, 2933, 1477, 1366, 1325, 1040, 924 and 858 cm^{-1}. It is hydrolysed to $HOCH_2CH_2OPO_3H_2$ in 30 minutes in H_2O at 100° [IR: Cox & Westheimer *J Am Chem Soc* **80** 5441 *1958*]. [*Beilstein* **1** IV 2419.]

2-Chlorophenyl diphenyl phosphate *[115-85-5]* **M 360.7, b 236°/4mm, n_D^{25} 1.5707.** Purify it by vacuum distillation, percolate it through a column of alumina, then pass it through a packed column maintained by a countercurrent stream of N_2 at reduced pressure [Dobry & Keller *J Phys Chem* **61** 1448 *1957*].

Chlorosulfonic (chlorosulfuric) acid *[7790-94-5]* **M 116.5, b 151-152°/750mm, d_4^{20} 1.753, n_D^{25} 1.4929, pK^{25} -5.9 (aqueous H_2SO_4).** Distil it in an all-glass apparatus, taking the fraction boiling at 156-158°. It reacts **EXPLOSIVELY** with water [Cremlyn *Chlorosulfonic acid: A Versatile Reagent*, Royal Society of Chemistry UK, 2002, 308 pp, ISBN 0854044981]. **LACHRYMATORY and CORROSIVE, wear gloves and face shield.**

Chlorotriphenylsilane (triphenylchlorosilane) *[76-86-8]* **M 294.9, m 90-92°, 91-93°, 94-95°, 97-99°, b 156°/1mm, 161°/0.6mm.** Likely impurities are tetraphenylsilane, small amounts of hexaphenyldisiloxane and traces of triphenylsilanol. Purify it by distillation at 2mm, then crystallise it from EtOH-free $CHCl_3$, and from petroleum ether (b 30-60°) or hexane by cooling in a Dry-ice/acetone bath. [Allen & Modena *J Chem Soc* 3671 *1957*, Curran et al. *J Am Chem Soc* **72** 4471 *1950*, Speier & Zimmerman *J Am Chem Soc* **77** 6395 *1955*, Thomas & Rochow *J Am Chem Soc* **79** 1843 *1957, Beilstein* **16** IV 1484.]

Chromeazurol S (Mordant Blue 29) *[1667-99-8]* **M 539.3, λ_{max} 540nm, ε 7.80 x 10^4 (10M HCl), CI 43825, pK_1^{25} <0, pK_2^{25} 2.25, pK_3^{25} 4.88, pK_4^{25} 11.75.** The crude *phenolic triphenylmethanecarboxysulfonic acid triNa salt* (40g) is dissolved in water (250ml) and filtered. Then conc HCl (50ml) is added to the filtrate, with stirring. The precipitate is filtered off, washed with HCl (2M) and dried. It is redissolved in water (250ml), and precipitation is repeated twice more in a water bath at 70°. It is dried under vacuum over solid KOH (first), then P_2O_5 [Martynov et al. *Zh Analyt Khim* **32** 519 *1977*]. It has also been purified by paper chromatography using *n*-butanol, acetic acid and water (7:3:1). First and second spots were extracted. It chelates Al and Be. It is used also for estimating fluoride. [*Beilstein* **11** IV 707.]

Copper (I) thiophenolate *[1192-40-1]* **M 172.7, m *ca* 280°, pK_1^{25} 6.62 (for PhS^-).** The Cu salt can be extracted from a thimble (Soxhlet) with boiling MeOH. It is a green-brown powder that gives a yellow-green solution in pyridine. Wash it with EtOH and dry it in a vacuum. It can be precipitated from a pyridine solution by adding H_2O, collecting the precipitate, washing it with EtOH and drying in a vacuum. [Posner et al. *Synthesis* 662 *1974*, Krebs et al. *Chem Ber* **90** 425 *1957*, *Beilstein* **6** IV 1465.]

Cupferron ammonium salt (*N*-nitroso-*N*-phenylhydroxylamine ammonium salt) *[135-20-6]* **M 155.2, m 150-155°(dec), 162.5-163.5°, 163-164°, pK^{25} 4.16 (free base).** Recrystallise it twice from EtOH after treatment with Norite and finally once with EtOH. The crystals are washed with diethyl ether and air dried, then stored in the dark over solid ammonium carbonate. A standard solution (*ca* 0.05M prepared in air-free H_2O) is prepared daily from this material for analytical work and is essentially 100% pure. [Olsen & Elving *Anal Chem* **26** 1747 *1954*.] It can also be washed with Et_2O, dried and stored as stated. In a sealed, dark container it can be stored for at least 12 months without deterioration. The UV has λ_{max} at 260nm ($CHCl_3$). [Marvel *Org Synth* Coll Vol **I** 177 *1941*, Elving & Olson *J Am Chem Soc* **78** 4206 *1956*, *Beilstein* **16** IV 891.] *Possible* **CARCINOGEN.**

Cupric trifluoromethylsulfonate (copper II triflate) *[34946-82-2]* **M 361.7, pK^{25} <-3.0 (for triflic acid).** Dissolve it in MeCN, add dry Et_2O until cloudy and cool at -20° in a freezer. The light blue precipitate is collected and dried in a vacuum oven at 130°/20mm for 8 hours. It has λ_{max} at 737nm (ε 22.4 M^1cm^{-1}) in AcOH. [Salomon & Kochi *J Am Chem Soc* **95** 330 *1973*]. It has also been dried in a vessel at 0.1Torr by heating with a Fischer burner [Andrist et al. *J Org Chem* **43** 3422 *1978*]. It has been dried at 110-120°/5mm for 1 hour before use and forms a *benzene complex which should be handled in a dry box because it is air sensitive [Kobayashi et al. *Chem Pharm Bull Jpn* **28** 262 *1980*, Salomon & Kochi *J Am Chem Soc* **95** 330 *1973*]. [*Beilstein* **3** IV 34.]

Cuprous (I) bromide dimethylsulfide complex *[54678-23-8]* **M 205.6, m *ca* 135°(dec).** Purify it by recrystallisation in the presence of Me_2S. A solution of the complex (1.02g) in Me_2S (5ml) is slowly diluted with hexane (20ml), and the pure colourless prisms of the complex (0.96g) separate and are collected and dried, **m** 124-129°(dec). The complex is insoluble in hexane, Et_2O, Me_2CO, $CHCl_3$ and CCl_4. It dissolves in DMF and DMSO, but the solution becomes hot and green indicating decomposition. It dissolves in $*C_6H_6$, Et_2O, MeOH and $CHCl_3$ if excess of Me_2S is added and a colourless solution is obtained. [House et al. *J Org Chem* **40** 1460 *1975*.] Prior to use, the complex is dissolved in Me_2S and evaporated to dryness in the weighed reaction flask [Bourgain-Commerçon et al. *J Organomet Chem* **228** 321 *1983*]. If this reagent is to assist in methylations with MeMgBr (e.g. of fullerenes) it is always best to make a fresh preparation. CuBr (25g) is washed with MeOH (4 x 50ml) to remove coloured impurities and dried *in vacuo* for 1 hour. This white green-tinged CuBr is dissolved in Me_2S (60ml, redistilled b 38°, use efficient fume cupboard) and insoluble impurities are filtered off. Hexane (200ml) is added and the precipitated light-sensitive white crystalline complex is filtered off and washed with hexane (5 times) under suction and N_2. It should be dried under a stream of dry N_2, and should not be kept or stored under reduced pressure as it will lose the some of the disulfide ligand and its efficiency. [Wuts *Synth Commun* **11** 139 *1981*, Nakamura et al. *Org Synth* **83** 80, *2006*.]

Cuprous iodide trimethylphosphite *[34836-53-8]* **M 314.5, m 175-177°, 192-193°.** Cuprous iodide dissolves in a $*C_6H_6$ solution containing trimethylphosphite to form the complex. The complex crystallises from $*C_6H_6$ or petroleum ether. [Arbusoff *Chem Ber* **38** 1171 *1905*, Nishizawa *Bull Chem Soc Jpn* **34** 1170, 1177 *1961*.]

Decaborane (14) ($B_{10}H_{14}$) *[17702-41-9]* **M 122.2, m 99.6-99.7°, 99.7-100°, b 100°/19mm, 213°/atm, d_4^{25} 0.94.** Purify decaborane by vacuum sublimation at 80°/0.1mm, followed by crystallisation from methylcyclohexane, CH_2Cl_2, or dry olefin-free-*n*-pentane, the solvent being subsequently removed by storing the crystals in a vacuum desiccator containing $CaCl_2$. It is soluble in H_2O but is slowly decomposed to give H_2. It is soluble in alkali, and on acidification it liberates H_2. **TOXIC.** [Greenwood in *Comprehensive Chemistry (Ed Bailar et al.)* Pergamon Press Vol **1** pp 818-837 *1973*.]

Di-*n*-amyl *n*-amylphosphonate *[6418-56-0]* **M 292.4, b 150-151°/2mm, n_D^{20} 1.4378.** Purify it by three crystallisations of its uranyl nitrate complex from hexane (see *tributyl phosphate*). It extracts Zr^{2+} from NaCl solutions.

Di-*n*-butyl boron triflate (di-*n*-butylboryl trifluoromethanesulfonate) *[60669-69-4]* **M 274.1, b 37°/0.12mm, 60°/2mm, pK^{25} <–3.0 (for triflic acid).** Distil it in a vacuum under argon and store it under argon. It should be used within 2 weeks of purchase or after redistillation. Use a short path distillation system. It has IR bands in CCl_4 with ν_{max} at 1405, 1380, 1320, 1200 and 1550cm^{-1}, and ^{13}C NMR ($CDCl_3$) with δ at 118.1, 25.1, 21.5 and 13.6. [Gage & Evans *Org Synth* **68** 83 *1990*, Evans et al. *J Am Chem Soc* **103**, 3099 *1981*.] **TOXIC**

Di-*n*-butyl *n*-butylphosphonate *[78-46-6]* **M 250.3, b 150-151°/10mm, 160-162°/20mm, n^{25} 1.4302.** Purify by three recrystallisations of its compound with uranyl nitrate, from hexane. For method, see *tributyl phosphate*.

Di-*n*-butyl cyclohexylphosphonate *[1085-92-3]* **M 245.4.** The compound with uranyl nitrate is recrystallised three times from hexane. For method see *tributyl phosphate*.

Di-*tert*-butyl dichlorosilane ($DTBCl_2$) *[18395-90-9]* **M 213.2, m -15°, b 190°/729mm, 195-197°/atm, d_4^{20} 1.01.** Purify it by fractional distillation. It is a colourless liquid with a pleasant odour and does not fume in moist air, but does not titrate quantitatively with excess of dilute alkali. [Tyler et al. *J Am Chem Soc* **70** 2877 *1948*.]

Di-*tert*-butylphosphine *[819-19-2]* **M 146.2, b 34-35°/2mm, 38-40°/13mm, d_4^{25} 0.951, pK_{Est} ~8.7.** It is prepared by reaction of *tert*-butylmagnesium bromide with PCl_3 in the presence of $LiAlH_4$, and purified by distillation in a vacuum. *Alternatively*, the intermediate *di*-tert-*butylchlorophosphine* [13716-10-4] is reduced separately and the product is purified by fractional distillation *in vacuo*. [Hoffmann & Schellenbeck *Chem Ber*

99 1134 *1966*, Hoffmann & Schellenbeck *Chem Ber* **100** 692 *1967*, Crofts et al. *J Chem Soc C* 331 *1970*.]

Di-*tert*-butyl silyl bis(trifluoromethanesulfonate) *[85272-31-7]* **M 440.5, b 73.5-74.5°/0.35mm, d_4^{20} 1.36 (see pK for triflic acid).** Purify it by fractional distillation at high vacuum. It is a pale yellow liquid that should be stored under argon. It is less reactive than the diisopropyl analogue. The presence of the intermediate monochloro compound can be detected by ^{1}H NMR, ($CHCl_3$): *tert*-$Bu_2Si(OTf)_2$ [δ 1.25s], but impurities have δ 1.12s for *tert*-$Bu_2Si(H)OTf$ and δ 1.19s for *tert*-$Bu_2HSi(Cl)OTf$. [Deslongchamps *Tetrahedron Lett* **23** 4871 *1982*, Deslongchamps *Aldrichimica Acta* **17** 72 *1984*.] **TOXIC.**

2,6-Dichlorophenol-indophenol sodium salt ($2H_2O$) *[620-45-1]* **M 326.1, ε 2.1 x 10^4 at 600nm and pH 8, pK^{30} 5.7 (oxidised form), pK_1^{30} 7.0, pK_2^{30} 10.1 (reduced form).** Dissolve it in 0.001M phosphate buffer, pH 7.5 (alternatively, about 2g of the dye is dissolved in 80ml of M HCl), and extracted into diethyl ether. The extract is washed with water, extracted with aqueous 2% $NaHCO_3$, and the sodium salt of the dye is precipitated by adding NaCl (30g/100ml of $NaHCO_3$ solution), then filtered off, washed with dilute NaCl solution and dried. It has λ_{max} at 605nm. [Hiromi et al. *Anal Biochem* **101** 421 *1980*.] The *acetate* [24857-20-3] **M 310.1** has **m** 101-103° (from Et_2O/petroleum ether) and 99.5-100.5° (from Et_2O). [*Beilstein* **13** IV 1078-1079.]

Dicyclopentylphosphine *[39864-68-1]* **M 170.2, b 76-78°/0.8mm, d_4^{25} 0.933, pK_{Est} ~4.5.** Purify dicyclopentylphosphine by distillation in a vacuum in a stream of N_2 or Ar as it is air sensitive and must be stored in an inert atmosphere. [*cf* Neidergall *Chem Ber* **95** 64 *1962*, *Beilstein* **16** IV 947 *for dicyclohexylphosphine*.]

***O,O*-Diethyl-*S*-2-diethylaminoethyl phosphorothiolate** *[78-53-5]* **M 269.3, m 98-99°.** Recrystallise it from isopropanol/diethyl ether. [Ailman & Magee in *Organo Phosphorus Compound* (Kosolapoff & Maier eds) Wiley Vol **7** pp 487-871 *1976*.]

Diethylmethylsilane *[760-32-7]* **M 102.3, b 78.4°/760mm, 77.2-77.6°/atm, d_4^{20} 0.71.** Fractionally distil it through a *ca* 20-plate column, and the fraction boiling within a range of less than 0.5° is collected. It is a **flammable irritating** liquid. [Price *J Am Chem Soc* **69** 2600 *1947*, *Beilstein* **4** III 1847.]

***N,N*-Diethyltrimethylsilylamine** *[996-50-9]* **M 145.3, b 33°/26mm, 126.8-127.1°/738mm, 126.1-126.4°, d_4^{20} 0.763, n_D^{20} 1.411.** Fractionate it through a 2ft vacuum-jacketed column containing Helipak packing with a reflux ratio of 10:1. [Sauer & Hasek *J Am Chem Soc* **68** 241 *1946*, Langer et al. *J Org Chem* **23** 50 *1958*, Rühlmann *J Prakt Chem* **9** 315 *1959*, *Beilstein* **4** IV 4010.]

Diethyl trimethylsilyl phosphite *[13716-45-5]* **M 210.3, b 61°/10mm, 66°/15mm, d_4^{20} 0.9476, n_D^{20} 1.4113.** Fractionate it under reduced pressure and has ^{31}PMR: δ_P -128ppm relative to H_3PO_4. [Sekine et al. *J Org Chem* **46 2**097 *1981*, Chernyshev et al. *J Gen Chem USSR (Engl Transl)* **45** 231 *1975*.]

Dihexadecyl phosphate (DHP) *[2197-63-9]* **M 546.9, m 75°, pK_{Est} ~1.2.** Recrystallise it from MeOH. Solutions of DHP were made in $CHCl_3$ or CH_2Cl_2 for making vesicles. It has been used for making surfactant vesicles in studies of the viscosity-dependent variations of the fluorescence yield ϕ_F and the polarity induced shift of the emission band maximum $\lambda_{F(max)}$ of a derivative of a [*p*-(dialkylamino)benzylidene]malononitrile [74677-08-0] fluorescence probe. [Lukac *J Am Chem Soc* **106** 4387 *1984*]. [*Beilstein* **1** IV 1880.]

1,2-Dihydroxybenzene-3,5-disulfonic acid, di-Na salt (TIRON) *[149-45-1]* **M 332.2, ε 6.9 x 10^4 at 260nm, pH 10.8, pK_1 and pK_2 <2 (for SO_3^-), pK_3 7.7, pK_4 12.6 (for OHs of disulfonate dianion).** Recrystallise it from water [Hamaguchi et al. *Anal Chim Acta* **9** 563 *1962*]. It is an indicator colour reagent for Fe, Mn, Ti and Mo ions and complexes with Al, Cd, Co, Co, Fe (III), Mn, Pd, UO_2^{2+}, VO^{2+} and Zn. [*Beilstein* **11** IV 630.]

(±)-Diisooctyl phenylphosphonate (bis[2-ethylhexyl] phenylphosphonate) *[49637-59-4]* **M 378.5, b 204-207°/4mm, d_4^{20} 0.970, n_D^{25} 1.4780.** Distil it in a vacuum, percolate it through a column of alumina, then pass it through a packed column maintained at 150° to remove residual traces of volatile materials in a countercurrent

stream of N_2 under reduced pressure [Dobry & Keller *J Phys Chem* **61** 1448 *1957*]. [*Beilstein* **16** III 884.]

Diisopropyl chlorosilane (chlorodiisopropylsilane) *[2227-29-4]* **M 150.7, b 59°/8mm, 80°/10mm, 200°/738mm, d_4^{20} 0.9008, n_D^{20} 1.4518.** Impurities can be readily detected by ^{1}H NMR spectroscopy. Purify it by fractional distillation [Gilman & Clark *J Am Chem Soc* **69** 1499 *1947*, Allen et al. *J Chem Soc* 3668 *1957*].

Dilongifolyl borane *[77882-24-7]* **M 422.6, m 169-172°.** Wash it with dry Et_2O and dry it in a vacuum under N_2. It has **m** 160-161° in a sealed evacuated capillary. It is sparingly soluble in pentane, tetrahydrofuran, carbon tetrachloride, dichloromethane, and chloroform, but the suspended material is capable of causing asymmetric hydroboration. Disappearance of solid indicates that the reaction has proceeded. [Jadhav & Brown *J Org Chem* **46** 2988 *1981*.]

Dimethyldichlorosilane *[75-78-5]* **M 129.1, m -75.5°, b 68.5-68.7°/750mm, 70.5°/760mm, d_4^{20} 1.0885, n_D^{20} 1.4108.** Other impurities are chlorinated silanes and methylsilanes. Fractionate it through a 3/8in diameter 7ft Stedman column rated at 100 theoretical plates at almost total reflux. See purification of $MeSiCl_2$. Solutions in heptane, 1,1,1-trichloroethane or 1-chloronaphthalene are used for the silanization of glassware and pipettes. [Sauer & Hadsell *J Am Chem Soc* **70** 3590 *1948, Beilstein* **4** IV 4110.]

2,6-Dimethyl-1,10-phenanthrolinedisulfonic acid, di-Na salt (H_2O) (bathocuproine-disulfonic acid di-Na salt) *[52698-84-7]* **M 564.5, m ~300°, pK_{Est}~0 (for free acid).** Inorganic salts and some coloured species can be removed by dissolving the crude material in the minimum volume of water and precipitating by adding EtOH. The purified reagent can be obtained by careful evaporation of the filtrate. Recrystallise it from EtOH and dry it in a vacuum at room temperature in the dark. [Lorenzo et al. *J Electroanalyt Chem* **356** 43 *1993*, Watkins et al. *Microchem J* **16** 14 *1971*.]

Dimethylphenylsilyl chloride (DMPSCl, chlorodimethylphenylsilane, phenyl dimethyl chlorosilane) *[768-33-2]* **M 170.7, b 79°/15mm, 85-87°/32mm, 196°/760mm, d_4^{20} 1.017, n_D^{20} 1.509.** Fractionate it through a 1.5 x 18inch column packed with stainless steel helices, or a spinning band column. [Daudt & Hyde *J Am Chem Soc* **74** 386 *1952*, Lewis et al. *J Am Chem Soc* **70** 1115 *1948*, Eaborn *J Chem Soc* 494 *1953*.] It is used for standardising MeLi or MeMgBr that form Me_3PhSi which is estimated by GC. [Maienthal et al. *J Am Chem Soc* **76** 6392 *1954*, House & Respess *J Organomet Chem* **4** 95 *1965*, *Beilstein* **16** IV 1475.] **TOXIC** and **MOISTURE SENSITIVE**.

Dimethyl thiophosphonate (dimethyl hydrogen phosphonothiolate) *[5930-72-3]* **M 126.1, b 53-53.5°/16.5mm, 56-59°/9mm, 59°/16mm, d_4^{25} 1.1892, n_D^{20} 1.4768.** Fractionally distil the ester in a stream of dry N_2 or Ar at as high a vacuum as possible. Store in a sealed ampoule under Ar as it has a foul odour. The IR (film) has ν_{max} at ~800 cm^{-1} (12.6 μ, P-S). [IR: McIvor et al. *Canad J Chem* **34** 1611 *1956*, McIvor et al. *Canad J Chem* **36** 820, 1818 *1958*, Tongcharoensirikul et al. *J Org Chem* **69** 2322 *2004*, *Beilstein* **1** IV 1258.]

Dioctyl phenylphosphonate *[1754-47-8]* **M 378.8, b 207°/4mm, d_4^{20} 1.485, n^{25} 1.4780.** Purify it as described for diisooctyl phenylphosphonate and distil under high vacuum. [*Beilstein* **16** IV 1069.]

(1,3-Dioxalan-2-ylmethyl)triphenylphosphonium bromide *[52509-14-5]* **M 429.3, m 191.5-193°, 193-195°.** Wash the crystals with Et_2O, dry them in a vacuum and recrystallise them from CH_2Cl_2/dry Et_2O to give prisms with **m** 172-174°, which is raised to 191.5-193° on drying at 56°/0.5mm. [Cresp et al. *J Chem Soc, Perkin Trans 1* 37 *1974*.]

Diphenyldiselenide *[1666-13-3]* **M 312.1, m 62-64.** Crystallise it twice from hexane [Kice & Purkiss *J Org Chem* **52** 3448 *1987*]. [*Beilstein* **6** IV 1781.]

Diphenyl hydrogen phosphate (diphenyl phosphate) *[838-85-7]* **M 250.2, m 99.5°, pK^{20} 0.26.** Crystallise it from $CHCl_3$/petroleum ether. [Cherbuliez in *Organo Phosphorus Compounds* (Kosolapoff & Maier eds) Wiley Vol **6** pp 211-577 *1973*, *Beilstein* **6** IV 714.]

4,7-Diphenyl-1,10-phenanthrolinedisulfonic acid, di-Na salt $3H_2O$ (bathophenanthroline-disulfonic acid di-Na salt) *[52746-49-3]* **M 590.6, m 300°, pK$_{Est}$~0 (for free acid).** Dissolve crude sample in the minimum volume of water and add EtOH to precipitate the contaminants. Carefully evaporate the filtrate to obtain pure material. It forms a dark red complex with Fe^{2+} with λ_{max} 535nm (ε 2.23 x 10^4mol^{-1} cm^{-1}) [Imasaka et al. *Anal Chim Acta* **115** 407 *1980*]. It is prepared by sulfonating bathophenanthroline with $ClSO_3H$: to 100g of bathophenanthroline is added 0.5ml of Fe free $ClSO_3H$ and heated over a flame for 30 seconds (**CARE**). Cool and carefully add 10ml of pure distilled H_2O and warm on a water bath with stirring till all solid dissolves. A stock solution is made by diluting 3ml of this reagent to 100ml with 45% aqueous NaOAc, filter off the solid and store in a dark bottle. In this way it is stable for several months. [Landers & Bennie *Am J Clinical Pathology* **29** 590 *1958*.]

Diphenylphosphinic acid *[1707-03-5]* **M 218.2, m 194-195°, pK^{20} 1.72.** Recrystallise it from 95% EtOH and dry it under vacuum at room temperature. [see Kosolapoff *Organophosphorus Compounds* J Wiley, NY, *1950*, Kosolapoff and Maier *Organic Phosphorus Compounds* Wiley-Interscience, NY, *1972-1976*, *Beilstein* **16** IV 1036.]

Diphenyl phosphorazidate (DPPA, diphenyl phosphoryl azide, phosphoric acid diphenyl ester azide) *[26386-88-9]* **M 275.2, b 134-136°/0.2mm, 137°/0.17mm, d $_4^{25}$ 1.277, n $_D^{20}$ 1.551.** This azide and nitrene source is prepared by stirring a mixture of diphenyl phosphorochloridate (56.8g, 210mmol, freshly distilled at 165-168°/5mm, see [2524-64-3]), sodium azide (16.3g, 250mmol) and anhydrous Me_2CO (300ml, dried over K_2CO_3 and freshly distilled) in a dry atmosphere at 20-25° for 21 hours. The ***lachrymatory*** mixture is filtered in a fume cupboard, and the filtrate is concentrated in vacuum. The residue is purified by distillation through a short Vigreux column keeping the bath temperature below 200° to avoid decomposition of the *azidate*, and collecting the fraction with b 134-136°/0.2mm (49-52g, 84-89%). It is a colourless non-explosive oil which can be stored for long periods if it is protected from moisture and light. It has IR (neat) with ν_{max} at 3060 (w, C-H), 2170 (s, $-N_3$), 1590 (m), 1490 (s, arene C=C), 1270 (m, P=O) and 960 (s, P-O-aryl) cm^{-1}; and the ^{1}H NMR ($CDCl_3$) has δ at 7.0-7.3 (br s, aryl-H). [Shioiri & Yamada *Org Synth* Coll Vol **VII** 206 *1990*.]
It is a useful activating agent and a versatile reagent in organic synthesis (see references cited in *Org Synth* Coll Vol **VII** 206 *1990* above). It is commercially available on a 100-200 mesh, 1% cross-linked polydivinylbenzene support and bound (*via para* linkage) through one of its phenyl rings (PS-DPPA, 1.0-1.5mmol/g N_3 loading).

Diphenyl phosphoro chloridate (diphenyl phosphoryl chloride) *[2524-64-3]* **M 268.6, b 141°/1mm, 194°/13mm, 314-316/272mm, d $_4^{30}$ 1.2960, n $_D^{35}$1.5490.** Fractionally distil it in a good vacuum; better use a spinning band column. [Walsh *J Am Chem Soc* **81** 3023 *1959*, IR: Bellamy & Beecher *J Chem Soc* 475 *1952*, *Beilstein* **6** IV 737.]

Diphenylsilane *[775-12-2]* **M 184.3, b 75-76°/0.5mm, 113-114°/9mm, 124-126°/11mm, 134-135°/16mm, d $_4^{20}$ 1.0027, n $_D^{20}$ 1.5802.** Dissolve it in Et_2O, mix slowly with ice-cold 10% AcOH. The Et_2O layer is then shaken with H_2O until the washings are neutral to litmus. Dry over Na_2SO_4, evaporate the Et_2O and distil the residual oil under reduced pressure using a Claisen flask with the take-off head modified into a short column. Ph_2SiH_2 boils at 257°/760mm, but it cannot be distilled at this temperature because exposure to air leads to flashing, decomposition and formation of silica. It is a colourless, odourless oil, miscible with organic solvents but not H_2O. A possible impurity is Ph_3SiH which has **m** 43-45° and would be found in the residue. [West & Rochow *J Org Chem* **18** 303 *1953*, Benkhesser et al. *J Am Chem Soc* **74** 648 *1952*, Gilman & Zuech *J Am Chem Soc* **81** 5925 *1959*, *Beilstein* **16** IV 1366.]

Diphenylsilanediol *[947-42-2]* **M 216.3, m 148°(dec).** Recrystallise it from $CHCl_3$/methyl ethyl ketone. [*Beilstein* **16** IV 1523.]

Diphenyl *p*-tolyl phosphate *[26444-49-5]* **M 340.3, m 18-29°, b 156-158°/0.002mm, n_D^{25} 1.5758.** Distil it in a vacuum, then percolate it through a column of alumina. Finally, pass it through a packed column maintained at 150° to remove traces of volatile impurities in a countercurrent stream of nitrogen under reduced pressure. [Dobry & Keller *J Phys Chem* **61** 1448 *1947*, *Beilstein* **6** IV 2130.]

Disodium 4,5(1,8)-dihydroxynaphthalene-2,7(3,6)-disulfonate $2H_2O$ (Chromotropic acid di-Na salt) *[5808-22-0]* **M 400.3, m >300°, pK_1 0.61(SO_3^-), pK_2 0.7(SO_3^-), pK_3 5.45(OH), pK_4 15.5(OH).** Recrystallise it from H_2O or H_2O by adding EtOH. It complexes with Ag, ClO_3^-, Cr, Hg, NO_2^-, NO_3^- and Ti. [*Beilstein* **11** H 72, **11** I 307, **11** II 174, **11** III 174, **11** IV 576.]

Disodium ethylenebis(dithiocarbamate) (Nabam) *[142-59-6]* **M 436.5, pK_{Est} ~3.0.** It crystallises (as *hexahydrate*) from aqueous ethanol. It is a skin irritant. [*Beilstein* **4** III 149, **4** IV 234.]

Disodium-β-glycerophosphate *[819-83-0 (4H_2O), 13408-09-8 (5H_2O)]* **M 216.0, m 102-104°, pK_2^{25} 6.66 (free acid).** Crystallise it from water. [Attwood et al. *Biochem J* **253** 389 *1988*, *Beilstein* **1** IV 2766.]

Disodium naphthalene-1,5-disulfonate *[1655-29-4]* **M 332.3, pK_{Est} ~0.** Recrystallise it from aqueous acetone. It darkens at high temperatures. [Okahata et al. *J Am Chem Soc* **108** 2863 *1986*, *Beilstein* **11** IV 561.]

Disodium 4-nitrophenylphosphate ($6H_2O$) *[4264-83-9]* **M 371.1.** Dissolve it in hot aqueous MeOH, filter and precipitate it by adding Me_2CO. Wash the solid with Me_2CO and repeat the purification. Aqueous MeOH and Et_2O can also be used as solvents. The white fibrous crystals contain less than 1% of free 4-nitrophenol [assay: Axelrod *J Biol Chem* **167** 57 *1947*]. [*Beilstein* **6** IV 1327.]

Disodium phenylphosphate ($2H_2O$) *[3279-54-7, 66778-08-3 (2H_2O)]* **M 254.1, pK_1^{25} 1.46, pK_2^{25} 6.29 [for $PhPO(OH)_2$].** Dissolve it in a minimum amount of methanol, filtering off any insoluble residue of inorganic phosphate, then precipitate it by adding an equal volume of Et_2O. Wash the solid with Et_2O and dry it in a vacuum [Tsuboi *Biochim Biophys Acta* **8** 173 *1952*]. [*Beilstein* **6** IV 708.]

Di-*p*-tolyl phenylphosphonate *[94548-75-1]* **M 388.3, n_D^{25} 1.5758.** Purify as described under diisooctyl phenylphosphonate.

1,3-Divinyl-1,1,3,3-tetramethyldisiloxane *[2627-95-4]* **M 186.4, m -99.7°, b 128-129°/atm, 139°/760mm, d_4^{20} 0.811, n_D^{20} 1.4122.** Dissolve it in Et_2O, wash it with H_2O, dry it over $CaCl_2$, evaporate the solvent and distil the residue. It is an **IRRITANT**. [Kantor et al. *J Am Chem Soc* **77** 1685 *1955*, Bazant & Matousek *Col Czech Chem Comm* **24** 3758 *1959*, *Beilstein* **4** IV 4080.]

Eriochrome Black T [3-hydroxy-7-nitro-4-(1-hydroxy-2-naphthylazo)naphthalene-1-sulfonic acid Na salt] *[1787-61-7]* **M 416.4. $A_{1cm}^{\%}(\lambda_{max})$ 656(620nm) at pH 10, using the dimethylammonium salt, pK_2^{25} 5.81, pK_3^{25} 11.55.** The sodium salt (200g) is converted to the free acid by stirring with 500ml of 1.5M HCl, and, after several minutes, the slurry is filtered on a sintered-glass funnel. The process is repeated and the material is air dried after washing with acid. It is then extracted with *benzene for 12 hours in a Soxhlet extractor, the *benzene solution is evaporated and the residue is air dried. A further desalting with 1.5M HCl (1L) is followed by crystallisation from dimethylformamide (in which it is very soluble) by forming a saturated solution at the boiling point, and allowing to cool slowly. The crystalline dimethylammonium salt so obtained is washed with *benzene and treated repeatedly with dilute HCl to give the insoluble *free acid* which, after air drying, is dissolved in alcohol, filtered and evaporated. The final material is air dried, then dried in a vacuum desiccator over $Mg(ClO_4)_2$. The purified acid is converted to the dimethylammonium salt with Me_2NH. [Diehl & Lindstrom *Anal Chem* **31** 414 *1959*]. It is an indicator in the complexometry of alkaline earth metals. [*Beilstein* **16** IV 429.]

Eriochrome Blue Black B (Mordant Black, 3, 3-hydroxy-4-(1-hydroxy-2-naphthylazo)-naphthalene-1-

sulfonic acid Na salt] *[3564-14-5]* **M 416.4, pK $_2^{25}$ 7.0, pK $_3^{25}$ 13.5.** Free it from metallic impurities by three precipitations from aqueous solution by addition of HCl. The precipitated dye is dried at 60° under vacuum and converted into the Na salt with the calculated amount of alkali. It is an indicator in the complexometry of Al, Fe and Zr. [*Beilstein* **16** III 319.]

Eriochrome Blue Black R (Palatine Chrome Black 6BN, Mordant Black 17, 3-hydroxy-4-(2-hydroxy-1-naphthylazo)naphthalene-1-sulfonic acid Na salt] *[2538-85-4]* **M 416.4, pK $_2^{25}$ 7.0, pK $_3^{25}$ 13.5.** Free it from metallic impurities by three precipitations from aqueous solution by addition of HCl. The precipitated dye is dried at 60° under vacuum and converted into the Na salt with the calculated amount of alkali. It is an indicator in the complexometry of Al, Fe and Zr. [*Beilstein* **16** H 297, **16** IV 428.]

Ethoxycarbonylmethylene triphenylphosphonium bromide *[1530-45-6]* **M 429.3, m 155-155.5°, 158°(dec).** Wash it with petroleum ether (b 40-50°) and recrystallise it from $CHCl_3$/Et_2O and dry it in a high vacuum at 65°. [Isler et al. *Helv Chim Acta* **40** 1242 *1957*, Wittig & Haag *Chem Ber* **88** 1654, 1664 *1955*.]

(Ethoxycarbonylmethylene)triphenylphosphorane [ethyl (triphenylphosphoranylidene)-acetate] *[1099-45-2]* **M 348.4, m 116-117°, 128-130°.** Crystallise it by dissolving it in AcOH and adding petroleum ether (b 40-50°) to give colourless plates. Its UV has λ_{max} ($A^{1\%}_{1mm}$) at 222nm (865) and 268nm (116) [Isler et al. *Helv Chim Acta* **40** 1242 *1957*, *Beilstein* **16** IV 977.]

Ethylarsonic acid *[507-32-4]* **M 154.0, m 94-95°, 99.5°, pK$_1$ 4.72 (As(OH)O$^-$), pK$_2$ 8.00 [AsO_2^{2-}].** Crystallise it from ethanol. Also it dissolves in excess EtOH, filter off the insoluble matter (salts?), evaporate the filtrate to dryness and recrystallise the residue from small volumes of EtOH or H_2O. [Quick & Adams *J Am Chem Soc* **44** 805 *1922*, Banks et al. *J Am Chem Soc* **69** 927 *1947*, *Beilstein* **4** H 614, **4** II 997, **4** III 1823, **4** IV 3682.]

Ethyl Orange (sodium 4,4'-diethylaminophenylazobenzenesulfonate) *[62758-12-7]* **M 355.4, pK$_{Est}$ ~ 3.8.** Recrystallise it twice from water. [*Beilstein* **16** IV 511.]

Ethyl trimethylsilylacetate *[4071-88-9]* **M 160.3, b 75.5°/42mm, 157°/730mm, d $_4^{20}$ 0.8762, n $_D^{20}$ 1.4149.** Purify it by distilling *ca* 10g of reagent through a 15cm, Vigreux column and then redistilling it through a 21cm glass helices-packed column [Hauze & Hauser *J Am Chem Soc* **75** 994 *1953*]. *Alternatively*, dissolve it in Et_2O, wash with H_2O, dilute Na_2CO_3, dry over Na_2CO_3, evaporate Et_2O, and distil it through a column of 15 theoretical plates. [Gold et al. *J Am Chem Soc* **70** 2874 *1948*, *Beilstein* **4** IV 3974.]

Ethyl 3-(trimethylsilyl)propionate *[17728-88-0]* **M 174.3, b 93°/40mm, 178°-180°/atm, d $_4^{20}$ 0.8763, n $_D^{20}$ 1.4198.** Dissolve it in Et_2O, wash this with H_2O, dilute Na_2CO_3, dry (Na_2SO_4), evaporate Et_2O and fractionally distil. [Sommer & Marans *J Am Chem Soc* **72** 1935 *1950*, *Beilstein* **4** IV 3975.]

Ethyl triphenylphosphonium bromide *[1530-32-1]* **M 371.3, m 203-205°.** Recrystallise it from H_2O and dry it in high vacuum at 100°. Its IR has bands at 1449, 1431 and 997cm^{-1}. [Wittig & Wittenberg *Justus Liebigs Ann Chem* **606** 1 *1957*, Bergmann & Dusza *J Org Chem* **23** 1245 *1958, Beilstein* **16** IV 982.]

Ethynyl trimethylsilane *[1066-54-2]* **M 98.2, b 53°/atm, 52.5°/atm, d $_4^{20}$ 0.71, n $_D^{20}$ 1.3871.** Distil it through an efficient column. The IR has bands at ν_{max} 2041 (C≡C) and 3289 (≡C-H) cm^{-1}. [Kröhnke & Goss *Chem Ber* **92** 30 *1959*, *Beilstein* **4** IV 3937.]

Fluorotrimethylsilane (trimethylsilyl fluoride, TMSF) *[420-56-4]* **M 92.2, m -74°, b 16°/760mm, 19°/730mm, d^0 0.793.** It is a **FLAMMABLE** gas which is purified by fractional distillation through a column at low temperature and with the exclusion of air. Preferably work in a vacuum line. [Booth & Suttle *J Am Chem Soc* **68** 2658 *1946*, Reid & Wilkins *J Chem Soc* 4029 *1955*, *Beilstein* **4** IV 4007.]

Hexaethyldisiloxane *[924-49-0]* **M 246.5, b 114-115°/16mm, 235.5°/760mm, d_4^{20} 0.8443, n_D^{20} 1.4330.** Distil in a vacuum, but it can be distilled at atmospheric pressure without decomposition. It is characterised by completely dissolving in conc H_2SO_4. [Eaborn *J Chem Soc* 3077 *1950*, *Beilstein* **4** IV 4055.]

2,2,4,4,6,6-Hexamethylcyclotrisiloxane *[1009-93-4]* **M 219.5, m -10°, b 81-82°/19mm, 111-112°/85mm, 188°/756mm, d_4^{20} 0.9196, n_D^{20} 1.448.** Purify it by fractional distillation at atmospheric pressure until the temperature reaches 200°. It is *moisture sensitive*. The residue in the flask is mostly octamethylcyclotetrasilazane. [Brewer & Haber *J Am Chem Soc* **70** 3888 *1948*, *Beilstein* **4** III 1887.]

Hexamethyldisilane *[1450-14-2]* **M 164.4, m 9-12°, b 113.1°/750mm, d_4^{20} 0.7272, n_D^{20} 1.4229.** The most likely impurity is trimethylchlorosilane (*cf* boiling point). Wash it with H_2O, cold conc H_2SO_4, H_2O again, then aqueous $NaHCO_3$, dry over $CaSO_4$ and fractionate at atmospheric pressure. [Brown & Fowles *J Chem Soc* 2811 *1958*.] A grossly impure sample (25% impurities) was purified by repeated spinning band distillation. This lowered the impurity level to 500 ppm. The main impurity was identified as 1-hydroxypentamethyldisilane. [*Beilstein* **4** IV 4277.]

Hexamethyldisilazane [HMDS, $(Me_3Si)_2NH$) *[999-97-3]* **M 161.4, b 125-125.6°/atm, 126°/760mm, d_4^{20} 0.7747, n_D^{20} 1.407.** A possible impurity is Me_3SiCl. Wash it well with petroleum ether and fractionate it through a vacuum jacketed column packed with Helipac using a reflux ratio of 10:1. [Langer et al. *J Org Chem* **23** 50 *1958*, *Beilstein* **4** IV 4014.] It forms a lithium salt, $(Me_3Si)_2NLi$ [4039-32-1], which is soluble in THF and hexane; and ~ 1M solutions in these solvents are available commercially.

Hexamethyldisiloxane (HMDSO) *[107-46-0]* **M 162.4, m -59°, b 99.4°/760mm, 100.4°/764mm, d_4^{20} 0.7633, n_D^{20} 1.3777.** Fractionally distil through a column packed with glass helices with *ca* 15 theoretical plates. It is highly **flammable** and is an **irritant**. [Mills & McKenzie *J Am Chem Soc* **76** 2672 *1954*, Csakvari et al. *J Organometal Chem* **107** 287 *1976*, *Beilstein* **4** IV 4018.]

Hexamethylphosphoric triamide (HMPA) *[680-31-9]* **M 179.2, f 7.2°, b 68-70°/1mm, 235°/760mm, d_4^{20} 1.024, n_D^{20} 1.460.** The industrial synthesis is usually by treatment of $POCl_3$ with excess of dimethylamine in isopropyl ether. Impurities are water, dimethylamine and its hydrochloride. It is purified by refluxing over BaO or CaO at about 4mm pressure in an atmosphere of nitrogen for several hours, then distilled from sodium at the same pressure. The middle fraction (**b** *ca* 90°) is collected, refluxed over sodium under reduced pressure under nitrogen and distilled. It is kept in the dark under nitrogen, and stored in solid CO_2. It can also be stored over 4A molecular sieves.
Alternatively, it is distilled under vacuum from CaH_2 at 60° and is crystallised twice in a cold room at 0°, seeding the liquid with crystals obtained by cooling in liquid nitrogen. After about two-thirds are frozen, the remaining liquid is drained off [Fujinaga et al. *Pure Appl Chem* **44** 117 *1975*]. For tests of purity see Fujinaga et al. in *Purification of Solvents*, Coetzee Ed., Pergamon Press, Oxford, 1982. For efficiency of desiccants in drying HMPA see Burfield and Smithers [*J Org Chem* **43** 3966 *1978*, and Sammes et al. *J Chem Soc, Faraday Trans 1* 281 *1986*]. [*Beilstein* **4** IV 284.] **CARCINOGEN.**

Hexamethylphosphorous triamide [HMPT, tris(dimethylamino)phosphine] *[1608-26-0]* **M 163.2, m 7.2°, b 49-51°/12mm, 162-164°/12mm, d_4^{20} 0.989, n_D^{20} 1.466.** It may contain more than 1% of phosphoric triamide. The yellow oil is first distilled at atmospheric pressure, then under reduced pressure and stored under N_2. It is air sensitive, **TOXIC**, *and should not be inhaled*. It is absorbed through the skin. [Mark *Org Synth* Coll Vol **V** 602 *1973*, *Beilstein* **4** IV 274.]

Hydroquinone-2-sulfonic acid K salt *[21799-87-1]* **M 228.3, m 250°(dec), $pK_{Est(1)}$~1, $pK_{Est(2)}$~8.5, $pK_{Est(3)}$~11.** Recrystallise it from water or EtOH. [*Beilstein* **11** I 70, **11** II 170, **11** III 570.]

Hydroxynaphthol Blue tri-Na salt *[63451-35-4]* **M 620.5, m dec on heating, pK_{Est} <0.** The crude material is treated with hot EtOH to remove soluble impurities, then dissolve in 20% aqueous MeOH and chromatographed on a cellulose powder column with propanol/EtOH/water (5:5:4) as eluent. The upper of three

zones are eluted to give the pure dye which is precipitated as the *monosodium salt trihydrate* by adding conc HCl to the concentrated eluate [Ito & Ueno *Analyst* **95** 583 *1970*]. It can be converted to the trisodium salt with the calculated amount of alkali.

Indigocarmine (2[1,3-dihydro-3-oxo-5-sulfo-2*H*-indol-2-ylidene]-2,3-dihydro-3-oxo-1*H*-indole-5-sulfonic acid di-Na salt) *[860-22-0]* **M 466.4, pK $_1^{20}$ 2.8, p K $_2^{20}$ 12.3.** Its solubility in H_2O is 1g/100ml at 25°. It has been purified by dissolving in H_2O, filtering and adding EtOH to cause the salt to separate. Wash the solid with EtOH, Et_2O and dry *in vacuo.* [Vörlander & Schubert *Chem Ber* **34** 1860 *1901*, UV: Smit et al. *Anal Chem* **27** 1159 *1955,* Preisler et al. *J Am Chem Soc* **81** 1991 *1959*, *Beilstein* **25** IV 1975.]

Iodomethyl trimethylsilane *[4206-67-1]* **M 214.1, b 139.5°/744mm, d $_4^{20}$ 1.44, n $_D^{25}$ 1.4917.** If slightly violet in colour, wash it with aqueous 1% sodium metabisulfite, H_2O, dry (Na_2SO_4) it and fractionally distil it at 760mm. [Whitmore & Sommer *J Am Chem Soc* **68** 481 *1946*, *Beilstein* **4** IV 3878.]

Iodotrimethylsilane (trimethylsilyl iodide, TMSI) *[16029-98-4]* **M 200.1, b 106.8°/742mm, 107.5°/760mm, d $_4^{20}$ 1.470.** Add a little antimony powder and fractionate with this powder in the still. Stabilise the distillate with 1% wt of Cu powder. [Eaborn *J Chem Soc* 3077 *1950*, *Beilstein* **4** IV 4009.]

Isopropyldimethyl chlorosilane *[3634-56-8]* **M 140.7, b 109.8-110.0°/738mm, d $_4^{20}$ 0.88, n $_D^{20}$ 1.4158.** Probable impurity is Me_3SiCl (**b** 56.9°/783mm) which can be removed by efficient fractional distillation. [Sommer et al. *J Am Chem Soc* **76** 801 *1954*, *Beilstein* **4** IV 4067.]

***N*-Lauroyl-*N*-methyltaurine sodium salt (sodium *N*-decanoyl-*N*-methy-2-aminoethane sulfonate)** *[4337-75-1]* **M 343.5, pK_{Est} ~1.5.** It is prepared from methyldecanoate (at 180° under N_2) or decanoyl chloride and sodium *N*-methylethane sulfonate and purified by dissolving it in H_2O and precipitating by addition of Et_2O. It decomposes on heating. [Desseigne & Mathian *Mém Services Chim Etat Paris* **31** 359 *1944*, cf. *Chem Abstr* **41** 705 *1947*.]

Lawesson's Reagent [LR, 2,4-bis(4-methoxyphenyl)1,3,2,4-dithiadiphosphetane 2,4-disulfide, *p*-methoxyphenylthiophosphonic acid cyclic di(thioanhydride)] *[19172-47-5]* **M 404.5, m 228-229.5° (sintering at 215°), 228-230°.** The reagent has been washed with anisole or C_6H_6* and dried in a vacuum over paraffin wax and P_2O_5, and heated above room temperature. It does not lose the solvents completely (possibly due to formation of clathrates). It loses anisole on heating at ~230°. Analytically pure reagent was obtained by recrystallisation from *o*-dichlorobenzene, washing the crystals with C_6H_6* and drying *in vacuo* at 150°. It is extremely moisture sensitive, liberating H_2S, and should be stored in sealed containers, and preferably weighed in a dry-box. Its molecular weight is consistent with the formula $(C_7H_7OPS_2)_2$ but slowly polymerises in solution at ~80-85°. Polymerisation is more rapid in polar than non-polar solvents. It s a very useful thiating reagent particularly for converting hydroxy to thiol substituents. [Nishio *J Chem Soc, Perkin Trans I* 1113 *1993*, *Tetrahedron Lett* **47** 9329 *2006*, *Beilstein* **16** IV 1113.]

Lead diethyldithiocarbamate *[17549-30-3]* **M 503.7, pK $_1^{25}$ 3.36 (for *N,N*-diethyldithio-carbamate).** Wash it with H_2O and dry it at 60-70°, or dissolve it in the minimum volume of $CHCl_3$ and add the same volume of EtOH. Collect the solid that separates and dry it as before. *Alternatively*, recrystallise it by slow evaporation of a $CHCl_3$ solution at 70-80°. Filter the crystals, wash them with H_2O until all Pb^{2+} ions are eluted (check by adding chromate) and then dry it at 60-70° for at least 10 hours. [Lo et al. *Analyt Chem* **49** 1146 *1977*.]

Lissamine Green B {1-[bis-(4,4'-dimethylaminophenyl)methyl]-2-hydroxynaphthalene-3,6-disulfonic acid sodium salt, Acid Green 50} *[3087-16-9]* **M 576.6, m >200°(dec), CI 44090, λ_{max} 633nm.** Crystallise it from EtOH/water (1:1, v/v). **Irritant**. [*Beilstein* **14** II 574.]

Lissapol C (mainly sodium salt of 9-octadecene-1-sulfate) *[2425-51-6]***.** Reflux the salt with 95% EtOH, then

filter to remove insoluble inorganic electrolytes. The alcoholic solution is then concentrated, and the residue is poured into dry acetone. The precipitate is filtered off, washed in acetone and dried under vacuum [Biswas & Mukerji *J Phys Chem* **64** 1 *1960*].

Lissapol LS (mainly sodium salt of anisidine sulfate) *[28903-20-0]***.** Reflux the salt with 95% EtOH, then filter to remove insoluble inorganic electrolytes. The alcoholic solution is then concentrated, and the residue is poured into dry acetone. The precipitate is filtered off, washed in acetone and dried under vacuum [Biswas & Mukerji *J Phys Chem* **64** 1 *1960*].

Lithium dodecylsulfate *[2044-56-6]* **M 272.3.** Recrystallise this detergent twice from absolute EtOH and dry it under vacuum. Critical Micellar Concentration (CMC) in H_2O is 8.77 x 10^{-3}M. [Mukerjee et al. *J Phys Chem* **71** 4166 *1967*, Mysels & Dulin *J Colloid Sci* **10** 461 *1955*, *Beilstein* **1** IV 1847.]

Lithium trimethylsilanolate (trimethylsilanol Li salt) *[2004-14-0]* **M 96.1, m 120°(dec in air).** Wash it with Et_2O and petroleum ether. It sublimes at 180°/1mm as fine transparent needles. [Tatlock & Rochnow *J Org Chem* **17** 1555 *1952*, *Beilstein* **4** IV 3992.] Suspected **CARCINOGEN**.

Magnesium dodecylsulfate *[3097-08-3]* **M 555.1.** Recrystallise it three times from EtOH and dry it in a vacuum. [*Beilstein* **1** I 1788, **1** IV 1849.]

Magnesium trifluoromethanesulfonate *[60871-83-2]* **M 322.4, m >300°.** Wash it with CH_2Cl_2 and dry it at 125°/2 hour and 3mmHg. [Corey & Shimoji *Tetrahedron Lett* **24** 171 *1983*, *Beilstein* **3** IV 34.]

Manganous ethylenebis(dithiocarbamate) (Maneb) *[12427-38-2]* **M 265.3, pK_{Est} ~3.0 (for —NCSSH).** Crystallise this fungicide from EtOH. It is soluble in $CHCl_3$. It is a skin **irritant**. [*Beilstein* **4** III 149, **4** IV 234.]

1*R*,2*S*,5*R*-Menthyl phosphorochloridite ($MenOPCl_2$) *[95456-31-8]* **M 257.1, b 110-112°/2.0mm, (62°/150mm ? also reported).** $MenOPCl_2$ is prepared by adding a solution (1*R*,2*S*,5*R*)(-)-menthol (78g, 0.50mol) in in CH_2Cl_2 (50ml, or THF) dropwise to a solution of PCl_3 (137.5g, 1.0mol) in CH_2Cl_2 (50ml, or THF) during 30 minutes. The mixture is stirred for 1 hour under a N_2 atmosphere, the volatiles are removed at ~25°/100mm, pure *$MenOPCl_2$* distilled at ~62°/150mm quantitatively. It has ^{1}H NMR (400MHz, C_6D_6, TMS) with δ at 0.64 (m, 1H, H-4), 0.77 (m, 10H, H-3, H-8, H-9, H-10), 1.15 (M, 3H, H-2, H-5, H-6), 1.44 (m, 2H, H-3, H-4), 1.98 (M, 1H, H-7), 2.30 (M, 1H, H-6), 4.40 (m, 1H, H-1); the $^{13}C\{^1H\}$ NMR (100MHz, C_6D_6, TMS) with δ at 16.1 (s, C-8), 21.2 (s, C-9), 22.0 (s, C-10), 22.8 (s, C-3), 25.1 (s, C-7), 31.4 (s, C-5), 33.8 (s, C-4), 43.3 (s, C-6), 48.7 (s, C-2), 83.5 (d, $^2J_{PC}$ = 9.8Hz, C-1); and the ^{31}P NMR (121.4MHz, THF, external ref 85% H_3PO_4) with δ at 175.6 or (at 162MHz, C_6D_6) with δ at 176.1 (d, $^3J_{PH}$ = 13.5Hz). [Alexander et al. *Organometallics* **19** 2700 *2000*, Brunel & Buono *J Org Chem* **58** 7313 *1993*, Totland et al. *Macromolecules* **29** 6114 *1996*]. Note that Hey-Hawkins and co-workers found that a 5 molar excess of PCl_3 in a solvent-free system gave 98% of dichloridite; but when a 1:1 ratio of menthol to PCl_3 was used a mixture of mono- and di- menthyl phosphorochloridites were obtained [Hey-Hawkins et al. *Eur J Inorg Chem* 2776 *2009*].

2-Mercaptopyridine *N*-oxide sodium salt (pyridinethione or pyrithione sodium salt) *[3811-73-2]* **M 149.1, m ~250°(dec), pK_1 -1.95, pK_2 4.65.** When recrystallised from water, it assayed as 98.7% based on $AgNO_3$ titration [Krivis et al. *Anal Chem* **35** 966 *1963*; see also Krivis et al. *Anal Chem* **48** 1001 *1976*, and Barton & Crich *J Chem Soc, Perkin Trans 1* 1603, 1613 *1986*]. [*Beilstein* **21/7** V 151.]

Metanil Yellow (3[{4-phenylamino}phenylazo]-benzenesulfonic acid) *[587-98-4]* **M 375.4, pK_{Est} <0.** It can be salted out from water three times with sodium acetate, then repeatedly extracted with EtOH [McGrew & Schneider *J Am Chem Soc* **72** 2547 *1950*]. [*Beilstein* **16** II 168.]

(Methoxycarbonylmethyl)triphenylphosphorane [methyl (triphenylphosphoranylidene)-acetate] *[2605-67-6]* **M 334.4, m 162-163°, 169-171°.** Crystallise it by dissolving in it AcOH and adding petroleum ether (b

40-50°) to give colourless plates. Its UV has λ_{max} ($A^{1\%}_{1mm}$) at 222nm (865) and 268nm (116) [Isler et al. *Helv Chim Acta* **40** 1242 *1957*]. [*Beilstein* **16** IV 977.]

Methoxycarbonylmethyltriphenylphosphonium bromide *[1779-58-4]* **M 415.3, m 163°, 165-170°(dec).** Wash it with petroleum ether (b 40-50°), recrystallise it from $CHCl_3$/Et_2O and dry it at high vacuum at 65°. [Isler et al. *Helv Chim Acta* **40** 1242 *1957*, Wittig & Haag *Chem Ber* **88** 1654, 1664 *1955*, *Beilstein* **16** IV 981.]

Methoxymethyl trimethylsilane (trimethylsilylmethyl methyl ether) *[14704-14-4]* **M 118.3, b 83°/740mm, d_4^{25} 0.758, n_D^{25} 1.3878.** It forms an azeotrope with MeOH (**b** 60°). If it contains MeOH (check IR for bands above 3000cm^{-1}), then wash with H_2O and fractionate. A possible impurity could be chloromethyl trimethylsilane (**b** 97°/740mm). [Speier *J Am Chem Soc* **70** 4142 *1948*, *Beilstein* **4** III 1844.] It is an IRRITATING FLAMMABLE liquid.

1-Methoxy-2-methyl-1-trimethylsiloxypropene (dimethyl ketene methyl trimethylsilyl acetal) *[31469-15-5]* **M 174.3, b 121-122°/0.35mm, 125-126°/0.4mm, 148-150°/atm, d_4^{20} 0.86.** Add Et_2O, wash with cold H_2O, dry (Na_2SO_4), filter, evaporate Et_2O, and distil the oily residue in a vacuum. [Ainsworth et al. *J Organometal Chem* **46** 59 *1972*.]

***trans*-1-Methoxy-3-(trimethylsilyloxy)-1,3-butadiene (Danishefsky's diene)** *[54125-02-9]* **M 172.3, b 68-69°/14mm, 70-72°/16mm, d_4^{20} 0.885, n_D^{20} 1.4540.** It may contain up to 1% of the precursor 4-methoxybut-4-ene-2-one. It is easily purified by distilling through a Vigreux column in a vacuum and taking the middle fraction. [Danishefsky & Kitihara *J Am Chem Soc* **96** 7807 *1974*, Danishefsky *Acc Chem Res* **14** 400 *1981*.]

Methylarsonic acid *[124-58-3]* **M 139.9, m 159.8°, 161°, pK_1^{25} 4.58, pK_2^{25} 7.82 [$As(OH)_2$].** Recrystallise this herbicide from Me_2CO or absolute EtOH (white plates; its solubility is 28g/100ml EtOH). [Quick & Adams *J Am Chem Soc* **44** 809 *1922*, *Beilstein* **4** H 613, **4** I 577, **4** II 996, **4** III 1822, **4** IV 3682.]

Methyl dichlorosilane (dichloro methylsilane) *[75-54-7]* **M 115.0, m -92.5°, b 41°/748mm, 40.9°/760mm, 40-45°/atm, d_{27}^{27} 1.105.** Impurities are generally other chloromethyl silanes. Distil it through a conventional Stedman column of 20 theoretical plates or more. It should be protected from H_2O by storing over P_2O_5. [Stock & Somieski *Chem Ber* **52** 695 *1919*, Sauer *J Am Chem Soc* **68** 962 *1946*, *Beilstein* **4** IV 4096.]

Methyl Orange (sodium 4,4'-dimethylaminophenylazobenzenesulfonate) *[547-58-0]* **M 327.3, pK_1^{25} 3.56, pK_2^{25} 6.49.** Recrystallise it twice from hot water, then wash it with a little EtOH followed by diethyl ether. It is an indicator: pH 3.1 (red) and pH 4.4 (yellow). [*Beilstein* **16** IV 510.]

Methylphenyl dichlorosilane (dichloro methyl phenylsilane) *[149-74-6]* **M 191.1, b 114-115°/50mm, 202-205°/atm, d_4^{20} 1.17.** Purify it by fractionation using an efficient column. It hydrolyses *ca* ten times more slowly than methyltrichlorosilane and *ca* sixty times more slowly than phenyltrichlorosilane. [Shaffer & Flanigen *J Phys Chem* **61** 1591 *1957*, *Beilstein* **16** III 1211, **16** IV 1517.]

Methylphosphonic acid *[993-13-5]* **M 96.0, m 104-106°, 105-107°, 108°, pK_1^{25} 2.12, pK_2^{25} 7.29.** If it tests for Cl^-, then add H_2O and evaporate to dryness, repeat several times till free from Cl^-. The residue solidifies to a wax-like solid. *Alternatively*, dissolve the acid in the minimum volume of H_2O, add charcoal, warm, filter and evaporate to dryness in a vacuum over P_2O_5. [Kosolapoff *J Am Chem Soc* **75** 3379 *1953*.] The *di-Na salt* is prepared from 24g of acid in 50ml of dry EtOH, and a solution of 23g Na dissolved in 400ml EtOH is added. A white precipitate is formed, but the mixture is refluxed for 30 minutes to complete the reaction. Filter off the solid and recrystallise it from 50% EtOH. Dry the crystals in a vacuum desiccator. [Thompson *J Chem Soc* 3292 *1952*, *Beilstein* **4** IV 3498.]

Methylphosphonic dichloride *[676-97-1]* **M 132.9, m 33°, 33-37°, b 53-54°/10mm, 64-67°/20.5mm, 86°/44mm, 162°/760mm, d_4^{40} 1.4382.** Fractionally redistil it until the purity as checked by hydrolysis and

acidimetry for Cl^- is correct and the distillate should solidify on cooling. [Kinnear & Perren *J Chem Soc* 3437 *1952*, Crofts & Kosolapoff *J Am Chem Soc* **75** 3379 *1952,* for IR see McIvor et al. *Can J Chem* **34** 1611 *1956*, *Beilstein* **4** IV 3509.]

Methyl Thymol Blue, sodium salt {MTB, 3,3′-bis[*N*,*N*′-di(carboxymethyl)amino]thymolsulfonephthalein sodium salt} *[1945-77-3]* **M 844.8, ε 1.89 x 10^4 at 435nm, pH 5.5, pK_1^{25} 3.0, pK_2^{25} 3.3, pK_3^{25} 3.8, pK_4^{25} 7.4 (pK_4^{25} 7.2), pK_5^{25} 11.5 pK_6^{25} 13.4.** The starting material for synthesis is Thymol Blue. Purify it as for Xylenol Orange in "Heterocyclic Compounds" in this Chapter. [Tereshin et al. *J Anal Chem USSR (Engl Trans)* **20** 1138 *1965*, Körbl & Kakác *Col Czech Chem Commun* **23** 889 *1958*, *Beilstein* **19/8** V 619.]

Methyl trichlorosilane *[75-79-6]* **M 149.5, b 13,7°/101mm, 64.3°/710.8mm, 65.5°/745mm, 66.1°/atm, d_4^{20} 1.263, n_D^{20} 1.4110.** If not very pure, distil it before use. The purity is checked by ^{29}Si NMR (δ in MeCN is 13.14 ppm with respect to Me_4Si). Possible contaminants are other silanes which can be removed by fractional distillation through a Stedman column of >72 theoretical plates with total reflux and 0.35% take-off. This apparatus should be under N_2 gas at a rate of 12 bubbles/minute fed into the line using an Hg manometer to control the pressure. It is sensitive to H_2O. [Gillam et al. *J Am Chem Soc* **73** 4252 *1951*, Olah et al. *J Org Chem* **48** 3667 *1983*, *Beilstein* **4** IV 4212.]

Methyl triethoxysilane *[2031-67-6]* **M 178.31, b 142-144.5°/742mm, 141°/765mm, 141.5°/775mm, d_4^{20} 0.8911, n_D^{20} 1.3820.** Purify by fractionating it repeatedly in a stream of N_2 through a 3' Heligrid packed Todd column. It is hydrolysed by H_2O and yields cyclic polysiloxanes on hydrolysis in the presence of acid in $*C_6H_6$. [Bee et al. *J Am Chem Soc* **77** 1292 *1955*, Sprung & Guenther *J Am Chem Soc* **77** 3990 *1955*, *Beilstein* **4** IV 4204.]

Methyl trimethoxysilane *[1185-55-3]* **M 136.2, b 102°/760mm, d_4^{20} 1.3687, n_D^{20} 1.3711.** Likely impurities are 1,3-dimethyltetramethoxy disiloxane (**b** 31°/1mm) and cyclic polysiloxanes, see previous entry methyl triethoxysilane. [Tamborski & Post *J Org Chem* **16** 1400 *1952*, Seyferth & Rochow *J Org Chem* **20** 250 *1955*, *Beilstein* **4** IV 4203.]

***N*-Methyl-*N*-trimethylsilylacetamide** *[7449-74-3]* **M 145.3, b 48-49°/11mm, 84°/13mm, 105-107°/35mm (solid at room temperature), d_4^{20} 0.90, n_D^{20} 1.4379.** A likely impurity is $Et_3N.HCl$ which can be detected by its odour. If it is completely soluble in $*C_6H_6$, then redistil; otherwise dissolve it in this solvent, filter and evaporate first in a vacuum at 12mm, then fractionate; all operations should be carried out in a dry N_2 atmosphere. [Klebe et al. *J Am Chem Soc* **88** 3390 *1966*, Ried & Suarez-Rivero *Chem Ber* **96** 1473 *1963*, *Beilstein* **4** IV 4011.]

Methyl trimethylsilylacetate *[2916-76-9]* **M 146.3, b 65-68°/50mm, d_4^{20} 0.89.** Dissolve it in Et_2O, shake with 1M HCl, wash with H_2O, aqueous saturated $NaHCO_3$, H_2O again, and dry it (a precipitate may be formed in the $NaHCO_3$ solution and should be drawn off and discarded). The solvent is distilled off, and the residue is fractionated through a good column. The IR ($CHCl_3$) has ν_{max} 1728cm^{-1}. [Fessenden & Fessenden *J Org Chem* **32** 3535 *1967*, Matsuda et al. *J Org Chem* **45** 237 *1980*, *Beilstein* **4** III 1855, **4** IV 3974 for Et ester.]

Methyl 2-(trimethylsilyl)propionate *[55453-09-3]* **M 160.3, b 155-157°/atm, d_4^{20} 0.89.** Dissolve it in Et_2O, wash it with aqueous $NaHCO_3$, H_2O, 0.1M HCl, H_2O again, dry ($MgSO_4$), evaporate and distil it. [Emde & Simchen *Synthesis* 867 1977, Oppolzer et al. *Tetrahedron* **39** 3695 *1983*, Crimmin et al. *J Chem Soc Perkin Trans 1* 541 *1985*.]

***N*-Methyl-*N*-trimethylsilyl trifluoroacetamide** *[24589-78-4]* **M 199.3, b 78-79°/130mm.** Fractionate the amide through a 40mm Vigreux column. Usually it contains *ca* 1% of methyl trifluoroacetamide and 1% of other impurities which can be removed by gas chromatography or fractionating using a spinning band column. [Donike *J Chromatogr* **42** 103 *1969*, Donike *J Chromatogr* **103** 91 *1975*, *Beilstein* **4** IV 4011.]

Methyl triphenoxyphosphonium iodide *[17579-99-6]* **M 452.2, m 114°** (sealed tube), **146°.** Gently heat the impure iodide with good grade Me_2CO. The saturated solution obtained is decanted rapidly from undissolved

salt and treated with an equal volume of dry Et_2O. The iodide separates as flat needles which are collected by centrifugation, washed several times with dry Et_2O, and dried in a vacuum over P_2O_5. For this recrystallisation it is essential to minimise the time of contact with Me_2CO and to work rapidly and with rigorous exclusion of moisture. If the crude material is to be used, it should be stored under dry Et_2O, and dried and weighed *in vacuo* immediately before use. [Landauer & Rydon *J Chem Soc* 224 *1953*, Hudson et al. *J Chem Soc Perkin Trans 1* 982 *1974*, *Beilstein* **6** IV 704.]

Methyl triphenylphosphonium bromide *[1779-49-3]* **M 357.3, m 229-230°(corr), 227-229°, 230-233°.** If the solid is sticky, wash it with $*C_6H_6$ and dry it in a vacuum over P_2O_5. [Marvel & Gall *J Org Chem* **24** 1494 *1959*, *Chem Ber* **87** 1318 *1954*, Milas & Priesing *J Am Chem Soc* **79** 6295 *1957*, Wittig & Schöllkopf *Org Synth* **40** 66 *1960*.] The *iodide*, on recrystallisation from H_2O, has **m** 187.5-188.5° [Mann et al. *J Chem Soc* 1130 *1953*, Wittig & Geissler *Justus Liebigs Ann Chem* **580** 44 *1953*]. [*Beilstein* **16** IV 981.]

Methyl vinyl dichlorosilane (dichloro methyl vinyl silane) *[124-70-9]* **M 141.1, b 43-45.5°/11-11.5mm, 91°/742mm, 92.5°/743.2mm, 92.5-93°/atm, d_4^{20} 1.0917, n_D^{20} 1.444.** Likely impurities are dichloromethyl-silane, butadienyl-dichloromethylsilane. Fractionate the silane through a column packed with metal filings (20 theoretical plates) at atmospheric or reduced pressure. [*Izv Akad Nauk SSSR Ser Khim* 1474 *1957* and 767 *1958*, *Beilstein* **4** III 1894, **4** IV 4184.]

Milling Red SWB {1-[4-[4-[4-toluenesulfonyloxy]phenylazo](3,3'dimethyl-1,1'-biphenyl)-4'-azo]-2-hydroxynaphthalene-6,8-disulfonic acid di-Na salt, Acid Red 114} *[6459-94-5]* **M 830.8, m dec >250°, CI 23635, λ_{max} ~514nm.** Salt out three times with sodium acetate, then repeatedly extract it with EtOH and dry the solid in air. [McGrew & Schneider *J Am Chem Soc* **72** 2547 *1950*, *Beilstein* **16** II 140.] See Solochrome Violet R [2092-55-9] in "Aromatic compounds" in this Chapter.

Milling Yellow G *[51569-18-7]***.** Salted out three times with sodium acetate, then repeatedly extracted with EtOH. [McGrew & Schneider *J Am Chem Soc* **72** 2547 *1950*, *Beilstein* **16** II 125.] See Solochrome Violet R [2092-55-9] in "Aromatic compounds" in this Chapter.

Naphthalene Scarlet Red 4R [1-(4-sulfonaphthalene-1-azo)-2-hydroxynaphthalene-6,8-disulfonic acid tri-Na salt, New Coccine, Acid Red 18] *[2611-82-7]* **M 604.5, m >250°(dec), CI 16255, λ_{max} 506nm.** Dissolve the dye in the minimum quantity of boiling water, filter and enough EtOH is added to precipitate *ca* 80% of the dye. This process is repeated until a solution of the dye in aqueous 20% pyridine has a constant extinction coefficient. [*Beilstein* **16** I 306.]

Naphthol Yellow S (citronin A, flavianic acid sodium salt, 8-hydroxy-5,7-dinitro-2-naphthalene sulfonic acid disodium salt) *[846-70-8]* **M 358.2, decomposes on heating.** It is a water-soluble greenish yellow powder. The *free sulfonic acid* can be recrystallised from dilute HCl (**m** 150°) or AcOH/EtOAc (**m** 148-149.5°). The disodium salt is then obtained by dissolving the acid in two equivalents of aqueous NaOH and evaporating to dryness and drying the residue in a vacuum desiccator. The sodium salt can be recrystallised from the minimum volume of H_2O or from EtOH [Dermer & Dermer *J Am Chem Soc* **61** 3302 *1939*]. [*Beilstein* **11** III 542.]

1,2-Naphthoquinone-4-sulfonic acid sodium salt (3,4-dihydro-3,4-dioxo-1-naphthlene sulfonic acid sodium salt) *[521-24-4]* **M 260.2, pK_{Est} <0.** It forms yellow crystals from aqueous EtOH and should be dried at 80° *in vacuo*. Its solubility in H_2O is 5% [Martin & Fieser *Org Synth* Coll Vol **III** 633 *1955*, Danielson *J Biol Chem* **101** 507 *1933*, UV: Rosenblatt et al. *Anal Chem* **27** 1290 *1955*]. [*Beilstein* **11** IV 668.]

1-Naphthyl phosphate disodium salt *[2183-17-7]* **M 268.1, pK_1^{25} 0.97, pK_2^{25} 5.85 (for free acid).** The free acid has **m** 157-158° (from $Me_2CO/*C_6H_6$). The *free acid* is recrystallised several times by adding 20 parts of boiling $*C_6H_6$ to a hot solution of 1 part of *free acid* and 1.2 parts of Me_2CO. It has **m** 157-158°. [Chanley & Ferguson *J Am Chem Soc* **77** 4002 *1955*.] The *monosodium salt* is precipitated from a solution of the acid phosphate in MeOH by addition of an equivalent of MeONa in MeOH. [Friedman & Seligman *J Am Chem Soc*

72 624 *1950*, *Beilstein* **6** IV 4226.] See also entry on p 877 in Chapter 7.

2-Naphthyl phosphate monosodium salt *[14463-68-4]* **M 246.1, m 203-205°, pK_1^{25} 1.25, pK_2^{25} 5.83 (for free acid).** Recrystallise it from H_2O (10ml) containing NaCl (0.4g). The salt is collected by centrifugation and dried in a vacuum desiccator, **m** 203-205° (partially resolidifies and re-melts at 244°). It crystallises from MeOH (**m** 222-223°). The free acid is recrystallised several times by addition of 2.5 parts of hot $CHCl_3$ to a hot solution of the free acid (1 part) in Me_2CO (1.3 parts), **m** 177-178°. [Friedman & Seligmann *J Am Chem Soc* **73** 5292 *1951*, Chanley & Feaggeson *J Am Chem Soc* **77** 4002 *1955*, *Beilstein* **6** H 647, **6** III 2989, **6** IV 428.] See also entry on p 877 in Chapter 7.

2-Nitrophenol-4-arsonic acid (4-hydroxy-3-nitrophenylarsonic acid) *[121-19-7]* **M 263.0, $pK_{Est(1)}$~4.4 As(O)-(OH)-(O^-), $pK_{Est(2)}$~7.4 (phenolic OH), $pK_{Est(3)}$~7.7 (As(O)-2(O^-).** It crystallises from water and is used for the spectroscopic detection of Zn. [*Beilstein* **16** II 468, **16** III 1073, **16** IV 1188.]

1-Nitroso-2-naphthol-3,6-disulfonic acid, di-Na salt, hydrate (Nitroso-R-salt) *[525-05-3]* **M 377.3, m >300°, $pK_{Est(1)}$<0 (SO_3^-), $pK_{Est(2)}$~7 (OH).** Purify the salt by dissolution in aqueous alkali and precipitation by addition of HCl. The pKa is 7.13. [Oka & Miyamoto *J Chem Soc Jpn* (Pure Chem Sectn) **76** 672 *1955* (*Chem Abstr* 11882 *1956I)*, *Beilstein* **11** IV 669.]

Nuclear Fast Red (1-amino-2,4-dihydroxy-5,10-anthraquinone-3-sulfonic acid Na Salt) *[6409-77-4]* **M 357.3, m >290°(dec), λ_{max} 518nm.** A solution of 5g of the dye in 250ml of warm 50% EtOH is cooled to 15° for 36 hours, then filtered on a Büchner funnel, washed with EtOH until the washings are colourless, then with 100ml of Et_2O and dry it over P_2O_5 *in vacuo*. It is a biological stain that is also used for the estimation of Ca. [Kingsley & Robnett *Anal Chem* **33** 552 *1961*.]

Octadecyl trichlorosilane *[112-04-9]* **M 387.9, b 159-162°/13mm, 185-199°/2-3mm, d_4^{30} 0.98.** Purify it by fractional distillation at high vacuum. [Winstein & Seubold *J Am Chem Soc* **69** 2916 *1947*, *Beilstein* **4** IV 4256.]

Octamethyl cyclotetrasiloxane *[556-67-2]* **M 296.6, m 17-19°, 17.58°, 18.5°, b 74°/20mm, 176.4°/760mm, $d_4^{29.3}$ 0.9451, n_D^{30} 1.3968.** The solid exists in two forms, **m** 16.30° and 17.65°. Dry it over CaH_2 and distil it. Further fractionation can be effected by repeated partial freezing and discarding the liquid phase. [Osthoff & Grubb *J Am Chem Soc* **76** 399 *1954*, Hoffman *J Am Chem Soc* **75** 6313 *1953*, *Beilstein* **4** IV 4125.]

Octamethyl trisiloxane *[107-51-7]* **M 236.5, m -80°, b 151.7°/747mm, 153°/760mm.** Distil it twice, the middle fraction from the first distillation is again distilled, and the middle fraction of the second distillation is used. [Patnode & Wilcock *J Am Chem Soc* **68** 358, Wolcock *J Am Chem Soc* **68** 691 *1946*, Thompson *J Chem Soc* 1908 *1953*, *Beilstein* **4** IV 4115.]

Octaphenyl cyclotetrasiloxane *[546-56-5]* **M 793.2, m 201-202°, 203-204°, b 330-340°/1mm.** Recrystallise it from AcOH, EtOAc, *C_6H_6 or *C_6H_6/EtOH. It forms two stable isomorphs and both forms, as well as the mixture, melt at 200-201°. There is a metastable form which melts at 187-189°. [Burkhard et al. *J Am Chem Soc* **67** 2174 *1945*, Hyde et al. *J Am Chem Soc* **69** 488 *1947*, *Beilstein* **16** IV 1530.]

Octyl trichlorosilane *[5283-66-9]* **M 247.7, b 96.5°/10mm, 112°/15mm. 119°/28mm, 229°/760mm, d_4^{20} 1.0744, n_D^{20} 1.4453.** Purify the silane by repeated fractionation using a 15-20 theoretical plate glass column packed with glass helices. This can be done more efficiently using a spinning band column. Its purity can be checked by analysing for HCl (*ca* 0.5-1g of sample is dissolved in 25ml of MeOH, diluted with H_2O and the HCl formed by hydrolysis is titrated with standard alkali). It is moisture sensitive. [Whitmore *J Am Chem Soc* **68** 475 *1946*, El-Abbady & Anderson *J Am Chem Soc* **80** 1737 *1958*, *Beilstein* **4** III 1907.]

Orange I [tropaeolin 000 Nr1, 4-(4-hydroxy-1-naphthylazo)benzenesulfonic acid sodium salt] *[523-44-4]* **M 350.3, m >260°(dec).** Purify the dye by dissolving it in the minimum volume of H_2O, adding, with stirring, a

large excess of EtOH. The salt separates as orange needles. It is collected by centrifugation or filtration, washed with absolute EtOH (3x) and Et_2O (2x) in the same way, and dried in a vacuum desiccator over KOH. The *free acid* can be recrystallised from EtOH. [Slotta & Franke *Chem Ber* **64** 86 *1931*, *Beilstein* **16** H 275, **16** II 117, **16** IV 410.] The purity can be checked by titration with titanium chloride [Klotz *J Am Chem Soc* **68** 2299 *1946*].

Orange II [tropaeolin 000 Nr2, 4-(2-hydroxy-1-naphthylazo)benzenesulfonic acid sodium salt] *[633-96-5]* **M 350.3.** Purification is as for Orange I. Its solubility in H_2O is 40g/L at 25°. [Müller et al. *Helv Chim Acta* **35** 2579 *1952*.] Also purify it by extracting it with a small volume of cold water, then crystallising it by dissolving in boiling water, cooling to *ca* 80°, adding two volumes of EtOH and cooling. When cold, the precipitate is filtered off, washed with a little EtOH and dried in air. It can be salted out from aqueous solution with sodium acetate, then repeatedly extracted with EtOH. Meggy and Sims [*J Chem Soc* 2940 *1956*], after crystallising the sodium salt twice from water, dissolved it in cold water (11ml/g) and added conc HCl to precipitate the *acid* dye which was separated by centrifugation, redissolved and again precipitated with acid. After washing the precipitate three times with 0.5M acid, it was dried over NaOH, recrystallised twice from absolute EtOH, washed with a little Et_2O, dried over NaOH and stored over conc H_2SO_4 in the dark. It can then be converted to the pure salt with the calculated amount of NaOH or Na_2CO_3. [*Beilstein* **16** IV 408.]

Orange G (1-phenylazo-2-naphthol-6,8-disulfonic acid di-Na salt) *[1936-15-8]* **M 452.4, pK_{Est}~9.** Recrystallise this dye from 75% EtOH, dry it for 3 hours at 110° and keep it in a vacuum desiccator over H_2SO_4. The *free acid* crystallises from EtOH or conc HCl in deep red needles with a green reflex. [Conant & Pratt *J Am Chem Soc* **48** 2483 *1923*, Drew & Landquist *J Chem Soc* 292 *1938*, *Beilstein* **16** H 301, **16** I 305, **16** II 141, **16** III 327.]

Orange RO {acid orange 8, 1,8-[bis(4-*n*-propyl-3-sulfophenyl-1-amino)]anthra-9,10-quinone di-Na salt} *[5850-86-2]* **M 364.4, CI 15575, λ_{max} 490nm.** Salt it out three times with sodium acetate, then extract it repeatedly with EtOH and dry *in vacuo*.

Pentafluorophenyl dimethylchlorosilane (Flophemesyl chloride) *[20082-71-7]* **M 260.7, b 89-90°/10mm, d_4^{30} 1.403, n_D^{30} 1.447.** If it goes turbid on cooling due to separation of some LiCl, then dissolve it in Et_2O, filter and fractionate it in a vacuum. [Morgan & Poole *J Chromatogr* **89** 225 *1974*, Birkinshaw et al. *J Chromatogr* **132** 548 *1977*.]

Phenylarsonic acid (benzenearsonic acid) *[98-05-5]* **M 202.2, m 155-158°(dec), 158-162°(dec), pK_1^{25} 3.65, pK_2^{25} 8.77.** Crystallise it from H_2O (3ml/g) between 90° and 0°. *Alternatively*, dissolve 600g of the acid in 500ml of boiling H_2O, add 20g of Norite, filter hot, cool, filter off the crystals and dry them. On heating at ~154-160° it is converted to the *anhydride*. [Bullard & Dickery *Org Synth* Coll Vol **II** 494 *1943*, for the 4-nitro derivative see Ruddy & Starkey *Org Synth* Coll Vol **III** 665 *1955*, *Beilstein* **16** H 868, **16** I 448, **16** II 457, **16** III 1057, 16 IV 1183.]

Phenylboronic acid (benzeneboronic acid) *[98-80-6]* **M 121.9, m ~43°, 215-216° (anhydride), 217-220°, pK_1^{25} 8.83.** It recrystallises from H_2O, but it can convert spontaneously to *benzeneboronic anhydride* or phenylboroxide on standing in dry air. A possible impurity is dibenzeneborinic acid which can be removed by washing with petroleum ether. Heating in an oven at 110°/760mm for 1 hour converts it to the *anhydride* **m** 214-216°. Its solubility in H_2O is 1.1% at 0° and 2.5% at 25°, and in EtOH it is 10% (w/v). [Gilman & Moore *J Am Chem Soc* **80** 3609 *1958*.] If the acid is required, not the anhydride, the acid (from recrystallisation in H_2O) is dried in a slow stream of air saturated with H_2O. The *anhydride* is converted to the acid by recrystallisation from H_2O. The acid gradually dehydrates to the *anhydride* if left in air at room temperature with 30-40% relative humidity. The melting point is usually that of the anhydride because the acid dehydrates before it melts [Washburn et al. *Org Synth* Coll Vol **IV** 68 *1963*]. [*Beilstein* **16** IV 1654.]

1,2-Phenylenephosphorochloridate (2-chloro-1,3,2-benzodioxaphosphole-2-oxide) *[1499-17-8]* **M 190.5, m 52°, 58-59°, 59-61°, b 80-81°/1-2mm, 118°/10mm, 122°/12mm, 125°/16mm, 155°/33mm.** After distilling it in a vacuum, it sets to a colourless solid. It is soluble in petroleum ether, *benzene and slightly soluble in Et_2O.

[Khwaja et al. *J Chem Soc (C)* 2092 *1970*, Anschütz & Broeker *Justus Liebigs Ann Chem* **454** 109 *1927*, *Beilstein* **6** IV 5602.]

Phenylphosphinic acid [benzenephosphinic acid, PhPH(O)(OH)] *[1779-48-2]* **M 142.1, m 70°, 71°, 83-85°, 86°, pK_1^{25} 1.75.** Crystallise it from H_2O (solubility is 7.7% at 25°). Also purify it by placing the solid in a flask covered with dry Et_2O, and allowed it to stand for 1 day with intermittent shaking. Et_2O is decanted off and the process repeated. After filtration, excess Et_2O is removed in a vacuum. It has also been recrystallised from $*C_6H_6$. [Michaelis *Justus Liebigs Ann Chem* **181** 265 *1876*, Banks & Skoog *Anal Chem* **29** 109 *1957*, NMR: Van Wazer et al. *J Am Chem Soc* **78** 5715 *1956*, *Beilstein* **16** IV 1033.]

Phenylphosphonic acid *[1571-33-1]* **M 158.1, m 164.5-166°, pK_2^{25} 7.43 (7.07).** It is best to recrystallise it from H_2O by concentrating an aqueous solution to a small volume and allowing it to crystallise. Wash the crystals with ice cold H_2O and dry them in a vacuum desiccator over H_2SO_4. [Lecher et al. *J Am Chem Soc* **76** 1045 *1954*.] pK^{25} values in H_2O are 7.07, and in 50% EtOH 8.26. [Jaffé et al. *J Am Chem Soc* **75** 2209 *1953*, IR: Daasch & Smith *Anal Chem* **23** 853 *1951*, *Beilstein* **16** IV 1068.]

Phenylphosphonic dichloride (P,P-dichlorophenyl phosphine oxide) *[824-72-6]* **M 195.0, m 3°, b 83-84°/1mm, 135-136°/23mm, d_4^{30} 1.977, n_D^{30} 1.5578.** Fractionally distil it using a very efficient or a spinning band column. [Lecher et al. *J Am Chem Soc* **76** 1045 *1954*, NMR: Müller et al. *J Am Chem Soc* **78** 3557 *1956*, Van Wazer et al. *J Am Chem Soc* **78** 5715 *1956*, IR: Daasch & Smith *Anal Chem* **23** 853 *1951*, *Beilstein* **16** IV 1074.]

Phenylphosphonous acid [$PhP(OH)_2$] [tautomer of phenylphosphinic acid – above] *[121-70-0]* **M 141.1, m 71°, pK_{Est} <0, pK^{17} 2.1.** Crystallise it from hot H_2O or $*C_6H_6$. [*Beilstein* **16** IV 1033.]

Phenylphosphonous dichloride (P,P-dichloro phenyl phosphine) *[644-97-3]* **M 179.0, m -51°, b 68-70°/1mm, 224-226°/atm, d_4^{30} 1.9317, n_D^{35}1.5962.** Distil it in a vacuum by fractionating through a 20cm column packed with glass helices (better to use a spinning band column) [Buchner & Lockhart *J Am Chem Soc* **73** 755 *1951*, NMR: Müller et al. *J Am Chem Soc* ***78*** 3557 *1956*, IR: Daasch & Smith *Anal Chem* **23** 853 *1951*]. It forms a yellow *Ni complex:* $Ni(C_6H_5Cl_2P)_4$ (**m** 91-92°, from H_2O) [Quin *J Am Chem Soc* **79** 3681 *1957*] and a yellow complex also with molybdenum carbonyl: $Mo(CO)_3.(C_6H_5Cl_2P)_3$ (**m** 106-110° dec) [Abel et al. *J Chem Soc* 2323 *1959*]. [*Beilstein* **16** IV 972.]

Phenyl phosphoryl dichloride *[770-12-7]* **M 211.0, m -1°, b 103-104°/2mm, 110-111°/10mm, 130-134°/21mm, 241-243°/atm, d_4^{30} 1.4160, n_D^{30} 1.5216.** Fractionally distil it under as high a vacuum as possible using an efficient fractionating column or a spinning band column. It should be redistilled if the IR is not very satisfactory [IR: Bellamy & Beecher *J Chem Soc* 475 *1952*, Freeman & Colver *J Am Chem Soc* **60** 750 *1938*, Orloff et al. *J Am Chem Soc* **80** 727 *1958*]. [*Beilstein* **6** IV 737.] **HARMFUL VAPOURS.**

Phenylsilane ($PhSiH_3$) *[694-53-1]* **M 108.2, b 62°/100mm, 120°/atm, d_4^{25} 0.877, n_D^{20} 1.5125.** It is best prepared by reduction of $PhSiCl_3$ with $LiAlH_4/Et_2O$: stir at room temperture overnight, pour onto crushed ice, extract with Et_2O, dry the extract (Drierite), filter, evaporate and distil the residual oil preferably in a vacuum [Beukesser et al. *J Am Chem Soc* **74** 648 *1952*, Koch et al. *Rec Trav Chim Pays Bas* **114** 206 *1995*, Finholt et al. *J Am Chem Soc* **69** 2692 *1947*].
It is a useful reagent for deoxygenating phosphine oxides to phosphines, and will reduced chiral phosphine oxides to chiral phosphines with retention of configuration [Marsi *J Org Chem* **39** 265 *1974*]. It is a reducing agent in radical reactions [Perez et al. *J Org Chem* **52** 5570 *1967*], and deoxygenates primary and secondary alcohols *via* their xanthate or thionocarbonate esters (prepared from aryl-OCSCl and an inhibitor, e.g benzoyl peroxide) in 60-100 minutes in >87% yields [Barton et al. *Synlett* 435 *1991*]. [*Beilstein* **16** III 1198, **16** IV 1360.]

Phenylthio trimethylsilane (trimethyl phenylthio silane) *[4551-15-9]* **M 182.4, b 95-99°/12mm, d_4^{30} 0.97.** Purification is as for phenyl trimethylsilylmethyl sulfide.

Phenyl trimethoxysilane (trimethoxysilyl benzene) *[2996-92-1]* **M 198.3, b 103°/20mm, 130.5-131°/45mm, d_4^{35} 1.022, n_D^{35} 1.4698.** Fractionate it through an efficient column but note that it forms an azeotrope with MeOH which is a likely impurity. [Kantor *J Am Chem Soc* **75** 2712 *1953 Beilstein* **16** IV 1556.]

Phenyl trimethylsilylmethyl sulfide [(phenylthiomethyl)trimethylsilane] *[17873-08-4]* **M 196.4, b 48°/0.04mm, 113-115°/12mm, 158.5°/52mm, d_4^{30} 0.9671, n_D^{30} 1.5380.** If the sample is suspect, then add H_2O, wash it with 10% aqueous NaOH, H_2O again, dry (anhydrous $CaCl_2$) and fractionally distil it through a 2ft column packed with glass helices. [Cooper *J Am Chem Soc* **76** 3713 *1954*.]

Phosphine *[7803-51-2]* **M 34.0, m -133°, b -87.5°/760mm, -87.7°/760mm, critical temperature 51.3°, d^{25} 1.5307, pK^{25} ~ -14 (extremely weak base).** Phosphine is a gas with a very strong odour of fish and is **POISONOUS**. The gas is poorly soluble in H_2O (0.26ml/ml at 20°), and ignites spontaneously in air with a luminous glow. It has been prepared in various ways. A convenient preparation is to make aluminium phosphide by mixing 2 parts of Al powder and 1 part of red P on a piece of paper. By igniting the paper, the mixture becomes white-hot resulting in a spongy mass of aluminium phosphide [Hoffman *J Am Chem Soc* **43** 1684 *1921*, Bodoux *Bull Soc Chim Fr* **27** (3) 568 *1902*]. This phosphide reacts with cold H_2O to give a steady stream of PH_3. [Use an efficient fume cupboard in these experiments.] Fortunately, the gas is available in metal cylinders, but all due precautions should be taken. [Klement in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 525-530 *1963*, Gokhale and Jolly *Inorg Synth* **9** 56 *1967*, for basicity see Henderson & Streuli *J Am Chem Soc* **82** 5791 *1960*.]

Polystyrenesulfonic acid sodium salt (-$CH_2CH(C_6H_4SO_3Na)$-) *[25704-18-1]***.** Purify the polymer by repeated precipitation of the sodium salt from an aqueous solution by MeOH, with subsequent conversion to the free acid by passage through an Amberlite IR-120 ion-exchange resin. [Kotin & Nagasawa *J Am Chem Soc* **83** 1026 *1961*.] Recrystallise it from EtOH. *Alternatively*, purify it by passage through cation and anion exchange resins in series (Rexyn 101 cation exchange resin and Rexyn 203 anion exchange resin), then titrated it with NaOH to pH 7. The sodium form of polystyrenesulfonic acid is precipitated by addition of 2-propanol. Dry it in a vacuum oven at 80° for 24 hours, and finally increasing to 120° before to use. [Kowblansky & Ander *J Phys Chem* **80** 297 *1976*.]

Pontacyl Carmine 2G (Acid Red 1, Amido Naphthol Red G, Azophloxine, 1-acetamido-8-hydroxy-7-phenylazonaphthalene-3,7-disulfonic acid di-Na salt) *[3734-67-6]* **M 510.4, CI 18050, λ_{max} 532nm.** Salt it out three times with sodium acetate, then repeatedly extract it with EtOH. See Solochrome Violet R [2092-55-9] in "Aromatic compounds" in this Chapter. [McGrew & Schneider *J Am Chem Soc* **72** 2547 *1950*.]

Pontacyl Light Yellow GX [Acid Yellow 17, 1-(2,5-dichloro-4-sulfophenyl]-3-methyl-4-(4-sulfophenylazo)-5-hydroxypyrazole di-Na Salt] *[6359-98-4]* **M 551.3, CI 18965, λ_{max} 400nm.** Purify as for Pontacyl Carmine 2G above.

Potassium 4-acetylphenyltrifluoroborate *[252726-24-2]* **M 226.1, m >250°, 290°(dec).** The salt is prepared by adding an aqueous solution of KHF_2 (41ml, 4.5M solution, 185mmol) to a solution of 4-acetylphenylboronic acid (10g, 61mmol) in MeOH (40ml) at ~25°, when a heavy precipitate deposits, but the suspension is stirred for 1 hour at 25° and the solid is filtered off, washed with MeOH and recrystallised from the minimum volume of Me_2CO to provide *p*-AcC_4H_4-BF_3^- K^+ (12, 87%), m >250°. Its ^1H NMR [$(CD_3)_3CO$, 500MHz] has δ at 7.74(d, *J* = 7.8Hz, 2H), 7.59 (d, *J* = 7.8Hz, 2H), 2.49 (s, 3H); the ^{13}C NMR [$(CD_3)_3CO$, 125MHz] has δ at 198.1, 134.2, 131.3 (d, *J* = 1.5Hz), 126.2, 26.4; the ^{19}F NMR (DMSO-d_6, 470MHz) has δ at -140.3 (br s), and the ^{11}B NMR (DMSO-d_6, 64MHz) has δ at 3.27 (br s), and has the correct elemental analysis for C and H. It has been used for inserting a 4-acetylphenyl group into the position of a halogen or triflate group of various arenes and various heterocycles in Pd-catalysed Suzuki-Miyaura cross-coupling reactions [Molander & Biolatto *J Org Chem* **68** 4302 *2003*.]

Potassium 3,5-bis(trifluoromethyl)phenyltrifluoroborate *[166328-09-2]* **M 320.0, m >250°.** This salt was prepared by the same procedure as the preceding salt in 89% yield and recrystallised from the minimum volume of Me_2CO. Its ^1H NMR (DMSO-d_6, 500MHz) has δ at 7.87(s, 2H), 7.71 (s, 1H), 2.49 (s, 3H); the ^{13}C NMR

(DMSO-d_6, 125MHz) has δ at 131.2, 128.1 (q, J = 31Hz), 124.2 (q, J = 272Hz), 118.6 (s); the ^{19}F NMR (DMSO-d_6, 470MHz) has δ at -61.7, -141.6 (br d, J = 71Hz), and the ^{11}B NMR (DMSO-d_6, 64MHz) has δ at 2.57 (br s), and has the correct elemental analysis for C and H. It has been used for inserting a 3,5-bis(trifluoromethyl)phenyl group into the position of a halogen or triflate group of various arenes and various heterocycles in Pd-catalysed Suzuki-Miyaura cross-coupling reactions [Molander & Biolatto *J Org Chem* **68** 4302 *2003*, Vedejs et al. *J Org Chem* **60** 3020 *1995*.]

Potassium 2,6-difluorophenyltrifluoroborate *[267006-25-7]* **M 220.0, m <300°.** This salt was prepared by the same procedure as the preceding bis(trifluoromethyl) salt in 90% yield except that the crystalline precipitate was washed with H_2O then Et_2O and dried at high vacuum in a Schlenk line, and had m >250°. Its ^{1}H NMR (DMSO-d_6, 500MHz) has δ at 6.66 (m, 2H), 7.10 (m, 1H); the ^{13}C NMR (DMSO-d_6, 125MHz) has δ at 168.7 (dd, J = 242Hz, 18H), 127.5 (t, J = 11Hz), 110.0 (dd, J = 23Hz, 8H), 118.6 (s); the ^{19}F NMR (DMSO-d_6, 470MHz) has δ at -103.7 (q, J = 9.4Hz), -132.6 (qt, J = 43.9Hz); and the ^{11}B NMR (DMSO-d_6, 64MHz) has δ at 2.17 (q, J = 44Hz), and has the correct elemental analysis for C and H. It has been used for inserting a 2,6-difluorophenyl group into the position of a halogen or triflate group of various arenes and various heterocycles in Pd-catalysed Suzuki-Miyaura cross-coupling reactions [Molander & Biolatto *J Org Chem* **68** 4302 *2003*.]
Potassium 2,4-difluorophenyltrifluoroborate *[871231-41-3]* ***M 220.0, m >300°*** can be prepared by the same procedure as above and applied in similar reactions.

Potassium 2,6-dimethylphenyltrifluoroborate *[561328-67-4]* **M 212.1, m >250°.** This salt was prepared by the same procedure as the preceding difluorophenyl) salt in 88% yield except that the crystalline precipitate was washed with H_2O then Et_2O and dried at high vacuum in a Schlenk line and had m >250°. Its ^{1}H NMR (acetone-d_6, 500MHz) has δ at 6.83 (t, J = 7.4Hz, 1H), 6.75 (d, J = 7.4Hz, 2H), 2.40 (s, 6H); the ^{13}C NMR (acetone-d_6, 125MHz) has δ at 142.5, 127.7, 125.9, 23.8; the ^{19}F NMR (acetone-d_6, 470MHz) has δ at -132.5 (q, J = 48Hz); and the ^{11}B NMR (acetone-d_6, 64MHz) has δ at 4.94 (br d, J = 49Hz), and has the correct elemental analysis for C and H. It has been used for inserting a 2,6-dimethylphenyl group into the position of a halogen or triflate group of various arenes and various heterocycles in Pd-catalysed Suzuki-Miyaura cross-coupling reactions [Molander & Biolatto *J Org Chem* **68** 4302 *2003*, cf Vedejs et al. *J Org Chem* **60** 3020 *1995*.] ***Potassium 4-tert-butylphenyltrifluoroborate*** *[423118-47-2]* **M 240.1, m >230°,** can be similarly prepared from 4-*tert*-butylphenylboronic acid and used in Pd catalysed Suzuki cross-coupling reactions.

Potassium ethyl xanthate (potassium *O*-ethyl dithiocarbonate, potassium ethyl xanthogenate) *[140-89-6]* **M 160.3, m ~210°(dec), > 215°(dec), pK^{25} 2.16 (for –S$^-$).** It forms white to pale yellow crystals, prepared by adding ethanolic KOH dropwise to an ethanolic solution of CS_2 to form the salt which can be coaxed further out of solution by adding Et_2O. Crystallise it from absolute EtOH, ligroin/ethanol or acetone by adding Et_2O. Wash it with ether, then dry it in a desiccator. Its solubility at 56° in EtOH is >1% and in Me_2CO is 8% (the Na salt has 44%), and very high in H_2O at 25°. Dry it *in vacuo*, if it contains H_2O, and store it in a tightly stoppered bottle away from light. [Warren & Matthews *Anal Chem* **26** 1985 *1954*, *Beilstein* **3** H 209, **3** I 84 **3** II 152, **3** III 336, **3** IV 402.]

Potassium 2-furantrifluoroborate *[166328-14-9]* **M 174.0, m 200°(dec), >293-303°.** This salt has been prepared from furan (5.0ml, 68.7mmol, dried over 3Å Molecular Sieves) in dry THF (50ml) which was treated under N_2 with BuLi (42.0ml, 1.64M in pentane, 68.9mmol) and stirred at -5° for 3.5 hours to form furyllithium. The latter was treated with B(*iso*-PrO)$_3$ and allowed to warm to ~25°, quenched with 10% aqueous HCl (~50ml), diluted with Et_2O (50ml) and the organic layer was extracted with 1N NaOH (2 X 50ml). The alkaline extracts were combined, acidified to pH 3 with 10% aqueous HCl, and the acid layer was then extracted with Et_2O (3 x 50ml). The combined Et_2O extracts were dried (Na_2SO_4) and evaporated to dryness. The residual 2-furanboronic acid was dissolved in MeOH (200ml) and H_2O (40ml) was treated with 3 equivalents of KHF_2 (16g, 206mmol), refluxed overnight and evaporated to dryness *in vacuo*. The residue was extracted with MeCN (2 x 30ml), filtered and the filtrate was evaporated to dryness, the residue was washed with Et_2O, dried and recrystallised from MeCN/EtOAc to give pure 2-furan-BF_3^- K^+ (5.8g, 48%) as yellow crystals. Attempted TLC on Silica Gel with EtOAc caused hydrolysis of the salt to 2-furylboronic acid. Its IR (KBr) had bands at ν_{max} 1575 (C=C), 1005 (B-F), 970 (B-F) cm^{-1}, the ^{1}H NMR (CD_3CN, 200MHz) had δ at 7.44-7.33 (m, 1H), 6.25-

6.17 (m, 1H), 6.17-6.10 (m, 1H); and the ^{11}B NMR (CD_3CN, 160MHz) has δ (from $BF_3.OEt_2$, 0 ppm) 1.8 (q, *J* 49Hz) and it had the correct elemental analysis for C and H. It is air stable and has been used successfully in Pd-catalysed Suzuki-Miyaura cross-coupling reactions [Vedejs et al. *J Org Chem* **60** 3020 *1995*].

Potassium isoamyl xanthate (potassium *O*-isoamyl dithiocarbonate) *[61792-26-5]* **M 202.4, pK^{25} 1.82 (pK^0 2.8 free acid).** Crystallise it twice from acetone/diethyl ether. Dry it in a desiccator for two days and store it under refrigeration. Its solubility in Me_2CO is 2.3% at 56°. [See potassium ethyl xanthate above for storage, Warren & Matthews *Anal Chem* **26** 1985 *1954*, *Beilstein* **3** III 340, **3** IV 404.]

Potassium 4-methoxyphenyltrifluoroborate *[192863-36-8]* **M 214.0, m >300°.** The salt is prepared by mixing 4-methoxyphenylboronic acid (0.65g, 4.3mmol) and KHF_2 (0.76g, 9.7mmol) in H_2O (1ml) and MeOH (1.8ml) at ~25° for 2 hours and the resulting yellow slurry is taken up in Me_2CO (10ml) and evaporated under a vacuum. The residue is dissolved consecutively in hot Me_2CO and THF, filtered and Et_2O is added to give a yellow solid which is filtered off, washed with Et_2O until free from the yellow colour, and the crystalline material is dried in a Schlenk vacuum line to give *p*-$MeOC_4H_4$-BF_3^- K^+ (0.83g, 92%). Its ^{1}H NMR (acetone-d_6, 500MHz) has δ at 7.38 (d, *J* = 8.2Hz, 2H), 7.69 (d, *J* = 8.2Hz, 2H), 3.70 (s, 3H); the ^{13}C NMR (acetone-d_6, 125MHz) has δ at 158.9, 133.5, 112.8, 55.1; the ^{19}F NMR (acetone-d_6, 470MHz) has δ (from $CFCl_3$, 0ppm) at -142.28 (br d, *J* = 66Hz); and the ^{11}B NMR (acetone-d_6, 64MHz) has δ (from $BF_3.OEt_2$, 0ppm) at 4.8 (br s, *J* = 17Hz), and it has the correct elemental analysis for C and H. It is air stable and has been used successfully in Pd-catalysed Suzuki-Miyaura cross-coupling reactions [Molander & Biolatto *Org Lett* **4** 1867 *2002*].
Potassium 3-methoxyphenyltrifluoroborate *[438553-44-7]* ***M 214.0, m >300°*** was prepared in the same manner from 3-methoxyphenylboronic acid in 89% yield and had IR (KBr) with bands at ν_{max} 1241 (? C=C), 987 (B-F) cm^{-1}; the ^{1}H NMR (acetone-d_6, N, 500MHz) had δ: 7.03 (m, 3H), 6.61 (m, 1H), 3.67 (s, 3H); the ^{13}C NMR (acetone-d_6, 125MHz) had δ at 159.6, 128.2, 124.9, 117.6, 112.0 55.0; the ^{19}F NMR (acetone-d_6, 470MHz) had δ (from $CFCl_3$, 0ppm) at -142.8 (br d, *J* = 66Hz); and the ^{11}B NMR (acetone-d_6, 64MHz) had δ (from $BF_3.OEt_2$, 0ppm) at 4.2 (br s, *J* 43Hz), and it had the correct elemental analysis for C and H [Molander & Biolatto *Org Lett* **4** 1867 *2002*, cf Vedejs et al. *J Org Chem* **60** 3020 *1995*].
Potassium 2-methoxyphenyltrifluoroborate *[236388-46-8]* ***M 214.0, m >300°*** can be prepared in the same manner from 2-methoxyphenylboronic acid and used successfully in Pd-catalysed Suzuki-Miyaura cross-coupling reactions.

Potassium methyltrifluoroborate *[13862-28-7]* **M 121.94, m 168-183°, 183°.** This salt, which was used successfully in Pd-catalysed Suzuki-Miyaura cross-coupling is air stable, more robust and easier to handle than methylboronic acid. It is prepared by adding trimethyl boroxine (5.14g, 41mmol, 3 equivs, [823-96-1]) at room temperature to KHF_2 (19.0g, 243mmol, 6 equivs) in MeCN (200ml), and the mixture is cooled to 0° and stirred for 30 minutes. Then H_2O (4.5ml) is added and after stirring for 3 hours the solvent is evaporated and the resulting solid is dried thoroughly *in vacuo*. The residue is triturated with Me_2CO/MeOH (1:1, 100ml), filtered off, washed with the same mixture of solvents (100ml) and once with Me_2CO/MeOH (1:2, 100ml), and the remaining insoluble white solid is dried at high vacuum in a Schlenk line to give $MeBF_3^-$ K^+ (12.0g, 80%) as a white powder m 183°. Its ^{1}H NMR (D_2O, 500MHz) has δ at -0.15 (s), the ^{13}C NMR (D_2O, 125MHz) has δ at 1.40 to -1.14 (br s), ^{19}F NMR (D_2O, 470MHz) has δ at -132.3 (q, *J* = 64Hz), and ^{11}B NMR (D_2O, 64MHz) has δ at 7.25 (q, *J* = 64Hz). and has the correct elemental analysis for C and H. It has been used for inserting a methyl group in the position of a halogen or triflate group of various arenes. [Molander et al. *J Org Chem* **68** 5534 *2003*.]

Potassium nonafluorobutane sulfonate *[29420-49-3]* **M 338.2.** Wash it with H_2O and dry it *in vacuo*. When the K salt is distilled with 100% H_2SO_4, it gives the *free acid* which can be distilled (**b** 105°/22mm, 210-212°/760mm) and then converted to the pure K salt. [Gramstad & Haszeldine *J Chem Soc* 2640 *1957*, *Beilstein* **2** IV 818.]

Potassium phenol-4-sulfonate (4-hydroxybenzene-1-sulfonic acid K salt) *[30145-40-5]* **M 212.3.** Crystallise it several times from distilled water at 90°, after treatment with charcoal, and cooling to *ca* 10°. Dry it at 90-100°, *in vacuo*. [*Beilstein* **11** H 55, **11** I 242, **11** II 137, **11** III 498, **11** IV 582.]

Potassium phenyltrifluoroborate *[329976-74-1]* **M 212.1, m 290°, 296°(dec).** The salt is obtained by adding excess of saturated aqueous KHF_2 (125ml, *ca* 4.5M solution, 563mmol) dropwise to a solution of phenylboronic acid (20g, 169mmol, [98-80-6]) in MeOH (50ml) with vigorous stirring. The precipitate is collected after 15 minutes, washed with cold MeOH and recrystallised from the minimum volume of MeCN and dried *in vacuo* to give Ph-BF_3^- K^+ (25.5g, 82%), m 296°(dec.). Its ^{1}H NMR (CD_3CN, 200MHz) has δ at 7.44-7.41 (m, 2H), 7.22-7.05 (m, 3H); the ^{19}F NMR (CD_3CN, vs $CF_3C_6H_5$, 470MHz) has δ at -79 (1:1:1:1 q, *J* = 57Hz); and the ^{11}B NMR (CD_3CN, 160MHz) has δ: 4.1 (q, *J* = 57Hz), and it has the correct elemental analysis for C and H. [Vedejs et al. *J Org Chem* **60** 3020 *1995*, Thierig & Umland *Naturwissenschaften* **54** 563 *1967*.] It is air stable and has been used successfully in Pd-catalysed Suzuki-Miyaura cross-coupling reactions [Vedejs et al. *J Org Chem* **60** 3020 *1995*, Molander & Biolatto *J Org Chem* **68** 4302 *2003*]. ***Potassium 2-naphthalenetrifluoroborate*** *[668984-08-5]* ***M 234.1, m >300°*** can be prepared in the same manner from 2-naphthaleneboronic acid and used successfully in Pd-catalysed Suzuki-Miyaura cross-coupling reactions.

Potassium pyridine-3-trifluoroborate *[561328-69-6]* **M 185.0, m 228-232°.** The 3-pyridine salt is prepared under N_2 from 3-bromopyridine (3.46g, 21.9mmol) and triisopropyl borate (6.1ml, 26.4mmol) in a mixture of dry toluene (40ml) and dry THF (10ml) at -60° to which is added *n*-BuLi (39ml, 1.6M in hexane, 62mmol) dropwise, the mixture is stirred for 2 hours and allowed to warm to room temperature overnight. This mixture containing the pyridine-3-boronic lithium salt is cooled to 0° and an aqueous solution of KHF_2 (4.5M, 58mmol) is added dropwise and stirred for 4 hours then the mixture is evaporated to dryness. The residue is dissolved in MeOH, filtered, evaporated to dryness and the residual oil gave a solid (90%) under high vacuum. Its ^{1}H NMR (MeOD-d_3, 500MHz) has δ at 8.57 (br s, 1H), 8.26 (br d, *J* = 4.6Hz, 1H), 7.90 (d, *J* = 7.3, 1H), 7.23 (dd, *J* = 5.5, 6.6Hz, 1H); the ^{13}C NMR (DMSO-d_6, 125MHz) has δ: 153.0, 145.7, 138.8, 122.0; the ^{19}F NMR (DMSO-d_6, 470MHz) has δ: -134.9 (s); and the ^{11}B NMR (MeOD-d_3, 64MHz) has δ: 4.0 (br s). It has been used for inserting a 2,6-dimethylphenyl group into the position of a halogen or triflate group of various arenes and various heterocycles in Pd-catalysed Suzuki-Miyaura cross-coupling reactions [Molander & Biolatto *J Org Chem* **68** 4302 *2003*.]

Potassium tetraphenylborate *[3244-41-5]* **M 358.3.** Precipitate it from a solution of KCl acidified with dilute HCl, then crystallise it twice from acetone, wash it thoroughly with water and dry it at 110° [Findeis & de Vries *Anal Chem* **28** 1899 *1956*]. It has also been recrystallised from conductivity water. [*Beilstein* **16** IV 1625.]

Potassium 3-thiophenyltrifluoroborate *[192863-37-9]* **M 190.0, m >260°(dec).** This salt, which was used successfully in Pd-catalysed Suzuki-Miyaura cross-coupling is air stable, more robust and easier to handle than 3-thienyl boronic acid. 3-Thiophenylboronic acid (4.97g, 26.2mmol) and KHF_2 (5.14g, 65.8mmol) in a Nalgene (polyethylene) bottle (100ml) are stirred vigorously with MeOH (7.5ml) and H_2O (14ml) for 2 hours, and the amber solid formed is set aside at 4° for 2 hours. The solid was collected washed with the minimum of cold MeOH and dissolved in hot Me_2CO filtered, and the filtrate was cooled to 25° and Et_2O was added in portions with stirring, until the supernatant showed no cloudiness. The mixture was set aside at 4° for 1 hour until crystallisation was complete. The crystals were collected washed with a little cold Et_2O and dried *in vacuo* to give C_4H_3S-BF_3^- K^+ (4.68g, 94%). Its ^{1}H NMR [$(CD_3)_3CO$, 500MHz] has δ at 7.20 (s, 1H), 7.14 (m, 2H); the ^{13}C NMR [$(CD_3)_3CO$, 125MHz] has δ at 131.8, 125.2, 122.3; the ^{19}F NMR [$(CD_3)_3CO$, 470MHz] has δ at -139.5 (d, *J* = 75Hz), and it has the correct elemental analysis for C and H. It has been used for inserting a thiophenyl group into the position of a halogen or triflate group of various arenes and various heterocycles. [Molander & Biolatto *J Org Chem* **68** 4302 *2003*.] ***Potassium 5-methyl-2-thiophenyltrifluoroborate*** *[871231-40-2]* ***M 204.1, m >220°, >250° (dec also reported)*** can be similarly prepared from 5-methylthiophenyl-2-boronic acid and used in Pd catalysed Suzuki cross-coupling reactions.

Potassium trimethylsilanolate (trimethylsilanol K salt) *[10519-96-7]* **M 128.3, m 131-135° (cubic form), d^{25} 1.11, 125°dec (orthorhombic form).** Recrystallise it from H_2O and dry it at 100°/1-2mm. [Hyde et al. *J Am Chem Soc* **75** 5615 *1953*, IR: Tatlock & Rochow *J Org Chem* **17** 1555 *1952*, *Beilstein* **4** IV 3992.]

Propargyl triphenyl phosphonium bromide *[2091-46-5]* **M 381.4, m 179°.** It recrystallises from 2-propanol as white plates. It also crystallises from EtOH with **m** 156-158°. Its IR has ν_{max} at 1440, 1110cm^{-1} (P-C str). [Elter & Dediger *Justus Liebigs Ann Chem* **682** 62 *1965*, Schweizer et al. *J Org Chem* **42** 200 *1977*].

Propenyloxy trimethylsilane *[1833-53-0]* **M 130.3, b 93-95°/atm, d_4^{20} 0.786.** Purify it by fractional distillation using a very efficient column at atmospheric pressure. It usually contains 5% of hexamethyl-disiloxane that boils at 99-101°, but is generally non-reactive and need not be removed. [Hauser & Hance *J Am Chem Soc* **71** 5091 *1952*.] It has been distilled under N_2 through a 15cm column packed with glass helices. Fraction **b** 99-104° is further purified by gas chromatography through a Carbowax column (Autoprep A 700) at a column temperature of 87°, and has a retention time of 9.5 minutes. [Krüger & Rochow *J Organomet Chem* **1** 476 *1963-4*.]

1-Propenyltrimethylsilane (*cis and trans* mixture) *[17680-01-2]* **M 114.3, b 85-88°, n_D^{20} 1.4121.** Dissolve ~20g in THF (200ml), shake it with H_2O (2x 300 ml), dry (Na_2SO_4) and fractionate. This is a mixture of *cis* and *trans* isomers which can be separated by gas chromatography on an $AgNO_3$ column (for preparation: see Seyferth & Vaughan *J Organomet Chem* **1** 138 *1963*) at 25° with He as carrier gas at 9 psi. The *cis*-isomer has n_D^{25} 1.4105, and the *trans*-isomer has n_D^{25} 1.4062. [Seyferth et al. *Pure Appl Chem* **13** 159 *1966*.]

Propylphosphonic acid (1-propanephosphonic acid) *[4672-38-2]* **M 124.1, m 73°, pK_1^{25} 2.49, pK_2^{25}8.18 (H_2O).** The phosphonic acid is purified by recrystallisation from hexane, heptane or $*C_6H_6$ to give long colourless needles, and is dried *in vacuo* over KOH. It is best prepared from di-*n*-butylphosphite (50mmol), which is converted into its sodium salt in dry hexane (150ml, by stirring under reflux until Na has dissolved, ~3-5 hours), treated with an equivalent of *n*-propylbromide and refluxed gently for 5-6 hours. After cooling, the mixture is washed thoroughly with H_2O, the organic layer is dried by distillation under a vacuum, and the residual dibutyl *n*-propylphosphonate is refluxed with 50-70ml of concentrated HCl overnight, and distilled from an oil bath to remove, BuCl and BuOH until *ca* 30ml is left, then carefully evaporated *in vacuo* and the residual solid is recrystallised from $*C_6H_6$ and/or hexane to give *n*-propylphosphonic acid (~80% yield) m 72.5-74.5°. ***Diethyl propanephosphonate*** [18812-51-6] **M 180.2** has **b 88-89°/9mm, d_4^{25} 1.010, n_D^{20} 1.4172**, and its ^{13}C NMR (25MHz, MeCO d_6, TMS) has δ_C at 61.8 (ester ***C***H_3, $^3J_{P,C-3}$ = 5.9 Hz), 61.3 (ester ***C***H_2, $^2J_{P,C-2}$ = 6.2 Hz), 28.2 (P-***C***H_2, $^1J_{P,C-1}$ = 140.4 Hz), 16.7 (-CH_2-***C***H_2-CH_3, $^2J_{P,C-2}$ = 5.2 Hz) and 15.4 (propane ***C***H_3, $^3J_{P,C-3}$ = 16.2 Hz) ppm [Ernst *Org Mag Res* **9** 35 *1977*]. [Kosolapoff *J Am Chem Soc* **67** 1180 *1945*, *Beilstein* **4** H 596.]

Propylphosphonic anhydride (2,4,6-tripropyl-1,3,5,2,4,6-trioxatriphosphorinane-2,4,6-trioxide, T3P) *[68957-94-8]* **M 318.2 (cyclic trimer), b 200°/0.3mm 200-350°/0.01-50mm.** This reagent is prepared by heating *n*-propylphosphonic acid with acetic anhydride at 70-100°, and the polymeric phosphonic acid anhydride intermediate gives the trimeric cyclic anhydride on distilling at 200-350°/0.01-50mm. The anhydride is immediately made into 50% w/w solutions in DMF, CH_2Cl_2, EtOAc or BuOAc, which are also commercially available. It was originally used as a peptide coupling reagent, but has found many applications which require removal of the elements of water from organic molecules. It allows the synthesis of a variety of heterocyclic compounds, acylation reactions which involves C-C coupling, in the presence of DMSO alcohols can be oxidised to ketones; and with $NH_2OH.HCl$ and Et_3N in MeCN, TBDMSCl is a selective reagent for hydroxyamidation of carboxylic acids. [Llanes Garcia *Synlett* 1328 *2007*, Wehner et al. PCT Int. Appl. WO 2005014604 *2005*, *Chem Abstr* **142** 198208 *2005*, Wissmann & Kleiner *Angew Chem Int Ed Engl* **19** 133 *1980*, Escher & Bünning *Angew Chem Int Ed Engl* **25** 277 *1986*.]

3-(2-Pyridyl)-5,6-diphenyl-1,2,4-triazine-*p,p'*-disulfonic acid, monosodium salt (H_2O) [Ferrozine] *[63451-29-6]* **M 510.5, m >350°(dec).** Purify it by recrystallisation from water or by dissolving it in the minimum volume of water, followed by addition of EtOH to precipitate the pure salt. It is light sensitive and complexes with Fe. [Stookey *Anal Chem* **42** 779 *1970*.]

Pyrocatechol Violet (tetraphenolictriphenylmethanesulfonic acid Na salt) *[115-41-3]* **M 386.4, ε 1.4 x 10^4 at 445nm in acetate buffer pH 5.2-5.4, $pK_{Est(1)}$>0 (SO_3H), $pK_{Est(2)}$~9.4, $pK_{Est(3)}$~13.** It is recrystallised from glacial acetic acid. It is very *hygroscopic* and is an indicator standard for metal complex titrations. [Mustafin et al. *Zh Anal Khim* **22** 1808 *1967*, *Beilstein* **19/3** V 703.]

Pyrogallol Red (tetraphenolic xanthyliumphenylsulfonate) *[32638-88-3]* **M 418.4, m >300°(dec), ε 4.3 x 10^4 at 542nm, pH 7.9-8.6, pK_1 2.71, pK_2 6.60, pK_3 10.41, pK_4 12.16 (5% aqueous EtOH).** It is recrystallised from aqueous alkaline solution (Na_2CO_3 or NaOH) by precipitation on acidification. Filter the dye off and dry

it in a vacuum. [Suk *Col Czech Chem Commun* **31** 3127 *1966*, *Beilstein* **19** H 407, **19** II 417, **19** III/IV 599, **19/10** V 226.]

Rose Bengal [Acid Red 94, 4,5,6,7-tetrachloro-2'.4',5',7'-tetraiodofluorescein di-Na or di-K salt] *[di-Na salt 632-69-9]* **M 1017.7 (di-Na salt)** *[di-K salt 11121-48-5]* **M 1049.8 (di-K salt).** This biological stain can be purified by chromatography on silica TLC using a 35:65 mix of EtOH/acetone as eluent. [*Beilstein* **19** II 261, **19** III/IV 2926.]

Selenopyronine *[85051-91-8]* **M 365.8, λ_{max} 571nm (ε 81,000).** Purify it as the hydrochloride from hydrochloric acid [Fanghanel et al. *J Phys Chem* **91** 3700 *1987*]. [*Beilstein* **18** II 434.]

Selenourea *[630-10-4]* **M 123.0, m 200°(slow heating), 202-205°, 205-207°(dec), 214-215°(dec), 235°(dec).** Recrystallise it from the least volume of H_2O using Norite (preferably under N_2) to form colourless needles which are dried over P_2O_5. It is air and light sensitive. It slowly turns moderately dark on storage even below 0°. [King & Hlavacek *J Am Chem Soc* **73** 1864 *1951*, Dunbar & Painter *J Am Chem Soc* **69** 1833 *1947,* Bacher & Bos *Rec Trav Chim Pays Bas* **62** 580 *1943*, Hope *Acta Chem Scand* **18** 1800 *1964*.] The *Se-methyl iodide* provides yellow crystals from EtOH/Et_2O with **m 187-188°(dec)**. The *N,N-dimethyl* derivative crystallises from H_2O or EtOH as colourless needles which slowly turn pink, then gray on standing, and although slightly soluble in *benzene it can be recrystallised from it and has **m 167-170°(dec)** [Zingaro et al. *J Org Chem* **18** 292 *1953*, IR: Jensen & Nielsen *Acta Chem Scand* **20** 597 *1966*, *Beilstein* **3** IV 435.]

Silicon tetraacetate *[562-90-3]* **M 264.3, m 110-111°, b 148°/5-6mm, pK_1^{25} 9.7, pK_2^{25} 11.9 (for H_4SiO_4 free acid).** It can be crystallised from mixtures of CCl_4 and petroleum ether or Et_2O, or from acetic anhydride and then dried in a vacuum desiccator over KOH. Ac_2O adheres to the crystals and is removed first by drying at room temperature, then at 100° for several hours. It is soluble in Me_2CO, is very *hygroscopic* and effervesces with H_2O. It decomposes at 160-170°. [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 701 *1963*, *Beilstein* **2** H 171.]

Silver diethyldithiocarbamate *[1470-61-7]* **M 512.3, m 172°, 174°, 176-78°, pK_1^{25} 3.36 (for *N,N*-diethyldithio-carbamate).** Purify it by recrystallisation from pyridine or CO_2. Store it in a desiccator in a cool and dark place. [*Beilstein* **4** III 224, **4** IV 391.]

Silver tosylate *[16836-95-6]* **M 279.1.** The anhydrous salt is obtained by recrystallisation from H_2O. Store it in the dark. [Claesson & Wallin *Chem Ber* **12** 1851 *1879*, *Beilstein* **11** H 97, 99.]

Silver trifluoromethanesulfonate *[2923-28-6]* **M 256.9.** Recrystallise it twice from hot CCl_4 [Alo et al. *J Chem Soc, Perkin Trans 1* 805 *1986*]. Store it in the dark. [*Beilstein* **3** IV 34.]

Sodium *n*-alkylsulfates. Recrystallise these salts from EtOH/Me_2CO [Hashimoto & Thomas *J Am Chem Soc* **107** 4655 *1985*].

Sodium amylpenicillin *[575-47-3]* **M 350.4, m 188°(dec, anhydrous) $[\alpha]_D^{23}$ +319° (c 1, H_2O).** The *monohydrate* crystallises from moist acetone or moist ethyl acetate. Dry it in a vacuum. [Wintersteiner in "The Chemistry of Penicilin", Clarke, Johnson and Robinson eds, Princeton University Press, p 470 *1949*.]

Sodium 9,10-anthraquinone-1,5-disulfonate (H_2O) *[853-35-0]* **M 412.3.** Separate it from insoluble impurities by continuous extraction with water. Recrystallise it twice from hot water and dry it under vacuum. [*Beilstein* **11** II 195, **11** III 634.]

Sodium 9,10-anthraquinone-1-sulfonate (H_2O) *[107439-61-2]* **M 328.3.** Recrystallise it from hot water (4ml/g) after treatment with active charcoal, or from water by addition of EtOH. Dry it under vacuum over $CaCl_2$, or in an oven at 70°. Store it in the dark. [*Beilstein* **11** II 192, **11** III 626, **11** IV 670.]

Sodium 9,10-anthraquinone-2-sulfonate (H_2O) (9,10-anthraquinone-2-sulfonic acid [Na salt, H_2O]) *[131-08-8]* **M 328.3, pK_{Est} ~<0 (SO_3H).** It crystallises from H_2O or MeOH (charcoal). [Costa and Bookfield *J Chem Soc, Faraday Trans 1* **82** 991 *1986*, *Beilstein* **11** IV 671.]

Sodium benzenesulfinate (benzenesulfinic acid Na salt) *[873-55-2]* **M 164.2, m >300°, pK^{25} 2.16 (2.74, for $PhSO_2H$).** Dissolve it in the minimum volume of O_2 free H_2O (prepared by bubbling N_2 through for 2 hours) and adding O_2 free EtOH (prepared as for H_2O), set aside at 4° overnight under N_2, filter, wash with EtOH, then Et_2O and dry *in vacuo*. The Na salt is relatively stable to air oxidation, but is best kept under N_2 in the dark. Also recrystallise it from EtOH and dry it at 120° for 4 hours in a vacuum. [Kornblum & Wade *J Org Chem* **52** 5301 *1987*, *Beilstein* **11** II 2, **11** IV 3.]

Sodium benzenesulfonate *[515-42-4]* **M 150.1, pK_1^{25} 0.70 (2.55) (for $PhSO_3H_2$).** Crystallise it from EtOH or aqueous 70-100% MeOH, and dry it under a vacuum at 80-100°. [*Beilstein* **11** H 28, **11** I 10, **11** II 18, **11** III 33, **11** IV 27.]

Sodium bis(trimethylsilyl)amide (hexamethyl disilazane sodium salt) *[1070-89-9]* **M 183.4, m 165-167°(sintering at 140°).** It can be sublimed at 170°/2mm (bath temperature 220-250°) onto a cold finger, and can be recrystallised from $*C_6H_6$ (its solubility is: 10g in 100ml at 60°). It is slightly soluble in Et_2O and is decomposed by H_2O. [Wannagat & Niederprüm *Chem Ber* **94** 1540 *1961*.] It is available commercially under N_2 in Sure/Seal bottles in tetrahydrofuran (various concentrations) and at ~0.6M in toluene. [*Beilstein* **4** IV 4014.]

Sodium 4-bromobenzenesulfonate *[5015-75-8]* **M 258.7.** Crystallise it from MeOH, EtOH or distilled water. [*Beilstein* **11** H 570, **11** I 14, **11** II 30, **11** III 97.]

Sodium cacodylate ($3H_2O$) *[124-65-2]* **M 214.0, m 60°.** Recrystallise it from aqueous EtOH. [*Beilstein* **4** H 612, **4** I 576, **4** IV 1818, see cacodylic acid above.]

Sodium 4-chlorobenzenesulfonate *[5138-90-9]* **M 214.6, pK_{Est} <0 (for SO_3H).** Crystallise it twice from MeOH and dry it under vacuum. [*Beilstein* **11** IV 107.]

Sodium 3-chloro-5-methylbenzenesulfonate *[5138-92-1]* **M 228.7, pK_{Est} <0 (for SO_3H).** Crystallise it twice from MeOH and dry it under vacuum. [*Beilstein* **2** I 22.]

Sodium *p*-cymenesulfonate *[77060-21-0]* **M 236.3.** Dissolve the salt in water, filter and evaporate to dryness. Recrystallise it twice from absolute EtOH and dry it at 110°.

Sodium 1-decanesulfonate *[13419-61-9]* **M 244.33.** Recrystallise it from absolute EtOH and dry it over silica gel. [*Beilstein* **4** IV 62.]

Sodium *n*-decylsulfate *[142-87-0]* **M 239.3.** Rigorously purify it by continuous Et_2O extraction of a 1% aqueous solution for two weeks. [*Beilstein* **1** IV 1818.]

Sodium dibenzyldithiocarbamate *[55310-46-8]* **M 295.4, m 230°(dec), pK^{20} 3.13 (for monobenzyldithiocarbamic acid).** The free acid, when recrystallised twice from dry Et_2O, has **m** 80-82°. The Na salt is reprecipitated from aqueous EtOH or EtOH by addition of Et_2O or Me_2CO [Lindler *Anal Chem* **50** 896 *1978*]. The *NH_4 salt* has **m** 130-133°, the *Cu salt* (yellow crystals) has **m** 284-286°, and the *Ti salt* has **m** 64-70°. [*Beilstein* **12** IV 2275.]

Sodium 2,5-dichlorobenzenesulfonate *[5138-93-2]* **M 249.0, pK_{Est} <0 (for SO_3H).** Crystallise it from MeOH, and dry it under vacuum. [*Beilstein* **11** III 93.]

Sodium diethyldithiocarbamate ($3H_2O$) *[20624-25-3]* **M 225.3, m 94-96°(anhydrous), 98°, pK^{20} 3.65**

(diethyldithiocarbamic acid). Recrystallise it from water. [*Beilstein* **4** III 224, **4** IV 390.]

Sodium di(ethylhexyl)sulfosuccinate (Aerosol-OT, sodium docusate) *[577-11-7]* **M 444.6.** Dissolve it in MeOH and the inorganic salts which precipitate are filtered off. Water is added and the solution is extracted several times with hexane. The residue is evaporated to one-fifth its original volume, *benzene is added and azeotropic distillation is continued until no water remains. The solvent is evaporated. The white residual solid is crushed and dried *in vacuo* over P_2O_5 for 48 hours [El Seoud & Fendler *J Chem Soc, Faraday Trans 1* **71** 452 *1975*]. [*Beilstein* **4** IV 114.] It solubilises major myelin trans membrane proteolipids, and forms reverse micelles in hydrocarbon solvents.

Sodium 2,2'-dihydroxy-1-naphthaleneazobenzene-5'-sulfonate. See Solochrome Violet R [2092-55-9] in "Aromatic Compounds" in this Chapter.

Sodium 2,4-dihydroxyphenylazobenzene-4'-sulfonate (Tropaeolin O, Acid Orange 6) *[547-57-9]* **M 316.3.** Recrystallise it from absolute EtOH. It has λ_{max} at 490nm and CI (colour index) 14270. [*Beilstein* **16** H 275.]

Sodium *p*-(*p*-dimethylaminobenzeneazo)-benzenesulfonate *[23398-40-5]* **M 327.3.** Recrystallise it from water and dry it *in vacuo*. [*Beilstein* **16** H 331, **16** I 317, **16** II 169, **16** III 370, **16** IV 510.]

Sodium 2,4-dimethylbenzenesulfonate *[827-21-4]* **M 208.2.** Crystallise it from MeOH and dry it under vacuum. [*Beilstein* **11** III 339.]

Sodium 2,5-dimethylbenzenesulfonate (sodium *p*-xylenesulfonate) *[827-19-0]* **M 208.2.** Dissolve it in distilled water, filter it, then evaporate it to dryness. Recrystallise it twice from absolute EtOH or MeOH and dry it at 110° under vacuum. [*Beilstein* **11** III 93, **11** IV 502.]

Sodium dimethyldithiocarbamate hydrate *[128-04-1 (hydrate), 207233-95-2 (anhydrous)]* **M 143.2, m 106-108°, 120-122°, pK^{25} 3.36 (diethyldithiocarbamic acid).** Crystallise it from a small volume of H_2O, or dissolve it in the minimum volume of H_2O and add cold Me_2CO, collect it and dry it in air. The solubility in Me_2CO is ~12.5g/100ml. The *dihydrate* loses H_2O on heating at 115° to give the *hemi-hydrate* that decomposes on further heating [Kulka *Can J Chem* **34** 1096 *1956*]. [*Beilstein* **4** IV 233.]

Sodium *N*,*N*-dimethylsulfanilate *[2244-40-8]* **M 223.2, m >300°.** It crystallises from water. [See *Beilstein* **4** IV 270.]

Sodium 1-dodecanesulfonate *[2386-53-0]* **M 272.4, m >300°.** Recrystallise it twice from EtOH and dry it in an oven at 105° for 2 hours. It picks up moisture to form the $3.5H_2O$. Its *hydrate* crystallises in several phases. [Tartar & Wright *J Am Chem Soc* **61** 543 *1939*, Reed & Tartar *J Am Chem Soc I* ***57*** *571* 1935*, Beilstein* **4** III 27, **4** IV 64.]

Sodium 4-dodecylbenzenesulfonate *[25155-30-0]* **M 348.5.** It crystallises from propan-2-ol or H_2O. [Gray et al. *J Org Chem* **20** 515 *1955*, *Beilstein* **11** IV 514.]

Sodium dodecylsulfate (SDS, sodium laurylsulfate) *[151-21-3]* **M 288.4, m 204-207°.** Purify this detergent by Soxhlet extraction with petroleum ether for 24 hours, followed by dissolution in acetone/MeOH/H_2O 90:5:5(v/v) and recrystallisation [Politi et al. *J Phys Chem* **89** 2345 *1985*]. It has been purified by two recrystallisations from absolute EtOH, aqueous 95% EtOH, MeOH, isopropanol or a 1:1 mixture of EtOH/isopropanol to remove dodecanol, and dried under vacuum [Ramesh & Labes *J Am Chem Soc* **109** 3228 *1987*]. SDS has also been purified by repeatedly foaming whereby a 0.15% aqueous solution is made to foam and the foam is discarded, then the H_2O is removed *in vacuo* and the residue is diluted to the required concentrations [see Cockbain & McMullen *Trans Faraday Soc* **47** 322 *1951*], or by liquid-liquid extraction [see Harrold *J Colloid Sci* **15** 280 *1960*]. Dry it over silica gel. For DNA work it should be dissolved in excess MeOH passed through an activated charcoal column and evaporated until it crystallises out.
It has also been purified by dissolving in hot 95% EtOH (14ml/g), filtering and cooling, then drying in a vacuum

desiccator. *Alternatively*, it is crystallised from H_2O, vacuum dried, washed with anhydrous Et_2O and dried in vacuum again. These operations are repeated five times [Maritato *J Phys Chem* **89** 1341 *1985*, Lennox and McClelland *J Am Chem Soc* **108** 3771 *1986*, Dressik *J Am Chem Soc* **108** 7567 *1986*]. [*Beilstein* **1** IV 1847.]

Sodium ethylmercurithiosalicylate (Thimerosal) *[54-64-8]* **M 404.8, m ~230°.** Recrystallise this antibacterial from EtOH/Et_2O. **HIGHLY TOXIC.** [Trikojus *Nature* **158** 472 *1940*, *Beilstein* **10** III 213.]

Sodium ethylsulfate *[546-74-7]* **M 166.1.** Recrystallise it three times from MeOH/Et_2O and dry it in a vacuum. [*Beilstein* **1** H 326, **1** I 164, **1** III 1317, **1** IV 1325.]

Sodium formaldehyde sulfoxylate dihydrate (sodium hydroxymethylsulfinate, Rongalite) *[149-44-0]* **M 134.1, m 63-64° (dihydrate).** It crystallises from H_2O as the *dihydrate* and decomposes at higher temperatures. Store it in a closed container in a cool place. It is insoluble in EtOH and Et_2O and is a good reducing agent. [X-ray structure: Tuter *J Chem Soc* 3064 *1955*.] Note that this compound {$HOCH_2SO_2Na$} should not be confused with formaldehyde sodium bisulfite adduct {$HOCH_2SO_3Na$} from which it is prepared by reduction with Zn. [*Beilstein* **1** IV 3052.]

Sodium hexadecylsulfate *[1120-01-0]* **M 344.5.** Recrystallise it from absolute EtOH or MeOH and dry it in vacuum [Abu Hamdiyyah & Rahman *J Phys Chem* **91** 1531 *1987*].

Sodium 2-hydroxy-4-methoxybenzophenone-5-sulfonate *[6628-37-1]* **M 330.3.** Crystallise it from MeOH and dry it under vacuum.

Sodium *p*-hydroxyphenylazobenzene-*p'*-sulfonate *[2623-36-1]* **M 288.2.** Recrystallise it from 95% EtOH.

Sodium 2-mercaptoethanesulfonate (MESNA) *[19767-45-4]* **M 164.2, pK_1^{20} <0 (SO_3^-), pK_2^{20} 9.53 (SH).** It can be recrystallised from H_2O and does not melt below 250°. It is purified further by converting to the free acid by passing a 2M solution through an ion-exchange (Amberlite IR-120) column in the acid form, evaporating the eluate in a vacuum to give the acid as a viscous oil (readily decomposes) which can be checked by acid and SH titration. It is then dissolved in H_2O, carefully neutralised with aqueous NaOH, evaporated and the salt recrystallised from H_2O [Schramm *J Am Chem Soc* **77** 6231 *1955*]. [*Beilstein* **4** IV 85.]

Sodium metanilate *[1126-34-7]* **M 195.2.** It crystallises from hot water. [*Beilstein* **14** H 688.]

Sodium methanethiolate [sodium methylmercaptide] *[5188-07-8]* **M 70.1, pK^{25} 10.33 (MeS^-).** Dissolve the salt (10g) in EtOH (10ml) and add Et_2O (100ml). Cool and collect the precipitate, wash it with Et_2O and dry it in a vacuum. It is a white powder which is very soluble in EtOH and H_2O. [Billmann & Jensen *Bull Soc Chim Fr* **3** 2318 *1936*, *Beilstein* **1** III 1212.]

Sodium 3-methyl-1-butanesulfonate *[5343-41-9]* **M 174.1.** It crystallises from 90% MeOH.

Sodium 1-naphthalenesulfonate *[130-14-3]* **M 230.2.** Recrystallise it from water or aqueous acetone [Okadata et al. *J Am Chem Soc* **108** 2863 *1986*]. [*Beilstein* **11** IV 521.]

Sodium 2-naphthalenesulfonate *[532-02-5]* **M 230.2.** It crystallises from hot 10% aqueous NaOH or water and is dried in a steam oven. [*Beilstein* **11** IV 521.]

Sodium 2-naphthylamine-5,7-disulfonate (Amido-G-acid) *[79004-97-0]* **M 235.4.** Crystallise it from water (charcoal) and dry it in a steam oven. [*Beilstein* **14** H 784, **14** II 473, **14** IV 2811.]

Sodium 1-octanesulfonate H_2O *[5324-84-5]* **M 216.2.** Recrystallise it from absolute EtOH. [*Beilstein* **4** IV 58.]

Sodium phenol-4-sulfonate ($2H_2O$) (4-hydroxybenzenesulfonic acid Na salt) *[825-90-1]* **M 232.2.** It crystallises from hot water (g/1m) by cooling to 0°, or from MeOH, and is dried in vacuum. [*Beilstein* **11** II 134.]

Sodium piperazine-*N,N'*-bis(2-ethanesulfonate) H_2O (PIPES-Na salt) *[76836-02-7]* **M 364.3.** It crystallises from water and EtOH. [*Beilstein* **23/2** V 380.]

Sodium *iso*propyl xanthate (sodium *O-iso*propyldithiocarbonate) *[140-93-2]* **M 158.2, pK^{25} 2.16 (for $-S^-$).** It crystallises from ligroin/ethanol.

Sodium sulfanilate (sodium *p*-aminobenzenesulfonic acid) *[515-74-2]* **M 195.2.** It crystallises from water. [*Beilstein* **14** IV 2655.]

Sodium taurocholate [2-(3α,7α,12α-trihydroxy-24-oxo-5-β-cholan-24-ylamino)ethanesulfonic acid sodium salt monohydrate] *[145-42-6*; *312693-83-7; 345909-26-4 (x H_2O)]* **M 555.7 (monohydrate), m 168°dec (hydrate), $[\alpha]_D^{20}$ +23.9° (c 2.5, H_2O), pK of acid is 1.4.** The non-sulfated bile salt has been synthesised from *ethyl cholate* (**m 162-163°**, crystallised from EtOAc/petroleum ether b 30-60° 2:8) *via* the *hydrazide* (**m 210°**, sintering at 202°), which was diazotised to the *azide* ($NaNO_2$/HCl at 0-2°) and condensed with taurine in aqueous N NaOH at 8-14°/45 minutes. The acidified product was converted to *Na taurocholate* which was prepared and purified by precipitation with saturated aqueous NaCl and Et_2O (84% recovery; note that crystallisation does not occur unless enough H_2O is present) [Cortese *J Am Chem Soc* **59** 2532 *1937*]. It was also purified by recrystallisation from aqueous EtOH/Et_2O, or by gel chromatography using Sephadex LH-20. It is a useful anionic detergent for solubilising proteins and bilirubin [Wosiewitz & Schroebler *Experientia* **35** 717 *1979*]. It has a CMC of 3-11 mM at 20-25°, with an average micellar weight of 2100. It is hydrolysed by mineral acids to cholic acid and taurine. [Tanaka *Z physiol Chem* **220** 39 *1933*, *Beilstein* **10** III 1655, **10** IV 2078.]

Sodium tetradecylsulfate (sodium myristyl sulfate) *[1191-50-0]* **M 316.4.** It recrystallises from absolute EtOH [Abu Hamdiyyah & Rahman *J Phys Chem* **91** 1531 *1987*]. It is *hygroscopic*. [*Beilstein* **1** H 716, **1** IV 1866.]

Sodium tetrakis-(4-fluorophenyl)borate hydrate *[207683-22-5]* **M 450.2.** This gravimetric reagent for Cs is purified by passing a solution (10g in 100ml H_2O) through a column of Dowex 50Wx4 (Na form) and eluting with dilute NaCl. Extract the 250-275ml eluate with Et_2O (3 x 50ml), add dry xylene (200ml), evaporate the Et_2O off *in vacuo*, immerse the xylene in a bath at 50° and the salt crystallises out. It is *hygroscopic*. [Moore et al. *Anal Chim Acta* **35** 1 *1966*, Tsubouci et al. *Anal Chem* **57** 783 *1985*.]

Sodium tetraphenylborate [tetraphenyl boron Na] *[143-66-8]* **M 342.2.** Dissolve the borate in dry MeOH and add dry Et_2O. Collect the solid and dry it in a vacuum at 80°/2mm for 4 hours. It can also be extracted (Soxhlet) using $CHCl_3$, and it crystallises from $CHCl_3$ as snow-white needles. It is freely soluble in H_2O, Me_2CO but insoluble in petroleum ether and Et_2O. An aqueous solution has pH ~5 and can be stored for days at 25° or lower, and for 5 days at 45° without deterioration. Its solubility in polar solvents increases with decrease in temperature [Wittig & Raff *Justus Liebigs Ann Chem* **573** 204 *1950*]. The salt can also be recrystallised from acetone/hexane or $CHCl_3$, or from Et_2O/cyclohexane (3:2) by warming the solution to precipitate the compound. Dry it in a vacuum at 80°. It dissolves in Me_2CO at 50-60° to give a clear solution. After standing at this temperature for 10 minutes the mixture is filtered rapidly through a pre-heated Büchner funnel, cooled and the crystals are collected and dried in a vacuum desiccator at room temperature for 3 days [Abraham et al. *J Chem Soc, Faraday Trans 1* **80** 489 *1984*]. If the product gives a turbid aqueous solution, the turbidity can be removed by treating with freshly prepared alumina gel and filtering. [*Beilstein* **16** IV 1624.]

Sodium thioglycolate *[367-51-1]* **M 114.1.** It crystallises from 60% EtOH (charcoal). It is *hygroscopic*. [*Beilstein* **3** IV 600.]

Sodium 4-toluenesulfinate *[824-79-3]* **M 178.2, pK^{25} 2.80 (1.99)(for $-SO_2^-$).** Recrystallise the salt from

water (to constant UV spectrum) and dry it under vacuum, or extract it with hot *benzene, then dissolve it in EtOH/H_2O and heat with decolorising charcoal. The solution is filtered and cooled to give crystals of the *dihydrate*. [*Beilstein* **11** I 718.]

Sodium 4-toluenesulfonate *[657-84-1]* **M 194.2, pK^{25} -1.34 (for -SO_3^-).** Dissolve it in distilled water, filter it to remove insoluble impurities and evaporate it to dryness. Then recrystallise it from MeOH or EtOH, and dry it at 110°. Its solubility in EtOH is not high (maximum 2.5%), so that Soxhlet extraction with EtOH may be preferable. Sodium *p*-toluenesulfonate has also been crystallised from Et_2O and dried under a vacuum at 50°. [*Beilstein* **11** I 4, **11** II 6, *cf* Gibson & Reid *J Chem Soc* 879 *1923*.]

Sodium 2,2',4-trihydroxyazobenzene-5'-sulfonate *[3564-26-9]* **M 295.3.** Purify the dye by precipitating the free acid from aqueous solution using concentrated HCl, then wash it and extract it with EtOH in a Soxhlet extractor. Evaporation of the EtOH leaves the purified acid which is converted to the sodium salt with an equivalent of NaOH or Na_2CO_3.

Sodium 2,4,6-trimethylbenzenesulfonate *[6148-75-0]* **M 222.1.** Crystallise it twice from MeOH and dry it under vacuum. [*Beilstein* **11** III 345.]

Sodium trimethylsilanolate (sodium trimethylsilanol) *[18027-10-6]* **M 112.2, m 230°(dec).** It is very soluble in Et_2O and *C_6H_6 but moderately soluble in petroleum ether. It is purified by sublimation at 130-150° in a high vacuum. [Hyde et al. *J Am Chem Soc* **75** 5615 *1953*, Tatlock & Rochow *J Org Chem* **17** 1555 *1952*, *Beilstein* **4** III 1856.]

Sodium 3,5-xylenesulfonate *[30587-85-0]* **M 208.2.** Dissolve it in distilled water, filter, then evaporate it to dryness and recrystallise it twice from absolute EtOH and then dry it at 110°. [*Beilstein* **11** H 126, **11** I 34.]

Strontium thiosalicylate ($5H_2O$) *[15123-90-7]* **M 289.8.** It crystallises from hot water (0.5g/ml) by cooling to 0°. [*Beilstein* **10** IV 272.]

Sulfur trioxide pyridine complex *[26412-87-3]* **M 159.2, m 155-165°, 175°.** Wash the solid with a little CCl_4, then H_2O to remove traces of pyridine sulfate, and dry it over P_2O_5. [Baumgarten *Chem Ber* **59** 1166 *1926*, Olah et al. *Synthesis* 59 *1979*, *Beilstein* **20/5** V 184].

Tetrabutylammonium borohydride *[33725-74-5]* **M 257.3, m 128-129°.** Purify it by recrystallisation from EtOAc followed by careful drying under vacuum at 50-60°. Samples purified in this way showed no signs of loss of *active* H after storage at room temperature for more than 1 year. Nevertheless samples should be stored at *ca* 6° in tightly stoppered bottles if they are to be kept for long periods. It is soluble in CH_2Cl_2. [Raber & Guida *J Org Chem* **41** 690 *1976*, Brändström et al. *Tetrahedron Lett* 3173 *1972*.]

Tetrabutylammonium tetrafluoroborate *[429-42-5]* **M 329.3, m 161.8°, 161-163°, pK^{25} -4.9 (for HBF_4).** Recrystallise it from H_2O, aqueous EtOH or from EtOAc by cooling in Dry-ice. Also recrystallise it from ethyl acetate/pentane or dry acetonitrile. Dry it at 80° under vacuum. [Detty & Jones *J Am Chem Soc* **109** 5666 *1987*, Hartley & Faulkner *J Am Chem Soc* **107** 3436 *1985*.] The *acetate* has **m** 118±2° (from BuCl), the *bromide* has **m** 118° (from EtOAc) and the *nitrate* has **m** 120° (from *C_6H_6). [Witschonka & Kraus *J Am Chem Soc* **69** 2472 *1947*, Wheeler & Sandstedt *J Am Chem Soc* **77** 2024 *1955*, *Beilstein* **4** IV 558.]

Tetraethoxysilane (tetraethyl orthosilicate) *[78-10-4]* **M 208.3, m -77°, b 165-166°/atm, d_4^{20} 0.933, n_D^{25} 1.382.** Fractionate it through an 80cm Podbielniak type column with a heated jacket and partial take-off head. It is soluble in EtOH, and is slowly decomposed by H_2O and. *It is **flammable**–it irritates the eyes and mucous membranes*. [Sumrell & Ham *J Am Chem Soc* **78** 5573 *1956*, Bradley et al. *J Chem Soc* 5020 *1952*, *Beilstein* **1** IV 1360.]

Tetraethylammonium hexafluorophosphate *[429-07-2]* **M 275.2, m >300°, 331°(dec), pK_1^{25} ~ 0.5, pK_2^{25}**

5.12 (for fluorophosphoric acid H_2PO_3F). Dissolve the salt (0.8g) in hot H_2O (3.3ml) and cool to crystallise. Yield of prisms is 0.5g. Its solubility in H_2O is 8.1g/L at 19° [Lange & Müller *Chem Ber* **63** 1067 *1930*]. [*Beilstein* **4** III 199.]

Tetraethylammonium tetrafluoroborate *[429-06-1]* **M 217.1, m 235°, 356-367°, 275-277°, 289-291°. pK^{25} -4.9 (for HBF_4).** Dissolve the salt in hot MeOH, filter and add Et_2O. It is soluble in ethylene chloride [Thompson & Kraus *J Am Chem Soc* **69** 1016 *1947*, Wheeler & Sandstadt *J Am Chem Soc* **77** 2025 *1955*]. It has also been recrystallised three times from a mixture of ethyl acetate/hexane (5:1) or MeOH/petroleum ether, then stored at 95° for 48 hours under vacuum [Henry & Faulkner *J Am Chem Soc* **107 3436** *1985*, Huang et al. *Anal Chem* **58** 2889 *1986*]. It is used as a supporting electrolyte. [*Beilstein* **4** IV 333.]

Tetraethylsilane *[631-36-7]* **M 144.3, b 153.8°/760mm, d_4^{30} 0.77, n_D^{30} 1.427.** Fractionate it through a 3ft vacuum-jacketed column packed with 1/4" stainless steel saddles. The material is finally percolated through a 2ft column packed with alumina and maintained in an inert atmosphere. [Staveley et al. *J Chem Soc* 1992 *1954*, Altshaller & Rosenblum *J Am Chem Soc* **77** 272 *1955*, *Beilstein* **4** H 625.]

1.1.3.3-Tetraisopropyldisiloxane *[18043-71-5]* **M 246.5, b 129-130°/6mm, d_4^{30} 0.89, n_D^{30} 1.47.** Fractionate it under reduced pressure in a N_2 atmosphere. [Gilman & Clark *J Am Chem Soc* **69** 1500 *1947*.]

Tetrakis(hydroxymethyl)phosphonium chloride (THPC) *[124-64-1]* **M 190.6, m 151°.** THPC is prepared in an efficient fume cupboard by placing a mixture of 40% formaldehyde (90ml) and concentrated aqueous HCl (40ml, sp. gr. 1.2) into a 100ml 3-bulb Ladenburg flask (filling about half of the neck of the flask), the latter is provided with a stopper through which is passed a gas delivery tube that reaches the bottom. The flask is inclined to an almost horizontal position, when PH_3 (from a cylinder) is passed to displace the air, and the solution is heated to ~80° [note that at lower temperatures the reaction is slower, and at higher temperatures the vapour pressure of the solution decreases gas absorption]. The bulbs of the flask help to hold back the gas which results in a more complete reaction. The complete reaction may take up to many hours. Some H_2 and PH_3 which escape from the side neck of the flask should be vented through the flue of the fume cupboard. The mixture is then evaporated with stirring on a steam bath or *in vacuo* (~50 to 60°) until a white granular solid is obtained (50g ~ 88%). Its purity is good enough for most purposes. However, it can be purified to analytical purity by recrystallising 1g of THPC from 50ml of AcOH. The low melting flat needles obtained which contain AcOH of crystallisation are converted to the pure substance, **m 151°**, by blowing dry air at 100° over the crystals, or by drying them at 100° *in vacuo* to give a constant weight. It can also be recrystallised from absolute EtOH. [For a Kg scale laboratory preparation see Reeves et al. *J Am Chem Soc* **77** 3923 *1955*.] It is very deliquescent and should be kept in the presence of a desiccant. It is readily soluble in MeOH, slightly soluble in $CHCl_3$, but insoluble in Et_2O. It is quite stable, its aqueous solutions can be boiled without decomposition, and it is unaffected by dilute acids. The ^1H NMR (60MHz, D_2O, DSS) has δ for $4CH_2$ at 4.77 (s, J_{PCH} = 1.7Hz and $J_{^{13}CH}$ = ~153Hz), and the ^{31}P NMR (40MHz, D_2O, external 85% H_3PO_4) has δ at -25.8. With the stoichiometric amount of alkali, the free *tris(hydroxymethyl)phosphine* (see [2767-80-8] above) is obtained as an oil together with formaldehyde. However with excess of alkali on THPC, H_2 evolution occurs with the liberation of HCHO and formation of *tris(hydroxymethyl)phosphine oxide* (see [1067-12-5] below) **m 54-55°**. The reaction with alkali becomes more complicated when the mixture is heated, and *bis(hydroxymethyl)phosphinic acid* is formed. An 80% w/v aqueous solution of THPC with d_4^{20} 1.33 is available commercially. Also a 70-75% aqueous solution of *bis[tetrakis(hydroxymethyl)phosphonium] sulfate* [55566-30-8] M 406.3 is commercially available. [Hoffman *J Am Chem Soc* **43** 1684 *1921*, Hoffman *J Am Chem Soc* **52** 2995 *1930*, *Beilstein* **1** IV 3062.]

Tetramethoxysilane (tetramethyl orthosilicate) *[681-84-5]* **M 152.2, m 4.5°, b 122°/760mm.** Purification is as for tetraethoxysilane. It has a vapour pressure of 2.5mm at 0°. [IR: Sternbach & MacDiarmid *J Am Chem Soc* **81** 5109 *1959*. *Beilstein* **1** IV 1266.]

Tetramethylammonium borohydride *[16883-45-7]* **M 89.0.** Recrystallisation of the borohydride from H_2O three times yields *ca* 94% pure compound. Dry in high vacuum at 100° for 3 hours. The solubility in H_2O is 48% (20°), 61% (40°), in EtOH it is 0.5% (25°), and in MeCN it is 0.4% (25°). It decomposes slowly in a

vacuum at 150°, but rapidly at 250°. The rate of hydrolysis of $Me_4N.BH_4$ (5.8M) in H_2O at 40° is constant over a period of 100 hours at 0.04% of original wt/hour. The rate decreases to 0.02%/hour in the presence of Me_4NOH (5% of the wt of $Me_4N.BH_4$). [Banus et al. *J Am Chem Soc* **74** 2346 *1952*, *Beilstein* **4** IV 148.]

Tetramethylammonium hexafluorophosphate *[558-32-7]* **M 219.1, m >300°, d_4^{25} 1.617, pK_1^{25} ~ 0.5, pK_2^{25} 5.12 (for fluorophosphoric acid H_2PO_3F).** The salt (0.63g) is recrystallised from boiling H_2O (76ml), yielding pure (0.45) $Me_4N.PF_6$ after drying at 100°. It is a good supporting electrolyte. [Lange & Müller *Chem Ber* **63** 1067 *1930*, *Beilstein* **4** III 110.]

Tetramethylammonium triacetoxyborohydride *[109704-53-2]* **M 263.1, m 93-98°, 96.5-98°.** If impure, wash it with freshly distilled Et_2O and dry it overnight in a vacuum to give a free flowing powder. Check ^1H NMR, and if still suspect prepare it freshly from Me_4NBH_4 and AcOH in $*C_6H_6$ and store it away from moisture [Banus et al. *J Am Chem Soc* **74** 2346 *1952*, Evans & Chipman *Tetrahedron Lett* **27** 5939 *1986*]. It is an **IRRITANT** and **MOISTURE SENSITIVE**.

Tetramethylammonium triphenylborofluoride *[437-11-6]* **M 392.2.** Crystallise it from acetone or acetone/ethanol. [*Beilstein* **4** IV 15.]

2,4,6,8-Tetramethylcyclotetrasiloxane (TMCTS) *[2370-88-9]* **M 240.5, m -69°, b 134°/750mm, 134.5-134.9°/755mm, d_4^{20} 0.99, n_D^{20} 1.3872.** It is purified by repeated redistillation, and fractions with the required ^1H NMR data are collected. [Sokolov *J Gen Chem USSR (Engl Transl)* **29** 262 *1959*, Sauer et al. *J Am Chem Soc* **68** 962 *1946*]. [*Beilstein* **4** IV 4099.]

1,1,3,3-Tetramethyldisiloxane *[3277-26-7]* **M 134.3, b 70.5-71°/731mm, 71-72°/atm, d_4^{30} 0.75, n_D^{25} 11.367.** Possible impurity is 1,1,5,5-tetramethyl-3-trimethylsiloxytrisiloxane **b** 154-155°/733mm. Fractionate it, collect fractions boiling below 80° and re-fractionate it. Its purity can be analysed by alkaline hydrolysis and measuring the volume of H_2 liberated followed by gravimetric estimation of silica in the hydrolysate. It is unchanged when stored in glass containers in the absence of moisture for 2-3 weeks. Small amounts of H_2 are liberated on long storage. ***Care** should be taken when opening a container due to developed pressure.* [Speier et al. *J Am Chem Soc* **79** 974 *1958*, Emeléus & Smythe *J Chem Soc* 609 *1958*, IR: Kriegsmann *Z Anorg Chem* **299** 78 *1959*, *Beilstein* **4** IV 3991.]

***N,N,N′N′*-Tetramethylphosphonic diamide (methylphosphonic bis-dimethylamide)** *[2511-17-3]* **M 150.2, b 60.5°/0.6mm, 138°/32mm, 230-230°/atm, d_4^{30} 1.0157, n_D^{30} 1.4539.** Dissolve it in heptane or ethylbenzene, shake this with 30% aqueous NaOH, stir for 1 hour, separate the organic layer and fractionate. [Kosolapoff & Payne *J Org Chem* **21** 413 *1956*.] Its IR (film) has ν□□□ at 1480, 1460, 1300, 1184, 1065 and 988-970cm^{-1} [Harvey & Mayhood *Can J Chem* **33** 1552 *1955*].

Tetramethylsilane (TMS) *[75-76-3]* **M 88.2, b 26.3°, d_4^{20} 0.639, n_D^{20} 1.359.** Distil it from conc H_2SO_4 (after shaking with it) or $LiAlH_4$, through a 5ft vacuum-jacketed column packed with glass helices into an ice-cooled condenser, then percolate it through silica gel to remove traces of halide. [For preparation on a 250g scale see Whitmore & Sommer *J Am Chem Soc* **68** 481 *1946*, *Beilstein* **4** IV 3875.]

2,4,6,8-Tetramethyl tetravinyl cyclotetrasiloxane *[2554-06-5]* **M 344.7, m -43.5°, b 111-112°/10mm, 145-146°/13mm, 224-224.5°/758mm, d_4^{30} 0.98, n_D^{30} 1.434.** A 7ml sample can be distilled in a small Vigreux column at atmospheric pressure without polymerisation or decomposition. It is soluble in cyclohexane. [Kantor et al. *J Am Chem Soc* **77** 1685 *1955*, *Beilstein* **4** IV 4184.]

Tetraphenylarsonium chloride hydrate *[507-28-8]* **M 418.8, m 258-260°, 261-263°.** A neutralised aqueous solution is evaporated to dryness. The residue is extracted into absolute EtOH, evaporated to a small volume and precipitated by addition of absolute Et_2O. It is again dissolved in a small volume of absolute EtOH or ethyl acetate and re-precipitated with Et_2O. *Alternatively*, it is purified by adding conc HCl to precipitate the chloride dihydrate. Redissolve in water, neutralise with Na_2CO_3 and evaporate to dryness. The residue is extracted with

$CHCl_3$ and finally crystallised from CH_2Cl_2 or EtOH by adding Et_2O. If the aqueous layer is somewhat turbid treat it with Celite and filter it through filter paper. It can be dehydrated before use in a vacuum. The *tetrafluoroborate* salt has **m** 293-295° (needles from MeCN), and the *picrate* salt has **m** 203-204° (from EtOH). [Blicke et al. *J Am Chem Soc* **57** 702 *1935*, Duke & Brown *J Am Chem Soc* **76** 1443 *1954*, Popov & Humphrey *J Am Chem Soc* **81** 2043 *1959*, Singhal & Raj *Synth Inorg Met-org Chem* **23** 1011 *1993*, *Beilstein* **16** III 1006, **16** IV 1170.] **POISONOUS.**

Tetraphenylarsonium iodide *[7422-32-4]* **M 510.2.** It crystallises from MeOH. [Blicke et al. *J Am Chem Soc* **57** 702 *1935*, Chatt et al. *J Chem Soc* 1192 *1940*.] **POISONOUS.**

Tetraphenylarsonium perchlorate *[3084-10-4]* **M 482.8, pK^{25} -2.4 to -3.1 (for $HClO_4$).** It crystallises from MeOH. [Horner et al. *Chem Ber* **101** 2903 *1968*.] **POISONOUS and possibly explosive.**

Tetraphenylbiphosphine (Ph_2P-PPh_2) *[1101-41-3]* **M 370.4, m 120.5° (evacuated tube), 120-122° (sealed tube), b 258-260°/1mm. pK_{Est} >0.0.** This useful precursor of diphenylphosphine compounds is made by heating a mixture of diphenylphosphine (6.0g, 32.5mmol, 829-85-6) and chlorodiphenylphosphine (7.1g, 32.5mmol, 1709-66-9) in petroleum ether (100ml, b 90-100°, freshly distilled over Na) under N_2 at reflux for 3.5 hours during which time all the HCl has evolved. The white crystalline biphosphine that separates (~80%) on cooling is collected, washed with ligroin, dried *in vacuo* and recrystallised or distilled at high vacuum, preferably in a N_2 atmosphere. It is soluble in $*C_6H_6$, toluene, CCl_4, and pyridine (yellow solution), and slightly soluble in Et_2O, EtOH and ligroin. The determined molecular weight was 391.6, 374.9 (method of Rast). When it is heated for 3 hours at 250-300° under N_2, phosphorus is liberated. The brown residue is boiled for 1 hour with dilute aqueous NaOH and 3% of H_2O_2, filtered, cooled, the solid that is collected gives *Ph_3PO* (m 153° and mixed m with authentic Ph_3PO) after crystallisation from petroleum ether (b 90-100°). *Diphenylphosphonic acid* [**m 191-192°** and mixed melting point with authentic $Ph_2P(O)OH$] can be isolated from the mother liquors, making a total yield of products almost quantitative. Reaction of a suspension of the biphosphine (3.3g) in CCl_4 under N_2 with Br (1ml) in CCl_4 is decolourised as it becomes clear. The mixture is then distilled and the oily residue is redistilled to give *bromodiphenylphosphine* (**b 146.5-148°/2.5mm**) as a colourless oil in almost quantitative yield. Bubbling dry air through a suspension of the biphosphine (3.3g) in dry toluene (30ml) at ~0° for 3 hours causes the mixture to become yellow in colour, and after dilution with toluene (30ml) and boiling for a short period it becomes clear. On cooling, and recrystallising the solid that separates from fresh toluene provides the white *dioxide $Ph_2P(O)$-$P(O)Ph_2$* (**m 167°**, evacuated tube, 1.9g, 53%), with a molecular weight of 418.5, 409.8 (measured by the method of Rast; the required value is 402.4). [Kuchen & Buchwald *Chem Ber* **91** 2871 *1958*, *Beilstein* **16** H 2871.]
Sodium dipenylphosphine (Ph_2PNa) is readily prepared by adding Na to a solution of the diphosphine in dry Et_2O or THF (exothermic!), whereby the colour becomes yellow and the orange Na salt separates. It is sensitive to moisture (giving Ph_2PH) and to CO_2 (giving Ph_2PCOOH); and the necessary precautions have to be taken. It is a useful reagent for preparing a variety of Ph_2P-R derivatives and it is best to prepare it freshly when required. [Kuchen & Buchwald *Chem Ber* **92** 227 *1959*.]

Tetraphenylboron potassium see potassium tetraphenylborate.

Tetraphenylphosphonium chloride *[2001-45-8]* **M 374.9, m 273-275°.** Crystallise the chloride from acetone and dry at 70° under vacuum. It can also be recrystallised from a mixture of 1:1 or 1:2 dichloromethane/petroleum ether, the solvents having been dried over anhydrous K_2CO_3. The purified salt is dried at room temperature under a vacuum for 3 days, and at 170° for a further 3 days. It also crystallises from isoPrOH/Et_2O or EtOH/Et_2O. *Extremely hygroscopic.* [Wittig & Geissler *Justus Liebigs Ann Chem* **580** 44, 50 *1953*, Willard et al. *J Am Chem Soc* **70** 737 *1948*, *Beilstein* **16** III 851, **16** IV 984.]

Tetraphenylsilane *[1048-08-4]* **M 336.4, m 231-233°, 234-235°, 236-238°.** It crystallises from *benzene as clear colourless bladed needles. It decomposes at ~360°/~760mm on attempted distillation. [George et al. *J Am Chem Soc* **77** 6647 *1955*, Polis *Chem Ber* **98** 1540 *1885*, Drew & Landuist *J Chem Soc* 1480 *1935*,s *Beilstein* **16** H 901, **16** I 525, **16** II 606, **16** III 1199, **16** IV 1372.]

Tetrasodium pyrene-1,3,6,8-tetrasulfonate *[59572-10-0]* **M 610.5.** Recrystallise this salt from aqueous acetone [Okahata et al. *J Am Chem Soc* **108** 2863 *1986*].

Thexyl dimethyl chlorosilane (dimethyl-[2,3-dimethyl-2-butyl] chlorosilane) *[67373-56-2]* **M 178.8, b 55-56°/10mm, 158-159°/720mm, d_4^{20} 0.970, n_D^{20} 1.428.** Purify this chlorosilane by fractional distillation, and store it in small aliquots in sealed ampoules. It is very sensitive to moisture and is estimated by dissolving an aliquot in excess of 0.1M NaOH and titrating with 0.1M HCl using methyl red as indicator [Szabó et al. *Helv Chim Acta* **67** 2128 *1984*].

***N*-(Thexyl dimethylsilyl)dimethylamine (*N*-[2,3-dimethyl-2-butyl]dimethylsilyl dimethyl-amine)** *[81484-86-8]* **M 187.4, b 156-160°/720mm.** Dissolve the amine in hexane, filter, evaporate and distil. It is a colourless oil which is extremely sensitive to moisture. It is best to store small quatities in sealed ampoules after distillation. For estimation of purity, crush an ampoule in excess 0.1N HCl and titrate the excess acid with 0.1M NaOH using methyl red as indicator. [Szabó et al. *Helv Chim Acta* **67** 2128 *1984*.]

Tribenzyl chlorosilane *[18740-59-5]* **M 336.9, m 139-142°, 141-142°, b 300-360°/100mm.** It is recrystallised three times from petroleum ether (in slender colourless needles, **m** 141°). It is sparingly soluble in cold petroleum ether but is soluble in Et_2O. It does not fume in moist air but is decomposed by H_2O to give *tribenzyl silanol* **m** 106° (from petroleum ether). [Robinson & Kipping *J Chem Soc* **93** 439 *1908*, Jenkins & Post *J Org Chem* **15** 556 *1950*, *Beilstein* **16** H 906, **16** IV 1498.]

Tribenzyl phosphine *[76650-89-7]* **M 304.4, m 96-101°, b 203-210°/0.5mm, pK_{Est}~8.8.** Dissolve it in Et_2O, dry it over Na_2SO_4, evaporate and distil it in an inert atmosphere. The distillate solidifies on cooling and is sublimed at 140°/0.001mm. This has **m** 92-95° (evacuated capillary). When air is bubbled through an Et_2O solution, it is oxidised to *tribenzyl phosphine oxide*, **m** 209-212° (evacuated capillary) (it crystallises from Me_2CO). [Hinton & Mann *J Chem Soc* 2835 *1959*, *Beilstein* **16** H 771, **16** IV 961.]

Tri-*n*-butyl borate *[688-74-4]* **M 230.2, b 110°/11mm, 136°/30mm, 232.4°, d_4^{20} 0.857, n_D^{20} 1.4092.** The chief impurities are *n*-butyl alcohol and boric acid (from hydrolysis). It must be handled in a dry-box and can readily be purified by fractional distillation, under reduced pressure. [O'Brien *Aust J Chem* **10** 91 *1957*, Gerrard & Lappert *J Chem Soc* 2545, 2547 *1951*, *Beilstein* **1** IV 1544.]

Tri-*n*-butyl chlorosilane *[995-45-9]* **M 234.9, b 93-94°/4.5mm, 134-139°/16mm, 250-252°/atm, 142-144°/29mm, d_4^{20} 0.88, n_D^{20} 1.447.** Fractionally distil this silane, and store it in small aliquots in sealed ampoules. [Gilman et al. *J Am Chem Soc* **74** 1361 *1952*, Osthoff & Clark *J Org Chem* **24** 219 *1959*, *Beilstein* **4** IV 4072.]

Tri-*n*-butyl phosphate (butyl phosphate) *[126-73-8]* **M 266.3, m -80°, b 47°/0.45mm, 98°/0.1mm, 121-124°/3mm, 136-137°/5.5mm, 166-167°/17mm, 177-178°/27mm, 289°/760mm (some dec), d_4^{20} 0.980, n_D^{20} 1.44249.** The main contaminants in commercial samples are organic pyrophosphates, mono- and di- butyl phosphates and butanol. It is purified by washing successively with 0.2M HNO_3 (three times), 0.2M NaOH (three times) and water (three times), then fractionally distilled under vacuum. [Yoshida *J Inorg Nucl Chem* **24** 1257 *1962*.] It has also been purified *via* its uranyl nitrate addition compound, obtained by saturating the crude phosphate with uranyl nitrate. This compound is crystallised three times from *n*-hexane by cooling to -40°, and then decomposed by washing with Na_2CO_3 and water. Hexane is removed by steam distillation; the water is then evaporated under reduced pressure, and the residue is distilled under reduced pressure. [Siddall & Dukes *J Am Chem Soc* **81** 790 *1959*.]
Alternatively, wash it with water, then with 1% NaOH or 5% Na_2CO_3 for several hours, then finally with water. Dry it under reduced pressure and fractionate it carefully under vacuum. It is a stable colourless oil, sparingly soluble in H_2O (1ml dissolves in 165ml of H_2O), but freely miscible in organic solvents. [Kuivila & Masterton *J Am Chem Soc* **74** 4953 *1952*, Cox & Westheimer *J Am Chem Soc* **80** 5441 *1958*, ^{31}P NMR: Van Wazer *J Am Chem Soc* **78** 5715 *1956*, Fertig et al. *J Chem Soc* 1488 *1957*, *Beilstein* **1** IV 1531.]

Tri-*n*-butyl phosphine (TBP) *[998-40-3]* **M 202.3, b 109-110°/10mm, 115-116°/12mm, 149.5°/50mm, 240.4-**

242.2°/atm, d_4^{20} 0.822, n_D^{20} 1.4463, pK_{Est}~7.6. Fractionally distil TBP under reduced pressure in an inert atmosphere (N_2) through an 8 inch gauze-packed column (**b** 110-111°/10mm), and redistil it in a vacuum, then seal it in thin glass ampoules. It is easily oxidised by air to *tri-n-butylphosphine oxide,* **b** 293-296°/745mm. It has a characteristic odour, it is soluble in EtOH, Et_2O, and $*C_6H_6$, but is insoluble in H_2O; and is less easily oxidised by air than the lower molecular weight phosphines. It forms complexes, e.g. with CS_2 (1:1) **m** 65.5° (from EtOH). [Davies & Jones *J Chem Soc* 33 *1929*, Chernick & Skinner *J Chem Soc* 1401 *1956*, *Beilstein* **4** IV 3436.] Unlike with Ph_3P, $(MeO)_3P$, $(Me_2N)_3P$ or Me_3P, when $(n\text{-}Bu)_3P$ is complexed with DEAD, best results are achieved in the Mitsunobu lactonisation of the final stage in the synthesis of the strained lactone (-)-Echinosporin (XK-213) [Smith et al. *J Am Chem Soc* **114** 2567 *1992*].

Tri-*tert*-butylphosphine *[*13716-*12-6]* **M 202.3, m ~30-35°, 62.3°, b 103-103°/13mm, d_4^{20} 0.834, pK^{25} 11.4.** It is prepared from *tert*-butylmagnesium chloride and PCl_3 in Et_2O and finally purified by vacuum fractionation and distillation. [Ger Pat, IG Farbenind DRP 730 638 *1939*, DRP *Org Chem* **3** 1144.] A 1.0M solution in toluene is commercially available (**d^{25} 0.861 g/l**). [*Beilstein* **4** III 1771.]
It is used with $Pd_2(dba)_3$ and Bu_3SnF in the Pd-catalysed regiocontrolled α-arylation of trimethylsilyl enol ethers with aryl halides [Iwama & Rawal *Org Lett* **8** 5725 *2006*], is a useful ligand for Pd-catalysed Suzuki-type coupling of arylboronic acids with phenyliodonium ylides of hydroxyquinones [Kazantzi et al. *Synlett* 2597 *2006*] and is a good ligand for $Ni(acac)_2$ in catalysing the cross-coupling of aryl- and heteroaryl- halides with aryl Grignard reagents [Böhm et al. *Angew Chem. Int Ed* **39** 1602 *2000*].

Tri-*tert*-butylphosphine oxide *[*6866-*70-2]* **M 218.3, m 64-69°, 70°, 77°.** The oxide has been prepared by treating $t\text{-}Bu_3P$ (1.7g, 85mmol) in Et_2O (20ml) containing a catalytic amount of KI (0.1g) with 30% of H_2O_2 until the colour of iodine disappears. The mixture is diluted with H_2O, basified with aqueous NaOH, the ethereal layer is evaporated, and the phosphine oxide (1.5g, 81%, **m 77°**) is obtained by sublimation at 50°/0.1mm. It is a crystalline hygroscopic solid that is soluble in most organic solvents, and is stable to 250°. Its IR (Nujol) has ν_{max} at 1160 (P=O, s) and 815 (P-C, br s) cm^{-1}; the ^1H NMR (C_6D_6, TMS) has δ_H at 0.59 (d, $^3J_{P\text{-}H}$ = 12.1Hz, C-Me_3); the ^{13}C NMR (C_6D_6, TMS) has δ_C at 29.08 (s, CH_3), 38.95 (d, $^1J_{P\text{-}C}$ = 51.27, C), and its ^{31}P NMR (C_6D_6, external H_3PO_4) has δ at 60.86. [Schmidbauer & Blaschke *Z Naturforsch* **33B** 1556 *1978*, Rankin et al. *JCS Dalton Trans* 827 *1985*.]

Tri-*n*-butyl phosphite *[102-85-2]* **M 250.3, b 114-115°/5mm, 122°/12mm, 130°/17mm, 137°/26mm, d_4^{20} 0.926, n_D^{20} 1.4924.** Fractionate the phosphite through an efficient column. It is stable in air but is slowly hydrolysed by H_2O. [Gerrard *J Chem Soc* 1464 *1940*, Fertig et al. *J Chem Soc* 1488 *1957*, Fields *J Am Chem Soc* **80** 2358 *1958*, Gillis et al. *J Am Chem Soc* **80** 2999 *1958*, *Beilstein* **1** IV 1527.]

B-Trichloroborazine [B-trichloroborazole) *[933-18-6]* **M 183.1, m 83.9-84.5°(sealed evacuated cappillary), 87°, b 88-92°/21mm, d_4^{25} 1.58.** Purify the borazine by distillation from mineral oil. It sublimes at 70°/1mm. [Brown & Laubangayer *J Am Chem Soc* **77** 3699 *1955*, Emeléus & Videla *J Chem Soc* 1306 *1959*.] It is extremely sensitive to moisture and reacts with H_2O exothermically to give boric acid and NH_4Cl. Store it in sealed tubes. It is soluble in $*C_6H_6$, cyclohexane, CS_2, $CHCl_3$, CCl_4, and C_6H_5Cl without decomposition, but in MeOH or EtOH it reacts vigorously, liberating HCl. It is insoluble in pyridine and $C_6H_5NO_2$. [*Beilstein* **4** III 174, **1** IV 305.]

Trichloromethyl trimethylsilane (trimethylsilyl trichloromethane) *[5936-98-1]* **M 191.6, m 130-132°, b 146-156°/749mm.** This silane distils at atmospheric pressure without decomposition and readily sublimes at 70°/10mm. It has one peak in the ^1H NMR spectrum (CD_2Cl_2) with δ at 0.38. [Speier *J Am Chem Soc* **73** 824 *1951*, Hergott & Simchen *Synthesis* 626 *1980*, *Beilstein* **4** IV 3892.]

Trichlorosilane ($SiHCl_3$, silicochloroform) *[10025-78-2]* **M 135.4, m -126°, b 31,8°/atm, 32-34°/atm, 36.5°/atm, d_4^{25} 1.342, n_D^{20} 1.4020.** This volatile trichlorosilane can be obtained from silane and HCl in the presence of $AlCl_3$, and is purified by fractional distillation at atmospheric pressure in the strict absence of moisture. However, $SiHCl_3$ is best prepared by placing finely powdered silicon (purified by boiling with HCl

and dilute HF) ground with *ca* 10% of $CuCl_2$ in a pyrex glass tube (fitted with an adapter and condenser which should extend into the middle of the distilling flask) and heating (carefully at first) in a furnace while a slow stream of absolutely dry HCl gas (from a gas cylinder, or generated from NaCl and concentrated H_2SO_4) is passed over the mixture with a furnace temperature of 300°. The receiver is cooled by an acetone/Dry-ice mixture, and the crude product is distilled from the receiver. HCl comes off first then $SiHCl_3$ distils over at 36.5° in 50% yield. With careful fractionation, the forerun SiH_2Cl_2, can be recovered. At 300°, $AlCl_3$ disproportionates $SiHCl_3$ to SiH_2Cl_2 and $SiCl_4$. [Note that by using an 4:1 mixture of H_2/HCl the yield of ***SiH_2Cl_2***, *[4109-96-0]* **M 101.0, m -122°, b 8.5°/atm, $d^{-122°}$ 1.22**, can be greatly improved; and ***SiH_3Cl***, has **m -118°, b -30.5°/atm, $d^{-113°}$ 1.15**. *$SiHCl_3$* is a water clear, very volatile liquid which fumes in moist air as it is hydrolysed by H_2O, but is remarkably inert towards metals even the alkali metals such as Na. It is a good reducing agent, is soluble in most organic solvents, e.g. $*C_6H_6$, $CHCl_3$, and CS_2, but not in protic solvents in which it may decompose. It is **TOXIC, should not be inhaled**, and should be handled under an efficient fume hood. [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 691-692 *1963*, Fritz *Z Anorg Allg Chem* **280** 134 *1955*.]

Tricyclohexylphosphine *[2622-14-2]* **M 280.4, m 82-83°, pK_{Est}~9.5.** It recrystallises from EtOH [Boert et al. *J Am Chem Soc* **109** 7781 *1987*]. [*Beilstein* **16** IV 947.]

Triethoxysilane *[998-30-1]* **M 164.3, m -170°, b 131.2-131.8°/atm, 131.5°/760mm, d_4^{20} 0.98753, n_D^{20} 1.4377.** Fractionate it using a column packed with glass helices of *ca* 15 theoretical plates in an inert atmosphere. Store it in aliquots in sealed ampoules because it is sensitive to moisture. [Spauschus et al. *J Am Chem Soc* **72** 1377 *1950*, MacKenzie et al. *J Am Chem Soc* **72** 2032 *1950*, Havill et al. *J Org Chem* **13** 280 *1948*, *Beilstein* **1** IV 1359.]

Triethylborane *[97-94-9]* **M 146.0, m –92.5°, b 94-97°, 94-95°, n_D^{20} 1.378, d_4^{20} 0.678.** This borane distils at 56-57°/220mm. It can also be purified *via* its *ammonia addition complex* which is distilled in a high vacuum, decomposed with dry HCl, and the Et_3B is distilled out. It is commercially available as a 15% solution in hexane or as 1M solution in hexane. [Brown *J Am Chem Soc* **67** 376 *1945*, Bamford et al. *J Chem Soc* 471 *1946*, Lin et al. *J Organomet Chem* **312** 277 *1986*, *Beilstein* **4** III 1957, **4** IV 4359.]

Triethyl borate *[150-46-9]* **M 146.0, b 44.5°/45mm, 118°, n_D^{20} 1.378, d_4^{20} 0.864.** Dry the ester over sodium, then distil it. Also fractionate it through a gauze packed column. [Charnlet et al. *J Chem Soc* 2288 *1952*, as for tributyl borate Johnson & Tompkins *Org Synth* Coll Vol **II** 106 *1943*, *Beilstein* **1** III 1339, **1** IV 1365.]

Triethyl phosphate *[78-40-0]* **M 182.2, b 40-42°/0.25-0.3mm, 98-98.5°/8-10mm, 90°/10mm, 130°/55mm, 204°/680mm, 215-216°/760mm, d_4^{25} 1.608, n_D^{20} 1.4053.** Dry the phosphate by refluxing it with solid BaO and then fractionally distil it under reduced pressure. It is kept over Na and distilled. Store it in the receiver protected from light and moisture. *Alternatively*, it is dried over Na_2SO_4 and distilled under reduced pressure. The middle fraction is stirred for several weeks over anhydrous Na_2SO_4 and again fractionated under reduced pressure until the specific conductance reaches a constant low value of κ^{25} 1.19 x 10^8, κ^{40} 1.68 x 10^8, and κ^{55} 2.89 x 10^8 ohm^{-1} cm^{-1}. It has also been fractionated carefully under reduced pressure through a glass helices-packed column. It is soluble in EtOH, Et_2O and H_2O (dec). [Estok & Wendlandt *J Am Chem Soc* **77** 4767 *1955*, Hoffmann et al. *J Am Chem Soc* **78** 6413 *1956*. (P NMR), Muller et al. *J Am Chem Soc* **78** 3557 *1956*, French et al. *J Chem Soc* 3582 *1959*, IR: Bellamy & Beecher *J Chem Soc* 475 *1952* and McIvor *Can J Chem* **36** 820 *1958*, Kosolapoff *Organophosphorus Compounds*, Wiley p 258 *1950*, *Beilstein* **1** IV 1339.]

Triethylphosphine *[554-70-1]* **M 118.2, b 100°/7mm, 127-128°/744mm, d_4^{15} 0.812, n_D^{18} 1.457, pK^{25} 8.69 (also available as a 1.0M solution in THF). All operations should be carried out in an efficient fume cupboard because it is flammable, toxic and has a foul odour.** Purify the phosphine by fractional distillation at atmospheric pressure in a stream of dry N_2, as it is oxidised by air to the oxide. In 300% excess of CS_2 it forms Et_3PCS_2 (**m** 118-120° crystallising from MeOH) which decomposes in CCl_4 to give Et_3PS as a white solid **m** 94° when recrystallised from EtOH. [Sorettas & Isbell *J Org Chem* **27** 273 *1962*, Henderson & Streuli *J Am*

Chem Soc **82** 5791 *1960*, pK: Henderson & Streuli *J Am Chem Soc* **82** 5791 *1960*, see also trimethylphosphine.] Store it in sealed vials under N_2.
Alternatively, dissolve it in Et_2O and shake it with a solution of AgI and KI to form the insoluble complex**.** Filter off the complex, dry it over P_2O_5 and the Et_3P is regenerated by heating the silver iodide complex in a tube attached to a vacuum system. It has the odour of hyacinths. [Hewitt & Holliday *J Chem Soc* 530 *1953*, Schettas & Isbell *J Org Chem* **27** 2573 *1962*, Kosolapoff *Organophosphorus Compounds*, Wiley p 31 *1950*, *Beilstein* **4** IV 3431.]

Triethyl phosphite *[122-52-1]* **M 166.2, b 48-49°/11mm, b 52°/12mm, 57.5°/19mm, 157.9°/757mm, d_4^{20} 0.9687, n_D^{20} 1.4135.** Treat the ester with Na (to remove water and any dialkyl phosphonate), then decant and distil it under reduced pressure, with protection against moisture; or distil it in a vacuum through an efficient Vigreux column or a column packed with Penn State 0.16 x 0.16inch protruded nickel packing and a variable volume take-off head. [Ford-Moore & Perry *Org Synth* Coll Vol **IV** 955 *1963*, Kosolapoff *Organophosphorus Compounds*, Wiley p 203 *1950*, *Beilstein* **1** IV 1333.]

Triethyl phosphonoacetate (triethyl carboxymethyl phosphonate) *[867-13-0]* **M 224.2, b 83-84°/0.5mm, 103°/1.2mm, 143-144°/11mm, 260-262°/atm, d_4^{20} 1.1215, n_D^{20} 1,4310.** Purify the phosphono-acetate by fractional distillation, preferably *in vacuo*. The ^{31}P NMR has a P resonance at 19.5 relative to orthophosphate. [Kosolapoff & Powell *J Am Chem Soc* **68** 1103 *1946*, Kosolapoff & Powell *J Am Chem Soc* **72** 4198 *1950*, Speziale & Freeman *J Org Chem* **23** 1586 *1958*, *Beilstein* **4** IV 3613.]

Triethyl phosphonoformate *[1474-78-8]* **M 210.2, b 70-72°/0.1mm, 122.5-123°/8mm, 130-131°/10mm, 138.2°/12.5mm, d_4^{20} 1.22, n_D^{20} 1.423.** Dissolve it in Et_2O, shake this with H_2O (to remove any trace of NaCl impurity), dry (Na_2SO_4), evaporate and distil it using an efficient fractionating column. [Nylén *Chem Ber* **57** 1035 *1924*, Reetz et al. *J Am Chem Soc* **77** 3813 *1955*, Monson *Advanced Organic Synthesis* Academic Press p 89 *1972*, *Beilstein* **3** II 103.]

Triethyl 2-phosphonopropionate [ethyl 2-(diethoxyphosphinyl)propionate] *[3699-66-9]* **M 238.2, b 76-77°/0.2mm, 137-138.5°/17mm, d_0^{20} 1.096, n_D^{20} 1.432.** Purify the ester by fractional distillation with high reflux ratio, preferably using a spinning band column. [Kosolapoff & Powell *J Am Chem Soc* **72** 4198 *1950*, Kresze et al. *Justus Liebigs Ann Chem* **756** 112 *1972*, *Beilstein* **4** IV 3617.]

Triethylsilane *[617-86-7]* **M 116.3, b 105-107°, 107-108°, d_0^{20} 0.734. n_D^{20} 1.414.** Reflux triethylsilane over molecular sieves, then distil it. It is passed through neutral alumina before use [Randolph & Wrighton *J Am Chem Soc* **108** 3366 *1986*]. [*Beilstein* **4** IV 3895.]

Triethylsilyl-1,4-pentadiene (1,4-pentadien-3-yloxy-trimethylsilane) *[62418-65-9]* **M 198.4, b 72-74°/12mm, d_4^{20} 0.842, n_D^{20} 1.439.** Dissolve the diene in pentane, wash this with H_2O, dry (Na_2SO_4), evaporate, and distil it under vacuum. R_F values on Kieselgel 60 are 0.15 (pentane) and 0.60 (*C_6H_6). [IR, NMR, MS: Oppolzer et al. *Helv Chim Acta* **64** 2002 *1981*.]

Tri-*n*-hexylborane *[1188-92-7]* **M 265.3, b 127°/1.5mm, b 185-188°/30mm.** Treat the borane with hex-1-ene and 10% anhydrous Et_2O for 6 hours at gentle reflux under N_2, then distil it in a vacuum through an 18 inch glass helices-packed column under N_2 taking the fraction **b** 130°/2.1mm to 137°/1.5mm. The distillate may still contain some di-*n*-hexylborane [Brown & Subba Rao *J Am Chem Soc* **81** 6423 *1959*, Mirviss *J Am Chem Soc* **83** 3051 *1961*]. [*Beilstein* **4** IV 4362.]

Triisoamyl phosphate *[919-62-0]* **M 308.4, b 143°/3mm.** Purify the ester by repeated crystallisation of its addition compound with uranyl nitrate from hexane. Decompose the complex, and distil the ester at high vacuum. [Siddall *J Am Chem Soc* **81** 4176 *1959*.] [see *tributyl phosphate* and Cherbuliez in *Organo Phosphorus Compounds* (Kosolapoff & Maier eds) Wiley Vol **6** pp 211-577 *1973*.]

Triisobutyl phosphate *[126-71-6]* **M 266.3, b 119-129°/8-12mm, 192°/760mm, d_4^{20} 0.962, n_D^{20} 1.421.** Purify the phosphate by repeated crystallisation of its addition compound with uranyl nitrate from hexane. (see *tributyl*

phosphate.) [Siddall *J Am Chem Soc* **81** 4176 *1959*; see Cherbuliez in *Organo Phosphorus Compounds* (Kosolapoff & Maier eds) Wiley Vol **6** pp 211-577 *1973*.]

Triisooctyl thiophosphate *[30108-39-5]* **M 450.6.** Purify the ester by passing its solution in CCl_4 through a column of activated alumina. [See Ailman & Magean in *Organo Phosphorus Compound* (Kosolapoff & Maier eds) Wiley Vol **7** pp 487-465 *1973*, and tri-*p*-tolyl phosphate below.]

Tri-isopropyl borate [(iso-PrO)$_3$B, boric acid tri-isopropyl ester, Boron iso-propoxide] *[5419-55-6]* **M 188.1, b 75°/76mm, 90°/120mm, 139-141°/760mm, d_4^{25} 0.815, n_D^{20} 1.376.** The borate ester is prepared in 85% yield from *iso*-propanol (250ml) and $NaBH_4$ (6.84g) followed by dropwise addition of AcOH (0.18g) over a period of 11 minutes, and then refluxing for 4 hours (fume cupboard and a "Dry-Ice" condenser as 16.15L of H_2 are released, CARE due to its flammability). Then fractionate the ester through a Widmer column. [Brown et al. *J Am Chem Soc* **78** 3613 *1956*.] The ester is a good reagent for borylation, e.g. *ortho*-borylating 1-substituted naphthalenes, by reacting with 1-halo- or cyano- naphthalenes (after treatment with LiTMP) to form 2-boryl esters which are later used in Pd-catalysed cross-coupling reactions [Lysén et al. *Synthesis* 3478 *2006*]. [*Beilstein* **1** H 363, **1** II 382, **1** III 1468, **1** IV 1488.]

Triisopropyl phosphite *[116-17-6]* **M 208.2, b 58-59°/7mm, 63-64°/7mm, n_D^{25} 1.4082.** Distil the phosphite from sodium, under vacuum, through a column packed with glass helices. (This removes any dialkyl phosphonate.) [Ford-Moore & Williams *J Chem Soc* 1465 *1947*, Arbuzov *Chem Ber* **38** 1171 *1905*, see Verkade & Coskren in *Organo Phosphorus Compound* (Kosolapoff & Maier eds) Wiley Vol **2** pp 1-187 *1972*, *Beilstein* **1** IV 1476.]

Trimesitylphosphine *[23897-15-6]* **M 388.5, m 205-206°, pK_{Est}~8.0.** It recrystallises from EtOH [Boert et al. *J Am Chem Soc* **109** 7781 *1987*]. The *P-methyl iodide* has **m** 269° (yellow powder from EtOH or H_2O). [*Beilstein* **16** H 774.]

Trimethallyl phosphate *[14019-81-9]* **M 260.3, b 134.5-140°/5mm, n^{25} 1.4454.** Purify it as for triisoamyl phosphate. [Cherbuliez in *Organo Phosphorus Compounds* (Kosolapoff & Maier eds) Wiley Vol **6** pp 211-577 *1973*.]

Trimethoxysilane *[2487-90-3]* **M 122.2, m -114.8°, 81.1°/760mm, 84°/atm, d_4^{20} 0.957, n_D^{20} 1.359.** Likely impurities are $Si(OMe)_4$ and $H_2Si(OMe)_2$. Efficient fractionation is essential for removing these impurities [IR: Sternbach & MacDiarmid *J Am Chem Soc* **81** 5109 *1959*, Heilfrich & Hausen *Chem Ber* **57** 795 *1924*, *Beilstein* **1** IV 1266.]

Trimethyl borate (methylborate, trimethoxyboron) *[121-43-7]* **M 103.9, m -34°, b 67-68°/742mm, d_4^{20} 0.928, n_D^{20} 1.3610.** Carefully fractionate the borate through a gauze-packed column. Re-distil and collect it in weighed glass vials and seal them. Keep it away from moisture. It undergoes alkyl exchange with alcohols and forms azeotropes, e.g. with MeOH the azeotrope consists of 70% $(MeO)_3B$ and 30% MeOH with **b** 52-54°/760mm, d 0.87. [Charnley et al. *J Chem Soc* 2288 *1952*, Gerrard & Lappert *Chem Ind (London)* 53 *1952*, Schlesinger et al. *J Am Chem Soc* **75** 213 *1953*.] It has also been dried with Na and then distilled. [*Beilstein* **1** IV 1269.]

Trimethyl boroxine ($Me_3B_3O_3$) *[823-96-1]* **M 125.5, m -38°, b 80°/742mm, 79.3°/755mm, d_4^{20} 0.902, n_D^{20} 1.362.** Possible impurity is methylboronic acid. If present, then add a few drops of conc H_2SO_4 and distil it immediately, then fractionate it through an efficient column. [McCusker et al. *J Am Chem Soc* **79** 5179 *1957*, IR: Goubeau & Keller *Z Anorg Allgem Chem* **272** 303 *1953*, *Beilstein* **4** IV 4378.]

Trimethylphenylsilane (phenyltrimethylsilane) *[768-32-1]* **M 150.3, b 67.3°/20mm, 98-99°/80mm, 170.6°/738mm, d_4^{25} 0.8646, n_D^{20} 1.491.** Fractionally distil the silane at atmospheric or reduced pressure (Podbielniak column) and estimate it by GC with a column packed with Silicone Fluid No 710 on Chromosorb P support. [Gilman et al. *J Org Chem* **18** 1743 *1953*, Maienthal et al. *J Am Chem Soc* **76** 6392 *1954*, House & Respess *J Organomet Chem* **4** 95 *1965*, Roberts et al. *J Am Chem Soc* **71** 2923 *1949*, Freiser et al. *J Am Chem*

Soc **75** 2821 *1953*, *Beilstein* **16** I 525, **16** II 605, **16** III 1198, **16** IV 1361.]

Trimethyl phosphate *[512-56-1]* **M 140.1, b 77°/12mm, 94°/22mm, 110°/60mm, 197.2°/atm, d_4^{20} 1.0213, n_D^{20} 1.3961.** Purify the phosphate by fractionation through an efficient column at high reflux ratio. It is quite soluble in H_2O; the solubility is 1:1 at 25°. [Becker *J Am Chem Soc* **74** 2923 *1952*, IR: Bergmann et al. *J Chem Soc* 847 *1952*, McIvor et al. *Can J Chem* **36** 820 *1958*, Kosolapoff *Organophosphorus Compounds*, Wiley p 258 *1950*, and Cherbuliez in *Organo Phosphorus Compounds* (Kosolapoff & Maier eds) Wiley Vol **6** pp 211-577 *1973*, *Beilstein* **1** IV 1259.]

Trimethylphosphine *[594-09-2]* **M 76.1, m -86°, b 38-39°/atm, pK^{25} 8.65, (also available as a 1.0M solution in THF or toluene). All operations should be carried out in an efficient fume cupboard because it is flammable, toxic and has a foul odour.** Distil trimethylphosphine at atmospheric pressure in a stream of dry N_2 (apparatus should be held together with springs to avoid loss of gas from increased pressure in the system) and the distillate run into a solution of AgI in aqueous KI whereby the silver complex $[Me_3PAgI]_4$ separates steadily. Filter off the complex, wash it with saturated aqueous KI solution, then H_2O and dry it in a vacuum desiccator over P_2O_5. The dry complex is heated in a flask (in a stream of dry N_2) in an oil bath at 140°, when pure Me_3P distils off (bath temperature can be raised up to 260°). The vapour pressure of Me_3P at 20° is 466mm and the **b** is 37.8° [Thomas & Eriks *Inorg Synth* **IX** 59 *1967*]. *Alternatively*, freshly distilled Me_3P (6g) is shaken with a solution of AgI (13.2g, 1.1mol) in saturated aqueous KI solution (50ml) for 2 hours. A white solid, not wetted with H_2O, separates rapidly. It is collected, washed with the KI solution, H_2O, and dried [Mann et al. *J Chem Soc* 1829 *1937*]. The silver complex is stable if kept dry in the dark, in which state it can be kept indefinitely. Me_3P can be generated from the complex when required. Store it under N_2 in a sealed container. It has been distilled in a vacuum line at -78° *in vacuo* and condensed at -96° [IR and NMR: Crosbie & Sheldrick *J Inorg Nucl Chem* **31** 3684 *1969*]. The pK^{22} by NMR was 8.80 [Silver & Lutz *J Am Chem Soc* **83** 786 *1961*, pK^{25} 8.65: Henderson & Strueuli *J Am Chem Soc* **82** 5791 *1960*].
The **$[Me_2PAgI]_4$** *complex [12389-34-3]* is a flammable solid which has **m** 140-142°. It is decomposed by heating gently in one arm of an inverted U tube. The other arm is kept in a freezing mixture. The complex dissociates, and pure Me_3P collects in the cold arm and is used at once. It should not be allowed to come in contact with air [for $AsMe_3$ see Mann & Wells *J Chem Soc* 708 *1938*]. The CS_2 complex has **m** 119° (crystallising from 95% EtOH) and decomposes in CCl_4 to give Me_3PS **m** 154° (from EtOH) [Sorettas & Isbell *J Org Chem* **27** 273 *1962*].
Trimethylphosphine hydrochloride is unstable and volatilises at 75°/0.4mm (120°/14mm). [Brown *J Am Chem Soc* **67** 503 *1945*, IR: Wagstaffe & Thompson *Trans Faraday Soc* **40** 41 *1944*, Kosolapoff *Organo-phosphorus Compounds,* Wiley p 31 *1950*, *Beilstein* **4** IV 3429.]

Trimethyl phosphite *[121-45-9]* **M 124.1, b 22°/23mm, 86-86.5°/351mm, 111-112°/760mm, 111°/atm, d_4^{20} 1.0495, n_D^{20} 1.408.** Treat the phosphite with Na (to remove water and any dialkyl phosphonate), then decant and distil it with protection against moisture. It has also been treated with sodium wire for 24 hours, then distilled in an inert atmosphere onto activated molecular sieves [Connor et al. *J Chem Soc, Dalton Trans* 511 *1986*]. It can be fractionally distilled using a spinning band column at high reflux ratio. It is a colourless liquid which is slowly hydrolysed by H_2O. [Gillis et al. *J Am Chem Soc* **80** 2999 *1958*, ^{31}P NMR: Callis et al. *J Am Chem Soc* **79** 2719 *1957*, Kosolapoff *Organophosphorus Compounds*, Wiley p 203 *1950*, *Beilstein* **1** IV 1256.]

Trimethylsilyl acetamide *[13435-12-6]* **M 131.3, m 38-43°, 52-54°, b 84°/13mm, 185-186°/atm.** Distil the amide repeatedly in an inert atmosphere with all operations to be performed in an anhydrous atmosphere. In the presence of moisture, trimethylsilanol (**b** 31-34°/26mm) is formed and is a likely impurity (check by NMR). [Birkofer et al. *Chem Ber* **96** 1473 *1963*, *Beilstein* **4** IV 4011.]

Trimethylsilyl acetonitrile (TMSAN) *[18293-53-3]* **M 113.2, b 49-51°/10mm, 65-70°/20mm, d_4^{20} 0.8729, n_D^{20} 1.4420.** Check if NMR and IR spectra show impurities; if present dissolve it in $*C_6H_6$ (10 volumes), wash it with buffer (AcOH/AcONa pH *ca* 7) several times, dry ($CaCl_2$) it, filter, evaporate and distil it. Its IR (CCl_4) has

ν_{max} at 2215 (CN) cm^{-1}, and ^1H NMR (CCl_4) with δ at 0.23 (s, 9H, $SiMe_3$), and 1.53 (s, 2H, CH_2CN). [Matsuda et al. *J Chem Soc, Perkin Trans 1* 26 *1979*, *Beilstein* **4** IV 3974.]

Trimethylsilyl azide *[4648-54-8]* **M 115.2, b 92-95°/atm, 95-99°/atm, d_4^{20} 0.878, n_D^{20} 1.441.** Distil the azide through a Vigreux column in a N_2 atmosphere maintaining the oil bath temperature thermostat at 135-140°. Check the purity by ^1H NMR [$CHCl_3$, δ: single peak at 13cps from Me_4Si]. Likely impurities are siloxane hydrolysis products. The azide is thermally stable even at 200° when it decomposes slowly without explosive violence. All the same, it is advisable to carry out the distillation behind a thick safety screen in a fumehood because unforseen **EXPLOSIVE** azides may be formed on long standing. [Birkofer & Wagner *Org Synth* Coll Vol **VI** 1030 *1988*.]

Trimethylsilyl chloride (TMCS trimethyl chlorosilane, chlorotrimethylsilane) *[75-77-4]* **M 108.6, b 56-57°/atm, 58°/760mm, d_4^{20} 0.86, n_D^{20} 1.388.** Likely impurities are other chlorinated methylsilanes and tetrachlorosilane (**b** 57.6°), some of which can form azeotropes. To avoid the latter, very efficient fractional distillation is required. It has been fractionated through a 12 plate glass helices-packed column with only the heart-cut material being used. It has also been fractionated through a 90cm, 19mm diameter Stedman column. Purify it by redistilling from CaH_2 before use. [Sauer et al. *J Am Chem Soc* **70**, 4254 *1948*, Sauer & Hadsell *J Am Chem Soc* **70** 4258 *1948*, Langer et al. *J Org Chem* **23** 50 *1958*, *Beilstein* **4** IV 4007.] **FLAMMABLE and CORROSIVE.**

Trimethylsilyl chloroacetate *[18293-71-5]* **M 166.7, m -20°, b 57-58°/14mm, 70-71°/ 30mm, 159°/760mm, d_4^{20} 1.057, n_D^{20} 1.4231.** Purify the chloroacetate by repeated fractionation, and taking the fractions with clean NMR spectra. [Anderson *J Am Chem Soc* **74** 2371 *1952*, *Beilstein* **4** IV 4004.]

Trimethylsilyl cyanide *[7677-24-9]* **M 99.2, m 8-11°, 10.5-11.5°, 11-12°, 12-12.5°, b 54-55°/87mm, 67-71°/168mm, 114-117°/760mm, 118-119°/760mm, d_4^{20} 0.79 n_D^{20} 1.43916.** The material should have only one sharp signal in the ^1H NMR (in CCl_4 with $CHCl_3$ as internal standard) with δ at 0.4, and the IR with ν_{max} at 2210cm^{-1} (C=) [McBride & Beachall *J Am Chem Soc* **74** 5247 *1952*, Prober *J Am Chem Soc* **77** 3224 *1955*]; otherwise purify it by fractionating through an 18 x 1/4inch column. [Evers et al. *J Am Chem Soc* **81** 4493 *1959*.] It has also been carefully distilled using a 60cm vacuum jacketed column. If the volume of sample is small, the cyanide can be chased (in the distillation) with xylene that had been previously distilled over P_2O_5. It is **HIGHLY TOXIC** and **FLAMMABLE**. [Evans et al. *J Org Chem* **39** 914 *1974*, *Beilstein* **4** IV 3893.]

Trimethylsilyldiazomethane (diazomethyl)trimethylsilane) *[18107-18-1]* **M 114.2, distils between 0°/100mm and 40°/15mm.** This diazo-silane is non-explosive, and non-mutagenic [Aoyama & Shiori *Chem Pharm Bull Jpn* **29** 3249 *1981*] and the careful precautions used in preparing diazomethane are not strictly necessary here. It is a good safe and stable substitute for diazomethane and excess of reagent can be evaporated off. It is available commercially as 2.0M solutions in Et_2O or hexane. Solutions in hexane can be stored for periods of more than 6 months at 0° in the absence of light without noticeable decomposition. Care should be taken, however, when opening a container, as it may become pressurised by N_2 which may be released, and should be done at ~0°.
Several methods were used for preparing this diazo-silane and some start from trimethylsilylmethylmagnesium chloride, e.g. by reaction with diazomethane (7-74%, Lappert et al. *J Chem Soc (A)* 2954 1970, Martin *Synth Commun* **13** 809 1983), or with TsN_3 (~17%, Mori et al. *Chem Pharm Bull Jpn* **30** 3380 *1982*, Barton & Hoekman *React Inorg. Met-Org Chem* **9** 297 *1979*], but the transfer of the azo group is most practical, high yielding and used on a large scale when diphenyl phosphorazidate is used, and is described here.
Trimethylsilylmethylmagnesium chloride [13170-43-9] is prepared in an inert atmosphere (e.g. argon) under strictly anhydrous conditions from Mg turning (10.7g, 0.44g-atom), anhydrous Et_2O (40ml) and 1,2-dibromoethane (0.1ml to initiate reaction) which are stirred at ~25° for 15 minutes, then 10ml of a mixture of trimethylsilylmethyl chloride (45.4g, 370mmol, freshly distilled at 97°/atm, see [2344-80-1] below) in anhydrous Et_2O (100ml) is added with stirring all at once to start the reaction followed by the rest in a dropwise manner at such a rate as to maintain gently reflux during the addition (~2 hours). After the exothermic reaction subsides, reflux and stirring are continued for 1 hour then the mixture is cooled to ~25°, and this Grignard

reagent is used in the next step. Under strictly anhydrous conditions and in a maintained argon atmosphere, a solution of diphenyl phosphorazidate (91.2g, 330mmol, freshly distilled at 134-136°/0.2mm see [26386-88-9] above) in anhydrous Et_2O (350ml) is cooled and stirred in an ice-NaCl bath until the temperature is -10°, and the preceding Grignard reagent is added dropwise (*via* a funnel or a cannula) at such a rate as to maintain the inner temperature of the solution below 0° (addition requires ~ 1.5 hours, forming a large amount of white precipitate when two-thirds of the reagent is added). After addition is complete, the ice-salt bath is replaced by an ice bath while stirring for 2 hours, then stirring is continued for 14-16 hours. The mixture is again cooled in an ice-salt bath until the inner temperature drops to -15°, and cold H_2O (35ml) is added dropwise while keeping the inner temperature below 0° (requiring ~ 1 hour), and the resulting yellow silyldiazomethane mixture is stirred for a further 0.5 hours. The mixture is filtered, the white solid is washed with Et_2O (3 x 100ml), the combined filtrate and washings are washed with cold H_2O (2 x 100ml), dried (Na_2SO_4), and the filtrate is placed in a 1L flask equipped with a Teflon-coated magnetic stirrer bar and a 30cm Vigreux column (1.5cm diameter). The mixture is slowly concentrated to *ca* 200ml by distillation at ~760mm with a bath temperature below 45° during ~6 hours (the colour of the distilled Et_2O is yellow due to some co-distillation of the diazo-silane. This rate of distillation is important as a faster rate results in decreased yields of the diazo-silane. The concentration time can be reduced to ~ 4 hours if a 30cm Widmer column is used. The remaining deep-yellow solution is then distilled, in the same equipment, by reducing the pressure to 100mm at 0° (bath temperature) and then at 15mm and 40° (bath temperature) while the distillate is collected in a receiver in a Dry-ice/Me_2CO bath until distillation is complete. The distillate is dried ($MgSO_4$), filtered and diluted with redistilled hexane (100ml). This solution is then concentrated again by distillation through the 30cm Vigreux column until the temperature of the vapour reaches 68° (with final oil bath temperature at 87°) which requires ~3 hours. About 80-110ml of the residual yellow hexane solution contains 220-230mmol of *trimethylsilyldiazomethane* (67-70% based on the phosphorazidate). Its IR (hexane) has ν_{max} at 2075, 1260 and 885 cm^{-1}, the ^1H NMR (100MHz, hexane, $CHCl_3$ as internal standard) has δ at 0.16 (s, 9H, -Si(C**H**$_3$)$_3$) and 2.58 (s, 1H, -C**H**N_2), and the ^1H NMR (100MHz, *C_6H_6) has δ at -0.03 (s, 9H, -Si(C**H**$_3$)$_3$) and 2.23 (s, 1H, -C**H**N_2).

The concentration of *trimethylsilyldiazo-methane* in hexane can be determined by adding 91mg (0.5mmol) of dibenzyl (see [103-29-7], Aromatic compounds) in 1ml of the hexane solution containing it, and measuring the ^1H NMR. The concentration of the azo-silane (*x* mmol/ml) is calculated from the formula: $x = 2a/b$, where *a* is the integral value (mm) of the methine proton (δ: 2.58) of *trimethylsilyldiazomethane*, and *b* is the integral value (mm) of the methylene protons (δ: 2.99) of dibenzyl. [Shioiri & Aoyama *Org Synth* Coll Vol **VIII** 612 *1993*, Mori et al. *Chem Pharm Bull Jpn* **30** 3380 *1982*].

It has been used for stereo and/or regio selective dipolar cycloadditions, e.g. with chiral acrylamides it produces $^2\Delta$-pyrazoline carboxylic acids (azaprolines) after protio-desilylation [Mish et al. *J Am Chem Soc* **119** 8379 *1997*], or with diethyl *trans*-glutaconate where the pyrazoline ester is oxidised to the respective pyrazole [Di & Rein *Tetrahedron Lett* **45** 4703 *2004*]. It also acts as a carbene source in stereoselective [1 + 4] annulation reactions with silylvinylketenes to form a variety of cyclopent-2-enones in good to excellent yields [Moser et al. *J Org Chem* **71** 6542 *2006*].

2-Trimethylsilyl-1,3-dithiane *[13411-42-2]* **M 192.2, b 54.5°/0.17mm, 100°/8mm, d_4^{20} 1.04, n_D^{20} 1.533.** Fractionally distil the dithiane through an efficient column and collect the fractions that have the correct NMR and IR spectra. Its ^1H NMR (CCl_4) has τ at 6.36 ($SiMe_3$), 9.87 (SCHS) and dithiane H at 7 and 8 (ratio 1:9:4:2) from Me_4Si; the UV has λ_{max} at 244nm (ε 711), sh 227nm (ε 800). [Corey et al. *J Am Chem Soc* **89** 434 *1967*.]

2-(Trimethylsilyl)ethanesulfonyl chloride (SES-Cl) *[106018-85-3]* **M 200.8, b 60°/0.1mm, 146.8°/760mm, d_4^{25} 1.059, n_D^{25} 1.4444.** Check IR; if the bands at ~3200 (OH) cm^{-1} are strong, then much of the SES-Cl had hydrolysed, and it should be treated with $POCl_3$ (with cooling) and stirred at ~25° for about 1 hour, poured into ice cold H_2O, extracted with CH_2Cl_2, washed with $NaHCO_3$, dried (Na_2SO_4), evaporated, and it distils as a yellow oil in a vacuum. This procedure is used for converting the Na salt [18143-30-1] to SES-Cl. It reacts with amines to form amides, e.g. SES-NRR', which on heating with CsF (i.e. F^- ions) in DMF at 95° provide the amine (NHRR'), SO_2 and $CH_2{=}CH_2$ [Weinreb et al. *Tetrahedron Lett* **27** 2099 *1986*]. [Ribiere et al. *Chem Rev*

106 2249 *2006*.]

Trimethylsilyl ethanol *[2916-68-9]* **M 118.3, b 53-55°/11mm, 75°/41mm, 95°/100mm, d_4^{25} 0.8254, n_D^{25} 1.4220.** If the NMR spectrum is not clean, then dissolve the alcohol in Et_2O, wash it with aqueous NH_4Cl solution, dry (Na_2SO_4), evaporate and distil it. The *3,4-dinitrobenzoyl* derivative has **m** 66° (from EtOH). [NMR: Speier et al. *J Am Chem Soc* **79** 974 *1957*, *Z Naturforsch* **14b** 137 *1959*, *Beilstein* **4** IV 3951.]

2-(Trimethylsilyl)ethoxymethyl chloride (SEMCl) *[76513-69-4]* **M 166.7, b 57-59°/8mm, d_4^{20} 0.942, n_D^{20} 1.4350.** Dissolve SEMCl in pentane, dry it ($MgSO_4$), evaporate and distil the residual oil in a vacuum. Stabilise it with 10 ppm of diisopropylamine. Store it under N_2 in a sealed container in a refrigerator. [Lipshutz & Pegram *Tetrahedron Lett* **21** 3343 *1980*.]

2-(Trimethylsilyl)ethoxymethyltriphenylphosphonium chloride *[82495-75-8]* **M 429.0, m 140-142°, 145-149°.** Wash the solid with AcOH and recrystallise it from CH_2Cl_2/EtOAc. Dry it in a vacuum desiccator. *Hygroscopic*. The ^1H NMR ($CDCl_3$) has δ at -0.2 (s, Me_3Si), 0.8 (t, 8Hz, CH_2Si), 3.83 (t, 8Hz, OCH_2), 5.77 (d, J_{PH} = 4Hz, P^+-CH_2O) and 7.70 (m, aromatic H). [Schönauer & Zbiral *Justus Liebigs Ann Chem* 1039 *1983*.]

Trimethylsilylethyl phenylsulfone (phenyl-2-trimethylsilylethylsulfone) *[73476-18-3]* **M 242.4, m 52°.** Dissolve the sulfone in Et_2O, wash it with saturated HCO_3^- followed by saturated NaCl, H_2O and dried ($MgSO_4$). Filtration followed by evaporation leaves residual crystals with **m** 52°. [Hsiao & Shechter *Tetrahedron Lett* **23** 1963 *1982*, Bortolini et al. *J Org Chem* **53** 2688 *1985*.]

Trimethylsilyl isocyanate *[1118-02-1]* **M 115.2, b 90-92°/atm, b 91.3-91.6°/atm, d_4^{20} 0.850 n_D^{20} 1.43943.** Purify it by repeated fractionation as for the isothiocyanate below. [Eaborn *J Chem Soc* 3077 *1950*, *Beilstein* **4** III 1861, **4** IV 4011.]

Trimethylsilyl isothiocyanate *[2290-65-5]* **M 131.3, m -33°, b 142.6-143.1°/759mm, 143.8°/760mm, n_D^{20} 1.4809.** The ^1H NMR spectrum should have only one peak; if not, purify it by repeated fractionation in an all-glass system using a 50cm (4mm internal diameter) column without packing. [Anderson *J Am Chem Soc* **69** 3049 *1947*, Fehér & Blümcke *Chem Ber* **90** 1934 *1957*, Neidleim & Hege *Synthesis* 51 *1975*, *Beilstein* **4** III 1861, **4** IV 4011.]

(Trimethylsilyl)methanol *[3219-63-4]* **M 104.2, b 120-122°/754mm, 122-123°/768mm, d_4^{20} 0.83 n_D^{20} 1.4176.** If the NMR indicates impurities (should have only two signals), then dissolve it in Et_2O, shake this with aqueous 5N NaOH, M H_2SO_4, saturated aqueous NaCl, dry ($MgSO_4$) and distil it using an efficient column at atmospheric pressure. The *3,5-dinitrobenzoate* has **m** 70-70.5° (from 95% EtOH). [Huang & Wang *Acta Chem Sin* **23** 291 *1957*, cf. *Chem Abstr* **52** 19911 *1958*, Speier et al. *J Am Chem Soc* **81** 1844 *1959* and Speier et al. *J Am Chem Soc* **70** 1117 *1948*, *Beilstein* **4** III 1844, **4** IV 2876.]

(Trimethylsilyl)methylamine (aminomethyl trimethylsilane) *[18166-02-4]* **M 103.2, b 101.6°/735mm, d_4^{20} 0.77, n_D^{20} 1.416.** A possible contaminant is hexamethyldisiloxane. It should have two ^1H NMR signals in $CDCl_3$; if not, dissolve it in $*C_6H_6$, shake it with 15% aqueous KOH, separate, dry (Na_2SO_4), filter, evaporate and distil it using a still of *ca* 10 theoretical plates. The water azeotrope has **b** 83°/735mm; hence it is important to dry the extract well. The *hydrochloride* has **m** 198-199° (from MeOH or Me_2CO). [Noll et al. *J Am Chem Soc* **73** 3867 *1951*, *Beilstein* **4** IV 3878.]

(Trimethylsilyl)methyl chloride (chloromethyltrimethylsilane, silico-neopentyl chloride) *[2344-80-1]* **M 122.7, b 97.1°/734mm, 98.2-98.7°/747mm d_4^{25} 0.979, n_D^{20} 1.4180.** This chloride is prepared by stirring a mixture of TMS (174g, 2 moles, Me_4Si see [75-76-3]) in dry CCl_4 (150ml) and PCl_5 (3g) [use suitably placed traps of Dry-ice/Me_2CO to prevent loss of TMS] under a reflux condenser and irradiated with a 450 watt GE sunlight lamp while dry chlorine is bubbled through for 4 hours at a rate of 0.5 mole per hour (check weight of flask occasionally). The mixture is then fractionated using a 15-plate glass helix packed column to give the *trimethylsilylmethyl chloride* (53g, 0.44 mole), b 97.1°/734mm, *polychlorinated tetramethylsilane* (93g) and

recovered TMS (62g, 0.7 mole). The *chloride* can be analysed by placing ~0.2g in a gelatin capsule in a Parr bomb and fused with Na_2O_2 (15g) and sucrose (1g). The melt is treated with H_2O, acidified with HNO_3 and the chloride ion is determined by titration using the Volhard method. [Whitmore & Sommer *J Am Chem Soc* **68** 481 *1946*, *Beilstein* **4** IV 3877.] It has also been prepared by reaction of chloro-dimethyl-chloromethyl-silane and MeMgBr in Et_2O [Whitmore et al. *J Am Chem Soc* **69** 1976 *1947*, Roedel *J Am Chem Soc* **71** 271 *1949*]. [*Beilstein* **4** III 1844, **4** IV 3877.]
It is readily converted to *trimethylsilylmethylmagnesium chloride* (see [13170-43-9] above) in ~90% yield. It reacts with *n*-BuLi in pentane to give *trimethylsilylmethylLi* [Sommer et al. *J Am Chem Soc* **71** 2750 *1949*], which reacts with anhydrous cerium (III) chloride to form *trimethylsilylmethyl cerium dichloride*. The latter reacts with acyl halides to provide bis-β-silylethyl tertiary alcohols that efficiently undergo a trimethylchlorosilane-promoted Peterson reaction to generate allylsilanes in high overall yields [Anderson & Fuchs *Synth Commun* **17** 621 *1987*]. It is useful also for Peterson olefination and homologation of aldehydes and ketones *via* 1,2-epoxysilanes [Lee et al. *Tetrahedron* **45** 5877 *1989*]. *Trimethylsilylmethyl bromide* [18243-41-9] has **M 167.1, b 115.5° /atm, d_4^{25} 1.17, n_D^{20} 1.444 [***Beilstein* **4** IV 3878], and *trimethylsilylmethyl iodide* [4206-67-1] has **M 214.1, b 139-141°/atm, d_4^{25} 1.433, n_D^{20} 1.491 [***Beilstein* **4** IV 3878], and both should be stored in the dark.

Trimethylsilylmethyl phenylsulfone (phenyltrimethylsilylmethylsulfone) *[17872-92-3]* **M 228.4, m 28-32°, b 121°/0.01mm, 160°/6mm, n_D^{20} 1.5250.** Fractionate the sulfone at high vacuum and recrystallise it from pentane at -80°. If too impure (*cf* IR), dissolve it in CH_2Cl_2 (*ca* 800ml for 100g), wash this with 2M aqueous NaOH (2 x 200ml), brine, dry, evaporate and distil it. [Craig et al. *J Chem Soc, Perkin Trans 1* 1949 *1985*, IR and NMR: Cooper *J Am Chem Soc* **76** 3713 *1954*.]

1-Trimethylsilyloxy-1,3-butadiene *[6651-43-0]* **M 142.3, b 131°/760mm (mixture of isomers), 49.5°/25mm (*E*-isomer), d_4^{20} 0.8237, n_D^{20} 1.447.** Purify the butadiene by fractional distillation, and collect the fractions with the required ^1H NMR. Store it under N_2 — it is a flammable and moisture-sensitive liquid. [Caseau et al. *Bull Soc Chim Fr* 16658 *1972*, Belge Patent 670,769, *Chem Abstr* **65** 5487d *1966*.]

1-(Trimethylsilyloxy)cyclopentene *[19980-43-9]* **M 156.3, b 45°/11mm, 75-80°/20-21mm, d_4^{20} 0.878, n_D^{20} 1.441.** If too impure as seen by the NMR spectrum, then dissolve it in 10 volumes of pentane, shake with cold $NaHCO_3$ (3 x 500ml), then 1.5M HCl (200ml) and aqueous $NaHCO_3$ (200ml) again, dry (Na_2SO_4), filter, evaporate and distil it through a short Vigreux column. Its ^1H NMR ($CDCl_3$) has δ at 0.21 (s, 9H), 1.55 (m, 2H), 1.69 (m, 2H), 2.05 (br d, 4H) and 4.88 (br s, 1H). GLPC in a 6ft x 1/8inch with 3% SP2100 on 100-120 mesh Supelcoport column should give one peak. Store dry. [For the cyclohexene analogue see Varghese et al. *Org Synth* Coll Vol **VIII** 460 *1993*.]

2-(Trimethylsilyloxy)furan *[61550-02-5]* **M 156.3, b 34-35°/9-10mm, 42-50°/17mm, 40-42°/25mm, d_4^{20} 0.950, n_D^{20} 1.436.** Fractionally distil the furan using a short path column. Its ^1H NMR in CCl_4 has δ at 4.90 (dd, J = 1.3Hz, 3H), 6.00 (t, J = 3Hz, 4H) and 6.60 (m, 5H). [Yoshii et al. *Heterocycles* **4** 1663 *1976*.]

4-Trimethylsilyloxy-3-penten-2-one (*cis*) (acetylacetone enol trimethylsilyl ether) *[13257-81-3]* **M 172.3, b 66-68°/4mm, 61-63°/5mm, d_4^{20} 0.917, n_D^{20} 1.452.** Fractionally distil the enone, and store it in glass ampoules which are sealed under N_2. It hydrolyses readily in contact with moisture giving, as likely impurities, hexamethyldisiloxane and 2,4-pentanedione. [West *J Am Chem Soc* **80** 3246 *1958*, *Beilstein* **4** IV 4003.]

1-(Trimethylsilyl)-2-phenylacetylene (1-phenyl-2-trimethylsilylacetylene) *[78905-09-6]* **M 174.3, b 45-46°/0.1mm, 67°/5mm, 87.5°/9mm, d_4^{20} 0.8961 n_D^{20} 1.5284.** Dissolve the acetylene in Et_2O, wash with H_2O, dry and fractionate it through a Todd column. [Benkeser & Hicker *J Am Chem Soc* **80** 5298 *1958*.]

3-(Trimethylsilyl)propyne *[13361-64-3]* **M 112.3, b 99-100°/760mm, d_4^{20} 0.7581, n_D^{20} 1.4091.** Fractionally distil the propyne, and add 2,6-di-*tert*-butyl-*p*-cresol (~0.5%) to stabilise it. [Petrov et al. *Doklady Acad Nauk USSR* **93** 293 *1953*, cf *Chem Abstr* **48** 13616 *1954*, *Beilstein* **4** IV 3938.]

2-Trimethylsilylpyridine *[13737-04-7]* **M151.3, b 47-49°/5mm, 69°/14.5mm, 74°/21mm, d_4^{25} 0.9113, n_D^{20}**

1.489. Purify it by distillation in a vacuum, but if it is discoloured then dissolve it in Et_2O or $*C_6H_6$, wash it with H_2O, dry over Na_2SO_4, filter, evaporate and distil the residue. It is more readily hydrolysed than the 3- or 4-trimethylsilyl isomers and the relative rates of hydrolysis in H_2O:MeOH:EtOH are 740:120:1; pyridine being liberated. Acids inhibit the reaction but bases have little effect. [Anderson et al. *J Chem Soc* B 450 *1958*, Effenberger & Häbich *Justus Liebigs Ann Chem* **512** 149-151 *1934*, Itami *Tetrahedron* **57** 5045 *2001*.]

3-Trimethylsilylpyridine *[13779-37-2]* **M151.3, b 94°/30mm, d_4^{25} 0.9113, n_D^{20} 1.4913.** Purify it as for the 1-isomer above except that less care needs be taken as it is hydrolyses more slowly. [Anderson et al. *J Chem Soc* B 450 *1958*.]

4-Trimethylsilylpyridine *[18301-46-7]* **M151.3, b 107°/48mm, d_4^{25} 0.9113, n_D^{20} 1.4868.** Purify it as for the 1-isomer above except that less care needs be taken as it hydrolyses more slowly. [Anderson et al. *J Chem Soc* B 450 *1958*.]

1-Trimethylsilyl-1,2,4-triazole *[18293-54-4]* **M 141.3, b 74°/12mm, d_4^{20} 0.99, n_D^{20} 1.4604.** Fractionally distil it at atmospheric pressure in an inert atmosphere because it is moisture sensitive. [Birkofer et al. *Chem Ber* **93** 2804 *1960*.]

Trimethylsilyl trifluoromethane (trifluoromethyl trimethylsilane, Ruppert's reagent) *[81290-20-2]* **M 142.2, b 54-55°, 55-55.5°, d_4^{20} 0.962, n_D^{20} 1.332.** Purify the silane by distilling it from trap to trap in a vacuum of 20mm using a bath at 45° and Dry-ice/Me_2CO bath for the trap. The liquid in the trap is then washed with ice cold H_2O (3x), the top layer is collected, dried (Na_2SO_4), and the liquid is decanted and fractionated through a helices-packed column at atmospheric pressure. ^1H, ^{13}C, ^{19}F, and ^{29}Si NMR can be used for assessing the purity of fractions. [Ruppert et al. *Tetrahedron Lett* **25** 2195 *1984*, Krishnamurti et al. *J Org Chem* **56** 984 *199*, *Beilstein* **4** IV 3892.]

2,8,9-Trimethyl-2,5,8,9-tetraaza-1-phosphabicyclo[3.3.3]undecane (Verkade Superbase, 2,8,9-trimethyl-*pro*-azaphosphatrane) *[120666-13-9]* **M 216.3, m 110-115°, pKa 26.8 (DMSO).** The free superbase can be prepared in three ways. When tris(dimethylamino)phosphine **(**8.8g, 54mmol, toxic see [1608-26-0]) and tris[2-(methylamino)-ethyl]amine (10.0g, 53mmol), see [65604-89-9]**)** are dissolved in dry xylene and refluxed for 21 days, then the solvent is removed *in vacuo*, a residual thick oil is obtained. On heating this oil at 105°/0.05mm the *pro-azaphosphatrane* (53g, 24.5mmol, 46%) sublimes out as a colourless waxy solid.
In a second preparation the *trimethyl-pro-azaphosphatrane hydrochloride* (0.87g, 3.4mmol, see [138800-17-6] below) dissolved in MeCN (10ml) is added dropwise to a suspension of freshly sublimed *tert*-BuOK (0.41g, 3.7mmol) in MeCN (20ml), stirred for 30 minutes, the solvent is removed *in vacuo*, the residue is extracted with hexane (2 x 30ml), evaporated, and the residue is sublimed at 60°/0.01mm to give the pure *superbase* (80%) as a white solid. [Schmidt et al. *Z Anorg Allg Chem* **578** 75 *1989*.]
In a third preparation the *trimethyl-azaphosphatrane hydrochloride* is heated slowly with a large excess of anhydrous NaOH under vacuum. No reaction occurs below 200°, but above this temperature sudden sublimation of the free superbase occurs. Extraction of the sublimate, and/or the reaction mixture, with $*C_6H_6$ followed by evaporation of the solvent provided pure free base (53% yield). Sometimes charring occurs during this reaction resulting in lower yields. [Lensink et al. *J Am Chem Soc* **111** 3478 *1959*.]
The *free base* is an unusually strong Lewis base. It deprotonates phenol (pKa 10), protonated "Proton Sponge" [1,8-(bismethylamino)naphthalene HI (pKa 12.3, Alder et al. *J C S, Chem Commun* 723 *1968*), diethyl malonate (pKa 13, Pearson & Dillon *J Am Chem Soc* **75** 2439 *1953*), H_2O (pKa 13.99, Harned & Robinson *Trans Farad Soc* **36** 2747 *1940*; or ? pKa 15.74 Reeve et al. *Can J Chem* **57** 2747 *1979*), but does not react with *tert*-BuOH (pKa 16.5, Reeve et al. *Can J Chem* **57** 2747 *1979*), to give the protonated base as the only product. In the presence of 1 equivalent of H_2O an equilibrium mixture of free base to cation of *ca* 4:1 is obtained (from NMR studies) [Lensink et al. *J Am Chem Soc* **111** 3478 *1989*.] The un-methylated analogous free base is not very stable although its hydrochloride is quite stable and it is a *stronger base* than the 2,8,9-trimethyl- or the respective 2,8,9-tribenzyl- derivative. The upper limit of the pKa of the trimethyl compound in DMSO is ~26.8 (by ^{13}P NMR) [Laramay & Verkade *J Am Chem Soc* **112** 9421 *1990*]. The *free base* has IR (Nujol) with ν_{max} at 1332 s,1303 m,1244 s,1226 s,1197m, 1145 s, 1128 s, 1053 s, 1004 s, 960 w, 887m, 850s, 767w, 650s and 634 s

cm^{-1}; the ^1H NMR (300MHz, CD_3CN, TMS) has δ at 2.60 (d, 9H, $^3J_{PH}$ = 11.0 Hz, CH_3) and 2.76 (br s, 12H, CH_2); the ^{13}C NMR (75MHz, C_6D_6, TMS) has δ at 37.2 ($^2J_{PC}$ = 41.0 Hz, CH_3), 49.4 (d, $^2J_{PC}$ = 6.7 Hz, $N_{eq}\boldsymbol{C}H_2$) and 51.3 (s, $N_{ax}\boldsymbol{C}H_2$); the ^{31}P NMR (122MHz, C_6D_6, 85% H_3PO_4) has δ at 120.8; and the HRMS has *m/z* 216.15088 (calc for M is 216.15039). [Schmidt et al. *Z Anorg Allg Chem* **578** 75 *1989*, Lensink et al. *J Am Chem Soc* **111** 3478 *1989*, Laramay & Verkade *J Am Chem Soc* **112** 9421 *1990*, Laramay & Verkade *Z Anorg Allg Chem* **608** 163 *1991*, Schmidt et al. *Inorg Chem* **29** 2214 *1990*]. In addition to being easily protonated (see following entry), the free base has been readily converted to P-substituted adducts (*five-coordinated phosphatranes*), where the P-H is replaced by P-X, where -X is -O (by using Me_3SiO_2), -S (by using S_8), -Se (by using Se), $-N_3P$ (by using PhN_3), -NPh (by using PhN_3 and heating), $-CS_2$ (by using CS_2) and $-PtCl_2$ [by using $(Et_2S)_2$-$PtCl_2$] in 60 to >80% yields [Schmidt et al. *Z Anorg Allg Chem* **578** 75 *1989*]. ***Note*** that the difference between the *pro-phosphatranes* and the *phosphatranes* is that the latter possess an apical N→P bond as evidenced by the shorter bond distance in X-Ray diffraction analyses and the large decrease in the δ ^{31}P chemical shifts in the NMR spectra.

2,8,9-Trimethyl-2,5,8,9-tetraaza-1-phosphabicyclo[3.3.3]undecane hydrochloride (Verkade Superbase HCl, 2,8,9-trimethylazaphosphatrane HCl) *[138800-17-6]* **M 252.7, m 132-136°.** Like the preceding free base it is prepared in different ways — two are described here. A solution of PCl_3 (1.22g, 8.85mmol) in CH_2Cl_2 (5.0ml) is added to a solution of P(NMe) (2.89g, 17.7mmol, toxic see [1608-26-0]) in CH_2Cl_2 (5.0ml), then cooled to 5°, and TREN (3.88g, 26.5mmol, see [4097-89-6]) in CH_2Cl_2 (25ml) is added during ~15 minutes. The precipitate formed is filtered off, washed with CH_2Cl_2 (25ml) and dried to give the pure *hydrochloride* (5.58g, ~100%). Crystals for X-Ray diffraction can be grown from concentrated MeOH solutions. The *2,8,9-tribenzyl hydrochloride* can be similarly prepared in 89% yield by using tris-(*N-benzylaminoethyl*)amine in place of TREN. [Laramay & Verkade *Z Anorg Allg Chem* **605** 163 *1991*].
In the second preparation tris[2-(methylamino)-ethyl]amine (1.67g, 11.4mmol), see [65604-89-9]**)** in CH_2Cl_2 (20ml) is added with stirring to a mixture of $ClP(NMe_2)_2$ (1.76g, 11.4mmol, TOXIC) and Et_3N (1.5g, 15mmol) in CH_2Cl_2 (30ml) during 5 minutes, then the mixture is stirred at ~25° for 1 hour, the volatiles are evaporated off *in vacuo* to give the *hydrochloride* quantitatively. It can be recrystallised from hexane/$CHCl_3$ (82% yield) in colourless crystals. When the hydrochloride salt is treated with $AgBF_4$ in CH_2Cl_2 the *HBF_4 salt* is obtained quantitatively. The salts are very difficult to deprotonate (see preceding entry). The X-ray crystal structure shows a short intra-annular bond between the apical N atom and the P atom with a robust P—H bond, the positive charge being on the apical N atom. [Laramay & Verkade *J Am Chem Soc* **112** 9421 *1990*, Lensink et al. *J Am Chem Soc* **111** 3478 *1989*.] It has ^1H NMR (300MHz, $CDCl_3$, TMS) with δ at 2.61 (d, 9H, $^3J_{PH}$ = 17.4 Hz, CH_3) and 3.03 (dt, 6H, $N_{ax}CH_2$, $^3J_{PH}$ = 11.0 Hz, $^3J_{HH}$ = 6.2 Hz), 3.58 (dt, 6H, $N_{eq}CH_2$, $^3J_{PH}$ = 4.7 Hz, $^3J_{HH}$ = 6.2 Hz), 5.20 (d, 1H, $^1J_{PH}$ = 6.2 Hz); the ^{13}C NMR (75MHz, $CDCl_3$) has δ at 34.4 (d, $^2J_{PC}$ = 17.1 Hz, $\boldsymbol{C}H_3$), 41.3 (d, $^2J_{PC}$ = 6.1 Hz, $N_{ax}\boldsymbol{C}H_2$) and 47.3 (d, $^2J_{PC}$ = 7.3 Hz, $N_{eq}\boldsymbol{C}H_2$); the ^{31}P NMR (122MHz, $CDCl_3$, 85% H_3PO_4) has δ at -10.6 [Lensink et al. *J Am Chem Soc* **111** 3478 *1989*].

Trimethyl vinyl silane *[754-05-2]* **M 100.2, b 54.4°/744mm, 55.5°/767mm, d_4^{25} 0.6865, n_D^{25} 1.3880.** If the ^1H NMR spectrum shows impurities, then dissolve it in Et_2O, wash it with aqueous NH_4Cl solution, dry over $CaCl_2$, filter, evaporate and distil it at atmospheric pressure in an inert atmosphere. It is used as a co-polymer and may polymerise in the presence of free radicals. It is soluble in CH_2Cl_2. [Nagel & Post *J Org Chem* **17** 1379 *1952*, *Beilstein* **4** IV 3922.]

Tri(4-nitrophenyl)phosphate *[3871-20-3]* **M 461.3, m 155-156°, 156°, 156-158°, 157-159°.** This phosphate has been recrystallised from AcOH, dioxane, AcOEt and Me_2CO and dried it in a vacuum over P_2O_5. [Katelaar & Gersmann *J Am Chem Soc* **72** 5777 *1950*, Moffatt & Khorana *J Am Chem Soc* **79** 3741 *1957*.]

Tri(*n*-octyl)phosphine oxide *[78-50-2]* **M 386.7, m 59.5-60°, pK_{Est} <0.** Mason, McCarty and Peppard [*J Inorg Nuclear Chem* **24** 967 *1962*] purified the oxide by stirring a 0.1M solution in *benzene with an equal volume of 6M HCl at 40° in a sealed flask for 48 hours, then washed the *benzene solution successively with water (twice), 5% aqueous Na_2CO_3 (three times) and water (six times). The *benzene and water were then evaporated under reduced pressure at room temperature. Zingaro and White [*J Inorg Nucl Chem* **12** 315 *1960*]

treated a petroleum ether solution of the oxide with aqueous $KMnO_4$ (to oxidise any phosphinous acids to phosphinic acids), then with sodium oxalate, H_2SO_4 and HCl (to remove any manganese compounds). The petroleum ether solution was slurried with activated alumina (to remove phosphinic acids), filtered, evaporated and the residue was recrystallised from petroleum ether or cyclohexane at -20°. It can also be recrystallised from EtOH. [*Beilstein* **4** IV 3466.]

Tri(*neo*-pentyl) phosphate *[14540-59-1]* **M 320.4.** Crystallise it from hexane. [See Cherbuliez in *Organo Phosphorus Compounds* (Kosolapoff & Maier eds) Wiley Vol **6** pp 211-577 *1973*.]

Triphenylarsine *[603-32-7]* **M 306.2, m 60-62°.** Recrystallise Ph_3As from EtOH or aqueous EtOH [Dahlinger et al. *J Chem Soc, Dalton Trans* 2145 *1986*, Boert et al. *J Am Chem Soc* **109** 7781 *1987*]. [*Beilstein* **16** H 829, **16** I 431, **16** II 407, **16** III 921, **16** IV 1139.] **HIGHLY TOXIC.**

Triphenylarsine oxide *[1153-05-5]* **M 322.2, m 194-196°** (*anhydrous)***.** The anhydrous oxide crystallises from *C_6H_6, whereas the *monohydrate* separates from EtOH with **m** 118° (**m** 114-117° was also reported). [*Beilstein* **16** H 846, **16** I 433, **16** II 433, **16** III 1022, **16** IV 1139.] **HIGHLY TOXIC.**

Triphenyl borane (borane triphenyl, triphenyl boron) *[960-71-4]* **M 242.1, m 134-140°, 137°, 139-141°, 142-142.5°, 147.5-148°, 151°, b 203°/15mm.** Recrystallise the borane three times from Et_2O or *C_6H_6 under N_2 and dry it at 130°. It can be distilled in a high vacuum at 300-350° and has been distilled **(b** 195-215°/~15mm) in vacuum using a bath temperature of 240-330°. N_2 is introduced into the apparatus before dismantling. It forms complexes with amines. [Nielsen et al. *Chem Ind (London)* 1069 *1957*, Wittig et al. *Justus Liebigs Ann Chem* **563** 110 *1949*, Bent & Dorfman *J Am Chem Soc* **57** 1259 *1935*, *Beilstein* **16** IV 1623.]

Triphenyl phosphate *[115-86-6]* **M 326.3, m 49.5-50°, b 245°/11mm.** Crystallise the phosphate from EtOH or petroleum ether (b 60-80°)/EtOH. [Cox & Westheimer *J Am Chem Soc* **80** 5441 *1958*, Krishnakumar & Sharma *Synthesis* 558 *1983*, Cherbuliez in *Organo Phosphorus Compounds* (Kosolapoff & Maier eds) Wiley Vol **6** pp 211-577 *1973*, *Beilstein* **6** III 658, **6** IV 720.] It has been used as an effective ligand with phase transfer catalysts [Nakoji et al. *J Org Chem* **67** 7418 *2002*].

Triphenylphosphine *[603-35-0]* **M 262.3, m 77-78°, 79°, 79-81°, 80.5°, 80-81°, b >360°(377°, in inert gas), d_4^{25} 1.194, d_4^{80} 1.075 (liq), pK^{25} 2.73.** The phosphine crystallises from hexane, MeOH, diethyl ether, CH_2Cl_2/hexane or 95% EtOH. Dry it at 65°/<1mm over $CaSO_4$ or P_2O_5. Chromatograph it through alumina using (4:1) *benzene/$CHCl_3$ as eluent. [Blau & Espenson et al. *J Am Chem Soc* **108** 1962 *1986*, Buchanan et al. *J Am Chem Soc* **108** 1537 *1986*, Randolph & Wrighton *J Am Chem Soc* **108** 3366 *1986*, Asali et al. *J Am Chem Soc* **109** 5386 *1987*.] It has also been crystallised twice from petroleum ether and 5 times from Et_2O/EtOH to give crystals with **m** 80.5°. *Alternatively*, dissolve it in conc HCl, and upon dilution with H_2O it separates because it is weakly basic, it is then crystallised from EtOH/Et_2O. It recrystallises unchanged from AcOH. [Forward et al. *J Chem Soc* Suppl. p121 *1949*, Muller et al. *J Am Chem Soc* **78** 3557 *1956*.] *$3Ph_3P.4HCl$* crystallises out when HCl gas is bubbled through an Et_2O solution, it has **m** 70-73°, but recrystallises very slowly and is deliquescent. *$Ph_3P.HBr$* [6399-81-1] has **m** 196° (dec). The *hydriodide*, made by adding Ph_3P to hydriodic acid, is not hygroscopic and decomposes at ~100°. The *chlorate* (1:1) *salt* has **m** 165-167°, but decomposes slowly at 100°. All salts hydrolyse in H_2O to give Ph_3P [IR, UV: Sheldon & Tyree *J Am Chem Soc* **80** 2117 *1958,* pK: Henderson & Streuli *J Am Chem Soc* **82** 5791 *1960*, Kosolapoff, *Organophosphorus Compounds*, Wiley *1950*]. [*Beilstein* **16** IV 951.]
§ It is also available commercially on a support of polystyrene cross-linked with 2% divinylbenzene as the free base [39319-11-4], loading of ~3.2 nmol/g, 100-200 mesh], and as the *hydrobromide* [loading 2.5-3.0 mmol Br, 200-400 mesh].

Triphenylphosphine dibromide *[1034-39-5]* **M 422.1, m 235°, 245-255°(dec).** The dibromide recrystallises from MeCN/Et_2O. Although it has been recrystallised from EtOH, this is not recommended as it converts alcohols to alkyl bromides as it has brominating power. It deteriorates on keeping, and it is best to prepare it afresh. [Anderson & Freenor *J Am Chem Soc* **86** 5037 *1964*, Horner et al. *Justus Liebigs Ann Chem* **626** 26 *1959*, *Beilstein* **16** III 864.]

Triphenylphosphine oxide *[791-28-6]* **M 278.3, m 152.0°, 156-157°, pK_{Est} ~–2.10 (aqueous H_2SO_4), pK^{25} 2.9 (in $MeNO_2$).** It crystallises from absolute EtOH and is dried *in vacuo*. The *gold chloride complex* has **m** 177.5-178.5°. [Addison & Sheldon *J Chem Soc* 2705 *1956*, Cox & Westheimer *J Am Chem Soc* **80** 5441 *1958*, *Beilstein* **16** III 864, **16** 1011.]

Triphenyl phosphite *[101-02-0]* **M 310.3, m 16-20°, 21-23°, b 181-189°/1mm, 183-184°/1mm, d_4^{20} 1.183.** Its ethereal solution is washed successively with aqueous 5% NaOH, distilled water and saturated aqueous NaCl, then dried with Na_2SO_4 and distilled under vacuum after evaporating the diethyl ether. [Walsh *J Am Chem Soc* **81** 3023 *1959*, Verkade & Coskren in *Organo Phosphorus Compounds* (Kosolapoff & Maier eds) Wiley Vol 6 pp 211-577 *1973*, *Beilstein* **6** IV 695.] It has been used as an effective ligand with phase transfer catalysts [Nakoji et al. *J Org Chem* **67** 7418 *2002*].

Triphenylphosphorylidene acetaldehyde (formylmethylenetriphenylphosphorane) *[2136-75-6]* **M 304.3, m 185-187°, 186-187°(dec).** Recrystallise it from Me_2CO, or dissolve it in $*C_6H_6$, wash with N NaOH, dry ($MgSO_4$), evaporate, and crystallise the residue from Me_2CO. It can be prepared from its precursor, formylmethyltriphenylphosphonium chloride (which crystallises from $CHCl_3$/EtOAc), by treatment with Et_3N and extraction with $*C_6H_6$. [Tripett & Walker *J Chem Soc* 1266 *1961*.]

(Triphenylphosphoranylidene)ketene [Bestmann ylide (triphenylphosphoranylidene)ethenone, ketenylidene(triphenyl)phosphorane) *[15596-07-3]* **M 302.3, m 167-173°, 173°.** This versatile reagent is prepared in a dry inert atmosphere (N_2 or argon) by first mixing $NaNH_2$ (19.5g, 0.5mole) in toluene (1.3L, dried by passage through alumina) and bis(trimethylsilyl)amine (81g, 105ml, 0.5mol, toxic and corrosive), and heated (70-80° bath temperature) under a reflux condenser until a clear and colourless solution of sodium hexamethyldisilazanide (see hexamethyl disilazane sodium salt [1070-89-9]) is obtained, and evolution of NH_2 ceased (2-4 hours). Note that repeated purging with argon or N_2 reduces the reaction time. The condenser is removed and under argon or N_2, (methoxycarbonylmethylene)triphenylphosphorane (167g, 0.5mol, [2605-67-6]) is added in large portions, and the mixture is again heated (70-80° bath temperature) with stirring for 24-30 hours until the colour of the solution assumes a bright yellow hue [and the IR band of a film of aliquots between KBr plates, with ν_{max} at 1616 cm^{-1} of the starting ylide has disappeared, and is replaced by a strong band of the product with ν_{max} at 2090 cm^{-1} of constant intensity, indicating completion of reaction]. While still hot, and under argon or N_2, the mixture is filtered rapidly [through a 20/40 standard taper vacuum filtration adapter and a 350ml fritted funnel of coarse porosity open to the atmosphere through a 2 cm thick layer of basic Al_2O_3 (III) and a 1cm Celite pad on top, and occasional scraping the top of the pad] into a 2L 24/40 single necked flask. The filtration requires 30-60 minutes and the funnel temperature should be kept between 30-50° to avoid crystallisation. The filtrate is flushed with inert gas and evaporated (rotavap) to dryness. The residue is recrystallised from hot dry toluene (1g/5ml) followed by cooling at -20° overnight. While the mixture is cold, the solids are filtered off, washed with cold toluene (3 x 100ml at 0°). The combined filtrates are evaporated in the same way at low temperature as before to give a second crop. The combined crops are dried to constant weight at high vacuum (0.01mm) to give pure *(triphenylphosphoranylidene) ketene* (106.8-114.9g, 74-76% and ~99.97% pure by ^1H NMR) as a pale yellow, flaky powder with m 173°. It is remarkably stable, it can be stored at ~25° under argon or N_2 for months and can be handled at ~25° without obvious deterioration. It has IR (KBr) with ν_{max} at 2090 (s), 1625 (m), 1436 (m) and 1110 (m) cm^{-1}; the ^1H NMR (400MHz, $CDCl_3$) has δ at 7.44-7.54 (m, 6H), 7.55-7.63 (m, 3H) and 7.64-7.77 (m, 6H); the ^{13}C NMR (100MHz, $CDCl_3$) has δ at -10.5 (d, $^3J_{P-C}$ = 185.4 Hz, Cα), 128.8 (d, $^3J_{P-C}$ = 12.9 Hz, C-*ortho*), 129.6 (d, $^1J_{P-C}$ = 98.5 Hz, C-*ipso*), 132.2 (s, C-*para*), 132.3 (s, C-*meta*) and 145.6 (d, $^2J_{P-C}$ = 63.0 Hz, Cβ); and the ^{31}P NMR (162MHz, $CDCl_3$) has δ at 6.0. Possible detectable impurities are starting ester ylide and toluene detected by ^1H NMR spectroscopy which have singlets at δ 3.60 and 2.36 respectively. It is a nucleophilic-only C_2-building block that reacts with a range of electrophiles in a variety of ways. It also undergoes cycloaddition reactions at the polar P-Cα bond as well as at the Cα=Cβ double bond, and multi-component and domino reactions. [Schobert *Org Synth* **82** 140 *2005*.]

Triphenyl silane *[789-25-3]* **M 260.4, m 45°, b 148-151°/1mm.** Purify it by recrystallisation from MeOH. [Gilman & Zuech *J Am Chem Soc* **81** 5925 *1959*, Westermark *Acta Chem Scand* **9** 947 *1955*, IR: Kaplan *J Am Chem Soc* **76** 5880 *1954*, *Beilstein* **16** II 605, **16** III 1199, **16** IV 1369.]

Triphenylsilanol (hydroxytriphenylsilane) *[791-31-1]* **M 276.4, m 150-153°, 151-153°, 154-155°, 156°.** It is purified by dissolving in petroleum ether, passing through an Al_2O_3 column, eluting thoroughly with CCl_4 to remove impurities and then eluting the silanol with MeOH. Evaporation gives crystals with **m** 153-155°. It can be recrystallised from petroleum ether, CCl_4 or from *benzene or Et_2O/petroleum ether (1:1). It has also been recrystallised by partial freezing from the melt to constant melting point. [George & Gilman *J Am Chem Soc* **81** 3288 *1959*, IR: Tatlock & Rochow *J Org Chem* **17** 1555 *1952* and Richards & Thompson *J Chem Soc* 124 *1949*, *Beilstein* **16** IV 1480.]

Triphenyl vinyl silane *[18666-68-7]* **M 286.5, m 58-59°, 57-59.5°, 67-68°, b 190-210°/3mm.** The vinylsilane has been recrystallised from EtOH, 95% EtOH, EtOH/*C_6H_6, petroleum ether (b 30-60°) and Et_2O, and has been distilled under reduced pressure. [Cason & Brooks *J Am Chem Soc* **74** 4582 *1952*, Nagel & Post *J Org Chem* **17** 1379 *1952*, *Beilstein* **16** IV 1371.]

Tri(*n*-propyl) borate *[688-71-1]* **M 188.1, b 64°/9mm, 175-177°/atm, d $_4^{20}$ 0.857, n $_D^{20}$ 1.395.** Dry the ester over sodium and then distil it, preferably in a vacuum. (cf tributyl borate.) [Charnley et al. *J Chem Soc* 2288 *1952*, *Beilstein* **1** IV 1436.]

Tri(*iso*-propyl) borate [(*iso*-PrO)$_3$B, boric acid tri-*iso*-propyl ester, Boron *iso*-propoxide] *[5419-55-6]* **M 188.1, b 75°/76mm, 90°/120mm, 139-141°/760mm, d $_4^{25}$ 0.815, n $_D^{20}$ 1.376.** The borate ester is prepared in 85% yield from *iso*-propanol (250ml) and $NaBH_4$ (6.84g) followed by dropwise addition of AcOH (0.18g) over a period of 11 minutes, and then refluxing for 4 hours (fume cupboard and a "Dry-ice" condenser as 16.15L of H_2 are released, CARE due to its flammability). Then fractionate the ester through a Widmer column. [Brown et al. *J Am Chem Soc* **78** 3613 *1956*.] The ester is a good reagent for borylation, e.g. *ortho*-borylating 1-substituted naphthalenes, by reacting with 1-halo- or cyano- naphthalenes (after treatment with LiTMP) to form 2-boryl esters which are later used in Pd-catalysed cross-coupling reactions [Lysén et al. *Synthesis* 3478 *2006*]. [*Beilstein* **1** H 363, **1** II 382, **1** III 1468, **1** IV 1488.]

Tri(quinol-8-yl) phosphate *[52429-99-9]* **M 479.4, m 193-197°, 202-203°.** Purify the phosphate by recrystallisation from dimethylformamide. The purity is checked by paper chromatography, R_F 0.90 [*i*-PrOH/saturated $(NH_4)_2SO_4/H_2O$, 2:79:19 as eluent], its IR (KBr) has ν_{max} at 1620**,** 1570 (C=C, C=N) and 1253 (P=O) cm^{-1}. [Takaku et al. *Bull Chem Soc Jpn* **47** 779 *1974*.]

Tri-*o*-tolylphosphine *[6163-58-2]* **M 304.4, m 129-130°, pK$_{Est}$ ~1.0.** Like PPh_3, it crystallises from hexane, MeOH, diethyl ether, CH_2Cl_2/hexane or 95% EtOH. Dry it at 65°/<1mm over $CaSO_4$ or P_2O_5. Purify further by chromatography through alumina using (4:1) *benzene/$CHCl_3$ as eluent. Of the phosphine ligands studied, P(*o*-Tol)$_3$ (6 mol%) was the best in the $Ru_3(CO)_{12}$ (2 mol%) catalysed *N*-alkylation of primary amines and secondary alcohols (e.g. hexylamine with 1-phenylethanol to give *N*-octyl 1-phenethylamine) in high yields at 90-110° [Tillack et al *Tetrahedron Lett* **47** 8881 *2006*]. The Heck reaction between aryl halides and *n*-butyl acrylates to provide substituted styrenes in ~80 to >90% yields at ~120° is catalysed by $Pd(OAc)_2$ (2 mol%) and P(*o*-Tol)$_3$ (8 mol%) without extensive P-C bond cleavage [Herrmann et al. *J Mol Catal A: Chem* **103** 133 *1995*]. [*Beilstein* **16** III 835.]

Tris(2-biphenylyl) phosphate *[132-28-5]* **M 554.6, m 115.5-117.5°.** Crystallise it from MeOH containing a little acetone. (*cf* triphenyl phosphate.)

Tris(2,4-di-*tert*-butylphenyl)phosphite *[31570-04-4]* **M 646.9, m 181-184°.** If the ester is suspect, e.g. partly hydrolysed, dissolve it in Et_2O, wash the solution successively with aqueous 5% NaOH, H_2O and saturated aqueous NaCl, then shake with charcoal, filter, dry with Na_2SO_4, filter again, evaporate and add petroleum ether when the volume has decreased considerably to crystallise the ester. [Verkade & Coskren in *Organophosphorus*

Compounds (Kosolapoff & Maier eds) Wiley Vol 6 pp 211-577 *1973*.] It is used as a processing stabiliser for polymers.

Tris(1,2-dioxyphenyl)cyclotriphosphazine {trispiro[1,3,5,2,4,6-triazatriphosphorine]-2,2':-2,4":2,6"'-tris(1,3,2)benzodioxaphosphole} *[311-03-5]* **M 459.0, m 244-245°, 245°, 245-246°.** Recrystallise this phosphazine from *C_6H_6 or chlorobenzene, then triple sublime it (175°/0.1mm, 200°/0.1mm, 230°/0.05mm). Its UV has λ_{max} nm (log ε) at 276 (3.72), 271 (3.79) 266sh (3.68) and 209 (4.38) in MeCN. Its IR has ν_{max} at 1270 (O-Ph), 1220 (P=N), 835 (P-O-Ph) and 745 (Ph) cm^{-1}. [Alcock *J Am Chem Soc* **86** 2591 *1964*, Alcock et al. *J Am Chem Soc* **98** 5120 *1976*, Meirovitch *J Phys Chem* **88** *1522 1984*.]

(±)-Tris(2-ethylhexyl) phosphate (TEHP, tri-isooctylphosphate, "trioctyl" phosphate, *[78-42-2, 25103-23-5]* **M 434.6, b 186°/1mm, 219°/5mm, d^{25} 0.92042, n_D^{20} 1.44464.** TEHP, in an equal volume of diethyl ether, is shaken with aqueous 5% HCl, and the organic phase is filtered to remove traces of pyridine (used as a solvent during manufacture) as its hydrochloride. This layer is shaken with aqueous Na_2CO_3, then water, and the ether is distilled off at room temperature. The ester is then filtered, dried for 12 hours at 100°/15mm, and again filtered, then shaken intermittently for 2 days with activated alumina (100g/L). It is decanted through a fine sintered-glass disc (with exclusion of moisture), and distilled under vacuum. [French & Muggleton *J Chem Soc* 5064 *1957*.] *Benzene can be used as a solvent (to give 0.4M solution) instead of ether. Its IR has ν_{max} at 1702, 1701, 481 and 478cm^{-1} [Bellamy & Becker *J Chem Soc* 475 *1952*]. The *uranyl nitrate* salt is purified by partial crystallisation from hexane [Siddall & Dukes *J Am Chem Soc* **81** 790 *1959*, Siddall *J Am Chem Soc* **81** 4176 *1959*]. [*Beilstein* **1** IV 1786.]

Tris(hydroxymethyl)phosphine (phosphinidynetrimethanol) *[2767-80-8]* **M 121.1, m 48-56°, 55°, b 111-113°/2.5mm, n_D^{20}1.5497, pK 5.5 (half neutralisation point, glass electrode).** It is obtained in two ways by neutralising precisely the THPC (Tetrakis(hydroxylmethyl)phosphonium chloride, [124-64-1]). In the *first* method, NaOH (1.6g, 40mmol) in H_2O (25ml) is added rapidly to THPC (7.6g, 40mmol, see above [124-64-1]) in H_2O (50ml) under N_2 at room temperature in a closed system connected to a glass buret. No evolution of gas should be observed on stirring for 20 hours indicating that the stoichiometric amount of alkali has been added. Any liberation of gas (H_2) would indicate that excess of alkali had been added which would liberate H_2 with the formation of the corresponding phosphine oxide (see next entry, and Hoffman *J Am Chem Soc* **52** 2995 *1930*). The solvent is then removed *in vacuo* at 50-60°, EtOH (under N_2) is added, the solid NaCl is filtered off, and the EtOH is removed *in vacuo* (45°) to give the *free base* (4.8g, 97%) as a clear viscous liquid which can be distilled at high vacuum in an atmosphere of N_2 (N_2 bleed). An IR (film) should indicate the absence of P=O and the presence of primary OH and P-CH_2 bands [Grayson *J Am Chem Soc* **85** 79 *1963*].
In the *second* method, under N_2 flushing and stirring, a solution of THPC (25g, 131mmol) in distilled H_2O (100ml), into which is immersed a glass pH electrode, is treated with ~ 150ml (0.21 equivalents) of 20-50 mesh Dowex-1 x 8 resin (in the OH^- form) during 45 minutes until the pH was ~8.3-8.5. The resin is filtered off, washed with H_2O, the combined aqueous solutions are evaporated (rotavap) at 65-70°, then under high vacuum for 30 minutes, then further at -30° to give the *free base* as a viscous liquid which formed a waxy solid. Its IR (film between NaCl plates) should have no bands at ν_{max} 1052 (of THPC), or 1043 or 1135 (for P=O), but intense broad absorption at 1010 cm^{-1}. The ^1H NMR (60MHz, D_2O, internal TMS, or DSS at 0) has δ for CH_2 at 4.15 (J_{PCH} = 5.5Hz, $J_{^{13}CH}$ = ~148Hz); and the ^{31}P NMR (40MHz, D_2O, external 85% H_3PO_4) has δ at -25.8. [Ellzey et al. *J Org Chem* **37** 3453 *1972*.] With *n*-butyl iodide it formed *n-butyl phosphonium iodide* which gave, on treatment with sodium tetraphenylboron, the *n-butyl tris(hydroxymethyl)phosphonium tetraphenylboron complex*, **m 145-146°(dec)** after drying and recrystallising from Me_2CO/*C_6H_6; and the *methiodide* gave with Ph_4BNa, the *methyl tris(hydroxymethyl)phosphonium tetraphenylboron complex*, **m 170-171°(dec)** after drying and recrystallising from Me_2CO/*C_6H_6 [Grayson *J Am Chem Soc* **85** 79 *1963*.]

Tris(hydroxymethyl)phosphine oxide *[1067-12-5]* **M 137.1, m 50-52°, 54-55° (69° and 70° have also been reported).** The oxide is prepared by slowly adding about 130% excess (over an equimolar amount) of 20-50 mesh Dowex-1 x 8 resin (in the OH^- form) to an aqueous solution of tris(hydroxymethyl)phosphine (25.0g, see preceding entry) which led to vigorous evolution of H_2. After standing overnight the resin is filtered off, and the filtrate is evaporated (rotavap, vacuum) to give the *oxide* (16.1g, 88%) which is recrystallised from absolute EtOH to yield hygroscopic crystals (11.9g). Store in a dry atmosphere. The IR has strong bands at ν_{max} 1043

and 1134 cm^{-1}; the ^1H NMR (60MHz, D_2O, internal TMS, or DSS at 0) has δ for CH_2 at 4.20 (J_{PCH} = 3.1Hz, $J_{^{13}CH}$ = ~146Hz); and the ^{31}P NMR (40MHz, D_2O, external 85% H_3PO_4) has δ at -48.7. [Ellzey et al. *J Org Chem* **37** 3453 *1972*, Anteunis et al. *Bull Soc Chim Belg* **74** 622 *1965*.] The *tribenzoate*, prepared by boiling THPC with excess of aqueous NaOH solution until no further evolution of H_2 occurred followed by treatment with a slight excess of PhCOCl, gave fine needles **m 111°** upon recrystallisation from MeOH [Hoffman *J Am Chem Soc* **43** 1684 *1921*].

Trisodium 8-hydroxy-1,3,6-pyrenetrisulfonate (Pyranine Solvent Green 7) *[6358-69-6]* **M 524.4, m >300(dec), CI 59040, λ_{max} 403nm.** Purify the salt by chromatography through an alumina column, and elute with *n*-propanol/water (3:1, v/v). Recrystallise it from aqueous acetone (5:95, v/v) using decolorising charcoal. [*Beilstein* **1** III 565.] **IRRITANT.**

Trisodium 1,3,6-naphthalenetrisulfonate *[5182-30-9]* **M 434.2.** The *free acid* is obtained by passing the salt through an ion-exchange column and converting it to the lanthanum salt by treatment with La_2O_3. This salt is crystallised twice from hot water. [The much lower solubility of $La_2(SO_4)_3$ and its retrograde temperature dependence allows a good separation from sulfate impurity]. The lanthanum salt is then passed through an appropriate ion-exchange column to obtain the free acid, the sodium or potassium salt. (The sodium salt is *hygroscopic*.) [Atkinson et al. *J Am Chem Soc* **83** 1570 *1961*.] It can also be recrystallised from aqueous acetone [Okahata et al. *J Am Chem Soc* **108** 2863 *1986*].

Tris(2,2,2-trifluoroethyl) phosphite *[370-69-4]* **M 328.1, b 130-131°/743mm, d_4^{20} 1.487, n_D^{20} 1.324.** Fractionate the phosphite through a 10 inch Helipak column [Krogh et al. *J Org Chem* **19** 1124 *1954*].

Tris(trimethylsilyl)silane (TTMSS) *[1873-77-4]* **M 248.7, b 73°/5mm, d_4^{20} 0.808, n_D^{20} 1.49.** Purify it by fractional distillation and taking the middle cut. Store it under N_2 or Ar as it is **PYROPHORIC** and is an **IRRITANT**. [Chatgilialoglu et al. *J Org Chem* **53** 3641 *1988*, Balestri et al. *J Org Chem* **56** *678 1991,* Chatgilialoglu *Acc Chem Res* **25** 188 *1992*, NMR: Gilman et al. *J Organomet Chem* **4** 163 *1965*.]

Tri(-*p*-tolyl) phosphate *[20756-92-7, 1330-78-5 (isomeric tritolyl phosphate mixture)]* **M 368.4, m 77°, b 232-234°, d^{25} 1.16484, n_D^{20} 1.56703.** Dry the ester with $CaCl_2$, percolate it through a column of alumina, then distil it under a vacuum. *Alternatively*, pass it through a packed column of alumina at 150°, with a counter-current stream of nitrogen, under reduced pressure, to remove residual traces of volatile impurities. It also crystallises from petroleum ether (b 60-80°). [Cherbuliez in *Organic Phosphorus Compounds* (Kosolapoff & Maier eds) Wiley-Interscience Vol **6** pp 454-457 *1973*.]

Tropaeolin 00 {4-[(4-anilinophenyl)azo]benzenesulfonic acid Na salt} *[554-73-4]* **M 375.4, $pK_{Est(1)}$~ 2.3, $pK_{Est(2)}$~ 5.8, $pK_{Est(3)}$~ 10.3.** Recrystallise it twice from water [Kolthoff & Gus *J Am Chem Soc* **60** 2516 *1938*]. It is an indicator which is red at pH 1.4 and orange-yellow at pH 3.2. [*Beilstein* **16** II 171.]

Vinyl chlorosilane *[75-94-5]* **M 161.5, b 17.7°/46.3mm, 82.9°/599.4mm, 92°/742mm, 91-91.5°/atm, d_4^{20} 0.1.2717, n_D^{20} 1.435.** Fractionally distil the chlorosilane at atmospheric pressure. It is water sensitive and is stored in the dark and it is likely to polymerise. [Müller & Schnurrbusch *Chem Ber* **91** 1805 *1958*, Munkelt & Müller *Chem Ber* **92** 1012 *1959*, Polarography: Abrahamson & Reynolds *Anal Chem* **24** 1827 *1952*, *Beilstein* **4** IV 4258.]

3-Vinylphenylboronic acid ([3-ethenylphenyl]-dihydroxyborane) *[15016-43-0]* **M148.0, m 141-147°, 145-160°, $pK_{Est(1)}$ ~8.8.** This binder for paper or glass crystallises in white plates from H_2O (**m** 144-145°), and its IR has ν_{max} at 919 and 995 ($CH_2CH{=}CH_2$), 1350 (B-O) and 3220 (OH) cm^{-1}. The *dibromo* derivative crystallises in white needles from H_2O with **m** 196-197.5°. [Wesley & Rush *J Org Chem* **27** 2598 *1962*, *Beilstein* **16** III 1279, **16** IV 1677.]

Vinylphosphonic acid *[1746-03-8]* **M 108.0, m 41-45°, d^{25} 1.389, pK_1^{20} 3.48, pK_2^{20} 8.54 (50% EtOH).** This fireproofing agent, and ingredient for making polymers, is obtained as a syrup on hydrolysing vinylphosphonyl dichloride with cold H_2O and solidifies on prolonged drying over P_2O_5/KOH. When distilled at 235-240°/0.0006mm, it gives the *anhydride* (d_4^{20} 1.304, n_D^{20} 1.5874) [Kabachnik & Medvedi *Izvest Akad Nauk SSSR, Ser Khim* 868 *1953*, *Chem Abstr* **54** 10834 *1960*]. It is best kept as the *sodium salt* (**m** 350°) which precipitates when a solution of EtOH containing NaOEt (from 2g of Na) is added to vinylphosphonic acid (3.2g), and is recrystallised from EtOH (5.1g, quantitative). The *p-anisidinium salt* forms mauve prisms **m** 250° (from EtOH/Et_2O). The *dimethyl ester*, [4645-32-3] **M** 136.1, $\mathbf{d_4^{20}}$ 1.1405, $\mathbf{n_D^{20}}$ 1.4330, has **b** 72.5°/10mm and 197-202°/760mm. [Kabachnik et al. *J Gen Chem USSR* (Engl Trans) **33** 375 *1963*, *Beilstein* **4** IV 3568.]

Xylenol Orange (sodium salt). See entry in "Heterocyclic Compounds" in this Chapter.

Zinc diethyldithiocarbamate *[14324-55-1]* **M 561.7, m 178-181°, pK^{25} 3.04 (for $Et_2NCS_2^-$).** Crystallise this herbicide several times from hot toluene or from hot $CHCl_3$ by addition of EtOH. It also crystallises from xylene, **m** 180°. [*Beilstein* **4** II 613.] **TOXIC.**

Zinc dimethyldithiocarbamate *[137-30-4]* **M 305.8, m 151-152°, 248-250°, pK^{25} 3.36 (for $Me_2NCS_2^-$).** Crystallise this herbicide several times from hot toluene or from hot $CHCl_3$ by addition of EtOH. [*Beilstein* **4** III 149, **4** IV 234.]

Zinc ethylenebis(dithiocarbamate) (Zineb) *[12122-67-7]* **M 249.7.** Crystallise this herbicide several times from hot toluene or from hot $CHCl_3$ by addition of EtOH. It is a skin irritant. [*Beilstein* **4** III 149, **4** IV 234.]

Zinc phenol-*o*-sulfonate ($8H_2O$) (Phenozin) *[127-82-2]* **M 555.8.** Phenozin crystallises from warm water by cooling to 0°. It effloresces in dry air, and loses all its H_2O at 120°. Its solubility in H_2O is 63% at 20° and 250% at boiling point, and in EtOH it is 55% at 50°. [*Beilstein* **11** H 53, **11** I 234, **11** IV 574.]

Zinc trifluoromethanesulfonate *[54010-75-2]* **M 363.5, m >300°.** This zinc salt should be dried at 125° for 2 hours at 3mm before use. It is soluble in CH_2Cl_2 but insoluble in petroleum ether. [Corey & Shimoji *Tetrahedron Lett* **24** 169 *1983*.]

CHAPTER 5

PURIFICATION OF INORGANIC AND METAL-ORGANIC CHEMICALS

INTRODUCTION

The most common method of purification of inorganic species is by recrystallisation, usually from water. However, especially with salts of weak acids or of cations other than the alkaline and alkaline earth metals, care must be taken to minimise hydrolysis. This can be achieved, for example, by recrystallising acetates in the presence of dilute acetic acid. Nevertheless, there are many inorganic chemicals that are too insoluble or are hydrolysed by water so that no general purification method can be given. It is convenient that many inorganic substances have large temperature coefficients for their solubility in water, but in other cases recrystallisation is still possible by partial solvent evaporation.
Organo-metallic compounds, on the other hand, behave very much like organic compounds, e.g. they can be redistilled and may be soluble in organic solvents. A note of **caution** should be made about handling organo-metallic compounds, e.g. arsines, because of their **potential toxicities**, particularly when they are volatile. Generally the suppliers of such compounds provide details about their safe manipulation. These should be read carefully and adhered to closely. If in any doubt, always assume that the materials are lethal and treat them with utmost care. The same **safety precautions** about the handling of substances as stated in Chapter 4 should be followed here (see Chapter 1).

For information on **ionization (pK)** see Chapter 1, pp 34-36, and Chapter 4, p 103. In order to avoid repetition, the literature (or predicted) pK values of anionic and/or cationic species are usually reported at least once, and in several cases are entered for the free acid or free base; e.g. Na_2SO_4 will have a pK value for Na^+ at the entry for NaOH and the pK values for SO_4^{2-} at the entries for H_2SO_4. When the pK values of the organic counter-ions are not given in this chapter, as in the case of sodium benzoate, the reader is referred to the value(s) in Chapter 4, Aromatic Compounds, e.g. of benzoic acid.

Abbreviations of titles of periodicals are defined as in the Chemical Abstracts Service Source Index (CASSI).

Benzene, which has been used as a solvent successfully and extensively in the past for reactions and purification by chromatography and crystallization, is now considered a **very dangerous substance**, so it has to be used with extreme care. We emphasised that an alternative solvent to benzene (e.g. toluene, toluene-petroleum ether, or a petroleum ether to name a few) should be used first. However, if benzene has to be used, then all operations have to be performed in well-ventilated fumehoods and precautions taken to avoid inhalation and contact with skin and eyes. Whenever benzene is mentioned in the text, an asterisk, e.g. *C_6H_6 or *benzene, is inserted to remind the user that special precaution should be adopted.

Organic dyes which are *not* complexed, or are salts of metals, are included in Chapter 4 (use the CAS Registry Numbers to find them). Commercially available polymer-supported reagents are indicated with **§** under the appropriate reagent.

This chapter is subdivided into two sections: the **Purification of Inorganic Compounds** and the **Purification of Metal-Organic Compounds** which includes ammonium and metal salts of organic acids.

Purification of Laboratory Chemicals. http://dx.doi.org/10.1016/B978-0-12-382161-4.00005-4

INORGANIC COMPOUNDS

Alumina (aluminium oxide) (neutral) *[1344-28-1]* **M 102.0 (anhydrous).** Stir the oxide with hot 2M HNO_3, either on a steam bath for 12 hours (changing the acid every hour) or three times for 30 minutes, then wash it with hot distilled water until the washings have pH 4, and follow by three washings with hot MeOH. The product is dried at 270° [Angyal & Young *J Am Chem Soc* **81** 5251 *1959*]. For the preparation of alumina for chromatography see Chapter 1. [For α, β and γ Al_2O_3 see Becher in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 822-823 *1963* and Wagner in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1662 *1965*.]

Aluminium ammonium sulfate decahydrate *[7784-26-1]* **M 453.3, m 93°, m 95°, pK_1^{25} 4.89, pK_2^{25} 5.43, pK_3^{25} 5.86 (Al^{3+} aquo), pK_4^{25} 11.22 [aluminate $Al(OH)_4^-$].** Crystallise it from hot H_2O and cool in ice. When the melt is heated, it loses NH_3 and H_2SO_4, and gives pure alumina at red heat. Solubility (%) in H_2O is 3.9% (0°), 15.0 (20°) and 135 (100°).

Aluminium bromide *[7727-15-3]* **M 266.7, m 97°, b 114°/10mm, d_4^{18} 3.205.** Reflux it and then distil it from pure aluminium chips in a stream of nitrogen into a flask containing more of the chips. It is then redistilled under vacuum into ampoules [Tipper & Walker *J Chem Soc* 1352 *1959*]. Anhydrous conditions are essential, and the white to very light brown solid distillate can be broken into lumps in a dry-box (under nitrogen). It fumes in moist air. [Becher in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 812-813 *1963*.]

Aluminium caesium sulfate dodecahydrate *[7784-17-0 ($12H_2O$), 14284-36-7]* **M 568.2.** Recrystallise it from hot water (3ml/g).

Aluminium chloride (anhydrous) *[7446-70-0]* **M 133.3, m 192.6°, d_4^{17} 2.465.** Sublime it several times in an all-glass system under nitrogen at 30-50mm pressure. It has also been sublimed in a stream of dry HCl and has been subjected to a preliminary sublimation through a section of granular aluminium metal [for manipulative details see Jensen *J Am Chem Soc* **79** 1226 *1957*]. It fumes in moist air. Used in Friedel-Crafts reaction.

Aluminium fluoride (anhydrous) *[7784-18-4]* **M 84.0, m 250°.** The technical material may contain up to 15% alumina, and minor impurities such as aluminium sulfate, cryolite, silica and iron oxide. Reagent grade AlF_3 (hydrated) contains only traces of impurities, but its water content is variable (and may be up to 40%). It can be dried by calcining at 600-800° in a stream of dry air (some hydrolysis occurs), followed by vacuum distillation at low pressure in a graphite system, heated to approximately 925° (condenser at 900°) [Henry & Dreisbach *J Am Chem Soc* **81** 5274 *1959*]. Its solubility in H_2O is 0.5%. [Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 225-226 *1963*.]

Aluminium nitrate nonahydrate *[7784-27-2 ($9H_2O$); 13473-90-0]* **M 375.1.** Crystallise the nitrate from dilute HNO_3, and dry it by passing dry nitrogen through the crystals for several hours at 40°. After 2 recrystallisations of ACS grade, it had S, Na and Fe at 2.2, 0.01 and 0.02 ppm, respectively.

Aluminium potassium sulfate dodecahydrate (alum) *[7784-24-9]* **M 474.4, m 92°.** Crystallise it from weak aqueous H_2SO_4 (*ca* 0.5ml/g). Its solubility (%) in H_2O is 5.7 (0°), 12.0 (20°) and 136.9 (100°).

Aluminium rubidium sulfate dodecahydrate *[7784-29-4]* **M 496.2.** Crystallise the double salt from aqueous H_2SO_4 (*ca* 2.5ml/g).

Aluminium sulfate (anhydrous) *[10043-01-3]* **M 342.2, m 765°(dec), Al_2O_3 14-18 H_2O** *[17927-65-0]*, **Al_2O_3 18 H_2O** *[7784-31-8]*. It crystallises from hot dilute H_2SO_4 (l ml/g) on cooling in ice. When a solution of alumina (Al_2O_3) in conc H_2SO_4 is slowly cooled, Al_2SO_4 17 or $18H_2O$ deposits as a crystalline mass. Al_2SO_4 $17H_2O$ is the stable form in equilibrium with its saturated aqueous solution at 25° [Smith *J Am Chem Soc* **64** 41

1942]. This is purified by dissolving it in a small volume of H_2O and adding EtOH until the sulfate readily crystallises from the oily supersaturated solution. It forms Al_2O_3 $16H_2O$ between 0-112°. On gradual heating, the hydrate melts, giving the anhydrous salt at *ca* 250°. Several hydrates up to $27H_2O$ have been described. Further heating to red heat (~ 600-800°) causes decomposition to $Al_2O_3 + SO_3 + SO_2$ and O_2 [Cobb *J Soc Chem Ind* **29** 250 *1910*]. The ACS reagent is Al_2O_3 $18H_2O$ (98+%).

Ammonia (gas) *[7664-41-7]* **M 17.0, pK^{25} 9.25.** Major contaminants are water, oil and non-condensable gases. Most of these impurities are removed by passing the ammonia through a trap at -22° and condensing it at -176° under vacuum. Water is removed by distilling the ammonia into a tube containing a small lump of sodium. Also dry it by passage through porous BaO, or over alumina followed by glass wool impregnated with sodium (prepared by soaking the glass wool in a solution of sodium in liquid ammonia and evaporating off the ammonia). It can be rendered oxygen-free by passage through a solution of potassium in liquid ammonia. [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 460-463 *1963*.] **AMMONIA (gas, liquid or aqueous solution) is very irritating and should not be inhaled in any quantity as it can lead to olfactory paralysis (temporary or permanent).**

Ammonia (liquid) *[7664-41-7]* **M 17.0, m -77.8°, b -33.35°, n $^{20}_{D}$ 1.325, d $^{20}_{4}$ 0.597, d^{-79} 0.817g/ml.** Dry the liquid, and store it, with sodium in a steel cylinder, then distil and condense it by means of liquid air, the non-condensable gases being pumped off. In order to obtain liquid NH_3 from a cylinder, turn the cylinder upside-down (i.e. with the valve at the bottom, use a metal stand to secure it in this position; a special stand can be constructed for it) and lead a plastic tube from the tap to a measuring cylinder placed in an efficient fume cupboard which is kept running. Turn the tap on and allow the ammonia to be released. At first, gas and liquid will splatter out (make sure that the plastic tube is secure), but soon the liquid will drip into the measuring cylinder. The high latent heat of evaporation will cool the ammonia so that the liquid will remain cool and not boil vigorously. If the ammonia is required dry, the necessary precautions should be taken, i.e. the gas is allowed to flow through tubes packed with coarse CaO pellets. **AMMONIA (gas, liquid or aqueous solution) is very irritating and should not be inhaled in any quantity as it can lead to olfactory paralysis (temporary or permanent).**

Ammonia (aqueous) *[7664-41-7]* **M 17.0 + H_2O, d $^{20}_{4}$ 0.90 (saturated, 27% w/v, 14.3 N), pK^{25} 9.25 (pK$_b$ at 25° = 4.75, i.e. 14.00-9.25, and $K_b = 1.81 \times 10^{-5}$).** Obtained metal-free by saturating distilled water, in a cooling bath, with ammonia (from a cylinder) gas. *Alternatively*, isothermal distillation can be used by placing a dish of concentrated aqueous ammonia and a dish of pure water in an empty desiccator and leaving to equilibrate for several days. **AMMONIA (gas, liquid or aqueous solution) is very irritating and should not be inhaled in any quantity as it can lead to olfactory paralysis (temporary or permanent).**

Ammonium bisulfate (ammonium hydrogen sulfate $(NH_4)_2HSO_4$) *[7803-63-6]* **M 115.1, m ~147°, d $^{20}_{4}$ 1.79, pK^{25} 1.96 (HSO_4^-).** It crystallises from water at room temperature (1ml/g) on adding EtOH and cooling. (NH_4) HSO_4 is formed as deliquescent rhombic crystals on cooling a solution of $(NH_4)_2SO_4$ in hot conc H_2SO_4 but EtOH decomposes it to $(NH_4)_3H(SO_4)_2$ [Dunnicliff *J Chem Soc* **123** 476 *1923*]. When powdered $(NH_4)_2SO_4$ is heated below 100°, it loses NH_3, and at 300° it is completely converted to fused (NH_4) HSO_4, **m** 140°, but >300° it decomposes to SO_2 and N_2 [Smith *J Chem Soc* **30** 253 *1911*].

Ammonium bromide *[12124-97-9]* **M 98.0, m 450°(sublimes), d $^{20}_{4}$ 2.43.** It crystallises from 95% EtOH and is slightly hygroscopic.

Ammonium chloride *[12125-02-9]* **M 53.5, m 338°(sublime point, without melting), d $^{20}_{4}$ 1.53.** Crystallise it several times from conductivity water (1.5ml/g) between 90° and 0°. It sublimes. The salt is fully ionised in aqueous solution, i.e. $K \approx \infty$. A 1M aqueous solution of NH_4Cl has a pH of ~4.7, i.e. is acidic. After one crystallisation, ACS grade has: metal(ppm) As (1.2), K (1), Sb (7.2), V (10.2). [Becher in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 812 *1963*.]

Ammonium chromate *[7788-98-9]* **M 152.1, m 185°(dec), d_4^{20} 1.81, pK_1^{25} 0.74, pK_2^{25} 6.49 (for H_2CrO_4).** Crystallise it from weak aqueous ammonia (*ca* 2.5ml/g) by cooling from room temperature. It loses NH_3 on heating to form ammonium dichromate. **POISONOUS.**

Ammonium dichromate *[7789-09-5]* **M 252.1, m 170°(dec), d_4^{20} 1.26.** It crystallises from weak aqueous HCl (*ca* 1ml/g). It decomposes rapidly on heating. (Possible **carcinogen and is POISONOUS**).

Ammonium dihydrogen arsenate *[13462-93-6]* **M 159.0, m 300°(dec).** Crystallise it from water (1ml/g). **POISONOUS**.

Ammonium dihydrogen orthophosphate *[7722-76-1]* **M 115.0, m 190°, d_4^{20} 1.80.** Crystallise it from water (0.7ml/g) between 100° and 0°.

Ammonium ferric sulfate dodecahydrate *[7783-83-7 ($12H_2O$), 10138-04-2 (anhydrous)]* **M 482.2, m ~37°, d_4^{20} 1.71.** Crystallise it from aqueous ethanol.

Ammonium ferrous sulfate hexahydrate [Mohr's salt] *[7783-85-9 ($6H_2O$), 10045-89-3 (anhydrous)]* **M 392.1, m 100°(dec), d_4^{20} 1.86.** A solution in warm water (0.67g/ml) is cooled rapidly to 0°, and the resulting light bluish-green monoclinic crystals are filtered at the pump, washed with cold distilled water and pressed between sheets of filter paper to dry it. The solubility at 25° is 0.36g/ml. It separates as an almost white powder when a saturated aqueous solution is diluted with EtOH.

Ammonium hexachloroiridate (IV) *[16940-92-4]* **M 441.0.** It is precipitated several times from aqueous solution by saturation with ammonium chloride. This removes any palladium and rhodium. It is then washed with ice-cold water and dried over conc H_2SO_4 in a vacuum desiccator. If osmium or ruthenium is present, it can be removed as the tetroxide by heating with conc HNO_3, followed by conc $HClO_4$, until most of the acid has been driven off. (This treatment is repeated.) The near-dry residue is dissolved in a small amount of water and added to excess $NaHCO_3$ solution and bromine water. On boiling, iridic (but not platinic) hydroxide is precipitated. It is dissolved in HCl and precipitated several times, then dissolved in HBr and treated with HNO_3 and HCl to convert the bromides to chlorides. Saturation with ammonium chloride and cooling precipitates ammonium hexachloroiridate which is filtered off and purified as above [Woo & Yost *J Am Chem Soc* **53** 884 *1931*].

Ammonium hexacyanoferrate II hydrate *[14481-29-9]* **M 284.1, m dec on heating.** The pale yellow *trihydrate* powder can be washed with 10% aqueous NH_3, filtered, then washed several times with EtOH and Et_2O, and dried at room temperature. It decomposes in a vacuum above 100° and should be stored away from light and under N_2. In light and air it decomposes by losing NH_3. [Lux in *Handbook of Preparative Inorganic Chem (Ed. Brauer)* Academic Press Vol **II** p 1509 *1965*.]

Ammonium hexafluorophosphate *[16941-11-0]* **M 163.0, d_4^{18} 2.181, pK_1^{25} ~0.5, pK_2^{25} 5.12 (for fluorophosphoric acid H_2PO_3F).** It crystallises from H_2O in square plates and decomposes on heating before melting. Its solubility in H_2O at 20° is 74.8% w/v, and it is very soluble in Me_2CO, MeOH, EtOH and MeOAc, but is decomposed by boiling mineral acids. [Lange & Müller *Chem Ber* **63** 1063 *1930*, Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 195 *1963*.]

Ammonium hexafluorosilicate *[16919-19-0]* **M 178.1, pK_2 1.92 (for H_2SiF_6).** Crystallise the salt from water (2ml/g). After 3 recrystallisations, the Technical grade salt has Li, Na, K and Fe at 0.3, 0.2, 0.1 and 1.0 ppm respectively.

Ammonium hypophosphite *[7803-65-8]* **M 83.0.** Crystallise it from hot EtOH.

Ammonium iodate *[13446-09-8]* **M 192.9, pK^{25} 0.79 (IO^{3+}).** Ammonium iodate crystallises from water (8ml/g) on cooling from 100° to 0°.

Ammonium iodide *[12027-06-4]* **M 144.9, sublimes with dec ~405°, d $_4^{20}$ 2.51.** The iodide crystallises from EtOH on addition of ethyl iodide, and is very *hygroscopic*. Store it in the dark. Its solubility is 177g in 100g of H_2O at 25°. [Schmeisser in *Handbook of Preparative Inorganic Chem (Ed. Brauer)* Academic Press Vol I p 289-290 *1963*.]

Ammonium magnesium chloride hexahydrate *[60314-43-4]* **M 256.8.** It crystallises from water (6ml/g) by partial evaporation in a desiccator over KOH (deliquescent).

Ammonium magnesium sulfate hexahydrate *[20861-69-2]* **M 360.6.** It crystallises from water (1ml/g) between 100° and 0°.

Ammonium manganous sulfate hexahydrate *[13566-22-8]* **M 391.3.** It crystallises from water (2ml/g) by partial evaporation in a desiccator.

Ammonium molybdate *[13106-76-8]* **M 196.0, pK $_1^{25}$ 0.9 (proton addition), pK $_2^{25}$ 3.57, pK $_3^{25}$ 4.08 (for H_2MoO_4).** Crystallise the salt from water (2.5ml/g) by partial evaporation in a desiccator. When a solution of MoO_3 in excess of hot concentrated NH_3 is cooled, *normal* ammonium molybdate $(NH_4)_2MoO_4$ crystallises out. However, when this solution is made to evaporate which allows the pH to drop to 6, the *common* hydrated ammonium *para*molybdate $(NH_4)_6Mo_7O_{24}$ $4H_2O$ {or $3[(NH_4)_2O]$, $7MoO_3$, $4H_2O$, [12054-85-2] M 1235.9} crystallises out. This was an old formula which was confirmed by Sturdivant. [Sturdivant *J Am Chem Soc* **59** 630 *1937*, Grüttner & Jauder in *Handbook of Preparative Inorganic Chem (Ed. Brauer)* Academic Press Vol **II** p 1711 *1965*.]

Ammonium nickel sulfate hexahydrate *[7785-20-8 ($6H_2O$), 15699-18-0 (anhydrous)]* **M 395.0, d $_4^{20}$ 1.923.** Crystallise this salt from water (3ml/g) on cooling from 90° to 0°.

Ammonium nitrate *[6484-52-2]* **M 80.0, m 165°(moist salt), 210°(dec explosively), d $_4^{20}$ 1.72.** It is crystallised twice from distilled water (1ml/g) by adding EtOH, or from warm water (0.5ml/g) by cooling in an ice-salt bath. Dry it in air, then under vacuum. After 3 recrystallisations of ACS grade, it contained Li and B at 0.03 and 0.74 ppm, respectively. It is deliquescent. [Early & Lowry *J Chem Soc* **115** 1387 *1919*, **121** 963 *1922*, Hendricks et al. *J Am Chem Soc* **54** 2766 *1932*.]

Ammonium perchlorate *[7790-98-9]* **M 117.5, d $_4^{20}$ 1.95, pK^{25} -2.4 to -3.1 (for $HClO_4$).** It is recrystallised twice from distilled water (2.5ml/g) between 80° and 0°, and dried in a vacuum desiccator over P_2O_5. Drying at 110° might lead to slow decomposition to the chloride. **POTENTIALLY EXPLOSIVE**.

Ammonium peroxydisulfate (ammonium persulfate) *[7727-54-0]* **M 228.2, m dec when heated wet liberating oxygen, d $_4^{20}$ 1.98.** Recrystallise it at room temperature from EtOH/water. It gradually loses NH_3 on exposure to air. Its solubility is 0.5g/ml at 20°, and 2g/ml at 100°.

Ammonium reineckate {Reineckate salt, $NH_4[Cr(NH_3)_2(SCN)_4]$} *[13573-16-5]* **M 336.4 (anhydrous), m 270-273°(dec).** Crystallise it from water, between 30° and 0°, while working under artificial light. Solutions of reineckate salt (aqueous or alcoholic) decompose slowly at room temperature in the dark (~2 weeks) and more rapidly at higher temperatures or in diffuse sunlight. The solutions are blue in colour and liberate HCN **(POISONOUS)**. Store it dry in the dark under a vacuum. [Dakin *Org Synth* Coll Vol **II** 555 *1943*.]

Ammonium selenate *[7783-21-3]* **M 179.0, d $_4^{20}$ 2.19, m dec on heating.** Crystallise the selenate from water at room temperature by adding EtOH and cooling. Its solubility in H_2O is 117% at 7° and 197% at 100°. [King *J Phys Chem* **41** 797 *1937*.]

Ammonium sulfamate *[7773-06-0]* **M 114.1, m 132-135°, dec at 160°.** Crystallise it from water at room temperature (1ml/g) by adding EtOH and cooling. [Sisler & Audrieth *Inorg Synth* **II** 180 *1946*.]

Ammonium sulfate *[7783-20-2]* **M 132.1, m 230°(dec), 280°(dec), d $_4^{20}$ 1.77.** Crystallise it twice from hot

water containing 0.2% EDTA to remove metal ions, then finally from distilled water. Dry it in a desiccator for 2 weeks over $Mg(ClO_4)_2$. After 3 recrystallisations, ACS grade had Ti, K, Fe, Na at 11, 4.4, 4.4, 3.2 ppm respectively.

Ammonium tetrafluoroborate *[13826-83-0]* **M 104.8, pK^{25} 2.77 (for HBF_4).** Crystallise it from conductivity water (1m/g) between 100° and 0°.

Ammonium thiocyanate *[1762-95-4]* **M 76.1, m 138°(dec), 149°(dec), pK^{25} -1.85 (for HSCN), 149.** Crystallise it three times from dilute $HClO_4$ to give material optically transparent at wavelengths longer than 270nm. It has also been crystallised from absolute MeOH or from acetonitrile.

Ammonium tungstate (VI) *[11120-25-5]* **M 283.9, pK $_1^{25}$ 2.20, pK $_2^{25}$ 3.70 (for tungstic acid, H_2WO_4).** It crystallises from warm water on adding EtOH and cooling.

Ammonium (meta) vanadate *[7803-55-6]* **M 117.0, d $_{10}^{20}$ 2.326.** Wash the salt with H_2O until free from Cl^- ions and dry it in air. It is soluble in H_2O (5.18g/100ml at 15°, 10.4g/100ml at 32°) but is more soluble in dilute NH_3. It crystallises from conductivity water (20ml/g). When heated at relatively low temperature, it loses H_2O and NH_3 to give vanadium oxide (V_2O_5), and at 210° it forms lower oxides. [Baker et al. *Inorg Synth* **III** 117 *1950*.] Its solubility in H_2O is 0.52% (15°), 1% (32°) and 1.6% (50°). After washing the technical grade salt with H_2O, it had Na, Mn and U at 0.06, 0.2 and 0.1 ppm, respectively. [Brauer in *Handbook of Preparative Inorganic Chem (Ed. Brauer)* Academic Press Vol **II** p 1272-1273 *1965*.]

Antimony (V) pentafluoride *[7783-70-2]* **M 216.7, m 7.0°, 8.3°, b 141°, 150°, 148-150°, d $_4^{20}$ 2.99, pK^{25} 2.55 [for $HSb(OH)_6 = Sb(OH)_6^- + H^+$].** Purify it by vacuum distillation, preferably in a quartz apparatus, and store it in quartz or aluminum bottles. It is a *hygroscopic* viscous liquid which reacts *violently* with H_2O and is hydrolysed by alkalis. *It is* **POISONOUS** *and attacks the skin*. [Woolf & Greenwood *J Chem Soc* 2200 *1950*, Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 200 *1965*.]

Antimony trichloride *[10025-91-9]* **M 228.1, m 73°, b 283°, pK $_1^{25}$ 1.4, pK $_2^{25}$ 11.0 (11.8), pK $_3^{25}$ 12.95 (for Sb^{3+} aquo).** Dry the trichloride over P_2O_5 or by mixing it with toluene or xylene and distilling (water is carried off with the organic solvent), then distil it twice under dry nitrogen at 50mm, and sublime it twice in a vacuum into ampoules and seal. It can be crystallised from CS_2 and is *deliquescent*. It fumes in moist air and is decomposed by H_2O with precipitation of the basic chloride, but forms a clear solution in dilute HCl.

Antimony trifluoride *[7783-56-4]* **M 178.8, m 292°, b 376°, d $_4^{20}$ 4.379.** It crystallises from MeOH to remove oxide and oxyfluoride, then it is sublimed under vacuum in an aluminium cup on to a water-cooled copper condenser. Its solubility is 443g/100g in H_2O at 20° and 562g/100g in H_2O at 30° with partial hydrolysis. [Woolf *J Chem Soc* 279 *1955*, Kwasnik in *Handbook of Preparative Inorganic Chem (Ed. Brauer)* Academic Press Vol **I** p 199 *1963*].

Antimony triiodide *[7790-44-5]* **M 502.5, m 167°, 170°, b 401°.** It sublimes under vacuum as a red solid with an orange vapour. It hydrolyses to the yellow oxyiodide with H_2O. [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 614 *1963*.]

Antimony trioxide *[1309-64-4]* **M 291.5, m 656°.** Dissolve the trioxide in the minimum volume of dilute HCl, filter, and add six volumes of water to precipitate the basic antimonous chloride (free from Fe and Sb_2O_5). The precipitate is redissolved in dilute HCl, and added slowly, with stirring, to a boiling solution (containing a slight excess) of Na_2CO_3. The oxide is filtered off, washed with hot water, then boiled and filtered. The process is repeated until the filtrate gives no test for chloride ions. The product is dried in a vacuum desiccator [Schuhmann *J Am Chem Soc* **46** 52 *1924*]. After one crystallisation (precipitation?), the oxide from a Chinese source had: metal (ppm) Al (8), Ag (0.2), As (56), Cr (6), Ge (0.4), Mn (0.2), Na (16), Ni (2.2) Pb (2.4), Sn (0.4) and V (32). It sublimes in a vacuum at 400°, being yellow on heating and pale buff in colour on cooling. [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 615-616 *1963*.]

Aqua regia. This is prepared by slowly adding concentrated HNO_3 (1 volume) to concentrated hydrochloric acid (3 volumes) in a glass container. This mixture is used to dissolve metals, including noble metals and alloys, as well as minerals and refractory substances. It is done by suspending the material and boiling (**EFFICIENT FUME CUPBOARD — EYE PROTECTION**] to dryness and repeating the process until the residue dissolves in H_2O. If the aqua regia is to be stored for long periods it is advisable to dilute it with one volume of H_2O which will prevent it from releasing chlorine and other chloro and nitrous compounds which are objectionable and toxic. Store it cool in a fume cupboard. However, it is good laboratory practice to prepare it freshly and dispose of it down the fume cupboard sink with copious amounts of water.

Argon *[7440-37-1]* **M 39.95, b -185.6°.** Argon is rendered oxygen-free by passage over reduced copper at 450°, or by bubbling through alkaline pyrogallol and H_2SO_4, then dried with $CaSO_4$, $Mg(ClO_4)_2$, or Linde 5A molecular sieves. Other purification steps include passage through Ascarite (**CARE: asbestos** impregnated with sodium hydroxide), through finely divided uranium at about 800° and through a -78° cold trap.
Alternatively, the gas is passed over CuO pellets at 300° to remove hydrogen and hydrocarbons, over Ca chips at 600° to remove oxygen and, finally, over titanium chips at 700° to remove nitrogen. It has also been purified by freeze-pump-thaw cycles and by passage over sputtered sodium [Arnold & Smith *J Chem Soc, Faraday Trans 2* **77** 861 *1981*].

Arsenic acid (arsenic pentoxide hydrate, arsenic V oxide hydrate, orthoarsenic acid) *[12044-50-7]* **M 229.8 + xH_2O, pK_1^{25} 2.26, pK_2^{25} 6.76, pK_3^{25} 11.29 (H_3AsO_4).** The acid crystallises from concentrated solutions of boiling conc HNO_3 as rhombic crystals. Dry it in a vacuum to give the *hemihydrate* (hygroscopic). Heating above 300° yields As_2O_5. [Thaler *Z Anorg Allgem Chem* **246** 19 *1941*, Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 601 *1963*.] **POISONOUS.**

Arsenic tribromide *[7784-33-0]* **M 314.6, m 31.1°, b 89°/11mm, 221°/760mm, d_4^{20} 3.67.** Distil it under vacuum. It hydrolyses in H_2O, but less readily than $AsCl_3$. **POISONOUS.** [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 597 *1963*.]

Arsenic trichloride (butter of arsenic) *[7784-34-1]* **M 181.3, m 31.2°, b 25°/11mm, 130.0°/atm, d_4^{20} 2.2.** Reflux the trichloride with arsenic for 4 hours, then fractionally distil it. The middle fraction is stored with sodium wire for two days, then again distilled [Lewis & Sowerby *J Chem Soc* 336 *1957*]. It fumes in moist air forming the solid hydroxy-chloride [$AsCl(OH)_2$] and is readily hydrolysed by H_2O to form arsenious acid. **POISONOUS.** [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 596 *1963*.]

Arsenic triiodide *[7784-45-4]* **M 455.6, m 146°, b 400°/atm, d_4^{25} 4.688.** It crystallises from acetone and sublimes below 100°. It is very slowly hydrolysed by H_2O (much more slowly than the chloride). **POISONOUS.** [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 597-598 *1963*.]

Arsenic III oxide (arsenic trioxide, arsenious oxide) *[1327-53-3]* **M 197.8, three forms: m ~200°(amorphous glass), m 275°(sealed tube, octahedral, common form, sublimes > 125° without fusion but melts under pressure), and m ~312°, pK_1^{20} 9.27, pK_2^{20} 13.54, pK_3^{20} 13.99 (for H_3AsO_3).** It crystallises in an *octahedral form* (common form) from H_2O or from dilute HCl (1:2), and is then washed, dried and sublimed (193°/760mm). Analytical reagent grade material is suitable for use as an analytical standard after it has been dried at 105° for 1-2 hours or has been left in a desiccator for several hours over conc H_2SO_4.
Alternatively, As_2O_3 (15g) is dissolved by heating in a mixture of H_2O (60ml) and HCl (90g, s.g. 1.1), and crystallisation occurs on cooling, accompanied by brilliant flashes of light [Bandrowski *Z Phys Chem* **17** 234 *1895*].
The *amorphous* form is a colourless transparent glass (**m 200°**) which is obtained when the vapour is slowly condensed below the vaporisation temperature, and should be kept in a sealed tube because it changes to the *octahedral* form (**m 275°**) in the presence of moisture. [Rushton & Daniels *J Am Chem Soc* **48** 384 *1926*.]
A third *monoclinic* form, is obtained by heating the oxide in a sealed tube at 400° (the vitreous, amorphous form

remains at the bottom of the tube) with the *monoclinic* form subliming onto the intermediate part of the tube at 200° (**m 312°)**, and the *octahedral* form deposits at the top of the tube. The transition temperature between the last two forms is ~250°. **POISONOUS (particularly the vapour, handle in a ventilated fume cupboard).** [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 600 *1963*.]

Barium (metal) *[7440-39-3]* **M 137.3, m 727°, b 1640°(1537°)/760mm, d_4^{20} 3.56(3.76).** Barium is cleaned by washing with diethyl ether to remove adhering paraffin, then filed in an argon-filled glove box, washed first with ethanol containing 2% conc HCl, then with dry ethanol. It is dried in a vacuum and stored under argon [Addison et al. *J Chem Soc* 3868 *1962*]. It has also been purified by double distillation under 10mm of argon pressure.

Barium bromide dihydrate *[7791-28-8]* **M 333.2, m at 75° loses first H_2O and at 120° it loses the second H_2O and melts at 847°.** It crystallises from H_2O (1ml/g) by partial evaporation in a desiccator. [Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 930 *1963*.]

Barium chlorate monohydrate *[10294-38-9 (hydrate), 13477-00-4 (anhydrous)]* **M 322.3, m 414°.** It crystallises from H_2O (1ml/g) between 100° and 0°, and loses $1H_2O$ at 120°. [Schmeisser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 314 *1963*.]

Barium chloride dihydrate *[10326-27-9]* **M 244.3, m ~120°(dec, hydrate), 963° (anhydrous).** It is crystallised twice from water (2ml/g) and dried in an oven to constant weight. The solubilities of the hydrate (% of anhydrous wt) in H_2O are 31.6 at 0°, 35.7 at 20° and 58.7 at 100°.

Barium dithionate dihydrate *[13845-17-5]* **M 333.5, m >150° loses SO_2, pK^{25} 0.49 (for $H_2S_2O_6$, theory pK_1 -3.4, pK_2 -0.2).** It crystallises from water. Its solubility in H_2O is 7.9% (0°), 15.7% (20°) and 19.9% (30°). [Pfanstiel *Inorg Synth* **II** 170 *1946*, Fehér in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 397 *1963*.]

Barium ferrocyanide hexahydrate *[13821-06-2]* **M 594.8, m 80°(dec), pK_3^{25} 2.57, pK_4^{25} 4.35 (for ferrocyanide).** It crystallises from hot water (100ml/g).

Barium fluoride *[7787-32-8]* **M 175.3, m 1353°, 1368°, b 2260°, d_4^{20} 4.83.** Wash it well with distilled H_2O and dry it in a vacuum. Its solubility in H_2O is 1.6g (10°), 1.6g (20°) and 1.62g (30°) per L, and is soluble in mineral acids and aqueous NH_4Cl. It may be stored in glass bottles. [Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 234 *1963*.]

Barium hydroxide octahydrate *[12230-71-6]* **M 315.5, m 78°, pK_1^{25} 13.13, pK_2^{25} 13.36.** It crystallises from water (1ml/g) and readily absorbs CO_2 from air. It effloresces to the *monohydrate*. It dehydrates to $Ba(OH)_2$ in dry air at 100°. An aqueous solution (***baryta water***) absorbs CO_2 to form a white precipitate of $BaCO_3$.

Barium hypophosphite monohydrate *[14871-79-5]* **M 285.4.** It precipitates from aqueous solution (3ml/g) on adding EtOH. Its solubility in H_2O is 28.6% at 17° and 33.3% at 100°. [Klement in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 557 *1963*.]

Barium iodate monohydrate *[7787-34-0]* **M 487.1, m 130°(loses H_2O), 476°(dec).** It crystallises from a large volume of hot water on cooling. Its solubility in H_2O is 1g/3.35L at 25° and 1g/0.625L at the boiling point. [Lambert & Yasada *Inorg Synth* **VII** 13 *1963*.]

Barium iodide dihydrate *[7787-33-9 ($2H_2O$), 13718-50-8 (anhydrous)]* **M 427.2, m 740°(dec).** It crystallises from water (0.5ml/g) by partial evaporation in a desiccator. **POISONOUS.**

Barium manganate (barium permanganate) *[7787-35-1]* **M 256.3, d_4^{20} 3.77.** Wash the salt with conductivity

H_2O by decantation until the supernatant gives a faint test for Ba^{2+}. Remove excess H_2O in a vacuum (IMPORTANT), then heat at 100° and the last traces of H_2O are removed in a vacuum desiccator over P_2O_5. Store it over KOH. It disproportionates in hot H_2O or dilute acid into $Ba(MnO_2)_2$ and MnO_2, and is a mild oxidant. [Schlezinger & Siems *J Am Chem Soc* **46** 1965 *1924*, Nyholm & Woolliams *Inorg Synth* **XI** 56 *1968*.]

Barium nitrate *[10022-31-8]* **M 261.4, m 593°(dec).** Crystallise it twice from water (4ml/g) and dry it overnight at 110°. It decomposes at higher temperatures to give mostly the oxide and the peroxide with only a little of the nitrite. **POISONOUS.** [Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 941 *1963*.]

Barium nitrite monohydrate *[7787-38-4]* **M 247.4, m 217°(dec).** Barium nitrite crystallises from water (1ml/g) on cooling in an ice-salt bath. **POISONOUS.**

Barium perchlorate *[13465-95-7]* **M 336.2, m 505°, pK^{25} -2.4 to -3.1 (for $HClO_4$).** Recrystallise the perchlorate twice from water. [Schmeisser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 320 *1963*.]

Barium sulfate *[7722-43-7]* **M 233.4, m >1580°.** Wash the sulfate five times by decantation with hot distilled water, dialyse it against distilled water for one week, then freeze-dry and dry in an oven at 105° to constant weight (~12 hours). It is almost insoluble in H_2O (its solubility is 0.0024g/L at 25°).

Barium tetrathionate *[82203-66-5]* **M 361.6.** Purify the tetrathionate by dissolving it in a small volume of water and precipitating it with EtOH below 5°. After drying, the salt is stored in the dark at 0°. [see Frehér in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 399-401 *1963* for potassium tetrathionate $K_2S_4O_4$.]

Barium thiocyanate dihydrate *[2092-17-3]* **M 289.6, pK^{25} -1.85 (for HSCN).** It is crystallised from water (2.5ml/g) by partial evaporation in a desiccator. It is deliquescent. [Herstein *Inorg Synth* **III** 24 *1950*.]

Barium thiosulfate *[35112-53-9]* **M 249.5, m 220°(dec), pK_1^{25} 0.6, pK_2^{25} 1.74 (for $H_2S_2O_3$).** It is very slightly soluble in water and is washed repeatedly with chilled water and dried in air at 40°.

Beryllium carbonate ($BeCO_3$) *[744998-97-8]* **M 69.0.** The commercial carbonate contains more than 1% of impurities. It is best purified by converting it to the basic acetate (see [1332-52-1]) which should be sublimed, converted into the nitrate with HNO_3 see below [13587-99-4]) and evaporated in a Pt dish until free from excess acid. The residual nitrate salt is dissolved in a small volume of H_2O and enough ammonium carbonate solution is added to redissolve the beryllium carbonate that precipitates and gives a clear solution. This is then evaporated in a Pt dish until course $BeCO_3$ separates. It is washed thoroughly with pure H_2O, then distilled EtOH and dried *in vacuo*. $Be(OH)_2$, BeO and Be salts are generally insoluble in NH_3 but dissolve in **aqueous** $(NH_4)_2CO_3$ solution to form the carbonate. [Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 893 *1963*.] Beryllium compounds are potentially **carcinogenic**.

Beryllium chloride ($BeCl_2$) *[7787-47-5]* **M 79.9, m 399°, 405°, b 488°/atm, d^{25} 1.89.** The anhydrous chloride is obtained by heating Be powder or chips (or BeO + C) with Cl_2 gas in a furnace at 300-350° for *ca* 40 hours when anhydrous $BeCl_2$ sublimes out as a white to faintly yellow crystalline mass or orthorhombic crystals. It is purified further by sublimation at ~300° *in vacuo*. It is very hygroscopic and reacts exothermically with H_2O which becomes acidic. The solid should be stored in a tightly stoppered vessel and handled in a dry atmosphere much like anhydrous $AlCl_3$ and has similar catalytic properties to it. It is insoluble in $*C_6H_6$ and toluene but is soluble EtOH, Et_2O, pyridine and CS_2 with which it probably complexes. The conductivity of fused $BeCl_2$ is ~0.001 of that of fused NaCl implying that 1 molecule in 1000 is ionised. [Tannenbaum *Inorg Synth* **5** 22 *1957*, Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 889 *1963*.] Beryllium compounds are potentially **carcinogenic**.

Beryllium hydroxide [$Be(OH)_2$] *[13327-32-7]* **M 43.0, d^{25} 1.89.** The hydroxide exists in two forms, a meta-

stable α-form and a stable β-form. The former is obtained in amorphous form by precipitating a Be salt with NH_3 in the absence of CO_2 and allowing it to age by prolonged heating (~24 hours) with NH_4OH solution. β-$Be(OH)_2$ is made by boiling a saturated solution of the amorphous α-form in 10N aqueous NaOH until a permanent turbidity is attained. On slow cooling fine crystals (regular double pyramids) of the β-form separate, and are purified by washing with warm H_2O until the washings are no longer alkaline, then drying at 80°. The mother liquours can be reused in the above process. It is very slightly soluble in H_2O and dilute NaOH, but both forms are amphoteric and are soluble in hot concentrated aqueous NaOH solutions and in acids. It dehydrates on strong heating to BeO. Several sodium beryllates are known. [Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 894, 895 *1963*.] Berylluim compounds are potentially **carcinogenic**.

Beryllium nitrate [$Be(NO_3)_2$] *[13587-99-4*; *$3H_2O$ 7787-55-5]* **M 133.0, m ~60° (for $3H_2O$).** The nitrate does not crystallise easily and is very deliquescent. It can be prepared from the metal by digesting it with conc HCl until most of it has dissolved, filter any insoluble material through a 0.45 micron acetate filter. Then at low boil, add conc HNO_3 with low heat to reduce to a slurry. Repeat with careful addition of HNO_3 as many times as necessary (3-6 additions) until the slurry tests negative for chloride ions with 0.1N aqueous $AgNO_3$. Then isolate the nitrate as described below [J. Papa personal communication. *2011*, see Chapter 1 p 38]. *Alternatively*, it is obtained by heating recrystallised, then sublimed, basic beryllium acetate {$Be_4O(OAc)_6$, see [1332-52-1]}, with pure concentrated HNO_3 in a degassed pyrex container until the volatiles are removed. Heat well below 1100°, so as not to decompose it to give pure BeO. It picks up moisture to give the white to pale yellow *trihydrate*. Store it in a well stoppered bottle in a cool place. [Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 893 *1963*.] Berylluim compounds are potentially **carcinogenic**.

Beryllium oxide *[1304-56-9]* **M 25.0, m 2530°, d^{25} 3.01.** It is prepared by calcining the nitrate at 1100° {see $Be(NO_3)_2$ above [13587-99-4]}, and this oxide always contains ~0.35ml of gas (N_2, O_2) per gram of oxide. *Alternatively*, freshly prepared beryllium carbonate is calcined in a Pt boat placed in an electric furnace at 900°. BeO is amphoteric, dissolving slowly in acids and in alkalis but if heated strongly it becomes refractory and difficult to dissolve except in hydrofluoric acid. Like ceramics it is a good electrical insulator, but it is a good conductor of heat like some metals. [Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 893 *1963*.] Beryllium compounds are potentially **carcinogenic**.

Beryllium potassium fluoride *[7787-50-0]* **M 105.1, m ~350°.** It crystallises from hot water (25ml/g). Beryllium compounds are potentially **carcinogenic**.

Beryllium sulfate tetrahydrate *[7787-56-6;]* **M 177.1, m ~100°(dec), d^{25} 1.713, pK_1^{25} 3.2, pK_2^{25} ~6.5 (Be^{2+}).** It crystallises from a concentrated solution of weak aqueous H_2SO_4 (with partial evaporation), and is dried in air. It is quite soluble in H_2O. The *tetrahydrate* loses H_2O at ~100° to give the *dihydrate*. [cf *Gmelin's Beryllium* (8th edn) **26** 169 1930.] Beryllium compounds are potentially **carcinogenic**.

Bismuth *[7440-69-9]* **M 209.0, m 271-273°, b 1450°.** Melt it in an atmosphere of dry helium, then filter it through dry Pyrex wool to remove any bismuth oxide present [Mayer et al. *J Phys Chem* **64** 238 *1960*].

Bismuth trichloride *[7787-60-2]* **M 315.3, m 233.6°, pK^{25} 1.58 *f*or hydrolysis (Bi_3^+ = $BiOH_2^+$ + H^+).** Sublime the trichloride under high vacuum, or dry it under a current of HCl gas, followed by fractional distillation, once under HCl and once under argon. It is *deliquescent*. [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 621 *1963*.]

Boric acid (orthoboric acid, boracic acid) *[10043-35-3]* **M 61.8, m 171°, pK^{25} 9.23.** Crystallise the acid three times from H_2O (3ml/g) between 100° and 0°, after filtering through sintered glass. Dry it to constant weight over metaboric acid in a desiccator. It is steam volatile. After two recrystallisations of ACS grade, it had Ag at 0.2 ppm. Its solubility (%) in H_2O is 2.66 at 0°, 4.0 at 12° and 24 at 80°. At 100° it loses H_2O to form *metaboric acid* (HBO_2). When it is heated to redness or slowly to 200°, or over P_2O_5 *in vacuo*, it dehydrates to *boric anhydride* (B_2O_3) [1303-82-6] to give a white hard glass or crystals with **m** ~294°. The glass softens on

heating and liquefies at red heat. It is an astringent, a fungicide and an antibacterial. [McCulloch *J Am Chem Soc* **59** 2650 *1937*, Kelly *J Am Chem Soc* **63** 1137 *1941*, Taylor & Cole *J Chem Soc* 70 *1926*, Conti *J Soc Chem Ind* **44** 343T *1925*.]

Boron trichloride (trichloroborane) *[10294-34-5]* **M 117.2, m -107°, b 0°/476mm, 12.5°/atm, d ^{0} 1.3728, d $^{12}_{4}$ 1.35 (also available as a 1.0M solution in toluene, *p*-xylene, CH_2Cl_2, heptane or hexanes).** Purify it (from chlorine) by passage through two mercury-filled bubblers, then fractionally distil it under a slight vacuum. In a more extensive purification the nitrobenzene addition compound is formed by passage of the gas over nitrobenzene in a vacuum system at 10°. Volatile impurities are removed from the crystalline yellow solid formed by pumping at -20°, and the BCl_3 is recovered by warming the addition compound at 50°. Passage through a trap at -78° removes entrained nitrobenzene, the BCl_3 finally condensing in a trap at -112° [Brown & Holmes *J Am Chem Soc* **78** 2173 *1956*]. *Alternatively*, purify it by condensing it into a trap cooled in acetone/Dry-ice, where it is pumped for 15 minutes to remove volatile impurities. It is then warmed, recondensed and again pumped. [Gamble *Inorg Synth* **III** 27 *1950*.]
It fumes in moist air. **TOXIC, do not breath in the vapours.** It forms addition compounds with Et_2O; and with dimethyl sulfide it forms ***$Me_2S.BCl_3$*** *[5523-19-3]* **M 179.3,** which has **m 88-90°**, and is a convenient solid form of it (also commercially available as a 2.0M solution in CH_2Cl_2) — **beware** of the foul odour of Me_2S; work in an efficient fume cupboard and absorb the sulfide vapours by flushing them with a stream of N_2 into lead acetate solution which will precipitate insoluble black PbS. [Gamble *Inorg Synth* **3** 27 *1950*, Gerrard & Leppert *Chem Rev* **58** 1081 *1958*.]

Boron trifluoride *[7637-07-2]* **M 67.8**, **b -101°/760mm.** The usual impurities-bromine, BF_5, HF and non-volatile fluorides-are readily separated by distillation. Brown and Johannesen [*J Am Chem Soc* **72** 2934 *1950*] passed BF_3 into benzonitrile at 0° until the latter was saturated. Evacuation to 10^{-5}mm then removed all traces of SiF_4 and other gaseous impurities. [A small amount of the BF_3-benzonitrile addition compound sublimes and is collected in a U-tube cooled to -80°]. The pressure is raised to 20mm by admitting dry air, and the flask containing the BF_3 addition compound is warmed with hot water. The BF_3 that evolves is passed through a -80° trap (to condense any benzonitrile) into a tube cooled in liquid air. The addition compound with anisole can also be used. BF_3 can be dried by passing it through H_2SO_4 saturated with boric oxide. It fumes in moist air. [It is commercially available as a 1.3M solution in MeOH or PrOH.] [Booth & Wilson *Inorg Synth* **I** 21 *1939*, Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 219-222 *1963*.] **TOXIC.**

Bromine *[7726-95-6]* **M 159.8, m –7.2°, b 59°, d $^{20}_{4}$ 3.102, n $^{20}_{D}$ 1.661.** Reflux the brown liquid with solid KBr and distil; dry the distillate by shaking it with an equal volume of conc H_2SO_4, then redistil it. The H_2SO_4 treatment can be replaced by direct distillation from BaO or P_2O_5. A more extensive purification [Hildenbrand et al. *J Am Chem Soc* **80** 4129 *1958*] is to reflux about 1L of bromine for 1 hour with a mixture of 16g of CrO_3 in 200ml of conc H_2SO_4 (to remove organic material). The bromine is distilled into a clean, dry, glass-stoppered bottle, and chlorine is removed by dissolving *ca* 25g of freshly fused CsBr in 500ml of the bromine and standing overnight. To remove HBr and water, the bromine is then distilled back and forth through a train containing alternate tubes of MgO and P_2O_5. [Schmeisser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 275 *1963*.] **HIGHLY TOXIC.**

Bromine pentafluoride *[7789-30-2]* **M 174.9, m –60.5°, b 41.3°, d^{25} 2.466.** Purify it *via* its KF complex, as described for chlorine trifluoride. [Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 158-159 *1963*.] **HIGHLY TOXIC.**

Cadmium *[7440-43-9]* **M 112.4, m 321.1°, b 767°, d $^{20}_{4}$ 8.642.** Any oxide contaminant is removed by filtering the molten metal, under vacuum, through quartz wool. Its solubility in Hg is 5.2% (18°), and it is soluble in mineral acids. [Wagenknecht & Juza in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1092 *1965*.]

Cadmium bromide *[7789-42-6 (anhydrous), 13464-92-1 ($4H_2O$)]* **M 272.2, m 566°, b 863°, 963°, d $^{20}_{4}$5.192.**

Crystallise it from water (0.57g/ml at 10°, 1.26g/ml at 100°) between and 0°, and dry it at 110°. It forms the *monohydrate* below 36° and the *tetrahydrate* above 36°. It is hygroscopic. [Wagenknecht & Juza in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1096 *1965*.]

Cadmium chloride *[10108-64-2]* **M 183.3, m 568°, b 960°, d $_4^{20}$ 4.06.** Crystallise it from water (1ml/g) by addition of EtOH and cooling. [Pray *Inorg Synth* **V** 153 *1957*, Wagenknecht & Juza in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1093 *1965*.]

Cadmium fluoride *[7790-79-6]* **M 150.4, m >1000°, b 1748°, d $_4^{20}$ 6.35.** Crystallise it by dissolving it in hot water (25ml/g at room temperature) at 60°, filtering, then cooling. [Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 243 *1963*.]

Cadmium iodide *[7790-80-9]* **M 366.2, m 388°, b 787°, d $_4^{20}$ 5.66.** Crystallise it from ethanol (2ml/g) by partial evaporation. [Wagenknecht & Juza in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1096 *1965*.]

Cadmium nitrate tetrahydrate *[10022-68-1]* **M 308.5, m 59.5°.** Crystallise the nitrate from water (0.5ml/g) by cooling in ice-salt. [*Gmelin's Cadmium (8th edn)* **33** pp 76-78 *1925*, Suppl p 446 *1959*.]

Cadmium potassium iodide *[13601-63-3]* **M 532.2.** Crystallise it from ethanol by partial evaporation.

Cadmium sulfate *[7790-84-3 (for $3CdSO_4$ $8H_2O$), 10124-36-4 (anhydrous)]* **M 208.4 (anhydrous), 769.5 (hydrate).** The sulfate crystallises from distilled water as a *hydrate* by partial evaporation in a desiccator. It gives the *monohydrate* on heating at 80°. It is insoluble in EtOH, Me_2CO or EtOAc. It forms a white precipitate of $Cd(OH)_2$ with aqueous NH_3 which dissolves in excess of NH_3 to form soluble $[Cd(NH_3)_4]SO_4$. [*Gmelin's Cadmium (8th edn)* **33** p 121 *1925*, Suppl pp 609-610 *1959*.]

Calcium *[7440-70-2]* **M 40.1, m 845°.** Clean the metal by washing it with ether to remove adhering paraffin, file the surface in an argon-filled glove box, and wash it with ethanol containing 2% of conc HCl. Then wash it with dry ethanol, dry it in a vacuum and store it under pure argon [Addison et al. *J Chem Soc* 3868 *1962*].

Calcium bromide monohydrate *[62648-72-0, 71626-99-8 (xH_2O), 7789-41-5 (anhydrous)]* **M 217.9, d $_4^{20}$ 3.35.** Crystallise the bromide from EtOH or Me_2CO. It loses H_2O on heating, is anhydrous at 750°, then it loses Br at higher temperatures. It is *deliquescent*. [Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 930 *1963*.]

Calcium chloride (anhydrous) *[10043-52-4]* **M 111.0, m 772°, b >1600°, d $_4^{15}$ 2.15.** It is available as fused granules or cubic crystals. It is very *hygroscopic*, very soluble in H_2O (exothermic), and EtOH. Store it in a tightly closed container. [Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 931 *1963*.]

Calcium chloride dihydrate *[10035-04-8]* **M 147.0, m 175°(dehydrates), 772°(dec).** Crystallise it from ethanol. It is *hygroscopic*. It loses H_2O at 200° so it can be dried at high temperatures to dehydrate it. The *hexahydrate [7774-34-7]* has **m** 30° and **d** 1.67.

Calcium dithionite *[13812-88-9]* **M 168.2, m dec on heating.** Crystallise it from water, or water followed by acetone and dry it in air at room temperature.

Calcium hexacyanoferrate (II) undecahydrate [*13821-08-4]* **M 490.3.** Recrystallise it three times from conductivity H_2O and dry it in air to constant weight over the partially dehydrated salt. [James *Trans Faraday Soc* **45** 855 *1949*.] *Alternatively*, the Ca salt can be purified by precipitation with absolute EtOH in the cold (to avoid oxidation) from an air-free saturated aqueous solution. The pure lemon yellow crystals are centrifuged, dried in a vacuum desiccator first over dry charcoal for 24 hours, then over partly dehydrated salt and stored in a dark glass stoppered bottle. No deterioration occurrs after 18 months. No trace of Na, K or NH_4 ions can be

detected in the salt from the residue after decomposition of the salt with conc H_2SO_4. Analyses indicate 11mols of H_2O per mol of salt. The solubility in H_2O is 36.45g (24.9°) and 64.7g (44.7°) per 100g of solution. [Farrow *J Chem Soc* 50 *1926*.]

Calcium hydroxide *[1305-62-0]* **M 74.1, m loses H_2O on heating, pK^{25} 12.7 (for Ca^{2+}).** Heat analytical grade calcium carbonate at 1000° during 1 hour. Allow the resulting oxide to cool and add slowly to water. Heat the suspension to boiling, cool and filter through a sintered glass funnel of medium porosity (to remove soluble alkaline impurities). Dry the solid at 110° and crush it to a uniformly fine powder. [Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 934 *1963*.]

Calcium iodate *[7789-80-2 (H_2O)]* **M 389.9, m >540°, pK^{25} 0.79 (for HIO_3).** Crystallise it from water (100ml/g at 100° and 100ml/0.1g at 0°). [Bahl & Singh *J Indian Chem Soc* **17** 397 *1940*.]

Calcium iodide x-hydrate *[71626-98-7 (xH_2O), 10102-68-8 (anhydrous)]* **M 293.9 (for $4H_2O$), m 740°, b 1100°.** Dissolve the salt in acetone, which is then diluted and evaporated. This drying process is repeated twice, then the CaI_2 is recrystallised from acetone/diethyl ether and stored over P_2O_5. It is very *hygroscopic* when anhydrous and is light sensitive [Cremlyn et al. *J Chem Soc* 528 *1958*]. The yellow *hexahydrate* has **m** 42°. It is soluble in H_2O, MeOH, EtOH and Me_2CO but insoluble in Et_2O.

Calcium nitrate tetrahydrate *[13477-34-4]* **M 236.1, m 45°(hydrate), 560°(anhydrous).** Crystallise the nitrate four times from water (0.4ml/g) by cooling in a $CaCl_2$-ice freezing mixture. The *tetrahydrate* is dried over conc H_2SO_4 and stored over P_2O_5, to give the *anhydrous salt*. It is *deliquescent*. After 3 recrystallisations of ACS grade salt, it had Co, Fe, Mg, Sr and Zn at 0.2, 1. 0, 0.02, 10 and 0.02 ppm resp. [Bassett & Taylor *J Chem Soc* **105** 1926 *1914*.]

Calcium nitrite dihydrate *[13780-06-8 (30% w/w aqueous solution)]* **M 150.1(hydrate), m dec on heating, d_D^{20} 2.22.** Crystallise it from hot water (1.4ml/g) by adding ethanol and cooling to give the hydrate. It is *deliquescent*. [Ray & Ogg *J Am Chem Soc* **79** 265 *1957*.]

Calcium permanganate tetrahydrate *[10118-76-0 (anhydrous)]* **M 350.0 (for $4H_2O$).** Crystallise it from water (3.3ml/g) by partial evaporation in a desiccator. It is *deliquescent*. Note that it loses oxygen more readily than the potassium salt. It is an oxidising agent.

Calcium sulfate dihydrate *[10101-41-4]* **M 172.1, m 150(dec), d_4^{20} 2.32.** It loses only part of its H_2O at 100-150° (see below). It is soluble in H_2O and very slowly soluble in glycerol. It is insoluble in most organic solvents.

Calcium sulfate hemihydrate *[10034-76-1]* **M 145.2.** Its solubility in H_2O is 0.2parts/100 at 18.75°. It dehydrates completely >650°. Dry it below 300° to give a solid with estimated pore size *ca* 38% of volume. *Anhydrous* $CaSO_4$ (**Drierite**) has a high affinity for H_2O and will absorb 6.6% of its weight of H_2O to form the *hemihydrate* (gypsum). It sets to a hard mass with H_2O; hence it should be kept in a tightly sealed container. The solubility of gypsum in H_2O is unusual: 0.176% at 0°, 0.209% at 30°, 0.210 at 40°, 0.204 at 50° and 0.200 at 60°. [Hulett *J Am Chem Soc* **27** 49 *1905*, James & Partington *J Chem Soc* **107** 1019 *1915*, Namba *J Soc Chem Ind* **40** 2797 *1920*.]

Calcium thiosulfate *[10124-41-1]* **M 152.2, m 43-49°, pK_1^{25} 0.6, pK_2^{25} 1.74 (for $H_2S_2O_3$).** Recrystallise the thiosulfate from water below 60° in a N_2 atmosphere, followed by drying with EtOH and Et_2O. Store it in a refrigerator. The *hexahydrate* can decompose spontaneously at 43-49°. Store it in a cool closed container. [Pethybridge & Taba *J Chem Soc, Faraday Trans 1* **78** 1331 *1982*.]

Carbon dioxide *[124-38-9]* **M 44.0, sublimes at -78.5°, pK_1^{25} 6.35, pK_2^{25} 10.33 (for H_2CO_3).** Pass the gas over CuO wire at 800° to oxidise CO and other reducing impurities (such as H_2), then over copper dispersed on Kieselguhr at 180° to remove O_2. Drying it at -78° removes the water vapour. Final purification is by vacuum

distillation at liquid nitrogen temperature to remove non-condensable gases [Anderson et al. *J Chem Soc* 3498 *1962*]. Sulfur dioxide contaminant can be removed at 450° using silver wool combined with a plug of platinised quartz wool. Halogens are removed by using Mg, Zn or Cu, heated to 450°. [Glemsner in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 647 *1963*.]

Carbon disulfide *[75-15-0]* **M 76.1, b 46.3°, d $_4^{20}$ 1.264, n $_D^{20}$ 1.627.** Shake it for 3 hours with three portions of $KMnO_4$ solution (5g/L), twice for 6 hours with mercury (to remove sulfide impurities) until no further darkening of the interface occurs, and finally with a solution of $HgSO_4$ (2.5g/L) or cold, saturated $HgCl_2$. Dry it with $CaCl_2$, $MgSO_4$, or CaH_2 (with further drying by refluxing over P_2O_5), followed by fractional distillation in diffuse light. **Alkali metals cannot be used as drying agents**. It has also been purified by standing with bromine (0.5ml/L) for 3-4 hours, shaking rapidly with KOH solution, then copper turnings (to remove unreacted bromine), and drying with $CaCl_2$. CS_2 is highly **TOXIC** has a **foul odour** and is highly **FLAMMABLE**. *Work in a good fumehood.*
Small quantities of CS_2 have been purified (including removal of hydrocarbons) by mechanical agitation of a 45-50g sample with a solution of 130g of sodium sulfide in 150ml of H_2O for 24 hours at 35-40°. The aqueous sodium thiocarbonate solution is separated from unreacted CS_2, then precipitated with 140g of copper sulfate in 350g of water, with cooling. After filtering off the copper thiocarbonate, it is decomposed by passing steam into it. The distillate is separated from H_2O and distilled from P_2O_5. [Ruff & Golla *Z Anorg Chem* **138** 17 *1924*, *Beilstein* **3** IV 395.]

Carbon monoxide *[630-08-0]* **M 28.0, m -200°, b -191.5°.** Iron carbonyl is a likely impurity in CO stored under pressure in steel tanks. It can be decomposed by passing the gas through a hot porcelain tube at 350-400°. Passage through alkaline pyrogallol solution removes oxygen (and CO_2). Removal of CO_2 and water are effected by passage through soda-lime followed by $Mg(ClO_4)_2$ or P_2O_5 and collected over Hg. Carbon monoxide can be condensed and distilled at -195°. It is sparingly soluble in H_2O but is readily absorbed by a solution of CuCl in HCl to give the white crystalline adduct $CuCl.CO.2H_2O$. It burns in air with a bright blue flame but a mixture of 2 volumes of CO and 1 volume of O_2 explode when kindled, although in a small jar the combustion is not violent. **HIGHLY POISONOUS gas** as it reacts with haemoglobin to form bright red carboxyhaemoglobin which is stable and not readily decomposed by oxygen. The **TOXIC LEVEL** of CO is 50ppm (~55mg/m^3). **The ANTIDOTE should be at hand and always available in laboratories using CO; and staff should be trained to administer it.** [Gilliland & Blanchard *Inorg Synth* **II** 81 *1946*, Glemser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 645-646 *1963*.]

Carbonyl bromide *[593-95-3]* **M 187.8, b 64.5°/760mm.** Purify it by distillation from Hg and from powdered Sb to remove free bromine, then distil it in a slight vacuum to remove volatile SO_2 (the major impurity) [Carpenter et al. *J Chem Soc, Faraday Trans 2* 384 *1977*]. **TOXIC.**

Carbonyl sulfide (COS) *[463-58-1]* **M 60.1, m -138°, b -47.5°, -50°.** Purify the gas by scrubbing it through three consecutive fritted washing flasks containing conc NaOH at 0° (to remove HCN), and then through conc H_2SO_4 (to remove CS_2) followed by a mixture of NaN_3 and NaOH solution; or passed through traps containing saturated aqueous lead acetate, then through a column of anhydrous $CaSO_4$. Then it is freeze-pumped repeatedly and distilled through a trap packed with glass wool and cooled to -130° (using an *n*-pentane slurry). It liquefies at 0°/12.5mm. Use stainless steel containers. The gas is stored over conc H_2SO_4. [Glemser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 654 *1963*.] **TOXIC.**

Ceric ammonium nitrate *[16774-21-3]* **M 548.2, pK_1^{25} -1.15, pK_2^{25} -0.72, pK_3^{25} 1.68, pK_4^{25} 2.29 (for aquo Ce^{4+}).** Ceric ammonium nitrate (125g) is warmed with 100ml of dilute HNO_3 (1:3 v/v) and 40g of NH_4NO_3 until it dissolves, and filtered through a sintered-glass funnel. The solid which separates on cooling in ice is filtered off on a sintered funnel (at the pump) and air is sucked through the solid for 1-2 hours to remove most of the nitric acid. Finally, the solid is dried at 80-85°.

Cerium(III) sulfate [cerous sulfate, $Ce_2(SO_4)_3$] *[13454-94-9 anhydrous*; *10450-59-6 8H_2O*; *13550-47-5 12 H_2O]* **M 568.4 (anhydr), d $_4^{25}$ 2.89, pK ^{25} 9.29 (for hydrolysis of Ce^{3+}).** To prepare cerous sulfate, cerium

oxide [CeO_2, 0.3g) or chloride is dissolved in hot 6N H_2SO_4 (20ml), filtered through a sintered glass funnel and allowed to crystallise over concentrated H_2SO_4 in a vacuum dessicator. The crystals are filtered off, washed twice with H_2O (10ml) and once with EtOH (10ml), and dried in air for 4 hours to provide the *pentahydrate*. *Alternatively*, a neutral or slightly acidic (with H_2SO_4) aqueous solution of the sulfate is treated with ¾ of its volume of EtOH. The salt is thus obtained rapidly and quantitatively without the evaporation stage. The *anhydrous* sulfate is formed by heating any sulfate hydrate salt at 400-500°, but is hygroscopic. The hydrate loses most of its H_2O at *ca* 250°, and above 650° it loses SO_3 also to give the basic salt. [Wendlandt *J Inorg Nucl Chem* **7** 51 *1958*, Wetzel in *Handbook of Preparative Inorganic Chem (Ed. Brauer)* Academic Press Vol **II** p 1156 *1965*.] When a fairly concentrated solution of the anhydrous salt in ice H_2O, is allowed to evaporate at 40-50°, the *octahydrate* salt separates as colourless rhombic pyramids [Koppel *Z Anorg Chem* **41** 385 *1904*]. The *dodecahydrate* is obtained in fine needles when a clear fairly concentrated solution of cerous sulfate is allowed to evaporate over concentrated H_2SO_4 in a desiccator in a refrigerator [Koppel *Z Anorg Chem* **41** 385 *1904*]. [Vanino *Handbuch der Präparativen Chemie* Vol **I**, 3rd Edn, pp 754-755, Stuttgart *1925*.]

Cerium(IV) sulfate [ceric sulfate, $Ce(SO_4)_2$] *[13590-82-4 anhydrous]* **M 332.2, d $_4^{25}$ 3.01, pK $_1^{25}$-1.15, pK $_2^{25}$ -0.72, pK $_3^{25}$1.68, pK $_4^{25}$2.29 (for hydrolysis of Ce^{4+}).** Ceric sulfate is prepared by heating pure ceric oxide (CeO_2) with an excess of concentrated H_2SO_4 for an hour, cooling, adding glacial acetic acid, stirring, allowing to settle and decanting off. The process is repeated several times and the yellow orthorhombic crystals of the sulfate are filtered off (sintered glass), washed with glacial acetic acid and dried in a vacuum desiccator over NaOH/KOH and/or soda lime. [Vanino *Handbuch der Präparativen Chemie* Vol **I**, 3rd Edn, pp 754-755, Stuttgart *1925*, Meyer & Aufrecht *Chem Ber* **37** 140 *1904*.] It is a strong oxidising agent (oxidation potential of a 1 to 8N H_2SO_4 solution at 25° is 1.42 ±0.1 volts), and like ceric ammonium sulfate is used in volumetric analysis. Solutions in dilute H_2SO_4 are standardised by titration with pure arsenious oxide, iron or ferrous ammonium sulfate. Although it is its own end-point indicator (Ce^{4+} ions are yellow and C^{3+} ions are colourless), the end point is not as sharp as that of permanganate, and it is best to use 0.005M *N*-phenylanthranilic acid as indicator (colour change from yellow-green to purple at end point) [J. Mendham, R.C. Denney, J.D. Barnes and M.J.K. Thomas, *Vogel's Quantitative Chemical Analysis*, 6th Edn, Prentice Hall, Harlow, 2000. ISBN 0582226287].
Ceric sulfate tetrahydrate is obtained thus: pure ceric ammonium nitrate *[16774-21-3]* in a small volume of H_2O is treated with ammonia, $Ce(OH)_4$ separates, is collected and is dissolved in concentrated H_2SO_4. This solution is evaporated to dryness and the residue is crystallised from H_2O (perhaps a small amount of H_2SO_4 should be added to avoid hydrolysis). A small volume of H_2O should be used as boiling with a large volume of H_2O leads to separation of the basic salt. The yellow-orange powder or orthorhombic crystals lose H_2O to give the anhydrous salt at 180-200°, but decomposes >350° to give the basic salt $CeOSO_4$. [Vanino *Handbuch der Präparativen Chemie* Vol **I**, 3rd Edn, pp 755-756, Stuttgart *1925*, Muthmann & Stützel *Chem Ber* **33** 1763 *1900*.]

Cesium bromide *[7787-69-1]* **M 212.8, m 636°, b *ca* 1300°, d $_4^{20}$ 4.44.** It is very soluble in H_2O, soluble in EtOH but insoluble in Me_2CO. Dissolve it in the minimum volume of H_2O, filter and precipitate it by adding Me_2CO. Filter off the solid and dry it at 100°. Also recrystallise it from water (0.8ml/g) by partial evaporation in a desiccator.

Cesium carbonate *[534-17-8]* **M 325.8, m 792°(at red heat).** Crystallise it from ethanol (10ml/g) by partial evaporation. [Dönges in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 988 *1963*.]

Cesium chloride *[7647-17-8]* **M 168.4, m 645°, b 1303°, d $_4^{20}$ 3.99.** It is soluble in H_2O but can be purified by crystallisation from H_2O [solubility in g percent: 162.3(0.7°), 182.2(16.2°) and 290(at bp 119.4°)] and dried in a high vacuum. It is soluble in EtOH and is *deliquescent*; keep it in a tightly closed container. [Dönges in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 951-955 *1963*.] For further purification of CsCl, a concentrated aqueous solution of the practically pure reagent is treated with an equivalent weight of I_2 and Cl_2 is bubbled into the solution until precipitation of $CsCl_2I$ is complete. Recrystallisation yields a salt that is free from other alkali metals. It is then decomposed to pure CsCl on heat-

ing. [Harned & Schupp *J Am Chem Soc* **52** 3886 *1930*.] It can also be recrystallised from acetone/water, or from water (0.5ml/g) by cooling in a $CaCl_2$/ice bath. Dry it at 78° under vacuum.

Cesium chromate *[56320-90-2]* **M 381.8, pK_1^{25} 0.74, pK_2^{25} 6.49 (for H_2CrO_4).** Crystallise the chromate from water (1.4ml/g) by partial evaporation in a desiccator. [Boer et al. *Z Anorg Allgem Chem* **191** 113 *1930*, Hein & Herzog in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1389 *1963*.]

Cesium fluoride *[13400-13-0]* **M 151.9, m 703°.** Crystallise it from aqueous solution by adding ethanol.

Cesium iodide *[7789-17-5]* **M 259.8, m 621°, b~1280°, d_4^{20} 4.5.** Crystallise it from warm water (1ml/g) by cooling to -5°.

Cesium nitrate *[7789-18-6]* **M 194.9, m 414°(dec), d_4^{20} 3.65.** It crystallises from water (0.6ml/g) between 100° and 0°. After 1 crystallisation of 99.9% grade salt, it had K, Na and Se at 0.8, 0.4 and 0.2 ppm respectively.

Cesium perchlorate *[13454-84-7]* **M 232.4, pK^{25} -2.4 to -3.1 (for $HClO_4$).** Crystallise it from water (4ml/g) between 100° and 0°.

Cesium sulfate *[10294-54-9]* **M 361.9, m 1005°, d_4^{20} 4.24.** Crystallise it from water (0.5ml/g) by adding ethanol and cooling.

Chlorine *[7782-50-5]* **M 70.9, m -101.5°, b -34.0°, d_4^{20} 2.898.** Pass the gas in succession through aqueous $KMnO_4$, dilute H_2SO_4, conc H_2SO_4, and a drying tower containing $Mg(ClO_4)_2$. Or bubble it through water, dry it over P_2O_5 and distil it from bulb to bulb in a vacuum line. One volume of water dissolves 4.6 volumes of Cl_2 at 0°, 2.15 volumes at 20°, 1.22 volumes at 50° and 0.39 volumes at 90°. [Schmeisser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 272 *1963*.] **HIGHLY TOXIC.**

Chlorine trifluoride *[7790-91-2]* **M 92.5, b 12.1°.** Impurities include chloryl fluoride, chlorine dioxide and hydrogen fluoride. Pass it first through two U-tubes containing NaF to remove HF, then through a series of traps in which the liquid is fractionally distilled. It can be purified *via* the KF complex; $KClF_4$, formed by adding excess ClF_3 to solid KF in a stainless steel cylinder in a dry-box and shaking overnight. After pumping out the volatile materials, pure ClF_3 is obtained by heating the bomb to 100-150° and condensing the evolved gas in a -196° trap [Schack et al. *Chem Ind (London)* 545 *1967*]. It attacks glass very vigorously. **HIGHLY TOXIC.**

Chlorosulfonic (chlorosulfuric) acid *[7790-94-5]* **M 116.5, b 151-152°/750mm, d_4^{20} 1.753, n_D^{20} 1.4929, pK^{25} -5.9 (aqueous H_2SO_4).** Distil the acid at atmospheric pressure in an all-glass apparatus, taking the fraction boiling at 156-158°. It reacts **EXPLOSIVELY** with water, **wear gloves and face protection.** [Cremlyn *Chlorosulfonic acid: A Versatile Reagent*, Royal Society of Chemistry UK, *2002*, p 308, ISBN 0854044981, Fehér in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 385 *1963*].

Chromic chloride (anhydrous) *[10025-73-7]* **M 158.4, m 1152°, pK_1^{25} 3.95, pK_2^{25} 5.55, pK_3^{25} 10.5 (for Cr^{3+}).** Sublime the chloride in a stream of dry HCl. *Alternatively*, the impure chromic chloride (100g) is added to 1L of 10% aqueous $K_2Cr_2O_7$ and several millilitres of conc HCl, and the mixture is brought to a gentle boil with constant stirring for 10 minutes. (This removes a reducing impurity.) The solid is separated and washed by boiling with successive 1L lots of distilled water until the wash water no longer gives a test for chloride ion, then dry it at 110° [Poulsen & Garner *J Am Chem Soc* **81** 2615 *1959*, Hein & Herzog in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1338 *1965*].

Chromium ammonium sulfate dodecahydrate *[34275-72-4 (hydrate), 13548-43-1 (anhydrous)]* **M 478.4, m 94° loses $9H_2O$ then dehydrates at 300°, d_4^{20} 1.72.** Crystallise the double salt from a saturated aqueous solution at 55° by cooling slowly with rapid mechanical stirring. The resulting fine crystals are filtered on a Büchner funnel, partly dried on a porous plate, then equilibrated for several months in a vacuum desiccator

over crude chromium ammonium sulfate (partially dehydrated by heating at 100° for several hours before use) [Johnson et al. *J Am Chem Soc* **75** 3922 *1953*].

Chromium (II) chloride (anhydrous) *[10049-05-5]* **M 122.9, m 824°, d_4^{14} 2.75.** It is obtained from the *dihydrate* by heating *in vacuo* at 180°. It is a very *hygroscopic* white powder which dissolves in H_2O to give a sky blue solution. It is stable in dry air but oxidises rapidly in moist air and should be stored in air tight containers. It sublimes at 800° in a current of HCl gas and should be cooled in the presence of HCl gas. *Alternatively*, it can be washed with air-free Et_2O and dried at 110-120°. [Burg *Inorg Synth* **III** 150 *1950*, Balthis & Bailar (4 H_2O) *Inorg Synth* **I** 125 *1939*, Hein & Herzog in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** pp 1336-1338 *1965*.]

Chromium hexacarbonyl *[13007-92-6]* **M 220.1, m 130°(dec), d_4^{20} 1.77.** Wash the complex with cold EtOH, then Et_2O, and allow it to dry in air. *Alternatively*, recrystallise it from dry Et_2O. This is best accomplished by placing the hexacarbonyl in a Soxhlet extractor and extracting exhaustively with dry Et_2O. Pure $Cr(CO)_6$ is filtered off and dried in air. Completely colourless refracting crystals are obtained by sublimation at 40-50°/<0.5mm in an apparatus where the collecting finger is cooled by Dry-ice and in which there is a wide short bore between the hot and cold sections to prevent clogging by the crystals. Loss of product in the crystallisation and sublimation is slight. It is important not to overdo the drying as the solid is appreciably volatile and **TOXIC** [vapour pressure is 0.04(8°), 1.0(48°) and 66.5(100°) mm]. Also, do not allow the Et_2O solutions to stand too long as a brown deposit is formed which is sensitive to light, and to avoid the possibility of violent decomposition. It sinters at 90°, decomposes at 130°, and **EXPLODES** at 210°. [Owen et al. *Inorg Synth* **III** 156 *1950*, Podall et al. *J Am Chem Soc* **83** 2057 *1961*.] **POISONOUS**.

Chromium (III) nitrate nonahydrate *[7789-02-8]* **M 400.2, m ~60° (dec >100°).** The pure deep violet nonahydrate salt is best prepared freshly from pure recrystallised (3 times) chromium (VI) trioxide and pure nitric acid. A solution is prepared by dissolving 1g of CrO_3 in 3ml of H_2O and 2ml of pure HNO_3, and carefully, with stirring (behind a screen) pure MeOH (0.5-1.0ml) is added dropwise carefully (shield) with cooling to avoid a violent reaction. A bluish colour develops as Cr(VI) is reduced to Cr(III). When this solution is diluted to 130,000ppm of the salt, analysis detected by ICP/MS gave the following trace elements (ppm in brackets): Sr (33), Na (3.5), Mo, Ni, Cu, Si and Mg (0.13 each), Se, Zn, Al (0.026 each), Ti (1.5), Fe (4.9), Co (0.07), Sn (0.065), Ba (0.013 and W (0.078). Evaporation of the methanolic solution in high vacuum over $CaCl_2$ eventually yields pure deep violet rhombic crystals of chromium (III) nitrate *nonahydrate*. An aqueous solution of this salt becomes green on heating but reverts to the violet colour on cooling.
The pale green ***anhydrous* chromium (III) nitrate**, *[13548-38-4]* **M** 238.0, **m** dec >60°, is best obtained pure by mixing a solution of chromium hexacarbonyl in CCl_4 with excess of N_2O_5 in CCl_4 under N_2 for 12 hours, whereby evolution of gases occurs. Filter off the salt and wash it with CCl_4 in a closed system under N_2, and dry it *in vacuo*. It is very soluble in H_2O, EtOAc and Me_2SO but insoluble in $*C_6H_6$, CCl_4 and $CHCl_3$. The *deliquescent* powder reacts vigorously with Et_2O. [Addison & Chapman *J Chem Soc* 539 *1964*.] **Cr(VI)** ions are **CARCINOGENIC** as they cause DNA breaks, and Cr(III) ions affect DNA synthesis.

Chromium potassium sulfate dodecahydrate *[7788-99-0]* **M 499.4, pK_1^{25} 0.74, pK_2^{25} 6.49 (for H_2CrO_4, chromic acid).** Crystallise it from hot water (2ml/g) by cooling.

Chromium trioxide (chromic anhydride) *[1333-82-0]* **M 100.0, m 197°, dec at 250° to Cr_2O_3, d 2.70 (pK_1^{25} 0.74, pK_2^{25} 6.49, for H_2CrO_4, chromic acid).** It forms red crystals from water (0.5ml/g) between 100° and -5°, or from water/conc HNO_3 (1:5). It separates when potassium or sodium dichromate are dissolved in conc H_2SO_4. Dry it in a vacuum desiccator over NaOH pellets. It is a *hygroscopic*, powerful oxidant and can ignite with organic compounds. It is a skin and pulmonary **IRRITANT**. [Keyes et al. *Industrial Chemicals* (Lowenheim & Moran eds.) 4th edn J. Wiley pp 270-274 *1975*.] **CANCER SUSPECT.**

Chromyl chloride *[14977-61-8]* **M 154.9, b 115.7°, d_4^{20} 1.911.** Purify it by distillation under reduced pressure. It hydrolyses violently with H_2O and is a powerful oxidant which explodes with P, and ignites in contact with S, NH_3, EtOH and many organic compounds. **TOXIC.**

Claisen alkali (alkali Claisen). Prepare this from KOH (35g) in H_2O (25ml) and dilute it to 100ml with MeOH. **STRONGLY CAUSTIC.**

Cobaltous ammonium sulfate hexahydrate *[13596-46-8]* **M 395.5, d $_4^{20}$ 1.90.** Crystallise it from boiling water (2ml/g) by cooling. Wash it with ethanol and dry it in a vacuum.

Cobaltous bromide hexahydrate *[85017-77-2 (xH_2O), 7789-43-7 (anhydrous)]* **M 326.9 ($6H_2O$), m 47°(dec), b 100°(dec), d $_4^{20}$ 4.9.** Crystallise it from water (1ml/g) by partial evaporation in a desiccator. The *anhydrous* salt is soluble in EtOH, Me_2CO, MeOAc to form blue-coloured solutions. [Glemser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1517 *1965*.]

Cobaltous hexahydrate *[7791-13-1 ($6H_2O$), 7646-79-9 (anhydrous)]* **M 237.9, m 87°(dec), d $_4^{20}$ 1.92.** A saturated aqueous solution at room temperature is fractionally crystallised by standing overnight. The first half of the material that crystallises in this way is used in the next crystallisation. The process is repeated several times, water being removed in a dry-box using air filtered through glass wool and dried over $CaCl_2$ [Hutchinson *J Am Chem Soc* **76** 1022 *1954*]. It has also been crystallised from dilute aqueous HCl. The *hexahydrate* **m 86°** forms pink to red deliquescent crystals. It loses $4H_2O$ on heating at 52-56° and forms the violet *dihydrate* which loses further H_2O at 100° to form the violet *monohydrate* which loses the last H_2O at 120-140° to give the pale blue *anhydrous* deliquescent salt **m 735°** and **b 1049°.** A pink solution of $CoCl_2$ in H_2O becomes blue on heating to 50° or adding conc HCl which may precipitate the *mono* or *dihydrate*. The solid *dihydrate* gives a blue-purple solution with EtOH. Note: $CoCl_2$ in H_2O is a "*sympathetic ink*", i.e. writing with an aqueous solution is almost invisible on paper, but becomes blue on warming the paper. On cooling or standing, the writing becomes invisible again. The *anhydrous* salt is soluble in H_2O, EtOH, Et_2O, Me_2CO and pyridine. [Glemser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1515 *1965*.]

Cobaltous nitrate hexahydrate *[10026-22-9]* **M 291.0, m ~55°($6H_2O$), 100-105°(dec), d $_4^{20}$ 1.88.** Crystallise the nitrate from water (1ml/g), or ethanol (1ml/g), by partial evaporation. After 3 crystallisations from H_2O it contains: metal (ppm) As (8), Fe (1.2), K (1), Mg (4), Mn (4), Mo (4), Na (0.6), Ni (18), Zn (1.6). The *hexahydrate* gives the pink *anhydrous* salt by the action of HNO_3 and N_2O_5. The *hexahydrate* melts at ~55° to give a red liquid which decomposes on further heating at 100-105° to form Co_3O_4.

Cobaltous perchlorate hexahydrate *[13478-33-6]* **M 365.9, pK^{25} -2.4 to -3.1 (for $HClO_4$).** Crystallise it from warm water (0.7ml/g) by cooling.

Cobaltous potassium sulfate *[13596-22-0]* **M 329.4.** Crystallise it from water (1ml/g) between 50° and 0°, and dry it in a vacuum desiccator over conc H_2SO_4.

Cobaltous sulfate heptahydrate *[10026-24-1 ($7H_2O$), 60459-08-7 (xH_2O), 10124-43-3 (anhydrous)]* **M 281.1, m (see text), d $_4^{20}$ 2.03.** Crystallise it three times from conductivity water (1.3ml/g) between 100° and 0° depending on which hydrate is required. The *heptahydrate* crystallises below 44° and is efflorescent with **m 97°**. Between 44° and 70° the monoclinic *hexahydrate* $CoSO_4.6H_2O$ **m 41.5°** is formed, and above 70° the *monohydrate* $CoSO_4.H_2O$ **m 71°** is obtained. The pale reddish or lavender-coloured *anhydrous* salt is obtained by heating the hydrate above 250°, boiling with conc H_2SO_4 or by heating with $(NH_4)_2SO_4$.

Cupric ammonium chloride dihydrate *[10534-87-9 (hydrate), 15610-76-1 (anhydrous)]* **M 277.5, m 110-120°(anhydrous) then dec at higher temperature, d $_4^{20}$ 2.0.** Crystallise it from weak aqueous HCl (1ml/g). It crystallises out of a hot solution of $CuCl_2$ saturated with NH_3 gas.

Cupric bromide *[7789-45-9]* **M 223.4, m 498°, b 900°, d $_4^{20}$ 4.7.** Crystallise it twice by dissolving it in water (140ml/g), filtering to remove any Cu_2Br_2, and concentrating under vacuum at 30° until crystals appear. The cupric bromide is then allowed to crystallise by leaving the solution in a vacuum desiccator containing P_2O_5 [Hope et al. *J Chem Soc* 5226 *1960*, Glemser & Sauer in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1009 *1965*].

Cupric chloride *[7447-39-4]* **M 134.4, m 498°, 630°(dec).** Crystallise the chloride from hot dilute aqueous HCl (0.6ml/g) by cooling in a $CaCl_2$-ice bath. It is dehydrated by heating on a steambath under vacuum. It is deliquescent in moist air but efflorescent in dry air. The *dihydrate* is emerald green but blue when free from solvent. Concentrated solutions are yellow-green in colour but are blue when free from solvent. Concentrated solutions are yellow-green and become yellow on adding conc HCl. A very dilute solution is pure blue due to $Cu(H_2O)_4^{2+}$ [Donan & Bassett *J Chem Soc* **81** 939 *1902*]. $CuCl_2$ is very deliquescent and is soluble in MeOH or EtOH to give green crystals of $Cu(ROH)_2Cl_2$. [Glemser & Sauer in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1008 *1965*.]

Cupric nitrate trihydrate *[10031-43-3 (3H_2O), 3251-23-8 (anhydrous)]* **M 241.6, m 114°, b 170°(dec), d $_4^{20}$ 2.0.** Crystallise it from weak aqueous HNO_3 (0.5ml/g) by cooling from room temperature. The *anhydrous* salt can be prepared by dissolving copper metal in a 1:1 mixture of liquid NO_2 and ethyl acetate and purified by sublimation [Evans et al. *J Chem Soc, Faraday Trans 1* **75** 1023 *1979*]. The *hexahydrate* dehydrates to the *trihydrate* at 26°, and the *anhydrous salt* sublimes between 150 and 225°, but melts at 255-256° and is *deliquescent*.

Cupric perchlorate hexahydrate *[10294-46-9 (hydrate), 13770-18-8]* **M 370.5, m 230-240°, pK^{25} -2.4 to -3.1 (for $HClO_4$).** Crystallise it from distilled water. The *anhydrous salt* is hygroscopic.

Cupric sulfate (blue vitriol, bluestone) *[7758-98-7]* **M 159.6, m >560°.** After adding 0.02g of KOH to a litre of nearly saturated aqueous solution of the sulfate, it is left for two weeks, then the precipitate is filtered on to a fibreglass filter with pore diameter of 5-15 microns. The filtrate is heated to 90° and allowed to evaporate until some $CuSO_4.5H_2O$ crystallises out. The solution is then filtered hot and cooled rapidly to give crystals which are freed from mother liquor by filtering under suction [Geballe & Giauque *J Am Chem Soc* **74** 3513 *1952*]. *Alternatively*, crystallise the sulfate from water (0.6ml/g) between 100 and 0°. The *pentahydrate* is slowly efflorescent, losing $2H_2O$ at 30°, two more H_2O are lost at 110° and a white anhydrous powder (dessicant) is obtained on heating above 250°.

Cuprous bromide *[7787-70-4]* **M 143.4, m 497°, b 1345°, d $_4^{20}$ 4.72.** Purify it as for cuprous iodide but using aqueous NaBr. [Keller & Wycoff *Inorg Synth* **II** 3 *1946*, Glemser & Sauer in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1006 *1965*.]

Cuprous chloride *[7758-89-6]* **M 99.0, m 430°, b~1400°.** Dissolve it in strong HCl, precipitate it by diluting with water and filter it off. Wash the solid with ethanol and diethyl ether, then dry it and store it in a vacuum desiccator [Österlöf *Acta Chem Scand* **4** 375 *1950*]. *Alternatively*, to an aqueous solution of $CuCl_2.2H_2O$ is added, with stirring, an aqueous solution of anhydrous sodium sulfite. The colourless product is dried at 80° for 30 minutes and stored under N_2. Cu_2Cl_2 can be purified by zone-refining [Hall et al. *J Chem Soc, Faraday Trans 1* **79** 343 *1983*]. [Glemser & Sauer in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1005 *1965*.]

Cuprous cyanide *[544-92-3]* **M 89.6, m 474°.** Wash the cyanide thoroughly with boiling H_2O, then with EtOH. Dry it at 100° to a fine soft powder. It dissolves in excess alkali cyanide solutions to form the very soluble complex ion $Cu(CN)_4^{3-}$. [Bassett & Corbett *J Chem Soc* **125** 1660 *1924*, Barber *J Chem Soc* 79 *1943*.]

Cuprous iodide *[7681-65-4]* **M 190.5, m 605°, b 1336°, d$_4^{25}$ 5.63.** It can be freshly prepared by dissolving an appropriate quantity of CuI in boiling saturated aqueous NaI over 30 minutes. Pure CuI is obtained by cooling and diluting the solution with water, followed by filtering and washing sequentially with H_2O, EtOH, EtOAc, Et_2O and pentane, then drying *in vacuo* for 24 hours [Dieter, *J Am Chem Soc* **107** 4679 *1985*]. *Alternatively*, wash it with H_2O, then EtOH and finally with Et_2O containing a little iodine. Traces of H_2O are best removed first by heating at 110° and then at 400°. Exess of I_2 is removed completely at 400°. It dissolves in Et_2O if an amine is present to form the amine complex. On heating it becomes red, then black, but changes to white on cooling. It is sparingly soluble in H_2O or alkali iodide solutions but readily soluble in NH_3 (which absorbs CO) and in cyanide or thiosulfate solutions. [Glemser & Sauer in *Handbook of Preparative Inorganic Chemistry (Ed Brauer)* Academic Press Vol **II** p 1007 *1965*, Bawn & Ledwith *Chem Ind (London)* 1180 *1957*.]

Cuprous thiocyanate *[18223-42-2]* **M 121.6, pK^{25} -1.85 (for HSCN).** Purify it as for cuprous iodide but using aqueous NaSCN. [Demmerle et al. *Ind Eng Chem* **42** 2 *1950*, Newman *Analyst* **88** 500 *1963*.]

Cyanamide *[420-04-2]* **M 42.0, m 43º, 45º, 46º, b 85-87º/0.5mm, pK$_1^{20}$ -0.36 (1.1 at 29º), pK$_2^{20}$ 10.27.** Purify it by placing *ca* 15g in a Soxhlet thimble and extracting exhaustively (2-3 hours) with two successive portions of Et_2O (400ml, saturated with H_2O by shaking before use) containing two drops of 1N acetic acid. Two successive portions of Et_2O are used so that the NH_2CN is not heated for too long. Each extract is dried over Na_2SO_4 (30g), then combined and evaporated under reduced pressure. The NH_2CN may be stored unchanged at 0º in Et_2O solution in the presence of a trace of AcOH. Extracts from several runs may be combined and evaporated together. The residue from evaporation of an Et_2O solution is a colourless viscous oil which sets to a solid and can be recrystallised from a mixture of 2 parts of $*C_6H_6$ and 1 part of Et_2O. Concentrating an aqueous solution of NH_2CN at high temperatures causes **EXPLOSIVE** polymerisation. [Kurzer & Lawson *Org Synth* Coll Vol **IV** 645 *1963*, Pinck & Salisbury *Inorg Synth* **III** 39 *1950*, Soloway & Lipschitz *J Org Chem* **23** 613 *1958*.] *Hygroscopic*. [*Beilstein* **3** IV 145.]

Cyanogen bromide *[506-68-3]* **M 105.9, m 49-51º, b 60-62º/atm.** *All operations with this substance should be performed in a very efficient fume cupboard—it is very* **POISONOUS** *and should be handled in small amounts. Fresh commercial material is satisfactory for nearly all purposes and does not need to be purified. It is a white crystalline solid with a strong cyanide odour. If it is reddish in colour and partly liquid or paste-like, then it is too far gone to be purified, and fresh material should be sought.* It can be purified by distillation using small amounts at a time, and using a short wide-bore condenser because it readily solidifies to a crystalline white solid which may clog the condenser. *An appropriate gas mask should be used when transferring the molten solid from one container to another, and the operation should be done in an efficient fume cupboard.* The melting point (**m** 49-51º) should be measured in a sealed tube. [Hartman & Dreger *Org Synth* Coll Vol **II** 150 *1948*.]

Cyanogen iodide *[506-78-5]* **M 152.9, m 146-147º.** *This compound is* **POISONOUS**, *and the precautions for cyanogen bromide (above) apply here.* The reagent (*ca* 5.9g) is dissolved in boiling $CHCl_3$ (15ml), filtered through a plug of glass wool into a 25ml Erlenmeyer flask. Cool to room temperature for 15 minutes, then place it in an ice-salt bath and cool to -10º. This cooling causes a small aqueous layer to separate as ice. The ice is filtered with the CNI, but melts on the filter and is also removed with the $CHCl_3$ used as washing liquid. The CNI which is collected on a sintered glass funnel is washed 3x with $CHCl_3$ (1.5ml at 0º) and freed from last traces of solvent by placing it on a watch glass and exposing it to the atmosphere in a good fume cupboard at room temperature for 1 hour to give colourless needles (*ca* 4.5g), **m** 146-147º (sealed capillary totally immersed in the oil bath). The yield depends slightly on the rapidity of the operation; in this way loss by sublimation can be minimised. If desired, it can be sublimed under reduced pressure at temperatures at which CNI is only slowly decomposed into I_2 and $(CN)_2$. The vacuum will need to be renewed constantly due to the volatility of CNI. [Bak & Hillebert *Org Synth* Coll Vol **IV** 207 *1963*.]

Decaborane *[17702-41-9]* **M 122.2, m 99.7-100º, b 100º/19mm, 213º/atm.** Purify decaborane by vacuum sublimation at 80º/0.1mm, followed by crystallisation from methylcyclohexane, CH_2Cl_2, or dry olefin-free-*n*-pentane, the solvent being subsequently removed by storing the crystals in a vacuum desiccator containing $CaCl_2$. It is soluble in H_2O but is slowly decomposed to give H_2. It is soluble in alkali, and on acidification it liberates H_2. **TOXIC.** [Greenwood in *Comprehensive Chemistry (Ed Bailar et al.)* Pergamon Press Vol **1** pp 818-837 *1973*.]

Deuterium *[7782-39-0]* **M 4.** Pass the gas over activated charcoal at -195º [MacIver & Tobin *J Phys Chem* **64** 451 *1960*]. Purify it also by diffusion through nickel [Pratt & Rogers, *J Chem Soc, Faraday Trans I* **92** 1589 *1976*]. Always check deuterium for radioactivity to determine the amount of tritium in it (see D_2O below).

Deuterium oxide *[7789-20-0]* **M 20, f 3.8º/760mm, b 101.4º/760mm, d$_4^{20}$ 1.105.** Distil it from alkaline $KMnO_4$ [de Giovanni & Zamenhof *Biochem J* **92** 79 *1963*]. **NOTE that D_2O invariably contains tritiated water and will therefore be RADIOACTIVE; always check the radioactivity level of D_2O in a scintillation**

counter before using.

***cis*-Diamminedichloroplatinum(II) (Cisplatin)** *[15663-27-1]* **M 300.1, m 270°(dec).** Recrystallise it from dimethylformamide and check the purity by IR and UV-VIS spectroscopy. [Raudaschl et al. *Inorg Chim Acta* **78** 143 *1983*.] **HIGHLY TOXIC, SUSPECTED CARCINOGEN.**

Diammonium hydrogen orthophosphate *[7783-28-0]* **M 132.1.** Crystallise it from water (1ml/g) between 70 and 0°. Its solubility in H_2O is 59% at room temperature and 200% at boiling point. It slowly evolves NH_3 and should be stored in a well-stoppered container. After one crystallisation, ACS grade salt had Fe, Mo, Na, Se and Ti at 1, 0.2, 1.4, 0.2 and 0.8ppm, respectively. [Gmelin's, Ammonium (8th edn) **23** pp422-426 *1936*.]

Dinitrogen tetroxide (nitrogen dioxide, N_2O_4) *[10544-72-6]* **M 92.0 m -11.2°, b 21.1°.** Purify it by oxidation at 0° in a stream of oxygen until the blue colour changes to red-brown. *Alternatively* distil it from P_2O_5, then solidify it by cooling in a deep-freeze (at –78°, giving nearly colourless crystals). Oxygen can be removed by alternate freezing and melting. **TOXIC VAPOUR.** [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 488-489 *1963*.]

Disodium hydrogen orthophosphate (anhydrous) *[7558-79-4]* **M 142.0 (see pK of H_3PO_4).** Crystallise the salt twice from warm water, by cooling. Dry in air, then in an oven overnight at 130°. It should be dried before use as it is slightly *hygroscopic*. It forms di-, hepta- and deca- hydrates.

Ferric Bromide *[10031-26-2]* **M 395.6, m >130°(dec).** Sublime it in a sealed tube with Br_2 at 120°-200°. [Lux in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1494 *1965*.]

Ferric chloride (anhydrous) *[7705-08-0]* **M 162.2, m >300°(dec).** Sublime it at 200° in an atmosphere of chlorine. It is an "iron-black" coloured powder with green irridescence. It is soluble in $*C_6H_6$, EtOH, Et_2O, Me_2CO and pyridine in which the monomeric species "$FeCl_3$" exist whereas in the vapour state it exists in the dimeric "Fe_2Cl_6" form. Store it in a weighing bottle inside a desiccator as it absorbs moisture from air to form the yellow *hexahydrate* (see next entry). [Tarr *Inorg Synth* **III** 191 *1950*, Pray *Inorg Synth* **V** 153 *1957*, Epperson *Inorg Synth* **VII** 163 *1963*.]

Ferric chloride hexahydrate *[10025-77-1]* **M 270.3, m 37°(dec), pK_1^{25} 2.83, pK_2^{25} 4.59 (for hydrolysis of Fe^{3+}).** An aqueous solution, saturated with the salt at room temperature, is cooled to -20° for several hours. Separation of the crystals is slow, even with scratching and seeding, and it is generally necessary to stir this overnight. The presence of free HCl retards crystallisation. [Linke *J Phys Chem* **60** 91 *1956*].

Ferric nitrate nonahydrate *[7782-61-8]* **M 404.0, m 47°(dec).** It crystallises from aqueous solutions of moderately strong HNO_3 as the pale violet *nonahydrate* **m 40°** and is soluble in EtOH and Me_2CO. With more concentrated aqueous solutions (containing some HNO_3), the *hexahydrate* crystallises out **m 60.5°**. The *anhydrous* salt is slightly deliquescent and decomposes at 47°. [Lambert & Thomson *J Chem Soc* **97** 2426 *1920*, *Gmelin's, Iron* (8th edn) **59** Part B pp 161-172 *1932*.]

Ferric perchlorate nonahydrate *[13537-24-1]* **M 516.3, pK^{25} -2.4 to -3.1 (for $HClO_4$).** Crystallise it twice from conc $HClO_4$, the first time in the presence of a small amount of H_2O_2 to ensure that the iron is fully oxidised [Sullivan *J Am Chem Soc* **84** 4256 *1962*]. Extreme care should be taken with this preparation because it is potentially **EXPLOSIVE**.

Ferric sulfate x-hydrate *[10028-22-5]* **M 399.9 + xH_2O.** Dissolve the sulfate in the minimum volume of dilute aqueous H_2SO_4 and allow it to evaporate at room temperature until yellowish-white crystals start to form. Do not concentrate by boiling off the H_2O as basic salts will be formed. Various *hydrates* are formed; the common ones are the dodeca and nona *hydrates* which are violet in colour. The anhydrous *salt* is colourless

and is quite *hygroscopic*, but it dissolves in H_2O slowly unless ferrous sulfate is added. [*Gmelin's, Iron* (8th edn) pp 439-462 *1932*.]

Ferrous bromide *[20049-65-4]* **M 215.7 + xH_2O, m 684°, d^{25} 4.63.** It crystallises from air-free H_2O to provide the *hexahydrate* as pale green to bluish-green rhombic prisms. On heating at 49° H_2O is lost and the *tetrahydrate* is formed. On further heating at 83° more H_2O is lost and the *dihydrate* is formed as a light yellow to dark brown *hygroscopic* powder. The ferrous iron in aqueous solutions of these salts readily oxidise to ferric iron. The salts should be stored over H_2SO_4 under N_2 in tightly closed containers. They have some solubility in EtOH. [Baxter *Z Anorg Chem* **38** 236 *1904*, Kühln & Ernst *Z Anorg Allgem Chem* **317** 84 *1962*, Lux in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1493 *1965*.]

Ferrous chloride tetrahydrate *[13478-10-9]* **M 198.8, m 105°(dec), pK$_1^{25}$ 6.7, pK$_2^{25}$ 9.3 (for aquo Fe^{2+}).** A 550ml round-bottomed Pyrex flask is connected, *via* a glass tube fitted with a medium porosity sintered-glass disc, to a similar flask. To 240g of $FeCl_2.4H_2O$ in the first flask is added conductivity water (200ml), 38% HCl (10ml), and pure electrolytic iron (8-10g). A stream of purified N_2 gas is passed through the assembly, escaping through a mercury trap. The salt is dissolved by heating which is continued until complete reduction has occurred. By inverting the apparatus and filtering (under N_2 pressure) through the sintered glass disc, unreacted iron is removed. After cooling and crystallisation, the unit is again inverted, and the crystals of ferrous chloride are filtered free from mother liquor by applied N_2 pressure. Partial drying by overnight evacuation at room temperature gives a mixed hydrate which, on further evacuation on a water bath at 80°, loses water of hydration and absorbed HCl (with vigorous effervescence) to give a white powder of $FeCl_2.2H_2O$ (see below). [Gayer & Wootner *J Am Chem Soc* **78** 3944 *1956*, ($2H_2O$) Gayer & Woontner *Inorg Synth* **V** 179 *1957*.]

Ferrous chloride *[7758-94-3]* **M 126.8, m 674°, b 1023°, d^{25} 3.16.** It sublimes in a stream of HCl at *ca* 700°, or in H_2 below 300°. Its vapour pressure at 700° is 12mm. It forms white *hygroscopic* rhombohedral crystals with a green tint which oxidise in air to $FeCl_3$ and Fe_2O_3. It is soluble in H_2O, EtOH Me_2CO but insoluble in Et_2O. The *tetrahydrate* is pale green to pale blue in colour and loses $2H_2O$ at 105-115°. The *dihydrate* loses H_2O at 120°. [*Anhydrous* $FeBr_2$ can be obtained by carefully dehydrating the *tetrahydrate* in a stream of HBr and N_2, and it can be sublimed under N_2.] The ferrous iron in aqueous solutions of these salts readily oxidises to ferric iron. (See above.) [Kovacuumic & Brace *Inorg Synth* **VI** 172 *1960*, Lux in *Handbook of Preparative Inorganic Chemistry (Ed Brauer)* Academic Press Vol **II** p 1491 *1965*.]

Ferrous perchlorate hexahydrate *[13933-23-8]* **M 362.9, pK^{25} -2.4 to -3.1 (for $HClO_4$).** Crystallise it from $HClO_4$. [**CARE, see ferric perchlorate above.**]

Ferrous sulfate heptahydrate (green vitriol) *[7782-63-0]* **M 278.0, m ~60°(dec).** Crystallise the sulfate from 0.4M H_2SO_4, or precipitate it from an aqueous solution with EtOH. It is *efflorescent* in dry air, and is converted to the *tetrahydrate* at 57°, then to the *monohydrate* at 65° (or by heating the heptahydrate in a vacuum at 140°). It forms a brown-black complex, $FeSO_4.NO$, with nitric oxide and is used in a qualitative test for nitrates ("**brown ring" test**).

Fluorine *[7782-41-4]* **M 38.0, b -129.2°.** Pass the gas through a bed of NaF at 100° to remove HF and SiF_4. [For description of stills used in fractional distillation, see Greenberg et al. *J Phys Chem* **65** 1168 *1961*; Stein et al. *Purification of Fluorine by Distillation, Argonne National Laboratory,* ANL-6364 1961 (from Office of Technical Services, US Dept of Commerce, Washington 25).] **HIGHLY TOXIC.**

Fluoroboric acid (tetrafluoroboric acid, fluoboric acid) *[16872-11-0]* **M 87.8, b 130°(dec), pK^{25} -4.9.** Crystallise fluoroboric acid several times from conductivity water. It can be stored in a glass vessel at room temperature. It is available commercially as ~48% aqueous solution. It is most useful for preparing *tetrafluoroborate salts* which are generally insoluble. For example, addition of the acid to aryldiazonium salt solutions precipitates the more stable aryldiazonium tetrafluoroborate salts which can be washed with H_2O to remove impurities, followed by EtOH and Et_2O, and stored for short periods of time before further use. It is a catalyst for preparing acetals. [Mathers et al. *J Am Chem Soc* **37** 1516 *1915*, Wamser & Christian *J Am Chem*

Soc **70** 1209 *1940*, Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 221-222 *1963*.] **STRONG IRRITANT and is TOXIC.**

Gallium *[7440-55-3]* **M 69.7, m 29.78°, b 2403°, $d^{29.6}$ 5.904, $d^{29.8}$ 6.095.** Dissolve the metal in dilute HCl and extract it with Et_2O. Bubbling H_2S through the solution removes many metals, and a second extraction with Et_2O frees Ga further from metal impurities, except for Mo, Th(III) and Fe which are largely removed by precipitation with NaOH. The solution is then electrolysed in 10% NaOH with a Pt anode and cathode (2-5A at 4-5V) to deposit Ga, In, Zn and Pb, from which Ga was obtained by fractional crystallisation of the melt [Hoffman *J Res Nat Bur Stand* **13** 665 *1934*]. Ga is also purified by heating to boiling in 0.5-1M HCl, then heating to 40° in water and pouring the molten Ga with water under vacuum through a glass filter (30-50 μ pore size), to remove any unmelted metals or oxide film. The Ga is then fractionally crystallised from the melt under water. [Dönges in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 837 *1963*.]

Gallium (III) Chloride *[13450-90-3]* **M 176.1, m 77.8°, b 133°/100mm, 197.7°/700mm, d_4^{20} 2.47, pK_1^{25} 2.91, pK_2^{25} 3.70, pK_3^{20} 4.42 (for Ga^{3+}).** The pure compound can be obtained by redistillation in a stream of Cl_2 or Cl_2/N_2 followed by vacuum sublimation or zone refining. It forms colourless needles which give *gallium dichloride* [$Ga(GaCl_4)$, **m** 172.4°] on heating. It dissolves in H_2O with liberation of heat. It is soluble in Et_2O and can be extracted from an HCl solution with Et_2O. [Laubengayer & Schirmer *J Am Chem Soc* **62** 1579 1940, Dönges in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 846 *1963*.]

Gallium (III) nitrate nonahydrate *[63462-65-7]* **M 417.9, m *ca* 65°.** Recrystallise the nitrate from H_2O (solubility is 295g/100ml at 20°). It forms a white *deliquescent*, colourless powder soluble in H_2O, absolute EtOH and Et_2O. It loses HNO_3 upon heating at 40°. Addition of Et_2O to a warm ethanolic solution (40-50°) of $Ga(NO_3)_3$ $9H_2O$ precipitates $Ga(OH)_2NO_3.Ga(OH)_3.2H_2O$. If the salt has partly hydrolysed, dissolve it in conc HNO_3, reflux, dilute with H_2O and concentrate on a sand bath. Wash the solid several times by adding H_2O and evaporating until there is no odour of acid. Dilute the residue to a Ga concentration of 26g/100ml. At this concentration, *spongy* $Ga(NO_3)_3.xH_2O$ separates from the viscous solution. After standing for several days the crystals are collected and dried in a stream of dry air first at room temperature, then at 40°. *Dehydration* is complete after 2 days. Recrystallise it from H_2O and dry it at water pump vacuum at room temperature. [Reimmann & Tanner *Z Naturforsch* **20B** 71 *1965*, Dönges in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 856 *1963*.]

Gallium (III) sulfate *[13494-91-2 (anhydrous), 13780-42-2 (hydrate)]* **M 427.6.** Recrystallisation from H_2O gives the 16-18H_2O hydrate (solubility at 20° is 170g/100ml). *Alternatively*, dissolve it in 50% H_2SO_4 and evaporate (60-70°), cool and precipitate it by adding EtOH/Et_2O. On heating at 165° it provides the *anhydrous* salt, which is a white *hygroscopic* solid. [Reimmann & Tanner *Z Naturforsch* **20B** 71 *1965*.]

Germanium *[7440-56-4]* **M 72.6, m 937°, 925-975°, b 2700°, d_4^{20} 5.3.** Copper contamination on the surface and in the bulk of single crystals of Ge can be removed by immersion in molten alkali cyanide under N_2. The Ge is placed in dry K and/or Na cyanide powder in a graphite holder in a quartz or porcelain boat. The boat is then inserted into a heated furnace which, after a suitable time, is left to cool to room temperature. At 750°, a 1mm thickness of metal requires about 1 minute, whereas 0.5cm needs about half hour. The boat is removed from the furnace, and the solid samples are taken out with plastic-coated tweezers, carefully rinsed in hot water and dried in air [Wang *J Phys Chem* **60** 45 *1956*, Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 712 *1963*]. **Care with the use of cyanide.**

Germanium (IV) oxide *[1310-53-8]* **M 104.6, m 1080°(soluble form), d^{25} 6.239; m 1116°(insoluble form) d^{25} 4.228, pK_1^{25} 9.02, pK_2^{25} 12.82 (for germanic acid H_2GeO_3).** The oxide (GeO_2) is usually prepared by hydrolysing redistilled $GeCl_4$ and igniting it in order to remove H_2O and chloride. It can be further purified by dissolving in hot H_2O (solubility is 4g/L cold) evaporating and drying the residual crystalline solid. When the *soluble* form (which is produced in H_2O at 355°) is heated for 100 hours, it is converted to the *insoluble* form.

This form is stable at temperatures up to 1033°, and fusion at 1080° for 4 hours causes complete de-vitrification and it reverts to the *soluble* form. [Müller & Blank *J Am Chem Soc* **46** 2358 *1924*, Dennis & Laubengayer *J Am Chem Soc* **47** 1945 *1925*, Laubengayer & Morton *J Am Chem Soc* **54** 2303 *1932*, Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol I p 706 *1963*.]

Germanium tetrabromide *[13450-92-5]* M392.2, **m 26°, b 185.9°/atm, d_4^{29} 3.123.** Purify it by simple distillation or fractionation depending on purity. It is soluble in EtOH, $CHCl_3$, $*C_6H_6$ and Et_2O. It fumes in moist air and is readily hydrolysed by water. [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 718 *1963*]. **LACHRYMATORY.**

Germanium tetrachloride *[10038-98-9]* **M 214.4, m -49.5° (α), -52.0° (β), b 83.1°/760mm, 86.5°/760mm corr, d_4^{20} 1.84.** Traces of Cl_2 and HCl can be removed from the liquid by blowing dry air through it for a few hours at room temperature or by shaking it with Hg or Hg_2Cl_2 and then fractionating it in a vacuum. It decomposes on heating at 950°. It has a sharp penetrating odour and fumes in moist air to give a chalky coat of GeO_2. It is slowly hydrolysed by H_2O to give GeO_2, but distils from conc HCl. [Foster et al. *Inorg Synth* **II** 109 *1946*, Dennis & Hance *J Am Chem Soc* **44** 304 *1922*, Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 715 *1963*.] **LACHRYMATORY.**

Glass powder (100-300 mesh). Washed with 10% HNO_3, water and dry in air.

Gold powder *[7440-57-5]* **M 196.97, m 1064.79°, b 2808° (2700°), d_4^{20} 19.3, resistivity at 0° is 2.05 μΩ-cm.** Massive gold reacts very slowly and it is best converted to the powder which is more readily reactive. While working in a well vented fume cupboard, solid gold (10g, 51mmol) is dissolved in *Aqua Regia*, made from concentrated hydrochloric acid (12M HCl, 50ml) and concentrated nitric acid (16M HNO_3, 13ml), by heating to 90° which will hasten dissolution, but will require topping up with *Aqua Regia*. *Alternatively*, the suspension is allowed to stand at ~25° until the solid has dissolved. The solution is evaporated to *ca* 10ml, concentrated hydrochloric acid (30ml) is added and evaporation is repeated. The solution is diluted with H_2O (20ml), filtered through a medium sintered-glass funnel, and the filter is washed with small volumes of H_2O. The filtrate and washings, which contain $HAuCl_4$, are heated to boiling and hydroquinone (10g, 91mmol) in hot H_2O (100ml) is slowly added. The mixture is kept at 90° for 1 hour (sufficient time to reduce all the $HAuCl_4$ to Au), cooled and filtered through an extraction thimble. The thimble is placed in a Soxhlet apparatus and extracted with MeOH. Afer 15 minutes, when the circulating MeOH in the thimble is colourless, the thimble is removed and the contents are collected and dried in air to give Au powder quantitatively. [Block *Inorg Synth* **4** 15 *1953*.]

Gold (III) bromide (gold tribromide) *[10294-28-7]* **M 436.7, m 150°(dec).** Purify it by adding pure Br_2 to the dark powder, securely stopper the container, warm a little and shake while keeping away from light for *ca* 48 hours. Remove the stopper and place it over NaOH until free Br_2 is no longer in the apparatus (48-60 hours). The bright yellow needles of the tribromide are stable over NaOH in the dark. It is soluble in H_2O and in EtOH where it is slowly reduced. Keep it in a cooled, closed container and protect it from light as decomposition causes free gold to be formed. *Auribromic acid* can be obtained by adding the calculated amount of conc HBr to $AuBr_3$ (actually Au_2Br_6) until all dissolves, whereby the acid crystallises out as $HAuBr_4.5H_2O$; a *deliquescent* solid soluble in EtOH with **m** *ca* 27°, and store it as above. [Gibson & Colles *J Chem Soc* 2411 *1931*, Burawoy & Gibson *J Chem Soc* 217 *1935*, Burawoy & Gibson *J Chem Soc* 219 *1935*.]

Gold (I) chloride [aurous chloride, Au(I)Cl] *[10294-29-8]* **M 232.4, m 289°(dec), d^{25} 7.4.** It is best prepared by heating $AuCl_3.\sim 3H_2O$, or $HAuCl_4$ (see next entry) at 100° in a high vacuum until the vapour pressure drops considerably when most of the H_2O has been expelled. As the $HAuCl_4$ liquefies again in this process much spluttering will occur. The solid residue (mostly anhydrous $AuCl_3$) is then heated to 156° (bromobenzene bath) and further to 170-205° when decomposition to AuCl is complete. Another preparation includes heating $AuCl_3$ in air at 185° [Thomsen *J Prakt Chem* **13** 337 *1876*], but purer salt is obtained by heating $AuCl_3$ in a stream of dry HCl at 175° [Diemer *J Am Chem Soc* **35** 552 *1913*]. It forms pale yellow crystals which are not deliquescent, slightly soluble in cold EtOH, dissolve in alkali chloride solutions to form chloroaurates(I), e.g. $KAuCl_2$, but it decompose in H_2O to give gold and hydrolysed Au(III) species. [Blitz & Wein *Z Anor Allgem Chem* **148** 192 *1925*, Glemser & Sauer *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic

Press Vol **II** p 1055 *1965*.]

Gold (III) chloride (hydrate) *[16903-35-8]* **M 339.8 + xH_2O, x ~3, m 229°, b 354°(dec), d $^{20}_{4}$ 3.9.** It is obtained as a dark red crystalline mass by dissolving Au in *aqua regia* and evaporating. When sublimed at 180°, the anhydrous crystals are ruby red. The anhydrous salt is *hygroscopic*, soluble in H_2O but sparingly soluble in EtOH and Et_2O. *Aurichloric acid* (chloroauric acid, $HAuCl_4$) is formed when $AuCl_3$ is dissolved in HCl. [Diemer *J Am Chem Soc* **35** 553 *1913*, Block *Inorg Chem* **4** 14 *1953*, Glemser & Sauer *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1056 *1965*.]

Gold (I) cyanide *[506-65-0]* **M 223.0, m dec on heating.** The lemon yellow powder is sparingly soluble in H_2O and EtOH but soluble in aqueous NH_3. It is obtained by heating $H[Au(CN)_2]$ at 110°. Wash it well with H_2O and EtOH and dry it at 110°. It has an IR band at ν_{max} 2239 cm^{-1} typical for C≡N stretching vibration. [Glemser & Sauer *Handbook of Preparative Inorg anic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1064 *1965*.] **CARE**: may evolve HCN.

Gold (I) iodide *[10294-31-2]* **M 323.9, m 120°(dec), d $^{20}_{4}$ 8.25.** It has been prepared by heating gold and iodine in a tube at 120° for 4 months. Since it decomposes to Au and I_2 in the presence of UV light and heat, then the main impurity is Au. The salt is therefore purified by heating at 120° with I_2 for several weeks. The crystals should be kept dry and in a cool place in the dark. [Weiss & Weiss *Z Naturforsch* **11B** 604 *1956*.]

Gold (III) oxide hydrate *[1303-58-8]* **M 441.9 + xH_2O, evolves O_2 at 110°, pK $^{25}_{1}$ <11.7, pK $^{25}_{2}$ 13.36, pK $^{25}_{3}$ >15.3 [for $Au(OH)_3$].** The most probable impurities are SO_4^{2-} and Cl^- ions. Dissolve it in strong boiling KOH solution (*ca* 5M) and precipitate (**care**) with excess of 3N H_2SO_4. Then shake and centrifuge, resuspend in H_2O and repeat the washing several times until free from SO_4 and Cl ions. This gives a *wet* oxide which is dried in air, but decomposes to free gold in sunlight. It is advisable to keep it wet as it decomposes on drying (analyse wet sample). Store it away from light in the presence of H_2O vapour. It evolves O_2 at 110°. It is insoluble in H_2O but soluble in HCl and conc HNO_3. [Roseveare & Buehrer *J Am Chem Soc* **49** 1221 *1927*.]

Graphite (black lead, mineral carbon, plumbago) *[7782-42-5]* **m 3652-3697°, d^{25} 2.09, 2.23.** This carbon allotrope is obtained by mining (e.g. in Shrilanka, Canada). It is normally soft, forms black/gray scales, and although even small crystals of it are rare it is composed of crystallised carbon containing traces of SiO_2, Fe and other minerals. Treat graphite with hot 1:1 HCl. Then filter, wash and the dried powdered is heated in an evacuated quartz tube at 1000° until a high vacuum is obtained. Cool this and store it in an atmosphere of helium [Craig et al. *J Phys Chem* **60** 1225 *1956*]. See also entry in Chapter 8.

Helium *[7440-59-7]* **M 4.0, m –272.2°/26atm, b –268.9°, d$^{-270.3}$ 0.147.** Dry the gas by passing it through a column of Linde 5A molecular sieves and $CaSO_4$, then through an activated-charcoal trap cooled in liquid N_2, to adsorb N_2, argon, xenon and krypton. Also pass it over CuO pellets at 300° to remove hydrogen and hydrocarbons, over Ca chips at 600° to remove oxygen, and then over titanium chips at 700° to remove N_2 [Arnold & Smith *J Chem Soc, Faraday Trans 2* **77** 861 *1981*]. Its solubility in 100ml of H_2O is 0.94ml at 25°, 1.05ml at 50° and 1.21ml at 75°.

Hexachloroplatinic acid hydrate (H_2PtCl_6, chloroplatinic acid, platinum IV chloride soution) *[16941-12-1]* **M 409.8 + H_2O, m 60° (deliquescent solid).** If it is to be purified, or regenerated from Pt recovered from catalytic hydrogenations, it should be dissolved in *aqua regia* followed by evaporation to dryness and dissolution in the minimum volume of H_2O. Then the aqueous solution is treated with saturated ammonium chloride until all the ammonium hexachloroplatinate [16919-58-7] separates. The $(NH_4)_2PtCl_6$ is filtered off and dried at 100°. Igniting this salt gives **Pt *sponge***; dissolve the Pt sponge in *aqua regia*, boil to dryness, dissolve the residue in concentrated HCl, boil to dryness again and repeat the process. Protect it from light. [Wickers *J Am Chem Soc* **43** 1268 *1921*, Adams et al. *Org Synth* Coll Vol **I** 463, 466 *1941*, Bruce *J Am Chem Soc* **58** 687 *1936*.]

Hexammine cobalt(III) chloride *[10534-89-1]* **M 267.5.** It crystallises from warm water (8ml/g) on cooling.

[Bjerrum & McReynolds *Inorg Synth* **II** 217 *1946*.]

Hexammine ruthenium(III) chloride *[14282-91-8]* **M 309.6.** Crystallise it twice from 1M HCl.

Hexarhodium hexadecacarbonyl *[28407-51-4]* **M 1065.6, m 220°(dec, in air), d $_4^{20}$ 2.87.** It slowly loses CO when heated in air, but may be regenerated by heating at 80-200° in the presence of CO at 200 atmospheres pressure for 15 hours, preferably in the presence of Cu. It forms black crystals which are insoluble in hexane. It has bands at 2073, 2026 and 1800 cm^{-1} in the IR. [Hieber & Lagally *Z Anorg Allgem Chem* **251** 96 *1963*, Corey & Dahl *J Am Chem Soc* **85** 1202 *1963*, Doyle et al. *Tetrahedron Lett* **22** 1783 *1981*.] **POISONOUS**.

Hydrazine monohydrate ($N_2H_4.H_2O$) *[7803-57-8]* **M 50.1, m 198°, b 118-122°/atm. d $_4^{20}$ 1.03.** It is best obtained by heating hydrazine sulphate (200g), NaOH (160g) and H_2O (75ml, exothermic) in a copper flask under reflux for 1.5 hours then distilled off (using a flame to remove all the hydrazine). The distillate (175ml) is a clear liquid which contains ~40-45% of N_2H_4. Note that hydrazine attacks glass, rubber and cork, and stainless steel equipment should be used. The percentage of hydrazine is determined by titration with standard acid (methyl orange indicator) or against standard iodine (starch indicator). *Hydrazine monohydrate* should contain 64% of N_2H_4. The ~40-45% solution may be concentrated by mixing it (144ml) with xylene (230ml) and distilling it through an efficient fractionating column (e.g. Hempel column). All the xylene passes over with about 85ml of H_2O. On distilling the residue, hydrated hydrazine (50ml) is obtained containing 80-85% of N_2H_4. This can be diluted with conductivity H_2O to 64% N_2H_4 to give the *monohydrate*. Hydrazine and its hydrates have **VERY IRRITATING** and **TOXIC** vapours and should be used in an efficient fume cupboard. [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 469-472 *1963*.]

Hydrazine hydrate ($N_2H_4.x\,H_2O$) *[10217-52-4]* **M 32.05 + x 18.02.** Hydrated hydrazine can be obtained as above and diluted as required. Solutions containing various amounts of H_2O are available commercially.

Hydrazine (anhydrous) *[302-01-2]* **M 32.1, m 1.5-2.0°, b 47°/26mm, 56°/71mm, 113-113.5°/atm, n 1.470, d 1.91, pK $_1^{25}$ -0.88, pK $_2^{25}$ 8.11.** Hydrazine hydrate is dried by refluxing with an equal weight of KOH pellets for 3 hours, then distilled from fresh solid NaOH or BaO in a current of dry N_2. Use stainless steel or copper equipment. Hydrazine and its hydrates have **VERY IRRITATING** and **TOXIC** vapours and should be used in an efficient fume cupboard. Store in a well-stoppered vessel, preferably under N_2. It is a useful reducing agent. [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 469-472 *1963*.]

Hydrazine dihydrochloride *[5341-61-7]* **M 105.0, m 198°, d $_4^{20}$ 1.42.** It is recrystallised from aqueous EtOH and dried under vacuum over $CaSO_4$.

Hydrazine monohydrochloride *[2644-70-4]* **M 68.5, m 89°.** Prepare it by dropwise addition of cold conc HCl to cold liquid hydrazine in equimolar amounts. The crystals are harvested from water and are twice recrystallised from absolute MeOH and dried under a vacuum. [Kovack et al. *J Am Chem Soc* **107** 7360 *1985*.]

Hydrazine sulfate *[10034-93-2]* **M 130.1, m 254°.** Crystallise it from H_2O. Its solubility in H_2O is 3% at room temperature, but is very soluble in hot H_2O. It is a suspected **carcinogen**. [Adams & Brown *Org Synth* Coll Vol **I** 309 *1941*, Audrieth & Nickles *Inorg Synth* **I** 90 *1939*.]

Hydrazoic acid (hydrogen azide, triazoic acid) *[7782-79-8]* **M 43.0, m -80°, b 37°/atm, pK^{25} 4.72.** The free acid is **HIGHLY EXPLOSIVE** and **POISONOUS**, so it is prepared and used in solution, and in an **efficient fume cupboard**. It is a very useful reagent for Schmidt and related reactions [Wolff *Organic Reactions* **3** 307 *1946*]. Solutions in $*C_6H_6$ or $CHCl_3$ are prepared by making a paste from NaN_3 (65g, 1mole) in warm H_2O (65ml), and added to $*C_6H_6$ or $CHCl_3$ (400ml), cooled to 0°, and concentrated H_2SO_4 (26.6mls, 0.5mol) is dropped into the stirred mixture while carefully controlling the temperature between 0° and 5°. The organic layer is separated, dried (Na_2SO_4), and stored in a cold room. Its concentration is determined by shaking a small

aliquot with ten times its volume of H_2O in a glass-stoppered flask, and titrating it against standard alkali. It can then be diluted to the desired concentration. [Audrieth & Gibbs *Inorg Synth* **1** 77 *1939*, Frost et al. *J Am Chem Soc* **55** 3516 *1933*, Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 472-474 *1963*.] The pure acid is a mobile, pungent explosive liquid, and ***poisonous***, causing irritation of membranes, headaches, palpitation, lowering blood pressure and ataxia — *handle with great care*.

Hydriodic acid *[10034-85-2]* **M 127.9, b 127°(aqueous azeotrope), d $_4^{20}$ 1.701, pK^{25} -8.56.** Iodine can be removed from aqueous HI, probably as the amine hydrogen triiodide, by three successive extractions using a 4% solution of Amberlite LA-2 (a long-chain aliphatic amine) in CCl_4, toluene or petroleum ether (10ml per 100ml of acid). [Davidson & Jameson *Chem Ind (London)* 1686 *1963*.] Extraction with tributyl phosphate in $CHCl_3$ or other organic solvents is also suitable. *Alternatively*, a De-acidite FF anion-exchange resin column in the OH^--form using 2M NaOH, then into its I^--form by passing dilute KI solution through, can be used. Passage of an HI solution under CO_2 through such a column removes polyiodide. The column can be regenerated with NaOH. [Irving & Wilson *Chem Ind (London)* 653 *1964*]. The earlier method was to reflux with red phosphorus and distil in a stream of N_2. The colourless product is stored in ampoules in the dark [Bradbury *J Am Chem Soc* **74** 2709 *1952*, Heisig & Frykholm *Inorg Synth* **I** 157 *1939*]. It fumes in moist air. **HARMFUL VAPOURS.**

Hydrobromic acid *[10035-10-6]* **M 80.9, b 125°(aqueous azeotrope, 47.5% HBr)/atm, d $_4^{20}$ 1.38 (34% HBr), pK^{25} -8.69.** A solution of aqueous HBr *ca* 48% (w/w, constant boiling) is purified by distilling twice with a little red phosphorus, and the middle half of the distillate is taken. (The azeotrope at 760mm contains 47.8% (w/w) HBr.) [Hetzer et al. *J Phys Chem* **66** 1423 *1962*]. Free bromine can be removed by Irvine and Wilson's method for HI (see above), except that the column is regenerated by washing with an ethanolic solution of aniline or styrene. Hydrobromic acid can also be purified by aerating with H_2S, distilling and collecting the fraction boiling at 125-127°. [Heisig & Andur *Inorg Synth* **I** 155 *1939*.] **HARMFUL VAPOURS.**

Hydrochloric acid (muriatic acid) *[7647-01-0]* **M 36.5, b 108.6°(aqueous azeotrope, 20.2% HCl), d $_4^{20}$ 1.09(20%), pK^{25} -6.1.** It is readily purified by fractional distillation as the constant boiling point acid, following dilution with H_2O. The constant-boiling fraction contains 1 mole of HCl in the following weights of distillate at the stated pressures: 179.555g (730mm), 179.766g (740mm), 179.979 (750mm), 180.193 (760mm), 180.407 (770mm). [Foulk & Hollingsworth *J Am Chem Soc* **45** 1220 *1923*.] **HARMFUL VAPOURS.**

Hydrofluoric acid *[7664-39-3]* **M 20.0, b 112.2°(aqueous azeotrope, 38.2% HF), d $_4^{20}$ 1.15 (47-53% HF), pK^{25} 3.21.** It is freed from lead (Pb *ca* 0.002ppm) by co-precipitation with SrF_2, by addition of 10ml of 10% $SrCl_2$ solution per kilogram of the concentrated acid. After the precipitate has settled, the supernatant is decanted through a filter in a hard-rubber or paraffin lined-glass vessel [Rosenqvist *Am J Sci* **240** 358 *1942*]. Pure aqueous HF solutions (up to 25M) can be prepared by isothermal distillation in polyethylene, polypropylene or platinum apparatus [Kwestroo & Visser *Analyst* **90** 297 *1965*]. It attacks glass and is used for etching glass. **HIGHLY TOXIC.**

Hydrogen *[1333-74-0]* **M 2.0, m -259.1°, b -252.9°, d 0.0889g/L (gas), 0.070g/L (liquid).** It is usually purified by passing through a suitable absorption train of tubes. Carbon dioxide is removed with KOH pellets, soda-lime or NaOH pellets. Oxygen is removed with a "De-oxo" unit or by passage over Cu heated to 450-500° and Cu on Kieselguhr at 250°. Passage over a mixture of MnO_2 and CuO (Hopcalite) oxidises any CO to CO_2 (which is removed as above). Hydrogen can be dried by passage through dried silica-alumina at -195°, through a dry-ice trap followed by a liquid-N_2 trap packed with glass wool, through $CaCl_2$ tubes, or through $Mg(ClO_4)_2$ or P_2O_5. Other purification steps include passage through a hot palladium thimble [Masson *J Am Chem Soc* **74** 4731 *1952*], through an activated-charcoal trap at -195°, and through a non-absorbent cotton-wool filter or small glass spheres coated with a thin layer of silicone grease. *Potentially* **VERY EXPLOSIVE** *in air or with O_2.*

Hydrogen bromide (anhydrous) *[10035-10-6]* **M 80.9, b -66.8°/atm.** Dry it by passing it through $Mg(ClO_4)_2$ towers. This procedure is **hazardous** [Stoss & Zimmermann *Ind Eng Chem* **17** 70 *1939*]. *Alternatively*, shake it with mercury, distil it through a -78° trap and condense it at -195°/10^{-5}mm. It fumes in moist air. **HARMFUL VAPOURS**. It is soluble in H_2O. A constant boiling aqueous solution of HBr has **b 126°/760mm,** and its HBr concentration is 47.4% (see hydrobromic acid above). It is soluble in AcOH. [Schneider & Johnson *Inorg Synth*

I 152 *1939*, Schmeisser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 282-286 *1963*.]

Hydrogen chloride *[7647-01-0]* **M 36.5, b -85°/760mm.** Pass it through conc H_2SO_4, then over activated charcoal and silica gel. It fumes in moist air. Hydrogen chloride in gas cylinders contains ethylene, 1,1-dichloroethane and ethyl chloride. The latter two may be removed by fractionating the HCl through a trap cooled to -112°. Ethylene is difficult to remove. HCl fumes in moist air. **HARMFUL VAPOURS.** Its solubility in H_2O is 82% at 0°. A constant boiling aqueous solution (azeotrope) has **b 108.6°/760mm** with an HCl concentration of ~20%, and is called *Hydrochloric acid (muriatic acid)* (see above). [Schmeisser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 280-282 *1963*.]

Hydrogen cyanide (anhydrous) *[74-90-8]* **M 27.0, b 25.7°/760mm, pK^{25} 9.21 (aqueous acid).** HCN is prepared from NaCN and H_2SO_4, and dried by passage through H_2SO_4 and over $CaCl_2$, then distilled in a vacuum system and degassed at 77°K before use [Arnold & Smith *J Chem Soc, Faraday Trans 2* **77** 861 *1981*]. Cylinder HCN may contain stabilisers against explosive polymerisation, together with small amounts of H_3PO_4, H_2SO_4, SO_2, and water. It can be purified by distillaton over P_2O_5, then frozen in Pyrex bottles at Dry-ice temperature for storage. [Zeigler *Org Synth* Coll Vol **I** 314 *1941*, Glemser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 658-660 *1963*.] Liquid HCN, like liquid ammonia, evaporates very slowly since the latent heat of evaporation is high and keeps it in the liquid state because the temperature of the liquid is lowered to below its boiling point. **EXTREMELY POISONOUS; all due precautions should be taken.**

Hydrogen fluoride (anhydrous) *[7664-39-3]* **M 20.0, b 19.4°.** It can be purified by trap-to-trap distillation, followed by drying over CoF_2 at room temperature and further distillation. *Alternatively*, it can be absorbed on NaF to form $NaHF_2$ which is then heated under vacuum at 150° to remove volatile impurities. The HF is regenerated by heating at 300° and is stored with CoF_3 in a nickel vessel, being distilled as required. (Water content should be *ca* 0.01%.) To avoid contact with base metal, use can be made of nickel, polychlorotrifluoroethylene and gold-lined fittings [Hyman et al. *J Am Chem Soc* **79** 3668 *1957*]. An aqueous solution is *hydrofluoric acid* (see above). It is **HIGHLY TOXIC and attacks glass.**

Hydrogen iodide (anhydrous) *[10034-85-2]* **M 127.9, b -35.5°.** After removal of free iodine from aqueous HI, the solution is frozen, then covered with P_2O_5 and allowed to melt under vacuum. The gas evolved is dried by passing through P_2O_5 on glass wool. It can be freed from iodine contamination by repeated fractional distillation at low temperatures. It fumes in moist air, and an aqueous solution is *hydriodic acid* (see above). **HARMFUL VAPOURS.**

Hydrogen peroxide *[7722-84-1]* **M 34.0, d_4^{20} 1.110, pK^{25} 11.65.** The 30% material has been steam distilled using distilled water. Gross and Taylor [*J Am Chem Soc* **72** 2075 *1950*] made 90% H_2O_2 approximately 0.001M in NaOH and then distilled it under its own vapour pressure, keeping the temperature below 40°, the receiver being cooled with a Dry-ice/isopropyl alcohol slush. The 98% material has been rendered anhydrous by repeated fractional crystallisation in all-quartz vessels. **EXPLOSIVE IN CONTACT WITH ORGANIC MATERIAL.**

Hydrogen peroxide urea adduct (UHP, urea hydrogen peroxide 1:1 complex, carbamide peroxide, Debrox, Hyperol) *[124-43-6]* **M 94.1, m. 85-90°(dec), 90°(dec).** It is a safe alternative to H_2O_2 in various oxidation reactions. It is commercially available in tablets ("rapidly soluble", equivalent to ~30% H_2O_2) or as a white powder (with 15-17% active oxygen). It is usually used without purification after assaying for active oxygen. This is done by titration with potassium permanganate or by iodometry, i.e. titration of liberated iodine when glacial acetic acid containing Fe^{3+} and NaI are added. It can be recrystallised from 30% H_2O_2 in a molar ratio of ~2:3 by heating in a pyrex dish for a few minutes at ~60°, cooling and allowed to crystallise slowly by evaporation in a crystallising dish. It forms elongated white needles, but if the solution is seeded just before crystallisation and shaken gently for as few seconds, then small plates are formed. Preferably collect the crystals by centrifugation at low temperature and dry them at 0° *in vacuo*. When dry, it is stable at room temperature and

it has been reported that the available oxygen content had not decreased noticeably after 12 months. However, it is best to store it dry at low temperature. It is soluble in organic solvents e.g. EtOH, Et_2O, $CHCl_3$, CH_2Cl_2 and Me_2CO with slow decomposition, and its solubility in H_2O is 40% where it also decomposes slowly. It decomposes slowly at 40-60°/20mm and at 55-70°/760mm in air, but decomposition appears to accelerate above 80°. It is very useful (and in many cases superior to *p*-chloroperbenzoic acid) in the oxidation of alkenes, (epoxides), aromatic hydrocarbons (to phenols), ketones (Baeyer-Villiger), sulfides (to sulfones) and N-heterocycles (to N-oxides) when using 5 to 10 molar ratios of oxidant in the presence of acetic or trifluoroacetic anhydrides. Care should be used with this reagent as it is **potentially explosive**. [Lu et al. *J Am Chem Soc* **63** 1508 *1941*, Cooper et al. *Synlett* 533 *1990*, *Beilstein* **3** H 54, **3** I 25, **3** II 45, **3** III 105, **3** IV 102.]

Hydrogen sulfide *[7783-06-4]* **M 34.1, b -59.6°, pK_1^{25} 7.05, pK_2^{25} 12.89.** Wash it, then pass the gas through a train of tubes containing saturated $Ba(OH)_2$ (2x), water (2x), and dilute HCl [Goates et al. *J Am Chem Soc* **73** 707 *1951*]. It is available in gas cylinders. **HIGHLY POISONOUS.**

Hydroxylamine *[7803-49-8]* **M 33.0, m 33.1°, b 56.5°/22mm, d_4^{20} 1.226, pK^{20} 5.96 (7.97).** Crystallise it from *n*-butanol at -10°, collect it by vacuum filtration and wash it with cold diethyl ether. **Harmful vapours.** [Hurd *Inorg Synth* **I** 87 *1939*, Semon in *Org Synth* Coll Vol **I** 318 *1932*.]

Hydroxylamine hydrochloride *[5470-11-1]* **M 69.5, m 151°.** Crystallise the salt from aqueous 75% ethanol or boiling methanol, and dry it under vacuum over $CaSO_4$ or P_2O_5. It has also been dissolved in a minimum of water and saturated with HCl; after three such crystallisations, it is dried under a vacuum over $CaCl_2$ and NaOH. Its solubility at 20° is 85% in H_2O, 6% in EtOH and 12% in MeOH. [Hurd *Inorg Synth* **I** 87 *1939*, Semon in *Org Synth* Coll Vol **I** 318 *1941*.]

Hydroxylamine sulfate *[10039-54-0]* **M 164.1, m 170°(dec).** Crystallise it from boiling water (1.6ml/g) by cooling to 0°.

Hydroxylamine-*O*-sulfonic acid *[2950-43-8]* **M 113.1, m 210-211°, 215°(dec), pK^{45} 1.48.** Stir the solid vigorously with anhydrous Et_2O and filter it off using large volumes of dry Et_2O. Drain dry at the pump for 5 minutes and then for 12-14 hours in a vacuum. Store it in a vacuum desiccator over conc H_2SO_4. Determine the purity by oxidation of iodide to I_2. It must be stored in a dry atmosphere at 0-4°. It decomposes slowly in H_2O at 25° and more rapidly above this temperature. [Matsuguma & Andrieth *Inorg Synth* **V** 122 *1957*.]

Hydroxyurea *[127-07-1]* **M 76.1, m 70-72° (unstable form), m 133-136°, 141° (stable form), pK^{25} 10.6.** Recrystallise hydroxyurea from absolute EtOH (10g in 150ml). Note that the rate of solution in boiling EtOH is slow (15-30 minutes). It should be stored in a cool dry place, but some decomposition could occur after several weeks. [Deghenghi *Org Synth* Coll Vol **V** 645 *1973*.] It is very soluble in H_2O and can be crystallised from Et_2O. [Kfod *Acta Chem Scand* **10** 256 *1956*, *Beilstein* **3** IV 170.]

Hypophosphorous acid (Phosphinic acid) *[6303-21-5]* **M 66.0, m 26.5°, d_4^{30} 1.217, 1.13 and 1.04 for 50, 30-32, and 10% aqueous solutions resp, pK^{25} 1.31 (H_3PO_2).** Phosphorous acid is a common contaminant of commercial 50% hypophosphorous acid. Jenkins and Jones [*J Am Chem Soc* **74** 1353 *1952*] purified this material by evaporating about 600ml in a 1L flask at 40°, under reduced pressure (in N_2), to a volume of about 300ml. After the solution was cooled, it was transferred to a wide-mouthed Erlenmeyer flask which was stoppered and left in a Dry-ice/acetone bath for several hours to freeze (if necessary, with scratching of the wall). When the flask was then left at *ca* 5° for 12 hours, about 30-40% of it liquefied, and was again filtered. This process was repeated, then the solid was stored over $Mg(ClO_4)_2$ in a vacuum desiccator in the cold. Subsequent crystallisations from *n*-butanol by dissolving it at room temperature and then cooling in an ice-salt bath at -20° did not appear to purify it further. The free acid forms *deliquescent* crystals **m** 26.5° and is soluble in H_2O and EtOH. The NaH_2PO_2 salt can be purified through an anion exchange resin [Klement *Z Anorg Allgem Chem* **260** 267 *1949*.]

Indium *[7440-74-6]* **M 114.8, m 156.6°, b 2000°, d $_4^{20}$ 7.31.** Before use, the metal surface is cleaned with dilute HNO_3, followed by thorough washing with water and an alcohol rinse. [Dönges in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 856 *1963*.]

Indium (III) chloride *[10025-82-8]* **M 211.2, m 586°, d $_4^{20}$ 4.0, pK$_1^{25}$ 3.54, pK$_2^{25}$ 4.28, pK$_3^{25}$ 5.16 (for aqueous In^{3+}).** The anhydrous salt forms yellow deliquescent crystals which can be sublimed at 600° in the presence of Cl_2/N_2 (1:1) [does not melt]. It is resublimed in the presence of Cl_2/N_2 (1:10) and finally heated to 150° to expel excess Cl_2. It is soluble in H_2O and should be stored in a tightly closed container. [Baxter & Alter *J Am Chem Soc* **55** 1943 *1933*.]

Indium (III) oxide *[1312-43-2]* **M 277.6, d $_4^{20}$ 7.18, m sublimes at 850°.** Wash it with H_2O and dry it below 850°. It volatilises at 850° and dissolves in hot mineral acids to form salts. Store it away from light because it darkens due to the formation of free In.

Indium sulfate *[13464-82-9]* **M 517.8.** Crystallise it from dilute aqueous H_2SO_4. It is *hygroscopic*; store it in a well-stoppered vessel.

Indium (III) sulfate pentahydrate *[17069-79-3]* **M 607.9, d $_4^{20}$ 3.44.** Dissolve the salt in strong H_2SO_4 and slowly evaporate at *ca* 50°. Wash the crystals with glacial AcOH and then heat them in a furnace at a temperature of 450-500° for 6 hours. Its solubility in H_2O is 5%. The *pentahydrate* is converted to an *anhydrous hygroscopic* powder on heating at 500° for 6 hours; but heating above this temperature over N_2 yields the oxide-sulfate. Evaporation of neutral aqueous solutions provides basic sulfates. [Baxter & Alter *J Am Chem Soc* **55** 1943 *1933*, Hattox & Vries *J Am Chem Soc* **58** 2126 *1936*.]

Iodic acid *[7782-68-5]* **M 175.9, m 118°(dec), d $_4^{20}$ 4.628, pK^{25} 0.79.** Dissolve iodic acid in the minimum volume of hot dilute HNO_3, filter and evaporate in a vacuum desiccator until crystals are formed. Collect the crystals and wash them with a little cold H_2O and dry them in air in the dark. It is soluble in H_2O: 269g/100ml at 20° and 295g/100ml at 40°. It is soluble in dilute EtOH and darkens on exposure to light. It is converted to $HIO_3.I_2O_5$ on heating at 70°, but at 220° complete conversion to HIO_3 occurs. [Lamb et al. *J Am Chem Soc* **42** 1636 *1920*, Bray & Caulkins *J Am Chem Soc* **53** 44 *1931*.]

Iodine *[7553-56-2]* **M 253.8, m 113.6°.** It is usually purified by vacuum sublimation. Preliminary purifications include grinding with 25% by weight of KI, blending with 10% BaO and subliming, subliming with CaO, grinding to a powder and treating with successive portions of H_2O to remove dissolved salts, then drying, and recrystallising from *benzene. Barrer and Wasilewski [*Trans Faraday Soc* **57** 1140 *1961*] dissolved I_2 in concentrated KI and distilled it, then steam distilled it three times and washed it with distilled H_2O. Organic material is removed by sublimation in a current of O_2 over platinum at about 700°, the iodine being finally sublimed under vacuum. **HARMFUL VAPOURS.**

Iodine monobromide *[7789-33-5]* **M 206.8, m 42°.** The brown-black crystals are purified by repeated fractional crystallisation from its melt. The vapour dissociates on heating [Yost et al. *J Amer Chem Soc* **55** 552 *1933*, Schmeisser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 291-292 *1963*].

Iodine monochloride *[7790-99-0]* **M 162.4, m 27.2°(α-form), 13.9°(β-form).** Purify it by repeated fractional crystallisation from its melt at low temperatures. The black crystals melt to a red-brown liquid. [Cornog & Karges *Inorg Synth* **I** 165 *1939*.]

Iodine pentafluoride *[7783-66-6]* **M 221.9, m -8.0°, b 97°.** Rogers et al. [*J Am Chem Soc* **76** 4843 *1954*] removed dissolved iodine from IF_5 by agitating with a mixture of dry air and ClF_3 in a Fluorothene beaker using a magnetic stirrer. The mixture is transferred to a still, and the more volatile impurities are pumped off as the pressure is reduced below 40mm. The still is gradually heated (kept at 40mm) to remove the ClF_3 before IF_5 distilled. Stevens [*J Org Chem* **26** 3451 *1961*] pumped IF_5 under vacuum from its cylinder, trapping it at -78°, then allowing it to melt in a stream of dry N_2. **HARMFUL VAPOURS.** [Kwasnik in *Handbook of Preparative*

Inorganic Chemistry (Ed. Brauer) Academic Press Vol **I** pp 159-160 *1963*.]

Iodine trichloride *[865-44-1]* **M 233.3, m 33°, b 77°(dec).** Purify ICl_3 by sublimation at room temperature. **Irritant vapours.** [Booth & Morris *Inorg Synth* **I** 167 *1939*.]

Iridium *[7439-88-5]* **M 192.2, m 2450°, b ~4500°, d $_4^{20}$ 22.65.** Iridium is a silver white hard solid which oxidises on the surface in air. Scrape the outer tarnished layer until silver clear and store it under paraffin. It is stable to acids but dissolves in aqua regia. [Gilchrist *Chem Rev* **32** 277 *1943*.]

Iridium (IV) chloride hydrate (hexachloroiridic acid) *[16941-92-7 ($6H_2O$), 207399-11-9 (xH_2O)]* **M 334.0+H_2O.** If it contains nitrogen, then repeatedly concentrate a conc HCl solution until free from nitrogen, and dry free from HCl in a vacuum over CaO until crystals are formed. The olive-green solid (yellow at ~700°) is very *hygroscopic*. [Woo & Yost *J Am Chem Soc* **53** 884 *1931*, Grube in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p1592 *1965*.]

Iron (wire) *[7439-89-6]* **M 55.9, m 1535°.** Clean it in conc HCl, rinse in de-ionised water, then reagent grade acetone and dry it under vacuum.

Iron enneacarbonyl (di-iron nonacarbonyl) *[15321-51-4]* **M 363.7, m 100°(dec).** Wash it with EtOH and Et_2O, then dry it in air. It sublimes at 35° in a high vacuum. It forms dark yellow plates which are stable for several days when kept in small amounts. Large amounts, especially when placed in a desiccator, spontaneously ***ignite*** in a period of one day. It decomposes in moist air. It is insoluble in hydrocarbon solvents but forms complexes with several organic compounds. [Sheline & Pitzer *J Am Chem Soc* **72** 1107 *1950*, Speyer & Wolf *Chem Ber* **60** 1424 *1927*.] **TOXIC.**

Iron pentacarbonyl (pentacarbonyl iron) *[13463-40-6]* **M 195.9, m -20°, b 102.8°/749mm, 103°/760mm, n 1.520, d 1.490.** It is a pale yellow viscous liquid that is **PYROPHORIC** and readily absorbed by the skin. **HIGHLY TOXIC (protect from light and air)**. It should be purified in a vacuum line by distilling and collecting in a trap at -96° (toluene-Dry-ice slush). It has been distilled at atmospheric pressure (use a very efficient fume cupboard). At 180°/atmospheric pressure it decomposes to give Fe and CO. In UV light in petroleum ether it forms $Fe_2(CO)_9$ (see previous entry). [Hagen et al. *Inorg Chem* **17** 1369 *1978*, Ewens et al. *Trans Faraday Soc* **35** 6811 *1939*.]

Lanthanum *[7439-91-0]* **M 138.9, m 920°, b 3470°, d $_4^{20}$ 6.16.** It is a shiny metal that slowly tarnishes in air due to oxidation. It slowly decomposes by H_2O in the cold and more rapidly on heating to form the hydroxide. The metal is cleaned by scraping off the tarnished areas until the shiny metal is revealed and stored under oil or paraffin. It burns in air at 450°. It exists in three forms: α-form, β-form and γ-form with transition temperatures of 310° and 864°, respectively. [Spedding et al. *Ind Eng Chem* **44** 553 *1952*.]

Lead (II) bromide *[10031-22-8]* **M 367.0, m 373°.** Crystallise it from water containing a few drops of HBr (25ml of water per gram $PbBr_2$) between 100° and 0°. A neutral solution is evaporated at 110°, and the crystals that separate are collected by rapid filtration at 70° and dried at 105° (to give the *monohydrate*). Its solubility in H_2O is 0.5% (at ~10°) and 5% (at ~100°). To prepare the *anhydrous* bromide, the hydrate is heated for several hours at 170° and then in a Pt boat at 200° in a stream of HBr and H_2. Finally it is fused [Clayton et al. *J Chem Soc, Faraday Trans 1* **76** 2362 *1980*]. **POISONOUS.**

Lead (II) chloride *[7758-95-4]* **M 278.1, m 501°.** Crystallise it from distilled water at 100° (33ml/g) after filtering through sintered-glass and adding a few drops of HCl, by cooling. After three crystallisations the solid is dried under vacuum or under anhydrous HCl vapour by heating slowly to 400°. The solubility in H_2O is 0.07% at ~10°, and 0.43% at ~ 100°. **POISONOUS.**

Lead (II) iodide *[10101-63-0]* **M 461.0, m 402°.** It crystallises from a large volume of water. The solubility in

H_2O is 1.1% at ~10°, and 3.3% at ~100°. **POISONOUS.**

Lead monoxide *[1317-36-8]* **M 223.2, m 886°.** Higher oxides are removed by heating under vacuum at 550° with subsequent cooling under vacuum. It is red at room temperature but becomes yellow at high temperatures (~480°) reversibly. [Ray & Ogg *J Am Chem Soc* **78** 5994 *1956*, Kwestroo et al. *J Inorg Nucl Chem* **29** 39 *1967*.] **POISONOUS.**

Lead nitrate *[10099-74-8]* **M 331.2, m 470°.** Precipitate it twice from a hot (60°) concentrated aqueous solution by adding HNO_3. The precipitate is sucked dry on a sintered-glass funnel, then transferred to a crystallising dish which is covered by a clock glass and left in an electric oven at 110° for several hours [Beck et al. *Trans Faraday Soc* **55** 331 *1959*]. After two recrystallisations of ACS grade, no metals above 0.001ppm were detected. **POISONOUS.**

Lithium (metal) *[7439-93-2]* **M 6.9, m 180.5°, b 1342°, d $_4^{20}$ 0.534.** After washing with petroleum ether to remove storage oil, lithium is fused at 400° and then forced through a 10-micron stainless-steel filter with argon pressure. It is again melted in a dry-box, skimmed, and poured into an iron distillation pot. After heating under a vacuum to 500°, cooling and returning it to the dry-box for a further cleaning of its surface, the lithium is distilled at 600° using an all-iron distillation apparatus [Gunn & Green *J Am Chem Soc* **80** 4782 *1958*].

Lithium aluminium hydride *[16853-85-3]* **M 37.9, m 125°(dec).** Extract it with Et_2O, and, after filtering, the solvent is removed under vacuum. The residue is dried at 60° for 3 hours, under high vacuum [Ruff *J Am Chem Soc* **83** 1788 *1961*]. It is a strong reducing agent. Store it in aliquots in a strictly dry atmosphere, and use in these aliquot quantities. **It IGNITES in the presence of a small amount of water and reacts with it EXPLOSIVELY.** [Becher in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 805 *1963*.]

Lithium amide *[7782-89-0]* **M 23.0, m 380-400°, d$^{17.5}$ 1.178.** Purify it by heating at 400° while NH_3 is passed over it in the upper of two crucibles (the upper crucible is perforated). The $LiNH_2$ will drip into the lower crucible through the holes in the upper crucible. The product is cooled in a stream of NH_3. Protect it from air and moisture, store it under N_2 in a clear glass bottle sealed with paraffin. Store it in small quantities so that all the material is used once the bottle is opened. If the colour of the amide is yellow, it should be destroyed as it is likely to have oxidised and to **EXPLODE.** On heating above 450° it is decomposed to Li_2NH, which is stable up to 750-800°. [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 463 *1963*, Greenlee & Henne *Inorg Synth* **II** 135 *1953*.]

Lithium azide *[19597-69-4]* **M 49.0, m 115-298° (dec), d $_4^{20}$ 1.008, pK^{25} 4.72 (HN_3).** Digest ~1g with 15ml of 96% EtOH at 35°, filter and dry it in air at temperatures below 80°. Store it in a cool place and treat it as potentially explosive. Its solubility in H_2O is 66.4% at 16°, and 20.26% at 16° in EtOH. [Hofmann-Bang *Acta Chem Scand* **11** 581 *1957*, Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 581 *1963*.]

Lithium borohydride *[16949-15-8]* **M 21.8, m 268°, b 380°(dec), d $_4^{20}$ 0.66.** It is crystallised from Et_2O, and pumped free of ether at 90-100° during 2 hours [Schaeffer et al. *J Am Chem Soc* **78** 729 *1956*]. Store it dry as it decomposes slowly in moist air. [Becher in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 775 *1963*.]

Lithium bromide *[7550-35-8]* **M 86.8, m 550°.** Crystallise it several times from water or EtOH, then dry it under high vacuum for 2 days at room temperature, followed by drying at 100°. Its solubility in H_2O is 167% at ~20°, and 250% at ~100°. It is *deliquescent* and should be stored in a tightly stoppered vessel.

Lithium carbonate *[554-13-2]* **M 73.9, m 552°, 618°.** Crystallise it from water. Its solubility decreases as the temperature is raised. The solubility in H_2O is 1.3% at ~10°, and 0.7% at ~100°. [Dönges in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 987 *1963*, Caley & Elving *Inorg Synth* **I** 1 *1939*.]

Lithium chloride *[7447-41-8]* **M 42.4, m 600°, 723°.** Crystallise it from water (1ml/g) or MeOH and dry it for several hours at 130°. Other metal ions can be removed by preliminary crystallisation from hot aqueous 0.01M disodium EDTA. It has also been crystallised from conc HCl, fused in an atmosphere of dry HCl gas, cooled under dry N_2 and pulverised in a dry-box. Kolthoff and Bruckenstein [*J Am Chem Soc* **74** 2529 *1952*] precipitated it with ammonium carbonate, washed it with Li_2CO_3 five times by decantation and finally with suction, then dissolved it in HCl. The LiCl solution is evaporated slowly with continuous stirring in a large evaporating dish, the dry powder being stored (while still hot) in a desiccator over $CaCl_2$.

Lithium fluoride *[7789-24-4]* **M 25.9, m 842°, 848°, b 1676°, 1681°, d_4^{20} 2.640.** Possible impurities are $LiCO_3$, H_2O and HF. These can be removed by calcining it at red heat, then pulverizing it with a Pt pestle and storing it in a paraffin bottle. Its solubility in H_2O is 0.27% at 18°. It volatilises between 1100-1200°. [Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 235 *1963*].

Lithium hydride. *[7580-67-8]* **M 7.95, m 680°, d_4^{20} 0.76-0.77.** It should be a white powder; otherwise replace it. It darkens rapidly on exposure to air and is decomposed by H_2O to give H_2 and LiOH, and reacts with lower alcohols. One gram in H_2O liberates 2.8L of H_2 (could be explosive). [Dönges in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 987 *1963*.]

Lithium hydroxide monohydrate *[1310-66-3 (H_2O), 1310-65-2 (anhydrous)]* **M 42.0, m 471°, d 1.51, pK^{25} 13.82.** It crystallises from water (3ml/g) as the *monohydrate*. It *dehydrates* at 150° in a stream of CO_2-free air, and sublimes at 220° with some decomposition [Cohen *Inorg Synth* **V** 3 *1957*, Bravo *Inorg Synth* **VII** 1 *1963*].

Lithium iodate *[13765-03-2]* **M 181.9.** Crystallise it from water and dry it in a vacuum oven at 60°.

Lithium iodide *[10377-51-2]* **M 133.8, m 73° ($3H_2O$), 469°, b 1171°, d_4^{20} 4.06.** Crystallise it from hot water (0.5mL/g) by cooling in a $CaCl_2$-ice EtOH or from an acetone- Dry-ice bath. Dry it under a vacuum over P_2O_5 for 1 hour at 60° and then at 120°. It is *deliquescent* and should be stored in dark tightly stoppered vessels.

Lithium nitrate *[7790-69-4]* **M 68.9, m 253°, d_4^{20} 2.38.** It crystallises from water or EtOH. Dry it at 180° for several days by repeated melting under vacuum. If it is crystallised from water keeping the temperature above 70°, formation of *trihydrate* is avoided. The *anhydrous* salt is dried at 120° and stored in a vacuum desiccator over $CaSO_4$. After the 99% pure salt was recrystallised 3 times, it contained: metal (ppm) Ca (1.6), K (1.1), Mo (0.4), Na (2.2). [Donnan & Burt *J Chem Soc* **83** 335 *1903*.]

Lithium nitrite monohydrate *[13568-33-7]* **M 71.0.** Crystallise it from water by cooling from room temperature.

Lithium perchlorate *[7791-03-9]* **M 106.4, m 236°, pK^{25} -2.4 to -3.1 (for $HClO_4$).** Crystallise it from water or 50% aqueous MeOH. It is rendered *anhydrous* by heating the *trihydrate* at 170-180° in an air oven. It can then be recrystallised twice from acetonitrile and again dried under vacuum [Mohammad & Kosower *J Am Chem Soc* **93** 2713 *1971*]. **SKIN IRRITANT.**

Lithium sulfate (anhydrous) *[10377-48-7]* **M 109.9, loses H_2O at 130° and m 859°, d_D^{20} 2.21.** Crystallise it from H_2O (4ml/g) by partial evaporation, and dry it above 130° *in vacuo*.

Lithium tetrafluoroborate *[14283-07-9]* **M 93.7, pK^{25} 13.82 (Li^+), pK^{25} -4.9 (for HBF_4).** Dissolve it in THF just below its solubility, filter from insoluble material and evaporate it to dryness in a vacuum below 50°. Wash the residue with dry Et_2O, and pass dry N_2 gas over the solid and finally heat it in an oven at 80-90°. Its solubility in Et_2O is 1.3g in 100ml at 25°; in THF it is 71g in 100ml at 25°. It is *hygroscopic* and is an **IRRITANT.** [Elliott et al. *J Am Chem Soc* **74** 5211 *1952*, **75** 1753 *1953*.]

Lithium thiocyanate (lithium rhodanide) *[556-65-0]* **M 65.0, pK^{25} -1.85 (for HSCN).** It crystallises from H_2O as the *dihydrate*, but on drying at 38-42° it gives the *monohydrate*. It can be purified by allowing an aqueous solution to crystallise in a vacuum over P_2O_5. The crystals are collected, dried out *in vacuo* at 80°/P_2O_5

in a stream of pure N_2 at 110°. [Coates & Taylor *J Chem Soc* 1245 *1936*.]

Magnesium *[7439-95-4]* **M 24.3, m 651°, b 1100°, d $_4^{20}$ 1.739.** It slowly oxidises in moist air and tarnishes. If dark in colour, do not use. The shiny solid should be degreased by washing with dry Et_2O, dry it *in vacuo* and keep it in a N_2 atmosphere. It can be activated by stirring it in Et_2O containing a crystal of I_2 then filtering it off, before drying and storing. [Gmelin's Magnesium (8th edn) **27A** 121 *1937*.]

Magnesium bromide (anhydrous) *[7789-48-2]* **M 184.1, m 711°, d $_4^{20}$ 3.72.** Crystallise it from EtOH or H_2O (3.3g/ml). Dry it in a vacuum at ~150°, or heat the *hydrate* in a stream of HCl. It is very *deliquescent*. [Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 909 *1963*.]

Magnesium chloride hexahydrate *[7791-18-6]* **M 203.3, m ~100°(dec), pK_1^{25} 10.3, pK_2^{25} 12.2 (for Mg^{2+} hydrolysis).** Crystallise it from hot water (3.3g/ml) by cooling. Dry it in a vacuum at ~175°, or heat the *hydrate* in a stream of HCl. When the hydrate is heated above 180° it is hydrolysed to the oxychloride (Mg_2OCl_2). It is *deliquescent*; store it in a well-stoppered vessel. [Bryce-Smith *Inorg Synth* **VI** 9 *1960*, Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 908 *1963*.]

Magnesium iodate tetrahydrate *[7790-32-1]* **M 446.2.** Crystallise from water (0.2g/ml) between 100° and 0°.

Magnesium iodide *[10377-58-9]* **M 278.1, m 634°.** Crystallise it from water (0.8g/ml) by partial evaporation in a desiccator. It is deliquescent and should be stored in the dark. [Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 910 *1963*.]

Magnesium nitrate hexahydrate *[13446-18-9]* **M 256.4, m ~95°(dec).** Crystallise the nitrate from water (2.5mlg) by partial evaporation in a desiccator. It is *deliquescent* and is soluble in EtOH. After two recrystallisations, ACS grade salt has: metal (ppm) Ca (6.2), Fe (8.4), K (2), Mo (0.6), Na (0.8), Se (0.02).

Magnesium perchlorate (Anhydrone, Dehydrite) *[10034-81-8 (anhydrous)]* **M 259.2, m >250°, pK^{25} -2.4 to -3.1 (for $HClO_4$).** Crystallise it from water to give the *hexahydrate* **M 331.3** *[13346-19-0]*. Coll et al. [*J Am Chem Soc* **81** 1284 *1959*] removed traces of unspecified contaminants by washing it with small portions of Et_2O and drying in a vacuum **(CARE)**. The anhydrous salt is commercially available as an ACS reagent, and is as efficient a dehydrating agent as P_2O_5 and is known as "Dehydrite" or "Anhydrone". [Smith et al. *J Am Chem Soc* **44** 2255 *1922* and *Ind Eng Chem* **16** 20 *1924*.] It is *hygroscopic*; keep it in a tightly closed container. It is **EXPLOSIVE** *in contact with organic materials, and is a* **SKIN IRRITANT**.

Magnesium sulfate (anhydrous) *[7487-88-9]* **M 120.4, m 1127°.** Crystallise it from warm H_2O (1g/ml) by cooling. Dry the *heptahydrate (Epsom salt)* at ~250° until it loses 25% of its weight. Its solubility in H_2O is 36% at 20°, 55% at 60° and 74% at 100°; above 110° the solubility decreases with rise of temperature. Store it in a sealed container.

Manganese decacarbonyl $Mn_2(CO)_{10}$ *[10170-69-1]* **M 390.0, m 151-152°, 154-155°(sealed tube) , d^{25} 1.75.** Golden yellow crystals which in the absence of CO begin to decompose at 110°, and on further heating yield a metallic mirror. In the presence of 3000psi of CO it does not decompose on heating to 250°. It is soluble in common organic solvents, insoluble in H_2O, not very stable in air, to heat or UV light. It dissolves in a lot of $*C_6H_6$ and can be crystallised from it. It distils with steam at 92-100°. It can be purified by sublimation under reduced pressure (<0.5mm) at room temperature to give well-formed golden yellow crystals. If the sample is orange coloured, this sublimation leads to a mixture of golden-yellow and dark red crystals of the carbonyl and carbonyl iodide, respectively, which can be separated by hand picking under a microscope. Separation followed by resublimation provides the pure compounds. **POISONOUS.** [Brimm et al. *J Am Chem Soc* ***76*** 3831 *1954*, Closson et al. *J Am Chem Soc* **80** 6167 *1958*, **82** 1325 *1960*.]

Manganous bromide (anhydrous) *[13446-03-2]* **M 214.8, m 695° ($4H_2O$)** *[10031-20-6]* **M 286.8, m 64°(dec).** It forms rose-red *deliquescent* crystals which are soluble in EtOH. The H_2O is removed by heating at

100° then in HBr gas at 725°, or dry it in an atmosphere of N_2 at 200°.

Manganous chloride tetrahydrate *[13446-34-9, 7773-01-5 (anhydrous)]* **M 197.9, m 58°, 87.5°, 650° (anhydrous), b 1190° (anhydrous), d_4^{20} 2.01.** It crystallises from water (0.3ml/g) on cooling. The red-rose *tetrahydrate* melts at ~52° and forms the *dihydrate salt* which loses all its H_2O at 198° to give $MnCl_2$. It is soluble in EtOH.

Manganous sulfate monohydrate *[10034-96-5 (H_2O), 15244-36-7 (xH_2O)]* **M 169.0, d_4^{20} 2.75.** Crystallise it from water (0.9ml/g) at 54-55° by evaporating about two-thirds of the water. It *dehydrates* above 400°.

Mercuric bromide *[7789-47-1]* **M 360.4, m 238.1°, b 320°, d_4^{20} 5.73.** Crystallise it from hot saturated ethanolic solution, dry and keep it at 100° for several hours under a vacuum, then sublime it. [Garrett *J Am Chem Soc* **61** 2744 *1939*.] Its solubility in H_2O is 0.6% at 20°, and 22% at 100°; in EtOH it is 30% at 25°; and in MeOH it is 69.6% at 25°. [Wagenknecht & Juza *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1109 *1965*.] **POISONOUS.**

Mercuric chloride *[7487-94-7]* **M 271.5, m 276°, b 304°, d_4^{20} 5.6.** Crystallise it twice from distilled water, dry it at 70° and sublime it under high vacuum. Its solubility in H_2O is 4.3% at ~0°, 6.6% at ~10° and 54% at ~100°. It is soluble in EtOH and is extracted into Et_2O from an aqueous solution. It is **very POISONOUS** and 0.2-0.4g is fatal. The antidote is immediate administration of white of egg as an emetic.

Mercuric cyanide *[592-04-1]* **M 252.6, m 320°(dec), d_4^{20} 4.00.** Crystallise it from water. The solubility in H_2O is 8% at ~20° and 33% at ~100°; in EtOH it is 8% at ~20° and in MeOH it is 25% at ~20°. [Blitz *Z Anorg Allgem Chem* **170** 161 *1928*.] **POISONOUS.**

Mercuric iodide (red) *[7774-29-0]* **M 454.4, m 259°(yellow >130°), b ~350°(subl), d_4^{20} 6.3.** Crystallise it from MeOH or EtOH and wash it repeatedly with distilled water (solubility is 0.006% at ~25°). It has also been mixed thoroughly with excess 0.001M iodine solution, filtered, washed with cold distilled water, rinsed with EtOH and Et_2O, and dried in air. It changes colour reversibly to yellow at ~130°. [Friend *Nature* **109** 341 *1922*.] **POISONOUS.**

Mercuric oxide (yellow) *[21908-53-2]* **M 216.6, m 500°(dec).** Dissolve it in $HClO_4$ and precipitate it with NaOH solution. It is yellow when cold and changes to red at ~130° reversibly. **POISONOUS.**

Mercuric thiocyanate *[592-85-8]* **M 316.8, m 165°(dec), pK^{25} -1.85 (for HSCN).** Recrystallise it from H_2O, and it can give various crystal forms depending on conditions. Its solubility in H_2O is 0.069% at 25°, but is more soluble at higher temperatures. It decomposes to Hg above 165°. **POISONOUS.** [Mason & Forgeng *J Phys Chem* **35** 1121 *1931*, Birckenbach & Kolb *Chem Ber* **68** 919 *1935*.]

Mercurous nitrate dihydrate *[7782-86-7 ($2H_2O$), 7783-34-8 (H_2O), 10415-75-5 (anhydrous)]* **M 561.2, m 70°(dec), d_4^{20} 4.78, pK^{25} 2.68 (for Hg_2^{2+} hydrolysis).** Its solubility in H_2O containing 1% HNO_3 is 7.7%. Recrystallise it from a warm saturated solution of dilute HNO_3 and cool to room temperature slowly to give elongated prisms. Rapid cooling gives plates. The colourless crystals should be stored in the dark. **POISONOUS.** [Grdenic *J Chem Soc* 1312 *1956*.]

Mercurous sulfate *[7783-36-0]* **M 497.3, d_4^{20} 7.56.** The white-yellow powder is recrystallised from dilute H_2SO_4., dried in a vacuum under N_2, and stored in the dark. Its solubility in H_2O is 0.6% at 25°. It is hydrolysed by excessive washing with H_2O to form the greenish-yellow *basic salt* $Hg_2SO_4.Hg_2O.H_2O$. **POISONOUS.**

Mercury *[7439-97-6]* **M 200.6, m -38.9°, b 126°/1mm, 184°/10mm, 261°/100mm, 356.9°/atm, d_4^{20} 13.534.** After air has been bubbled through mercury for several hours to oxidise metallic impurities, it is filtered to remove coarser particles of oxide and dirt, then sprayed through a 4-ft column containing 10% HNO_3. It is washed with distilled water, dried with filter paper and distilled under vacuum. [Schenk in *Handbook of*

Preparative Inorganic Chemistry (Ed. Brauer) Academic Press Vol **I** p 8 *1963*.]

Molybdenum *[7439-98-7]* **M 95.9, m 2622°, b ~4825°, d^{25} 10.3g/ml, resistivity of 5.0 μΩ-cm at 20°.** The dark-gray metal is commercially available in varying degrees of purity from 98 to 99.99%, as foil with thickness from 0.025mm (5.8g 150 x 150mm) to 1.0mm (25.6g, 50mm x 50mm or 102.4g, 100mm x 100 mm), or black powder from <150μm to 1-2μm particle size as well in nanopowder form of <100nm (BET) size. It is also available as wire of 1.0mm in diameter. The metal is stable in air but is oxidised at red heat to MoO_3; is ureactive towards dilute acids or alkalis but reacts with strong HNO_3, H_2SO_4, fused $KClO_3$ or KNO_3, F_2 (at ~ 25°), Cl_2 and Br_2 (at red heat). [**CARE**: it is potentially quite toxic—particularly the nano sized particles.]

Molybdenum (VI) dichloride dioxide (MoO_2Cl_2) *[13637-68-8]* **M 198.8, d^{25} 6.31g/ml.** It is prepared from MoO_2 (40.0g, 313mmol) by placing it in a test tube with a wide side arm and a central tube which ends ~2cm above the surface of the oxide. The side arm is connected to a large round bottomed flask which vents through a bubbler containing H_2SO_4. The apparatus is flushed with argon, and the tube containing the oxide is immersed in an oil bath which is kept at 140° for 12 hours to dry the oxide. The temperature of the tube is then raised to 160° and a stream of Cl_2 gas (pre-dried by bubbling through two H_2SO_4 traps) is allowed to flow over the hot oxide for 10 hours. The wide tube connecting the test tube and the flask is wrapped with a heating tape to encourage the MoO_2Cl_2 to sublime into the flask as it is formed. Stirring the contents of the flash (magnetic stirrer bar) hinders the clogging entry and exit tubes. MoO_2Cl_2 collects as ivory flakes that are quite pure for most purposes, but can be resublimed if necessary. All due **PRECAUTIONS** should be taken as chlorine is a **TOXIC GAS** and concentrated H_2SO_4 is used in the bubblers. [Schrock et al. *J Am Chem Soc* **112** 3875 *1990*, Epperson et al. *Inorg Synth* **7** 168 *1963*.] Commercial fluffy MoO_2Cl_2 gives poor yields of substitution products (e.g. with $ArNHSiMe_3$), but the THF complex $MoO_2Cl_2(THF)_2$ *[556907-19-8; 12081-12-8]* is easier to handle, reacts in a similar way, and gives much higher yields of substitution products. It is readily prepared in solution by carefully adding solid MoO_2Cl_2 to dry THF at -30°. Addition of THF to MoO_2Cl_2 is too exothermic to keep under control. [Schrock et al. *J Am Chem Soc* **112** 3875 *1990*.] Krauss & Huber prepared it by adding MoO_2Cl_2 (2.0g, 10mmol) in four portions to THF (7ml. 6.5g, 90mmol) while shaking. The yellow solution is diluted with light petroleum (5ml), filtered, the filtrate is diluted further with light petroleum (10ml) when the complex crystallises out. The supernatant is decanted off, the solid is washed several times with light petroleum (10ml lots), and dried at room temperature in a stream of N_2 to give analytically pure $MoO_2Cl_2(THF)_2$ (3.2g, 93%) as very pale yellow needles, **m > 50° (dec)**, that are soluble in THF, slightly soluble in Et_2O but insoluble in light petroleum [Krauss & Huber *Chem Ber* **94** 2864 *1961*]. It is very useful for preparing a variety of Mo complexes and catalysts.

Molybdenum hexacarbonyl *[13939-06-5]* **M 264.0, m 150°(dec), b 156°.** Sublime it in a vacuum before use [Connor et al. *J Chem Soc, Dalton Trans* 511 *1986*]. **TOXIC.**

Molybdenum hexafluoride *[7783-77-9]* **M 209.9, m 17.5°, b 35°/760mm, d_4^{20} 2.543.** Purify the hexafluoride by low-temperature trap-to-trap distillation over pre-dried NaF. It is *hygroscopic*, fumes in moist air and is hydrolysed readily by H_2O. [Oppengard et al. *J Am Chem Soc* **82** 3825 *1960*, Anderson & Winfield *J Chem Soc, Dalton Trans* 337 *1986*, Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 259 *1963*.] **Poisonous vapours.**

Molybdenum (IV) oxide [molybdenum (IV) dioxide, MoO_2] *[18868-43-4]* **M 127.9, d^{25} 6.47.** It is prepared by grinding together ~10-15g of a mixture in a 2:1 ratio of MoO_3 (dried by heating in at 500° for 1 hour) and Mo metal powder in a quartz combustion tube under argon, or in an evacuated tube (CARE when opening), at 800° for 70 hours. It forms a brown-violet powder, oblong needles or thick platelets with a metallic lustre. [Conroy & Ben-Dor *Inorg Synth* **14** 149 *1973*, **30** 105 *1997*, Herzog et al. in *Handbuch der Preparativen Anorganische Chemie (Ed. Brauer)* Enke Verlag Stuttgart Vol **3** p 1542 *1981*.] Beware of TOXIC vapours.

Molybdenum trichloride *[13478-18-7]* **M 202.3, m 1027°, d_4^{20} 3.74.** Boil it with 12M HCl, wash it with absolute EtOH and dry it in a vacuum desiccator. It is a brown-red powder soluble in H_2O, EtOH or Et_2O and gives a blue solution in conc H_2SO_4. [Hein & Herzog *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1404 *1965*.]

Molybdenum trioxide [molybdenum (VI) oxide, MoO_3] *[1313-27-5]* **M 143.9, m 795°, b 1155°, d $_4^{20}$ 4.60.** MoO_3 is prepared by adding HNO_3 to an aqueous solution of ammonium molybdate and stirring for several hours which precipitates H_2MoO_4. The acid is filtered off, washed with H_2O, heated at 150° for 1-2 hours and the hydrated oxide is dried at 450°. It recrystallises in rhombs from water (1g/50ml) between 70° and 0°, and is dried in air at ~500° for 1 hour before use. Its solubility in H_2O is 0.1% at 18°, and 2% at 70°. It is a white powder which turns yellow reversibly on heating. It sublimes readily at >780°/760mm in a quartz tube to give pure MoO_3. [Hein & Herzog *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1412 *1965*, Herzog et al. in *Handbuch der Preparativen Anorganische Chemie (Ed. Brauer)* Enke Verlag Stuttgart Vol **3** p 1544 *1981*.] It is used in the synthesis of Mo compounds, and of the ternary reduced molybdenum oxide $Pr_4Mo_9O_{18}$, which contains the previously unknown Mo_7, Mo_{13}, and Mo_{19} clusters; and is a precursor for the preparation of fast ion conductors and superconductors [Arulraj *Chem Mater* **14** 2492 *2002*, Lacorre *Nature* **404** 856 *2000*]. The oxide forms hydrates and alcoholates which have different IR spectra [Krauss & Huber *Chem Ber* **94** 2864 *1961*]. Beware of **TOXIC** vapours.

Molybdic acid (H_2MoO_4) *[7782-91-4]* **M 162.0, 180.0 (monohydrate), d ^{25} 3.124 (for monohydrate), pK $_1^{25}$ 0.9 (proton addition), pK $_2^{20}$ 4.00, pK $_3^{20}$ 4.21.** Treatment of an aqueous solution of 0.4N Na_2MoO_4 [1L, or of $(NH_4)_2MoO_4$ as in the preceding entry] at 60° with 30% HNO_3 (1L, prepared from 300ml of concentrated acid, d 1.42, in 1L of H_2O with cooling) and allowing to stand at 25° for several days deposited the theoretical amount of canary yellow monoclinic crystals which are collected, washed with ice water and dried *in vacuo* over H_2SO_4 for 2 weeks to give $H_2MoO_4.H_2O$. This is referred to as ***α-molybdic acid*** which on warming in H_2O at 70° is transformed to the white anhydrous ***β-molybdic acid***. These acids have different X-Ray spectra and vapour pressures. ***Colloidal molybdic acid*** is obtained by dialysing an aqueous solution of $(NH_4)_2MoO_4$ and HCl, and forms a gum on evaporation. By heating these acids, or the ammonium salts, provide white MoO_3 which on heating further at 500° in the presence of H_2 gives reddish-brown MoO_2, and at 1200° a grey powder of metallic Mo is obtained (see preceding entries). Polymeric forms are known such as ***tetramolybdic acid*** **[$H_2Mo_4O_{16}$**, pK_1 1.4, pK_2 1.2, Chauveau et al. *Bull Soc Chim Fr* 1190 *1959***]** and ***heptamolybdic acid*** **[$H_6Mo_7O_{24}$**, pK $_5^{25}$ ~3.7, pK $_6^{25}$ 4.33, Sasaki et al *J Inorg Nucl Chem* **9** 93 *1959*]. Note that in aqueous alkaline solution the main Mo(VI) acid species are MoO_4^{2-}, but in neutral and acidic media polynuclear species exist [cf Sasaki & Sillén *Arkiv Kemi* **29** 253 *1968*, and Sasaki et al *J Inorg Nucl Chem* **9** 93 *1959*]. [Herzog et al. in *Handbuch der Preparativen Anorganische Chemie (Ed. Brauer)* Enke Verlag Stuttgart Vol **3** p 1544 *1981*, Rosenheim *Z Anorg Chem* **50** 320 *1906*, Peters et al. *Z Anor Allgem Chem* **365** 14 *1969*; and for pKs see also Sasaki & Sillén *Acta Chem Scad* **18** 1014 *1964*, Rohwer & Cruywagen *J S African Chem Inst* **16** 26 *1963*, Rohwer & Cruywagen *J S African Chem Inst* **17** 145 *1964*.]

Monocalcium phosphate dihydrate (monobasic) *[7789-77-7 ($2H_2O$), 7757-93-9 (anhydrous)]* **M 154.1, m 200°(dec, loses H_2O at 100°), d $_4^{20}$ 2.2.** Crystallise it from a near-saturated solution in 50% aqueous reagent grade phosphoric acid at 100° by filtering through fritted glass and cooling to room temperature. The crystals are filtered off, and this process is repeated three times using fresh acid. For the final crystallisation the solution is cooled slowly with constant stirring to give thin plate crystals that are filtered off on a fritted glass funnel, washed free of acid with anhydrous acetone and dry in a vacuum desiccator [Egan et al. *J Am Chem Soc* **78** 1811 *1956*].

Neodynium chloride hexahydrate *[13477-89-9]* **M 358.7, m 124°, pK$_1^{25}$ 8.43 (for Nd^{3+} hydrolysis).** Neodynium chloride forms large purple prisms from concentrated solutions of dilute HCl. They are soluble in H_2O (2.46 parts in 1 part of H_2O) and EtOH, and lose H_2O at 160°.

Neodymium(II) iodide *[61393-36-0]* **M 398.1.** This one electron reductant can be prepared in large quantities (~40g) by direct reaction of the metal and iodine at 600° [Evans et al. *Inorg Chem* **42** 3097 *2003*]. The black solid NdI_2 can be kept at room temperature for months in the absence of solvent. Solutions can be stored under argon for several hours at -15° but should be used as soon as possible. The stability is considerably reduced if N_2 is used as inert atmosphere, instead of argon, even at -30°. In tetrahydrofuran under argon it promotes a pseudo-Barbier reaction, i.e. rapid reductive coupling of primary and secondary (but not tertiary) halides with ketones, e.g. butylchloride and cyclohexanone provide almost quantitative yield of 1-butylhexan-1-ol [Evans et

al. *Org Lett* **5** 2041 *2003*]. Thus behaving somewhat like a Grignard reagent. This solution also has Birch reduction-type reactivity, e.g. reduces naphthalene to 1,4-dihydronaphthalene.
NdI_2 (THF)$_x$ solution is prepared by transferring pre-cooled THF (45ml, at -15°) *via* a cannula into a septum-capped flask containing black NdI_2 (1.0g, 2.5mmol) and a magnetic stirrer bar at -15° whereby the colour of the solution becomes purple, and is stirred for 45 minutes. An aliquot should show the concentration to be 0.05M by complexiometric titration [method of Evans & Allen *J Am Chem Soc* **122** 2118 *2000*]. This solution is used for reactions and should be performed under argon.

Neodymium(III) iodide (anhydrous) *[13813-24-6]* **M 524.7. m 775°, b 1370°.** It is an almost black crystalline powder (green when ground) that is soluble in hot and cold H_2O. It can be prepared by the method of Bochkarev [Bochkarev & Fagin *Chem Eur J* **5** 2990 *1999*] where a small quantity of Nd metal is placed in a quartz crucible in a quartz reactor [see Evans et al. *Inorg Chem* **42** 3097 *2003*], heated to 600°, and I_2 is added, then small amounts of metal and I_2 are added alternately. Every addition of I_2 results in an orange glow in the mixture. When addition is complete (total ≥3 equivalents) the apparatus is cooled, and the crucible containing NdI_3 is transferred to an argon filled glovebox and the salt is ground (with a pestle and mortar) to a green powder. The metal content is analysed by titration (complexometric metal analysis is performed by dissolving the salt in H_2O at ~25°, evaporating, ashing the residue at 500°, dissolving in HCl and the analysis is carried out in hexamethylenetetramine buffer with xylenol orange as indicator and EDTA as titrant: Schwarzenbach & Flaschka "Complexometric Titrations" Metheun, London p 194 *1969*; Evans et al. *J Am Chem Soc* **103** 6672 *1981*). It should contain at least 27.5% Nd (theoretical is 29.5% Nd). [Evans & Workman *Organometallics* **24** 1989 *2005*.]
Potassium graphite KC_8 with NdI_3 has also been used for reductive coupling and is prepared *in situ*. [Weitz & Rabinovitz *J Chem Soc, Perkin Trans I* 117 *1993*]. KC_8 can be prepared in a Schlenk line, or in a glove box, by adding K metal (0.541g, 13.8mmol) to a scintillating vial containing a Teflon stirbar then Graphite (1.242g, 12.9mmol), and the mixture is stirred and heated until a bronze-coloured powder results. The NdI_3/KC_8/THF is prepared by adding precooled (-15° *via* a cannula) THF into a septum-capped Schlenk flask (~25ml) containing NdI_3, KC_8 and a Teflon stirbar thus producing a purple solution which is stirred at -15° for 40 minutes and is ready for the reaction. The alkyl halide is injected, stirred for 1 minute, and is followed by the aldehyde or ketone. [Evans & Workman *Organometallics* **24** 1989 *2005*.]

Neodynium nitrate hexahydrate *[16454-60-7]* **M 438.4, m 70-72°.** It crystallises with 5 and 6 molecules of H_2O from concentrated solutions in dilute HNO_3 by slow evaporation; 1 part is soluble in 10 parts of H_2O.

Neodymium oxide *[1313-97-9]* **M 336.5, m 2320°.** Dissolve it in $HClO_4$, precipitate it as the oxalate with doubly recrystallised oxalic acid, wash it free of soluble impurities, dry it at room temperature and ignite it in a platinum crucible at higher than 850° in a stream of oxygen. It is a blue powder. [Tobias & Garrett *J Am Chem Soc* **80** 3532 *1958*.]

Neon *[7440-01-9]* **M 20.2.** Pass the gas through a copper coil packed with 60/80 mesh 13X molecular sieves which is cooled in liquid N_2, or through a column of Ascarite (NaOH-coated silica/asbestos adsorbent).

Nickel bromide *[13462-88-9]* **M 218.5, m 963°(loses H_2O at ~ 200°).** Crystallise it from dilute HBr (0.5ml/g) by partial evaporation in a desiccator. The *anhydrous* salt is yellow, but the *trihydrate* is green.

Nickel chloride hexahydrate *[7791-20-0 ($6H_2O$), 69098-15-3 (xH_2O), 7718-54-9 (anhydrous)]* **M 237.7.** It crystallises from dilute HCl to form the green *hexahydrate*. At 70° this dehydrates to the *tetrahydrate*, and at higher temperatures it forms the *anhydrous* salt. It sublimes in yellow hexagonal scales in a stream of HCl. Store it in a desiccator as it is *deliquescent*. [Hart & Partington *J Chem Soc* 104 *1943*.]

Nickel nitrate hexahydrate *[13478-00-7]* **M 290.8, m 57°.** Crystallise it from water (3.3g/ml) by partial evaporation in a desiccator. Store it in a desiccator as it is *deliquescent*.

Nickel(II) perchlorate hexahydrate [$Ni(ClO_4)_2$. $6H_2O$] *[13520-61-1]* **M 365.7, m 140°, 200°, 209° (sealed tube), d^0 1.570, d^{20} 1.583, d^{40} 1.597, d^{50} 1.646, d^{60} 1.597.** The greenish blue hexagonal prisms of this salt are

obtained by double decomposition between $NiSO_4$ and $Ca(ClO_4)_2$ in aqueous solution, filtering off the insoluble $BaSO_4$, and concentrating the filtrate. It recrystallises from H_2O, and drying the crystals in a vacuum desiccator over H_2SO_4 or $CaCl_2$ provides the *hexahydrate*. *Alternatively*, it is prepared from freshly precipitate NiO or $NiCO_3$ and aqueous $HClO_4$, filtering off the excess of $NiCO_3$ and concentrating the filtrate to crystallisation. The solubility of $Ni(ClO_4)_2.6H_2O$ in H_2O (g/100ml) is 217 (0°), 236 (10°), 245 (20°), 267 (30°), 280 (35°), 273 (40°), 311 (50°), 295 (55°), 280 (60°). The salt form hydrates with 2, 4, 5, 6, 7, and 9 molecules of H_2O. The *hexahydrate* is normally obtained by crystallisation from H_2O and is the more stable hydrate. It forms the *tetrahydrate* at 110°/760mm/36 hours or 70°/1mm/66 hours, which yields the *dihydrate* at 130°/760mm/42 hours or 100°/1mm/72 hours. It should be kept in a desiccator over $CaCl_2$ as it is quite *hygroscopic*. The UV in EtOH has λ_{max} (logε) at 395 (~0.68), 660 (~0.22), 720 (~0.25) nm. Evaporation of a solution in ether with dry air gives $Ni(ClO_4)_2.Et_2O$ as a yellow powder, and with dioxan it forms $Ni(ClO_4)_2.2C_4H_8O_2$. A solution in Me_2CO at ~2 x 10^{-4}M is green with a characteristic absorption at 410nm [Katzin *Nature* **182** 1013 *1958*]; it complexes also with acetylacetone [Fernelius et al. *J Chem Phys* **59** 235 *1955*], ethylene, trimethylenediamine [Cotton & Harris *J Phys Chem* **59** 1203 *1955*], DMF [Pflaum, & Popov *Anal Chim Acta* **13** 167, 169 *1955*], and with pyridine it forms blue crystals of $[Ni(C_5H_5N)_6](ClO_4)_2.4H_2O$ [Weinland et al. *Arch Pharm* **265** 352 *1927*], $Ni(ClO_4)_2.4(C_5H_5N)$ and $Ni(ClO_4)_2.6(C_5H_5N)$ [Sinha *J Indian Chem Soc* **35** 865 *1958*, Sinha & Ray *J Indian Chem Soc* **20** 32 *1943*]. [Salvadori *Gazzetta* **42** I 458 *1912*, Veeraiah & Qureshi *J Indian Chem Soc* **21** 127 *1944*, Bernath et al. *J Prakt Chem* **143** [2] 302 *1935*, Freund & Schneider *J Am Chem Soc* **81** 4780 *1959*, Gmelin's *Handbuch der Anorganischen Chemie, Nickel Teil B-Lieferung 2I,* Verlag Chemie GMBH Weinheim, System 57, pp 596-601 *1966*.]

Nickel sulfate hexahydrate *[10101-97-0]* **M 262.9, m loses $5H_2O$ at 100°, becomes anhydrous at ~280°, d^{25} 2.07.** It crystallises from H_2O in bluish-green tetragonal crystals of the α-form which undergo a transition at 53.3° to the β-form that has green transparent monoclinic crystals. The crystals are stable at ~40°, become blue in colour and then opaque in air due to slow efflorescence. Its solubility in H_2O is 0.6/ml at 0° and 3.4g/ml at 100°. It is sparingly soluble in EtOH, slightly more soluble in MeOH, soluble in aqueous NaOH, and very soluble in aqueous ammonia to give the bluish-green monoclinic $(NH_4)_2Ni(SO_4)_2\ 6H_2O$ double salt. The pH of an aqueous solution is about 4.5, i.e. weakly acidic. (See also the heptahydate below.)

Nickel sulfate heptahydrate *[10101-98-1, 7786-81-4 (anhydrous)]* **M 280.9, m loses $5H_2O$ at 100°, anhydrous m at ~280°, d^{25} 1.948.** The sulfate crystallises from warm water (4g/ml) or dilute H_2SO_4 as bright green monoclinic crystals on cooling. It is isomorphous with Epsom salt (see $MgSO_4\ 7H_2O$ above). Prolonged exposure to air gives the blue *tetrahydrate*. On heating above 118°, it is converted to the *dihydrate*, which at >280° is converted to the *yellow anhydrous* $NiSO_4$ which does not react with HCl.

Nickel(II) sulfide M 90.8 (NiS, *mellirite***, bronze-yellow, d^{25} 5.3-5.6), 240.2 (Ni_3S_2** *[12035-72-2] Heazelwoodite*, **d^{25} 5.8) and (Ni_3S_2/NiS black powder** *[16812-54-7]* **d^{25} 5.3-5.6), m 790°, 797°.** The sulfide is generally obtained as a highly insoluble black precipitate by adding NH_4OH and NH_4SH to a nickel salt. It dissolves slowly in excess of $(NH_4)_2S_x$ and re-precipitates on boiling, exposure to air or addition of acid. A black dense sulfide is also obtained by boiling a nickel salt with $Na_2S_2O_3$. It is insoluble in dilute HCl, slowly soluble in concentrated HCl, readily in HNO_3 and aqua regia. The sulfides should be washed well with H_2O, dried, and analysed for Ni. Various forms have been prepared [Dunn & Rideal *J Chem Soc* **123** 1242 *1923*.]

Niobium (Colombium) (V) chloride *[10026-12-7]* **M 270.2, m 204.7-209.5°, b ~250°(begins to sublime at 125°), d_4^{20} 2.75**. It forms yellow, very deliquescent crystals which decompose in moist air to liberate HCl. Keep it in a dry box flushed with N_2 in the presence of P_2O_5. Wash it with CCl_4 and dry it over P_2O_5. The yellow crystals can contain a few small, dirty white pellets among the yellow needles. These should be easily picked out. Upon grinding in a dry box, however, they turn yellow. $NbCl_5$ has been sublimed and fractionated in an electric furnace. [Epperson *Inorg Synth* **VII** 163 *1963*, Alexander & Fairbrother *J Chem Soc* suppl 233 *1949*.]

Nitric acid (*Aqua fortis*) *[7697-37-2]* **M 63.0, m -42°, b 83°, d^{25} 1.5027, [Constant boiling acid has composition w/w of 68% HNO_3 + 32% H_2O, b 120.5°, d_4^{20} 1.41], pK^{25} -1.27 (1.19).** The acid is obtained

colourless (approx. 92%) by direct distillation of fuming HNO_3 under reduced pressure at 40-50° with an air leak at the head of the fractionating column. ***Concentrated nitric acid*** is an aqueous solution containing 70-71% of HNO_3 (**d_4^{20} 1.4134**). Store it in a desiccator that is kept in a refrigerator away from light which causes the formation of NO_2. Nitrite-free HNO_3 can be obtained by vacuum distillation from urea. [Ward et al. *Inorg Synth* **III** 13 *1950*, Kaplan & Schechter *Inorg Synth* **IV** 53 *1953*.] If ***"fuming nitric acid"*** (90%) is yellow in colour (due to the presence of oxides of nitrogen), then treat 100mls with urea (0.5g) and bubble dry air through it until it is colourless (~20 minutes) [Freeman & Shepard *Org Synth* **43** 84 *1932*]. Acid that is free from oxides does not discolour drops of 1N $KMnO_4$. ***Anhydrous*** **HNO_3 (100%, d_4^{20} 1.5129)** is obtained on distilling a mixture of equal volumes of "fuming nitric acid" and concentrated H_2SO_4 [Liang *Org Synth* Coll Vol **III** 804 *1955*]. It is an oxidising agent, its vapours irritate and cauterise tissues, and cause the skin to turn yellow in colour. The "fuming acid" is particularly dangerous, should be handled in an efficient fume cupboard, and is used more as an oxidant than for acidification — use EYE PROTECTION.

Nitric oxide *[10102-43-9]* **M 30.0, b -151.8°.** Bubble the gas through 10M NaOH which removes NO_2. It can also be freed from NO_2 by passage through a column of Ascarite followed by a column of silica gel held at −197°K. The gas is dried with solid NaOH pellets or by passing through silica gel cooled at -78°, followed by fractional distillation from a liquid N_2 trap. This purification does not eliminate nitrous oxide. Other gas scrubbers sometimes used include one containing conc H_2SO_4 and another containing mercury. It is freed from traces of N_2 by the freeze and thaw method. [Blanchard *Inorg Synth* **II** 126 *1946*, Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 485-487 *1963*.] **TOXIC.**

Nitrogen *[7727-37-9]* **M 28.0, b -195.8°.** Cylinder N_2 can be freed from oxygen by passage through ***Fieser's solution*** [which comprises 2g sodium anthraquinone-2-sulfonate and 15g sodium hydrosulfite dissolved in 100ml of 20% KOH; see Fieser, *J Am Chem Soc* **46** 2639 *1924*] followed by scrubbing with saturated lead acetate solution (to remove any H_2S generated by the Fieser solution), conc H_2SO_4 (to remove moisture), then soda-lime (to remove any H_2SO_4 and CO_2). *Alternatively*, after passage through Fieser's solution, N_2 can be dried by washing with a solution of the metal ketyl from benzophenone and Na wire in absolute diethyl ether. [If ether vapour in N_2 is undesirable, the ketyl from liquid Na-K alloy under xylene can be used.]
Another method for removing O_2 is to pass the nitrogen through a long, tightly packed column of Cu turnings, the surface of which is constantly renewed by scrubbing it with ammonia (sg 0.880) solution. The gas is then passed through a column packed with glass beads moistened with conc H_2SO_4 (to remove ammonia), through a column of packed KOH pellets (to remove H_2SO_4 and to dry the N_2), and finally through a glass trap packed with chemically clean glass wool immersed in liquid N_2. Nitrogen has also been purified by passage over Cu wool at 723°K and Cu(II) oxide [prepared by heating $Cu(NO_3)_2.6H_2O$ at 903°K for 24 hours] and then into a cold trap at 77°K.
A typical dry purification method consists of a mercury bubbler (as trap), followed by a small column of silver and gold turnings to remove any mercury vapour, towers containing anhydrous $CaSO_4$, dry molecular sieves or $Mg(ClO_4)_2$, a tube filled with fine Cu turnings and heated to 400° by an electric furnace, a tower containing soda-lime, and finally a plug of glass wool as filter. Variations include tubes of silica gel, traps containing activated charcoal cooled in a Dry-ice bath, copper on Kieselguhr heated to 250°, and Cu and Fe filings at 400°. [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 458-460 *1963*.]

Nitrosyl chloride *[2696-92-6]* **M 65.5, m -64.5°. b -5.5°.** It is an orange gas with a suffocating odour. It has been fractionally distilled at atmospheric pressure in an all-glass, low-temperature still, taking the fraction boiling at -4° and storing it in sealed tubes. *Alternatively*, the gas is dried by $CaCl_2$ and passed through H_2SO_4 when Cl_2 passes on, but NOCl is absorbed to form ***nitrososulfuric acid*** ($NO.HSO_4$) which on warming with NaCl evolves pure NOCl [Tilden *J Chem Soc* **27** 630 *1874*.] It is decomposed by H_2O and alkali, and forms compounds with metal chlorides e.g. $FeCl_3.NOCl$. [Coleman *Inorg Synth* **I** 55 *1939*.]

Nitrous oxide (laughing gas) *[10024-97-2]* **M 44.0, b -88.5°.** Wash the gas with concentrated alkaline pyrogallol solution, to remove O_2, CO_2, and NO_2, then dry it by passing it through columns of P_2O_5 or Drierite, and collecting in a dry trap cooled in liquid N_2. It is further purified by freeze-pump-thaw and distillation cycles

under vacuum [Ryan & Freeman *J Phys Chem* **81** 1455 *1977*, Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 484-485 *1963*].

Osmium tetroxide (osmic acid) *[20816-12-0]* **M 524.2, m 40.6°, b 59.4°/60mm, 71.5°/100mm, 109.3°/400mm, 130°/760mm, d_D^{20} 5.10, pK_1^{25} 7.2, pK_2^{25} 12.2, pK_3^{25} 13.95, pK_4^{25} 14.17 (H_4OsO_6).** It is **VERY TOXIC** and should be manipulated in a very efficient fume cupboard. It attacks the eyes severely **(use also eye and face protection)** and is a good oxidising agent. It is volatile and has a high vapour pressure (11mm) at room temperature. It sublimes and volatilises well below its boiling point. It is soluble in $*C_6H_6$, H_2O (7.24% at 25°), CCl_4 (375% at 25°), EtOH and Et_2O. It is estimated by dissolving a sample in a glass-stoppered flask containing 25ml of a solution of KI (previously saturated with CO_2) and acidified with 0.35M HCl. After gentle shaking in the dark for 30 minutes, the solution is diluted to 200ml with distilled H_2O saturated with CO_2 and titrated with standard thiosulfate using starch as indicator. This method is not as good as the gravimetric method. Hydrazine hydrochloride (0.1 to 0.3g) is dissolved in 3M HCl (10ml) in a glass-stoppered bottle. After warming to 55-65°, a weighed sample of OsO_4 solution is introduced, and the mixture is digested on a water bath for 1 hour. The mixture is transferred to a weighed glazed crucible and evaporated to dryness on a hot plate. A stream of H_2 is started through the crucible, and the crucible is heated over a burner for 20-30 minutes. The stream of H_2 is continued until the crucible in cooled to room temperature, and then the H_2 is displaced by CO_2 in order to avoid rapid combustion of H_2. Finally the crucible is weighed. [Grube in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** pp 1603 *1965*, Anderson & Yost *J Am Chem Soc* **60** 1822 *1938*.]
§ Available commercially on a polymer support.

Oxygen *[7782-44-7]* **M 32.00, m -218.4°, b -182.96°, d^{-183} 1.149, $d^{-252.5}$ 1.426.** Purify it by passing the gas over finely divided platinum at 673°K and Cu(II) oxide (see under nitrogen) at 973°, then condensed in a liquid N_2-cooled trap. **HIGHLY EXPLOSIVE in contact with organic matter.**

Palladium (II) chloride *[7647-10-1]* **M 177.3, m 678-680°.** The *anhydrous* salt is insoluble in H_2O and dissolves in HCl with difficulty. The *dihydrate* forms red *hygroscopic* crystals that are readily reduced to Pd. Dissolve it in conc HCl through which dry Cl_2 is bubbled. Filter this solution which contains H_2PdCl_4 and H_2PdCl_6 and on evaporation it yields a residue of pure $PdCl_2$. [Grube in *Handbook of Preparative Inorganic Chemistry (Ed Brauer)* Academic Press Vol **II** p 1582 *1965*, Mozingo *Org Synth* Coll Vol **III** 685 1955.] *Alternatively* (fume cupboard), Pd metal is dissolved in *aqua regia*, and converted to the chloride by repeated evaporation with concentrated HCl. The dark red palladous chloride is dried at 150-180° in a stream of dry chlorine gas to give the *anhydrous* salt. [Kharasch, Seyler and Mayo *J Am Chem Soc* **60** 882 *1938*.]

Palladium (II) cyanide *[2035-66-7]* **M 158.1.** The yellow solid should be washed well with H_2O and dry in air. [Bigelow *Inorg Synth* **II** 245 *1946*]. **POISONOUS.**

Perchloric acid *[7601-90-3]* **M 100.5, d_4^{20} 1.665, pK^{25} -2.4 to -3.1 ($HClO_4$).** The 72% acid has been purified by double distillation from silver oxide under vacuum: this frees the acid from metal contamination. Distillation at atmospheric pressure is **dangerous** and **explosive**. The *anhydrous* acid is obtained by adding gradually 400-500ml of oleum (20% fuming H_2SO_4) to 100-120ml of 72% $HClO_4$ in a reaction flask cooled in an ice-bath. The pressure is reduced to 1mm (or less), with the reaction mixture at 20-25°. The temperature is gradually raised during 2 hours to 85°; the distillate is collected in a receiver cooled in Dry-ice. For further details of the distillation apparatus see Smith [*J Am Chem Soc* **75** 184 *1953*]. **It is HIGHLY EXPLOSIVE; a strong protective screen should be used at all times.** [Schmeisser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 318-320 *1963*.]

Perrehenic acid (HRe_2O_4) *[13768-11-1]* **M 251.2, d^{25} 2.16, pK^{25} -1.25.** The acid is commercially available as a 65-70% w/w solution in H_2O. It can be prepared freshly from a solution of pure finely powdered KRe_2O_4 (10.0g, 35.6mmol) in hot H_2O (120ml) at 100° which is placed on the top of a Dowex 50W-X1 cation exchange

resin column (40 x 20mm, 50g of 50-100 mesh with a 1cm layer of Pyrex wool). This resin is first washed with 6 M HCl (20ml) and flushed with pure hot H_2O at 100° until the effluent is colourless and does not become turbid on addition of $AgNO_3$ solution (i.e. chloride free). The hot KRe_2O_4 solution is applied to the resin in four 30ml portions (to keep the temperature high, boiling if necessary for the salt to remain in solution), and the hot column is rinsed with pure hot H_2O. The rate of flow should be kept at 15-20ml/minute, the first effluent (*ca* 50ml) is discarded and the acidic fraction (to litmus, *ca* 150ml) is collected. This solution is concentrated to as small a volume as possible, preferably *in vacuo* over P_2O_5, and an aliquot is diluted and titrated against standard alkali to obtain the concentration of HRe_2O_4 in the residue. It is a strong acid. It is then diluted with pure H_2O as required. The theoretical amount of acid in the residue should be 8.68g. [Watt & Thompson *Inorg Synth* **VII** 187 *1963*.] It is also prepared by dissolving rhenium heptoxide (Re_2O_7, 1314-68-7) in H_2O. [Smith & Long *J Am Chem Soc* **70** 354 *1948*, Melaven et al. *Inorg Synth* **III** 188 *1950*.]

Phosgene *[75-44-5]* **M 98.9, m -118°, b 8.2°/756mm.** Dry the gas with Linde 4A molecular sieves, de-gas it and distil it under vacuum at low temperature. This should be done in a closed system such as a vacuum line. It is hydrolysed slowly by H_2O, but does not fume in moist air. It is available in cylinders and as a ~20% solution in toluene. **It is HIGHLY TOXIC and should not be inhaled. If it is inhaled, the operator should lie still and, be made to breathe in ammonia vapour which reacts readily with phosgene to give urea.** [Pope et al. *J Chem Soc* **117** 1410 *1920*, *Beilstein* **3** IV 41.]

Phosphine *[7803-51-2]* **M 34.0, m -133°, b -87.7°, pK^{25} -14, pK_b 28.** PH_3 is best purified in a gas line (in a vacuum) in an efficient fume cupboard. It is spontaneously flammable, has a strong odour of decayed fish and is **POISONOUS**. The gas is distilled through solid KOH towers (two), through a Dry ice-acetone trap (-78°, to remove H_2O, and P_2H_4 which spontaneously ignites with O_2), then through two liquid N_2 traps (-196°), followed by distillation into a -126° trap (Dry-ice/methylcyclohexane slush), allowed to warm in the gas line and then sealed in ampoules preferably under N_2. Its IR as ν_{max} at 327 (m), 1121 (m) and 900 (m) cm^{-1}. [Klement in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 525-530 *1963*, Gokhale & Jolly *Inorg Synth* **IX** 56 *1967*.] PH_3 has also been absorbed into a solution of cuprous chloride in hydrochloric acid (when $CuCl.PH_3$ is formed). PH_3 gas is released when this solution is heated, and the gas is purified by passage through KOH pellets and then over P_2O_5. It ignites spontaneously in air with a luminous flame. Its solubility is 0.26ml/1 ml of H_2O at 20°, and a crystalline *hydrate* is formed on releasing the pressure on an aqueous solution.

Phosphonitrilic chloride (tetramer) *[1832-07-1]* **M 463.9.** Purify it by zone melting, then recrystallise it from petroleum ether (b 40-60°) or *n*-hexane. [van der Huizen et al. *J Chem Soc, Dalton Trans* 1317 *1986*.]

Phosphonitrilic chloride (trimer) (hexachlorocyclotriphosphazine) *[940-71-6]* **M 347.7, m 112.8°, 113-114°.** Purify it by zone melting, by crystallisation from petroleum ether, *n*-hexane or *benzene, and by sublimation. [van der Huizen et al. *J Chem Soc, Dalton Trans* 1311 *1986*, Meirovitch et al. *J Phys Chem* **88** 1522 *1984*, Alcock et al. *J Am Chem Soc* **106** 5561 *1984*; Winter & van de Grampel *J Chem Soc, Dalton Trans* 1269 *1986*.]

Phosphonous acid (phosphonic acid, $H\text{-}P{=}O(OH)_2$) *[13598-36-2]* **M 82.0, m 73.6°, d_4^{25} 1.651, pK_1 1.43, pK_2 6.67.** Phosphonous acid is best prepared by adding PCl_3 to concentrated HCl, when HCl gas is liberated and the solution is evaporated (fume-cupboard) until the temperature reaches 180° (all HCl gas is driven off). On cooling the acid separates as white hygroscopic (and deliquescent) crystals. It has a garlic taste, melts at 73.6°, and decomposes at 200° to give phosphine and phosphoric acid (note that PH_3 ignites in air with bright flashes, see above). It is a dibasic acid that slowly oxidises to phosphoric acid in air. Store it under dry N_2, or as a 20% aqueous solution under N_2. [Simon & Fehér *Z Anorg Allgem Chem* **230** 298 *1937*, Voight & Gallais *Inorg Synth* **IV** 55 *1953*.]

Tautomerism of phosphonous acid. This acid is tautomeric with trihydroxyphosphine with the latter tautomer being in extremely small concentrations, e.g. 1 in 10^{12}. The diester [e.g. $(MeO)_2P(H){=}O$] has the H linked to the P atom. The tautomerism is not like that of keto-enol tautomerism in carbon chemistry, and dialkylphosphites $(RO)_2P(H){=}O$ do *not* react with sulfur to form the corresponding P-SH derivatives, but they do form solid salts such as $(RO)_2PONa$ which *do* add sulfur readily. Also this acid does form triesters such as $(MeO)_3P$ which is

trimethylphosphite or trimethoxyphosphine, and behave more like phosphines. [cf. F.A. Cotton, G, Wilkinson, C.A. Murillo and M. Bochmann, *Advanced Inorganic Chemistry*, 6th Edn, Interscience Publ, *1999*, ISBN 0-471-19957-5.]

Phosphoric acid *[7664-38-2]* **M 98.0, m 42.3°, pK $_1^{25}$ 2.15, pK $_2^{25}$ 7.21, pK $_3^{25}$ 12.37.** Pyrophosphate can be removed from phosphoric acid by diluting with distilled H_2O and refluxing overnight. By cooling to 11° and seeding with crystals obtained by cooling a few millilitres in a Dry-ice/acetone bath, 85% orthophosphoric acid crystallises as $H_3PO_4.H_2O$. The crystals are collected on a sintered glass filter. [Weber & King *Inorg Synth* **I** 101 *1939*.]

Phosphorus (red) *[7723-14-0]* **M 31.0, m 590°/43atm, ignites at 200°, d $_4^{20}$ 2.34.** Heat it for 15 minutes in boiling distilled H_2O, allow it to settle and wash it several times with boiling H_2O. Transfer it to a Büchner funnel, wash it with hot H_2O until the washings are neutral, then dry it at 100° and store it in a desiccator.

Phosphorus (white) *[7723-14-0]* **M 31.0, m 44.1°, b 287°, d $_4^{20}$ 1.82.** Purify white phosphorus by melting it under dilute H_2SO_4—dichromate (possible **carcinogen**) mixture and allow to stand for several days in the dark at room temperature. It remains liquid, and the initial milky appearance due to insoluble, oxidisable material gradually disappears. The phosphorus can then be distilled under vacuum in the dark [Holmes *Trans Faraday Soc* **58** 1916 *1962*]. It sublimes *in vacuo*. Other methods of purification include extraction with dry CS_2 followed by evaporation of the solvent, or washing with 6M HNO_3, then H_2O, and drying under vacuum. It ignites in air at ~50°, or by friction if dry. Store and cut it under H_2O. **POISONOUS, use gloves.**

Phosphorus oxychloride *[10025-87-3]* **M 153.3, b 105.5°, d $_4^{20}$ 1.675, n $_D^{20}$ 1.461.** Distil the liquid under reduced pressure to separate it from the bulk of the HCl and the phosphoric acid (from hydrolysis); the middle fraction is re-distilled into ampoules containing a little purified mercury. These ampoules are sealed and stored in the dark for 4-6 weeks with occasional shaking to facilitate reaction of any free chloride with the mercury. The $POCl_3$ is then again fractionally distilled and stored in sealed ampoules in the dark until required [Herber *J Am Chem Soc* **82** 792 *1960*]. Lewis and Sowerby [*J Chem Soc* 336 *1957*] refluxed their distilled $POCl_3$ with Na wire for 4 hours, then removed the Na and again distilled. *Use Na only with almost pure $POCl_3$ to avoid explosions.* **HARMFUL VAPOURS; work in an efficient fume cupboard.**

Phosphorus pentabromide *[7789-69-7]* **M 430.6, m <100°, b 106°(dec).** Dissolve it in pure nitrobenzene at 60°, filtering off any insoluble residue on to sintered glass funnel, then allow it to crystallise by cooling. Wash the collected solid with dry Et_2O and remove excess ether in a current of dry N_2. (All manipulations should be performed in a dry-box.) [Harris & Payne *J Chem Soc* 3732 *1958*]. It fumes in moist air because of hydrolysis. **HARMFUL VAPOURS** (wash burning eyes with aqueous $NaHCO_3$)**.**

Phosphorus pentachloride *[10026-13-8]* **M 208.2, m 179-180°(sublimes).** [All operations should be carried out in an efficient fume cupboard.] Sublime it at 160-170° in an atmosphere of chlorine. Excess chlorine is then displaced by dry N_2 gas. All subsequent manipulations should be performed in a dry-box [Downs & Johnson *J Am Chem Soc* **77** 2098 *1955*]. It fumes in moist air and attacks the eyes and the mucous membranes of the nose. It should not be breathed in and has very **HARMFUL VAPOURS** (wash burning eyes with aqueous $NaHCO_3$).

Phosphorus pentasulfide *[1314-80-3]* **M 444.5, m 277-283°, 290°, b 513-515.** Purify P_2S_5 by extraction and crystallisation with CS_2, using a Soxhlet extractor, and is heated in a CO_2 atmosphere at 150° to remove solvent. It liberates H_2S in moist air. **HARMFUL VAPOURS.** [Klements in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 568 *1963*.]

Phosphorus pentoxide *[1314-56-3]* **M 141.9, m 562°, b 605°.** It has been sublimed at 250° under vacuum into glass ampoules. It fumes in moist air and reacts violently with water. It is an excellent drying agent for use in desiccators. **HARMFUL VAPOURS and attacks skin, use gloves.** [Manley *J Chem Soc* **121** 331 *1922*, Klements in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 541 *1963*.]

Phosphorus sesquisulfide P_4S_3 *[1314-85-8]* **M 220.1, m 172°.** Extract $P_4S_3$with CS_2, filter it and evaporate it to dryness. *Alternatively*, place it in H_2O, and pass steam through it for an hour. The H_2O is then removed, the solid is dried, and recrystallised from CS_2 (with the usual CS_2 precautions) [Rogers & Gross *J Am Chem Soc* **74** 5294 *1952*].

Phosphorus sulfochloride (phosphorus thiochloride) *[3982-91-0]* **M 169.4, m -35°, b 122-124°, 125°(corr), d_4^{30} 1.64, n_D^{30} 1.556.** Possible impurities are PCl_5, H_3PO_4, HCl and $AlCl_3$. Gently mix it with H_2O to avoid a heavy emulsion; the product decolourises immediately and settles to the bottom layer. It is soluble in *C_6H_6 and CCl_4. [Duval *Inorg Synth* **IV** 73 *1953*.] **HARMFUL VAPOURS.**

Phosphorus tribromide *[7789-60-8]* **M 270.7, m -41.5°, b 168-170°/725mm, 171-173°/atm, 172.9°/760mm(corr), d_4^{30} 2.852.** It is decomposed by moisture, it should be kept dry and is *corrosive*. Purify it by distillation through an efficient fractionating column [see Whitmore & Lux *J Am Chem Soc* **54** 3451] in a slow stream of dry N_2, i.e. under strictly dry conditions. [Gay & Maxson *Inorg Synth* **II** 147 *1946*, *Org Synth* Col Vol **II** 358 *1943*.] Dissolve it in CCl_4, dry it over $CaCl_2$, filter and distil it. Store it in sealed ampoules under N_2 and keep it away from light. It is also commercially available as a 1.0M solution in CH_2Cl_2 (d^{25} 1.488). **HARMFUL VAPOURS.**

Phosphorus trichloride *[7719-12-2]* **M 137.3, b 76°, d_4^{20} 1.575, n 1.515.** Heat it under reflux to expel dissolved HCl, then distil it. It has been further purified by vacuum fractionation several times through a -45° trap into a receiver at -78°. [Forbes *Inorg Synth* **II** 145 *1946*.] **HARMFUL VAPOURS.**

Phosphorus triiodide *[13455-01-1]* **M 411.7, m 61°.** It decomposes in moist air and must be kept in a desiccator over $CaCl_2$. It is crystallised from sulfur-free CS_2; otherwise the **m** decreases to *ca* 55°. It is best to prepare it freshly. [Germann & Traxler *J Am Chem Soc* **49** 307 *1927*, Klement in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 541 *1963*.] **HARMFUL VAPOURS.**

12-Phosphotungstic acid *[12501-23-4]* **M 2880.2, m ~96°.** A few drops of conc HNO_3 are added to 100g of phosphotungstic acid dissolved in 75ml of water, in a separating funnel, and the solution is extracted with diethyl ether. The lowest of the three layers, which contains a phosphotungstic acid-ether complex, is separated, washed several times with 2M HCl, then with water and again extracted with ether. Evaporation of the ether under vacuum with mild heating on a water bath gives crystals which are dried under vacuum and ground [Matijevic & Kerker, *J Am Chem Soc* **81** 1307 *1959*].

Platinum (IV) ammonium chloride [ammonium hexachloroplatinate (IV), $(NH_4)_2$ $PtCl_6$] *[16919-58-7]* **M 443.9.** This salt is a useful Pt compound and is a very good source for preparing many amine complexes. It provides spongy Pt at high temperature. It is prepared by dissolving the less expensive spongy Pt (9.76g, 50mmol) in *aqua regia* (200ml, 1HNO_3:4HCl by volume, and allowed to stand for 30 minutes until orange-red in colour) by heating and concentrating in an evaporating dish (***use an efficient fume hood and care as it is a dangerous operation***) to a thick syrup which is then taken almost to dryness on a water bath. Avoid drying at higher temperatures as it becomes incompletely soluble in H_2O. The orange-red crusty residue is dissolved in H_2O (100ml), filtered; and to it is add slowly a solution of NH_4Cl (8g, 150mmol) in H_2O (100ml) with stirring, when a yellow finely crystalline precipitate separates. Set the mixture aside for 30 minutes in an ice bath. Filter off the platinate salt and wash it several times with 1% aqueous NH_4Cl (30ml portions), then with EtOH (which removes any corresponding Pd salt impurity) and Et_2O. Dry the salt first in air, powder the crystals and dry further at 120° for 1 hour to provide an almost quantitative yield. Note that although the filtrates may be yellow in colour they only contain minute traces of Pt as the colour can be imparted at as low concentrations as 1 part in 20,000 parts of H_2O. The salt is not hygroscopic. Its solubility (by weight) in H_2O is 0.5% at 20° and 3.37% at 100°, and it is still less soluble in 1M NH_4Cl (0.0028%). It decomposes above 185° and yields ***spongy Pt*** at higher temperatures. It is reduced to the metal by H_2 at 120° and yields H_2PtCl_6 with Cl_2. [Kauffman *Inorg Synth* **9** 182 *1967*.]

Platinum (II) chloride *[10025-65-7]* **M 266.0, d $_4^{20}$ 5.87.** It is purified by heating at 450° in a stream of Cl_2 for 2 hours. Some sublimation occurs because the $PtCl_2$ sublimes completely at 560° as red (almost black) needles. This sublimate can be combined to the bulk chloride, and while still at *ca* 450° it should be transferred to a container and cooled in a desiccator. A probable impurity is $PtCl_4$. To test for this add a few drops of H_2O (in which $PtCl_4$ is soluble) to the salt, filter and add an equal volume of saturated aqueous NH_4Cl to the filtrate. If no precipitate is formed within 1 minute, then the product is pure. If a precipitate appears, then the whole material should be washed with small volumes of H_2O until the soluble $PtCl_4$ is removed. The purified $PtCl_2$ is partly dried by suction and then dried in a vacuum desiccator over P_2O_5. It is insoluble in H_2O, but soluble in HCl to form chloroplatinic acid (H_2PtCl_4) by disproportionation. [Cohen *Inorg Synth* **VI** 209 *1960*.]

Potassium bicarbonate *[298-14-6]* **M 100.1.** It is crystallised from water at 65-70° (1.25ml/g) by filtering and then cooling to 15° (~0.4ml/g). During all operations, CO_2 is passed through the stirred mixture. The crystals are sucked dry at the pump, washed with distilled water, dried in air and then over H_2SO_4 in an atmosphere of CO_2. It is much less soluble than the carbonate in H_2O (see below).

Potassium biiodate *[13455-24-8]* **M 389.9.** Crystallise the biiodate three times from hot water (3ml/g), and stirring continuously during each cooling. After drying at 100° for several hours, the crystals are suitable for use in volumetric analysis.

Potassium bisulfate *[7646-93-7]* **M 136.2, m 214°, 218°.** Crystallise it from H_2O (1ml/g) between 100° and 0°. It is also formed when a warm solution of K_2SO_4 in conc H_2SO_4 is cooled down.

Potassium borohydride *[13762-51-1]* **M 53.9, m ~500°(dec).** Crystallise it from liquid ammonia. It is slowly hydrolysed by H_2O. Its solubility at ~20° in H_2O or liquid NH_3 is 20%, in MeOH it is 0.7%, in Me_2NCHO it is 15% and in MeOH/H_2O (1:4) it is 13%. [Jons & Wallbridge *Progr Inorg Chem* **11** 99-231 *1970*.]

Potassium bromate *[7758-01-2]* **M 167.0, m 350°(dec at 370°), d $_4^{20}$ 3.27.** Crystallise $KBrO_3$ from distilled H_2O (2ml/g) between 100° and 0°. To remove bromide contamination, a 5% solution in distilled H_2O, cooled to 10°, is bubbled with gaseous chlorine for 2 hours, then filtered and extracted with reagent grade CCl_4 until colourless and odourless. After evaporating the aqueous phase to about half its volume, it is cooled again slowly to about 10°. The crystalline $KBrO_3$ that separates, is washed with 95% EtOH and dried in a vacuum [Boyd et al. *J Am Chem Soc* **74** 237 *1952*]. Another way to remove Br^- ions is by stirring several times in MeOH and then drying at 150° [Field & Boyd *J Phys Chem* **89** 3767 *1985*].

Potassium bromide *[7758-02-3]* **M 119.0, m 734°, d $_4^{20}$ 2.75.** Crystallise the bromide from distilled water (1ml/g) between 100° and 0°. Wash it with 95% EtOH, followed by Et_2O. Dry it in air, then heat it at 115° for 1 hour, pulverise it, then heat it in a vacuum oven at 130° for 4 hours. It has also been crystallised from aqueous 30% EtOH, or EtOH, and dried over P_2O_5 under vacuum before heating in an oven.

Potassium carbonate *[584-08-7]* **M 138.2, m 898°, d $_4^{20}$ 2.3.** It crystallises from water between 100° and 0°. The solubility in H_2O is 105% at 0°, 127% at 60° and 205% at 135° (**b** of saturated solution). After two recrystallisations of technical grade material, it had B, Li and Fe at 1.0, 0.04 and 0.01 ppm, respectvely. [Dönges in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 987 *1963*.]

Potassium chlorate *[3811-04-9]* **M 122.6, m 368°.** It has been recrystallised from water (1.8ml/g) between 100° and 0°, and the crystals were filtered onto sintered glass. Keep away from organic material as it oxidises them readily.

Potassium chloride *[7447-40-7]* **M 74.6, m 771°, d $_4^{20}$ 1.98.** Dissolve it in conductivity water, filter it, and saturate it with chlorine (generated from conc HCl and $KMnO_4$). Excess chlorine is boiled off, and the KCl is precipitated by HCl (generated by dropping conc HCl into conc H_2SO_4). The precipitate is washed with water, dissolved in conductivity water at 90-95°, and crystallised by cooling to about -5°. The crystals are drained at the centrifuge, dried in a vacuum desiccator at room temperature, then fused in a platinum dish under N_2, cooled

and stored in a desiccator. Potassium chloride has also been sublimed in a stream of pre-purified N_2 gas and collected by electrostatic discharge [Craig & McIntosh *Can J Chem* **30** 448 *1952*].

Potassium chromate *[7789-00-6]* **M 194.2, m 975°, d $_4^{20}$ 2.72, pK$_1^{25}$ 0.74, pK$_2^{25}$ 6.49 (for H_2CrO_4).** Crystallise it from conductivity water (0.6g/ml at 20°), and dry it between 135° and 170°.

Potassium cobalticyanide *[13963-58-1]* **M 332.4, m dec on heating, d $_4^{25}$ 1.878.** Crystallise it from water to remove traces of HCN. Its solubility in 87-88% EtOH is 1 in 7500 at 20°. [Glemser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1542 *1965*.]

Potassium cyanate *[590-28-3]* **M 81.1, d $_4^{20}$ 2.05, pK^{25} 3.46 (for HCNO).** Common impurities include ammonia and bicarbonate ion (from hydrolysis). Purify it by preparing a saturated aqueous solution at 50°, neutralising with acetic acid, filtering, adding two volumes of EtOH and keeping for 3-4 hours in an ice bath. (More EtOH can lead to co-precipitation of $KHCO_3$.) Filter, wash it with EtOH and dry it rapidly in a vacuum desiccator (P_2O_5). The process is repeated [Vanderzee & Meyers *J Chem Soc* **65** 153 *1961*].

Potassium cyanide *[151-50-8]* **M 65.1, m 634°, d $_4^{20}$ 1.52.** A saturated solution in H_2O-ethanol (1:3) at 60° is filtered and cooled to room temperature. Absolute EtOH is added, with stirring, until crystallisation ceases. The solution is again allowed to cool to room temperature (during 2-3 hours), then the crystals are filtered off, washed with absolute EtOH, and dried, first at 70-80° for 2-3 hours, then at 105° for 2 hours [Brown et al. *J Phys Chem* **66** 2426 *1962*]. It has also been purified by melting in a vacuum and by zone refining. Its solubility is 33% (H_2O), 66% (boiling H_2O), 33% (glycerol), 4% (MeOH) and 1% (EtOH). It hydrolyses in H_2O, and a 0.1M aqueous solution of KCN has a pH of 11, i.e. CO_2 in the H_2O makes it acidic enough to liberate a lot of the more poisonous HCN. To keep the HCN in solution it must be made quite alkaline (pH <11). LD_{50} oral toxicity in rat is ~10mg/Kg. **HIGHLY POISONOUS work in an efficient fume cupboard.**

Potassium dichromate *[7778-50-9]* **M 294.2, m 398°(dec), d $_4^{20}$ 2.68.** Crystallise it from water (g/ml) between 100° and 0° and dry it under vacuum at 156°. (Possible **CARCINOGEN**.)

Potassium dihydrogen phosphate *[7778-77-0]* **M 136.1.** Dissolve it in boiling distilled water (2ml/g), keep on a boiling water-bath for several hours, then filter it through paper pulp to remove any turbidity. Cool rapidly with constant stirring, and the crystals are collected on to hardened filter paper, using suction, washed twice with ice-cold water, once with 50% EtOH, and dried at 105°. Alternative crystallisations are from water, then 50% EtOH, and again water, or from concentrated aqueous solution by addition of EtOH. It is freed from traces of Cu by extracting its aqueous solution with diphenylthiocarbazone in CCl_4, followed by repeated extraction with CCl_4 to remove traces of diphenylthiocarbazone.

Potassium dithionate *[13455-20-4]* **M 238.3, pK$_{Est(1)}$ -3.4, pK$_2^{25}$ 0.49 (for dithionic acid).** Crystallise it from water (1.5ml/g) between 100° and 0°.

Potassium ferricyanide *[13746-66-2]* **M 329.3, pK^{25} <1 (for ferricyanide).** It has been recrystallised repeatedly from hot water (1.3ml/g) and dried under vacuum in a desiccator.

Potassium ferrocyanide trihydrate *[14459-95-1]* **M 422.4, pK$_3^{25}$ 2.57, pK$_4^{25}$ 4.35 (for ferrocyanide).** It is purified by repeated crystallisation from distilled water, and never heating above 60°. The *anhydrous* salt is prepared by drying at 110° over P_2O_5 in a vacuum desiccator. To obtain the *trihydrate*, it is necessary to equilibrate the salt in a desiccator over a saturated aqueous solution of sucrose and NaCl. It can also be precipitated from a saturated solution at 0° by adding an equal volume of cold 95% EtOH, setting aside for several hours, then centrifuge and wash with cold 95% EtOH. It is finally sucked air dry with water-pump vacuum. The *anhydrous* salt is obtained by drying the hydrate in a platinum boat at 90° in a slow stream of N_2 [Loftfield & Swift *J Am Chem Soc* **60** 3083 *1938*].

Potassium fluorosilicate *[16871-90-2]* **M 220.3, d $_4^{20}$ 2.3, pK^{25} 1.92 (for H_2SiF_6).** Crystallise it several times from conductivity water (100ml/g) between 100° and 0°.

Potassium hexachloroiridate (III) (**K_3IrCl_6**) *[14024-41-1]* **M 483.1.** Crystallise it from hot aqueous solution, and the solution should be olive-green in colour. If it has a tinge of red, then some would have oxidised to (K_2IrCl_6) [see following entry]. In this case make a concentrated solution in H_2O, and bubble H_2S through until the solution is clearly olive-green in colour due to Ir(III). Add KCl and $K_3IrCl_6.3H_2O$ deposits on evaporating under N_2. Filter it off, wash it with a little H_2O, then EtOH and dry it *in vacuo* away from air. [Grube in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** pp 1595 *1965*.]

Potassium hexachloroiridate (IV) (**K_2IrCl_6**) *[16920-56-2]* **M 522.2.** Crystallise it from hot aqueous solution containing a few drops of HNO_3 to keep it in the oxidised state. It forms small shiny red-black octahedral crystals which are dried at 100° and give a red powder on grinding [Grube in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** pp 1593-1594 *1965*].

Potassium hexachloroosmate (IV) *[16871-60-6]* **M 481.1.** Crystallise it from hot dilute aqueous HCl. [Turner et al. *Anal Chem* **30** 1708 *1958*.]

Potassium hexachloroplatinate (IV) *[16921-30-5]* **M 486.0, m 250°(dec).** It crystallises from water (20ml/g) between 100 and 0°. Its solubility in H_2O is 0.7% at 0°, 1.12% at 20°, 2.16% at 50° and 5.13% at 100°. [Grube in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1571 *1965*.]

Potassium hexacyanochromate (III) (**$K_3[Cr(CN)_6]\ 3H_2O$**) *[13601-11-1]* **M 418.5.** It forms yellow crystals from water. Recrystallise it two or three times from H_2O and dry it over H_2SO_4. Its solubility at 20° is 30.96g/100g H_2O, and it is insoluble in EtOH. Aqueous solutions tend to decompose especially in the presence of light or on heating when $Cr(OH)_3$ separates. [Hein & Herzog in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** pp 1373-1374 *1965*.]

Potassium hexafluorophosphate *[17084-13-8]* **M 184.1, pK_1^{25} ~0.5, pK_2^{25} 5.12 (for fluoro-phosphoric acid H_2PO_3F).** Crystallise it from alkaline aqueous solution, using polyethylene vessels, or from 95% EtOH, and dry it in a vacuum desiccator over KOH. [Kloditz *Z Anorg Allgem Chem* **284** 144 *1956*, Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 196 *1963*.]

Potassium hexafluorozirconate (**K_2ZrF_6**) *[16923-95-8]* **M 283.4, d_4^{20} 3.48.** Recrystallise it from hot water (solubility is 0.78% at 2° and 25% at 100°).

Potassium hydrogen fluoride *[7789-29-9]* **M 78.1, m 225°(dec).** It crystallises from water. It is very soluble in hot H_2O and 41% at 21°. [Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 237 *1963*.]

Potassium hydroxide (solution) *[1310-58-3]* **M 56.1, pK^{25} 16 (for aquo K^+).** Its carbonate content can be reduced by rinsing KOH sticks rapidly with water prior to dissolving them in boiled out distilled water. *Alternatively*, a slight excess of saturated $BaCl_2$ or $Ba(OH)_2$ can be added to the solution which, after shaking well, is set aside so that the $BaCO_3$ is allowed to separate out. Davies and Nancollas [*Nature* **165** 237 *1950*] rendered KOH solutions carbonate free by ion exchange using a column of Amberlite IR-100 in the OH^- form.

Potassium iodate *[7758-05-6]* **M 214.0, pK^{25} 0.80 (for HIO_3).** It has been crystallised twice from distilled water (3ml/g) between 100 and 0°, dried for 2 hours at 140° and cooled in a desiccator. Analytical reagent grade material dried in this way is suitable for use as an analytical standard.

Potassium iodide *[7681-11-0]* **M 166.0, pK^{25} -8.56 (for HI).** Crystallise it from distilled water (0.5ml/g) by filtering the near-boiling solution and cooling. To minimise oxidation to iodine, the process can be carried out under N_2 and the salt is dried under a vacuum over P_2O_5 at 70-100°. Before drying, the crystals can be washed with EtOH or with acetone followed by petroleum ether. It has also been recrystallised from water/ethanol. After 2 recrystallisations, ACS/USP grade had Li and Sb at <0.02 and <0.01 ppm respectively. [Lingane & Kolthoff *Inorg Synth* **I** 163 *1939*.]

Potassium nickel sulfate hexahydrate *[13842-46-1]* **M 437.1.** Crystallise it from H_2O (1.7ml/g) between 75 and 0°.

Potassium nitrate (saltpetre) *[7757-79-1]* **M 101.1, m 336°.** It crystallises from hot H_2O (0.5ml/g) on cooling (*cf* KNO_2 below). Dry it for 12 hours under vacuum at 70°. The solubility in H_2O is 13.3% at 0°, 110% at 60°, and 246% at 100°. After two recrystallisations, technical grade salt had <0.001 ppm of metals. The fused salt is a powerful oxidising agent.

Potassium nitrite *[7758-09-0]* **M 85.1, m 350°(dec), pK^{20} 3.20 (for HNO_2).** A saturated solution at 0° is warmed and partially evaporated under vacuum. The crystals so obtained are filtered off from the warm solution. (This procedure is designed to reduce the level of nitrate impurity and is based on the effects of temperature on solubility. The solubility of KNO_3 in water is 13g/100ml at 0°, 247g/100ml at 100°; for KNO_2 the corresponding figures are 280g/100ml and 413g/100ml.) *Alternatively*, dissolve it in H_2O and precipitate by adding of EtOH.

Potassium nitrosodisulfonate (Fremy's Salt) *[14293-70-0]* **M 268.3.** It forms yellow needles (dimeric) which dissolve in H_2O to give the violet monomeric free radical. It is purified by dissolving (~12g) in 2M KOH (600ml) at 45°, filtering the blue solution and keeping it in a refrigerator overnight. The golden yellow crystals (10g) are filtered off, washed with MeOH (3x), then Et_2O and stored in a glass container in a vacuum over KOH. It is stable indefinitely when dry. [Cram & Reeves *J Org Chem* **80** 3094 *1958*, Schenk *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 505 *1963*.]

Potassium osmate (VI) dihydrate *[19718-36-6]* **M 368.4.** It forms *hygroscopic* **POISONOUS** crystals which are soluble in H_2O but insoluble in EtOH and Et_2O. It decomposes slowly in H_2O to form the *tetroxide* which attacks the eyes. The solid should be kept dry and in this form it is relatively safe. [Lloyd et al. *Synthesis* 610 *1972*, Grube in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1604 *1965*.]

Potassium perchlorate *[7778-74-7]* **M 138.6, m 400(dec), d_4^{20} 2.52, pK^{25} -2.4 to -3.1 (for $HClO_4$).** It crystallises from boiling water (5ml/g) on cooling. Dry it under vacuum at 105°.

Potassium periodate (potassium metaperiodate) *[7790-21-8]* **M 230.0, m 582°, d_4^{20} 3.62.** Crystallise it from distilled water. Its solubility in H_2O is 0.2% at 0°, 0.4% at 20°, 4.4% at 80° and 7.9% at 100°. [Hill *Inorg Synth* **I** 171 *1939*, Schmeisser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 325 *1963*.]

Potassium permanganate *[7722-64-7]* **M 158.0, m 240(dec), d_4^{20} 2.7, pK^{25} -2.25 (for $HMnO_4$).** Crystallise it from hot water (19ml/g at 15°, 4ml/g at 65°), then dry it in a vacuum desiccator over $CaSO_4$. Phillips and Taylor [*J Chem Soc* 4242 *1962*] cooled an aqueous solution of $KMnO_4$, saturated at 60°, to room temperature in the dark, and filtered it through a No.4 porosity sintered-glass filter funnel. The solution was allowed to evaporate in air in the dark for 12 hours, and the supernatant liquid was decanted from the crystals, which were dried as quickly as possible with filter paper. It is a secondary analytical standard. It is a useful oxidant and is used as a topical antiseptic.

Potassium peroxydisulfate (potassium persulfate, $K_2S_2O_8$) *[7727-21-1]* **M 270.3.** Crystallise the persulfate twice from distilled water (10ml/g) and dry it at 50° in a vacuum desiccator. Its solubility in H_2O is 1.6% at 0°, 4.5% at 20°, and 7.2% at 30°. An aqueous solution decomposes on long standing with evolution of O_2 and formation of $KHSO_4$. It is a powerful oxidising agent. Store it at ~10°. [Fehér in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 390 *1963*.]

Potassium peroxymonosulfate (Oxone, potassium monopersulfate triple salt; $2KHSO_5.KHSO_4.K_2SO_4$), *[37222-66-5, 70693-62-8 (triple salt)]* **M 614.8.** This is a stable form of Caro's acid and should contain >4.7% of active oxygen. It can be used in EtOH/H_2O and EtOH/AcOH/H_2O solutions. If active oxygen is too low. it is

best to prepare it afresh from 1mole of $KHSO_5$, 0.5mole of $KHSO_4$ and 0.5mole of K_2SO_4. [Kennedy & Stock *J Org Chem* **25** 1901 *1960*, Stephenson US Patent 2,802,722 *1957*.] A rapid preparation of ***Caro's acid*** is made by stirring finely powdered potassium persulfate (**M** 270.3) into ice-cold conc H_2SO_4 (7ml) and when homogeneous add ice (40-50g). It is stable for several days if kept cold. Keep away from organic matter as it is a **STRONG OXIDANT**. A detailed preparation of **Caro's acid** (***hypersulfuric acid,*** **H_2SO_5,** *[7722-86-3])* in crystalline form **m** ~45° from H_2O_2 and chlorosulfonic acid was described by Fehér in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 388 *1963*.

Potassium perrhenate ($KReO_4$) *[10466-65-6]* **M 289.3, m 550°, b 1360-1370°, d_4^{25} 4.887, n_D^{25} 1.643. pK^{25} -1.25 (for $HReO_4$).** It forms white tetrahedral crystals from H_2O where its solubility is 12.1g/L at 20° and 140g/L at 100°. The salt is then fused in a platinum crucible in air at 750°. [Smith & Long *J Am Chem Soc* **70** 354 *1948*, Watt & Thompson *Inorg Synth* **7** 187 *1963*.]

Potassium reineckate *[34430-73-4]* **M 357.5.** Crystallise it from KNO_3 solution, then from warm water [Adamson *J Am Chem Soc* **80** 3183 *1958*].

Potassium(VI) ruthenate *[31111-21-4]* **M 243.3.** Dissolve the ruthenate in H_2O and evaporate until crystals are formed. The crystals are iridescent green prisms which appear red in thin films. A possible impurity is RuO_4; in this case wash with CCl_4 (which dissolves RuO_4). The concentration of an aqueous solution of RuO_4^{2-} (orange colour) can be estimated from the absorbance at 385nm (ε 1030 M^{-1} cm^{-1}), or at 460nm (ε 1820 M^{-1} cm^{-1}). [Lee et al. *Can J Chem* **50** 3741 *1972*, Connic & Hurley *J Am Chem Soc* **74** 5012 *1952*, Grube et al. *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1600 *1965*].

Potassium selenocyanate *[3425-46-5]* **M 144.1.** Dissolve it in acetone, filter and precipitate it by adding Et_2O.

Potassium sulfate *[7778-80-5]* **M 174.3, m 1069°, d_4^{20} 2.67.** It crystallised from distilled water (4ml/g at 20°; 8ml/g at 100°) between 100° and 0°.

Potassium tetrachloroplatinate(II) *[10025-99-7]* **M 415.1, m 500°(dec).** It forms crystals from aqueous 0.75M HCl (20ml/g) between 100° and 0°. Wash them with ice-cold water and dry.

Potassium tetracyanopalladate (II) trihydrate *[10025-98-6]* **M 377.4.** *All operations should be carried out in an efficient fume cupboard*. ***Cyanide is very*** **POISONOUS**. Dissolve the complex (*ca* 5g) in a solution of KCN (4g) in H_2O (75ml) with warming and stirring, and evaporate hot till crystals appear. Cool, filter off the crystals and wash them with a few drops of cold H_2O. Further concentration of the mother liquors provides more crystals. The complex is recrystallised from H_2O as the colourless *trihydrate*. It *effloresces* in dry air and dehydrates at 100° to the *monohydrate*. The *anhydrous salt* is obtained by heating at 200°, but at higher temperatures it decomposes to $(CN)_2$, Pd and KCN. [Bigelow *Inorg Synth* **II** 245 *1946*.]

Potassium tetrafluoroborate (potassium borofluoride) *[14075-53-7]* **M 125.9, m 530°, d_4^{30} 2.505, pK^{25} -4.9 (for HBF_4).** Crystallise it from H_2O (solubility% (temperature): 0.3 (3°), 0.45 (20°), 1.4 (40°), 6.27 (100°), and dry it under vacuum. It is a non-hygroscopic salt. A 10% solution is transparent blue at 100°, green at 90° and yellow at 60°. [Vörlander et al. *Chem Ber* **65** 535 *1932*, Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 223 *1963*.]

Potassium thiocyanate *[333-20-0]* **M 97.2, m 172°, pK^{25} -1.85 (for HSCN).** Crystallise it from H_2O if much chloride ion is present in the salt, otherwise from EtOH or MeOH (optionally by addition of Et_2O). Filter off on a Büchner funnel without paper, and dry it in a desiccator at room temperature before heating for 1 hour at 150°, with a final 10-20 minutes at 200° to remove the last traces of solvent [Kolthoff & Lingane *J Am Chem Soc* **57** 126 *1935*]. Store it in the dark.

Potassium thiosulfate hydrate *[13446-67-8, 10294-66-3 (75% aqueous solution)]* **M 190.3, pK $_1^{25}$ 0.6, pK $_2^{25}$ 1.74 (for $H_2S_2O_3$).** Crystallise it from warm water (0.5ml/g) by cooling in an ice-salt mixture. It is a good reducing agent used in analytical chemistry. [Foerster & Mommen *Chem Ber* **57** 258 *1924*.]

Potassium tungstate (*ortho* dihydrate) *[37349-36-3; 7790-60-5]* **M 362.1, m 921°, d $_4^{20}$ 3.12, pK $_1^{25}$ 2.20, pK $_2^{25}$ 3.70 (for H_2WO_4).** Crystallise it from hot water (0.7ml/g).

Praseodymium trichloride hexahydrate *[10361-79-2]* **M 355.4, pK $_1^{25}$ 8.55 (for Pr^{3+} hydrol).** Its 1M solution in 6M HCl is passed twice through a Dowex-1 anion-exchange column. The eluate is evaporated in a vacuum desiccator to half its volume and allowed to crystallise [Katzin & Gulyas *J Phys Chem* **66** 494 *1962*].

Praseodymium oxide (Pr_6O_{11}) *[12037-29-5]* **M 1021.4.** Dissolve the oxide in acid (perchloric acid), precipitate it as the oxalate and the salt is ignited at 650° to give the oxide.

Reinecke salt. See ammonium reineckate above.

Rhodium (I) carbonyl chloride (di-μ-chloro-tetracarbonyl dirhodium I, $[Rh(CO)_2Cl]_2$) *[14532-22-9]* **M 388.8, m 121°, 124-125°.** This catalyst is soluble in most organic solvents, but not petroleum ethers, and forms orange-red crystals from hexane. It sublimes at 80°/0.1mm to a red solid. It decomposes on exposure to air when in organic solvents but the solid is stable in dry air. It is moisture sensitive and should be stored in ampoules under N_2 or argon. It catalyses ring-opening silylformylation of olefins. [McCleverty & Wilkinson *Inorg Synth* **8** 211 *1966*, Dahl et al. *J Am Chem Soc* **83** 1761 *1961*, Cramer *Inorg Synth* **15** 14 *1974*, Fukumoto et al. *J Org Chem* **58** 4187 *1993*, Colton et al. *Aust J Chem* **23** 1351 *1970*.]

Rhodium (III) chloride *[10049-07-7]* **M 209.3, m >100°(dec), b 717°.** Probable impurities are KCl and HCl. Wash the chloride well with small volumes of H_2O to remove excess KCl and KOH and dissolve it in the minimum volume of conc HCl. Evaporate it to dryness on a steam bath to give wine-red coloured $RhCl_3.3H_2O$. Leave it on the steam bath until the odour of HCl is lost – do not try to dry further as it begins to decompose above 100° to the oxide and HCl. It is not soluble in H_2O but soluble in alkalis or CN solutions and forms double salts with alkali chlorides. [Anderson & Basolo *Inorg Synth* **VII** 214 *1963*.]

Rubidium bromide *[7789-39-1]* **M 165.4, m 682°, b 1340°, d $_4^{20}$ 3.35.** The bromide is a white crystalline powder which crystallises from H_2O (solubility: 50% in cold and 67% in boiling H_2O to give a neutral solution). It also crystallises from near-boiling water (0.5ml/g) by cooling to 0°.

Rubidium chlorate *[13446-71-4]* **M 168.9, d $_4^{20}$ 3.19.** It crystallises from water (1.6ml/g) by cooling from 100°.

Rubidium chloride *[7791-11-9]* **M 120.9, m 715°, m 1383°, d $_4^{20}$ 2.80.** Crystallise it from water (0.7ml/g) by cooling to 0° from 100°. Its solubility in H_2O is 77.3% at 0.6°, 90.3% at 70° and 147% at boiling point. [Dönges in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 951-955 *1963*.]

Rubidium nitrate *[13126-12-0]* **M 147.5, m 305°, d $_4^{20}$ 3.11.** Crystallise the nitrate from hot water (0.25ml/g) by cooling to room temperature.

Rubidium perchlorate *[13510-42-4]* **M 184.9, d $_4^{20}$ 2.80, pK^{25} -2.4 to -3.1 (for $HClO_4$).** Crystallise the perchlorate from hot water (1.6ml/g) by cooling to 0°.

Rubidium sulfate *[7488-54-2]* **M 267.0, m 1050°, d $_4^{20}$ 6.31.** Crystallise the sulfate from water (1.2ml/g) between 100° and 0°.

Ruthenium (III) chloride dihydrate (β–form) *[14898-67-0]* **M 207.4 + H_2O, m >500°(dec), d $_4^{20}$ 3.11, pK $_1^{25}$ 3.40 (for aquo Rh^{3+} hydrolysis).** Dissolve the salt in H_2O, filter and concentrate to crystallisation in the

absence of air to avoid oxidation. Evaporate the solution in a stream of HCl gas while being heated just below its boiling point until a syrup is formed and finally to dryness at 80-100° and dried in a vacuum over H_2SO_4. When heated at 700° in the presence of Cl_2 the insoluble α-form is obtained [Grube in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1598 *1965*, Carlsen et al. *J Org Chem* **46** 3936 *1981*].

Ruthenium (IV) oxide *[12036-10-1]* **M 133.1, d $_4^{20}$ 6.97.** Free the oxide from nitrates by boiling in distilled water and filtering. A more complete purification is based on fusion in a KOH/KNO_3 mix to form the soluble ruthenate and perruthenate salts. The melt is dissolved in water, and filtered, then acetone is added to reduce the ruthenates to the insoluble hydrated oxide which, after making a slurry with paper pulp, is filtered and ignited in air to form the *anhydrous* oxide [Campbell et al. *Anal Chem* **33** 58 *1961*].

Samarium (II) iodide (SmI_2) *[32248-43-4]* **M 404.2, m 520°, b 1580.** A possible impurity is SmI_3 from which it is made. If present, grind the solid to a powder and heat it in a stream of pure H_2. The temperature (~ 500-600°) should be below the **m** (~628°) of SmI_3, since the molten compounds react very slowly. [Wetzel in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** pp 1149, 1150 *1965*.] It promotes a pseudo-Barbier reaction between aldehydes and ketones with aliphatic or alycyclic halides (see NdI_2) [Namy et al. *J Organomet Chem* **328** 81 *1987*.] It is a one-electron reducing agent [Brendt et al. *Aldrichim Acta* **24** 15 *1991*.]
SmI_2 in THF for reactions is prepared in a dry box, or dry gloves, filled with N_2 (not generally necessary for synthetic purposes, but should be used for Grignard-type conditions, i.e. exclusion of moisture) from samarium powder (3g, 20mmol, or distilled metal or ingot), placed in a flask fitted with a dropping funnel containing 1,2-diiodoethane (22.82g, 10mmol) in THF (250ml) which is added dropwise. The reaction has no induction period if the solvent is pure. [Excess metal can be re-used later.] An intense blue-green solution results with a SmI_2 concentration of 4 x 10^{-2} M in THF that can be diluted to 10^{-1} M. These solutions can be stored for a long time without loss of Sm^{2+} concentration if kept in an inert atmosphere in the presence of a small amount of metal. However, it is best to use them within a few days to ensure reproducible results. In addition to promoting coupling reactions, it is also a powerful and selective reducing agent for olefins [Girard et al. *J Am Chem Soc* **102** 2693 *1980*, see also Asano et al. *Synthesis* 1309 *2007*], promotes the reaction of chlorofluoroacetonitrile [359-05-7] with aldehydes to form cyanofluorohydrins in the presence of HMPA [Asano et al. *Synthesis* 1309 *2007*], intramolecular cyclisation reactions [Molander & McKie *J Org Chem* **59** 3186 *1994*], and intermolecular ketone-olefin coupling reactions [Kawatsura et al. *J Org Chem* **59** 6900 *1994*].

Selenious acid *[7783-00-8]* **M 129.0, m 70°(dec), d $_D^{20}$ 3.0, pK_1^{25} 2.62, pK_2^{25} 8.32 (H_2SeO_3).** Recrystallise the acid from water. On heating it loses water and SeO_2 sublimes. [Waitkins & Clark *Chem Rev* **36** 235 *1945*.]

Selenium *[7782-49-2]* **M 79.0, m 217.4°, d $_4^{20}$ 4.81.** Dissolve selenium in small portions in hot conc HNO_3 (2ml/g), filter and evaporate to dryness to give selenious acid which is then dissolved in conc HCl. Pass SO_2 gas through the solution whereby selenium (but not tellurium) precipitates. It is filtered off and washed with conc HCl. This purification process is repeated. The selenium is then converted twice to the selenocyanate by treating with a 10% excess of 3M aqueous KCN (CARE), heated for half an hour on a sand-bath and filtered. Add an equal weight of crushed ice to the cold solution, followed by an excess of cold, conc HCl, with stirring (in an efficient fume cupboard as HCN is evolved) which precipitates selenium powder. This is washed with water until colourless, and then with MeOH and is heated in an oven at 105°. Finally it is fused for 2 hours *in vacuo*. It is cooled, crushed and stored in a desiccator [Tideswell & McCullough *J Am Chem Soc* **78** 3036 *1956*].

Selenium dioxide *[7446-08-4]* **M 111.0, m 340°.** Purify it by sublimation at 315°, or by solution in HNO_3, precipitation of selenium which, after standing for several hours or boiling, is filtered off, then re-oxidised by HNO_3 and cautiously evaporated to dryness below 200°. The dioxide is dissolved in H_2O and again evaporated to dryness. In H_2O it forms selenious acid (see selenious acid above). Its solubility in H_2O is 70%w/w at 20°, and it is soluble in EtOH. It is a useful and selective oxidant. [Waitkins & Clark *Chem Rev* **36** 235 *1945*, Fehér in *Handbook of Preparative Inorganic Chemistry (Ed Brauer)* Academic Press Vol **I** p 421 *1963*.]

Silica *[7631-86-9 (colloidal), 60676-86-0 (Quartz, Cristobalite, sand), 112945-52-5 (fumed)]*. Purification of silica for high technology applications uses isopiestic vapour distillation from concentrated volatile acids and is absorbed in high purity water. The impurities remain behind. Preliminary cleaning to remove surface contaminants uses dip etching in HF or a mixture of HCl, H_2O_2 and deionised water [Phelan & Powell *Analyst* **109** 1299 *1984*].

Silica gel *[63231-67-4, 112926-00-8]*. Before use as a drying agent, silica gel is heated in an oven, then cooled in a desiccator. Conditions in the literature range from heating at 110° for 15 hours to 250° for 2-3 hours. Silica gel has been purified by washing with hot acid (in one case successively with *aqua regia*, conc HNO_3, then conc HCl; in another case it was digested overnight with hot conc H_2SO_4), followed by exhaustive washing with distilled water (one week in a Soxhlet apparatus has also been used), and prolonged oven drying. *Alternatively*, silica gel has been extracted with acetone until all soluble material was removed, then dried in a current of air, washed with distilled water and oven dried. Silica gel has also been washed successively with water, M HCl, water, and acetone, then activated at 110° for 15 hours.

Silicon monoxide *[10097-28-6]* **M 44.1, m > 1700°, d $_4^{20}$ 2.18.** Purify the monoxide by sublimation in a porcelain tube in a furnace at 1250° (4 hours) in a high vacuum (10^{-4}mm) in a stream of N_2. It is obtained as brownish black scales. [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 696 *1963*.]

Silicon tetrachloride *[10026-04-7]* **M 169.9, m -70°, b 57.6°, d $_4^{20}$ 1.483.** Distil it under vacuum and store it in sealed ampoules under N_2. It fumes in moist air and is very sensitive to moisture. It is soluble in organic solvents. It is a **strong irritant**. [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 682-683 *1963*.]

12-Silicotungstic acid (tungstosilicic acid; $H_4SiW_{12}O_{40}$) *[12027-43-9]* **M 2914.5.** Extract the acid with diethyl ether from a solution acidified with HCl. The diethyl ether is evaporated under vacuum, and the free acid is crystallised twice [Matijevic & Kerker *J Phys Chem* **62** 1271 *1958*].

Silver (metal) *[7440-22-4]* **M 107.9, m 961.9°, b 2212°, d $_4^{20}$ 10.5.** For purification by electrolysis, see Craig et al. [*J Res Nat Bur Stand* **64A** 381 *1960*]. For purification of crude, or silver residues to pure silver see Glemser & Sauer in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 1028-1030 *1963*, and for the preparation of *colloidal silver* see *ibid (Ed. Brauer)* p 1034.

Silver acetate *[563-63-3]* **M 166.9, dec on heating, d^{25} 3.259.** The salt is a white (or slightly gray if exposed to light) crystalline powder or lustrous needles, which should not be exposed to light for long periods. It can be purified by recrystallisation from H_2O (preferably containing a little AcOH) as its solubility (w/v) in cold H_2O is 1% and in boiling H_2O it is 35%. *Alternatively*, it is boiled with Ac_2O, the insoluble salt is collected and recrystallised from glacial AcOH. It is freely soluble in dilute HNO_3. Store in dark bottles away from light. [*Beilstein* **2** H 110, **2** I 48, **2** II 116, **2** III 189, **2** IV 112.]
It oxidises a green solution of U(IV) acetate in liquid NH_3 to the yellow U(VI) in a few hours with the formation of the tris complex $(NH_4)U(VI)O_2(AcO)_3$ [isolated], acetamide and Ag metal [Kline & Kershner *Inorg Chem* **5** 932 *1966*].
At a 0.2-2 mole%, AgOAc catalyses efficient cycloaddition reactions of methyl isocyanoacetate with olefin Michael-acceptors at ambient temperature to produce Δ^1- or Δ^2-pyrrolines in good yields. Isocyanoacetates undergo AgOAc catalysed cyclodimerisation to imidazoles in excellent yields in the absence of a suitable olefin. Also, when combined with azomethine ylide, AgOAc catalyses a 1,3-dipolar cycloaddition reaction in a one-pot sequential cascade process to yield the 7-azabicyclo[2.2.1]heptane ring system which is characteristic of the naturally occurring potent non-opioid analgesic epibatidine [originally isolated from the skin of the Ecuadoran poison frog *Epipedobates tricolor,* Spande et al. *J Am Chem Soc* **114** 3475 *1992*]. [Grigg et al. *Tetrahedron* **55** 2025 *1999*.]
When combined with I_2, AgOAc in aqueous or anhydrous AcOH reacts with olefins to form *vicinal* diols (glycols). The hydroxylations are not always *cis* [Woodward & Brutcher *J Am Chem Soc* **80** 209 *1958*, Ginsberg *J Am Chem Soc* **75** 5746 *1953*, Barkley et al. *J Am Chem Soc* **76** 5014 *1954*, Klass et al. *J Am Chem Soc* **77** 2329

1955, Slates & Wendler *J Am Chem Soc* **78** 3749 *1956*, Jefferies & Milligan *J Chem Soc* 2363 *1956*, Gunstone & Morris *J Chem Soc* 487 *1957*, Ellington et al. *J Chem Soc* 1327 *1966*], but can produce *cis/trans* diol mixtures depending on the olefin [Bunton & Carr *J Chem Soc* 770 *1963*].

Silver bromate *[7783-89-3]* **M 235.8, m dec on heating, d $_4^{20}$ 5.21.** It crystallises from hot water (80ml/g). It reacts with bromine water to form bromic acid ($HBrO_3$) which is a strong oxidising agent. Store it in the dark.

Silver bromide *[7785-23-1]* **M 187.8, m 432°, d $_4^{20}$ 6.47.** Purify it from Fe, Mn, Ni and Zn by zone melting in a quartz vessel under vacuum. It is insoluble in dilute HNO_3 or dilute NH_3 but is soluble in conc NH_3. Store it in the dark.

Silver chlorate *[7783-92-8]* **M 191.3, m 230°, b 270°(dec), d $_4^{20}$ 4.43.** Recrystallise the chlorate three times from water (10ml/g at 15°; 2ml/g at 80°). Store it in the dark. [Nicholson & Holley *Inorg Synth* **II** 4 *1946*, Glemser & Sauer in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 1037 *1963*.]

Silver chloride *[7783-90-6]* **M 143.3, m 455°, b 1550°, d $_4^{20}$ 5.56.** Recrystallise it from conc NH_3 solution by acidifying with HCl, filtering off the solid, washing it with H_2O and drying it in a vacuum. It is soluble in NH_3 and should be kept in the dark.

Silver chromate *[7784-01-2]* **M 331.8, d^{25} 5.625, pK$_1^{25}$ 0.74, pK$_2^{25}$ 6.49 (for H_2CrO_4).** Wash the red-brown powder with H_2O, dry it in a vacuum, then powder well and dry again in a vacuum at 90°/5 hours. Its solubility in H_2O is 0.0014% at 10°. Store it in the dark. [Cardillo & Shimizu *J Org Chem* **42** 4268 *1977*.]

Silver cyanide *[506-64-9]* **M 133.9, m dec at 320°, d $_4^{20}$ 3.95.** It is a **POISONOUS** white or grayish white powder. Stir it thoroughly with H_2O, filter, wash well with EtOH and dry it in air in the dark. It is very insoluble in H_2O (0.000023g in 100ml H_2O), but is soluble in HCN or aqueous KCN to form the soluble $Ag(CN)_2^{2-}$ complex. [Schnitz-Dumont *Chem Ber* **72** 298 *1939*, Randall & Halford *J Am Chem Soc* **52** 184 *1930*.]

Silver difluoride *[7783-95-1]* **M 145.9, m 690°, d $_4^{20}$ 4.7.** It is highly **TOXIC** because it liberates HF and F_2. It is very *hygroscopic* and reacts violently with H_2O. It is a powerful oxidising agent and liberates O_3 from dilute acids, and I_2 from I^- solution. Store it in quartz or iron ampoules. It is white when pure; otherwise it is brown-tinged. It is thermally stable up to 700°. [Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 241 *1963*.]

Silver fluoride *[7775-41-9]* **M 126.9, m 435°, b *ca* 1150°, d $_4^{20}$ 5.852.** The fluoride is a *hygroscopic* solid with a solubility of 135g/100ml of H_2O at 15°, and forms an insoluble basic fluoride in moist air. Purify it by washing with AcOH and dry $*C_6H_6$, then keep it in a vacuum desiccator at room temperature to remove $*C_6H_6$, and store it in opaque glass bottles. The flaky *hygroscopic* crystals darken on exposure to light. It *attacks* bone and teeth. [Sharpe *J Chem Soc* 4538 *1952*, Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 240 *1963*.]

Silver iodate *[7783-97-3]* **M 282.8, m >200°, d $_4^{20}$ 5.53.** Wash the iodate with warm dilute HNO_3, then H_2O and dry it at 100°, or recrystallise it from NH_3 solution by adding HNO_3, filtering, washing with H_2O and drying at 100°.

Silver nitrate *[7761-88-8]* **M 169.9, m 212°, b 444°(dec), d $_4^{20}$ 4.35.** Purify it by recrystallisation from hot water (solubility of $AgNO_3$ in water is 992g/100ml at 100° and 122g/100ml at 0°). It has also been purified by crystallisation from hot conductivity water by slow addition of freshly distilled EtOH.
CAUTION: avoid using EtOH for washing the precipitate; and avoid concentrating the filtrate to obtain further crops of $AgNO_3$ owing to the risk of EXPLOSION (as has been reported to us) caused by the presence of silver fulminate. When using EtOH in the purification, the apparatus should be enveloped in a strong protective shield. [Tully, *News Ed (Am Chem Soc)* **19** 3092 *1941*; Garin & Henderson *J Chem Educ*

47 741 *1970*, Bretherick, *Handbook of Reactive Chemical Hazards* 4th edn, Butterworths, London, 1985, pp 13-14.] Before being used as a standard in volumetric analysis, analytical reagent grade $AgNO_3$ should be finely powdered, dried at 120° for 2 hours, then cooled in a desiccator.
Recovery of silver residues as $AgNO_3$ **[use protective shield during the whole of this procedure]** can be achieved by washing with hot water and adding 16M HNO_3 to dissolve the solid. Filter this through glass wool and concentrate the filtrate on a steam bath until precipitation commences. Cool the solution in an ice-bath and filter the precipitated $AgNO_3$. Dry it at 120° for 2 hours, then cool it in a desiccator in a vacuum. Store it over P_2O_5 in a vacuum in the dark. *AVOID contact with hands due to formation of black stains.*

Silver nitrite *[7783-99-5]* **M 153.9, m 141°(dec), d $_4^{20}$ 4.45.** Crystallise the salt from hot conductivity water (70ml/g) in the dark. Dry it in the dark under vacuum. [Glemser & Sauer in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 1048 *1963*.]

Silver(I) oxide *[20667-12-3]* **M 231.7, m ~200°(dec), d $_4^{20}$ 7.13.** Leach the oxide with hot water in a Soxhlet apparatus for several hours to remove any entrained electrolytes. [Glemser & Sauer in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1037 *1965*.]

Silver (II) oxide *[1301-96-8]* **M 123.9, m >100°(dec), d^{25} 7.22.** It is soluble in 40,000 parts of H_2O, and should be protected from light. Stir it with an alkaline solution of potassium peroxysulfate ($K_2S_2O_8$) at 85-90°. The black AgO is collected, washed free from sulfate with H_2O made slightly alkaline and dried in air in the dark. [Hammer & Kleinberg *Inorg Synth* **IV** 12 *1953*.]

Silver perchlorate monohydrate *[14242-05-8 (H_2O), 7783-93-9 (anhydrous)]* **M 207.3, pK^{25} -2.4 to -3.1 (for $HClO_4$).** Reflux it with *benzene (6ml/g) in a flask fitted with a Dean and Stark trap until all the water is removed azeotropically (*ca* 4 hours). The solution is cooled and diluted with dry pentane (4ml/g of $AgClO_4$). The precipitated $AgClO_4$ is filtered off and dried in a desiccator over P_2O_5 at 1mm for 24 hours [Radell et al. *J Am Chem Soc* **83** 3958 *1961*]. It has also been recrystallised from perchloric acid. [**Caution** *due to its* **EXPLOSIVE** *nature in the presence of organic matter*.] Store it in the dark.

Silver permanganate *[7783-98-4]* **M 226.8, d $_4^{20}$ 4.49.** The salt forms violet crystals which can be crystallised from hot H_2O (soluble is 9g/L at 20°). Store it in the dark. This oxidising agent is decomposed by light. [Lux in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 1463 *1963*.]

Silver sulfate *[10294-26-5]* **M 311.8, m 652°, b 1085°(dec), d $_4^{20}$ 5.45.** Crystallise the sulfate form hot conc H_2SO_4 containing a trace of HNO_3, and dilute with H_2O while being strongly cooled. The precipitate is filtered off, washed with H_2O and dried at 120°. Its solubility in H_2O is 0.8% at 17°, and 1.46% at 100°. Store it in the dark. [Glemser & Sauer in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1042 *1965*.]

Silver tetraoxorhenate [$Ag(ReO_4)$] *[7784-00-1]* **M 358.1, pKa -1.25.** It is prepared by adding slowly, with ice cooling, H_2O_2 (35%, 100ml) to a stirred suspension of Re powder (10g, 54mmol) in H_2O (20ml) during 4 hours, stirring at ~25° for 30 minutes, and then at 80° for 3 hours. The mixture is filtered from a small amount of insoluble material, and the clear solution is treated with $Ag(NO_3)$ (10g, 59mmol), when $Ag(ReO_4)$ immediately separates as a white precipitate which is filtered off, washed with Et_2O (3 x 25ml) to remove H_2O and H_2O_2, and dried *in vacuo* to give the silver salt (18.7g, 97%). [Herrmann & Kratzer *Inorg Synth* **33** 111 *2002*, Herrmann et al. *Angew Chem, Int Ed. Engl* **36** 2652 *1997*.]

Silver thiocyanate *[1701-93-5]* **M 165.9, m 265°(dec), d $_4^{20}$ 3.746, pK^{25} -1.85 (for HSCN).** Digest the solid salt with dilute aqueous NH_4NCS, filter, wash it thoroughly with H_2O and dry it at 110° in the dark. It is soluble in dilute aqueous NH_3. *Alternatively*, dissolve it in strong aqueous NH_4NCS solution, filter and dilute with large volumes of H_2O when the Ag salt separates. The solid is washed with H_2O by decantation until free from NCS^- ions, collected, washed with H_2O, EtOH and dried in an air oven at 120°. It has also been purified by dissolving in dilute aqueous NH_3 when single crystals are formed by free evaporation of the solution in air. Store it in the

dark. [Garrick & Wilson *J Chem Soc* 835 *1932*, Occleshaw *J Chem Soc* 2405 *1932*, IR and Raman: *Acta Chem Scand* **13** 1607 *1957*, Lindqvist *Acta Cryst* **10** 29 *1957*.]

Sodium (metal) *[7440-23-5]* **M 23.0, m 97.5°, d $_4^{20}$ 0.97.** The metal is placed on a coarse grade of sintered-glass filter, melted under vacuum and forced through the filter using argon. The Pyrex apparatus is then re-evacuated and sealed off below the filter, so that the sodium could be distilled at 460° through a side arm and condenser into a receiver bulb which is then sealed off [Gunn & Green *J Am Chem Soc* **80** 4782 *1958*]. **EXPLODES and IGNITES in water.**

Sodium amide *[7782-92-5]* **M 39.0, m 210°.** It reacts *violently* with H_2O and is soluble in liquid NH_3 (1% at 20°). It should be stored in wax-sealed containers in small batches. It is very *hygroscopic* and absorbs CO_2 and H_2O. If the solid is discoloured by being yellow or brown in colour, then it should be destroyed as it can be highly **EXPLOSIVE.** It should be replaced if discoloured. It is best destroyed by covering it with much toluene and slowly adding dilute EtOH with stirring until all the ammonia is liberated (FUME CUPBOARD). [Dennis & Bourne *Inorg Synth* **I** 74 *1939*, Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 465 *1963*, Bergstrom *Org Synth* Coll Vol **III** 778 *1955*.]

Sodium ammonium hydrogen phosphate *[13011-54-6]* **M 209.1, m 79°(dec), d $_4^{20}$ 1.55.** Crystallise it from hot water (1ml/g).

Sodium arsenate heptahydrate *[10048-95-0]* **M 312.0, m 50 (loses $5H_2O$), m 130°, d $_4^{20}$ 1.88 pK_1^{25} 2.22, pK_2^{25} 6.98 (for H_3AsO_4).** Crystallise it from water (2ml/g).

Sodium azide *[26628-22-8]* **M 65.0, m 300°(dec, explosive), pK^{25} 4.72 (for HN_3).** Crystallise sodium azide from hot water or from water by adding absolute EtOH or acetone. Also purify it by repeated crystallisation from an aqueous solution saturated at 90° by cooling it to 10°, and adding an equal volume of EtOH. The crystals are washed with acetone, and the azide is dried at room temperature under vacuum for several hours in an Abderhalden pistol. Its solubility in H_2O is 42% at 18°, and in EtOH it is 0.22% at 0°. [Das et al. *J Chem Soc, Faraday Trans 1* **78** 3485 *1982*, Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 474-475 *1963*, Browne *Inorg Synth* **1** 79 *1939*, Frierson *Inorg Synth* **II** 139 *1946*.] **HIGHLY POISONOUS and potentially explosive.**

Sodium bicarbonate *[144-55-8]* **M 84.0, m ~50°(dec, -CO_2).** Crystallise it from hot water (6ml/g). The solid should not be heated above 40° due to the formation of carbonate.

Sodium bisulfite *[7631-90-5]* **M 104.1, d $_4^{20}$ 1.48.** Crystallise it from hot H_2O (1ml/g). Dry it at 100° under vacuum for 4 hours.

Sodium borate (borax) *[1330-43-4]* **M 201.2, m 741°, d $_4^{20}$ 2.37.** Most of the water of hydration is removed from the *decahydrate* (see below) by evacuation at 25° for three days, followed by heating to 100° and evacuation with a high-speed diffusion pump. The dried sample is then heated gradually to fusion (above 966°), allowed to cool gradually to 200°, then tranferred to a desiccator containing P_2O_5 [Grenier & Westrum *J Am Chem Soc* **78** 6226 *1956*]. [Becher in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 794-795 *1963*.]

Sodium borate (decahydrate, hydrated borax) *[1303-96-4]* **M 381.2, m 75°(loses $5H_2O$ at 60°), d $_4^{20}$ 1.73.** Crystallise the borate from water (3.3ml/g), keeping below 55° to avoid formation of the pentahydrate. Filter it off at the pump, wash it with water and equilibrate it for several days in a desiccator containing an aqueous solution saturated with respect to sucrose and NaCl. Borax can be prepared more quickly (but its water content is somewhat variable) by washing the recrystallised material at the pump with water, followed by 95% EtOH, then Et_2O, and dried in air at room temperature for 12-18 hours on a clock glass. [Becher in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 794-795 *1963*.]

Sodium borohydride *[16940-66-2]* **M 37.8, m ~400°(dec), d $_4^{20}$ 1.07.** After adding $NaBH_4$ (10g) to freshly distilled diglyme (120ml) in a dry three-necked flask fitted with a stirrer, nitrogen inlet and outlet, the mixture is

stirred for 30 minutes at 50° until almost all of the solid has dissolved. Stirring is stopped, and, after the solid has settled, the supernatant liquid is forced under N_2 pressure through a sintered-glass filter into a dry flask. [The residue is centrifuged to obtain more of the solution which is added to the bulk.] The solution is cooled slowly to 0° and then decanted from the white needles that separated. The crystals are dried by evacuating for 4 hours to give anhydrous $NaBH_4$. *Alternatively*, after the filtration at 50° the solution is heated at 80° for 2 hours to give a white precipitate of substantially anhydrous $NaBH_4$ which is collected on a sintered-glass filter under N_2, then evacuated at 60° for 2 hours [Brown et al. *J Am Chem Soc* **77** 6209 *1955*].
$NaBH_4$ has also been crystallised from isopropylamine by dissolving it in the solvent at reflux, cooling, filtering and allowing the solution to stand in a filter flask connected to a Dry-ice/acetone trap. After most of the solvent has passed over into the cold trap, crystals are removed with forceps, washed with dry diethyl ether and dried under vacuum. [Kim & Itoh *J Phys Chem* **91** 126 *1987*.] Somewhat less pure crystals were obtained more rapidly by using Soxhlet extraction with only a small amount of solvent and extracting for about 8 hours. The crystals that formed in the flask are filtered off, then washed and dried as before. [Stockmayer et al. *J Am Chem Soc* **77** 1980 *1955*.] Other solvents used for crystallisation include water and liquid ammonia.

Sodium bromate *[7789-38-0]* **M 150.9, m 381°, d $_4^{20}$ 3.3.** It is crystallised from hot water (1.1ml/g) to decrease contamination by NaBr, bromine and hypobromite. [Noszticzius et al. *J Am Chem Soc* **107** 2314 *1985*.]

Sodium bromide *[7647-15-6]* **M 102.9, m 747°, b 1390°, d $_4^{20}$ 3.2.** Crystallise the bromide from water (0.86ml/g) between 50° and 0°, and dry it at 140° under vacuum (this purification may not eliminate chloride ion).

Sodium carbonate *[497-19-8]* **M 106.0, m 858°, d $_4^{20}$ 2.5.** It crystallises from water as the *decahydrate* which is redissolved in water to give a near-saturated solution. By bubbling CO_2, $NaHCO_3$ is precipitated. It is filtered off, washed and ignited for 2 hours at 280° [MacLaren & Swinehart *J Am Chem Soc* **73** 1822 *1951*]. Before being used as a volumetric standard, analytical grade material should be dried by heating at 260-270° for 0.5 hour and allowed to cool in a desiccator. It has a transition point at 450°, and its solubility in water is 21.58% at 20° (*decahydrate* in solid phase), 49.25% at 35° (*heptahydrate* in solid phase) and 44.88% at 75° (*monohydrate* in solid phase) [Dönges in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 987-988 *1963*]. After three recrystallisations, technical grade Na_2CO_3 had Cr, Mg, K, P, Al, W, Sc and Ti at 32, 9.4, 6.6, 3.6, 2.4, 0.6, 0.2 and 0.2 ppm respectively; another technical source had Cr, Mg, Mo, P, Si, Sn and Ti at 2.6, 0.4, 4.2, 13.4, 32, 0.6, 0.8 ppm respectively.

Sodium chlorate *[7775-09-9]* **M 106.4, m 248°, b >300°(dec), d $_4^{20}$ 2.5.** It is crystallised from hot water (0.5ml/g). It is a strong oxidising agent, and should be kept clear from organic matter.

Sodium chloride *[7647-14-5]* **M 58.4, m 800.7°, b 1413°, d $_4^{20}$ 2.17.** It is recrystallised from a saturated aqueous solution (2.7ml/g) by passing in HCl gas, or by adding EtOH or acetone. It can be freed from bromide and iodide impurities by adding chlorine water to an aqueous solution and boiling it for some time to expel free bromine and iodine. Traces of iron can be removed by prolonged boiling of solid NaCl in 6M HCl; the crystals are then washed with EtOH and dried at *ca* 100°. Sodium chloride has been purified by sublimation in a stream of pre-purified N_2 and collected by electrostatic discharge [Ross & Winkler *J Am Chem Soc* **76** 2637 *1954*]. For use as a primary analytical standard, analytical reagent grade NaCl should be finely ground, dried in an electric furnace at 500-600° in a platinum crucible, and allowed to cool in a desiccator. For most purposes, however, drying at 110-120° is satisfactory.

Sodium chlorite *[7758-19-2]* **M 90.4, m ~180°(dec).** Crystallise the chlorite from hot water and store it in a cool place. It has also been crystallised from MeOH by counter-current extraction with liquid ammonia [Curti & Locchi *Anal Chem* **29** 534 *1957*]. A major impurity is chloride ion which can be removed by recrystallisation from 0.001M NaOH. [Schmeisser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 312 *1963*.]

Sodium chromate tetrahydrate *[10034-82-9]* **M 234.0, m ~20°(for $10H_2O$), d $_4^{20}$ 2.7, pK $_1^{25}$ 0.74, pK $_2^{25}$ 6.49 (for H_2CrO_4).** Crystallise the chromate from hot water (0.8ml/g). It is *deliquescent*.

Sodium cyanate *[917-61-3]* **M 65.0, m 550°, d $_4^{20}$ 1.893, pK^{25} 3.47 (for HCNO).** It forms colourless needles from EtOH. Its solubility in EtOH is 0.22g/100g at 0°C. It is soluble in H_2O but can be recrystallised from small volumes of it.

Sodium cyanoborohydride *[25895-60-7]* **M 62.8, m 240-242°(dec), d^{28} 1.20.** It is a very *hygroscopic* solid, soluble in H_2O (212% at 29°, 121% at 88°), tetrahydrofuran (37% at 28°, 42.2% at 62°), very soluble in MeOH, slightly soluble in EtOH, but insoluble in Et_2O, *C_6H_6 and hexane. It is stable to acid up to pH 3 but is hydrolysed in 12N HCl. The rate of hydrolysis at pH 3 is 10^{-8} times that of $NaBH_4$. The fresh commercially available material is usually sufficiently pure. If very pure material is required, one of the following procedures can be used [Lane *Synthesis* 135 *1975*]: (a) The $NaBH_3CN$ is dissolved in tetrahydrofuran (20% w/v), filtered and the filtrate is treated with a fourfold volume of CH_2Cl_2. The solid is collected and dried in a vacuum [Wade et al. *Inorg Chem.* **9** 2146 *1970*]. (b) $NaBH_3CN$ is dissolved in dry $MeNO_2$, filtered, and the filtrate is poured into a 10-fold volume of CCl_4 with vigorous stirring; the white precipitate is collected, washed several times with CCl_4 and dried in a vacuum (yield 75%) [Berschied & Purcell *Inorg Chem* **9** 624 *1970*]. (c) When the above procedures fail to give a clean product, then dissolve $NaBH_3CN$ (10g) in tetrahydrofuran (80ml) and add N MeOH/HCl until the pH is 9. Pour the solution with stirring into dioxane (250ml). The solution is filtered and heated to reflux. A further volume of dioxane (150ml) is added slowly with swirling. The solution is cooled slowly to room temperature, then chilled in ice and the crystalline dioxane complex is collected, dried in a vacuum for 4 hours at 25°, then 4 hours at 80° to yield the amorphous dioxane-free powder (6.7g) with purity >98% [Borch et al. *J Am Chem Soc* **93** 2897 *1971*]. The purity can be checked by iodometric titration [Lyttle et al. *Anal Chem* **24** 1843 *1952*].

Sodium dichromate *[7789-12-0]* **M 298.0, m 84.6° (2H_2O), 356° (anhydrous); b 400°(dec), d $_4^{25}$ 2.348.** Crystallise the dichromate from small volumes of H_2O by evaporation to crystallisation. Its solubility in H_2O is 238% at 0° and 508% at boiling. The red *dihydrate* is slowly dehydrated by heating at 100° for long periods. It is *deliquescent* and is a powerful oxidising agent—*do not place it in contact with skin— wash immediately as it is* ***caustic.*** (Possible **carcinogen**.)

Sodium dihydrogen orthophosphate dihydrate *[13472-35-0 (2H_2O), 10049-21-5 (H_2O), 7558-80-7 (anhydrous)]* **M 156.0, m 60°(dec), d $_4^{20}$ 1.91.** Crystallise it from warm water (0.5ml/g) by chilling.

Sodium dithionite dihydrate *[7631-94-9]* **M 242.1, m 110°(loses 2H_2O), 267°(dec), d $_4^{20}$ 2.19, pK$_{Est(1)}$ -3.4, pK $_2^{25}$ 0.49 (for dithionic acid).** Crystallise it from hot water (1.1ml/g) by cooling.

Sodium ferricyanide monohydrate *[14217-21-1, 13601-19-9 (anhydrous)]* **M 298.9, pK^{25} <1 (for ferricyanide).** Crystallise the ferricyanide from hot water (1.5ml/g) or by precipitation from 95% EtOH.

Sodium ferrocyanide decahydrate *[13601-19-9]* **M 484.1, m 50-80° (loses 10H_2O), 435°(dec), d $_4^{20}$ 1.46, pK$_3^{25}$ 2.57, pK$_4^{25}$ 4.35 (for ferrocyanide).** Crystallise it from hot water (0.7ml/g), until free of ferricyanide as shown by the absence of formation of Prussian Blue colour with ferrous sulfate solution.

Sodium fluoride *[7681-49-4]* **M 42.0, m 996°, b 1695°, d $_4^{20}$ 2.56.** Crystallise NaF from water by partial evaporation in a vacuum desiccator, or dissolve it in water, and precipitate *ca* half of it by adding EtOH. The precipitate is dried in an air oven at 130° for one day, and then stored in a desiccator over KOH. Its solubility in H_2O is 4% at 15° and 4.3% at 25°. [Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 235 *1963*].

Sodium fluoroborate *[13755-29-8]* **M 109.8, m 384°, d $_4^{20}$ 2.47, pK^{25} -4.9 (for fluoroboric acid $H_3O^+BF_4^-$).** Crystallise the fluoroborate from hot water (50ml/g) by cooling to 0°. *Alternatively*, free it from insoluble material by dissolving it in a minimum amount of water; then fluoride ions are removed by adding concentrated lanthanum nitrate in excess. After removing lanthanum fluoride by centrifugation, the supernatant is passed through a cation-exchange column (Dowex 50, Na^+-form) to remove any remaining lanthanum [Anbar & Guttman *J Phys Chem* **64** 1896 *1960*]. It has also been recrystallised from anhydrous MeOH and dried in a vacuum at 70° for 16 hours. Keep it dry as it is *hygrosopic*. [Delville et al. *J Am Chem Soc* **109** 7293 *1987*.]

Sodium fluorosilicate *[16893-85-9]* **M 188.1.** Crystallise it from hot water (40ml/g) by cooling.

Sodium hexafluorophosphate *[21324-39-0]* **M 167.9, pK_1^{25} ~0.5, pK_2^{25} 5.12 (for fluoro-phosphoric acid H_2PO_3F).** Recrystallise it from acetonitrile and dry it in a vacuum for 2 days at room temperature. It is an **irritant** and is *hygroscopic*. [Delville et al. *J Am Chem Soc* **109** 7293 *1987*.]

Sodium hexanitrocobaltate III ($Na_3[Co(NO)_6]$) *[13600-98-1]* **M 403.9.** Dissolve the salt (*ca* 60g) in H_2O (300ml), filter to obtain a clear solution, add 96% EtOH (250ml) with vigorous stirring. Allow the precipitate to settle for 2 hours, filter it off, wash it with EtOH (4 x 25ml), twice with Et_2O and dry it in air [Glemser in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1541 *1965*]. It forms yellow to brown crystals which are very soluble in H_2O, are decomposed by acid and form an insoluble K salt. Used for estimating potassium.

Sodium hydride (NaH) *[7646-69-7]* **M 24.00, m ~425°(dec), 800°(dec), d 1.396.** NaH is a granular gray powder which ignites in moist air and should be stored in an inert atmosphere. It is prepared in the laboratory by passing H_2 through a dispersion of Na in an industrial white oil at *ca* 250° [Mattson & Whaley *Inorg Synth* **5** 10 *1957*]. Like sodium it is very reactive with H_2O liberating hydrogen and NaOH. Fortunately it is commercially available as a 50 to 60% (w/w) dispersion in oil, which protects the NaH from the atmosphere, moderates its reaction with moisture, and can be handled routinely without recourse to using dry box techniques. In this form its reaction with H_2O (and alcohols) can be controlled safely, unlike the dry solid. The oil is freely soluble in petroleum ethers, hexanes, Et_2O, $*C_6H_6$, toluene and THF without affecting NaH reactivity. Removal of the oil is achieved by adding any of these solvents, decanting them off, repeating the process, then adding the desired reaction solvent to cover the NaH. NaH is insoluble in inert organic solvents and in liquid NH_3. When the dispersion is kept for long periods, or if the lid of the container in which it is kept is removed a considerable number of times, the NaH may have deteriorated and the mixture will contain a high percentage of NaOH and/or $NaHCO_3$ or Na_2CO_3. In this case a new batch should be used as laboratory purification is not practicable. The NaH content can, however, be determined by carefully adding H_2O to a known weight of the dispersion oil in a flask and measuring the volume of H_2 released using a manometer. The aqueous solution can then be titrated with standard acid (phenolphthalein indicator) to provide the total Na content. [For numerous examples of the use of NaH in organic synthesis see the various volumes of Fieser and Fieser's *Reagents in Organic Synthesis*.]

Sodium hydroxide (anhydrous) *[1310-73-2]* **M 40.0, m 323°, b 1390°, d_4^{20} 2.13.** Common impurities are water and sodium carbonate. Sodium hydroxide can be purified by dissolving 100g in 1L of pure EtOH, filtering the solution under vacuum through a fine sintered-glass disc to remove insoluble carbonates and halides. (This and subsequent operations should be performed in a dry, CO_2-free box.) The solution is concentrated under vacuum, using mild heating, to give a thick slurry of the mono-alcoholate which is transferred to a coarse sintered-glass disc and evacuated free of mother liquor. After washing the crystals several times with purified alcohol to remove traces of water, they are dried in a vacuum, with mild heating, for about 30 hours to decompose the alcoholate, leaving a fine white crystalline powder [Kelly & Snyder *J Am Chem Soc* **73** 4114 *1951*]. **CAUSTIC.**

Sodium hydroxide solutions (*caustic*), pK^{25} 14.77. Carbonate ion can be removed by passage through an anion-exchange column (such as Amberlite IRA-400; OH^--form). The column should be freshly prepared from the chloride form by slow prior passage of sodium hydroxide solution until the effluent gives no test for chloride ions. After use, the column can be regenerated by washing with dilute HCl, then water. Similarly, other metal ions are removed when a 1M (or more dilute) NaOH solution is passed through a column of Dowex ion-exchange A-1 resin in its Na^+-form.
Alternatively, carbonate contamination can be reduced by rinsing sticks of NaOH (analytical reagent quality) rapidly with H_2O, then dissolving in distilled H_2O, or by preparing a concentrated aqueous solution of NaOH and drawing off the clear supernatant liquid. (Insoluble Na_2CO_3 is left behind.) Carbonate contamination can be reduced by adding a slight excess of concentrated $BaCl_2$ or Ba $(OH)_2$ to a NaOH solution, shaking well and allowing the $BaCO_3$ precipitate to settle. If the presence of Ba in the solution is unacceptable, an electrolytic purification can be used. For example, sodium amalgam is prepared by the electrolysis of 3L of 30% NaOH

with 500ml of pure mercury for cathode, and a platinum anode, passing 15 Faradays at 4Amps, in a thick-walled polyethylene bottle. The bottle is then fitted with inlet and outlet tubes, the spent solution being flushed out by CO_2-free N_2. The amalgam is then washed thoroughly with a large volume of deionized water (with the electrolysis current switched on to minimise loss of Na). Finally, a clean steel rod is placed in contact in the solution with the amalgam (to facilitate hydrogen evolution), reaction being allowed to proceed until a suitable concentration is reached, before being transferred to a storage vessel and diluted as required [Marsh & Stokes *Aust J Chem* **17** 740 *1964*].

Sodium hypophosphite monohydrate *[10039-56-2]* **M 106.0 (see pK of hypophosphorous acid).** Dissolve it in boiling EtOH, cool and add dry Et_2O till all the salt separates. Collect and dry it in vacuum. It is soluble in 1 part of H_2O. It liberates PH_3 on heating and can *ignite* spontaneously when heated. The anhydrous salt is soluble in ethylene glycol (33% w/w) and propylene glycol (9.7%) at 25°.

Sodium iodate *[7681-55-2]* **M 197.9, m dec on heating, d_4^{20} 4.28.** Crystallise sodium iodate from water (3ml/g) by cooling.

Sodium iodide *[7681-82-5]* **M 149.9, m 660°, b 1304°, d_4^{20} 3.67.** Crystallise NaI from water/ethanol solution and dry it for 12 hours under vacuum, at 70°. *Alternatively*, dissolve it in acetone, filter it and cool it to -20°; the resulting yellow crystals are filtered off and heated in a vacuum oven at 70° for 6 hours to remove acetone. The NaI is then crystallised from very dilute NaOH, dried under vacuum, and stored in a vacuum desiccator [Verdin *Trans Faraday Soc* **57** 484 *1961*].

Sodium-mercury amalgam (sodium amalgam) *[11110-52-4]* **M depends on Na%, m (Na-Hg/m): 0.5%/0°, 1.0%/50°, 1.5%/100°, 2.0%/130°, 2.5%/156°, 3.3%/250°, 4.0%/320°.** The composition of the amalgam depends on the amount of Na added to the Hg. The reaction is exothermic and can be violent on first mixing. Generally 1-3% of Na in Hg is used, but higher amalgams can be obtained or prepared. Amalgams with more than 1% are solids with melting points that increase with the percentage of Na reaching > 360° at > 5% Na. Unless it has been prepared recently, it is always best to prepare the amalgam afresh. Three general procedures can be adopted. Use a fume cupboard as Hg vapour is **TOXIC**.
Method 1: For a ~1.2% amalgam, clean dry Na (9g) is placed in a 500ml flask with a reflux condenser, covered with dry toluene (20ml), and warmed gently until the Na has melted. Hg is added dropwise (separating funnel) with swirling. The exothermic reaction during the addition of the first few mls of Hg will cause the toluene to reflux, and Hg is added at such a rate as to keep the toluene refluxing gently. When addition is complete, allow the solvent to evaporate and the amalgam will solidify. Note that it is low melting (~50°) but will solidify on cooling. The solid amalgam is pulverised in a mortar (under N_2; to avoid spluttering of small quatities of solid Na-Hg, the mortar is covered with a thick filter paper, or cardboard, with a hole in the centre to allow the pestle to go through), and stored away from moisture in a tightly stoppered container. Up to a ~2%Na amalgam can be prepared by this method and using 15.2g Na and 750ml of Hg.
Method 2: To a flask with dry N_2 or Argon flushing continuously through it, clean freshly cut Na (22.8g) is added followed by Hg (10ml) from a separating funnel. The flask is warmed gently until the reaction commences then more Hg (total 750g) is added, with shaking, at such a rate as to keep the amalgam molten. After half the Hg is added, the amalgam begins to solidify and should be kept liquid by external heating. When addition is complete, the molten amalgam is poured (under N_2 or Argon) into a cold mortar and powdered (see Method 1 above). This provides a 3% amalgam. It should be stored as before. A 5%Na amalgam corresponds to a composition of $NaHg_2$, and a 20% amalgam corresponds to a composition of Na_2Hg.
Method 3: This method is convenient and commonly used. To the required volume of Hg in a wide-necked flask continuously flushed with N_2 or Argon, is added Na which is cut into small cubes, *ca* 5mm, and each cube is speared with a pointed glass rod and pushed into the liquid Hg. If traces of metal are not a concern, then it is better to use a stainless steel spike or a long tweezers to pick the Na cubes. A vigorous reaction occurs (perhaps with a flash of light occasionally) as each piece of Na dissolves into the Hg or amalgam. The temperature rises and the amalgam is kept in liquid form by the heat released on adding the Na. Do not allow the amalgam to solidify before all the Na is added. If it does, then heat the flask with a burner to keep the amalgam in a liquid state. To avoid damage from flying pieces of Na resulting from the vigorous reaction, the glass rod or metal pick spearing the Na cubes is inserted through a hole in the centre of a thick cardboard sheet which is placed over the mouth of the flask. The amalgam is then powdered and stored as above.

The amalgams are good reducing agents, and react with H_2O releasing "nascent H" and H_2, but much less vigorously than Na metal. [Brauer in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1802 *1965*, Audrieth *Inorg Synth* Vol **I** 5 *1939*, Babcock *Inorg Synth* **I** 10 *1939*, Holleman *Org Synth* Coll Vol **I** 555 *1941*, Renfrow & Hauser *Org Synth* Coll Vol **II** 609 *1943*, Deulofeu & Guerrero *Org Synth* Coll Vol **III** 589 *1955*.]

Sodium metaperiodate ($NaIO_4$) *[7790-28-5]* **M 213.9, m ~300°(dec), d $_4^{20}$ 4.17.** Recrystallise it from hot water. [Willard *Inorg Synth* **I** 170 *1939*, Bernays *Inorg Synth* **II** 212 *1946*.]

Sodium metasilicate pentahydrate *[6834-92-0]* **M 212.1, m 1088°, d $_4^{20}$ 2.4.** Crystallise it from aqueous 5% NaOH solution. [Schwartz *Z Anorg Allgem Chem* **126** 62 *1923*.]

Sodium molybdate dihydrate *[10102-40-6]* **M 241.9, m 100°(loses $2H_2O$), 687°, d $_4^{20}$ 3.28, pK^{25} 4.08 (for H_2MoO_4).** Crystallise it from hot water (1ml/g) by cooling to 0°.

Sodium nitrate *[7631-99-4]* **M 85.0, m 307°, b 380°, d $_4^{20}$ 2.26.** Crystallise $NaNO_3$ from hot water (0.6ml/g) by cooling to 0°, or from a concentrated aqueous solution by adding MeOH. Dry it under a vacuum at 140°. After two recrystallisations, technical grade sodium nitrate had K, Mg, B, Fe Al, and Li at 100, 29, 0.6, 0.4, 0.2 and 0.2 ppm respectively. (See KNO_3.)

Sodium nitrite *[7632-00-0]* **M 69.0, m 271°, b 320°, d $_4^{20}$ 2.17.** Crystallise $NaNO_2$ from hot water (0.7ml/g) by cooling to 0°, or from its own melt. Dry it over P_2O_5. (See KNO_2.)

Sodium oleate *[143-19-1]* **M 304.4, m 233-235°.** It is recrystallised from EtOH, and is dried in an oven at 100°. [*Beilstein* **2** H 465, **2** I 201, **2** II 434, **2** III 1405, **2** IV 1645.]

Sodium percarbonate ($Na_2CO_3.1.5H_2O_2$, hydrogen peroxide sodium carbonate adduct) *[15630-89-4]* **M 157.0, dec >120°.** This is not a per-salt, but is crystalline Na_2CO_3 with H_2O_2 of crystallisation with a specific composition. The crystals are consistent in having 1.5 molecules of H_2O_2 for each molecule of Na_2CO_3. It is a stable, inexpensive, a non-toxic source of H_2O_2 that is easily handled in the laboratory. It is prepared by the addition of excess of H_2O_2 (~3 to 15%) to a saturated aqueous solution of analytically pure Na_2CO_3 or $NaHCO_3$ at room temperature, stirring for 30 minutes then absolute EtOH is added. The percarbonate separates as white needle-shaped crystals. These are filtered off, washed with EtOH then Et_2O and dried in air. Its available oxygen content is determined by titration with standard $KMnO_4$ after acidification, and is ~13-15%. [Galwey & Hood *J Phys Chem* **83** 1810 *1979*.] Its solubility in H_2O at ~25° is ~1 mol/L and the pH is ~10.5. The kinetics of thermal decomposition have been studied in detail and are autocatalytic, and best represented by the equation $Na_2CO_3.1.5H_2O_2 = Na_2CO_3 + 1.5\ H_2O + 0.75O_2$. [Galwey & Hood *J Chem Soc, Faraday Trans* **78** 2815 *1982*.] It is a useful oxidising agent; converting nitriles to amides [Kabalka et al. *Synth Commun* **20** 1445 *1990*], oxidises α-diketones to dicarboxylic acids [Yang et al. *Synth Commun* **23** 1183 *1993*], it promotes the Baeyer-Villiger reaction in TFA at 0° [Olah et al. *Synthesis* 739 *1991*], forms epoxides with olefins, hydroxylates arenes, forms *N*-oxides, and converts sulfides into sulfones [Review: Muzart *Synthesis* 1325 *1995*], and converts selectively primary and secondary alcohols to their respective carbonyl compounds in the presence of catalytic amounts of $K_2Cr_2O_7$ and Adogen 464 [see 72749-59-8] [Muzart et al. *Tetrahedron Lett* **35** 1989 *1994*, Mohand & Muzart *Synth Commun* **25** 2373 *1995*]. It is a useful disinfectant and antiseptic, and is best stored blow 10°.
For X-ray crystallography, the crystals were prepared by slowly evaporating in air a solution of Na_2CO_3 in 10% H_2O_2, or in an excess of 15% H_2O_2 or D_2O_2 by standing for 1 hour at -5° before precipitating with EtOH, washing with EtOH and Et_2O, and drying in air. $Na_2{}^{13}CO_3$ was similarly used. The X-ray structure revealed the presence of H_2O_2 molecules hydrogen bonded to the CO_3 ions in the crystal, with two types of H_2O_2 molecules. The IR and Raman spectra of the normal, ^{13}C and ^{2}H isotopically substituted "percarbonates" are consistent with the X-ray data where the two H_2O_2 sites are different. The IR (nujol, 25°) of $Na_2CO_3.1.5H_2O_2$ has ν_{max} at 3050w, 2900m, 2720sh, 2490s, 2350m, 1550m, 985m, 960s, 973vw, 868w cm^{-1}, and $Na_2CO_3.1.5^2H_2O_2$ has ν_{max} at 2470w, 2210m, 1940sh, 1890s, 1820m, 1130m, 1040s, 1035m, 873vw, 869w, 660m, 635s cm^{-1} [Carrondo et al. *J Chem Soc, Dalton Trans* 2323 *1977*.]

Sodium perchlorate (anhydrous) *[7601-89-0]* **M 122.4, m 130°(for monohydrate), d $_4^{20}$ 2.02, pK^{25} -2.4 to -3.1 (for $HClO_4$).** Because its solubility in water is high (2.1g/ml at 15°) and it has a rather low-temperature coefficient of solubility, sodium perchlorate is usually crystallised from acetone, MeOH, water/ethanol or dioxane/water (33g dissolved in 36ml of water and 200ml of dioxane is added). After filtering and recrystallising, the solid is dried under vacuum at 140-150° to remove solvent of crystallisation. Basic impurities can be removed by crystallisation from hot acetic acid, followed by heating at 150°. If $NaClO_4$ is precipitated from distilled water by adding $HClO_4$ to the chilled solution, the precipitate contains some free acid. **EXPLOSIVE.**

Sodium phosphoamidate *[3076-34-4]* **M 119.0.** Dissolve it in water below 10°, and acetic acid is added dropwise to pH 4.0 so that the monosodium salt is precipitated. The precipitate is washed with water and Et_2O, then dried in air. Addition of one equivalent of NaOH to the solution gives the sodium salt, the solution being adjusted to pH 6.0 before use [Rose & Heald *Biochem J* **81** 339 *1961*].

Sodium-potassium alloy *[11135-81-2]* **M depends on composition, liquid.** This is generally in the form of a liquid globule from which an aliquot can be pipetted under dry N_2. It is available commercially in two ratios, *viz* K (78wt%), Na (22 wt%) and K (56 wt%), Na (44 wt%), in ampoules. A fresh *ca* ~5:1 $NaK_{2.8}$ liquid alloy can be prepared from clean K metal (77g, 2.0mol) and clean Na (16g, 0.7mol) by heating gently in xylene (100ml, freshly distilled from Na) until the metals coalesce, then dry oxygen-free diglyme (50ml) is added in order to keep the alloy in one globule (stir with a glass rod). Small globules of the alloy can be united by adding a few drops of *iso*-PrOH to the mixture. Cool to room temperature, and this can be stored under dry N_2 indefinitely. An aliquot can be safely pipetted out from the central globule by syringe equipped with a metal stopcock. The alloy can be more safely disposed of than the Na/Hg alloy, but must be handled carefully as it ignites in moist air. Residues are readily destroyed by a 1:1 muxture of *iso*-PrOH/petroleum ether (b 60-100°). [Ellis & Flom *J Organomet Chem* **99** 263 *1975*, Gilman & Young *J Org Chem* **1**, 315 *1936*.] When it reacts, e.g. in THF, to form metal carbonyl anions, and with some hydrocarbons, e.g. cyclopentadienes, diphenyl ether, it always forms the K-metallide, i.e. cyclopentadienylpotassium and C_6H_5K, and not the Na-metallide [Bryce-Smith & Turner *J Chem Soc* 861 *1953*, Ziegler & Schnell *Justus Liebigs Annalen Chemie* **437** 227 *1924*, Müller & Bunge *Chem Ber* **69** 2164 *1936*].

Sodium pyrophosphate decahydrate *[13472-36-1]* **M 446.1, d $_4^{20}$ 1.82, pK $_1^{25}$ 1.52, pK $_2^{25}$ 2.36, pK $_3^{25}$ 6.60, pK $_4^{25}$ 9.25 (for pyrophosphoric acid, $H_4P_2O_7$).** Crystallise the salt from hot H_2O and dry it in air at room temperature.

Sodium selenate *[13410-01-0]* **M 188.9, d $_4^{20}$ 3.21, pK $_1^{25}$ ~0, pK $_2^{25}$ 1.66 (for selenic acid, H_2SeO_4).** Crystallise sodium selenate from hot water. [Fehér in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 433 *1963*].

Sodium selenite *[10102-18-8]* **M 172.9, m >350°, pK $_1^{25}$ 2.62, pK $_2^{25}$ 8.32 (for H_2SeO_3).** Crystallise sodium selenite from a saturated aqueous solution where its solubility is 68% at 20° to give the *pentahydrate* salt. This yields the *anhydrous* salt on heating at 40°. [Fehér in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 431 *1963*].

Sodium silicate solution *[1344-09-8]* **pK $_1^{25}$ 9.51, pK $_2^{25}$ 11.77 (for silicic acid, H_4SiO_4)** Purify by contact filtration with activated charcoal.

Sodium sulfate decahydrate *[7727-73-3 ($10H_2O$), 7757-82-6 (anhydrous)]* **M 322.2, m 32°(dec), 884° (anhydrous), d $_4^{20}$ 2.68 (anhydrous).** Crystallise sodium sulfate from water at 30° (1.1ml/g) by cooling to 0°. It becomes anhydrous at 32°.

Sodium sulfide nonahydrate *[1313-84-4 ($9H_2O$), 1313-82-2 (anhydrous)]* **M 240.2, m ~50(loses H_2O), 950(anhydrous), d $_4^{20}$ 1.43 ($10H_2O$), 1.86 (anhydrous), pK $_1^{25}$ 7.04, pK $_2^{25}$ 11.96 (for H_2S).** Some purification of the hydrated salt can be achieved by selecting large crystals and removing the surface layer (contaminated with oxidation products) by washing with distilled water. Other metal ions can be removed from Na_2S solutions

by passage through a column of Dowex ion-exchange A-1 resin, Na^+-form. The hydrated salt can be rendered *anhydrous* by heating it in a stream of H_2 or N_2 until water is no longer evolved. (The resulting cake should not be heated to fusion because it is readily oxidised.) Recrystallise it from distilled water [Anderson & Azowlay *J Chem Soc, Dalton Trans* 469 *1986*]. Note that sodium sulfide hydrolyses in H_2O to form NaHS + H_2O, and is therefore alkaline. A 0.1N solution in H_2O is 86% hydrolysed at room temperature. Its solubility in H_2O is 8% at 0°, 12% at 20° and 30% at 50°. The *anhydrous* salt is obtained by allowing it to stand in a vacuum over conc H_2SO_4 or P_2O_5 at 45° to start with, then at 30-35° when the salt contains 4% of water. The last traces of water are removed by heating to 700° in a glass or porcelain tube in a stream of H_2 to give pure H_2S. [Fehér in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 358-360 *1963*.]

Sodium sulfite *[7757-83-7]* **M 126.0, d $_4^{20}$ 2.63.** Crystallise the sulfite from warm water (0.5ml/g) by cooling to 0°. Also purify it by repeated crystallisation from deoxygenated water inside a glove-box, and finally drying it under vacuum. [Rhee & Dasgupta *J Phys Chem* **89** 1799 *1985*.]

Sodium tetrametaphosphate *[13396-41-3]* **M 429.9, pK $_1^{25}$ 2.60, pK $_2^{25}$ 6.4, pK $_3^{25}$ 8.22, pK $_4^{25}$ 11.4 (tetrametaphosphoric acid, $H_4P_4O_{12}$).** Crystallise it twice from water at room temperature by adding EtOH (300g of $Na_4P_4O_{12}.H_2O$, 2L of water, and 1L of EtOH), wash it first with 20% EtOH then with 50% EtOH and dry it in air [Quimby *J Phys Chem* **58** 603 *1954*].

Sodium thioantimonate ($Na_3SbS_4.9H_2O$, Schlippe's salt) *[13776-84-6]* **M 481.1, m 87°, b 234°, d $_4^{20}$ 1.81.** Crystallise it from warm water (2ml/g made weakly alkaline with a few drops of dilute aqueous NaOH) by cooling to 0°. It forms a yellow *nonahydrate* which readily *effloresces* in air. [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 619 *1963*.]

Sodium thiocyanate *[540-72-7]* **M 81.1, m 300°, pK^{25} -1.85 (for HSCN).** It is recrystallised from EtOH or Me_2CO, and the mother liquor is removed from the crystals by centrifugation. It is very *deliquescent* and should be kept in an oven at 130° before use. It can be dried in a vacuum at 120°/P_2O_5 [Partington & Winterton *Trans Faraday Soc* **30** 1104 *1934*]. Its solubility in H_2O is 113% at 10°, 178% at 46°, 225.6% at 101.4°; in MeOH 35% at 15.8°, 51% at 48°, 53.5% at 52.3°; in EtOH 18.4% at 18.8°, 24.4% at 70.9°; and in Me_2CO 6.85% at 18.8° and 21.4% at 56° [Hughes & Mead *J Chem Soc* 2282 *1929*].
Sodium thiocyanate has also been recrystallised from water, acetonitrile or from MeOH using Et_2O for washing, then dried at 130°, or dried under vacuum at 60° for 2 days. [Strasser et al. *J Am Chem Soc* **107** 789 *1985*, Szezygiel et al. *J Am Chem Soc* **91** 1252 *1987*.] (The latter purification removes material reacting with iodine.) Sodium thiocyanate solutions can be freed from traces of iron by repeated batch extractions with Et_2O.

Sodium thiosulfate pentahydrate *[10102-17-7 (hydrate), 7772-98-7 (anhydrous)]* **M 248.2(anhydrous), m 48(rapid heat), d $_4^{20}$ 1.69, pK $_1^{25}$ 0.6, pK $_2^{25}$ 1.74 (for $H_2S_2O_3$).** Crystallise it from EtOH/H_2O solutions or from water (0.3ml/g) below 60° by cooling to 0°, and dry it at 35° over P_2O_5 under vacuum. [Foerster & Mommsen *Chem Ber* **57** 258 *1924*.] This salt is used as a secondary standard in volumetric analysis [Kilpatrick *J Am Chem Soc* **45** 2132 *1923*], and is used as "**Hypo**" in photography [Hargreaves & Dunningham *J Soc Chem Ind* **42** 147T *1923*.]

Sodium trimetaphosphate hexahydrate *[7785-84-4]* **M 320.2, m 53°, d $_4^{20}$ 1.79, pK $_2^{25}$ 1.64, pK $_3^{25}$ 2.07 (for trimetaphosphoric acid, $H_3P_3O_9$).** It is precipitated from an aqueous solution at 40° by adding EtOH. It is dried in air.

Sodium tripolyphosphate *[7758-29-4]* **M 367.9, pK $_1^{25}$ ~1, pK $_2^{25}$ 2.0, pK $_3^{25}$ 2.13, pK $_4^{25}$ 5.78, pK $_5^{25}$ 8.56 (for tripolyphosphoric acid, $H_5P_3O_{10}$).** Purify it by repeated precipitation from aqueous solution by slow addition of MeOH and dried in air. Also a solution of anhydrous sodium tripolyphosphate (840g) in water (3.8L) is filtered, MeOH (1.4L) is added with vigorous stirring to precipitate $Na_5P_3O_{10}.6H_2O$. The precipitate is collected on a filter, air dried by suction, then left to dry in air overnight. It is crystallised twice more in this way, using a 13% aqueous solution (w/w), and leaching the crystals with 200ml portions of water [Watters et al. *J Am Chem Soc* **78** 4855 *1956*]. Similarly, EtOH can be added to precipitate the salt from a filtered 12-15% aqueous solution, the final solution containing *ca* 25% EtOH (v/v). Air drying should be at a relative humidity of 40-

60%. Heat and vacuum drying should be avoided. [Quimby *J Phys Chem* **58** 603 *1954*, Klement in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 547 *1963*.]

Sodium tungstate dihydrate *[10213-10-2]* **M 329.9, m 698°, d $_4^{20}$ 4.18, pK $_1^{25}$ 2.20, pK $_2^{25}$ 3.70 (for tungstic acid, H_2WO_4).** The salt crystallises from hot water (0.8ml/g) on cooling to 0°. [Grüttner & Jender in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1727 *1965*].

Stannic chloride (tin IV chloride, stannic tetrachloride) *[7646-78-8]* **M 260.5, m -33°, -30.2°, b 114°/760mm, d $_4^{20}$ 2.23, pK^{25} 14.15 (for aquo Sn^{4+} hydrolysis).** $SnCl_4$ fumes in moist air due to formation of a hydrate. Fractionate it in a ground glass still and store it in the absence of air. Possible impurities are SO_2 and HCl [Baudler in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 729 *1963*]. It forms a solid *pentahydrate [10026-06-9]* which smells of HCl and is obtained when the *anhydrous* salt is dissolved in a small volume of H_2O. Also reflux it with clean mercury or P_2O_5 for several hours, then distil it under (reduced) N_2 pressure into a receiver containing P_2O_5. Finally redistil it. *Alternatively*, distil it from Sn metal under vacuum in an all-glass system and seal off in large ampoules. $SnCl_4$ is available commercially as 1M solutions in CH_2Cl_2 or hexane. **HARMFUL VAPOURS.**

Stannic iodide (SnI_4) *[7790-47-8]* **M 626.3, m 144°, b 340, d $_4^{20}$ 4.46.** It is recrystallised from anhydrous $CHCl_3$, dry it under vacuum and store it in a vacuum desiccator. It sublimes at 180°.

Stannic oxide (SnO_2) *[18282-10-5]* **M 150.7, m 1630°, d $_4^{20}$ 6.95.** Reflux it repeatedly with fresh HCl until the acid shows no tinge of yellow. The oxide is then dried at 110°.

Stannous chloride (anhydrous) *[7772-99-8]* **M 189.6, m 247°, b 606°, d $_4^{20}$ 3.95, pK $_1^{25}$ 1.7, pK $_2^{25}$ 3.7 (for aquo Sn^{2+} hydrolysis).** Analytical reagent grade stannous chloride *dihydrate* is dehydrated by adding it slowly to vigorously stirred, redistilled acetic anhydride (120g salt per 100g of anhydride) in a fume cupboard. After *ca* an hour, the anhydrous $SnCl_2$ is filtered on to a sintered-glass or Büchner funnel, washed free from acetic acid with dry Et_2O (2 x 30ml), and dried under vacuum. It is stored in a sealed container. [Stephen *J Chem Soc* 2786 *1930*, Williams *Org Synth* Coll Vol **III** 627 *1955*.]

Strontium bromide *[10476-81-0]* **M 247.4, m 643°, d $_4^{20}$ 4.22.** Crystallise the bromide from water (0.5ml/g). It is *deliquescent*. [Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 930 *1963*.]

Strontium chloride hexahydrate *[1025-70-4]* **M 266.6, m 61°(rapid heating), 114-150°(loses $5H_2O$), 868°(anhydrous).** It crystallises from warm water (0.5ml/g) on cooling to 0°. It dehydrates at 150-160° in a vacuum. [Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 930 *1963*.]

Strontium chromate *[7789-06-2]* **M 203.6, d $_4^{20}$ 3.9, pK $_1^{25}$ 0.74, pK $_2^{25}$ 6.49 (for H_2CrO_4).** Crystallise strontium chromate from water (40ml/g) by cooling.

Strontium hydroxide octahydrate *[1311-10-0 ($8H_2O$), 18480-07-4 (anhydrous)]* **M 265.8, m 100° (loses H_2O), d $_4^{20}$ 1.90, m 375 (anhydrous), d 3.63 (anhydrous).** Crystallise the hydroxide from hot water (2.2ml/g) by cooling to 0°.

Strontium nitrate *[10042-76-9]* **M 211.6, m 570°, b 645°, d $_4^{20}$ 2.99.** Crystallise it from hot water (0.5ml/g) by cooling to 0°.

Sulfamic acid *[5329-14-6]* **M 97.1, m 205°(dec), pK^{25} 0.99 (NH_2SO_3H).** Crystallise NH_2SO_3H from water at 70° (300ml per 25g), after filtering, by cooling a little and discarding the first batch of crystals (about 2.5g) before standing in an ice-salt mixture for 20 minutes. The crystals are filtered off by suction, washed with a small quantity of ice cold water, then twice with cold EtOH and finally with Et_2O. Dry it in air for 1 hour, then

store it in a desiccator over $Mg(ClO_4)_2$ [Butler et al. *Ind Eng Chem (Anal Ed)* **10** 690 *1938*]. For the preparation of primary standard material see *Pure Appl Chem* **25** 459 *1969*.

Sulfamide *[7803-58-9]* **M 96.1, m 91.5°.** Crystallise sulfamide from absolute EtOH. It decomposes at 250°. [Schenk in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 482-483 *1963*.]

Sulfur *[7704-34-9]* **M 32.1, m between 112.8° and 120°, depending on form.** Murphy, Clabaugh & Gilchrist [*J Res Nat Bur Stand* **64A** 355 *1960*] have obtained sulfur of about 99.999% purity by the following procedure: Roll sulfur was melted and filtered through a coarse-porosity glass filter funnel into a 2L round-bottomed Pyrex flask with two necks. Conc H_2SO_4 (300ml) was added to the sulfur (2.5kg), and the mixture was heated to 150°, stirring continuously for 2 hours. Over the next 6 hours, conc HNO_3 was added in about 2ml portions at 10-15 minutes intervals to the heated mixture. It was then allowed to cool to room temperature and the acid was poured off. The sulfur was rinsed several times with distilled water, then remelted, cooled, and rinsed several times with distilled water again, this process being repeated four or five times to remove most of the acid entrapped in the sulfur. An air-cooled reflux tube (*ca* 40cm long) was attached to one of the necks of the flask, and a gas delivery tube (the lower end about 2.5cm above the bottom of the flask) was inserted into the other. While the sulfur was boiled under reflux, a stream of helium or N_2 was passed through to remove any water, HNO_3 or H_2SO_4, as vapours. After 4 hours, the sulfur was cooled so that the reflux tube could be replaced by a bent air-cooled condenser. The sulfur was then distilled, rejecting the first and the final 100ml portions, and transferred in 200ml portions to 400ml glass cylinder ampoules (which were placed on their sides during solidification). After adding about 80ml of water, displacing the air with N_2, the ampoule was cooled, and the water was titrated with 0.02M NaOH, the process being repeated until the acid content was negligible. Finally, entrapped water was removed by alternate evacuation to 10mm Hg and refilling with N_2 while the sulfur was kept molten. The ampoules were then sealed. Other purifications include crystallisation from CS_2 (which is less satisfactory because the sulfur retains appreciable amounts of organic material), *benzene or *benzene/acetone, followed by melting and degassing. It has also been boiled with 1% MgO, then decanted, and dried under a vacuum at 40° for 2days over P_2O_5. [For the purification of S_6, "recrystallised S_8" and "Bacon-Fanelli sulfur" see Bartlett et al. *J Am Chem Soc* **83** 103, 109 *1961*.]

Sulfur dichloride (sulfur chloride, SCl_2**)** *[10545-99-0]* **M 103.0, m -78°, b 59°/760mm(dec), d $_4^{20}$ 1.621.** Distil sulfur chloride twice in the presence of a small amount of PCl_3 through a 12in Vigreux column, the fraction boiling between 55-61° being redistilled (in the presence of PCl_3), and the fraction distilling between 58-61° retained. (The PCl_3 is added to inhibit the decomposition of SCl_2 into S_2Cl_2 and Cl_2). The SCl_2 must be used as quickly as possible after distillation — within 1 hour at room temperature. The sample contains 4% of S_2Cl_2. On long standing this reaches 16-18%. [Fehér in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 371-372 *1963*.] **HARMFUL VAPOURS.**

Sulfur dioxide *[7446-09-5]* **M 64.1, m -72°, b -10°.** Dry it by bubbling through conc H_2SO_4 and by passage over P_2O_5, then through a glass-wool plug. Freeze it with liquid air and pump it to a high vacuum to remove dissolved gases. It is easily liquefied by compression (2.5 atmospheres at 15°), or by passing it through a glass spiral column in a freezing mixture of ice and salt. It is a colourless liquid with a density of 1.434 at 0°, which on rapid evaporation forms a snow white solid. It could be used as a solvent in certain reactions. **HARMFUL SUFFOCATING VAPOURS.**

Sulfuric acid (oil of vitriol) *[7664-93-9]* **M 98.08, d $_4^{20}$ 1.836 (96-98%), 1.805 (100%), m 3.0° (98%), 10.36° (100%), b 330.0 ±0.5° (100%), dec > 340.0°, *dihydrate* M 134.11, m -38.9°, b 167°, pK $_1^{25}$ ~ -8.3, pK $_2^{25}$ 1.99.** Sulfuric acid, and also 30% fuming H_2SO_4, can be distilled in an all-Pyrex system, optionally from potassium persulfate. It has been purified by fractional crystallisation of the *monohydrate* from the liquid. It has a very strong dehydrating action and attacks skin—wash immediately with cold H_2O ***and protect eyes***; otherwise the skin can be scarred for life ***and could be blinding***. It is very *hygroscopic* and has been used as a desiccant in desiccators. Dilution with H_2O is highly exothermic, and because the concentrated acid is much more dense than H_2O it is diluted by running the concentrated acid down the side of the container of H_2O with slow stirring while cooling the outside of the container in an ice bath. If these precautions are not taken, the H_2O is likely to splatter and boil vigorously over. **CORROSIVE.**

Sulfuric acid (fuming) (oleum) *[8014-95-7]* **M 98.08 (+ *x* SO_3).** This is sulfuric acid with various amounts of SO_3 dissolved in it up to 80% free SO_3. The specific gravities, **Sp gr** d_4^{20}, of oleums (% free SO_3) are: 1.899 (15%), 1.915 (20%), 1.952 (30%), 2.001 (50%), 2.102 (60% maximum density) and 1.949 (80%). They are an almost colourless viscous liquids which emit choking fumes of SO_3, and should be handled with great care: **use eye and body protection**. It reacts explosively with H_2O to form strong sulfuric acid, and is a strong sulfonating agent.

Sulfur monochloride (sulfur monochloride, S_2Cl_2**)** *[10025-67-9]* **M 135.0, m -77°; b 19.1°, 29-30°/12mm, 72°/100mm, 138°/760mm, d** d_4^{20} **1.677, n** n_D^{20} **1.67.** It is a *pungent, irritating golden yellow liquid.* When impure its colour is orange to red due to SCl_2 formed. It fumes in moist air and liberates HCl, SO_2 and H_2S in the presence of H_2O. Distil it and collect the fraction boiling above 137° at atmospheric pressure. Fractionate this fraction over sulfur at *ca* 12mm using a ground glass apparatus (**b** 29-30°). *Alternatively*, purify it by distillation below 60° from a mixture containing sulfur (2%) and activated charcoal (1%), under reduced pressure (e.g. 50mm). It is soluble in EtOH, $*C_6H_6$, Et_2O, CS_2 and CCl_4. Store it in a closed container in the dark in a refrigerator. [Fehér in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 371 *1963*.] **HARMFUL VAPOURS.**

Sulfuryl chloride (SO_2Cl_2) *[7791-25-2]* **M 135.0, m -54.1°**, **b 69.3°/760mm, d** d_4^{20} **1.67, n** n_D^{20} **1.44.** It is a *pungent, irritating colourless liquid.* It becomes yellow with time due to decomposition to SO_2 and HCl. Distil it and collect fraction boiling below 75°/atm which is mainly SO_2Cl_2. To remove HSO_3Cl and H_2SO_4 impurities, the distillate is poured into a separating funnel filled with crushed ice and *briefly* shaken. The lower cloudy layer is removed, dried for some time in a desiccator over P_2O_5 and finally fractionate it at atmospheric pressure. The middle fraction boils at 69-70° and is pure SO_2Cl_2. It decomposes gradually in H_2O to H_2SO_4 and HCl. It reacts **violently** with EtOH and MeOH and is soluble in $*C_6H_6$, toluene, Et_2O and acetic acid.
[Fehér in *Handbook of Preparative Inorganic Chemistry (Ed Brauer)* Academic Press Vol **I** p 383 *1963*, Allen & Maxson *Inorg Synth* **I** 114 *1939*]. **HARMFUL VAPOURS.**

Tantalium (V) chloride (tantalium pentachloride) *[7721-01-9]* **M 358.2, m 216.2°, 216.5-220°, b 239°/atm, d** d_4^{20} **3.68.** Purify it by sublimation in a stream of Cl_2. It forms colourless needles when pure (yellow when contaminated with even less than 1% of $NbCl_5$). It is sensitive to H_2O; even in conc HCl it decomposes to tantalic acid. It is soluble in EtOH. [Rolsten *J Am Chem Soc* **80** 2952 *1958*, Brauer in *Handbook of Preparative Inorganic Chemistry (Ed Brauer)* Academic Press Vol **II** p 1302 *1965*.]

Telluric acid *[7803-68-1]* **M 229.6, pK** K_1^{25} **7.70, pK** K_2^{25} **11.04 (H_6TaO_6).** Crystallise it once from nitric acid, then repeatedly from hot water (0.4ml/g). [Fehér in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** pp 451-453 *1963*.]

Tellurium *[13494-80-9]* **M 127.6, m 450°.** Purify tellurium by zone refining and repeated sublimation to an impurity of less than 1 part in 10^8 (except for surface contamination by TeO_2). [Machol & Westrum *J Am Chem Soc* **80** 2950 *1958*.] Tellurium is volatile at 500°/0.2mm. It has also been purified by electrode deposition [Mathers & Turner *Trans Amer Electrochem Soc* **54** 293 *1928*].

Tellurium dioxide *[7446-07-3]* **M 159.6, m 733°, d** d_4^{20} **6.04.** Dissolve it in 5M NaOH, filter it and precipitate it by adding 10M HNO_3 (CARE) to the filtrate until the solution is acid to phenolphthalein. After decanting the supernatant, the precipitate is washed five times with distilled water, then dried for 24 hours at 110° [Horner & Leonhard *J Am Chem Soc* **74** 3694 *1952*].

Terbium oxide *[12037-01-3]* **M 747.7, pK^{25} 8.16 (for Tb^{3+} hydrolysis).** Dissolve it in acid (e.g. perchloric acid), precipitate it as its oxalate and ignite the oxalate at 650°.

Thallium (III) nitrate trihydrate [TTN, thallic nitrate trihydrate, $Tl(NO_3)_3\ 3H_2O$] *[13453.38-8]* **M 444.4, m 102-105°.** It is prepared from Tl(III)oxide (45g, [1314-32-5]) by stirring it in hot concentrated HNO_3 (120ml) at ~50° for 30 minutes when all the oxide dissolves to give a clear colourless solution. On cooling to 0°, a white solid crystallises out. It is filtered off, washed with a little cold H_2O, dilute HNO_3, dried in a vacuum desiccator over P_2O_5 to give TTN (75g, 85%) as hard, colourless crystals which should be stored in a cold tightly sealed container. Treat carefully as it is **POISONOUS**. [McKillop et al. *J Am Chem Soc* **95** 3635 *1973*.]

Thallous bromide *[7789-40-4]* **M 284.3, m 460°.** Thallous bromide (20g) is purified by refluxing for 2-3 hours with water (200ml) containing 3ml of 47% HBr. It is then washed until acid-free, heated to 300° for 2-3 hours and stored in brown bottles. It solubility in H_2O (w/w) is 0.034% at 0°, 0.048% at 20°, and 0.204% at 100°. [Dönges in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 870 *1963*]. **POISONOUS.**

Thallous carbonate *[6533-73-9]* **M 468.7, m 268-270°.** It crystallises from hot water (4ml/g) on cooling. **POISONOUS.**

Thallous chlorate *[13453-30-0]* **M 287.8, d_4^{20} 5.05.** It crystallises from hot water (2ml/g) on cooling. Its solubility in H_2O (w/w) is 0.17% at 0°, 0.32% at 20°, and 2.4% at 100°. [Dönges in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 870 *1963*]. **POISONOUS.**

Thallous chloride *[7791-12-0]* **M 239.8, m 429.9°, b 806°, d_4^{20} 7.0.** Recrystallise it from 1% HCl and wash it until acid-free, or crystallise it from hot water (50ml/g), then dry it at 140° and store it in brown bottles. Also purify it by subliming it in a vacuum, followed by treatment with dry HCl gas and filtering while molten. (It is soluble in 260 parts of cold water and 70 parts of boiling water). **POISONOUS.**

Thallous hydroxide *[12026-06-1]* **M 221.4, m 139°(dec), pK^{25} 13.2 (for Tl^+).** It crystallises from hot water (0.6ml/g) on cooling. **POISONOUS.**

Thallous iodide *[7790-30-9]* **M 331.3, m 441.8°, b 824°, d_4^{20} 7.1.** Reflux it for 2-3 hours with water containing HI, then wash it until acid-free, and dry it at 120°. Store it in brown bottles. [Dönges in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 870 *1963*.] **POISONOUS.**

Thallous nitrate *[10102-45-1]* **M 266.4, m 206°, b 450°(dec), d_4^{20} 5.55.** The nitrate crystallises from warm water (1ml/g) on cooling to 0°. **POISONOUS.**

Thallous perchlorate *[13453-40-2]* **M 303.8, pK^{25} -2.4 to -3.1 (for $HClO_4$).** It crystallises from hot water (0.6ml/g) on cooling. Dry it under vacuum for 12 hours at 100° (protect from possible **EXPLOSION**).

Thallous sulfate *[7446-18-6]* **M 504.8, m 633°, d_4^{20} 6.77.** The sulfate crystallises from hot water (7ml/g) by cooling; then dry it under vacuum over P_2O_5. It is **POISONOUS.**

Thionyl chloride *[7719-09-7]* **M 119.0, b 77°, d_4^{20} 1.636.** Crude $SOCl_2$ can be freed from sulfuryl chloride, sulfur monochloride and sulfur dichloride by refluxing it with sulfur and then fractionally distilling twice. [The $SOCl_2$ is converted to SO_2 and sulfur chlorides. The S_2Cl_2 (**b** 135.6°) is left in the residue, whereas SCl_2 (**b** 59°) passes over in the forerun.] The usual purification is to distil it from quinoline (50g $SOCl_2$ to 10g quinoline) to remove acid impurities, followed by distillation from boiled linseed oil (50g $SOCl_2$ to 20g of oil). Precautions must be taken to exclude moisture.
Thionyl chloride is used extensively in organic syntheses and can be prepared by distillation of technical $SOCl_2$ in the presence of diterpene (12g/250ml $SOCl_2$), and avoiding overheating. Further purification is achieved by redistillation from linseed oil (1-2%) [Rigby *Chem Ind (London)* 1508 *1969*]. Gas chromatographically pure material is obtained by distillation from 10% (w/w) triphenyl phosphite [Friedman & Wetter *J Chem Soc (A)* 36 *1967*, Larsen et al. *J Am Chem Soc* **108** 6950 *1986*]. **HARMFUL VAPOURS.**

Thorium chloride *[10026-08-1]* **M 373.8, pK_1^{25} 10.45, pK_2^{25} 10.62, pK_3^{25} 10.80, pK_4^{25} 11.64 (for aquo Th^{4+}).** It is freed from anionic impurities by passing a 2M solution of $ThCl_4$ in 3M HCl through a Dowex-1 anion-resin column. The eluate is partially evaporated to give crystals which are filtered off, washed with Et_2O and stored in a desiccator over H_2SO_4 to dry. *Alternatively*, a saturated solution of $ThCl_4$ in 6M HCl is filtered through quartz wool and extracted twice with ethyl, or isopropyl ether (to remove iron), then evaporated to a small volume on a hot plate. (Excess silica precipitates and is filtered off. The filtrate is cooled to 0^o and saturated with dry HCl gas.) It is shaken with an equal volume of Et_2O, shaken with HCl gas, until the mixture becomes homogeneous. On standing, $ThCl_4.8H_2O$ precipitates out and is filtered off, washed with Et_2O and dried [Kremer *J Am Chem Soc* **64** 1009 *1942*].

Thorium sulfate tetrahydrate *[10381-37-0]* **M 496.2, m 42^o(loses H_2O), d_4^{20} 2.8.** Crystallise it from water. The solubility of the *decahydrate* increases with increase in temperature, whereas the solubility of the *tetrahydrate* decreases with increase of temperature.

Tin (powder) *[7440-31-5]* **M 118.7.** Tin powder is purified by adding it to about twice its weight of 10% aqueous NaOH and shaking vigorously for 10 minutes. (This removes oxide film and stearic acid or similar material that is sometimes added for pulverisation.) It is then filtered, washed with water until the washings are no longer alkaline to litmus, rinsed with MeOH and dried in air. [Sisido et al. *J Am Chem Soc* **83** 538 *1961*.]

Titanium tetrabromide *[7789-68-6]* **M 367.5, m 28.3^o, b 233.5^o, d_4^{20} 3.3.** Purify it by distillation. The distillate forms light orange hygroscopic crystals. Store it in the dark under N_2 preferably in sealed brown glass ampules. [Olsen & Ryan *J Am Chem Soc* **54** 2215 *1932*.]

Titanium tetrachloride *[7550-45-0]* **M 189.7, b 136.4^o, 154^o, d 1.730, pK_1^{25} 0.3, pK_2^{25} 1.8, pK_3^{25} 2.1, pK_4^{25} 2.4 (for aquo Ti^{4+} hydrolysis).** Reflux it with mercury or a small amount of pure copper turnings to remove the last traces of colour [due to $FeCl_3$ and VCl_4], then distil it under N_2 in an all-glass system, taking precautions to exclude moisture. Clabaugh et al. [*J Res Nat Bur Stand* **55** 261 *1955*] removed organic material by adding aluminium chloride hexahydrate as a slurry with an equal amount of water (the slurry being *ca* one-fiftieth the weight of $TiCl_4$), refluxed it for 2-6 hours while bubbling in chlorine, the excess of which is subsequently removed by passing a stream of clean dry air. The $TiCl_4$ is then distilled, refluxed with copper and again distilled, taking precautions to exclude moisture. Volatile impurities are then removed using a technique of freezing, pumping and melting. The *titanium tetrachloride 2-tetrahydrofuran complex,* $TiCl_4(THF)_2$, [31011-57-1] **M 333.9,** has **m 126-128^o** and is easier to handle than $TiCl_4$ [Hamilton et al. *Organometallics* **75** 2881 *1953*, Abrahamson et al. *Organometallics* **3** 1379 *1984*, *Beilstein* **17/1** V 33]. [Baxter & Fertig *J Am Chem Soc* ***45*** 1228 *1923*, Baxter & Butler *J Am Chem Soc* ***48*** 3117 *1926*.] **HARMFUL VAPOURS.**

Titanium trichloride *[7705-07-9]* **M 154.3, m >500^o, pK_1^{25} 2.55 (for hydrolysis of Ti^{3+} to $TiOH^{2+}$).** It is a brown purple powder that is very reactive to H_2O and pyrophoric when dry. It should be manipulated in a dry box. It is soluble in CH_2Cl_2 and tetrahydrofuran, and is used as a M solution in these solvents in the ratio of 2:1, and stored under N_2. It is a powerful reducing agent. [Ingraham et al. *Inorg Synth* **VI** 52 *1960*.]

Titanyl sulfate ($TiOSO_4.2H_2O$) *[13825-74-6]* **M 160.0.** Dissolve it in water, filter and crystallise it three times from boiling 45% H_2SO_4, washing with EtOH to remove excess acid, then with Et_2O. Dry it in air for several hours, then in an oven at 105-110^o. [Hixson & Fredrickson *Ind Eng Chem* **37** 678 *1945*.]

Triiron dodecacarbonyl *[17685-52-8]* **M 503.7, m 140^o(dec).** It usually contains 10% by weight of MeOH as stabiliser. This can be removed by keeping it in a vacuum at 0.5mm for at least 5 hours. It can be sublimed slowly at high vacuum and is soluble in organic solvents. [Landesberg et al. *J Org Chem* **37** 930 *1972*, Case & Whiting *J Chem Soc* 4632 *1960*, King & Stone *Inorg Synth* **VII** 193 *1963*.] **TOXIC.**

Trisodium orthophosphate dodecahydrate *[10101-89-0]* **M 380.1, pK_1^{25} 2.15, pK_2^{25} 7.21, pK_3^{25} 12.33 (for H_3PO_4).** It crystallises from warm dilute aqueous NaOH (1ml/g) on cooling to 0^o.

Tritium *[10028-17-8]* **M 6.0.** Purify tritium from hydrocarbons and ^3H by diffusion through the wall of a hot nickel tube [Landecker & Gray *Rev Sci Instrum* **25** 1151 *1954*]. **RADIOACTIVE.**

Tungsten (rod) *[7440-33-7]* **M 183.6. m 3410°, b 5900°, d $_4^{20}$ 19.0.** Clean the solid with conc NaOH solution, rub it with very fine emery paper until its surface is bright, wash it with previously boiled and cooled conductivity water and dry it with filter paper. [Hein & Herzog in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1417 *1965*.]

Tungsten hexacarbonyl *[14040-11-0]* **M 351.9, d $_4^{20}$ 2.650.** Sublime it *in vacuo* before use [Connoe et al. *J Chem Soc, Dalton Trans* 511 *1986*]. **TOXIC.**

Tungsten (VI) trichloride *[13283-01-7]* **M 396.6, m 265°(dec), 275°, b 346°, d $_4^{25}$ 3.520, pK$_1^{25}$ 2.20, pK$_2^{25}$ 3.70 (for tungstic acid, H_2WO_4).** Sublime it in a stream of Cl_2 in a high temperature furnace and collect it in a receiver cooled in a Dry-ice/acetone bath in an inert atmosphere because it is sensitive to moisture. It is soluble in CS_2, CCl_4, $CHCl_3$, $POCl_3$, $*C_6H_6$, petroleum ether and Me_2CO. Its solutions decompose on standing. Good crystals can be obtained by heating WCl_6 in CCl_4 to 100° in a sealed tube, followed by slow cooling (tablets of four-sided prisms). Store it in a desiccator over H_2SO_4 in the dark. [Leitzke & Holt *Inorg Synth* **III** 163 *1950*, Parterfield & Tyree *Inorg Synth* **IX** 133 *1967*, Hein & Herzog in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1420 *1965*.]

Uranium hexafluoride *[7783-81-5]* **M 352.0, b 0°/17.4mm, 56.2°/765mm, m 64.8°, pK^{25} 1.68 (for hydrolysis of U^{4+} to UOH^{3+}).** Purify uranium hexafluoride by fractional distillation to remove HF. Also purify it by low-temperature trap-to-trap distillation over pre-dried NaF [Anderson & Winfield *J Chem Soc, Dalton Trans* 337 *1986*].

Uranium trioxide *[1344-58-7]* **M 286.0, d $_4^{20}$ 7.29.** The oxide is dissolved in $HClO_4$ (to give a uranium content of 5%), and the solution is adjusted to pH 2 by addition of dilute ammonia. Dropwise addition of 30% H_2O_2, with rapid stirring, precipitated U(VI) peroxide, the pH being held constant during the precipitation, by addition of small amounts of the ammonia solution. Then H_2O_2 is added until further quantities caused no change in pH. After stirring for 1 hour, the slurry is filtered through coarse filter paper in a Büchner funnel, washed with 1% H_2O_2 acidified to pH 2 with $HClO_4$, then heated at 350° for three days in a large platinum dish [Baes *J Phys Chem* **60** 878 *1956*].

Uranyl nitrate ($UO_2(NO_3)_2$ $6H_2O$) *[13520-83-7]* **M 502.1, m 60.2°, b 118°, d^{25} 2.807, pK^{25} 5.82 (for aquo UO_2^{2+}).** Crystallise the nitrate from water by cooling to -5°, taking only the middle fraction of the solid which separates. Dry the *deliquescent* rhombic yellow crystals of the *hexahydrate* over 35-40% H_2SO_4 in a vacuum desiccator. The crystals reflect a greenish lustre. They are remarkable because on crushing, rubbing or shaking they show *triboluminescence* with occasional detonation. They are very soluble in EtOH, and solutions of the nitrate in Et_2O can explode in the presence of sunlight.

Vanadium (metal) *[7440-62-2]* **M 50.9, m 1910°, d $_4^{20}$ 6.0.** Clean the metal by rapid exposure consecutively to HNO_3, HCl, HF, de-ionised water and reagent grade acetone, then dry it in a vacuum desiccator. [Brauer in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** pp 1252-1255 *1965*.]

Vanadyl trichloride ($VOCl_3$) *[7727-18-6]* **M 173.3, m-79.5°, b 124.5-125.5°/744mm, 127.16°/760mm, d^0 1.854, d^{32} 1.811.** $VOCl_3$ should be lemon yellow in colour. If it is red, it may contain VCl_4 and Cl_2. Fractionally distil it, and then redistil it over metallic Na, but be careful to leave some residue because the residue can become **EXPLOSIVE** in the presence of the metal. **USE A SAFETY SHIELD** *and avoid contact with moisture.* It readily hydrolyses to vanadic acid and HCl. Store it in a tightly closed container or in sealed ampoules under N_2. [Brown & Griffitts *Inorg Synth* **I** 106 *1939*, Brown & Griffitts *Inorg Synth* **IV** 80 *1953*.]

Water *[7732-18-5]* **M 18.0, m 0°, b 100°, pK^{25} 14.00.** Conductivity water (specific conductance *ca* 10^{-7} mho) can be obtained by distilling water in a steam-heated tin-lined still, then, after adding 0.25% of solid NaOH and 0.05% of $KMnO_4$, distilling once more from an electrically heated Barnstead-type still, taking the middle fraction into a Jena glass bottle. During these operations suitable traps must be used to protect against entry of CO_2 and NH_3. Water, only a little less satisfactory for conductivity measurements (but containing traces of organic material) can be obtained by passing ordinary distilled water through a mixed bed ion-exchange column containing, for example, Amberlite resins IR 120 (cation exchange) and IRA 400 (anion exchange), or Amberlite MB-1. This treatment is also a convenient one for removing traces of heavy metals. (The metals Cu, Zn, Pb, Cd and Hg can be tested for by adding pure concentrated ammonia to 10ml of sample and shaking vigorously with 1.2ml of 0.001% dithizone in CCl_4. Less than 0.1µg of metal ion will impart a faint colour to the CCl_4 layer.) For almost all laboratory purposes, simple distillation yields water of adequate purity, and most of the volatile contaminants such as ammonia and CO_2 are removed if the first fraction of distillate is discarded. Most laboratories have glass stills that "doubly" or "triple" distil water. [See "water" in Chapter 1.]

Wood's Metal *[76093-98-6]* **M ~1486, m ~75°, 73-77°.** It is a fusible alloy of Bi, Pb, Sn, Cd with the atomic composition of 4:2:1:1 (**m 71°**) It is commonly used as a metal bath for heating reaction flasks as it melts at a convenient temperature. Its temperature rises rather rapidly when heated with a Bunsen burner in a crucible (e.g. steel or nickel), so care should be taken when heating a reaction or distilling flask containing chemical reactants immersed into it. Heating should be applied slowly, and the temperature should be monitored continuously with a thermometer immersed in the molten metal. The temperature of the metal can be taken up to ~350°, and it is better to work in an efficient fume cupboard as the vapours are toxic. At higher temperature some oxidation of the metal takes place. A bath that has been heated at high temperatures and then the metal cooled back to the solid, and melted again has a solid scum of the oxides on its surface. These can be easily removed with a nickel spatula to leave a nice clean surface. The melting point of the re-used alloy is not seriously affected, and the alloy can be used over and over again without considerable loss in weight. It is commercially available in a granular form or as sticks with the composition of Bi(50 wt%), Pb (25 wt%), Sn (12.5 wt%) and Cd (12.5 wt%). Other such alloys are **Rose's metal** (**m 93.75°**) with the composition of Bi, Pb, Sn in the ratio of 2:1:1, and **Lipowtiz alloy** (**m 60-65°**) with the composition of Bi, Pb, Sn, Cd in the ratio 15:8:4:3, but they are not commonly used in the laboratory. Alloys of Bi, Pb and Sn which melt slightly above 100° have been used as melting plugs in automatic sprinkler fire alarms.

Zinc (dust) *[7440-66-6]* **M 65.4.** Commercial zinc dust (1.2kg) is stirred with 2% HCl (3L) for 1 minute, then the acid is removed by filtration, and washed in a 4L beaker with a 3L portion of 2% HCl, three 1L portions of distilled water, two 2L portions of 95% EtOH, and finally with 2L of absolute Et_2O. (The wash solutions were removed each time by filtration.) The material is then dried thoroughly, and if necessary, any lumps are broken up in a mortar. [Wagenknecht & Juza *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1067 *1965*.]

Zinc (metal) *[7440-66-6]* **M 65.4, m 420°, d $_4^{20}$ 7.141.** Fuse it under vacuum, cool it, then wash it with acid to remove the oxide.

Zinc bromide *[7699-45-8]* **M 225.2, m 384, b 697.** Heat $ZnBr_2$ to 300° under vacuum ($2x10^{-2}$ mm) for 1 hour, then sublime it. [Wagenknecht & Juza *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1072 *1965*.]

Zinc chloride *[7646-85-7]* **M 136.3, m 283°, 290°.** The anhydrous material can be sublimed under a stream of dry HCl, followed by heating to 400° in a stream of dry N_2. It sublimes at high vacuum. Also purify it by refluxing (50g) in dioxane (400ml) with 5g zinc dust, filtering hot and cooling to precipitate $ZnCl_2$. Crystallise it from dioxane and store it in a desiccator over P_2O_5. It has also been dried by refluxing in thionyl chloride. [Weberg et al. *J Am Chem Soc* **108** 6242 *1986*.] *Hygroscopic: minimal exposure to the atmosphere is necessary*. [Wagenknecht & Juza *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1070 *1965*.]

Zinc-Copper Couple *[53801-63-1]* **m 419-420°.** It is available in the form of a powder made of Zn and Cu. If the Zn contains some ZnO, then it should be treated with dilute HCl for a very short period, washed H_2O, a little EtOH then Et_2O, and dried *in vacuo* (see also zinc dust above). The *couple* can be prepared in either of the following ways. (1) Zinc dust (120g, MW of Zn is 65.4) and powdered copper oxide (10g, MW of Cu is 63.6) in a round-bottomed flask (~200ml) are heated gently over a flame in a current of H_2 and N_2 with stirring or rotating the flask until the CuO is reduced, and a uniformly gray mixture is obtained. The temperature should be maintained below the point of fusion during heating (~500°) and the mixture is stored in a desiccator. (2) Zinc powder (24.6g) is stirred with 3% aqueous HCl (20ml) for 1 minute, washed by decantation with 3% aqueous HCl (3 x 20ml), with H_2O (5 x 20ml), with 2% aqueous $CuSO_4$ (2 x 40ml), distilled H_2O (5 x 20ml), with EtOH (4 x 20ml), with Et_2O (2 x 20ml), filtered off on a Büchner funnel, sucked dry then stored in a desiccator over P_2O_5 overnight. [Corbin et al. *Org Synth* **44** 30 *1964*, Coll Vol **V** 328 *1973*; *Smith* & Simmons *Org Synth* **41** 72 *1961*, Coll Vol **V** 855 *1973*.] (3) A suitable zinc/copper alloy with 5—8% of Cu can be prepared by melting zinc (m 419.5°) with clean brass turnings (*ca* 2Cu/1Zn) and casting into bars, which can be turned into fine shavings prior to use. [Noller *Org Synth* Coll Vol **II** 185 *1943*.] Note that the couple loses activity in moist air, so it should be kept dry, and used as soon as possible after it is prepared for best results.
When it is required to reduce organic halides to the respective hydrocarbon or deuterated derivative, it is best to prepare the Zn-Cu couple in an oxygen-free system. Thus Zn dust (6.5g, 100mmol) suspended in H_2O (10ml) is vigorously stirred with acidic cupric chloride solution (15ml of 0.15M in 5% hydrochloric acid) until evolution of gas ceases, the black solid is filtered off, and washed with H_2O until the filtrate gives a negative chloride test with 6% $AgNO_3$ solution. The *couple* is washed twice with Me_2CO, and in order to obtain the highest deuterium incorporation, the Me_2CO wash should be followed by a D_2O wash, two Me_2CO washes, two Et_2O washes and dried *in vacuo* at ~25°. This preparation of the *couple* is exceptional for replacing the halogen in a variety of organic halides by H or D in water-containing ether solvents, under mild conditions, and in reproducibly moderate to high yields (e.g. 1,4-dideuterobutadiene from 1,4-dichloro-1,3-butadiene, or 2-butanone-3-d_1 from 3-bromo-2-butanone). The deuterium derivatives provide a convenient ^{13}C NMR method for deuterium analysis. [Stephenson et al. *J Org Chem* **42** 212 *1977*.]

Zinc cyanide *[557-21-1]* **M 117.4, m 800°(dec), d_4^{20} 1.852.** It is a **POISONOUS** white powder which becomes black on standing if $Mg(OH)_2$ and carbonate are not removed in the preparation. Thus, wash it well with H_2O, then well with EtOH, Et_2O and dry it in air at 50°. Analyse it by titrating the cyanide with standard $AgNO_3$. Other likely impurities are $ZnCl_2$, $MgCl_2$ and traces of basic zinc cyanide; the first two salts can be washed out. It is soluble in aqueous KCN solutions. However, if purified in this way $Zn(CN)_2$ is not reactive in the Gattermann synthesis. For this, the salt should contain at least 0.33 mols of KCl or NaCl which will allow the reaction to proceed faster. [Adams & Levine *J Am Chem Soc* **45** 2375 *1923,* Arnold & Sorung *J Am Chem Soc* **60** 1699 *1938*, Fuson et al. *Org Synth* Coll Vol **III** 549 *1955*.]

Zinc fluoride *[7783-49-5]* **M 103.4, m 872°, b 1500°, d^{25} 5.00.** A possible impurity is H_2O which can be removed by heating at 100° or by heating to 800° in a dry atmosphere. Heating in the presence of NH_4F produces larger crystals. It is sparingly soluble in H_2O (1.51g/100ml) but more soluble in HCl, HNO_3 and NH_4OH. It can be stored in glass bottles. [Kwasnik in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 242 *1963*.]

Zinc iodide *[10139-47-6]* **M 319.2, m 446, b 624°(dec), d_4^{20} 4.74.** Heat the iodide to 300°/2 x 10^{-2}mm) for 1 hour, then sublime it. Its solubility in H_2O is 0.3ml/g, and it is soluble in EtOH. Store it in the dark.

Zinc perchlorate hexahydrate *[13637-61-1]* **M 372.4, m 105-107°, pK^{25} -2.4 to -3.1 (for $HClO_4$).** Crystallise it from a small volume of H_2O. It is soluble in EtOH. **Potentially EXPLOSIVE.**

Zinc-Silver Couple *[37350-66-6]***.** It is best to prepare the couple fresh when used to replace a vinylic bromine atom in organic compounds by a hydrogen atom, deuterium atom or a tritium atom. The zinc dust to be used should first be cleaned from any zinc oxide or greasy material. Zinc dust (22g) is stirred under N_2 at ~25° as a suspension in 10% aqueous HCl (110ml) for 20 minutes. Acetone (50ml) is added to the mixture, the liquid is decanted from the metal, and the gray slurry is washed thoroughly with Me_2CO (6 x 50ml) by decantation. The residual Zn is treated with a boiling suspension of AgOAc (~6.6g) in AcOH (125ml), stirred rapidly without

further heating, the liquid is decanted off and the black granular solid that is formed is washed with AcOH (2 x 60ml), Me_2CO (2 x 20ml), and finally dry THF (2 x 50ml). Store it under N_2 in the dark. If it is used for deuterium replacement of bromine it is best to stir the couple with D_2O (5ml) in dry THF (50ml) for 15 minutes, decant, repeat the process a second time and then wash the solid with dry THF (50ml). This reduces the amount of proton incorporation while maximising deuterium incorporation. [Fryzuk & Bosnich *J Am Chem Soc* **101** 3043 *1979*, Clark & Heathcock *J Org Chem* **41** 636 *1976*.]

Zinc sulfate heptahydrate (white vitriol) *[7446-20-0 (7 H_2O) 7446-19-7 (H_2O), 7733-02-0 (anhydrous)]* **M 287.5, m 100°(dec), 280°(loses all 7H_2O), >500(anhydrous), d $_4^{20}$ 1.97.** Crystallise it from aqueous EtOH or dilute H_2SO_4 below 39° when it forms the *heptahydrate*, and between 39° and 70° it forms the *hexahydrate*, and above 70° the *monohydrate* is stable. The *anhydrous salt* is obtained from the hydrates by heating at 280° or lower temperatures in a current of dry air. It decomposes to ZnO and SO_2 at 767°. The solubility of the *heptahydrate* in H_2O is 5.88% at 0°, 61.92% at 30°, 66.61% at 35° and 70.05% at 39°.

Zirconium tetrachloride *[10026-11-6]* **M 233.0, m 300°(sublimes), pK $_1^{25}$ -0.32, pK $_2^{25}$ 0.06, pK $_3^{25}$ 0.35, pK $_4^{25}$ 0.46 (for hydrolysis of aquo Zr^{4-}).** Crystallise it repeatedly from conc HCl. It is hydrolysed by H_2O to form white $ZrOCl_2$ (see below) and HCl. [Krebs *Z Anorg Allgem Chem* **378** 263 *1970*.]

Zirconyl chloride hexahydrate *[7699-43-6]* **M 286.2, m 150°(loses 6H_2O).** Crystallise it repeatedly from 8M HCl to give $ZrOCl_2.8H_2O$ (see below). On drying, $ZrOCl_2.6H_2O$, **m** 150°, is formed. The product is not free from hafnium. [Blumenthal *J Chem Ed* **39** 607 *1962*.]

Zirconyl chloride octahydrate *[13520-92-8]* **M 322.3, m 150° (loses 6H_2O), 210° (loses all H_2O). 400° (anhydrous dec), d $_4^{20}$ 1.91.** Recrystallise the chloride several times from water [Ferragina et al. *J Chem Soc, Dalton Trans* 265 *1986*]. Recrystallisation from 8M HCl gives the *octahydrate* as white needles on concentrating. It is also formed by hydrolysing $ZrCl_4$ with water. After one recrystallisation from H_2O, 99+% grade zirconyl chloride had Ag, Al, As, Cd, Cu, Hf, Mg, Na, Sc and V at 20, 1.8, 0.6, 0.6, 0.4, 8.4, 0.4, 2.4, 80 and 3 ppm, respectively. (See above.)

METAL-ORGANIC COMPOUNDS

This section contains metal-organic compounds, ammonium and metal derivatives of organic alcohols, amines and carboxylic acids (salts), as well as ionophores that form complexes with metal ions. Note that there is a large number of metal-organic catalysts, and reagents for preparing some of these catalysts, in Chapter 6, and can be considered as an extension of this section. (For Introduction see p 555.)

Acetylenedicarboxylic acid monopotassium salt *[928-04-1]* **M 152.2.** It is very soluble in H_2O, but can be crystallised from a small volume of H_2O in small crystals. These are washed with EtOH and dried over H_2SO_4 at 125°. [Bandrowski *Chem Ber* **10** 841 *1877*, Lossen *Justus Liebigs Ann Chem* **272** 133 *1893*, *Beilstein* **2** H 801, **2** I 317, **2** II 670, **2** III 1991, **2** IV 2290.]

Acetylferrocene (ferrocenyl methylketone) *[1271-55-2]* **M 228.1, m 86°, 86-87°.** Orange-red crystals are obtained when it is recrystallised from isooctane or *C_6H_6, and then sublimed at 100°/1mm. The *oxime* has **m** 167-170° (from Et_2O or aqueous EtOH). The *semicarbazone* has **m** 198-201° (from EtOH). [Richmond & Freiser *J Am Chem Soc* **77** 2022 *1955*, Weinmayer *J Am Chem Soc* **77** 3009 *1955*, Broadhead et al. *J Chem Soc* 650 *1958*, *Beilstein* **16** IV 1798.]

Allylpalladium(II) chloride dimer *[12012-95-2]* **M 365.9, m ~160°.** It crystallises from benzene and is soluble in MeOH, Et_2O and $CHCl_3$. [Hüttel et al. *Chem Ber* **94** 766 *1961*, Dent et al. *J Chem Soc* 1585 *1964*, Armstrong *J Org Chem* **31** 618 *1966*.]

Allyl tri-*n*-butylstannane (allyl tributyl tin) *[24850-33-7]* **M 331.1, b 88-92°/0.2mm, 115°/17mm, d_4^{20} 1.068, n_D^{20} 1.487.** A possible impurity is tributylchlorostannane — test for Cl as Cl ion after hydrolysing. Dissolve it in *C_6H_6 (or toluene), shake this with dilute aqueous NaOH, dry ($CaCl_2$), filter, evaporate and distil the residue in a vacuum [Jones et al. *J Chem Soc* 1446 *1947*, Bristow *Aldrichimica Acta* **17** 75 *1984*, Yamamoto *Aldrichimica Acta* **20** 45 *1987*]. [*Beilstein* **4** IV 4317.]

Aluminum acetylacetonate (tris[2,4-pentandionate]aluminium) *[13963-57-0]* **M 324.3**, **m 192-194°, 195°.** Recrystallise it several times from *benzene or aqueous MeOH, λ_{max} 216 and 286mn. [Charles & Pawlikowski *J Phys Chem* **62** 440 *1958*.] It can be purified by sublimation and has the following solubilities in g percent: *C_6H_6 35.9 (20°), 47.6 (40°), toluene 15.9 (20°), 22.0 (40°) and acetylacetone 6.6 (20°), 10.4 (40°). [Fernelius & Bryant *Inorg Synth* **V** 105 *1957*, *Beilstein* **1** IV 3668.]

Aluminum ethoxide *[555-75-9]* **M 162.2, m 154-159°, 146-151°, b 187-190°/7mm, 210-214°/13mm.** Crystallise it from CS_2 [**m** 139°, CS_2 complex] and distil it in a vacuum. The molecular weight corresponds to $[Al(OEt)_3]_4$ [Robinson & Peak *J Phys Chem* **39** 1127 *1935*, Vilani & Nord *J Am Chem Soc* **69** 2605 *1947*]. [*Beilstein* **1** H 313, **1** I 158, **1** II 3008, **1** III 1284, **1** IV 1289.]

Aluminium isopropoxide *[555-31-7]* **M 204.3, m 119°, b 94°/0.5mm, 135°/10mm.** Redistil it under vacuum. *Hygroscopic*. [Robinson & Peak *J Phys Chem* **39** 1127 *1935*, *Beilstein* **1** IV 1468.]

Aluminum triethyl (triethyl aluminum) *[97-93-8]* **M 114.2, b 69°/1.5mm, 76°/2.5mm, 129-131°/55mm, d_4^{20} 0.695, n_D^{20} 1.394.** Purify $Al(Et)_3$ by fractionation in an inert atmosphere under a vacuum in a 50cm column containing a heated nichrome spiral, taking the fraction **b** 112-114°/27mm. It is very sensitive to H_2O and should be stored under N_2. It should not contain chloride ions which can be shown by hydrolysis and testing with $AgNO_3$. [Baker & Sisler *J Am Chem Soc* **75** 4828 5193 *1953*, NMR: Brownstein et al. *J Am Chem Soc* **81** 3826 *1959*, *Beilstein* **4** IV 4398.]

Aluminium tri-*tert*-butoxide *[556-91-2]* **M 246.3, m 208-210°(dec), >300°.** Crystallise $Al(O\text{-}tBu)_3$ from *C_6H_6 and sublime it at 180°. [McElvain & Davie *J Am Chem Soc* **73** 1400 *1951*, *Beilstein* **1** IV 1612.]

Aluminium trimethanide (trimethyl aluminium) *[75-24-1]* **M 72.1, m 15.2°, b 111.5°/488.2mm, 124.5°/atm, d_4^{20} 0.725.** Distil $Al(Me)_3$ through a 10-20 theoretical plates column under 1 atmosphere pressure of N_2 (better with very slow take-off). It attacks grease (use glass joints). It has been distilled over Al in absence of grease, into small glass vials and sealed under N_2. The purity is measured by its freezing point. It reacts with H_2O, is non-conducting in $*C_6H_6$ and is **HIGHLY FLAMMABLE**. [Bamford et al. *J Chem Soc* 468 *1946*, Pitzer & Gutowsky *J Am Chem Soc* **68** 2204 *1946*, *Beilstein* **4** IV 4397.]

4-Aminophenylmercuric acetate *[6283-24-5]* **M 371.8, m 168°, 175°(dec), 180°(dec).** Recrystallise it from hot dilute AcOH and dry it in air. Highly **TOXIC**. [Mahapatra et al. *J Indian Chem Soc* **32** 613 *1955,* Albert & Schneider *Justus Liebigs Ann Chem* **465** 269 *1928*, *Beilstein* **16** III 1411, **16** IV 1754.]

Ammonium acetate *[631-61-8]* **M 77.1, m 112-114°, d_4^{20} 1.04.** Crystallise it twice from anhydrous acetic acid, and dry under vacuum for 24 hours at 100° [Proll & Sutcliff *Trans Faraday Soc* **57** 1078 *1961*].

Ammonium benzoate *[1863-63-4]* **M 139.2, m 198°, 200°(dec), d_4^{20} 1.26.** Crystallise it from EtOH. [*Beilstein* **9** IV 273.]

Ammonium dodecylsulfate (ammonium laurylsulfate) *[2235-54-3]* **M 283.4.** Recrystallise it first from 90% EtOH and then twice from absolute EtOH, and finally dry it in a vacuum. [*Beilstein* **1** III 1786.]

Ammonium ferric oxalate trihydrate *[13268-42-3]* **M 428.1, m ~160°(dec), d_4^{20} 1.77.** Crystallise it from hot water (0.5ml/g). [*Beilstein* **3** III 1103.]

Ammonium formate *[540-69-2]* **M 63.1, m 116°, 117.3°, d_4^{45} 1.280.** Heat the solid in NH_3 vapour and dry it in a vacuum till the NH_3 odour is faint (note that it can evaporate completely in a vacuum). Recrystallise it from absolute EtOH and then keep it in a desiccator over 99% H_2SO_4 *in vacuo*. It is very *hygroscopic*. It exists in two forms, stable needles and less stable plates. It also forms acid salts, i.e. $HCO_2NH_4.3HCO_2H$ and $HCO_2NH_4.HCO_2H$. [Kensall & Adler *J Am Chem Soc* **43** 1473 *1921*, *Beilstein* **2** IV 18.]

Ammonium ionophore I (Nonactin) *[6833-86-7]* **M 736.9, m 147-148°, $[\alpha]_D^{20}$ 0° (c 1.2, $CHCl_3$).** Crystallise it from MeOH (colourless needles), and it is dried at 20° in high a vacuum. It is a selectophore with high sensitivity for NH_4^+ ions. [Corbaz et al. *Helv Chim Acta* **38** 1445 *1955*, Domingues et al. *Helv Chim Acta* **45** 129 *1962*, Nawata & Ando *Helv Chim Acta* **55** 1371 *1972*, *Beilstein* **19/12** V 751.]

Ammonium oxalate dihydrate *[6009-70-7]* **M 142.1, d_4^{20} 1.50.** Crystallise it from water (10ml/g) at 50°. [*Beilstein* **2** IV 1846.]

Ammonium picrate *[131-74-8]* **M 246.1, m EXPLODES above 200°.** Crystallise it from EtOH and acetone. [Mitchell & Bryant *J Am Chem Soc* **65** 128 *1943*, *Beilstein* **6** II 262, **16** III 879, **16** IV 1392.]

***n*-Amylmercuric chloride** *[544-15-0]* **M 307.2, m 110°.** Crystallise it from EtOH. The *bromide* has **m** 122°. [Larock & Brown *J Am Chem Soc* **92** 2467 *1970*, Marvel et al. *J Am Chem Soc* **47** 3009 *1925*, *Beilstein* **14** H 706, 725.]

Aurothioglucose (gold thioglucose) *[12192-57-3]* **M 392.2.** Purify it by dissolving it in H_2O (0.05g in 1ml) and precipitating it by adding EtOH. It yields yellow crystals with a slight mercaptan odour. It decomposes slowly in H_2O, and is soluble in propylene glycol but insoluble in EtOH and other common organic solvents. [Caterson & Taylor *FEBS Lett* **98** 351 *1979*, Cooney et al. *Biochem J* **259** 651 *1989*.]

Barium acetate *[543-80-6]* **M 255.4.** Crystallise the salt twice from anhydrous acetic acid and dry it under vacuum for 24 hours at 100°. [*Beilstein* **2** I 49, **2** II 117, **2** III 192, **2** IV 114.]

Barium ionophore I [*N,N,N′,N′*-tetracyclohexyloxy-bis-(*o*-phenyleneoxy)diacetamide] *[96476-01-6]* **M**

644.9, m 156-158°. Purify the ionophore by chromatography on a Kieselgel column, elute it with CH_2Cl_2/EtOAc (5:1), and recrystallise the residue from the evaporated effluent from EtOH/Me_2CO to give colourless crystals. It is an electrically neutral ionophore with high selectivity for Ba^{2+} ions and with high lipophilicity. [Kleiner et al. *Chem Ber* **118** 1071 *1985*, Läubli et al. *Anal Chem* **57** 2756 *1985*.]

Barium propionate (H_2O) *[5908-77-0]* **M 301.5, d_4^{27} 1.44, pK^{24} 4.88 (for propionic acid).** Crystallise it from warm water (50ml/g) by adding EtOH and cooling. [*Beilstein* **2** III 517, **2** IV 702.]

Benzenechromium(0) tricarbonyl *[12082-08-5]* **M 214.1, m 162-163°, 163-166°.** Purify the complex by sublimation *in vacuo*. A possible impurity is 2-picoline which can be removed by washing with pentane and drying. It is then purified further by sublimation at 80-85°/10^{-3}mm, or by recrystallisation from Et_2O to give yellow crystals. ^{1}H NMR in $CDCl_3$ should give a single peak at τ 4.68. [Rausch *J Org Chem* **39** 1787 *1974*, Pauson in Houben-Weyl *Meth Org Chem* V, E 18 Pt I p226 Theme Verlag, Stuttgart *1986*, *Beilstein* **5** IV 625.]

Beryllium acetate [$Be(OAc)_2$] *[543-81-7]* **M 127.1, m 65-100° (slow heating), 155-180° (rapid heating).** It is obtained by dissolving the *basic acetate* (4g, see below) in boiling glacial AcOH containing acetyl chloride (4.5g) and refluxing for ~15 minutes. The $Be(OAc)_2$ which separates during this time, is filtered off, washed with AcOH, cold $CHCl_3$ and dried *in vacuo* to give 90-94% yield of the salt. It is stable for several weeks in a tightly stoppered container at ~25°. It slowly loses Ac_2O**,** and more rapidly on heating, to give the basic acetate which sublimes out. Strong heating partially decomposes it to give Ac_2O and BeO. It is not readily attacked by cold H_2O but forms a hydrate on warming, and is insoluble in most solvents. [Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 901 *1963*, Besson & Hardt *Z Anorg Allg Chem* **277** 188 *1954*.] Beryllium compounds are potentially **carcinogenic**.

Beryllium acetate (basic) [$Be_4O(OAc)_6$] *[1332-52-1]* **M 406.3, m 283°, 285-286°, b 330-331°/atm.** On evaporating $Be(OH)_2$ with AcOH this covalent basic acetate is produced. *Alternatively*, $BeCO_3$ (40g, see [744998-97-8]) and AcOH (80ml) are heated with stiring until evolution of CO_2 ceases. When the reaction is complete, white semi-translucent crystals separate. After cooling to ~25°, the basic acetate crystals are filtered off and dried in air. These are treated with warm $CHCl_3$ (60-80ml), any insoluble material is filtered off, and the colourless octahedral crystals of the basic acetate which separate on cooling (with partial evaporation) are collected and freed from any $CHCl_3$ *in vacuo* to give pure basic salt (28g, ~47%, **m 284°**). It is readily volatile, it can be distilled, and it sublimes in a vacuum leaving a small residue of 0.3-0.5% of BeO. It is very soluble in $CHCl_3$, soluble in non-polar organic solvents such as boiling $*C_6H_6$, toluene, xylene, tetralin, and in AcOH; less so in CCl_4, Ac_2O and AcCl, but is sparingly soluble (~0.3%) in Et_2O. It dissolves in anhydrous boiling MeOH but soon liberates Ac_2O to form highly aggregated basic acetates. It is quite stable in cold H_2O, but is rapidly hydrolysed in hot H_2O. [Moeller et al. *Inorg Synth* **III** 9 *1950*, Ehrlich in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 901 *1963*, and for the basic formate or propionate salts see Besson & Hardt *Z Anorg Allg Chem* **277** 188 *1954*, Hendus & Hardt *Z Anorg Allg Chem* **277** 127 *1954*, Hendus & Hardt *Z Anorg Allg Chem* **286** 265 *1956*, and Hardt *Z Anorg Allg Chem* **286** 254 *1956*, *Beilstein* **2** H 111, **2** I 48, **2** II 116, **2** III 190, **2** IV 112.] The X-ray crystal structure shows that the four beryllium atoms are arranged at the corners of a regular tetrahedron with oxygen at the centre, and the six edges are occupied by acetate groups. Thus the four Be atoms at the apexes of the tetrahedron are coordinated to the carboxyl oxygen atoms of the six acetate groups, i.e. each Be atom is coordinated to three oxygen atoms. [Bragg & Morgan *Proc Roy Soc* **104** 437 *1923*, for partial structure see also F.A. Cotton and G. Wilkinson *Advanced Inorganic Chemistry (A Comprehensive Text)* p. 175, Interscience Publ. *1962*, Library of Congress Catalog Number 62-14818.] Berylluim compounds are potentially **carcinogenic**.

Beryllium acetylacetonate [$Be(acac)_2$] *[10210-64-7]* **M 207.2, m 108°, 108.5-109°, b 270°, d^{20} 1.168.** This complex has been prepared by adding 3M aqueous NaOH (100ml) to a solution of $BeSO_4$ $4H_2O$ (10g, see [7787-50-0]) in distilled H_2O (100ml) to give a strong basic solution to which is added freshly distilled acetylacetone (30ml) dropwise with stirring, and a white precipitate separates. This is collected, washed with H_2O and dried *in vacuo* to give the complex (5.1g 43%) which is recrystallised by dissolving in a small volume of $*C_6H_6$ and adding gradually petroleum ether until crystallisation is complete. The crystals are collected, washed with

petroleum ether and dried *in* vacuo. It can be recrystallised further from a small volume of $*C_6H_6$ or a large volume of petroleum ether. It has also been prepared in 70% yield from basic beryllium carbonate (3g) in H_2O (45ml) by conversion to the chloride with 6N aqueous HCl (*ca* 20ml) until slightly acidic. To this is added dropwise a clear solution of acetylacetone (10g suspended in 45ml of H_2O to which is added 6N ammonia until completely clear) and stirred until precipitation of the complex is complete (pH should be near neutral). The solid is collected washed with H_2O, dried, and crystallised as before. It is also sublimed through a plug of glass wool at a vacuum of 0.1mm by heating in a bath at 80 to100°. It is very soluble in most organic solvents such as EtOH, Et_2O, Me_2CO, $*C_6H_6$ and in CS_2 but considerably less in petroleum ethers. However, it is practically insoluble in H_2O which hydrolyses it on boiling; and it is also hydrolysed by acids and alkalis. [Jones *J Am Chem Soc* **81**, 3188 *1959*, Arch & Young *Org Synth* **II** 17 *1946*.] Berylluim compounds are potentially **carcinogenic**.

Bicyclo[2.2.1]hepta-2,5-diene rhodium (I) chloride dimer (norbornadiene rhodium chloride complex dimer) *[12257-42-0]* **M 462, m 240°(dec).** It recrystallises from hot $CHCl_3$/petroleum ether as fine crystals soluble in $CHCl_3$ and $*C_6H_6$ but is almost insoluble in Et_2O or petroleum ether. [Abel et al. *J Chem Soc* 3178 *1959*.]

2,2'-Bipyridinium chlorochromate *[76899-34-8]* **M 292.6.** Wash it with cold conc HCl, then H_2O (sintered glass funnel) and dry it in a vacuum ($CaCl_2$) to give a free-flowing yellow-brown powder. Store it in the dark. [Guziec & Luzzio *Synthesis* 691 *1980*, Chakraborty & Chandrasekaran *Synth Commun* **10** 951 *1980*.] **SUSPECTED CARCINOGEN.**

2,2'-Biquinolin-4,4'-dicarboxylic acid dipotassium salt *[63451-34-3]* **M 420.51.** Recrystallise it from H_2O. The *Cu salt* has UV with λ_{max} at 562nm. [Mopper & Gindler *Anal Biochem* **56** 440 *1973*, *Beilstein* **25** IV 1148.]

Bis(1,2,3,4,5-η-cyclooctadienyl)ruthenium [$Ru(COD)_2$] *[63395-36-8]* **M 315.4, m 89-90°, 113-114°.** The bis-complex is prepared by adding a solution of $RuCl_3.3H_2O$ (624mg, 1.33mol) in EtOH (20ml) under argon (or N_2) slowly over 30 minutes to a stirred suspension of Zn powder (7g), EtOH (5ml) and redistilled 1,2-5,6-cyclooctadiene (11ml, 80mol), COD see [111-78-4, 1552-12-1], then stirring at room temperature for 2 hours, and filtering the mixture under N_2. The filtrate is concentrated on a vacuum line to remove volatiles, and the residual brown oil is placed on top of an Al_2O_3 column in hexane after flushing with N_2. The yellow band is eluted with hexane, concentrated *in vacuo*, the eluate is evaporated, pentane is added to dissolve the residue and the solution is cooled at -78° for several hours, to provide very pale yellow (almost colourless) crystals of the analytically pure *complex* (283mg, 35%). The ^1H NMR (60MHz, C_6D_6, TMS) has τ at 4.42 (t, 2H), 6.15 (dd, 4H), 6.45 (m, 4H) and 7.49-8.95 (m, 12H); and the ^{13}C NMR (22.6MHz, C_6D_6, TMS) has δ at 22.5, 27.3, 36.7, 35.3, 38.9, 62.4, 76.7, 87.6. [Pertici et al. *J Chem Soc, Perkin Trans* 1961 *1980* (gave m 89-90°), Itoh et al. *J Organomet Chem* **272** 179 *1984* (gave m 113-114°)].

Bis(η^5-2,4-cyclopentadien-1-yl)samarium II [$SmCp_2$, samarocene] *[80695-16-5]* **M 280.5, decomposes at high temperatures.** Samarium dicyclopentadienyl can be prepared in Schlenk equipment under argon by adding SmI_2 (0.1M in THF, 60ml, 6mmol) to a 0.4M solution of sodium pentadienide in THF (30ml, 12mmol) when the complex separates immediately and is decanted within 1 hour. The red powder of $SmCp_2$ is collected, washed twice with THF to remove NaI, dried *in vacuo* and stored under argon. The red powder and the purple solid THF complex (**M 352.6**) are ***pyrophoric*** in air. $SmCp_2$ can also be stored for a few days in a Schlenk tube under THF without decomposition. Freshly prepared suspensions of $SmCp_2$ have been used in pseudo-Barbier couplings between carbonyl compounds and aliphatic or allylic halides and are more efficient than SmI_2 [Namy et al. *J Organometal Chem* **328** 81 *1986*].

$SmCp_2$-THF has been prepared in one arm of a U-tube by stirring in an anhydrous oxygen-free helium atmosphere) tris(cyclopentadienyl)samarium III ($SmCp_3$, 0.499g), K metal (0.527g, naphthalene (0.128g, 25% molar deficiency) and THF (25ml, freshly distilled under reduced pressure from Na-benzophenone) for 48 hours. Purple $SmCp_2$-furanate was separated by decantation, washed by successive back-distillation with THF and the

solvent is removed at 24°/10^{-3}mm during 18 hours. It is *pyrophoric* and should be handled in an anhydrous oxygen-free atmosphere. Its IR has ν_{max} (Nujol) at 3080 (C-H stretch), 1475, 1347, 1308, 1263, 1163, 1070, 1008 (C-H bend parallel), 775, 740 (C-H bend perpendicular) and 350 (antisym metal-ring vibration) cm^{-1}, and other bands at 2980, 2880, 1375, 725 and 565 cm^{-1} due to coordinated THF with intensities similar to the weaker metallocene bands. On exposure to traces of air this complex immediately changes in colour from deep purple to yellow-gray with drastic reduction in the paramagnetism. [Watt & Gillow *J Am Chem Soc* **91** 775 *1969*.]

Bis(2,9-dimethyl-1,10-phenanthroline) copper(I) perchlorate (Cuproine) *[54816-44-5]* **M 579.6, pK^{25} -2.4 to -3.1 (for $HClO_4$) and 6.15 (for dimethylphenanthroline).** Crystallise it from acetone. It has UV with λ_{max} in isopentanol or hexan-1-ol at 454nm. [Smith & McCurdy *Anal Chem* **24** 371 *1952*, Gahler *Anal Chem* **26** 577 *1954*, *Beilstein* **23** III/IV 1737.]

1,1'-Bis(diphenylphosphino)ferrocene *[12150-46-8]* **M 554.4, m 181-183°, 184-194°.** Wash the ferrocene with distilled H_2O and dry it in a vacuum. Dissolve it in *ca* 5 parts of hot dioxane and cool to give orange crystals **m** 181-183°. Recrystallisation from *C_6H_6/heptane (1:2) gives a product with **m** 183-184°. [Bishop et al. *J Organomet Chem* **27** 241 *1971*.]

Bis(ethyl)titanium(IV) chloride *[2247-00-9]* **M 177.0.** Recrystallise it from boiling toluene. [See Marek (ed) *Titanium and Zirconium in Organic Synthesis* Wiley-VCH *2002* ISBN 3-527-304-28-2, Wailes et al. *Organometallic Chemistry of Titanium, Zirconium and Hafnium* Academic Press *1974* ISBN 0-127303502.]

Bis(ethyl)zirconium(IV) chloride *[92212-70-9]* **M 220.3.** Recrystallise it from boiling toluene. [See Marek (ed) *Titanium and Zirconium in Organic Synthesis* Wiley-VCH *2002* ISBN 3-527-304-28-2, Wailes et al. *Organometallic Chemistry of Titanium, Zirconium and Hafnium* Academic Press *1874* ISBN 0-127303502.]

***N,N'*-Bis(salicylidene)ethylenediamine cobalt (II) [Co(SALEN)$_2$, salcomine]** *[14167-18-1]* **M 325.2.** The powder should have an oxygen capacity of 4.7-4.8% as measured by the increase in weight under O_2 at 100 pounds pressure at *ca* 20°. The O_2 is expelled on heating the material to 65°. It crystallises from pyridine, $CHCl_3$ or *C_6H_6, and the solvent may be removed by heating at 120° in a vacuum. However, this heating may mean reduced O_2 capacity. In the dry state it absorbs O_2, turning from a maroon colour to black. [Diehl & Hack *Inorg Synth* **III** 196 *1950*.]

Bis(tetrabutylammonium) dichromate *[56660-19-6]* **M 700.9, m 139-142°.** Wash the dichromate with water and dry it in a vacuum. Recrystallise it from hexane (**m** 79-80°). [Santaniello & Ferraboschi *Synth Commun* **10** 75 *1980*, *Beilstein* **4** IV 556.] (Possible **CARCINOGEN**.)

***n*-Butylmercuric chloride** *[543-63-5]* **M 293.1, m 130°.** Crystallise it from 95% EtOH. [Larock & Brown *J Am Chem Soc* **92** 2467 *1970*, Marvel et al. *J Am Chem Soc* **47** 3009 *1925*.]

***n*-Butylstannoic acid [PhSn(OH)$_3$, trihydroxy-*n*-butylstannane]** *[22719-01-3]* **M 208.8.** Purify it by adding excess KOH in $CHCl_3$ to remove *n*-BuSn(OH)Cl_2 and *n*-BuSn(OH)$_2$Cl, and isolate it by acidification [Holmes et al. *J Am Chem Soc* **109** 1408 *1987*].

Cadion [1-(4-nitrophenyl)-3-(4-phenylazophenyl)-triazene] *[5392-67-6]* **M 346, m 189°(dec).** Commercial cadion is purified by recrystallisation from 95% EtOH and is dried *in vacuo*. It is stable in 0.2 N KOH (in 20% aqueous EtOH) at 25°. It is a sensitive reagent for Cd, and the Cd complex has UV with λ_{max} (EtOH) at 475nm. [Chavanne & Geronimi *Anal Chim Acta* **19** 377 *1958*, *Beilstein* **16** III 664.]

Cadmium acetate dihydrate *[5743-04-4]* **M 230.5, m 255°(anhydrous), d_4^{20} 2.01 (hydrate), 2.34 (anhydr), pK_1^{25} 9.7, pK_2^{25} ~11.0 (for Cd^{2+}).** Recrystallise it twice from anhydrous acetic acid and dry it under vacuum for 24 hours at 100°. [*Beilstein* **2** IV 114.]

Cadmium ionophore I [*N,N,N',N'*-tetramethyl-3,6-dioxooctanedi-(thioamide)] *[73487-00-0]* **M 432.7, m**

35-36°. Wash it well with petroleum ether, then several times with 2N HCl (if it has a slight odour of pyridine), then H_2O and dry it in a vacuum over H_2SO_4. It is a polar selectrophore for Cd. [Schneider *Helv Chim Acta* **63** 217 *1980*, Simon & Carafoli *Methods Enzymol* **56** 439 *1977*.]

Cadmium lactate *[16039-55-7]* **M 290.6.** Recrystallise the lactate from water (10ml/g) by partial evaporation in a desiccator. [*Beilstein* **3** H 277, **3** III 465, **2** IV 637.]

Cadmium salicylate *[19010-79-8]* **M 248.5, 242°(dec).** Recrystallise it from distilled H_2O by evaporation in a desiccator. It is an antiseptic. [Prasad et al. *J Indian Chem Soc* **35** 267 *1958*, *Beilstein* **10** H 60, **10** I 25, **10** II 33, **10** III 94, **10** IV 128.]

Calcein sodium salt [2',7'-bis-{*N,N*-di(carboxymethyl)aminomethyl}fluorescein Na salt, Fluorexon, Fluorescein Complexon] *[108750-13-6 diNa salt, 1461-15-0 free acid]* **M 666.5, $pK_{Est(1)}$~1.9, $pK_{Est(2)}$~2.5, $pK_{Est(3)}$~8.0, $pK_{Est(4)}$ ~10.5 (all for N-CH_2COOH), and $pK_{Est(5)}$ ~3.5 (for benzoic COOH).** Dissolve it in distilled H_2O and acidify with dilute HCl to pH 3.5. Filter off the solid acid and wash it well with H_2O. Redissolve *ca* 10g in 300ml H_2O containing 12g of NaOAc. Precipitate it again by adding HCl, filtering and washing with H_2O. Add the solid to 200ml of EtOH stir for 1 hour and filter. Repeat the EtOH wash and dry the bright yellow solid in a vacuum. This acid decomposes on heating at *ca* 180°. See below for the preparation of the Na salt. [Diehl & Ellingboe *Anal Chem* **28** 882 *1956*].
Alternatively, dissolve it in H_2O and acidify with 3N HCl to pH 3.5. Collect the solid and wash it with H_2O. The air-dried precipitate is extracted with 70% aqueous EtOH, filtered hot and cooled slowly. Fine yellow needles of the acid crystallise out; they are filtered off and dissolved in the minimum quantity of 0.01N NaOH and re-precipitated by adding N HCl to pH 3.5. It is then recrystallised from 70% aqueous EtOH (3x). The final product (acid) is dried at 80° in a vacuum for 24 hours, **m** >300°(dec). It contains one molecule of water per molecule of acid ($C_{30}H_{36}N_4O_{13}.H_2O$). The product is pure as revealed by electrophoresis at pH 5.6 and 8.6, and by TLC in *i*-BuOH/*i*-PrOH/AcOH/H_2O (60:60:5:5 by volume) or *i*-PrOH or pH 8.0 borate buffer. [Wallach et al. *Anal Chem* **31** 456 *1959*.]
The Na salt is prepared by dissolving the pure acid in H_2O containing 2 mols of NaOH per mol of acid reagent and lyophilising. It complexes with Ca and Mg ions. [*Beilstein* **19** III/IV 4338.]

Calcium acetate monohydrate *[5743-26-0 (H_2O), 62-54-4 (xH_2O)]* **M 176.2 (H_2O), m 150° (loses H_2O), pK^{25} 12.7 (for Ca_2^+).** Recrystallise the acetate from water (3ml/g) by partial evaporation in a desiccator. [*Beilstein* **2** IV 113.]

Calcium benzoate trihydrate *[2090-05-3]* **M 336.4.** Recrystallise the benzoate from water (10ml/g) between 90° and 0°. [*Beilstein* **9** I 60, **9** H 85, **9** III 377, **9** IV 280.]

Calcium butyrate *[5743-36-2]* **M 248.2, d_4^{30} 1.271.** Recrystallise the butyrate from water (5ml/g) by partial evaporation in a desiccator and dry it in a vacuum to constant weight. [Pathak & Bhide *J Indian Chem Soc* **30** 47, 48 *1953*.] Its dissociation constant at 25° is 0.29 [Colman-Porter & Monk *J Chem Soc* 4363 *1952*, *Beilstein* **2** IV 785].

Calcium carbamate *[543-88-4]* **M 160.1.** Recrystallise calcium carbamate from aqueous ethanol. [*Beilstein* **4** H 75, **4** I 336, **4** II 557, **4** III 149, **4** 234.]

Calcium formate *[544-17-2]* **M 130.1, m dec on heating, d_4^{20} 2.01.** Recrystallise calcium formate from water (5ml/g) by partial evaporation in a desiccator. [*Beilstein* **2** IV 16.]

Calcium D-gluconate monohydrate *[299-28-5, 18016-24-5]* **M 448.4, m dec on heating, $[\alpha]_{546}^{20}$ +11.0°, $[\alpha]_D^{20}$ +9.0° (c 1.2, H_2O).** Calcium gluconate is soluble in H_2O (3.5g in 100g at 25°). Dissolve it in H_2O, filter and precipitate it by adding MeOH. Filter off the solid and dry it in a vacuum at 85°. *Alternatively*, dissolve it in H_2O, filter (from insoluble inorganic Ca) and evaporate it to dryness under vacuum at 85°. [March et al. *J Am Pharm Assoc* **41** 366 *1952*, *Beilstein* **3** IV 1255.]

Calcium D-heptagluconate dihydrate *[17140-60-2]* **M 526.4, $[\alpha]_{546}^{20}$ +5.2°, $[\alpha]_{D}^{20}$ +4.4° (c 5, H_2O).** Purify it in the same way as for calcium D-gluconate. [*Beilstein* **3** III 1112.]

Calcium ionophore I (ETH 1001) *[58801-34-6]* **M 685.0.** This is a neutral Ca selectophore. It can be purified by thick layer (2mm) chromatography (Kieselgel F_{245}) and eluted with $Me_2CO/CHCl_3$ (2:1). [Ammann et al. *Helv Chim Acta* **56** 1780 *1973*, Simon & Carafoli *Methods Enzymol* **56** 439 *1977*.]

Calcium ionophore II (ETH 129) *[74267-27-9]* **M 460.7, m 153-154°.** Recrystallise it from Me_2CO. It forms 1:2 and 1:3 metal/ligand complexes with Mg^{2+} and Ca^{2+} ions, respectively, and induces selectivity in membranes for Ca^{2+} over Mg^{2+} by a factor of *ca* 10^4. [Pretsch et al. *Helv Chim Acta* **63** 191 *1980*, Simon & Carafoli *Methods Enzymol* **56** 439 *1977*.]

Calcium ionophore III [A23187 calcimycin] *[52665-69-7]* **M 523.6, m 181-182°, $[\alpha]_{D}^{25}$-56.0° (c 1, $CHCl_3$).** It recrystallises from Me_2CO as colourless needles. Protect it from light and moisture, store in a refrigerator. It is soluble in Me_2SO or EtOH and can be stored for 3 months without loss of activity. The Mg and Ca salts are soluble in organic solvents and cross biological membranes. It has a pKa of 6.9 in 90% Me_2SO. The Ca complex crystallises from 50% EtOH as colourless prisms. It is *highly* **TOXIC.** [Pressman *Ann Rev Biochem* **45** 501 *1976*, Chaney et al. *J Am Chem Soc* **96** 1932 *1974*, Chaney et al. *J Antibiotics* **29** 124 *1976*, Suzuki et al. *Anal Biochem* **61** 382 *1989*, Simon & Carafoli *Methods Enzymol* **56** 439 *1977*.]

Calcium isobutyrate *[533-90-4]* **M 248.2.** Crystallise it from water (3ml/g) by partial evaporation in a desiccator. It forms a *pentahydrate* at low temperatures, but the crystals filtered from a saturated solution at 80° are the *monohydrate*; the transition temperature is 62.5°. [Lumsden *J Chem Soc* **81** 359 *1902*.] It has a dissociation constant of 0.31 [Colman-Porter & Monk *J Chem Soc* 4363 *1952*]. [*Beilstein* **2** H 290, **2** II 290, **2** IV 845.]

Calcium lactate ($5H_2O$) *[814-80-2, 15743-47-5]* **M 308.3, m anhydrous at 120°, $[\alpha]_{D}^{20}$ -4.2° (c 5, H_2O).** Crystallise calcium lactate from warm water (10ml/g) by cooling to 0°. [*Beilstein* **3** IV 636.]

Calcium propionate *[4075-81-4]* **M 186.2, m dec on heating.** Crystallise this antifungal salt from water (2ml/g) by partial evaporation in a desiccator. [*Beilstein* **2** H 238, **2** II 218, **2** III 516.]

Calcium salicylate ($2H_2O$) *[824-35-1]* **M 350.4, pK_1^{20} 3.08, pK_2^{20} 13.43 (for acid).** Recrystallise calcium salicylate from water (3ml/g) between 90° and 0°. [*Beilstein* **10** H 60, **10** II 33, **10** III 94, **10** IV 128.]

Carbonate ionophore I [ETH 6010] (heptyl 4-trifluoroacetylbenzoate) *[129476-47-7]* **M 316.3, b 170°/0.02mm, d_4^{20} 0.909.** Purify the ionophore by flash chromatography (2g of reagent with 30g of Silica Gel 60) and elute with EtOAc/hexane (1:19). The fractions that absorb light at 260nm are pooled, evaporated and dried at room temperature (10.3 Torr). The oily residue is distilled in a bubble-tube apparatus (170°/0.02 Torr). Its IR ($CHCl_3$) has peaks at 1720, 1280, 940cm^{-1}, and its solubility in tetrahydrofuran is 50mg/0.5ml. It is a lipophilic neutral ionophore selective for carbonate as well as being an optical humidity sensor. [Behringer et al. *Anal Chim Acta* **233** 41 *1990*.]

Cerous acetate *[537-00-8]* **M 317.3, pK_1^{25} 8.1 (9.29), pK_2^{25} 16.3, pK_3^{25} 26.0 (for Ce^{3+}).** Recrystallise it twice from anhydrous acetic acid, then pumped dry under a vacuum at 100° for 8 hours. [*Beilstein* **2** I 50, **2** II 119, **2** III 196, **2** IV 115.]

Cesium oleate *[31642-12-3]* **M 414.4.** Recrystallise cesium oleate from EtOAc, dry it in an oven at 40° and store it over P_2O_5. [Finkle et al. *J Am Chem Soc* **45** 2785 I1923, *Beilstein* **2** II 437, **2** III 1405.]

Cesium perfluoro-octanoate (Cesium pentadecafluorooctanoate) *[17125-60-9]* **M 546.0.** Recrystallise it from a butanol/petroleum ether mixture, dry it in an oven at 40° and store it over P_2O_5 under vacuum. [*Beilstein* **2** IV 994.]

Chloro-tri-isopropoxy titanium *[20717-86-6]* **M 260.6, m 45-50°, b 61-65°/0.1mm.** When distilled under vacuum, the distillate sets slowly to a solid on standing. Stock reagents are made by dissolving the warm liquid in pentane, toluene, Et_2O, THF, CH_2Cl_2, and can be stored in a pure state or in solution under dry N_2 for several months. The reagent is *hygroscopic* and is hydrolysed by H_2O. [Reetz et al. *Chem Ber* **118** 1421 *1985*.]

Chromocene [bis(cyclopentadienyl) chromium II) *[1271-24-5]* **M 182.2, m 173°.** Chromocene forms *pyrophoric* red crystals on sublimation at 50°/0.1mm followed by resublimation at 75-90°/0.1mm. Although it is stable at least to 300°, it is readily oxidised in air, and effervesces slowly in H_2O to give cyclopentadiene. All operations should be carried out in a dry box. It decomposes in CCl_4 or CS_2, and for IR even grinding with nujol, KBr or KI causes some decomposition. [Wilkinson et al. *J Inorg Nucl Chem* **95** 109 *1956*, Wilkinson *J Am Chem Soc* **76** 209 *1954*, *Beilstein* **16** IV 1774.]

Chromoionophore I [ETH 5294] [9-diethylamino-5-octadecanoyl-imino-5-*H*-benzo[a]-phenoxazine] *[125829-24-5]* **M 583.9.** Purify it by flash chromatography (Silica Gel) and elute with EtOAc. The coloured fractions are pooled, evaporated and recrystallised from EtOAc. It is a lipophilic fluorescent chromoionophore and is a selectophore for K and Ca ions. [Morf et al. *Anal Chem* **62** 738 *1990*.]

Cobalt (II) *meso*-5.10,15,20-tetraphenylporphine complex *[14172-90-8]* **M 671.7.** It yields brown crystals from Et_2O or $CHCl_3$/MeOH (*cf iron chloride complex)*. It crystallises on extraction (Soxhlet) with $*C_6H_6$. It is soluble in most organic solvents except MeOH and petroleum ether. [UV, IR: Rothemund & Manott *J Am Chem Soc* **70** 1808 *1948*, Thomas & Martell *J Am Chem Soc* **81** 5111 *1959*.]

Cobaltic acetylacetonate *[21679-46-9]* **M 356.3.** Recrystallise it from $*C_6H_6$/petroleum ether and dry it in a vacuum. [Charles & Pawlikowski *J Phys* Chem **62** 440 *1938*, *Beilstein* **1** H 783.]

Cobaltous acetate tetrahydrate *[6147-53-1]* **M 249.1, pK_1^{25} 9.85 (for Co^{2+}).** Several recrystallisations from 50% aqueous acetic acid give the *tetrahydrate*. It is converted to the *anhydrous* salt by drying at 80°/1mm for 60 hours. [*Beilstein* **2** IV 120.]

Cobaltous acetylacetonate *[14024-48-7, 123334-29-2 x H_2O]* **M 257.2, m 165-170°, 172°.** Recrystallise the complex from acetone or MeOH and dry it in a vacuum. [*Beilstein* **1** H 783.]

12-Crown-4 (lithium ionophore V, 1,4,7,10-tetraoxacyclododecane) *[294-93-9]* **M 176.2, m 17°.** The distilled crude ionophore has to be recrystallised from pentane at -20° to remove acyclic material. It is then dried over P_2O_5. It complexes Li. [Anet et al. *Acta Chem Scand* **27** 3395 *1973*, *Beilstein* **19/11** V 334.]

Cupric acetate monohydrate *[6046-93-1 (H_2O), 142-71-2 (anhydrous)]* **M 199.7, m 115°, 240°(dec), d_4^{20} 1.88, pK_1^{25} 8.0, pK_2^{25} 13.1 (for Cu^{2+}).** Recrystallise $Cu(OAc)_2$ twice from warm dilute acetic acid solutions (5ml/g) by cooling. [*Beilstein* **2** IV 111.]

Cupric benzoate *[533-01-7]* **M 305.8.** Recrystallise it from hot water. Its solubility in EtOH/$*C_6H_6$ (90%) at 25° is 0.1%. [Crawford & Stewart *J Chem Soc* 228, 289 *1953*, *Beilstein* **9** H 84, **9** I 60, **9** III 376, **9** IV 280.]

Cupric lactate monohydrate *[814-81-3]* **M 295.7.** The *monohydrate* crystallises from hot H_2O (3ml/g) on cooling. [*Beilstein* **3** II 203, **3** III 465, **3** IV 636.]

Cupric oleate *[1120-44-1]* **M 626.5.** Crystallise cupric oleate from diethyl ether. [*Beilstein* **2** H 465, **2** I 196, **2** I202, **2** II 436, **2** III 1404, **2** IV 1646.]

Cupric phthalocyanine *[147-14-8]* **M 576.1.** Precipitate it twice from conc H_2SO_4 by slow dilution with water. It has also been purified by two or three sublimations at 580° in an argon flow at 300-400Pa. [*Beilstein* **26** III/IV 4256.]

(1,5-Cyclootadiene)(1,3,5-cyclooctatetraene)ruthenium [Ru(COD)(COT)] *[127382-91-6]* **M 315.4, m 88-**

94°, 92-94°. It can been prepared directly under argon and pressure equalisation, by adding freshly distilled cycloocta-1,5-diene (12.5ml, COD, see [111-78-4, 1552-12-1]) to MeOH (5ml) to Zn dust (6g) in a flask which is placed in an ultrasound bath (Branson, Bransonic Model B220) thermostated at 70°. A solution of $RuCl_3.3H_2O$ (530mg) in MeOH (12ml) is slowly added during 20 minutes to the refluxing COD mixture under N_2 flow and ultrasound. After addition is complete the mixture is sonicated for a further 2 hours under reflux at 70°. The solids are filtered off and the filtrate is evaporated with a vacuum line. The residual brown oil is extracted with the minimum volumes of hexane (3 x, total ~70ml), placed on an Al_2O_3 (Merck 1079, or Brockman Activity II-III) column under N_2 and eluted with hexane. The yellow band is collected, the volatiles are removed *in vacuo* to give orange crystals (590mg, 93%). Analytically pure ***Ru(COD)(COT)*** [$C_{16}H_{22}Ru$] is obtained as yellow crystals upon recrystallisation (70-90% recovery) from hexane at ~ -78°/~6 hours preferably under N_2 or argon. [Itoh et al. *J Organomet Chem* **272** 179 *1984*, Pertici et al. *J Chem Soc, Dalton Trans* 1961 *1980*.] The ^1H NMR (60MHz, $*C_6D_6$, TMS) has τ at 4.78 (dd, 2H), 5.22 (m, 2H), 6.21 (m, 2H), 7.08 (m, 4H), 7.78 (m, 8H), 8.36 (m, 2H) and 9.10 (m, 2H); compare with the ^1H NMR (60MHz, $*C_6D_6$, TMS) of $\underline{Ru(COD)_2}$ (see below) which has τ at 4.42 (t, 2H), 6.15 (dd, 4H), 6.45 (m, 4H), and 7.49—8.95 (m, 12H).
Alternatively, thermal isomerisation of **$\underline{Ru(COD)_2}$** (75mg, see [63395-36-8]) in $CDCl_3$ (0.5ml) in an NMR tube filled with argon occurs when the sealed tube is heated at 70° for 12 minutes as observed by the spectrum. Evaporation of the solution and purification as above gave yellow-orange crystals of Ru(COD)(COT) in >85% yield with no deuterium incorporation as observed by NMR. Isomerisation in $*C_6D_6$ is very slow at 70° giving a mixture of three isomers after 5 hours [Itoh et al. *J Organomet Chem* **272** 179 *1984*, see also Petrici et al. *J Chem Soc, Dalton Trans* 1961 *1980*]. A synthesis *via* a Grignard reduction of $[RuCl_2(COD)]_n$ has also been described [Pelzer et al. *Chem Mater* **16** 4937 *2004*]. For its catalytic activity see Chapter 7, Catalysts-Part 1. It is a key precursor for the preparation of stabilised Ru nanoperticles [Pan et al. *J Am Chem Soc* **123** 7584 *2001*, cf Chapter 8].

Cyclopentadienyl iron(II) dicarbonyl dimer [di(cyclopentadienyl)tetracarbonyl-diiron), $(C_5H_5Fe)_2(CO)_4$] *[38117-54-3]* **M 353.9, m 194° (dec) (sealed tube).** This key precursor to a variety of cyclopentadienyl-carbonyl complexes is prepared from $Fe(CO)_5$ (10ml, [13463-40-6], **CARE**, poisonous, work in an efficient fume cupboard) by refluxing with an excess of dicyclopentadiene (10ml, cyclopentadiene dimer see 77-73-6) for *ca* 40 hours under a N_2 or argon atmosphere in the absence of light, removing the solvent, adding $CHCl_3$ (50ml), and removing any $Fe_2(CO)_9$ and insoluble material by centrifugation. The decanted supernatant is cooled in a Dry-ice/Me_2CO bath, the crystals are collected by centrifugation and recrystallised from $CHCl_3$ to give a ~30% yield (based on CO) of analytically pure dark reddish-purple crystals of *$(C_5H_5Fe)_2(CO)_4$*, **m 194° (dec)** (sealed tube). The solid is stable to air and light, but solutions deteriorate under these conditions. It forms ferrocene (in 75% yield based on C_5H_5) when heated at 210°. It is readily soluble in EtOH, $CHCl_3$, pyridine, less soluble in CCl_4 and CS_2, and sparingly soluble in light petroleum giving red solutions in each case. It is insoluble in H_2O and is unaffected by it. The measured molecular weight by isothermal distillation is 368. The IR has strong bands at λ_{max} at 4.95μ, 5.1μ and 5.6μ (in CCl_4) and 12.1μ (CS_2). In the presence of O_2 a solution of the complex in EtOH/$CHCl_3$/concHCl/3hours provides red crystals of *$C_5H_5Fe(CO)_2Cl$* (from $CHCl_3$/petroleum ether 85:15, decomposing >87°). This chloride is not ionic but gives the orange cation *$C_5H_5Fe(CO)_2^+$* with $AgNO_3/HNO_3$, and yellow crystals of *$C_5H_5Fe(CO)_2CN$* (from $CHCl_3$, decomposing >120°) by reaction with NaCN/MeOH/24 hours in 46% yield. [Piper, Cotton and Wilkinson *J Inorg Nucl Chem* **1** 165 *1955*, *Beilstein* **16** IV 1826.] When *$(C_5H_5Fe)_2(CO)_4$* is treated with NaHg it provides the anion *$C_5H_5Fe(CO)_2^-$* that can be alkylated with MeI to furnish *$C_5H_5Fe(CO)_2Me$* and related alkyl derivatives. [Aktogu et al. *J Organomet Chem* **262** 49 *1984*, R.B. King *Organometallic Synthesis Vol 1*, p 45, Academic Press, NY, *1965*.]

2,4-Cyclopentadien-1-yl lithium (lithium cyclopentadienide, CpLi) *[16733-97-4]* **M 72.0.** CpLi is a white air and moisture sensitive solid which should be stored under N_2 preferably at low temperature. Like CpNa [4984-82-1] and CpK, it is handled in a dry box or Schlenk equipment in an inert atmosphere (compare with CpTl below). To avoid excessive manipulation, the reagents are sometimes prepared *in situ* in the reactions without being isolated. The solid is prepared in Schlenk equipment under a N_2 atmosphere by adding dropwise redistilled cyclopentadiene (2.34ml, 28.5mmol) to a solution of EtLi (28.5mmol) in *benzene (50ml) and stirred magnetically until precipitation of a voluminous white solid is complete. This is filtered, or centrifuged, off

under N_2, washed with dry Et_2O and dried *in vacuo*. It is sparingly soluble in Et_2O but is soluble in THF. [Wagner & Ebel *Tetrahedron* **26** 5155 *1970*.] For the preparation of a standard solution (use drybox, or Schlenk equipment under N_2) cyclopentadiene (~10.0mmol) in dry THF (7ml) is refluxed with excess of lithium metal (see Ford *J Am Chem Soc* **82** 2857 *1970*) for 4 hours, filtered through a sintered glass funnel and diluted to a total volume of 10ml with THF which provides a 1.00M solution for further use. [Ford *J Organomet Chem* **32** 27 *1971*.] Its UV in THF has no maxima above 210nm, and its IR has ν_{max} (solid in Nujol) at 3048 (m), 2906 (w), 1742 (m), 1629 (m), 1548 (w), 1513 (w), 1426 (m), 1364 (sw), 1304 (w), 1258 (w), 1166 (w), 1110 (w), 1003 (s), 935 (sw), 887 (sw) and 746 (ss) cm^{-1}; the ^1H NMR [100MHz, shift relative to β-CH_2 of THF (1.767ppm of 2% TMS in THF) at 27°] has a peak at δ 5.59 (at 1.0M) or 5.70 (at 0.01M) [Ford *J Organomet Chem* **32** 27 *1971*; the ^{13}C NMR (22.6MHz, $MeOCH_2CH_2OMe/*C_6D_6$ 3:1, under N_2 at 30°, TMS) has a multiplet with δ centered at 103.59 (m, $^1J_{^{13}C\text{-}H}$ 159.4 and 6.9Hz). [Fischer et al. *J Organomet Chem* **116** 65 *1976*.]

Cyclopentadienyl thallium [(η^5-2,4-cyclopentadien-1-yl)thallium, thallium(I) cyclopentadienide, CpTl) *[34822-90-7]* **M 269.5, blackens at ~60° in air and at ~230° in a sealed capillary, but does not melt below 270°.** CpTl is purified by repeated sublimation through a glass plug at ~80°/0.005mm, 75°/0.1mm or 100-110°/10mm to give pale yellow acicular (small pointed needles) crystals. It is moderately stable in air but darkens superficially after several months. As it is somewhat light sensitive, it should be stored in dark brown screw cap containers, and thus keeps for prolonged periods of time. It reacts with some solvents, e.g. $CHCl_3$ and CCl_4 (forming TlCl), and CS_2 (forming black and red materials), or is very poorly soluble, e.g. in THF, Et_2O and $*C_6H_6$. However, it is soluble enough in the latter solvents, even at low temperatures (e.g. -20°), to react almost completely to give high yields of products. *It is a more convenient reagent for cyclopentadienylation than CpNa, CpK or CpLi because it is less basic, can be prepared in aqueous medium, can be prepared on a large scale, and is stable in air at room temperature for long periods*. The cyclopentadiene ring of CpTl has IR in accord with C_{5v} symmetry, exhibiting one C—H stretching band at ν_{max} 3101 cm^{-1} in the gas phase at 150° to 249° which compares with ferrocene (3109 cm^{-1}), nickelocene (3107 cm^{-1}), di-cyclopentadienylmanganese (3101 cm^{-1}), di-cyclopentadienyl-magnesium(II) (3095 cm^{-1}), and benzene (3099 cm^{-1}), and is supported by theoretical considerations. The five membered ring is flat and ionic with the positive charge delocalised within it, and the Tl bears the counter negative charge and is centered on top of it. [Cotton & Raynolds *J Am Chem Soc* **80** 269 *1958*, Roberts et al. *J Mol Spectr* **35** 476 *1970*, Fritz *Chem Ber* **92** 780 *1959*.]
CpTl is conveniently prepared by dissolving or suspending a thallium(I) salt [TlCl 3.6g, TlBr 5.26g, TlI does not react, TlSCN 3.94g, $TlNO_3$ 4.00g or Tl(I) acetylacetonate 4.55g] in a solution of KOH (10g) in H_2O (100ml) in a Waring Blender (900ml jar capacity), adding cyclopentadiene (2.0ml, freshly distilled [542-92-7]) and stirring for 30 seconds. Longer stirring gives a fine suspension that is difficult to collect. The white product is filtered off, washed with EtOH (2 x 10ml), dried in a desiccator over anhydrous $CaSO_4$ to give CpTl in 91, 93, 0, 99, 97 and 87% yields respectively which is usually used without purification. The preparation can be scaled up to give ~50g of CpTl, and the preferred salt is TlBr. If desired, further purification can be performed by high vacuum sublimation as described above. [Hunt & Doyle *Inorg Nucl Chem Lett* **2** 283 *1966*, Cotton & Raynolds *J Am Chem Soc* **80** 269 *1958*, Corey et al. *J Am Chem Soc* **93** 1489 *1971*.] ***Note that all thallium compounds are POISONOUS and due precautions have to be exercised.***
CpTl is a source of the C_5H_5 ligand, and reactions are performed under N_2 with highly purified solvents. The following are a few of the many reported reactions of CpTl. It has been used to prepare ferrocene, cobaltocene, nickelocene, also complexes such as Cp_2TiCl_2 with $TiCl_4$ in $*C_6H_6$, or of $Cp(MeOCp_2)Pd(II)$ from $[CpPd(OMe)Cl]_2$ with CpTl in $*C_6H_6$ [Hunt & Doyle *Inorg Nucl Chem Lett* **2** 283 *1966*], as well as compounds like the 1-methoxymethylcyclopenta-2,4-diene key intermediate for the synthesis of prostaglandins [Corey et al. *J Am Chem Soc* **93** 1489 *1971*]; it reacts with $[CpMo(NO)I_2]_2$ in THF to give $Cp_2Mo(NO)I$ where the iodine can be replaced [King *Inorg Chem* **7** 90 *1968*], CpTl reacted with electrophilic olefins, e.g. tetracyanoethylene, in MeCN or THF to form compounds of the type $Tl^+[Cp(CN)C(CN)_2]^-$ [Freeman & Sneddon *Inorg Chem* **19** 1125 *1980*], and the reaction of CpTl (10-80% molar excess) with 7-chloronorbornadiene in dry diglyme at 150°/3-4 hours gave, after filtration of Tl salts, the hydrocarbon *hexahydro-3,4,7-methenocyclopenta[a]pentalene* in 8-12% yield from a one-step synthesis (a hydrocarbon which would have required several synthetic steps to prepare) [Battiste & Timberlake *J Org Chem* **42** 176 *1977*]. [Meister *Angew Chem* **69** 533 *1957*, *Beilstein* **16** IV 1690.]

6,6-Dibenzyl-14-crown-4 (lithium ionophore VI, 6,6-dibenzyl-1,4,8,11-tetra-oxa-cyclo-tetradecane) *[106868-21-7]* **M 384.5, m 102-103°.** Dissolve it in $CHCl_3$, wash this with saturated aqueous NaCl, dry ($MgSO_4$), evaporate and purify it by chromatography on silica gel and gradient elution with *C_6H_6/MeOH followed by preparative reverse phase HPLC on an octadecyl silanised silica (ODS) column and eluting with MeOH. It can be recrystallised from MeOH (IR has ν_{max} at 1120 cm^{-1}, C-O-C in KBr). [Kimura et al. *Anal Chem* **59** 2331 1987, see also Maruyama et al. *J Chem Soc Perkin Trans 1* 2069 *1986* and Tsukube et al. *J Chem Soc Perkin Trans 1* 1033 *1986*.] It complexes selectively with Li ions.

Di-*n*-butyltin oxide *[818-08-6]* **M 248.9, m >300°.** The oxide is prepared by hydrolysis of di-*n*-butyltin dichloride with KOH. Hence wash it with a little aqueous M KOH, then H_2O and dry at ~80°/10mm until the IR is free from OH bands. [Cummings *Aust J Chem* **18** 98 *1965*, *Beilstein* **4** I 588.]

Dicarbonyl(cyclopentadienyl)Co (I) *[12078-25-0]* **M 180.1, b 75°/22mm, b 139-140°(dec)/710mm.** Best distilled in an atmosphere of CO in a vacuum. The red brown liquid decomposes slightly on distillation even in a vacuum to liberate some CO. Operations should be performed in an efficient fume cupboard. It is soluble in organic solvents and stable in air but decomposes slowly in sunlight and rapidly under UV. [Piper et al. *J Inorg Nucl Chem* **1** 165 *1955*, *Beilstein* **16** IV 1827.] **TOXIC.**

Dichloro(2,2′:6′, 2″-terpyridine)platinum(II) dihydrate *[151120-25-1]* **M 535..3, decomposes at 240-260°.** The aqueous filtrate from the reaction between terpyridyl (2.3g) and potassium platinochloride (4.0g) in H_2O at 90° for 6 hours, is evaporated, cooled, and treated with HCl whereby the red chloride separates as the *dihydrate*, whereas the black *trihydrate* slowly crystallises from a cold aqueous solution and is air-dried. It is converted to the *dihydrate* in a desiccator over H_2SO_4, by washing with EtOH, heating in H_2O (slowly), or by precipitating from a warm aqueous solution with hydrochloric acid. This salt is not decomposed by boiling HCl, and is insoluble in most organic solvents. [Morgan & Burstall *J Chem Soc* 1498 *1934*, Lippard *Acc Chem Res* **118** 211 *1987*, *Beilstein* **26** IV 260.]

Diethyl aluminium chloride *[96-10-6]* **M 120.6, m -75.5°, b 106.5-108°/24.5mm, d_4^{20} 0.96.** Distil it from excess dry NaCl (to remove ethyl aluminium dichloride) in a 50-cm column containing a heated nichrome spiral. [*Beilstein* **4** IV 4403.]

***N,N′*-Diheptyl-*N,N′*-5,5-tetramethyl-3,7-dioxanonanediamide [lithium ionophore I (ETH 149)]** *[58821-96-8]* **M 442.7.** Purify it by chromatography on Kieselgel using $CHCl_3$ as eluent (IR has ν_{max} at 1640cm^{-1}). [Kirsch et al. *Helv Chim Acta* **60** 2326 *1977*, Simon & Carafoli *Methods Enzymol* **56** 439 *1977*.]

Diphenylmercury *[587-85-9]* **M 354.8, m 125.5-126°, 128-129°.** Sublime Ph_2Hg, then crystallise it from nitromethane or ethanol. If phenylmercuric halides are present, they can be converted to phenylmercuric hydroxide which, being much more soluble, remain in the alcohol or *benzene used for crystallisation. Thus, crude material (10g) is dissolved in warm ethanol (*ca* 150ml) and shaken with moist Ag_2O (*ca* 10g) for 30 minutes, then heated under reflux for 30 minutes and filtered hot. Concentrating the filtrate by evaporation gives diphenylmercury, which is then recrystallised from *benzene [Blair et al. *J Chem Soc* 3174 *1959*]. [*Beilstein* **16** IV 1702.] **TOXIC.**

Disodium calcium ethylenediaminetetraacetate *[39208-14-5]* **M 374.3, (see pKs for EDTA in entry below).** Dissolve it in a small amount of water, filter it and precipitate it with excess EtOH. Dry it at 80°. [*Beilstein* **4** IV 2451.]

Disodium dihydrogen ethylenediaminetetraacetic acid ($2H_2O$) *[6381-92-6]* **M 372.2, m 248°(dec), pK_1^{25} 0.26 pK_2^{25} 0.96, pK_3^{25} 2.60, pK_4^{25} 2.67, pK_5^{25} 6.16, pK_6^{25} 10.26 (see EDTA).** Analytical reagent grade material can be used as primary standard after drying at 80°. Commercial grade material can be purified by crystallisation from water or by preparing a 10% aqueous solution at room temperature, then adding ethanol slowly until a slight permanent precipitate is formed, filtering, and adding an equal volume of ethanol. The precipitate is filtered off onto a sintered-glass funnel, is washed with acetone, followed by diethyl ether, and

dried in air overnight to give the *dihydrate*. Drying at 80° for at least 24 hours converts it to the *anhydrous* form. [*Beilstein* **4** IV 2451.]

Disodium magnesium ethylenediaminetetraacetate *[14402-88-1]* **M 358.5, pK_1^{25} 0.26 pK_2^{25} 0.96, pK_3^{25}2.60, pK_4^{25} 2.67, pK_5^{25} 6.16, pK_6^{25} 10.26 (see EDTA).** Dissolve it in a small amount of water, filter and precipitate it with an excess of MeOH. Dry it at 80°. [*Beilstein* **4** IV 2450.]

Disodium succinate *[150-90-3]* **M 162.1.** Crystallise it twice from water (1.2ml/g) and dry it at 125°. It has been freed from other metal ions by passage of a 0.1M solution through a column of Dowex resin A-1 (Na form). It is *hygroscopic*. [*Beilstein* **2** H 606, **2** IV 1908.]

Di-*p*-tolylmercury *[50696-65-6, 537-64-4]* **M 382.8, m 244-246°.** Crystallise it from xylene. [Whitmore et al. *Org Synth* Coll Vol **I** 231 *1941*, *Beilstein* **16** H 947, **16** I 667, **16** III 1329, **16** IV 1705.]

Di-*p*-tolyl phenylphosphonate *[94548-75-1]* **M 388.3, n_D^{25} 1.5758.** Purify as described under diisooctyl phenylphosphonate.

Eosin B (Bluish, Eosin Scarlet, 4',5'-dibromo-2',7'-dinitrofluorescein disodium salt) *[548-24-3]* **M 624.1, λ_{max} 514nm, CI 45400.** Free it from inorganic halides by repeated crystallisation from butan-1-ol. [*Beilstein* **19/6** V 469.]

Eosin Y (as di-Na salt) (2′,4′,5′,7′-tetrabromofluorescein di-Na salt) *[17372-87-1]* **M 691.9.** Dissolve it in water and precipitate it by adding dilute HCl. The precipitate is washed with water, crystallised from ethanol, then dissolved in the calculated amount of dilute NaOH solution and evaporated to dryness on a water-bath. The purified disodium salt is then crystallised twice from ethanol [Parker & Hatchard *Trans Faraday Soc* **57** 1894 *1961*]. [*Beilstein* **19** III/IV 2917.] [Same as below.]

Ethylmercuric chloride *[107-27-7]* **M 265.1, m 192.5°, 193-194°.** Mercuric chloride can be removed by suspending ethylmercuric chloride in hot distilled water, filtering with suction onto a sintered-glass crucible and drying it. Then crystallise it from ethanol and sublime it under reduced pressure. It can also be crystallised from water. [Marvel et al. *J Am Chem Soc* **47** 3009 *1925*.]

Ethylmercuric iodide *[2440-42-8]* **M 356.6, m 182°, 186°.** Crystallise it once from water (50ml/g). [See previous entry, Marvel et al. *J Am Chem Soc* **4** 3009 *1925*.]

Ethylzinc (zinc diethyl) *[557-20-0]* **M 123.5, m -28°, -33.8°, b 116.8°/761mm, d_4^{25} 1.205, n_D^{20} 1.498.** The presence of EtI in the liquid can be detected by its absorption spectrum. This can be removed by 2 or 3 passages over a Zn/Cu couple at ~150°. Any hydrocarbon impurities are removed by distillation at ~760mm in an inert atmosphere as it is flammable. It is moisture sensitive, hydrolysing to give ethane so store it in sealed ampoules under N_2 or argon.
It is also available as a ~15% solution in toluene (d_4^{20} 0.915) or ~ 1M *n*-hexane (d_4^{20} 0.726). Solutions should be stored under dry N_2 or argon, and if they contain some precipitate, the solutions should be filtered through a sintered frit under inert gas pressure. *Alternatively*, siphon carefully the required volume of supernatant. [Noller *Org Synth* Coll Vol **II** 184 *1943*, Bamford et al. *J Chem Soc* 471 *1946*, *Beilstein* **4** H 672, **4** I 609, **4** II 1044, **4** III 1999, **4** IV 4423.]

Ethynyl tributylstannane *[994-89-8]* **M 315.1, b 76°/0.2mm, 130-135°/0.7mm, 200°/2mm, d_4^{20} 1.1113, n_D^{20} 1.4770.** Purify the stannane by dissolving the reagent (*ca* 50g) in heptane (250ml), washing it with H_2O (100ml), drying ($MgSO_4$), evaporating and distilling in a vacuum. It has IR with ν_{max} at 3280 (≡ C–H), 2950, 2850, 2005 (C≡C), 1455, 1065 and 865cm^{-1}. [Bottaro et al. *J Org Chem* **46** 5221 *1981*, Stille & Simpson *J Am Chem Soc* **109** 2138 *1987*, Zavgorodnii et al. *J Gen Chem USSR (Engl Edn)* **37** 1469 *1967*.]

Europium (III) acetate dihydrate *[62667-64-5]* **M 383.1, pK_1^{25} 8.31 (for aquo Eu^{3+}).** Recrystallise it several times from water [Ganapathy et al. *J Am Chem Soc* **108** 3159 *1986*]. [*Beilstein* **2** II 119.] For europium shift reagents see lanthanide shift reagents in "Aliphatic Compounds", Chapter 4.

Ferrocene *[102-54-5]* **M 186.0, m 173-174°.** Purify ferrocene by crystallisation from pentane or cyclohexane (also $*C_6H_6$ or MeOH can be used). It is moderately soluble in Et_2O and sublimes readily above 100°. Crystallisation from EtOH gave material **m** 172.5-173°. [Wilkinson *Org Synth* Coll Vol **IV** 473 *1963*, Miller *J Chem Soc* 632 *1952*.] It has also been crystallised from methanol and sublimed *in vacuo*. [Saltiel et al. *J Am Chem Soc* **109** 1209 *1987*, *Beilstein* **16** IV 1783.]

Ferrocene carboxaldehyde *[12093-10-6]* **M 214.1, m 117-120°, 118-120°, 121°, 124.5°.** The aldehyde forms red crystals from heptane/CH_2Cl_2, EtOH or petroleum ether and sublimes at 70°/1mm. The *cyanohydrin* has **m** 104° (from $*C_6H_6$/EtOH). The *semicarbazone* has **m** 217-219°(dec) after recrystallisation from aqueous EtOH. The *oxime* provides two isomers from petroleum ether *viz* **m** 96-99° and **m** 155°. The *O-acetyloxime* has **m** 80-81° after recrystallisation from hexane [Lindsay & Hauser *J Org Chem* **22** 355 *1957*]. The *2,4-dinitrophenylhydrazone* has **m** 248°(dec). [*Beilstein* **16** IV 1798, Graham et al. *J Am Chem Soc* **79** 3416 *1957*, Broadhead et al. *J Chem Soc* 650 *1958*.]

Ferrocene carboxylic acid *[1271-42-7]* **M 230.1, m 210°(dec), 225-230°(dec), pK^{20} 4.4 (H_2O), 6.29 (68% aqueous MeOH).** The acid crystallises as yellow crystals from petroleum ether (**m** 225-230°dec), $CHCl_3$ (**m** 208.5°dec), toluene/petroleum ether (**m** 195-205°dec), or aqueous ethanol. [Matsue et al. *J Am Chem Soc* **107** 3411 *1985*.] The *acid chloride* **m** 49° crystallises from pentane, and has UV with λ_{max} at 458nm [Lau & Hart *J Org Chem* **24** 280 *1959*]. The *methyl ester* crystallises from aqueous MeOH with **m** 70-71°. The *anhydride* has **m** 143-145° when recrystallised from petroleum ether [Acton & Silverstein *J Org Chem* **24** 1487 *1959*]. The *amide* has **m** 168-170° when crystallised from $CHCl_3/Et_2O$ or **m** 167-169° when crystallised from $*C_6H_6$/MeOH. [Reeves *Org Synth* **56** 28 *1977*, Arimoto & Haven *J Am Chem Soc* **77** 6295 *1955*, Benkeser et al. *J Am Chem Soc* **76** 4025 *1954*.] [*Beilstein* **16** IV 1807.]

Ferrocene-1,1'-dicarboxylic acid *[1293-87-4]* **M 274.1, m >250°(dec), >300°, pK_1^{25} 3.9, pK_2^{25} 5.3.** The dicarboxylic acid crystallises in orange-yellow crystals from AcOH and sublimes above 230°. The *monomethyl ester* has **m** 147-149° [Nesmeyanov & Reutov *Dokl Acad Nauk USSS* **115** 518 *1957*]. The *dimethyl ester* has **m** 114-115° [Woodward et al. *J Am Chem Soc* **74**, 3458 *1953*]. The *diacid chloride* has **m** 92-93° when recrystallised from petroleum ether. [Nesmeyanov & Reutov *Dokl Acad Nauk SSSR* **120** 1267 *1958*, Kazitsyna et al. *Dokl Acad Nauk SSSR* **127** 333 *1959*, *Beilstein* **16** IV 1811.]

Ferrocene-1,1,-dimethanol *[1291-48-1]* **M 246.1, m 107-108°.** The diol is obtained from the diacid by $LiAlH_4$ reduction and recrystallised from Et_2O/petroleum ether. [Reinhart et al. *J Am Chem Soc* **82** 4111 *1960*, *Beilstein* **16** IV 1795.]

1-(Ferrocenyl)ethanol (α-methylferrocenemethanol) *[1277-49-2]* **M 230.1, m 73-75°, 76-77°, 76-79°.** This versatile reagent is obtained by reduction of acetylferrocene (22.8g, see [1271-55-2]) in dry Et_2O (500ml) with $LiAlH_4$ (1.9g) solution in anhydrous Et_2O and refluxing for 2 hours. Excess of hydride is destroyed with EtOAc, the mixture is treated with a solution of NH_4Cl (28g) in H_2O, stirred for 0.5 hours at 0°, filtered, the organic layer is washed twice with H_2O, dried ($MgSO_4$), and evaporated to dryness. The residue (20.5g, 89%) is recrystallised from Et_2O/petroleum ether to give the *carbinol* as orange rods. It is free from a C=O band but has a strong broad OH band in the IR spectrum. The *acetyl derivative* (Ac_2O/pyridine/0°/15 hours), after sublimation at 60°/0.2mm, has **m 67-68°** and an IR band at 5.78μ (s, C=O), but no band in the OH region. [Arimoto & Haven *J Am Chem Soc* **77** 6295, *Beilstein* **16** IV 1975.]

Germanium tetraethoxide *[14165-55-0]* **M 252.8, m -72°, b 54.5°/5mm, 71-72°/11mm, 188-190°/722mm, d^{25} 1.1288.** Distil $Ge(OEt)_4$ through a 10cm Vigreux column under reduced pressure. *Alternatively*, distil it through a Fenske glass helices column fitted with a total condensation variable take-off stillhead. Fractionate it under reduced pressure using a reflux ratio of 10:1. [Johnson & Fritz *J Am Chem Soc* **75** 718 *1953*, Bradley *J Chem Soc* 4916 *1956*, *Beilstein* **1** IV 1308.]

Hexabutyldistannane **{hexabutylditin, bis[(tributyl)tin}** *[813-19-4]* **M 580.4, b 160-162°/0.3mm, d_4^{20} 1.148, n_D^{20} 1.512.** Purify bis[(tributyl)tin] by distilling it in a vacuum and store it in the dark. [Shirai et al. *Yakugaku Zasshi* **90** 59 *1970*, *Chem Abstr* **72** 90593 *1970*, *Beilstein* **4** I 590.]

Hexamethylditin {hexamethyldistannane, bis[(trimethyl)tin]} *[661-69-8]* **M 327.6, m 23.5°, b 85-88°/45mm, 182°/756mm, d^{25} 1.57.** Wash bis[(trimethyl)tin] with H_2O and extract with $*C_6H_6$, dry by filtering through powdered Na_2SO_4, remove $*C_6H_6$ on a rotary evaporator and fractionally distil the oily residue under vacuum (**b** 85-88°/45mm). *It boils at ca 182° at atmospheric pressure, but it cannot be distilled in air because the hot vapours flash in the condenser.* [Kraus & Session *J Am Chem Soc* **47** 2361 *1925*, Morris & Selwood *J Am Chem Soc* **63** 2509 *1941*, Pedley et al. *Trans Faraday Soc* **53** 1612 *1957*, *Beilstein* **4** IV 4346.]

Iron(II) acetylacetonate **[iron(II) bis(2,4-pentanedionato-κO2,κO4), $Fe(2^+)(acac)_2$]** *[14024-17-0]* **M 254.1, m 175°.** The preparation and handling of this complex should be done in a dry box or Schlenk equipment under dry pre-purified N_2; and solvents should be de-gassed prior to use. $Fe(acac)_2$ is prepared by adding $FeCl_2.4H_2O$ (25g) in degassed H_2O (50ml) containing a small amount of sodium dithionite to reduce any Fe(III) impurities, to a degassed aqueous solution (300ml) containing piperidine (27.3ml) and redistilled acetylacetone (28.1ml, [123-54-6]). After 15 minutes the resulting precipitate is filtered off and washed with degassed H_2O, EtOH then Et_2O and the yellow-brown powder [presumed to be $Fe(acac)_2.2H_2O$ Emmert & Jarczynski *Chem Ber* **64** 1072 *1931*] is transferred into a sublimation apparatus with a large cold finger and pumped dry at 10^{-3} mm for 6 hours; and the hydrated complex is then heated at 90°/10^{-3}mm for at least 12 hours to dehydrate it and the orange-brown solid is sublimed twice at 165-175°/10^{-3}mm. The small orange-brown crystals that sublime at first become darker as the crystals grow, giving finally larger black clusters which are analytically pure anhydrous solid. Note that the complex is very sensitive to O_2 in air, darkens in colour upon oxidation, and great care should be exercised to avoid oxidation when using it. It maybe ***pyrophoric*** when dry. Its molecular weight (cryoscopic and ebullioscopic) in $*C_6H_6$ increases as the concentration increases reaching a maximum for a hexamer, and the data are supported by the UV absorption spectra. [Buckingham et al. *Aust J Chem* **20** 281 *1967*, Dwyer & Sargeson *Pr J Soc NSWales* **90**, 141, 142 *1956*; for the formation constant see Izatt et al. *J Phys Chem* **59** 80 *1955*, *Beilstein* **1** III 3122, **1** IV 3675.] *Note*: **iron(1+) bis(2,4-pentanedionato-κO2,κO4)** has [*20149-10-4*], see Chapter 6, Catalysts-Part 1 for $Fe(III)(acac)_3$, [14024-18-1].

Iron(II) bis(1,1,1,5,5,5-hexafluoropentan-2,4-dionate) [iron(II) bis(1,1,1,5,5,5-hexafluoro-2,4-pentane-dionato-κO2,κO4), $Fe(2^+)(facac)_2$, $Fe(hfacac)_2$] *[28736-68-7]* **M 470.1, mp 40°.** The preparation and handling of this complex [cf $Fe(acac)_2$ 14024-17-0] should be carried out in a dry box or Schlenk equipment under dry pre-purified N_2; and solvents should be de-gassed prior to use. $Fe(hfacac)_2$ is prepared by adding $FeSO_4.7H_2O$ (11.8g) in H_2O (50ml) slowly to a mixture of redistilled hexafluoroacetylacetone (12.2ml, see [1522-22-1]) and piperidine (8.5ml), whereby a dark violet precipitate separates immediately. This solid is filtered off, washed with a large volume of H_2O (1000 ml), placed in a sublimation apparatus and evacuated at 10^{-3}mm at ~25° for hours. The temperature is slowly raised to 40° and kept at 45-50° and 10^{-3}mm for 3 days, and the dark violet crystals that formed on the cold finger are collected, and if necessary are ground to a fine powder and re-sublimed to give analytically pure $Fe(hfacac)_2$ (IR is free of bands at 3300-3500 cm^{-3}, i.e. absence of H_2O). It requires a much longer period of evacuation than $Fe(acac)_2$ for dehydration. The strong electron withdrawing effects of the CF_3 groups make this complex relatively more stable to aerial oxidation than $Fe(acac)_2$. It can be recrystallised from very dry $*C_6H_6$ without alteration, where its molecular weight (cryoscopic and ebullioscopic) increases with increase in concentration up to a value of 1.7 (compare with 6 for $Fe(acac)_2$ above). [Buckingham et al. *Aust J Chem* **20** 281 *1967*.]

Iron(II) dicyanobis(2.2′-dipyridine) trihydrate [$Fe(bpy)_2(CN)_2.\ 3H_2O$] *[15603-10-8]* **M 474.3, dec. on heating.** The iron complex is prepared from 2,2′-dipyridine (4.7g, 30mmol) and ferrous ammonium sulfate hexahydrate (3.9g, 10mmol) in H_2O (400ml) which are heated to just below boiling, and a freshly prepared solution of KCN (10g) in H_2O (20ml) is added all at once to it, stirred, and the hot mixture is allowed to cool to room temperature. The complex separates as very dark violet (almost black) fine crystals rapidly, but is allowed to stand for 1 hour. The solid is collected and washed liberally with H_2O. Unused bipyridine is recovered from the filtrate by extraction with Et_2O. The iron complex can be purified by dissolving it in concentrated H_2SO_4 (25ml) and slowly diluting it with H_2O (800ml, CARE as it will warm up) with stirring. The crystalline solid is collected washed free from H_2SO_4 with small volumes of H_2O, sucked dry, rinsed with Me_2CO and dried *in vacuo* to give analytically pure *trihydrated complex* (3.5g, 75%). It is soluble in H_2O to give a pale red solution, in EtOH to give a deep red-violet liquid, and in $CHCl_3$ to give a deep blue colour; but is only very slightly soluble in basic solution. Large amounts can be dissolved in concentrated H_2SO_4 to give the yellow di-protonated species which on gradual dilution with H_2O the solution changes its hue to orange then to red and finally to the dark violet colour of the original crystals. It is a diamagnetic Fe(II) complex which is readily oxidised to the corresponding Fe(III) complex and can be titrated with Ce(IV) sulfate in H_2SO_4. On titration with $HClO_4$ in anhydrous AcOH (**Care** due to possible explosion; Schilt *J Am Chem Soc* **82** 5779 *1960*), the first equivalence point leads to a mono-protonated orange species, and at the second equivalence point (not quite as sharp as the first) it provides the yellow di-protonated species. The electronic (Schilt *J Am Chem Soc* **82** 3000 *1960*, Schilt *J Am Chem Soc* **82** 5779 *1960*, Madeja & König *J Inorg Nucl Chem* **25** 377 *1963*), and vibrational spectra (Schilt *Inorg Chem* **3** 1323 *1964)* have been reported, and the *cis*-configuration has been deduced from IR (Hamer & Orgel *Nature* **190** 439 *1961*, Schilt *Inorg Chem* **3** 1323 *1964*) and stereochemical (Madeja *Chem Zvesti* **19** 186 *1965*) considerations. [Schilt *Inorg Synth* **12** 249 *1970*.]

Iron(III) ethoxide [$Fe(OEt)_3$] *[5058-42-4]* **M 91.0, m 120°, volatilies at 155°/0.1mm in a molecular still.** The ethoxide is prepared by adding excess of ammonia to a solution of anhydrous $FeCl_3$ (15g) in $*C_6H_6$ (170ml) and EtOH (76ml), which results in an exothermic reaction at the end of which the mixture is evaporated to dryness *in vacuo*. The residue is extracted with $*C_6H_6$ (150ml), the NH_4Cl is filtered off, the filtrate is evaporated to dryness *in vacuo* to leave a viscous brown residue. This is dissolved in hot EtOH (30ml) and brown crystals of analytically pure *ferric ethoxide* (4.2g) deposit slowly. It is trimeric in $*C_6H_6$ solution (molecular weight by ebullioscopy) and is for preparing other useful ferric trialkoxides by alcohol exchange in benzene solution, e.g. with *n*-PrOH, *n*-BuOH, *iso*-BuOH or *n*-amyl alcohol, *via* the azeotropic removal of EtOH. It is commercially available as a 1M solution in EtOH. [Bradley et al. *J Chem Soc* 126 *1955*, *Beilstein* **1** IV 1243.]

Iron(III) *meso*-5,10,15,20-tetraphenylporphine chloride complex [5,10,15,20-tetraphenyl-21*H*, 23*H*-porphine iron(III) chloride] *[16456-81-8]* **M 704.0, λ_{max} 418nm.** Purify the complex by extraction from a thimble (Soxhlet) with $CHCl_3$. Concentrate the extract to *ca* 10ml and add *ca* 80ml of hot MeOH. Dark blue crystals separate on cooling. It can be recrystallised several times from $CHCl_3$/MeOH. Avoid prolonged heating. It is quite soluble in organic solvents but insoluble in petroleum ether. [Rothemund & Manotti *J Am Chem Soc* **70** 1808 *1948,* UV: Dorough et al. *J Am Chem Soc* **73** 4315 *1951*, *Beilstein* **26** III 1960.] [As catalyst for silylation of OH groups see Firouzabadi et al. *Synth Commun* **27** 2709 1997.]

Lanthanide shift reagents

See in "Aliphatic Compounds", Chapter 4, europium (III) acetate above and $Eu(tmc)_3$ and $Eu(tfc)_3$ below.

Lead II acetate (sugar of lead) *[301-04-2 (anhydrous), 6080-56-4 ($3H_2O$)]* **M 325.3, m 280°, pK_1^{25} 7.1 (for Pb^{2+}), pK_2^{25} 10.1 ($HPbO_2^-$), pK_3^{25} 10.8 (PbO_2^{2-}).** Crystallise $Pb(OAc)_2$ twice from anhydrous acetic acid and dry it under vacuum for 24 hours at 100°. The solubility in H_2O is 63% (at ~20°) and 200% (at boiling point). [*Beilstein* **2** IV 118.]

Lead (bis-cyclopentadienyl) (plumbocene) *[1294-74-2]* **M 337.4.** Purify it by vacuum sublimation. Handle and store it under N_2. [Dave et al. *J Chem Soc* 3686 *1979*, *Beilstein* **16** IV 1614.]

Lead tetraacetate *[546-67-6]* **M 443.2, m 175-180°.** Colourless prisms or needles purified by dissolving in hot glacial acetic acid containing a little acetic anhydride, treated with decolorising charcoal, collected on a hot water funnel or preheated Büchner funnel with minimum contact with moist air, and dried in a vacuum desiccator over KOH pellets. Store it in a well-stoppered vessel as it is decomposed by moisture to form brown PbO_2. It attacks skin, is soluble in hot AcOH, $*C_6H_6$, $CHCl_3$, tetrachloroethane and is used as a powerful oxidising agent. [Bailar *Inorg Synth* **I** 42 *1939*, Baudler in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 767 *1963*, *Beilstein* **2** IV 118.] **TOXIC.**

Lithium benzoate *[553-54-8]* **M 128.1.** Crystallise the salt from EtOH (13ml/g) by partial evaporation. [*Beilstein* **9** I 107, **9** IV 279.]

Lithium diisopropylamide *[4111-54-0]* **M 107.1, b 82-84°/atm, 84°/atm, d^{22} 0.722, flash point -6°.** LiN(*iso*-Pr)$_2$ is purified by refluxing over Na wire or NaH for 30 minutes and then distilled into a receiver under N_2. Because of the low boiling point of the amide, a dispersion of NaH in mineral oil can also be used directly in this purification without prior removal of the oil. It is **HIGHLY FLAMMABLE,** and is decomposed by air and moisture. [Wittig & Hesse *Org Synth* **50** 69 *1970*, *Beilstein* **4** H 154, **4** I 369, **4** II 630, **4** III 274, **4** IV 510.]

Lithium formate monohydrate *[6108-23-2 (H_2O), 556-63-8 (anhydrous)]* **M 70.0, d_4^{20} 1.46.** Crystallise HCO_2Li from hot water (0.5ml/g) by chilling. [*Beilstein* **2** III 22, **2** IV 13.]

Lithium methylate (lithium methoxide) *[865-34-9]* **M 38.0.** The most probable impurity is LiOH due to hydrolysis by moisture. It is important to keep the sample dry. It can be dried by keeping in a vacuum at 60-80° under dry N_2 using an oil pump for a few hours. Store it under N_2 in the cold. It should not have bands above 3000cm^{-1}, and its IR (KBr) should have ν_{max} at 1078, 2790, 2840 and 2930cm^{-1}. [Suebold *J Org Chem* **21** 156 *1956*, *Beilstein* **1** IV 1220, 1241.]

Lithium pentamethylcyclopentadienide (LiCp′, 1,2,3,4,5-pentamethyl-2,4-pentadiene-1-yllithium) *[51905-34-1]* **M 142.2, m >230°.** In the necessary Schlenk equipment under argon or dry N_2 an equimolar amount of 4M *n*-BuLi in hexane is added dropwise to a stirred solution of equimolar pentamethylcyclopentadiene (Cp′) in dry THF (30ml per g of Cp′) at 0° which gives a pulpy pale yellow suspension. Magnetic stirring is continued for 2 hours while the temperature is allowed to rise to ~25°; and this can be used directly for coordinating a Cp′ ligand to metals. If LiCp′ is to be isolated, then the solvent to be used is petroleum ether (~15ml per g of Cp′), addition of the *n*-BuLi solution is done within a few minutes without cooling as the reaction is slower than in THF, and stirring is continued for 24 hours. The solvent is removed *in vacuo*, or the colourless to pale grey solid (>90% yield) is filtered off, washed with petroleum ether under N_2 and dried *in vacuo*. [Kohl et al. in *Organometallic Synthesis* (R. Bruce King and J.J. Eisch) **vol 3** 381, Elsevier Amsterdam *1986*]. LiCp′ is air and moisture sensitive, and should be stored and weighed in an inert atmosphere. [King & Bisnette *J Organomet Chem* **8** 287 *1967*.] This reagent has been prepared also *in situ* from Cp′ with MeLi/THF at 0° [White et al. *Synth Commun* **3** 425 *1973*], with *n*-BuLi in dimethoxyethane [Manriques & Bercaw *J Am Chem Soc* **96** 6229 *1974*], or as a slurry of LiCp′ in Et_2O at ~25° [Beachley et al. *Organometallics* **4** 1675 *1985*]. The metal-Cp′ bond in LiCp′ has a more covalent nature than that in KCp′ and NaCp′ which are more ionic [Jutzi et al. *Chem Ber* **118** 1959 *1985*].

Lithium picrate *[18390-55-1]* **M 221.0.** Recrystallise the picrate three times from EtOH and dry it under vacuum at 45° for 48 hours [D'Aprano & Sesta *J Phys Chem* **91** 2415 *1987*]. [*Beilstein* **6** H 276, **6** II 263, **6** III 880, **6** IV 1390.] The necessary precautions should be taken in case of **EXPLOSION**.

Lithium salicylate *[552-38-5]* **M 144.1.** Recrystallise the salicylate from EtOH (2ml/g) by partial evaporation. [*Beilstein* **10** H 59, **10** II 32, **10** III 93, **10** IV 126.]

Magnesium acetate *[142-72-3 (anhydrous), 16674-78-5 ($4H_2O$)]* **M 214.5, m 80°.** Crystallise it from anhydrous acetic acid, then dry it under vacuum for 24 hours at 100°. [Nencollas *J Chem Soc* 744 *1956*,

Beilstein **2** IV 113.]

Magnesium benzoate trihydrate *[553-70-8]* **M 320.6, m ~200°.** Crystallise it from water (6ml/g) between 100° and 0°. [*Beilstein* **9** III 376, **9** IV 280.]

Magnesium ethylate (magnesium ethoxide) *[2414-98-4]* **M 114.4.** Dissolve *ca* 1g of solid in 12.8ml of absolute EtOH and 20ml of dry xylene, and reflux in a dry atmosphere (use $CaCl_2$ in a drying tube at the top of the condenser). Add 10ml of absolute EtOH and cool. Filter the solid under dry N_2 and dry it in a vacuum. *Alternatively*, dissolve it in absolute EtOH and pass it through molecular sieves (40 mesh) under N_2, evaporate under N_2, and store it in a tightly stoppered container. [Smith & Wiley *J Am Chem Soc* **68** 889 *1946*, *Beilstein* **1** III 1283.]

Magnesium D-gluconate *[3632-91-5]* **M 414.6, $[\alpha]_{546}^{20}$ +13.5°, $[\alpha]_{D}^{20}$ +11.3° (c 1, H_2O).** Crystallise it from dilute EtOH to give *ca trihydrate*, and then dry it at 98° in high vacuum. It is insoluble in EtOH, and the solubility in H_2O is 16% at 25°. [Prescott et al. *Ind Eng Chem* **45** 338 *1953*, *Beilstein* **3** IV 1256.]

Magnesium ionophore I (ETH 1117), (*N,N′*-diheptyl-*N,N′*-dimethyl-1,4-butanediamide) *[75513-72-3]* **M 340.6.** Purify it by flash chromatography (at 40 kPa) on silica and eluting with EtOH/hexane (4:1). Its IR ($CHCl_3$) has ν_{max} at 1630 cm^{-1}. [Eene et al. *Helv Chim Acta* **63** 2271 *1980*.] It is a good magnesium selectophore compared with Na, K and Ca [Lanter et al. *Anal Chem* **52** 2400 *1980*].

Magnesium ionophore II (ETH 5214), [*N,N*′-octamethylene-bis(*N′*-heptyl-*N*′-methyl methylmalonamide)] *[119110-37-1]* **M 538.8.** The reagent (*ca* 700mg) can be purified by flash chromatography on Silica Gel 60 (30g) and eluting with CH_2Cl_2/Me_2CO (4:1). [Hu et al. *Anal Chem* **61** 574 *1989*.]

Magnesium lactate *[18917-37-1]* **M 113.4.** Recrystallise the salt from water (6ml/g) between 100° to 0°. [*Beilstein* **3** IV 636.]

Magnesium succinate *[556-32-1]* **M 141.4.** Recrystallise the salt from water (0.5ml/g) between 100° and 0°. [*Beilstein* **2** IV 1912.]

Magon [3-hydroxy-4-(hydroxyphenylazo)-2-naphthoyl-2,4-dimethylanilide, Xylidyl Blue II] *[523-67-1]* **M 411.5, m 246-247°.** Suspend it in H_2O and add aqueous NaOH until it dissolves, filter and acidify with dilute HCl. Collect the dye, dissolve it in hot EtOH (solubility is 100mg/L at *ca* 25°) concentrate to a small volume and allow to cool. The solubility of the Na salt in H_2O is 0.4mg/ml. [Mann & Yoe *Anal Chim Acta* **16** 155 *1957*, Mann & Yoe *Anal Chem* **28** 202 *1956*.]

Manganese (II) acetylacetone *[14024-58-9]* **M 253.2, m ~250°, 261°(dec).** Purify it by stirring 16g of reagent for a few minutes with 100ml absolute EtOH and filter by suction as rapidly as possible through coarse filter paper. Sufficient EtOH is added to the filtrate, to make up for the loss of EtOH and to redissolve any solid that separates. Water (15ml) is added to the filtrate, and the solution is evaporated with a stream of N_2 until reduced to half its volume. Cool for a few minutes and filter off the yellow crystals, dry them under a stream of N_2, then in a vacuum at room temperature for 6-8 hours. These conditions are important for obtaining the *dihydrate*. A vacuum to several mm of Hg or much lower pressure for several days produces the *anhydrous complex*. The degree of hydration can be established by determining the loss in weight of 100g of sample after heating for 4 hours at 100° and <20mmHg. The theoretical loss in weight for $2H_2O$ is 12.5%. The material sublimes at 200°/2mm. It is soluble in heptane, MeOH, EtOH or $*C_6H_6$ at 30°. [Charles *Inorg Synth* **VI** 164 *1960*, Fernelius & Biswas *Inorg Synth* **V** 105 *1957*, *Beilstein* **3** II 3122.]

Manganous acetate tetrahydrate *[6156-78-1 ($4H_2O$), 638-38-0 (anhydrous)]* **M 245.1, m 80°, d_4^{20} 1.59, pK^{25} 10.59 (for Mn^{2+} hydrolysis).** Crystallise it from water acidified with acetic acid. [*Beilstein* **2** IV 120.]

Manganous lactate trihydrate *[6505-50-6 3 H_2O, 51877-53-3 (xH_2O)]* **M 287.1.** Recrystallise the lactate

from water. [IR: Ranade & Biswas *J Indian Chem Soc* **44** 314 1967, *Beilstein* **3** IV 637.]

Mercuric(II) acetate [$Hg(OAc)_2$] *[1600-27-7]* **M 318.7, m 178-180°, 179-182°, pK_1^{25} 2.47, pK_2^{25} 3.49 (for Hg^{2+} hydrolysis).** It is prepared from HgO and acetic acid. Recrystallise it from glacial acetic acid. Its solubility in H_2O is 1g/2.5ml at ~20° and 1g/ml at 100°, and it is soluble in EtOH. The solid is light sensitive and is hydrolysed slowly in H_2O to yield a yellow oxide. Store it in a tightly stoppered bottle away from light. It is a reagent for mercuration of alkenes (and aromatic cmpounds, cf mercury trifluoroacetate below) [Larock *Tetrahedron* **38** 1713 *1928*]; de-mercuration being achieved with $NaBH_4$. [Wagenknecht & Juza in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **II** p 1120-1121 *1965*, *Beilstein* **2** IV 114.] **POISONOUS.**

Mercury(II) bis(cyclopentadienyl) *[18263-08-6]* **M 330.8 starts to dec at ~60° but melts at 83-85°.** The pale yellow crystals can be purified by low-temperature (−78°) recrystallisation from Et_2O. Store it at low temperature in the dark as it decomposes slowly at room temperature even in the dark. It reacts with $FeCl_2$ in tetrahydrofuran to give ferrocene quantitatively. It is soluble in Et_2O, $*C_6H_6$, $CHCl_3$, CCl_4, and most organic solvents. [Campbell et al. *J Am Chem Soc* **94** 8387 *1972*, Wilkinson & Piper *J Inorg Nucl Chem* **2** 32, 36 *1956*, Piper & Wilkinson *J Inorg Nucl Chem* **3** 104,106 *1956*, *Beilstein* **16** IV 1702.]

Mercury dibromofluorescein {mercurochrome, merobromin, [2',7'-dibromo-4'-(hydroxy-mercurio)-fluorescein di-Na salt] *[129-16-8]* **M 804.8, m>300°.** The Na salt is dissolved in the minimum volume of H_2O, or the free acid suspended in H_2O and dilute NaOH is added to cause it to dissolve, filter and acidify it with dilute HCl. Collect the precipitate, wash it with H_2O by centrifugation and dry it in a vacuum. The di Na salt can be purified by dissolving it in the minimum volume of H_2O and is precipitated by adding EtOH, filter, wash it with EtOH or Me_2CO and dry it in a vacuum. Its solubility in 95% EtOH is 2% and in MeOH it is 16%. [White *J Am Chem Soc* 42 2355 *1920*.]

Mercury Orange [1-(4-chloromercuriophenylazo)-2-naphthol] *[3076-91-3]* **M 483.3, m 291.5-293°(corr) with bleaching.** Wash it several times with boiling 50% EtOH and recrystallise it from 1-butanol (0.9g/l of boiling alcohol). The fine needles are insoluble in H_2O but slightly soluble in cold alcohols, $CHCl_3$ and soluble in aqueous alkalis. [Chaikin *J Am Chem Soc* **70** 3522 *1948*.]

Mercury(II) trifluoroacetate *[13257-51-7]* **M 426.6, m 171-173°.** It is prepared from HgO and trifluoroacetic acid and is recrystallised from trifluoroacetic anhydride/trifluoroacetic acid. It is a useful reagent for mercuration of aromatic compounds [Lau & Kochi *J Am Chem Soc* **108** 6720 *1986*]. Store it in a tightly stoppered bottle away from light. [cf Aylett in *Comprehensive Inorganic Chemistry (Bailer et al. eds)* **Vol 3** p187 *1973*, *Beilstein* **2** IV 458.] It is very **TOXIC** and *hygroscopic.*

Methylmercuric chloride *[115-09-3]* **M 251.1, m 167°, 170°.** Recrystallise it from absolute EtOH (20ml/g). Its UV has λ_{max} at 206nm (ε 1.37). [See EtHgCl above; Breitinger et al. *J Organomet Chem* **256** 217 *1983*, Slotta et al. *J Prakt Chem* **120** 249 *1929*, Waugh et al. *J Phys Chem* **59** 395 *1955*, *Beilstein* **16** IV 1729.]

Milling Yellow G *[51569-18-7]***.** Salted out three times with sodium acetate, then repeatedly extracted with EtOH. [McGrew & Schneider *J Am Chem Soc* **72** 2547 *1950*, *Beilstein* **16** II 125.] See Solochrome Violet R [2092-55] in "Aromatic compounds", Chapter 4.

Monoperoxyphthalic acid magnesium hexahydrate salt. (MMPP) *[84665-66-7]* **M 494.7, m ~93°(dec).** MMPP is a safer reagent than *m*-chloroperbenzoic acid for oxidation reactions because it is not as explosive and has advantages of solubility. It is soluble in H_2O, low-molecular-weight alcohols, *i*-PrOH and DMF. The product of reaction, Mg phthalate, is soluble in H_2O. It has been used in aqueous phase to oxidise compounds in e.g. $CHCl_3$ and using a phase transfer catalyst, e.g. methyltrioctylammonium chloride [Brougham *Synthesis* 1015 *1987*]. The oxidising activity can be checked (as for perbenzoic acid in Silbert et al. *Org Synth* Coll Vol **V** 906 *1973*], and if found to be low it would be best to prepare afresh from phthalic anhydride (1mol), H_2O_2 (1mol) and MgO at 20-25° to give MMPP. [Hignett, European Pat Appl 27 693 *1981*, *Chem Abstr* **95** 168810 *1981*, *Beilstein* **9** IV 3260.]

Neopentoxy lithium *[3710-27-8]* **M 94.1.** Recrystallise alkoxide from hexane [Kress & Osborn *J Am Chem Soc* **109** 3953 *1987*]. [*Beilstein* **1** H 406, **1** I 201, **1** II 435. **1** III 1448, **1** IV 1690, *for alcohol and Al and Fe neopentoxides*.]

New Methylene Blue N (2,8-dimethyl-3,7-bis(ethylamino)phenothazinium chloride 0.5 $ZnCl_2$) *[6586-05-6]* **M 416.1, m >200°(dec), pK_1 3.54, pK_2 4.82.** Crystallise the dye from *benzene/MeOH (3:1). [*Beilstein* **27** IV 5163.]

Nickel (II) acetate ($4H_2O$) *[6018-89-9]* **M 248.9, d_4^{20} 1.744, pK_1^{25} 8.94 (from Ni^{2+} hydrolysis).** The acetate crystallises from aqueous AcOH as the green *tetrahydrate salt*. It is soluble in 6 parts of H_2O. It forms lower hydrates and should be kept in a well-sealed container. [Hardt & Pohlmann *Z Anorg Allgem Chem* **343** 92 *1966, Beilstein* **2** IV 120.]

Nickelocene [bis-(cyclopentadienyl)nickel II] *[1271-28-9]* **M 188.9, m 173-174°(under N_2).** Dissolve the complex in Et_2O, filter and evaporate in a vacuum. Purify it rapidly by recrystallisation from petroleum ether using a solid CO_2/Me_2CO bath, and has **m 171-173°** (in an evacuated tube). Also purify it by vacuum sublimation. [Wilkinson et al. *J Am Chem Soc* **76** 1970 *1954*, *Beilstein* **16** IV 1831.]

Nickel (II) phthalocyanine *[14055-02-8]* **M 571.3, m >300°.** Wash it well with H_2O and boiling EtOH and sublime it at high vacuum in a slow stream of CO_2. A special apparatus is used (see reference), with the phthallocyanine being heated to red heat. The sublimate is in the form of needles with an extremely bright red lustre. The powder is dull greenish blue in colour. [Barrett et al. *J Chem Soc* 1719 *1936, Beilstein* **26** III/IV 4255.]

Nickel 5,10,15,20-tetraphenylporphyrin *[14172-92-0]* **M 671.4, λ_{max} 414(525)nm.** Purify it by chromatography on neutral (Grade I) alumina, followed by recrystallisation from CH_2Cl_2/MeOH [Yamashita *J Phys Chem* **91** 3055 *1987*]. [*Beilstein* **26** III/IV 1960.]

Octadecyl isonicotinate See hydrogen ionophore IV, ETH 1778 in "Heterocyclic Compounds" [103225-02-1], Chapter 4.

Phenylmercuric acetate (PhHgOAc) *[62-38-4]* **M 336.7, m 148-151°, 149°, 151.8-152.8°.** This acetate forms small colourless lustrous prisms from EtOH. Its solubility in H_2O is 0.17%, but it is more soluble in EtOH, Me_2CO and $*C_6H_6$. [Maynard *J Am Chem Soc* **46** 1510 *1925*, Coleman et al. *J Am Chem Soc* **59** 2703 *1937*, *J Am Pharm Assoc* **25** 752 *1936, Beilstein* **16** IV 1720.] See PhHgOH below.

Phenylmercuric hydroxide (PhHgOH) *[100-57-2]* **M 294.7, m 195-203°, pK^{25} 10 (~4.5).** Crystallise it from dilute aqueous NaOH. [Waugh et al. *J Phys Chem* **59** 395 *1955*, *Beilstein* **16** IV 1721.]

Phenylmercuric nitrate ($PhHgNO_3$) *[8003-05-2]* **M 634.4, m 178-188°.** When recrystallised from water or aqueous EtOH, it has **m 191-191.5°**, and from 95% EtOH it has **m 186.5°** [Challanger & Rothstein *J Chem Soc I 1258* 1934]. When recrystallised from $*C_6H_6$ or $CHCl_3$, it has **m 131-131.5°** [Morton et al. *J Am Chem Soc* **69** 908 *1947*.] [*Beilstein* **16** III 1348, **16** IV 1721.]

Phthalocyanine *[574-93-6]* **M 514.6.** Purify phthalocyanine by sublimation (two to three times) in an argon flow at 300-400Pa; and similarly for the Cu(II), Ni(II), Pb(II), VO(II) and Zn(II) phthalocyanine complexes. [*Beilstein* **26** III/IV 4255.]

Platinum (II) acetate (diacetatoplatinum) *[38928-89-1]* **M 313.2 (monomer), m 245°dec.** Purify the purple crystals by dissolving them in $CHCl_3$, filtering, mixing with half its volume of glacial acetic acid and set aside to evaporate at room temperature. The resulting large, almost black, crystals are collected, washed with H_2O and

dried in air. It dissolves in $CHCl_3$, $*C_6H_6$ and toluene to give purple solutions. Its molecular weights (ebullioscopically) in $CHCl_3$, $*C_6H_6$ and chlorobenzene are 950 (±2), 937 and 888, respectively, indicate that it is trimeric in solution. [Stephenson et al. *J Chem Soc* 3632 *1965*.]

Platinum (II) acetylacetonate *[15170-57-7]* **M 393.3, m 249-252°.** It crystallises from $*C_6H_6$ as yellow crystals and is dried in air or in a vacuum desiccator. [Werner *Chem Ber* **34** 2584 *1901*, Fernelius & Bryant *Inorg Synth* **V** 105 *1957*, *Beilstein* **1** H 783, **1** IV 3678.]

Potassium 4-aminobenzoate *[138-84-1]* **M 175.2.** Crystallise the aminobenzoate from EtOH. [*Beilstein* **14** II 246, **14** IV 1128.]

Potassium antimonyltartrate monohydrate *[28300-74-5]* **M 333.9, $[\alpha]_D$ +141° (c 2, H_2O).** Crystallise "**tartar emetic**" from water (3ml/g) between 100° and 0°. Dry it at 100°. [Chinoporos & Papathanosopolos *J Phys Chem* **65** 1643 *1961*, *Beilstein* **3** III 1014, **3** IV 1227.]

Potassium benzoate *[582-25-2]* **M 160.2.** Crystallise it from water (1ml/g) between 100° and 0°. [*Beilstein* **9** III 375, **9** IV 279.]

Potassium *tert*-butoxide *[865-47-4]* **M 112.2.** It sublimes at 220°/1mm. The last traces of *tert*-BuOH are removed by heating at 150-160°/2mm for 1 hour. It is best prepared afresh as likely impurities are *tert*-BuOH, KOH and K_2CO_3 depending on its exposure to air. Its solubility at 25-26° in hexane, toluene, Et_2O, and THF is 0.27, 2.27, 4.34 and 25.0%, respectively. [Feuer et.al. *J Am Chem Soc* **78** 4364, Doering & Urban *J Am Chem Soc* **78** 5938 *1956*, *Beilstein* **1** IV 1612.]

Potassium citrate tribasic monohydrate (tripotassium citrate monohydrate) *[6100-05-6]* **M 324.4, m 275°(dec).** Its solubility in H_2O is 154g/100ml and it loses H_2O at 180°. [*Beilstein* **3** III 1091.]

Potassium dihydrogen citrate *[866-83-1]* **M 230.2.** It crystallises from H_2O with a solubility of 11.5% at 100°. Dry it at 80°, or in a vacuum desiccator over Sicapent. [*Beilstein* **3** I 209, **3** III 336, **3** IV 402.]

Potassium hydrogen D-glucarate (D-tetrahydroxyadipic acid mono K salt, D-glucosaccharic acid mono K salt) *[18404-47-2]* **M 248.2, m 188°(dec), $[\alpha]_D^{20}$ +4.95° (c 1.2, H_2O), pK_1^{25} 5.0 (free acid).** Crystallise it from water. [Wolfrom & Neely *J Am Chem Soc* **75** 2778 *1953*, *Beilstein* **3** H 579, **3** II 378, **3** III 1119, **3** IV 1291.]

Potassium hydrogen malate *[4675-64-3]* **M 172.2.** A saturated aqueous solution at 60° is decolorised with activated charcoal, and filtered. The filtrate is cooled in a water-ice bath, and the salt is precipitated by adding EtOH. After five recrystallisations from ethanol-water mixtures, it is dried overnight at 130° in air [Eden & Bates *J Res Nat Bur Stand* **62** 161 *1959*]. [*Beilstein* **3** H 419, **3** III 915, **3** IV 1123.]

Potassium hydrogen oxalate (H_2O) *[127-95-7]* **M 137.1, m ~300°(dec).** Crystallise the acid oxalate from H_2O by dissolving 20g in 100ml H_2O at 60° containing 4g of potassium oxalate, filtering and allowing to cool to 25°. The crystals, after washing three or four times with water, are allowed to dry in air. [*Beilstein* **2** III 1552.]

Potassium hydrogen phthalate *[877-24-7]* **M 204.2.** Crystallise it first from a dilute aqueous solution of K_2CO_3, then H_2O (3ml/g) between 100° and 0°. Before being used as a standard in volumetric analysis, analytical grade potassium hydrogen phthalate should be dried at 120° for 2 hours, then allowed to cool in a desiccator. [*Beilstein* **9** IV 3169.]

Potassium hydrogen *d*-tartrate *[868-14-4]* **M 188.2, $[\alpha]_{546}^{20}$ +37.5° (c 10, M NaOH).** It crystallises from water (17ml/g) between 100° and 0°. Dry it at 110°. [*Beilstein* **3** IV 1222.]

Potassium ionophore I (valinomycin) See valinomycin in "Miscellaneous Compounds", Chapter 7.

Potassium laurate (potassium dodecanoate) *[10124-65-9]* **M 338.4.** Recrystallise potassium laurate three times from EtOH [Neto & Helene *J Phys Chem* **91** 1466 *1987*]. [*Beilstein* **2** H 360, **2** I 156, **2** II 318, **2** III 880, **2** IV 186.] See purification of sodium dodecanoate below.

Potassium nonafluorobutane sulfonate *[29420-49-3]* **M 338.2.** Wash it with H_2O and dry it *in vacuo*. When the K salt is distilled with 100% H_2SO_4, it gives the *free acid* which can be distilled (**b** 105°/22mm, 210-212°/760mm) and then converted back into the pure K salt. [Gramstad & Haszeldine *J Chem Soc* 2640 *1957*, *Beilstein* **2** IV 818.]

Potassium oleate *[143-18-0]* **M 320.6.** Recrystallise potassium oleate from EtOH (1g/ml). [*Beilstein* **2** H 465, **2** I 196, **2** I 202, **2** II 436, **2** III 1404, **2** IV 1646.]

Potassium oxalate *[6487-48-5]* **M 184.2, m 160°(dec), d_4^{20} 2.13.** Recrystallise the oxalate from hot water. It forms various K + oxalic acid salts [e.g. potassium hydrogen oxalate $KH(C_2O_4)$—see above, and $KH_3(C_2O_4)_2$ which is, surprisingly, called potassium tetraoxalate—see below]. [*Beilstein* **2** H 513, **2** I 224, **2** II, 485, **2** III 1552, **2** IV 1823.]

Potassium pentamethylcyclopentadienide (KCp′, 1,2,3,4,5-pentamethyl-2,4-pentadiene-1-ylpotassium) *[94348-92-2]* **M 174.3, m >230°.** In an efficient fume cupboard, liquid NH_3 (1.3L) is condensed into a flask containing freshly cut K metal (11.7g, 300mg-atoms) under an argon or N_2 atmosphere, stirred at -78°, and a small crystal of $Fe(NO_3)_3.9H_2O$ is added to the blue coloured solution. The mixture is made to warm to room temperature allowing refluxing until the blue solution turns into a light grey suspension. Cp′ (40.9g, 300mmol) is added *via* a syringe, the mixture is stirred at reflux (MeOH condenser cooled at -78°) for 4 hours, and the NH_3 is allowed to evaporate using a stream of N_2. The residue is dried *in vacuo* and stored in a N_2 atmosphere as it is air and moisture sensitive, and unlike other Cp′Ms it can be spontaneously flammable in air. It is more soluble in THF than Cp′Li but less soluble than Cp′Na. It is a Cp′ ligand source for complexing with a large number of metals and non-metal halides. [Kohl et al. in *Organometallic Synthesis* (R. Bruce King and J.J. Eisch eds) **vol 3** 381, Elsevier Amsterdam *1986*].

Potassium phthalimide (phthalimide K salt) *[1074-82-4]* **M 185.2, m >300°.** The solid may contain phthalimide and K_2CO_3 from hydrolysis. If too much hydrolysis has occurred (this can be checked by extraction with cold Me_2CO in which the salt is insoluble, evaporate the Me_2CO and weigh the residue), it would be better to prepare it afresh. If little hydrolysis has occurred, then recrystallise it from a large volume of EtOH, and wash the solid with a little Me_2CO and dry it in a continuous vacuum to constant weight. [Salzerg & Supriawski *Org Synth* Coll Vol **I** 119 *1941*, Raman & IR: Hase *J Mol Struct* **48** 33 *1978*, Dykman *Chem Ind (London)* 40 *1972*, IR, NMR: Assef et al. *Bull Soc Chim Fr* II 167 *1979*, *Beilstein* **21/10** V 270.]

Potassium picrate *[573-83-1]* **M 267.2, m 250°.** Recrystallise it from water or 95% EtOH, and dry it at room temperature in vacuum. It is soluble in 200 parts of cold water and 4 parts of boiling water. [*Beilstein* **3** III 880, **3** IV 1390.] **THE DRY SOLID EXPLODES WHEN STRUCK OR HEATED.**

Potassium propionate *[327-62-8]* **M 112.2.** Recrystallise $C_2H_5CO_2K$ from water (30ml/g) or 95% EtOH. [*Beilstein* **2** II 217, **2** III 516, **2** IV 701.]

Potassium sodium tartrate tetrahydrate *[6381-59-5 ($4H_2O$), 304-59-6 (R,R)]* **M 282.3.** Recrystallise the tartrate from distilled water (1.5ml/g) by cooling to 0°. [*Beilstein* **3** IV 1223.]

Potassium *d*-tartrate monohydrate *[921-53-9 , 6381-59-5]* **M 235.3, m loses H_2O at 150°, d_4^{20} 1.98.** Recrystallise it from distilled water (solubility: 0.4ml/g at 100°, 0.7ml/g at 14°). [*Beilstein* **3** IV 1223.]

Potassium tetraoxalate dihydrate [oxalic acid hemipotassium salt] *[6100-20-5 ($2H_2O$), 127-96-8]* **M 254.2.** Crystallise it from water below 50°. Dry it below 60° at 760mm. [See potassium oxalate above, *Beilstein* **2** IV 1823.]

Potassium trifluoroacetate *[2923-16-2]* **M 152.1, m 140-142°, pK^{25} 0.52 (for CF_3CO_2H).** To purify it, dissolve the salt in trifluoroacetic acid with *ca* 2% of trifluoroacetic anhydride, filter it and evaporate it carefully to dryness (avoid over heating), and finally dry it in a vacuum at 100°. It can be recrystallised from trifluoroacetic acid (solubility in the acid is *ca* 50.1%). [Simons & Lorentzen *J Am Chem Soc* **74** 4746 *1952*, Hara & Cady *J Am Chem Soc* **76** 4285 *1954*, Watt & Muga *J Inorg Nucl Chem* **9** 166 *1959*, *Beilstein* **2** IV 458.]

Pyridinium chlorochromate *[26299-14-9]* **M 215.6, m 205°(dec).** Dry it in a vacuum for 1 hour. It is not hygroscopic and can be stored for extended periods at room temperature without change. If the purity is very suspect, it can be readily prepared. [Corey & Scuggs *Tetrahedron Lett* 2647 *1975*, Piancatelli et al. *Synthesis* 245 *1982*.] (Possible **CARCINOGEN**.)
§ Available commercially on a polymer support.

Pyridinium dichromate *[20039-37-6]* **M 376.2, m 145-148°, 152-153°.** Dissolve it in the minimum volume of H_2O and add 5 volumes of cold Me_2CO and cool to -20°. After 3 hours the orange crystals are collected, washed with a little cold Me_2CO and dried in a vacuum. It is soluble in dimethylformamide (0.9g/ml at 25°), and in H_2O, and has a characteristic IR with ν_{max} at 930, 875, 765, 730 and 730 cm^{-1}. [Corey & Schmidt *Tetrahedron Lett* 399 *1979*, Coats & Corrigan *Chem Ind (London)* 1594 *1969*.] (Possible **CARCINOGEN**.)
§ Available commercially on a polymer support.

Pyronin B [di-(3,6-bis(diethylamino)xanthylium chloride) diFeCl$_5$ complex] *[2150-48-3]* **M 358.9 (Fe free), m 176-178° (diFe complex), CI 45010, λ_{max} 555nm, pK^{25} 7.7.** Recrystallise it from EtOH. It forms an Fe stain. [*Beilstein* **18/10** V 182.]

Quinolinium chlorochromate *[108703-35-1]* **M 265.6, m 127-130°.** It is a yellow-brown solid which is stable in air for long periods. If it has deteriorated or been kept for too long, it is best to prepare it freshly. Add freshly distilled quinoline (13ml) to a mixture of chromic acid (CrO_3) (10g) and ~5M HCl (11ml of conc HCl and 10ml of H_2O) at 0°. A yellow-brown solid separates, it is filtered off on a sintered glass funnel, dried for 1 hour in a vacuum, and can be stored for extended periods without serious loss in activity. It is a good oxidant for primary alcohols in CH_2Cl_2. [Singh et al. *Chem Ind (London)* 751 *1986*, method of Corey & Suggs *Tetrahedron Lett* 2647 *1975*, *Beilstein* **20/7** V 276.]

Resorufin (7-hydroxy-3H-phenoxazine-3-one Na salt) *[635-78-9]* **M 213.2, pK$_1^{30}$ 6.93, pK$_2^{30}$ 9.26, pK$_3^{30}$ 10.0.** Wash Resorufin with water and recrystallise it several times from EtOH. [*Beilstein* **27** II 108, **27** III/IV 2263.]

Rhodizonic acid sodium salt (5,6-dihydroxycyclohex-5-ene-1,2,3,4-tetraone di-Na salt) *[523-21-7]* **M 214.0, pK$_1^{30}$4.1 (4.25), pK$_2^{30}$ 4.5 (4.72).** The *free acid* is obtained by acidifiying and extracting with Et_2O, drying ($MgSO_4$), filtering, evaporating and distilling in a vacuum (**b** 155-160°/14mm). The *free acid* solidifies on cooling, and the colourless crystals can be recrystallised from tetrahydrofuran/petroleum ether or *C_6H_6. It forms a *dihydrate* **m** 130-140°. The pure di Na salt is formed by dissolving the acid in 2 equivalents of NaOH and evaporating in a vacuum. It forms violet crystals which give an orange solution in H_2O that is unstable for extended periods even at 0°, and should be prepared freshly before use. Salts of rhodizonic acid **cannot** be purified by recrystallisation without great loss due to conversion to crotonate, so that the original material must be prepared anew if pure salt is required. It can be washed with NaOAc solution, then EtOH, to remove excess NaOAc, dried under vacuum and stored in the dark. [UV and tautomerism: Schwarzenbach & Suter *Helv Chim Acta* **24** 617 *1941*, Polarography: Preisler & Berger *J Am Chem Soc* **64** 67 *1942*, Souchay & Taibouet *J Chim Phys* **49** C108 *1952*, *Beilstein* **8** H 535, **8** II 572, **8** III 4214, **8** IV 3609.]

Ruthenium (III) acetylacetonate *[14284-93-6]* **M 398.4, m 240°(dec).** Purify the complex by recrystallisation from *benzene. [Wilkinson *J Am Chem Soc* **74** 6146 *1952*, *Beilstein* **1** IV 3677.]

Ruthenocene [bis-(π-cyclopentadienyl)ruthenium] *[1287-13-4]* **M 231.2, m 195.5°, 199-210°.** If it has to

be prepared *ab initio*, then in a flask (500ml), under continuous flushing with N_2, and stirring, dry 1,2-dimethoxyethane (300ml) is added followed by Na (7.2g, 0.312 g.atom) cut in small pieces then cyclopentadiene (31.0ml, 0.376 mole; see [542-92-7], prepared from the dimer, [cf. Wilkinson *Org Synth* Coll Vol **IV** 475 *1963*] is added dropwise. After H_2 evolution stops, the mixture is kept just below boiling for 1-2 hours until all the Na has dissolved. If some metal remains undissolved, cool, and add a few milliliters of cyclopentadiene, and heat again until complete dissolution of the metal occurs. To this solution of sodium pentadienide [see also 4989-82-1], under N_2 and stirring, is added a mixture of $RuCl_3$ (14.6g, 0.07 mole) and Ru metal (2.4g, 0.024 g.atom), and heated just below reflux for 80 hours. The solvent is removed under reduced pressure, the flask is filled with N_2, the solid residue is transferred (use a dry-box) to a sublimator, and sublimed at 0.1mm and 130° (bath temperature). It is advantageous to use a Dry-ice sublimation finger. The sublimate is dissolved in $*C_6H_6$, passed through a column of activated Al_2O_3 (2.5 x 30cm), and evaporated to give pure *non-pyrophoric* ruthenocene (12.2-15.1g, 56-69%), m 199-200°. The residue from sublimation is, however, *pyrophoric*, but this residue can be destroyed by adding H_2O under N_2. It can be further sublimed in high vacuum at 120°. It forms yellow crystals which can be recrystallised from CCl_4 as transparent plates. [Bublitz et al. *Org Synth* Coll Vol **V** 1001 *1973*, Wilkinson *J Am Chem Soc* **74** 6146 *1952*, *Beilstein* **16** IV 1833.] It is generally less reactive than ferrocene towards electrophiles.
Two other alternative syntheses have been adopted using Schlenk techiques in an atmosphere of N_2 or argon, with dry and de-oxygenated solvents. In the *first*, [Sn-*n*-$Bu_3(C_5H_5)$] (32.0g, 90mmol, prepared from Sn-*n*-Bu_3Cl, 1461-22-9, and LiC_5H_5 as per Davison & Rakita *Inorg Chem* **9** 289 *1970*) is added to a suspension of [$RuCl_2(COD)_n$] (8.4g, 30mmol, see [50982-12-2]) in EtOH (150ml), and the mixture is stirred and refluxed for 48 hours whereby the Ru polymer dissolved. The hot solution is filtered in air, and on cooling the pale yellow *ruthenocene* that crystallises out is filtered off, washed thoroughly with cold EtOH (2 x 20ml) then Et_2O (2 x 20ml), and recrystallised to analytical purity (5.2g, 75%) from hot EtOH or Me_2CO. Its ^1H NMR (500MHz, $CDCl_3$) has δ at 4.55 (s, C_5H_5), and its ^{13}C NMR (125MHz, $CDCl_3$) has δ at 20.1 (s, C_5H_5) (any *n*-butyl signals from impurities would be at their usual shifts). In the *second*, [$RuCl_2(COD)_n$] (1.4g, 50mmol) and cyclopentadienyl thallium (2.7g, 10mmol, see [34822-90-7]) in dimethoxyethane (~50ml) are refluxed for 1 hour, filtered hot (in air), the solvent is removed *in vacuo*, the residue is extracted with Et_2O (4 x 20ml), filtered, evaporated, and the residue is recrystallised and/or sublimed, as above, to give pure *ruthenocene* (0.9g, 78%). [Albers et al. *Organometallics* **5** 2321 *1986*.] The Raman spectrum of the melt has ν_{max} at 160w, 325s(p), 396m, 590vw, 815m(p), 830w, 1060m, 1098s(p), 1195vw 1360w, 1410m cm^{-1} (p is with polarized light) [Lokshin et al. *J Organomet Chem* **124** 293 *1977*].

Silver acetate *[563-63-3]* **M 166.9, pK^{25} >11.1 (for aquo Ag^+ hydrolysis).** Shake AgOAc with acetic acid for three days, and the process is repeated with fresh acid. The solid is then dried in a vacuum oven at 40° for 48 hours. It has also been recrystallised from water containing a trace of acetic acid, and dried in air. Store it in the dark. [*Beilstein* **2** IV 112.]

Silver lactate *[128-00-7]* **M 196.9, m ~ 100°.** Recrystallise it from H_2O by adding EtOH. The solid is collected, washed with EtOH, then Et_2O, and dried at 80° to give the *dihydrate*. It is a white powder soluble in 15 parts of H_2O but only slightly soluble in EtOH. Store it in the dark. [Engelhardt & Maddrell *Justus Liebigs Ann Chem* **63** 89 *1847*, Karrer et al. *Helv Chim Acta* **2** 251 *1919*, *Beilstein* **3** III 464.]

Silver tetrafluoroborate [$AgBF_4$] *[14104-20-2]* **M 194.7, m 70-73°, dec >200° (to form a silver mirror).** The anhydrous salt has been freshly prepared under dry N_2, by suspending AgF (34g, 268mmol) in dry $MeNO_2$ (30.5ml) while BF_3 is passed through with stirring. The temperature rises to 60°, and is maintained by occasional dipping into an ice bath. After about 30 minutes most of the AgF dissolves and ~280mmoles of BF_3 will have dissolved. Excess BF_3 is removed by bubbling dry N_2 for 1 hour through the murky solution which is then filtered (through a sintered glass frit, under N_2), and the $MeNO_2$ is distilled off at 70°/5mm into a liquid N_2 trap. The off-white solid is ground in a mortar under dry *n*-pentane in a glove box flushed with dry N_2, and the solvent is evaporated under N_2 at ~25°. The residual salt (237mmole, 88.5%) is pumped dry at 70° and stored under *n*-pentane. [Olah & Quin *J Inorg Nucl Chem* **14** 295 *1960*.] The synthesis has been carried out in $*C_6H_6$

with which it forms a 1:2 complex [Heyns & Paulsen *Angew Chem* **72** 349 *1960*], although 1:1 [Meerwein et al. *Arch Pharm* **291** 541 *1958*] and 2:3 complexes [Sharp & Sharpe *J Chem Soc* 1855 *1956*] were reported. $AgBF_4$ is very soluble in H_2O, Et_2O, toluene, $MeNO_3$, moderately soluble in $*C_6H_6$, cyclohexene but insoluble in pentane and cyclohexane. The solubility in unsaturated hydrocarbons is attributed to π-bond complexing. A solution obtained by dissolving Ag_2O (1.0g) in 45% fluoroboric acid (7.2g) has been used for the synthesis of a tropone [Birch & Keeton *J Chem Soc (C)* 09 *1968*].
The salt is used for making tetrafluoroborate salts of complexes and other salts (see examples in this chapter) by displacing chloride from precious metal complexes, e.g. $Ru(Me_2SO_4)Cl_2$ with excess $AgBF_4$ under N_2 in refluxing EtOH (*ca* 1 hour) and repeatedly recrystallising from H_2O/EtOH to give a 60% yield of $[Ru(Me_2SO_4)(H_2O)_2]$ BF_4, which is used for the oxidation of alcohols by persulfate [Bressan et al. *J Mol Catal* **79** 85 *1993*]. It provides a silver-ion template for improved macrolactamisation of linear dipeptides, e.g. to form cyclohexadepsipeptides [Yanjie et al. *Synlett* 1901 *2007*].

Silver trifluoroacetate *[2966-50-9]* **M 220.9, m 251-255°.** Extract the salt (Soxhlet) with Et_2O. The extract is filtered and evaporated to dryness, then the powdered residue is completely dried in a vacuum desiccator over silica gel. Its solubility in Et_2O is 33.5g in 750ml. It can be recrystallised from $*C_6H_6$ (solubility is: 1.9g in 30ml of $*C_6H_6$, and 33.5g will dissolve in 750ml of anhydrous Et_2O). [Traynham & Dehn *J Org Chem* **23** 1545 *1958*, Haszeldine *J Chem Soc* 584 *1951*.] Store it in the dark. It is also soluble in trifluoroacetic acid (15.2% at 30°), toluene, *o*-xylene and dioxane [Hara & Cady *J Am Chem Soc* **76** 4285 *1954*]. [*Beilstein* **2** IV 461.]

Sodium acetate (anhydrous) *[127-09-3]* **M 82.0, m 324°, d $_4^{20}$ 1.53.** Crystallise it from acetic acid and keep it under vacuum for 10 hours at 120°. *Alternatively*, it crystallises from aqueous EtOH as the *trihydrate*. This material can be converted to *anhydrous* salt by heating slowly in a porcelain, nickel or iron dish, so that the salt liquefies. Steam is evolved and the mass again solidifies. Heating is now increased so that the salt melts again. (NB: if it is heated too strongly, the salt can char; avoid this.) After several minutes, the salt is allowed to solidify and is cooled to a convenient temperature (in a desiccator) before being powdered and bottled. The water content should now be less than 0.02%. [*Beilstein* **2** II 113, **2** III 184, **2** IV 109.]

Sodium acetylacetonate [Na(acac), 2,4-pentanedione ion (1-) sodium (1:1)] *[15435-71-9]* **M 122.1, m 217-219° and is quite stable to heating below 191°, d $_4^{20}$ 1.213.** It is prepared by two different procedures. In the *first*, 2,4-pentanedione (100g, 1.0 mole) in H_2O or EtOH is slowly added to NaOH (40g. 1.0 mole) in the minimum amount of H_2O while keeping the temperature below 70°. On cooling Na(acac) (98g, 80%) crystallises out. Note that addition of solid NaOH resulted in a product containing NaOH. Recrystallisation from aqueous EtOH, Me_2CO or EtOAc gives pearly plates of the *dihydrate* (most probably a coordinated compound) which is soluble EtOAc but not in toluene. It gives off H_2O on heating, and the anhydrous form (salt form ?) is no longer soluble in EtOAc.
In the *second* procedure, 2,4-pentanedione (50g, 0.5 mole) is added to Na metal (11.5g, 0.5 mole) in toluene (100ml) while the temperature is maintained at 100° to keep the metal in the molten state (CARE, as the experiment may be dangerous; N_2 should be flushing through the apparatus until the metal has dissolved). Na(acac) (101g, 83%) separates during the reaction. Note that using lower temperatures provide Na(acac) contaminated with Na. The product can be recrystallised from EtOH (see above) or by dissolving in EtOH and adding $*C_6H_6$. Its solubility in *n*-hexane, cyclohexane, or $*C_6H_6$ is less than 0.01% at 70°. However, although quite insoluble in $*C_6H_6$ or toluene, a suspension of Na(acac) will dissolve in these solvents on warming if excess of 2,4-pentanedione, or other related dicarbonyl compounds, e.g. benzoylacetone or ethyl acetoacetate, are added. Note that on heating the anhydrous or hydrated material decomposition and charring occurs if the sample in a soft glass tube is used. However, if the tube is placed in a bath at ~212° and the temperature is raised slowly, a sharp and reproducible melting point (**217-219°**) can be obtained with very little decomposition. [Hatch & Sutherland *J Org Chem* **13** 249 *1948*, Sidgwick & Brewer *J Chem Soc* **127** 2379 *1925*.] The ratios of mole of decomposition product/mole of "salt" after 50 hours when heated under N_2 at 27° and 191° are both 0.07, i.e. it is reasonably stable at high temperatures. [Charles & Pawlikowski *J Phys Chem* **62** 440 *1958*.] Its UV (EtOH) has λ_{max} at 277 (ε 800 x 10^3) nm [Hatch & Sutherland *J Org Chem* **13** 249 *1948*]; and its electrical molecular conductivities (dilution) are: 5.794 (8), 8.254 (16), 11.187 (32), 14.426 (64), 18.116 (128), 21.82 (256), 25.636 (512), 29.927 (1024), and do not approach complete dissociation when nearing maximum dilution as hydrolysis may well be occurring [White *J Chem Soc* 1413 *1928*]. Like K(acac) and Cs(acac), Na(acac) is

unstable in aqueous solution or in moist conditions and is decomposed by hot H_2O into Me_2CO and the alkali acetate [Morgan & Moss *J Chem Soc* **105** 189 *1914*]. Store it in a dry atmosphere. [Marchi *Inorg Synth* **II** 10 *1946*, Frenelius & Bryant *Inorg Synth* **V** 105 *1957*.]

Sodium acetylide *[1066-26-8]* **M 48.0.** It disproportionates at *ca* 180° to sodium carbide. It sometimes contains diluents, e.g. xylene, butyl ether or dioxane that can be removed by filtration followed by a vacuum at 65-60°/5mm. *Alternatively*, the acetylide is purged with HC≡CH at 100-125° to remove diluent. NaC_2H adsorbs 2.2x, 2.0x and 1.6x its wt of xylene, butyl ether and dioxane, respectively. Powdered NaC_2H is yellow or yellow-gray in colour and is relatively stable. It can be heated to *ca* 300° in the absence of air. Although no explosion or evolution of gas occurs, it turns brown due to disproportionation. At 170-190° in air it ignites slowly and burns smoothly. At 215-235° in air it "flash-ignites" and burns quickly. It can be dropped into a *slight* excess of H_2O without flashing or burning, but vigorous evolution of HC≡CH (**HIGHLY FLAMMABLE IN AIR**) occurs. A sample had been stored in the absence of air for one year without deterioration. Due to the high flammability of HC≡CH, the salt should be stored dry and should be treated with care. After long storage, NaC≡CH can be redissolved in liquid NH_3 and used for the same purposes as the fresh material. However, it may be slightly turbid due to the presence of moisture. [Rutledge *J Org Chem* **22** 649 *1957*, Greenlee & Henne *J Am Chem Soc* **77** 5013 *1955*, Campbell & Campbell *Inorg Synth* **II** 76, 81 *1946*, *Org Synth* **30** 15 *1950*, *Beilstein* **1** H 238.] It is available commercially under N_2 in Sure/Seal bottles as an 18 wt% solution in xylene/mineral oil. See "Aliphatic Compounds", Chapter 4, for its preparation.

Sodium alginate (Algin) *[9005-38-3]*. Free Algin from heavy metal impurities by treatment with ion-exchange resins (Na^+-form), or with a dilute solution of the sodium salt of EDTA. *Alternatively*, dissolve it in 0.1M NaCl, centrifuge and fractionally precipitate it by gradual addition of EtOH or 4M NaCl. The resulting gels are centrifuged off, washed with aqueous EtOH or acetone, and dried under vacuum. [Büchner et al. *J Chem Soc* 3974 *1961*.]

Sodium 4-aminobenzoate *[555-06-6]* **M 159.1.** Recrystallise it from water. [Hermann *Helv Chim Acta* **9** 786 *1926*, *Beilstein* **14** II 247.]

Sodium 4-aminosalicylate dihydrate *[6018-19-5]* **M 175.1.** Recrystallise it from water at room temperature (2ml/g) by adding acetone and cooling. [*Beilstein* **14** III 1436, **14** IV 1969.]

Sodium antimonyl tartrate *[34521-09-0]* **M 308.8.** It crystallises from water. [*Beilstein* **3** III 1014, **3** IV 1227.]

Sodium barbitone (sodium 5,5-diethylbarbiturate) *[144-02-5]* **M 150.1, pK_1^{25} 3.99, pK_2^{25} 12.5 (barbituric acid).** Crystallise it from water (3ml/g) by adding an equal volume of EtOH and cooling to 5°. Dry it under vacuum over P_2O_5. [*Beilstein* **24** III/IV 1904.]

Sodium benzoate *[532-32-1]* **M 144.1.** Crystallise it from EtOH (12ml/g). [*Beilstein* **9** IV 27.]

Sodium *tert*-butoxide *[865-48-5]* **M 96.1.** It sublimes at 180°/1mm. Its solubility in *tert*-BuOH is 0.208M at 30.2° and 0.382M at 60°, and it is quite soluble in tetrahydrofuran (32g/100g). It should not be used if it has a brown colour. [Feuer *J Am Chem Soc* **78** 4364 *1956*, Hurd *Inorg Synth* **I** 87 1939, IR: Seubold *J Org Chem* **21** 156 *1956*, *Beilstein* **1** IV 1609.]

Sodium butyrate *[156-54-7]* **M 110.1.** Prepare it by neutralising the acid with Na_2CO_3, and recrystallising it from EtOH. [*Beilstein* **2** IV 779.]

Sodium carboxymethylcellulose *[9004-32-4]*. Dialyse it for 48 hours against distilled water and freeze-dry if a solid is required.

Sodium decanoate (sodium caproate) *[1002-62-6]* **M 194.2.** Neutralise sodium hydroxide by adding a slight excess of free decanoic acid and recovering the excess acid by Et_2O extraction. The salt is recrystallised from

the aqueous solution by adding pure acetone and repeating the steps several times, then drying the salt in an oven at *ca* 110° [Chaudhury & Awuwallia *Trans Faraday Soc* **77** 3119 *1981*]. [*Beilstein* **2** IV 1041.]

Sodium deoxycholate monohydrate *[302-95-4, 145224-92-4]* **M 432.6, $[\alpha]_D^{20}$ +48° (c 1, EtOH).** Recrystallise it from EtOH and dry it in an oven at 100°. The solution is freed from soluble components by repeated extraction with acid-washed charcoal. [*Beilstein* **10** IV 1608.]

Sodium diethyloxaloacetate *[63277-17-8, 40876-98-0]* **M 210.2.** Extract it several times with boiling Et_2O (until the solvent remains colourless), and then the residue is dried in air. [*Beilstein* **3** H 789.]

Sodium diformylamide *[18197-26-7]* **M 95.0.** Grind the amide under dry tetrahydrofuran (fumehood), filter and wash it with this solvent, then dry it *in vacuo*. It is soluble in EtOH and H_2O but insoluble in Et_2O and petroleum ether. [IR and preparation: Rakshit *J Chem Soc* **103** 1557 *1913*, Yinglin & Hongwen *Synthesis* 122 *1990*, Allenstein & Beyl *Chem Ber* **100** 355 *1967*, Allenstein et al. *Chem Ber* **102** 4089 *1969*, *Beilstein* **2** II 22.]

Sodium *p*-dimethylaminoazobenzene-*o*'-carboxylate (Methyl Red) *[845-10-3]* **M 291.2.** It can be precipitated from aqueous solution as the free acid which is recrystallised from 95% EtOH, then reconverted to the sodium salt. In H_2O it is pink at pH 4.2 and yellow at pH 6.2 and has UV with λ_{max} at 437nm. *Methyl Red Hydrochloride* [63451-28-5] has **M 305.8**, **m 175°(dec)** and UV with λ_{max} at 493nm. [*Beilstein* **16** H 329.]

Sodium *p*-dimethylaminoazobenzene-*p*'-carboxylate *[845-46-5]* **M 219.2.** It has been precipitated from aqueous solution as the free acid which was recrystallised from 95% EtOH, then reconverted to the sodium salt. [*Beilstein* **16** H 329.]

Sodium dodecanoate (sodium laurate) *[629-25-4]* **M 222.3, pK^{20} 5.3 (COOH).** Neutralise it by adding a slight excess of dodecanoic acid and removing it by ether extraction. The salt is recrystallised from the aqueous solution by adding pure Me_2CO and repeating the process (see sodium decanoate above). It has also been recrystallised from MeOH. [*Beilstein* **2** IV 1085.]

Sodium ethoxide *[141-52-6]* **M 68.1.** It is a *hygroscopic* powder which should be stored under N_2 in a cool place. A likely impurity is EtOH which can be removed by warming at 60-80° under high vacuum. It is hydrolysed by H_2O to yield NaOH and EtOH. Other impurities, if kept in air for long periods are NaOH and Na_2CO_3. In this case the powder cannot be used if these impurities affect the reactivity, and a fresh sample would be acquired. It is prepared by adding Na to absolute EtOH under N_2 and evaporated *in vacuo*, or used *in situ*. [IR: Seubold *J Org Chem* **21** 156 *1956*]. [*Beilstein* **1** H 311, **1** IV 1289.]

Sodium ethylmercurithiosalicylate (Thimerosal) *[54-64-8]* s**M 404.8, m ~230°.** Recrystallise this antibacterial from EtOH/Et_2O. **HIGHLY TOXIC.** [Trikojus *Nature* **158** 472 *1940*, *Beilstein* **10** III 213.]

Sodium fluoroacetate (FCH_2CO_2Na) *[62-74-8]* **M 100.0, m 200-205°(dec).** It is a free-flowing white **HIGHLY POISONOUS** powder which is purified by dissolving it in *ca* 4 parts of H_2O, and the pH is checked. If it is alkaline, add a few drops of FCH_2CO_2H to make the solution just acidic. Evaporate (fumehood) on a steam bath until crystals start to separate, cool and filter the solid off. More solid can be obtained by adding EtOH to the filtrate. Dry it at 100° *in vacuo*. The p-*nitrobenzyl ester* crystallises from EtOH with **m** 76°. The free acid interferes with the citric acid cycle. [Saunders & Stacey *J Chem Soc* 1778 *1948*, *Beilstein* **2** IV 446.]

Sodium formate (anhydrous) *[141-53-7]* **M 68.0, m 253°, d_4^{20} 1.92.** A saturated aqueous solution at 90° (0.8ml water/g) is filtered and allowed to cool slowly. (The final temperature should be above 30° to prevent formation of the hydrate.) After two such crystallisations, the crystals are dried in an oven at 130°, then under high vacuum. [Westrum et al. *J Phys Chem* **64** 1553 *1960*, Roecker & Meyer *J Am Chem Soc* **108** 4066 *1986*.] The salt has also been recrystallised twice from 1mM DTPA (diethylenetriaminepentaacetic acid, which was recrystallised 4x from MilliQ water and dried in a vacuum), then twice from water [Bielski & Thomas *J Am Chem Soc* **109** 7761 *1987*]. [*Beilstein* **2** IV 3.]

Sodium D-gluconate *[527-07-1]* **M 218.1, m 200-205°dec, $[\alpha]_{546}^{20}$ +14°, $[\alpha]_{D}^{20}$ +12° (c 20, H_2O).** Crystallise it from a small volume of H_2O (solubility is 59g/100ml at 25°), or dissolve it in H_2O and add EtOH since it is sparingly soluble in EtOH. It is insoluble in Et_2O. It forms a Cu complex in alkaline solution and a complex with Fe in neutral solution. [Sawyer & Bagger *J Am Chem Soc* **81** 5302 *1959*, *Beilstein* **3** I 188.]

Sodium glycochenodeoxycholate *[16564-43-5]* **M 472.6, m 245-250°, $[\alpha]_{D}^{23}$ +41.2° (c 1, H_2O).** Dissolve it in EtOH, filter it and concentrate it to crystallisation, and recrystallise from a little EtOH. It also recrystallises from EtOH/Et_2O. [*Beilstein* **10** IV 1611.]

Sodium glycocholate *[863-57-0]* **M 488.6, m 230-240°, $[\alpha]_{D}^{23}$ +29.2° (c 1, H_2O).** Dissolve it in EtOH, filter it and concentrated to crystallisation, and recrystallise from a little EtOH. It also crystallises from 95% EtOH/Et_2O. [*Beilstein* **3** IV 573.]

Sodium glycolate dehydrate (sodium hydroxyacetate) *[2836-32-0]* **M 98.0, pK^{25} 3.83 (for acid).** Precipitate it from aqueous solution by adding EtOH and dry it in air. Also recrystallise it from H_2O, where its solubility is 38% at 0° and 61% at100°. [*Beilstein* **3** III 370, **3** IV 573.]

Sodium hydrogen diglycollate (2,2′-oxydiacetic acid monosodium salt) *[50795-24-9]* **M 156.1, pK_1^{20} 2.70, pK_2^{20} 4.22 (for acid).** Crystallise it from hot water (7.5ml/g) by cooling to 0° with constant stirring. The crystals are filtered off on to a sintered-glass funnel and dried at 110° overnight. Its solubility in water is 2.6% (at 0°) and 20% (at 90°). [*Beilstein* **3** III 377, **3** IV 577.]

Sodium hydrogen oxalate dihydrate *[1186-49-8]* **M 130.0, m 100°(loses H_2O), b 200°(dec).** Crystallise it from hot water (5ml/g) by cooling. Its solubility in H_2O is 1.7% at 15.5° and 21.3% at boiling. [Souchay & Lenssen *Justus Liebigs Ann Chem* **99** 34 *1856, Beilstein* **2** H 513, **2** I 223, IV 1817.]

Sodium hydrogen succinate *[2922-54-5]* **M 140.0.** Crystallise it from hot water and dry it at 110°. Its solubility in H_2O is 17% at 0°, 40% at 25° and 86% at 75°. [Marshall & Bain *J Chem Soc* **97 [I]** 1074, 1084 *1910*, Stokes **70** 1945 *1948*, *Beilstein* **2** H 606, **2** I 262, **2** III 16557, **2** IV 1911.]

Sodium hydrogen *d*-tartrate *[526-94-3]* **M 190.1, m 100°(loses H_2O), m 253°dec, $[\alpha]_{546}$ +26° (c 1, H_2O) and $[\alpha]_{D}^{20}$ +24° (c 1, H_2O).** It crystallises from warm water (10ml/g) by cooling to 0°. [*Beilstein* **3** IV 1219.]

Sodium 2-hydroxy-4-methoxybenzophenone-5-sulfonate *[6628-37-1]* **M 330.3.** Crystallise it from MeOH and dry it under vacuum.

Sodium *p*-hydroxyphenylazobenzene-*p*'-sulfonate *[2623-36-1]* **M 288.2.** Recrystallise it from 95% EtOH.

Sodium ionophore I (ETH 227) (*N,N′,N″*-triheptyl-*N,N′,N″*-trimethyl-4,4',4"-propylidyne-tris(3-oxabutyramide) *[61183-76-4]* **M 642.0.** It is purified (*ca* 200mg) by TLC on Kieselgel F_{254} with $CHCl_3$/Me_2CO (1:1) as solvent, followed by HPLC (50mg) with an octadecyltrimethylsilane modified column (Mercksorb SI 100, 10µm) [IR, NMR, MS: Güggi et al. *Helv Chim Acta* **59** 2417 *1976*]. [See Simon & Carafoli *Methods Enzymol* **56** 439 *1977*.]

Sodium ionophore V (ETH 4120) [4-octadecanoyloxymethyl-*N,N,N′,N′*-tetracyclohexyl-1,2-phenylenedioxydiacetamide] *[129880-73-5]* **M 849.3.** Purify it by recrystallisation from EtOAc [Preparation and properties: Géhrig et al. *Anal Chim Acta* **233** 295 *1990*].

Sodium ionophore VI {bis[(12-crown-4)methyl]dodecyl methyl malonate} *[80403-59-4]* **M 662.9.** Purify it by gel permeation or column chromatography. [Preparation and NMR data: Shono et al. *J Electroanal Chem* **132** 99 *1982*, Cram & Cram *Science* **183** 803 *1974*.]

Sodium *RS*-mandelate *[114-21-6]* **M 174.1, pK^{25} 3.41 (for the acid).** It crystallises from 95% EtOH and is dried in a vacuum. [Ross & Morrison *J Chem Soc* 1019 *1933*, Banks & Davies *J Chem Soc* 74 *1938*, *Beilstein* **10** III 450.]

Sodium methoxide *[124-41-4]* **M 54.0.** It behaves in the same way as sodium ethoxide. It is *hygroscopic* and is hydrolysed by moist air to NaOH and MeOH. Material that has been kept under N_2 should be used. If erratic results are obtained, even with recently purchased NaOMe, it should be freshly prepared thus: Clean Na (37g) cut in 1-3g pieces is added in small portions to stirred MeOH (800ml) in a 2L three-necked flask equipped with a stirrer and a condenser with a drying tube. After all the Na has dissolved, the MeOH is removed by distillation under vacuum, and the residual NaOMe is dried by heating at 150° under vacuum and kept under dry N_2 until required [Burness *Org Synth* **39** 51 *1959*]. [*Beilstein* **1** IV 1227.]

Sodium monensin *[22373-78-0]* **M 693.8.** Crystallise it from EtOH/H_2O [Cox et al. *J Am Chem Soc* **107** 4297 *1985*].

Sodium oleate *[143-19-1]* **M 304.4, m 233-235°.** Sodium oleate crystallises from EtOH, and is dried in an oven at 100°. [*Beilstein* **2** H 465, **2** I 201, **2** II 434, **2** III 1405, **2** IV 1645.]

Sodium oxalate *[62-76-0]* **M 134.0, m 250-270°(dec), d_4^{20} 2.34.** It crystallises from hot water (16ml/g) by cooling to 0°. Before use as a volumetric standard, analytical grade quality sodium oxalate should be dried for 2 hours at 120° and allowed to cool in a desiccator. [*Beilstein* **2** IV 1819.]

Sodium palmitate *[408-35-5]* **M 278.4, m , 270°, 285-201°.** It crystallises from EtOH and is dried in an oven. [*Beilstein* **2** IV 1157.]

Sodium pentamethylcyclopentadienide (NaCp′, 1,2,3,4,5-pentamethyl-2,4-pentadiene-1-ylsodium) *[40585-51-1]* **M 158.2, m >230°.** It is prepared, handled and stored as for KCp′ but is not as flammable. A 0.5M solution in THF is commercially available. It is a Cp′ ligand source for complexing with a large number of metals and non-metal halides. [Kohl et al. in *Organometallic Synthesis* (R. Bruce King and J.J. Eisch eds) ***Vol 3*** 381, Elsevier Amsterdam *1986*].

Sodium phenoxide *[139-02-6*, *156150-40-2 (3H_2O)]* **M 116.1, m 61-64°.** The ground powder is washed with Et_2O, then heated at 60°/1mm for 12 to 24 hours to remove any free phenol and solvent. [Kornblum & Lurie *J Am Chem Soc* **81** 2710 *1959*, *Beilstein* **6** I 718.]

Sodium phenylacetate *[114-70-5]* **M 158.1.** Its aqueous solution is evaporated to crystallisation on a steam bath; the crystals are washed with absolute EtOH and dried under vacuum at 80°. [*Beilstein* **9** IV 1614.]

Sodium *o*-phenylphenolate tetrahydrate *[132-27-4]* **M 264.3.** Crystallise the salt from acetone and dry it under vacuum at room temperature. [*Beilstein* **16** IV 4600.]

Sodium phenylpyruvate *[114-76-1]* **M 186.1, m >300°.** The salt should have no OH broad bands in the IR at ~3000cm^{-1}. If these are present, then they are due either to water contamination or to the presence of free acid. For the first case dry the solid thoroughly in a vacuum over P_2O_5, and in the latter case wash the salt well with Et_2O *in vacuo* till free of acid. *Alternatively*, add a slight excess of the free acid (cf p 375, see[156-06-9]) in EtOH to ethanolic NaOH, evaporate to dryness and extract excess acid from the salt with dry Et_2O. [*Beilstein* **10** I 325.]

Sodium phytate monohydrate [*myo*-inositolhexakis(H_2PO_4) Na salt] *[14306-25-3]* **M 857.9.** Crystallise sodium phytate from hot water. [*Beilstein* **6** IV 7927.]

Sodium polyacrylate (NaPAA) *[9003-04-7]***.** Commercial polyacrylamide is first neutralised with an aqueous solution of NaOH, and the polymer is precipitated with acetone. The precipitate is redissolved in a small amount of water and freeze-dried. The polymer is then repeatedly washed with EtOH and water to remove traces of low-molecular-weight material, and finally dried in vacuum at 60° [Vink *J Chem Soc, Faraday Trans 1* **75** 1207 *1979*]. It has also been dialysed overnight against distilled water, then freeze-dried.

Sodium poly (α-L-glutamate). Wash it with acetone, dry it in a vacuum, dissolve it in water and precipitate it with isopropanol at 5°. Impurities and low-molecular-weight fractions are removed by dialysis of the aqueous solution for 50 hours, followed by ultrafiltration through a filter impermeable to polymers of molecular weights greater than 10^4. The polymer is recovered by freeze-drying. [Mori et al. *J Chem Soc, Faraday Trans 1 2583 1978*.]

Sodium propionate *[137-40-6]* **M 96.1, m 287-289°.** Recrystallise it from H_2O (solubility 10%) and dry by heating at 100° for 4 hours. The solubility of the anhydrous salt in MeOH is 13% at 15° and 13.77% at 68°. It is insoluble in $*C_6H_6$ and Me_2CO. [Henstock *J Chem Soc* 1341 *1934*, *Beilstein* **2** IV 701.]

Sodium stearate *[822-16-2]* **M 306.6.** It is better to prepare it by adding a slight excess of octadecanoic acid to ethanolic NaOH, evaporating and extracting the residue with dry Et_2O. [*Beilstein* **2** III 1003.]

Sodium *R*-tartrate dihydrate *[6106-24-7]* **M 230.1, m 120°(loses H_2O), d $_4^{20}$ 1.82, [α] $_D^{20}$ +26° (c 1, H_2O).** It crystallises from warm dilute aqueous NaOH on cooling. [*Beilstein* **3** H 524.]

Sodium trifluoroacetate *[2923-18-4]* **M 136.0, m 206-210°(dec), pK^{25} 0.52 (for $CF_3CO_2^-$).** A possible contaminant is NaCl. The solid is treated with CF_3CO_2H and evaporated twice. Its solubility in CF_3CO_2H is 13.1% at 29.8°. The residue is crystallised from dilute EtOH, and the solid is dried in vacuum at 100°. [Hara & Cady *J Am Chem Soc* **76** 4285 *1954*.] It can be precipitated from EtOH by adding dioxane, then recrystallising several times from hot absolute EtOH. Dry it at 120-130°/1mm. [*Beilstein* **2** IV 461.]

Stannous bis-cyclopentadienyl *[26078-96-6]* **M 248.9.** Purify it by vacuum sublimation. Handle and store it under dry N_2. The related thallium and indium compounds are similarly purified.

Strontium acetate *[543-94-2]* **M 205.7, d 2.1, pK^{25} 13.0 (for aquo Sr^{2+} hydrolysis).** Crystallise it from AcOH, then dry it under vacuum for 24 hours at 100°. [*Beilstein* **2** II 91.]

Strontium lactate trihydrate *[29870-99-3]* **M 319.8, m 120°(loses $3H_2O$).** It crystallises from aqueous EtOH. [*Beilstein* **3** IV 633.]

Strontium oxalate monohydrate *[814-95-9]* **M 193.6, m 150°.** It crystallises from hot water on cooling. The solubility at ~25° in H_2O is 1g/20L, and in 3.5% AcOH and 25% AcOH it is 1g/1.9L and 1g/1.1L respectively. **IRRITANT**. [*Beilstein* **2** H 515, **2** IV 1826.]

Strontium salicylate *[526-26-1]* **M 224.7.** It crystallises from hot water (4ml/g) or EtOH. [*Beilstein* **10** IV 125.]

Strontium tartrate *[868-19-9]* **M 237.7.** It crystallises from hot water. [*Beilstein* **3** IV 1219.]

Tantalium pentaethoxide *[6074-84-6]* **M 406.3, b 147°/0.2mm, 202°/10mm, pK$_1^{25}$ 9.6, pK$_2^{25}$ 13.0 (for tantalic acid).** Purify it by distillation under reduced pressure. It aggregates in $*C_6H_6$, EtOH, MeCN, pyridine and diisopropyl ether. [Bradley et al. *J Chem Soc* 726 *1955*, Bradley et al. *J Chem Soc* 5 *1956*, *Beilstein* **1** IV 1312.]

Tetraallyltin (tetraallylstannane) *[7393-43-3]* **M 283.0, b 52°/0.2mm, 69-70°/15mm, d $_4^{20}$ 1.179, n $_D^{20}$ 1.536.** Possible contaminants are allyl chloride and allyltin chloride. Check the ^{1}H NMR and IR [Fishwick & Wallbridge *J Organomet Chem* **25** 69 *1970*], and if impure, dissolve it in Et_2O and shake it with a 5% aqueous solution of NaF which precipitates allyltin fluoride. Separate the Et_2O layer, dry ($MgSO_4$), and distil it at ~0.2mm. It decomposes slightly on repeated distillation. [O'Brien et al. *Inorg Synth* **XIII** 75 *1972*, Fishwick et al. *J Chem Soc (A)* 57 *1971*, *Beilstein* **4** III 1922.]

Tetrabutylammonium borohydride *[33725-74-5]* **M 257.3, m 128-129°.** Purify it by recrystallisation from EtOAc followed by careful drying under vacuum at 50-60°. Samples purified in this way showed no signs

of loss of *active* H after storage at room temperature for more than 1 year. Nevertheless samples should be stored at *ca* 6° in tightly stoppered bottles if kept for long periods. It is soluble in CH_2Cl_2. [Raber & Guida *J Org Chem* **41** 690 *1976*, Brändström et al. *Tetrahedron Lett* 3173 *1972*.]

Tetrabutyl orthotitanate monomer (titanium tetra-*n*-butoxide) *[5593-70-4]* **M 340.4, b 142°/0.1mm, 134-136°/0.5mm, 160°/0.8mm, 174°/6mm, 189°/13mm, d $_4^{35}$ 0.993, n $_D^{25}$ 1.49.** Dissolve it in *C_6H_6, filter if solid is present, evaporate and vacuum fractionate through a Widmer 24 inch column. The ester hydrolyses when exposed to air to give hydrated ortho-titanic acid. The titanium content can be determined thus: weigh a sample (*ca* 0.25g) into a weighed crucible and cover it with 10ml of H_2O and a few drops of conc HNO_3. Heat (hot plate) carefully till most of the H_2O has evaporated. Cool and add more H_2O (10ml) and conc HNO_3 (2ml), and evaporate carefully (no spillage) to dryness and ignite the residue at 600-650°/1 hour. Weigh the residual TiO_2. [Bradley et al. *J Chem Soc* 2773 *1952*, Speer *J Org Chem* **14** 655 *1949*, *Beilstein* 1 II 398, **1** III 1515, **1** IV 1415.]

Tetrabutyl tin (tin tetrabutyl) *[1461-25-2]* **M 347.2, m -97°, b 94.5-96°/0.28mm, 145°/11mm, 245-247°/atm, d $_4^{20}$ 1.0559, n $_D^{24}$ 1.473.** Dissolve it in Et_2O, dry it over $MgSO_4$, filter, evaporate and distil it under reduced pressure. Although it does not crystallise easily, once the melt has crystallised, then it will recrystallise more easily. It is soluble in Et_2O, Me_2CO, EtOAc and EtOH, but insoluble in MeOH and H_2O, and shows no apparent reaction with H_2O. [Johnson & Fritz *J Org Chem* **19** 74 *1954*, Staveley *J Chem Soc* 1992 *1954*, Van der Kerk & Luitzen *Org Synth* Coll Vol **IV** 822 *1963*, *Beilstein* **4** III 1920, **4** IV 4312.]

Tetraethyl lead *[78-00-2]* **M 323.5, m -38°, b 84-85°/15mm, 200°, 227.7°(dec), d $_4^{20}$ 1.653, n $_D^{20}$ 1.5198.** Its more volatile contaminants can be removed by exposure to a low pressure (by continuous pumping) for 1 hour at 0°. Purify it by stirring with an equal volume of H_2SO_4 (d 1.40), keeping the temperature below 30°, repeating this process until the acid layer is colourless. It is then washed with dilute Na_2CO_3 and distilled water, dried with $CaCl_2$ and fractionally distilled at low pressure under H_2 or N_2 [Calingaert *Chem Rev* **2** 43 *1926*]. It prevents "knocking" in petrol combustion engines. [Milde & Beatty *Adv Chem Res* **23** 306-318 *1959*, *Beilstein* **4** H 639.] **VERY POISONOUS.**

Tetraisopropyl orthotitanate (titanium tetraisopropoxide) *[546-68-9]* **M 284.3, m 18.5°, 18-20°, b 80°/2mm, 78°/12mm, 228-229°/755mm.** Dissolve it in dry *C_6H_6, filter if a solid separates, evaporate and fractionate. It is hydrolysed by H_2O to give solid $Ti_2O(iso\text{-}OPr)_2$ **m** *ca* 48°. [Bradley et al. *J Chem Soc* 2027, *1952*, Bradley et al. *J Chem Soc* 469 *1957*, *Beilstein* **1** II 328, **1** IV 1469S.]

Tetrakis(diethylamino) titanium [(titanium tetrakis(diethylamide)] *[4419-47-0]* **M 336.4, b 85-90°/0.1mm, 112°/0.1mm, d $_4^{30}$ 0.93, n $_D^{30}$ 1.54.** Dissolve it in *C_6H_6, filter if a solid separates, evaporate under reduced pressure and distil it. It is an orange liquid which reacts violently with alcohols. [Bradley et al. *J Chem Soc* 3857 *1960*, *Beilstein* **4** IV 313.]

Tetramethyloxorhenium [$(CH_3)_4ReO$] *[53022-7-1]* **M 262.4, m ~45° (no dec <150°).** It is best prepared by adding a 1M solution of MeLi in Et_2O (80ml, 80mmol) slowly to a stirred suspension of $ReOCl_3(PPh_3)_2$ (8.32g, 10mmol, cf [17442-18-1]) in Et_2O (120ml) at -78°, and the mixture is allowed to warm slowly to ~25° to form a dark brown solution which is stirred further for 0.5 hours. The excess of MeLi is destroyed by dropwise addition, at -78°, of H_2O (~10ml), and allowed to warm to ~25°, and then cooled again, to -30°; and H_2O_2 (2.5g, 30% diluted in 20ml of H_2O) is added slowly dropwise with vigorous stirring. The colour of the solution changes to red rapidly and stirring is continued for 0.5 hours after the temperature has risen to ~25°. This mixture is then cooled to -78°, the Et_2O layer is filtered free from ice, dried first with $CaCl_2$ at ~25° then with molecular sieves, cooled again to -78°, filtered, and the solvent is carefully evaporated at -50°. The red-purple (carmine) crystalline residue is sublimed onto a probe at -78°, in a 1mm vacuum, to give Me_4ReO (1.26g, ~48%; but can be as high as 70% by very careful removal of solvent). Lower yields are obtained if due care is not taken during the removal of solvent *in vacuo*. The low melting solid is extremely volatile subliming readily even at -35°/10^{-3}mm; it co-distils at low temperatures with Et_2O or petroleum ether, and always occurs during removal of solvents (see earlier), hence the temperature has to be kept as low as possible, and a cold probe should be

included in the system to avoid losses. In an alternative method $ReOCl_4$ (3mmol) is reacted with MeLi (12mmol) in Et_2O at -78º to give a 20% yield of Me_4ReO, although this low yield may well be due to evaporative losses.
Me_4ReO is thermally stable and can be stored indefinitely *in vacuo*. It is very soluble in petroleum ethers, Et_2O, CS_2, CCl_4, but these solutions slowly decompose with time even in the absence of air. However, solutions in THF and aromatic hydrocarbons are more stable. It is surprisingly unreactive at ~25º in Et_2O, H_2O, mineral acids, alcohols, H_2, CO, CO_2, SO_2, HCl gas, butadiene, tertiary phosphines, amines, tetramethylthiuram disulfide and 1,1-diphenyl-2-picrylhydrazyl. It is however, highly reactive with air and oxygen producing instantly white fumes and crystals of $MeReO_3$ (methyltrioxorhenium, MTO, the carrier catalyst, see [70197-13-6]). In $*C_6H_6$ solution with air, it slowly oxidises to form yellow-orange products (cf yellow cis-Me_3ReO_3 [56090-01-8]). In the mass spectrum, ions of Re isotopes are identified (^{185}Re 37%, ^{187}Re 63%) with the natural isotopic abundance. The solid state IR (at ~ -250º co-condensed with argon) has ν_{max} at 2974s(CH str), 1231s(CH def), 1018s(Re=O str), 1004sh,br, 746m(Me rock), 552m and 529s(ReC str) cm^{-1}, and IR (de-oxygenated CS_2) has ν_{max} at 2980s, 1370m, 1002s, 749w, 520m cm^{-1}. [Mertis, Williamson and Wilkinson *JCS, Dalton Trans* 607 *1975*, Mertis & Wilkinson *JCS, Dalton Trans* 1488 *1976*, Beattie & Jones *Inorg Chem* **18** 2318 *1979*.]

Tetramethyltin (tetramethylstannane, tin tetramethyl) *[594-27-4]* **M 178.8, m -55º, b 76.6º/748mm, 74-75º/atm, 78º/atm, d ^{25} 1.291, n $^{20}_{D}$ 1.441.** Organotin compounds are **HIGHLY TOXIC,** and all due precautions should be taken when handling them. Me_4Sn is an ethereal smelling liquid that is highly flammable with a flash point of less than 20º, and should be stored at low temperatures. An improved preparation of Me_4Sn has been achieved by carrying out the reaction in the higher boiling di-*n*-butyl ether, and preparing the Grignard reagent *in situ*. Under strictly anhydrous conditions, to Mg turnings (50g, 2.06g.atoms) in dry *n*-Bu_2O (600ml, containing a few crystals of I_2) is added dropwise a solution of MeI (225g, 1.59moles, freshly distilled) in *n*-Bu_2O (600ml) with gentle stirring. After the initial reaction has started, the MeI solution is added at such a rate as to keep the solution refluxing gently, requiring *ca* 3 hours. Cool the solution to ~25º and add to it, dropwise, anhydrous $SnCl_4$ (75g, 0.29 moles) while sustaining gentle reflux (*ca* 2-2,5 hours). The mixture is then refluxed steadily (85-95º) for 1 hour, and set aside at ~25º for several hours. The reflux condenser is replaced by a Claisen head and the mixture is distilled; whereby Me_4Sn and *n*-Bu_2O distil together at ~85-95º/atm. It dissolves stopcock silicone greases. The Me_4Sn is purified by fractionation through a Todd column (35-40 plates) to give pure *stannane* with **b 76.6º/748mm** in 91% yield. [Edgell & Ward *J Am Chem Soc* **76** 1169 *1954*.] Its IR (liquid film) has ν_{max} at 2920 (vs) and 3000 (vs) C-H str, 1443 (s) and 1198 (s) CH_3 deformation, 770 (vs) CH_3 rocking, **528 (s) C-Sn** str cm^{-1}, and from Raman spectrum 160 (vs) and 145 (vs) cm^{-1} for **C-Sn-C** bending [Taimsalu & Wood *Trans Farad Soc* **59** 1754 *1963*, Edgell & Ward *J Am Chem Soc* **77** 6486 *1955*]. The ^{119}Sn NMR (15.5 MHz, at 28ºC, 12mm tube not spinning, neat $SnCl_4$ as external standard) has δ at -147.8 ($J_{H\text{-}^{119}Sn}$ = 54.0Hz from 60MHz proton spectrum) [Lassigne & Wells *Can J Chem* **55** 927 *1977*, for ^{1}H and ^{13}C NMR spectra see Singh *J Organomet Chem* **99** 251 *1975*.] [*Beilstein* **4** H 631, **4** I 583, **4** II 1010, **4** III 1917, **4** IV 4307.]

Tetraphenyltin *[595-90-4]* **M 427.1, m 224-225º, 226º.** $SnPh_4$ forms yellow crystals from $CHCl_3$, petroleum ether (b 77-120º), xylene or *benzene/cyclohexane, and is dried at 75º/20mm. [Gilman & Rosenberg *J Am Chem Soc* **74** 531 *1952*, *Beilstein* **16** IV 1592.]

Tetra-*n*-propylammonium perruthenate (TPAP, tetrapropyl tetraoxoruthenate) *[114615-82-6]* **M 351.4, m 160º(dec).** It is a dark green solid that is stable at ~25º for long periods without much deterioration, and is best kept in a refrigerator. It is a strong oxidant, and should not be heated directly as it may explode. Small amounts decompose in a flame at ~155º in air. It can be washed with aqueous *n*-propanol, then H_2O and dried over KOH in a vacuum. It is soluble in CH_2Cl_2 and MeCN. Generally, at ambient temperatures in these solvents it is most useful, when in conjunction with *N*-methylmorpholine *N*-oxide, for the oxidation of primary and secondary alcohols, including allylic and benzylic alcohols, lactol oxidation, heteroatom oxidation, and some cleavage reactions. [Dengel et al. *Transition Met Chem* **10** 98 *1985*, Griffith et al. *J Chem Soc, Chem Commun* 1625 *1987*, for a review see Ley et al. *Synthesis* 639 *1994*, and for its catalytic activity see chapter on "Catalysis".]
§ Polymer supported reagent is available commercially.

Thallium (I) acetate (TlOAc) *[563-68-8]* **M 263.4, m 131°.** Thallous (I) acetate crystallises from EtOH (needles) or Me_2CO. The salt forms white deliquescent crystals (specific gravity 3.68) which are soluble in H_2O and EtOH. Store it in sealed containers. It forms TlOAc.AcOH crystals which melt at 64°. [*Beilstein* **2** H 115, **2** II 119, **2** III 195.] **POISONOUS — HANDLE CAREFULLY WITH GLOVES, and work in a well-ventilated fume hood.**

Thallium (III) triacetate [$Tl(OAc)_3$] *[2570-63-0]* **M 381.5, m 182°(dec.).** The salt is prepared by stirring thallic oxide (50g) in AcOH (300ml) at 65° until all the brown-black solid has dissolved (~24 hours), then filter and cool to obtain the salt as white crystals which are collected by decantation and dried over P_2O_5 *in vacuo* as they turn brown in air. A second crop can be obtained by concentrating the filtrate (total yield 73g, 99%). On a large scale (457g) of the brown trioxide was treated with AcOH (2L) containing Ac_2O (110ml) by stirring at 80-90°, the walls of the flask were washed down with a further volume of AcOH (500ml). Heating (90-100°) and stirring was continued for 2 hours (all the brown oxide had dissolved), the hot solution was filtered using a sintered glass funnel, cooled to ~20°, and collected onto a glass frit. The solid was dissolved in the minimum volume of AcOH (~800ml) at 80-90°, filtered through a glass frit and allowed to cool first to ~20° then to ~15°, and collected by filtration. The $Tl(OAc)_3$ was dried by spreading it in a large dish in a desiccator over KOH pellets overnight to give ~97% pure salt (467g, 61% yield). It promotes the quantitative photochemical decarboxylation of a variety of aliphatic acids to yield a high proportion of the corresponding alkanes with some alkenes, dialkyls and other minor products at wavelength 3500Å; whereas at wavelength 2537Å the alkyldimers are formed in high yields. [Kochi & Bethea *J Org Chem* **33** 75 *1968*.] [*Beilstein* **2** H 115, **2** III 195.] **POISONOUS — HANDLE CAREFULLY WITH GLOVES, and work in a well-ventilated fume hood.**

Thallium (III) trifluoroacetate [$Tl(tfl)_3$, $Tl(OCOCF)_3$] *[23586-53-0]* **M 543.4, m dec slowly >100°, 213° (dec.).** This thallation reagent is prepared in 90-100% yield by heating a suspension of thallium(III) oxide in TFA containing 10-20% of H_2O until clear. This colourless solution can be used directly in thallation reactions or a granular solid salt can be isolated by evaporation *in vacuo*, and then used in inert solvents such as MeCN. The salt does not have a sharp melting point and decomposes slowly >100°. It is water sensitive but can be stored at ~25° in a stoppered container away from light without appreciable decomposition for long periods. A solution of the salt in TFA, however, can tolerate up to ~20% of H_2O to give a 0.8M solution before serious hydrolysis of the salt occurs. It thallated aromatic rings (e.g. PhCl, PhF, toluene, xylene, *o*-benzoic acid) in TFA to produce the corresponding Aryl$Tl(tfl)_2$ at low temperatures which can be isolated in 70-100% yields, or reacted further (e.g. with KI) to displace the $Tl(tfl)_2$ group and form the respective iodides. [McKillop et al. *J Am Chem Soc* **93** 4841 *1971*, Taylor et al. *Org Synth* Coll Vol **VI** 709 *1988*, see Fieser & Fieser's *Organic Reagents* for further applications, *Beilstein* **2** II 186.] **POISONOUS — HANDLE CAREFULLY WITH GLOVES, and work in a well-ventilated fume hood.**

Thallous (I) ethoxide (TlOEt) *[20398-06-5]* **M 249.4, d_4^{25} 3.522, n_D^{20} 1.676.** The alkoxide is prepared by refluxing dry EtOH in a modified Soxhlet extractor whereby the hot alcohol leaches thallium shot or turnings (see below) placed in the vapours of refluxing alcohol while oxygen flows through the apparatus which is protected from moisture with a soda lime drying tube at the top of the condenser. The apparatus devised by Fieser and Fieser can be used. Thallium shot (m 303°) is made by holding a clean piece if metal with tongs and heated with a blow torch allowing the molten metal to drip in ~2L of cold H_2O. *Alternatively*, thallium turnings made with a pencil sharpener from thallium rods can be used. A Soxhlet flask (500ml) containing dry EtOH (300ml) is placed under Tl shot (100ml, dried by pressing with filter paper) in the crucible above, and the EtOH is refluxed while a rapid stream of dry O_2 is made to flow just beneath the metal. The volume of boiling EtOH in the flask is maintained at ~300ml by further addition of dry EtOH. When all the metal has been converted to TlOEt (12-16 hours), and all the oily alkoxide has run into the flask which will form a separate heavy oily liquid layer (note that TlOEt had d = 3.522), boiling is stopped and the volume of the alkoxide solution is adjusted to 300ml which would give a saturated solution containing 9g of TiOEt/100ml. Store away from moisture. *Alternatively*, the oily layer can be sucked out with a vacuum into a container, but great care should be taken to avoid contact with moisture. Thallium in the ethoxide solution can be determined as TlOH by cooling it in an ice bath without separating the excess of EtOH (to avoid partial conversion of TlOH to black Tl_2OH), and adding an equal volume of boiled and re-cooled H_2O (i.e. free from O_2) and evaporating *in vacuo* to give yellow

adding an equal volume of boiled and re-cooled H_2O (i.e. free from O_2) and evaporating *in vacuo* to give yellow crystalline TlOH. [Fieser & Fieser's *Reagents for Organic Synthesis* **2** 409 *1969*, Dönges in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Academic Press Vol **I** p 877-878 *1963*, Freudenberg & Uthemann *Chem Ber* **52** 1508 *1919*.] **POISONOUS— handle with gloves, and work in a good fume hood.**

Tin (II) acetate (stannous acetate) *[638-39-1]* **M 236.8, m 180-182°, 182.55-183°, b 239-241° (some dec under N_2), d 2.31.** It is prepared by dissolving blue-black SnO_2 (25g) in refluxing 50%v/v AcOH (200ml), evaporating *in vacuo* (over KOH) and subliming the white residue *in vacuo* at 150-155° (~96% yield of white orthorhombic crystals). *Alternatively*, finely divided Sn is refluxed in glacial AcOH for 80-90 hours [not less as $Sn(OAc)_2$ 2AcOH is formed] and isolated as before. It hydrolyses slowly in H_2O to give blue Black SnO_2, Me_2CO, CO_2 and H_2, can be stored for long periods under N_2, and is soluble in EtOH (2.9%), Me_2CO (1.4%) and 2N AcOH (33%). It is a useful reducing (and acetylating) agent. [Donaldson et al. *J Chem Soc* 5942 *1964*.]

Titanium (IV) methoxide *[992-92-7]* **M 172.0, m 200-210°, b 243°/52mm.** It is extremely sensitive to moisture. Dissolve it in H_2O-free $*C_6H_6$, filter, evaporate and distil it *in vacuo* under N_2. It is **FLAMMABLE** and **TOXIC**. [Bradley et al. *Metal Alkoxides* Academic Press *1978,* ISBN 0121242501.]

Titanocene dichloride *[1271-19-8]* **M 248.9, m 260-280°(dec), 289.2°, 298-291°, d_4^{20} 1.60.** It forms bright red crystals from toluene or xylene/$CHCl_3$ (1:1) and sublimes at 190°/2mm. It is moderately soluble in EtOH and insoluble in Et_2O, $*C_6H_6$, CS_2, CCl_4, petroleum ether and H_2O. The crystalline *dipicrate* explodes on melting at 139-140°. [Wilkinson et al. *J Am Chem Soc* **75** 1011 *1953*, IR: Wilkinson & Birmingham *J Am Chem Soc* **76** 4281 *1954*, NMR and X-ray: Glivicky & McCowan *Can J Chem* **51** 2609 *1973*, Clearfield et al. *J Am Chem Soc* **53** 1622 *1975*, *Beilstein* **16** IV 1769.]

Tri-*n*-butyl tin chloride *[1461-22-9]* **M 325.5, b 98-100°/0.4mm, 140-152°/10mm, 172°/25mm, d_4^{20} 1.21, n_D^{20} 1.492.** Fractionate it in an inert atmosphere and seal it in small aliquots in glass ampoules. It is sensitive to moisture. [Jones et al. *J Chem Soc* 1446 *1947*, Kocheshkov *J Gen Chem USSR* **4** *1359 1934,* Kocheshkov *J Gen Chem USSR* **5** 211 *1935*, *J Appl Chem* **6** 93 *1936*, *Beilstein* **4** III 1926, **4** IV 4330.]

Tributyl tin hydride *[688-73-3]* **M 291.1, b 76°/0.7mm, 81°/0.9mm, d_4^{20} 1.098, n_D^{20} 1.473.** Dissolve it in Et_2O, add quinol (500mg for 300ml, to stabilise it), dry over Na_2SO_4, filter, evaporate and distil it under dry N_2. It is a clear liquid if dry and decomposes very slowly. In the presence of H_2O, traces of tributyl tin hydroxide are formed in a few days. Store it in sealed glass ampoules in small aliquots. It is estimated by reaction with aqueous NaOH when H_2 is liberated. **CARE**: stored samples may be under pressure due to liberated H_2. [Van Der Kerk et al. *J Appl Chem* **7** 366 *1937*, Ono et al. *Tetrahedron* **41** 4013 1985, Neuman *Synthesis* 665 *1987*, Curran *Synthesis* 417 *1988*, *Beilstein* **4** IV 4312.]

Triethyltin hydroxide *[994-32-1]* **M 222.9, m 49-50°, b 153-155°/20mm.** Treat it with HCl, followed by KOH, and filter it to remove diethyltin oxide [Prince *J Chem Soc* 1783 *1959*]. [*Beilstein* **4** H 633, **4** I 585, **4** II 1012, **4** III 1924, **4** IV 4325.]

Trimethyloxonium tetrafluoroborate *[420-37-1]* **M 147.9, m 141-143°(sinters, open capillary), 179.6-180.0°(dec), 210-220°(dec).** The salt must be a white crystalline solid **m** ~179.6-180.0° (dec, sealed tube). Under a N_2 atmosphere (e.g. Dry Box), wash it twice with CH_2Cl_2, then twice with Na-dried Et_2O, and dry by passing dry N_2 over the salt until free from Et_2O [Curphey *Org Synth* Coll Vol **VI** 1019 *1988*]. The oxonium salt, purified in this way, can be handled in air for short periods. The sample kept in a desiccator (Drierite) for 1 month at -20° had an unaltered melting point, and samples stored in this way for >1 year are satisfactory for alkylations. ^1H NMR in liquid SO_2 in a sealed tube had a single peak at δ 4.54 (impurities have δ at 3.39). [Meerwein *Org Synth* Coll Vol **V** 1096 *1973*.] If the sample looks good, dry it in a vacuum desiccator for 2 hours (25°/1mm) and store it under N_2 at -20°. The melting point depends on heating rate. [*Beilstein* **1** IV 1248.]

***Cis*-Trimethylrhenium dioxide [*cis*-trimethyldioxorhenium(VII), *cis*-$(CH_3)_3ReO_2$]** *[56090-01-8]* **M 263.3, m 10-11°.** This yellow dioxide is best prepared, in ~60% yield, from Me_4ReO (preceding oxide [53022-7-1],

e.g. 0.5g) in Et_2O (e.g. 40ml) at -78° by exposing the solution to nitric oxide when the red colour disappears while allowing to warm to ~25° with stirring. After 1 hour (without isolating the nitroso intermediate), the Et_2O is removed at -40° *in vacuo* and the yellow crystalline residue is sublimed at 10^{-3}mm onto a probe at -78° to give *cis*-$(CH_3)_3ReO_2$, which can be recrystallised from petroleum ether solution on cooling to -78°, or distilled *in vacuo*. It is reasonably stable at room temperature, and like the starting material it fumes in air forming needles of MTO, the carrier catalyst (see above). Store it under N_2 or argon in a sealed ampoule. Its IR spectrum is consistent with the trigonal bipyramidal structure, where bands due to methyl vibrations are present together with two strong bands at ν_{max} 992 and 951 cm^{-1} attributable to *cis*-ReO_2. This structure is also consistent with the ^1H NMR in CS_2 or deuteriotoluene which has two sharp resonances at δ 2.07 and 2.50 in the ratio 1:2 in which the higher field band is assumed to be from the axial methyl group. The lines do not broaden on cooling to -78° or heating to 85° in toluene solution which is consistent with a rigid molecule. The MS is as predicted from the two isotopes of Re (see above). [Mertis & Wilkinson *JCS, Dalton Trans* 1488 *1976*, Beattie & Jones *Inorg Chem* **18** 2318 *1979*.]

Trimethyltin chloride (chlorotrimethylstannane) *[1066-45-1]* **M 199.3, m 37.5-39.5°, 42°, b 45-47°/10mm, 152°/760mm, 154-156°/atm.** Me_3SnCl forms colourless needles that have **HIGHLY TOXIC** vapours and is best purified by distillation at atmospheric pressure or in a vacuum. It has been prepared by dropwise addition of a solution of Et_2O saturated with dry HCl (20ml) to freshly distilled (dimethylamino)trimethylstannane (2.21g, b 126°/atm, d^{25} 1.274, n_D^{20} 1.463 [993-50-0]) in dry Et_2O (10ml). $Me_2NH.HCl$ precipitated out, was filtered, the solvent was evaporated at <20°/15mm, and the residue was distilled at 760mm providing the colourless crystalline solid *Me_3SnCl* (1.80g, 89.7%). It sublimes slowly at ~25°/20mm. [Jones & Lappert *J Organomet Chem* **3** 295 *1965*, for ^1H and ^{13}C NMR see Singh *J Organomet Chem* **99** 251 *1975*.] It is also available commercially as 1.0M solutions in hexanes or THF. Like the reaction of Me_2N-$SnMe_3$, the *Me_3SnCl* reacts with H_2O on heating to give *Me_3SnOH* (almost quantitatively, [56-24-6]) as white crystals **m 118°**, which sublime at their melting point. It has IR (Nujol mull) with ν_{max} at 3620 (m), 2985 (m), 2915 (m), 1405 (w), 1195 (m), 920 (s), 765 (s), **540** (s) **Sn-C** str, 370 (s) and 316 (w) cm^{-1}; it exists as a *dimer* $[Me_3SnOH]_2$ in the solid state (IR mull) and in $*C_6H_6$, CCl_4 and in $CHCl_3$ solutions (ebullioscopy) [Okawara & Yasuda *J Organomet Chem* **1** 356 *1964*].

Triphenylantimony *[603-36-1]* **M 353.1, m 52-54°.** Recrystallise Ph_3Sb from acetonitrile [Hayes et al. *J Am Chem Soc* **107** 1346 *1985*]. [*Beilstein* **16** H 891, **16** IV 1198.]

Triphenylbismuth (bismuth triphenyl) *[603-33-8]* **M 440.3, m 75-76°, 77-78°, 78.5°, b 124°/7mm, $d_4^{98.5}$ 1.6427(melt).** Dissolve Ph_3Bi in EtOH, precipitate it with H_2O, extract with Et_2O, dry and evaporate till the residue crystallises. It has been recrystallised from EtOH and Et_2O/EtOH and is a stable compound. [Forward et al. *J Chem Soc* suppl p121 *1949*, Pfeiffer et al. *Chem Ber* **37** 4620 *1904*, Gilman & Yablunky *J Am Chem Soc* **62** 665 *1940*, UV: Jaffé *J Chem Phys* **22** 1430 *1954*, *Beilstein* **4** III 1841.]

Triphenyltin chloride (chlorotriphenylstannane, triphenylchlorostannane) *[639-58-7]* **M 385.5, m 103-106°(dec), 108°(dec), b 240°/13.5mm.** Purify it by distillation, followed by recrystallisation from MeOH by adding petroleum ether (b 30-60°), **m** 105-106° [Kozeschow et al. *Chem Ber* **67** 1348 *1934*], or by crystallisation from Et_2O, or 5 parts of EtOH and a small volume of petroleum ether. [Krause *Chem Ber* **51** 914 *1918*.] It sublimes in a vacuum. [*Beilstein* **16** H 914, **16** I 540, **16** II 625, **16** III 1240, **16** IV 1606.] **HIGHLY TOXIC.**

Triphenyltin hydroxide *[76-87-9]* **M 367.0, m 122-123.5°, 124-126°.** West, Baney and Powell [*J Am Chem Soc* **82** 6269 *1960*] purified a sample which was grossly contaminated with tetraphenyltin and diphenyltin oxide by dissolving it in EtOH, most of the impurities remaining behind as an insoluble residue. Evaporation of the EtOH extract gave the crude hydroxide which was converted to *triphenyltin chloride* (above) by grinding in a mortar under 12M HCl, then evaporating the acidic solution. The chloride, after crystallisation from EtOH, had **m** 104-105°. It was dissolved in Et_2O and converted to the hydroxide by stirring with excess aqueous ammonia. The ether layer was separated, dried, and evaporated to give triphenyltin hydroxide which, after crystallisation from EtOH (or MeCN) and drying under vacuum, was in the form of white crystals (**m** 119-120°), which retained some cloudiness in the melt above 120°. The hydroxide retains water (0.1-0.5 moles of water per mole)

tenaciously. [Glidewell & Liles *Acta Cryst* (B) **34** 129 *1978*, *Beilstein* **16** H 914, **16** I 540, **16** II 625, **16** III 1240, **16** IV 1606.]

Tris(2,2'-bipyridine)ruthenium(II) dichloride ($6H_2O$) *[50525-27-4]* **M 748.6.** Recrystallise it from water, then from MeOH [Ikezawa et al. *J Am Chem Soc* **108** 1589 *1986*].

Tris(η^5-2,4-cyclopentadien-1-yl)samarium III [$SmCp_3$] *[1298-55-1]* **M 345.6, m 365°.** $SmCp_3$ was prepared by stirring $SmCl_3$ with cyclopentadienyl sodium [see 4989-82-1] in THF, the solvent is removed and the residue is heated at 200-250° in a high vacuum. Crystalline $SmCp_3$ is stable up to 400° and sublimes at 220°/10^{-4}mm (also 145°/10^{-3}mm) to give orange or yellow-orange crystals that are soluble in THF and are hydrolysed in H_2O. The IR is similar to that of $SmCp_2$. [Wilkinson & Birmingham *J Am Chem Soc* **76** 6210 *1954*, Birmingham & Wilkinson *J Am Chem Soc* **78** 42 *1956*, Watt & Gillow *J Am Chem Soc* **91** 775 *1969*.] It is used in the selective reduction of specific double bonds, i.e. has regioselectivity [Qian et al. *J Organomet Chem* **344** 175 *1988*].
The ***acetonitrile $SmCp_3$ complex*** [100439-84-7] M 386.7 forms bright yellow crystals soluble in MeCN, the ***cyclohexylisocyanide $SmCp_3$ complex*** [37299-04-0] is soluble in *C_6H_6 and has **m 148°**, and the ***pyridine $SmCp_3$ complex*** [114269-11-3] **M 424.7** is obtained as a yellow crystalline solid by dissolving it in pyridine and evaporating to dryness and is soluble in pyridine and MeCN. [Deacon et al. *Aust J Chem* **40** 895 *1987*.]

Tris(d,d-dicampholylmethanato) europium (III) [$Eu(dcm)_3$] *[52351-64-1]* **M 108.5, m 220-227.5°, 229-232°, $[\alpha]_D^{25}$ +28.6° (c 5.4, CCl_4, and varies markedly with concentration).** Dissolve it in pentane, filter it from any insoluble material, evaporate to dryness and dry the residue (white powder) at 100°/0.1mm for 36 hours. Its IR has ν_{max} at 1540cm^{-1}. [McCreary et al. *J Am Chem Soc* **96** 1038 *1974*.]

Trisodium citrate dihydrate *[68-04-2, 6132-04-3]* **M 294.1, m 150°(loses H_2O).** Crystallise the salt from warm water by cooling to 0°. [*Beilstein* **3** III 1100, **3** IV 1274.]

Tris-[(3-trifluoromethylhydroxymethylene)-d-camphorato] europium (III) [$Eu(tfc)_3$] *[34830-11-0]* **M 893.6, m 195-299° (dec), ~220°, $[\alpha]_D^{24}$ +152° (c 2, CCl_4, and varies markedly with concentration).** Purify it by extraction with pentane, filter and the filtrate is evaporated and the residual bright yellow amorphous powder is dried at 100°/0.1mm for 36 hours. A sample purified by fractional molecular distillation at 180-200°/0.004mm gave a liquid which solidified and softened at ~130°, melted at ~180° and was analytically pure. Its IR (CCl_4) has ν_{max} at ν_{max} 1630-1680 cm^{-1} and the ^1H NMR (CCl_4) has δ at -1.3 to 0.5 (br), -0.08 (s), 0.41 (s), 1.6-2.3 and 3.39 (s). [McCreary et al. *J Am Chem Soc* **96** 1038 *1974*, Goering et al. *J Am Chem Soc* **93** 5913 *1971*.]

Vanadium (III) acetylacetonate (vanadyl tris[2,4-pentadienato-O,O′], $V[AcAc]_3$) *[13476-99-8]* **M 348.3, m 181-184°, 185-190°, pK_1^{25} 2.92, pK_2^{25} 3.5 (for aquo V^{3+} hydrolysis).** It crystallises from acetylacetone in brown plates. It can be distilled in small quantities without decomposition. It is soluble in $CHCl_3$ and *C_6H_6, and evaporation of a $CHCl_3$ solution yields brown crystals which are washed with cold EtOH and dried in vacuum or at 100° in a CO_2 atmosphere. Under moist conditions it readily oxidises [$V(AcAc)_3$ to $V(AcAc)_2O$]. [Fernelius & Bryant *Inorg Synth* **V** 105 *1957*, McKaveney & Freiser *Anal Chem* **30** 526 *1958*, UV: *J Am Chem Soc* **80** 5686 *1958*, *Beilstein* **1** IV 3672.]

Vanadyl (IV) acetylacetonate (vanadyloxa bis[2,4-pentadienato-O,O′], $VO[AcAc]_2$) *[3153-26-2]* **M 265.2, m 256-259°.** It crystallises from acetone. [*cf* Fernelius & Bryant *Inorg Synth* **V** 105 *1957*, *Beilstein* **1** IV 3672.]

Vinylferrocene (ferrocenylethene) *[1271-51-8]* **M 212.1, m 51-52.5°, b 80-85°/0.2mm.** Dissolve vinylferrocene in Et_2O, wash it with H_2O and brine, dry (Na_2SO_4), and evaporate to a small volume. Purify it through an Al_2O_3 (Spence grade H) column by eluting the yellow band with petroleum ether (b 40-60°). The low melting orange crystals can be sublimed. The *tetracyanoethylene adduct [49716-63-4]* crystallises from *C_6H_6/pentane and has **m** 137-139°(dec). [Horspool & Sutherland *Can J Chem* **46** 3453 *1968*, Berger et al. *J Org Chem* **39** 377 *1974*, Rauch & Siegel *J Organomet Chem* **11** 317 *1968*, *Beilstein* **16** III 1787.]

Vinyltributylstannane (vinyltributyltin) *[7486-35-3]* **M 317.1, b 104-106°/3.5mm, d_4^{20} 1.081, n_D^{20} 1.4751.** Fractionate the stannane under reduced pressure and taking the middle fraction to remove impurities such as $(n\text{-Bu})_3SnCl$. [Seyferth & Stone *J Am Chem Soc* **79** 515 *1957*, *Beilstein* **16** III 1279.]

Xylenol Orange (sodium salt) See entry [1611-35-4] in "Heterocyclic Compounds", Chapter 4.

Zinc acetate dihydrate *[5970-45-6]* **M 219.5, m 100° (loses $2H_2O$), 237°, d_4^{20} 1.74, pK^{25} 8.96 (for hydrolysis of Zn^{2+} to $ZnOH^+$).** It crystallises (in poor yield) from hot water or, better, from EtOH. [*Beilstein* **2** III 193, **2** IV 114.]

Zinc acetonylacetate *[14024-63-6, 108503-47-5 (x H_2O)]* **M 263.6, m 138°.** The zinc complex crystallises from hot 95% EtOH. [Fernelius & Bryant *Inorg Synth* **V** 105 *1957*, Wakita et al. *J Organometal Chem* **301** C17 *1986*, *Beilstein* **2** IV 144.]

Zinc caprylate (zinc n-hexanoate) *[557-09-5]* **M 351.8, m 142°.** It crystallises from EtOH in plates. [Howarth *J Chem Soc* 1406 *1929, Beilstein* **2** H 284.]

Zinc formate dihydrate *[557-41-5]* **M 191.4, m 140°(loses H_2O), d_4^{20} 2.21.** It crystallises from water (3ml/g). [*Beilstein* **2** H 16, **2** I 14, **2** II 21, **2** III 25, **2** IV 17.]

Zinc *RS*-lactate trihydrate *[554-05-2, 16039-53-5 (L)]* **M 297.5.** It crystallises from water (6ml/g). [*Beilstein* **3** I 107, **3** II 204, **3** III 464, **3** IV 637.]

Zincon (*o*-[1-(2-hydroxy-5-sulfo)-3-phenyl-5-formazono]-benzoic acid) *[135-52-4]* **M 459.4.** Main impurities are inorganic salts which can be removed by treatment with dilute acetic acid. Organic contaminants are removed by refluxing with ether. It can be recrystallised from dilute H_2SO_4 and complexes with Zn ions (see below). [Fichter & Schiess *Chem Ber* **33** 751 *1900*, *Beilstein* **16** IV 421.]

Zincon disodium salt (*o*-[1-(2-hydroxy-5-sulfo)-3-phenyl-5-formazono]-benzoic acid di-Na salt) *[135-52-4, 56484-13-0]* **M 484.4, m ~250-260° (dec).** Zincon solution is prepared by dissolving 0.13g of the powder in aqueous N NaOH (2ml diluted to 100ml with H_2O). This gives a deep red colour which is stable for one week. It is a good reagent for zinc ions but also forms stable complexes with transition metal ions. [UV-VIS: Bush & Yoe *Anal Chem* **26** 1345 *1954*, Hunter & Roberts *J Chem Soc* 820 *1941*, Platte & Marcy *Anal Chem* **31** 1226 *1959*] The *free acid* (see above) has been recrystallised from dilute H_2SO_4. [Fichter & Scheiss *Chem Ber* **33** 751 *1900*, *Beilstein* **16** IV 421.]

Zinc phthalocyanine *[14320-04-8]* **M 580.9.** Sublime it in oxygen-free N_2. [*Beilstein* **26** III/IV 4257.]

Zinc 5,10,15,20-tetraphenylporphyrin *[14074-80-7]* **M 678.1, λ_{max} 418(556)nm.** Purify the porphyrin by chromatography on neutral (Grade I) alumina, followed by recrystallisation from CH_2Cl_2/MeOH [Yamashita et al. *J Phys Chem* **91** 3055 *1987*].

Zirconium (IV) acetonylacetonate *[17501-44-9]* **M 487.7, m 190-193° (sealed capillary) 194.5-195°. 192-195°.** The zirconium complex crystallises from hot 95% EtOH (**m** 190-191°) or petroleum ether and sublimes *in vacuo* at 140° with slight decomposition. The *decahydrate* effloresces in air and dehydrates in a 0.1mm vacuum. Its solubility in 1L at 20° is 30g in CS_2, 47g in CCl_4, 44g in ethylene dibromide, 56g in acetonylacetone and 200g in $*C_6H_6$. [Young & Arch *Inorg Synth* **II** 122 *1964*, *Beilstein* **1** H 782, **1** II 835, **1** III 3121, **1** IV 3672.]

Zirconium (IV) propoxide *[23519-77-9]* **M 327.6, b 198°/0.03mm, 208°/0.1mm, d_4^{20} 1.06, n_D^{20} 1.454.** Although it was reported that it could not be crystallised or sublimed even at $150°/10^{-4}$mm [Bradley & Wardlaw *J Chem Soc* 280 *1951*], the propoxide, when properly prepared, has been purifed by distillation in a high vacuum [Bradley et al. *J Chem Soc* 2025 *1953*]. [*Beilstein* **1** IV 1420.]

CHAPTER 6

CATALYSTS

INTRODUCTION

Catalysts, and the process of catalysis, are almost as old as the chemical and physical sciences. Over the centuries a large number of metals and their derivatives, and a large variety of organic compounds, have been found to catalyse reactions successfully. The importance of catalysis in the sciences can be judged by the number of Nobel Prizes that have been awarded over the years for discoveries in this field of research. During the past decade much research emphasis has concentrated on combining metals with organic ligands, by complexation, in order to achieve greater metal solubility in a variety of solvents, not only for more efficient catalysis but also, by using chiral ligands, to achieve high, if not almost complete, regioselectivity and/or stereoselectivity. This is evidenced by the award of the 2001, 2005 and 2010 Nobel Prizes for Chemistry respectively for *Catalytic Asymmetric Synthesis* (to W. S. Knowles, R. Nyori and K. B. Sharpless), for *Catalytic Olefin Metathesis* (to Y. Chauvin, R. H. Grubbs and R. R. Schrock) and for *Catalytic Cross-Coupling Reactions* (to R. Heck, E-I Negishi and A. Suzuki). In addition to the many recently published reviews and monographs on various aspects of catalysis, a journal entitled *ChemCatChem* began in 2009, and is published by Wiley-VCH on behalf of ChemPubSoc Europe [www.chempubsoc.eu]. Original research papers, and reviews, on "cutting edge" discoveries in homogeneous, heterogeneous and enzymes catalysis are published particularly in this periodical, allowing proximity and cross communication in these fields of work.

Commercial suppliers of chemicals have availed themselves of this surge in new catalysts, and are now providing a large variety of recently discovered catalysts to the scientific community. The present chapter addresses a selection of these commercially available catalysts. Generally they can be used as supplied. However, some samples may have been kept for too long, or their shelf life may not be long, or they may have partially deteriorated; so knowledge about their purification, or assessment of purity is essential. Purification details have been provided for these, and in many cases published details of their preparations have also been included. Knowledge of the methods of preparation can provide information about probable impurities, and dictate the best purification procedures. Since several catalysts (and some ligands) have high and/or not well defined melting points, spectroscopic details have been included; such as IR, ^{1}H NMR, ^{13}C NMR and ^{11}B NMR, ^{31}P NMR (when these elements are present), optical properties if they are chiral, and occasionally MS.

This chapter is divided into two sections. The first section is devoted to heterogeneous and homogeneous catalysts. The second section contains ligands and reagents used for the preparation of these catalysts and of these ligands, as well as sections on phase transfer catalysts, and a section containing a small number of chiral auxiliaries. There are a number of substances mentioned in this chapter, or could possibly have been included here, but whose purifications are described in chapters 4, 5 and 7, that are not repeated here. However, they are referred to *via* their Chemical Abstracts Registry Numbers (CASRN), and their place in the book can be located from the CASRN index which gives their respective page entry.

It should be pointed out that great care should be taken to ascertain that the catalyst is indeed the metal or reagent used, and not some trace of unsuspected contaminating metal. This point has been clearly made in the article by J.M. Crow *entitled "When is a catalyst not a catalyst" (Chemistry World* ***8*** 46 *2011). He draws attention to the papers of* Buchwald & Bolm *Angew Chem, Int Ed* **48** 5586 *2009*, Larsson et al. *Angew Chem, Int Ed* **48** 5691 *2009*, Leadbeater & Marco *Angew Chem, Int Ed* **42** 1407 *2003*, Arvela et al. *J Org Chem* **70** 161 *2005*, *and the measurement of trace impurities at the ppb (parts per billion) and/or ppt (parts per trillion) levels in* Gonda, Tolnai and Novák *Chem Eur J* **16** 11822 *2010, and the possibility of co-catalysis.*

Purification of Laboratory Chemicals. http://dx.doi.org/10.1016/B978-0-12-382161-4.00006-6

CATALYSTS—PART 1

HETEROGENEOUS METAL CATALYSTS

Copper Chromite (Lazier catalyst, copper chromium oxide, $2CuO.Cr_2O_3$) *[12053-18-8]* **M 311.1.** It is also known as **Adkins catalyst** (with very slight difference in preparation). The catalyst is prepared by adding $Cu(NO_3)_2.3\ H_2O$ (109g) to a warm solution of $Ba(NO_3)_2$ (13g) in H_2O (140ml) at 70° and stirring until clear. Ammonium chromate solution, made by dissolving ammonium dichromate (63g) in H_2O (300ml) and adding concentrated aqueous ammonia (75ml, sp.gr. 0.90), is stirred in a thin stream into the solution of the above nitrates, stirred for 5 minutes further and the red-brown precipitate of copper barium ammonium chromate is filtered off, washed with H_2O, drained well and dried at 110°. The salt is placed in a suitable container and heated in a muffle furnace at 350-450° for 1 hour. Note that a spontaneous exothermic reaction occurs on heating with evolution of gas. The ignited blue-black residue (~80g), composed of copper and barium chromates and CuO, is pulverised thoroughly, suspended in aqueous 10% AcOH (600ml), stirred for 10 minutes, allowed to settle during 15 minutes, the supernatant is decanted, and the process is repeated. Filter off the solid, dry it at 110° and grind it in a mortar to give the catalyst (~70g) as a fine black powder. It is not affected by air or moisture and no special storing precautions are necessary. Other than the use of $Na_2Cr_2O_7$ (Adkin) instead of $(NH_4)_2Cr_2O_7$ (Lazier), there seems to be very little difference in the preparation procedure or the actvity of the catalyst [see Fieser & Fieser's *Reagents for Organic Synthesis* **2** 82 *1969*]. Note that the inclusion of barium is for protection against sulfate which is a catalyst poison, and stabilises it against reduction. If a barium free catalyst is required, then it is omitted in the preparation and the amount of $Cu(NO_3)_2.3\ H_2O$ should be increased to 121g without altering the preparation procedure. [Lazier & Arnold *Org Synth* Coll Vol **II** 142 *1943*, Adkins et al. *J Am Chem Soc* **72** 2626 *1950*]. It is an effective catalyst for the reduction of aldehydes, ketones and esters to the corresponding alcohols, aliphatic but not aromatic double bonds, the reduction of amides to amines, and for the decarboxylation of carboxylic acids [see Fieser & Fieser *Reagents for Organic Synthesis* **1** 186 *1967*]. These reactions however may have to be carried out in stainless steel bombs or autoclaves as several reactions require high temperatures (100-260°) and pressures (up to 5000psi).

Nickel *[7440-02-0]* **M 58.7, m 1455°, b 2730°, d^{25} 8.90.** The catalytic use of the metal can be divided into (a) the Raney nickel type and (b) the non-Raney nickel type.

***Raney Nickel type*:** This catalyst was introduced by the Raney Catalyst Division of Grace & Co and is made from a Ni-Al alloy (~1:1, e.g. by fusion at 1200-1500°). The catalyst is prepared by treating the alloy with alkali, which dissolves the Al, and the alkali is washed off as thoroughly as possible. The method was developed by Adkins and coworkers at the University of **W**isconsin (USA) and the catalyst was designated as **W**-1 to **W**-6 (chronological, not activity, order) [Billica & Atkins *Org Synth* Coll Vol **III** 176 *1955*, and for comparison of Ws see Adkins & Krsek *J Am Chem Soc* **70** 412 *1948*]. The catalyst has been used very extensively for reduction reactions, as well as for replacing sulfur by hydrogen in compounds; and there is a large volume of literature on this subject [see Fieser & Fieser's *Reagents for Organic Synthesis* **1** 440, 723, **2** 289, 293, **4** 267, **5** 263, 381, 570, 736, **6** 502, **7** 321, **8** 433, **9** 405, **10** 339, **11** 457, **12** 175, 218, 338, 422, **13** 265, **14** 270, **16** 278, **17** 296]. The reactions normally require stirring or shaking at ambient temperatures, and pressures of H_2 not greater than 100psi. A variety of equipment for this purpose is available commercially. The catalyst is essentially prepared by adding the Ni-Al alloy (150g) in small portions to aqueous sodium hydroxide (190g in 750ml of H_2O) with stirring in an ice bath at 10° at such a rate that the temperature is kept below 25°, *ca* 2 hours. *n*-Octanol may be added to prevent excessive foaming. This reaction should be carried out in an efficient fume cupboard as H_2 is liberated during the reaction (with the possibility of igniting), and it is preferable to use magnetic stirring to avoid sparking from an electric motor. When addition of the alloy is complete, allow the temperature of the mixture to rise to ~25°, and then heat it gradually (avoiding frothing over) on a boiling water bath until evolution of H_2 is complete (8-12 hours). Add distilled H_2O to restore the original volume, stir, allow the Ni to settle down, then decant the supernatant liquid. Transfer the Ni to a graduated cylinder with H_2O, allow it to settle, decant the supernatant liquid, add aqueous NaOH (25g, in 250ml H_2O), shake the mixture thoroughly, allow the Ni to settle again and decant off the supernatant alkaline liquid. Wash the Ni with H_2O (~750ml each time) by shaking, allow it to settle and decant the supernatant H_2O. Repeat the process until the washings are neutral to litmus and then a further 10 times. This may require 30 to 40 washings. Repeat the washing process three times with 95%

EtOH, then again three times with absolute EtOH. Store the Ni catalyst in bottles which are filled with absolute EtOH to the brim and stopper them. Keep them in a cold store room. Yield of Raney Ni is usually ~75g. The metal should be kept moist, or under liquid, at all times because the dry solid is highly **pyrophoric**. The more active the catalyst, the more readily it ignites. For this reason it is best to spoon the catalyst out from the settled material. When prepared as above it contains ~0.6g of Ni per ml of settled solid, and a level tablespoonful contains ~3g of Ni. [Mozingo *Org Synth* Coll Vol **III** 181 *1955*]. The activity of Raney Ni deteriorates slowly with time, but if prepared properly and stored as above it should be quite active for about 6 months. Its activity can be enhanced immensely by addition of a very small amount of triethylamine and chloroplatinic [Levering & Lieber *J Am Chem Soc* **71** 1515 *1949*]. It has been used both as a catalytic oxidation catalyst (with an appropriate donor), as well as a reduction catalyst [Kleiderer & Kornfeld *J Org Chem* **13** 455 *1948*].

***Non-Raney Nickel type*:** This includes a catalyst of the composition Ni/Al_2O_3 formed by treating Ni-Al alloy with H_2O at 70° [Tyman *Chem & Ind* 404 *1964*], and the commercially available Ni on silica (with 60 wt% loading on Kieselguhr) and Ni on silica/alumina (with~65 wt% loading). All Ni coordination compounds which have catalytic activity can come under this heading.

Palladium *[7440-05-3]* **M 106.4, m 1555°, b 3167°/atm, d_4^{20} 0.951, electrical resistivity at 0° is μΩ-cm.** Pd is a silver-white metal which also occurs as a black powder or in a compressible spongy form. It is reactive towards HNO_3, H_2SO_4, HCl and $HClO_3$, particularly in the presence of air or oxygen; and forms dihalides with halogen at high temperatures. It has the capacity of adsorbing and absorbing large volumes of H_2. It is extremely useful in chemical reactions as displayed in a limited way in this chapter. Apart from its extensive value in metal coordination chemistry it has out-classed many related metals in the field of catalysis. As well as its use in catalysis as the free metal in precipitated form, pellet or granular form, it has found extensive use in catalysis when diluted with C [7440-44-0], $BaSO_4$, $CaSO_4$, $SrSO_4$, Kieselguhr, and Al_2O_3 (see below). The following catalyst preparations have been used for many decades:

***Palladium on charcoal (5% Pd)*—** A clear solution of $PdCl_2$ (8.2g, 46mmol) in concentrated HCl (20ml, 240mmol) and H_2O (50ml), obtained by heating on a steam bath for 2 hours or until complete dissolution, is added with stirring to a suspension of charcoal (93g, HNO_3—washed)† in H_2O (1.2L) at 80° followed by 37% formaldehyde solution (80ml, 100mmol). The solution is made slightly alkaline to litmus (pH ~8.0) by careful addition of aqueous 30% sodium hydroxide with stirring which is continued further for 5 minutes longer. The catalyst is filtered off and washed with H_2O (10 x 250ml), drained well then dried at 25°, first in air then over KOH or $CaCl_2$ in a desiccator. The dry catalyst (93-98g), which is in a reduced state is stored in a tightly closed vessel. [*Do not dry at high temperatures as ignition may occur*.]

† *Darco G-60, Norit or other carbons can be used and should be heated on a steam bath with 10% aqueous HNO_3 for 2-3 hours, washed free from acid (check pH of washings), and dried at 100-110° before use* (see chapter on Aliphatic Compounds).

A comparison of the rates of hydrogenation with 5% Pd/C, 5% Pt/C, 5% Rh/C and 5% Ru/C catalysts towards reduction of C=C, C=O, C-OH and benzene rings in various solvents at 25° and initial H_2 pressure of 1 atmosphere were made by Breitner, Roginski & Rylander [*J Org Chem* **24** 1855 *1959*.]

Note that palladised charcoal has also been used for ***dehydrogenation***, e.g. tetralin is converted to naphthalene by boiling for 4 hours in the presence of Pd/C in a slow stream of CO_2, and α-tetralone is dehydrogenated to naphthalene by boiling (1 hour, with internal temperature of 235°) in the presence of Pd/C and a slow stream of CO_2 in 75% yield.

***Palladium on charcoal (10% Pd)*—** A clear solution of $PdCl_2$ (8.3g) in concentrated HCl (5.5ml) and H_2O (40ml), prepared as above, is poured into a solution of $NaOAc.3H_2O$ (135g) in H_2O (500ml) in a hydrogenation bottle, and charcoal (45g, HNO_3—washed, see above†) is added and the mixture is hydrogenated until absorption ceases (1-2 hours). The catalyst is collected on a filter funnel, washed with H_2O (5 x 400ml), drained well, dried in air and then in a desiccator over KOH or $CaCl_2$; and the reduced catalyst (48-50g) is stored as above.

***Palladium chloride on charcoal (5% Pd)*—** A clear solution of $PdCl_2$ (8.2g, 46mmol) in concentrated HCl (20ml, 240mmol) and H_2O (50ml), obtained by heating on a steam bath for 2 hours or until complete dissolution, is diluted with H_2O (140ml) and poured over charcoal (92g, HNO_3—washed, see above†) in a 20cm evaporating dish, thoroughly mixed and dried, firstly on a steam bath and then in an oven at 100° with occasional stirring until the catalyst (98-100g) is completely dry and is then stored in a stoppered bottle until required.

When required, the desired aliquot of catalyst is transferred to a hydrogenation bottle (or flask) and reduced in the solvent used for hydrogenation by shaking with H_2 in the hydrogenation apparatus. When absorption of H_2 is complete, the catalyst is filtered off, washed with fresh solvent to remove HCl, returned to the hydrogenation bottle (which should have been rinsed with the same fresh solvent), the material for reduction is added and hydrogenation is carried out in the usual way.

Palladium on barium sulfate (5% Pd)— To a rapidly stirred hot (80°) solution of reagent grade $Ba(OH)_2$ $8H_2O$ (126.2g, 400mmol) in H_2O (1.2L), 6N H_2SO_4 (120ml, 360mol) is added all at once then more 6N H_2SO_4 is added to the $BaSO_4$ suspension that is formed in order to be just acidic to litmus (pH ~5). A clear solution of $PdCl_2$ (8.2g, 46mmol) in concentrated HCl (20ml, 240mmol) and H_2O (50ml), obtained by heating on a steam bath for 2 hours or until complete dissolution, is subsequently added to the hot (80°) stirred $BaSO_4$ suspension# followed by 37% formaldehyde solution (8ml, 100mmol). The suspension is made alkaline to litmus (pH ~8.0) by careful addition of aqueous 30% sodium hydroxide with stirring, which is continued further for 5 minutes longer, and allowed to settle. The clear colourless supernatant liquid is decanted off, replaced by H_2O, resuspended, and washed ten times by decantation. The catalyst is collected on a 90mm medium porosity sintered glass funnel, drained until the filter cake begins to crack, washed again with H_2O (95 x 250ml), drained as completely as possible and placed in an oven at 80° until a dry catalyst (93-98g) is obtained. Store it as above. [This catalyst is particularly useful for Rosenmund catalytic reductions of acid chlorides (RCOCl) to aldehydes (RCHO), cf Hersberg & Cason *Org Synth* Coll Vol **III** 627 *1955*.]

#An equivalent weight of precipitated $BaCO_3$ (93g) may be used instead for $BaSO_4$; but the volume of concentrated HCl in preparing the $PdCl_2$ solution should be reduced to 8.2ml (to avoid decomposition of the carbonate) to give ***5% Pd on calcium carbonate*** catalyst. [Mozingo *Org Synth* Coll Vol **III** 685 *1955*.]

Note that at the completion of hydrogenations with these catalysts, the used catalysts that are filtered off should be kept moist with solvent or H_2O as they may be **pyrophoric** when dry. Also, with the catalysts that have been prepared using the formaldehyde (HCHO) procedure, the spent catalysts from reduction reactions in which MeOH is used as solvent are particularly flammable, possible because MeOH/HCHO form an oxidation-reduction couple since there is no guarantee that the catalyst is completely free from HCHO.

Other commonly used supports for Pd include **$CaCO_3$** [Busch & Stöve *Chem Ber* **49** 1063 *1916*], **$SrCO_3$** [Martin & Robinson *J Chem Soc* 491*1943*], **Al_2O_3** [Alan C. Johnson US pat 2,366,409, *Chem Abstr* **39** 2001 *1945*], **Kieselguhr** [Rosenmud & Langer *Chem Ber* **56** 2262 *1923*, Sabalitschka & Moses *Chem Ber* **60** 786 *1927*], **silica-gel** [Fester & Brude *Chem Ber* **56** 2247 *1923*], **asbestos** [Zelinsky & Borisoff *Chem Ber* **57** 150 *1924*, Zelinsky & Turowa-Pollak *Chem Ber* **58** 1295 *1925*] and **polyvinyl alcohol** [Kavanagh & Nord *J Am Chem Soc* **66** 2126 *1944*].

Platinum *[7440-06-4]* **M 195.1, m 1772°, b 3827°, d^{20} 21.45.** Platinum, when used directly or on a carbon, alumina or silica support, or *via* its oxide, is generally an excellent catalyst for the reduction of compounds. Hydrogenations using Pt catalysts are usually carried out at ambient temperatures, and atmospheric pressure of H_2, and the reaction can be followed by using a manometer and noting the absorption of gas. They may require, as in the reduction of aromatic rings to alicyclic rings, somewhat elevated pressures (a few to several atmospheres) and temperatures. Specialised equipment is used in such cases (see Ni catalysts above).

***Platinum Black*:** It is obtained by reducing a solution of chloroplatinic acid *[16941-12-1]* with alkaline formaldehyde and shaking vigorously to coagulate the colloidal metal formed [Feulgen *Chem Ber* **54** 360 *1921*]. In addition to its use as a catalyst, it destroys H_2O_2 in liquids or solvents by shaking them with the metal until liberation of O_2 ceases [Cope & Cignek *Org Syn* Coll Vol **IV** 612 *1963*].

***Platinum Sponge*:** Ammonium hexachloroplatinate is precipitated when recovered Pt residues are dissolved in *aqua regia* (see below), evaporated to dryness then dissolved in the minimum volume of H_2O and treated with saturated ammonium chloride. The $(NH_4)_2PtCl_6$ is filtered off and dried at 100°. Ignition of this salt gives Pt *sponge*. [Wickers *J Am Chem Soc* **43** 1268 *1921*.]

Brown & Brown Catalyst: This is usually prepared *in situ* by adding a solution of $NaBH_4$ in EtOH stabilised with NaOH to a suspension of charcoal (see palladium catalysts above) in a solution of chloroplatinic acid in EtOH (or aqueous EtOH) to form the supported catalyst. Excess HCl is added, followed by the substrate for reduction, then $NaBH_4$ in EtOH stabilised with NaOH is added dropwise at such a rate as to maintain atmospheric pressure of H_2.Here the supported catalyst and H_2 are generated *in situ* resulting in more effective reductions. [Brown et al. *J Org Chem* **28** 214 *1963*.]

Platinum on support: The catalyst is prepared from a cooled solution of the metal (5.0g, or $PtCl_4$ or H_2PtCl_6) in H_2O (50ml) and concentrated HCl (5ml) and support [11g, acid washed charcoal (see Pd above), neutral alumina, silica or asbestos (Gooch asbestos, termolyte not chrysolite, boil with concentrated HNO_3, filter, wash free from acid with H_2O and dry at 100º)] in a freezing mixture and treat with formalin (50ml, 40% formaldehyde). The mixture is then stirred while aqueous KOH (50g in 50ml of H_2O) solution is added slowly and keeping the temperature below 5º. The temperature is then allowed to rise to 60º in 15 minutes. The catalyst is washed thoroughly with H_2O by decantation, finally with dilute AcOH, collected onto a suction filter and washed with H_2O until free from chloride ions and alkali, and drained well. Dry the solid at 100º and store it in a desiccator. This method gives a catalyst containing *ca* 30-40% of metal, but the amount can be adjusted by varying the ratio of metal to support. [Brown & Brown *J Am Chem Soc* **28** 2827, 2829 *1962*.]
A comparison of the rates of hydrogenation with 5% Pd/C, 5% Pt/C, 5% Rh/C and 5% Ru/C catalysts towards reduction of C=C, C=O, C-OH and benzene rings in various solvents at 25º and initial H_2 pressure of 1 atmosphere were made by Breitner, Roginski & Rylander [*J Org Chem* **24** 1855 *1959*.]
Platinum (IV) oxide (Adams catalyst, PtO_2) *[1H_2O 12137-21-2; xH_2O 52785-06-5]* **M 227.1, M 245.1 (1 H_2O), m >450º.** Adams catalyst can be prepared in three ways.
Firstly*,** from ammonium hexachloroplatinate (IV) [16919-58-7] [3.0g, $(NH_4)_2PtCl_6$] and KNO_3 (30g, Analytical Grade; $NaNO_3$ yields slightly less active catalyst) which are thoroughly mixed in a porcelain dish (fume cupboard, use a head shield for protection***) and heated gently at first until the rapid evolution of gas subsides, then strongly until the temperature reaches 300º (15 minutes, no splattering). The liquid mass is heated further at 500-530º for 30 minutes and allowed to cool. Add H_2O (50ml) to the residue, stir and allow the brown platinum oxide (PtO_2. H_2O) to settle. Wash it once or twice with H_2O by decantation, collect it on a filter, wash it free from nitrates (stop washing if the solid starts to become colloidal#; traces of $NaNO_3$ do not affect catalytic activity) and dry the oxide in a desiccator. Store it in small aliquots.
If colloidal Pt filters through, it can be checked by testing a small volume of the filtrate for Pt by acidifying it with HCl, adding a few drops of stannous chloride when a yellow or brown colour results depending on the amount of Pt present. The yellow colour is soluble in Et_2O rendering the test more sensitive. If Pt is present in the filtrate then heat the filtrate with excess formalin and aqueous NaOH, cool, and the platinum black which separates is filtered off and worked up with other Pt residues. The weight of PtO_2 obtained is about equal to half the weight of $(NH_4)_2PtCl_6$.
Secondly, purest possible chloroplatinic acid [3.5g, H_2PtCl_6] in H_2O (10ml) is mixed with KNO_3 (35g, Analytical Grade; $NaNO_3$ yields slightly less active catalyst) in a porcelain dish, evaporate gently to dryness and heat at 350-370º for 10 minutes (use a strong heat source, ***fume cupboard, use a head shield for protection***) when brown oxides of nitrogen evolve and brown PtO_2 separates. Stir more vigorously if frothing occurs and direct an additional burner at the top of the mixture. [Take care not to allow the top of the mixture to solidify, e.g. by removing the burner that is underneath, otherwise frothing over occurs]. The temperature is raised to 400º in the following 15 minutes, after which liberation of fumes decreases considerably, and the temperature is raised further to 500-550º (*ca* 2 minutes); at this stage evolution of brown gases practically ceases but there is still a gentle evolution of gas. Maintain at this temperture (with burner at full heat) for 30 minutes by which time fusion is complete. Allow the container to cool slowly to ~20-25º, add H_2O (50ml) and isolate the catalyst as above.
Thirdly*,** Pt metal and or Pt metal residues are dissolved in *aqua regia* [prepared by adding slowly concentrated HNO_3 (1 volume) to concentrated hydrochloric acid (3 volumes) in a glass container in an efficient fume cupboard and head protection***] using gentle heat if necessary, evaporate several times almost to dryness with concentrated HCl, dissolve the final residue in a small volume of H_2O and precipitate the metal as $(NH_4)_2PtCl_6$ with saturated aqueous NH_4Cl. Filter off the precipitate, dry it at 100º and continue as in the first procedure (see above). [Adams et al. *Org Synth* Coll Vol **I** 463, 466 *1941*, Bruce *J Am Chem Soc* **58** 687 *1936*.]
Reactions catalysed by Adams catalyst can be carried out in alcoholic solution which is sometimes enhanced by the presence of HCl; a variety of other organic solvents have been used which include EtOAc, EtOAc+15% AcOH, EtOAc+8%EtOH, and glacial AcOH; and neat CF_3CO_2H is a particularly good solvent for the reduction of C=N in heterocyclic compounds.
PtO_2 on silisic acid has been prepared in much the same way as above (***fume cupboard and head protection***)

from chloroplatinic acid (7g) in H_2O (25ml) and silicic acid (20g, 200 mesh) in a borosilicate beaker (100ml) which are stirred into a smooth paste and heated on a burner until desiccated. Heat to ~360° and add powdered $NaNO_3$ (70g) in portions while stirring and mixing vigorously with a glass rod (evolution of brown fumes occurs at each addition with frothing) and heat until gas evolution ceases. Add further molten $NaNO_3$ (20g) to the beaker with heating while scratching its sides. Cool, and transfer to a 2L beaker containing H_2O (1.5L), stir for 2 hours, allow to settle, decant the supernatant and collect on a medium porosity sintered glass funnel. Wash the solid well with H_2O, then with 95% EtOH (2 x) and Et_2O, dry it in air for 1 hour then in a vacuum desiccator (P_2O_5). The dry powder is then pulverised in a mortar and sieved (200 mesh) until all the solid has passed through (use a Camel's-hair brush to help the solid through) to give the catalyst as a light brown powder (21.0g) containing ~0.14g of Pt per gram of solid. Store it in screw caped vials. It can be exposed to light and air without loss of activity. It gives very reproducible hydrogenation results and has been used analytically for the estimation of reducible groups [Vandenheuvel *Anal Chem* **28** 362 *1956*.]; and for the hydrogenation of methyl esters in EtOH without causing trans-esterification [Ackman & Brugher *J Lipid Res* **5** 130 *1964*].

Other applications*:** Prior to the development of catalysts in which Pt is coordinated to a plethora of ligands in order to achieve particular specificities (e.g. Pt with phosphine ligands below), some specificites were obtained by manipulating the metal. Examples include a ***platinum-tin chloride catalyst made from ***H_2PtCl_6 and $SnCl_2$*** for specific reduction of olefins [Cramer et al. *J Am Chem Soc* **85** 1691 *1963*], ***PtO_2/Pt black+$FeCl_2$/Zn(OAc)$_2$*** for reduction of unsaturated aldehydes to unsaturated alcohols, e.g. cinnamaldehyde to cinnamyl alcohol [Tulley & Adams *J Am Chem Soc* **47** 3061 *1925*], and ***PtS_2/C*** which is less active than the oxide but is insensitive to poisons (e.g. sulfur compounds) and will reduce a nitro group without affecting halogen substituents, e.g. chloronitrobenzenes to chloroanilines [Dovell & Greenfield *J Am Chem Soc* **87** 2767 *1965*].

Rhenium metal (Re) used in preparing the following catalysts has *[7440-15-5]* **M 186.2, m 3180°, b 5596°, d^{20} 21.02.**

Rhenium(II) oxide ($ReO.2H_2O$) *[12143-03-2]* **M 238.2.** This catalyst is prepared in a fume cupboard by the reduction of ammonium perrhenate with either Na/liqNH_3, Li/liqNH_3, or Li/EtNH_2 which give consistently $ReO.2H_2O$. In dried apparatus used typically for Na/liqNH_3 reduction, liquid NH_3 or EtNH_2 (50-75ml) and NH_4ReO_4 (1-2g, weighed) are stirred in a dry atmosphere until the salt dissolves; then Na or Li (15-30g) are added in chunks as rapidly as possible. The colourless solution becomes typically blue-black and is stirred until the colour disappears (15 minutes to 2 hours). The NH_3 or EtNH_2 are allowed to evaporate while the total volume is kept constant by addition of EtOH. The residue is transferred to a fritted glass thimble in a Soxhlet apparatus and extracted with dilute HCl (~2N) for 24 hours (the pot acquiring a brown colour), then with EtOH for an equal time. When the brown acid extract, that decolorises aqueous $KMnO_4$, is basified with aqueous NH_4OH black $ReO.2H_2O$ precipitates, and the supernatant now does not decolorise aqueous $KMnO_4$. The solid is collected, washed with cold EtOH, and dried at 100° *in vacuo* over P_2O_5 (conditions under which it is stable and does not dehydrate) to provide the hydrated oxide (75-85%) as a very finely divided black powder. Note that any solid left in the thimble has the same composition as this oxide. It is stored as a suspension in EtOH which tends to settle rather readily, or as a suspension in distilled H_2O which requires more than 24 hours to settle out completely. Aliquots of suspensions (with or without evaporating to dryness) are used as the heterogeneous catalyst. The amount of rhenium can be determined as described by Broadbent and Selin [*J Org Chem* **28** 2343 *1963*].

$ReO.2H_2O$ catalyses the hydrogenation of a wide variety of organic substrates in high yields with unusual selectivity, being particularly efficient for carboxylic acids. Hydrogenations are carried out in a rocking Parr reactor under pressures of ~200 atmospheres and temperatures varying from ~20° to ~200°, and reduction times from 0.5 to ~10 hours. The catalyst prepared by the Li/liqNH_3 method is only marginally better than by the other methods. [Broadbent & Seegmiller *J Org Chem* **28** 2347 *1963*.]

Rhenium(III) oxide (Re_2O_3) *[12060-05-8]* **M 420.5.** Re_2O_3 is prepared from a mixture of ammonium perrhenate (2.04g, 160mmol, NH_4ReO_4), a solution of 8*N* NH_4Ac (20ml, 160mmol) and glacial AcOH (2ml, 35mmol) in H_2O (100ml) in an ice-water bath to which is added dropwise, with vigorous stirring, an ice-cold solution of $NaBH_4$ (3.4g, 90mmol) in H_2O (100ml) over a 1 hour period. After half of the $NaBH_4$ solution is added, a further amount of AcOH (2ml, 35mmol) is added in one lot. Stirring is continued for 15 minutes and the solution is centrifuged at full speed in an ultracentrifuge, the supernatant is decanted off, the oxide is washed

twice by suspension in H_2O and finally re-suspended in H_2O, and stored as such before use. The fine solid remains in suspension for 12-24 hours. Analysis indicated that reduction was ~85% complete giving a yield of 70-90% (~1.35g). The activity is checked by its ability to effect hydrogenation of styrene at room temperature in 6-10 hours. It catalyses a range of substrates including aliphatic olefins, maleic acid, benzene, nitrobenzene, bromonitrobenzene, naphthalene, pyridine, ketones and nitriles mostly in yields approaching 100% with (e.g. H_2O or EtOH), and without solvents. Typically the substrate (0.2mol, with or without solvent) and catalyst (0.2g of Re) in a 420ml rocking Parr bomb under hydrogen pressures up to 3000psi (204 atmospheres) are heated (40-50° increments) until the pressure starts to drop. Reductions occur in the temperature range of 25-250°. [Broadbent & Johnson *J Org Chem* **27** 4400 *1962*.]

Rhenium(IV) oxide (ReO_2. $2.5H_2O$) *[12036-09-8]* **M 218.2.** When a vigorously stirred mixture of a solution of ammonium perrhenate (1.2g) in H_2O (150ml) and an excess of granular zinc (5-10g, previously treated with a little dilute acid, to remove any surface oxide, and washed thoroughly to clean the surface) is treated dropwise over a period of several hours with 3N H_2SO_4 (64ml) at such a rate that black finely divided rhenium oxide is suspended into the solution which is periodically decanted from the zinc; the oxide is centrifuged off, the supernatant is returned to the reaction flask and addition of acid is resumed. The acid should not be added rapidly as the finely divided rhenium oxide coats the zinc and slows (or prevents) further reaction, and does not produce a Zn-free product. At the end of the reaction all the rhenium oxide residues from centrifugation are combined, washed with H_2O by decantation until the washings are free from sulfate. Conversion from perrhenate to rhenium (IV) oxide is >60%, and nearer 100% if an excess of Zn is maintained in the reaction by further addition of the metal. ReO_2. $2.5H_2O$ analyses as a hydrate, is very stable, resists dehydration at 95° *in vacuo* over P_2O_5, and loses H_2O only very slowly at 250°; however when the hydrated oxide is heated at 250° in $*C_6H_6$ under hydrogenation conditions anhydrous ReO_2 can be isolated from the experiment. It exists in two crystallographic forms: the α-form is obtained when synthesised below 300° ($Re + 2ReO_3 = 3ReO_2$), and is irreversibly transformed into the orthorhombic β-form which is obtained when synthesised above 300° [Rogers et al. *Inorg Synth* **XIII** 142-145 *1972*, Rogers et al. *Inorg Synth* **XXX** 102 *1995*].
ReO_2. $2.5H_2O$ has catalytic activity for the hydrogenation of a variety of organic substrates, and although generally less active than Nickel or palladium catalysts (i.e. requires higher temperatures and/or pressures), it is however much more effective than these for the reduction of the carboxylic acid function. It has a potentially valuable selectivity, and very few other elements exhibit this characteristic to such a degree. [Broadbent & Selin [*J Org Chem* **28** 2343 *1963*.]

Rhenium(VI) oxide (ReO_3) *[1314-28-9]* **M 234.2, b 750°, d^{20} 6.9-7.4.** ReO_3 is prepared from the heptoxide (1.0g, see below) by adding it directly to *p*-dioxane (10-25ml) or tetrahydrofuran and warming gently to produce a colourless to dark green solution, and the excess solvent is removed *in vacuo* to give a sticky, tarry, black complex. The complex decomposes when carefully heated to *ca* 145° to give gaseous products and a pure, red, crystalline residue of ReO_3 (84-95%yield). This is finely ground and stored dry in a screw-cap vial. It forms non-hygroscopic, red/maroon-coloured crystals (with a green luster) which are air stable below 100°, and disproportionates in a vacuum to rhenium(IV) and rhenium(VII) oxides at 400°. It is inert to H_2O, dilute alkali, and is thus more convenient to handle and store than the hygroscopic heptoxide which also has high catalytic activity. Analysis showed it to have the formula of the anhydrous oxide ReO_3. It is oxidised by HNO_3 to $HReO_4$. It has catalytic activity when used as such or when prepared *in situ* by using Re_2O_7 and allowing it to be reduced to ReO_3 during the hydrogenation process. This oxide, when used directly or prepared *in situ*, is the most effective hydrogenation catalyst of all the Re catalysts. It is very efficient in reducing carboxylic and carboxamide groups without reducing the aromatic ring, with the latter producing amines. Benzoic acid, ethyl benzoate, benzaldehyde, and *m*-nitrobenzaldehyde are reduced to the respective carbinols without hydrogenolysis to the toluenes as in most catalytic hydrogenations. Like the preceding rhenium oxide catalysts hydrogenations are carried out in shaking Parr-Bomb reactors under pressures of *ca* 200 atmospheres and temperatures ranging from ~100° to ~200° depending on when the substrates begin to absorb H_2 at a reasonable rate. [Broadbent & Bartley *J Org Chem* **28** 2345 *1963*, Nechamkin & Hiskey *Inorg Synth* **III** 186 *1950*.] It is also obtained in quant-

itative yield from Re_2O_7 (purified by sublimation) in a CO atmosphere by heating at 175° until the oxide is blue, the temperature is raised slowly to 225°, then increased to 280° after the colour of the oxide has turned to red [Melaven et al. *Inorg Synth* **III** 187 *1950*].

Rhenium(VII) oxide (rhenium heptoxide Re_2O_7) *[1314-68-7]* **M 484.4, m 300.3°, b 360.3°, d^{20} 6.103.** Dirhenium heptoxide is prepared by heating the metal or its lower oxides in a stream of oxygen or air at 400° to 425°. It forms canary-yellow crystals which are as deliquescent as P_2O_5, and sublimes at 250°/760mm and melts at 297° in a sealed tube [Ogawa *Bull Chem Soc Jpn* **7** 265 *1932*]. Great care should be taken to avoid moisture during handling and storage. It is very soluble in H_2O to form perrhenic acid $HReO_4$. It is also soluble in most organic solvents such as ethers, esters, alcohols, dioxane and pyridine. [Melaven et al. *Inorg Synth* **III** 188 *1950*.] Reduction of Re_2O_7 during hydrogenation reactions generates rhenium "blacks" which mainly consist of ReO_3 and is among the best catalyst for reducing a variety of carboxylic acids to alcohols (at ~160°/*ca* 200 atmospheres/few hours) in very good yields. The alcohols are occasionally accompanied with esters; unreduced acids rarely survive, amides are reduced to the respective amines and the usual functional groups that are reduced by Ni and Pt catalysts are also reduced with this rhenium catalyst. [Broadbent et al. *J Org Chem* **24** 1847 *1959*.] It is a precursor for organorhenium oxides which catalyse olefin oxidation, metathesis and other transformations. It is a *Lewis-acdic metal oxide* which forms adducts of the formula $Re_2O_7.n$L with a variety of O, N and S ligands such as 1,2-dimethoxyethane, 4,4′-di-*tert*-butyl-2,2′-bipyridine, and 1,4,7-trithiacyclononane respectively [Herrmann et al. *Inorg Chem* **34** 4701 *1995*].

Rhenium(VII) sulfide (rhenium heptasulfide, Re_2S_7) *[12038-67-4]* **M 596.9.** The heptasulfide is obtained by bubbling H_2S through a 3% solution of potassium perrhenate in 5-6 N HCl maintained at the boiling point until precipitation is complete. The suspension is allowed to stand overnight, then it is filtered through a sintered glass funnel, the solid is washed with 1:4 aqueous HCl, H_2O, dried for several days in a desiccator over $CaCl_2$, powdered in a mortar and stored in a common screw capped vial. The catalyst is not adversely affected by occasional exposure to air, is prepared with high catalytic reproducibility, is insoluble in concentrated non-oxidising acids, is stable under all the conditions of hydrogenation used (1000-3600psi/25° to 335°/0.5 to 3 hours), and is not reduced to form H_2S. It is remarkably resistant to "poisoning". It catalyses the reduction of a variety of organic substrates in high yields including sulfides, with desulfurisation [e.g. diphenylsulfide to benzene (94%), and thiophenol to a mixture of benzene (60%) and cyclohexane (40%)]; and without desulfurisation [e.g. allyl phenyl sulfide to propyl phenyl sulfide (100%), and of thiophene to thiophane (70%)]. [Broadbent et al. *J Am Chem Soc* **76** 1519 *1954*.] When the heptasulfide is heated for 16 hours at 350-400° in a tube furnace under a stream of CO_2 to blow out sulfur vapours, and cooled in a desiccator, it gives ***rhenium disulfide*** *[12038-63-0]*. The catalytic activity of ReS_2 parallels that of Re_2S_7 but to a lesser extent, and is more active than related molybdenum or cobalt catalysts. [Broadbent et al. *J Am Chem Soc* **76** 1519 *1954*.]

Rhodium metal (Rh) used in preparing the following catalysts has [*[7440-16-6]* **M 102.9, m 1966°, b 3727°, d^{20} 12.41].**

Rhodium on alumina (5% Rh loading). Rh-Al_2O_3 has been used as a general catalyst for the complete reduction of the aromatic ring in phenols, e.g. gallic acid to *cis*-3,4,5-trihydroxycyclohexane carboxylic acid [Burgstahler & Bithos *Org Synth* **42** 62 *1962*] requiring high pressures (2200psi) and temperatures (~100°) for 8-12 hours [see also Smith & Stump *J Am Chem Soc* **83** 2739 *1961*, Kaye & Matthews *J Org Chem* **28** 324 *1963*], the hydrogenation of 1-naphthol to *cis*-1-hydroxydecalin [6psi, 25°, 12 hours; Meyers et al. *J Org Chem* **29** 3427 *1964*], resorcinol gives cyclohexane-1,3-dione [50psi, 25°, 16-18 hours; Sircar & Meyers *J Org Chem* **30** 3206 *1965*], D-mandelic acid gives pure D-hexahydromandelic acid but L-mandelic acid gives (±)-hexahydromandelic acid [3-4 atmospheres, 25°, 1.5 hours, AcOH is mandatory; Stocker *J Org Chem* **27** 2288 *1962*], reduction of vinylic and allylic double bonds [500psi, 100°, 15 minutes; Ham & Coker *J Org Chem* **29** 194 *1964*], reduction of oximes or aliphatic nitriles to primary amines [1-2 atmospheres, ~25°, 1-2 hours; Freifelder et al. *J Org Chem* **27** 2209 *1962*, Freifelder *J Am Chem Soc* **82** 2386 *1960*], hydrogenolysis of ketals to the corresponding dialkyl ethers [Howard & Brown *J Org Chem* **26** 1026 *1961*], hydrogenation of heterocyclic compounds e.g. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid to *cis*-decahydroisoquinoline-3-carboxylic acid [40psi, ~25°, 3 hours;

Rapala et al. *J Am Chem Soc* **79** 3770 *1957*], nicotinic acid to hexahydronicotinic (nipecotinic) acid without decarboxylation [2 atmospheres, ~25°, 4 hours; Freifelder *J Org Chem* **27** 4046 *1962*, Freifelder *J Org Chem* **28** 602, 1135 *1963*], complete hydrogenation of quinoxaline [Broadbent at al. *J Am Chem Soc* **82** 189 *1960*], reduction of the 4,5-double bond of pyrimidine nucleosides and nucleotides [Cohn & Doherty *J Am Chem Soc* **78** 2863 *1956*], dehydrogenation e.g. hydrogen transfer from hexahydrohexahelicene to benzene in order to provide hexahelicene and cyclohexane in 73% yield [Newman & Lednicer *J Am Chem Soc* **78** 4765 *1956*, cf also Anderson & Anderson *J Org Chem* **22** 1197 *1957*], and hydrogenation of anilines to cyclohexylamine with little hydrogenolysis [Freifelder et al. *J Org Chem* **30** 2485 *1965*].

Rhodium on carbon (5% and 10% Rh loading). A 10%-Rh, 0.1%Pd on carbon catalyst has been prepared from a mixture of $RhCl_3.3H_2O$ (5.26g), $PdCl_2$ (0.34g) and carbon (18g, e.g. Darco G-60, or any acid washed charcoal can be used) in H_2O (200ml) is rapidly stirred and heated to 80°. Lithium hydroxide hydrate (2.7g) dissolved in H_2O (10ml) is added in one lot and heating is stopped but the mixture is stirred overnight, filtered, and washed with 0.5% v/v aqueous AcOH (100ml) then dried *in vacuo* at 65° to give 20.6-21g of catalyst. One gram of this catalyst will absorb 0.0022-0.0028 mole of H_2 in aqueous suspension. It has been used, for example, in the reduction of *p*-aminobenzoic acid to a mixture of *cis*- and *trans*- 4-aminocyclohexanecarboxylic acid [at 50psi/~25°/~24 hours] which was converted to 2-azabicyclo[2.2.2]octan-3-one (3-isoquinuclidone) in 81-84% yield. *The point was made that when fresh catalyst is added to the reaction vessel, it should be moistened with the solvent; and that hydrogen should be removed by evacuation at the end of the reduction in order to avoid having a hydrogen-air atmosphere which could be explosive*. [Pearlman *Org Synth* Coll Vol **V** 670 *1973*, Pearlman *Tetrahedron Lett* 1663 *1967*.] It is a useful catalyst (even without the trace of Pd) for the reduction of nitriles to primary amines, and the hydrogenation of aromatic and pyridine rings, aldehydes and sugars. It is superior to $Rh\text{-}Al_2O_3$ for reduction of the pyridine ring and larger amounts of catalyst have to be added to overcome the poisoning effect of the piperidine products [Freifelder et al. *J Org Chem* **27** 284 *1962*]. It is useful for the stepwise reduction of 3-*H*-pyrrolizine to 3,4-dihydropyrrolizine, and then to the fully reduced pyrrolizidine [Scweizer & Light *J Am Chem Soc* **86** 2963 *1964*]; and in boiling norbornadiene complete conversion to a mixture of dimers and trimers occurs [Mrowca % Katz *J Am Chem Soc* **88** 4012 *1966*]. A comparison of the rates of hydrogenation with 5% Pd/C, 5%Pt/C, 5% Rh/C and 5% Ru/C catalysts towards reduction of C=C, C=O, C-OH and benzene rings in various solvents at 25° and initial H_2 pressure of 1 atmosphere were made by Breitner, Roginski & Rylander [*J Org Chem* **24** 1855 *1959*.]

Ruthenium (1,5-Cyclooctadiene)(1,3,5-cyclooctatetraene) [Ru(cod)(cot)] *[127382-91-6]* **M 315.4, m 88-94°, 92-94°.** For preparation see Chapter 5, Metal-Organic Compounds. Purify the ruthenium complex (~ 0.3g) by dissolving it in *n*-pentane (~ 70ml) and filtering the solution through a column of alumina (Merck, Brockman activity II—III, 20cm). Collect the yellow band and reduce its volume to ~ 5ml then cool it at -70°, preferably under N_2 or Ar. After ~ 6 hours collect the yellow solid (~ 0.2g) and dry it *in vacuo*. Recrystallisation from *n*-pentane results in a 75-85% recovery. [Itoh et al. *J Organomet Chem* **272** 179 *1984*, Petrici et al. *J Chem Soc, Dalton Trans* 1961 *1980*]. It is a highly selective catalyst for amine alkylations in which, unlike other ruthenium catalysts, alkylates the amino group of e.g., 2-, 3-, or 4- aminopyridines as well as 2-aminopyrimidine to give the respective monoethylamino derivatives by using EtOH in high yields with very little, if any, of diethylamino derivatives. Thus it stops almost exclusively at monoalkylation. [Watanabe et al. *J Org Chem* **61** 4214 *1996*]. It also catalyses the dimerisation of 2,5-norbornadiene *via* [2+2] cycloaddition reactions and eyne generation in the presence of dimethylfumarate in THF at 40° for 1 hour to form the "cup-shaped" molecule pentacyclo[$6.6.0.0^{2,6}.0^{3,13}.0^{10,14}$]tetradeca-4,11-diene in 96% yield. An alicyclic compound which would otherwise require many steps to synthesis. [Mitsudo et al. *J Am Chem Soc* **121** 1839 *1999*.]

Ruthenium metal (Ru) used in preparing the following catalysts has *[7440-18-8]* **M 101.1, m 2310°, b 3900°, d^{20} 12.5].**

Ruthenium-aluminium oxide/hydroxide catalyst (~2.5wt% Ru loading). The preparation of this catalyst is described in Chapter 8 because it consists of Ru(0) nanoparticles encapsulated in an aluminium oxy-hydroxide

matrix and is superior as a catalyst to the commercially available material. It is a recyclable catalyst for the efficient oxidant-free alcohol dehydrogenation (compare with $RuCl_3.3H_2O$ or xH_2O above) of a wide range of alcohols including benzylic alcohols, secondary long chain fatty alcohols, secondary allylic alcohols, 3-pyridylmethanol, 2-thiophenylmethanol and 4-methylthiobenzyl alcohol in dry toluene to the respective carbonyl compounds under argon at dehydrogenation temperatures of 80° to 110°, using 3-6 mol% of Ru, in yields of >90%. It is 5 times superior to the commercial Ru/Al_2O_2 catalyst and is re-usable, after washing with Me_2CO and drying in air, at least 10 times without loss of activity. [Kim, Park and Park *Org Lett* **8** 2543 *2006*.]

Ruthenium on alumina (5% Ru reduced loading). Ru/Al_2O_3 can be freshly prepared by treating alumina powder with a ruthenium compound, e.g. $RuCl_3.xH_2O$ in H_2O, $Ru(acac)_3$ or $Ru_3(CO)_{12}$ in *benzene (to give a solid that is ~5wt% in Ru), followed by evaporating the solvent and reducing the solid in a stream of H_2 at 500°. This catalyst will oxidise dibenzothiophene or dibenzothiophene oxide (Ru molar ratio 11:1) in $*C_6H_6$ to dibenzothiophene sulfone at 100° in air (70 atmospheres) for 12 hours in 97% yield. Slow poisoning of Ru occurs during the oxidation. The activity of the catalyst depends on the preparation, but is much more active than the following catalysts in the sequence $Ru_3(CO)_{12}$ > $Ru(acac)_3$ > $RuCl_3.xH_2O$. Ru/C or Ru/SiO_2, and the commercially available Ru/Al_2O_3 are less active than the above preparation. Pt/Al_2O_3 or Ir/Al_2O_3 gives only a trace of the sulfone, and Pd/Al_2O_3, Rh/Al_2O_3, Os/Al_2O_3 or Cu/Al_2O_3 are totally inactive. It should be noted that with this catalyst oxidation of *n*-Bu_2S (0.2M in $*C_6H_6$; in the ratio of Ru/sulfide 21:1) provides 44 and 9% molar yields of *n*-Bu_2SO and *n*-Bu_2SO_2 respectively, with full recovery of unreacted *n*-Bu_2S. [Ledlie & Howell *Tetrahedron Lett* 785 *1976*.]

Ruthenium on carbon (5% Ru loading). A comparison of the rates of hydrogenation with 5% Pd/C, 5%Pt/C, 5% Rh/C and 5% Ru/C catalysts towards reduction of C=C, C=O, C-OH and benzene rings in various solvents at 25° and initial H_2 pressure of 1 atmosphere were made by Breitner, Roginski & Rylander [*J Org Chem* **24** 1855 *1959*.] Ru/C is a superior catalyst than Pd/C and Pd/C for the hydrogenation of ketones in basic and neutral media and in some cases (e.g. tetramethylcyclobutan-1,3-dione at 1000-1500psi of H_2/125°/1 hour) >90% yields of diols were obtained [Hseck et al. *J Org Chem* **27** 700 *1961*], C=C (with some selectivity), and acetylenes were reduced to alkanes [Berkowitz & Rylander *J Org Chem* **24** 708 *1959*], nitrobenzene was reduced to hydrazobenzene in alcoholic KOH in 80% yield without over-reduction to aniline [Peitra & Res *Ann Chim (Rome)* **48** 299 *1958*], and 10% Ru/C was better than other catalysts for reducing phenolic rings in polycyclic compounds [Walton et al. *J Am Chem Soc* **78** 4760 *1956*].

Ruthenium(IV) oxide (RuO_2) *[12036-10-1]* **M 133.1, d^{25} 6.97.** The dioxide is prepared by heating Ru metal in a silca boat in a silica combustion tube placed horizontally in a furnace, and a slow stream of dry oxygen is allowed to flow over it while it is being heated at 1000° for 24 hours. During heating a little of the oxide volatilises and small crystals may condense on the walls at the downstream end of the tube. A 90-95% yield of polycrystalline RuO_2 remains in the boat. It forms tetragonal dark blue crystals which are insoluble in organic solvents, H_2O and acids but soluble in fused alkali. [Schäfer & Heitland *Z Anorg Allgem Chem* **304** 249 *1960*, Schäfer et al. *Z Anorg Allgem Chem* **319** 327 *1963*, Rogers et al. *Inorg Synth* **XIII** 137 *1972*, **XXX** 96 *1995*.]
It is a good catalyst, no doubt by being converted to the metal *in situ* which promotes catalysis. It has been used for the reduction of aromatic rings to cyclohexane rings [e.g. at 1350psi/147°/16 hours, or 70psi/90°/1 hour; Freifelder & Stone *J Am Chem Soc* **80** 5270 *1958*, Freifelder & Stone *J Org Chem* **26** 3805 *1961,* Freifelder & Stone *J Org Chem* **27** 3568 *1962*, Johnson et al. *J Am Chem Soc* **84** 2181 *1962*], and phenolic compounds to the respective cyclohexanols [Rapala & Farkas *J Org Chem* **23** 1404 *1958*, Counsel *Tetrahedron* **15** 202 *1961*, Ireland & Schiess *J Org Chem* **28** 6 *1963*]; but with some enones only the double bond was reduced without affecting the carbonyl function [Rapala & Farkas *J Am Chem Soc* **80** 1008 *1958*].

HOMOGENEOUS METAL CATALYSTS

Allylpalladium(II) chloride dimer {di-μ-chloro-η^3-allylpalladium(II), $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$} *[12012-95-2]* **M 365.9, m 155-156°(dec.), ~160°(dec.).** It is prepared from allyl chloride, $PdCl_2$, and NaCl in the presence of carbon monoxide and is extracted into $CHCl_3$, washed with H_2O, dried ($CaCl_2$), filtered and evaporated to

dryness to give the complex as yellow crystals (use a very efficient fume cupboard). These can be used as such, but by recrystallisation from a mixture of CH_2Cl_2 and hexane analytically pure catalyst can be obtained (**m 155-156º dec.)**. It also crystallises from benzene and is soluble in MeOH, Et_2O, Me_2CO and $CHCl_3$. The ^1H NMR ($CDCl_3$) has two doublets at δ_H 3.03 (anti CH_2, J = 12.0Hz) and 4.10 (syn CH_2, J = 7.1Hz), and a triplet at δ_H 5.48 (CH) 2:2:1. [Tatsuno et al. *Inorg Synth* **28** 342 *1990*, Shaw *Proc Chem Soc* 247 *1960*, Hüttel et al. *Chem Ber* **94** 766 *1961*, Dent et al. *J Chem Soc* 1585 *1964*.]
It is a labile Pd complex, but is very useful for preparing a variety of stable catalytic Pd(0) complexes with a wide selection of ligands to perform stereoselective reactions. A particularly useful ligand is *cis,cis,cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane [Tedicyp] [Laurenti et al. *J Org Chem* **66** 1633 *2001*]. The catalyst with this ligand is typically prepared under argon, in a Schlenk type system, by dissolving $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (4.2mg, 11.6μmol) and Tedicyp (20mg, 23.2μmol, see [333380-86-2] in Part 2) in dry tetrahydrofuran (10ml) and stirring for 10 minutes before use. It gives a solution of 2.32μmol/ml of catalyst, which has ^{31}P NMR (162MHz, $CDCl_3$) with δ at 25 (vbrs, *width* 80Hz), 19.4 (vbrs, *width* 110Hz). It is very efficient in catalysing allylic substitutions with high turnover numbers (up to 9,800,000) and frequencies (up to 190,000 h^{-1}).
$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ is used for cross-coupling reactions [Wallow & Novak *J Org Chem* **59** 5034 *1994*], the Heck reactions with olefins [Fall et al. *Synthesis* 1683 *2007*] and enol ethers [Battace et al. *Eur J Org Chem* 3122 *2007*], and the formation of ethyl cyclopropane carboxylates with ethyl diazoacetate and olefins [Armstrong *J Org Chem* **31** 618 *1966*] to name a few.

Bis(acetonitrile)dichloropalladium(II) [Pd(II)Cl_2(MeCN)$_2$ complex] *[14592-56-4]* **M 259.4, dec > 200º.** It is prepared by mixing anhydrous $PdCl_2$ (1mol) and MeCN (2mols) until clear and precipitating the complex with petroleum ether. *Alternatively*, MeCN (3ml) is added to a solution of K_2PdCl_4 (2g) in H_2O (40ml) and stirred at ~25º until separation of yellow prisms is complete (could take up to 8 days). Filter these off, wash them with H_2O, EtOH, Et_2O, and dry them *in vacuo*. Further purification, if necessary, can be achieved by dissolving it in anhydrous solvents (which are not likely to displace the ligands) such as MeOH, toluene, THF, precipitating it with light petroleum, and drying the solid *in vacuo*. It is also soluble in $*C_6H_6$ to the extent of 100mg/4.0ml. In addition to its use as a source of metal for palladium complexes and catalysts such as $PdCl_2$(*R*)-BINAP [115826-95-4] (see Ozawa et al. *Organometallics* **12** 4188 *1993*), it also catalyses Overman rearrangements (aza-Claisen rearrangement, Overman & Garpenter *Org React* **66** 1 *2005*, see below). A particularly interesting example of the rearrangement being the high diastereoselectivity which is directed by a δ-methoxymethylether group in δ-substituted allylic trichloroacetamidates, where the ether oxygen atoms coordinate with Pd to direct the orientation of the reaction [Jamieson & Sutherland *Tetrahedron* **63** 2123 *2007*]. The IR spectrum shows, from the RCN and M-X vibrations, that the MeCN groups have a *trans*-planar configuration, unlike related Pt complexes which have the *cis*-configuration. The IR (Nujol) has ν_{max} at 1417m, 1358m, ~1160wbr, 1030m, 970wbr cm^{-1} [Walton *Spectrochim Acta* **21** 1795 *1965*].

Bis(benzonitrile)dichloropalladium(II) [Pd(II)Cl_2(PhCN)$_2$ complex] *[14220-64-5]* **M 383.6, m 131º.** It is prepared and purified in the same manner as the Pd(II)Cl_2(MeCN)$_2$ complex above. *Alternatively*, anhydrous $PdCl_2$ (2g) suspended in benzonitrile (50ml) is stirred at 100º. Most of the $PdCl_2$ dissolves after 20 minutes to give a red solution which is filtered while hot, and the hot filtrate is poured slowly into petroleum ether (b 40-60º). The light yellow complex which crystallises out is collected, washed with petroleum ether and dried *in vacuo* (4.0g, 93%). It can be purified further by dissolving it in the minimum volume of $*C_6H_6$, and the hot red solution is filtered and diluted with petroleum ether to allow the complex to crystallise out. [Doyle, Slade and Jonassen *Inorg Synth* **VI** 218 *1960*, Kharasch et al. *J Am Chem Soc* **60** 882 *1938*.] Pd(II)Cl_2(PhCN)$_2$ is an effective catalyst for the regiospecific cycloaddition cross-coupling reactions of aziridines with carbodiimides to form imidazolidin-2-imines in 40-94% yields [Baeg & Aler *J Org Chem* **57** 157 *1992*]. In the presence of a Buchwald ligand (e.g. 2-di-*t*-butyl-2'4'6'-tri-*i*-propylbiphenyl) in CH_2Cl_2, it catalyses the stereoselective formation of α-*O*-glycosides from protected glycalimidates with a variety of phenols or protected glycosides in high yields at room temperature [Schuff, Mercer and Nguyen *Org Lett* **9** 3174 *2007*]. Also, in the presence of Xantphos {4,5-bis(diphenylphospheno)-9,9-dimethylxanthene, see [161265-03-8]}, it promotes Stille-type cross coupling reactions between alkynyl-$SnBu_3$ and α-halo esters or amides under neutral conditions in THF to provide 3-alkynoates or alkynoamides in high yields without homocoupling of the alkynyltin reagents [Shi et al.

Chem Commun 2342 *2007*]. The IR spectrum shows, from the RCN and M-X vibrations, that the PhCN groups have a *trans*-planar configuration, unlike related Pt complexes which have the *cis*-configuration. The IR (Nujol) has ν_{max} at 3096w, 3057w, 3033w, 3002vwm 2287s, 1480m-w, 1440s, 760s, 678s cm^{-1} [Walton *Spectrochim Acta* **21** 1795 *1965*].

Bis(cyclopentadienyl)cobalt(II) (cobaltocene, $C_5H_5CoC_5H_5$, Cp_5Co) *[1277-43-6]* **M 189.1, m 173-174° (under N_2), 176-180°(dec).** Cp_2Co is prepared by adding anhydrous $CoCl_2$ (0.5 mol, prepared by dehydrating the salt at 200° in a vacuum) to a cold solution of 1 mol of sodium cyclopentadienide [4984-82-1] in THF (see below), stirring for 2 hours, removing the solvent and subliming the product directly from the mixture at 150-200°/10^{-4} mm in 75-80% yields; or by using $CoBr_2$ and refluxing for 3 hours. *Alternatively* (method of Wi et al. *J Inorg Nucl Chem* **2** 110 *1956*), cyclopentadiene (42ml, 0.5mol) and Et_2NH (~100ml, 1mol) are added slowly to $CoBr_2$ (0.25mol) with cooling, and then stirring at ~25° for 6-8 hours; the solvent is removed *in vacuo* and the residue is extracted with petroleum ether, filtered, and the solvent is evaporated to give dark violet monoclinic crystals m 171-173°.
When anhydrous *cobalticenium chloride* (5g, prepared from sodiocyclopentadienide and anhydrous $CoCl_2$ in THF as above but stirring at the boiling point for 2 hours, evaporating the solvent and adding 1:1 hydrochloric acid) in dry 1,2-dimethoxyethane (150ml) is treated with excess of $NaBH_4$ (5g, or LAH) in small portions while stirring (H_2 is evolved), then warm to 60°, or add H_2O (2ml), the mixture becomes deep wine-red in colour. After 1 hour the solution is filtered, the solid is washed with Et_2O and the filtrate is evaporated to a few mls *in vacuo*, diluted with petroleum ether (b ~40-60°), concentrated again and applied on to an alumina column (20 x 2cm). The first red band that elutes with petroleum ether is evaporated, and the residue is sublimed *in vacuo* onto a cold finger at -70° to give wine-red crystals of ***π-cyclopentadienyl(cyclopentadiene)cobalt*** **[π-$C_5H_5CoC_5H_6$]** (yield 80%) with **m 98-99°**, has **M 193** (ebulioscopic in $*C_6H_6$), and a UV with λ_{max} nm(ε) at 263.8 (1.78 x 10^5), 327 (9.27 x 10^3), and 395 (5.27 x 10^3). It has a camphorous odour and should be kept under argon as it is stable in air for only a few minutes, but for a few hours in degassed solutions of organic solvents. [Green et al. *J Chem Soc* 3753 *1959*.]
Sodium cyclopentadienide [4984-82-1] is prepared under N_2 by slowly adding cyclopentadiene (37ml) to a cooled suspension of sodium (10g) in THF (150ml) when H_2 evolves rapidly and a solution of sodium cyclopentadienide is formed. The colour of the soluton depends on the purity of the solvent and the amount of air in the system. Clear pale orange or red solutions are obtained with good conditions, but dark red to purple colours are obtained in the presence of traces of air without, however, seriously decreasing the yields of the complexes formed. [Wilkinson et al. *J Inorg Nucl Chem* **2** 95 *1956*, Reynolds & Wilkinson *J Nuclear Chem* **9** 86 *1959*, *Beilstein* **16** IV 1698.] It is available commercially as a 2.0M solution in THF as sodium cyclopentadienylide. The dry solid is **pyrophoric**.
Cp_2Co catalyses the condensation of acetylene and mono-substituted acetylenes (but not di-substituted acetylenes) with nitriles at 150° to give 30-70% yields of substituted pyridines [Wakatsuki & Yamazaki *Synthesis* 26 *1976*]. This synthesis has been applied successfully in a 2+2+2 cycloaddition reaction between di(trimethylsilyl)propargyl ether and acetonitrile to prepare a pyridine intermediate which was used to obtain pyridoxine (vitamin B_6) [Greiger et al. *Helv Chim Acta* **67** 1274 *1984*].

The above are general procedures for preparing **Bis(cyclopentadienyl)chromium (II) [Cp_2Cr]** *[1271-24-5]* **M 182.2, m 168-170° [***Beilstein* **16** IV 1774, Wilkinson et al. *J Inorg Nucl Chem* **2** 95 *1956*.], **Bis(cyclopentadienyl)magnesium(II) [Cp_2Mg]** *[1284-72-6]* **M 154.5, m 176-178°, 180°(dec) [***Beilstein* **16** IV 1695, Wilkinson et al. *J Inorg Nucl Chem* **2** 95 *1956*, Barber *J Inorg Nucl Chem* **4** 373 *1957*], *and* **Bis(cyclopentadienyl)vanadium(II) [Cp_2V]** *[1277-47-0]* **M 181.1, m 165-167° [***Beilstein* **16** IV 1771]. [Wilkinson et al. *J Inorg Nucl Chem* **2** 95 *1956*.]

Bis(dibenzylideneacetone)palladium(0) [$Pd(dba)_2$] *[32005-36-0]* **M 575.0.** The precise nature of this complex is not clear but a product with reproducible stoichiometry [$C_{34}H_{28}O_2Pd$] is prepared first by stirring $PdCl_2$ (8.87g, 50mmol) and NaCl (2.92g, 50mmol) in MeOH (250ml) at 25° for 16 hours, filtering through a cotton wool plug, diluting the filtrate to ~1.5L with MeOH, and heating to 60° to form $Na_2[PdCl_6]$. Dibenzylideneacetone (36.5g, 150mmol, see [538-58-9], cf Organic Compounds in Chapter 4) is then added to this warm solution stirred solution of $Na_2[PdCl_6]$, and stirring for a further 15 minutes and anhydrous NaOAc (75g) is added. The reaction begins immediately, heating is stopped but stirring is continued until the reaction

cools to room temperature. The dark brown precipitate that is formed is washed with MeOH (2 x 25ml), H_2O (5 x 50ml), Me_2CO (5 x 15ml) and dried in air to constant weight (923g, 80% yield) [Rettig & Maitlis *Inorg Synth* **17** 134 *1977*]. See the related complex **Pd(dm-dba)$_2$** below for the structure of these complexes in $CDCl_3$ solution. Catalysis with these complexes occurs at room temperature in the presence the ligand DIPHOS [dpe, 1,2-bis-[diphenylphospheno]ethane (see [1663-45-2] in Metal-Organic Compounds in Chapter 5) which is more efficient than with the less stable $Pd(PPh_3)_4$. It is used for the synthesis of allylic substituted cyclopentadienes [Fiaud & Mallerson *Tetrahedron Lett* **21** 4437 *1980*] and is a homogeneous catalyst [Fiaud & Mallerson *Tetrahedron Lett* **22** 1399 *1981*, Black *Aldrichimica Acta* **15** 13 *1982*] which catalyses the alkylation of a variety of nucleophiles under mild conditions [Ferroud et al. *Tetrahedron Lett* **25** 4379 *1984*.] Together with cyclic thiourea ligands such as *1N,3N*-bis(1,4-di-*tert*-butylphen-2-yl*)*imidazoline-2-thione, it catalyses efficient aerobic oxidations of alcohols to aldehydes and ketones in toluene in yields >95% [Yang et al. *Synlett* 3057 *2006*.]

Bis(3,5,3′,5′-dimethoxybenzylideneacetone)palladium(0) {bis[1,3-bis(3′,5′-methoxybenzylidene)acetone palladium(0), [Pd(dm-dba)$_2$]} *[811862-77-8]* **M 815.2, m 170-178º.** This Pd catalyst with the dimethoxy-dba ligand is prepared and purified as for $Pd(dba)_2$ above but using 1,5-bis(3′,5′-dimethoxyphenyl)penta-1*E*,4*E*-diene-3-one (dm-dba, [39777-58-7]),***** instead of dba. *Alternatively*, Fairland's method can be used, whereby NaCl (3.3g, 56mmol) is added to $PdCl_2$ (5g, 28mmol) in MeOH (140ml) and stirred under argon at 25º for 24 hours, filtered and evaporated *in vacuo* to half its volume. To this solution at 60º is added dm-dba (20.6g, 88mmol), stirred at 60º for 15 minutes, anhydrous NaOAc (42.3g) is added and allowed to cool to 25º. The mixture is stirred at 25º for 2 hours as the dark red precipitate of the complex separates. The solid is collected, washed with MeOH (2 x 100ml), H_2O (2 x 100ml) then Me_2CO (2 x 20ml), partially dried by suction, placed in a Schlenk flask and stirred under a flow of N_2 overnight to give the complex as a maroon/purple microcrystalline solid (11g 68%). It was found to have higher activity than those of the complex with the unsubstituted ligand [i.e. $Pd(dba)_2$] in Suzuki-Miyaura cross-coupling reactions of organic halides with arylboronic acids. ***Note*** that a solution of the complex, as in the case of $Pd(dba)_2$ above, in $CDCl_3$, was found to contain one dm-dba ligand coordinated to Pd and one free in solution. Addition of two equivalents of Ph_3P to the complex in THF and $(CD_3)_2CO$ resulted in the formation of the η^2-(dm-dba)$Pd^{(0)}(Ph_3P)_2$ complex as shown by the presence of two phosphorous doublets in the ^{31}P NMR spectrum. [Fairlamb et al. *Org Lett* **6** 4435 *2004*, cf *Handbook of Organopalladium for Organic Synthesis* Negishi ed. Wiley, Hoboken NJ *2002*, ISBN 0-471-31506-0.]
For **Pd$_2$(*p,p'*-dimethoxy-dba)$_3$** see **Pd$_2$(dba)$_3$**($CDCl_3$) below.

Bis(di-*tert*-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium(II) [(A-^{ta}Phos)$_2$PdCl$_2$] *[887919-35-9]* **M 708.1.** The catalyst is prepared by mixing one equivalent of di-*tert*-butylphosphine, 1 equivalent of 4-dimethylaminophenyl bromide and 1 mol% of Pd_2dba_3 at 90º for 12 hours. The mixture is cooled to 25º, filtered through a short silica gel plug, the plug is rinsed with toluene and the combined filtrate is evaporated under vacuum. The residue is dissolved in tetrahydrofuran and 0.35 equivalents of solid $PdCl_2$(COD) are added followed by stirring at 25º for 12 hours. The product is filtered off, and the yellow solid collected is washed with pentane and dried *in vacuo* to give ~85% yield of (A-^{ta}Phos)$_2PdCl_2$ which provides the correct microanalysis for C and H. It has ^1H NMR (CD_2Cl_2) with δ at 7.5 (s br, 4 H, ArH), 6.42 (d, J = 8.3Hz, 4H, ArH), 2.75 (s, 12H, NMe_2), 1.38 (t, J_{PH} = 6.6Hz, 36H, *tert*-Bu); and ^{31}P NMR ($CDCl_3$) with δ at 52.1.
Similarly ***bis[di-*tert*-butyl(p-trifluoromethylphenyl]phosphine)dichloropalladium(II)*** can be prepared which has ^1H NMR ($CDCl_3$) with δ at 8.0 (s br, 4 H, ArH), 7.59 (d, J = 7.9Hz, 4H, ArH), 1.62 (t, J_{PH} = 7.0Hz, 36H, *tert*-Bu); ^{31}P NMR ($CDCl_3$) with δ at 55.7; and ^{19}F NMR ($CDCl_3$) with δ at -63.4. Also ***bis[di-tert-butyl(phenyl)phosphine]dichloro-palladium (II)*** was prepared in the same way and has ^1H NMR ($CDCl_3$) with δ at 7.9-7.8 (m, 4 H, ArH), 7.36-7.30 (m, 6H, ArH), 1.56 (t, J_{PH} = 6.9Hz, 36H, *tert*-Bu); ^{31}P NMR ($CDCl_3$) with δ at 54.4. These are air-stable active catalysts for Suzuki-Miyaura cross-coupling with aryl halides including 5- and 6-membered heteroaryl halides in the presence of bases such as K_2CO_3, Na_2CO_3, KOAc, K_3PO_4 with high turn over numbers (TON) of 100 to 100,000 [Guram et al. *Org Lett* **8** 1787 *2006*].

2-[Bis(2,4-di-*tert*-butylphenoxy)phosphinooxy]-3,5-di(*tert*-butyl)phenyl-palladium(II) chloride dimer {Bedford's Catalyst, 2[bis(2,4-di-*tert*-butylphenoxy)phosphino-κP-oxy)-3,5-di-*tert*-butylphenyl-κC]di-μ-chloro-dipalladium} *[217189-40-7]* **M 1575.6.** The thoroughly characterised Bedford catalyst, an *ortho*-metallated dimer, is prepared in 96% yield from the bulky tris(2,4-di-*tert*-butylphenyl)phosphite and $PdCl_2$. The catalyst is remarkably stable to moisture and air, showing no signs of deterioration after several weeks, can be kept in air for at least 6 months and is not decomposed on heating at 130° in toluene for 24 hours. It is very efficient for coupling aryl halides with either arylboronic acids (Suzuki reaction) or aryltin compounds (Stille reaction) in solvents such as toluene or tetrahydrofuran to form biaryls with very high turn over numbers (TONs up to 1,000,000 moles of product/mol of Pd) at even very low Pd catalyst concentrations, and in moderate to high yields [Albisson et al. *J Chem Soc, Chem Commun* 2095 *1998*]. Bedford's catalyst also proved to be extremely active in the arylation (with e.g. aryl bromides) of alkenes (e.g. acrylate, styrene) with turn over numbers of up to 5,750,000 (mole product/mol Pd), and turn over frequencies of 300,000 (mol product/mol Pd/hour) [Albisson et al. *Tetrahedron Lett* **39** 9793 *1998*].

***R,R*-(+) *and S,S*-(-) *N,N′*-Bis(3,5-di-*tert*-butylsalicylidene)-1,2-*trans*-cyclohexanediamine Manganese(III) Chloride [Jacobsen's catalyst]** *[R,R-138124-32-0, S,S-135620-04-1]* **M 635.2, m 330-332°, 324-326°, $[\alpha]_D^{20}$ ±580° (c 0.01, EtOH).** This complex is commonly referred to as the Mn(salen) catalyst. If this enantioselective catalyst for the epoxidation of olefins requires purification, the brown powder (*ca* 6g) is dissolved in CH_2Cl_2 (100ml), extracted with H_2O (2 x 100ml), the organic phase is dried (Na_2SO_4), filtered, evaporated to dryness and the solid residue is dried in a vacuum desiccator over $CaSO_4$. [Jacobsen et al. *J Am Chem Soc* **113** 7063 *1991*]. For large scale preparation see Larrow et al. *J Org Chem* **59** 1939 *1994*, Deng & Jacobsen *J Org Chem* **57** 4320 *1992*. For epoxidation of indenes see Hughes et al. *J Org Chem* **62** 2222 *1997*, and for the epoxidation of isoflavones see Adams et al. *Tetrahedron: Asymmetry* **9** 1121 *1998*, Chang et al. *Tetrahedron* **58** 6939 *1993*, Jacobsen et al. *Tetrahedron* **50** 4323 *1994*, Jacobsen's Asymmetric Catalytic Epoxidation of Unfunctionalized Olefins in *Catalytic Asymmetric Synthesis Vol I,* p. 159, Ojima Ed. VCH, NY *1993* (see also Bibliography in Part 2), and for enantioselective hydrolysis of epoxides see Furrow et al. *J Org Chem* **63** 6776 *1998*.
On a large scale, the brown *R,R-(+)- catalyst* (300-400g) is washed with hot H_2O (2 x 800ml, at 50°), and dried on the filter for 2 hours then under vacuum (50-100mm) at 60-70° for 12 hours, m 324-326° (product of acceptable purity has m ~320°), $[\alpha]_D^{23}$ +580° (c 0.01, EtOH), and IR with ν_{max} (KBr) at 1535, 1612, 2950-2958 cm^{-1}. [Larrow et al. *J Org Chem* **59** 1939 *1994*.]
The related chiral complexes of Al(II)-Cl *[R,R 250611-13-3; S,S 307926-51-8]*, of Cr(III)-Cl *[R,R 164931-83-3; S,S 219143-92-7]* and of the Co(III)-Cl *[R,R-(+) 176762-62-5; S,S-(-) 188264-84-8]* (Tokunaga et al. *Science* **277** 936 *1977*, Jacobsen et al. *Tetrahedron Lett* **38** 733 *1997)* are similarly prepared and are available commercially.

NOTE: It was shown that addition of pyridine *N*-oxides, and particularly 4-(3-phenylpropyl)pyridine-1-oxide (P_3NO, see [34122-28-6] in Part 2), stabilise and improve the catalytic activity of Mn(salen) catalysts [Larrow & Jacobsen *J Am Chem Soc* **116** 12129 *1994*, Srinivan et al. *J Am Chem Soc* **108** 2309 *1986*, Senanayake *Aldrichimica Acta* **31** 3 *1998*.] Thus in a typical epoxidation MnLCl (0.56mmol, salen Mn catalyst) and P_3NO (2.32mmol) in chlorobenzene (10ml) are added to a 2M solution of NaOCl (26.5mmol) cooled to 0° under N_2, and stirred at 0° for 15 minutes, followed by simultaneous addition of indene (10ml) and further NaOCl (79.5mmol) (syringe pumps) during 30 minutes. The reaction is complete within 1 hour at 0°, and can be performed on a multi-kilogram scale to provide indene epoxide in 89% yield and with an optical purity of 88% e.e. [Senanayake et al. *Tetrahedron Lett* **37** 3271 *1996*.]

A **dimeric Jacobsen ligand**, formed by linking two units with a methylene bridge has been prepared and crystallised from CH_2Cl_2/pentane. Its **bis-Mn catalyst** exhibited improved retention in a poly-dimethylsiloxane membrane for the asymmetric epoxidation of olefines [Janssen et al. *Tetrahedron: Asymmetry* **8** 3481 *1997*].

[*(R)*-(+)-2,2′-Bis(diphenylphosphino)-1,1′-binaphthyl]palladium(II) dichloride ([*R*-BINAP]$_2$PdCl$_2$) *[115826-95-4]* **M 800.0, m 255-260° (dec), $[\alpha]_D^{24}$ +682° (c 0.5, $CHCl_3$).** This catalyst is prepared by dissolving a mixture of *R*-BINAP (500mg, 0.803mmol, see [76189-55-4]), η-allyl-η-cyclopentadienyl-Pd(II) (84,2mg, 0.396mmol, see [1271-03-0], *cf* Tatsuno et al. *Inorg Synth* **19** 220 *1979*) in $*C_6H_6$ (5ml), in a Schlenk tube

under N_2 (dried over P_2O_5), and heated at 80° for 3 hours to give a deep red solution which is then evaporated to dryness. The red solid is then dissolved in CH_2Cl_2 (10ml), filtered and the filtrate is evaporated *in vacuo* down to *ca* 4ml, diluted with Et_2O (40ml) and cooled to 4° whereby red-purple crystals of [*R*-BINAP]$_2$Pd(0) separate, which on washing with cold Et_2O and drying *in vacuo* give analytically pure ***[R-BINAP]$_2$Pd(0)-Et$_2$O*** (480mg, 90%). The 1:1 ratio of Et_2O to Pd is confirmed by ^{1}H NMR spectroscopy. It has ^{1}H NMR (90MHz, *C_6D_6, TMS) with δ_H at 5.88 (t, *J* = 7.6Hz, 8H), 6.19 (t, *J* = 7.3Hz, 4H), 6.8-7.6 (m, 40H), 7.83 (d, *J* = 8.2Hz, 4H), 8.36 (brs, 8H); and the ^{31}P{^{1}H} NMR (36MHz, *C_6D_6, referenced to external 85% H_3PO_4 at δ 0.0) has δ_P at 27.3. This Pd(0) complex catalyses asymmetric arylation in the Heck reaction. ***[R-BINAP]$_2$PdCl$_2$*** is obtained by stirring *R*-BINAP (249mg, 0.40mmol) in *C_6H_6 (4.0ml) with $PdCl_2(MeCN)_2$ (104mg, 0.40mmol) in *C_6H_6 (4.0ml) overnight. The yellow precipitate is collected by filtration, washed with *C_6H_6 and dried *in vacuo*. It is crystallised by dissolving in Me_2CO, layering with hexane and setting aside at ~25° to give red crystals of [*R*-BINAP]$_2$PdCl$_2$ (238mg, 75%, m 255-260°) of analytical purity, and suitable for X-ray crystallographic structure determination which confirmed its structure. [Ozawa et al. *Organometallics* **12** 4188 *1993*, *cf* review by Shimizu, Nagasaki & Saito *Tetrahedron* **61** 5405 *2005*].

Bis(trifluoromethanesulfonyl)amine metal salts [NTf$_2$, bis-(trifluoromethanesulfon)amide metal salts, (CF$_3$SO$_2$)$_2$NMetal] see *[82113-65-3]*. **NTf$_2$** readily forms salts, e.g. with Li, Ba, Ca, Al, Zn, Al and lanthanides, which act as *Lewis Acids* in effectively catalysing Diels-Alder reactions [Kobayashi et al. *Chem Lett* 307 *1995*, Handy et al. *Synlett* 565 *1995*] and acylation reactions [Mikami et al. *Synlett* 171 *1996*]. It forms an *N-trimethylsilyl derivative* ($TMSNTf_2$ prepared from allylTMS and NTf_2, see above) which catalyses Diels-Alder reactions between methyl acrylate and various dienes [Mathieu & Ghosez *Tetrahedron Lett* **38** 5497 *1997*], as well as Friedel-Crafts acylation reactions of anisole, and allylation and bis-allylation of carbonyl derivatives [Oshii et al. *Synlett* 1145 *1997*]. **NTf$_2$** is a weakly coordinating counter ion which confers stability to catalytic metal complexes such as the gold catalyst $[Ph_3PAu(I)]^+ [NTf_2]^-$, see [866395-16-6].

***R*(-)- and *S*(+)- 4,12-Bis(diphenylphosphino)-[2.2]-paracyclophane {*R*- and S- PHANEPhos, (*R*)- and (*S*)-5,11-bis(phenylphosphino)-tricyclo[8.2.2.2^{4,7}]hexadeca-hexaene}** *[(R) 364732-88-7; (S) 192463-40-4]* **M 576.6, m 222-226°, 224-276°, $[\alpha]_D^{25}$ *R* -34°, *S* +34° (c 1, CHCl$_3$).** These are chiral ligands for the rhodium precatalysts **(COD)Rh{(*R*)-[2.2]PHANEPhos}$^+$ OTf$^-$** and **(COD)Rh{(*S*)-[2.2]PHANEPhosS}$^+$ OTf$^-$** (see preparation and purification below) which are highly enantioselective in the hydrogenation of dehydroamino acid methyl esters generally, and also of methyl 1-Ac-4-Boc-1,4,5,6-tetrahydropyrazine-1-carboxylate which is difficult to reduce. When they are pre-reduced in MeOH, they form **(MeOH)$_2$Rh{(*R*)-[2.2]PHANEPhos}$^+$ OTf$^-$** whose activity is more pronounced and reduction is complete in less than 60 minutes by passing H_2 gas through the MeOH solution at temperatures between -45° to +50°, with high substrate to catalyst ratios.
The preparations of these ligands (described briefly here for convenience) involve di-bromination of *p*-cyclophane, separation of the *meso*- from the *racemic*-isomers (latter are more soluble in triglyme), reaction of the *rac*-isomer (1 equivalent) with *tert*-BuLi (4.2 equivalents), and $MgBr_2.Et_2O$ (2.3 equivalents) in THF then diphenylphosphinyl chloride (Ph_2POCl, 2.2 equivalents) to give *rac*-4,12-bis(diphenylphosphinyl)-[2.2]-paracyclophane (76% yield). Optical resolution of this racemate (in $CHCl_3$) with (+)-dibenzoyl-D-tartaric acid (in EtOAc) at 60°, then cooling to ~25° over 18 hours, gave a white precipitate from which the *R*(-)-*enantiomer* (>99.5% ee) is isolated. The absolute configuration was obtained from the X-ray crystallographic structure determination of the *R*-dibenzoyl-D-tatrate salt (for definition of the chiral descriptor notation see R.S. Chan, C.K. Ingold and V. Prelog *Angew Chem Int Edn Engl* **5** 385 *1966*). From the mother liquors the *S*(+)-*enantiomer* (>99.5% ee) was isolated by washing the diastereomeric tartrate salt (in $CHCl_3$) with 0.5M aqueous NaOH. They are white solids which are separated by SFC (supercritical fluid chromatography using a 25cm Hewlett Packard Chiracel AD column with 15% MeOH/supercritical CO_2 at 1.0ml/minute) with retention times of 13.0 minutes for the *R*-isomer and 17.8 minutes for the *S*-isomer, and they have $[\alpha]_D^{25}$ -104° and $[\alpha]_D^{25}$ +104° (c 0.1, EtOH) respectively. When *R*-4,12-bis(diphenylphosphinyl)-[2.2]-paracyclophane (4.0g, 6.58mmol) is treated with Cl_3SiH (10ml, 99mmol, 10025-78-2] in *p*-xylene (80ml), and slowly heated to 140°, kept at this temperature for 18 hours, a further aliquot of Cl_3SiH (5ml, 49.5mmol) is added, and heating is continued for 24

hours, the reduction appears complete. The mixture is then cooled to -10°, quenched with 30% aqueous NaOH (60ml, care violent reaction), extracted with EtOAc (3 x 80ml), the extract is dried ($MgSO_4$), filtered and evaporated to dryness. Degassed MeOH (30ml, by sonication) is added to the residue which is filtered and dried to give the pure diphosphino *R*-[2.2]PHANEPhos as a white solid. It has ^{1}H NMR (400MHz, $CDCl_3$, with residual $CHCl_3$ as reference at δ 7.27) with δ_H at 7.54, (m, 2H), 7.45 (m, 3H), 7.41 (m, 2H), 7.24 (m, 3H), 6.62 (*ortho and meta*, 2H), 6.58 (dd, *J* = 7.6 and 5.0Hz, 1H), 3.13 (m, 1H), 3.03 (*ortho and meta*, 2H), 2.65 (m, 1H); and ^{13}C NMR (100MHz, $CDCl_3$, with residual $CHCl_3$ as reference at δ 77.0) with δ_C at 143.2 (d, *J* = 16.1Hz), 139.6 (d, *J* = 11.2Hz), 139.2 (*J* = 2.4Hz), 137.4 (d, *J* = 12.0Hz), 137.2 (d, *J* = 10.4Hz), 135.8 (d, *J* = 22.5Hz), 134.3 (d, *J* = 4.0Hz), 133.3 (t, *J* = 4.0Hz), 132.9 (d, *J* = 20.1Hz), 132.7, 129.4, 128.44, 128.39 (d, *J* = 8.8Hz), 128.2 (d, *J* = 8.0Hz), 35.8, 33.2; and ^{31}P NMR (160MHz, $CDCl_3$, referenced to external 85% H_3PO_4 at δ 0.0) with δ_P at -0.53. The enantiomeric *S*-[2.2]PHANEPhos is similarly obtained.

Rh(COD){(*R*)-[2.2]PHANEPhosS}$^+$ OTf$^-$ is prepared using Schlenk equipment under N_2 from the red solution of *R*-[2.2]PHANEPhos (630mg, 1.09mmol) and $[(Rh\ COD)]_2^+$ OTf^- (512mg, 1.09mmol, see 12092-47-6 for chloride), in CH_2Cl_2 (10ml) which is stirred for 30 minutes, evaporated *in vacuo*, MeO-*t*-Bu (10ml) is added to the residue, sonicated for 30 minutes, stirred vigorously for 30 minutes, filtered and the solid is dried under N_2 to give the orange *R*- precatalyst (860mg, 85%). It has ^{1}H NMR (400MHz, $CDCl_3$, with residual $CHCl_3$ as reference at δ 7.27) with δ_H at 8.58 (m, 2H), 7.85 (m, 1H), 7.31 (m, 2H), 7.59 (m, 1H), 7.43 (m, 1H), 7.36 (m, 2H), 7.19 (m, 2H), 6.55 (br d, *J* = 8.0Hz, 1H), 6.43 (dd, *J* = 8.0 and 4.0Hz, 1H), 4.50 (br s, 2H), 2.77 (m, 1H), 2.67 (m, 1H), 2.54 (m, 1H), 2.48 (m, 1H), 2.20 (om, 3H), 2.03 (m, 1H); and ^{13}C NMR (100MHz, $CDCl_3$, with residual $CHCl_3$ as reference at δ 77.0), due to the non-equivalence of the P atoms, some carbon signals are second order multiplets which are noted as multiplets with δ_C at 142.2, 139.9 (m), 139.3 (m), 139.0 (t, *J* = 4.0Hz), 138.3 (m), 134.6, 133.7, 132.2 (t, *J* = 4.0Hz), 131.2 (m), 130.8 (m), 130.59, 130.58 (m), 129.2 (t, *J* = 4.2Hz), 128.9 (t, *J* = 4.4Hz), 100.5 (dt, *J* = 8.8 and 3.2Hz), 91.6 (dt, *J* = 8.0 and 7.0Hz), 35.1. 34.5, 32.5, 28.8; and ^{31}P NMR (160MHz, $CDCl_3$, referenced to external 85% H_3PO_4 at δ 0.0) with δ_P at 32.7 (d, $J_{P\text{-}Rh}$ = 146.1Hz). The enantiomeric **Rh(COD){(*S*)-[2.2]PHANEPhosS}$^+$ OTf$^-$** is similarly prepared. [Pye, Rossen et al. *J Am Chem Soc* **119** 6207 *1997*.] For the catalytic hydrogenation of β-keto esters to β-hydroxy esters using **Ru(II){[2.2]PHANEPhos}(trifluoroacetate)$_2$** with up to 96% ee, see Pye, Rossen et al. *Tetrahedron Lett* **39** 4441 *1998*.

***R*(-)- and *S*(+)- 4,12-Bis[di(3,5-xylyl)phosphino)-[2.2]-paracyclophane {*R*- and *S*- xylyl-PHANEPhos, (*R*)- and (*S*)-5,11-bis[di(3,5-xylyl)phenylphosphino)-tricyclo-[8.2.2.2^{4,7}]hexadeca-hexaene}** *[(R) 325168-89-*6; *(S) 325168-88-5]* **M 688.9, m 234-238°, $[\alpha]_D^{22}$ *R* -61.0°, *S* +61.0 (c 0.1, EtOH).** These chiral ligands are prepared and purified in much the same way as for [2.2]PHANEPhos above except that 3,5-dimethylphenylphosphinyl chloride is used to introduce the phosphorous group into the *p*-cyclophane. When these enantiomers are complexed with ruthenium and chiral ethylenediamine-type bases, they form powerful precatalysts that in the presence of H_2, will catalyse the reduction of a range of simple aromatic, heteroaromatic as well as α,β-unsaturated ketones with high ee values. Only one example, **R-{[xylyl-PHANEPhos]-Ru$_2$Cl(S,S)-DPEN}** is described here. It is prepared from the red solution of $[(C_6H_6)RuCl_2]_2$ (218mg, 0.436mmol, see [37366-09-9]), *R*-xylyl-PHANEPhos (0.60mg, 0.871mmol) in dry DMF (6ml) by heating at 100° for 4 hours, to which is then added *S,S-1,2-diphenylethylene-1,2-diamine* (185mg, 0.871mmol, *S,S*-DPEN, [29841-69-8]), and heating, and stirring is continued at 100° for 1.5 hours. The mixture is filtered, the filtrate is evaporated *in vacuo*, treated with Et_2O (10ml) and MeOH (100), the yellow catalyst is filtered off, washed with MeOH (12ml) and dried (420mg, 45% yield). It has ^{1}H NMR (400MHz, $CDCl_3$) with δ_H at 1.78 (ddd, *J* = 15.0, 10.5, 4.5Hz, 1H), 2.07 (s, 6H), 2.27 (s, 6H), 2.59 (s, 1H), 2.78 (m, 1H), 4.01 (m, 1H), 4.40 (m, 1H), 4.49 (m, 1H), 6.36 (d, *J* = 8.0Hz), 6.42 (d, *J* = 8.0Hz), 6.60 (m, 2H), 6.79 (m, 1H), 6.96 (m, 2H), 7.06 (s, 1H), 7.13 (m, 3H), 8.04 (m, 2H), 8.21 (m, 1H); and ^{31}P NMR (162MHz, $CDCl_3$, referenced to external 85% H_3PO_4 at δ 0.0) with δ_P at +46.06 (s). The crude catalysts performed equally as well as the purified precatalysts. [Burk et al. *Org Lett* **2** 4173 *2000*.]

{1,2-Bis[(4*S*)-4-isopropyl-2-oxazolin-2-yl]benzene}zinc(II) Chloride *[131380-93-3]* **M436.7, m 202°.** The zinc complex is obtained by adding a solution of the free ligand (300mg, 1mmol, see [131380-80-8]) in dry THF (5ml) to a solution of fused anhydrous $ZnCl_2$ (136mg, 1mmol, dried by melting in high vacuum and cooling under argon] in dry THF (10ml) and collecting the crystals, but if crystals are not readily formed, evaporate to

dryness and recrystallise the residue from EtOH to give the colourless complex (420mg, 98%). It has IR (KBr) with ν_{max} at 1655 (C=N) cm^{-1}; the ^1H NMR (300MHz, CD_3CN) has δ at 0.84 (d, J = 6.9Hz, 6H, $CH(CH_3)_2$), 0.95 (d, J = 7.1Hz, 6H, $CH(CH_3)_2$), 2.52-2.62 (m, 2H, $CH(CH_3)_2$), 4.50-4.62 (m, 6H, OCH_2CHN), 7.77-7.81 (m, 2H, 4-H and 5-H), 7.85-7.89 (m, 2H, 3-H and 6-H) from TMS; and the ^{13}C NMR (100MHz, CD_3CN) has δ at 14.85 (q), 18.59 (q), 30.92 (d), 71.08 (d), 71.39 (t), 126.57 (s), 132.25 (d), 134.05(d), 168.99 (s). [Bolm et al. *Chem Ber* **124** 1173 *1991*.] Like many chiral bis(oxazolin-2-yl) complexes it can be involved in a variety of metal catalysed asymmetric synthesis such as allylation, aziridination, cyclopropanation, Diels-Alder and retro Diels Alder, Mukaiyama aldol condensation and hydrosilylation [see reviews by Ghosh et al. *Tetrahedron: Asymmetry* **9** 1 *1998*, Pflatz *Acta Chem Scand* **50** 189 *1996*, Johnson & Evans *Acc Chem Res* **33** 325 *2000*, Jørgensen et al. *Acc Chem Res* **32** 605 *1999*.]

1,3-Bis(2,4,6-trimethylphenyl)-imidazol-2-ylidenegold(I) chloride (IMesAuCl) *[852445-81-9]* **M 537.1, m ~280-286°.** The gold complex is prepared by adding Ag_2O (0.5mmol) to $IMes^+ Cl^-$ (1mmol) in CH_2Cl_2 and the suspension is stirred for 3 hours at ~25° whereby it became clear; then a solution of $Au(Me_2S)Cl$ (1mmol, see [29892-37-3]) in CH_2Cl_2 is added dropwise and stirred for a further 4 hours. After filtration through Celite, the filtrate is evaporated to a small volume and hexane is added to allow the complex to separate. It is collected and dried (49% yield). Its ^1H NMR (400MHz, $CDCl_3$, TMS) has δ_H at 7.08 (s, 2H), 6.97 (bs, 4H), 2.33 (s, 6H), 2.09 (s, 12H), and its ^{13}C NMR (100MHz, THF-d_8, TMS) has δ_C at 134.68, 129.49, 122.12, 21.13, and 17.75 (one signal is missing, coincident signals?). HRMS-FAB Calc for $C_{21}H_{25}AuN_2Cl$ (M^++H) is 537.1372; and found 537.1361. It catalyses the intramolecular [4+2] cycloadditions of 1-en-6-ynes, or aralkynes with alkenes, in the presence of $AgSbF_6$; also the related ***1-methyl-3-(2,4,6-trimethylphenyl)-imidazol-2ylgold(I) chloride*** is almost equally effective [Nieto-Oberhuber *J Am Chem Soc* **127** 6178 *2005*].
The saturated 4,5-dihydro- analogue **1,3-bis(2,4,6-trimethylphenyl)-imidazolin-2-ylidenegold(I) chloride (ISMeAuCl)** *[852445-82-0]* **M 539.1,** behaves in much the same manner as IMesAuCl, chemically and catalytically. It has recently been shown that both IMesAuCl and SIMesAuCl can be made by metal exchange from the cheaper respective IMesCuCl and SIMesCuCl (see below) in 71-90% yields. Thus a mixture of [$AuCl(SMe_2)$] (0.4-0.47mmol, [29892-37-3]) and [CuCl(NHC)] (1 equivalent) in CH_2Cl_2 (5ml) is stirred at 40° for 1-2 hours, then filtered through Celite and the solvent is removed *in vacuo*. CH_2Cl_2 (3ml) and petroleum ether (10ml) are added to the residue, the almost pure Au complex is filtered off, washed with petroleum ether (3 x 5ml) until colourless, and dried *in vacuo*. Their catalytic activities from these different preparations are the same. [Furst & Cazin *Chem Commun* **46** 6924 *2010*.]

Chloro[(1,1′-biphenyl-2-yl)di-*tert*-butylphosphine]gold(I) (JohnPhos-gold(I) chloride, JohnPhos-AuCl) *[854045-93-5]* **M 530.8, m 237-240°.** The gold complex is made from sodium tetrachloroaurate(III) dihydrate [13874-02-7] or hydrogen tetrachloroaurate(III) [see 16961-25-4] (1 mmol) in H_2O and the yellow solution is cooled in ice, to which is added bis(2-hydroxyethyl)sulfide [see 111-48-8] (3mmol) dropwise over ~45 minutes with stirring. Then a solution of JohnPhos [224311-51-7] (1mmol) in EtOH is added dropwise, whereby the gold complex separates as a white solid which is filtered off (43% yield), washed with MeOH and dried *in vacuo*. The ^1H NMR (400MHz, $CDCl_3$) has δ_H at 7.87 (td, J = 7.7, 1.7Hz, 1H), 7.51 (m, 5H), 7.31 (m, 1H), 7.13 (dd, J = 8.0, 1.0Hz, 2H), 1.41 (d, J = 15.6Hz, 18H); the ^{31}P NMR (160MHz, $CDCl_3$) has δ_P at 63.11; and the ^{13}C NMR (100MHz, $CDCl_3$) has δ_C at 150.16 (d, $^2J_{(^{13}C-^{31}P)}$ = 13.5Hz), 142.10 (d, $^3J_{(^{13}C-^{31}P)}$ = 6.3Hz), 133.46 (d, $^4J_{(^{13}C-^{31}P)}$ = 3.0Hz), 133.22 (d, $^3J_{(^{13}C-^{31}P)}$ = 7.5Hz), 129.19, 128.67, 128.22, 126.67 (d, $^3J_{(^{13}C-^{31}P)}$ = 6.8Hz), 126.06 (d, $^1J_{(^{13}C-^{31}P)}$ = 45.3Hz), 37.75 (d, $^1J_{(^{13}C-^{31}P)}$ = 25.7Hz), 30.84 (d, $^2J_{(^{13}C-^{31}P)}$ = 6.7Hz); HRMS-ESI calc for CHAuNP (M + MeCN-Cl): 536.1781, found: 536.1779. [Nieto-Oberhuber et al. *J Am Chem Soc* **127** 6168 *2005*, Al-Sa'Ady et al. *Inorg Synth* 191 *1985*.]
The acetonitrile complex salt derivative ***(acetonitrile)(2-biphenyl)-di-tert-butylphosphinogold(I) hexafluoro-antimonate*** **[866641-66-9] M 772.1,** has **m 198-203°(dec).** It catalyses a highly efficient intramolecular addition of β-ketoamide to unactivated olefins leading to highly substituted lactams in the presence of AgOTf (e.g. *N*-allyl *N*-benzyl benzoylacetamide to *cis*-3-benzoyl-1-benzyl-4-methylpyrrolidin-2-one in 99% yield) [Zhou & Che *J Am Chem Soc* **129** 5828 *2007*]. JohnPhos-AuCl and related complexes, in the presence of $AgSbF_6$ (i.e. the SbF_6^- salts), catalyse intramolecular [4+2] cycloadditions of 1,3-enynes or arylalkynes and alkenes with high efficiency [Nieto-Oberhuber et al. *J Am Chem Soc* **127** 6168 *2005*].

Chloro[2-dicyclohexyl(2′,4′,6′-tri-isopropylbiphenyl)phosphine]gold(I) [X-Phos-gold(I) chloride, X-Phos-

AuCl)] *[854045-94-6]* **M 709.1, m 243-250°.** This complex is prepared in much the same way as JohnPhos-AuCl but using a solution containing 1mmol of X-Phos [564483-18-7] in EtOH instead and giving a 61% yield of the X-Phos-AuCl as a white solid. The ^{1}H NMR (400MHz, $CDCl_3$) has δ_H at 7.57-7.55 (m,2H), 7.23 (m, 1H), 7.05 (s, 2H), 2.95 (hept, *J* = 7.0Hz, 1H), 2.21 (hept, *J* = 6.7Hz, 2H), 2.05-2.01 (m, 4H), 1.83-1.71 (m, 6H), 1.67-1.61 (m, 2H), 1.53-1.42 (m, 3H), 1.35 (s, 3H), 1.34 (s, 3H), 1.28 (s, 3H), 1.26 (s, 3H), 1.23-1.13 (m, 7H), 0.92 (s, 3H), 0.91 (s, 3H); the ^{31}P NMR (160MHz, $CDCl_3$) has δ_P at 38.48; and the ^{13}C NMR (100MHz, $CDCl_3$) has δ_C at 150.6, 145.48, 133.82 (d, $^{3}J_{(^{13}C-^{31}P)}$ = 8.1Hz), 132.04 (d, $^{1}J_{(^{13}C-^{31}P)}$ = 3.2Hz), 130.35 (d, $^{1}J_{(^{13}C-^{31}P)}$ = 1.8Hz), 127.08 (d, $^{1}J_{(^{13}C-^{31}P)}$ = 7.1Hz), 121.70, 37.23 (d, $^{1}J_{(^{13}C-^{31}P)}$ = 33.5Hz), 34.30, 30.93, 30.81, 27.01 (d, $^{1}J_{(^{13}C-^{31}P)}$ = 13.5Hz), 26.69 (d, $^{1}J_{(^{13}C-^{31}P)}$ = 12.9Hz), 24.36, 23.21 HRMS-ESI calc for $C_{33}H_{49}AuPNa$ (M^+ + Na): 731.2823, found: 731.2789. [Nieto-Oberhuber et al. *J Am Chem Soc* **127** 6168 *2005*, Al-Sa'Ady et al. *Inorg Synth* 191 *1985*.] Its catalytic activities are similar to those of JohnPhos-AuCl above.

Chloro(triphenylphosphine)gold(I) *[14243-64-2]* **M 495.7, m 240-241°, 242-243°.** Ph_3PAuCl is prepared under argon by adding a solution of hydrogen tetrachloroaurate (2.0g, 5.87mmol, $H[AuCl_4].nH_2O$, *n* ~3, "brown gold chloride" see [16903-35-8]) in EtOH (10ml), which has been filtered to remove any insoluble Au-containing material, to a stirred solution of Ph_3P (3.08g, 11.7mmol) in absolute EtOH (50ml of 100%, warm if necessary to dissolve). The solution immediately becomes colourless and after stirring for 15 minutes the white microcrystalline solid is collected (fritted glass filter, porosity 4), washed with EtOH (2 x 5ml), then Et_3O (3 x 15ml), and dried *in vacuo* (0.1mm) to give the analytically pure complex (1.9-2.3g 67-80%, or up to 92% if equipment is thoroughly dried, solvents degassed, and working in a strict inert atmosphere). It (~1.g) crystallises from CH_2Cl_2 (10ml) by slow addition of *n*-pentane (60ml) and cooling to -25° to give small slender white needles within a few minutes, and it also crystallises from $CHCl_3$ solution by addition of heptane. [Braunstein et al. *Inorg Synth* **27** 218 *1990*, Bruce et al. *Inorg Synth* **26** 324 *1986*, cf JohnPhos-AuCl above]. Ph_3PAuCl has also been prepared by adding Ph_3P (1.5g) in Me_2CO (5ml) to a solution of $HAuCl_4$ (1g, 0.5mol equivalents, "chlorogold(III) acid" see [16903-35-8]) in Me_2CO at 20°. The volume of the solution is reduced to *ca* 5ml and the complex that separates (1.2g, 83%) is collected and dried or crystallised as before [Burgess et al. *JCS, Dalton Trans* 1161 *1983*].
Alternatively, to the orange solution of sodium tetrachloroaurate(III).$2H_2O$ (1mmol, [13874-02-7]) dissolved in $2H_2O$, cooled in ice, is slowly added 2,2′-thiodiethanol {3mmol, i.e. bis(2-hydroxyethyl)sulfide [see 111-48-8]} at 0° during ~45 minutes, followed dropwise by a solution of the Ph_3P ligand (1mmol, or other PX_3 ligand) in EtOH which causes a white solid to separate. This is filtered off, washed with MeOH, and dried *in vacuo* (0.1mm) to give Ph_3PAuCl (or other PX_3AuCl) as a white solid in ~88% yield. It is recrystallised as described above. [Li et al. *J Org Chem* **73** 4323 *2008*,]. The ^{1}H NMR (400MHz, $CDCl_3$) has δ_H at 2.03-1.93 (m, 9H), 1.89-1.85 (m, 6H), 1.75-1.72 (m, 3H), 1.52-1.41 (m, 6H), 1.35-1.21 (m, 9H); the ^{31}P NMR (160MHz, $CDCl_3$) has δ_P at 57.12 (34.224ppm reported also at 300MHz, $CDCl_3$, from external H_3PO_4); and ^{13}C NMR (100MHz, $CDCl_3$) has δ_C at 33.28 (d, $^{1}J_{(^{13}C-^{31}P)}$ = 31Hz), 30/75, 26.96 (d, $^{2}J_{(^{13}C-^{31}P)}$ = 12.2Hz), 25.80 (d, $^{3}J_{(^{13}C-^{31}P)}$ = 1.5Hz), HRMS-ESI calc for $C_{20}H_{36}AuPNa$ (M^+ + MeCN-Cl): 518.2251, found: 518.2241. [Nieto-Oberhuber et al. *J Am Chem Soc* **127** 6168 *2005*, Al-Sa'Ady et al. *Inorg Synth* 191 *1985*, Li et al. *J Org Chem* **73** 4323 *2008*.] Its catalytic activities are similar to those of JohnPhos-AuCl above. It has also been used in the cyclisation of *O*-propargyl carbamates to alkylideneoxazolidiones at room temperature, *via* a 5-exo-digonal pathway [Ritter et al. *Synlett* 3309 *2006*]. It is soluble in Me_3CO, CH_2Cl_2, $CHCl_3$, $*C_6H_6$ and THF, but not in EtOH or hexane, and is used for the preparation of a variety of Ph_3PAu salts and cluster complexes. It is stable indefinitely in air, and note that ^{31}P NMR studies of Ph_3PAuCl showed no change in the chemical shift (at 33.8ppm in THF) after bubbling O_2 through the solution of 24 hours, indicating how stable it is compared with cationic Ph_3PAu^+ species in the presence of O_2 [Liu et al. *J Am Chem Soc* **128** 11332 *2006*]. X-Ray crystallography showed that the molecule of Ph_3PAuCl is linear with a P-Au-Cl angle of 179.68° and Au-P distance of 2.235Å [Baezinger et al. *Acta Cryst* **B32** 962 *1976*].

Chlorotris(triphenylphosphine)rhodium(I) (Wilkinson's catalyst) *[14694-95-2]* **M 925.2, m 138°(dec), 140°(dec), 157-158°(dec).** It is prepared by adding PPh_3 (12g, recrystallised from EtOH to remove any PPh_3O)

in hot EtOH (350ml) to $RhCl_3.3H_2O$ (2g) in 95% EtOH (70ml) in a flask purged with N_2, refluxed in the presence of N_2 for 2 hours, and the red solid that is formed is collected on a sintered glass funnel and washed with small volumes of dry Et_2O (50ml) to give the catalyst (6.25g, 88%). It forms dark burgundy crystals from hot EtOH after refluxing for 30 minutes. When the solution is heated for only 5 minutes, orange crystals are formed. Heating the orange crystals in EtOH yields red crystals. Crystallisation from Me_2CO gives the orange crystals. The dimorphic forms have similar IR spectra, but the X-ray diffraction patterns are slighly different. Excess of PPh_3 can be recovered by adding H_2O to the EtOH filtrates from recrystallisation and, collecting it after standing for 2-3 days. [Osborne et al. *J Chem Soc (A)* 1711 *1966*, Osborne & Wilkinson *Inorg Synth* **10** 67 *1967*, Bennett & Donaldson *Inorg Chem* **16** 655 *1977*.] The solubilities are as follows: in CH_2Cl_2 ~2% (25º), in toluene 0.2% (25º), and less soluble in Me_2CO, MeOH, BuOH and AcOH, but insoluble in petroleum ethers and cyclohexane. It reacts with donor solvents such as pyridine, DMSO and MeCN. Solutions of $RhCl[(PPh_3)_3]$ are air sensitive, absorb O_2, and as well as the solid should be stored under O_2-free N_2 or argon. On heating solutions in $*C_6H_6$, toluene or methyl ethyl ketone the chlorine-bridged *dimer* $[(PPh_3)_3RhCl_2Rh(PPh_3)_3]$ is formed as salmon-red crystals which absorb oxygen even in the solid state, but can be converted to the *monomer* in refluxing EtOH containing PPh_3. Red solution of $RhCl[(PPh_3)_3]$ absorb H_2 reversibly at 760mm/25º, become yellow in colour, and are effective in catalysing the reduction of C-C double bonds and triple bonds, often in a selective manner. [Osborn & Wilkinson *Inorg Synth* **28** 77 *1990*.] The stoichiometric and catalytic reactions of $RhCl[(PPh_3)_3]$ have been reviewed [Jardine *Prog Inorg Chem* **28** 63 *1981*]. In the presence of 1.5 mol of Et_2Zn, 1 mol of 4-phenylbut-3-ene-2-one (and related α-ene-ones) reacts with 1.7mol of CF_3Cl in THF at 5º to give 4-phenyl-3-(trifluoromethyl)butan-2-one (and related ketones) in moderate yields in the presence of catalytic amounts of $RhCl[(PPh_3)_3]$ (~0.02mol) [Sato, Omote, Ado and Kumadaki *Org Synth* **83** 177 *2006*].

Chromium (III) acetylacetonate [Cr(acac)$_3$] *[21679-31-2]* **M 349.3, m 212-216º, 216º, b 340º, pK^{25} 4.0 (see chromic chloride).** Purify it by dissolving 6g in hot $*C_6H_6$ (20ml) and adding petroleum ether (75ml) slowly. Cool to room temperature then chill on ice, filter off and dry in air to give 2.9g. It also crystallises from EtOH. It is soluble in heptane, $*C_6H_6$, toluene and pentane-2,4-dione at 20-40º. It forms a 1:2 complex with $CHCl_3$. [Fernelius & Blanch *Inorg Synth* **V** 130 *1957*, Steinbach & Burns *J Am Chem Soc* **80** 1839 *1958*, *Beilstein* **1** H 782, **1** II 836, **1** IV 3673.] $Cr(acac)_3$ catalyses the oxidation of methacrylic acid esters in the presence of H_2O_2 which provides a new route to pyruvic esters [Inoue et al. *Chem Lett (Jpn)* **18** 99 *1989*]. **TOXIC** — potential carcinogen.

Cobalt Oxazoline Palladacycles (COPs) are organocobalt-palladium complexes which catalyse the asymmetric rearrangements of non-chiral allylic trichloroacetamidates with very high enantiomeric selectivity (>90%) to provide chiral allylic amines [it is an aza-Claisen rearrangement, '***The Overman Rearrangement***' Overman & Carpenter *Org React* **66** *2005*, Kirsch, Overman and Watson *J Org Chem* **69** 8101 *2004*]; and in the presence of phenols stereospecific cross-coupling also occurs to provide chiral phenoxyallyl ethers with very high (>90%) enantiomeric selectivity [Kirsch, Overman and White *Org Lett* **9** 911 *2007*, Overman & Carpenter *Org React* **66** *2005*].

(*S*)-(+)-COP-OAc dimer catalyst {*S*(COP-OAc)$_2$; di-μ-acetobis[η^5-(*S*)-(*pR*)-2-(2′-(4′-methylethyl)-oxazolinyl)cyclopentadienyl, 1-*C*-3′-*N*)(η^4-tetraphenylcyclobutadiene)cobalt]dipalladium} *[222400-03-5]* **M 1512-2, m 189-194º (250-257º dec.), [α] $^{24}_{D}$ +942º (c 0.215, $CHCl_3$).** This COP is prepared in a Schlenk flask flushed with argon containing (η^5-(*S*)-2-(4'-methylethyl)-oxazolinylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt (9.6g, 16.2mmol, see 22240-02-4) in glacial acetic acid (96ml) to which is added palladium(II) acetate (3.6g, 16.2mmol, must be recrystallised from $*C_6H_6$), and the red solution is heated at 95º for 30 minutes when an orange precipitate separates. After cooling to ~25º, the solid is collected, washed with glacial acetic acid (50ml) and dried *in vacuo* to give almost analytically pure *S*-$(COP\text{-}Ac)_2$ (8.9g, 73%) as mustard coloured crystals. It has IR (thin film) with ν_{max} at 3061, 2961, 1583 (C=N), 1501, 1417 (acetate bridge), 1366, 1181, 1069 cm^{-1}; ^{1}H NMR (500MHz, $CDCl_3$) with δ_H at -0,01 (d, *J* = 6.6Hz, 3H, C*H*$_3$), 0.46 (d, *J* = 7.1Hz, 3H, C*H*$_3$), 1.72-1,81 (m, 1H, C*H*), 1.96 (s, 3H, C*H*$_3$), 2.98 (td, *J* = 9.0, 3.1Hz, 1H, C*H*), 3.36 (t, *J* = 9.0Hz, 1H, C*H*$_2$), 4.08 (dd, *J* = 8.6, 3.9Hz, 1H, C*H*$_2$), 4.23 (t, *J* = 2.4Hz, 1H, C*H*), 4.62 (d, *J* = 1.4Hz, 1H, C*H*), 4.68 (d, *J* = 2.0Hz, 1H,

C*H*), 7.20-7.29 (m, 12H, ArH), 7.64 (m, 8H, ArH); and the ^{13}C NMR (125MHz, $CDCl_3$) has δ_C at 13.3, 18.8, 24.2, 29.1, 65.0, 71.2, 76.2, 79.4, 85.0, 85.4, 86.8, 98.1, 126.2, 128.1, 129.5, 136.1, 170.8, and 180.9.

The **(*R*)-(-)-COP-OAc dimer enantiomer** *[849592-74-1]* **M 1512.2, m 241-251º dec.** is prepared in the same way but using the enantiomeric starting material. [Stevens & Richards *Organometallics* **18** 1346 *1999*, Anderson et al. *Org Synth* **84** 148 *2007*.] The reactions of trichloroacetimidate derivatives of *Z*-2-alken-1-ols with phenolic nucleophiles in the presence of chiral COP-OAc dimer catalysts yield 3-aryloxy-1-alkenes in high yield (63-90%) and high enantiomeric purity (90-97% ee); and are compatible with the presence of base-labile substituents in either reactant [Kirsch, Overman and White *Org Lett* **9** 911 *2007*].

(*S*)-(+)-COP-Cl dimer catalyst {*S*(COP-Cl)$_2$; di-μ-chlorobis[η^5-(*S*)-(*pR*)-2-(2′-(4′-methylethyl)-oxazolinyl)cyclopentadienyl, 1-*C*-3′-*N*)(η^4-tetraphenylcyclobutadiene)cobalt]dipalladium} *[581093-92-7]* **M 1464.98, m 204-205º, $[\alpha]_D^{20}$ +1201º (c 0.1, CH_2Cl_2).** It is obtained from the above *S*-(COP-OAc)$_2$ (8.9g, 5.9mmol) in acetone (59ml) by stirring vigorously at ~25º with aqueous NaCl (2M, 30ml) to give a homogeneous mixture until the reaction is complete (~4 hours, checked periodically by sampling a filtered aliquot and examining the ^{1}H NMR spectra). The yellow complex which separates is filtered off, washed with H_2O (125ml) then Me_2CO (20ml) and dried *in vacuo* to give almost pure (COP-Cl)$_2$ (8.2g, 95%) as a mustard coloured solid. It can be purified further by filtering a solution in CH_2Cl_2 through a short plug of Celite and eluting with CH_2Cl_2 to give an analytically pure orange solid (97% recovery) which exists as a 1.0:0.7 mixture of dimers. It has IR (thin film) with ν_{max} at 3061, 2961, 1602, 1502, 1370, 1185 cm^{-1}; the ^{1}H NMR (500MHz, $CDCl_3$) has δ_H at 0.70-0.74 (m, 6H, C*H*$_3$), 0.76 (d, *J* = 6.8Hz, 3H, C*H*$_3$), 0.80 (d, *J* = 7.0Hz, 3H, C*H*$_3$), 2.20-2.33 (m, 2H, C*H*), 3.03-3.15 (m, 2H, C*H*), 3.34 (t, *J* = 9.0Hz, 1H, *CH*$_2$), 3.43 (t, *J* = 8.9Hz, 1H, C*H*$_2$), 4.16-4.22 (m, 2H, C*H*$_2$), 4.28 (t, *J* = 2.5Hz, 1H, C*H*), 4.40 (t, *J* = 2.5Hz, 1H, C*H*), 4.70 (d, *J*= 2.0Hz, 1H, C*H*), 4.73 (d, *J* = 2.0Hz, 1H, C*H*), 4.98 (d, *J* = 1.5Hz, 1H, C*H*), 4.99 (d, *J* = 1.5Hz, 1H, C*H*), 7.16-7.22 (m, 12H, ArH), 7.23-7.30 (m, 12H, ArH), 7.58-7.62 (m, 8H, ArH), 7.66-7.71 (m, 8H, ArH); and the ^{13}C NMR (125MHz, $CDCl_3$) has δ_C at 14.3, 14.5, 19.0 (2C), 29.0, 29.2, 65.6, 66.0, 71.4, 71.5, 76.5, 76.8, 81.0, 84.2, 84.5, 84.8, 84.9, 85.7, 87.1, 98.6, 98.7, 126.4, 126.5, 128.2, 128.3, 129.4, 129.5, 135.5, 135.6, 171.1, 171.2. The enantiomeric purity was determined by conversion into the acetylacetonate derivative ***COP-acac*** (see below) and the enantiopurity was shown to be >99% by HPLC [Diacel Chiralpak AD-H (0.46cm x 25cm) column, with1.0ml/minute flow rate and eluted with 95:5 hexanes:*iso*-PrOH]. The retention time for *S*-COP-acac is 5.1 minutes whereas that of *R*-COP-acac would have been ~3.1 minutes [Anderson, Kirsch and Overman *Org Synth* **84** 148 *2007*.]

(*R*)-(-)-COP-Cl dimer catalyst {*R*(COP-Cl)$_2$; di-μ-chlorobis[η^5-(*R*)-(*pR*)-2-(2′-(4′-methylethyl)-oxazolinyl)cyclopentadienyl, 1-*C*-3'-*N*)(η^4-tetraphenylcyclobutadiene)cobalt]dipalladium} *[612065-00-6]* **M 1464.98, m 205-208º, $[\alpha]_D^{20}$ +1240º (c 0.1, CH_2Cl_2)** is obtained and purified as for its *S*-enantiomer above but using the *R*-enantiomeric intermediates. These planar chiral COP-Cl dimers catalyse the [3+3]-sigmatropic rearrangements of a wide range of non-chiral *E*-allylic trichloroacetim**idates** into the corresponding transposed chiral allylic trichloroact**amides** (from which the free base can be obtained) in high yields and very high enantioselectivities [Anderson & Overman *J Am Chem Soc* **125** 12412 *2003*, Anderson, Overman and Watson *Org Synth* **82** 134 *2005*]. The reactions of trichloroacetimidate derivatives of *Z*-2-alken-1-ols with phenolic nucleophiles in the presence of chiral COP-Cl dimer catalysts yield 3-aryloxy-1-alkenes in high yield (63-90%) and high enantiomeric purity (90-97% ee); and are compatible with the presence of base-labile substituents in either reactant [Kirsch, Overman and White *Org Lett* **9** 911 *2007*].

(*S*)-(+)-COP-acac monomer catalyst {acetylacetonato[η^5-(*S*)-(*pR*)-2-(2′-(4′-methylethyl)-oxazolinyl)cyclopentadien-yl,1-*C*-3′-*N*)-(η^4-tetraphenylcyclobutadiene)cobalt]palladium} *[805315-09-7]* **M 796.1, m 100-104º(dec.), $[\alpha]_D^{28}$ +246.1º, $[\alpha]_{577}^{28}$ +250.2º, $[\alpha]_{546}^{28}$ +175.5º, $[\alpha]_{435}^{28}$ -59.8º, $[\alpha]_{405}^{28}$ -91.4º (c 1.00, $CHCl_3$).** (*S*)-(+)-COP-acac is obtained as a monomer from the above dimer *S*-(COP-OAc)$_2$ (1.0g, 0.66mmol), sodium acetonylacetonate (954mg, 6.8mmol, see [15435-71-9]), Me_2CO (6.6ml) and H_2O (3.3ml) by stirring vigorously for 24 hours at ~25º. The mixture is then extracted with CH_2Cl_2 (10ml), the extract is separated, dried ($MgSO_4$), filtered and concentrated to give almost pure (*S*)-(+)-COP-acac (1.0g, quantitative) as an orange solid. It can be further purified by filtering through a silica-gel column and eluting with *iso*-PrOH:hexanes (5:95) and evaporating the orange band to give an analytically pure complex. See above *S*(COP-Cl)$_2$ for HPLC data; and it has R_F 0.59 (silica gel, hexanes-EtOAc, 80:20). It has IR (thin film) with ν_{max} at 3058, 2960, 1597, 1579, 1508,

1399, 1265, 1183, 1067 cm^{-1}; the ^1H NMR (400MHz, $CDCl_3$) has δ_H at 7.64 (d, *J*= 7.6Hz, 8H), 7.20-7.30 (m, 12H), 5.26 (s, 1H), 5.17 (s, 1H), 4.89 (d, *J* = 1.6Hz, 1H), 4.47 (s, 1H), 4.27 (dd, *J* = 8.4, 5.6Hz, 1H), 3.67 (t, *J* = 9.0Hz, 1H), 3.29-3.31 (m, 1H), 2.26-2.27 (m, 1H), 2.00 (s, 3H), 1.94 (s, 3H), 0.84 (d, *J* = 7.6Hz, 3H), 0.82 (d, *J* = 8.0Hz, 3H); and the ^{13}C NMR (100MHz, $CDCl_3$) has δ_C at 14.8, 18.6, 27.2, 27.6, 29.0, 65.1, 71.6, 76.0, 80.0, 85.1, 85.8, 86.3, 99.4, 126.0, 127.8, 128.1, 129.2, 136.0, 172.0, 184.9, 186.3. [Kirsch et al. *J Org Chem* **69** 8101 *2004*, Anderson, Kirsh and Overman *Org Synth* **84** 148 *2007*.].

The isomer **(*R*)-(-)-COP-acac monomer catalyst {acetylacetonato[η5-(*R*)-(*pR*)-2-(2′-(4′-methylethyl)-oxazolinyl)cyclopentadien-yl,1-*C*-3′-*N*)-(η4-tetraphenylcyclobutadiene)cobalt]palladium}** *[CASRN is the same as preceding S-(+)-enantiomer]* **M 796.1, m 100-104°(dec), $[\alpha]_D^{28}$ -246.1°, $[\alpha]_{577}^{28}$ -250.2°, $[\alpha]_{546}^{28}$ –175.5°, $[\alpha]_{435}^{28}$ +59.8°, $[\alpha]_{405}^{28}$ +91.4° (c 1.00, $CHCl_3$)** can be obtained and purified as for its *S*-enantiomer above but using the *R*-enantiomeric intermediates. These monomeric COPs catalyse the asymmetric rearrangements of non-chiral allylic trichloro-acetim**idates** into chiral transposed allylic trichloroact**amides** in good yield with high asymmetric induction (>90% ee). These are more soluble catalysts than the COP dimers, and because they are soluble in a much wider variety of solvents, the reactions can be carried out at high substrate concentration (e.g. at ~2.6M) [Kirsch et al. *J Org Chem* **69** 8101 *2004*]. The reactions of trichloroacetimidate derivatives of *Z*-2-alken-1-ols with phenolic nucleophiles in the presence of chiral COP-acac monomer catalysts yield 3-aryloxy-1-alkenes in high yield (63-90%) and high enantiomeric purity (90-97% ee); and are compatible with the presence of base-labile substituents in either reactant [Kirsch, Overman and White *Org Lett* **9** 911 *2007*].

(*S*)-(+)-COP-hfacac {hexafluoroacetylacetonato[η5-(*S*)-(*pR*)-2-(2′-(4′-methylethyl)oxazolinyl)-cyclopentadienyl, 1-*C*-3′-*N*)(η4-tetraphenylcyclobutadiene)cobalt]palladium} *[805315-08-6]* **M 904.0, m 108-110°(dec.) $[\alpha]_D^{28}$ +271.2°, $[\alpha]_{577}^{28}$ +277.6°, $[\alpha]_{546}^{28}$ +214.8°, $[\alpha]_{435}^{28}$ -57.7°, $[\alpha]_{405}^{28}$ -86.8° (c 1.02, $CHCl_3$).** (*S*)-(+)-COP-hfacac is obtained as a monomer from the above dimer *S*-$(COP\text{-}OAc)_2$ (1.0g, 0.66mmol), sodium hexafluoroacetonylacetonate (1.6g, 6.8mmol, see [22466-49-5]), Me_2CO (6.6ml) and H_2O (3.3ml) by stirring vigorously at ~25° for 9-11 hours (check periodically by sampling a filtered aliquot and examining the ^1H NMR spectra until completion). The solid that separates is filtered off, washed with H_2O (10-20ml) and dried *in vacuo* over P_2O_5 to give (*S*)-(+)-COP-hfacac monomer (1.1g, 91%). A pure sample can be obtained by filtration through a short plug of silica gel with CH_2Cl_2 as eluent (in an 89% yield). It has R_F 0.63 (silica gel, hexanes-EtOAc, 80:20). It has IR (thin film) with ν_{max} at 3061, 2964, 1629, 1598, 1509, 1475, 1258, 1208, 1150 cm^{-1}; the ^1H NMR (500MHz, $CDCl_3$) has δ_H at 7.54-7.56 (m, 8H, Ar*H*), 7.19-7.29 (m, 12H, Ar*H*), 5.95 (s, 1H, C*H*), 4.68 (d, *J* = 2.3Hz, 1H, C*H*), 4.90 (d, *J* = 2.3, 1H, C*H*), 4.53 (t, *J* = 2.3Hz, 1H, C*H*), 4.33 (*J* = 8.6, 5.3Hz, 1H, CH_2), 3.72 (t, *J*= 9.4Hz, 1H, CH_2), 3.45 (td, *J* = 9.4, 5.1Hz, 1H, C*H*), 2.05-2.08 (m, 1H, C*H*), 0.83 (d, *J* = 7.0Hz, 3H, CH_3), 0.79 (d, *J* = 6.9Hz, 3H, CH_3); and the ^{13}C NMR (125MHz, $CDCl_3$) has δ_C at 14.9, 18.4, 29.3, 65.3, 72.3, 76.7, 78.9, 84.1, 84.8, 87.7, 90.1, 97.6, 116.6, 118.8, 126.5, 127.9, 128.9, 135.5, 173.3, 173.6, 174.1. [Kirsch et al. *J Org Chem* **69** 8101 *2004*, Anderson et al. *Org Synth* **84** 148 *2007*.]

Enantiomer **(*R*)-(-)-COP-hfacac {hexafluoroacetylacetonato[η5-(*R*)-(*pR*)-2-(2′-(4′-methylethyl)-oxazolinyl)-cyclopentadienyl, 1-*C*-3′-*N*)(η4-tetraphenylcyclobutadiene)cobalt]palladium}** *[CASRN is the same as preceding S-(+)-enantiomer]* **M 904.0, m 108-110°(dec.) $[\alpha]_D^{28}$ -271.2°, $[\alpha]_{577}^{28}$ -277.6°, $[\alpha]_{546}^{28}$ –214.8°, $[\alpha]_{435}^{28}$ +57.7°, $[\alpha]_{405}^{28}$ +86.8° (c 1.02, $CHCl_3$)** can be obtained and purified as for its *S*-enantiomer above but using the *R*-enantiomeric intermediates. These COP-hfacac complexes, like the related COP-acac complexes, are monomeric and more soluble than the dimeric COPs above. They can be used in a variety of solvents, e.g. THF, MeCN, which allow catalytic asymmetric allylacetimidate rearrangements to be performed at high concentrations and using as little as 1 mole% of catalyst. [Anderson Kirsch and Overman *Org Synth* **84** 148 *2007*, Kirsch, Overman and Watson *J Org Chem* **69** 8101 *2004*]. The reactions of trichloroacetimidate derivatives of *Z*-2-alken-1-ols with phenolic nucleophiles in the presence of chiral COP-acac catalysts yield 3-aryloxy-1-alkenes in high yield (63-90%) and high enantiomeric purity (90-97% ee); and are compatible with the presence of base-labile substituents in either reactant [Kirsch, Overman and White *Org Lett* **9** 911 *2007*].

Copper(I) [1,3-bis(2,6-di-*iso*-propylphenyl)imidazol-2-ylidene] chloride [1,3-bis(2,6-di-*iso*-propyl-phenyl)imidazol-2-ylidene copper(I) chloride, (IPr)=CuCl] *[578743-87-0]* **M 487.59, m >300°.** This NHC (N-heterocyclic carbene) precatalyst is readily prepared in analytical purity in a Schlenk flask and under an argon atmosphere. Dry THF (100ml) is added to a mixture of freshly prepared Cu(I)Cl (1.0g, 10.1mmol), 1,3-bis(2,6-

di-*iso*-propylphenyl)imidazolinium chloride (4.29g, 10.1mmol, IPr.HCl see [250285-32-6]) and Na *tert*-butoxide (0.97g, 10.1mmol), and stirred mechanically under argon at ~25º for 20 hours. The mixture is then filtered through a plug of Celite, and the filtrate is evaporated *in vacuo* to give the complex as a white powder (4.59g, 9.40mmol, 94%), m >300º. Suitable crystals were grown from CH_2Cl_2/hexane solutions and subjected to single-crystal diffraction studies. The molecular structure was as expected with the imidazole C2, Cu and Cl atoms in the same plane, with the C2-Cu bond length of 1.953Å, the Cu-Cl bond length 2.089Å, and the C2—Cu—Cl angle of 180.00º, i.e. is linear. [Kaur et al. *Organometallics* **23** 1157 *1160*]. It has IR (neat on a DiComp probe) with ν_{max} at 2968, 2927, 2871, 1680, 1647, 1470, 1457, 809, 764, and 743 cm^{-1}; the ^1H NMR (500MHz, Me_2CO-d_6, downfield from TMS) has δ_H at 7.26 (s, 2H), 7.57-7.54 (dd, J = 15.5 and 8.0Hz, 2H), 7.43-7.41 (d, J = 8.0Hz, 4H), 2.70-2.65 (m, 4H), 1.32-1.31 (d, J = 7.0Hz, 12H), 1.27-1.25 (d, J = 6.5 Hz, 12H); the ^{13}CNMR (125MHz, $CDCl_3$ with 77.23 ppm of $CDCl_3$ reference) has δ_C at 180.2, 146.0, 135.1, 130.6, 124.2, 24.4 and 23.3; and the HRMS (EI, *m/z*) has: found 389.2962, and calculated for $C_{14}H_{16}O$: 389.2951 (M -CuCl) [Jurkauskas et al. *Org Lett* **5** 2417 *2003*.]

(IPr)=CuCl catalyses the conjugate reduction of α,β-unsaturated carbonyl compounds with catalytic amounts of the Cu complex, Na *tert*-BuO and poly(methylhydrosiloxane) as the stoichiometric reductant in >81% yields [Jurkauskas et al. *Org Lett* **5** 2417 *2003*], it catalyses the methenylation of a variety of aliphatic and aromatic aldehydes and ketones in the presence of trimethylsilyldiazomethane ($TMSCHN_2$), Ph_3P and 2-propanol efficiently, and is a cheaper alternative to the corresponding rhodium catalyst [LeBel et al. *J Org Chem* **72** 144 *2007*], it catalyses the efficient hydrosilylation of ketones with Et_3SiH to yield the corresponding saturated triethylsilylethers [Kaur et al. *Organometallics* **23** 1157 *1160*], it catalyses the transfer of the ':$CHCO_2Et$' group (from ethyl diazoacetate) to saturated and unsaturated substrates, e.g. olefins, amines or alcohols, in very high yields [Fructos et al. *J Am Chem Soc* **126** 10846 *2004*], and has been used for the total synthesis of (-)-Angelastin A by catalysing the aziridiylation (using TsN=IPh) [55962-05-5]) of a difficult rather electron-deficient cyclopentene intermediate [Trost & Dong *J Amer Chem Soc* **128** 6054 *2006*].

NOTE: More recently it has been shown that the above IPr=CuCl (IPrCuCl) and its 4,5-dihydro-derivative SIPrCuCl, are readily prepared by refluxing ~1.9-2.3mmol of 1,3-bis-(2,6-diisopropylphenyl)imidazolium chloride (IPrCl, see [250285-32-6]) or 1,3-bis-(2,6-diisopropylphenyl)imidazoliniuum chloride (SIPrCl, see [25278-25-0]) with Cu_2O (~1.4-1.5mmol, ~95% purity, *ca* 0.65 equivalents) for 24 hours, then excess of Cu_2O is removed to provide the following respective yields in the solvents indicated: IPrCuCl (78% from toluene, 88% conversion; 94% from H_2O with 96% conversion; 74% from dioxan) or SIPrCuCl (88% from toluene, 99% conversion; 72% from H_2O, 78% conversion). [Cazin and coworkers: Citadella et al. *Dalton Trans* **39** 4489 *2010*, Son and coworkers: Chun et al. *Organometallics* **29** 1518 *2010*].

Similarly the analogous **[1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene copper(I) chloride, [(IMes)=CuCl]]** and the ***4,5-dihydro derivative*** **[1,3-bis(2,4,6-trimethylphenyl)imidazolin-2-ylidene copper(I) chloride [(SIMes)=CuCl**, **S** is for saturated**]** can be prepared from the respective *IMesCl* an *SIMesCl* with 0.65 equivalents of Cu_2O by refluxing in toluene for 24 hours (in 86% and 71% yields respectively, with 100% conversion), and by refluxing in H_2O for 24 hours (in 98% and 99% yields respectively, with 100% conversion). [Cazin and coworkers: Citadella et al. *Dalton Trans* **39** 4489 *2010*]. These are generally slightly less catalytically specific than their IPr counter-parts because the latter have slightly greater steric hindrance.

Copper(I) bis-[1,3-bis(2,6-di-*iso*-propylphenyl)imidazol-2-ylidene] tetrafluoroborate [$(IPr)_2Cu^+$ BF_4^-] *[886061-48-9]* **M 927.5, m >300º.** This copper catalyst is prepared in an oven dried septum screw capped vial (in a glove box) by mixing tetrakis(acetonitrile)copper (I) tetrafluoroborate (186mg, 0.5mmol), IPr.Cl (157mg, 0.5mmol, see [250285-32-6]) and *ter*-BuONa (96mg, 1mmol), sealing, then injecting THF (10ml) and stirring outside the box at ~25º for 6 hours. The mixture is filtered through a plug of Celite (THF), and the Cu complex salt is precipitated by adding excess hexane, filtered off, and dried *in vacuo* to give the pure white *tetrafluoroborate* (452mg, 92%). It has ^1H NMR (400MHz, Me_2CO-d_6) with δ at 7.54 (t containing a singlet at 7.55, J = 7.5 Hz, 8H, *p*-C*H* + NC*H*), 7.25 (d, J = 7.5 Hz, 8H, *m*-C*H*), 2.40 (septet, J = 6.8Hz, 8H, C*H*$(CH_3)_2$), 1.04 (d, J = 6.8Hz, 24H, CH_3), 0.94 (d, J = 6.8Hz, 24H, CH_3); and its ^{13}CNMR (100MHz, $CDCl_3$) has δ at 177.4 (N-*C*-N), 145.0 (*C*H aromatic), 134.7 (*C* aromatic), 130.6 (*C* aromatic), 125.3 (=*C*H-N), 124.5 (*C*H aromatic), 28.6 (*C*H$(CH_3)_2$), 24.3 (*C*H_3), 24.2 (*C*H_3). The ***hexafluorophosphate salt*** is similarly prepared in 96% yield starting from tetrakis(acetonitrile)copper (I) hexafluorophosphate [64443-05-6]. The structure of these salts was shown by X-ray crystal analysis (crystals grown from CH_2Cl_2-methyl *tert*-butyl ether solution) to consist of two *N-heterocyclic carbenes* attached to one Cu atom.

These salts are air- and moisture- stable and are highly active catalysts for the hydroxysilylation of ketones with varying steric constraints, aldehydes and enolisable aldehydes, and esters in THF at ~25º, in the presence of Et_3SiH and *ter*-BuONa in >90% yields [Díez-González et al. *Organometallics* **25** 2355 *2006*].

Diacetato[*(R)*-(+)- and *(S)*-(–)- 2,2′-Bis(diphenylphospheno)-1,1′-binaphthyl]ruthenium(II) [*R*- and *S*-(BINAP)$_2$ Ru(II) (OAc)$_2$] *[(R) 132071-87-5*; *(S) 261948-85-0, 104713-03-3]* **M 841.8, m 185-187º(dec,), 186-188º(dec.), 188-190º(dec.), *R*- λ_{max} 335nm ($\Delta\varepsilon$/mol^{-1}.dcm^3.cm^{-1} +4.5) and λ_{max} 450nm ($\Delta\varepsilon$/mol^{-1}. dcm^3.cm^{-1} +2.5); *S*- λ_{max} 335nm ($\Delta\varepsilon$/mol^{-1}.dcm^3.cm^{-1} -4.5) and λ_{max} 450nm ($\Delta\varepsilon$/mol^{-1} dcm^3 cm^{-1} -2.5); (c 6.5 x 10^{-5} M, CH_2Cl_2).** Typically, the *S-enantiomer* is prepared in a Schlenk tube under dry argon, by dissolving (*S*)-BINAP (1.37g, 2.20mmol, see [76189-56-5]) and $[RuCl_2(COD)]_n$ (0.56g, 2.0mmol, calc based on monomer weight, see [50982-12-2]) in dry toluene (55ml) containing Et_2NH (1.2ml, 8.6mmol), and the brown suspension is refluxed with stirring for 12 hours. The clear reddish brown solution is cooled to ~25º, the solvent is removed *in vacuo* and the brown solid residue is dissolved in CH_2Cl_2 (40ml), filtered through a Celite pad and the filtrate is evaporated *in vacuo*. A solution of anhydrous NaOAc (0.88g, 11mmol) in *t*-BuOH (107ml) is added to the residue, stirred under reflux for 12 hours in an argon atmosphere, the solvent is removed *in vacuo* and the residue is extracted with absolute Et_2O (3 × 20ml) and evaporated again *in vacuo*. The brown residue is extracted several times with absolute EtOH (70ml total) and evaporated *in vacuo* to give a yellow-brown solid (1.58g) which is recrystallised from toluene (12ml)/hexane (30ml) mixture to afford purer complex (1.23g, 68% yield). This sample is pure enough for providing good catalytic activity for asymmetric hydrogenations. Analytical purity (to give 0.9g, 50%, 188-190º dec.) can be achieved by further recrystallisation from toluene (14ml)/hexane (13ml), and another amount (0.3g, 17%) can be recovered from the mother liquors by evaporation and recrystallisation of the residue (from 8ml of toluene and 10ml of hexane). Crystals of analytical material were subjected to Xray structure determination that gave the required absolute configuration of the complex, and the circular dichroism spectrum of it and its enantiomer were consistent with the Xray structure. It has IR (CH_2Cl_2) with ν_{max} at 1452, 1518 cm^{-1}; and ^{1}H NMR (400MHz, $CDCl_3$, TMS) with δ_H at 1.80 (s, 2 $OCOCH_3$), 6.47-7.84 (m, aromatic H); and $^{13}C\{^1H\}$ NMR (100MHz, $CDCl_3$, TMS) with δ at 23.5 ($OCOCH_3$), 125.2-138.3 (aromatic *C*), 188.8 ($OCOCH_3$). The *R-enantiomer* can be prepared and purified in the same way.

The enantiomers of this complex catalyse the asymmetric hydrogenation of pro-chiral ketones and olefins in high yields and ee values. [Ohta, Takaya and Noyori *Inorg Chem* **27** 566 *1988*, Kumbobyashi et al. *Synlett* 1055 *2001*.] RhBINAP complexes with ligands other than acetate, e.g. Cl_2, $*C_6H_6$, $(OCO\text{-}t\text{-}Bu)_2$, $(OCOCMe{=}CHMe)_2$ also catalyse asymmetric hydrogenations, isomerisations and asymmetric Heck reactions [Shimizu, Nagasaki and Saito *Tetrahedron* **61** 5405 *2005*.] An excellent asymmetric hydrogenation catalyst for α-(acylmino)acrylic acids to give the corresponding chiral α-aminoacylpropionic acids with high ee-ratios is **(*S*)-[(BINAP)Rh$^+$(OMe)$_2$] ClO_4^-**. It is obtained (together with norbornane) when a solution of ***(S)-[(BINAP)Rh$^+$(norbornadiene)] ClO_4^-*** in MeOH is exposed to H_2 at room temperature. Exactly 2mols are absorbed, and it is isolated as deep red prisms [whose ^{1}H NMR (CD_2Cl_2, TMS) has δ_H at 7,50 (m) and 6.82 (BINAP), 3.42 (s, CH_3O); and ^{31}PNMR (CD_3OD with 5% H_3PO_4 in CD_3OD as external standard) has δ at 53.1 (d, $J_{Rh\text{-}P}$ = 206Hz)]. It loses MeOH *in vacuo* to give an equally active catalyst. [Myashita et al. *J Am Chem Soc* **102** 7932 *1980*.]

Dichloro(1,5-cyclooctadiene)palladium(II) [Pd(COD)Cl$_2$] *[12107-56-1]* **M 285.5, m 210º (dec).** This air-stable catalyst can be prepared by adding 1,5-cyclooctadiene (3ml, 2.2mol, [111-78-4]) to a cooled and filtered solution of $PdCl_2$ (2.0g, 1 mol) and concentrated HCl (150ml, warm) in EtOH (150ml), whereby the yellow complex separates immediately. After keeping for 10 minutes the solid is filtered off, washed with Et_2O (3 x 30ml) and dried *in vacuo* (3.1g, 96%). The yellow powder is recrystallised by boiling in CH_2Cl_2 (200ml), and evaporating until the onset of crystals. ***Dibromo(1,5-cyclooctadiene)palladium(II) [Pd(COD)Br$_2$)]*** [12145-47-0] **M 374.4, m 213º (dec)**, is obtained from the dichloride and NaBr in Me_2CO, or as above from $PdCl_2$/HCl in the presence of NaBr before adding the diene. [Drew & Doyle *Inorg Synthesis,* Coll Vol **28** 348 *1990*, **13** 52 *1972*.] *Alternatively*, a solution of sodium chloropalladite tetrahydrate (2g) in MeOH (75ml) and the diene (2ml) can used, and the pale orange-yellow complex is collected after 1 hour and is recrystallised from glacial AcOH. **[Pd(COD)Br$_2$]** can also be prepared from the dichloride (0.45g) and LiBr (0.1g) in Me_2CO (20ml), boiled under

reflux for 2 hours, filtered and the filtrate is evaporated to dryness in a vacuum (15mm), the residue is washed with H_2O, dried (0.22g) and is recrystallised from AcOH (orange-red needles). [Chatt et al. *J Chem Soc* 3413 *1957*.] The *dichloro-complex* is sparingly soluble in cold EtOH and $*C_6H_6$, but is more soluble in hot $*C_6H_6$, $CHCl_3$, Me_2CO, MeEtCO, $(EtO)_2CO$, tetrahydrothiophene 1,1-dioxide (sulfolane) and nitrobenzene. It reacts with Me_2SO to form *Pd(II)Cl$_2$(Me$_2$SO)$_2$*. The IR (Nujol) has ν_{max} at 1489, 1419, 1337, 1088, 999, 867, 825, 794, 768 325 and 295 cm^{-1}; and the ^1H NMR ($CDCl_3$) has δ at 2.69 (CH_2 protons) and 6.32 (CH=CH protons). The *dibromo-complex* is similarly air-stable and has similar solubility in solvents, and its IR (Nujol) has ν_{max} at 1472, 1417, 1333, 1172, 1083, 992, 905, 864, 823, 787, 764, 678, 310, 265, 221, 213, 178 and 126 cm^{-1}; and the ^1H NMR ($CDCl_3$) has δ at 2.60 (CH_2 protons) and 6.32 (CH=CH protons). [*Beilstein* **5** IV 404.]

Dichloro(1,5-cyclooctadiene)platinum(II) [Pt(COD)Cl$_2$]* *[12080-32-9]* **M 374.2, m 220-278º (dec), 285º (dec).** The colourless air-stable dichloro-complex is obtained by adding 1,5-cyclooctadiene* (6ml) to a warm solution (75º) of hydrated chloroplatinic acid (5g) in AcOH (15ml), stirring, and cooling to ~25º then diluting with H_2O (50ml), and the black suspension is kept at ~25º for 1 hour. The black solid is collected, washed with H_2O (50ml), Et_2O (100ml), then suspended in CH_2Cl_2 (400ml), heated to boiling and kept at this temperature for 5 minutes. The solution is cooled, mixed with chromatographic grade silica gel (5g) and allowed to settle. The supernatant should be colourless, otherwise portions (~1g) of silica gel should be added until the supernatant is colourless. The solid is filtered off, washed with CH_2Cl_2 (2 x 50ml) and the combined CH_2Cl_2 solutions (~500ml) are evaporated until crystallisation (75ml) occurs. The hot CH_2Cl_2 solution is then poured into petroleum ether (b 60-70º) producing a fine white powder which is collected, washed with petroleum ether (50ml) and dried (2.55g, 80%). Recrystallisation in the same way (dissolving in boiling CH_2Cl_2 and evaporating till crystallisation sets in) yields white macroscopic crystals. It also crystallises from AcOH (charcoal) as white needles. Its solubilities in solvents are similar to those of Pd(COD)Cl_2 above, i.e. being insoluble in most organic solvents except boiling CH_2Cl_2, $CHCl_3$ and AcOH, and decomposes slowly in Me_2SO (cf related Pd compound above). Its IR (Nujol) has ν_{max} at 1334, 1179, 1333, 1009, 1083, 871, 834, and 782 cm^{-1}; and the ^1H NMR ($CDCl_3$) has δ at 2.71 (CH_2 protons) and 5.62 ($J_{Pt\text{-}H}$ = 65Hz, CH=CH protons). [Drew & Doyle *Inorg Synthesis,* Coll Vol **28** 346 *1990*, **13** 47 *1972*.]

Dibromo(1,5-cyclooctadiene)platinum(II) [Pt(COD)Br$_2$] *[12145-48-1]* **M 463.1, m 220-278º (dec)** can be obtained from sodium chloroplatinate hydrate (4g), diene (4ml) and LiBr (2g) in EtOH (80-100ml), kept at ~20º for 2 days, and the precipitate is crystallised from AcOH (charcoal) in pale yellow needles. It is slightly more soluble than the chloro-analogue in organic solvents. [Chatt et al. *J Chem Soc* 2496 *1957*, *Beilstein* **5** IV 404.]

* *Dichloro(1,3,5,7-cyclooctatetraene)Platinum(II)*, *dichloro(dicyclopentadiene)Platinum(II)* and *dichloro(2,5-norbornadiene)Platinum(II)* have been prepared successfully by this procedure and using the respective olefins.

Dichloro[(1,2,3,6,7,10,11,12-η□□ıdodecatriene-1,12-diyl]ruthenium(IV), [(dichloro-2,6,10-dodecatrienylene-ruthenium(IV)] *[12170-97-7]* **M 334.2, decomposes >200º with part melting at 220º.** This complex is much more stable than the corresponding Ni complex, and is prepared by bubbling butadiene for 7 hours through a solution of $RuCl_3$. $3H_2O$ (0.43g, [13815-94-6]) in 2-methoxyethanol (25ml) at 90º in a hot water bath. The deep red solution deposits yellow-brown prisms when cooled. These are filtered off and recrystallised from CH_2Cl_2/petroleum ether (b 40-60º) to give the analytically pure complex (0.30g, 54.5%) as orange crystals. The IR shows a medium intensity band at ν = 1522 cm^{-1} assigned to the *trans* C=C co-ordinated to the Ru atom; the ^1H NMR (60MHz, $CDCl_3$/TMS) has δ at ~5.4 (m, w = 65Hz, 6H, vinylic and non terminal allylic H), 4.9 (d, *J* = 7.5Hz, 2H, terminal allylic H), 3.76 (d, *J* = 11.2Hz, 2H, terminal allylic H), 3.1 (m, w = 20Hz, 4H, methylene H) and 2.37 (m, w = 35Hz, 4H, methylene H); and the measured molecular weight (osmometry in 1.45% $*C_6H_6$ solution) is 340. [Nicholson & Shaw *J Chem Soc (A)* 807 *1966*.] The ^1H NMR is consistent with a Ru atom enveloped by dodeca-2,6,10-triene and co-ordinated to the two terminal allylic double bonds, i.e. butadiene trimerised about the metal atom, and this structure is confirmed by an X-Ray determination. This showed that Ru is bipyramidal, with the Cl atoms at the apices of the pyramids with three co-ordinate bonds (to the allylic and the C6=C7 double bonds) in the central plane. [Lydon et al. *Proc Chem Soc* 421 *1964*].

The *dichloro-dodecatriene-ruthenium* complex is a highly efficient catalyst for the *one-pot* internal redox process that converts allylic alcohols (RC=C-C(OH) into carbonyl compounds (RC-C-C=O, ketones or aldehydes) in the presence of $CsCO_3$ under N_2 with high yields and turnover frequencies (TOF) in THF or H_2O [Cadierno et al. *Chem Commun* 232 *2004*, see also van der Drift et al. *J Organomet Chem* **650** 1 *2002*]. It is also an efficient catalyst for the de-protection of *N*-allylic and *N*-diallylic substrates (with ~3mol% of Ru) in aqueous solution at

90° under N_2 in very high yields (typically >95%) to give the free amine and propionaldehyde (allyl product); and can be carried out on a preparative scale [Cadierno et al. *Chem Commun* 4086 *2005*].

Dichloro(η^5-pentamethylcyclopentadienyl)iridium(III) dimer {di-μ-chloro-dichlorobis(η^5-pentamethylcyclopentadienyl)diiridium (III), [Rh(η^5-C_5Me_5)Cl_2]$_2$} *[12354-84-6]* **M 796.7, m >230°.** The complex is prepared by stirring $IrCl_3$. xH_2O (10g, 26mmol), pentamethylcyclopentadiene (5g, 36mmol, Cp′ see [4045-44-7]) and MeOH (300ml), purging the apparatus with N_2 for 5 minutes then refluxing the solution also under N_2 for 48 hours. After cooling to room temperature the orange crystals are filtered off in air through a glass sinter, the filtrate is concentrated *in vacuo* to ~50ml and cooled to give a second crop of crystals which are combined with the first crop, washed with Et_2O (3 x 50ml) and air dried. The *Ir-dimer* (10.7g, 85%) can be obtained as an orange microcrystalline solid in analytical purity by recrystallisation using the minimum volume of $CHCl_3$ to dissolve it, filtering off insoluble material if present, and adding slowly twice that volume of hexane. The complex is stable in air at room temperature without obvious decomposition for several years. It is soluble in chlorinated solvents, much less so in Me_2CO, EtOH or hydrocarbon solvents, but is somewhat soluble in H_2O. The halogen atoms undergo metathesis and can be replaced by PF_6 and MeCN to form complexes such as [Ir(η^5-C_5Me_5)$(NCMe)_3$] $[PF_6]_2$. Its reactions can be studied by following the ^{1}H NMR ($CDCl_3$) signal of the single C_5Me_5 resonance at δ 1.73s. [White et al. *Inorg Synth* **29** 229 *1992*.] The *Ir-dimer* directly catalyses the C3 alkylation of a variety of indoles using aliphatic and benzylic alcohols in >80% yields [Grigg et al. *Tetrahedron* **65** 4375 *2009*]. It is used as a precursor of N-3-substituted-*N*-1-pyrimidyl-imidazolinium-Ir-pentamethylcyclopentadiene which catalyses transfer hydrogenation from isoPrOH to ketones, e.g. cyclohexanone, and imines, e.g. benzylideneaniline, to form the respective alcohols and amines [Gnanamagri et al. *Organometallics* **28** 321 *2009*]. It has also been used as a precursor to efficient phosphine-free Ir-Cp′ chiral catalysts, e.g. with *N*-sulfonyl *S*,*S*-1,2-diphenylethylenediamine, for the hydrogenation of 2-substituted quinolines to produce chiral 2-substituted 1,2,3,4-tetrahydroquinolines in >90% yields with up to 99% ee [Li et al. *Org Lett* **20** 5265 *2008*].

Dichloro(η^5-pentamethylcyclopentadienyl)rhodium(III) dimer {di-μ-chloro-dichlorobis(η^5-pentamethylcyclopentadienyl)dirhodium (III), [Rh(η^5-C_5Me_5)Cl_2]$_2$} *[12354-85-7]* **M 618.1, m >230°.** The complex is readily prepared by stirring $RhCl_3$. $3H_2O$ (10g, 42mmol), pentamethylcyclopentadiene (6g, 44mmol, Cp′ see [4045-44-7]) and MeOH (300ml), purging the apparatus with N_2 for 5 minutes then refluxing the solution also under N_2 for 48 hours. After cooling to room temperature the dark red crystals are filtered off in air through a glass sinter, the filtrate is concentrated *in vacuo* to ~50ml and cooled to give a second crop of crystals which are combined with the first crop, washed with Et_2O (3 x 50ml) and air dried to give the *Rh-dimer* (11.25g, 95%). It can obtained in analytical purity by recrystallisation using the minimum volume of $CHCl_3$ to dissolve it, filtering off insoluble material if present, and adding slowly twice that volume of hexane. The complex is stable in air at room temperature without obvious decomposition for several years. It is soluble in chlorinated solvents, much less so in Me_2CO, EtOH or hydrocarbon solvents, but is somewhat soluble in H_2O. The halogen atoms undergo metathesis and can be replaced by PF_6 and MeCN to form complexes such as [Rh(η^5-C_5Me_5)$(NCMe)_3$][PF_6]$_2$. Its reractions can be studied by following the ^{1}H NMR ($CDCl_3$) signal of the single C_5Me_5 resonance at δ 1.60s. [White et al. *Inorg Synth* **29** 229 *1992*.] In the presence of base the rhodium dimer is a good catalyst for the hydrogenation of olefins [Gill et al. *J Chem Soc, Dalton Trans* 617 *1978*], for hydrosilylation of olefins [Millan et al. *J Mol Catal* **26** 89 *1984,* Millan et al. *J Chem Soc, Chem Commun* 673 *1981*], and for the disproportionation of aldehydes [Cook et al. *J Chem Soc, Dalton Trans* 2342 *1981*].

Dicobalt octacarbonyl (cobalt carbonyl) *[10210-68-1]* **M 341.9, m 51°, 51-52° (dec), d 1.87.** $Co_2(CO)_8$ has been identified as the cobalt catalyst in hydroformylation, hydrogenation and homologation reactions involving H_2 and CO (synthesis gas). The earlier preparation [Glimont & Blanchard *Inog Synth* **2** 238 *1946*] has been improved due to the availability of steel pressure vessels and CO under pressure. Thus Raney Co (4 to 6g) was placed with Et_2O (145ml) under CO at 3200psi in a steel pressure bomb and heated with shaking for 5 or 6 hours at 150°. The pressure during the heating process dropped from 4900 to 4300psi and then to 2200psi when the bomb was cooled to ~25°. The insoluble material was removed by centrifugation, and the reddish-brown clear solution (160ml, which includes washings and transfers) contained 8.9g of $Co_2(CO)_8$. It is kept in a closed pressure-adjusted Pyrex bottle and aliquots siphoned as required because it decomposes slowly to liberate CO in an open vessel and should be stored in the cold. The solubility of the catalyst in Et_2O at ambient temperture is 7.5g per 100ml of solution. Cobalt on Kieselguhr "Co-100 powder" which contains 12 to 15% of Co can be substituted for Raney Co. [Adkins & Kresk *J Am Chem Soc* **70** 383 *1948*.] The above preparation can also be

carried out in $^*C_6H_6$ which has the advantage of being less volatile than Et_2O, and in which reactions could be carried out at lower temperatures. It has been kept at a concentration of 1.0 x 10^{-2} M in 50ml of $^*C_6H_6$. [Adkins & Kresk *J Am Chem Soc* **71** 3051 *1949*.] It forms orange-brown *air-sensitive* crystals on recrystallisation from *n*-hexane under a carbon monoxide atmosphere. It has been sublimed *in vacuo* (orange platelets*)*, and is available commercially as a solid moistened with 5-10% of hexane. It is insoluble in H_2O, but soluble in organic solvents such as alcohols, Et_2O, $^*C_6H_6$, CS, slowly decomposed by HCl, and H_2SO_4, but more rapidly by HNO_3. [Wender et al. *J Am Chem Soc* **71** 4160 *1949*, Ojima et al. *J Am Chem Soc* **109** 7714 *1987*; see also Hileman in *Preparative Inorganic Reactions,* Ed. Jolly, Vol **1** p 101 1987].
Carbon monoxide is **VERY POISONOUS** as it complexes with haemoglobin. Great care should be exercised when using the catalyst as well as CO, and all operations should be carried out in an efficient fume cupboard. The **TOXIC LEVEL** of CO is 50ppm (~55mg/m^3). **The ANTIDOTE should be at hand and always available in laboratories using CO; and staff should be trained to administer it.** On completion of reactions the autoclave should be filled with H_2 at 1000-1300psi and heated at 110-135^o for 45 minutes where cobalt compounds are transformed to the metal. If the product of reaction does not contain oxidisable compounds, the mixture is heated in air on a steam bath when copious evolution of CO occurs and the metal is deposited as a cobalt mirror. A third procedure to decompose $Co_2(CO)_8$ and related CO compounds is to shake or stir the mixture with dilute H_2SO_4 until evolution of gas ceases. [Wender et al. *J Am Chem Soc* **72** 4375 *1950*.]

2,6-Di-*iso*-propylphenylimino-neophylidene[(*S*)-(-)-BIPHEN]molybdenum(VI) {(*S*)-Schrock-Hoveyda Catalyst; Mo(*N*-2,6-di-*iso*-$Pr_2C_6H_3$)(CHCMe$_2$Ph)(*syn*-(*S*)(-)-*tert*-Bu_2Me_4(BIPHEN); molybdenum, [(*S- or R-)* 3,3′-bis(1,1′-dimethylethyl)-5,5′,6,6′-tetramethyl[1,1′-biphenyl]-2,2′-diolato(2-)-κO,κO′][2,6-bis(1-methylethyl)benzenaminato(2-)](2-methyl-2-phenylpropylidene)- } *[S- 205815-80-1; R- 329735-77-5; RS-300344-02-9]* **M 755.9.** The key intermediate is ***2,6-di-iso-propylphenylimino-neophylidene-bistriflate-dimethoxyethane-molybdenum (VI) complex*** {*molybdenum, [2,6-bis(1-methylethyl)benzenaminato(2-)][1,2-dimethoxy-κO)ethane][2-methyl-2-phenylpropylidene)bis(1,1,1-trifluoromethanesulfonato-κO)-*; [Mo(=N-2,6-isoPr$_2$C$_6$H$_3$)(=CHMePh)-(OTf)$_2$-DME] *[126949-63-1]* which is prepared in three steps. ***Firstly*** (preferred method): A solution of $MoO_2Cl_2(THF)_2$ (10.2g, 29.0mmol, see [13637-68-8, *556907-19-8; 12081-12-8*]**)** in DME (200ml) at -30^o is stirred vigorously while the following are added sequentially (i) a solution of 2,6-lutidine (12.4g, 116mmol) in DME (10ml at -30^o**)** during 3-5 minutes, (ii) a solution of Me_3SiCl (31.5g, 290mmol, see [75-77-4]) in DME (40ml, at -30^o**)** over a period of 3-5 minutes, and (iii) a solution of 2,6-di-*iso*-propylaniline (10.3g, 58mmol, see [24544-04-5]**)** in DME **(**15ml at -30^o**)** during 15 minutes. The colour of the solution alters from pale yellow to bright red-orange to deep red-orange as a solid separated. The mixture is stirred as it warmed to room temperature during 6 hours. The mixture is then heated to 50^o for 5 hours, filtered through Celite, to remove 2,6-lutidine hydrochloride, which is washed with Et_2O until the washings are clear; all filtrates are combined and evaporated *in vacuo* to give *bis(2,6-di-iso-propylphenylimino)dichloro-dimethoxyethane molybdenum* [Mo(=N-2,6-isoPr$_2$C$_6$H$_3$)$_2$Cl$_2$DME] (16.7g, 27.5 mmol, 95%) as a brick red solid which is almost of analytical purity (elemental C, H, N and Cl for $MoC_{28}H_{44}Cl_2N_2O_2$), and used in the next step. Its ^{1}H NMR (400MHz, C_6D_6, TMS) has δ at 7.01 (d, 4, arom H_m), 6.89 (t, 2, arom H_p), 4.29 (sept, 4, C***H***Me$_2$), 3.44 (s, 6, ***Me***OCH$_2$CH$_2$O***Me***), 3.18 (s, 4, MeOC***H***$_2$C***H***$_2$OMe), 1.25 (d, 24, CH***Me***$_2$) and the ^{13}C NMR (100MHz, C_6D_6, TMS) has δ at 154.1 (arom C_{ipso}), 145.5 (arom C_p), 128.0 (arom C_m), 123.9 (arom C_o), 71.3 (***Me***OCH$_2$CH$_2$O***Me***), 62.8 (MeO***C***H$_2$***C***H$_2$OMe), 28.2 (***C***HMe$_2$), 25.2 (CH***Me***$_2$). ***Secondly*****:** Neophyl magnesium chloride (100ml, 0.5M, 50mmol, see [35293-35-7]) in Et_2O is added dropwise to a stirred solution of the preceding complex [Mo(=N-2,6-isoPr$_2$C$_6$H$_3$)$_2$Cl$_2$DME] (15.1g, 25mmol) in Et_2O (250ml) at -30^o (all the complex need not have dissolved). The colour of the solution alters from red to orange as $MgCl_2$ separates, the mixture is allowed to thaw to 25^o and is stirred at this temperature for 3 hours. The mixture is filtered through Celite, the filtrate is concentrated *in vacuo*, kept at -40^o to provide orange crystals (usually three crops) of almost analytically pure (elemental C, H and N for $MoC_{44}H_{60}N_2$) *bis(2,6-di-iso-propylphenylimino)-bis(neophyl) molybdenum* [Mo(=N-2,6-isoPr$_2$C$_6$H$_3$)$_2$(-CH$_2$C Me$_2$Ph)$_2$] (14.3g, 80%). Its ^{1}H NMR (400MHz, C_6D_6, TMS) has δ at 7.45 (d, 4H, aromatic), 7.24 (t, 4H, aromatic), 7.10 (t, 2H, aromatic), 7.00-6.92 (m, 6H, aromatic), 3.65 (sept, 4H, C***H***Me$_2$), 1.72 (s, 4H, C***H***$_2$CMe$_2$Ph), 1.49 (s, 12H, CH$_2$C***Me***$_2$Ph), 1.11 (d, 24H, CH***Me***$_2$) and the ^{13}C NMR (100MHz, C_6D_6, TMS) has δ at 153.3, 142.7, 128.6, 126.8, 126.4, 126.0, 123.2, 78.6, 39.5, 32.0, 27.9, 23.5. ***Thirdly*****:** A solution of triflic acid (4.42g, 29.45mmol) in DME (15ml) is added slowly to an orange solution of the preceding

Mo (=N-2,6-isoPr$_2$C$_6$H$_3$)$_2$(-CH$_2$C Me$_2$Ph)$_2$ (14.2g, 20mmol) in DME (150ml) at -30º, then allowed to thaw to ~25º, stirred overnight, and the deep yellow solution is evaporated to dryness *in vacuo*. The yellow residue is extracted with chilled (~0º) toluene (100ml), filtered, evaporated *in vacuo*, and the dark yellow residue is recrystallised from Et$_2$O to provide the desired almost analytically pure (elemental C, H, and N for MoC$_{28}$H$_{39}$F$_6$NO$_8$S$_2$) key intermediate *2,6-di-iso-propylphenylimino-neophylidene-bis(triflate)-dimethoxyethane molybdenum(IV) complex* [Mo(=N-2,6-isoPr$_2$C$_6$H$_3$)(=CHMePh)(OTf)$_2$DME] (5.94g, 76%, in three crops). Its ^{1}H NMR (400MHz, C$_6$D$_6$, TMS) has δ at 14.45 (s, 1H, C***H***CMe$_2$Ph), 7.57 (d, 2H, aromatic), 7.18 (t, 2H, aromatic), 6.97-6.89 (m, 4H, aromatic), 3.84 (sept, 2H, C***H***Me$_2$), 3.73 (s, 3H, OC***H***$_3$), 3.18 (M, 2H, OC***H***$_2$), 2.84-2.78 (m, 5H, OC***H***$_3$, OC***H***$_2$), 1.91 (s, 6H, CHC***Me***$_2$Ph), 1.37 (d, 6H, CH***Me***$_2$), 1.21 (d, 6H, CH***Me***$_2$) and the ^{13}C NMR (100MHz, C$_6$D$_6$, TMS) has δ at 328.4, 152.1, 151.8, 148.7, 130.6, 128.7, 126.6, 124.3, 72.8, 70.0, 65.7, 61.9, 58.8, 31.1, 28.3, 25.6, 22.8. [Schrock et al. *J Am Chem Soc* **112** 3875 *1990*.]

The **Schrock-Hoveyda** catalyst is prepared in a glove box or in Schlenk equipment under an argon or N$_2$ atmosphere by adding solid KH (360mg, 9mmol, 3 equivalents) in portions to a stirred solution of H$_2$[*S*-BIPHEN] (1.06g, 3mmol, see [*R*- 329735-68-4, *S*- 205927-03-3, *RS*- 101203-31-0] in Part 2) in THF (100ml), whereby H$_2$ gas evolves while the K$_2$[BIPHEN] salt is being formed. After stirring for 18 hours at ~25º, the suspension is filtered through Celite to remove excees of KH, and the key intermediate above [Mo(=N-2,6-isoPr$_2$C$_6$H$_3$)(=CHMePh)(OTf)$_2$DME] (2.24g, 2.83mmol, 0.94 equivalents) is added as a solid during 2 minutes. The mixture is stirred for 3 hours at ~25º, the volatiles are removed *in vacuo*, and the residual red powder is treated with *C$_6$H$_6$ (40ml), and the slurry is filtered through Celite to remove insoluble CF$_3$SO$_3$K and washed with *C$_6$H$_6$ until the washings are no longer red in colour. The red *C$_6$H$_6$ solutions are combined, evaporated *in vacuo*, and the spongy red solid is recrystallised from Et$_2$O (~4ml) to give the desired catalyst, mainly in the *syn* configuration at the alkylidene group, as dark orange red crystals (1.35g, 64%). Its ^{1}H NMR (400MHz, *C$_6$D$_6$, TMS) has δ at 10.98 (s, 1H, J_{CH} = 123Hz, *syn* alkylidene C=C***H***CMe$_2$Ph), 7.42 (m, 3H, biphenyl and Ph C***H***s), 7.16 (m, 3H, biphenyl and Ph C***H***s), 7.05 (br t, J = 7.6Hz, 1H, aromatic), 6.92 (s, 3H, aromatic), 3.70 (heptet, J = 7.0Hz, 2H, *iso*-C***H***Me$_2$), 2.13 (s, 3H), 2.15 (s, 3H), 1.85 (s, 3H), 1.74 (s, 3H), 1.66 (s, 3H) {these signals 2.13—1.66 ppm are from 4 biphenyl-***Me***s and one methyl from C***Me***MePh}, 1.59 (s, 9H, *tert*-C***Me***$_3$), 1.54 (s, 9H, *tert*-C***Me***$_3$), 1.14 (d, J = 7.0Hz, 6H, *iso*-CH***Me***$_2$), 1.13 (s, 3H, CMe***Me***Ph), 0.90 (d, J = 7.0Hz, 6H, *iso*-CH***Me***$_2$), and the ^{13}C{^{1}H} NMR (100MHz, C$_6$D$_6$, TMS) has δ at 277.1 (d, J_{CH} = 123Hz, *syn* alkylidene carbon), 155.4, 154.5, 154.3, 151.3, 146.8, 140.0, 138.0, 136.5, 135.7, 132.0, 131.1, 130.9, 130.6, 129.6, 128.2, 127.9, 126.3, 123.8, 53.7, 35.95, 35.7, 34.7, 33.1, 33.0, 30.9, 30.4, 29.2, 24.6, 23.0, 20.8, 20.7, 17.2, 16.7, 14.6. [Alexander et al. *J Am Chem Soc* **120** 4041 *1998*.] See also a slightly modified preparation in which the red spongy powder is dissolved in Et$_2$O (18ml), transferred to a 20ml vial, kept uncapped in a well purged glovebox (with N$_2$) until the volume decreased to 5ml, the red solution is decanted from the red crystal blocks which were washed with cold Et$_2$O and dried *in vacuo* to provide a 72% yield of analytically pure (elemental C, H, and N for MoC$_{46}$H$_{61}$NO$_2$) *syn*-(*S*)-catalyst. The X-ray crystal structure proved the absolute configuration of the biphenolate ligand. Related complexes in which the 2,6-di-*iso*-propylphenylimino ligand is replaced by various other ligands have been similarly prepared. [Alexander et al. *Organometallics* **19** 3700 *2000*.] Schrock-Hoveyda catalysts with *R*-BIPHEN and *racemic*-BIPHEN also form red crystals, and have been similarly prepared. All are *air and moisture sensitive, and have to be stored cold and in the dark*. NMR data revealed that the *syn*-alkylidene conformer predominates in solution with a *syn-anti* exchange rate of ~1 s^{-1}. However, evidence from ROM (ring-opening metathesis) polymerisation suggests that reactions with the *anti* conformer are catalytically more active than with the *syn* conformer by some orders of magnitude [Oskam & Schrock *J Am Chem Soc* **115** 11831 *1993*].

The related catalyst where the *tert*-buyl groups in the biphenol ligand are replaced by 1-adamantyl groups **Mo(*N*-2,6-di-*iso*-Pr$_2$C$_6$H$_3$)(CHCMe$_2$Ph)(*syn*-(*S*)(-)-*tert*-Bu$_2$Me$_4$(BIAD))** has been prepared in 54% yield as orange crystals from the above key intermediate [Mo(=N-2,6-isoPr$_2$C$_6$H$_3$)(=CHMePh)(OTf)$_2$DME] and (*S*)-H$_2$(BIAD) (see in Part 2) except that benzylpotassium was used instead of KH to prepare the phenolate salt. X-ray crystallography of the catalyst also confirmed the *S*-absolute configuration of (-)-H$_2$(BIAD). [Alexander et al. *Organometallics* **19** 3700 *2000*; and for the X-ray chrystallographic structures of related Mo-2,2′-dihydroxy-1,1′-

biaryls see Totland et al. *Macromolecules* **29** 6114 *1996*.]
These and related chiral molybdenum complexes are remarkable catalysts that effect efficient asymmetric enantioselective ring-closing olefin metathesis (RCM) [Alexander et al. *J Am Chem Soc* **120** 4041 *1998*, Weatherhead et al. *Tetrahedron Lett* **41** 9553 *2000*], ring-opening metathesis/cross metathesesis (ROM/CM) [La et al. *J Am Chem Soc* **123** 7767 *2001*], as well as ring-opening olefin metathesis (ROM) polymerisation [Totland et al. *Macromolecules* **29** 6114 *1996*] reactions. These complexes catalyse olefin metathesis reactions in which the starting olefin is a racemic mixture, and in the reaction process *kinetic resolution* occurs, whereby the products, and any unreacted starting material, are of one chirality, i.e. the asymmetric centre in the racemic mixture is converted into one enantiomer at the expense of the other enantiomer. The above Mo-(*S*)-[BIPHEN] complex also catalyses efficient and enantioselective *desymmetrisation* reactions, e.g. (±)-3-allyloxy-2,4-dimethylpenta-1,4-diene and its 1,5-dimethyl derivative (4-allyloxy-3,5-dimethyl-hepta-2,5-diene) are cyclised to 2-(prop-2′en-2′yl)-3(*R*)-methyl-2,5-dihydrofuran and 2-(but-2-en-2-yl)-3(*R*)-methyl-2,5-dihydro-furan in the absence of solvent, 1-2 mol% catalyst, at 22° in 5 minutes in 85% and 93% yields, and 93%ee and 99%ee respectively [La et al. *J Am Chem Soc* **120** 9720 *1998*]. [For a review on olefin metathesis see Grubbs *Tetrahedron* **60** 7117 *2004*, and R.H. Grubbs (Ed.), *Handbook of Metathesis*, Vols 1-3, Wiley-VCH, *2003*. ISBN 3527306161.]

Ferric (III) acetylacetonate [Fe(acac)$_3$, iron(III) tris(2,4-pentadionate)] *[14024-18-1]* **M 353.2, m 181.3-182.3°**. When recrystallised twice from *benzene/petroleum ether, it has **m** 181.3-182.3° corr [Finn et al. *J Chem Soc* 1256 *1938*]. However, when recrystallised from EtOH or Et_2O it has **m** 179° [Hantzsch & Desch *Justus Liebigs Ann Chem* **323** 13 *1902*]. Recrystallisation from absolute EtOH also gives material with **m** 159.5° [Emmert & Jacob *Chem Ber* **67** 286 *1934*]. Dry it for 1 hour at 120°. [*Beilstein* **1** I 404, **1** II 836, **1** IV 3675.]
$Fe(acac)_3$ catalyses a large variety of chemical reactions such as aromatic substitution, cross-coupling, Friedel-Crafts etc [see B. Pleitker (ed), *Iron Catalysis in Organic Chemistry* Wiley-VCH, *2008*, ISBN 978-3-527-31927].

Ferrous (II) acetylacetonate [Fe(acac)$_2$, iron(II) bis(2,4-pentadionate)] *[14024-17-0]* **M 254.1, m 175°.** For catalytic properties see B. Pleitker (ed), *Iron Catalysis in Organic Chemistry* Wiley-VCH, *2008*, ISBN 978-3-527-31927, and for the preparation see Chapter 5, Metal-Organic Compounds. [*Beilstein* **1** III 3122, **1** IV 3676]

Iridium(I) bis(1,5-cyclooctadiene) tetrafluoroborate complex [bis(1,5-cyclooctadiene)iridium (I) tetrafluoroborate, Ir(COD)$_2^+$.BF$_4^-$] *[35138-23-9]* **M 495.4, m ~190° (dec).** This iridium complex is prepared and purified exactly as for the corresponding $Rh(COD)_2^+.BF_4^-$ [35138-22-8, below] from the dimer {$[Ir(COD)Cl]_2$ [12112-67-3] below, Herde et al. *Inorg Synth* **15** 18 *1974*]} with COD and $AgBF_4$ in 93% yield. [Schenck et al. *Inorg Chem* **24** 2334 *1985*.]

Iridium(I) chloride 1,5-cyclooctadiene complex dimer {chloro(1,5-cyclooctadiene)iridium dimer, di-μ-chlorobis[(1,2,5,6-η)-1,5-cyclooctadiene]diiridium (I), [Ir(COD)Cl]$_2$} *[12112-67-3]* **M 671.7, m 205°(dec).**
The complex is an orange-red, air-stable solid that is soluble in $*C_6H_6$ and $CHCl_3$, less so in Me_2CO and insoluble in Et_2O. It can be prepared from $IrCl_3.3H_2O$ (3g) in 95% EtOH (34ml), H_2O (17ml) and cycloocta-1,5-diene (6ml), through which is bubbled (with magnetic stirring) a slow stream of N_2 while boiling under reflux for 24 hours, during which time a brick-red product precipitates. The mixture is cooled and $Ir(COD)Cl]_2$ is filtered off, washed with ice-cold MeOH to remove unreacted COD and dried *in vacuo* at 25° for 8 hour (yield 1.5g, 72%, decomp >200°). [Herde et al. *Inorg Synth* **15** 18 *1974*.] *Alternatively*, to a mixture of H_2O (100ml), isoPrOH (35ml) and 1,5-cyclooctadiene (18ml) is added $(NH_4)_2IrCl_6$ (20g), and the mixture is refluxed under N_2 for 18 hours when the colour changes to orange-red, and a red or orange solid separated on cooling. This is filtered off (frit), and washed with EtOH (2 x 5ml at 0°) to give the complex in high purity (14.0g, 92%). Recrystallisation (if required) is best carried out by slowly adding an equal volume of EtOH to a saturated stirred solution of the solid in CH_2Cl_2, followed by gentle removal of half of the mixed solvent under reduced pressure. The stirred solution is cooled spontaneously to -30° during the process and the complex is filtered off, washed with EtOH (2 x 5ml at 0°) and dried *in vacuo*. It is identified by the characteristic IR bands (Nujol) at 907, 970, 980 and 1002 cm^{-1}; and the vinyl CH resonance in the ^{1}H NMR ($CDCl_3$) spectrum at δ 4.3. [Crabtree et al. *Synth React Inorg Met-Org Chem* **12** 407 *1982*.]
It is the metal complex precursor with allyamines for asymmetric allylic substitutions; for resting state and kinetic studies [cf Markovic & Hartwig *J Am Chem Soc* **129** 11680 *2007*].

Iridium(I) (1,5-cyclooctadiene)-η^5-(indenyl) {(1,5-cyclooctadiene)-η^5-(indenyl)iridium (I), [(COD)(C_9H_7)Ir(I)], [(Ind)Ir(I) (COD)]} *[102525-11-1]* **M 414.5, m 126-131°.** The complex is obtained by adding solid indenyllithium (0.73g, 5.98mmol) to a solution of the preceding dimer $[Ir(COD)Cl]_2$ (2.0g, 2.98mmol) in THF (50ml) and stirring at ~20° for 1 hour. The solvent is removed *in vacuo*, extracted with pentane (6 x 50ml) and the combined extracts are slowly evaporated to deposit pale yellow crystals (2.15g, 86%). It has ^{1}H NMR (200MHz) with δ at 1.65-1.86 (m, 8H, COD C*H*$_2$), 3.99 (m, 4H, COD C*H*), 5.00 (d, 2H, indenyl H1/H3), 5.76 (t, 1H, indenyl H2), 6.98-7.16 (m, 4H, indenyl H4-H7); and ^{13}C NMR (50MHz) with δ at 34.36 (COD *C*H$_2$), 51.35 (COD *C*H), 72.80 (indenyl C1/C3), 85.15 (indenyl C2), 110.23 (indenyl C8/C9), 121.75 and 124.89 (indenyl C4-C7). [Merola & Kacmarcik *Oganometallics* **8** 778 *1989*, Abad *Inorg Chim Acta* **121** 213 *1986*, Crabtree et al. *Synth React Inorg Met-Org Chem* **12** 407 *1982*, Naderer Siebel *Organomet Chem* **518** 181 *1996*.] [Uson & Oro *Inorg Synth* **23** 126 *1985*.]

[(Ind)Ir(I) (COD)] is a powerful C-H activation catalyst for preparing phenols from arenes in the presence of pinacolborane and bis(diphenylphosphino)ethane that borylate arenes to the intermediate pinacol arylboryl esters which are then converted to the respective phenols by reaction with *oxone* [$2KHSO_5.KHSO_4.K_2SO_4$] in Me_2CO at 25° within ~7 minutes in 51 to 88% yields depending on the substituents [Maleczka et al. *J Am Chem Soc* **125** 7792 *2003*.]

Iridium(I) μ-chloro-bis(cyclooctene) dimer {di-μ-chlorotetrakis(cyclooctene)diiridium(I), $[Ir(COE)_2Cl]_2$} *[12246-51-4]* **M 967.2, m 150°(dec).** This solid yellow iridium complex is air sensitive and decomposes to a dark green solid which eventually turns black. However, it can be stored *in vacuo* in a desiccator for prolonged periods of time. It is preferable to store it in aliquots in sealed ampoules under an inert atmosphere or in a vacuum. It is soluble in Me_2CO, $CHCl_3$ and $*C_6H_6$, but it oxidises more readily in solution than in the solid state, and the necessary precautions to strictly exclude air should be exercised.

It is prepared by stirring (stirrer bar) a mixture $IrCl_3.3H_2O$ (2.0g), *iso*-propanol (22ml), H_2O (8ml) and cyclooctene (40ml), while a slow stream of dry N_2 is bubbled through the solution, and refluxed at 78° for 3 hours. During this time the colour of the solution changes from dark red to orange-yellow and the complex separates from the solution which is cooled to ~25°. It is collected rapidy by filtration, washed rapidly with ice-cold MeOH to remove excess of cyclohexene (this is done preferably in a dry box under N_2). Drying *in vacuo* at 25° for 4 hours gives pure di-μ-chlorotetrakis(cyclooctene)diiridium(I) (1.5g, 59%), which decomposes at 150° and has the correct elemental analysis for C, H, Cl and Ir. [Herde et al. *Inorg Synth* **15** 18 *1974*, Herde & Senoff *Inorg Nucl Chem Lett* **7** 1029 *1971*.] By using $(NH_4)_3IrCl_6$ (6g) suspended in an oxygen-free suspension of *iso*-PrOH (30ml) and H_2O (90ml), and cyclooctene (12ml), and refluxing with stirring for 3-4 hours under N_2, followed by cooling, provides an orange oil which solidifies, is collected, washed with cold EtOH, and allowed to crystallise from EtOH, collected, dried *in vacuo*, all under N_2, to give of the $[Ir(COE)_2Cl]_2$ (80-92% yield) as yellow needles. It should be stored under N_2 at room temperature. [van der Ent & Onderdelinden *Inorg Synth* **28** 91 *1989*.]

Although this compound is air sensitive, with the correct stoichiometry, it forms a less sensitive stable tris-boryl complex with pinacolborane (Bpin) and 4,4′-di-*tert*-butyl-2,2′-dipyridine (dtbpy) which has been crystallised, and its X-ray analysis shows that it has the composition $[Ir(dtbpy)(COE)(Bpin)_3]$‡. These complexes are catalytically active in the C-H borylation of arenes. Thus dissolution of the latter complex in $*C_6D_6$ (or $*C_6H_6$) provided $*C_6D_5$-Bpin within minutes at room temperature and in 80% yield. Kinetic studies revealed a kinetic isotope effect k_H/k_D of 3.8. The iridium complexes containing dtbpy are easily prepared and are air-stable. The reaction of bis(pinacolato)diboron (B_2pin_2) and ½$[IrCl(COE)_2]_2$/dtbpy (5 mol% of Ir) in 60 equivalents of $*C_6H_6$ at 25° for 4.5 hours gives Ph-Bpin in 83% yield; and with ½$[IrCl(COE)_2]_2$/dtbpy (0.02 mol% of Ir) at 100° for 16 hours gives Ph-Bpin in 80% yield with 8000 turnovers. These catalysts provide a simple and direct route for the synthesis of arylboronates—which were previously obtained by transmetalation with aryl lithium or arylmagesium reagents and trialkylborates. [Ishiyama et al. *J Am Chem Soc* **124** 390 *2002*, cf Ishiyama et al. *Angew Chem In Ed* **41** 3056 *2002*.]

‡***[Ir(dtbpy)(COE)(Bpin)$_3$]*** is prepared in a dry box under N_2; a glass flask containing a mixture of $[Ir(COE)_2Cl]_2$ (350mg, 390mmol), dtbpy (209mg, 778mmol) and B_2pin_2 (494mg, 1.95mmol), to which is added mesitylene (or xylene) (50ml) and heated with very slow stirring at 50° for 5 hours. The solvent is evaporated off at ~25°, the residue is dissolved in Et_2O and allowed to evaporate slowly at ~25° to afford red cubes (blocks) of the complex

in 28% yield (52mg). Its ^{1}H NMR (400MHz, cyclohexane-d_{12}) has δ at 1.15 (s, 12H), 1.17 (s, 12H), 1.18 (s, 12H), 1.33 (m, 12H), 1.41 (s, 18H). 3.74 (d, 2H, J = 10.8Hz), 7.09 (dd, 2H, J = 6.4, 2.0Hz), 7.93, (s, 2H), 9.45 (d, 2H, J = 6.4Hz) from Me_4Si; and its ^{11}B NMR (128MHz, $CDCl_3$) has δ at 37 from external BF_3OEt_2. [Ishiyama et al. *J Am Chem Soc* **124** 390 *2002*.]

Iridium(I) (methoxy)(1,5-cyclooctadiene) dimer {bis(η^4–1,5-cyclooctadiene) di-μ-methoxy diiridium (I) dimer, [(COD)(OMe)Ir(I)]$_2$} *[12148-71-9]* **M 662.9, m 154-179^o (dec).** Deoxygenated solvents should be used and reactions should be carried out under N_2 or argon. The methoxylated catalyst is prepared in Schlenk equipment in an inert atmosphere by adding a suspension of $[Ir(COD)Cl]_2$ (148mg, 222mmol, [12112-67-3]) in MeOH (10ml) to KOH (25mg, 445mmol) in MeOH (5ml), whereby the colour becomes orange-red and a yellow crystalline solid is formed. Stir for 30 minutes then add H_2O (40ml), collect the solid, wash it with H_2O (6 x 5ml), and dry it over P_2O_5 *in vacuo* to give $[Ir(COD)(OMe)]_2$ (124mg, 85%, decomposing at 145-155^o becoming black at 155^o) as a yellow air-stable solid. It is soluble in chlorinated solvents to give solutions which are air sensitive. It is soluble in MeOH, Me_2CO, hexane, $*C_6H_6$ and Et_2O but insoluble in H_2O. Its IR (Nujol) has ν_{max} at 1325m, 1300m, 1232w, 1208m, 1172w, 1158w, 1060vs, 1005m, 972s, 913m, 824w, 827w, 811w, 783w, 574s, 560sh, 532m, 512w, 434w, 337m cm^{-1}; the ^{1}H NMR ($CDCl_3$) has δ at 3.57 (8H, vinyl), 2.22 (8H, allylic H), 1.45 (8H, allylic H) and 3.28 (sharp singlet, 6H, MeO). [Uson et al. *Inorg Synth* **23** 127 *1981*.]
Alternatively, $[Ir(COD)(OMe)]_2$ can be prepared by boiling $[Ir(COD)Cl]_2$ (1g) in MeOH (40ml) under reflux with anhydrous Na_2CO_3(0.6g) for 1 hour, filtering hot, cooling, and the yellow plates of the desired complex are filtered off, washed with MeOH and dried *in vacuo*. [Chatt & Venanzi *J Chem Soc* 4735 *1975*.]
It has been used successfully, by preparing it *in situ*, on adding NaOMe to the solution containing $[Ir(COD)Cl]_2$ (see below).
[Ir(I) (OMe)(COD)]$_2$, like the preceding complex, is a powerful C-H activation catalyst for preparing phenols from arenes in the presence of pinacolborane and 3,3′-di-*tert*-butyl-1,1′-bipyridyl which borylates arenes to the intermediate pinacol arylboryl esters which are then converted to the respective phenols by reaction with *oxone* [$2KHSO_5.KHSO_4.K_2SO_4$] in Me_2CO at 25^o within 7 minutes in ~70% yields depending on the substituents [Maleczka et al. *J Am Chem Soc* **125** 7792 *2003*.] The catalyst, prepared *in situ*, in the presence of bipyridines has been used as in the previous reference for borylation of arenes in high yields and should be useful for preparing arylboronates [Ishiyama et al. *Angew Chem, Int Edn* **41** 3056 *2002*.]

Iridium(III) (1,1,1,5,5,5-trifluoroacetylacetonato)(bis-cyclooctene) [(hfacac)(COE)$_2$Ir] *[58616-58-3]* **M 620.5, m 96-97^o.** It is prepared by adding Tl(hfacac)† (600mg) to a suspension of $[Ir(COE)_2Cl]_2$ (920mg, see above) in pentane (100ml) at ~25^o, and stirring for 3 hours then filtering. The red filtrate is concentrated to 10ml, kept at -30^o for 24 hours and the red crystals of [**(hfacac)(COE)$_2$Ir]** (786.5g, 70%) are collected and dried *in vacuo* to give analytically pure complex (C and H). It is a monomeric complex in $*C_6H_6$ and has IR (KBr) with ν_{max} at 2960m, 2910s, 2840s, 2660w, 1620m, 1580s, 1540s, 1500w, 1440s, 1340s, 1310w, 1250s, 1210w, 1140s, 1040w, 1015w, 970w, 950m, 945w, 910s, 895w, 875w, 860w, 850w, 810m, 795s, 740m, 680s, 630m, 590s, 570m, 545s, 435m cm^{-1}; and the ^{1}H NMR (60MHz, $CDCl_3$) has δ at 6.26 (s, 1H), 2.8-2.4 (br m, 4H), 2.3-1.8 (br m, 8H), 1.7-1.3 (br m, 16H) from TMS.
(**Acac)(COE)$_2$Ir** is similarly prepared from Tl(acac) *{[25955-51-6], M 303.5, m 134^o obtained as for Tl(hfacac) below}* and $[Ir(COE)_2Cl]_2$ in 86% yield forming orange-yellow crystals with **m 114-115^o, M 512.6**, and has IR (KBr) with ν_{max} at 2970s, 2910s, 2890s, 2830s, 1620m, 1570s, 1540m, 1510s, 1460s, 1440m, 1410w, 1370m, 1340w, 1310w, 1270w, 1185w, 1140w, 1015s, 970w, 930w, 910w cm^{-1}; and the ^{1}H NMR (60MHz, $CDCl_3$) has δ at 5.43 (s, 1H), 1.92 (s, 6H), 2.4-1.7 (br m, 8H), 1.7-1.0 (br m, 20H) fromTMS. [Diversi et al. *J Organomet Chem* **125** 253 *1977*.]
†**Thallium 1,1,1,5,5,5-hexafluoroacetylacetonate [Tl(hfacac)]** is obtained when to a solution of thallous ethoxide (8g, prepared as in Fieser & Fieser's *Reagents for Organic Synthesis* **2** 407 *1969*, see [20398-06-5] in Chapter 5, Metal-Organic Compounds] in EtOH (60ml) is added hexafluoroacetylacetone (6.7g, [see 1522-22-1]) at ~ 25^o, and after 30 minutes the solvent is removed *in vacuo* and the residue is washed with pentane and dried to give Tl(hfacac) (11.8g, 95%) as a microcrystalline solid. [Ingrosso et al. *J Organomet Chem* **84** 75 *1975*.]

Iron(0) 2,2′-bipyridine [bpyFe(0)] *[bpy*Fe(1^+) *500295-31-8*; *bpy*Fe(2^+) *73871-24-6*; *bpy*Fe(3^+) *51232-88-3]* **M 212.0.** This iron catalyst mediates *ene-carbocyclisations* such as formal [4+4] ene reaction of trienes [Takacs & Anderson *J Am Chem Soc* **109** 2200 *1987*, Takacs et al. *Tetrahedron* **46** 5507 *1990*], regio- and chemo- selective diene to olefin cross coupling reactions [Takacs et al. *Organometallics* **5** 2395 *1986*], stereoselective and regiocontrolled formation of substituted tetrahydropyrans [Takacs et al. *Tetrahedron Lett* **28** 5627 *1987*]. The "active bpyFe(0) catalyst" is prepared *in situ* from $Fe(acac)_2$ (see [14024-17-0]) generated by a minimum of 3.0 equivalents of Et_3Al and $Fe(acac)_3$ (see [14024-18-1], in $*C_6H_6$ at 0°), and 2,2′-bipyridine (1:1 with respect to Fe, sublimed at 65°/0.01mm) to which is added the olefin(s) at or near room temperature. [The $Fe(acac)_3$ is recrystallised from EtOH or $*C_6H_6$/hexanes, dried at 25°/0.01mm, or sublimed at 100°/0.05mm.] Prior to the reduction of the iron, 1.1 equivalents of 2,2′-bipyridine and 10 equivalents of "addend" (furan or 2-methylfuran) are added to the $Fe(acac)_3$ in $*C_6H_6$. After reduction, the substrate(s) are added and the reaction is allowed to proceed at 25° and monitored. The "addend" is added mainly to slow down the disproportionation of the active bpyFe(0) into inactive bpy_2(Fe(0) and Fe_{metal} [Takacs et al. *Tetrahedron* **46** 5507 *1990*]. **Note:** The catalytically active 1:1 complex bpyFe(0) has not been isolated, but is assumed to be in solution and is most probably stabilised in solution by coordinating with some entity such as ethylene (derived from Et_3Al), or perhaps even furan or methylfuran as these are required for its stability (see below).
The reduction of $FeCl_3$ by 3.1 equivalents of *iso*-PrMgBr in the presence of 1.1 equivalents of 2.2′-bipyridine and 2,3-dimethylbutadiene yields an active catalyst by forming the ***bpyFe(0)2,3-butadiene complex*** [104714-94-5] in which the olefin may be involved in the reaction [Takacs et al. *Organometallics* **5** 2395 *1986*].
Carbocyclisations are also mediated by Pd, Ni, Co, and Rh complexes [for bibliography see Takacs et al. *Tetrahedron* **46** 5507 *1990*]. *Note:* the Fe(0) valence is dubious.

(2,3-*O*-Isopropylidene)-2,3-dihydroxy-1,4-bis-(diphenylphosphino)butane (DIOP) *[4R,5S-(-)- 32305-98-9, 4S,5R-(+)- 37002-48-5]* **M 498.5, m 88-89°, 88-90°, $[\alpha]_D^{19}$ (-) and (+) 26° (c 2.3, $CHCl_3$), also 4*R*,5*S*- has $[\alpha]_D^{22}$ (-) 12.3° (c 4.6, $*C_6H_6$), pK_{Est} ~0.0.** These are quite stable in air and have been recrystallised from $*C_6H_6$/petroleum ether. After 2 recrystallisations from EtOH, they are generally pure by TLC on silica gel using Me_2CO/hexane as solvent. The optical purity can be determined by GC [Chiral Select 1000 column 15m x 0.25mm using He carrier gas (1ml/minute); or Chirasil-L-Val fused silica 25m x 0.25mm] or by HPLC using an (*S,S*)-Whelk-01 column (5.0µm, 25cm x 0.46cm). [Details of the general preparation of **DIOP** are described under **3,4-O-isopropylidene-(3*S*,4*S*)-dihydroxy-(2*R*,5*R*)-bis(diphenylphosphino)hexane (*RSSR*-dimeDIOP**, see [258873-45-9]) in Part 2. The rhodium(I) complexes described below catalyse the asymmetric hydrogenation of β-substituted α-acetamidoacrylic acids to the corresponding chiral α-amino acid derivatives with high stereoselectivity. [Kagan & Dang *J Am Chem Soc* **94** 6429 *1972*.]
The DIOP derived catalysts used are **$Rh(I)^+$(DIOP)(COD) X^-** where X^- **is Cl^-, BF_4^-, SbF_6^-** or **PF_6^-** and are prepared *in situ* by reaction of $Rh(I)^+(COD)_2$ X^- with the DIOP ligand in a solvent (CH_2Cl_2, MeOH, $PhCH_3$, THF or $*C_6H_6$), using a DIOP/Rh ratio of <2 (preferably 1.1:1.0) to avoid the formation of $Rh(I)^+(DIOP)_2$ which exhibits very little, if any, catalytic activity due to its inability to coordinate with the olefinic substrate. A **typical hydrogenation** is carried out in a Fisher-Porter tube which is filled (in a dry-box) with the enamide substrate (0.25mmol), the appropriate solvent (5ml), and pre-formed $Rh(I)^+$(DIOP)(COD) X^- [Rh precursor, $Rh(I)^+(COD)_2$ X^- (0.005mol) in the appropriate solvent (3ml), DIOP (0.055ml of 0.1M solution in, e.g. $PhCH_3$, 0.0055mmol) and stir for 10 minutes]. After sealing, the tube is removed from the dry-box, placed behind a proper body shield, and *ca* five vacuum/refilling cycles of H_2 are performed. Hydrogenation is performed at room temperature, with the desired pressure of H_2 (1.1 to 50 bar, usually ~30psi), and is stirred vigorously for ~10 hours (but could be up to 60 hours). The reaction is completed by releasing the H_2, the catalyst is filtered off through a short silica column, and the filtrate is worked up in the appropriate manner. [Kagan & Dang *J Am Chem Soc* **94** 6429 *1972*, Li & Zhang *J Org Chem* **65** 5871 *2000*, Yan & RajanBabu *Org Lett* **26** 4137 *2000*.] A variety of DIOP derivatives have been synthesised and tested with pre-Rh catalyst salts having different X^- counter ions in several solvents. The combination which gave high yields and ee excesses of ~98% was the all-equatorial *3,4-O-isopropylidene-(3S,4S)-dihydroxy-(2R,5R)-bis(diphenylphosphino)hexane*, i.e. *RSSR*-dimeDIOP, $X^- = BF_4^-$ and $Rh(I)^+(COD)_2$ BF_4^- [35138-22-8], in CH_2Cl_2, at 20-40psi and 10 hours [Yan & RajanBabu *Org Lett* **26** 4137 *2000*].
Other examples of the application of Rh-catalysed reactions requiring the DIOP ligand include regioselective hydroformylation of methyl *N*-aminoacrylate [and involving RhH(CO)(DOP)] [Gladiali & Pinna *Tetrahedron:*

Asymmetry **1** 693 *1990*], 1,4-disilylation of α, β-unsaturated ketones [Matsumoto & Hayashi *Tetrahedron* **50** 335 *1994*], the Heck reaction with alkenyl iodides [Sato et al. *Tetrahedron* **50** 371 *1994*], as well as the asymmetric hydrogenation of enamides [Morimoto et al. *Tetrahedron: Asymmetry* **6** 23 *1995*, Morimoto et al. *Tetrahedron Asymmetry* **6** 75 *1995*].

Lanthanide trifluoromethanesulfonate (triflate) salts. These behave mostly as water-tolerant *Lewis acids* which catalyse a variety of organic functional group transformations. The lanthanide triflates below have been prepared and purified by the general procedure described here unless otherwise stated. The salts are prepared by adding excess of lanthanide(III) or (IV) oxide (>99% purity, 30mmol) to an aqueous solution of trifluoromethanesulfonic acid (50% v/v, 21.2ml) and heating to boiling for 30 minutes to 1 hour (*alternatively*, at 100° for 2 hours). The mixture is filtered to remove the unreacted oxide. The water is then removed under a vacuum. The resulting hydrated salt is dried by heating under vacuum at 180 to 200° for 48 hours (200°/0.5mm for 40 hours was also reported). These salts are quite hygroscopic and all manipulations of reactions using these salts should be carried out using Schlenk equipment or glove boxes under an inert atmosphere (N_2, He or Ar) to prevent contamination with H_2O which will lead to the formation of insoluble lanthanide hydroxides, and to maximise the activity of the catalyst. [Forsberg et al. *J Org Chem* **52** 1017 *1987*, Kobayashi & Hachiya *J Org Chem* **59** 3590 *1994*.]

Cerium(IV) trifluoromethanesulfonate [cerium triflate, $Ce(OSO_2CF_3)_4$ H_2O, $Ce(OTf)_4$ H_2O] *[698999-65-4]* M 736.4 (anhydrous), slowly decomposes above 120° to give trivalent cerium species. Preparation of $Ce(OTf)_4$ from CeO_4 or $Ce(OH)_4$ and trifluoromethanesulfonic acid as above for lanthanide triflates is usually unsuccessful. It is best prepared by adding, with vigorous stirring, a solution of K_2CO_3 (17.3g, 120mmol) in H_2O (95ml) to a solution of cerium(IV) ammonium nitrate (27.4g, 50mmol) [16774-21-3] in H_2O (80ml), whereupon a pale yellow carbonate separates. This is filtered off and washed several times with H_2O. CF_3SO_3H (triflic acid, 17.7ml, 200mmol) is slowly added at 0° to this "wet" cerium(IV) carbonate whereby it dissolves, and the resulting orange coloured solution is evaporated under reduced pressure, and the residue is dried *in vacuo* at 70° for 10 hours to give $Ce(OTf)_4$ as a yellow powder (36.2g). [Note that a "wet" carbonate is important as very dry carbonate does not react readily with triflic acid at 0°.] The IR (KBr) has characteristic bands at $\nu_{S=O}$ 1230 and ν_{C-F} 1010 cm^{-1} and it analyses as a *monohydrate* (by Karl Fischer). The salt is hygroscopic and should be stored under N_2 and preferably in aliquots in sealed containers. It is soluble in H_2O, EtOH, THF, 1,2-dimethoxyethane and dioxane, but almost insoluble in hexane, $*C_6H_6$ and $CHCl_3$. It has very good oxidising ability, thus converting benzylic alcohols to aldehydes or ketones, and benzylic type CH_2 to CO, e.g. substituted toluenes to their corresponding benzaldehydes, ethylbenzene to acetophenone and diphenylmethane to benzophenone in high yields. [Imamoto et al. *Chem Lett* 1445 *1990*].
$Ce(OTf)_4$ is an efficient catalyst for the ring opening of epoxides with high regio and stereo selectivity. Ring opening, e.g. of styrene oxides (phenyloxiranes), yields essentially *trans* products with the OH, OR or OAc entering groups (when H_2O, alcohols or AcOH are used) attacking the 'benzylic carbon' atom and with high optical purity when the reaction is carried out at ~–10° [e.g. *R*(+)-styrene oxide provides *S*(+)-$PhCH(OMe)CH_2OH$]. Ring opening of thiiranes with H_2O, alcohols or AcOH also yield *trans* products which dimerise to the corresponding dithianes. [Iranpoor et al. *Synth Commun* **28** 347 *1998*, cf Vougiokas & Kagan *Tetrahedron Lett* **28** 6065 *1987*.]

Gadolinium(III) trifluoromethanesulfonate [$Gd(OTf)_3$] *[52093-29-5]* M 604.5, decomposes >120°. $Gd(OTf)_3$ is prepared by the general method described above. If suspect, then add aqueous triflic acid (50% v/v) and proceed as above. It catalyses the aminolysis of epoxides in an extraordinarily efficient manner in aprotic solvents (e.g. toluene, CH_2Cl_2) with complete *trans* stereoselectivity and high regioselectivity [Chini et al. *Tetrahedron Lett* **35** 433 *1994*]. It also catalyses the reactions between nitriles and amines to yield a variety of amidines which, depending on the amine, can be used to prepare cyclic amidines, pyrimidines and *s*-triazines [Forsberg et al. *J Org Chem* **52** 1017 *1987*]. It is a water-tolerant *Lewis acid* used in aldol reactions of silyl enol-ethers and aldehydes in ~79-89% yields (see below) [Kobayashi & Hachiya *J Org Chem* **59** 3590 *1994*].

Hafnium(IV) trifluoromethanesulfonate hydrate [$Hf(OTf)_4$] *[161337-67-3]* M 774.8 (anhydrous),

m >350°. $Hf(OTf)_4$ is prepared by the general method described above. If suspect, then add aqueous triflic acid (50% v/v) and proceed as in the general method above. It is an efficient catalyst in the Fries rearrangement of acyloxy benzene or naphthalene derivatives, and for the regioselective direct acylation of phenol and naphthol derivatives with acid chlorides [Kobayashi et al. *Tetrahedron Lett* **37** 2053 *1996*]. It is an excellent and recyclable catalyst for mono-nitration of *o*-nitrotoluene [Waller et al. *Tetrahedron Lett* **39** 1641 *1998*].

Neodymium(III) trifluoromethanesulfonate [$Nd(OTf)_3$] *[34622-08-7]* **M 698.3, decomposes >120°.** $Nd(OTf)_3$ is prepared by the general method described above. If suspect, then add aqueous triflic acid (50% v/v) and proceed as above. It catalyses the aminolysis of epoxides in an extraordinarily efficient manner in aprotic solvents (e.g. toluene, CH_2Cl_2) with complete *trans* stereoselectivity and high regioselectivity [Chini et al. *Tetrahedron Lett* **35** 433 *1994*]. It also catalyses the reactions between nitriles and amines to yield a variety of amidines, which, depending on the amine, can be used to prepare cyclic amidines, pyrimidines and *s*-triazines [Forsberg et al. *J Org Chem* **52** 1017 *1987*]. It is a water-tolerant *Lewis acid* used in aldol reactions of silyl enol-ethers and aldehydes in ~83-85% yields (see below) [Kobayashi & Hachiya *J Org Chem* **59** 3590 *1994*].

Ytterbium(III) trifluoromethanesulfonate hydrate [$Yb(OTf)_3$ x H_2O] *[252976-51-5]* **M 620.3 (anhydr), decomposes >120°.** $Yb(OTf)_3$ is prepared by the general method described above. If suspect, then add aqueous triflic acid (50% v/v) and proceed as above. It can be recrystallised from $MeCN/CH_2Cl_2$. It has IR (KBr) bands at 3650, 3350, 2300, 1650, 1300, 1040 cm^{-1}; and ^{13}C NMR (270MHz, D_2O) at δ 122.4 (q, J = 317Hz) using sodium 2,2-dimethyl-2-silapentane-5-sulfonate as internal standard.
It catalyses the aminolysis of epoxides in an extraordinarily efficient manner in aprotic solvents (e.g. toluene, CH_2Cl_2) with complete *trans* stereoselectivity and high regioselectivity [Chini et al. *Tetrahedron Lett* **35** 433 *1994*]. It also catalyses the *trans* addition of indole (at position 3) to epoxides (e.g. to phenoxymethyloxirane) in >50% yields at 60° (42 hours) under pressure (10 Kbar) and was successfully applied for an enantioselective synthesis of (+)-diolmycin A2 [Kotsuki *Tetrahedron Lett* **37** 3727 *1996*]. Of the ten lanthanide triflates, $Yb(OTf)_3$ gave the highest yields (> 90%, see above) of condensation products by catalytically activating formaldehyde, and a variety of aldehydes, in hydroformylations and aldol reactions, respectively, with trimethylsilyl enol-ethers in THF at room temperature. All the lanthanide triflates can be recovered from these reactions for re-use. [Kobayashi & Hachiya *J Org Chem* **59** 3590 *1994*.]

Methyltrioxorhenium (MTO, trimethylrhenium(VII) trioxide, Me_3ReO_3) *[70197-13-6]* **M 249.2, m 110°, 111°, pK_a^{25} 7.53.** MTO is an air-stable carbon-rhenium oxide which is prepared from tetramethylrhenium oxide (Me_4ReO, [53022-70-1]) or trimethylrhenium dioxide (Me_3ReO_2, [56090-01-8]) (100mg) in a 1L evacuated bulb, and dry air is admitted up to a pressure of ~760mm (atmospheric). After a few days long needles of Me_3ReO_3 are formed, and after 4 weeks in excess of 50% yields of the trioxide are abtained. These can be resublimed to analytical purity *in vacuo* (at ~25°/1mm or 65°/0.001mm), have a sharp melting point (110°), are not decomposed in the gas phase <300°. ***Alternatively on a larger scale*,** silver tetraoxorhenate (14.0g, 39mmol, $AgReO_4$ [7784-00-1]) is dissolved in MeCN (150ml) followed by addition of Me_3SiCl (10.8ml, 85mmol, TMSCl [75-77-4]) whereby a white precipitate of AgCl separates and the solution becomes orange in colour. The suspension is treated with Me_4Sn (6.0ml, 43mmol, [594-27-4]), stirred for 24 hours, filtered into a Schlenk sublimation tube (~0.75L) and evaporated in a vacuum (20mbar), using a liquid N_2 trap (for volatile Sn compounds). A cold finger is then inserted into the tube and the Me_3SnCl [1066-45-1] is sublimed out at ~25°/20mbar; this compound is removed and the vacuum is increased to 0.01mbar when MTO sublimes out as a yellow-white crystalline solid. Traces of toxic Sn compounds may be present in this MTO (causing a pungent odour), but are removed by spreading it on filter paper in a fume hood for 1-3 hours, and the purity is checked by elemental analysis. MTO (7.8g) is thus obtained in 80% yield. Similar results are obtained on a 100g scale. The recovered Me_3SnCl can be converted to $SnMe_4$ by methylating with MeMgCl (23% in THF). High-purity MTO can be obtained by recrystallisation from CH_2Cl_2/hexane (73%). The white solid turns gray on standing without alteration in its activity, but can be minimised by storing it away from light under N_2. The Sn compounds are **HIGHLY TOXIC, and all work should be carried out in an efficient fume cupboard**. [Herrmann & Kratzer *Inorg Synth* **33** 111 *2002*, Herrmann et al. *Angew Chem, Int Ed. Engl* **36** 2652 *1997*.]
MTO forms colourless needles which develop a greyish tint on prolonged storage in light. It differs from methylperrhenate in being stable to hydrolysis by H_2O. It is soluble in MeCN, $*C_6H_6$, $CHCl_3$, EtOH and H_2O, but sparingly soluble in CS_2 and hexane. Its MS has parent ion peaks of $MeReO_3^+$ at 248 and 250 mass units for

the species containing ^{185}Re and ^{187}Re in a ratio consistent with the relative isotopic abundances. The UV/VIS (Et_2O) has λ_{max} (ε) at 260nm (1400, $Lmol^{-1}cm^{-1}$) and 232nm (1900, $Lmol^{-1}cm^{-1}$). ^{1}H, ^{13}C and ^{17}O NMR ($CDCl_3$, 25°) spectroscopy shows signals with δ_H at 2.61 (sharp), δ_C at 19.03 (^2J = 138Hz, C-H) and δ_O at 829 respectively; and the IR (hexachlorobutadiene mull) has ν_{max} at 1360ms (*CH deformation*), 2895 and 2980 (*CH stretching*) cm^{-1}; the IR in gaseous state (at 70°) has ν_{max} at 1003w(*ReO_3 sym str*), 985w, 975vs, 962vs(*ReO_3 antisym str*), 743mw(*CH_3-rock*), 574w(*Re-C*), 324w(*ReO_3 deformation*) cm^{-1}, and the IR (argon matrix) 1000ms(*ReO_3 sym str*), 970vs and 966m(*ReO_3 antisym str*), 566w(*Re-C*) cm^{-1}. Its Raman spectrum in CS_2 has ν_{max} at 999s(*ReO_3 sym str*) cm^{-1}, and in the solid state it has ν_{max} at 999s(*ReO_3 sym str*), 964m(*ReO_3 antisym str*), 530m(*Re-C*), 330m and 242m(*ReO_3 deformation*) cm^{-1}. [Beattie & Jones *Inorg Chem* **18** 2318 *1979*.]
MTO is a *catalytic oxygen carrier* in conjunction with an oxidant, e.g. H_2O_2, UHP (urea-H_2O_2 complex). For example 3.7mmol of 3,4,6-tri-*O*-acetyl-D-glucal in MeOH is oxidised by 7.4mmol of H_2O_2 in the presence of a catalytic amount of MTO (3.6 x 10^{-2}mmol) at ~25° in 2 hours to give the corresponding β-D-*gluco*- and α-D-*manno*- pyranosides (2:1) in 78% isolated yields *via* the intermediate epoxide. [Boyd et al. *Green Chem* **5** 679 *2003*.] **MTO** is a versatile oxidation catalyst and very effective in olefin epoxidation, olefin isomerisation, olefin metathesis, Baeyer-Villiger oxidation of ketones to lactones, aromatic oxidation to *p*-quinones, and in Diels-Alder reactions [Summarised in Herrmann *J Organomet Chem* **500** 149 *1995*]. It is a catalytic oxidant for the conversion of imines to nitrones [Soldaini et al. *Org Lett* **9** 473 *2007*, Baldwin & Long *Org Lett* **6** 1653 *2004*], and catalyses the efficient and stereospecific desulfurisation of thiirane (episulfides) by Ph_3P at ~25°, and more so if MTO is pre-treated with H_2S, probably due to the formation of Re(V)S species as the active catalyst [Jacob & Espenson *JCS, Chem Commun* 1003 *1999*].

Molybdenum dioxo bis(2,4-dipentandionato-κO2,κO4) [bis(acetylacetonato)dioxomolybdenum (IV), dioxobis(2,4-pentadionato)molybdenum (IV), MoO_2 (acac)$_2$] *[17524-05-9]* M 326.2, m 179°, 184-185°, 184° (dec). This complex is readily prepared by dissolving powdered ammonium *para*molybdate {$(NH_4)_6Mo_7O_{24}$ $4H_2O$, 3.0g, 2.4mmol, see [12054-85-2]} in 15% aqueous NH_3 (6.0ml, or 6.0.ml of 58%) with stirring. The clear solution (but if some solid remains undissolved, it will dissolve when nitric acid is finally added) is treated with 2,4-pentanedione (7.0ml, 6.8mmol) with stirring and the colour turns yellow. Concentrated HNO_3 (5.0ml, d 1.42) is slowly added with stirring to the mixture which warms up and the colour turns greenish yellow. The yellow complex separates as the mixture is allowed to cool to room temperature. After ~0.5 hours the solid is filtered off washed well with H_2O, then with EtOH, and dried *in vacuo* to give a 72% yield (4.0g) of the complex which can be increased to 93% if the hot solution is kept in a freezer at -10° in 18 hours. It can be recrystallised by dissolving ~2.0g in hot 2,4-pentanedione (6.0ml) at ~90° then keeping at -10° in 18 hours. The yellow crystals are filtered off with suction, washed with EtOH and dried *in vacuo* to give 1.8g of product. Note that if all the 2,4-pentanedione is not removed the crystals slowly develop a reddish tint. It decomposes slowly when stored in air or under fluorescent light, and turns blue. However, it is stable when stored *in vacuo* or under N_2. It is insoluble in H_2O, but slightly soluble in EtOH, $CHCl_3$, CH_2Cl_2 and soluble in MeCN. [Chakravarti & Bandyopadhyay *Inorg Synth* **29** 130 *1992*, and from MoO_3 and 2,4-pentanedione see Fernelius et al. *Inorg Synth* **6** 146 *1960*.] Its IR (KBr) has ν_{max} at 1560, 1500, 1350, 1260, 1015, 930 (Mo=O symm), 900 (Mo=O antisymm), 795, 665, 570 and 445 cm^{-1}; the ^{1}H NMR (CD_2Cl_2, TMS) has δ at 2.12, 2.14 and 5.83; and the ^{13}C NMR (CD_2Cl_2, TMS) has δ at 196.7, 185.2, 104.9, 28.0 and 25.7.
MoO_2 (acac)$_2$ catalyses: (a) the oxidation of primary (e.g. cinnamyl alcohol) or secondary alcohols (e.g. 1-phenylpropan-1-ol) to their respective aldehydes or ketones in high yields using sodium percarbonate (see [15630-89-4]) as oxidant and Adogen 464 (0.2 equivalents, as phase transfer catalyst see [72749-59-8]) in boiling (6-24 hours) CH_2Cl_2 [Maignein et al. *Synlett* 439 *1996*]; (b) the mild and efficient deprotection of acetals (e.g. benzaldehyde dimethyl acetal, dodecanal dimethyl acetal) in > 70-95% yields using ~10% of catalyst in MeCN under N_2 for ~4 hours [Kantam et al. *Synth Commun* **25** 2529 *1995*], (c) the oxidation of 3-β-cholesteryl esters to the corresponding 5,6-β-epoxides in the presence of isobutyraldehyde and O_2 in CH_2Cl_2 in yields >75% [Kantam et al. *Synth Commun* **24** 961 *1994*], and (d) the methoxymethylation of primary, secondary and tertiary alcohols (R-OH) to their corresponding methoxymethyl ethers (R-OCH_2OCH_3) in 75-95% yields using excess of methylal {$CH_2(OMe)_2$ see [109-87-5]} in refluxing $CHCl_3$ [Kantam & Ssnthi *Synlett* 429 *1993*].

(2*S*)-3-exo-(Morpholino)isoborneol [(-)MIB] *[287105-48-0]* **and (2*R*)-3-exo-(morpholino)iso-borneol [(+)MIB] (Nugent's reagent) M 239.4, m 60-65°, 65-67°, $[\alpha]_D^{25}$ ±6° (c 1, MeOH).** The (2*R*)-*enantiomer* is prepared from (2*R*)(+)-*cis*-3-exo-(amino)isoborneol (4.53g, 26.8mmol; Chittenden & Cooper *J Chem Soc C* 49

1970) in DMSO (25ml) and Et_3N (10ml), to which is added dropwise, with stirring, a solution of di(2-bromoethyl) ether (8.07g, ~90% pure, 31.3mmol) in DMSO (20ml). After 72 hours the mixture is poured into H_2O (250ml), basified with aqueous M NaOH (60ml), extracted with Et_2O (3 x 100ml), and the extract is evaporated *in vacuo*. The residue is then dissolved in Et_2O, extracted into aqueous M HCl (50ml), basified with aqueous NaOH and re-extracted into Et_2O which is dried ($MgSO_4$), filtered, evaporated *in vacuo*, and the residue is dissolved in hot hexanes (4ml/g crude), filtered and cooled to -30° to give analytically pure (C, H and N) (+)MIB (2.95g, 46%). It is a white crystalline solid, **m 65-67°**, that can be stored at ambient temperature for 3 months with no alteration in spectroscopic properties, or catalytic performance when compared with freshly prepared material. It has ^{1}H NMR (*C_6D_6) with δ_H at 0.69 (s, 3H), 0.73 (m, 1H), 0.88 (m, 1H), 1.04 (s, 3H), 1.31 (td, 1H), 1.52 (m, 1H), 1.67 (d, 1H), 1.99 (d, 1H), 2.13 (br, 2H), 2.31 (br, 2H), 3.32-3.42 (m, 5H total), 3.92 (br d, 1H); and the ^{13}C NMR (*C_6D_6) has δ_C at 11.88, 21.10, 22.19, 27.99, 32.56, 45.35, 46.64, 49.52, 66.82, 73.37, 79.03 (and one resonance is too broad to be observed at ~25°). [Nugent *J Chem Soc. Chem Commun* 1369 *1999*.]
MIB acts as an efficient catalyst for the enantioselective addition of the ethoxy vinyl zinc reagent to aldehydes providing hydroxy vinyl ethers, which in turn, are easily converted to chiral hydroxy aldehydes [Jeon et al. *Org Lett* **7** 1729 *2005*]. It generally catalyses the addition of organo-zinc reagents (e.g. from transmetalation of allylic boranes with alkylZn compounds) to aldehydes with very high enantiomeric preference, *viz* (*R*)-MIB providing the (*R)*-alcohol from the corresponding aldehyde [Nugent *J Chem Soc. Chem Commun* 1369 *1999*, Jeon et al. *Org Lett* **7** 1729 *2005*], and this catalytic method has been adopted for the preparation of α-amino acids [Chen et al. *J Am Chem Soc* **124** 12225 *2002*], of γ-unsubstituted β-amino acids [Lurain & Walsh *J Am Chem Soc* **125** 10683 *2003*] and for epoxy-alcohols with up to three contiguous stereocentres [Lurain et al. *J Am Chem Soc* **126** 10683 *2004*, Lurain et al. *J Org Chem* **70** 1262 *2005*].

Nickel(II) acetylacetonate [$Ni(acac)_2$] *[3264-82-2]* **M 256.9, m 229-230°, b 220-235°/11mm, d^{17} 1.455.** It is obtained by adding a solution of acetylacetone (50g, 0.5mole) in MeOH (100ml) to $NiCl_2.6H_2O$ (59.4g, 0.25mole) in H_2O (250ml) with stirring, followed by a solution of $NaOAc.3H_2O$ (68g, 0.5mole) in H_2O (150ml), heating briefly on a hot plate, cooling in a refrigerator for several hours, and filtering the crystals off. Wash the emerald green solid with H_2O, dry it in a vacuum desiccator and recrystallise it from MeOH. [Charles & Pawlikowski *J Phys Chem* **62** 440 *1958*.] The complex can be conveniently dehydrated by azeotropic distillation with toluene, and the crystals can be isolated by concentrating the toluene solution. [Wilkinson et al. *J Am Chem Soc* **76** 1970 *1954*, *Beilstein* **1** IV 3677.] It is soluble in organic solvents such as EtOH, $CHCl_3$, and *C_6H_6 but insoluble in Et_2O and hexanes. Its UV spectrum has λ_{max} nm(logε) at 265 (4.44) and 298 (4.34) (10^{-4} M in $CHCl_3$). It is a *trimer* in the solid state and a *monomer* in the vapour phase. When the metal in $Ni(acac)_2$ is coordinated with the carbenes derived from IPr.Cl, IPr.BF_4, (see below) or related 1,3-dimesityl-imidazolium chloride [141556-45-8], or with tri-*tert*-butylphosphine, it efficiently catalyses the cross-coupling of aryl- and heteroaryl-halides with aryl Grignard reagents [Böhm et al. *Angew Chem. Int Ed* **39** 1602 *2000*].

Nickel(II) bis(triphenylphosphine) dichloride [bis(triphenylphosphine)nickel(II) dichloride] *[14264-16-5]* **M 654.2, m 247-250°(dec), 250°(dec).** It is best prepared by adding $NiCl_2.6H_2O$ (2.38g, 10mmol) in H_2O (2ml) to a solution of Ph_3P (5.25g, 20mmol) in glacial AcOH (25ml) when an olive-green precipitate separates, but changes to dark blue crystals after standing in the mother liquors for 24 hours. These are filtered off washed with glacial AcOH and dried in a vacuum desiccator (H_2SO_4 and KOH) until AcOH is removed to give 84% of dark blue crystals. [Venanzi *J Chem Soc* 719 *1958*, Cotton et al. *J Am Chem Soc* **83** 344 *1961*, Kocienski et al. *J Org Chem* **54** 1215 *1989*, *Beilstein* **16** IV 953]. With butyl chloride at 150-180° in a sealed tube followed by crystallisation from BuOH, it provides blue crystals with m 176° of **[Ni(BuCl)($Ph_3P)_2Cl_2$].** [Yamamoto *Bull Chem Soc Jpn* **27** 501 *1954*, *Beilstein* **16** IV 953.]
In small amounts it catalyses the formation of terminal alkenes, e.g. from alkyl bromides or iodides in the presence of BuLi/DBU in THF at 25° in 50-80% yields [Jerapoulos & Smith *JCS Chem Commun* 1621 *1986*]. It also catalyses the replacement of OH groups in allyl acohols with the alkyl group of alkylmagnesium bromide thus forming a C-C bond, and also causes dehydrohalogenation of alkylhalides to form the corresponding terminal olefin [Chuit et al. *JCS Chem Commun* 1604 *1986*].

Nickel(0) bis(1,5-cyclooctadiene) [bis-(1,5-cyclooctadiene)nickel(0), $Ni(COD)_2$] *[1295-35-8]* **M 275.1, m 60° (dec), 142°(dec).** It is available in sealed ampoules under N_2. All procedures should be carried out in a dry box

and in an atmosphere of N_2 or argon in subdued light because the complex is light and oxygen sensitive, and flammable. The solid is washed with dry Et_2O (under argon) and separates from toluene as yellow crystals. Filter this under argon gas pressure, place the crystals in a container and dry them under a vacuum of 0.01mm to remove adhered toluene, flush with argon and seal them under argon or N_2 in glass ampoules. It catalyses cycloaddition reactions of 1,3-dienes [Semmelhack *Org Reactions* **19** 115 and 178 *1972*, Wilke et al. *Justus Liebigs Ann Chem* **699** 1 *1966*, Wender & Jenkins *J Am Chem Soc* **111** 6432 *1989*, Fieser & Fieser's *Reagents for Org Synth* **4** 33, **16** 29, **17** 32]. It also catalyses the addition of allyl phenyl sulfide to alkynes leading to 1,4-dienes. The reaction with acetylenes affords high yields, and in the presence of chiral phosphine ligands, with high stereoselectivity. The reaction tolerates a variety of functional groups [Hua et al. *Org Lett* **9** 263 *2007*]. **SUSPECTED CARCINOGEN**.

Oxime Palladacycle dimers (Nájera Catalysts, OPs) are Pd complexes of aromatic oximes, e.g. where palladium(II) is complexed with the oxime nitrogen atom and co-metalated with the *o*-position of the aromatic ring. They catalyse a variety of coupling reactions such as Suzuki-Miyaura, Heck, Stille, Sonogashira (all cross coupling) reactions and the Ullmann (homocoupling) reactions. *Note that the concentration of Pd in the products from Suzuki-Miyaura coupling reactions can be reduced from ~100ppm to 8000ppm by treating the reaction mixture with toluene and 20% aqueous $NaHSO_3$ at ~60° for ~1 hour* [Bullock, Mitchell and Toczko *Organic Process Research & Development* **12** 896 *2008*].

Oximes are prepared by a common procedure: A solution of the required aryl-ketone (22mmol) in MeOH (10ml) is added to a solution of hydroxylamine hydrochloride (3.06g, 44mmol), anhydrous NaOAc (3.6g, 44mmol) in H_2O pre-heated at 60° for 1 hour. If some solid separates, add enough MeOH to obtain a clear solution, then stir at this temperature overnight. On cooling to ~25°, the oximes that separate in >90% yield are filtered off, washed with H_2O and recrystallised to ^{1}H NMR purity (>98%). *Acetophenone oxime* has **m 59.1-59.7°** (from MeOH then cyclohexane, Pearson & Ball *J Org Chem* **14** 125 *1949*), *4,4'-dichlorobenzophenone oxime* has **m** 135.2-136.9° (from MeOH, Sieger & Klein *J Org Chem* **22** 953 *1957*), *4,4'-dihydroxybenzophenone oxime* has **m 266-267°dec.** (from EtOH, Zigeuner & Ziegler *Monatsh für Chemie* **89** 359 *1949*), *4-hydroxyacetophenone oxime* has **m 144-145°** (from aqueous MeOH), *4-methoxyacetophenone oxime* has **87°** (from petroleum ether, v. Auwers et al. *Chem Ber* **58** 41 *1925*), *4-methylacetophenone oxime* has **m 87-88°** (from MeOH then cyclohexane, Pearson & Ball *J Org Chem* **14** 125 *1949*), and *9-fluorenone oxime* has **m 195°**, **198°** (yellow crystals from $*C_6H_6$ or xylene, Anet et al. *Can J Chem* **35** 180 *1957*, Wislicenus & Waldmuller *Chem Ber* **41** 3335 *1908*).

Oxime palladacyles are generally dimers that can be prepared by a general procedure. A solution of the oxime (10mmol) in methanol (20ml) containing NaOAc.$3H_2O$ (1.63g, 10mmol) is added to a 0.5M solution of Li_2PdCl_4 (20ml, i.e. 2.62g, 10mmol, see [123334-21-4] in this Chapter Part 2) and stirred at ~25° for 2 to 3 days. Small quantities of precipitate may form and the colour of the reddish black solution turns to yellow. This is filtered and H_2O (10ml) is added to precipitate the palladacycles as yellow solids (~90% yields) that are filtered off, washed with a little MeOH and H_2O, and dried *in vacuo*. [Botella & Nájera *J Organomet Chem* **663** 46 *2002*, Onoue, Minami and Nakagawa *Bull Chem Soc Jpn* **43** 3480 *1970*; for preparation *via* ligand exchange see Ryabov et al. *Inorg Chem* **31** 3083 *1992*.] They can be used directly to catalyse reactions, their solubilities vary with the complex, but some can be crystallised from CH_2Cl_2-*n*-hexane, $*C_6H_6$-*n*-hexane or $CHCl_3$. They catalyse Heck couplings (in *N*-methylpyrrolidone with Et_3N as base), Heck couplings under Jeffrey's conditions (DMF with Bu_4NBr), Sonogashira reactions (with acetylenes in pyrrolidine and CuI), Stille coupling (in toluene), Suzuki coupling (in toluene with K_2CO_3 as base), and Ullmann-type homocoupling (in DMF, in the necessary presence of hydroquinone), and typical reaction conditions are described [Alonso, Nájera and Pacheco *Org Lett* **2** 1823 *2000*, Iyer & Ramesh *Tetrahedron Lett* **41** 8981 *2000*].

Di-chloro-bis[5-chloro-2-[(4-chlorophenyl)(hydroxyimino)methyl]phenyl-C]-di-palladium {Nájera Catalyst I, di-μ-chlorobis[5-chloro-2-[(4-chlorophenyl)(hydroxyimino-κN)methyl]phenyl-κC]-palladium (II) dimer} *[287410-78-0]* has **M 814.0** and **m 208-210°.** [Alonso, Nájera and Pacheco *Org Lett* **2** 1823 *2000*].

Di-chloro-bis[5-hydroxy-2-[1-(hydroxyimino)ethyl]phenyl-C]-di-palladium {Nájera Catalyst II, di-μ-chlorobis[5-chloro-2-[1-(hydroxyimino-κN)ethyl]phenyl-κC]-palladium(II) dimer} *[419581-64-9]* has **M 584.1** and **m >250°, 251-255°.** It has IR (KBr) with ν_{max} at 3425 (OH), 1662 (C=N) cm^{-1}; the ^{1}H NMR (300MHz, DMF-d_7, TMS) has δ_H at 9.96 (brs, 2H, 2 x OH), 9.71(brs, 2H, 2 x OH), 7.20 (brs, 2H, ArH), 7.07 (d, J = 8.5Hz, 2H, ArH), 6.50 (dd, J = 7.9, 2.4 Hz, 2H, ArH), 2.24 (s, 6H, 2 x CH_3); and its ^{13}C NMR (75MHz, DMF-d_7, TMS) has δ_C at 167.3, 157.4, 152.7, 134.2, 127.2, 123.4, 111.3, 111.1. Botella & Nájera [*J Organomet*

Chem **663** 46 *2002*] obtained high turnover numbers and turnover frequencies in Suzuki-Miyaura cross-coupling reactions at room temperature conditions with this catalyst. Botella & Nájera [*J Org Chem* **70** 4360 *2005*] also studied this catalyst for Mirozoki-Heck couplings in aqueous *N,N*-dimethylacetamide in air using *N*-methyldicyclohexylamine (see [7560-83-0]) as base with or without Bu_4NBr.

Di-chloro-bis[2-[1-(hydroxyimino)ethyl]phenyl-C]-di-palladium {di-μ-chlorobis[-2-[1-(hydroxy-imino-κN)ethyl]phenyl-κC]-palladium(II) dimer} *[32679-19-9]* has **M 568.1** and **m 210°, 209-212°.** It has IR (KBr) with ν_{max} at 3426 (OH), 1640 (C=N) cm^{-1}. [Alonso, Nájera and Pacheco *Org Lett* **2** 1823 *2000*, Onoue, Minami and Nakagawa *Bull Chem Soc Jpn* **43** 3480 *1970*.]

Di-chloro-bis[5-hydroxy-2-[(4-hydroxyphenyl)(hydroxyimino)methyl]phenyl-C]-di-palladium, {di-μ-chlorobis[5-hydroxy-2-[(4-hydroxyphenyl)(hydroxyimino-κN)methyl]phenyl-κC]-palladium(II) dimer} *[419581-64-9]* has **M 777.0** and **m >250°.** It has IR (KBr) with ν_{max} at 3405 (OH), 1612 (C=N) cm^{-1}; the ^1H NMR (300MHz, DMF-d_7, TMS) has δ_H at 10.50-9.40 (brs, 6H, 6 x OH), 7.41 (d, J = 8.5Hz, 4H, ArH), 7.26 (brs, 2H, 2 x OH), 7.20 (brs, 2H, ArH), 7.02 (d, J = 8.5Hz, 4H, ArH), 6.69 (d, J = 8.5Hz, 4H, ArH), 6.48 (dd, J = 7.9, 2.7 Hz, 2H, ArH); and its ^{13}C NMR (75MHz, DMF-d_7, TMS) has δ_C at 167.8, 160.0, 157.5, 152.9, 134.3, 131.5, 129.4, 123.7, 121.0, 115.8, 111.5. [Botella & Nájera *J Organomet Chem* **663** 46 *2002*.]

Di-chloro-bis[5-chloro-2-[(4-phenyl)(hydroxyimino)methyl]phenyl-C]-di-palladium, {di-μ-chloro-bis[5-chloro-2-[(4-phenyl)(hydroxyimino-κN)methyl]phenyl-κC]-palladium(II) dimer} *[1145982-32-6; 30471-18-2 for stereoisomer]* has **M 743.0** and **m 139-141°.** It has IR (KBr) with ν_{max} at 3373 (OH), 1645 (C=N), 1569, 1435, 1340, 1024 cm^{-1}; the ^1H NMR (300MHz, DMSO-d_6, TMS) has δ_H at 6.69 (m, 4H), 7.09 (m, 4H), 7.35-8.10 (m, 10H). [Alonso, Nájera and Pacheco *Org Lett* **2** 1823 *2000*, Onoue, Minami and Nakagawa *Bull Chem Soc Jpn* **43** 3480 *1970*.]

Di-chloro-bis[5-methoxy-2-[(4-methoxyphenyl)(hydroxyimino)methyl]phenyl-C]-di-palladium {di-μ-chlorobis[5-methoxy-2-[(4-methoxyphenyl)(hydroxyimino-κN)methyl]phenyl-κC]-palladium(II) dimer} *[287410-79-1]* has **M 803.0** and **m 135-137°.** It has IR (KBr) with ν_{max} at 3390 (OH), 1607 (C=N), 1579, 1559, 1253, 1233, 1177, 1026 cm^{-1}; the ^1H NMR (300MHz, DMSO-d_6, TMS) has δ_H at 3.71 (s, 6H), 3.83 (s, 6H), 6.71 (m, 4H), 7.08-7.25 (m with d at 7.10, J = 8.6Hz, 5H), 7.30-7.55 (m with d at 7.43, J = 8.6Hz, 5H). [Alonso, Nájera and Pacheco *Org Lett* **2** 1823 *2000*].

Palladium(II) acetate [$Pd(OAc)_2$] *[3375-31-3]* **M 244.5, m 205°(dec.), pK_1^{25} 1.0, pK_2^{25} 1.2 (for Pd_2^{2+}).** It recrystallises from $CHCl_3$ as purple crystals. It can be washed with AcOH and H_2O and dried in air. Large crystals are obtained by dissolving it in $*C_6H_6$, adding half its volume of AcOH and allowing it to evaporate slowly at room temperature. It forms green adducts with nitrogen donors, it dissolves in KI solution to form solid PdI_2 and a red solution of PdI_4^{2-}, but is insoluble in aqueous saturated NaCl, and NaOAc. It dissolves in HCl to form $PdCl_4^{2-}$. It is soluble in $CHCl_3$, CH_2Cl_2, Me_2CO, MeCN, Et_2O, but it is insoluble in H_2O, and decomposes when warmed in alcohols in which it is also insoluble. [Morehouse et al. *Chem Ind (London)* 544 *1964*, Stephenson et al. *J Chem Soc* 3632 *1965,* Skapski & Smart *J Chem Soc (D)* 658 *1970*, Heck *Acc Chem Res* **12** 146 *1979*.] **$Pd(OAc)_2$** should be an orange/red solid. Sometimes **commercial** samples, or old samples, give lower yields in catalytic reactions and it is found that good results are obtained after recrystallisation from $*C_6H_6$ [Anderson et al, *Org Synth* **84** 150 *2007*].
It is useful as a catalyst for coupling reactions [Kang et al. *J Am Chem Soc* **128** 6194 *2006*], and is a precursor for preparing heterogeneous and homogeneous catalysts [Jujjuri et al. *J Catal* **239 (2)** 486 *2006*, Xu et al. *J Nano Res* **7** 449 *2005*].

Palladium(II) acetylacetone [$Pd(acac)_2$] *[14024-61-4]* **M 304.6, m 200-250°(dec).** It can be recrystallised from $*C_6H_6$/petroleum ether and sublimes *in vacuo*. It is soluble in heptane, $*C_6H_6$ (1.2% at 20°, 2.2 at 40°), toluene (0.56% at 20°, 1.4% at 40°) and acetylacetone (1.2% at 20°, 0.05% at 40°). [West & Riley *J Inorg Nucl Chem* **5** 295 *1957/8*, Fernelius & Bryant *Inorg Synth* **V** 105 *1957*, *Beilstein* **1** IV 3676.] It is a soluble Pd source for the preparation of various soluble Pd catalysts by transferring the metal to a variety of phosphorus and other ligands for homogeneous catalysis [cf *Handbook of Organopalladium for Organic Synthesis* Negishi ed. Wiley, Hoboken NJ *2002*, ISBN 0-471-31506-0.]
A complex consisting of Cu 1.10-phenanthroline [which mediates decarboxylation of arylcarboxylic acids with formation of aryl Cu species] and $Pd(acac)_2$ [for coupling] was made and used to catalyse the decarboxylative cross-coupling of the Cu species with aryl halides. This bimetallic system allows direct coupling of a variety of aryl, heteroaryl or vinyl carboxylic acids with aryl or heteroaryl bromides, chlorides or iodides at 160° in *N* methylpyrrolidine in the presence of K_2CO_3. [Goossen et al. *J Am Chem Soc* **129** 4824 *2007*].

Palladium EnCat. Ley and co-workers [Ramarao et al. *J Chem Soc, Chem Commun* 1132 *2002*, Pears & Smith *Aldrichimica Acta* **38** 23 *2005*] have described a method of encapsulating $Pd(OAc)_2$ in the matrix of 20-250μm microcapsules prepared from a dispersion of an aromatic polyfunctional isocyanate and $Pd(OAc)_2$ in CH_2Cl_2 into H_2O containing stabilisers and surfactants. At the point when the oily dispersion reaches the desired size, e.g. 20-250μm, polymerisation is initiated (evolution of heat) whereby part of the isocyanate groups are hydrolyse to carbamate then to amino groups. The latter condense with the unhydrolysed isocyanate groups to form a crosslinked polyurea matrix entrapping the metal catalyst. After the necessary washing etc., polyurea microcapsules (MC average size ~150μm) are formed which are hard, porous and highly crosslinked spheres. These beads are catalytically active, robust and recyclable and have been used in conventional and supercritical media (e.g. liquid CO_2). They catalyse MC-[Pd] mediated Heck coupling (*p*-aryl and 4-heteroaryl nitro, methoxy and fluoro compounds with acrylic esters), carbonylation of 4-substituted arenes or heterocycles, Suzuki-type ($ArB(OH)_2$ + Ar to form crossed biaryls) and Stille couplings without requiring supplementary ligands [Ley et al. *J Chem Soc, Chem Commun* 1134 *2002*]. For **$EnPd(OAc)_2$ [Pd EnCat™]** and **$Pd^{(0)}$ EnCat™** see entries in Chapter 8.
Encapsulated Pd catalysts such as **Pd EnCat™** are available commercially. These particles are defined by their matrix content e.g. 30 or 40%, the latter having the smaller pore size. [See also Bremeyer et al. *Synlett* 1843 *2002*, Yu et al. *J C S Chem Commun* 678 *2003*, Vickerstaffe et al. *Org Biomol Chem* **1** 2419 *2003*.]

Palladium(II) trifluoroacetate *[42196-31-6]* **M 332.4, m ~210°(dec).** Suspend it in trifluoroacetic acid and evaporate it on a steam bath a couple of times. The residue is then dried in vacuum (40-80°) to give a brown powder. It is *hygroscopic* and should be stored in a dry atmosphere, preferably aliquoted in sealed vials [Stephenson et al. *J Chem Soc* 3632 *1965*, Trost & Metzner *J Am Chem Soc* **102** 3572 *1980*.]
$Pd(CF_3CO)_2$ catalyses the decarboxylation of electron-rich aromatic acids (e.g. with OMe groups) in DMSO/DMF at 70-90° (1 to 24 hours) in high yields and is not affected by steric hinderance [Dickstein et al. *Org Lett* **9** 2441 *2007*], and (in the presence of $Cu(OAc)_2$ with Cesium pivalate + 3-nitropyridine as additives at 110-140° in a microwave) it catalysed direct cross-coupling between unactivated arenes and *N*-acetylindoles with coupling mostly at C3 of indoles but with no homo-coupling [Stuart & Fangou *Science* **316** 1172 *2007*].
In the presence of AcOH, benzoquinone (as oxidant) and *o*-methoxyacetophenone or Ph_3P as ligands, $Pd(tfa)_3$ catalyses selective allylic oxidation of olefins into their allyl acetates [McMurry & Kocovsky *Tetrahedron Lett* **25** 4187 *1984*].

Phosferrox ligands and SK-Naud catalysts. The ligands are (diphenylphosphinoferrocenyl)oxazolines and are complexes where one of the cyclopentadienyl rings has two different substituents. These molecules have "***planar chirality***", i.e. are asymmetric, and exist in two enantiomeric forms. The oxazolines are 4,5-dihydro-oxazoles which for this use have a 4-substituent, usually alkyl or aryl, thus introducing a chiral centre at C-4 of the heterocyclic ring. Phosferrox ligands are prepared by lithiation of chiral 4-alkyloxazolin-2-ylferrocene in which lithiation is directed predominantly to one of the *ipso* positions of the cyclopentadienyl ring, generating "***planar asymmetry***" in the ferrocene moiety. It is highly diastereoselective with *ortho*-lithiation yield of ~84–99% de, producing the *S*-stereochemistry at the ferrocene moiety as shown by X-ray analysis and CD spectra of the products. Reaction of the lithiated ferrocene with Ph_2PCl furnishes the desired chiral phosferrox ligand. The stereochemistry of the reaction has been studied in detail [Sammakia et al. *J Org Chem* **60** 10 *1995*, Sammakia & Latham *J Org Chem* **60** 6002 *1995*, Richards & Mulvaney *Tetrahedron: Asym* **7** 1419 *1996*, Nishibayashi et al. *J Organomet Chem* **545-546** 381 *1997*]. Advantage is taken of the diastereoselectivity of the lithiation reaction in order to obtain the enantiomeric *R*-ferrocene. Thus, after lithiation, the lithium is displaced by a trimethylsilyl group (by reaction with Me_3SiCl), the *S*-TMS derivative is lithiated again, but at the other *ipso* position of the same cyclopentadienyl ring, followed by reaction with Ph_2PCl to form the 1-diphenylphosphino-3-TMS-2-(oxazolin-2-yl)ferrocene. Finally, removal of the TMS group, e.g. with *tetra-n-butylammonium fluoride* (*TBAF,* see [429-41-4; 3 H_2O 87749-50-6]), provides the phosferrox where the stereochemistry at the ferrocene moiety is now *R*. Chiral phosferrox ligands react with $RuCl_2(Ph_3P)_3$ [15529-49-4] to from *Nauk catalysts* which are *phosferrox-$RuCl_2(Ph_3P)$* complexes that reduce aryl ketones in the presence of *i*-PrOH/*i*-PrOK to form the respective alcohols with high stereoselectivity [Sammakia & Stangeland *J Org Chem* **62** 6104 *1997*, Nishibayashi et al. *Organometallics* **18** 2291 *1999*].

***S*-2-[(*S*)-2-(Diphenylphosphino)ferrocenyl]-4-(1-methylethyl)oxazoline (*S,S-i*-Pr-Phosferrox)** *[163169-29-7]* **M 481 , m 157-158°, $[\alpha]_D^{24}$ +112° (c 0.1, EtOH).** This phosferrox is prepared in a Schlenk tube at -78° under N_2, by adding dropwise *n*-BuLi (0.38ml, 0.7mmol) to a yellow-orange stirred solution of *S*-2-ferrocenyl-4-(1-methylethyl)oxazoline (0.158g, 0.53mmol) and TMEDA (0.10ml, 0.7mmol) in Et_2O (6ml) which had formed a yellow precipitate, and is stirred for 2 hours; the tube containing the orange non-homogeneous mixture is transferred to an ice-bath and stirred for 5 minutes further. To this now orange-red homogeneous solution is added Ph_2PCl (0.12ml, 0.7mmol, see [1079-66-9]), the mixture is allowed to warm to ~25°, and after 15 minutes it is quenched with saturated aqueous $NaHCO_3$ (10ml), the layers are separated, the aqueous layer is extracted with Et_2O (10ml), the combined Et_2O solutions are dried (Mg SO_4), filtered, and evaporated to give an orange crystalline solid. This is purified by column chromatography (pre-adsorbed on silica, eluting with 10% EtOAc/petroleum ether) to give a yellow-orange crystalline solid (0.163g, 64%) that provided ***S,S-i*-Pr-Phosferrox** as an analytically pure single diastereomer upon recrystallisation from hexane. It has CD ($CHCl_3$) λ_{max} ($\Delta\varepsilon$) 456 (+2.20), 368 (+0.49), 342 (-1.00), 315 (+216) nm; the IR has ν_{max} (nujol) at 1652 (C=N) cm^{-1}; the ^1H NMR (360Mz, $CDCl_3$) has δ_H at 0.68 (3H, d, *J* = 7 Hz, -C*H*$_3$), 0.82 (3H, d, *J* = 7 Hz, -C*H*$_3$), 1.61-1.69 (1H, m, C*H*(C*H*$_3$)$_2$), 3.61 (1H, brs, Fc), 3.67 (1H, t, *J* = 8 Hz, -OC*H*H), 3.83-3.90 (1H, m, -NC*H*-), 4.22 (5H, s, C_5H_5), 4.22-4.30 (1H, m, -OCH*H*-), 4.37 (1H, brs, Fc), 4.99 (1H, brs, Fc), 7.18-7.24 (5H, m, Ph), 7.36-7.37 (3H, m, Ph), 7.46-7.51 (2H, m, Ph); the ^{13}C NMR (90Mz, $CDCl_3$) has $\delta_C\{^1H\}$ at 17.52 (-*C*H$_3$), 18.61 (-*C*H$_3$), 32.05 (*C*H(CH$_3$)$_2$), 69.57 (-O*C*H$_2$-), 70.72 (C_5H_5), 72.02, 72.14, 73.81, 73.85, 75.32 (d, *J* = 16 Hz, Fc), 78.55 (d, *J* = 15 Hz, Fc), 127.81 (Ph), 127.92 (Ph), 127.99 (Ph), 128.10 (Ph), 128.18 (Ph), 128.89 (Ph), 132.40 (d, *J* = 20 Hz, Ph), 134.86 (d, *J* = 22 Hz, Ph), 138.21 (d, *J* = 13 Hz, Ph-*ipso*), 139.54 (d, *J* = 12 Hz, Ph-*ipso*); the ^{31}P NMR ($CDCl_3$) has a single peak with δ_P at -16.92, and the MS (EI) has *m*/*z* 481 (M^+, 100%), 410 (68), 404 (44), 170 (38), 121 (76). [Richards & Mulvaney *Tetrahedron: Asym* **7** 1419 *1996*].

S*-2-[(*R*)-2-(Diphenylphosphino)ferrocenyl]-4-(1-methylethyl)oxazoline [*S*-(*R-i*-Pr-Phosferrox)]** *[163169-10-6]* **M 481, m 132-132.5°, $[\alpha]_D^{20}$ -53° (c 0.15, EtOH).** This diastereomer is obtained by de-trimethylsilylation of *S*-2-[*R*-2-(diphenylphosphino)-5-(trimethylsilyl)ferrocenyl]-4-(1-methylethyl)oxazoline (0.14g 0.25mmol) with a yellow solution of 1M TBAF (see [429-41-4; 3 H_2O 87749-50-6], in Part 2) in THF (10ml) containing *ca* 5% H_2O by boiling for 4 hours, evaporating *in vacuo* to a small volume, shaking with Et_2O (10ml) and H_2O (10ml), separating, the aqueous layer is extracted with Et_2O, the ethereal layers are combined, dried (Mg SO_4), filtered, evaporated *in vacuo*, and the residue is chromatographed in a silica column (eluted with 10% EtOAc/petroleum ether b 40-60°) to give ***S-(R-i-Pr-Phosferrox) as a yellow crystalline solid (0.090, 75%). Its CD ($CHCl_3$) has λ_{max} ($\Delta\varepsilon$) 492 (+0.45), 434 (-0.43), 361 (-0.31), 344 (+0.35), 314 (-2.38) nm; the IR has ν_{max} (nujol) at 1660 (C=N) cm^{-1}; the ^1H NMR (360Mz, $CDCl_3$) has δ_H at 0.63 (3H, d, *J* = 7 Hz, -C*H*$_3$), 0.65 (3H, d, *J* = 7 Hz, -C*H*$_3$), 1.50-1.58 (1H, m, C*H*(C*H*$_3$)$_2$), 3.62 (1H, brs, Fc), 3.89-4.08 (3H, m, -OC*H*$_2$CH-), 4.22 (5H, s, C_5H_5), 4.36 (1H, brs, Fc), 4.94 (1H, brs, Fc), 7.19-7.23 (5H, m, Ph), 7.35-7.37 (3H, m, Ph), 7.48-7.53 (2H, m, Ph); the ^{13}C NMR (90Mz, $CDCl_3$) has $\delta_C\{^1H\}$ at 17.88 (*C*H$_3$), 32.44 (-*C*H$_3$), 69.47 (-O*C*H$_2$), 70.44, 70.67 (C_5H_5), 72.09, 72.41, 74.07, 74.95 (d, *J* = 16 Hz, Fc), 78.12 (d, *J* = 14 Hz, Fc), 127.71 (Ph), 127.83 (Ph), 127.90 (Ph), 128.07 (Ph), 128.15 (Ph), 128.55 (Ph), 128.86 (Ph), 132.38 (d, *J* = 19 Hz, Ph), 134.98 (d, *J* = 22 Hz, Ph), 138.31 (d, *J* = 13 Hz, Ph-*ipso*), 139.37 (d, *J* = 12 Hz, Ph-*ipso*), 164.62 (*C*=N); the ^{31}P NMR ($CDCl_3$) has a single peak at δ_P -18.03; and the MS (EI) has *m*/*z* 481 (M^+, 32%), 410 (19), 170 (22), 121 (100). [Richards & Mulvaney *Tetrahedron: Asym* **7** 1419 *1996*].

Among other phosferrox ligands that were prepared are *S,S*-4′*Me*-Phosferrox, *S,R*-4′*Me*-Phosferrox, *S,S*-4′*Et*-Phosferrox, *S,S*-4′*n-Bu*-Phosferrox, *S,S*-4′*iso-Bu*-Phosferrox, *S,S*-4′*t-Bu*-Phosferrox, *S,S*-4′*Ph*-Phosferrox, and *S,S*-4′*benzyl*-Phosferrox [Sammakia & Stangeland *J Org Chem* **62** 6104 *1997*, Nishibayashi et al. *J Organomet Chem* **545-546** 381 *1997*].

S*-2-[S_p-2-(Diphenylphosphino)ferrocenyl]-4-*iso*-propyl-2-oxazoline triphenylphosphine ruthenium (II) dichloride complex [*S,S-i*-Pr-Phosferrox-Ru(II) Ph_3PCl_2 complex, SK-Naud Catalyst-N003-2z]** ***[*212133-11-4]* **M 915.6, $[\alpha]_D^{20}$ -1100° (c 0.2, $CHCl_3$).** This catalyst can be prepared *in* situ from the phosferrox and $RuCl_2(PhP_3)_3$, but it can also be isolated. Thus a mixture of $RuCl_2(PhP_3)_3$ (480mg, 0.50mmol) and *S,S-i*-Pr-Phosferrox (0.50mmol) and toluene (15ml) are stirred under N_2 at ~25° for 20 hours when the original purple solution changes to a red suspension. Addition of *n*-hexane caused the crystalline catalyst to separate, and the red crystals are recrystallised to analytical purity from CH_2Cl_2/*n*-hexane (~81% yield). The ^1H NMR (270Mz, $CDCl_3$) has δ_H at 0.57 (3H, d, *J* = 7 Hz, C*H*$_3$), 0.97 (3H, d, *J* = 7 Hz, C*H*$_3$), 2.12 (1H, dd, *J* = 8 and 8Hz), 3.21 (1H, m), 3.28 (1H, m), 3.80 (1H, dd, *J* = 3 and 8Hz), 4.02 (5H, s), 4.59 (1H, m), 4.68 (1H, m), 4.84 (1H, m), 6.5-8.4 (25H, m); and the ^{31}P NMR (107Mz, $CDCl_3$) indicated a diastereomerically pure complex with δ_P 40.1 (d, *J* =

45Hz) and 77.0 (d, *J* = 45Hz). It causes a high conversion with high stereoselectivity (with 88-<99% ee) in the Ru-catalysed asymmetric transfer hydrogenation of ketones using *i*-PrOH as H source, as well as catalysing the asymmetric oxidation of *sec*-alcohols to ketones [Nishibayashi et al. *Organometallics* **18** 2291 *1999*].

R*-2-[R_p-2-(Diphenylphosphino)ferrocenyl]-4-*iso*-propyl-2-oxazoline triphenylphosphine ruthenium(II) dichloride complex (SK-Naud Catalyst-N003-1z)** ***[*849921-25-1]* **M 915.6, $[\alpha]_D^{20}$ +1100° (c 0.5, $CHCl_3$)** can be prepared and purified as in the preceding entry.

S*-2-[S_p-2-(Diphenylphosphino)ferrocenyl]-4-phenyl-2-oxazoline triphenylphosphine ruthenium (II) dichloride complex [*S,S-Ph*-Phosferrox-Ru(II) Ph_3P Cl_2 complex]** ***[*212210-73-6]* **M 949.6.** As above (SK-Naud catalyst-N003-2z) the catalyst can be prepared *in situ*, but can also be isolated in pure crystalline form, and its structure has been confirmed by X-ray crystallography. A mixture of ***S,S*-4′*Ph*-Phosferrox** [257mg, 0.50mol, red solid purified by flash chromatography with silica gel and eluting with hexanes the 10:1 hexanes/EtOAc, and recrystallisation from hexane, **m 184-185° dec., $[\alpha]_D^{23}$ +25.6° (c 0.67, $CHCl_3$)**] and $RuCl_2(PhP_3)_3$ (480mg, 0.50mmol) in toluene (15ml) are stirred under N_2 at ~25° for 20 hours when the original purple solution changes to a red suspension. Addition of *n*-hexane causes the crystalline catalyst to separate, and the red crystals are recrystallised to analytical purity from CH_2Cl_2/*n*-hexane to provide the catalyst (with 1 mol of CH_2Cl_2) in 80% yield. The ^{1}H NMR (270Mz, $CDCl_3$) has δ_H at 2.68 (1H, dd *J* = 8 and 9Hz), 3.29 (1H, dd, *J* = 1 and 9Hz), 4.12 (5H, s), 4.23 (1H, dd, *J* = 1 and 8Hz), 4.71 (1H, m), 4.80 (1H, m), 5.04 (1H, m), 6.6-8.2 (30H, m); and the ^{31}P NMR (107Mz, $CDCl_3$) indicated almost diastereomerically pure complex with δ_P 40.8 (d, *J* = 45Hz) and 75.7 (d, *J* = 45Hz). It has similar catalytic activity as the SK-Naud catalysts [Nishibayashi et al. *Organometallics* **18** 2291 *1999*, Sammakia & Stangeland *J Org Chem* **62** 6104 *1997*].

Platinum(0) bis(1,5-cyclooctadiene) [Pt(COD)$_2$, Pt bis(1,2,5,6-η-1,5-octadiene)] *[12130-66-4]* **M 411.6, m>~200°.** $Pt(COD)_2$ is prepared in a dry, O_2-free, N_2 atmosphere by adding dropwise an ethereal solution of $Li_2(C_8H_8)$ [*ca* 40ml of a 0.24mol dm^{-3} of dilithium cyclooctatetraene [40698-91-7] in Et_2O (Katz *J Am Chem Soc* **82** 3784 *1960*, see also below)] to a finely powdered suspension of $Pt(COD)Cl_2$ (3.7g, 10mmol, see above entry) in 1,5-cyclooctadiene at -30°, stirring for 30 minutes as the temperature rises to -10°; and then the solvent is evaporated *in vacuo* to dryness. Extraction of the residue with toluene (6 x 50ml) gives a brown solution which is filtered through an Al_2O_3 column (8 x 2.5cm, Brockman Activity III), the filtrate is evaporated to ~15ml and the supernatant is decanted from the off-white product which is washed with several small volumes of cold toluene until the washings are almost colourless. This Pt catalyst (1.6-2.4g, 40-60%) is useful for most purposes. Analytically pure (C and H) white crystals can be obtained by dissolving it in petroleum ether (b 40°-60°) (~80ml for each mmol of catalyst), filtering through an Al_2O_3 column (6 x 2.5cm) and cooling to -78°. Its IR has ν_{max} at 3020m, 3000sh, 2930m, 2910sh, 2965m, 2825m, 1475m, 1465m, 1433m, 1327s, 1306w, 1238m, 1212m, 1178w, 1158w, 1090vw, 1075w, 1009w, 998m, 970sh, 962w, 890vw, 865sh, 855m, 829sh, 823m, 810m, 788m, 769vw, 580vw, 510vw, and 465vw cm^{-1}; the ^{1}H NMR (100MHz, *C_6D_6) has τ at 5.80 (m, 8H, CH=CH, $J_{Pt\text{-}H}$ = 55Hz) and 7.81 (m, 16H, CH_2); and the ^{13}C NMR (25.15MHz, *C_6D_6-^{1}H decoupled) has ^{13}C shifts with δ measured relative to $SiMe_4$ (positive values to high frequency) 73.3 (C=C, $J_{Pt\text{-}C}$ = 143Hz) and 33.2 (CH_2, $J_{Pt\text{-}C}$ = 15Hz). The white crystalline complex is stable in air and can be handled without difficulty. [Spencer *Inorg Synth* **19** 214 *1979*, Crascall & Spencer *Inorg Synth* **28** 127 *1990*.] *Note that attempts to prepare the corresponding Pd complex [Pd(COD)$_2$] in a similar manner failed; however, it was obtained by the reaction of [Pd(COD)Cl$_2$] with Li$_2$[C$_8$H$_8$] in the presence of excess of propene as a white crystalline solid which was stable below -20°, but decomposed rapidly to Pd and 1,5-cyclooctadiene at ambient temperatures.* [Green et al. *J Chem Soc, Dalton Trans* 271 *1977*, Crascall & Spencer *Inorg Synth* **28** 128 *1990*.] $Pt(COD)_2$ catalyses the *cis*-diborylation of olefins in >80% yields under ambient conditions with e.g. CatB-BCat (see below). [Iverson & Smith *Organometallics* **16** 2757 *1997*].

Platinum(0) bis(dibenzylideneacetone) [Pt(dba)$_2$, bis(C^3,O^3-η-1,5-diphenyl-1,4-pentadien-3-one)-platinum (0)] *[33677-56-4]* **M 683.7, m >170° (to Pt and dba).** $Pt(dba)_2$ is a deep purple air stable complex which is prepared in 41% yield from K_2PtCl_4 with 3 mol equivalents of dba in refluxing EtOH under N_2 in the presence of NaOAc. It crystallises from Me_2CO and is soluble in MeOH and $CHCl_3$. It is useful for preparing complexes with $(PPh_3)_2$, $(AsPh_3)_2$, $(PEt_3)_2$, $(AsEt_3)_2$, as well as with other ligands. The *tris complex Pt(dba)*$_3$ is formed as a yellow microcrystalline solid in 40% yield by carrying out the above reaction in refluxing aqueous MeOH *in the presence of air or oxygen*. It is stable in the solid form, and is soluble in organic solvents but gives green solutions that rapidly turns purple, from which $Pt(dba)_2$ and dba (1:1) can be isolated. Physical properties showed

that complete dissociation of $Pt(dba)_3$ had occurred. Both complexes decompose >170° on heating to Pt and dba, on treatment with CO, or when solutions are set aside for long periods. The IR ($CHCl_3$) of $Pt(dba)_2$ has ν_{max} at 1656w(CO), 1613vs, br(C=C), 1579m(C=C aromatic), 1544m, br(CO) cm^{-1}; and complex $Pt(dba)_3$ has ν_{max} at 1652w(CO), 1624vs(C=C), 1593s, br(C=C aromatic), 1579m(C=C aromatic), 1527m br(CO) cm^{-1}. The UV-VIS ($CHCl_3$) of $Pt(dba)_2$ has λ_{max} nm (logε) at 235 (4.48), 336 (4.54), 378sh(4.27) 538 (3.92, metal→ ligand: $d \rightarrow \pi^*$); of $Pt(dba)_3$ has λ_{max} nm (logε) at 235 (4.27), 336 (4.48), 568 (3.51, metal→ ligand: $d \rightarrow \pi^*$); and of dba has λ_{max} nm (logε) at 233 (3.90), 325 (4.38). The ^1H NMR (100MHz, $CDCl_3$) of $Pt(dba)_2$ and dba are surprisingly similar [see however: Müller & Gröser *Angew Chem. Int Edn* **6** 364 *1967*]. It is a useful catalyst for the oligomerisation of acetylenes [Moseley & Maitlis *J C S. Chem Commun* 982 *1971*, Cherwinski et al. *JCS, Dalton Trans* 1405 *1974*], and is used in the $Pt(dba)_2$-catalysed selective *cis*-addition of bis(pinacolato)borane to terminal alkenes and cyclic alkenes with internal strain to form bis(boryl)alkanes in 76-86% yields at 50° [Ishiyama et al. *J C S, Chem Commun* 689 *1997*] among other uses in catalysis.

Rhodium(II) acetate dimer ($2H_2O$) [dirhodium tetraacetate, tetrakis(acetato)dirhodium(II)] *[15956-28-2]* **M 478.0.** Dissolve 5g of the dimeric salt in boiling MeOH (*ca* 600ml) and filter. Concentrate the filtrate to 400ml and chill overnight at *ca* 0° to obtain dark green crystals of the MeOH adduct. Concentration of the mother liquors gives a further crop of *$[Rh(OAc)_2]_2.2MeOH$*. The adduct is then heated at 45° in a vacuum for 2 hours (all MeOH is lost) to leave the emerald green crystals of the acetate. [Legzdins et al. *J Chem Soc (A)* 3322 *1970*, Rempel et al. *Inorg Synth* **XIII** 90 *1972*.] *Alternatively*, dissolve the acetate in glacial AcOH and reflux for a few hours to give an emerald green solution. Evaporate most of the AcOH on a steam bath, then heat the residue at 120°/1 hour. Extract the residue with boiling Me_2CO. Filter, concentrate to half its volume and keep at 0°/18 hours. Collect the crystals, wash them with ice cold Me_2CO and dry them at 110°. It is moderately soluble H_2O, MeOH, Me_2CO (see above), and in many organic solvents to give green solutions. It forms adducts with MeOH, Me_3N and Me_2S, and gives solutions with different colours varying from green to orange and red depending on solvent and dilution. The IR(Nujol) has ν_{max} at 1580s, 1425s, and 1350m cm^{-1}, and the IR (hexachlorobutadiene) has ν_{max} at 1445s, 1415s and 1350m cm^{-1} among other bands. [UV: Johnson et al. *Inorg Chem* **2** 960 *1963, Beilstein* **1** H 124.]
It is a homogeneous catalyst [Black *Aldrichimica Acta* **15** 13 *1982*], is used in an efficient synthesis for β-hydroxy-α-acrylates involving the decomposition of diazoester intermediates with concomitant 1,2-arylmigration [Xiao et al. *Tetrahedron Lett* **48** 1147 *2007*], and is an effective catalyst for the formation of allylsulfonium ylides (e.g. from 3,3-dimethylallyl methyl sulfide and trimethylsilyldiazomethane) which undergo [2.3] sigmatropic rearrangement (e.g. to 2,2-dimethyl-1-methylthio-1-trimethylsilylbut-3,4-ene) [Carter & Van Vranken *Tetrahedron Lett* **40** 1617 *1999*]. The reaction of alkyl diazoacetates with carbodiimides (to form 2-imino-4-oxazolines) [Drapier et al. *Tetrahedron Lett* 559 *1979*], with acetylenes (to form cyclopropenes) [Petiniot et al. *Tetrahedron Lett* 1239 *1978*], and with ROH, HOH and R'COOH (replacing H to form the respective O-CH_2CO_2Alkyl) [Paulissen et al. *Tetrahedron Lett* 2233 *1973*]; are all catalysed by $[Rh(OAc)_2]_2$ at about room temperature.

Rhodium(III) acetylacetonate [2,4-pentanedione rhodium(III), $Rh(acac)_3$] *[14284-92-5]* **M 400.2, m 263-264°.** It is prepared from $Rh(NO_3)_3$ solution (0.1g in Rh) in 0.2*N* HNO_3 (10ml) which is neutralised with aqueous $NaHCO_3$ (10%) to pH 4, whereby the light yellow hydroxide (or basic nitrate) begins to separate. Acetylacetone (5ml) is added, the mixture is refluxed, and after a few minutes orange-yellow crystals begin to separate while the pH of the solution decreases. After 30 minutes reflux the pH of the solution is re-adjusted and reflux is continued for a further 15 minutes. The orange-yellow complex is collected and forms monoclinic plates (0.3g, 75%, m 260°) upon recrystallisation from aqueous MeOH, and sublimes at 240°/1.0mm. It decomposes above 280° depositing a rhodium mirror. It is insoluble in H_2O, sightly soluble in EtOH and petroleum ether, but freely soluble in $*C_6H_6$ and $CHCl_3$. It is stable in boiling dilute acids and 10% aqueous NaOH. Molecular weight determination (~490, by Rast in camphor) indicates that it is monomeric. [Dwyer & Sargeson *J Am Chem Soc* **75** 984 *1953*, *Beilstein* **1** IV 3677.] $Rh(acac)_3$ is a very effective catalyst (~90% yields) for the hydrogenation of monocarboxylic or ω-dicarboxylic acids to the respective alcohols in DME at 100 atmospheres (16 hours at 160°) when combined with $Re(CO)_{10}$ or $Mo(CO)_6$ [He et al. *Tetrahedron Lett* **36** 1059 *1995*].

Rhodium(I) bis(1,5-cyclooctadiene) tetrafluoroborate complex [bis(1,5-cyclooctadiene)rhodium(I) tertra-

fluoroborate, Rh(COD)$_2^+$.BF$_4^-$] *[35138-22-8]* **M 406.1, m ~190º (dec), the xHydrate** *[207124-65-0]* **has m 165º (dec).** This complex is prepared from the dimer [Rh(COD)Cl]$_2$ (1.47g, 2.98mmol, cf [12092-47-6]) in CH_2Cl_2 (20ml), to which is added COD (1.1ml, 8.97mmol) followed by $AgBF_4$ (1.33g, 6.83mmol) in Me_2CO (10ml) which results in a deep red solution containing a white precipitate. The mixture is stirred for 20 minutes, filtered through Celite, THF (20ml) is then added and the volume is reduced on a Rotovap at 25º down to 10ml. The deep red crystals are filtered off, washed with THF (2 x 5ml), Et_2O and dried in air (2.35g, 97%). [Schenck et al. *Inorg Chem* **24** 2334 *1985*.] A general purification procedure involves dissolving the complex in the minimum volume of CH_2Cl_2, adding an equal volume of EtOH and completing the crystallisation by dropwise addition of Et_2O, filtration, and drying the solid *in vacuo*.
It is used for preparing cationic COD-Rh complexes with phosphine ligands for enantioselective [2+2+2] cycloaddition of unsymmetrical diynes with styrene and norbornene derivatives to yield bi- and tetra-cyclic products with good (~50%) to very good (>90%) enantiomeric enrichment [Shibata et al. *Tetrahedron* **63** 12853 *2007*], for hydrogenation [Nagel et al. *Chem Ber* **119** 3326 *1986*, Ojima et al. *Tetrahedron* **45** 6901 *1989*, Sawamura et al. *J Am Chem Soc* **117** 9602 *1995*], and for hydrosilylation [Takeuchi et al. *J Org Chem* **60** 3045 *1995*].

[Rhodium(*S*,*S*-Chiraphos)(COD)] ClO_4.THF {[(1,2,5,6-η)-1,5-cyclooctdiene][1.2-dimethyl-1,2-ethanediyl-(di-phenylphosphine)-*P*,*P′*]rhodium(1$^+$) perchlorate. THF, η^4-1,5-cyclooctadiene[(*2S,3S*)-*2*,3-bis(diphenyl-phosphino)butane]rhodium(I) perchlorate.THF} *[61886-03-1, 61886-02-0 THF-free]* **M 809.1, 737.0 (THF-free).** The *S,S*-catalyst is obtained by adding 70% perchloric acid (0.080g, 1 equivalent) in pure THF (1ml) under N_2 to a mixture of *S,S*-chiraphos (0.244g, see [64896-28-2]) and *[Rh(COD)(acac)] (0.180) in THF (4ml); and the red mixture is allowed to stand at 25º for 14 hours. The bright orange block crystals are collected, washed with cold THF and dried in air to give analytically pure (C, H, P and Cl analysis) catalyst *perchlorate THF* (0.40g). The presence of solvent is confirmed by NMR. A single crystal X-ray (absolute) structural determination of this THF-pre-catalyst shows that it is as predicted, i.e. the chiral centres are *S* and the methyl groups are equatorial to give a δ-chelate ring [Ball & Payne *Inorg Chem* **16** 1187 *1977]*. The configuration in solution is assumed to be the same, being consistent with the stereochemistry of the catalytically produced products.
The above two complexes are efficient homogeneous catalysts for the hydrogenation of α-*N*-acylamioacrylic acids at room temperature and pressure in THF, dioxane or *C_6H_6, EtOH or aqueous EtOH to provide the amino acid derivatives in very high optical purity [e.g. of alanine (91%), DOPA (83%) and tyrosine (92%)], and in almost quantitative chemical yields with turnover numbers ranging from 3 x 10^{-2} to 6 x 10^{-4} sec^{-1}, from which essentially completely optically pure "non-natural" *R*-α-amino acids can be obtained by recrystallisation. [Fryzuk & Bosnich *J Am Chem Soc* **99** 6262 *1977*]. An ingenious application of this *S,S*-chiraphos catalyst using hydrogen, deuterium and tritium has been adopted for the asymmetric synthesis of chiral lactic acid in which the methyl group is chiral by virtue of its having a hydrogen, a deuterium and a tritium atom on the methyl carbon atom. [Fryzuk & Bosnich *J Am Chem Soc* **101** 3043 *1979*]. In the hydrogenation of selected Z-olefins with this pre-catalyst, addition of Et_3N appears to give higher optical yields of products [Onuma et al. *Bull Chem Soc, Jpn* **53** 2012 *1980*].
*** [Rh(COD)(acac)]** *[12245-39-5]* **M 310.2, m 138-140º,** is prepared from [Rh(COD)Cl]$_2$ (4.4g, 9 mmol, see [12092-47-6]) and acetylacetone (acacH, 0.9ml, 9 mmol) in CH_2Cl_2 (50ml) chilled to -80º by treating dropwise with a solution of Na_2CO_2 (5,7g) in H_2O (100ml) and shaking; then warming to 0º while shaking and more CH_2Cl_2 (50ml) is added. The layers are separated, and the organic layer is evaporated *in vacuo* until the complex crystallises out. [Fryzuk & Bosnich *J Am Chem Soc* **99** 6262 *1977*].

Rhodium(*S*,*S*-Chiraphos)(NBD)] ClO_4 {(bicyclo[2.2.1]heptadiene)[(*2S,3S*)-*2*,3-bis(diphenylphosphino) butane]-rhodium (I) perchlorate, [(1,2,5,6-η)bicyclo[2.2.1]hepta-2,5-diene][*S*,*S*-1.2-dimethyl-1,2-ethanediyl)-bis(diphenylphosphine)-*P*,*P′*]rhodium(1$^+$) perchlorate} *[65012-74-0; 65012-73-9 for cation; Rh(S,S-chiraphos)(MeOH)$_2^+$ has 71264-71-6]* **M 720.97.** This catalyst can be prepared by two methods. In the *first*, 7% $HClO_4$ (0.173g, 1 equivalent) in THF (6ml) is added to a solution of the complex *[Rh(NBD)(acac)] (0.356g) and *S,S*-chiraphos (0.516g, see [64896-28-2]) in dry, freshly distilled, THF (7.5ml) under N_2, and the deep red coloured solution is allowed to stand at 25º for 24 hours. The orange-red crystals that separate are collected, washed with cold THF, dried at 40º *in vacuo* to give the catalyst *perchlorate* (0.6g), which should be

stored at 0° under N_2 in a sealed container. In the *second*, *S,S*-chiraphos (0.308g) and the complex **[Rh(NBD)$_2$]ClO$_4$ (0.290g) are dissolved in CH_2Cl_2 (5ml) and THF (5ml) under N_2, followed by addition of hexane (6ml), allowing to stand at 25° for 1 hour, then at 5° for 2 hours. The orange-red needles of the catalyst *perchlorate* (0.43g) are collected, dried and stored as in the first method. Note that it loses catalytic activity if stored in air. [Fryzuk & Bosnich *J Am Chem Soc* **99** 6262 *1977*.] Its ^{31}P NMR ($CDCl_3$, with external H_3PO_4 as reference) has δ at +56.9 (d, J_{Rh-P} = 153Hz), i.e. downfield from H_3PO_4 [Slack et al. *Inorg Chem* **18** 3125 *1979*]. The **tetrafluoroborate *[79790-89-9]* M 708.3** forms orange-red crystals from CH_2Cl_2/Et_2O.

***[Rh(NBD)(acac)]** *[32354-50-0]* **M 294.2, m 176-177°,** is prepared from the dimer [Rh(NBD)Cl]$_2$ *[12257-42-0]* and Tl(acetylacetone) *([25955-51-6])* as described for [(hfacac)(COE)$_2$Ir] *[58616-58-3]* [see this chapter and Diversi et al. *J Organomet Chem* **125** 253 *1977*.]

****[Rh(NBD)$_2$]$^+$ClO$_4^-$** *[60576-59-1]* **M 386.6,** is also prepared from the dimer [Rh(NBD)Cl]$_2$ (0.35g, *[12257-42-0]*) and NBD (0.14g) in CH_2Cl_2 (15ml) under N_2, adding $AgClO_4$ (0.315g), stirring for 1 hour, filtering and adding THF (15ml). When the CH_2Cl_2 in the mixture is evaporated off under a vacuum, [Rh(NBD)$_2$]ClO$_4$ separates as orange needles which are collected, washed with cold THF and dried *in vacuo* to give now orange-brown crystals (0.5g). *Alternatively*, add Et_2O instead of THF (15ml), filter, wash with Et_2O, and dry *in vacuo* (yield 90%). Its ^{1}H NMR in $(CD_3)_2CO$ has δ at 5.23 (br, olefin H), 4.09 (bridgehead CH) and 1.50 (CH_2). [Fryzuk & Bosnich *J Am Chem Soc* **99** 6262 *1977*; cf Cramer *J Am Chem Soc* **86** 217 *1964*, Uson et al. *Trans Metallorg Chem* **4** 55 *1979*.] **[Rh(NBD)$_2$]$^+$BF$_4^-$** has *[36620-11-8]* **M 373.99, m 157-159°**, and is prepared as for the perchlorate, but replacing $AgClO_4$ by an equivalent of $AgBF_4$, and recrystallising from CH_2Cl_2/Et_2O. The cation **[Rh(NBD)$_2$]$^+$** has *[35015-46-4]* **M 287.2.** [Green et al. *J Chem Soc (A)* 2334 *1971*, Osborn et al. *J Am Chem Soc* **93** 3089 *1971*, Green et al. *JCS, Dalton Trans* 832 *1972*.]

[Rhodium(*R*,*R*-Chiraphos)(NBD)]ClO$_4$ {(bicyclo[2.2.1]heptadiene)[(*2R,3R*)-*2*,3-bis(diphenylphosphino) butane]-rhodium (I) perchlorate} *[74892-62-9]* M 720.97. This pre-catalyst is prepared and purified as its enantiomer above in 77% yield in orange-red crystals after recrystallising from CH_2Cl_2/hexane. Its catalytic properties are very similar to those of its enantiomer above except that optically pure "natural" *S*-α-amino acids are produced. [Köiiner & Gerber *Chem Ber* **113** 2323 *1980*.]

The mechanism of the above asymmetric hydrogenations has been studied in some detail [Brown & Chaloner *J Am Chem Soc* **102** 3040 *1980*, Brown et al. *J Organomet Chem* **216** 263 *1981*].

[Rhodium (*R*-Prophos)(NBD)] ClO$_4$. 0.5CH$_2$Cl$_2$ {(bicyclo[2.2.1]heptadiene)[*R*(+)-1,*2*-bis(diphenyl-phosphino)-butane]-rhodium(I) perchlorate. 0.5CH$_2$Cl$_2$, [(2,3,5,6-η)bicyclo[2.2.1]hepta-2,5-diene][(1-methyl-1,2-ethanediyl)bis(diphenylphosphine)-*P,P′*]rhodium(1$^+$) perchlorate. 0.5CH$_2$Cl$_2$} *[67881-59-8; 67884-58-7 for the cation; Rh(R-prophos)(MeOH)$_2^+$ has 71264-72-7]* **M 706.9, decomposes on heating.** The precatalyst is made from freshly recrystallised [Rh(NBD)$_2$]ClO$_4$ (0.388g, 1mmol, [12257-42-0]) and *R-prophos* (0.437g, 1.106mmol) in a mixture of CH_2Cl_2 (4ml) and pure THF (4ml) under N_2; and to this orange red solution is added hexane (4ml) dropwise, and the mixture is then allowed to stand at 25° for 5 hours then at 5° for 12 hours.

The orange-red solid is filtered off quickly, washed with ice-cold THF then hexane, and dried under a stream of dry N_2 to give analytically pure [Rh(*R*-Prophos)(NBD)]ClO$_4$ (with 0.5CH_2Cl_2 by NMR). It remains catalytically active indefinitely if kept at 0° under N_2. Its ^{31}P NMR ($CDCl_3$, with external H_3PO_4 as reference) has δ at +60.5 (d, J_{Rh-P} = 172Hz), +41.8 (q, J_{Rh-P} = 139Hz, J_{P-P} = 34Hz), i.e. downfield [Slack et al. *Inorg Chem* **18** 3125 *1979*]. Its absolute crystal X-ray structure has been determined and is the one predicted, i.e. the chelate ring is λ, the methyl group is equatorially disposed and the absolute configuration of the diphosphine is *R*. The configuration in solution is assumed to be the same, being consistent with the stereochemistry of the catalytically produced products.

Like the above rhodium complexes of *S,S-chiraphos*, this *R-prophos* rhodium complex is an efficient homogeneous catalyst for the production of α-amino acids, and the optical yields appear to be insensitive to the nature of the substituents on the substrates which provide the "natural" *S*-amino acids in 90±3% optical yields and high chemical yields (<87%) [compare with the *S,S-chiraphos* rhodium precatalysts above which gives the non-natural *R*- α-amino acids]. Furthermore, the catalyst *R-prophos* rhodium complex can breed its own chirality so that large quantities of *R*-prophos can be made from the catalytic hydrogenation of ethyl acetoxyacrylate, *via* ethyl *S-(-)*-O-acetyllactate, by the *R*-prophos catalyst itself. This procedure has been used to produce ***S-prophos***

if the pre-catalyst used is [Rh(S,S-chiraphos)(NBD)]ClO_4. [Fryzuk & Bosnich *J Am Chem Soc* **100** 5491 *1978*.] An ingenious application of this *R*-prophos rhodium pre-catalyst using hydrogen, deuterium and tritium has been adopted for the asymmetric synthesis of chiral lactic acid in which the methyl group is chiral by virtue of its having a hydrogen, a deuterium and a tritium atom on the methyl carbon atom. The orientations here being opposite to those obtained with the *S,S*-chiraphos rhodium precatalysts. [Fryzuk & Bosnich *J Am Chem Soc* **101** 3043 *1979*.]
Note that these rhodium catalysts are in fact *pre-catalysts* because in the presence of hydrogen their {e.g. [Rh(*S,S*-chiraphos)NDB]$^+$} strong deep red-orange colours are reduced to a light straw yellow colour of the true catalyst {e.g. [Rh(*S,S*-chiraphos)$(H)_2$]$^+$}. The mechanism of these asymmetric hydrogenations has been studied in some detail [Brown & Chaloner *J Am Chem Soc* **102** 3040 *1980*, Brown et al. *J Organomet Chem* **216** 263 *1981*].

Rhodium(III) chloride [$RhCl_3$ ± x H_2O] *[10049-07-7; 20765-98-4 x H_2O]* **M 209.3 (anhydrous), m 100° (hydrate, dec).** The anhydrous form is crystalline and is hydrophobic. It is a red powder insoluble in H_2O, but soluble in aqueous NaOH or cyanide solutions. The hydrate, however, is soluble in H_2O. [cf preparation of the trihydrate by Anderson & Basolo *Inorg Chem* **7** 214 *1963*.]
It catalyses the direct conversion of methane to AcOH [Sen et al. *Nature* **368** 613 *1994*], and is a catalyst for conjugate reduction of cinnamaldehydes followed by cross-coupling with arylboronic acids [Wang et al. *JCS,Chem Commun* 1192 *2004*]. It also catalyses the deuteration of saturated hydrocarbons [Takahashi et al. *J Am Chem Soc* **97** 7489 *1975*], and in the presence of Ph_3P (Wilkinson's catalyst) the trimethylsilylation of methacrylic esters to 1-alkoxy-1-trimethylsilyl oxyethylenes with rearrangement of a methyl group in the presence of Me_3SiH in THF is achieved [see Revis & Hilty *J Org Chem* **55** 2972 *1990*.]

Rhodium(II) pentafluorobenzoate dimer [tetrakis(pentafluorobenzoato)dirhodium(II)] *[75863-37-5]* **M 947.2.** This dimer is obtained from a solution of perfluorobenzoic acid (4.5g) and hydrated $RhCl_3$ (1g) in EtOH (80ml), to which is added NaOH (0.8g), and heated under reflux for 3 hours, cooled and the solid is filtered off. The solid is refluxed for a further hour with fresh EtOH (80ml) and is filtered again. The combined EtOH solutions are evaporated *in vacuo*, the solid green residue is extracted with several volumes of Et_2O until the extracts are colourless; the Et_2O is concentrated and chromatographed on SiO_2 (eluting with toluene/Et_2O 9:1). Some of the complex (1g) is collected in one of the fractions, and dried *in vacuo* for 3 hours [150° at 10^{-2} mm] and is analytically pure. The IR(KBr) has ν_{max} at 1655m, 1597s, 1525m, 1500s, 1433s, 1405s, 1297w, 1118m, 997s, 942w, 768m cm^{-1}. Like the triflate salt (following entry) it catalyses the addition of carbenes (drived from alkyl diazo diazoesters) to aromatic compounds, although its catalytic efficiency is unaffected by the bulk of the diazo ester alkoxy group [Anciaux et al. *J Org Chem* **46** 873 *1981*].

Rhodium(II) trifluoroacetate dimer [dirhodium tetra-trifluoroacetate, tetrakis(trifluoroacetato)-dirhodium(II), $Rh_2(Tfl)_4$] *[31126-95-1]* **M 657.9.** It can be purified in much the same way as the preceding acetate dimer (see [15956-28-2]) and is recrystallised from *C_6H_6 before use. It is a homogeneous catalyst [Black *Aldrichimica Acta* **15** 13 *1982*]. Tetrakis(perfluoroacetato)dirhodium(II) catalyses the addition of carbenes (generated from diazo esters) to aromatic compounds at room temperature to generate 1-carbalkoxycyclohepta-2,4,6-trienes (with high kinetic selectivity for the *non*conjugated isomers) in very good yields. A competitive reduction of the catalyst occurs simultaneously causing the reaction to slow down, and should be taken onto account [Anciaux et al. *J Org Chem* **46** 873 *1981*].

Ruthenium(III) acetylacetonate [$Ru(acac)_3$] *[14284-93-6]* **M 398.4, m 240°(dec).** Purify the complex by recrystallisation from *benzene. [Wilkinson *J Am Chem Soc* **74** 6146 *1952*, *Beilstein* **1** IV 3677.] It catalyses the hydrogenation of dimethyloxalate to ethylene glycol under mild conditions [70bar H_2 pressure at 100°] and the best ligand is $MeC(CH_2PPh_2)_3$ with a trace of Zn (0.07% of oxalate) in MeOH with yields of >84% and with turnover numbers of 875 (turnover frequency/hour of 53.5) [Teunissen & Elsevier *J Chem Soc, Chem Commun* 667 *1997*].

Ruthenium (benzylidine)dichloro-bis-(tricyclohexylphosphine) [phenylmethylene-bis-(tricyclohexyl-phosphine) dichlororuthenium (Grubbs catalyst—first generation) *[172222-30-9]* **M 823.0, m 153° (dec).** Wash

it repeatedly with Me_2CO and MeOH and dry it in a vacuum. *Alternatively*, dissolve it in warm CH_2Cl_2, concentrate it to half its volume, filter, add MeOH to precipitate it as purple microcrystals. Filter these off, wash several times with Me_2CO and MeOH and dry them in a vacuum for several hours. [Scwab et al. *J Am Chem Soc* **118** 100 *1996*, Miller et al. *J Am Chem Soc* **118** 9606 *1996*, Furstner & Langermann *J Am Chem Soc* **119** 9130 *1997*.] It is used to catalyse ring-closing metathesis [Schrodi & Pederson *Aldrichimica Acta* **40** 45 *2007*, Schmidt *Angew Chem. Int Ed* **42** 4997 *2003*], and promotes olefin metathesis with ruthenium based catalysts [Grubbs *Tetrahedron* **60** 7117 *2004*]

§ A polymer supported version is available [Schwab et al. *Angew Chem, Intl Edn* **34** 2039 *1995*].

Ruthenium(III) chloride ($RuCl_3$) *[3H_2O 13815-94-6; xH_2O 14898-67-0; Anhydrous 10049-08-8]* **M 207.4 (anhydrous), 261.5 (3H_2O), d^{20} 3.11.** The anhydrous salt exists in two forms. The α-form is produced by the slow reaction of Cl_2 with Ru metal in siliceous containers at >600° to give black lustrious hexagonal crystals which are antiferromagnetic and insoluble in H_2O or EtOH [Hill & Beamish *J Am Chem Soc* **72** 4855 *1950*]. The second β-form is prepared by heating Ru metal in a stream of CO and Cl_2 at 340°, to avoid the formation of carbonyl compounds such as $Ru(CO)_2Cl_2$ and is free from the metal or α-$RuCl_3$. It is formed in dark brown fluffy hexagonal crystals that are soluble in EtOH. It is the metastable form because at or about the transition temperature of 450° the β-form is slowly converted to the α-form (irreversibly, with $t_{0.5}$ ~1 hour), and is the best way to prepare the α-form. [Fletcher et al. *Nature* **199** α-form 1089 *1963*.]

Hydrated $RuCl_3$ is one of the most useful inorganic ruthenium compounds, and particularly for the preparation of Ru coordinated compounds. It is prepared by evaporating RuO_4 in concentrated hydrochloric acid in a stream of HCl gas. Unlike the anhydrous form, the hydrate is soluble in H_2O, but a fresh aqueous solution (brown to brown-green colour) does not precipitate AgCl with $AgNO_3$ solution because the halogen atoms (as well as one molecule of H_2O) are coordinated to the metal. However, on warming in H_2O the halogen atoms are displaced by H_2O molecules and the Cl^- ions can be precipitated (or titrated) with $AgNO_3$ [Grube & Fromm *Z Electrochem* **45** 661 *1940*, *cf* Connick & Fine *J Am Chem Soc* **83** 3414 *1961*].

It is a soluble catalyst used for the oxidative cyclisation of 1,7-dienes to oxepane diols [Piccialli et al. *Tetrahedron Lett* **48** 5131 *2007*], and promotes a site-specific hydroxylation of tertiary carbon-hydrogen bonds of cyclic ethers in the presence of periodate or bromate [Lee et al. *J Org Chem* **72** 5820 *2007*].

It also catalyses oxidation reactions with an oxidant, e.g. the methylene group in cyclopropylmethyl-compounds to a carbonyl group in the presence of metaperiodate [Hasegawa et al. *Chem Lett (Jpn)* 1385 *1985*, Carlsen et al. *J Org Chem* **46** 3936 *1981*, cf Review Gore *Platinum Metals Rev* **27** 111 *1983*]. It catalyses the synthesis of 2-ethyl-3-methylquinolines from primary aromatic amines and triallylamine [Cho et al. *Tetrahedron Lett* **40** 1499 *1999*], and has been used for the selective hydrogenation of unsaturated aldehydes [Fujita et al. *J Catal* **255** 95 *2004*].

Ruthenium [1,3-bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidine] dichloro (benzylidene) (tri-cyclohexyl-phosphine) {Benzylidene-[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydro-2-imidazolinylidene]dichloro-(tri-cyclohexylphosphine)-ruthenium, [(1,3-Bis(2,4,6-trimethylphenyl)-2-imidazolinylidene) dichloro (phenyl-methylene)(tricyclophosphine)ruthenium, (Grubbs catalyst—second generation)} *[246047-72-3]* **M 849.0, m 143.5-148.5°.** This catalyst is prepared by adding a solution of *tert*-BuOK (1.25g, 10.2mmol, 1.4 equiv) in dry THF (200ml) slowly to a suspension of 1,3-dimesityl-4,5-dihydroimidazolium tetrafluoroborate (4.2g, 10.2mmol, 1.4 equivalent) in dry THF (100ml) in a flame dried Schlenk flask (500ml) under N_2 (magnetic stirring) at ~20°. The BF_4^- salt dissolves immediately, the cloudy yellow mixture is stirred at ~20° for 1 hour, and then transferred (cannula) to a larger Schlenk flask (twice size) under argon. To this is added $RuCl_2(=CHPh)(PCy_3)_2$ (7.29, 7.29mmol, 1.0 equivalents) in dry $*C_6H_6$ (400ml) and heated at 80° for 30 minutes when the reaction is complete (by ^1H NMR). The volatiles are removed *in vacuo* and the residue is washed with dry MeOH, or pentane (4 × 100ml) to provide the active catalyst as a pink-brown microcrystalline powder (4.64g, 75%). It has ^1H NMR (400MHz, CD_2Cl_2) with δ at 19.16 (s, 1H), 7.37-7.05 (m, 9H), 3.88 (s, 4H), 2.56—0.15 (m, 51H); ^{31}P NMR (161.9MHz, CD_2Cl_2) with δ at 31.41 and HRMS (FAB) at 848.3306 for M^+ [Scholl et al. *Org Lett* **1** 953 *1999*].

It is used in ruthenium catalysed ring closure metathesis (RCM) and olefin metathesis [Kulkarni & Diver *J Am Chem Soc* **126** 8110 *2004*, Schmidt *Angew Chem*. *Int Ed* **42** 4996 *2003*, Scholl et al. *Org Lett* **1** 953 *1999*], and generate unsaturated sultones (e.g. 2,7-3*H*-dihydro-[1,2]oxathiepine-2,2-dioxide) from olefinic sulfonates (e.g. but-3-enyl allylsulfonate) *via* ring closure metathesis [Le Flohic et al. *Tetrahedron* **62** 9017 *2006*].

Ruthenium [(*R*-P-Phos)(acac)$_2$] {Ruthenium [*R*-(+)-2,2′,6,6′-tetramethoxy-4,4′-bis(diphenylphosphino)-3,3′-bipyridine)-bis(acetylacetonate)] is prepared by mixing equimolar amounts of *R*-P-Phos (see *R*-(+)- [221012-82-4] in Part-2 below) with Ru(acac)$_3$ [14284-93-6] in the presence of a reducing agent (Zn powder) in refluxing EtOH to give the solid catalyst in 97% yield which was characterized by ^{1}H, ^{31}P NMR, elemental analysis and X-ray crystallographic structure determination. **Ru[(*S*- P-Phos)Cl$_2$](DMF)$_n$** is prepared in a similar manner with the appropriate ingredients (using ***S*-(-)-P-Phos** [362524-23-0]) in DMF. [Pai et al. *J Am Chem Soc* **122** 11513 *2000*.] These (see also below) atropisomeric bi-heteroaromatic diphosphine (P-Phos and its variants) complexes with transition metals are effective in catalysing asymmetric reactions including asymmetric hydrogenation of 2-arylacrylates, β-ketoesters, arylketones, hydrosilylation and C-C bond formation with high stereospecificity. [Wu & Chan *Acc Chem Res* **39** 711 *2006*, Au-Yeung & Chan *Coordination Chemistry Reviews* **248** 2151 *2004,* Pai et al. *J Am Chem Soc* **122** 11513 *2000*.]

Ruthenium [(*R*-Xylyl-P-Phos)(C$_6$H$_6$)]Cl$_2$ {Ruthenium *R*-(+)-2,2′,6,6′-tetramethoxy-4,4′-bis[di(3,5-xylyl)phosphino]-3,3′-bipyridine)(benzene) dichloride] is prepared in 88% yield by mixing equimolar amounts of [RuCl$_2$(C$_6$H$_6$)]$_2$ [37366-09-9] with *R*-Xylyl-P-Phos (see *R*-(+)- [442905-33-1] in Part-2 below) in EtOH/*C$_6$H$_6$ (8:1) and heating at 50-60^o for 1 hour. This ruthenium complex is a highly active, enantioselective, air stable catalyst for the asymmetric hydrogenation of β-ketoesters (PH$_2$ = 200-350psi at 70-90^o for 1-15 hours) to optically active β-hydroxyesters with ~100% conversion and >91% enantiomeric enrichment. It is very stable in the solid state in air; and a stirred solution for 10 hours under air showed no loss of activity or stereoselectivity; and its ^{31}P NMR (200MHz, CDCl$_3$) is not different from that obtained for the original sample under N$_2$ which has an AB set of signals with δ_P at 33.49 (d, $J_{PA\text{-}PB}$ = 62.9Hz) and 39.96 (d, $J_{PA\text{-}PB}$ = 62.5Hz). The coordination of ruthenium to benzene makes the phosphorus atoms non-equivalent. The resonance observed in the ^{1}H NMR (500MHz, CDCl$_3$) at 5.65ppm is assignable to the 6H resonances of the η^6-coordinated benzene moiety [Wu et al. *Tetrahedron Lett* **43** 1539 *2002*].
Other P-Phos related ligands, such as the chiral 4-bis(tolylphosphino) (***Tol-P-Phos***) and chiral 4-bis(cyclohexylphosphino) (***Cy-P-Phos***) ligands, were prepared and purified in a similar, or slightly modified, manner using the appropriate phosphines. They also form ruthenium complexes that have related catalytic activities [Wu & Chan *Acc Chem Res* **39** 711 *2006*, Au-Yeung & Chan *Coordination Chemistry Reviews* **248** 2151 *2004*].

Ruthenium(II)-tris(triphenylphosphine) dichloride [tris(triphenylphosphine)ruthenium(II) dichloride] *[15529-49-4]* **M 958.8; 433 (in Me$_2$CO/N$_2$), m 132-134^o.** This catalyst is prepared by heating under reflux RuCl$_3$.3H$_2$O (0.26g, 1mmol) and Ph$_3$P (1.57g, 6mmol) in MeOH (65ml) under N$_2$ for 3 hours, when the reddish-brown tris-complex separates. It is washed well with MeOH, then Et$_2$O and dried *in vacuo* at 60^o (yield 75%). It is soluble in CHCl$_3$, Me$_2$CO, *C$_6$H$_6$, EtOAc and hot *i*-PrOH, but insoluble in H$_2$O, Et$_2$O and sparingly soluble in alcohol. When less Ph$_3$P is used in e.g. MeOH, complexes such as Ru(III)-di(Ph$_3$P)(MeOH)Cl$_2$ are formed. *Note that if the above mixture is shaken, not refluxed, Ru(II)-tetrakis(triphenylphosphine) dichloride is formed which turns green on exposure to air*. [Stephenson & Wilkinson *J Inorg Nucl Chem* **28** 945 *1966*, Sammakia & Stangeland *J Org Chem* **62** 6105 (footnote) *1997*.]
The *tris-complex* catalyses a variety of reactions including hydrogen transfer [Sasson & Blum *Tetrahedron Lett* 2167 *1971*, Regen & Whitesides *J Org Chem* **37** 1832 *1972*], insertion of *t*-BuOO- into the carbon atom α to the N-atom of, e.g. *N*-methoxycarbonylpyrrolidine and 1,2,3,4-tetrahydroisoquinoline with *t*-BuOOH [Kondo et al. *J Org Chem* **56** 487 *1991*], intramolecular cyclisation of unsaturated α,α-dichloroesters or amides [Hayes at al. *J Org Chem* **51** 5501 *1986*], and the reduction of –CHO by HCOOH/Et$_3$N/THF without affecting NO$_2$, RCOR', ester or *tert*-amide groups [Kai & Arcelli *Tetrahedron Lett* **26** 3365 *1985*]; and for other examples of catalysis by this Ru-complex see selected volumes of Fieser & Feiser's *Reagents in Organic Synthesis*, and *Angew Chem. Int Ed* **46** 1905 *2007*. When complexed further with chiral (phosphinoferrocenyl)oxazolines, hydrogen transfer is not only considerably enhanced but is also highly stereospecific [see further in this chapter].

Samarium (II) iodide (SmI$_2$) Samarium (II) iodide (SmI$_2$) see [32248-43-4], Chapter 5, Inorganic Compounds.
Silver acetate (AgOAc) see [563-63-3], Chapter 5, Inorganic Compounds.

Silver tetrafluoroborate [$AgBF_4$] see [14104-20-2], Chapter 5, Inorganic Compounds.
Tetrakis(triphenylphosphino)palladium(0) [palladium-tetrakis(triphenylphosphine)] *[14221-01-3]* **M 1155.6, m 100-105°, 115°, ~116° (dec, sealed tube under N_2), (m is unreliable and is not a criterion of purity because it varies).** This catalyst is prepared from $PdCl_2$ (5.9g, 0.1mol), Ph_3P (43.7g, 0.5ml) in Me_2SO (400ml) under a vacuum N_2 system with pressure release, and the yellow mixture is heated (oil bath) with stirring until dissolution (140°). The bath is removed, the mixture is stirred rapidly for 15 minutes and hydrazine hydrate (6.7g 0.4mol) is injected within 1 minute. A vigorous evolution of N_2 occurs and the dark solution is rapidly cooled with a cool water bath and crystallisation takes place (~125°). When the temperature reaches ~20° the solid is filtered off (coarse sintered glass) under N_2, washed with EtOH (2 × 50ml), Et_2O (2 × 50ml) and the yellow crystalline solid is dried by a slow stream of N_2 through the funnel overnight (37.4g 97%). *Alternatively*, it can be prepared freshly by mixing $Pd(NO_3)_2$ (2mmols) and PPh_3(2mmols) in hot $*C_6H_6$ when vigorous evolution of nitric oxide occurs (fume cupboard) and a solid mass separates. This is collected and crystallised from EtOH. It should not be heated excessively as it dissociates to $Pd(PPh_3)_3$ and PPh_3, and then further to $Pd(PPh_3)_2$ and PPh_3. It is also air sensitive as PPh_3 is oxidised to PPh_3O. It is stable only for short periods because on exposure to heat or air it turns from yellow to orange and dissociates in solution, so the solutions should be used directly. Its cryoscopic constant in $*C_6H_6$ (at 0.601g/20ml) corresponds to **M 1156** [Malatesta & Angoletti *J Chem Soc* 1186 *1957*]. Molecular weight determination in $*C_6H_6$ indicates considerable dissociation, and the solution absorbs O_2 rapidly to give an insoluble green oxygen complex [Nyman et al. *J Chem Soc A* 561 *1968*]. It is moderately soluble in $*C_6H_6$ (5g/100ml), CH_2Cl_2 and $CHCl_3$ but less soluble in Me_2CO, THF and MeCN. $Pd(Ph_3P)_4$ may be handled in air but it is best stored under N_2. [Coulson *Inorg Synth* **28** 121 *1990,* Malatesta & Angoletta *J Chem Soc* 1186 *1990*, *Beilstein* **16** IV 954.]
$Pd(Ph_3P)_4$ is a very versatile catalyst for promoting the dimerisation of butadiene to 1,3,7-octatriene [Takahashi et al. *Bull Chem Soc Jpn* **41** 454 *1968*], catalysing various coupling reactions, without homo-coupling occurring [Brocato et al. *Tetrahedron Lett* **33** 7433 *1992*, Arcadi et al. *Tetrahedron Lett* **34** 2813 *1993*, McClure & Danishefsky *J Am Chem Soc* **115** 6093 *1993*, Paquette & Astles *J Org Chem* **58** 165 *1993*, Schoo et al. *Org Lett* **8** 4141 *2006*], including Suzuki coupling [Trost *Tetrahedron* **33** 2615 *1977*]. [*Beilstein* **16** IV 954.]
This palladium catalyst bound to a polymer support (~0.06mmol/g) is also commercially available [*cf* Frnger & LeDrain *Tetrahedron Lett* **39** 4287 *2988*].

Tetra-*n*-propylammonium perruthenate (TPAP, tetrapropyl tetraoxoruthenate) *[114615-82-6]* **M 351.4, m 160°(dec).** This stable dark green solid is a useful catalyst for a variety of oxidation reactions at about room temperature. It is used at a concentration of about 5 mol% with an equivalent of *N*-methylmorpholine *N*-oxide which provides the required oxygen with typical turnovers of about 250. The reactions are carried out in CH_2Cl_2 and/or MeCN, although the latter assists the reactions in CH_2Cl_2 considerably. Care should be taken to add TPAP slowly as the reaction can be vigorous. Addition of finely ground 4Å molecular sieves moderate the rate and efficiency of the reaction. The reactions usually proceed to completion within 5 minutes to one hour. Cooling and slow addition of TPAP is necessary with reactions on a large scale. Workup is simple, and is carried out by passing the solution through a short silica-gel column and eluting with EtOAc followed by evaporation and crystallisation or distillation of the product. When MeCN is the solvent, or is present in the solvent, it is advisable to evaporate the solvent prior to passage through the silica-gel column. [Ley et al. *Synthesis* 639 *1994*; see entry in the "Metal-Organic Compounds" chapter for further information].

Triphenylphosphinegold(I) bis(trifluoromethanesulfonyl)imidate ($[Ph_3PAu(I)]^+$ $[NTf_2]^-$) *[866395-16-6]* **M 739.4, m >230°.** $AgNTf_2$ is first prepared by mixing Ag_2CO_3 (276mg, 1.0mmol) and $HNTf_2$ (562mg, 2.0mmol, 2 equivalents [82113-65-3]) in H_2O (10ml), and refluxing for 3 hours (to eliminate CO_2); then evaporating to dryness *in vacuo*. It can be used as a solid or dissolved in dry CH_2Cl_2 (5ml). [Li et al. *J Org Chem* **73** 4323 *2008*.] The versatile catalyst is then prepared by dissolving Ph_3PAuCl (2mmol, [14243-64-2]) in CH_2Cl_2 (5ml) and adding to it solid $AgNTf_2$ (786mg, 2mmol) or the preceeding CH_2Cl_2 (5ml) solution. Immediate separation of AgCl occurs. After stirring for 15 minutes the ^{31}PMR reveals a single peak of the Au salt. The AgCl is removed by filtration through Celite, the pale coloured solution is evaporated *in vacuo*, and the residue is dried *in vacuo* to give a quantitative yield of the catalyst. It forms small white crystals which are air stable, but should be preferably stored in a dry inert atmosphere. It is soluble in Me_2CO, CH_2Cl_2, and $CHCl_3$ but insoluble in petroleum ethers. Its IR (CCl_4) has ν_{max} at 1482, 1437, 1405, 1384, 1216, 1196, 1133, 1103 and 960, cm^{-1}; the ^{1}H NMR (400MHz, $CDCl_3$) has δ_H at 7.47-7.55 (m, 12H, aromatic H) and 7.56-7.62 (m, 3H, aromatic H close to

Au); the ^{13}C NMR (100MHz, $CDCl_3$) has δ_C at 118.4 (q, $J_{^{13}C-^{19}F}$ = 323.0Hz), 126.3 (d, $^1J_{^{13}C-^{31}P}$ = 65.8Hz), 128.5(d, $^2J_{^{13}C-^{31}P}$ = 12.5Hz), 133.5 (d, $^4J_{^{13}C-^{31}P}$ = 2.5Hz) and 133.1 (d, $^3J_{^{13}C-^{31}P}$ = 13.7Hz); and the ^{31}P NMR (121.5MHz, CD_2Cl_2) has δ_P at 30.7. [Mésailles et al. *Org Lett* **7** 4133 *2005*.] **NTf_2** is a weakly coordinating counter ion which confers stability to the complex. ^{31}P NMR spectra of pre-formed solutions of the complexes Ph_3PAuBF_4, Ph_3PAuPF_6 and $Ph_3PAuSbF_6$, using the respective Ag salts, showed that they were not very stable. Attempts to isolate the complexes were unsuccessful. [Mésailles et al. *Org Lett* **7** 4133 *2005*.]
At concentrations of 1-2mol% in CH_2Cl_2 or Me_2CO, $Ph_3PAu(I)]^+$ $[NTf_2]^-$ catalyses the stereoselective isomerisation of butynediol monobenzoates into functionalised 2,5-dihydrofurans (in a sequence of two steps) in high yields at room temperature and in 15 to ~30 minutes [Buzas et al. *Org Lett* **8** 1957 *2006*]. It is exceedingly active in catalysing a wide variety of eyne cycloisomerisations [Mésailles et al. *Org Lett* **7** 4133 *2005*]. Also under similar mild conditions, in the presence of electrophilic bromine (from *N*-bromosuccinimide) or iodine (from *N*-iodosuccinimide), it catalyses the formation of linear α-halo-enones from propargyl acetates [Yu et al. *Tetrahedron* **65** 1846 *2009*], and 4-haloalkylidene-1,3-dioxalan-2-ones with propargyl *tert*-butylcarbonates [Buzas et al. *Tetrahedron* **65** 1889 *2009*], products which are suitable substrates for Pd-catalysed cross coupling reactions. Like the following OTf^- Au catalyst, it promotes the glycosylation of 1,2-anhydrosugars as donors using protected sugars with one free sterically unhindered OH group [Li et al. *J Org Chem* **73** 4323 *2008*].

Triphenylphosphinegold(I) trifluoromethanesulfonate ($[Ph_3PAu(I)]^+$ $[OTf]^-$) *[156397-47-6]* **M 608.2, m >230°.** $Ph_3PAu(I)]^+$ $[OTf]^-$ differs from the preceding catalyst in the counter anion, and is much less air and moisture sensitive. Due precautions need to be taken in use and storage. It is prepared by dissolving Ph_3PAuCl (0.1mmol, [14243-64-2]) and silver trifluoromethanesulfonate (0.1mol, [2923-28-6]) in dry CH_2Cl_2 (1ml) and stirred for 5 minutes. Filtration from AgCl provides a 0.1M solution of catalyst in CH_2Cl_2. Generally the AgCl does not interfere in the catalytic process and so the catalyst can be prepared *in situ*. Colourless $Ph_3PAu(I)]^+$ $[OTf]^-$ can be obtained by evaporating the CH_2Cl_2 solution and stored appropriately. It is a superior catalyst than anhydrous $ZnCl_2$ for the well established glycolsylation reactions with 1,2-anhydrosugars as donors [Li et al. *J Org Chem* **73** 4323 *2008*], and it catalyses the intramolecular hydroamination of terminal alkenes in high yields with 1-5mol% of catalyst by heating in toluene at 100° for 12-48 hours, or the intra- and inter- molecular hydroamination in $ClCH_2CH_2Cl$ by microwave radiation as heat source in ~30 minutes in high yield [Liu et al. *Org Lett* **8** 2707 *2006*]. In a useful application, the catalyst $Ph_3PAu(I)]^+$ $[OTf]^-$ promotes a cascade cyclisation/oxidative cleavage of a carbon-carbon triple bond in Z-enynols, e.g. 5-Ph or 5-*n*-butyl-pent-2-ene-4-yne-1-ols, in the presence of molecular oxygen to give high yields of the corresponding 2,5-dihydrofuran-2-ones and releasing C-5 with its substituent as the aldehyde or acid. The reaction involves free radicals as it is completely suppressed in the presence of the radical scavenger 4-hydroxy-TEMPO [Liu et al. *J Am Chem Soc* **128** 11332 *2006*].

Tris(dibenzylideneacetone)dipalladium(0) chloroform adduct [$Pd_2(dba)_3(CDCl_3)$] *[52522-40-4]* **M 1035.1, m 122-124°; solvent free $Pd_2(dba)_3$** *[51364-51-3]* **M 95.7, m 152-155°.** When $PdCl_2$ (1.05g, 5.92mmol) is added to a solution of dibenzylidene acetone (dba, 4.60g, 19.6mmol) and NaOAc (3.9g, 47.5mmol) in MeOH (150ml at 50°) and mixed at 40° for 4 hours then cooled, a reddish-purple precipitate separates. This is collected, washed with H_2O then Me_2CO and dried *in vacuo*. The precipitate (3.39g) is purified by dissolving it in hot $CDCl_3$ (120ml), filtering, and to the deep violet filtrate is added slowly Et_2O (170ml) when the *chloroform adduct* separates as deep purple needles which are collected and dried *in vacuo* (80% yield, m 122-124°). Recrystallisation from $*C_6H_6$ instead of $CHCl_3$ gives deep-violet needles of **tris(dibenzylideneacetone)-dipalladium(0) benzene adduct** (62.5% yield, m 141-142°). By using toluene instead of $CHCl_3$, deep-violet needles of **tris(dibenzylideneacetone) dipalladium(0) toluene adduct** (36% yield, m 140-141°) are obtained. The solvates can be exchanged with each other (i.e. $CDCl_3$, $*C_6H_6$ or toluene) without affecting the coordinating reactivity of the complex with other ligands such as Ph_3P, Bipy, *o*-phen, olefins, *o*-quinones etc. [Ukai et al. *J Organomet Chem* **65** 253 *1974*, for applications see Fustero *Org Lett* **8** 4129 *2006*.]
If the procedure is used with bis(*p*-methoxybenzylidene)acetone and the complex crystallised from $CDCl_3/Et_2O$, **Pd_2(*p,p′*-methoxy-dba)$_3$** is obtained as deep violet needles (72.3% yield, m 141-143°) which do not complex with the solvent. [cf **$Pd(dba)_2$** above.] [Ukai et al. *J Organomet Chem* **65** 253 *1974*.]

Tris(dibenzylideneacetone)palladium [$Pd(dba)_3$]: When a fourfold excess of dba is added to solution of $Pd(dba)_2$ or $Pd_2(dba)_3$ in $*C_6H_6$, heated and reduced in volume, the dark red colour of $Pd(dba)_2$ turns to brown,

and on complete evaporation, orange brown crystals of **Pd(dba)$_3$** contaminated with yellow crystals of dba are obtained. Washing the crystals with *C_6H_6 leads to crystal decomposition. The IR of the complex has ν_{max} at 1651 (C=O) and olefine bands at 1598, 1580 and 1531 cm^{-1}. X-ray analysis of the Pd(dba)3—*C_6H_6 crystals showed that each pentadienone ligand is coordinated through one olefin group, and the Pd atom is trigonal with ~C_3 symmetry [Mazza & Pierpont *Inorg Chem* **12** 2955 *1973*, cf *Handbook of Organopalladium for Organic Synthesis* Negishi ed. Wiley, Hoboken NJ *2002*, ISBN 0-471-31506-0].

Tris[triphenylphosphinegold(I)]oxonium tetrafluoroborate ([Ph$_3$PAu(I)]$_3$O$^+$ [BF$_4$]$^-$) *[53317-87-6]* **M 1480.6, m 207º (dec), 207-208º (dec), 220-221º (dec).** The catalytic oxonium salt is prepared by adding a solution of $AgBF_4$ (0.2g, 1.03mmol) in MeOH (5ml) to a solution of Ph_3PAuCl (0.5g, 1.01mmol, [14243-64-2]) in THF (20ml) and the AgCl that precipitated is filtered off. A solution of KOH (0.1g, 1.78mmol) and $NaBF_4$ (0.5g, 4.55mmol) in MeOH (100ml) is added to the filtrate, stirred for 1 hour, the solvent is evaporated off *in vacuo*, the residue is extracted with $CHCl_3$ (2 x 30ml), the combined extract is filtered, and hexane (100ml) is added to precipitate the oxonium salt which gives analytically pure $[Ph_3PAu(I)]_3O^+$ $[BF_4]^-$ (0.42g, 84%), **m 220-221º (dec)**, after recrystallisation from a saturated $CHCl_3$ solution on adding ~1.5-fold volume of Me_2CO. ***Alternatively***, Ag_2O freshly prepared from $AgNO_3$ (5.0g, 29.5mmol), and $NaBF_4$ (5.0g, 45.5mmol, finely powdered) are added to a solution of Ph_3PAuCl (4.0g, 8.08mmol) in Me_2CO (600ml), stirred vigorously for 1 hour, and the solvent evaporated *in vacuo*. The residue is extracted with *C_6H_6 to removed unreacted Ph_3PAuCl, and the oxonium salt is extracted with $CHCl_3$ (3 x 40ml), filtered, and hexane (400ml) is added to crystallise $[Ph_3PAu(I)]_3O^+$ $[BF_4]^-$ (3.6g, 90%) out. It is soluble in $CHCl_3$ and CH_2Cl_2 but insoluble in hexane and Et_2O. Its IR (nujol mull) has ν_{max} at 1050-1070 (br, BF_4^-) cm^{-1}. It is a versatile air and moisture tolerant catalyst that has been used in a variety of reactions (see below). X-ray crystallography showed that in the crystals the oxonium ions are dimeric, with the two pyramidal monomeric $(Ph_3PAu)_3(\mu_3\text{-}O)^+$ fragments interacting *via* Au-Au' bonds (~3.16Å) involving two of the three Au atoms in each unit. The pyramidal structure has the O^+ atom centrally above the Au_3 triangular plane, and the resulting six-membered Au_2OAu_2O heterocycle has a chair conformation. The ***oxonium trifluoroacetate*** **m 209-210º (dec)** from $CHCl_3$/*C_6H_6, and the ***oxonium permanganate*** **m 131-131.5º (dec)** from $CHCl_3$/hexane (1.2:4.0 v/v) were prepared similarly. [Nesmeyanov et al. *J Organomet Chem* **201** 343 *1980*, cf Bruce et al. *Inorg Synth* **26** 326 *1988*.] Oxonium complexes with other phosphine ligands have been similarly prepared and if $H_2{}^{17}O$ is used in the preparations, then it is incorporated into the oxygen of the cation. $[Ph_3PAu(I)]_3{}^{17}O^+$ $[BF_4]^-$ has ^{31}P NMR (36MHz, CD_2Cl_2, external 85% H_3PO_4) with δ_P at 24.0, and ^{17}O NMR (CD_2Cl_2 and external H_2O) with $\delta_{^{17}O}$ at +19.7 (br s, *w/2* = 152Hz). [Yang et al. *Inorg Chem* **32** 1946 *1993*.]

[Ph$_3$PAu(I)]$_3$O$^+$ [BF$_4$]$^-$ catalyses the Claisen rearrangement of propargyl vinyl ethers, e.g. 1-phenylhept-2-yne-1-yl vinyl ether, to respective aldehydes which are usually reduced *in situ* with $NaBH_4$ to give the homoallenic alcohol, i.e. 1-phenyl-3-*n*-butyl-3-(2-hydroxyethyl)allene, in high yield with 1mole% of catalyst in CH_2Cl_2 at room temperature. Chirality is efficiently transferred in the rearrangement. [Sherry & Toste *J Am Chem Soc* **126** 15978 *2004*]. In the presence of sterically hindered secondary amines, e.g. (iso-Pr)$_2$NH or (iso-Pr)CyNH, it catalyses the 5-*exo-dig* cyclisation of formyl alkynes, e.g. 6-formyl-4,4-bis(methoxycarbonyl)hex-1-yne, to 1,1-(bismethoxycarbonyl)-3-formyl-4-exomethylenecyclopentane in $CDCl_3$, 70º/3-24 hours, in ~70% yields [Binder et al. *Org Lett* **10** 1025 *2008*]. In the presence of O_2 in THF at ~50º $[Ph_3PAu(I)]_3O^+$ $[BF_4]^-$ also catalyses the cascade cyclisation/oxidative cleavage of a carbon-carbon triple bond in Z-enynols efficiently [see$Ph_3PAu(I)]^+$ $[OTf]^-$ above, Liu et al. *J Am Chem Soc* **128** 11332 *2006*].

(Xantphos)Rh(H)(CO)(PPh$_3$) is prepared by stirring a solution of $(PPh_3)Rh(H)(CO)$ (100mg, 0.11mmol) and Xantphos (63.6mg, 0.11mmol, see [161265-03-8] in Catalysts—Part 2 below) in *C_6H_6 (10ml) at 30º for 4 hours, evaporating the solvent *in vacuo*, washing the residue with MeOH (1ml) and drying *in vacuo* to give the analytically pure complex with the formula $C_{58}H_{48}O_2P_3Rh$. The complex has IR ($CHCl_3$) with ν_{max} at 1996.9vs, 1909.6m cm^{-1}; the ^{1}H NMR (300MHz, C_6D_6) has δ at 7.82 (apparent q, 4H, *J* = 4.8Hz, ar), 7.66 (m, 6H, ar), 7.53 (apparent q, 4H, *J* = 4.9Hz, ar), 7.11 (dd, 2H, *J* = 7.3, 1.3Hz, CHC*H*CC), 7.0-6.9 (ar), 6.79 ('d', 4H), 1.48 (s, 3H, CC*H*$_3$), 1.38 (s, 3H, CC*H*$_3$), -9.14 ($J_{H\text{-}P}$ = 12.2Hz, $J_{H\text{-}P'}$ = 18.2Hz, $J_{H\text{-}Rh}$ = 1.7Hz); the ^{13}C{^{1}H}NMR (100MHz, C_6D_6) has δ at 156.9 (t, *J* = 5.6Hz), 141.9 (dt, *J* = 4.4, 31.1Hz), 140.1 (t, *J* = 18.9Hz), 137.6 (t, *J* = 18Hz), 135.6 (s), 134.9 (ar), 134.8 (ar), 134.6 (ar), 134.5 (ar), 134.4 (ar), 134.2 (ar), 36.9 (s, *C*(CH$_3$)$_2$), 31.0 (s, CH$_3$), 24.7 (s,

CH_3); and the $^{31}P\{^1H\}$NMR (121.5MHz, C_6D_6, referenced to external 85% H_3PO_4) has δ at 42.67 ($J_{P\text{-}Rh}$ = 151.1Hz, $J_{P'\text{-}P}$ = 119.1Hz, PPh_3), 25.65 ($J_{P\text{-}Rh}$ = 127.9Hz, $J_{P'\text{-}P}$ = 119.1Hz, Xantphos-P); and the MS has *m/z* at 961 (M-CO), 726 (M-PPh_3-2H), 698 (M-PPh_3-CO-2H); HR-MS found M is 578.1916 (calc for $C_{39}H_{32}OP_2$ is 578.1928). [Kranenburg, van der Burgt, Kramer and van Leewen *Organometallics* **14** 3081 *1995*.]

Xantphos-Ru complex formed *in situ* from equimolar amounts of Xantphos and $Ru(PPh_3)(CO)H_2$ in refluxing toluene containing piperidinium acetate is a good catalyst for akylating active methylene compounds, e.g. *t*-butyl cyanoacetate, and hydroxy compounds, e.g. $PhCH_2OH$, to provide α-substituted cyanoacetates, e.g. *t*-butyl 2-cyano-3-phenylpropionate [Slatford, Whittlesey and Williams *Tetrahedron Lett* **47** 6787 *2006*].

Xantphos-Pd complexes formed *in situ* from xantphos and $Pd(OAc)_2$ or $Pd_2(dba)_3$ catalyse the cross-coupling reactions between the amide nitrogen and aryl and heteroaryl halides [Manley & Bilodou *Org Lett* **14** 2433 *2004*] or *meso*-brominated porphyrins [Gao, Chen and Zhang *Org Lett* **11** 1837 *2004*] to form the corresponding aryl-N-CO- and *meso*-porphyrin-NCO- in high yields respectively in the presence of a base e.g. $CsCO_3$. Similar cross-coupling catalysis with *in situ* Xantphos and $Pd(OAc)_2$ between thenylbromides and 2-aminopyridines or aminoquinolines has been achieved in high yields [Begouin et al. *Synthesis* 2794 *2006*]. It should be *noted* that a detailed study of the mixing of Xantphos and $Pd_2(dba)_3$ identified the complexes ***(Xantphos)Pd(dba)*** and ***Pd(Xantphos)$_2$***. The former is a very active catalyst whereas the latter bis(xanthane based phosphine)$_2$Pd(0) is less soluble and inherently less active. It is therefore important, when forming the pre-catalyst, to keep the ratio of xantphos to Pd source less than 1.5:1 for a more effective catalyst involving cross-coupling between a nitrogen atom and an organic halide. [Lingensmith, Strieter, Barder and Buchwald *Organometallics* **25** 82 *2006*.]

(Xantphos)$_2$ Pd is prepared, in flame dried Schlenk equipment, evacuated/backfilled with argon three times, by stirring xantphos (579mg, 1.00mmol) and $Pd_2(dba)_3$ (229mg, 0.25mmol) in toluene (300ml) under argon for 4 hours. This is filtered *via* a cannula into a separate dry flask under argon, concentrated somewhat overnight and any palladium black which may have settled is filtered off and the filtrate is evaporated to dryness. The yellow residue is stirred overnight with toluene (100ml) to remove excess (or unused) dibenzylidene acetone and unreacted Xantphos. The remaining yellow Pd(Xantphos)$_2$ has **m 164° (dec.)**, is sparingly soluble in most common organic solvents, and is characterised by the correct elemental analyses for $C_{78}H_{64}O_2P_4Pd$. Its IR (KBr) has ν_{max} at 2924, 2854, 1461, 1398, 1377, 1222 cm^{-1}; and MALDI-MS: calcd for $C_{78}H_{64}O_2P_4Pd$: *theoretical:* 1260.2894 (22.9%), 1262.2909 (63.4%), 1262.2911 (100.0%), 1263.2907 64.6%), 1264.2914 (77.2%), 1265.2933 (47.5%), 1266.2931 (35.5%), 1267.2949 (25.1%); *Found:* 1260.3405 (24.0%), 1261.3285 (67.4%), 1262.3166 (100.0%), 1263.3162 (73.2%), 1264.3300 (79.3%), 1265.3424 (47.5%), 1266.3491 (35.5%), 1267.3104 (25.1%). [Lingensmith, Strieter, Barder and Buchwald *Organometallics* **25** 82 *2006*.]

Zirconocene chloride hydride (bis[cyclopentadienyl]zirconium(IV) hydride chloride, Cp_2ZrClH) (Schwartz' reagent) *[37342-97-5]* **M 257.9.** It is moisture and light sensitive. Determine its purity by reaction with a slight excess of Me_2CO whereby the active H reacts to produce $Cp_2ZrClOPr^i$ and the integrals of the residual Me_2CO in the ^1H NMR will show its purity. The presence of Cp_2ZrH_2 can be determined because it forms $Cp_2Zr(OPr^i)_2$. For a very active compound, it is best to prepare it freshly from the *dichloride*, see below by reduction with Vitride [$LiAl(OCH_2CH_2OH)_2H_2$], the white precipitate is filtered off, washed with tetrahydrofuran, then Et_2O and dried in a vacuum. Store it dry in the dark. [Carr & Schwartz *J Am Chem Soc* **101** 3521 *1979*, Negishi & Takahashi *Aldrichimica Acta* **18** 31 *1985*, Buchwald et al. *Tetrahedron Lett* **28** 3895 *1987*, Negishi & Takahashi *Synthesis* 1 *1988*, *Beilstein* **16** IV 1770.] It has been used for functionalising olefins and alkynes [Sun et al. *Org Synth* **71** 83 *1992,* Negishi & Takahashi *Aldrichimica Acta* **18** 31 *1985*, Ganem & Franke *J Org Chem* **72** 3981 *2007*]. It has also been used for mild and selective hydrozirconation of amides to aldehydes [Spletstoser et al. *J Am Chem Soc* **129** *3408* 2007].

Zirconocene dichloride (bis[cyclopentadienyl]zirconium dichloride, Cp_2ZrCl_2) *[1291-32-3]* **M 292.3, m 242-245°, 248°.** Recrystallise the dichloride from $CHCl_3$ or xylene and dry it in a vacuum. ^1H NMR ($CDCl_3$) has δ at 6.52 from Me_4Si. Store it dry in the dark under N_2. [Reid et al. *Aust J Chem* **18** 173 *1965*, *Beilstein* **16** IV 1770.]. Together with Zn and CH_2Cl_2 it is used for methylenation of carbonyl compounds [Tour et al.

Tetrahedron Lett **30** 3927 *1989*], and has been useful for the synthesis of a wide range of early transition-metal complexes and organometallic compounds [Negishi & Takahashi *Aldrichimica Acta* **18** 31 *1985*, see also selected volumes of Fieser & Fieser's *Reagents for Organic Synthesis*].

NANO METAL CATALYSTS: see section on Nano Metals in Chapter 8, "Nanomaterials and Nanotechnology".

ORGANOCATALYSTS

Organocatalysis has already been discussed in general terms (see Chapter 3), and this section deals with some individual examples that have proved useful.
Organocatalysts are small metal-free organic molecules, or metal-containing compounds but where the metal is not involved in the catalytic process, which efficiently and selectively catalyse a large variety of chemical reactions when used in small non-stoichiometric amounts. Several are commercially available and the purification of some are described here; the preparations of some also are mentioned as these assist in devising methods of purification. The purification of a number of organocatalysts is also described in other chapters. Examples include (-)-*quinine* [see 130-95-0] and (+)-*quinidine* [see 56-54-2] used to catalyse α-halogenation of carbonyl compounds, intramolecular Michael additions, cyclopropanation of enones, enolates etc, β-lactam synthesis from imines and ketenes, β-lactone synthesis from aldehydes and ketenes, Morita-Baylis-Hillman reactions, hydrophosphonylation of aldehydes, Diels-Alder reactions and desymmetrisation of *meso*-anhydrides; (-)-*cinchonidine* [see 405-71-2] and (+)-*cinchonine* [see 118-10-5] which catalyse additions to prochiral ketenes, desymmetrisation of *meso*-diols and of *meso*-epoxides; and their respective *N-benzyl salts* [see 69257-04-1, and 69221-14-3] are efficient chiral *phase transfer catalysts* (see below); *L-proline* [see 147-85-3] which catalyses intramolecular Michael addition, Mannich reactions, inter- and intra- molecular aldol reactions, addition to N=O (α-aminoxylation/hydroxylation of C=O compounds), addition to nitrones and to N=N double bonds (α-amination of C=O compounds); *L-phenylalanine* [see 63-91-2] which catalyses intramolecular aldol reactions; and the *metal-free Jacobsen's ligand N,N'*-Bis(3,5-di-*tert*-butylsalicylidene)-1,2-*trans*-cyclohexanediamine [see *R,R'*-135616-40-9 or *S,S'*-135616-36-3] which catalyses hydrocyanation (with TMS-CN) of aldehydes. It should be noted that the ***Phase Transfer Catalysts*** described in a later section of this Chapter are ***organocatalysts***. [For further examples see: A. Berkessel and H. Gröger *Asymmetric Organocatalysis* Wiley-VCH, Weinheim *2005*, ISBN-13 978-3-527-30517-9, ISBN-10 3-527-30517-3; B. List (Ed) *Topics in current chemistry* **Vol 291**: *Asymmetric Organocatalysis* Springer Verlag 2010, ISBN 9783642028144, 9783642028151; which include sections on *Noncovalent organocatalysis based on hydrogen bonding* (Etzenbach-Effers & Berkessel)*, Enamine catalysis* (Pihko et al.), *Carbene catalysis* (Moore & Rovis) *Brønsted base catalysts* (Ting et al.), *Chiral ketone and imminium catalysts for olefin epoxidation* (Wong & Shi), *Amine, alcohol and phosphine catalysts for acyl transfer reactions* (Spivey & Arseniyadis), *Secondary and primary amine catalysts for iminium catalysis* (Brazier & Tomkinson), *Lewis acid organocatalysts* (Sereda et al.) and *Chiral Brønsted acids for asymmetric organocatalysis* (Kampen et al.); P.I. Dalko (Ed), *Enantioselective Organocatalysis: reactions and experimental procedures*, Wiley-VCH, Weinheim, *2007*, ISBN 978-3-527-31522-2, 3-527-31522-5; M.C. Willis, review on *Enantioselective desymmetrisation, J Chem Soc, Perkin Trans 1* 1765 *1999*.] A whole issue of *Chem Rev (ACS)* [**107** 513-5841 *2007*] devoted to *Organocatalysis* with B. List as introductory guest writer has appeared.

***RS*-(±)-1,1'-Bi(2-naphthol) (± 1,1'-binaphthyl-2,2'-diol)** *[602-09-5]* **M 286.3, m 214-217°, 216-218°, 217-218°, 218°, $pK_{Est(1)}^{20}$~7.5, $pK_{Est(2)}^{20}$~11.8; *R*-(+)-1,1'-bi(2-naphthol) (*R*-(+)-BINOL)** *[18531-94-7]* **m 208-210°, 207.5-208.5°, $[\alpha]_D^{20}$ □□° (c 1, THF), $[\alpha]_{546}^{25}$+50.9° (c 1, THF); *S*-(−)-1,1'-bi(2-naphthol) (*S*-(−)-BINOL)** *[18531-99-2]* **m 207-208°, 208-210°, $[\alpha]_D^{22}$ −34° (c 1, THF), $[\alpha]_{546}^{25}$+51.3° (c 1, THF).** 1,1'-Bi(2-naphthol) is easily prepared by slowly adding a solution of $FeCl_3.6H_2O$ (28g, 104mmol, see [10025-77-1]) in H_2O (60ml) to a vigorously stirred and refluxing suspension of 2-naphthol (14.4g, 100mmol, see [135-19-3]) in H_2O (600ml) and boiled until the oily drops of 2-naphthol disappear and the *binaphthol* separates out in flakes. Boiling is continued for 10 minutes, and the solid is filtered off, washed with boiling H_2O and dried first in air then *in vacuo*, to give (±)-BINOL in almost quantitative yield. Recrystallisation from hot EtOH, toluene or $*C_6H_6$ (~150ml, using charcoal) gives colourless glistening plates m 218°. The (±)-*dimethyl ether* [75640-87-8, 75685-

01-7] has **m 190°** (from AcOH). [A.I.Vogel *Practical Organic Chemistry* Longmans, Green & Co, London, p 639 *1948*, Pummerer et al. *Ber* **59** 2159 *1926*, Walder *Ber* **15** 2166 *1882*.] The FT-IR (Nujol) has ν_{max} at 3486.6, 1617.9, 1508.8, 1322.7, 1252.4, 1177.2, 1126.4, 827.3 and 751.3 cm^{-1} (note below how it is different from its enantiomers). [*Beilstein* **6** H 1051, **6** I 519, **6** II 1026, **6** III 5877, **6** IV 7020.]

***R*- and *S*-BINOL** have been obtained by a variety of ways which attest to their usefulness. They have been prepared by resolution of the (±)-BNP-acid (see below), the (±)-BINOL-boron ester (*via* the quinine salt), the (±)-BINOL dibenzoate (*via* pancreas acetone powder), or by oxidative coupling of 2-naphthol in the presence of chiral amines [see Zimmer & Suhrbier *J Prakt Chem* **339** 758 *1997*]. The preparations involving reduction of the (±)-BNP acid directly with $LiAlH_4$, or *via* the methyl phosphate derivative with RedAl [sodium bis(2-methoxyethoxy)aluminium hydride] in 3.4M toluene solution [Truesdale *Org Synth* Coll Vol **VIII** 46 *1993*] appear to be most convenient, and do not involve racemisation. The former is described here as it does not require an esterification step. Pure *R*-(+)-BNP acid (115.4g, 331mmol) in dry THF at 0° under N_2, is treated with $LiAlH_4$ (31.4g, 830mmol) in small portions (exert extreme care here because of the large quantities used — fire hazard) during 1 hour with stirring. A further volume of dry THF (400ml) is added and the mixture is stirred at 25° under N_2, for 17 hours, cooled to 0° under N_2, and cold 6N aqueous HCl (250ml) is added very carefully. The upper phase is then decanted off, and the lower phase is mixed with 6N aqueous HCl (150ml) and THF (150ml), stirred, and is allowed to settle. The phases are separated and the lower phase is extracted with Et_2O. The combined organic phases are washed with brine, decolorised with charcoal and evaporated *in vacuo*. The residual oil is dissolved in $*C_6H_6$ (1L, toluene may be used) and evaporated until crystallisation sets in. The solid is collected (90.6g, 96%, m 202-207°), which upon crystallisation from $*C_6H_6$ or toluene gives optically pure BINOL (84.5g, 89%, **m 207-208°**) with (+) or (–) **$[\alpha]_{589}^{25}$ 34.3°, $[\alpha]_{578}^{25}$ 37.8°, $[\alpha]_{546}^{25}$ 51.3°, $[\alpha]_{436}^{25}$ 228° (c 1.1, THF)**. The FT-IR (Nujol) of the BINOL enantiomers are identical, though different from that of the racemate (see above), and have ν_{max} at 3509.9, 1617.9, 1511.5, 1319.1, 1220.9, 1148.9, 815.6, 749.6 and 566.0 cm^{-1}; and the ^1H NMR (1:1 $CDCl_3$/DMSO-d_6, TMS) has δ at 7.04 (d, 2H, J = 8.8Hz), 7.20-7.35 (m, 4H), 7.40 (d, 2H, J = 8.8Hz), 7.92 (d, 2H, J = 8.8Hz) and 9.21 (s, 2H). **Racemisation studies** showed that: BINOL (0.1g) is optically stable in an H_2O (10ml)/dioxane (12ml) mixture at 100° under N_2 during 26 hours; loses 44% and 66% of optical activity in BuOH (10ml) containing KOH (0.71mmol) per BINOL (0.33mmol) at 118° under N_2 in 13 and 23 hours respectively; and loses 37% and 72% of optical activity of BINOL (100mg) in a 20% aqueous HCl (10ml)/dioxane (12ml) mixture at 100° under N_2 during 7 and 26 hours respectively. [Kyba et al. *J Org Chem* **42** 4173 *1977*.]

BINOL and 3,3′-diaryl derivatives act as organocatalysts for Mirata-Baylis-Hillman reactions involving C-H activation, e.g. condensation of a variety of aldehyde with cyclohex-2-en-1-one to provide chiral 2-(1-substituted-1-hydroxymethyl)cyclohex-2-en-1-ones in 40 to 80% yields and "ee" values of ~90 in the presence of Et_3P [McDougal & Schaus *J Am Chem Soc* **125** 12094 *2003*], they catalyse hydrocyanation (with TMS-CN) of aldehydes with high "ee" at -78° [Holmes & Kagan *Tetrahedron Lett* **41** 7453 and 7457 *2000*], and the titanium complexes catalyse the stereoselective reduction [with $(MeO)_3SiH$] of carbonyl compounds [Schiffers & Kaga *Synlett* 1175 *1997*], as well as C-C forming reactions [Zimmer & Suhrbier *J Prakt Chem* **339** 758 *1997*] and Diels-Alder reactions [Mikami et al. *Tetrahedron*: *Asymmetry* **2** 643 *1991*]. The rare earth La-*S*-BINOL complex realises an asymmetric nitroaldol reaction with nitromethane in high product yield and enantomeric enrichment [Sasai et al. *J Am Chem Soc* **115** 10372 *1993*].

RS*-(±)-1,1'-Binaphthyl-2,2'-diylhydrogen phosphate (1,1'-binaphthyl-2,2'-phosphoric acid, BNP)** *[36193-63-6]* **M 348.3, m 217°, pK^{20} 0.74; *R*-(–)-1,1'-binaphthyl-2,2'-diylhydrogen phosphate** *[39648-67-4]* **m 217°, $[\alpha]_D^{20}$ –608° (c 1, MeOH), $[\alpha]_D^{22}$ –562.7° (c 0.97, $CHCl_3$), $[\alpha]_{546}^{22}$ –113° (c 0.95, $CHCl_3$); *S*-(+)-1,1'-binaphthyl-2,2'-diylhydrogen phosphate** *[35193-64-7]* **m 217°, $[\alpha]_D^{20}$ +608° (c 1, MeOH).** Recrystallise it from EtOH. Reflux for 3 hours in N NaOH is required to hydrolyse the cyclic phosphate. The ***R*-enantiomer** has been prepared by a general procedure in which ***R*-(+)-1,1'-binaphthyl-2,2'-ol** (1.90mmol, see *R*-BINOL [18531-94-7]) in pyridine (7.8ml) is treated with $POCl_3$ (250µl, 2.68mmol) and stirred at ~25° for 3 hours. The mixture is then quenched with H_2O (154µl) at 0°, stirred for 1 hour at ~25°, evaporated *in vacuo*, the residue is acidified with 6N HCl (20ml) at 0° then refluxed for 2 hours. After cooling to 0°, the *phosphoric acid* separates, is filtered off, washed with H_2O and dried *in vacuo*. Recrystallisation by dissolving in CH_2Cl_2 and pouring it into hexane provides pure crystals of the ***R*-(–)-*acid (1.58mmol, 83%). [Yamanaka et al. *J Am Chem Soc* **129** 6756 *2007*, for general procedure see Jacques & Fourquet *Org Synth* **67** 1 *1989*.] It has IR ($CHCl_3$) with ν_{max} at 3024, 3015, 1231, 1215, 1203, 1020, 951, 797, 779, 773, 762, 748, 737, 723, 716, 700 and 673 cm^{-1}; its ^1H NMR

(400MHz, $CDCl_3$, TMS) has δ at 8.01 (d, 2H, *J* = 8.8 Hz), 7.94 (d, 2H, *J* = 8.2 Hz), 7.55 (d, 2H, *J* = 8.8 Hz), 7.49-7.44 (m, 2H), 7.38 (d, 2H, *J* = 8.2 Hz), 7.32-7.27 (m, 2H) and 3.22 (s, 1H); and its ^{13}C NMR (100MHz, $CDCl_3$, $CDCl_3$ as internal standard with δ at 77.0) has δ at 147.2, 147.1, 132.2, 131.6, 131.0, 128.3, 127.0, 126.5, 125.5, 121.4 and 120.5. [Jacques et al. *Tetrahedron Lett* 4617 *1971*, Arnold et al. *Tetrahedron* **24**, 343 *1983*, *Beilstein* **6** II 1027.] ***Alternatively***, (and more useful as it can be carried out on a 100g scale), the *R*-(**–**) and *S*-(+) BNP *acids* are obtained by optical resolution of the diastereoisomeric *(+)-cinchonine salts* of the (±)-BNP *acid via* recrystallisation from hot MeOH. The crude *(+)-acid (+)-base salt* [which contains 91% of (+)-acid (+)-base and 9% of (–)-acid (+)-base] has $[\alpha]_{546}^{25}$ +424º (c 0.99, MeOH) and the more soluble crude *(–)-acid (+)-base salt* obtained by evaporation of the mother liquors [which contains 81% of (–)-acid (+)-base and 19% of (+)-acid (+)-base] has $[\alpha]_{546}^{25}$ –113º (c 0.95, MeOH). Pure *(+)-acid (+)-base salt* $[\alpha]_{546}^{25}$ +492º (c 1, MeOH) and pure *(–)-acid (+)-base salt*, $[\alpha]_{546}^{25}$ –256º (c 1, MeOH) as obtained from the pure enantiomeric BNP acids and (+)-cinchonine are recrystallised from MeOH/EtOAc and MeOH/Me_2CO/EtOAc respectively. The BNP acids are obtained from the respective salts (e.g. 77g) in boiling EtOH (e.g. 500ml) and adding 6N aqueous HCl (e.g. 570ml) with vigorous stirring during 30 minutes while keeping the temperature between 75º and 80º. After cooling the BNP acid is collected, washed with H_2O (e.g. 5 x 90ml), and air dried to give (~50 yield of ~99% ee) almost pure acid (by NMR and HPLC). BNP acids from the filtrates can be purified by recrystallisation from hot MeOH or EtOH and are sparingly soluble in H_2O. The solubilities at 25º in g/100ml are: 5.7±0.2 enantiomer (EtOH) and 10.3±0.5 racemate (EtOH); and 2.1±0.1 enantiomer (MeOH) and 2.5±0.1 raemate (MeOH). Two recrystallisations from EtOH of the BNP enantiomeric acids obtained did not alter the rotations at 25º which are (+) or (–): 595º ±7 (589nm), 624º ±7 (578nm), 720º ±8 (546nm), 1328 ±15 (436nm), 2050º ±25 (365nm) in MeOH; 574º ±16 (589nm), 602º ±17 (578nm), 694º ±20 (546nm), 1267 ±25 (436nm), 1828º ±40 (365nm) in EtOH. [Jacques & Fouquet *Org Synth* Coll Vol **VIII** 51 *1993*, see also Kyba et al. *J Org Chem* **42** 4172 *1977*].
The BNP acids, and their 3,3'-aryl derivatives, are useful asymmetric organocatalysts in being efficient *Brønsted acid catalysts* for enantioselective Mannich reactions. [Yamanaka et al. *J Am Chem Soc* **129** 6756 *2007*.]

2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) *[RS* see *98327-87-8]* **M 622.7, m 283-286º**, *[R-(+)-* see *76189-55-4]* **m 241-242º,** *[S-(-)-* see *76189-56-5]* **m 241-242º.** In addition to being ligands for Pd, Rh and Ru catalysts, *S*-BINAP also act as a organocatalysts for Mirata-Baylis-Hillman reactions involving C-H activation, e.g. in the condensation of 5-formylpyrimidine and derivatives with methyl acrylate to form methyl β-hydroxy-β–(pyrimidin-5-yl)- α-methylenepropionates with moderate enantiomeric excess at the chiral hydoxy centre [Hayase et al. *Chem Commun* 1271 *1998*].

Bode-Rovis-Enders NHC precatalysts
These are a group of 3,4-fused-2-aryl substituted 1,2,4-triazolium salt pre-catalysts, which when converted into the corresponding NHCs (N-heterocyclic carbenes) where C-5 of the heterocyclic ring becomes a carbene carbon atom, are ***organocatalysts*** that promote a wide variety of organic reactions. The carbene is usually generated *in situ* on addition of diisopropylamine or BTU. Among the reactions that these NHCs catalyse are cyclo-condensation reactions, enantioselective azadiene Diels-Alder reactions, aza-Claisen reactions, annulation reactions, formation of trisubstituted indanes *via* catalysed cascade annelations, desymmetrisation of cyclo-hexadienones, benzoin condensations, Stetter reaction, a^3 to d^3 Umpolung, transesterification, 1,2-additions, etc. [Bode *Speciality Chemicals Magazine* **27(6)** 28 pages *2007*, Moor & Rovis *Top Curr Chem* **290** 77-144 *2009*, Enders, Niemeier and Henseler *Chem Rev* **107** 5606-5655 *2007*.] Described below are such four chiral organoprecatalysts whose carbenes catalyse highly stereospecific reactions in good to very good yields and with very high enantiomeric excess(e,e), and two related non-chiral salts which also catalyse non-chiral reactions in high yields.

(4*aR*,9*aS*)-4,4*a*,9,9*a*-1-oxa-4-azafluorenone, **(4*aR*,9*aS*)-indeno[2,1-*b*]-1,4-oxazin-3(2*H*)-one)** *[862095-79-2]* **M 189.2, m 180-183º(dec), $[\alpha]_D^{23}$ –17.3º (c 1.08, MeOH)**. This is the key chiral intermediate *fluorine-3-one* that uses (+)-*cis-(1R,2S)-1-aminoindan-2-ol* (see [*136030-00-7*]) for the preparation of chiral *indeno-triazolo-oxazinium* pre-catalysts. Details of its synthesis are not given here because they have been reported in great detail by Rovis and coworkers [Vora et al. *Org Synth* **87** 350 2010], but the physical and spectroscopic properties, and final purification procedures are provided in order to assess the purity of the commercial product and to purify it further if necessary. Thus the aminoindanol is converted to the –ONa salt with NaH/THF which is reacted with $ClCH_2CO_2Et$ to form the *fluorenone*. The final purification is carried out by stirring vigorously the crude light brown solid with hexanes under a reflux condenser in an oil bath at 70º for

2 hours, cooling to ~25°, filtering the solid off and drying it at 70° *in vacuo* (2mm Hg) for 1 hour to give the *fluoreneone* as a white solid in 80-86% yield of almost analytical (C, H and N) purity. It has IR with ν_{max} at 3179, 3050, 2910, 1681, 1646, 1484, 1417 cm^{-1}; ^{1}H NMR (400MHz, Me_2CO-d_6) with δ at 2.97 (d, *J* = 16.8Hz, 1H), 3.23 (dd, *J* = 16.6, 4.9Hz, 1H), 3.89 (d, *J* = 16.2Hz, 1H), 4.05 (d, *J* = 16.2Hz, 1H), 4.57 (t, *J* = 4.6Hz, 1H), 4.82 (t, *J* = 4.0Hz, 1H), 7.23-7.29 (m, 3H), 7.46-7.49 (m, 1H), 8.21 (br s, 1H); ^{13}C NMR (100MHz, Me_2CO-d_6) with δ at 38.2, 59.4, 67.1, 77.1, 124.7, 125.7, 127.6, 128.4, 140.8, 143.1, 168.5; and HRMS (APCI$^+$) has *m/z* 190.0862, and the calculated value for $C_{11}H_{12}NO_2$ (M^+) is 190.0863. The enantiomeric **(4*aS*,9*aR*)-4,4*a*,9,9*a*-1-oxa-4-azafluorenone** can be similarly prepared by starting from (–)-*cis-(1S,2R)-1-aminoindan-2-ol* (see [*126456-43-7*]) and differs only in the sign of the specific rotation.

(5*aR*,10*bS*)–5*a*,10*b*-Dihydro-2-(2,4,6-trimethylphenyl)-4*H*,6*H*-indeno[2,1-*b*]-1,2,4-triazolo[4,3-*d*]-1,4-oxazinium chloride monohydrate *[903571-02-8 for anhydrous]* **M 385.9, m 217-219°, 226-230° (anhydrous ?), $[\alpha]_D^{20}$ –133.5° (c 1.00, EtOH), $[\alpha]_D^{20}$ –156.0° (c 1.00, $CHCl_3$).** Here also details of its synthesis are not given because they have been reported in great detail by Bode and coworkers [see Struble & Bode *Org Synth* **87** 362 2010], but the physical and spectroscopic properties, and final purification procedures are provided in order to assess the purity of the commercial products and to purify further if necessary. The preceding (4*aR*,9*aS*)-*fluorenone* is treated with Me_3OBF_4/CH_2Cl_2 (~25°/16 hours) then $NaHCO_3$, and dried in a high vacuum (12 hours) to give a 92-93% yield (95% purity) of **(4*aR*,9*aS*)-3-methoxy-2,4*a*,9,9*a*-tetrahydroindeno[2,1-*b*][1,4]oxazine** as a pale brown solid with **m 73-75°**, **$[\alpha]_D^{20}$ –15.7° (c 1.26, EtOH)**, and consistent IR, NMR and MS. This *methoxy-oxazine* is then added to a solution containing one equivalent of *2,4,6-trimethylphenylhydrazinium chloride** in MeOH and a catalytic amount of 4M HCl/dioxane (obligatory) and heated at 60° under a reflux condenser and N_2 atmosphere for 48 hours. The solvent is removed *in vacuo* and the crude orange solid residue is suspended in EtOAc (must be absolutely dry for high yields; dry by passing through an Al_2O_3 drying column in an argon atmosphere) with vigorous stirring at 90° (under N_2) for 30 minutes, cooled to 0°, and the light yellow solid is filtered off, washed with EtOAc and dried at ~25° (<1 mbar, 12 hours) to provide an 81-82% yield of **(*Z*)-2-mesityl-1-[(4*aR*,9*aS*)-4,4*a*,9,9*a*-tetrahydroindeno-[2,1*b*][1,4]-oxazin-3-(2*H*)ylidene)hydrazinium chloride** as a light yellow powder which has **m 200-201°(dec)**, **$[\alpha]_D^{20}$ +66.7° (c 1.42, EtOH),** and consistent IR, NMR and MS. The precatalyst is then obtained by cyclising the hydrazium chloride with triethylorthoformate (8 equivalents) in chlorobenzene (dried over 4Å molecular sieves) and anhydrous HCl (4M in dioxane, 1 equivalent) by stirring under N_2 at 120° for 1 hour, and the clear brown solution is evaporated *in vacuo*. The brown residue is treated with toluene, heated at 120° for 5 minutes, cooled in ice/water, the white solid is filtered off and the filtrate is evaporated at 60° *in vacuo* and dried at high vacuum (<0.75mm). The brown residue dissolves in toluene at 60° within 3-5 minutes then a white precipitate is formed rapidly. The cooled solution is filtered, the white solid is washed with a little toluene and dried at high vacuum (<1 mbar) to constant weight (>24 hours) to give a 60-64% yield of the desired *(5aR,10bS)-oxazinium chloride* pre-catalyst as an analytically pure (C, H and N) white powder with m 217-219°. It has IR with ν_{max} at 3435, 3482, 2904, 2853, 1580, 1466, 1222, 1097, 1083, 847, 749, 729, 662 cm^{-1}; the ^{1}H NMR (400MHz, DMSO-d_6) has δ at 212 (s, 6H), 2.37 (s, 3H), 3.16 (d, *J* = 17.0Hz, 1H), 3.50 (dd, *J* = 16.9, 4.8Hz, 1H), 4.99 (t, *J* = 4.4Hz, 1H), 5.08 (d, *J* = 16.0Hz, 1H), 5.26 (d, *J* = 16.0Hz, 1H), 6.12 (d, *J* = 4.0Hz, 1H), 7.21 (s, 2H), 7.33-7.45 (m, 3H), 7.65 (d, *J* = 7.2Hz, 1H), 11.34 (s, 1H); the ^{13}C NMR (100MHz, DMSO-d_6) has δ at 16.9, 20.6, 37.0, 59.7, 61.1, 76.8, 124.0, 125.3, 127.1, 129.2, 129.3, 131.2, 134.8, 136.1, 140.6, 141.3, 144.7, 150.0; and the HRMS (ESI) has *m/z* 332.1756 and the calculated value for $C_{21}H_{22}N_3O$ (M^+) is 332.1757.

The enantiomeric ***(5aS,10bR)–5a,10b-Dihydro-2-(2,4,6-trimethylphenyl)-4H,6H-indeno[2,1-b]-1,2,4-tri-azolo[4,3-d]-1,4-oxazinium chloride monohydrate*** **M 385.9, m 212-216°, $[\alpha]_D^{20}$ +158.0° (c 1.00, $CHCl_3$)** can be prepared similarly by starting from the enantiomeric ***(4aS,9aR)-4,4a,9,9a-1-oxa-4-azafluorenone*** and is purified in the same way.

*The purity of ***2,4,6-mesitylhydrazinium chloride*** [76195-82-9] **M 186.7** is critical for obtaining pure mesityl-pre-catalysts. The preparation from 2,4,6-trimethylaniline is described in great detail by Struble and Bode [*Org Synth* **87** 362 *2010*] who emphasise that it is imperative for diazotisation and reduction to be strictly monitored. It is paramount that $NaNO_2$ and $SnCl_2$ solutions be added at such a rate that the internal temperature is carefully monitored at <5°. The final purification is by suspending the salt (~7.5g) in absolute EtOH/Et_2O (1:1, 15ml), and sonicating (85W) for 5 minutes while maintaining the temperature below 30°. The pale orange solid is filtered off using a fine porosity filter, washed with EtOH/Et_2O (1:1, 3 x 5ml), and dried under high vacuum (~25°, <0.75mm) for 12 hours to give analytically pure (C, H and N) *2,4,6-mesitylhydrazinium chloride* (36-40% yield).

Note that the material may be very fine to filter in a short period, in which case it should be dissolved in dry MeOH and concentrated by evaporation to give a more crystalline product that can be filtered more easily. *Alternatively*, it should be collected by centrifugation, decantation of the supernatant, washed with EtOH/Et_2O (1:1, 3 x 5ml) also by decantation and sonication in the same way in between washes. It has **m 195-197°(dec)** (**167-173°** also reported); it has IR with ν_{max} at 3296, 3002, 2964, 2911, 2691, 1564, 1515, 1479, 846, 830, 575 cm^{-1}; the ^1H NMR (400MHz, DMSO-d_6) has δ at 2.20 (s, 3H), 2.35 (s, 6H), 6.60 (br s, 1H), 6.86 (s, 2H), 9.27 (variable br s, 3H, N*H,*N*H*$_2$); the ^{13}C NMR (100MHz, DMSO-d_6) has δ at 17.8, 20.4, 129.0, 134.9, 136.1, 137.9; and HRMS (ESI) has *m/z* 151.1228, and the calculated value for $C_9H_{15}N_2$ (M^+) is 151.1223. [Struble and Bode *Org Synth* **87** 362 *2010*]

(5*aR*,10*bS*)–5*a*,10*b*-Dihydro-2-(pentafluorophenyl)-4*H*,6*H*-indeno[2,1-*b*]-1,2,4-triazolo[4,3-*d*]-1,4-oxazinium tetrafluoroborate *[740816-14-2]* **M 467.1, m 223-226°, 235°(dec), $[\alpha]_D^{23}$ –130.8° (c 1.28, MeCN)**. Details of its synthesis are not given here because they have been reported in great detail by Rovis and coworkers [Vora et al. *Org Synth* **87** 350 2010], but the physical and spectroscopic properties, and final purification procedures are provided in order to assess the purity of the commercial product and to purify it further if necessary. The common intermediate ***(4aR,9aS)-4,4a,9,9a-1-oxa-4-azafluorenone*** (1.0 equivalent see [862095-79-2] above) is added with stirring, and under anhydrous conditions in an argon atmosphere, to a mixture of Me_3OBF_4 (1.0 equivalent *and no more*, care **Toxic**) in CH_2Cl_2 **(**containing <20ppm of H_2O, by filtering through activated Al_2O_3 under argon) and stirred at ~25° until the homogeneous reaction is complete (1-2 hours by ^1H NMR). Pentafluorophenylhydrazine (1.0 equivalent) is then added to the mixture under argon, stirred until the reaction is complete (~4 hours, when ^1H NMR signals of activated amidate disappear), the mixture is evaporated *in vacuo*, dried at 100°/2mm; then chlorobenzene (as solvent) followed by triethyl orthoformate (2.5 equivalents) are added and heated under reflux to 130° with stirring (open to the atmosphere) for 24 hours. A second portion of triethyl orthoformate (2.5 equivalents, syringe) is added and the mixture is stirred for a further 24 hours, and this process is repeated once more. Excess of toluene is added, the slurry is filtered, and the solid is washed with toluene and hexanes. It is then triturated with EtOAc and MeOH (4:1), filtered through a medium frit funnel, washed with cold EtOAc to give the ***oxazinium tetrafluoroborate*** pre-catalyst which, when dried at 100°/2mm to constant weight (~1 hour, 61-64% yield), gave an off white solid that analysed as the ~0.5 hydrate. It has IR with ν_{max} at 3147, 3106, 3028, 2967, 1595, 1530, 1517, 1487, 1461, 1056, 1046, 998 cm^{-1}; the ^1H NMR (400MHz, Me_2CO-d_6) has δ at 3.28 (d, *J* = 17.2Hz, 1H), 3.55 (dd, *J* = 17.1, 4.9Hz, 1H), 5.19 (t, *J* = 4.5Hz, 1H), 5.25 (d, *J* = 16.4Hz, 1H), 5.39 (d, *J* = 16.4Hz, 1H), 6.33 (d, *J* = 4.0Hz, 1H), 7.34 (t, *J* = 7.3Hz, 1H), 7.43 (q, *J* = 7.4Hz, 2H), 7.63 (d, *J* = 7.6Hz, 1H), 11.09 (br s, 1H); the ^{13}C NMR (100MHz, Me_2CO-d_6) has δ at 37.9, 60.8, 63.5, 78.2, 125.2, 126.4, 128.1, 130.4, 136.2, 141.7, 147.1, 152.5; and HRMS ($APCI^+$) has *m/z* 380.0816, and the calculated value for $C_{18}H_{11}N_3OF_5$ (M^+) is 380.0817. [Vora et al. *Org Synth* **87** 350 2010].

The enantiomeric ***(5aS,10bR)–5a,10b-Dihydro-2-(pentafluorophenyl)-4H,6H-indeno[2,1-b]-1,2,4-triazolo-[4,3-d]-1,4-oxazinium tetrafluoroborate*** can be prepared and purified in a similar way but starting with the enantiomeric ***(4aS,9aR)-4,4a,9,9a-1-oxa-4-azafluorenone.***

2-Pentafluorophenyl-6,7-dihydro-5*H*-pyrrolo[2,1-*c*][1,2,4]triazol-2-ium tetrafluoroborate (2-pentafluoro-2,5,6,7-tetrahydro[2,1-*c*][1.2.4]-tetrazol-4-ium tetrafluoroborate), *[862095-91-8]* **M 363.0, m 242-245°, 245°.** Details of its synthesis are not given here because they have been reported in great detail by Rovis and coworkers [Vora et al. *Org Synth* **87** 350 2010], but the physical and spectroscopic properties, and final purification procedures are provided in order to assess the purity of the commercial product and to purify it further if necessary. Starting with 2-pyrrolidinone (1.0 equivalent, [616-45-5]) which is converted into 2-methoxy-3,4-dihydro-5*H*-pyrrolidinium tetrafluoroborate by reaction with trimethyloxonium tetrafluoroborate (1.0 equivalent) in CH_2Cl_2 under argon with stirring at ~25° until homogeneous, then pentafluorophenylhydrazine (1.0 equivalent, [828-73-9]) is added with stirring for 4 hours (when amidate signals disappear in the ^1H NMR spectrum), the mixure is evaporated *in vacuo*, chlorobenzene and triethyl orthoformate (2.0 equivalents, syringe) are added and heated at 130° for 24 hours under a reflux condenser open to the atmosphere. Addition of triethyl orthoformate (2.0 equivalents, syringe) and heating is repeated for 24 hours, followed by evaporation to dryness *in vacuo*, excess of toluene is added to the residue and the slurry is filtered, and the solid is washed with toluene and hexanes, then with EtOAc. Final purification is by washing well with

cold EtOAc, and the off-white solid is thoroughly dried at 100° *in vacuo* (2mm) to constant weight (~1 hour) to give the *pre-catalyst tetrafluoroborate* in 74-76% yield. It has IR with ν_{max} at 3145, 3097, 2983, 1655, 1604, 1524, 1499, 1028, 994, 875 cm^{-1}; the ^1H NMR (400MHz, Me_2CO-d_6) has δ at 3.00 (ddd, *J* = 15.0, 7.7, 7.7Hz, 2H), 3.42 (t, *J* = 8.0Hz, 2H), 4.76 (t, *J* = 8.0Hz, 2H), 10.19 (s, 1H); the ^{13}C NMR (100MHz, Me_2CO-d_6) has δ at 22.6, 27.6, 49.5, 137.8, 140.4, 142.9, 143.3, 144.5, 145.6, 145.8, 165.8; and HRMS (APCI$^+$) has *m/z* 276.0556, and the calculated value for $C_{11}H_7N_3F_5$ (M^+) is 276.0555. [Vora et al. *Org Synth* **87** 350 2010].

2-Mesityl-6,7-dihydro-5*H*-pyrrolo[2,1-*c*][1,2,4]triazol-2-ium chloride (2-mesityl-2,5,6,7-tetrahydro[2,1-*c*][1.2.4]-tetrazol-4-ium chloride), M 263.8, m 202-205°. This is prepared and purified in much the same was as the preceding salt except for using triethyloxonium chloride for preparing the ethoxy pyrrolidinium chloride followed by reaction with mesitylhydrazinium chloride instead of perfluorophenylhydrazine.

Boron trifluoride diethyl etherate *[109-63-7]* **M 141.9, m -58°, b 46°/10mm, 126-129°/atm, d_4^{25} 1.15, n_D^{20} 1.344.** If the liquid has darkened due to oxidation by air it can be redistilled to give a colourless liquid. It is recommended that excess dry Et_2O (10ml) be added to the etherate (500ml) and distilled from CaH_2 (2g) in an all glass still at (b 46°/10mm) which removes volatile acids and avoids bumping [Zwiefel & Brown *Organic Reactions* **13** 28 *1963*]. It is a fuming liquid which hydrolyses in moist air forming highly toxic fluorides on decomposition. Store it under N_2 or argon and work in an efficient fume cupboard. It is a versatile *Lewis acid* for catalysis, acetylation, alkylation, dehydration, condensations, Beckmann rearrangements and polymerisation reactions. It catalyses the synthesis of cyclopentyl- and cycloheptyl[*b*]indoles from aryl cyclopropyl ketones *via* [3+2] cycloaddition [Venkatesh et al. *Eur J Org Chem* 5378 *2006*], and is a mild and efficient catalyst for Beckmann rearrangement in anhydrous MeCN [An et al. *Chin J Chem* **29** 947 *2011*]. [*Beilstein* **1** IV 1321.]

CBS (Corey-Bakshi-Shibata) Catalysts:

***R*-(+)-2-Methyl-CBS-oxazaborolidine (*R*-1-methyl-3,3-diphenyltetrahydro-1*H*,3*H*-pyrrolo[1,2-*c*][1,3,2]-oxazaborole, α,α–diphenyl-D-prolinolmethylboronic acid cyclamide)** *[112022-83-0]* **M 277.2, m 74-87°, 79-81°, 85-95°, $[\alpha]_D^{22}$ +76.8° (c 1, toluene) and *S*-(-)-2-Methyl-CBS-oxazaborolidine** *[112022-81-8]* **M 277.2, m 85-95°.** These CBS (**C**orey-**B**akshi-**S**hibata) catalysts effect the asymmetric reduction of *pro*-chiral ketones, the stereoselective synthesis of α-amino acids and α-hydroxy acids, the preparation of ferrocenyl diols and propargyl alcohols. The catalyst is usually best prepared *in situ* from the respective α,α–diphenyl-(*R* or *S*)-prolinol [22348-32-9 or 79815-20-6] and a slight excess of trimethylboroxine [823-96-1]. Their suitability is determined by capillary GC [DB-1. 200°, retention time 4.9 minutes] and ^1H NMR, where possible impurities have signals at δ ($CDCl_3$) for starting prolinol at ~4.3(t), trimethylboroxine at 0.45(s), the B—OH intermediate at 0.35 to -0.50 multiple B-Me singlet's, and/or the ring-B-O-B(Me)-OH intermediate at -0.25 B-Me brs. An analytical sample is obtained by dissolving it in toluene, filtering, then evaporating at 50°/0.001mm to give the catalyst as a white solid. Store it under dry N_2 or argon. The IR (CCl_4) has ν_{max} at 1000, 1235, 1310, 1330, 1440, 2880, 2960 cm^{-1}; and the ^1H NMR (0.2M in $CDCl_3$) has δ at 7.65-7.15 (m, 10 H, ArH), 4.4 (dd, *J* = 5.8, 10.0 Hz, 1 H, C3a-H), 3.45-3.30 (m, 1 H, C6-H), 3.15-3.00 (m, 1 H, C6-H), 1.90-1.55 (m, 3 H, C4-H, C5-H_2), 0.95-0.75 (m, 1 H, C4-H), 0.40 (s, 3 H, B-CH_3). They are also available commercially as 1M solutions in toluene or tetrahydrofuran. [Mathre et al. *J Org Chem* **56** 571 *1991*, Corey et al. *J Am Chem Soc* **124** 3808 *2002*, Ryu & Corey *J Am Chem Soc* **126** 8106 *2004*, Ryu et al. *J Am Chem Soc* **124** 9992 *2002*, Hu et al. *J Am Chem Soc* **126** 13708 *2004*, Quallich & Woodall *Tetrahedron Lett* **34** 785 *1993*.]

***R*-(+)- and *S*-(–)-2-*o*-Tolyl-CBS-oxazaborolidine {*R*- and *S*-3,3-diphenyl-1-*o*-tolyltetrahydro-1*H*,3*H*-pyrrolo[1,2-*c*] [1,3,2]-oxazaborole}** *[R-865812-10-8; S 463941-07-3]* **M 353.3, $[\alpha]_D^{20}$ +18° and –18° (c 1, toluene).** These Corey-Bakshi-Shibata (CBS) oxazaborolidines are available commercially as 0.5M solutions in toluene (d_4^{25}0.9009g/ml). They produce chiral *Lewis acids* when protonated with trifluoromethanesulfonamide and are used in enantioselective Diels-Alder reactions. They are prepared and purified as for the 2-methyl-CBS-oxazaborolidines above except that they are obtained as liquids on evaporation of the toluene solutions. [For applications see Ryu & Corey *J Am Chem Soc* **125** 6388 *2003*, Stemmler *Synlett* 997 *2007*, Corey et al. *J Am Chem Soc* **109** 7925 *1987*, Cho & Kim *Tetrahedron: Asymmetry* **12** 2043 *2001*, Cho et al. *J Chem Soc, Perkin Trans I* 1204 *2001*, Lebsack et al. *J Am Chem Soc* **123** 4851 *2001*, and references therein.]

2-Methyl-CBS-oxazaborolidines derived from 1*S*,2*R*-(-)- *[126456-43-7]* **and 1*R*,2*S*-(+)-*cis*-1-Amino-2-hydroxyindane** *[136030-00-7]* are best prepared *in situ* by reaction of *cis*-1-aminoindan-2-ol (1*S*,2*R*

see [126456-43-7]; 1*R*,2*S* see [136030-00-7]) with trimethylboroxine (see [823-96-1]) in a solvent (usually toluene), and they are sensitive to moisture and air. They catalyse the reduction of ketones and α-haloketones to their respective alcohols by BH_3 or some of its complexes, e.g. BH_3-DMS, BH_3-THF, with high stereospecificities (ee above 80%) at room temperature or below because of the steric effects of the methyl and indane groups around the heterocyclic boron atom. In a typical preparation, trimethylboroxine (0.19ml, 1.34mmol) is added to a solution of pure 1*R,*2*S*-1-aminoindan-2-ol (2.01mmol) in dry toluene (10ml), stirred at ~25° for 30 minutes, more toluene (10ml) is added and the solution is concentrated by distillation to *ca* 2ml. The procedure is repeated twice then the toluene is removed *in vacuo* to give the *CBS-catalyst* as a white solid. Dry THF (~2ml) is added to produce an approximately 1.0M solution of the catalyst in THF for later reactions. The solution should be stored under dry N_2 or argon and is stable for about 48 hours. For reduction reactions, the borane hydride (1.83mmol) is added to a solution of the chiral 2-methylaminoindanol (0.17ml, 0.166mmol) in the desired solvent (e.g. toluene) (2ml) stirred under N_2 at ~25° for 30 minutes, cooled to 0° and the ketone (1.67mmol) in the desired solvent (e.g. toluene, 1ml) is added *via* a cannula, stirred at ~25° for 30 minutes, quenched with MeOH (5ml), H_2O (20ml) is added, the MeOH is removed *in vacuo*, and the resulting optically active alcohol is isolated from the aqueous solution. [Gilmore & Jones *Tetrahedron: Asymmetry* **14** 2115 *2003*, Hong et al. *Tetrahedron Lett* **36** 6631 *1994*

4-Dimethylaminopyridine (DMAP) *[1122-58-3]* **M 122.2, m 108-109°, 112-113°, b 191°/atm (under N_2), $pK^{5.4}$ 10.14, pK^{20} 9.70, pK^{25} 9.61, pK^{35} 9.33 (in H_2O).** Recrystallise DMAP from toluene [Sadownik et al. *J Am Chem Soc* **108** 7789 *1986*]. DMAP can also be purified by recrystallisation from EtOH or $*C_6H_6$ and dried *in vacuo*. It is prepared easily from suitable 4-substituted pyridines, e.g. 4-chloropyridine and Me_2NH in EtOH (2 hours at 100°, or in a sealed tube for 12 hours at 100°, 115-130°, Wibaut & Brockman *Rec Trav Chim Pays Bas* **80** 309 *1961*), or in very high yield from 4-trimethylsilyloxypyridine with $Me_2NH/HgCl_2$ (48 hours at 120°, Vorbrüggen *Angew Chem Int Ed Engl* **11** 305 *1972*). This organocatalyst is a strong base and promotes a large variety of acylation reactions, e.g. of *m*-chloroaniline and of benzyl alcohol at relative rates that are 3.14×10^6 and 3.45×10^8 compared with those of the uncatalysed reactions. It is useful industrially. The acylating agent is an acid chloride or an acid anhydride. Typically, catalytic amounts of DMAP are used together with one equivalent of a tertiary base, e.g. Me_3N, to neutralise the anion formed, i.e. Cl^- from the acid chloride or AcO^- from the anhydride, and to avoid protonating the catalyst. [Scriven *Chem Soc Rev* **12** 129 *1983*.] Its *picrate* has **m 108°** (EtOH), and its *tetrafluoroborate salt* has **m 126°** (from MeCN/Et_2O). The UV has λ_{max} (ε) at 261nm (18,300 $cm^2.mole^{-1}$) for free base at pH >12.0, and 280.5nm (19,600 $cm^2.mole^{-1}$) for the mono-cation at pH <7.0 in H_2O (Essery & Schofield *J Chem Soc* 3939 *1961*); and the IR ($CHCl_3$) has ν_{max} (ε_A) at 2840 (sh, 45), 1448 (95, Me bend)), 1380 (155, CN str), 1346 (35), 1179 (35, Me_2 rock), 1108 (30, Me_2 rock), 1063 (35, NMe_2, C-N-C stretch) and 951 (55, NMe_2, C-N-C stretch) cm^{-1} (Katritzky & Jones *J Chem Soc* 3674 *1959*). [*Beilstein* **22** II 341, **22** III/IV 4101, **22/9** V 112.]
DMAP is an efficient ***desymmetrisation*** catalyst. [Willis *J Chem Soc, Perkin 1* 1765 *1999*.] Thus it allows the use of an achiral or *meso* molecule, e.g. 3-substituted glutaric anhydride to react with chiral alcohols e.g. *R*-1-(1′-naphthyl)ethanol to produce (1′*R*,3*R*)-1(1′-naphthyl)ethyl methyl 3-substituted-pentanoate di-esters (after treatment with diazomethane), which are now chiral at C-3. The achiral carbon atom at C-3 in the glutaric anhydride becomes chiral in the pentanoate (mono-ester of glutarate). [Theisen & Heathcock *J Org Chem* **53** 2374 *1988*, Theisen & Heathcock *J Org Chem* **58** 142 *1993*.]
§ It is commercially available in 0.04mmol impregnated tablets, and a polystyrene supported version (PS-DMAP) with a loading of ~3.0mmol/g is also available for recyclable acylation purposes.

***N,N′*-Dimethylethylenediamine [DMEDA, bis(methylamino)ethane]** *[110-70-3]* **M 88.2, b 110-112°/750mm, 119°/atm, d^{25} 0.819, n_D^{20} 1.431, pK_1^0 8.30, pK_2^0 10.89, pK_1^{25} 6.80 (7.01), pK_2^{25} 9.88 (10.03).** It has been prepared in several ways, but most commonly when ethylene dibromide (1mol), $MeNH_2$ (5mols) and H_2O (*ca* 3mols) are boiled under reflux for 15 hours. A 32% aqueous solution of NaOH is added, excess $MeNH_2$ is distilled out, and the rest of the liquid is distilled off. The diamine in the distillate is salted out with solid NaOH, dried (Na_2CO_3, or KOH), filtered and fractionally distilled (in *ca* 50% yield) until the NMR indicates that it is free from impurties. Store it in sealed containers under N_2 or argon as it is a strong base. The *N,N′-bis(p-toluenesulfonamide)* has **m 164°** (from AcOH), *N,N′-bis(benzenesulfonamide)* has **m 129-131°** (from EtOH and AcOH, or EtOAc), the *N,N′-bis(benzamide)* has **m 177-178°** (from $*C_6H_6$), the *monopicrate* has **m 140°** (plates

from EtOH or Me_2CO) and the *dihydrochloride* decomposes at **m 235°**. [Kermack & Wight *J Chem Soc* 1425 *1935*, Boon *J Chem Soc* 311 *1947*, Woodburn & O'Gee *J Org Chem* **17** 1241 *1953*, Bauer *J Am Chem Soc* **78** 1945 *1956*.]
In the presence of resublimed *tert*-BuOK (1.5mmol), DMEDA (0.1mmol) ***catalyses*** cross-coupling between aryl and substituted aryl halides (0.5mmol) with arenes, e.g, *benzene, naphthalene (0.5mmol) at 80°/~4 hours, to provide the corresponding biaryls in high yields (~70 to >90%). *Ortho* substitution leads to decreased yields, and replacing $KOBu^t$ with other bases (e.g. KOH, Na_2CO_3, KOAc, *tert*-BuONa, or *tert*-BuOK, *tert*-BuOLi) results in no reaction or extremely low yields. Of the amines studied DMEDA is the most effective catalyst and evidence is presented that a radical reaction is involved. It is the first example of a cross-coupling reaction which does not require a metal. [Liu et al. *J Am Chem Soc* **132** 16737 *2010*, *Beilstein* **4** H 250, **4** I 425, **4** II 689, **4** III 512, **4** IV 1171.]

***R*-(+)-Indoline-2-carboxylic acid** *[98167-06 -7]* **M 163.2, m 177°(dec), $[\alpha]_D^{20}$ +11.0° (c 0.3, MeOH).** Purify it as for the *S-enantiomer* below. The *R-(+)-hydrochloride* has [172152-19-1]. It is a proline based organocatalyst which promotes the enantioselective formation of cyclopropanes by reaction between 2-(dimethyl-λ^4-sulfanylidene)-1-phenyl-ethanone (for stable sulfonium ylides see Ratts & Yao *J Org Chem* **31** 1185 *1966*) and but-2-enals in high yields and very high stereoselectivity involving Direct Electrostatic Activation (DEA) [Kunz & Mac Millan *J Am Chem Soc* **127** 3240 *2005*.]

***S*-(-)-Indoline-2-carboxylic acid** *[79815-20-6]* **M 163.2, m 177°(dec), $[\alpha]_D^{20}$ -114° (c 1, N HCl).** It is purified as the racemate (see [78348-24-0] in Heterocyclic Compound, Chapter 4). The *S-(-)-hydrochloride* [82923-76-0] **M 199.7, m 133°(dec), $[\alpha]_D^{20}$ -70° (c 1, EtOH)** crystallises from Et_2O/propan-2-ol. It is a proline based organocatalyst which promotes the enantioselective formation of cyclopropanes by reaction between 2-(dimethyl-λ^4-sulfanylidene)-1-phenyl-ethanone (for stable sulfonium ylides see Ratts & Yao *J Org Chem* **31** 1185 *1966*) and but-2-enals in high yields and very high stereoselectivity involving Direct Electrostatic Activation (DEA) [Kunz & Mac Millan *J Am Chem Soc* **127** 3240 *2005*.]

α-Methyl-L-proline (*S*-2-methylproline) *[42856-71-3]* **M 129.2, m 248-252°(dec), $[\alpha]_D^{25}$ -75° (c 2.0, MeOH), and (*R*-2-methylproline)** *[58123-62-9]*. This derivative catalyses reactions similar to those of proline. The general three-step synthesis from proline devised by Seebach and co-workers provides enantiomerically pure compound [*Helv Chim Acta* **64** 2704 *1981*, *J Am Chem Soc* **105** 5390 *1983*, *Org Synth* **72** 62 *1993*]. It has been prepared on a 20-40g scale starting from *S*- or *R*- proline which is converted into ***2S,5S- (or 2R,5S)*- 2-*tert*-butyl-1-aza-3-oxabicyclo[3.3.0]octan-4-one** (*tert*-BuCHO, CF_3CO_2H as catalyst, pentane reflux for 114 hours with removal of H_2O) in 67-74% yield, which is methylated to ***2S,5S- (or 2R,5S)*- 2-*tert*-butyl-5-methyl-1-aza-3-oxabicyclo[3.3.0]octan-4-one** [86046-11-9] (MeI, *iso*-Pr_2NLi/THF/-78°) with complete retention of configuration at C-5 in 93-95% yield; and hydrolysed (1.3M HCl/reflux for 1 hour, or 15% aqueous HBr/~25° for 8 hours) to give the respective *2-methyl-proline hydrochloride* which is purified through a Dowex 50W x 8 (H^+ form) column by washing with H_2O, then eluting with 3N aqueous NH_3 and evaporating to give the free *2-methylproline* in 85-90% yield. The last step is apparently quite tedious to carry out and is time consuming. The following procedure is more convenient and gives better than 90% yields of pure *2-methylproline*. The above butyl-methyl-azaoxa-bicyclooctanone (13.4mmol) in MeOH/H_2O (6:1, 35ml) is treated with Silica gel 200-400 mesh, 60Å (3.0g) and stirred overnight. The silica gel is filtered off, washed with MeOH, the combined washings and filtrate are evaporated *in vacuo*, the pale yellow residue is dissolved in $CHCl_3$/MeOH (20:1), filtered through a 0.45μ filter disk (Acrodisk® CR PTFE), evaporated to dryness and the residue is triturated with Et_2O and dried *in vacuo*. Although it may be yellow in colour, it is almost spectroscopically pure, and can be purified further by dissolving in MeOH, treating with activated charcoal (5% w/w), filtering the whole suspension through Celite and evaporating. It can be crystallised by slow evaporation of the $CHCl_3$/MeOH solution, or from an MeOH/Et_2O mixture to give a first crop (50-70% yield) of white crystals leaving remaining *2-methylproline* and traces of yellow impurities in the mother liquors. Additional product crystallisation can be achieved by vapour diffusion of the supernatant against Et_2O in a closed desiccator. It also crystallises nicely from MeOH/EtOAc in colourless plates, unlike many α-amino acids. [Genin et al. *Tetrahedron Lett* **35** 4967 *1994*.]

S-2-Methylproline with $[\alpha]_D$ -72.1° (c 1.0, MeOH) was shown to have an enantiomeric excess "ee" of 99.0 ±0.5% by chiral capillary gas chromatography. For this purpose the amino acid (5mg) is heated with *iso*-propyl isocyanate (0.3ml) in CH_2Cl_2 (0.3ml) at 100° for 15 minutes, cooled, excess of volatiles are removed by a strong stream of dry air, the residue is dissolved in Et_2O (1ml), filtered through cotton wool and 10µl applied to the chiral capillary column. A Chirasil-Val fused-silica capillary column of Machery-Nagel (25m, 0.4mm) in a Carlo-Erba-Fraftovap 4160 HR GC unit has been used. The column was heated at 160° for 15 minutes then raised by 2°/min up to 200° (Argon as carrier gas ?). The amino acid has ^{1}H NMR (200MHz, D_2O, HDO at d 4.80) with δ at 1.52 (s, 3H, C***H***$_3$), 1.75-2.40 (m, 4H, 3-C***H***$_2$ + 4-C***H***$_2$), and 3.20-3.45 (m, 2H, 5-C***H***$_2$); and its ^{13}C{^{1}H decoupled}NMR (50MHz, D_2O) has δ at 179.87 (***C***O_2H), 73.2 (***C***-2), 48.06 (***C***H_3-2), 38.27 (N-***C***-5), 25-85 (***C***-3) and 23.99 (***C***-4). [Beck et al. *Org Synth* **72** 62 *1993*].

S-2-Methylproline hydrobromide [42856-71-3], prepared by hydrolysis with 15% aqueous HBr (see above) evaporating and triturating with dry Et_2O as colourless crystals (80%), has **m 136-137°(dec), $[\alpha]_D^{20}$ -28.9° (c 1.0, MeOH)** and its ^{1}H NMR (200MHz, D_2O, HDO at d 4.70) has δ at 1.60 (s, 3H, C***H***$_3$), 1.80-2.45 (m, 4H, 3-C***H***$_2$ + 4-C***H***$_2$), and 3.36 (t, 2H, J = 7 Hz, 5-C***H***$_2$) [Seebach et al. *J Am Chem Soc* **105** 5390 *1983*, Overberger & Jon *J Polym Sci, Polym Sci Ed* **15** 1413 *1977*].

α-Methyl-DL-proline (*RS*-2-methylproline) *[68078-09-1]* **M 129.2, m 263-264.5°.** The racemic 2-methylproline was prepared by hydrolysing 5-(3-chloropropyl)-5-methylhydantoin (2g, 10mmol) with $Ba(OH)_2$ (6.3g, 20mmol) and H_2O (50ml) in a pressure bomb at 160° for 30 minutes, cooling, adjusting the pH to 6 with 6N H_2SO_4, filtering off the $BaSO_4$, applying the filtrate through a column of Amberlite IRC 120 (H^+ form), washing with H_2O, eluting with 4N NH_4OH, and evaporating the eluate to give a white solid m 252-258° (1.2g, 90%). Recrystallisation of the solid from MeOH/Et_2O gave analytically pure *RS*-2-methylproline m 263-264.5°. It has IR (KBr) with ν_{max} at 3450 and 3200 (OH and NH), and 1600 (C=O) cm^{-1}; and its ^{1}H NMR (60MHz, CD_3OD, TMS) has δ at 1.6 (s, 3H, C***H***$_3$), 1.9 (m, 4H, 3-C***H***$_2$ + 4-C***H***$_2$), and 3.3 (m, 2H, 5-C***H***$_2$). [Ellington & Honigberg *J Org Chem* **39** 104 *1974*]. It should be possible to prepare it by Seebach's procedure (see preceding entry) and starting with *RS*-proline.

Tetra-*n*-butylammonium fluoride (TBAF) *[anhydrous, 1 M in THF 429-41-4; 3 H_2O 87749-50-6; hydrate 22206-57-1]* **M 261.5** (anhydrous), **315.5** (3 H_2O)**, m liquid** (anhydrous), **62-63°** (3 H_2O)**, 37°** (18 H_2O). It is a powerful catalyst for the regioselective ring opening of epoxides with thiols [Albanese et al, *Synthesis* 34 *1994*], the addition reactions of trimethylallylsilane [Majetich et al. *J Org Chem* **51** 1745 *1986*], Michael, Knoevenagel, aldol condensations, and by acting as a base in organic synthesis [Clark *Chem Rev* **80** 429 *1980*]. It is a mild and highly efficient source of nucleophilic fluoride ions, causing substitution of halogen or tosyl groups by fluorine. TBAF is also used for cleaving silyl ethers and silyl protecting groups [*cf* T.W. Greene and P.G.M. Wuts *Protective Groups in Organic Synthesis*, J. Wiley, NY *1991*]. When an aqueous solution of tetra-*n*-butylammonium hydroxide is titrated with hydrofluoric acid, a homogeneously melting *octadecahydrate* (m 37°) is obtained [Fowler et al. *J Am Chem Soc* **62** 1140 *1940*]. When the octadeca- or tri- hydrates are heated under high vacuum at temperatures of above 80°, decomposition occurs giving tetrabutylammonium bifluoride, tributylamine and 1-butene; with loss of a lot of it useful properties. When the *trihydrate* is warmed at 40° under high vacuum, almost "*anhydrous*" TBAF is obtained. This salt contained 0.1-0.3 molar equivalents of H_2O (by ^{1}H NMR). It is an oil at room temperature [Cox et al. *J Org Chem* **49** 3216 *1984*]. Virtually anhydrous TBAF in DMF can be prepared without heating by using aliquots (~10 to 30mg) of the trihydrate and placing them under high vacuum (<0.1mm Hg) for 0.5 hour at ~25°, the flask is flushed with N_2, and dry DMF (2ml) is added. The solution is transferred (syringe) to a round-bottomed flask (under N_2), containing 4Å Molecular sieves (which had been activated by flame-drying for 5 minutes under high vacuum), and stirred with a micro stirrer bar for 30 minutes [Majetich et al. *J Org Chem* **51** 1745 *1986*]. This is then used for catalytic or other reactions in anhydrous media.

TBAF is also available commercially as a 1 M solution in THF, 75% solution in H_2O, on alumina support 15wt% loading [429-41-4], on silica gel at ~1.5mmol/g F^- as a non-hygroscopic support for use as a source of "naked" fluoride ions [Ricci et al. *Tetrahedron Lett* **23** 577 *1982*, Gambacorta et al. *Synth Commun* **19** 2441 *1989*]. [*Beilstien* **4** III 292, For further applications see selected volumes of Fieser & Fieser's *Reagents for Organic Synthesis*.]

CATALYSTS—Part 2

LIGANDS & REAGENTS USED FOR MAKING LIGANDS THAT ASSIST CATALYSIS

Ligands and reagents in this section are mainly ones that are used within this and the former section Catalysts-Part 1. *Others will be found scattered in Chapters 4, 5 and 7, and can be identified by their CAS Registry Numbers through the index, or from their commonly used names.*

(η^3-Allyl)(η^5-cyclopentadienyl)palladium(II) [(allyl)(cyclopentadienyl)palladium(II)] *[1271-03-0]* **M 212.5, m 61° (dec).** This complex is volatile and should be handled in an efficient fume hood. Using Schlenk equipment under N_2 or argon and strictly dry conditions, a clear yellow solution of bis(η^3-allyl)di-μ-chloro-dipalladium(II) (9.9g, 27mmol, see [12012-95-2]) in THF (100ml) and $*C_6H_6$ (100ml) is prepared, and cooled in an ice-NaCl bath to -20°. A solution of sodium cyclopentadienyl (54mmol in 28ml of THF, [4984-82-1]) in a N_2 flushed syringe is added dropwise to the yellow solution at -20° with stirring, whereby the colour changes to dark red. The ice bath is removed after stirring for 1 hour, the temperature is allowed to rise to ~25°, stirring is continued for 30 minutes and the solvents are removed by evaporation *in vacuo* (30-60 torr; no higher than 20° because the Pd complex will begin to sublime at ~25°) to yield a dark red solid. The residue is extracted with hexane (80ml), the extract is filtered under N_2 (use fluted filter paper as a glass frit is likely to become clogged). The filtrate is evaporated as before (*in vacuo* at 30-60 torr) to give red needles of the palladium(II) complex (9.2g, 80%). Note that by using mechanical stirring the yield can be improved to 98%. This product is satisfactory for most preparations of Pd(0) complexes, but an analytical sample is readily obtained as red needle-like crystals by subliming it at 40°/30mm. It has an unpleasant odour, is relatively stable in air, decomposes gradually in air at ~25° to form a black solid which is not soluble in hexane, and is best stored below -20° under N_2 or argon. The ^{1}H NMR ($*C_6D_6$) has δ at 2.14 (d, *J* = 11Hz, 2H), 3.11 (d, *J* = 6Hz, 6H) and 4.63 (m, 1H) complex for allyl protons and 8.1 (s, 5H, cyclopentadienyl protons). [Tatsuno et al. *Inorg Synth* **XIX** 221 *1979*]. The complex is useful for preparing Pd(0) complexes [Shaw *J Chem Soc* 247 *1960*] by reaction with hindered alkyl phosphines [Otsuka et al. *J Am Chem Soc* **98** 5850 *1976*], reacts with isonitriles to form $Pd(CNR)_2$ complexes [Fischer & Werner *Chem Ber* **95** 703 *1962*, Otsuka et al. *J Am Chem Soc* **91** 6994 *1969*], and has been used to prepare BINAP complexes such as Pd[(*R*)-BINAP]$_2$ for asymmetric catalysis [Ozawa et al. *Organomet* **12** 4188 *1993*].

Ammonium perrhenate (NH_4ReO_4) *[13598-65-7]* **M 268.2, m 365°(dec.), d_4^{25} 3.97, pK^{25} -1.25 (for $HReO_4$).** The higher solubility of the ammonium salt in H_2O (17g/L at 0°, and 162g/L at ~50°) compared to that of the potassium salt (see [10466-65-6]) has made this salt preferable for use in the preparation of a variety of rhenium compounds. It is prepared from perrhenic acid (see [13768-11-1]) which is obtained from $KReO_4$ (10.0g, 0.036mol) using the procedure of Watt & Thompson (*Inorg Synth* **7** 187 *1963*) whereby a solution in H_2O (100ml, solubility is 14% at 100°) at 90° is passed through a column of cation exchange resin (Dowex 50-Wx2, but not x8) held at 90° (preferably coated with "Instatherm", Ace Glass Co., Inc Vineland, NJ, USA, to withstand the temperature), washed with H_2O, and the combined aqueous eluates are concentrated *in vacuo* down to the critical volume of 5ml. If it is concentrated further and the colour darkens, then one drop of 30% aqueous H_2O_2 should be added to decolourise it. The solution is cooled to ~0°, and while being stirred, a chilled mixture of 2-propanol (15ml, saturated with gaseous NH_3) and Et_2O (50ml) is added. The cold mixture is allowed to stand for 1 hour, and the white hexagonal plates (~90% yield) are filtered onto a sintered-glass funnel, washed three times with 2-propanol/Et_2O (1:9), dried *in vacuo*, then at 110° to give NH_4ReO_4 (8.9g, 96% yield) that is 99.4-99.95% pure by microanalysis and by passage through a cation-exchange resin in H_2O and titrating with standard base. [Thompson *Inorg Synth* **8** 171 *1966*, see also Smith & Long *J Am Chem Soc* **70** 354 *1948*.]

Benzotriazol-1-yloxy-tris(dimethylamino)phosphonium hexafluorophosphate ($BOP.PF_6$, Castro's reagent) *[56602-33-6]* **M 442.3, m >130°, 147-148°, 130°.** Castro's reagent is prepared by adding dropwise hexamethylphosphoric triamide (180g, 1 mol, see [680-31-9]) to a vigorously stirred solution of phosgene in toluene (180ml, 20%) during 4 hours (use a bubbler to control the evolution of CO_2). After stirring for 16 hours

at ~25°, excess of $COCl_2$ is removed under reduced pressure, CH_2Cl_2 (300ml) is added to ensure a homogeneous solution, and solid hydroxybenzotriazole monohydrate (153g, see [123333-53-9]) is added. The mixture is cooled to -5° (Me_2CO/Dry-ice) and Et_2NH (100ml, 1mol) is added during 15 minutes, and stirring is continued at 0° for 4 hours. The precipitated $Et_2NH.HCl$ is filtered off (sintered glass funnel), the solvent is evaporated *in vacuo*, H_2O (500ml) is added and the aqueous solution is extracted with Et_2O (3 x 100ml). This aqueous solution of BOP chloride is added to a filtered solution of KPF_6 (200g) in H_2O (2L) and the precipitated $BOP.PF_6$ is extracted into CH_2Cl_2. The organic layer is dried ($MgSO_4$), filtered and concentrated under reduced pressure. Addition of Et_2O causes the separation of the first crop of $BOP.PF_6$ which is collected, and further crops are obtained by addition of CH_2Cl_2 to the mother liquors, concentrating and adding Et_2O. The combined crops are washed with Et_2O and dried *in vacuo* to give the salt (354g, m 147-149°, 80%) which may be recrystallised further from Me_2CO/ Et_2O. The reagent is usually pure enough for efficient coupling of peptides without this recrystallisation. Its IR(KBr) has ν_{max} at 1010 (P-N), 840, 770, and 560 (PF_6^-) cm^{-1}; the ^1H NMR (acetone-d_6) has δ_H at 3.0 (d, 18H, $N(CH_3)_2$, $J_{H\text{-}P}$ = 10Hz), 7.9 (m, $4H_{arom}$); and the ^{31}P NMR (CH_2Cl_2/D_3PO_4) has δ at -43.7 (s, P^+), +144.2 (septet, PF_6^-). [Castro et al. *Synthesis* 751 *1976*.]

Benzotriazol-1-yloxy(tripyrrolidino)phosphonium hexafluorophosphate (PyBOP) *[128625-52-5]* **M 520.4, m 154-156°, 156-157°.** It can be prepared and purified in a similar manner as for BOP except that pyrrolidine replaced Et_2NH [cf Castro's reagent above, see [56602-33-6] and Dormoy & Castro *Tetrahedron Lett* 3321 *1979*] by recrystallisation from Me_2CO/ Et_2O and drying *in vacuo*. It is non-hygroscopic and can be stored at ~25°. It has ^{31}P NMR ($CDCl_3$) at δ: 31.8 (s) and -143.7 (heptet, J = 713Hz). It is an analogue of the BOP and a very good coupling agent which does not form the carcinogenic HMPA as byproduct [Coste *Tetrahedron Lett* **31** 205 *1990*, Seebach *Helv Chim Acta* **77** 1313 *1994*].

(2-Biphenyl)-di-*tert*-butylphosphine [JohnPhos, 2-(di-*tert*-butylphosphino)biphenyl] *[224311-51-7]* **M 298.4, m 86-88°.** This *Buchwald ligand* is prepared in Schlenk-type equipment under argon containing Mg turnings (617mg, 25.4mmol) and a small crystal of I_2 (to activate the metal) at ~25°, which is treated with a solution of 2-bromobiphenyl (5.38g, 23.1mol, see [2052-07-5]) in THF (40ml), the mixture is refluxed for 2 hours and allowed to cool to 25°. Anhydrous Cu(I) Cl (2.40g, 24.2mmol) is added, the flask is capped with a septum, purged with argon for 2 minutes and di-*tert*-butylchlorophosphine (5.0g, 24.2mmol; see [13716-10-4]) is injected *via* a syringe, and the mixture is refluxed for 8 hours. The mixture is cooled to ~25°, diluted with 1:1 hexanes/Et_2O (200ml) and the suspension is filtered, the solids are washed with hexanes (60ml), and the solid material is added to 1:1 hexanes/EtOAc (150ml) followed by H_2O (100ml) and 30% aqueous NH_4OH (60ml). This slurry is stirred at ~25° for 5 minutes, the layers are separated and the organic layer is washed with brine (100ml), dried (Na_2SO_4), filtered, evaporated *in vacuo* and the residue is recrystallised from MeOH (2 crops are collected) to provide *JohnPhos* as a white solid (4.46g, 67%) with **m 86-86.5°**. The IR (film) has ν_{max} at 2956, 1459, 1362, 1173 cm^{-1}. It has ^1H NMR (300MHz, $CDCl_3$) with δ_H at 7.95-7.85 (m, 1H), 7.40-7.21 (m, 8H), 1.15 (d, J = 11.6Hz, 18H); the ^{31}P NMR (121MHz, $CDCl_3$) has δ_P at -18.7; and ^{13}C NMR (75MHz, $CDCl_3$) at δ_C: 151.4, 150.9, 143.6, 143.5, 135.6, 135.2, 135.0, 130.4, 130.1, 128.3, 127.0, 126.7, 126.5, 126.2, 126.0, 125.6, 32.7, 32.6, 30.8, 30.6 (observed complexity from P-C coupling not assigned).
This ligand with $Pd(OAc)_2$ catalyses Suzuki coupling at ~25° between aryl halides (Br and Cl) with arylboronic acids with 0.5-1.0mol%Pd in high yields [Wolfe et al. *J Am Chem Soc* **121** 9550 *1999*, see cyclohexyl-JohnPhos below]. The ligand was used for the amination of aryl halides and aryltriflates **[**Wolfe et al. *J Org Chem* **65** 1158 *2000*]. This bulky biarylphosphine ligand was also used in the Pd-catalysed Stille cross-coupling reaction [Artamkina et al. *Synlett* **2** 235 *2006*] and in the Pd-catalysed 2,3-diarylation of α,α-disubstituted-3-thiophenemethanols *via* cleavage of C-H and C-C bonds [Nakano et al. *J Org Chem* **71** 8309 *2006*].

(2-Biphenyl)-dicyclohexylphosphine [cyclohexyl-JohnPhos, 2-(dicyclohexylphosphino)biphenyl] *[247940-06-3]* **M 350.5, m 102-106°.** This *Buchwald ligand* is prepared in a way similar to the preceding JohnPhos except that 2-bromobiphenyl in THF is converted to 2-lithiobiphenyl with *n*-BuLi at -78°/45 minutes, and followed by reaction with dicyclohexylchlorophosphine at -78°/15 minutes. The desired product is recystallised from MeOH to give cyclohexyl-JohnPhos (71%) as white crystals **m 103°**. The IR (film) has ν_{max} at 2916, 1441, 749 cm^{-1}; the ^1H NMR (300MHz, $CDCl_3$) has δ_H at 7.62-7.51 (m, 1H), 7.40-7.10 (m, 8H), 1.95-1.45 (m, 13H), 1.35-0.95 (m, 9H); and the ^{31}P NMR (121MHz, $CDCl_3$) has δ_P at -12.7; and the ^{13}C NMR (75MHz,

$CDCl_3$) has δ_C at 150.7, 150.4, 142.9, 142.8, 134.1, 133.8, 132.8, 130.61, 130.55, 130.5, 130.2, 130.1, 128.1, 127.3, 127.14, 127.05, 126.7, 126.4, 34.7, 34.5, 30.5, 30.2, 29.3, 29.1, 27.3, 27.2, 27.1, 26.4 (observed complexity from P-C coupling not assigned).
This ligand with $Pd(OAc)_2$ allows Suzuki coupling at low catalyst loadings (0.000001-0.02mol%Pd) between aryl halides (Br and Cl) with arylboronic acids in high yields, and tolerates a wide range of functional groups and substrate combinations including sterically hindered substrates. It was the most active catalyst system in terms of temperature of reaction, turnover numbers and steric tolerance in 1999 [Wolfe et al. *J Am Chem Soc* **121** 9550 *1999*.] This ligand was also used for the amination of aryl halides and aryltriflates **[**Wolfe et al. *J Org Chem* **66** 2560 *2001*], and was employed in the Pd-catalysed synthesis of 1,3,5-tris(2′aminophenyl)-benzene from *o*-aminophenylboronic acid and 1,3,5-triiodobenzene, which may be used as a three-directional core building block for potential ionic receptors [Piatek & Slomiany *Synlett* 2027 *2006*].

2,2′-Bipyridine (2.2′-dipyridyl, α,α′-dipyridyl) *[366-18-7]* **M 156.2, m 69.7º, b 272-273º/atm, pK^{25} 4.50.** The reaction of pyridine with Na produces a mixture of bipyridyls which can be separated by fractional distillation where the 2,2′-isomer distils at 272.5º/atm and solidifies on cooling (m 69.5º). The distilled oil can be purified further by dissolving in Et_2O, adding an equal volume of petroleum ether then the 2,3′- and 3,3′-isomers are washed out with several portions of H_2O. The organic layer is evaporated and the oily residue is recrystallised from aqueous EtOH. 2.2′-Bipyridyl also sublimes at 65º/0.01mm. Its solubility in H_2O is 0.5%, and it is very soluble in organic solvents. Its UV spectrum has λ_{max} nm(ε) 233 (10,200) and 280 (13,300) for the neutral species in H_2O. Unlike the other isomers it complexes with metals, e.g. it gives an intense red colour with ferrous salts. The *picrate* has **m 69.7º** (from aqueous EtOH). It is a metalloprotease inhibitor with high affinity for Fe^{2+} containing enzymes at 10^{-8} M. [Smith *J Am Chem Soc* **46** 414 *1924*; UV Krumholz *J Am Chem Soc* **73** 3487 *1951*, *Beilstein* **23/8** IV 28, **23/16** V 8.] **[TOXIC]**

1,3-Bis(1-adamantyl)-1,3-dihydro-2*H*-imidazol-2-ylidene (IAd) *[131042-77-8]* **M 336.3, m 240-241º.** This is a stable ***N*-heterocyclic carbene** (NHC) which has been prepared in 96% yield from IAdCl by de-protonation in THF with catalytic amounts of dismyl anion [$CH_3S(O)CH_2^-$] in the presence of 1 equivalent of NaH, or with *tert*-BuOK. In this reaction H_2 is liberated and NaCl is precipitated. The carbene is stable in the absence of oxygen and moisture and recrystallises from toluene to give clear, colourless rectangular prisms with a sharp melting point that is unaltered by melting and re-solidifying. The IR has (KBr) has ν_{max} at 2920, 1504, 1448, 1378, 1350, 1303, 1213, 1291, 833, 695 and 495 cm^{-1}; the ^{1}H NMR (*C_6H_6-d_6) has δ_H at 1.58 (s, $Ad_{4',6',10'}$, 12H), 2.01 (s, $Ad_{3',5',7'}$, 6H), 2.29 (s, $Ad_{2',8',9'}$, 12H), 6.91 (s, 3,4-C*H*, 2H); the ^{13}C NMR (*C_6H_6-d_6) [^{1}H] has δ_C at 211.43 (s, C_2), 113.88 (dd, $^1J_{CH}$ = 185.6Hz, $^2J_{CH}$ = 13.4Hz, $C_{4',5'}$), 55.99 (s, $Ad_{1'}$), 44.8 (tm, $^1J_{CH}$ = 131.3Hz, $Ad_{2',8',9'}$), 37.7 (tm, $^1J_{CH}$ = 126.8Hz, $Ad_{4',6',10'}$), 30.3 (dm, $^1J_{CH}$ = 128.9Hz, $Ad_{3',5',7'}$); the ^{15}N NMR (*C_6H_6-d_6, ref NH_4NO_3) has δ -160.5, and the EI-MS has *m/z* = 336.26. The X-ray crystal structure has been determined and showed a small N-C-N angle at the carbene centre. [Arduengo et al. *J Am Chem Soc* **113** 361 *1991*, see also Arduengo 336.3 et al. *J Am Chem Soc* **114** 5530 *1992*.] It is as effective, if not better in some cases, in many of the metal mediated catalytic reactions as other NHCs (Nitrogen Heterocyclic Carbenes). For further detail see the entry on IPr.Cl *[250285-32-6]*. [Arduengo USPatent 5 077 414 *1991, Chem Abstr* **116** 106289 *1002*, Kantchev, O'Brien & Organ *Aldrichimica Acta* **39** 97 *2006*, Phillips, Chan & Scheidt *Aldrichimica Acta* **42** 55 *2009*].

1,3-Bis(1-adamantyl)imidazolium tetrafluoroborate (IAd.BF_4) *[286014-42-4]* **M 424.3, m 277-282º.** This NHC (N-Heterocyclic Carbene) precursor is prepared by established procedures from 2 mols of amine, 1 mol of glyoxal and 1 mol of formaldehyde in toluene/H_2O in the presence of HBF_4. It is as effective, if not better in some cases, in many of the metal mediated catalytic reactions as other NHCs. For further detail see the entry on IPr.Cl *[250285-32-6]*. [Arduengo USPatent 5 077 414 *1991, Chem Abstr* **116** 106289 *1002*, Kantchev, O'Brien & Organ *Aldrichimica Acta* **39** 97 *2006*, Phillips, Chan & Scheidt *Aldrichimica Acta* **42** 55 *2009*].

2,2'-Bis(1,3,2-benzodioxaborole) [bis(catcholato)diboron, Cat-BB-Cat] *[13826-27-2]* **M 237.8, m 189-196º, 195-198º.** This borole is prepared by distilling B_2Cl_4 (3.95mmol [Wartik et al. *J Am Chem Soc* **71** 3265 *1949,* Urry et al. *J Am Chem Soc* **76** 5293 *1954*]) and CH_2Cl_2 (30ml) into a reaction vessel containing catechol (8.03mmol) at -196º, and then the reaction is allowed to proceed over the temperature range ~78 to 25º for 15 hours to give a clear solution (slightly less than 16mmol of HCl is liberated). CH_2Cl_2 and HCl are distilled off

from the reaction vessel *in vacuo* leaving a white residue which is sublimed at 120-130°/10^{-4}mm to give the pure borole in ~70% yield. A similar result is obtained by using $B_2[NMe_2]_4$ instead of B_2Cl_4. Cat-BB-Cat has one peak at -30.7ppm (from BF_3OEt_2 external reference) in the ^{11}B NMR (19MHz, CH_2Cl_2), and one peak for the aromatic protons at 2.69ppm (from solvent reference) in the ^{1}H NMR (60MHz, CH_2Cl_2); and its IR (KBr) has ν_{max} at 3058vw, 1610vw, 1597w, 1481s, 1464s, 1422m, 1400s, 1368s, 1346m, 1337m, 1285w, 1271m, 1263w, 1232s, 1214sh, 1157m. 1148s, 1140s, 1132s, 1117s, 1083m, 1037w, 1000w, 940w, 930m, 901w, 892m, 861m, 851w, 811s, 766m, 754s, 740s, 732s, 554s, 475w, 457w, and 419s cm^{-1}. Molecular weight determination in $*C_6H_6$ idicated that it is a *monomer*, and alkaline hydrolyses provided 0.96 mole of hydrogen per mole of B-B compound. [Welch & Shore *Inorg Chem* **7** 225 *1968*.] Cat-BB-Cat is efficient in olefin diboration catalysed by base-free Pt complexes such as $Pt(COD)_2$ and Pt(norbornene)$_2$ [Iverson & Smith *Organometallics* **16** 2757 *1997*], consequently producing useful synthons for cross-coupling reactions and related conversions to other functional groups [Miyaura & Suzuki *Chem Rev* **95** 2457 *1995*].

Bis[(*R,R,S*)-diazaPhos-SPE] {2,2′,2″,2‴-(1,2-phenylenebis(1*R*,3*R*)-tetrahydro-5,8-dioxo-1*H*-[1,2,4]-diaza-phospholo[1,2-*a*]pyridazine-2,1,3(3*H*)-triyl)tetrakis(*N*-[(1*S*)-1-phenethyl)benzamide} *[851609-33-1]* **M 1311.40, m 183-195°, $[\alpha]_D^{20}$ -82° (c 1, THF), and the diastereomeric bis[(*S,S,S*)-diazaPhos-SPE] {2,2′,2″,2‴-(1,2-phenylenebis(1*S*,3*S*)-tetrahydro-5,8-dioxo-1*H*-[1,2,4]-diaza-phospholo[1,2-*a*]pyridazine-2,1,3(3*H*)-triyl)-tetrakis(*N*-[(1*S*)-1-phenethyl)benzamide}** *[851770-14-4]* **M 1311.40, m 289-299°, $[\alpha]_D^{20}$ +15° (c 1, THF).** The central diazaphospholane tetracarbocylic acid in the two molecules are enantiomeric and these are converted to the phenethylamide using the same *S*-phenethylamine. Thus the two substances are diastereomeric. They are prepared by mixing the diazaphospholane tetracarboxylic acid (0.34mmol) with 5 equivalents of PyBOP [(benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate, m 154-156° cf [128625-52-5]] under N_2, adding degassed CH_2Cl_2 (100ml) followed by 5 equivalents of *N,N*-diisopropylethylamine and 5 equivalents of (α*S*)-α-methylbenzmethanamine (*S*-2-phenylethylamine), and stirring overnight. The solution is exposed to the atmosphere and washed with saturated $NaHCO_3$ (50ml), 2M HCl (50ml), saturated $NaHCO_3$ (50ml) again, then H_2O (50ml). The organic layer is dried ($MgSO_4$), filtered, and evaporated *in vacuo*. The residue is purified by flash chromatography (eluted with 2:1 CH_2Cl_2/EtOAc), and the separation of diastereoisomers is accomplished by liquid chromatography using a Zorbax Rx-Sil column (4.6 x 250 column). The *R,R,S- diastereomer* (21% yield) has ^{1}H NMR (500MHz, d-THF) with δ_H at 1.37 (d, 6H, *J* = 6.7Hz, CH_3), 1.56 (d, 6H, *J* = 6.7Hz, CH_3), 2.2-2.7 (m, 6H, CH_2CH_2), 2.65-3.0 (m, 2H, CH_2CH_2), 5.06 (dq, 2H, *J* = 7.5, 6.9Hz, C*H*CH_3), 5.41 (dq, 2H, *J* = 7.7, 6.9Hz, C*H*CH_3), 6.39 (d, 2H, *J* = 7.3Hz), 6.5-6.9 (m, 10H), 7.06-7.36 (m, 26H), 7.51 (m, 2H), 7.60 (d, 4H, *J* = 7.4Hz), 7.97 (d, 2H, *J* = 8.3Hz, N*H*CH CH_3), 9.23 (d, 2H, *J* = 7.8Hz, N*H*CH CH_3); the ^{13}C NMR (125MHz, d-THF) has δ_C at 23.2 (s, CH_3), 23.7 (s, CH_3), 29.6 (s, CH_3), 30.6 (s, CH_2), 50.0 (s, *C*HCH_3), 50.3 (s, *C*HCH_3), 56.9 (br, P*C*HN), 57.6 (t, br, P*C*HN), peaks at 125-150 have not been assigned, 166.7 (s, CO), 168.2 (s, CO), 168.4 (s, CO), 168.5 (s, CO); the ^{31}P NMR (202.4MHz, d-THF) has δ_C at 11.0 (br). The NMR spectra of the *S,S,S*-diastereomer is similar but not identical. [Clark et al. *J Am Chem Soc* **127** 5040 *2005*, Clark & Landis *J Am Chem Soc* **125** 11792 *2003*.]
It is a diazaphospholane ligand which displays high conversion and selectivity in Rh catalysed asymmetric hydroformylation reactions [Axtel et al. *Angew Chem. Int Ed Engl* **44** 5834 *2005*, Clark et al. *J Am Chem Soc* **127** 5040 *2005*, US Pat 7.071.357B.]

***R,R*-(-)- *and S,S*-(+)- *N,N′*-Bis(3,5-di-*tert*-butylsalicylidene)-1,2-*trans*-cyclohexanediamine (Jacobsen's ligand)** *[R,R- 135616-40-9, S,S- 135616-36-3]* **M 546.8, m 203-206°, 205-208°, 205-208°, $[\alpha]_D^{20}$ ±310° (c 1, CH_2Cl_2).** If this general ligand is to be purified, dissolve it in boiling EtOH and while cooling add H_2O to the yellow solution until a yellow solid separates. This is filtered off, washed with a little of 95% aqueous EtOH and dried *in vacuo*. It is the ligand for preparing Jacobsen's Catalysts [Jacobsen et al. *J Am Chem Soc* **113** 7063 *1991*, Deng & Jacobsen *J Org Chem* **57** 4320 *1992*].
On a large scale, the *R,R*-ligand (~60g) is dissolved in CH_2Cl_2 (500ml), washed with H_2O (2 x 300ml) and brine (100ml), dried (Na_2SO_4), and the solvent is removed to yield a yellow powder with m 200-203°, $[\alpha]_D^{20}$ ±315° (c 1, CH_2Cl_2), the required ^{1}H and ^{13}C NMR and IR with ν_{max} (KBr) at 1595, 1631, 2869, 2960 cm^{-1}. However, if it is felt that the product is of insufficient purity then it should be crystallised in two crops from Me_2CO (1:20 w/v with typical 86-93% recovery [Larrow et al. *J Org Chem* **59** 1939 *1994*.]
A **dimeric Jacobsen ligand**, formed by joining two units with a methylene bridge has been prepared and crystallised from CH_2Cl_2/pentane. Its **bis-Mn catalyst** exhibited improved retention in a poly-dimethylsiloxane

membrane for the asymmetric epoxidation of olefins [Janssen et al. *Tetrahedron Asymmetry* **8** 3481 *1997*].

1,5-Bis(3′,5′-dimethoxyphenyl)penta-1*E*,4*E*-dien-3-one (dm-dba)** ***[*39777-58-7****]*** **M 354.1, m 132-134°.** To a cooled (ice-water bath) solution of NaOH (1.8g, 2.5equivalents) in H_2O (18ml) diluted with EtOH (15ml) is added slowly 3′,5′-dimethoxybenzaldehyde (3g, 1equivalent) and analytical grade acetone (0.52g, 0.5equivalent) during 15 minutes, then it is stirred at 25° for 1 hour. A yellow solid separates, and after a further hour it is filtered off, then washed with Et_2O (3 x 50ml) and dried *in vacuo*. Purification by flash chromatography (*ca* 150 mesh Al_2O_3 deactivated with 6% v/w H_2O prior to use) and elution with petroleum ether (b 40°—60°)/EtOAc (4/1 v/v) gives *dm-dba* as a yellow solid (2.2g, 69%) which is recrystallised by layering a concentrated solution of CD_2Cl_2 with Et_2O (CD_2Cl_2/Et_2O, 1/3). The IR (CH_2Cl_2) has ν_{max} at 1652m (C=O), 1621vs (C=C), 1596w (C=C aromatic), 1572w (C=C aromatic) and 989m (CH trans) cm^{-1}; the UV has λ_{max} (THF) at 239 (π- π*) and 371 (n- π*) nm; the ^{1}H NMR (400MHz, $CDCl_3$) has δ_H at 6.48 (d, 1H, ^3J = 15.7Hz, H-2), 7.01 (1H, d, ^3J = 15.7Hz, H-1), 6.71 (2H, t, ^3J = 6.7Hz, 7.9Hz, H-6'), 7.62 (1H, d, ^3J = 8.2Hz, H-4′), 3.70 (s, 12H); and the ^{13}C NMR (100MHz, $CDCl_3$) has δ_C at 188.7 (4°), 160.9 (4°), 143.2 (CH), 136.5 (CH), 125.5 (CH), 106.1 (4°), 102.7 (4°) and 55.3 (CH_3). [Fairlamb et al. *Org Lett* **6** 4435 *2004*, *Beilstein* **7** IV 1747.]

2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) *[RS 98327-87-8]* **M 622.7, m 283-286°**, *[R-(+)- 76189-55-4]* **m 241-242°,** *[S-(-)- 76189-56-5]* **m 241-242°, $[\alpha]_D^{20}$ *R*+ and *S*- 233° (c 0.3, toluene).** It has been prepared from (±)-BINOL which is converted to (±)-2,2'-dibromo-1,1-binaphthyl (with Ph_3PBr_2) then to (±)-2,2′-bis(diphenylphosphinyl)-1,1-binaphthyl (BINAPO) [with Mg/$Ph_2P(O)Cl$] which is resolved into *S*-(−)- and *R*-(+)- BINAPO *via* separation of the diastereoisomeric (−)-2,3-di-*O*-benzoyl-L-tartrate salts in $CHCl_3$/EtOAc followed by treatment with 0.75N NaOH, extraction into $CHCl_3$, and isolation. The chiral BINAPO enantiomers are reduced to the respective *S*-(−)- and *R*-(+)- BINAP with excess of Cl_3SiH [see 10025-78-1] and Et_3N in toluene (100-120°) followed by treatment with 30% aqueous NaOH, extraction into toluene, isolation and purification as follows. Dissolve the enantiomer in toluene, wash it with 30% aqueous NaOH, three times with H_2O, dry (Na_2SO_4), evaporate to ~15% of its volume and add an equal volume of degassed MeOH. Collect the solid, wash it with MeOH and dry it at 80°/0.005mm for 6 hours. Recrystallise it from a 1:1 mixture of toluene/EtOH to optical purity (**m** 241-242°). Pure (99%) (*S*)-(−)-BINAP has ^{1}H NMR (300MHz, $CDCl_3$, TMS) with δ_H at 6.81 (d), 6.90 (t), 7.10 (m), 7.23 (s), 7.33 (t), 7.43 (dd), 7.82 (d) and 7.89 (d) where multiplicities are not necessarily coupled signals; and the ^{13}C NMR (75MHz, $CDCl_3$, TMS) has δ at 145.43, 145.38, 145.16, 144.93, 144.87, 137.93, 137.84, 137.77, 137.42, 137.35, 137.31, 137.24, 135.49, 135.46, 135.40, 135.38, 134.29, 134.23, 134.09, 133.94, 133.88, 133.31, 133.24, 133.12, 132.93, 132.89, 132.76, 132.63, 132.58, 130.44, 128.29, 127.99, 127.95, 127.91, 127.80, 127.57, 127.47, 127.39, 126.41 and 125.69 (40 signals of 44 carbons, i.e. 4 signals must overlap). The purity is determined by GLC analysis using an OV-101 5m capillary column at 200-280° (argon carrier gas ?). TLC analysis (Kieselgel 60 PF_{254}, with MeOH/$CHCl_3$ 1:19) is used to identify BINAP (R_F 0.83), BINAPO (R_F 0.4.2) and BINAP-monooxide (R_F 0.67). **(±)-BINAPO** [86632-33-9] crystallises from hot toluene (solubility is 3.6g/100ml at 110°) or from hexane/toluene, and analytically pure crystals have **m 304-306°** (299-300° also reported). ***S*-(−)-BINAPO** [94041-18-6] crystallises from a hexane/toluene mixture and has **m 261-262°**, **$[\alpha]_D^{24}$ −396° (c 0.47, C_6H_6)**, **$[\alpha]_D^{24}$ −168° (c 0.5, EtOH)**; and ***R*-(+)-BINAPO** [94041-16-4], similarly recrystallised, has **m 262-263°**, **$[\alpha]_D^{24}$ +396° (c 0.5, C_6H_6)**. [Takaya et al. *Org Synth* **67** 20 *1989*, Coll Vol **VIII** 57 *1993*]. [Noyori & Takaya *Acc Chem Res* **23** 345 *1990*, Kitamura et al. *Org Synth* **71** 1 *1993*, Takaya et al. *Org Synth* **72** 74 *1995*, Kitamura et al. *J Org Chem* **57** 4053 *1992*.]
§ A polymer supported version of BINAP is available.

2*R*,3*R*-(+)-2,3-Bis(diphenylphosphino)butane (*R*,*R*-CHIRAPHOS) *[74839-84-2]* **2*S*,3*S*-(-)-2,3-bis(diphenylphosphino)butane (*S*,*S*-CHIRAPHOS)** *[64896-28-2]* **M 426.5, m 108-109°, *R*- $[\alpha]_D^{20}$ (+) and *S*- $[\alpha]_D^{20}$ (-) 200° (c 1.5, $CHCl_3$). For *S*,*S*-CHIRAPHOS:** Ph_2PLi [*prepared in situ from Ph_3P (95g) and Li (5g) in THF (300ml) under N_2 at ~55°/1 hour then at 25°/2 hours, and the PhLi formed is decomposed with tert-BuCl (33g) for 45 minutes; the clear orange solution is boiled for 5 minutes then cooled to -4°*] solution is treated with ***(+)-(2R,3R)-butanediol bis(tosylate)*** (35g, [64896-27-1]) in dry THF (100ml) over 1 hour with stirring, the temperature is allowed to rise to 25° and stirring is continued for 30 minutes. N_2 purged H_2O (100ml) is added, the THF layer is separated and evaporated *in vacuo* to give impure ***S,S*-chiraphos** (note inversion of configuration) as a colourless oil. The oil is extracted under N_2 with Et_2O (2 x 150ml), dried (Na_2SO_4), and filtered (under N_2) into a solution of $Ni(ClO_4)_2.6H_2O$ (15g) in EtOH. The Na_2SO_4 is washed with Et_2O which

is added to the Ni solution. The oily red-brown deposit of the *Ni-chiraphos* sometimes contains some yellow solid of the Ni-perchlorate complex which is discarded (pyrophoric?). To the brown-oily (or part crystalline) mixture is added NaCNS (15g) in hot EtOH and stirred vigorously until a homogenous yellow-brown crystalline **[Ni(*S,S*-chiraphos)$_2$NCS]NCS** is obtained. It is collected, washed thoroughly with EtOH then finally Et_2O.
The Ni-NCS complex (15g), suspended in 95% EtOH (150ml) under N_2 is stirred, brought to the boil, and NaCN (4g) in H_2O (20ml) is added rapidly when the Ni complex slowly dissolves to give a clear blood-red solution which then turns cloudy beige in colour. The hot solution is stirred until all the complex which had dissolved is converted to the yellow slurry. After cooling in ice-water, the solid is collected, washed with H_2O (2 x 25ml) then rapidly with ice-cold EtOH (25ml) to give impure beige coloured *S,S-chiraphos*. This solid is purified by drying at 25°, dissolving in boiling absolute EtOH (~125ml), filtering through a frit under N_2 and allowing to stand at ~25° for 12 hours, whereby *S,S*-chiraphos deposits as lustruous colourless plates. A second crystallisation from absolute EtOH (60ml) provides optically pure **(-)-(2*S*,3*S*)-bis(diphenylphosphino)butane (*S,S*-CHIRAPHOS)** (5.5g), m 108-109° (sealed tube under N_2) as colourless plates with $[\alpha]_D^{27}$ -211° (c 1.5, $CHCl_3$), which is unchanged on further recrystallisation [Fryzuk & Bosnich *J Am Chem Soc* **99** 6262 *1977*]. Its ^{31}P NMR ($CDCl_3$, with external H_3PO_4 as reference) has δ at -10.7, i.e. upfield from H_3PO_4 [Slack et al. *Inorg Chem* **18** 3125 *1979*].
For *R,R*-CHIRAPHOS: This enantiomeric ligand is obtained essentially by the same synthesis as its enantiomer above. The **(-)-*(2S,3S)*-butanediol bis(tosylate)** *[74839-83-1]* is prepared in 94% yield, and has **m 63-64°**, **$[\alpha]_D^{25}$ -36.8° (c 2.1, $CHCl_3$)**, and ^1H NMR ($CDCl_3$) with δ at 1.20 (d, J = 6Hz; 6H, CH_3), 2.50 (s; 6H, tosyl-CH_3), 4.70 (q, J ~ 7Hz; 2H, CH), 7.70 (m; 8H, aromatic-H). This is converted to **bis[(2*R,3R*)-2,3-bis(diphenylphosphino)butan]thiocyanato-nickel(II) thiocyanate** in 56% yield after washing with EtOH and Et_2O, and decomposed with NaCN to give ***R,R*-CHIRAPHOS** in 32% yield with **m 106-107°**, **$[\alpha]_D^{27}$ +197° (c 1.5, $CHCl_3$)**, and ^1H NMR ($CDCl_3$) with δ at 1.10 (d, J = 7Hz; 3H, CH_3), 1.40 (d, J = 6Hz; 6H, CH_3), 2.60 (q, J ~ 7Hz; 2H, CH), 7.50 (m; 20H, aromatic-H). [Köiiner & Gerber *Chem Ber* **113** 2323 *1980*.]

1,4-Bis-(diphenylphosphino)butane (dppb) *[7688-25-7]* **M 426.5, m 135-136°, 136-137°.** Recrystallise it from EtOH [Trippett *J Chem Soc* 4263 *1961*]. [King *J Coord Chem* **1** 62 *1971*, Tolman *Chem Rev* **77** 313 *1977*.]

1,2-Bis-(diphenylphosphino)ethane (DIPHOS, ethylene bis(diphenylphosphine)) *[1663-45-2]* **M 398.4, m 139-140°, 140-142°, 143-144°, pK_{Est} ~4.5.** Recrystallise it from aqueous EtOH or *C_6H_6. The *dimethiodide*, when recrystallised from MeOH has **m** 305-307°, and the *dioxide* when recrystallised from toluene or DMF (needles), or *C_6H_6 (plates) has **m** 252-254° (276-278°) [Isslieb et al. *Chem Ber* **92** 3175 *1959*, NMR: Aquiar et al. *J Org Chem* **29** 1660 *1964*, Bäckvall et al. *J Org Chem* **52** 5430 *1987*]. [*Beilstein* **16** IV 958.]

***R*-(+)-1,2-Bis(diphenylphosphino)propane (*R*-PROPHOS)** *[67884-32-6]* **M 412.4, m 68.5° (sealed tube under N_2), 71-73°, $[\alpha]_D^{26}$ *R* +186.0°, *S* +61.0 (c 1.0, Me_3CO).** *S*-(-)-Propane-1,2-diol bis(*p*-toluenesulfonate) (51.9g, [60434-71-1]) in dry THF (75ml) is reacted with Ph_2PLi to give the *R-diol* which is converted to its Ni-perchlorate salt and then converted into its NiNCS complex (45-55g) essentially as described for *chiraphos* above. This NCS complex (22g) is decomposed with NaCN essentially as described for *chiraphos* above, and finally the crude oily *R-prophos* (note change in absolute configuration) is dissolved in absolute EtOH at 50° under N_2, allowed to cool to 25°, then held at 5° for 24 hours and the *diphosphine* (10g) that separated is collected and recrystallised from absolute EtOH (100ml) to give small colourless prisms of analytically pure *R-prophos* (7.5g) whose optical rotation is unchanged by further recrystallisation. [Fryzuk & Bosnich *J Am Chem Soc* **101** 3043 *1979*]. Its ^{31}P NMR ($CDCl_3$, with external H_3PO_4 as reference) has δ at -20.6 (d, $J_{P\text{-}P}$ = 20.6Hz), i.e. upfield, and +1.7 ppm, i.e downfield from H_3PO_4 [Slack et al. *Inorg Chem* **18** 3125 *1979*]. Pure *R-prophos* can be prepared in a similar way.

Bis(2-hydroxyethyl)sulfide (2.2′-thiodiglycol, thiodiglycol) *[111-48-8]* **M 112.2, m -16°, b 121-121.8°/0.01mm, 130°/2mm, 136-137°/3mm, 148°/4mm, 165°/20mm 168°/20mm, 185.5°/40mm, 194°/50mm, 282°/760mm, d_4^0 1.1973, d_4^{25} 1.1793, n_D^{20} 1.5203, n_D^{26} 1.5146.** The sulfide has been prepared on large scales for

the manufacture of "Mustard Gas". The thioglycol has been prepared from ethylene oxide and H_2S, and the crude compound prepared from chlorohydrin contains considerable quantities of dithiane and polymeric impurities. These can be removed by distillation at 150°/8mm and the polymeric material breaks down at ~160° [Masson *J Chem Soc* **49** 236 *1886*]. The distillate is then diluted with H_2O until its boiling point at atmospheric pressure is reduced to 165°, and superheated steam is passed through it. After evaporating off the H_2O, the thiodiglycol is distilled at 147°/6mm. It is soluble in H_2O, lower alcohols, $CHCl_3$, EtOAc; and at 25° its solubility (w/w) in $*C_6H_6$ is 1.07%, in absolute Et_2O it is 7.09 and in ligroin it is 0.06%. In organic acids, or alone, it is stable at 180° for many hours, but when heated at 100° with 2.5 parts of 0.1N aqueous NaOH for 30 minutes sulfide ions are formed, much more so (50%) with 1N NaOH at 140°/10 hours. $Pb(OAc)_2$, and $Cu(NO_3)_2$ decompose it at 100°, but it is stable with BaO, CaO and Al_2O_3 even at 180°/10 hours, in unsuccessful attempts to dehydrate it to vinyl sulfide. Of the several esters of aliphatic alcohols that were reported, the *diacetate* had **b 139.5°/8mm**, the *dibutyrate* had **b 172°/8mm**, and the *dicaproate* had **b 207°/7mm** [Clayton & Reid *J Am Chem Soc* **64** 908 *1942*]. The *bis-3,4-diphenylcarbamoyl derivative* had **m 141.4-142.5°** (from EtOH) [Beaver et al. *J Am Chem Soc* **79** 1236 *1957*], and the *bis-4-nitrobenzoate ester* had **m 107.7°** (from EtOH) [Major *Bull Soc Chim Fr* **41** 634 *1927*]. [Nenitzescu & Scarlatescu *Chem Ber* **68** 587 *1935*, *Beilstein* **1** H 470, **1** I 244, **1** II 525, **1** III 2122, **1** IV 2437.]

1,2-Bis[(*4S)*-4-isopropyl-2-oxazolin-2-yl]benzene [(4*S*,4′*S*)-2,2′-(phen-1,2-diyl)bis(4-isopropyl-4,5-dihydro-oxazole)] *[131380-80-8]* **M 300.4, b 175°/10^{-2} mbar, $[\alpha]_{589}^{25}$ -98.8° (c 2.13, CH_2Cl_2), $[\alpha]_{546}^{25}$ -119.4° (c 2.13, CH_2Cl_2), $[\alpha]_{365}^{25}$ -415.2° (c 2.13, CH_2Cl_2).** This ligand is prepared by melting a small amount of anhydrous $ZnCl_2$ (68mg, 0.50mmol, m 293°) in high vacuum under argon, cooling to ~25°, adding chlorobenzene followed by *o*-phthalonitrile (1.28g, 10mmol) and *S*-valinol (3.09g, 30mmol), and boiling under reflux for 24 hours. The cooled solution is extracted with H_2O (2 x 20ml), and the aqueous phase is extracted with CH_2Cl_2 (30ml). The combined organic extracts are dried (Na_2SO_4), filtered, evaporated *in vacuo*, and the residual oil is purified by flash chromatography and MPLC (pentane/EtOAc 4:1); and distilled at high vacuum to provide optically (by NMR and chiral HPLC on CHIRACEL OD) and analytically pure (C, H and N) colourless *bis-oxazoline* (2.68g, 89%). It has IR(film) with ν_{max} at 1655 (C=N) and 1250 (C-O) cm^{-1}; the ^{1}H NMR (300MHz, $CDCl_3$) has δ at 0.95 [d, *J* = 6.8Hz, 6H, CH(C*H*$_3$)$_2$], 1.04 [d, *J* = 6.8Hz, 6H, CH(C*H*$_3$)$_2$], 1.88 [sept, *J* = 6.8Hz, 2H, C*H*(CH$_3$)$_2$], 4.04-4.13 (m, 4H, OCH$_2$), 4.34-4.42 (m, 2H, CHN), 7.45-7.50 (m, 2H, 4- and 5-H), 7.74-7.77 (m, 2H, 3- and 6-H) from TMS; and the ^{13}C NMR (400MHz, $CDCl_3$) has δ at 17.92 (q), 18.78 (q), 32.39 (d), 70.46 (t, C-5′), 72.87 (d, C-4′), 128.61 (s, C-1, C-2), 129.97 (d, C-4, C-5), 130.36 (d, C-3, C-6), 163.95 (s, C-2′). [Bolm et al. *Chem Ber* **124** 1173 *1991*.] Like many chiral bis(oxazolin-2-yl) ligands it complexes with metals such as Zn (see its crystalline Zn complex [131380-93-3] in Part 1 above) and Cu, being involved in a variety of metal catalysed asymmetric synthesis such as allylation, aziridination, cyclopropanation, Diels-Alder and retro Diels-Alder, Mukaiyama aldol condensation and hydrosilylation [see reviews by Ghosh et al. *Tetrahedron: Asymmetry* **9** 1 *1998*, Pflatz *Acta Chem Scand* **50** 189 *1996*, Johnson & Evans *Acc Chem Res* **33** 325 *2000*, Jørgensen et al. *Acc Chem Res* **32** 605 *1999*.]

1,2-Bis[(*4S)*-4-isopropyl-2-oxazolin-2-yl]ethane [(4*S*,4*S*′)-2,2′-(ethane-1,2-diyl)bis(4-isopropyl-4,5-dihydro-oxazole)] *[131380-80-8]* **M 252.4, b 150°/2.10^{-2} mbar, $[\alpha]_{589}^{25}$ -93.6° (c 2.28, CH_2Cl_2), $[\alpha]_{546}^{25}$ -112.1° (c 2.28, CH_2Cl_2), $[\alpha]_{365}^{25}$ -335.5° (c 2.28, CH_2Cl_2).** This colourless bis-oxazolinylethane (1.49g, 59% yield) was prepared by the general method described in the preceding entry from anhydrous $ZnCl_2$ (68mg, 0.50mmol), 1,2-dicyanoethane (0.80g, 10mmol), and *S*-valinol (3.09g, 30mmol) in optical and analytical purity. It has IR(film) with ν_{max} at 1645 (C=N) cm^{-1}; the ^{1}H NMR (300MHz, $CDCl_3$) has δ at 0.87 [d, *J* = 6.7Hz, 6H, CH(C*H*$_3$)$_2$], 0.95 [d, *J* = 6.7Hz, 6H, CH(C*H*$_3$)$_2$], 1.74 [sept, *J* = 6.7Hz, 2H, C*H*(CH$_3$)$_2$], 2.63 [s, 4H, CH$_2$)$_2$], 3.84-3.98 (m, 4H, OCH$_2$), 4.22 (dd, *J* = 8.5, 8.5Hz, 2H, C*H*N) from TMS; and the ^{13}C NMR (100MHz, $CDCl_3$) has δ at 17.68 (q), 18.45 (q), 24.40 (t), 32.28 (d), 69.90 (t, C-5′), 71.92 (d, C-4′), 166.21 (s, C-2′). [Bolm et al *Chem Ber* **124** 1173 *1991*.] Like many chiral bis(oxazolin-2-yl) ligands it complexes with metals such as Zn (see the crystalline Zn complex in Part 1 above) and Cu, being involved in a variety of metal catalysed asymmetric synthesis such as allylation, aziridination, cyclopropanation, Diels-Alder and retro Diels-Alder, Mukaiyama aldol condensation and hydrosilylation [see reviews by Ghosh et al. *Tetrahedron: Asymmetry* **9** 1 *1998*, Pflatz *Acta Chem Scand* **50** 189 *1996*, Johnson & Evans *Acc Chem Res* **33** 325 *2000*, Jørgensen et al. *Acc Chem Res* **32** 605 *1999*.]

1,3-Bis[(*4S*)-4-isopropyl-2-oxazolin-2-yl]propane [(4*S*,4′*S*)-2,2′-(propane-1,3-diyl)bis(4-isopropyl-4,5-dihydrooxazole)] *[131380-90-0]* **M 266.4, b 120°/2.10^{-2} mbar, $[\alpha]_{589}^{25}$ -57.4° (c 3.05, CH_2Cl_2), $[\alpha]_{546}^{25}$ -68.4° (c 3.05, CH_2Cl_2), $[\alpha]_{365}^{25}$ -204.0° (c 3.05, CH_2Cl_2).** This colourless bis-oxazolinylpropane (1.12g, 42% yield) was prepared by the general method described in the preceding entries from anhydrous $ZnCl_2$ (68mg, 0.50mmol), 1,3-dicyanopropane (0.94g, 10mmol), and *S*-valinol (3.09g, 30mmol) in optical and analytical purity. It has IR(film) with ν_{max} at 1645 (C=N) cm^{-1}; the ^{1}H NMR (300MHz, $CDCl_3$) has δ at 0.88 [d, *J* = 6.7Hz, 6H, CH(C*H*$_3$)$_2$], 0.95 [d, *J* = 6.7Hz, 6H, CH(C*H*$_3$)$_2$], 1.74 [sept, *J* = 6.7Hz, 2H, C*H*(CH$_3$)$_2$], 2.33-2.61 [m, 6H, CH$_2$)$_3$], 3.85-3.98 (m, 4H, OC*H*$_2$CHN), 4.18-4.26 (m, 2H, NC*H*CH$_2$O) ppm from TMS; and the ^{13}C NMR (100MHz, $CDCl_3$) has δ at 17.77 (q), 18.37 (q), 21.66 (t), 26.21 (t), 32.27 (d), 69.87 (t), 71.94 (d), 165.53 (s). [Bolm et al. *Chem Ber* **124** 1173 *1991*.] Like many chiral bis(oxazolin-2-yl) ligands it complexes with metals such as Zn (see the crystalline Zn complex in the "Catalyst" section above) and Cu, being involved in a variety of metal catalysed asymmetric synthesis such as allylation, aziridination, cyclopropanation, Diels-Alder and retro Diels-Alder, Mukaiyama aldol condensation and hydrosilylation [see reviews by Ghosh et al. *Tetrahedron: Asymmetry* **9** 1 *1998*, Pflatz *Acta Chem Scand* **50** 189 *1996*, Johnson & Evans *Acc Chem Res* **33** 325 *2000*, Jørgensen et al. *Acc Chem Res* **32** 605 *1999*.]

2,2-Bis[(*4S*)-4-isopropyl-2-oxazolin-2-yl]propane {4,5-dihydro-2-[2(4,5-dihydro-(4*S*)-4-isopropyloxazol-2-yl)propan-2-yl)]-(4*S*)-4-isopropyloxazole, (4*S*,4′*S*)-2,2′-(propane-2,2-diyl)bis(4-isopropyl-4,5-dihydro-oxazole)} *[relative stereochemistry 929270-13-3; absolute stereochemistry 797757-81-4]* **M 266.4, b 95-100°/0.5 mm, d_4^{25} 0.9864, n_D^{20} 1.4665, $[\alpha]_D^{24}$ -107.5° (c 1, CH_2Cl_2).** The propane ligand for metal assisted asymmetric catalysis is prepared in two steps. The *first* is the synthesis of the bis-oxazoline precursor (-)-(*S,S*)-*N,N′*-bis(1-hydroxymethyl-2-methylpropyl),2,2-dimethylmalonamide which is prepared in a flask under nitrogen purge at 0° (ice bath) containing a mixture of *S*-valinol (5.13g, 50mmol) and dry $EtNH_2$ (17.4ml, 124mmol, distilled from CaH_2) to which 2,2-dimethylmalondioyl chloride (3.3ml, 250mmol; Evans et al. *J Org Chem* **63** 4541 *1998*] is added dropwise during 25 minutes (temperature rising from 0° to 10°), then allowing to warm to ~25°. After stirring for 45 minutes the colourless precipitate in the mixture is dissolved by adding CH_2Cl_2 (120ml). Aqueous N HCl (30ml) is then added, the mixture is extracted with CH_2Cl_2 (3 x 13ml), the combined organic layers are washed with saturated aqueous $NaHCO_3$ (30ml), brine (30ml), dried ($MgSO_4$), filtered and evaporated *in vacuo* to provide a yellow solid which is crystallised from EtOAc (~40ml) to give the malonamide (6.4g, 84% in three crops). The amide has m 98-99°, $[\alpha]_D^{24}$ -6.0° (c 0.5, CH_2Cl_2); it has IR(KBr) with ν_{max} at 3349, 3380, 2962, 2886, 1658, 1530, 1049, 1033 cm^{-1}; the ^{1}H NMR (300MHz, $CDCl_3$) has δ at 0.92 (d, *J* = 6.8Hz, 6H), 0.96 (d, *J* = 6.8Hz, 6H), 1.50 (s, 6H), 1.82 (oct, *J* = 6.8Hz, 2H), 2.66 (br s, 2H), 3.52 (m, 2H), 3.69-2.86 (m, 4H), 6.41 (d, *J* = 8.6Hz, 2H); and the ^{13}C NMR (75MHz, $CDCl_3$) has δ at 18.8, 19.6, 23.7, 29.1, 50.2, 57.1, 63.5, 174.5; and correct elemental analysis for C, H and N.

The *second* step is carried out, with stirring, under N_2 purge in a flask containing the preceding malondiamide (5.5g, 18.4mmol), 4-dimethylaminopyridine (204mg, 1.67mmol) in dry CH_2Cl_2 (130ml, filtered through activated Al_2O_3) at ~25°, and dry $EtNH_2$ (10.25ml, 73.4mmol, distilled from CaH_2) is added slowly (*via* syringe) followed by tosyl chloride (7.10g, 37mmol, 2 equivalents) dissolved in dry CH_2Cl_2 (15ml) dropwise during 30 minutes *via* a funnel which is rinsed with CH_2Cl_2 (2.5ml), and the mixture is stirred for 27 hours at ~25°. The mixture is then treated with saturated aqueous NH_4Cl (70ml), H_2O (40ml), the aqueous layer is separated, extracted with CH_2Cl_2 (3 x 55ml), the combined organic layers are dried ($MgSO_4$), filtered and evaporated. The oily residue is mixed with hot pentane (40ml), stirred for 5 minutes, the supernatant liquid is decanted, and the procedure repeated three times. The pentane layers are combined and evaporated *in vacuo* and the oily residue (4.05g 83%) is distilled (Kügelrohr) to give the analytically pure *bis-oxazole*. It has IR(film) with ν_{max} at 3308, 2960, 2874, 1746, 1525, 1353, 1303, 1037, 1017, 895, 815, 714 cm^{-1}; the ^{1}H NMR (300MHz, $CDCl_3$) has δ at 0.95 (d, *J* = 6.8Hz, 6H), 0.91 (d, *J* = 6.8Hz, 6H), 1.51 (s, 6H), 1.88-1.73 (m, 2H), 4.06-3.93 (m, 4H), 4.26-4.15 (m, 2H); and the ^{13}C NMR (75MHz, $CDCl_3$) has δ at 17.3, 18.5, 24.4, 32.2, 38.5, 69.9, 71.5, 168.7. [Evans et al. *Org Synth* **83** 97 *2006*]. Like many chiral bis(oxazolin-2-yl) ligands it complexes with metals such as Zn (see the crystalline Zn complex [131380-93-3] in the "Catalyst" section above) Cu, Ir, Pd, W, being involved (with or without further ligands) in a variety of metal catalysed asymmetric synthesis such as allylation, aziridination, cyclopropanation, Diels-Alder and retro Diels-Alder, Mukaiyama aldol condensation and hydrosilylation [see reviews by Ghosh et al. *Tetrahedron: Asymmetry* **9** 1 *1998*, Pflatz *Acta Chem Scand* **50** 189 *1996*, Johnson & Evans *Acc Chem Res* **33** 325 *2000*, Jørgensen et al. *Acc Chem Res* **32** 605 *1999*.]

1,3-Bis(2,6-isopropylphenyl)imidazolium chloride (IPr. Cl) *[250285-32-6]* **M 425.1, m 278°(dec).** IPr.Cl is a ligand precursor of an NHC (N-heterocyclic carbine — Kantchev, O'Brien & Organ *Aldrichimica Acta* **39** 97 *2006*, Phillips, Chan & Scheidt *Aldrichimica Acta* **42** 55 *2009*) which coordinates with transition metals to form soluble catalysts that promote a variety of reactions. IPr.Cl can be prepared in two steps. *1,4-Bis(2,6-diisopropylphenyl)diazabutadiene [1,2-bis(2,6-diisopropylphenylimino)-ethane]* is first prepared by dissolving 2,6-diisopropylaniline (100g, 560mmol) and glyoxal (31.5ml, 280mmol, in 40% H_2O) in absolute EtOH (500ml), and adding a few drops of formic acid as catalyst. The yellow coloured solution produces a yellow precipitate after a few hours, the mixture is stirred for 2 days, and the yellow solid is collected, washed with cold MeOH, and dried *in vacuo* to give analytically pure *diazabutadiene-ethane* (81.7g, 77.5%). It has ^{1}H NMR (400MHz, $CDCl_3$) with δ at 1.28 (d, *J* = 7.6 Hz, 24H, $CH(CH_3)_2$), 3.03 (sep, *J* = 6.4Hz, 4H, $CH(CH_3)_2$), 7.27 (m, 6H, $CH(CH_3)_2$-C_6H_3), 8.19 (s, 2H, NC*H*). In the second step the *diazabutadiene-ethane* (25g, 66mmol) in toluene (500ml) is treated with solid paraformaldehyde (2.0g, 66mmol) with stirring under N_2, heated to 100° until clear, then cooled to 40° and HCl (16.5ml, 66mmol, 4M in dioxane) is introduced with a syringe. The colour of the mixture turns to brown and a white precipitate separates within a few hours, but stirring is continued at ~25° for 36 hours. The solid is filtered off, washed with THF, and dried *in vacuo* to give off-white IPr.Cl (13.1g, 47%). It has ^{1}H NMR (400MHz, CD_2Cl_2) with δ at 1.24 (d, *J* = 7.2 Hz, 12H, $CH(CH_3)_2$), 1.27 (d, *J* = 7.2 Hz, 12H, $CH(CH_3)_2$), 2.42 (sep, *J* = 6.8Hz, 4H, $CH(CH_3)_2$), 7.18 (t, *J* = 7.2Hz, 2H, *p*-C_6H_3), 7.4 (m, 4H, *m*-C_6H_3), 7.80 (s, 2H, NC*H*), 11.0 (s, 1H, NC(*H*Cl)); and its ^{13}C NMR (100MHz, CD_2Cl_2) has δ_C{H} at 23.9 ($CH(CH_3)_2$), 26.1 ($CH(CH_3)_2$), 86.4 (NCHCHN), 125.2 (q C, phenyl), 125.8 (CH, phenyl), 128.7 (quaternary C, phenyl), 129.5 (CH, phenyl), 145.7 (CHCl).

IPr.Cl has been used, in dioxane under argon, as a ligand with $Pd_2(dba)_3$ (see above) to catalyse cross-coupling reactions between arylhalides and arylmagnesium bromides in a Kumada reaction to form diaryls efficiently [Huang & Nolan *J Am Chem Soc* **121** 9889 *1999*]; and in the presence of a base (*tert*-BuOK, or Cs_2CO_3) and $Pd(OAc)_2$ {or $PdCl_2$, $[Pd(allyl)Cl]_2$, $PdCl_2(PCy_3)_2$} and CO under pressure it catalyses the carbonylative cross-coupling of bromopyridines with arylboronic acids to provide high yields of arylpyridylketones [Maerten et al. *Tetrahedron* **63** 682 *2007*].

When IPr.Cl is treated with a base (e.g. Bu^{t}OK, Bu^{t}ONa, K_2CO_3 or Cs_2CO_3), the carbene **1,3-bis(2,6-diisopropylphenyl)-1,3-dihydro-2*H*-imidazol-2-ylidene** *[244187-81-3]* **M 388.6, m 213-217°**, is formed and is stable enough to be isolated, stored and is available commercially. The carbene-carbon atom at C2 coordinates with metals; and forms C-C bonds, by C-H insertion, with acetylene, MeCN, $HCCl_3$, $PhSOCH_3$, and the structures of some of the products have been confirmed by X-ray analysis [Arduengo et al. *Helv Chim Acta* **82** 2348 *1999*].

Bis(pinacolato)diboron [bis(pinacolylborane), 4, 4, 4′, 4′, 5, 5, 5′, 5′-octamethyl-2,2′-bi-1,2,3-dioxaborolane, B_2pin_2] *[73183-34-3]* **M 253.9, m 138°, 137-140°.** This versatile borylating agent is prepared in four steps* from BBr_3 by conversion to tris(dimethylamino)borane {$(Me_2N)_3B$, m -16°, b 45°/12mm, 147-148°/atm [4375-83-1]} upon treatment with Me_2NH/pentane, followed by further reaction with BBr_3/pentane to give bromobis(dimethylamino)borane {$(Me_2N)_2BBr$, b 20-28°/0.5mm, 56-58°/12mm [6990-27-8]}, which on reaction with Na in toluene under reflux for ~3 hours provides tetrakis(dimethylamino)diboron [$(Me_2N)_2B$-$B(Me_2N)_2$, b 55-57°/2.5mm, 92°/12mm, Brotheron et al. *J Am Chem Soc* **82** 6242, 6245 *1962*] in 72% yield. Then a mixture of $(Me_2N)_2B$-$B(Me_2N)_2$ [53.7g, 271mmol, one signal in the ^{1}H NMR at δ 2.67 (s, 24H) in $CDCl_3$] in dry toluene (510ml) and pinacol (64.4g, 545mmol) in dry toluene (340ml) under dry N_2 is stirred in an ice-water bath, and 5.4M HCl in Et_2O (203ml, 1.10 mol) is added dropwise during 2 hours. A white precipitate of Me_2NH.HCl separates immediately but the mixture is stirred further for 4 hours at ~25°; the precipitate is filtered off and the filtrate is evaporated to dryness. The white residue is dissolved in pentane (~700ml), washed with H_2O (3 x 500ml), dried ($MgSO_4$), filtered and evaporated to ~150ml. This is warmed to dissolved any solid and chilled in a freezer (-30°). The first crop of **B_2pin_2** is collected and washed with cold pentane (2 x 30ml). The mother liquor is concentrated to give further crops of **B_2pin_2** which are combined with the first crop, and dried for 16 hours at ~25°/0.1mm to give colourless plates, m 138°, in 79-91% yield. The diboron is air stable and is stored in a capped container. Its IR (KBr) has ν_{max} at 2978, 2930, 1372, 1289, 1189, 1177, 1127, 960, 850, 744, 660, 547 cm^{-1}; the ^{1}H NMR (300MHz, $CDCl_3$) has δ_H at 1.25 (s, 24H); the ^{13}C NMR (100MHz, $CDCl_3$) has δ_C at 83.4, 24.9; and the ^{11}B NMR (128.3MHz, toluene) has δ_B at 30.61 (BF_3. Et_2O as external reference with δ 0.00). [Ishiyama et al. *Org Synth* **77** 176 *2000*, Nöth *Naturforsch B: Anorg Chem, Org Chem* **39B** 1463 *1984*.] It borates ethylenes, acetylenes, allenes, conjugated olefins, replaces the halogen atom or a

triflate group in arenes with a $-B(OR)_2$ group effectively in the presence of catalysts such as $Pt(PPh_3)_4$, $Pt(dba)_2$, or $PdCl_2(dppf)$, $Pd(dba)_2$ [Ishiyama et al. *J Am Chem Soc* **115** 11018 *1993*, Lesley *Organometallics* **15** 5137 *1996*, Ishiyama et al. *J Chem Soc. Chem Commun* 689 *1997*, Iverson & Smith *Organometallics* **16** 2757 *1997*, Ishiyama et al. *J Chem Soc. Chem Commun* 2073 *1996*, Ishiyama et al. *Tetrahedron Lett* **39** 2357 *1998*, Ishiyama et al. *J Org Chem* **60** 7508 *1995*, Ishiyama et al. *Tetrahedron Lett* **38** 3447 *1997*].
* Caution: All operations should be carried out under N_2 in a well ventilated fume cupboard because bromoborane derivatives fume in air by hydrolysing rapidly with evolution of heat.

Bis(trifluoromethanesulfonyl)amine [NTf_2, bis(trifluoromethanesulfon)amide, $(CF_3SO_2)_2NH$] *[82113-65-3]* **M 281.2, m 49-50°, 46-57°, b 90-91°/atm, has a pK of a superacid [ΔG_{acid} = 291.8 kcal/mol].** NTf_2 is a very strong neutral *Brønsted acid* which is to be compared with CHF_2CO_2H (ΔG_{acid} = 323.8) < HBr (ΔG_{acid} = 318.3) < CF_3CO_2H (ΔG_{acid} = 316.3) and < CF_3SO_3H (ΔG_{acid} = 299.5) [Koppel et al. *J Am Chem Soc* **116** 3047 *1994*, see pK values in AcOH below]. For purification see at the end of its synthesis below. NTf_2 is a white crystalline solid that should be handled in closed systems (Schlenk equipment), or under very efficient ventilation as it is quite volatile, fumes in moist air and is very corrosive. However, it is soluble in H_2O, and it is stable in aqueous solutions where it can be titrated with NaOH as a typical acid with a pKa of ~1.7. In glacial acetic acid, the pK value by measuring δ(OH) chemical shifts in the ^1H NMR spectra gives a value of 7.8 for NTf_2, as compared with CF_3CO_2H (11.4), HNO_3 (10.1), H_2SO_4 (7.0), HI (5.8), $HClO_4$ (4.9) and CF_3SO_3H (4.2) measured in the same way. If these comparisons are valid then NTf_2 is a remarkably strong acid. [Foropoulos & DesMarteau *Inorg Chem* **23** 3270 *1984*, cf also Rode et al. *Z Phys Org Chem (Leipzig)* **253** 17 *1973*.]
The preparation of NTf_2 in several steps from CH_3SO_2Cl [Foropoulos & DesMarteau *Inorg Chem* **23** 2720 1984] has been improved from 48% to 80% overall yield [DesMarteuu & Witz *J Fluorine Chem* **52** 7 *1991*], and is described here.
Methanesulfonyl chloride (286g, [124-63-0], b 60°/21mm, 161°/atm, redistilled from P_2O_5, Hearst & Noller *Org Synth* Coll Vol **IV** 571 *1963*) is added slowly to solid KF (170g) and stirred for 1 hour at 25°, then CH_3SO_2F is distilled off, fraction b 123-124° is collected and redistilled from P_2O_5 to give pure acid fluoride (208g). Electrochemical fluorination of the methanesulfonyl fluoride in anhydrous HF at 4-5Volts and 7-9Amps continuously for 24 hours (as described by Gramstad & Haszeldine *J Chem Soc* 173 *1956*) gave CF_3SO_2F (~180g, [335-05-7]) is followed by isolation *via* condensation at -78° and redistillation at -21.7°.
CF_3SO_2F (76g) is bubbled into semi-frozen NH_3 (600ml, at ~ -77°) with dry N_2, during 0.5 hours while stirring with external cooling at -78°. Excess of NH_3 is allowed to evaporate under N_2 flow into a fume cupboard; NaOMe (54g) in MeOH (500ml) is added to the residual slush and the mixture is heated to 60° for a few minutes, the NaF is filtered off, the filtrate is evaporated, the residue is dried in a high vacuum to give CF_3SO_2NHNa (81g, 95%, [91742-21-1]). This Na salt (81g) is refluxed with hexamethyldisilazane (645ml, 500g, HMDS see [999-97-3]) under N_2 flow (oil bath temperature <145° to avoid excessive darkening) with strong mechanical stirring as the mixture thickens progressively. After release of NH_3 is complete (~12 hours), HMDS is distilled off (while increasing the vacuum), and the residual moisture sensitive solid is dried under high vacuum (in the same flask) to give $CF_3SO_2NNa(SiMe_3)$ (106g, 92%, [91742-20-0]). This salt (106g) in dry THF (370ml) is transferred to a stirrable stainless steel autoclave (~600ml) and gaseous CF_3SO_2F (67g, ~26% excess) is transferred under N_2 pressure *via* a metal vacuum system, as it is not usually possible to cool the autoclave to below -50°. The autoclave is sealed and the mixture is stirred at 100° overnight, the volatile products are vented into an efficient hood, the autoclave is washed out with H_2O, the combined H_2O/THF mixture is washed with CH_2Cl_2, evaporated in a rotavap, and the residual solid is dried under high vacuum at 110° to give $(CF_3SO_2)_2NNa$ (129g, 98%, [91742-21-1]). The Na salt (129g) and 96% H_2SO_4 (150ml) are heated in a single necked flask at 60-90°/2 x 001mm and the *$(CF_3SO_2)_2NH$* (NTf_2) (111g,93%) is collected in an ascending tube cooled at -22°. If necessary (cf spectra below), it is sublimed twice at 60° and/or recrystallised from $CFCl_3$ at -50°. The analytically pure crystalline white solid has m 49-50° and can be stored in a sealed container in a drybox.
NTf_2 has IR (gas in equilibrium with solid at 25°) with ν_{max} at 3395 (m), 3320 (br), 1463 (m), 1440 (m), 1300 (w), 1240 (s), 1224 (s), 1138 (s), 860 (m), 643 (vw), 614 (m), 570 (vw) and 505 (w) cm^{-1}; Raman (solid -180°) has ν_{max} at 3205 (w), 1464 (vw), 1458 (w), 1450 (w), 1343 (w), 1263 (s), 1142 (m, 839 (w), 778 (s), 646 (w), 591 (w), 566 (w), 537 (w), 510 (w), 392 (m), 386 (m), 346 (s), 311 (s), 276 (s), 212 (w), 195 (w) and 128 (m) cm^{-1}; the ^1H NMR (60MHz, external TMS) has peaks at 10.42 (in Me_2CO d_6), 7.92 (in $CFCl_3$) ppm; the ^{19}F NMR (20MHz, in $CFCl_3$ as solvent and internal standard) has a peak at -75.97 (s) ppm, i.e. is at higher field

than that of $CFCl_3$; the MS[EI] has *m/z* at 281 (M^+), 211 ($CF_3SO_2NSO_2^+$), 147 ($CF_3SO_2N^+$), 133 ($CF_3SO_2^+$) and 69 (CF_3^+); and the MS[CI] has major *m/z* at 282 (MH^+), 150 ($CF_3SO_3H^+$ or $CF_3SO_2NH_3^+$) and 115 ($CF_2SO_2H^+$ or $CF_2SONH_2^+$). [Foropoulos & DesMarteau *Inorg Chem* **23** 2720 *1984*.]
NTf_2 forms several derivatives including ***$(CF_3SO_2)_2NCl$*** (viscous acrid liquid, **m -96° to -93°**, [91742-17-5]), ***$(CF_3SO_2)_2NNO$*** (white solid, **m ~118°**, [91742-19-7]), ***$(CF_3SO_2)_2NNO_2$*** (white crystals **dec ~107°**, [91742-18-6]), ***$(CF_3SO_2)_2Si(Me)_3$*** (low-volatile colourless liquid, [82113-18-5]), and with CsF in MeCN it gives the cesium salt ***$(CF_3SO_2)_2NCs$*** (white crystals **m 115°**, [91742-16-4]) [Foropoulos & DesMarteau *Inorg Chem* **23** 2720 *1984*]. It forms an ***N-trimethylsilyl derivative*** (**$TMSNTf_2$** prepared from allylTMS and NTf_2, see above) which catalyses Diels-Alder reactions between methyl acrylate and various dienes [Mathieu & Ghosez *Tetrahedron Lett* **38** 5497 *1997*], as well as Friedel-Crafts acylations of anisole, and allylation and bis-allylation of carbonyl derivatives [Oshii et al. *Synlett* 1145 *1997*]. It readily forms the silver salt, **$AgNTf_2$**, e.g. with Ag_2CO_3.

1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride (IMes.Cl) *[141556-45-8]* **M 340.9, m >300°.** This NHC (N-Heterocyclic Carbene) precursor is prepared by established procedures from 2 mols of amine, 1 mol of glyoxal and one mol of formaldehyde [Arduengo USPatent 5 077 414 *1991, Chem Abstr* **116** 106289 *1002*, cf Hermann et al. *Chem Eur J* **2** 1627 *1996*] and washed with THF before use. It is useful for making IMesCuCl which in turn is used for making IMesAuCl and $[IMesPtCl]_2$ [Furst & Casin *Chem Commun* **46** 6924 *2010*].

1,3-Bis(2,4,6-trimethylphenyl)imidazol-2-ylidene (IMes) *[141556-42-5]* **M 304.4, m 150-155°(dec.).** By using Schlenk equipment and techniques under dry N_2, this NHC is prepared from the preceding IMes.Cl (10.0g, 29.3mmol) suspended in dry THF (80ml) and stirred for 15 minutes, then solid *tert*-BuOK (3.5g, 31.2mmol) is added at ~25° in one portion, the dark grey solution is stirred for 20 minutes, and the volatiles are removed *in vacuo*. The reside is extracted into warm toluene (2 x 50ml), filtered through Celite and the solvent is removed *in vacuo* to provide small crystals of the carbene (7.55g, 84%). The crystals are recrystallised from hexane to yield colourless crystals, **m 150-155°(dec)** which are analytically pure and suitable for X-ray structural analysis. Its ^1H NMR (300MHz, THF-d_8, TMS) has δ_H at 2.02 (s, 2′,6′-CH_3, 12H), 2.30 (s, 4′-CH_3, 6H), 6.94 (s, ArH, 4H), 7.04 (s, 4,5-C*H*, 2H); and its ^{13}C NMR (75MHz, THF-d_8, TMS) has δ_C at 18.04 (s, 2′,6′-*C*H_3), 21.04 (s, 4′-*C*H_3), 121.28 (s, *C*-4 and *C*-5), 129.69 (s, Mes *C*-3′,5′), 135.73 (s, Mes *C*-2′,6′), 137.55 (s, Mes *C*-4), 139.73 (s, Mes *C*-1), 219.69 (s, N*C*N carbene-*C*); and the ^{15}N NMR (30MHz, THF-d_8, $NH_4{}^{15}NO_3$) has δ at -178.85. [Arduengo et al. *J Am Chem Soc* **114** 5530 *1992*.] It is useful for making a variety metal complexes of ruthenium (among other metals) for catalysing olefin metathesis [Grubbs *Tetrahedron* **60** 7117 *2004*], and other metathesis reactions [Love et al. *Angew Chem. Int Ed* **41** 4035 *2002*, Schrodi & Pederson *Aldrichimica Acta* **40** 45 *2007*, Kanemitsu & Seeberger *Org Lett* **5** 4541 *2003*].

4-Bromobiphenylboronic acid MIDA ester {[2-(4-bromophenyl)-6-methyl-1,3,6,2-dioxazaborocane-4,8-dione], (4-bromophenyl)[*N*-[(carboxy-κ*O*)methyl]-*N*-methylglycinato(2-)-κ*N*,κ*O*] boron *[943552-04-3]* **M 311.9, m 238-240°, 248-253°.** This ester is obtained from 4-bromophenylboronic acid (24.99g, 124.4mmol) and MIDA (18.31g, 124.4mmol, see [4408-64-4]) to which is added a freshly prepared mixture of DMSO (6.3ml) and toluene (118.7ml) in a flask to give a white solid suspension in a clear colourless solution. The flask is fitted with a Dean-Stark trap and a reflux condenser, and the mixture is boiled under reflux with stirring (magnetic Teflon coated bar) for 6 hours during which time the mixture became clear and about 2.1ml of H_2O are collected in the trap. Heating is stopped and the reaction is allowed to cool, with stirring, to ~25° during 1 hour; the apparatus is washed down with toluene and the combined liquids are evaporated (40°/15mm) to remove most of the toluene and give a crude tan, chunky, solid. Acetone (15ml) is added to the residue and swirled vigorously to give a white solid in a tan solution. To this mixture is added Et_2O (150ml, dried through neutral Al_2O_3 columns) in small portions (25ml) with stirring each time to allow further separation of white solid, and is finally filtered onto a medium porosity glass frit. The solid is washed with Et_2O (3 x 50ml), dried by suction, and is dried further in a vacuum (~25°/1mm) for 4 hours to give *4-bromophenylboronic acid MIDA ester* as an air stable, free-flowing white powder (36.3g, 94%) with m 238-240°. *Alternatively*, the crude tan solid can be purified by silica gel chromatography to provide the white MIDA ester in almost quantitative yield. An analytical sample has IR (in Me_2CO, thin film) with ν_{max} at 3012, 1745, 1584, 1459, 1339, 1294, 1237, 1216, 1187, 1037, 995, 867, 812, 707 cm^{-1}; the ^1H NMR (400MHz, CD_3CN) has δ_H at 2.50 (s, 3H), 3.89 (d, *J* = 16.0Hz, 2H), 4.07 (d, *J* = 16.0Hz, 2H), 7.41 (d, *J* = 8.0Hz, 2H), 7.55 (d, *J* = 8.0Hz, 2H); the ^{13}C NMR (100MHz, CD_3CN) has δ_C at

48.2, 62.5, 124.1, 131.6, 135.2, 169.2; the ^{11}B NMR (100MHz, CD_3CN) has δ_B at 12.0; the LRMS (EI^+) has *m/z* (relative intensity): 314.0 (97%), 313.0 (20%), 312.0 (M^{++}H, 100%), 311.0 (23%), 283.0 (16%), 255.9 (16%); and the HMRS (EI+) has found: 312.0035, and calculated for $C_{11}H_{12}BBrNO_4$ $[M+H]^+$: 312.0037. [Ballmer, Gillis and Burke *Org Synth* **86** 344 *2009*.]

***trans*-(2-Bromovinyl MIDA boronate {*trans*-2-bromovinylboronic acid MIDA ester 6-methyl-2-*trans*-bromovinyl-1,3,6,2-dioxazabronane-4,8-dione, [(1*Z*)-2-bromoethenyl][*N*-[(carboxy-κ*O*)methyl]-*N*-methyl-glycinato(2-)-κ*N*,κ*O*]-boron}** *[trans E 1104636-68-1; cis Z has 1105069-27-9]* **M 261.9.** The ester is prepared using Schlenk equipment in subdued daylight under dry N_2 by adding dropwise *via* a syringe freshly distilled (*E*)-(2-bromoethenyl)dibromoborane (21.0g, 75.9mmol, prepared from BBr_2 and acetylene, Hyuga et al. *Chem Lett* 1757 *1987*) to a stirred mixture of MIDA (16.9g, 114mmol, 1.5 equivalents, see [4408-64-4]) and 2,6-lutidine (17.7g, 151.9mmol, 2 equivalents) in DMSO (250ml) at 0° over 15 minutes, and allowed to warm to ~25° then kept at that temperature for 48 hours. The yellow mixture is treated with H_2O (300ml) and extracted with 1:1 THF:Et_2O (3 x 500ml), the combined extracts are washed with brine (3 x 350ml), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The light yellow solid residue is purified by flash chromatography on silica gel and eluting with Et_2O/petroleum ether (1:1), then EtOAc, then EtOAc/MeCN (9:1) to give the desired boronate as colourless crystals (12g, 60%). On TLC it has R_F 0.46 (Merck silica gel plate grade 9385, 60Å, 230-400 mesh, eluting with EtOAc and visualised with $KMnO_4$). [A preparation similar to the one for vinyl MIDA boronate (this chapter) using the MIDA-di Na salt gave similar yields [cf Uno, Gillis and Burke *Tetrahedron* **65** 3230 *2009*]. Material stored under air at room temperature for 1.5 years showed no signs of deterioration. Crystals grown by slow evaporation of an EtOAc solution at ~25° were suitable for X-ray analysis which revealed a *trans* configuration while confirming the expected structure with a pyramidalised boron centre. Its IR (thin film) has ν_{max} at 3006, 2962, 1755, 1589, 1451, 1338, 1286, 1196, 1152, 1118, 1080, 1025, 1009, 961, 893, 872, 773, 678 cm^{-1}; the ^{1}H NMR (500MHz, CD_3CN, δ = 1.93 centre line, TMS) has δ_H at 6.69 (d, *J* = 15.0Hz, 1H), 6.63 (d, *J* = 14.5Hz, 1H), 3.97 (d, *J* = 17.0Hz, 2H), 3.82 (d, *J* = 17.0Hz, 2H), 2.80 (s, 3H); the ^{13}C NMR (125MHz, CD_3CN, δ = 1.93 centre line, TMS) has δ_C at 169.0, 118.8, 62.6, 47.9; the ^{11}B NMR (100MHz, CD_3CN, $BF_3.Et_2O$ internal standard) has δ at 10.5; and HRMS (EI+) found: 261.9874, calculated for $C_7H_{10}BBrNO_4$ $[M+H]^+$: 261,9886. It is very useful in the reactions stated for vinyl MIDA boronate and for iterative cross-coupling. [Lee, Gray, Peak and Burke *J Am Chem Soc* **130** 466 *2008*, Uno, Gillis and Burke *Tetrahedron* **65** 3230 *2009*, Gillis & Burke *Aldrichimica Acta* **42** 17 *2009*].

Chloro(dimethylsulfide)gold(I) [(dimethylsulfide)gold(I) chloride, aurochloro dimethylsulfide, AuCl.Me_2S] *[29892-37-3]* **M 295.6, m >100°(dec), 100-102°(dec), 120°(dec).** All procedures for preparing this complex should be carried out in an efficient fume cupboard because Me_2S is **toxic** and has a **foul** odour. The gold complex has been prepared by adding Me_2S (1 mole, see [75-18-3]) slowly to a stirred solution of NH_4AuCl_4 (1mole) in dilute *Aqua Regia* when the complex separates and is collected [Allen & Wilkinson *Spectrochimica Acta* **28B** 2257 *1972*]. *Alternatively*, Me_2S is added to a solution of auric chloride ($AuCl_3$) in HCl [which forms *aurichloric acid (chloroauric acid)* $HAuCl_4$ see [16903-35-8]) when much heat is evolved and a flocculent white precipitate of *AuCl.Me_2S* separates. It is filtered off, washed with H_2O (in which it is insoluble) and a little EtOH (in which it is slightly soluble), and dried at room temperature in air in the dark. It is air stable and can be recrystallised from $*C_6H_6$/Me_2CO. Clearly, the Me_2S reduces Au(III) to Au(I) before the complex separates. It is rapidly decomposed by sunlight to give metallic gold, Me_2S and HCl. In the absence of sunlight it can be kept in the solution in which it has been prepared for long periods, or in the presence of a slight excess of Me_2S in which colourless crystalline needles are formed. It is soluble in many organic solvents, e.g. CH_2Cl_2, $*C_6H_6$, but solutions deposit metallic gold in time. The gold content can be determined by exposing solutions to sunlight, and the gold that deposits can be collected and weighed. On heating in N_2, Me_2S begins to evolve above 100° until 200°, after which a residue of gold is obtained. [Phillips *J Am Chem Soc* **23** 250 *1901*.] In a third synthesis, a suspension of freshly prepared Au(I)Cl (0.23g, 1mmol, [10294-29-8]) in dry $*C_6H_6$ (25ml) is treated with an excess of Me_2S which causes the solid to dissolve on stirring at 20°. After half an hour, the solution is evaporated *in vacuo*, and the crystalline residue is recrystallised from $*C_6H_6$/Me_2CO (1:1) to give a 70% yield of the pure complex, **m 100-102°(dec)**. [Dash & Schmidbaur *Chem Ber* **106** 1221 *1973*.]
For the **Au(III) complex** aurochloric acid (10g) in H_2O (5ml) and a 1:1 v/v mixture of HNO_3 (d 1.4) and HCl (d 1.2) (1ml) are cooled in an ice bath for 10 minutes, and then Me_2S (0.5g) in Me_2CO (5ml) is added gradually (1ml at a time, at 3-5 minutes interval), heat is evolved and a yellow oil separates which soon solidifies to an

orange yellow solid (some white *aurochloro dimethylsulfide* separates simultaneously). After allowing to stand in contact with a further quantity of acid mixture, all the solid is converted to ***aurichloro dimethylsulfide*** (**$AuCl_3.Me_2S$**). This is filtered off, washed with a 1:1v/v mixture of N/10 HNO_3 and N/10 HCl then H_2O and finally with EtOH, and dried in air. It is recrystallised from $CHCl_3/Et_2O$ to give yellow prismatic crystals of analytically pure *auri complex* **$AuCl_3.Me_2S$** with **M 365.5** *[29826-91-3]* and **m 160°**, which is soluble in $CHCl_3$, Et_2O, Me_2CO, and warm $*C_6H_6$. When this auri complex is warmed with EtOH on a water bath, it is converted into the auro complex **$AuCl.Me_2S$** and the colour changes to white. The latter can be converted back to the former complex by treatment with aqua regia or chlorine water. [Ray & Sen *J Indian Chem Soc* **7** 67 *1930*.]
$AuCl.Me_2S$ is monomeric with M^+ at *m/e* at 294; its IR (Nujol mulls between polyethylene discs or CsI plates) has bands at 730vw (SC_2 *asym*), 675vw (SC_2 *sym*), 345s (Au-S, str), 326s and 319sh (Au-Cl str), 279m (SC_2 *def*), 198s (CSAu *def*), 109m, 93m and 83m (SAuCl *bend and lattice modes*) cm^{-1} [Goggin et al. *J Chem Soc, Dalton* 1904 *1972*], the ^1H NMR (100MHz, CH_2Cl_2, TMS) has one peak at τ = 8.1 ppm [Allen & Wilkinson *Spetrochim Acta* **28A** 2257 *1972*], and the ^1H NMR (60MHz, $CHCl_3$, TMS) has one peak at δ = –2.81 [Dash & Schmidbaur *Chem Ber* **106** 1221 *1973*].
It is a very useful compound for preparing a variety of gold complexes and gold catalysts [e.g. IMesAuCl in Part 1 of this Chapter].

Chlorotris(triphenylphosphine)cobalt [$CoCl(PPh_3)_3$] *[26305-75-9]* **M 881.2, m 135-139°(dec), 176-179°(dec), 177°(dec), 188°(dec).** The complex is prepared under N_2, and preferably in Schlenck-type equipment. $CoCl_2.6H_2O$ (9.6, 40.3mmol), PPh_3 (32g, 122mmol) and EtOH (600ml) are stirred while being purged with N_2 for several minutes, then vigorously at 60-70° for 30 minutes to ensure complete formation of the blue-coloured fine powder of $CoCl_2(PPh_3)_2$. Then under vigorous stirring the mixture is cooled to ~30° and $NaBH_4$ (1.28g, 33.9mmol) is added during ~10 minutes (in ~10 portions) whereby the colour of the solution changes from blue to green, then to brown. The green-brown precipitate is collected by filtration (in air), washed with portions of EtOH until the filtrate is no longer blue in colour, then with H_2O, EtOH again and finally with hexane, and dried *in vacuo* to give $CoCl(PPh_3)_3$ (24g, 67%). In the solid state it decomposes quite slowly in air, but is stable indefinitely under argon or N_2 in a refrigerator. It is soluble in $*C_6H_6$ and CH_2Cl_2 and the spectra in $*C_6H_6$ have λ_{max} at 745, ~940sh, 1100, 2200nm. [Wakatsuki & Yamazaki *Inorg Synth* **26** 190 *1989*, Aresta et al. *Inorg Chim Acta* **3** 227 *1969*.]
$CoCl(PPh_3)_3$ is a useful stoichiometric reagent for radical dimerisation of halogenated organic compounds as in the biomimetic synthesis of the bis-sesquiterpene lactones (±)-biatractylolide and (±)-biepiasterolide [Bagal et al. *J Org Chem* **69** 9100 *2004*], and alkaloid dimerisation in the total synthesis of the alkaloids (-)-calycanthine and (+)-chimonanthine [Movassaghi & Schmidt *Angew Chem Int Ed* **46** 3725 *2007*]. It is used for the preparation of COPs (**c**obalt **o**xazoline **p**alladacycles) catalysts [see above, Stevens & Richard *Organometallics* **18** 1346 *1999*].

(1,3,5,7-Cyclooctatetraene)dilithium (2,4,6-cyclooctatriene-1,2-diyl dilithium, $Li_2C_8H_8$) *[40698-91-7]* **M 118.1.** It is prepared by suspending lithium foil (1.0g, 144mmol) under N_2 in Et_2O (20ml) and stirring at 0° with 1,3,5,7-cyclooctatetraene (5.0g, 48mmol) for 16 hours. The small amount of white precipitate is allowed to settle, and an aliquot sample of the orange solution is sucked into a syringe, and the molarity of the solution is determined by hydrolysis with H_2O and titrating with standard acid. A saturated solution of $Li_2C_8H_8$ in Et_2O is ~0.24M. Store in the cold and away from air and moisture. The solution is not more flammable than an Et_2O solution, but the dry solid $Li_2C_8H_8$ is **pyrophoric** in air. [Spencer *Inorg Synth* **19** 214 *1979*, Crascall & Spencer *Inorg Synth* **28** 127 *1990*.]

(1*R*,2*R*)-(+)-1,2-Diaminocyclohexane-*N*,*N*′-bis(2-diphenylphosphinobenzoyl) [(*R*,*R*)-DACH-phenyl Trost ligand] *[138517-61-0]* **and (1*S*,2*S*)-(–)-1,2-diaminocyclohexane-*N*,*N*′-bis(2-diphenylphosphinobenzoyl) [(*S*,*S*)-DACH-phenyl Trost ligand]** *[169689-05-8]* **M 690.8, m 137-142°, $[\alpha]_D^{20}$ *R*,*R*- +134°, *S*,*S*- -134° (c 1.0, MeOH), $[\alpha]_D^{20}$ *R*,*R*- +55.1°, *S*,*S*- -55.1° (c 2.85, CH_2Cl_2).** The (1*R*,2*R*)-enantiomer is prepared from (1*R*,2*R*)-1,2-diaminocyclohexane (0.535g, 4.68mmol), 2-(diphenylphosphino)benzoic acid (3.02g, 9.83mmol, [17261-28-8]), DMAP (61.0g, 0.5mmol) and DCC (2.13g, 10.3mmol) in CH_2Cl_2 (30ml) for 6 hours. The residue is chromatographed on silica gel and eluted with a 15—30% gradient of EtOAc/hexanes followed by recrystallisation from CH_2Cl_2/Et_2O to give the (+)-DACH-phenyl Trost ligand (2.96g, 90%). It has an R_F of 0.43 on silica TLC (1:1 EtOAc-pentanes) and its IR (neat film from $CDCl_3$) has ν_{max} at 3303, 3070, 2935, 2857,

1955w, 18877w, 1817w, 1645s, 1538, 1478, 1434, 1328, 1306, 1162, 1091, 909 cm^{-1}; the ^1H NMR (200MHz, $CDCl_3$) has δ at 7.57 (m, 2H), 7.15-7.26 (m, 24H), 6.91 (m, 2H), 6.31 (br d, *J* = 7.7Hz, 2H, N-H), 3.77 (m, 2H), 1.87 (m, 2H), 1.62 (m, 2H), 0.9-1.3 (m 6H); the ^{13}C NMR (50MHz, $CDCl_3$) has δ at 169.46, 140.80 (d, *J* = 24.2Hz), 137.96 (d, *J* = 11.8Hz), 137.88 (d, *J* = 12.3Hz), 136.81 (d, *J* = 21.6Hz), 134.34, 133.97 (d, *J* = 20.3Hz), 130.23, 128.79, 128.66, 128.57, 128.51, 128.43, 127.63, 127.55, 53.58, 31.71, 24.4; and has correct elemental analyses for C, H, N and P. [Trost et al. *J Am Chem Soc* **114** 9327 *1992*.]
The Pd complexes have found extensive use in catalysing Asymmetric Allylic Alkylation (AAA) and palladium-catalysed Dynamic Kinetic Asymmetric Transfomations (DKYATs), i.e. kinetic resolutions [Trost & Fandrick *Aldrichimica Acta* **40** 59 *2007*].

(–)-*N*,*N*′-(1*R*,2*R*)-1,2-Diaminocyclohexanediylbis(2-pyridinecarboxamide) [(*R*,*R*)-DACH-pyridyl Trost ligand] ***[218290-24-5]*** **and (+)-*N*,*N*′-(1*S*,S*R*)-1,2-diaminocyclohexanediylbis(2-pyridinecarboxamide) [(*R*,*R*)-DACH-pyridyl Trost ligand]** ***[172138-95-3]*** **M 324.4, m 171-176°, 174-176°, $[\alpha]_D^{20}$ *R,R* -97.0°, *S,S* +97.0° (c 1.0, MeOH).** The (*RS,RS*)-1,2-diaminocyclohexanediylbis(2-pyridinecarboxamide) is readily prepared by treating a mixture of 1,2-diaminocyclohexane (5.7g, 50mmol) in pyridine (20ml) and pyridine-2-carboxylic acid (12.3g, 100mmol) in pyridine (40ml) with triphenylphosphite (31.0g, 100mmol), and heating on a steam bath for 12 hours. The resulting brown oil is extracted into $CHCl_3$, washed twice with aqueous $NaHCO_3$, and H_2O, dried ($MgSO_4$), filtered, evaporated to a small volume and set aside overnight whereby brown crystals of the product are obtained (7.6g, 47%). Recrystallisation from $CHCl_3$ gives analytically pure (±)-ligand as white crystals, m 201-202°, with IR (KBr) ν_{max} at 3300, 3050, 2940, 2850, 1655, 1535 cm^{-1}; and the ^1H NMR (60MHz, $CDCl_3$) has δ at 8.6 (m), 8.4 (br), 8.1 (m, combined 8H), 7.8 (m, 2H), 7.4 (m, 2H), 4.1(br, 2H), 2.3 (br), 1.6 (br, combined 6H) downfield from TMS (peaks are not well separated at 60MHz). [Barnes et al. *J Chem Eng Data* **23** 349 *1978*.] **(1*R*,2*R*)-DACH-pyridyl Trost ligand** and **[(1*S*,2*S*)-DACH-pyridyl Trost ligand** are prepared similarly, but starting from (*1R,2R)(-)-[20439-47-8] and* (*1S,2S)(+)-[21436-03-3]* 1,2-diaminocyclohexanes respectively [cf their resolution in Chapter 4, Alicyclic Compounds pp 242-243].
These ligands readily form complexes with Cu, Zn, Co, Pt and Pd [Mulqi et al. *Inorg Chim Acta* **53** L91c *1981*, Adolfson & Moberg *Tetrahedron:Asymmetry* **6** 2023 *1995*] and the Pd complexes have found extensive use in catalysing Asymmetric Allylic Alkylation (AAA) and palladium-catalysed Dynamic Kinetic Asymmetric Transfomations (DKYATs), i.e. kinetic resolutions [Trost & Fandrick *Aldrichimica Acta* **40** 59 *2007*].

Di-*tert*-butylchlorophosphine *[13716-10-4]* **M 180.7, b 48°/3mm, 72-73°/13mm, d_4^{25} 0.951, n_D^{20} 1.482.** This chlorophosphine is prepared from two equivalents of *tert*-butylmagnesium bromide and PCl_3 followed by the usual workup and fractional distillation in a vacuum, and redistillation of the desired fraction. With MeLi it provides *di*-tert-*butylmethylphosphine* **b 95-105°/3mm (170-172°/atm)**, which with MeI provides ***di*-tert-*butyl-dimethylphosphinium iodide* m 95-105°** (from EtOH). Hydrolysis of the chlorophosphine with H_2O provides ***di*-tert-*butylphosphine oxide*** [684-19-5] **M 162.2**, **m 55-59°** (hygroscopic crystals), **b 112°/9mm**, with IR which has ν_{max} ($CHCl_3$) 2950s, 2290, 1470s, 1394w, 1370, 1142s, 918, 815 (P-Bu^t) and 656 cm^{-1}; the ^1H NMR (CD_2Cl_2) has τ at 3.53 (d, J_{HP} = 453Hz), 8.65 (d, J_{HCCP} = 15Hz, Bu^t). Note that this phosphine oxide is tautomeric with *di*-tert-*butylphosphinous acid*. [Hoffmann & Schellenbeck *Chem Ber* **99** 1134 *1966*, Hoffmann & Schellenbeck *Chem Ber* **100** 692 *1967*, Issleib & Krech *J Organometal Chem* **13** 283 *1968*, Crofts et al. *J Chem Soc C* 331 *1970*.]
The complex from $Pd(OAc)_2$ and this bulky *di*-tert-*butylchlorophosphine* ligand, after condensation with *P*-imino-azaphosphatrane, catalyses efficiently the cross-coupling of arylboronic acids with aryl halides in the Suzuki-Miyaura reaction to provide specific unsymmetrical biphenyls in well over 90% yields [Kingston & Verkade *J Org Chem* **72** 2816 *2007*.]

4,4′-Di-*tert*-butyl-2.2′-bipyridyl (dtbpy) *[72914-19-3]* **M 268.4, b 235°/32mm, m 159-160°, 159-161°, pK_{Est} ~4.2.** The bipyridyl has been prepared by reaction of *tert*-butylpyridine with $NaNH_2$ (ratio 2:1) in xylene at 144-218° during 26 hours, then cooled, hydrolysed with H_2O, the organic layer is separated, dried, and distilled *in vacuo*. The bipyridyl solidified and can be sublimed. [McGill USP 4177349, *Chem Abstr* **92** 110871 *1980*, *Beilstein* **23/8** IV 181.] By coordinating with Ir(COD) and Ir(COE), complexes formed with **dtbpy** assist in C-H borylations [see Ir complexes above and Ishiyama et al. *Angew Chem. Int Edn* **41** 3056 *2002*, Ishiyama et al. *J Am Chem Soc* **124** 390 *2002*.]

Di-*tert*-butylneopentylphosphine [DTBNpP, ($PBu^t_2(-CH_2CMe_3)$] *[60633-21-8]* **M 216.3, b 40°/0.1 mm, d ^{25} 0.839, n $^{20}_{D}$ 1.478.** This ligand, with increased steric bulk, can be obtained by adding a solution of di-*tert*-butylchlorophosphine (108.4g, 114.0ml, 0.6mol, see [13716-10-4]) in THF (250ml) to neopentylmagnesium chloride (from 16g, 0,67g-atom of Mg turnings, 74ml, 64g, 0.6mol of neopentyl chloride in 250ml of dry THF containing a small amount of 1,2-dibromoethane as initiator, and stirred until all the Mg has dissolved, then cooled to 0°) at 0° with stirring, allowing to warm to ~25°, boiling under reflux for *ca* 15 minutes, then the solvent is removed at ~40°/40mm). The residue is diluted with Et_2O, the mixture is hydrolysed by stirring with saturated aqueous NH_4Cl, the layers are separated and the organic phase is dried ($MgSO_4$), filtered, the Et_2O is removed at ~25°/50mm, and the residual phosphine is distilled at high vacuum. There are also alternative syntheses for DTBNpP. *Work with protective gloves, with eyes and face protection, and in an efficient fume cupboard*. [*cf*: King et al. *J Org Chem* **41** 972 *1976*.] It is, however, better to store and use it in the form of its salts, e.g. DTBNpP.HBF_4 (see below). In that case an equivalent amount of base, e.g. *t*-BuONa, must be added to the reaction mixture to liberate the free ligand. With a Pd source, e.g. $Pd(OAc)_2$ or $Pd_2(dba)_3$, H—B coupling (Hartwig—Buchwald) of various aryl halides with a variety of aromatic primary or secondary amines, or saturated heterocyclic amines, e.g. morpholine, is catalysed to form di- or tri-substituted amines in toluene solutions at 23° to 140° in high yields. [Hill et al. *J Org Chem* **71** 5117 *2006*.]
Unlike with Pd complexes, when DTBNpP is mixed with $Pt(PhCN)_2Cl_2$ (1:1 mol per Pt atom) in CH_2Cl_2 at 20° for a few minutes, a white binuclear complex is formed. It was characterised by spectroscopic and Xray diffraction methods to have the structure **$[PtCl(PBu^t_2CH_2CMe_2CH_2)]_2$**, i.e. one of the methyl groups of the neopentyl moiety is folded back and is metallated by the Pt to form a five membered Pt heterocyclic ring — and the molecule is dimeric. Such metallation does not occur with $PBu^t_2Pr^n$ under similar conditions, and in this case the monomeric *cis* and *trans* $[PtCl_2(PhCN)(PBu^t_2Pr^n)]$ square planar complexes are formed. [Mason et al. *JCS Chem Commun* 292 *1976*.]

Di-*tert*-butylneopentylphosphonium tetrafluoroborate ($DTBNpP^+.HBF_4^-$) *[886059-84-3]* **M 304.2, m 258-262°(dec).** This air stable salt is prepared in the same manner as [(*tert*-Bu)$_3PH^+$ BF_4^-, [131274-22-1] by mixing DTBNpP and aqueous HBF_4. It is easier to handle [*cf*: Netherton & Fu *Org Lett* **3** 4295 *2001*], and is a useful ligand in Pd-catalysed cross-coupling amination reactions of aryl bromides and chlorides [Hill et al. *J Org Chem* **71** 5117 *2006*].

3,3′-Di-*tert*-butyl-5,5′,6,6′-tetramethyl-1,1′-biphenyl-2,2′-diol {H_2[BIPHEN], 1,1′-biphenyl-2,2′-diol, 3,3′(1,1′-dimethylethyl)-5,5′,6,6′-tetramethyl-} *[R- 329735-68-4, S- 205927-03-3, RS- 101203-31-0]* **M 354.5, m 160.5-161.5°.** This biphenyl is prepared by the oxidation of 2-*tert*-butyl-4,5-dimethylphenol. The oxidation is carried out by slowly adding a solution of $K_2Cr_2O_7$ (130g, 0.442 mole, i.e. 1.02 equivalents being twice the theoretical amount to form the biphenyl) in a mixture of concentrated H_2SO_4 (260ml) and H_2O (780ml, CARE as much heat is evolved on mixing) at ~25°, to a solution of 2-*tert*-butyl-4,5-dimethylphenol (231.7g, 1.3 moles, see [1445-23-4]) in AcOH (1300ml) over 10 minutes at 55-60° and keeping at this temperature range. The colour of the solution changes from orange to green and a tan coloured solid separates during the reaction which is cooled to room temperature. It is collected, washed sequentially with H_2O (2 x 250ml) and MeOH (3 x 200ml) until the solid is almost colourless, dried *in vacuo* and recrystallised from hot MeOH or dioxane/MeOH to give racemic *3,3'-di-tert-butyl-5,5',6,6'-tetramethyl-1,1'-biphenyl-2,2'-diol* [101203-31-0] **(~115g, ~50%) m 160.5-161.5°** (m 140-142° before recrystallisation). Its ^{1}H NMR (400MHz, $CDCl_3$, TMS) has δ at 7.12 (s, 2H, aromatic C*H*), 4.79 (s, 2H, OH), 2.24 (s, 6H, CH_3), 1.80 (s, 6H, CH_3), 1.38 (s, 18H, C(CH_3)$_3$); and its ^{13}C NMR (100MHz, C_6D_6, ref C_6D_6 at δ = 128.4) has δ at 151.24, 134.60, 134.13, 127.73, 128.79, 121.64, 35.15, 30.19, 20.46, 16.35. [Albert *J Am Chem Soc* **76** 1983 *1954*, Alexander et al. *J Am Chem Soc* **120** 4041 *1998*, Alexander et al. *Organometallics* **19** 3700 *2000*.]
Optical Resolution of H_2[BIPHEN]*:** Two procedures have been used: (i) preparation of the respective 2,2′-cyclic phosphoric acid (*via* reaction with $POCl_3$ with the di-Na salt in THF) followed by hydrolysis and recrystallisation of the (±)-acid (-)-Cinchonidine salt in EtOH, followed by hydrolysis of the optically salts, conversion of the optically active cyclic acids to their respective optically active cyclic methyl esters, and finally cleavage with "Red-Al" [Na $AlH_2(OCH_2CH_2OMe_2)$] in toluene to give optically pure *H_2[BIPHEN]*s. [Alexander et al. *J Am Chem Soc* **120** 4041 *1998*.]; and (ii) which is decribed here in some detail as it can be used generally for the resolution of racemic 2,2′-dihydroxybiphenyls. ***Firstly: A solution of (1*R*,2*S*,5*R*)(-)-menthol (44g, 282mmol) in CH_2Cl_2 (100ml) is added to a solution of PCl_3 (58g, 423mmol, 1.5

equivalents) in CH_2Cl_2 (200ml) at 0° during 30 minutes. The cold bath is removed, the mixture is kept at ~25° for 1 hour, and the volatiles are removed at <25°/100mm. The residual oil, which consists of *menthyl phosphorochloridite* (see [95456-31-8] in Chapter 4, p 516), is dissolved in CH_2Cl_2 (250ml), and a mixture of Et_3N (118ml, 847mmol, 3 equivalents) in CH_2Cl_2 (400ml) and H_2[Biphen] (100g, 282mmol) is added during 30 minutes. After 2 hours the mixture is filtered; H_2O_2 (30%, 200ml, *extremely violent reaction* take great CARE, wear body protection) is added very slowly with stirring, the biphasic mixture is then stirred vigorously for 2 hours, the layers are allowed to settle, the organic phase is washed with H_2O and brine (200ml), dried ($MgSO_4$), filtered and evaporated *in vacuo* to give a mixture of (*R*)- and (*S*)- BiphenP(O)(OMen) (124g, 85%) with ^{31}P NMR (121MHz, THF, external ref 85% H_3PO_4) which has δ at -4.89 and -3.37 respectively due to the diasereomeric menthyl phosphates. ***Secondly*:** The diastereomeric mixture of phosphates is dissolved in the minimum volume of refluxing AcOH (~450ml), allowed to cool, and after 16 hours white crystals were filtered off, washed with cold AcOH (2 × 50ml) and dried *in vacuo* to give *(S)-BiphenP(O)(OMen)* (42g, 97-99% de). Recrystallisation from refluxing **AcOH** gives pure *S*-diastereomer (37.8g, >99%de, in 61% yield), The mother liquors from the first crystallisation are evaporated to give *(R)-BiphenP(O)(OMen)* (26.8g, >99%de, 43% *R*-diastereomer) after two recrystallisations from refluxing **MeOH** and cooling to 0°. [Partly racemic ester from the mother liquors are re-used in subsequent resolution processes.] ***Thirdly*:** To the preceding (*S*)-biphenP(O)(OMen) (37.83g, 70.3mmol) in toluene (500ml) in a 2L Schlenk flask at 0° is treated dropwise with Red-Al (53ml, 65%wt in toluene, introduced into the separating funnel *via* a cannula) at 0°, and stirred for 16 hours. The mixture is carefully quenched with H_2O (75ml) then bleach (75ml), the slurry is filtered through a Celite pad, the pad is washed with toluene (250ml), the combined filtrates are allowed to settle, the toluene layer is separated, washed with bleach (200ml), brine (200ml), dried ($MgSO_4$), filtered, then the toluene is removed *in vacuo* at 0°, any menthol (minty odour) is removed by trituration with MeOH (50ml), to provide after drying, the resolved (*S*)-H_2[BIPHEN] (17.5g, 70%, >99% ee) which has $[\alpha]_D^{20}$ -53.0° (c 0.352, THF). The absolute configuration of this diastereoisomer was deduced from the X-ray crystallographic structure of its *syn*-Mo(*N*-2,6-di-*iso*-PrC_6H_3)(CHCMe$_2$Ph)[(*S*)-BIPHEN] complex (see Schrock-Hoveyda catalyst [205815-80-1] in Part 1). (*R*)-H_2[BIPHEN] is prepared from (*R*)-BiphenP(O)(OMen) using an identical procedure and the optical purity is deduced from that of its precursor as no racemisation occurs in these reactions. Note that the NMR spectra of the *RS*- (see above), *R*- and *S*-H_2[BIPHENS] are the same. About 20g each of the *R*- and *S*- H_2[BIPHENS] are usually obtained from 100g of *RS*-H_2[BIPHEN]Me; and ~60g of the latter are pooled from the mother liquors which can be recycled. [Alexander et al. *Organometallics* **19** 3700 *2000*, Alexander et al. *J Am Chem Soc* **120** 4041 *1998*.]

By using identical compounds and reactions, but in which the *tert*-butyl group is replaced by a 1-adamantyl group the corresponding ***1-adamantyl (H_2BIAD) derivatives*** are obtained in almost similar yields and used to prepare related molybdenum catalysts. For example **(*S*)-3,3′-bis(1-adamantyl)-5,5′,6,6′-tetramethyl-1,1'-biphenyl-2,2′-diol {(*S*)-H_2(BIAD) {*S*-(-)-3,3′-biphenyl-2,2′-diol, 5,5′,6,6′-tetramethyl-3,3′-bis(tricyclo-[3.3.1.13.7]dec-1-yl,** [*255728-57-5*]} with $[\alpha]_D^{20}$ -32.1° (c 3.3, THF), whose absolute configuration was also deduced by X-Ray crystallography of its related respective Mo complex catalyst, was prepared starting from 2-(1-adamantyl)-4,5-dimethylphenol **m 135-138°**. [Alexander et al. *Organometallics* **19** 3700 *2000*.]

Dicyclohexyl(2-methylphenyl)phosphine (Cy$_2$P-*o*-Tol) *[173593-25-4]* **M 288.4, m 90-93°, pK_{Est} ~4.0.** This phosphine is prepared and purified in the same way as Cy_2PPh (following entry), and is used in the same manner as a phosphorus ligand for catalyst systems in coupling reactions. It has the advantage that it is less susceptible to oxidation, has a higher melting point and is easier to handle.

Dicyclohexylphenylphosphine (Cy_2PPh) *[6476-37-5]* **M 274.4, m 56-57°, 57-58°, pK^{25} 3.40.** Cy_2PPh is a "foul smelling" solid which is a good ligand for Cr, Hg and Group VIII metals. It can be prepared by reaction of $PhPCl_2$ with CyMgCl in 50% yield [Issleib & Völker *Chem Ber* **64** 392 *1961*], or in 90% yield from $PhPCl_2$ and CyLi [Screttas & Isbell *J Org Chem* **27** 2573 *1973*], and is recrystallised from oxygen-free Me_2CO or EtOH. In detail: to the Grignard solution, at ice-salt bath temperature, made from Mg turnings (24.1g, 0.99mol) in dry Et_2O (350ml) and CyBr (162g, 122ml, 0.99mol) in dry Et_2O (130ml), is added dropwise (2 hours) to a solution of $PhPCl_2$ (81g, 61.4ml, 0.45mol) in dry Et_2O (100ml). The mixture is then boiled under reflux for 30 minutes and hydrolysed by stirring with saturated, deoxygenated, aqueous NH_4Cl. The Et_2O layer is separated and evaporated at ~20°/30mm leaving an oil that crystallises after all the solvent is removed. It may be recrystallised

by slowly cooling a hot, oxygen-free EtOH solution (1ml/g), with gentle stirring to prevent formation of an oil, to give analytically pure (Cy_2PPh) as white needles (98g, 79.5%). [Bianco & Doronzo *Inorg Synth* **18** 171 *1978*.] It is a phosphorus ligand used in catalytic systems for coupling reactions.
Dicyclohexylphenylphosphine oxide (Cy_2PPhO), crystallises from petroleum ether, EtOH or Me_2CO and melts at **157.5°** (m 165° was also reported).

Dicyclohexylphosphine (Cy_2PH) *[829-84-5]* **M 198.3, b 105-108°/3mm, 128°/8mm, 281-283°/atm, n_D^{25} 1.5142, pK_a 4.55.** This phosphine is a useful air sensitive ligand and should be used preferably in an inert atmosphere. It has been prepared in 80% yield by heating $Cy_2PSSPCy_2$ with excess Cu and distilling [Niederfeld & Langenfeld *Chem Ber* **95** 64 *1962*], or in 55% yield by the addition of PH_3 to cyclohexene under pressure in the presence of α, α-azobis(isobutyronitrile) followed by fractional distillation [Rauhut et al. *J Org Chem* **26** 5138 *1961*]. It is a phosphorus ligand in catalytic systems used in coupling reactions. It forms a pale yellow *Li salt* [19966-81-5] which is slightly soluble in dioxane but insoluble in Et_2O, $*C_6H_6$ and petroleum ether. [cf Edmundson *Dictionary of Organophosphus Compounds*, Chapman & Hall, London, *1988*, p 221, ISBN 0-412-25790-4.]

Dicyclohexylphosphine oxide **(Cy_2PHO)** *[14717-29-4]* **M 214.3**, **m 72.5-74.5°.** The oxide crystallises from hexane or $*C_6H_6$. It is tautomeric with dicyclohexylphosphinous acid (Cy_2P-OH), whose *Ethyl ester* ([80413-46-3] **M 242.3**, obtained from CyP_2Cl [16523-54-9] and EtOH) distils at **111-113°/1mm**, n_D^{20} **1.4950.** [Kabachnik et al. *Izv Akad Nauk SSSR, Ser Khim,* 949, 923 *(Engl Trans) 1967*]; and the *trimethylsilyl ester*, **M 286.5**, distils at **108-110°/1mm**, n_D^{20} **1.4919** [Foss et al. *Zh Obhsch Khim* **49** 2418, 2134 *(Engl Trans) 1979*, cf Edmundson *Dictionary of Organophosphus Compounds*, Chapman & Hall, London, *1988*, p 222, ISBN 0-412-25790-4.]

2-Dicyclohexylphosphino-2',6'-dimethoxybiphenyl (S-Phos) *[657408-07-6]* **M 410.5, m 162-162.5°, 164-166°.** This Buchwald phosphine can be synthesised in one pot under argon by adding *n*-BuLi (6.20ml, 2.5M solution in hexanes, 15.5mmol, 1.1 equivalents) *via* a syringe over 5 minutes to a cold (0°) solution of 1,3-dimethoxybenzene (2.00ml, 15.3mmol, 1.1 equivalents, [151-10-0]) in dry THF (35ml), allowing the temperature to rise to ~25°, then it is stirred for 3.5 hours. The mixture is re-cooled (0°) and 2-bromochlorobenzene (1.60ml, 13.7mmol, 1.0 equivalents, [694-80-4]) is added dropwise *via* a syringe over 15 minutes while stirring vigorously; and the burgundy coloured solution is stirred for a further 15 minutes at 0°. At this stage GC analysis of an aliquot quenched with Et_2O/H_2O should show that all the bromochlorobenzene has been used up and a clean conversion to 2-bromo-2′,6′-dimethoxybiphenyl has occurred. The mixture is cooled to -78° and *n*-BuLi (6.20ml, 2.5M solution in hexanes, 15.5mmol, 1.1 equivalents) is added dropwise *via* a syringe during 5 minutes and stirred further (with swirling if necessary) at -78° for further 30 minutes. Neat chlorodicyclohexylphosphine (3.03ml, 13.7mmol, 1.0 equivalents [16523-54-9]) is then added dropwise *via* syringe, stirred at -78° for 1 hour and allowed to warm to ~25°. The mixture is filtered through a pad of Flash silica gel topped with a layer of Celite, eluted with EtOAc (400ml) and the combined filtrates are evaporated *in vacuo* to give a yellow solid residue which is recrystallised from Me_2CO to give *S-Phos* (2.90g) as a white solid. A further crop can be obtained by concentrating the mother liquors and triturating with MeOH to provide a total yield of 3.32g (59%) as a white solid m 162-162.5°. Its IR (neat) has ν_{max} at 2921, 2848, 1588, 1470, 1459, 1430, 1245, 1109, 909, 722 cm^{-1}; and its ^1H NMR (300MHz, C_6D_6) has δ at 7.59 (dm, *J* for the doublet 7.2Hz, 1H), 7.39-7.42 (m, 1H), 7.15-7.25 (m, 3H), 6.43 (d, *J* = 8.5 Hz, 2H), 3.33 (s, 6H), 1.60-1.94 (m. 12H), 1.06-1.36 (m, 10H) from TMS; the ^{13}C NMR (75MHz, C_6D_6) has δ at 158.49, 158.48, 144.3, 143.9, 137.3, 137.3, 137.0, 132.82, 132.77, 132.4, 132.2, 129.2, 128.82, 128.81, 128.2, 126.8, 121.2, 121.1, 104.0, 55.2, 35.0, 34.8, 31.0, 30.8, 30.3, 30.1, 28.22, 28.15, 28.07, 28.05, 27.40, 27.39 (observed complexity due to P-C coupling; definitive assignment have not been made); the ^{31}P NMR (121MHz, C_6D_6) has δ at -8.6. [Barder et al. *J Am Chem Soc* **127** 4685 *2005*.]
Complexation of S-Phos to form a Pd-catalyst [e.g. with $Pd(OAc)_2$] provides a system with unprecedented scope, reactivity and stability for Suzuki-Miyaura coupling processes, e.g. it generates truly hindered highly chiral biaryls and heterobiaryls [Walker et al. *Angew Chem. Int Ed* **43** 1879 *2004*, and quinine-quinidine syntheses: Raheem et al. *J Am Chem Soc* **126** 706 *2004*, Huang et al. *J Am Chem Soc* **125** 6653 *2003*, Nguyen et al. *J Am Chem Soc* **125** 11818 *2003*, Gelman & Buchwald *Angew Chem. Int Ed* **42** 5993 *2003*], and is useful for C-N bond formation [Strieter & Buchwald *Angew Chem. Int Ed* **45** 925 *2006*].

2-Dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (X-Phos, 2,4,6-triisopropyl-2′-dicyclohexylphosphinobiphenyl) *[564483-18-7]* **M 476.7, m 182-184º, 187-190º.** This *Buchwald ligand* is prepared by reacting 2,4,6-triisopropylphenylmagnesium bromide with *o*-bromochlorobenzene in the presence of CuCl, and the resulting biphenyl is condensed with dicyclohexylphosphorus chloride. X-Phos is purified by solubilising it in Et_2O/CH_2Cl_2 (2:1, *ca* 30ml/g) by sonication, seeding it, and setting aside at -40º for 24 hours to give a first crop which is collected and washed with cold Et_2O. A second crop can be obtained by concentrating the mother liquors then mixing with hot MeOH (~10ml, at 65º), cooling and while sonicating Et_2O/CH_2Cl_2 is added until homogeneous and set aside as before. The combined crops are dried *in vacuo* for 24 hours to give white crystals m 182-184º. The IR (film) has ν_{max} at 2923, 1461, 1449, 876 and 768 cm^{-1}. It has ^1H NMR (300MHz, C_6D_6) with δ_H at 7.48-7.42 (m, 1H), 7.24-7.06 (m, 5H), 2.85 (septet, *J* = 6.9Hz, 1H), 2.71 (septet, *J* = 6.9Hz, 2H), 1.94-1.52 (m, 12H), 1.42 (d, *J* = 6.9Hz, 6H), 1.24 (d, *J* = 6.9Hz, 6H), 1.30-1.02 (m, 10H), 1.12 (d, *J* = 6.9Hz, 6H); the ^{31}P NMR (121MHz, C_6D_6) has δ_P at -11.5; and the ^{13}C NMR (75MHz, C_6D_6) has δ_C at 148.7, 148.6, 148.2, 147.01, 146.99, 137.8, 137.7, 137.60, 137.558, 132.92, 132.88, 132.3, 132.2, 128.2, 127.0, 121.0, 35.4, 35.3, 35.1, 32.1, 31.9, 31.68, 31.66, 30.3, 30.1, 28.6, 28.4, 28.3, 28.2, 27.4, 26.9, 25.0, 23.92, 23.90 (observed complexity from P-C coupling). [Huang et al. *J Am Chem Soc* **125** 6653 *2003*, Tomori et al. *J Org Chem* **65** 5334 *2000*.] X-Phos has been used for the amidation of arylsulfonates, in Pd catalysed Suzuki coupling [Johnson et al. *J Org Chem* **71** 7899 *2006*], annulation of *o*-haloanilines [Jia & Zhu *J Org Chem* **71** 7826 *2006*], and the synthesis of regioregular polythiophenes [Liversidge et al. *Tetrahedron Lett* **47** 5143 *2006*.]

R*-(+)- and *S*-(-)- *N,N*-Dimethyl-1-ferrocenylethylamine (α-ferrocenylethyldimethylamine)** *[(R) 31886-58-5; (S) 31886-57-4; (RS) 31904-34-4]* **M 257.2, *R or S* b 120-121º/0.7mm, d^{25} 1.222, n_D^{20} 1.589, *RS* b 111º/0.65mm (part dec), n_D^{25} 1.5883, *R* $[\alpha]_D^{25}$ + 14.1º (c 1, EtOH), *S* $[\alpha]_D^{25}$ -14.1º (c 1.6, EtOH).** The *RS*-amine has been prepared from ferrocenyldimethylaminoacetonitrile and MeMgI [Hauser & Lindsay *J Org Chem* **22** 906 *1957*], but it is easily obtained by adding a solution of 1-ferrocenylethanol (23.0g, see [1277-49-2]) in toluene (150ml) at -20º dropwise to a stirred solution of phosgene (12.5g) in toluene (100ml) at -20º during ~30 minutes, then allowing to warm to ~20º; and without isolating the chloro-derivative, the mixture is added to a solution of Me_2NH (22.5g) in propan-2-ol (200ml) at ~20º. The temperature is then allowed to rise to ~25º, the solution is filtered, evaporated to dryness, treated with $*C_6H_6$ which is washed with 8.5% aqueous H_3PO_4, more $*C_6H_6$ is added, neutralised with Na_2CO_3, the $*C_6H_6$ layer is dried (K_2CO_3), filtered and evaporated to give the *RS*-amine (24.2g, 95% crude), which after distillation (b 110º/0.45mm with some decomposition) gives the base as a clear amber oil (17.5g, 68%). Its *picrate* [39699-90-6] forms red plates **m 136-137º** from EtOH. The crude (±)-base is satisfactory for optical resolution. The ***resolution is carried out by stirring a solution of the (±)-base (51.4g) and *R*(+)-tartaric acid (30.0g) in MeOH (100ml) at 55º, seeding, lowering the temperature slowly (2º/hour), and after 24 hours the (-)-base-(+)-acid (30.0g) is obtained which gives the (-)-base (19.0g, $[\alpha]_D^{25}$ -11.0º, c 1.5, EtOH). This is purified further by mixing it again with the (+)-acid (11.1g), each in MeOH (50ml) at 55º, seeded, and cooled as before to give pure (-)-base-(+)-acid from which pure (-)-base (17.0g, b 120-121º/0.7mm, $[\alpha]_D^{25}$ -14.1º, c 1.6, EtOH) is isolated. From the mother liquors, the crude (+)-base is converted to the (+)base-(+)tartrate, recrystallised twice from Me_2CO/H_2O (10:1), from which pure (+)-base, $[\alpha]_D^{25}$ -14.1º is obtained as a clear amber oil. [Marquarding et al. *J Am Chem Soc* **92** 3589 *1970*.] The absolute configuration was determined by X-Ray analysis of the *(S,R,S)-2-(p-methoxyphenyl)hydroxymethyl-N,N-dimethyl-1-ferrocenylethylamine* [yellow powder from *n*-heptane has **m 110-111º**, **$[\alpha]_D^{22}$ -120.8º (c 1.6, EtOH)**] which is obtained by lithiation of the (+)-base, which is highly stereoselective, followed by reaction with *p*-anisaldehyde. [Battelle et al. *J Am Chem Soc* **95** 482 *1973*.]

This ferrocene is a very useful compound for preparing a variety of chiral ferrocene derivatives [see Marquarding et al. *J Chem Res (S)* 82 *1977* and *(M)* 0915 *1977*], and remarkable phosphine ligands for catalysts by virtue of its highly stereoselective lithiation (with BuLi) in the position *ortho* to the dimethylaminoethyl group that allows substitution to give chiral 2-phosphines [Hayashi et al. *Tetrahedron Lett* 4405 *1974*], 2—$SiMe_3$, 2—CH_2OH and 2—CPh_2OH derivatives [Marquarding et al. *J Am Chem Soc* **92** 3589 *1970*]. The chiral 2-lithio derivative (prepared with *sec*-BuLi/Et_2O) reacts with sulfur, selenium or tellurium to give the yellow, red or red-brown ***dichalcogenides*** *(R,S)*-{[E-C_5H_3-CHMe(NMe_2)]Fe(C_5H_5)}$_2$ (from the *R-(+)-base*) and *(S,R)*-{[E-C_5H_3-CHMe(NMe_2)]Fe(C_5H_5)}$_2$ (from the *R-(+)-base*), where E is S, Se or Te respectively. These dichalcogenides are effective chiral ligands for the rhodium(I) {using $[Rh(COD)Cl]_2$}–catalysed asymmetric hydrosilylation of alkyl and aryl ketones with high enantiomeric excesses. The iridium(I) catalyst exhibits lower selectivity [Nishibayashi et al. *JCS Chem Commun* 1375 *1994*].

The tellurium dichalcogenide ***(R,S)*-{[Te-C_5H_3-CHMe(NMe_2)]Fe(C_5H_5)}$_2$**, **[*R,S*-(-)-(Fc*Te)$_2$]** is prepared from lithiated *R*-(+)-*N*,*N*-dimethyl-1-ferrocenylethylamine (with *sec*-BuLi/Et_2O) in Et_2O under N_2 at 0° which is then treated with Te powder in portions, and the mixture is subjected to ultrasonic irradiation for 1 hour. The mixture is poured into H_2O, and air is bubbled through it for 3 hours at ~25°. The solid is collected and purified by column chromatography on activated Al_2O_3, and eluting with EtOAc/hexane to give analytically pure **[*R,S*-(-)-(Fc*Te)$_2$]** as a red-brown solid (42%) with **m 57-58°**, **[α]$_D^{25}$ -622° (c 1, $CHCl_3$)**, the ^{1}H NMR (270MHz, $CDCl_3$) has δ_H at 1.25 (d, *J* = 6.9Hz. 6H), 2.18 (s, 12H), 4.01 (q, *J* = 6.9Hz, 2H), 4.06 (s, 10H), 4.18 (q, *J* = 1.3Hz, 2H), 4.23 (q, *J* = 1.1Hz, 2H), 4.48 (q, *J* = 1.3Hz, 2H); the ^{13}C NMR (67.8MHz, $CDCl_3$) has δ_C at 9.6 (q), 39.7 (q), 50.2 (q), 59.5 (q), 67.1 (d), 67.7 (d), 70.7 (d), 76.2 (d), 93.7 (s). **[*S,R*-(+)-(Fc*Te)$_2$]** is prepared similarly, but from *S*-(-)-*N*,*N*-dimethyl-1-ferrocenylethylamine in 47% yield and has identical physical properties except for **[α]$_D^{25}$ +613° (c 1, $CHCl_3$)**. After conversion into their anions (e.g. Te^-Fc^*, with $NaBH_4$/EtOH), they react with allylic bromides, e.g. geranyl bromide, to form allylic-TeF*c which produce the corresponding allylic alcohols (on treatment with Bu^tOOH/toluene) in 14-22% enantiomeric excess by chirality transfer, possibly *via* a [2.3]-sigmatropic rearrangement [Chiba et al. *Tetrahedron Lett* **36** 1519 *1995*].

Similarly, but using Se instead of Te, *R*-(+)- and *S*-(-)-*N*,*N*-dimethyl-1-ferrocenylethylamine provide **[*R,S*-(Fc*Se)$_2$] (m 98-100°** from hexane) and **[*S,R*-(Fc*Se)$_2$] (m 103°** from hexane) respectively as red solids, and these catalysts induce highly enantioselective selenoxide elimination to produce axially chiral allene carboxylic esters with high enantiomeric excess [Nishibayashi et al. *Tetrahedron lett* **35** 3115 *1994*].

[*R,S*-(Fc*S)$_2$] (m 169-170° from hexane) is obtained as a yellow solid in the same way, but using S instead of Se or Te. [See above for the Rh(I)-catalysed asymmetric hydrosilylation reaction of ketones with these dichalcogenide ligands.]

(1*R*,2*R*)-(+)- and (1*S*,2*S*)-(-)-1,2-Diphenylethylenediamine [(1*R*,2*R*)-(+)- and (1*S*,2*S*)-(-)-1,2-diamino-1,2-diphenylenediamine, 1,2-diamino-1,2-diphenylethane, stilbenediamine, DPEN, STEIN) *[(R) 35132-20-8]; (S) 29841-69-8; (RS±) 16635-95-3]* **M 212.3, *R or S* m 79-83°, *RS* m 82°, [α]$_D^{20}$ *R,R* +102°, *S,S* -102° (c 1, EtOH), [α]$_D^{23}$ *R,R* +106°, *S,S* -106° (c 1.1, MeOH), pK$_{(Est1)}^{25}$ ~5.86, pK$_{(Est2)}^{25}$ ~8.92.** The racemate is prepared in two steps. In the first, a mixture of benzil (158g, 0.75mol, [134-81-6]), anhydrous NH_4OAc (400g) and cyclohexanone (80ml, 0.77mol) in glacial AcOH (1.0L) are stirred and heated under reflux (colour changing from light yellow to dark green) for 1.5 hours, and while hot it is poured into H_2O (3.0L) with vigorous stirring. After cooling to ~25° overnight, the crystals are collected, washed with H_2O (4 x 300ml), and crushed in a mortar (*in vacuo*) to give *2,2-**spirocyclohexane-4,5-diphenyl-2**H-**imidazole*** (***2,3-diphenyl-1,4-diazaspiro-*[4,5]*deca-1,3-diene,*** [5396-98-5]) (~208g, 96%) as yellow-green crystals, **m 107-108°**, on recrystallisation from hexane or aqueous MeOH. Its ^{1}H NMR (400MHz, $CDCl_3$, TMS) has δ_H at 1.65-1.92 (m, 6H), 1.95-2.00 (m, 4H), 7.33-7.53 (m, 10H); and its ^{13}C NMR (100MHz, $CDCl_3$) has δ at 24.1, 25.7, 34.7, 104.1, 128.3, 128.9, 129.9, 133.1, 164.0. In the second step, under argon and a Dry-ice condenser, the preceding crude spiro-imidazole (72.0g, 0.25mol) in dry THF (400ml, distilled from Na/benzophenone) is stirred until clear, cooled to -78° (Dry-ice/Me_2CO bath), a stream of gaseous NH_3 is passed through until the volume of homogeneous solution increases to 400ml. Lithium metal (6.94g, 1.0mol, *via* a powder funnel, from wire cut with scissors under a gentle stream of argon) is added at such a rate that the temperature is kept below -65°. The mixture is stirred for 30 minutes, absolute EtOH (30ml, 1.0mol) is added carefully, the mixture is stirred further for 20 minutes and NH_4Cl (70g) is added. The cooling bath is removed, the reaction temperature is made to rise to 0°, H_2O (400ml) is carefully added and the liquid phases are allowed to separate. The aqueous phase is extracted with Et_2O (3 x 300ml), the combined organic phases are washed with saturated aqueous NaCl (brine), dried (Na_2SO_4), filtered, evaporated down (to 200ml), and while being kept at 0°, 2 N aqueous HCl (300ml) is added slowly, then the two phases are stirred vigorously for 1 hour at ~25°, H_2O (500ml) is added and the phases are separated. The organic layer is treated with H_2O (150ml) and extracted with CH_2Cl_2 (to remove any cyclohexanone). All the aqueous acidic phases are combined, and carefully (cool if necessary) basified with 2N aqueous NaOH (300ml) and extracted with CH_2Cl_2 (4 x 300ml); the combined extracts are washed with brine, dried (Na_2SO_4), filtered and evaporated *in vacuo* to give crude ±*STEIN* (~40g, ~90%) as a light yellow solid **m 81-82°**. Its ^{1}H NMR (400MHz, $CDCl_3$, TMS) has δ_H at 1.59 (br s, 4H), 4.10 (s, 2H), 7.2-7.3 (m, 10H); and its ^{13}C NMR (100MHz, $CDCl_3$) has δ at 61.9, 126.8, 126.9, 128.2, 143.4.

The *optical resolution* is carried out by adding carefully a hot (70°) homogeneous solution of (L)-(+)-tartaric acid (30.0g, 0.20mol) in EtOH (230ml) to a hot (70°) solution of ±*STEIN* (42.5g, 0.20mol) in EtOH (230ml)

(care exothermic, EtOH may boil) with stirring. The tartrate salts separate immediately and the mixture is cooled to ~25°, the salts are filtered off, washed with EtOH (2 x 60ml), dried *in vacuo*, dissolved in boiling H_2O (230ml), EtOH (230ml) is added and the clear solution is cooled slowly to ~25°. The crystals are collected by filtration, washed with EtOH (40ml), dried *in vacuo*, and recrystallised twice as before [from boiling H_2O (230ml), and EtOH (230ml)] to give the colourless ***(-)-diamine-(+)-tatrate salt*** (~24g, ~66%) with $[\alpha]_D^{23}$ -10.8° (c 1.2, H_2O). To this (-)-(+)-salt suspended in H_2O (300ml) and vigorously stirred at 0-5°, is added dropwise an aqueous solution of 50% NaOH (23ml) followed by CH_2Cl_2 (150ml), and is stirred for 30 minutes; the phases are separated, the aqueous phase is extracted with CH_2Cl_2 (2 x 50ml), the organic layers are combined, washed with brine, dried (Na_2SO_4), filtered and evaporated *in vacuo* to give a colourless solid that is recrystallised from hexane to provide >98% optically pure ***S,S-(-)-diphenylethylenediamine*** as colourless crystals with the properties stated in the title and with NMR spectra same as the racemate.

To obtain the enantiomeric diamine, all the filtrates from above are combined, evaporated to dryness *in vacuo*, the residue is stirred vigorously in H_2O (250ml), treated with aqueous 50% NaOH (25ml) then CH_2Cl_2 (200ml), stirred further for 30 minutes, the phases are separated, the aqueous phase is extracted with CH_2Cl_2 (2 x 50ml), the combined extracts are washed with brine, dried (Na_2SO_4), filtered and evaporated *in vacuo* to give enriched *R,R*-(+)-diamine (~26g) as pale yellow crystals. This is treated with (D)-(-)-tartaric acid as in the above and gives relatively impure ***(+)-diamine-(-)-tartrate salt*** (~31g, ~85%, $[\alpha]_D^{23}$ +4° (c 1.2, H_2O). However, recrystallisation of this salt did not improve its optical purity, but treatment with 50% NaOH and extraction as above etc, and crystallisation from hexane gave optically pure ***R,R-(+)-diphenylethylenediamine*** as colourless crystals with $[\alpha]_D^{23}$ +106° (c 1.1, MeOH), and NMR spectra as obtained with the racemate. The optical purity can be confirmed by the ^{1}H NMR of their (L)-mandelate salts (*cf* Benson et al. *J Org Chem* **53** 5335 *1988*). These diamines were used successfully in highly stereoselective epoxidation [Zhang et al. *J Am Chem Soc* **112** 2801 *1990*], aldol, Diels-Alder [Corey et al. *J Am Chem Soc* **111** 5493 *1989*], allylation [Corey et al. *J Am Chem Soc* **111** 5495 *1989*], osmylation [Corey et al. *J Am Chem Soc* **111** 2943 *1989*] reactions; as well as enantioselective Michael additions [Bruner & Hammer *Angew Chem Inter Ed Eng* **23** *J Am Chem Soc* **111** 5493 *1989*] 312 *1984*] and asymmetric hydrogenation [Fiorini & Giongo *J Mol Cat* **5** 303 *1979*]. [Corey et al. *J Am Chem Soc* **111** 5493 *1989*, Pikul & Corey *Org Synth* **71** 22 *1993* and references herein.]

This diamine has been used successfully as a Trost ligand with $Pd(dba)_2$ to catalyse a Heck reaction, but it is not, albeit, as commonly used as DACH (*trans*-1,2-diaminocyclohexane) ligands.

***R*-(+) and *S*-(-)-2-[2-(Diphenylphosphino)phenyl]-4-isopropyl-2-oxazoline [*R*-(+)- and *S*-(-)-2-[2-(diphenylphosphino)phenyl]-4,5-dihydro-4-isopropyloxazole** *[R- 164858-78-0*; *S- 148461-14-7]* **M 373.4, m 85-89°, $[\alpha]_D^{20}$ *R* +48° and *S* -48° (c 1.4, $CHCl_3$).** The 4*S*-(-)- enantiomer can be obtained by decomposing the 4*S*-(+)-*Zinc II dichloride complex* [crystallises from *tert*-butyl-methyl-ether/$CHCl_3$ as colourless crystals m 221-223°, $[\alpha]_D^{20}$ +53° (c 1.52, $CHCl_3$)] (9.5g, 17.5mmol) in $CHCl_3$ (130ml) under argon with 2,2'-dipyridyl (2.72g, 1.74mmol) at ~25° for 1 hour (stirring), then the mixture is applied directly onto a silica-gel column (6 x 7 cm), eluted with $CHCl_3$ or EtOAc (800ml), and the eluate is evaporated to yield the desired 4*S*-(-)-*oxazoline*(6.78g 95%) as a colourless solid which can be recrystallised from petroleum ether/Et_2O. On TLC (silica gel 60 Merck, 0.25mm F245) it has R_F 0.40 (hexane/EtOAc 6/1); the IR ($CHCl_3$) has ν_{max} at 3070w, 3060m, 3010m, 2965s, 2905m, 2875m, 1950w, 1885w, 1815w, 1650s, 1585w, 1480m, 1470w, 1435s, 1355m, 1310m, 1245m, 1090s, 1050m, 1030m, 965m cm^{-1}; the ^{1}H NMR (300MHz, $CDCl_3$) has δ_H at 0.70 (d, J = 6.8Hz, 3H, CH(CH_3)$_2$), 0.81 (d, J = 6.8Hz, 3H, CH(CH_3)$_2$), 1.43-1.54 (m, 1H, CH(CH$_3$)$_2$), 3.80-3.90 (m, 2H, H_2C(5)), 4.09-4.19 (m, 1H, HC(4), 6.85-6.89 (m, 1H, HC (4')), 7.24-7.37(M, 12 H, arom. H), 7.88-7.92 (m, 1H, HC(6')); the ^{13}C NMR (75MHz, $CDCl_3$) has δ_C at 18.3 (CH(*C*H$_3$)$_2$), 18.9 (CH(*C*H$_3$)$_2$), 32.7 (*C*H(CH$_3$)$_2$), 70.0 (H_2C(5)), 73.1 (HC(4)), 127.8, 128.05, 128.16, 128.26, 128.27 (d, J_{PC} = 15Hz), 129.6 (d, J_{PC} = 3Hz), 130.1, 133.5 (d, J_{PC} = 20Hz), 133.7, 134.1 (d, J_{PC} = 21Hz)(arom CH), 131.7 (d, J_{PC} = 19Hz), 137.9 (d, J_{PC} = 10Hz), 138.1 (d, J_{PC} = 12Hz), 138.8 (d, J_{PC} = 25Hz)(arom. H), 162.7 (d, J_{PC} = 3Hz, C(2); and the ^{31}P NMR (121MHz, $CDCl_3$. triphenyl phosphate external standard at -18ppm) has δ at -5.8.

***S*-(+)-2-[2-(diphenylphosphino)phenyl]-4,5-dihydro-4-phenyloxazole** *[148461-15-6]* **M 407.4, m 89-93°, $[\alpha]_D^{20}$ +29.5° (c 1, $CHCl_3$)** and ***R*-(-)-2-[2-(diphenylphosphino)phenyl]-4,5-dihydro-4-phenyloxazole** *[167171-03-1]* **M 407.4, m 89-93°, $[\alpha]_D^{20}$ -29.5° (c 1, $CHCl_3$)** were prepared as for the 4-isopropyloxazole above and have R_F 0.27 (hexane/EtOAc 5/1). [Koch et al. *Rec Trav Chim Pays Bas* **114** 206 *1995*.]

With an iridium catalyst they promote asymmetric alkylation [Janssen & Helchen *Tetrahedron Lett* **38** 8025

1997], and are chiral ligands for asymmetric reduction reactions [lightfoot et al. *Angew Chem Int Ed Engl* **110** 3047 *1998*]. This ligands, when complexed with $Ni(COD)_2$, promote the regio and stereoselective addition of allylic sulfides to alkynes; a reaction which tolerates a variety of functional groups [Hua et al. *Org Lett* **9** 263 *2007*]. These types of ligands also promote Pd-catalysed allylic substitution reactions [von Matt & Pflatz *Angew Chem* **105** 614 *1993*, Williams et al. *Tetrahedron Lett* **34** 3149 *1993*].

Diphenylphosphine *[829-85-6]* **M 186.2, b 100-102º/1.5mm, 150-151º/12mm, 156-157º/16mm, 165º/25mm, 280º/atm, d ^{25} 1.07, n $^{20}_{D}$ 1.6269, pK 0.03.** This toxic and flammable phosphine is prepared under N_2 by adding dropwise a solution of chlorodiphenylphosphine (50g, [1079-66-9]) in dry Et_2O (75ml) to a solution/suspension of LiAlH (2.6g) in absolute Et_2O (75ml), then boiling the mixture under reflux for 1 hour, adding H_2O (6ml, carefully and with cooling) and stirring for 2-3 hours. The Et_2O layer is collected, dried ($CaCl_2$), decanted, evaporated and the residue is distilled *in vacuo* to give the phosphine (70%) as a colourless oil [Kucken & Buchwald *Chem Ber* **91** 2871 *1958*]. *Alternatively*, Ph_2ClP is reacted with Na in dry *n*-Bu_2O under N_2 to give Ph_2PNa which is treated with EtOH, boiled under reflux for 30 minutes, poured into H_2O, extracted with Et_2O which is separated, dried ($CaCl_2$), decanted, evaporated and the residue is distilled *in vacuo* to give the phosphine (72%) [Kucken & Buchwald *Chem Ber* **92** 227 *1959*]. [*Beilstein* **16** H 758, **16** II 371, **16** III 833, **16** IV 950.]

2-(Diphenylphosphino)benzoic acid [(2-carboxyphenyl)diphenylphosphine) *[17261-28-8]* **M 306.3, m 174-177º, 175-176º (187-188º), pK_{Est} ~2.7.** The benzoic acid is prepared by first adding Na (15.3g, 667mmol, cut in ~1g pieces) carefully to liquid NH_3 (1.5L) with stirring until a blue colour is persistent (**use an efficient fume cupboard**), then adding PPh_3 (87.4g, 330mmol) in small portions during 30-40 minutes with swirling to dissolve any Na on the sides of the flask. After 2.5 hours the red-orange colour of the solution of $NaPPh_2$ is treated with 2-chlorobenzoic acid (52.2g, 330mmol) in small portions over 30-40 minutes followed by anhydrous THF (500ml, using a syringe), and the resulting solution is allowed to warm to room temperature overnight under a blanket of argon. As the solution warms, the colour of the red solid turns to gold with mild evolution of heat results. The residue is dissolved in H_2O (1.4L) and extracted with Et_2O (400ml) which is discarded. The aqueous layer is acidified to pH 2 with concentrated HCl (~60ml), and extracted with CH_2Cl_2 (3 x 200ml), the extract is washed with H_2O (500ml), evaporated to *ca* 125ml, and MeOH (~50ml) is added to precipitate the pale-yellow crystalline acid (requiring inducement sometimes) which is collected and dried to give the phosphino-acid (50g, 49%) which provides analytically pure acid (C, H and P) on recrystallisation from a minimum amount of boiling MeOH. The air stable compound forms yellow needles from aqueous EtOH, is soluble in halogenated solvents and Et_2O, but is less soluble in other solvents. Its IR (Nujol) has ν_{max} at 3200 (OH), 1690 (CO), 1275 cm^{-1}. The *methiodide* crystallises from Me_2CO/*C_6H_6 with **m 169-173º(dec)**, and the *phosphine oxide* [2572-40-9] M 322.3 has **m 262-264º** (**252-254º** and **274-275º** are also reported), **pKa 5.06** and **5.37** (in 50% aqueous EtOH) and crystallises from EtOH, aqueous EtOH or aqueous AcOH. With diazomethane, *methyl 2-(diphenylphosphino)benzoate* is obtained in 85% yield; it forms colourless crystals from MeOH with **m 96-97º**, its IR (Nujol) has ν_{max} at 1712 (C=O) cm^{-1}, and the ^{1}H NMR (90MHz, $CDCl_3$) has δ_H at 7.6-6.9 (m, 14H), 3.70 (s, 3H), and the ^{31}P NMR (40.5MHz, $CDCl_3$) has δ at 5.10 upfield of 85% H_3PO_4. [Rauchfuss et al. *J Am Chem Soc* **103** 6769 *1981*, Hoots et al. *Inorg Chem* **21** 178 *1982*.] It is used for preparing the DACH-Trost phenyl ligand above.

S*-(-)-2-Ferrocenyl-4-(1-methylethyl)oxazoline [*S*-(-)-4-isopropyloxazo-2-yl ferrocene]** *[162157-03-1]* **M 297.0, m 71.5-72.5º (m 61-62º), [α] $^{22}_{D}$ -129º (c 1.5, EtOH), CD ($CHCl_3$) λ_{max} (Δε) 464 (-080), 358 (+1.0)nm.** This complex is prepared in three steps from ferrocenecarboxylic acid (1.33g, 4.49mmol, 1271-42-7), ***firstly by converting it into the acid chloride with oxalyl chloride (0.79g, 9mmol) in CH_2Cl_2 (15ml) under N_2 at ~25º until gas evolution ceased (~10 minutes), stirring for 10 minutes further, and the solution is evaporated to dryness *in vacuo*. ***Secondly*** the crude dark red oily acid chloride (that solidified on standing) is dissolved in CH_2Cl_2 (10ml) and added (syringe) to a solution of *S*-(+)-valinol (0.554g, 5.37mmol) and Et_3N (1.25ml, 9mmol) in CH_2Cl_2 (7ml) under N_2 at ~25º. After standing overnight, the mixture is washed with H_2O (2 x 20ml), dried (Na_2SO_4), filtered, and evaporated to dryness *in vacuo*. The residue is purified by column chromatography on SiO_2 (40-83mm), eluting with 3% MeOH/CH_2Cl_2, to give analytically pure **2*S*-*N*-(1-hydroxy-3-methylbutyl)-ferrocenamide** (1.184g, 84%) with **m 109-110º, [α] $^{21}_{D}$ -8º (c 1.34, EtOH)**. It has IR (nujol) with ν_{max} at 3284 (N-H), 3192 (O-H), 1611 (C=O amide I), 1551 (amide II) cm^{-1}; the ^{1}H NMR (360MHz, $CDCl_3$) has δ_H at 0.97

(d, 3H, *J* = 6.8Hz, -C*H*$_3$), 0.98 (d, 3H, *J* = 6.8Hz, -C*H*$_3$), 1.93 (octet, 1H, *J* = 6.8Hz, -C*H*(CH$_3$)$_2$), 2.71 (brt, 1H, -O*H*), 3.56-3.83 (m, 3H, -C*H*$_2$OH and –NHC*H*-), 4.16 (s, 5H, C$_5$*H*$_5$), 4.30 (brs, 2H, Fc), 4.60 (brs, 1H, Fc), 4.62 (brs, 1H, Fc), 5.80 (brd, 1H, -NH-); the ^{13}C NMR (90MHz, $CDCl_3$) has $\delta_C\{^1H\}$ at 19.04 (-C*H*$_3$), 19.69 (-C*H*$_3$), 28.99 (-*C*H(CH$_3$)$_2$), 57.01 (-NH*C*H-), 63.87 (-O*C*H$_2$-), 67.91 (Fc), 68.42 (Fc), 69.75 (*C*$_5$H$_5$), 70.46 (Fc), 70.51 (Fc), 75.95 (Fc –*ipso*), 171.37 (*C*=O); and the MS (EI) has *m/z* 315 (M$^+$, 100%), 213 (81%). ***Thirdly***, to a light orange solution of the preceding *S-(-)-amide* (0.817g, 2.59mmol) and Ph_3P (2.49g, 9.5mmol) in dry MeCN (60ml) is added Et_3N (1.6ml, 11.5mmol) followed by CCl_4 (2.2ml, 22.8mmol), and the mixture is stirred at ~25^o overnight. Water (80ml) is added to the mixture which is extracted with petroleum ether (5 x 50ml), the combined organic layers are dried ($MgSO_4$), filtered, and evaporated to dryness *in vacuo*. The residue is contaminated with Ph_3PO, and is purified through column chromatography (SiO_2, 40-83mm) and eluting with 30% EtOAc/petroleum ether (b 40-60^o) to give analytically pure ferrocenyl oxazoline as dark yellow crystals (0.685g, 89%) with **m 71.5-72.5^o**. *Note that much lower yields of product are obtained if the solvent is removed from the reaction mixture before work-up*. It has IR (nujol) with ν_{max} at 1657 (C=N) cm^{-1}; the ^{1}H NMR (360MHz, $CDCl_3$) has δ_H at 0.87 (d, 3H, *J* = 6.8Hz, -C*H*$_3$), 0.94 (d, 3H, *J* = 6.8Hz, -C*H*$_3$), 1.78 (hextet, 1H, *J* = 6.6Hz, -C*H*(CH$_3$)$_2$), 3.41 (q, 1H, *J* = 7.0Hz, –NHC*H*-), 3.89-3.95 (m, 1H, -OC*H*H-), 4.00 (t, 1H, *J* = 7.7Hz, -OCH*H*-), 4.06 (s, 5H, C$_5$*H*$_5$), 4.26 (brs, 2H, Fc), 4.66 (brs, 1H, Fc), 4.70 (brs, 1H, Fc); the ^{13}C NMR (90MHz, $CDCl_3$) has $\delta_C\{^1H\}$ at 17.79 (-C*H*$_3$), 18.81(-C*H*$_3$), 32.27 (-*C*H(C*H*$_3$)$_2$), 68.92, 68.95, 69.27, 69.51 (*C*$_5$H$_5$), 70.06, 70.09, 70.60 (Fc –*ipso*), 72.27, 165.56 (*C*=N); and the MS (EI) has *m/z* 297 (M$^+$, 100%), 254 (64%), 211 (47%), 121 (92%). [Richards & Mulvaney *Tetrahedron Asymm* **7** 1419 *1996*.] The *R*-enantiomer is prepared in the same way by using *R*-(+)-valinol. Similarly prepared while using the respective chiral *S*-2-aminoethanols were *S*-(-)-*4-methyloxazol-2-yl ferrocene* [red solid, 96% yield, **m 84-85^o**, **$[\alpha]_D^{27}$ -60^o [c 0.2, EtOH), CD ($CHCl_3$) λ_{max} ($\Delta\varepsilon$) 461 (+0.34), 336 (-0.25)nm**], *S*-(-)-*4-ethyloxazol-2-yl ferrocene* [orange solid, 34% yield, **m 47-48^o**], *S*-(-)-*4-tert-butyloxazol-2-yl ferrocene* [orange-red solid, 34% yield, **m 127-128^o**, **$[\alpha]_D^{24}$ -150^o (c 2.1, CH_2Cl_2)**], and *among others where the 4-alkyl group is replaced by isobutyl, sec-butyl, benzyl, phenyl, 4,5-diphenyl, 1-hydroxy-1-methylethyl, 1-methoxy-1-methylethyl, 1-hydroxy-1-ethylpropyl, 1-methoxy-1-ethylpropyl, hydroxymethyl, methoxymethyl, and several more* [Sammakia et al. *J Org Chem* **60** 10 *1995*, Nishibayashi et al. *J Organomet Chem* **545-546** 381 *1997*, Richards & Mulvaney *Tetrahedron Asymm* **7** 1419 *1996*.] An independent synthesis of the title compound from *S*-(-)-valinol, $ZnCl_2$, cyanoferrocene in refluxing chlorobenzene under N_2 for 72 hours followed by column chromatography (SiO_2, eluting with hexane/EtOAc) gave a red solid (40% yield based on cyanoferrocene) **m 61-62^o** [note difference in m.p.] but with similar ^{1}H and ^{13}C NMR. Other chiral derivatives, some mentioned above, were also obtained in this way. [Nishibayashi et al. *J Organomet Chem* **545-546** 381 *1997*.]

Iridium(III) acetylacetonate [tris(pentane-2,4-dionato)iridium, Ir(acac)$_3$] *[15635-87-7]* **M 489.5, m 269-271^o.** Iridium sulfate solution is made from freshly precipitated iridium dioxide (from 1.0g of potassium hexachloridate) by heating it with 1*N* H_2SO_4 (25ml) until the acid begins to fume. The solution is diluted to its original volume, and undissolved iridium oxide is removed by centrifugation. The light green solution is treated with 10% aqueous NaOH until the green iridium III hydroxide precipitate just begins to redissolve. This precipitation should be rapid in order to avoid oxidation; the pH of the solution is adjusted to 6, and the mixture is heated at 60^o with acetylacetone (2ml) for one hour. The solution becames red and deposits a yellow crystalline precipitate. This iridium complex is collected and crystallises from aqueous MeOH in rhombic plates (0.1g, 10%, m 269^o). It is insoluble in H_2O, sightly soluble in EtOH and petroleum ether, but freely soluble in *C_6H_6 and $CHCl_3$. It is stable in boiling dilute acids and 10% aqueous NaOH. It sublimes at 260^o/1mm, but decomposes above 290^o depositing an iridium mirror. Molecular weight determination (~400, by Rast in camphor) indicates that it is monomeric. [Dwyer & Sargeson *J Am Chem Soc* **75** 984 *1953*, *Beilstein* **1** IV 3678.] It is a useful precursor for making Iridium complexes.

3,4-O-isopropylidene-(3*S*,4*S*)-dihydroxy-(2*R*,5*R*)-bis(diphenylphosphino)hexane (*RSSR*-dimeDIOP, or *R*,S,S,*R*-DIOP*, DIOP starred, in dedication to Professor Kagan**)** *[258873-45-9]* **M 526.2, low melting oil, $[\alpha]_D^{24}$ (+) 41.8^o (c 0.88, $PhCH_3$), pK_{Est} ~0.0.** The starting material for this ligand is the readily available D-mannitol that is converted to the isopropyledine diepoxide, which in turn is converted to 3,4-*O*-isopropylidene-(3*S*,4*S*)-dihydroxy-(2*S*,5*S*)-hexane. The latter (2.2g, 11.6mmol), and Et_2NH (4.9ml, 34.8mmol) in CH_2Cl_2 (30ml) is added dropwise to a solution of $MeSO_2Cl$ (2.0ml, 25.8mmol) in CH_2Cl_2 (10ml) at 0^o, kept at 0^o for 30 minutes, stirred at ~25^o for 30 minutes, and treated with saturated aqueous NH_4Cl. The layers are separated, the

aqueous phase is extracted with CH_2Cl_2, the combined organic phases are dried (Na_2SO_4), evaporated and the residue is purified by flash chromatography on silica gel, eluting with CH_2Cl_2/Et_2O (9/1) to give ***3,4-O-isopropylidene-(3S,4S)-bis(mesyloxy)-(2S,5S)-hexane*** (3.85g, 96%) as a colourless oil. This is a useful intermediate for making a variety of phosphine ligands and has **$[\alpha]_D^{24}$ (-) 1.3° (c 1.04, $CHCl_3$)**; its ^1H NMR (360MHz, $CDCl_3$) has δ at 4.82-4.76 (m, 2H), 3.99-3.96 (m, 2H), 3.03 (s, 6H), 1.45 (d, *J* = 6.6, 6.0Hz), 1.37 (s, 6H); and the ^{13}C NMR (90MHz, $CDCl_3$) has δ at 110.14, 78.19, 76.26, 38.53, 26.75, 17.63; and HRMS has found *m/z* 347.0834, calcd for $C_{11}H_{23}O_8S_2$ (MH^+) is 347.0834. The preceding dimesylate (1.04g, 3.0mmol) in THF (20ml) is added to the orange solution at -78° of Ph_2PLi [prepared under N_2, from Ph_2PH (1.15ml, 6.6mmol) in THF (50ml) to which is added *via* a syringe *n*-BuLi in hexane (4.0ml, 6.4mmol) at -78° during 5 minutes, warmed to ~25° while stirring for 1 hour, and cooling to -78° again] during 20 minutes. The orange solution is warmed to ~25°, stirred overnight, the resulting white suspension is hydrolysed with saturated aqueous NH_4Cl, the aqueous layer is extracted with CH_2Cl_2, the combined organic layers are dried (Na_2SO_2), filtered, evaporated and the residue is purified by flash chromatography on silica gel, eluting with hexane/Et_2OAc (95/5), or hexane/Et_2O (95/5) to give (+)-*RSSR*-DIOP* (1.06g, 67%) as a colourless oil or low melting white solid respectively. Its ^1H NMR (360MHz, $CDCl_3$) has δ at 7.56-7.52 (m, 8H), 7.38-7.33 (m, 12H), 3.78-3.76 (m, 2H), 2.50-2.46 (m, 2H), 1.14 (s, 6H), 0.91 (d, *J* = 7.0Hz, 3H), 0.87 (d, *J* = 6.9Hz, 3H); the ^{13}C NMR (90MHz, CD_2Cl_2) has δ at 137.46 (d, *J* = 15.9Hz), 137.03 (d, *J* = 15.5Hz), 134.14 (d, *J* = 3.7Hz), 133.91 (d, *J* = 4.0Hz), 129.30 (d, *J* = 8.6Hz), 128.75 (d, *J* = 7.1Hz), 108.27 (dd, *J* = 12.0, 6.8Hz), 31.33 (d, *J* = 14.3Hz), 27.05, 10.74 (d, *J* = 17.6Hz); the ^{31}P NMR ($CDCl_3$) has δ at -6.3 (-5.42); and the HRMS has found *m/z* 527.2771, calculated for $C_{33}H_{37}O_2P_2$ (MH^+) is 527.2269. [Li & Zhang *J Org Chem* **65** 5871 *2000*, Yan & RajanBabu *Org Lett* **26** 4137 *2000*.]

Lithium tetrachloropalladate(II) hydrate (Li_2PdCl_4 xH_2O) *[123334-21-4]* **M 262.1 (anhydrous).** It is commercially available as a powder or in chunks. A 0.5M solution of water-free Li_2PdCl_4 in dry MeOH for the preparation of Pd catalysts (e.g. see *Oxime Palladacycles* above) is made by stirring anhydrous LiCl (42.4g, 1 mole, dried at 130° to constant weight, several hours, see [7447-41-8]) and anhydrous $PdCl_2$ (88.6g, 0.5 mole, see [7647-10-1]) in dry MeOH (1L) until the solution is homogeneous. Store the solution under N_2 or argon. [Onue, Minami and Nakagawa *Bull Chem Soc Jpn* **43** 3480 *1970*.]

η^5-(*S*)-(*pR*)-2-(2′-(4′-Methylethyl)-oxazolinyl)cyclopentadienyl,1-*C*-3′-*N*)(η^4-tetraphenylcyclobutadiene) cobalt *[222400-02-4]* **M 591.6, m 160-162°, $[\alpha]_D^{24}$ -55.2° (c 0.09, $CHCl_3$).** This cobalt complex is the key intermediate for the preparation of all the **c**obalt **o**xazoline **p**alladacycle (COP) catalysts described in Part 1. Although originally prepared in four distinct steps [Stevens & Richards *Organometallics* **18** 1346 *1999*], the synthesis has been slightly modified and can be completed in two steps without purifying intermediates. ***Firstly,*** *η^5-(carbomethoxycyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt* [*182627-81-2*] is prepared (using Schlenk equipment flushed with argon) in a triple-necked flask with two rubber septa containing sodium cyclopentadienide (20ml, 2.0M in THF, 40mmol, [4984-82-1], should be light red/orange in colour; discard if black or contains solid residues), anhydrous THF (20ml *via* a syringe, pre-filtered through activated Al_2O_3), then dimethyl carbonate (10.2ml, 120mmol, *via* a syringe), and the mixture is stirred and boiled under reflux for 4 hours before cooling to ~25°. [The intermediate can be isolated but this is not necessary.] To the cooled mixture is added dry toluene (160ml, *via* a syringe), followed by chlorotris(triphenylphosphine)cobalt(I) (30.8g, 34.8mmol, see above [26305-75-9], preferably freshly prepared for higher yields) and diphenylacetylene (14.2g, 80mmol, recrystallised from EtOH), and heated at reflux for 5 hours, cooled to ~25° before transferring to a single-necked flask and evaporating to dryness *in vacuo*. The residue is suspended in hexanes (150ml), the solid is filtered off, washed with hexanes (~3.5L) until the filtrate is colourless. The dark mustard-coloured solid is dissolved from the filter by washing with CH_2Cl_2 until the filtrate is colourless (discard any insoluble black solid) and evaporate the combined filtrates *in vacuo* to give the *Cobalt-ester* (12.7g, 67%) as a mustard-coloured solid. It can be purified by column chromatography on Matrix silica 60 (35-70μm, eluting with 20% EtOAc/petroleum ether b 40-60°) to give the *Cobalt-ester* as an orange crystalline solid **m 240-244°** [lit **m 246-248°** Mabrouk & Rauch *J Organomet Chem* **523** 111 *1996*]. It has IR (thin film) with ν_{max} at 3058, 2953, 1713, 1596, 1498, 1467, 1281, 1140 cm^{-1}; the ^1H NMR (500MHz, $CDCl_3$) has δ_H at 3.23 (s, 3H), 4.79 (t, *J* = 2.0Hz, 2H), 5.21 (t, *J* = 2.0Hz, 2H), 7.22-7.30 (m, 12H), 7.43-7.45 (m, 8H); and the ^{13}C NMR (125MHz, $CDCl_3$) has δ_C at 51.4, 76.5, 84.7, 86.6, 86.8, 126.9, 128.2, 129.0, 135.3, 166.6. [Anderson, Overman, Richards, Watson and

White *Org Synth* **84** 139 *2007*.]

Secondly, η^5-(*S*)-(*pR*)-2-(2′-(4′-methylethyl)oxazolinyl)cyclopentadienyl,1-*C*-3′-*N*)(η^4-tetraphenylcyclobutadiene)cobalt is prepared by stirring under argon the above crude *Cobalt-ester* (10g, 18.6mmol), lithium iodide (4.96g, 37.2mmol, see [10377-51-2]) and 2,4,6-collidine (100ml, b **175-178°**/atm, see [108-75-8]), then boiling under reflux (air condenser) for ~16 hours until the *Cobalt-ester* (R_F 0.8, silica plate eluted with 20% EtOAc:hexanes) has completely reacted. The solution is cooled to ~25°, diluted with CH_2Cl_2, washed with 2N aqueous HCl (4 x 150ml), dried (Na_2SO_4), filtered and evaporated *in vacuo* to give the solid orange coloured *Cobalt-acid* [^{1}H NMR (500MHz, $CDCl_3$) at δ_H: 4.84 (2d, *J* = 2.0Hz, 2H), 5.23 (2d, *J* = 2.0Hz, 2H), 7.20-7.24 (m, 12H), 7.42-7.44 (m, 8H)] which is used further. Under argon, with stirring, the preceding *cobalt-acid* in CH_2Cl_2 (124ml, pre-filtered through activated Al_2O_3), oxalyl chloride (3.25ml, 37.2mmol) followed by anhydrous DMF (3 drops sequentially, as evolution of gas occurs) are kept at ~25° for 30 minutes, evaporated *in vacuo*, CH_2Cl_2 (100ml) is added to dissolve the residue, evaporate again *in vacuo* and the process is repeated three times to give dry *Cobalt-acid chloride* as a red-brown residue. A Schlenk flask with a rubber septum, flushed with argon *via* inlet and outlet needles, is loaded with *S*-valinol hydrochloride (3.6g, 26mmol, prepared from the free base, see [2026-48-4], by treating with 2N HCl in Et_2O), then dry Et_3N (15.5ml, 112mmol) and CH_2Cl_2 (86ml) are added *via* the septum, followed, *via* a cannula, a solution of the preceding crude *Cobalt-acid chloride* in CH_2Cl_2 (100ml). The mixture is stirred at ~25° for 2 hours and cooled to 0° in an ice-bath. $MeSO_2Cl$ (3.6ml, 47mmol, [124-63-0]) is then added to the mixture in one portion *via* a syringe and allowed to warm to ~25°. After 16 hours the mixture is washed with saturated aqueous $NaHCO_3$ (150ml), brine (150ml), the organic layer is dried (Na_2SO_4), filtered, and concentrated *in vacuo*. The residue is purified by dissolving it in the minimum volume of CH_2Cl_2 (~50ml), adding it to a silica gel column and eluting with hexanes/EtOAc (9:1) to give *η⁵-(S)-(pR)-2-(2'-(4'-methylethyl)-oxazolinyl)cyclopentadienyl,1-C-3'-N)(η⁴-tetraphenylcyclobutadiene)cobalt* (8.2g, 75%) as a yellow solid, which can be recrystallised to analytical purity from 10% EtOAc/petroleum ether to m 160-162°. It has IR (thin film) with ν_{max} at 3058, 2958, 1652 (C=N), 1597, 1499, 1373, 1113, 1024 cm^{-1}; the ^{1}H NMR (400MHz, $CDCl_3$) has δ_H at 0.77 (d, *J* = 6.7Hz, 6H, C*H*$_3$), 0.97 (d, *J* = 6.7Hz, 3H, C*H*$_3$), 1.40 (oct, *J* = 6.7Hz, 1H, C*H*$(CH_3)_2$), 3.41-3.56 (m, 3H, -C*H*-C*H*$_2$-), 4.62 (brs, 1H, Cp*H*), 4.80 (brs, 1H, Cp*H*), 5.09 (brs, 1H, Cp*H*), 5.20 (brs, 1H, Cp*H*), 7.17-7.27 (m, 12H, *m*+*p*-Ph*H*), 7.44-7.47 (m, 8H, *o*-Ph*H*); and the ^{13}C NMR (100MHz, $CDCl_3$) has $\delta_C\{^1H\}$ at 20.4 (*C*H$_3$), 26.1 (*C*H$_3$), 35.0 (*C*H$(CH_3)_2$), 71.5 (-*C*H-CH$_2$-), 74.7 (-CH-*C*H$_2$-), 78.9 (C_4Ph$_4$), 84.1 (*ipso*-Cp*C*), 86.4 (Cp*C*), 87.0 (Cp*C*), 87.1 Cp*C*), 88.4 Cp*C*), 126.8 (*p*-Ph*C*), 128.3 (Ph*C*), 129.3 (Ph*C*), 135.8 (*ipso*-Ph*C*), 162.6 (*C*=N); and MS(EI) at *m/z* 591 (M^+, 100), 415 (82), 356 (8), 178 (60). The ***R-enantiomer*** is prepared in precisely the same way except that *R*-valinol hydrochloride is used, and it differs only in having optical rotation of opposite sign. [Stevens & Richards *Organometallics* **18** 1346 *1999*, Anderson, Overman, Richards, Watson and White *Org Synth* **84** 139 *2007*.]

***N*-Methyliminodiacetic acid (MIDA)** *[4408-64-4]* **M 147.1, m 220° (dec), 223-225° (dec), 226° (dec), pKa** (thermodynamic) **acidic: 2.138 (0°), 2.142 (10°), 2.146 (20°), 2.150 (30°), 2.154 (50°); basic: 10.474 (0°), 10.287 (10°), 10.088 (20°), 9.920 (30°), 9.730 (40°).** It has been prepared from $MeNH_2$ and formaldehyde cyanohydrin followed by hydrolysis of the dinitrile formed [Eschweiler *Justus Liebigs Ann Chem* **279** 29 *1894*] and in 63-71% yield from chloroacetic acid and $MeNH_2$ [Berchet *Org Synth Coll Vol* **II** 397 *1943*]. However, a more convenient preparation is from iminodiacetic acid [142-73-4] (13.3g), formic acid (4.6g), aqueous formaldehyde (10ml, 36%) and H_2O (5ml) at 100° until evolution of CO_2 ceases, and after 2 hours the mixture is refluxed for 10 minutes, diluted with excess EtOH, cooled and the precipitated acid is filtered off. Recrystallisation from aqueous EtOH (charcoal) provides pure colourless *MIDA* (14.7g, 90%). [Childs et al. *J Chem Soc* 2174 *1948*]. It has been purified *via* the Ba salt [Berchet *Org Synth Coll Vol* **II** 397 *1943*] and the stability constants of the complexes with Cu^{2+}, Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, and Ni^{2+} have been determined [Scwarzenbach et al. *Helv Chim Acta* **38** 1147 *1955*]. The *diethyl ester* has **b 92-94°/0.04mm** [Viscontini et al. *Helv Chim Acta* **35** 451 *1952*], and the *monoamide* has **m 168°** after crystallisation (needles) from aqueous EtOH [Eschweiler *Justus Liebigs Ann Chem* **279** 29 *1894*]. MIDA (**m 215-216° dec)** has been prepared on a ~100g scale by the method described by Childs et al. (above) with slight modification in 88% yield, and had IR (thin film) with ν_{max} at 2998, 2955, 1682 (C=N), 1477, 1380, 1328, 1223, 1172, 1126, 1065, 1018, 982, 958, 903, 886, 723 cm^{-1}; the ^{1}H NMR (400MHz, D_2O) has δ_H at 2.98 (s, 3H), 3.96 (s, 4H); the ^{13}C NMR (100MHz, 95:5 DMSO-d_6: D_2O, TMS) has δ_C at 170.0, 56.7, 41.7; the LRMS (ESI+) has *m/z* (relative intensity) 219.1 (24%), 148.1 (M^+, 100%), 102.1 (8%); and the HRMS (ESI+) for $C_5H_{10}NO_4$ [$M+H^+$] has calculated 148.0604, and found 148.0603. [Ballmer, Gillis and Burke *Org Synth* **86** 344 *2008*]. [*Beilstein* **4** H

367, **4** II 800, **4** III 1177, **4** IV 2428].

MIDA boronic esters: MIDA is a very useful protecting group for boronic acids and forms stable (more stable that the free acid) *boronates* which are readily prepared from the boronic acid, MIDA in toluene-DMSO (2.5:1) under reflux using Dean-Stark conditions to eliminate H_2O requiring ~3 hours. When these boronic acid surrogates are suitably substituted on boron they can be made to undergo Suzuki-Miyaura, Stille, Heck, Sonogashira and Negishi coupling, as well as Miyaura borylations. The boronates are easy to handle, stable in air, stable under cross-coupling conditions, surviving temperatures of up to 80°, and acidic reagents like trifluoromethanesulfonic, acetic acid and oxidizing agents such as Jones reagent. The MIDA group can be easily hydrolysed by mild aqueous base (see below) thus also allowing the use of controlled iterative cross-coupling (ICC) of protected haloboronic acids. [Gillis & Burke *Aldrichimica Acta* **42** 17 *2009*]. A variety of MIDA boronate synthons are available commercially.
Hydrolysis of 4-(*p*-tolyl)phenylboronic acid MIDA ester (m 214-216°) to the boronic acid is given here as a typical example for the hydrolysis procedure. The MIDA ester (10.1g, 31.3mmol, 1 equivalent) in THF (220ml), and aqueous 1M NaOH (93.5ml, 93.5mmol, 2.99 equivalents) gives a biphasic mixture with a clear colourless lower layer and a milky white upper layer. The container is capped, and the mixture is stirred vigorously at ~25° for 10 minutes whereby the lower colourless layer becomes clear and the upper layer becomes clear yellow. A saturated aqueous solution of NH_4Cl (250ml) is added (to act as acidifier) and the mixture is stirred vigorously for 5 minutes, shaken with Et_2O (4 x 50ml), and the aqueous layer is extracted with freshly prepared THF/Et_2O (1:1, 400ml). The combined organic layers are dried (MgSO), filtered through Celite, and concentrated by rotary evaporation in a vacuum (40°/20mm), and residual solvent is removed by three azeotropic cycles with MeCN (3 x 50ml) in a rotary evaporator (40°/20mm), and then at higher vacuum (25°/1mm) for 12 hours to give the boronic acid as a fine off-white powder (6.24g, 94% yield, **m 136-138° dec**) with the expected IR, NMR and Mass spectra which indicate ~92% purity. [Ballmer, Gillis and Burke *Org Synth* **86** 344 *2008*].

MIDA-disodium salt is prepared from MIDA (147g, 1 mol), which is dissolved (caution: exothermic) in NaOH (120g, 3 mol) in H_2O (300ml) to give a clear light yellow solution that is evaporated *in vacuo*. The residue is treated with MeOH (300ml), heated to reflux, filtered through a glass frit, heated to reflux and filtered again, and the process repeated once more. The filtrate is co-evaporated with MeCN (3 x) and lyophilised to give analytically pure **diNa salt** (173g, 91%) as a white powder with ^{1}H NMR (300MHz, CD_3OD, TMS) δ_H at 2.95 (s, 4H), 2.24 (s, 3H); and ^{13}C NMR (125MHz, CD_3OD, TMS) δ_C at 179.2, 63.7, 43.9. It is used for preparing MIDA-boronate esters [Uno et al. *Tetrahedron* **65** 3130 *2009*, cf also Coombs & Margerum *Inorg Chem* **9** 1711 *1970*, Davis & Richardson *Inorg Chem* **23** 184 *1984*, Stringfield & Shepherd *Inorg Chim Acta* **309** 28 *2000*].

Norbornadiene (NBD, bicycle[2.2.1]hepta-2,5-diene) *[121-46-0]* **M 92.1, m -19.1°, b 89.5-90°/atm, 90.3°/atm, d_4^{20} 0.9064, n_D^{25} 1.4684.** NBD is a versatile diene that coordinates with metals, helps in solubilising them in organic solvents, and is used for making a variety of pre-catalysts (see further in this chapter under "Homogeneous Catalysts" Part 1). It is prepared by a general method whereby *cis*- or *trans*- *1,2-bis(phenylsulfonyl)ethylene* (0.22g, 0.714mmol; *trans* [963-16-6] M 308.4, m 221-223°, 226.5-227°, 229.5° from EtOH or AcOH; *cis-isomer* has m 89.5-90°, 101-101.5°, from EtOH, *Beilstein* **6** IV 1500, Truce & McManimie *J Am Chem Soc* **75** 1672 *1953*) and freshly distilled cyclopentadiene (1.6g, 2.42mmol) in toluene (5ml) are heated at 130° for 24 hours, evaporated to dryness *in vacuo*, and the residue is recrystallised from *C_6H_6-EtOH (1:1) to give the Diels-Alder adduct *3,6-methano-4,5-bis(phenylsulfonyl)cyclohex-1,2-ene*, m 257-258°, in good yield. Lower yields are obtained in *C_6H_6 (~25°/40 hours). Elimination of the β-disulfone groups is achieved by stirring a mixture of the *bis(diphenylsulfonyl)* compound (2.5mmol) and $NaH_2PO_4.2\ H_2O$ (5g) in MeOH (~40ml) at room temperature overnight with freshly prepared sodium amalgam (from *ca* 0.4g, 17mmol of Na, [11110-52-4]). The mixture is extracted with pentane (b 36°/atm) and the extract is fractionated at atmospheric pressure to give NBD in 65% yield. Store and stabilise with 0.50.25% of BHT under N_2. [De Lucchi & Modena *JCS Chem Commun* 914 *1982*, cf Parham & Heberling *J Am Chem Soc* **77** 1175 *1955*.] Industrially it is prepared from cyclopentadiene and acetylene at 340°/6atm [Shell Devel. Co., USP 2 875256 *1953*].
NBD has UV with λ_{max} (logε) at 198.5 (3.78), 202infl (3.41), 213infl (3.24). 219infl (3.01), 227infl (2.41)nm (in EtOH), and 194.5 (3.53)nm (in cyclohexane) [Stich, Rotzler & Reichstein *Helv Chim Acta* **42** 1480 *1959*]; its IR (thin film) with ν_{max} of the more intense bands at 2987, 1543, 1311, 1228, 875, 799, 727, 502 cm^{-1}, and in CS_2

and CCl_4 it has ν_{max} at 3080(s), 2960 (vs), 2880 (s), 1646 (m), 1452 (ms), 1335 (ms), 1310 (vs), 1271 (m), 1229 (s), 1206 (s), 1150 (s), 1105 (ms), 1063 (m), 1016 (m), 935 (s), 911 (s), 885 (sh), 870 (vs), 795 (sh), 715 (vs), 650 (s) cm^{-1} [Abel, Bennett and Wilkinson *J Chem Soc* 3178 *1959*]; the ^1H NMR (60MHz, $CDCl_3$) has δ_H at 1.99 (s, 2H, CH_2). 3.56 (s, 2H, bridgehead H), 6.74 (s, 4H, olefin H) from TMS, and the ^{13}C NMR (15MHz, $CDCl_3$, TMS) has δ_C at 143.3, 75.3, 50.2. The photoelectron spectrum shows intense bands at 8.69, 9.55, 11.26, 12.51—12.75, 14.24 and weak bands at 15.66—17.16 eV; and the interaction between the two non-conjugated π-bonds has been shown to be 0.85eV [Bischof et al. *Helv Chim, Acta* **52** 1745 *1969*].

NBD-silver nitrate complex is formed by shaking for 5 minutes a mixture of $AgNO_3$ (1.36g) in H_2O (10ml) and NBD (3ml). The white complex is collected and recrystallised from EtOH to give pure **NBD-$(AgNO_3)_2$** (0.95g) which decomposes in air, in H_2O, and on heating to give a strong odour of NBD. Store it cold and under N_2. It is soluble in warm MeOH, EtOH, CCl_4, $CHCl_3$, and $*C_6H_6$, but insoluble in Me_2CO, Et_2O and light petroleum. Its IR (Nujol and hexachlorobutadiene mulls) has ν_{max} at 3020 (w), 2960 (w), 2885 (w), 1470 (m), 1385 (v, brs), 1325 (s), 1310 (s), 1243 (m), 1189 (m), 1046 (m), 1014 (w), 969 (m), 950 (vw), 929 (m), 890 (w), 877 (w), 808 (m), 795 (w), 790 (w), 725 (ms) cm^{-1} [Abel, Bennett and Wilkinson *J Chem Soc* 3178 *1959*.]

Similarly the **NBD-cuprous bromide** complex is formed by shaking for 5 minutes a mixture of anhydrous CuBr (2.6g) in EtOH (30ml) and NBD (5ml). The white crystalline complex is filtered off, and washed with EtOH (5ml) and Et_2O (5ml) to give **NBD-$(CuBr)_2$** as fine white crystals which slowly become green in air. The complex, which is insoluble in most organic solvents, leaves CuBr under reduced pressure, and is decomposed by H_2O to give Cu_2O. Its IR (Nujol and hexachlorobutadiene mulls) has ν_{max} at 3027 (vw), 3000 (vw), 2930 (m), 2860 (w), 1471 (w), 1453 (m), 1310 (ms), 1265 (w), 1245 (vw), 1234 (w), 1180—1080 (br-w), 1050 (vw), 993 (m), 976 (m), 950 (w), 938 (w), 918 (ms), 889 (w), 867 (w), 777 (w), 765 (w), 739 (m), 719 (m) cm^{-1} [Abel, Bennett and Wilkinson *J Chem Soc* 3178 *1959*]. [*Beilstein* **5** IV 879.]

For the *bis(phenylsulfonyl)ethylenes* see also Truce & McManimie *J Am Chem Soc* **76** 5745 *1954*, Montaniari *Gazetta* **86** 429 *1956*, Parham & Heberling *J Am Chem Soc* **77** 1175 *1955*, Modena & Montaniari *Gazetta* **86** 436 *1956*, Adams & Ferretti *J Am Chem Soc* **81** 4931 *1959*, and for UV see Angeletti & Montaniari *Boll Scient Fac Chim Ind Univ Bologna* **15** 44, 45 *1957*; in EtOH the *cis-isomer* has λ_{max} at 241-243nm, and the *trans-isomer* λ_{max} at 246nm.

Pentaphenylferrocenyl(di-*tert*-butyl)phosphine [$P(C_5H_4FeC_5Ph_5)(t\text{-butyl})_2$, Q-Phos] *[312959-24-3]* **M 710.7, m 211-219°.** This catalyst ligand is prepared in two steps in high yield, and all reactions are performed in a drybox. Firstly *(di*-tert-*butylphosphino)ferrocene* is prepared by adding *t*-BuLi (31.6ml, 53.8mmol) in THF to a solution of Cp_2Fe (10.0g, 53.8mmol) in THF (25ml) during 5 minutes at 0°, stirred for 20 minutes and the solvent is removed *in vacuo*. The residue is dissolved in pentane (100ml) and THF (5ml), $(t\text{-Bu})_2PCl$ (5.33g, 29.5mmol) is added and the mixture is stirred for 3 hours after which time degassed MeOH (1ml) is added, and most of the solvents are removed *in vacuo*. The residue is filtered through a plug of silica gel under N_2 and unreacted Cp_2Fe is eluted with pentane first and then the phosphine is eluted all at once with Et_2O, the solvent is removed *in vacuo*, and the required *phosphine* is crystallised from pentane (yield 7.58g, 78%). In the second step this *phosphine* (1.00g, 3.03mmol), $Pd(OAc)_2$ (0.35g, 0.156mmol) and *t*-BuONa (2.93g, 30.5mmol) are dissolved in PhCl (34.10g, 303.0mmol) and heated at 110° for 18 hours. The mixture is filtered through Celite, the PhCl is removed *in vacuo*, and the residue is subjected to chromatography on Silica gel, and eluting with pentane/Et_2O (80:1), to give $P(C_5H_4FeC_5Ph_5)(t\text{-butyl})_2$ (1.47g, 68%) as a pink-red solid. Its ^1H NMR (C_6D_6*) has resonances at δ: 1.07 (d, 11.0Hz, 18H, Me_3), 4.42 (t, 1.7Hz, 2H, C_5H_4), 4.67 (d, 1.0Hz, 2H, C_5H_4), 6.95-6.97 (m, 15H, *m,p*-C_6H_5), 7.44-7.48 (m, 10H, *o*-C_6H_5); the $^{13}C\{^1H\}$ NMR (C_6D_6*) has resonances at δ: 31.31 (d, 13.8Hz, CMe_3), 33.31 (d, 24.8Hz, CMe_3), 76.41 (d, 2.6Hz, C_5H_4), 78.58 (d, 11.4Hz, C_5H_4), 85.49 (d, 41.6Hz, *ipso*-C_5H_4), 88.38 (s, C_5Ph_5), 126.67 (s, C_5Ph_5), 127.47 (s, C_5Ph_5), 133.23 (s, C_5Ph_5), 136.32 (s, C_5Ph_5); and the $^{31}P\{^1H\}$ NMR (C_6D_6*) has a resonance at δ 25.49 (s). Similarly prepared were ***P[$C_5H_4FeC_5(C_6H_4$-p-$CF_3)_5$](t-butyl)$_2$*** (37.3% yield, from pentane), ***P[$C_5H_4FeC_5(C_6H_4$-p-OMe)$_5$](t-butyl)$_2$*** (36% yield, from Et_2O at -30°), ***P($C_5H_4FeC_5HPh_4$)(t-butyl)$_2$*** (47.4% yield, orange crystals from pentane at -35°), and ***P[$C_5H_4FeC_5$(3,5-$Me_2C_6H_3)_5$](t-butyl)$_2$*** (30% yield, red solid from pentane/Et_2O) by using *p*-trifluoromethylchlorobenzene, *p*-methoxychlorobenzene, a limited amount of PhCl and 5-bromo-*m*-xylene respectively. These are air-stable ferrocenyl dialkylphosphines for palladium-catalysed C-C, C-N and C-O bonding-forming cross-coupling reactions. The ligand $P(C_5H_4FeC_5Ph_5)(t\text{-butyl})_2$ exhibits turnovers of ~1000 for aminations with unactivated aryl bromides or chloride, catalysed the formation of selected aryl ethers under mild conditions, and aryl halides coupled with acyclic or cyclic secondary alkyl- and arylamines, and the latter amines coupled with aryl- and

primary alkylboronic acids. The ligand is air stable in the solid state and in solution, and produces highly active Pd catalysts which are stable in the solid state and react only slowly with oxygen in solution. [Kataoka et al. *J Org Chem* **67** 5553 *2002*, cf also Shelby et al. *J Am Chem Soc* **122** 10718 *2000*.]

4-(3-Phenylpropyl)pyridine 1-oxide (P_3NO) *[34122-28-6]* **M 213.3, m 58-65°, 60°, pK_{Est}~1.3.** The *N*-oxide is prepared by adding 4-(3-phenylpropyl)pyridine (12.5g, [2057-49-0]) during 5 minutes to a slurry of oxone (37.5g, [70693-62-8]), H_2O (63.5ml) and MeOH (125ml) (pH ~1.4) under N_2, and the stirred mixture is kept at pH 5.5 by addition of 5N aqueous NaOH while the temperature is kept at ≤ 35° (the temperature being controlled by external water cooling and by the rate of NaOH addition). The reaction is monitored by HPLC, and at completion, the salts are removed by filtration and the cake is washed with MeOH (50ml). The combined filtrate and washes are treated with 1M aqueous sodium metabisulfite solution (12ml), stirred for 0.5 hours and the pH is adjusted to 10.0 by addition of 5N aqueous NaOH, and set aside for 1 hour. The mixture is concentrated *in vacuo* (at 50°) to a final volume of ~75ml, cooled to 20°, the solid is filtered off, washed with H_2O (50ml), and dried under N_2 to give the desired *1-oxide* in 93% yield. *Alternatively*, it can be prepared by the oxidation of the *phenylpropylpyridine* with 30% H_2O_2/AcOH using the standard method of Ochiai [*J Org Chem* **18** 534 *1953*, see also Boekelheide & Linn *J Am Chem Soc* **76** 1286 *1954*]. Its ^{1}H NMR (300MHz, $CDCl_3$) has δ at 1.8-1.98 (m, 2H, 2′propyl-CH_2), 2.3-2.6 (m, 4H, ph-CH_2, py-CH_2), 7.05 (m, 2H, 3,5-pyridine), 7.12-7.30 (m, 5H, benzene H), 8.11 (m, 2H, 2,6-pyridine H). [Senanayake et al. *Tetrahedron Lett* **37** 3271 *1996*.] This reagent stabilises and enhances Jacobsen Mn-salen catalysts and is more readily obtained in quantity than the commonly used 4-phenylpyridine 1-oxide [see Jacobsen et al. *J Am Chem Soc* **113** 7063 *1991*].

Pinacolborane (4,4,5,5-tetramethyl-1,3,2-dioxaborolane) *[25015-63-8]* **M 128.0, b 42-43°/50mm, d_4^{25} 0.882, n_D^{20} 1.396.** This borolane is prepared by stirring a cooled solution (at 0°) of pinacol (2.36g, 20mmol [76-09-5]) in CH_2Cl_2 (2ml) to which is added, dropwise, BH_3-SMe_2 (20mmol, 10.0M in SMe_2) whereby effervescence occurs (use efficient fume hood, and gases have a foul odour, are flammable, and should be absorbed through alkaline solution or oxidising solutions containing H_2O_2 or $KMnO_4$). After stirring for ~1 hour at 0°, the mixture is warmed to ~25°, when evolution ceases (*ca* another 1 hour) and is distilled to give the borolane as a clear oil (1.61g, 63% yield). Its IR (CH_2Cl_2) has ν_{max} at 3272s, 2980s, 1530m, 1482s, 1333s, 1143s, 983s, 851s cm^{-1}; and the ^{1}H NMR (300MHz, $CDCl_3$) has δ at 1.27 (s, 12H); the ^{13}C NMR (75.5MHz, $CDCl_3$) has δ at 83.1, 24.5; and the ^{11}B NMR (115.5MHz, $CDCl_3$) has δ at 28.07. It is a very efficient hydroboration reagent, requires mild reaction conditions, has higher functional group tolerance, higher regio- and stereoselectivity, with excellent stability of the resulting pinacol boronic esters produced. [Tucker et al. *J Org Chem* **57** 3482 *1992*.]

Rhodium(I) chloride 1,5-cyclooctadiene complex dimer {chloro(1,5-cyclooctadiene)rhodium dimer, di-μ,μ′-chlorobis[(1,2,5,6-η)-1,5-cyclooctadiene]dirhodium (I), $[Rh(COD)Cl]_2$} *[12092-47-6]* **M 493.1, m ~243° (dec, see below).** The complex is prepared by refluxing a solution of $RhCl_3.3H_2O$ (1.93g, 7.3mmol), H_2O (3ml), EtOH (35ml) and COD (6ml, 48mmol) overnight. After cooling, the crude solid is collected, washed with a little H_2O, dried and recrystallised from CH_2Cl_2/hexane or acetic acid, then dried *in vacuo* to give 82% yield (1.5g) of dimer. On heating it darkens from about 220°, melts at ~256° and decomposes with effervescence at 258°. **M** by ebullioscopy in 0.9% $CHCl_3$ is **~513** confirming the dimeric stucture. It is soluble in CH_2Cl_2 and THF, moderately in $CHCl_3$, AcOH and Me_2CO, slightly soluble in hexane, Et_2O, MeOH, EtOH, and $*C_6H_6$ but insoluble in H_2O. Its magnetic susceptibility χ, is -0.52 x 10^{-6} ±4% per g. [Chatt & Venanzi *J Chem Soc* 4735 *1957*, Schenck et al. *Inorg Chem* **24** 2334 *1985*, cf Giordano & Crabtree *Inorg Synth* **19** 218 *1979*.]

Rhodium(I) chloride norbornadiene complex dimer {bicyclo[2.2.1]hepta-2,5-diene-rhodium(I) chloride dimer, di-μμ′-chlorobis[2,5-norbornadiene]dirhodium(I), $[Rh(NBD)Cl]_2$} *[dimer 12257-42-0; polymer 42740-82-9]* **M 460.99, m ~240° (dec).** The yellow dimer is obtained by shaking rhodium "trichloride" (0.7g, $RhCl_3.3H_2O$) and norbornadiene (2ml) in aqueous EtOH (10ml) for 2 days. It is collected and recrystallised from hot $CHCl_3$/light petroleum to give analytically pure complex (0.62g). **M** by ebullioscopy in $*C_6H_6$ is 481 consistent with a dimeric structure. The fine yellow crystals are soluble in $CHCl_3$ and $*C_6H_6$, but almost insoluble in light petroleum and Et_2O. Its IR (CS_2) has ν_{max} at 3060(m), 3000(m), 2960(m), 2920(m), 2855(m), 1307(s), 1171(m), 1157(w), 1068(w), 1029(w), 995(w), 932(m), 882(m), 721(w), 680(s), 630(s) cm^{-1}. [Abel,

Bennett & Wilkinson *J Chem Soc* 3178 *1959*.]

Ruthenium(II)benzenedichloride dimer {di-μ-chloro-bis[(η-benzene)chlororuthenium(II)], $Ru_2(C_6H_6)_2Cl_4$, $[Ru(C_6H_6)Cl_2]_2$} *[37366-09-9]* **M 500.2, m 242°.** This versatile reagent is prepared by refluxing $RuCl_3.3H_2O$ (2.0g) in EtOH (100ml) with cyclohexadiene (10ml, of 1,3- or 1-4 prepared by reduction of *benzene with Na/Liquid NH_3, Kaiser *Synthesis* 391 *1972*, Birch & Subba Rao *Adv Org Chem* **8** 1 *1972*) for 4 hours. The brown precipitate is filtered off, washed with MeOH and dried *in vacuo* to give the *complex* (1.83g, 95%). The complex is diamagnetic, it is *dimeric* in freezing $CHBr_3$, and is sparingly soluble in organic solvents except Me_2SO with which it forms a red complex with the *monomeric* structure $RuCl_2(C_6H_6)$(dmso). It dissolves in pyridine, tertiary phosphines, phosphites, tertiary arsines (L) which cleave the chlorine bridges of the dimer to form orange or red air stable complexes **$RuCl_2(C_6H_6)(L)$** which are *monomeric* in $CHCl_3$. Large excess of the ligand L should be avoided in the reaction, otherwise the benzene rings may be displaced. Its IR has Ru—Cl stretching bands with ν_{max} at 295, 259 and 248sh cm^{-1}; and the ^1H NMR ($CDCl_3$, TMS) has a singlet at τ_H 4.02 which is *ca* 2.0 ppm upfield of the free benzene H resonance. It is a useful precursor for the preparation of Ru(II) complexes, some of which are catalysts. [Bennett & Smith *J Chem Soc, Dalton Trans* 233 *1974*, Bennett et al. in *Comprehensive Organometallic Chemistry* Wilkinson ed, Vol 4 pp 748-750 Pergamon Press Oxford *1982*.]

The complex ***$Ru_2(C_6H_6)_2$*** has also been prepared by evaporating a coat of Ru powder (10-15%) in slow curing "Araldite" cement on a 1mm tungsten wire heated to ~2400°. The Ru vapour thus produced is co-condensed with *benzene to form thermally unstable orange-yellow crystals of $Ru_2(C_6H_6)_2$ which decompose below 0°. The ^1H NMR ($CFCl_3$) of the orange crystals show H resonances at τ 4.22 (2H), 4.84 (6H), 5.10 (2H) and 7.11(2H) consistent with the 1—4-η, 1—6-η formulation of the $Ru_2(C_6H_6)_2$ structure. [Timms & King *J C S, Chem Commun* 898 *1978*.]

Ruthenium dichloride 1,5-cyclooctadiene complex [dichloro-μ-(η^4-cycloocta-1,5-diene)ruthenium(II), $RuCl_2(COD)_n$] *[50982-12-2]* **M 280.2 (monomer).** Analytically pure complex is obtained by heating a mixture of pure $RuCl_3.3H_2O$ (50.0g, 0.2mol) and cycloocta-1,5-diene (50ml, 0.4mol, use a fume hood) in absolute EtOH (400ml) under reflux for 24 hours whereby the brown complex precipitates. After cooling, the solid is filtered off, washed with Et_2O ((50ml) and dried *in vacuo* to give pure [$RuCl_2$(COD)] (~52g, ~90%). It is stable in air, only slightly soluble in organic solvents, reacts by halogen-bridge cleavage and is a useful synthetic precursor of ruthenium((II) complexes. [Ohta, Takaya and Noyori *Inorg Chem* **27** 566 *1988*, Alders, Singleton and Yates *Inorg Synth* **26** 253 *1989*, Bennett et al. in *Comprehensive Organometallic Chemistry* Wilkinson ed., **Vol 4** pp 748-750 Pergamon Press Oxford *1982*.]

Tetrakis(acetonitrile)copper(I) hexafluorophosphate [$Cu(MeCN)_4^+$ PF_6^-] *[64443-05-6]* **M 372.7, m 160°(dec).** In an efficient fume cupboard, 60-65% aqueous hexafluorophosphoric acid (10ml, ~113mmol, [16940-81-1], M 146.0) is added in 2ml portions to a stirred suspension of Cu(I) oxide (4.0g, 28mmol) in MeCN (80ml) when a very exothermic reaction occurs (use a refux condenser), causing the solution to boil. After stirring for a further 3 minutes the solution is filtered (use a medium-porosity frit) from some black solid, and $Cu(MeCN)_4^+$ PF_6^- may begin to crystallise out, and is complete on standing at -20°, or by adding an equal volume of dry Et_2O and cooling to 0°. (If some white solid separates with the black solid it should be washed off with MeCN and the MeCN solutions combined and cooled at -20°, or diluted with Et_2O.) The salt is collected by filtration, washed with Et_2O and immediately dissolved in MeCN (100ml), filter off any undissolved blue Cu^{2+} species, add Et_2O (100ml) and set aside at -20° for several hours to crystallise out. The crystalline complex would need a second recrystallisation if it has a blue tinge. It may be recrystallised from MeCN (80ml) and Et_2O (80ml). The white complex salt is dried *in vacuo* for ~30 minutes immediately after washing with Et_2O to give the analytically pure salt (~12.5g, ~60% depending on crystallisation losses). It is a free-flowing white, microcrystalline powder which does not darken on long storage under N_2 or argon. On exposure to air for >1 hour minor surface oxidation occurs as it is slightly hygroscopic. The MeCN ligands are not removed easily *in vacuo* at ~25° (but dissociation occurs at ~5 torr/80° and ~25 torr/110°). The IR (Nujol) has ν_{max} at 2277m and 2305m cm^{-1} (for MeCN), and 850vs and 557s cm^{-1} for PF_6^-. The related salt,

$Cu(MeCN)_4^+$ BF_4^-, can be prepared similarly by using an equivalent amount of HBF_4 (as 48% aqueous acid [16872-11-0], M 87.9) instead of HPF_6. These complexes are suited for the non-aqueous-media synthesis of Cu(I) complexes [see $(IPr)_2Cu^+$ PF_6^- and $(IPr)_2Cu^+$ BF_4^- above]; as well as for preparing other complexes such as $[Rh(C_2H_4)_3(MeCN)_2]^+$ + CuCl by reaction of $Cu(MeCN)_4^+$ with $[Rh(C_2H_4)_2Cl]_2$ and C_2H_4 in CH_2Cl_2 [Maspero et al. *J Organomet Chem* **38** C43 *1972*]. The X-ray structure of the ClO_4^- salt showed that the copper is almost ideally tetrahedral with nearly linear MeCN molecules [Csoregh et al. *Acta Cryst* **B31** 314 *1975*]. [Kubas *Inorg Synth* **19** 90 *1979*, Kubas *Inorg Synth* **28** 68 *1990.*]

***cis-cis-cis*-1,2,3,4-Tetrakis(diphenylphosphinomethyl)cyclopentane [(1*R**,2*R**,3*S**,4*S**)-tetrakis-(diphenylphosphinomethyl)cyclopentane, Tedicyp]** *[333380-86-2]* **M 862.9, m 79°.** The intermediate cis-cis-cis-1*,2,3,4-tetrakis(boranatodiphenylphosphanylmethyl)cyclopropane* (white crystals **m 149°**, after chromatography on silica gel eluting with AcOEt/petroleum ether, 1:4) is obtained from Ph_2PLi (from Ph_2PCl see [1079-66-9] and Li) and *cis-cis-cis*-1,2,3,4-tetrakis(tosyloxymethyl)cyclopentane in THF under argon (~20°/5 hours), then borane in THF is added. This boranato intermediate formed is added to anhydrous Et_2NH, heated at 55-60° for 10 hours, evaporated to dryness, this process is repeated twice, and the residue is chromatographed on silica gel (eluted with Et_2O/petroleum ether, 1:4) to give white crystals of Tedicyp (98%) with **m 79°**. It is not very stable in air and must be stored under argon. It has ^1H NMR (400MHz, THF-d_8) with δ at 7.71-7.23 (40H, m), 2.91-2.52 (2H, m), 2.38-1.72 (10H, m), 1.25 (2H, m); the ^{13}C NMR (100MHz, THF-d_8, TMS) has δ at 141.6 (s, $^1J_{P,C}$ = 15.1Hz), 141.1 (s, $^1J_{P,C}$ = 14.1Hz), 140.0 (s, $^1J_{P,C}$ = 15.1Hz), 139.4 (s, $^1J_{P,C}$ = 16.0Hz), 134.6 (d, $J_{P,C}$ = 20.1Hz), 134.5 (d, $J_{P,C}$ = 19.1Hz), 133.5 (d, $J_{P,C}$ = 17.0Hz), 133.3 (d, $J_{P,C}$ = 18.0Hz), 129.6 (d, $J_{P,C}$ = 14.0Hz), 129.3-129.0 (d, $J_{P,C}$ = 15.0Hz), 45.4 (t, $^2J_{P,C}$ = 8.6Hz), 45.2 (d, $^2J_{P,C}$ = 8.7Hz), 40.4 (t, $^2J_{P,C}$ = 8.75Hz), 40.3 (t, $^2J_{P,C}$ = 9.2Hz), 3.91 (d, $^2J_{P,C}$ = 13.3Hz), 33.1 (d, $^1J_{P,C}$ = 10Hz), 26.5 (t, $^1J_{P,C}$ = 12.9Hz); the ^{31}P NMR (162MHz, THF-d_8) has δ at -16.3 and -17.7. It is used for preparing the Pd-Tedicyp catalyst with $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (see above) for promoting allylic alkylations [Laurenti et al. *J Org Chem* **66** 1633 *2001*], cross coupling reactions [Wallow & Novak *J Org Chem* **59** 5034 *1994*], and catalysing Heck reactions of α- or β-substituted enol ethers with aryl bromides [Battace et al. *Eur J Org Chem* 3122 *2007*] with high efficiency.
The tetra-phosphine oxide of cis-cis-cis-*1,2,3,4-tetrakis(diphenylphosphinoylmethyl)cyclopropane* is obtained by oxidising Tedicyp in THF with excess H_2O_2 (~20°/4 days) then purified by chromatography on silica gel (eluting with MeOH/CH_2Cl_2, 5:95) to yield (66%) white crystals of the *tetroxide* with **m 165°**. It has ^1H NMR (400MHz, $CDCl_3$) with δ at 7.79-7.62 (16H, m), 7.32-7.28 (8H, m), 2.85 (2H, br t, J = 12.9Hz), 2.28 (4H, d, J = 11.9Hz), 2.26-2.15 (2H, m), 2.10-2.05 (2H, m), 1.88 (2H, br q, J = 12.9Hz), 1.60 (1H, dt, J = 13.8, 7.5Hz), 1.36 (1H, dt, J = 13.8, 10.2Hz); the ^{13}C NMR (100MHz, $CDCl_3$) has δ at 134.3 ($^1J_{P,C}$ = 13.0Hz), 133.3 (m), 131.94 ($^1J_{P,C}$ = 5Hz), 131.62 ($^1J_{P,C}$ = 5Hz), 131.27-131.0 (m), 129.0-128,6 (m), 41.9 (d, $^2J_{P,C}$ = 10.0Hz), 38.0 (t), 35.2 (d), 33.0 (t, $^1J_{P,C}$ = 69.9Hz), 27.1 (t, $^1J_{P,C}$ = 70.0Hz) relative to TMS; and the ^{31}P NMR (162MHz, $CDCl_3$) has δ at 32.2. [Laurenti et al. *J Org Chem* **66** 1633 *2001*.]

R*-(+)- and *S*-(-)- 2,2′,6,6′-Tetramethoxy-4,4′-bis(diphenylphosphino)-3,3′-bipyridine (*R*-(+)- P-Phos and *S*-(-)- P-Phos)** *[R- 221012-82-4* and *S- 362524-23-0]* **M 644.6, m 261-265°, $[\alpha]_D^{20}$ +98° and -98° (c 1, $CHCl_3$).** This group of ligands have been prepared from (3-bromo-2,6-dimethoxypyrid-4-yl)(diphenyl)-phosphine oxide by an Ulmann reaction (Cu/DMF/140°) to give *RS- 2,2',6,6'-tetramethoxy-3,3'-bipyridine-4,4'-diphenylphosphine dioxide* (85%) which is resolved into the (+)- and (-)- enantiomers by HPLC on a preparative Diacel AD column (25m x 1.2m), eluting with 2-propanol/hexane (20:80) at a flow rate of 3.0ml/minute: t_R = 12.24 minutes, t_S = 25.06 minutes. The phosphine oxide groups are then each reduced by Cl_3SiH/Et_3N/toluene at 140° to give *R*-(+)- and *S*-(-)- R-Phos in 99% yields. *Alternatively*, the above *RS*- dioxide, which cannot be resolved easily, is converted into the *5,5'dibromo derivative* (Br_2/NaOAc/AcOH; 0°-60°, 97%) which can now be resolved *via* the (+) and (-)-di-*O*-benzoyl tartrate salts (in EtOAc/$CHCl_3$, 1/1) to provide the enantiomeric *5,5'-dibromo-dioxides* that are de-brominated, and reduced (Cl_3SiH/Et_3N/toluene during an extended period from 25° to 140°) to give ***R-(+)- and S-(-)- P-Phos in 91% yields. [Pai et al. *J Am Chem Soc* **112** 11513 *2000*.]

***R*-(+)- and *S*-(-)- 2,2′,6,6′-Tetramethoxy-4,4′-bis[di(3,5-xylyl)phosphino]-3,3′-bipyridine [*R*-(+)- Xylyl-P-Phos and *S*-(-)- Xylyl-P-Phos)** *[R- 442905-33-1* and *S- 443347-10-2]* **M 756.9, m (158-162°), 190-194°, $[\alpha]_D^{20}$ +125° and -125° (c 1, $CHCl_3$).** The Xylyl-P-Phos ligands are prepared in a slightly different way from P-Phos ligands above. Thus *3-bromo-2,6-dimethoxypyridine* is converted into *(3-bromo-2,6-dimethoxypyrid-4-yl)di(3,5-dimethylphenyl)phosphine* [*a*: LDA/THF/-78°; *b*: $(3,5\text{-dimethylphenyl})_2PCl$/-78°) in 56% yield, then

oxidised (H_2O_2/Me_2CO/0°) to the *phosphine oxide* (99%), followed by an Ulmann reaction as above (Cu/DMF/140°) to give *RS- 2,2',6,6'-tetramethoxy-3,3'-bipyridine-4,4'-di(3,5-dimethylphenyl)phosphine dioxide* (85% yield) that is resolved *via* (-)- and (+)- di-*O*-benzoyl tartrate salts (*a*: see above fractional crystallisation; *b*: 10% aqueous NaOH) to give the *R- (75%)* and *S- (88%) Xylyl-P-Phos dioxides* which are reduced (Cl_3SiH/Et_3N/toluene) to ***R*(+)- and *S- Xylyl-P-Phos*** in >90% yields. The absolute configuration *S*- was determined from the X-ray crystal stucture of the diastereoisometrically pure 1:1 salt of (-)-Xylyl-P-Phos and (+)-(2*S*,3*S*)-dibenzoyl-*O*-tartrate. The latter have ^{1}H NMR (500MHz, $CDCl_3$) with δ_H at 2.20 (s, 12H, PhC*H*$_3$), 2.25 (s, 12H, PhC*H*$_3$), 3.37 (s, 6H, O C*H*$_3$), 3.83 (s, 6H, O C*H*$_3$), 6.06 (d, *J* = 1.5Hz, 2H, Py*H*), 6.79-6.92 (m, 12H, Ph*H*); the ^{13}C NMR (125MHz, $CDCl_3$) with δ_C at 21.54 (d, *J* = 4.78Hz), 53.06, 53.43, 105.47, 115.39 (t, *J* = 37.07Hz), 130.47 (d, *J* = 33.81Hz), 131.46 (t, *J* = 20.99Hz), 132.42 (t, *J* = 21.74Hz), 135.69 (t, *J* = 10.05Hz), 136.88 (t, *J* = 12.82Hz), 137.39 (t, *J* = 8.04Hz), 137.71 (t, *J* = 7.16Hz), 154.64, 154.70, 154.75, 160.76 (t, *J* = 11.18Hz), 162.30; the ^{31}P NMR (200MHz, $CDCl_3$) with δ_P at -11.99; the LSMS [M^+] found 757, calculated for $C_{46}H_{50}N_2O_4P_2$ is 756.85; and the C, H and N elemental analyses fit for the latter empirical formula. [Wu et al. *Tetrahedron Lett* **43** 1539 *2002*.]

***6RS*(±)-*4*,4,6-Trimethyl-2-vinyl-1,3,2-dioxaborinane (vinylboronic acid 2-methyl-2,4-pentanediol ester)** *[4627-10-5]* **M 154.0, b 50-55°/0.46mm, d $^{25}_4$ 0.893, n $^{20}_D$ 1.429.** It is prepared by a modification of a published method [Hoffmann & Landmann *Chem Ber* **119** 2013 *1986*] where *n*-octanol is replaced by 2-methylpentane-2,4-diol (MPD). To a solution of $(MeO)_3B$ (30ml, 270mmol) in dry Et_2O (125ml) at -78° is added over 45 minutes a 2.1M solution of vinylmagnesium chloride (118ml, 248mmol) in THF with stirring, and allowing the temperature to rise to ~25°. The mixture is then acidified, under cooling, with aqueous HCl (concentrated, 21ml, 0.25mol in 62.5ml of H_2O), phenothiazine (0.1g, as stabiliser) is added, the phases are separated, the aqueous phase is extracted with MPD (3 x 50ml). The combined organic phases are evaporated *in vacuo* from a bath at 80° and the residual oil is distilled at high vacuum to give pure *borinane* in ~60% yield. [Note that all the liquids in the reaction mixture distil at lower temperatures than the desired racemic vinyl-dioxaborinane.] It is superior to vinylboronic pinacol ester in preparation, storage, stability, and reactivity, providing improved selectivity for Heck *versus* Suzuki coupling with aryl and heteroaryl bromides and iodides [Lightfoot et al. *Tetrahedron Lett* **44** 7645 *2003*]. By adopting different reaction conditions with $Pd(PPh_3)_4$/*t*-BuOK, selective Suzuki-Miyaura coupling with a range of aryl and heteroaryl halides (Cl, Br and I) was achieved [Lightfoot et al. *Synlett* 259 *2005*, cf Lightfoot et al. *Org Biomol Chem* **3** 3167 *2005*].

Tri-*tert*-butylphosphonium tetrafluoroborate [(*tert*-Bu)$_3$PH$^+$ BF$_4^-$] *[131274-22-1]* **M 290.1, m 261°(dec), pK^{25} 11.4 (phosphine).** The salt is prepared by adding HBF_4 (48% aqueous solution, 1.0ml, 7.6mmol) to a solution of pure (*t*-Bu)$_3$P (225mg, 1.11mmol, see above) in CH_2Cl_2 (15ml), stirring vigorously for 5 minutes, the organic layer is separated, dried ($MgSO_4$), filtered and evaporated to dryness to give analytically pure *salt* (302mg, 94%) as a white powder. It has ν_{max} (KBr) at 3002, 2217, 1478, 1405, 1381, 1181, 1059, 886 (br) cm^{-1}; the ^{1}H NMR (400MHz, $CDCl_3$) has δ_H at 6.07 (d, $^1J_{PH}$ = 465Hz, 1H), 1.65 (d, $^3J_{PH}$ = 15.3Hz, 27H); the ^{13}C NMR (75MHz, $CDCl_3$) has δ_C at 37.0 (d, $^1J_{PC}$ = 29Hz, 1H), 30.1; and the ^{31}P{^{1}H} NMR (121MHz, $CDCl_3$) has δ_P at 51.7. The salt is more air-stable than the free phosphine, and can be heated at 120° for 24 hours without decomposition (no change in NMR spectra), or loss of catalytic activity with transition metal complexes. It is ***not hygroscopic***. In the presence of $Pd_2(dba)_3$ in THF it catalyses Suzuki cross-coupling reactions between aryl halides and arylboronic acids, Stille cross-coupling reactions between aryl halides and tributylSn compounds, and Heck reactions between aryl halides and olefines [Netherton & Fu *Org Lett* **3** 4295 *2001*]. The salt has also been used successfully in the Heck coupling [with $PdCl_2$(COD), LiCl, Cy_2NMe] of non-activated alkenyl tosylates and phosphates as substrates with electron-poor alkenes and styrene derivatives [Hansen et al. *Angew Chem Int Ed* **45** 3349 *2006*].

Vinyl MIDA boronate {vinylboronic acid MIDA ester, 6-methyl-2-vinyl-1,3,6,2-dioxazaborocane-4,8-dione, [*N*-[(carboxy-κ*O*)methyl]-*N*-methylglycinato(2-)-κ*N*,κ*O*]ethenyl boron} ***[1104636-73-8]*** **M 183.0, m 152-156°.** The boronate is prepared in Schlenk equipment by adding dropwise vinyltrimethylsilane (4.49ml, 31.5mmol, freshly distilled see [754-05-2]) to a stirred solution of BBr_3 (1.0M in CH_2Cl_2, 30mmol) at 0°, and maintained at this temperature for 20 minutes, then allowed to warm to ~ 25° with stirring for a further 2 hours. This mixture is added *via* a cannula to a stirred suspension of MIDA sodium salt (5.73g, 30.0mmol, see above)

in MeCN (50ml) at 0º, at such a rate as to keep the temperature below 5º; then the temperature is allowed to warm to ~25º while stirring for 1 hour. The resulting white suspension is filtered through a pad of Celite and the filtrate cake is extracted 3 times with Me_2CO. Et_2O is added to the combined orange filtrates which allowed the colourless free flowing vinyl MIDA boronate (4.74g, 86%) to crystallise out. On TLC it has R_F 0.26 (Merck silica gel plate grade 9385, 60Å, 230-400 mesh, with EtOAc). Its IR (thin film) has ν_{max} at 3063, 2997, 2960, 1755, 1617, 1455, 1420, 1345, 1312, 1251, 1175, 1155, 1134, 1117, 1090, 1033, 987, 964, 951, 865 cm^{-1}; the ^1H NMR (500MHz, Me_2CO-d_6, δ = 2.04 centre line) has δ_H at 5.96 (dd, *J* = 19.0, 13.5Hz, 1H), 5.72-5.63 (m, 2H), 4.21 (d, *J* = 17.0Hz, 2H), 4.01 (d, *J* = 17.0Hz, 2H), 3.0 (s, 3H); the ^{13}C NMR (125MHz, Me_2CO-d_6, δ = 29.80 centre line) has δ_C at168.3, 128.7, 61.6, 46.7; and the HMRS (EI+) has found *m/z* 183.0700, calculated for $C_7H_{10}BBrNO_4$ $[M]^+$ is 183.0703.
Single crystal X-ray analysis confirmed the predicted structure as having a pyramidalised boron centre. The vinylboronate shows no signs of deterioration when kept on the benchtop in air for more than 3 months. It is a versatile reagent that can be prepared on a multigram scale. It readily reacts with $CH_2N_2/Pd(OAc)_2$ to provide cylopropyl MIDA boronate [Et_2O, 0-23º, 1 hour, 93%], and with *m*-CPBA it yields oxiranyl MIDA boronate [CH_2Cl_2, 0-23º, 18 hours, 74%] [Uno, Gillis and Burke *Tetrahedron* **65** 3230 *2009*]; and can be used in Suzuki, Heck, Stille, Negishi and Sonogashira couplings and Miyaura borylations [Gillis & Burke *Aldrichimica Acta* **42** 17 *2009*].

Xantphos [4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene] *[161265-03-8]* **M 578.2, m 221-222º, 224-228º.** Xantphos is prepared, using Schlenck techniques under N_2, by adding *sec*-BuLi (13.6ml of 1.3M in 98/2 cyclohexane/hexane, 14.3mmol) dropwise to a stirred solution of 9,9-dimethylxanthene (1.0g, 4.76mmol, see [19814-75-6]) and TMEDA (2.3ml, 13.3mmol) in dry Et_2O (54ml), and stirring for 16 hours at ~25º to form the 4,5-dilithium derivative. To this mixture is added a solution of chlorodiphenylphosphine (2.8ml, 14.3mmol, see [1079-66-9]) in hexane (16ml) dropwise, and stirring is continued for 16 hours, then the solvent is removed *in vacuo*. The residual thick oil is dissolved in CH_2Cl_2, washed with H_2O, dried ($MgSO_4$), filtered, the solvent is removed *in vacuo*, the residue is washed with hexanes, and recrystallised from propan-1-ol to give *xantphos* (2.05g, 74.6%) as an air stable yellow-white powder. Its IR ($CHCl_3$) has ν_{max} at 3.073w, 2974w, 1435s, 1405vs, 1243m, 695m cm^{-1}; the ^1H NMR (300MHz, $CDCl_3$) has δ at 7.4 (dd, 2H, *J* = 7.8, 1.0Hz, CPC*H*CH), 7.15-7.26 (aryl, 20H, $[P(C_6H_5)_2]_2$), 6.96 (t, 2H, *J* = 7.7Hz, CHC*H*CH), 6.54 (dd, 2H, *J* = 7.4, 1.4Hz, CHC*H*CC), 1.65 (s, 6H, CH_3); the $^{13}C\{^1H\}$NMR (100MHz, $CDCl_3$) has δ at 137.2 (t, *J* = 5.3Hz) through space P-P coupling ~60Hz, 133.7 (t, *J* = 10.1Hz), 131.9, 129.7, 128.0 (ar), 126.1, 125.7 (t, *J* = 9.8Hz), 123.1, 67.8 (CMe_2), 31.6 (CH_3); the $^{31}P\{^1H\}$NMR (121.5MHz, $CDCl_3$, referenced to external 85% H_3PO_4) has δ at -17.5; and exact mass (MS) is found to be 578.1916 (calculated for $C_{39}H_{32}OP_2$ is 578.1928). Out of several diphenylphosphino ligands studied, xantphos induced the highest selectivity in rhodium-catalysed hydroformylation of 1-alkenes to form linear aldehydes. The hydroformylation is carried out in a stainless steel bomb under pressure of ~10 bars of CO/H_2 (1:1) in toluene with phosphorus ligand and $Rh(acac)(CO)_2$ as metal source. [Kranenburg, van der Burgt, Kramer and van Leewen *Organometallics* **14** 3081 *1995*.]

PHASE TRANSFER CATALYSTS

Phase transfer catalysts (PTCs) are agents that are soluble in both lipophilic and hydrophilic solutions, i.e. soluble in aqueous solutions and in non-water soluble organic solvents, in varying degrees. They are mostly cationic species that assist the transfer of anions. e.g. CN^-, from the aqueous phase into the non-aqueous phase, e.g. hexane, $CHCl_3$, which would contain the reactive compound, e.g. 1-octyl chloride, to form the product, i.e. 1-octylnitrile, in the non-aqueous phase in high yields. However, the catalysts can also be essentially neutral as with *crown ethers, cryptands* (tricyclic ethers containing nitrogen atoms at the bridgehead allowing formation of three rings) and *ionophores* which are useful for transferring metal ions through the bilayer interface. Some PTCs are polymer-bound making it easy for their removal and recycling. Other reactions that are phase transfer catalysed include: β-eliminations, *N*-alkylations, nucleophilic aromatic substitutions, metal-organic reactions, oxidation and reduction reactions. The reactions may proceed in either phase and/or at the interphase of the phases. They invariably occur in the organic phase, but in *Reverse Phase Transfer* reactions they occur in the aqueous phase. This section provides a selection of such agents, some of which are chiral and are capable of

promoting stereoselective, or stereospecific reactions. [Starks *J Am Chem Soc* **93** 195 *1971*, Brändström *Adv Phys Org Chem* **15** 267 *1977*, G.W. Gokel *Crown Ethers and Cryptands*, Royal Society of Chemistry, Cambridge, *1991*, ISBN 0-85186-996-3; S. R. Cooper (Ed.), *Crown Compound*: *Towards Future Applications*, VCH, Weinheim, *1992*, ISBN 1-56081-024-6, 3-527-28073-1; B. Deitrich, P. Viout and J-M, Lehn, *Macrocyclic Chemistry*: *Aspects of Organic and Inorganic Supramolecular Chemistry*, VCH, Weinheim, *1993*, ISBN 3-527-28330-7; M. Hiraoka (Ed.), *Crown Ethers and Analogous Compounds*, Elsevier, Amsterdam, *1992*, ISBN 0-444-88191-3; Ooi & Maruoka *Aldrichimica Acta* **40** 77 *2007*; K. Maruoka (Ed.), *Asymmetric Phase Transfer Catalysis*, Wiley-VCH, Weinheim, *2008*, ISBN 978-3-527-31842-1.]

Adogen 464 [methyl trialkyl(C8—C10)ammonium chloride] *[72749-59-8]* **M 416.2, d ^{25} 0.898, n $^{20}_{D}$ 1.4665.** This is purified in the same way as Aliquat 336 in the following entry. [US Patent 3 992 432.]

Aliquat 336 (methyltricaprylylammonium chloride, tri-*n*-octylmethylammonium chloride) *[5137-55-3, a replacement product, Aliquat 128, has 63393-96-4]* **M 404.2, d ^{25} 0.884, n $^{20}_{D}$ 1.4665.** A 30% (v/v) of Aliquat 336 solution in *benzene is washed twice with an equal volume of 1.5M HBr. [Petrow & Allen, *Anal Chem* **33** 1303 *1961*.] It is purified by dissolving 50g in $CHCl_3$ (100ml) and shaking with 20% NaOH solution (200ml) for 10 minutes, and followed by 20% NaCl (200ml) for 10 minutes. It is then washed with a small volume of H_2O, and filtered through a dry filter paper. [Starks *J Am Chem Soc* **93** 195 *1971*, Adam & Pribil *Talanta* **18** 733 *1971*.]

***N*-Anthracenylmethyl)cinchonidinium chloride** *[199588-80-2]* **M 521.1, m ~158-161°.** The salt can be purified by recrystallisation from CH_2Cl_2/Et_2O and dried *in vacuo*. This chiral phase–transfer-catalyst (PTC) assists in the allyl alkylation of the α-carbon of glycine imino ester to yield finally α-allyl-substituted α-amino acids. Thus with a ratio of imino ester to allyl compound: achiral phosphines (e.g.1,2-bis[diphenyl-phosphino]ethane DIPHOS, DPPE [1663-45-2], its oxide, triphenoxyphosphine or its oxide) : base (KOH) : $[Pd(p\text{-allyl})Cl]_2$: PTC of 100:200:150:3.5:10 produced the α-allyl imino ester in varying yields and stereoselectivity. However, the derivative ***N*-(9-anthracenylmethyl)-*O*(9)-methyl-cinchonidinium iodide** (prepared from the chloride with MeI/50% aqueous NaOH/20°/4 hours) was a more effective PTC, providing better yields and with up to ~94% enantiomeric excess. The orange *iodide*, which is soluble in CH_2Cl_2, is crystallised from CH_2Cl_2/Et_2O and has $[\alpha]_D^{19}$ -288° (c 1, CH_2Cl_2), IR with ν_{max} ($CDCl_3$) at 3686, 3014, 2952, 1598, 1515, 1456, 1075, 986 cm^{-1}; the ^1H NMR (500MHz, $CDCl_3$) has δ_H at 1.38-1.55 (m, 2H), 1.95-2.03 (m, 1H), 2.12-2.21 (m, 1H), 2.35-2.43 (m, 1H), 2.64-2.72 (m, 1H), 3.09 (dd, 1H, *J* = 5.6, 5.6Hz), 3.83 (s, 3H), 4.42-4.51 (m, 1H), 4.84 (d, *J* = 4.8Hz, 1H), 5.07 (d, *J* = 5.2Hz, 1H), 5.19 (d, *J* = 8.5Hz, 1H), 5.25 (bs, 1H), 5.87-6.02 (m, 2H), 6.52 (bs, 1H), 6.97 (d, *J* = 6.9Hz, 1H), 7.54-7.60 (m, 3H), 7.69-7.73 (m, 2H), 7.82-7.89 (m, 2H), 7.97 (brs, 1H), 8.05 (d, *J* = 4.3Hz, 1H), 8.14 (d, *J* = 4.1Hz, 1H), 8.20 (d, *J* = 4.3Hz, 1H), 8.32 ((d, *J* = 4.6Hz, 1H), 8.65 (s, 1H), 9.06 (d, *J* = 2.3Hz, 2H), 9.65 (d, *J* = 4.4Hz, 1H); and the ^{13}C NMR (125MHz, CD_3OD) has δ_C at 150.9, 149.1, 143.0, 138.5, 134.7, 134.6, 133.8, 133.0, 132.9, 131.5, 131.2, 131.1, 130.4, 129.6, 129.4, 129.4, 127.2, 126.1, 126.57, 125.7, 124.8, 124.7, 121.8, 118.9, 117.8, 79.5, 70.0, 63.3, 57.7, 57.5, 53.7, 39.4, 27.2, 26.2, 23.2. This *iodide* in CH_2Cl_2 was converted to another useful PTC ***N*-(9-anthracenylmethyl)-*O*(9)-methyl-cinchonidinium hexafluorophosphate** [by addition of NH_4PF_6 in H_2O at 25°/1 hour, dilution with CH_2Cl_2 and H_2O, drying the organic layer ($MgSO_4$) and evaporating] which gave yellow crystals from $CH_2Cl_2/CHCl_3$ with **m 163-164°**, $[\alpha]_D^{23}$ -314° (c 1.1, CH_2Cl_2), and IR and NMR quite similar to those of the iodide. [Nakoji et al *J Org Chem* **67** 7418 *2002*.]

8*S*,9*R*-(-)-*N*-Benzylcinchonidinium chloride (BCDC) *[69257-04-1]* **M 421.0, m 212-213° (dec), $[\alpha]_D^{20}$ -180°, -183° (c 5, H_2O), pK_{Est} ~5.** Dissolve the chloride in the minimum volume of H_2O and add absolute Me_2CO. Filter it off and dry it in a vacuum. It can also be recrystallised from hot EtOH or $EtOH/Et_2O$. It is a good chiral phase transfer catalyst producing the opposite enantiomer to the one using *N*-benzylcinchoninium chloride as catalyst — see below. [Colonna et al. *J Chem Soc, Perkin Trans 1* 547 *1981*, Imperali & Fisher *J Org Chem* **57** 757 *1992*.] [*Beilstein* **23** H 446.] See cinchonidine [485-71-2].

8*R*,9*S*-(+)-*N*-Benzylcinchoninium chloride (BCNC, *N*-benzyl-9*S*-hydroxycinchoninium chloride) *[69221-14-3]* **M 421.0, m 265° (dec), $[\alpha]_D^{20}$ +169° (c 0.4, H_2O), pK_{Est} ~ 5.** Recrystallise the chloride from isoPrOH, toluene or small volumes of H_2O. It is a good chiral phase transfer catalyst producing the opposite enantiomer to

the one using the above *N*-benzylcinchonidinium chloride as catalyst — see above. [Julia et al. *J Chem Soc, Perkin Trans 1* 574 *1981*, Hughes et al. *J Am Chem Soc* **106** 446 *1984*, Hughes et al. *J Org Chem* **52** 4745 *1987*, *Beilstein* **23** IV 2832.] See cinchonine [118-10-5].

(11b*R*)-(–)- and (11b*S*)-(+)- 4,4-Dibutyl-4,5-dihydro-2,6-bis(3,4,5-trifluorophenyl)-3H-dinaphth[2,1-c:1′,2′-e]azepinium bromide [*R- 887938-70-7; S- 851942-89-7]* **M 748.6, m 223-228°, 224-229°, $[\alpha]_D^{29}$ ±11.7° (c 1.01, $CHCl_3$).** The precursor chiral 2,2′-bisbromomethyl -1,1′-binaphthyl (280mg, 0.4mmol), di-*n*-butylamine (140µl, 0.8mmol) and K_2CO_3 (82mg, 0.6mmol) in MeCN (5ml) is refluxed with stirring for 10 hours. The mixture was poured into H_2O, extracted with CH_2Cl_2, the extract is dried (Na_2SO_4), filtered and evaporated to dryness. The residue is purified by column chromatography on silical gel (eluting with $MeOH/CH_2Cl_2$, 1:20) to give the bromide salt (275mg, 92%) which may be recrystallised from $MeOH/Et_2O$. The *S-enantiomer* has IR with ν_{max} (film) at 2965, 2936, 2876, 1614, 1524, 1470, 1447, 1360, 1242, 1047, 923, 908, 870, 725 cm^{-1} and ^1H NMR (400MHz, $CDCl_3$) with δ_H at 7.97-7.95 (4H, m, Ar-H), 7.55-7.51 (2H, m, Ar-H), 7.27-7.23 (8H, m, Ar-H), 4.99 (2H, d, *J* = 14.1Hz, Ar-CH_2), 3.74 (2H, d, *J* = 14.1Hz, Ar-CH_2), 3.32 (2H, t, *J* = 12.5Hz, N-CH_2 –CH_2), 2.56 (2H, t, *J* = 12.3Hz, N-CH_2 –CH_2), 1.06-0.97 (6H, m, CH_2), 0.71 (6H, t, *J* = 6.9Hz, CH_3), 0.23 (2H, bs, CH_2); the ^{13}C NMR (100MHz, $CDCl_3$) has δ_C at 151.03 (d, $J_{C\text{-}F}$ = 294.1Hz), 139.63 (ddd, $J_{C\text{-}F}$ = 254.1, 15.1, 15.1Hz), 138.30, 136.86, 134.63 (dd, $J_{C\text{-}F}$ = 12.7, 7.8Hz), 133.43, 131.13, 130.83, 128.30, 128.29, 127.68, 127.36, 123.32, 115.40-113.94 (m), 57.54, 57.34, 24.59, 19.32, 13.26. [Kitamura et al. *Angew Chem, Int Ed* **44** 1549 *2005*, Ooi et al. *J Org Chem* **68** 4576 *2003*.]
These are potent phase transfer organocatalysts for asymmetric α-alkylation of *N*-arylideneglycine *tert*-butyl ester derivatives for the synthesis of chiral α-substituted α-amino acids at extremely low concentrations of catalyst [Ooi et al. *Tetrahedron Asymm* **17** 603 *2006*].

Cetyltrimethylammonium bromide (cetrimonium bromide, CTAB) *[57-09-0]* **M 364.5, m 227-235°(dec).** Crystallise it from EtOH, EtOH/*benzene or from wet acetone after extracting twice with petroleum ether. Shake it with anhydrous diethyl ether, filter and dissolve it in a little hot MeOH. After cooling in the refrigerator, the precipitate is filtered off at room temperature and re-dissolved in MeOH. Anhydrous ether is added and, after warming to obtain a clear solution, it is cooled and the crystalline material is collected. [Dearden & Wooley *J Phys Chem* **91** 2404 *1987*, Hakemi et al. *J Am Chem Soc* **91** 120 *1987*, *Beilstein* **4** IV 819.]

Cetyltrimethylammonium chloride *[112-02-7]* **M 320.0.** Crystallise the chloride from acetone/ether mixture, EtOH/ether, or from MeOH. [Moss et al. *J Am Chem Soc* **109** 4363 *1987*, *Beilstein* **4** IV 819.]

Decyltrimethylammonium bromide *[2082-84-0]* **M 280.3, m 239-242°.** Crystallise the salt from 50% (v/v) $EtOH/Et_2O$, or from acetone and wash with ether. Dry it under vacuum at 60°. Also recrystallise it from EtOH and dry it over silica gel. [McDonnell & Kraus *J Am Chem Soc* **73** 2170 *1952*, Dearden & Wooley *J Phys Chem* **91** 2404 *1987*, *Beilstein* **4** IV 784.]

Didodecyldimethylammonium bromide *[3282-73-3]* **M 463.6, m 157-162°.** Recrystallise the salt from acetone, acetone/ether mixture, then from ethyl acetate, wash with ether and dry it in a vacuum oven at 60° [Chen et al. *J Phys Chem* **88** 1631 *1984*, Rupert et al. *J Am Chem Soc* **107** 2628 *1985*, Halpern et al. *J Am Chem Soc* **108** 3920 *1986*, Allen et al. *J Phys Chem* **91** 2320 *1987*]. [*Beilstein* **4** IV 801.]

Dioctadecyldimethylammonium bromide *[3700-67-2]* **M 630.9, m 161-163°.** Crystallise the bromide from acetone, then MeOH [Lukac *J Am Chem Soc* **106** 4387 *1984*]. Also purify it by chromatography on alumina by washing with $*C_6H_6$ and eluting with Me_2CO, evaporating and crystallising from MeCN [Swain & Kreevoy *J Am Chem Soc* **77** 1126 *1955*]. [*Beilstein* **4** IV 829.]

***N,N*-Dioctadecyl methylamine (hydrogen ionophore III)** *[4088-22-6]* **M 536.0, m 40°, 44-46°, 48-49°, b 252-259°, pK_{Est} ~10.** It can be distilled at high vacuum, but by dissolving in $*C_6H_6$, filtering and evaporating, a waxy solid suitable for electrode use can be obtained. It recrystallises from Me_2CO or MeCN. [Hoerr et al. *J Org Chem* **9** 201 *1944*, Wu & Yu *Talanta* **34** 577 *1987*, *Beilstein* **4** III 435.]

Dodecyltrimethylammonium chloride *[112-00-5]* **M 263.9, m 246°(dec).** Dissolve the chloride in MeOH, treat with active charcoal, filter and dry it *in vacuo* [Waldenburg *J Phys Chem* **88** 1655 *1984*], or recrystallise it several times from 10% EtOH in acetone. It has also been repeatedly crystallised from EtOH/ether or MeOH. [Cella et al. *J Am Chem Soc* **74** 2062 *1952*, *Beilstein* **4** IV 79.]

Hexyltrimethylammonium bromide *[2650-53-5]* **M 224.3, m 186°.** Recrystallise it from acetone. It is extremely *hygroscopic*. [McDowell and Kraus *J Am Chem Soc* **73** 2170 *1951*, *Beilstein* **4** IV 710.]

Octadecyl trimethylammonium bromide (stearyl trimethylammonum bromide) *[1120-02-1]* **M 392.5, m ~250°dec, 230-240°(dec).** Crystallise it from EtOH or H_2O (solubility is 1 in 1000parts). It is very soluble in Me_2CO. It is a bactericide. [Sheldon et al. *J Am Chem Soc* **68** 754 *1946*, Grieger & Kraus *J Am Chem Soc* **70** 3805, 38007, *Beilstein* **4** IV 827.]

Tetra-*n*-amylammonium bromide (tetra-*n*-pentylammonium bromide) *[866-97-7]* **M 378.5, m 100-101°.** Crystallise it from petroleum ether, *benzene or acetone/ether mixtures and dry it *in vacuo* at 40-50° for 2 days. It is used in ion-paired chromatography. (Sagara et al. *J Chromatogr* **328** 289 *1985*). [*Beilstein* **4** IV 677.]

Tetra-*n*-amylammonium iodide *[2498-20-6]* **M 425.5, m 135-137°.** Crystallise the iodide from EtOH and dry it at 35° under a vacuum. It has also been purified by dissolving in acetone and precipitating by adding diethyl ether, and drying at 50° for 2 days. [*Beilstein* **4** IV 677.]

Tetradecyltrimethylammonium bromide (myristyl trimethylammonium bromide) *[1119-97-7]* **M 336.4, m 244-245°, 244-249°.** Crystallise the bromide from acetone or a mixture of Me_2CO and >5% MeOH, or Me_2CO/EtOH. Wash it with diethyl ether and dry it in a vacuum oven at 60°. It is a cationic detergent. Its solubility is 1g/5g H_2O. [Dearden & Wooley *J Phys Chem* **91** 2404 *1987*, Shelton et al. *J Am Chem Soc* **68** 754 *1946*, *Beilstein* **4** III 419, **4** IV 813.]

Tetra-*n*-heptylammonium iodide *[3535-83-9]* **M 537.7, m 102-103°.** Crystallise the iodide from EtOH or aqueous EtOH. [Eriksen et al. *J Org Chem* **25** 849 *1960*, *Beilstein* **4** IV 736 for triheptylamine.]

Tetra-*n*-hexylammonium bromide *[4328-13-6]* **M 434.6, m 99-100°.** Wash the bromide with ether, and dry it in a vacuum at room temperature for 3 days.

Tetra-*n*-hexylammonium chloride *[5922-92-9]* **M 390.1.** Crystallise the chloride from EtOH.

Tetra-*n*-hexylammonium iodide *[2138-24-1]* **M 481.6, m 99-101°, 102-103°.** Wash the iodide with diethyl ether and dry it at room temperature *in vacuo* for 3 days. It is soluble in CH_2Cl_2. [Eriksen et al. *J Org Chem* **25** 849 *1960*, *Beilstein* **4** IV 711 for trihexylamine.]

Tetrahexylammonium perchlorate *[4656-81-9]* **M 454.1, m 104-106°.** Crystallise the salt from acetone and dry it *in vacuo* at 80° for 24 hours.

Tetrapentylammonium bromide. See tetra-*n*-amylammonium bromide above.

Tetra-*n*-propylammonium bromide *[1941-30-6]* **M 266.3, m >280°(dec).** Crystallise it from ethyl acetate/EtOH (9:1), acetone or MeOH. Dry it at 110° under reduced pressure. [*Beilstein* **4** IV 471.]

Tetra-*n*-propylammonium iodide *[631-40-3]* **M 313.3, m >280°(dec).** Purify the iodide by crystallising it from EtOH, EtOH/diethyl ether (1:1), EtOH/water or aqueous acetone. Dry it at 50° under a vacuum and store it over P_2O_5 in a vacuum desiccator. Store it away from light. [*Beilstein* **4** IV 472.]

Tri-*n*-butylhexadecylphosphonium bromide (TBHDTB, hexadecyltributylphosphonium bromide) *[14937-45-2]* **M 507.7, m 54°, 56-58°.** It is made by heating 1-bromohexadecane (1 mol, 112-82-3) and tri-*n*-butylphosphine (1 mol, 998-40-3) at 65° for 3 days. The mixture solidifies on cooling, and the solid is recrystal-

lised from hexane and dried *in vacuo* to give 68% of the phosphonium salt. [Starks *J Am Chem Soc* **93** 195 *1971*, *cf* for preparing fluorides see Landini et al. *Synthesis* 37 and 428 *1974*, for preparing disulfides see Landini & Rolla *Synthesis* 565 *1974*.]

Tri-*n*-dodecylamine (Hydrogen ionophore I) *[102-87-4]* **M 522.0, m 15.7°, b 220-228°/0.03mm, d_4^{20} 0.833, n_D^{20} 1.4577, pK_{Est} ~11.0.** Distil tridodecylamine under high vacuum and N_2, and store it in the absence of CO_2. It can be recrystallised from 95%EtOH/*C_6H_6 at low temperature under vacuum. The *hydrochloride* has **m** 78-79°. [Ra et al. *J Org Chem* **9** 259 *1944*, *Beilstein* **4** III 413, **4** IV 801.]

Tri-*n*-dodecylammonium nitrate *[2305-34-2]* **M 585.0.** Crystallise the salt from *n*-hexane/acetone (95:5) and keep it in a desiccator over P_2O_5 under vacuum. [*Beilstein* **4** IV 801 for tridodecylamine.]

Tri-*n*-dodecylammonium perchlorate *[5838-82-4]* **M 622.4.** Recrystallise the salt from *n*-hexane or acetone and keep it in a desiccator over P_2O_5. (Potentially explosive.)

Tri-*n*-octylammonium chloride *[1188-95-0]* **M 384.2, m 78-79°, pK^{25} 8.35 (in 70% aqueous EtOH).** Crystallise it from Et_2O, then *n*-hexane (see above). [Burrows et al. *J Chem Soc* 200 *1947*, *Beilstein* **4** H 196.]

Tri-*n*-octylammonium perchlorate *[2861-99-6]* **M 454.2, m >300°(dec).** Crystallise the perchlorate from *n*-hexane. (Possibly explosive.) [*Beilstein* **4** IV 754.]

IMIDAZOLINIUM IONIC LIQUID CRYSTAL CATALYSTS

A general discussion on ionic liquid crystals has already been made (see Chapter 3), and this section includes some commercially available liquid crystal 1,3-dialkylimidazolinium salts that participate in the catalytic process, i.e. by coordination with the metal component of catalysts, as well as assisting in other ways such as acting as a solvent, affecting the dielectric, and in phase transference of reagents. Depending on the *N*-alkyl substituents and the counter anion the salts may be more, or less, soluble in water or organic solvents. They are non-volatile (i.e. environmentally friendly), stable to water and air and many may be heated to temperatures as high as 300°, making it possible to distil off some products from them. They can be recovered for re-use. [See P. Wasserscheid and T. Welton, *Ionic Liquids in Synthesis* (2 volume set), Wiley VCH, Weinheim, *2008*. ISBN-10: 3527312390, ISBN-13: 978-3527312399.]

Preparation: Alkylation of *N*-1 of imidazole can be carried out using alkyl halide and alkoxide as for 1-ethylimidazole [1072-62-4], and the second alkylation onto *N*-3 is performed by further reaction with the desired alkylbromide (slightly less than a molar equivalent) in a solvent, e.g. 1,1,1-trichloroethane, at reflux for 2 hours. The molten bromide salt is separated from the solvent, washed with trichloroethane, dried on a Rotavap at 70°/0.1mm to give the bromide salt as a white solid or a liquid in high yield (~>90%) and high state of purity if the starting reagents are pure. Check purity by ^{1}H NMR and elemental analysis. The imidazolinium bromide salts are most useful as they can be converted into other salts, e.g. AcO^- with AgOAc, TfO^- with AgOTf, bis(trifluoromethylsulfonyl)imide [NTf_2^-] with NTf_2Li, nonafluorobutanesulfonate [NfO^-] with NfOK, etc. Generally the imidazolinium bromide and the metal salt of the required anion are dissolved in the least volume of H_2O at 70°, stirred for 1 hour (if silver halide precipitates it is filtered off), and the imidazolinium salt can be extracted into an organic solvent, e.g. CH_2Cl_2 or 1,1,1-trichloroethane, and the extract is then evaporated *in vacuo* and dried at 50°/0.1mm for 2 hours or until there is no further loss in weight. *Alternatively*, where possible, the 1-alkylimidazole is alkylated with e.g. alkyl toluene-*p*-sulfonate ester to provide the 1,3-dialkylimidazolinium toluene-*p*-sulfonate directly. [Bonhôte et al. *Inorg Chem* **35** 1168 *1996*.]

The following liquid crystal salts can be readily prepared in small or large quantities:

1-Butyl-3-methylimidazolinium Salts ($BMIM^+$ X^-, see Park & Kazlauskas *J Org Chem* **66** 8395 *2001* for improved preparation, purification and use at ambient temperature of some of the folowing ionic liquids in lipase-catalysed enantio- and regioselective acylation reactions**:**

$BMIM^+$ AcO^- *[284049-75-8]* **M 198.6; $BMIM^+$ NTf_2^-** *[174899-83-3]* **M 419.4, n_D^{20} 1.428,** [good synthetic activity of soluble *Candida antarctica* lipase B in this ionic liquid was obtained towards the enantioselective and operational stability for butyl butyrate synthesis and kinetic resolution of 1-phenylethanol in supercritical CO_2,

Lozano et al. *JCS, Chem Commun* 692 *2002*]**; BMIM$^+$ Br$^-$** *[85100-77-2]* **M 219.1,** [used in Heck reactions with Pd(OAc) where Pd-Im bond is formed, Xu et al. *Organometallics* **19** 1123 *2000*]**; BMIM$^+$ Cl$^-$** *[79917-90-1]* **M 174.7, m ~70°,** [used with $AlCl_3$ in Friedel-Crafts alkylation reactions, Chauvin et al. *J Mol Catal* **92** 155 *1994*]**; BMIM$^+$ (*n*-BuO)$_2$P(O)O$^-$** *[663199-28-8]* **M 348.4, n $_D^{20}$ 1.472; BMIM$^+$ (NC)$_2$N$^-$** *[448245-52-1]* **M 205.3; BMIM$^+$ SbF$_6^-$** *[174645-81-9]* **M 375.0;** and **BMIM$^+$ PF$_6^-$** *[174501-64-5]* **M 284.2, n $_D^{20}$ 1.411,** [used in allylation of RCHO with (Allyl)Sn, Gordon & McCluskey *JCS, Chem Commun* 1431 *1999*; in coupling of aryl halides by $(Ph_3)_nNi(0)$, Howarth et al. *Tetrahedron Lett* **41** 10319 *2000*; and catalyse the addition of CN (from TMSCN) to arylimines (from ArCHO + RNH_2) to form α-aminonitriles, Yadav et al. *New J Chem* **27** 462 *2003*]**; BMIM$^+$ HCO$_3^-$** *[366491-15-8]* **M 200.2, as 50% in 2:3 MeOH:H$_2$O; BMIM$^+$ HSO$_4^-$** (as **BASIONIC® AC 28**) *[262297-13-2]* **M 236.3; BMIM$^+$ MeSO$_3^-$** (as **BASIONIC® ST 78**) *[342789-81-5]* **M 234.3;** and **BMIM$^+$ MeSO$_4^-$** *[401788-98-5]* **M 250.3, n $_D^{20}$ 1.478**, [catalyse the addition of CN (from TMSCN) to arylimines (from ArCHO + RNH_2) to form α-aminonitriles, Yadav et al. *New J Chem* **27** 462 *2003*]**; BMIM$^+$ BF$_4^-$** *[174501-65-6]* **M 226.0,** {specifically catalyses the Biginelli reaction (formation of 3,4-dihydropyrimidin-2(1*H*)-ones from aldehydes + urea + $MeCOCH_2COR$), Peng & Deng *Tetrahedron Lett* **42** 5917 *2001*; **BMIM$^+$ PF$_6^-$** *[174501-64-5]* **M 284.2,** [catalyses the addition of CN (from TMSCN) to arylimines (from ArCHO + RNH_2)**}** to form α-aminonitriles, Yadav et al. *New J Chem* **27** 462 *2003*; assists in the bi-phasic hydrogenation of arenes at room temperature using a ruthenium cluster catalyst which coordinates with it, Dyson et al. *JCS, Chem Commun* 25 *1999*; and the molten salt catalyses the asymmetric hydrogenation of 2-arylacrylic acids by immobilised Ru-BINAP complex, Montiero et al. *Tetrahedron Asymmetry* **8** 177 *1997*; and is used in Palladium $[Pd(Ph_3)_4]$ catalysed Suzuki cross-coupling (aryl halides and arylboronic acids) at ambient temperature, Mathews et al. *JCS, Chem Commun* 1249 *2000*; and it specifically catalyses the Biginelli reaction (formation of 3,4-dihydropyrimidin-2(1*H*)-ones from aldehydes + urea + $MeCOCH_2COR$), Peng & Deng *Tetrahedron Lett* **42** 5917 *2001*}**;** and **BMIM$^+$ CF$_3$SO$_3^-$** *[174899-66-2]* **M 288.3, n $_D^{20}$ 1.434; BMIM$^+$ octylOSO$_3^-$** *[445473-58-5]* **M 348.5,** [this ionic liquid inceases the yield and enzyme stability of β-galactosidase in enzyme-catalysed syntheses, Kaftzik et al. *Org Process Res Dev* **6** 553 *2002*]**.**

1-Ethyl-3-methylimidazolinium Salts (EMIM$^+$ X$^-$, see Park & Kazlauskas *J Org Chem* **66** 8395 *2001* for improved preparation and use of ambient temperature of some of the folowing ionic liquids in lipase-catalysed enantio- and regioselective acylation reactions)**:**
EMIM$^+$ Br$^-$ *[65039-08-9]* **M 191.1,** [it is highly conductive at ~25° [Bonhôte et al. *Inorg Chem* **35** 1168 *1996*]**; EMIM$^+$ Cl$^-$** *[65039-09-0]* **M 146.6, m 77-79°; EMIM$^+$ (*n*-BuO)$_2$P(O)O$^-$** *[869858-84-4]* **M 320.4, n $_D^{20}$ 1.469; EMIM$^+$ AcO$^-$** *[143314-17-4]* **M 170.2, n $_D^{20}$ 1.502; EMIM$^+$ (CF$_3$CF$_2$-SO$_2$)$_2$N$^-$** *[216299-76-2]* **M 491.3, m ≤1°,** [very stable fluorinated ionic liquids that are extremely hydrophobic]; **EMIM$^+$ NTf$_2^-$** *[174899-82-2]* **M 391.3, m ≥15°**, [it is a useful medium for the enantioselective cyclopropanation of styrene with ethyldiazoacetate, promoted by two different Cu-bis(oxazoline) complexes and its recovery, Fraile et al. *Tetrahedron Asymmetry* **12** 1891 *2001*; and good synthetic activity of soluble *Candida antarctica* lipase B in this ionic liquid was obtained towards the enantioselective and operational stability for butyl butyrate synthesis and kinetic resolution of 1-phenyl ethanol in supercritical CO_2, Lozano et al. *JCS, Chem Commun* 692 *2002*]; **EMIM$^+$ (CN)$_2$N$^-$** *[370865-89-7]* **M 177.2,** [its conductivity is ~26,000 μS/cm, and its electrochemical window is -2.4 to +3.3 V, cf Bonhôte et al. *Inorg Chem* **35** 1168 *1996*]**; EMIM$^+$ PF$_6^-$** *[155371-19-0]* **M 256.1, m 58-62°,** [it is prepared by mixing $EMIM^+$ Cl^- (29.3g, 200mmol) and 60% aqueous HPF_6 (9.g, 200mmol) in H_2O (300ml), the resulting mixture of white solid and liquid are cooled in an ice bath for 2 hours and the $EMIM^+$ PF_6^- (31.8g 62%) is dried *in vacuo*. Recrystalisation from MeOH provides crystals for X-ray structural analysis. [Fuller et al. *JCS. Chem Commun* 299 *1994*]**;** and **EMIM$^+$ BF$_4^-$** *[143314-16-3]* **M 198.0, m 15°, b >350°, d $_4^{25}$ 1.294, n $_D^{20}$ 1.413,** [its conductivity is ~11,500 μS/cm, and its electrochemical window is -2.2 to +3.5 V, cf Bonhôte et al. *Inorg Chem* **35** 1168 *1996*]; the salt is prepared by stirring Ag_2O (23.2g,100mmol) with 48% aqueous HBF_4 (36.9g, 200mmol) in H_2O (300ml) until the Ag_2O has reacted completely to give a clear solution, then $EMIM^+$ Cl^- (29.2g, 200mmol) dissolved in H_2O is added and the mixture is stirred for 2 hours, the AgCl is filtered off, the filtrate is evaporated *in vacuo* and the colourless residue is dried in a vacuum oven at 60° to give the BF_4^- salt (33.6g, 85%). [Fuller et al. *JCS, Chem Commun* 299 *1994*].

CHIRAL AUXILIARIES

These compounds are involved in reactions, which direct stereospecificity and are decomposed, e.g. by

hydro-lysis, reduction, to generate the desired chiral products and the remains of the original auxiliary which can be recycled. Unlike the case of catalysis, the auxiliary is involved stoichiometrically and is not recycled during the reaction. It is one of the products of the reaction and can, *via* other reactions if necessary, be used to regenerate the original auxiliary. These have been used for decades and are of necessity chiral molecules themselves. The auxiliaries have to be linked to the molecule that has a reactive group which can be operated on, e.g. carbonyl, to generate an asymmetric centre, e.g. a chiral alcohol. This section includes more recently available auxiliaries, although many useful ones such as cinchonine, cinchonidine, borneols, camphors, menthol derivatives, substituted sugars, substituted chiral heterocycles (e.g. pyrrolidines), sterols etc. will be found scattered in Chapters 4, 5 and 7. [see Evans *Aldrichimica Acta* **15** 23 *1982*, Ager et al. *Chem Rev* ***96*** 835 *1996*, Ager et al. *Aldrichimica Acta* **30** 3 *1997*, Mukaiyama *Aldrichimica Acta* **29** 59 *1996*, K. Rück-Braun and H. Kunz *Chiral Auxiliaries in Cycloaddition Reactions* Wiley-VCH, Weinheim *1999*, ISBN 3-527-29386-8.]

***R*-(-)- and *S*-(+)- Acetyl-cyclopentadienyl-ironcarbonyl triphenylphosphine complex [*R- and S-* (η^5-C_5H_5)Fe(CO)(CH_3CO) (PPh_3)]** *[R 36548-61-5; S 36548-60-4; RS 12101-02-9]* **M 454.3, m 142°, (+), 140° (–), 145° (±), *R*-[α] $^{27}_{436}$ –288°, [α] $^{22}_{546}$ –288° (c 0.045, C_6H_6), *S*- [α] $^{22}_{546}$ +288° (c 0.045, C_6H_6).** This racemic "chiral" auxilliary can be made on a large scale from [η^5-(C_5H_5)Fe(CO)$_2$]$_2$ [38117-54-3] which is cleaved with Na/Hg to give the anion [η^5-(C_5H_5)Fe(CO)$_2^-$ (Na^+)] that is methylated to η^5-(C_5H_5)Fe(CO)COMe (m **78-82°**, caramel coloured waxy crystals from sublimation *in vacuo* onto an ice-cooled glass finger) with MeI [Piper & Wilkinson *J Inorg Nucl Chem* **3** 104 *1956*, Aktogu et al. *J Organomet Chem* **262** 49 *1984*, King *Organometallic Synthesis Vol 1*, Academic Press, NY, p 145 *1965*]. This methyl complex provides the racemic title compound when treated with PPh_3. Thus (C_5H_5)Fe(CO)$_2$Me (1.0g, 5mmol) and PPh_3 (1.3g, 5mmol) in redistilled THF (10ml) are refluxed (65°) under N_2 until the Fe-Me band (IR: strong C-H deformation band at 1170 cm^{-1} in CS_2) disappears (~48 hours). The solution is filtered, the solvent is evaporated (to ~20mm), the residue is dissolved in pentane (10ml), passed through an Al_2O_3 column (5 x 20cm), and only one band (yellow orange to orange) is eluted with pentane which, on evaporation (at ~20mm), provides the analytically pure orange (±)-*η^5-C_5H_5)Fe(CO)(CH_3CO)(PPh_3)*, m 145° in ~98% yield. This reaction is solvent dependent, i.e. no reaction occurs in boiling hexane (68°), and is only 50% complete in boiling Et_2O (34°) after 48 hours. The solid is stable in air, is soluble in organic solvents, e.g. pentane, hexane, Et_2O, THF, CH_2Cl_2, $CHCl_3$, and *C_6H_6, but is insoluble in MeOH or H_2O. Solutions in $CHCl_3$, and *C_6H_6 decompose rapidly in air to produce brown intractable solids. Hence these solutions should be prepared and used under N_2 or argon. Its IR ($CHCl_3$) has bands with ν_{max} at 1598 (s, MeC=O) and 1920 (vs, br, Fe carbonyl) cm^{-1}; and the ^{1}H NMR (60MHz, $CDCl_3$, external TMS) has δ_H at 7.59 (m, Ph, 15H), 4.69 (s, C_5H_5, 5H) and 2.52 (s, COMe, 3H). [Bibler & Wojcicki *Inorg Chem* **5** 889 *1966*, Butler et al. *Inorg Chem* **6** 2074 *1967*.]

The versatility of this acetyl auxiliary has prompted its **optical resolution** into the pure enantiomers which proved to be very good chiral auxiliaries for preparing a variety of optically active molecules where high stereo control is achieved. Two independent resolutions were achieved, both involving 1*R,2S,5R*-(–)-2-isopropyl-5-methylcyclohexan-1-ol (*R-(l*-menthol). The first is from the reaction of sodium *R*-menthylate ($NaOC_{10}H_{19}$, *R*-menthyl refers to the radical produced by loss of the hydroxyl group) and (±)-*(η^5-C_5H_5)Fe(CO)$_2$(PPh_3)$^+PF_6^-$* (see below) recovered from hydrolysis, decomplexation, of derivatives of the racemic title compound Aktogu et al. [*J Organomet Chem* **262** 49 *1984*] to give a diastereoisomeric mixture of (+)-*(C_5H_5)Fe(CO)(PPh_3)-(–)CO $OC_{10}H_{19}$* {[α] $^{20}_{589}$ +30°, [α] $^{20}_{579}$ +35°, [α] $^{20}_{546}$ +70°, [α] $^{20}_{436}$ –1450° (in 10^{-3}M *C_6H_6)}, and (–)-*C_5H_5)Fe(CO)(PPh_3)-(–)COO$C_{10}H_{19}$* {[α] $^{20}_{589}$ –75°, [α] $^{20}_{579}$ –80°, [α] $^{20}_{546}$ –120°, [α] $^{20}_{436}$ +1550° (in 10^{-3}M *C_6H_6)}, (together with $NaPF_6$) which were separated by recrystallisation from pentane, with the latter being more soluble. [Brunner & Schmidt *J Organomet Chem* **21** P53 *1970*.] Then the ester with [α] $^{20}_{546}$ –120° (560mg, 0.93mmol) in THF (20ml) at –30°, is treated dropwise with MeLi (1ml of 1.5M Et_2O solution), followed by stirring at –30°/1 hour, then at ~25°/1 hour. After quenching the reaction and evaporating, the brown residue is extracted into *C_6H_6, and purified through a column of Al_2O_3/3%H_2O and eluted with *C_6H_6. The greenish zone gives a menthol-free yellow solid, which on sublimation provides analytically pure orange (+)-*η^5-(C_5H_5)Fe(CO)(CH_3CO)(PPh_3)* (47mg, 11% yield), m 142°, [α] $^{20}_{546}$ –228° (in 10^{-3}M *C_6H_6), found M 465 (osmometry in *C_6H_6). Similarly the menthyl ester with [α] $^{20}_{546}$ +70° gives pure (–)-*η^5-(C_5H_5)Fe(CO)(CH_3CO)(PPh_3)* (80mg, 30% yield), m 140°, [α] $^{20}_{546}$ +227° (in 10^{-3}M *C_6H_6), found M 464 (osmometry in *C_6H_6). From the CD and ORD spectra it was concluded that these reactions occurred with ***inversion*** of configuation at the tetrahedral iron centre [Brunner & Schmidt *J Organomet Chem* **36** C18 *1972*].

In the second resolution *R-(–)-chloromethylmenthyl ether* (***R-*** *is the configuration at* 1-C-OH *of menthol*, see [26127-08-2]) was reacted with the lithium salt of (±)-η^5-$(C_5H_5)Fe(CO)(CH_3CO)(PPh_3)$ (generated with *n*-BuLi) to give the diastereomeric ethers (–)-η^5-$(C_5H_5)Fe(CO)(PPh_3)(COCH_2CH_2O$-(–)-$C_{10}H_{19}$ {$[\alpha]_D^{20}$ +65° (c 0.4, *C_6H_6)}, and (+)-η^5-$(C_5H_5)Fe(CO)(PPh_3)(COCH_2CH_2O$-(–)-$C_{10}H_{19}$ {$[\alpha]_D^{20}$ –150° (c 0.4, *C_6H_6)} which are separable by chromatography and distinguishable by ^{1}H NMR (300MHz). Crystals of the latter diastereoisomer were subjected to x-ray crystallographic analysis which revealed that the absolute configuration at the tetrahedral Fe centre was ***R*** by virtue that the absolute configuration of the *R*-menthyl moiety had been established. Since the original formation of these ethers occurs with alteration in the configuration at the Fe centre, then the desired *S*-(+)- and *R*-(–)- configurations of (±)-η^5-$(C_5H_5)Fe(CO)(CH_3CO)(PPh_3)$ are established. It was also shown that Brunner & Schmidt's reactions of the *R*-menthyl esters with *n*-BuLi to provide the title enantiomers occurred with ***complete*** inversion of configuration (as determined by 500MHz ^{1}H NMR spectroscopy). The enantiomers can be discriminated in solution (9mg in 700µl of $CDCl_3$) containing the chiral shift reagent Eu(tfc) {tris[3-(trifluouomethylhydroxymethylene)-(+)-camphorato] europium (III), see [34834-11-0]} (0.48mg in 8µl) where a clear separation of the methyl singlets in the 300MHz ^{1}H NMR spectra occurs: the *S*-(+)-enantiomer has δ at 2.66 and the *R*-(–)-enantiomer has δ at 2.58 (from TMS). [Davies et al. *JCS Chem Commun* 607 *1986*.]

The chiral auxiliary properties of the complexes η^5-$C_5H_5)Fe(CO)(CH_3CO)(PPh_3)$ are displayed by deprotonation with *n*-BuLi ($isoPr_2NLi$ in THF has also been used) to give the blood-red enolate which undergoes a variety of reactions and sequences of reactions (homochiral synthesis) that are highly stereoselective. These include alkylation, homochiral succinylation, asymmetric aldol reactions, formation of α,β-unsaturated iron acyls and homochiral dienolates, asymmetric Michael addition reaction, asymmetric synthesis of β-amino acids and β-lactams, asymmetric synthesis of cyclopropanecarboxylic acids, asymmetric synthesis of chiral sulfoxides, and chirality recognition for homochiral synthesis. [Davies *Aldrichimica Acta* **23** 31 *1990*.] Decomplexation at the end of the reactions can be achieved by oxidative cleavage (Br/MeOH, H_2O or *n*-$BuNH_2$, NBS/EtOH) to provide the acid, amide or ester, also by alcoholysis (to provide different esters) from which the products can be isolated. From the aqueous solution η^5-$C_5H_5)Fe(CO)_2(PPh_3)^+PF_6^-$ (evaporated to 20ml, from 1mmol of complex product) can be recovered by addition of NH_4PF_6 (0.6g, 3.7mmol), stirring for 1 hour, evaporating to dryness, and the residue is extracted with CH_2Cl_2 (3 x 10ml). The combined extracts are evaporated to 5ml and Et_2O is added to give pale yellow crystals of the complex salt (0.38g, 65%, m 186°). It can also be recrystallised from Me_2CO/Et_2O or Me_2CO/hexane. It has IR (Nujol) with ν_{max} at 2055 and 2010 (terminal CO, in $CHCl_3$) and 1435s, 1090s, 995w, 880m, 850-820vs, br, 740m, 700m, 685m, 605m, 575m, 555m, 525m, 500w cm^{-1}; and the ^{1}H NMR (60MHz, Me_2CO, TMS) has δ_H at 5.62 (d, $J_{P,H}$ = 1.5Hz, C_5H_5) and 7.68 (m, Ph, 15H). [Aktogu et al. *J Organomet Chem* **262** 49 *1984*, Treichel et al. *Inorg Chem* **5** 1177 *1966*.]

1R,2S,5R*-(-)-Chloromethylmenthylether [*R-(-)-chloromethylmenthyl ether*]** *[26127-08-2]* **M 204.7, b 62°/0.1mm, 160-162°/13-16mm, d 0.9821, d^{25} 0.994, n_D^{20} 1.467, n_D^{27} 1.465, $[\alpha]_D^{24}$-177.0° (c 1, CH_2Cl_2),** and ***1S,2R,5S*-(+)-chloromethylmenthyl-ether [*S-(+)-chloromethylmenthyl ether*]** *[103128-76-3]* **M 204.7, b 72°/0.4mm, d^{21} 0.994, n_D^{20} 1.467, $[\alpha]_D^{24}$+181.0° (c 2, CH_2Cl_2).** The chloro methyl derivatives of *R-(l)-* and *S-(+)-* menthol respectively are useful chiral auxiliary resolving agents (see previous entry) as they can be readily removed by mild hydrolysis and the recovered menthol can be recycled. The *R*-(*l*)-enantiomer is prepared by melting *l*-menthol (100g, 0.64moles) on a water bath and stirring vigorously with 40% w/w aqueous formalin (50g, 0.67moles) while HCl gas is bubbled through. The mixture warms up at first and has to be cooled at 0° until no more gas dissolves. The clear mixture separates into two layers, the upper layer is removed and the lower layer is dried over Na_2SO_4. This is filtered and fractionated under reduced pressure from some unreacted menthol, formaldehyde trimer and HCl to give the *chloromethyl ether* (120-130g, 91-99%) as a slightly refracting oil which distils steadily at 160-162°/16mm (and 62°/0.1mm), but it decomposes at *ca* 230°/atm. The pure ether has $[\alpha]_D^{21}$ -172.75° (c 6.78 $CHCl_3$). On heating in EtOH/charcoal it forms the ***dimethylmethylal $\mathbf{C_{10}H_{19}OCH_2OC_{10}H_{19}}$ which crystallises from aqueous EtOH in greasy looking scales or from Et_2O in colourless needles m 57° (b 337°/atm), with $[\alpha]_D^{24}$ -77.94° (c 0.8 EtOH). The *chloromethylmenthyl ethers* hydrolyse in H_2O to menthol, HCHO and HCl so they should be stored in an inert atmosphere in the cold [Wedekind *Chem Ber* **34** 813 *1901*, Deutsches Reichspatent No. 119008, D.R.P. 189331 *Chem Zentralblatt* **1** 184 *1908*]. [*Beilstein* **6** H 32, **6** I 21.]

4*R*-(+)-4-Isopropyl-5,5-dimethyl-2-oxazolidinone (4*R*-(+)-4-isopropyl-5,5-dimethyl-1,3-oxazolidin-2-one) *[223906-38-5]* **and 4*S*-(-)-4-isopropyl-5,5-dimethyl-2-oxazolidinone (4*S*-(-)-4-isopropyl-5,5-dimethyl-1,3-**

oxazolidin-2-one) *[168297-86-7]* **M 157.2, m 86-87°, $[\alpha]_D^{20}$ ±47° (c 1, H_2O).** The starting chiral ethanolamine is prepared from the methyl esters of chiral α-aminoacids (*R*- or *S*- valine in this case) by reaction with MeMgI/Et_2O to give chiral 2,2-dimethylvalinol which is converted into the desired chiral 2-oxazolidinones with $(EtO)_2CO/K_2CO_3$ (as in the following entry), or by reaction with CCl_3COCl (in pyridine) or carbonyl-diimidazole (in CH_2Cl_2) as carbonyl equivalents. Similarly by using the esters of chiral alanine, norleucine or α-phenylglycine the respective optically active 5,5-dimethyl-2-oxazolidinones where the 4-isopropyl group is replaced by methyl, *n*-butyl and phenyl groups respectively can be prepared. These auxilliaries have been named "second series Quat auxilliaries", the first series being substituted 3,3-dimethyl-2-pyrrolidinones [Davies et al. *Tetrahedron Lett* **35** 2369, 2373 *1994*]. The present 2-oxazolidinones can be *N*-acylated, (e.g. with BuLi, then RCH_2COCl or MeCH=CHCOCl), and the *N*-acyl moieties can be the targets for highly stereoselective enolate alkylation and conjugate addition reactions. The products can be hydrolysed (e.g. with LiOH, THF/H_2O 3:1, 0° at ~25°) to provide the respective chiral acids and regenerated oxazolidin-2-one. The *gem*-dimethyl groups enhance the face-stereoselective shielding of the attached *N*-acyl moeity leading to very high diastereomeric excess in the products. [Davies & Sanganee *Tetrahedron Asymm* **6** 671 *1995*, *cf*: review by Mukaiyama *Aldrichimica Acta* **29** 59 *1996*.]

4*R*-(+)-4-Isopropyl-2-oxazolidinone (4*R*-(+)-4-isopropyl-1,3-oxazolidin-2-one) *[95530-58-8]* **and 4*S*-(-)-4-isopropyl-2-oxazolidinone (4*S*-(-)-4-isopropyl-1,3-oxazolidin-2-one)** *[17016-83-0]* **M 129.2, m 70-71.5°, 70-72°, 71-72°, *R*- $[\alpha]_D^{20}$ +18°, *S*- $[\alpha]_D^{20}$ -18°, (c 6, EtOH).** These compounds are *Evans' type* of chiral auxiliaries. The *S*-enantiomer was prepared by stirring 1mol of *S*-valinol, 1.1mol of diethyl carbonate and 1mol of anhydrous K_2CO_3 at 125-126° (internal temperature) until 2.0mols of EtOH had distilled off (4-6 hours). The cooled mixture (to 20°) is dissolved in Et_2O, filtered through a pad of Celite to remove the K_2CO_3, evaporated to a small volume and cooled slowly to 0° when the oxazolinone crystallises as white needles (m 69-70°, 85-95% yield). It is soluble in CH_2Cl_2 and recrystallises from hexanes/EtOAc (4:1, v/v) by allowing it to stand at 6° overnight. On TLC (0.25mm silica gel 60-F plates) it has R_F 0.19 (hexanes/EtOAc 6:4,v/v). It has $[\alpha]_{589}$ -16.6°, $[\alpha]_{577}$ -17.3°, $[\alpha]_{546}$ -20.2°, $[\alpha]_{435}$ -37.3°, $[\alpha]_{365}$ -63.7° (c 5.81, EtOH); the IR (CH_2Cl_2) has ν_{max} at 1240, 1400, 1760, 2980, 3060, 3240-3340, 3480 cm^{-}; and the ^1H NMR (90MHz, $CDCl_3$) has δ at 6.7 (br s, 1H, NH), 4.42 (t, *J* = 8.6Hz, 1H, C_5-H), 4.07 (d of d, *J* = 8.5, 6.5Hz, 1H, C_5–H), 3.58 (d of t, *J* = 8.6, 6.5Hz, 1H, C_4–H), 1.9-1.6 (m, 1H, C_4–H), 0.95 (overlapping d's, *J* = 6.0Hz, 6H, $CH(CH_3)_2$). [Evans et al. *J Org Chem* **50** 1830 *1985*, Evans et al. *J Am Chem Soc* **103** 2127 *1981*.]

The ***4S-(+)-4-isopropyl-3-propionyl-1:3-oxazolidine-2-one derivative*** *[77877-9-1]* **M 185.2,** has **b 102-106°/0.75mm, d_4^{25} 1.094, n_D^{20} 1.464, $[\alpha]_D^{25}$ +93° (c 8.7, CH_2Cl_2).** An auxiliary reagent also used as a chiral ligand in dirhodium (II) complexes [Doyle et al. *J Am Chem Soc* **115** 9968 *1993*], and in aldol addition reactions [Pridgen et al. *J Org Chem* **58** 5107 *1993*]. For a reviews on chiral auxiliaries for asymmetric synthesis see Ager et al. *Aldrichimica Acta* **30** 3 *1997*, and Mukaiyama *Aldrichimica Acta* **29** 59 *1996*.

4*R*-(+)-4-Isopropyl-2-oxazolidinethione [4*R*-(+)-4-isopropyl-1,3-oxazolidin-2-thione, (*4R*)-4-(1-methyl-ethyl)-2-oxazolidinethione) *[1217463-35-8]* **and** 4**S*-(-)-4-isopropyl-2-oxazolidinethione (4*S*-(-)-4-isopropyl-1,3-oxazolidin-2-thione)** *[104499-08-3]* **M 145.2, m 48-52°, 51-53°, *R*- $[\alpha]_D^{20}$ +23.2°, *S*- $[\alpha]_D^{20}$ -23.2°, (c 0.4, $CHCl_3$).** These compounds are *Evans type* of chiral auxiliaries. The *S*-(-)-enantiomer is synthesised by adding CS_2 (0.9ml, 15mmol) to a solution of *S*-valinol (10mmol [cf 2026-48-4]) in aqueous N Na_2CO_3 (20ml) and stirring at 100° (bath at 110° under efficient reflux and fume-cupboard) for 15 minutes, cooling to 20° and extracting with CH_2Cl_2 (2 x 50ml). The extract is dried (Na_2SO_4), filtered, evaporated to dryness and the residue is recrystallised from EtOAc/cyclohexane or EtOAc/hexane. It has UV (EtOH) with λ_{max} at 244 nm (ε 18,800); the IR has ν_{max} (KBr) at 3160 and 1515 cm^{-1}; and the ^1H NMR (300MHz, $CDCl_3$) has δ at 0.77 (d, 3H, *J* = 6.8Hz), 0.82 (d, 3H, *J* = 6.7Hz), 1.68 (m, 1H), 3.77 (d of t, 1H, *J* = 6.6 and 9.1Hz), 4.23 (d of d, 1H, *J* = 6.6 and 9.1Hz), 4.55 (t, 1H, *J* = 9.1Hz), 9.00 (br s, 1H); and the ^{13}C NMR (75.5MHz, $CDCl_3$) has δ at 189.54, 73.53, 62.52, 32.17, 18.04, 17.90. [Delaunay et al. *J Org Chem* **60** 6604 *1995*, Nagao et al. *J Chem Soc, Perkin Trans I* 2361 *1985*.] They are selective and efficient chiral auxiliaries [Velazquez & Olivio *Current Org Chem* **6** 303 *2000*] which can be directly reduced to their corresponding aldehydes and the chiral auxiliary by reductive cleavage with diisobutylaluminium hydride [Crimmins & Chaudhary *Org Lett* **2** 775 *2000*].

4*R*-(+)-4-Isopropyl-2-thiazolidinethione (4*R*-(+)-4-isopropyl-1,3-thiazolidin-2-thione) *[110199-16-1]* **and** 4**S*-(-)-4-isopropyl-2-thiazolidinethione (4*S*-(-)-4-isopropyl-1,3-thiazolidin-2-thione)** *[76186-04-4]* **M 161.3,**

m 66-67°, 67-68°, 69-71°, *R*- $[\alpha]_D^{20}$ +37°, *S*- $[\alpha]_D^{20}$ -37° (c 1, $CDCl_3$). These compounds are efficient *Evans type* of chiral auxiliaries. The *S*-(-)-enantiomer was synthesised by adding CS_2 (3ml, 50mmol) to a solution of *S*-valinol (10mmol (see [2026-48-4]) in aqueous N KOH (50ml) and stirring at 100° (bath at 110° under reflux and efficient fume-cupboard) for 16 hours, cooling to 20° and extracting with CH_2Cl_2 (2 x 50ml). The extract is dried (Na_2SO_4), filtered, evaporated to dryness and the residue is recrystallised from CH_2Cl_2 (colourless needles) or Et_2O. ***Note*** that unlike the preparation of the 1,3-oxazolidine-2-thione above, the preparation of the 1,3-thiazolidine-2-thione required a larger excess of CS_2, stronger base and much longer heating time to replace the alcoholic O by S. It has ^1H NMR (300MHz, $CDCl_3$) with δ at 1.00 (d, 3H, *J* = 7.2Hz), 1.03 (d, 3H, *J* = 8.5Hz), 2.01 (m, 1H), 3.32 (d of d, 1H, *J* = 8.2 and 11.0Hz), 3.53 (d of d, 1H, *J* = 8.2 and 11.0Hz), 4.11 (m, 1H), 9.05 (br s, 1H); and the ^{13}C NMR (75.5MHz, $CDCl_3$) has δ at 200.78, 70.20, 35.73, 31.98, 18.78, 18.18. [Delaunay et al. *J Org Chem* **60** 6604 *1995*, Nagao et al. *J Chem Soc. Chem Commun* 1418 *1985*, Nagao et al. *J Org Chem* **51** 2391 *1986*, McKinnon & Meyer *J Org Chem* **58** 3568 *1993*.] They are selective and efficient chiral auxiliaries [Velazquez & Olivio *Current Org Chem* **6** 303 *2000*], and the condensation products can be directly reduced to the corresponding aldehyde and the chiral auxiliary by reductive cleavage with diisobutylaluminium hydride [Crimmins & Chaudhary *Org Lett* **2** 775 *2000*].

1*R*(-)-Menthol [natural *l-(-)-*, 1*R*,2*S*,5*R*-(-)-1-hydroxy-2-*iso*propyl-5-methylcyclohexane] *[2216-51-5]* **M 156.3, m 42-45°, 43°, 44-46.5°, 89°/2mm, 100-101°/7mm, 212°/atm, d^{25} 0.89, n_D^{25} 1.458, n_D^{60} 1.446, $[\alpha]_D^{20}$ - 50° (c 10, EtOH), $[\alpha]_{546}^{18}$ - 58.7° (c 2, EtOH),** and **1*S*(+)-menthol [synthetic *d-(+)-*menthol, 1*S*,2*R*,5*S*-(+)-1-hydroxy-2-*iso*propyl-5-methylcyclohexane]** *[15356-60-2]* **m 43-44°, 103-104°/9mm, d^{25} 0.89, n_D^{25} 1.458, n_D^{60} 1.446, $[\alpha]_D^{23}$ + 48° (c 10, EtOH), $[\alpha]_{546}^{18}$ +58,6° (c 2, EtOH).** The natural *l*-isomer is present in peppermint oil and has a strong odour of peppermint, and is sometimes called peppermint camphor. Crystallise menthol from $CHCl_3$, petroleum ether or EtOH/water. It can be sublimed at 40° *in vacuo*, but distillation at 5-10mm is preferable with large quantities. It is best stored under N_2 in the dark. It is soluble in most organic solvents but is slightly soluble in H_2O. [Barrow & Atkinson *J Chem Soc* 638 *1939*, *Beilstein* **6** III 133, **6** IV 150.] *l*-(-)-Menthol is a very useful resolving agent for acids [Brunel & Buono *J Org Chem* **58** 7313 *1993*, see also resolution of the Fe complex [12101-02-9] above], and has been used in crystallisation-induced asymmetric transformation of malonate esters [Ihara et al. *J Chem Soc, Chem Commun* 9 *1988*]. It is a chiral auxiliary that can be recycled [Solladié et al. *Synthesis* 173 *1987*, Katagiri et al. *J Org Chem* **53** 227 *1988*]. Similar purification and applications are applicable for *non-natural d*-(+)-menthol, with the advantage of producing the optical enantiomers of the products. The *racemic* form ***1RS,2SR,5RS-(±)-1-hydroxy-2-isopropyl-5-methylcyclohexane (hexahydro-thymol) [****1490-04-6]* **M 156.3, m 28° and 38° (dimorphic), b 216.5°/atm, d^{30} 0.8911, n_D^{20} 1.4415, n_D^{60} 1.4461**, is obtained by catalytic hydrogenation of thymol [89-83-8] followed by distillation. **[**Huggett *J Soc Chem Ind* **60** 67 *1941*, Waters & Beal *J Am Pharm Assoc* **34** 52 *1945*, *Beilstein* **6** III 137, **6** IV 152.]

LEWIS AND BRØNSTED/LOWRY ACIDS AND BASES

A few words are warranted here because these terms are frequently used in current literature. The definition of acids (which produce H^+ ions) and bases (which produce HO^- ions) was adequate to explain reactions (e.g. salt formation) in aqueous solutions, and led to the concepts of pH (S.P.L. Sørensen *Biochem Z* **21** 131, 201 *1909*) and pK (ionisation, cf: Chapter 1 pp 34-36). The definition becomes unsatisfactory when applied to studies of reactions in non-aqueous media, particularly in the catalytic context. Independently, J.N. Brønsted [*Rec Trav Chim Pays Bas* **42** 718 *1923*, *Chem Rev* **5** 231 *1928*] and T.M. Lowry [*J Soc Chem Ind* (London) **42** 42 *1923*] developed the view that an acid is a substance that has a tendency to lose a proton, and a base is one that has a tendency to gain a proton. This led to the understanding of *conjugate* species, e.g. R_3NH^+ as potential acids, and defining the equilibrium: *Base* + H^+ ⇆ H-*Base*$^+$. They pointed out that the differences in nett charge is not as important as the chemical behaviour on which their definition is based. Basicity and acidity do not bear a simple relationship to the nett respective charges, and both their properties depend much more on the complex electronic constitutions of the reagents. Later G.N. Lewis (1928 and later work) began with the classical concept of acids and bases, and progressed to a broader definition of an acid as a substance that is able to accept a pair of electrons, and a base as a substance capable of supplying a pair of electrons. This broader definition has been used extensively for reactions in non-aqueous solutions as well as in aqueous solutions. [Note that these concepts originated from extensive studies of catalytic reactions, e.g. mutarotation, hydrolysis, etc]. Thus a

Lewis acid is a substance that is electron deficient (e.g. BF_3), and a Lewis base is a substance that can donate electrons (e.g. amines, phosphines, boranes, ethers, sulfides etc) to form bonds or complexes with Lewis acids.
In the *Brønsted/Lowry definition*, a base donates an electron pair to a proton to form a covalent B—H bond (a positive charge, if involved, will reside on B). In the *Lewis definition*, a base donates a pair of electrons to an electron deficient atom (other than a proton). An acid does not donate a proton but accepts a base to form a new bond. An electron pair is required for forming a covalent or a dative bond.
In the broadest form, an acid is an *electrophile* whereas a base is a *nucleophile*. When these species are regenerated during reactions then they become catalytic. For general reading see Michael B. Smith *Organic Chemistry*: *An Acid-Base Approach* CRC Press *October 2010*, ISBN 10: 1420079204, 13: 9781420079203.

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CHAPTER 7

PURIFICATION OF BIOCHEMICALS AND RELATED PRODUCTS

INTRODUCTION

Biochemicals are chemical substances produced by living organisms. They range widely in size, from simple molecules such as formic acid and glucose to macromolecules such as proteins and nucleic acids. Their *in vitro* synthesis is often impossibly difficult, and in such cases they are available (if at all) only as commercial tissue extracts which have been subjected to purification procedures of widely varying stringency. The desired chemical may be, initially, only a minor constituent of the source tissue which may vary considerably in its composition and complexity. Recent advances in molecular biology have made it possible to produce substantial amounts of biological materials, which are present in nature in extremely small amounts, by recombinant DNA technology and expression in bacteria, yeast, insect and mammalian cells. The genes for these substances can be engineered such that the gene products, e.g. polypeptides or proteins, can be readily obtained in very high states of purity, and in large amounts if necessary. However, many such products, which are still obtained from the original natural sources, are available commercially and may require further purification.

As a preliminary step the tissue might be separated into phases [e.g. whole egg into white and yolk, blood into plasma (or serum) and red cells], and the desired phase may be homogenised. Subsequent treatment usually comprises filtration, solvent extraction, salt fractionation, ultracentrifugation, chromatographic purification, gel filtration and dialysis. Fractional precipitation with ammonium sulfate gives crude protein species. Purification is finally judged by the formation of a single band of macromolecule (e.g. protein, DNA) on electrophoresis and/or analytical ultracentrifugation. Although these generally provide good evidence of high purity, nonetheless it does not follow that one band under one set of experimental conditions is an absolute indication of homogeneity [D.S. Vodopich and R. Moore, *Biology Laboratory Manual*, McGraw-Hill, *2007*, ISBN 9780072995220].

During the past 20 or 30 years a wide range of methods for purifying substances of biological origin have become available. For small molecules (including many sugars and amino acids) reference should be made to Chapters 1 and 2. The more important methods used for large molecules, polypeptides and proteins in particular, comprise:

1. *Centrifugation.* In addition to centrifugation for sedimenting proteins after ammonium sulfate precipitation in dilute aqueous buffer, the technique has been used for fractionation of large molecules in a denser medium or a medium of varying density. By layering sugar solutions of increasing densities in a centrifuge tube, proteins can be separated in a sugar-density gradient by centrifugation. Smaller DNA molecules (e.g. plasmid DNA) can be separated from RNA or nuclear DNA by centrifugation in aqueous cesium chloride (*ca* 0.975g/ml of buffer) for a long time (e.g. 40 hours at 40,000 x g). The plasmid DNA band appears at about the middle of the centrifuge tube and is revealed by the fluorescent pink band formed by the binding of DNA to ethidium bromide which is added to the CsCl buffer. *Microfuges* are routinely used for centrifugation in Eppendorf tubes (1.2-2ml) and can run up to speeds of 12,000 x g. *Analytical centrifugation*, which is performed under specific conditions in an analytical ultracentrifuge is very useful for determining purity, aggregation of protein subunits and the molecular weight of macromolecules. [D. Rickwood, T.C. Ford and J. Steensgaard (Eds), *Centrifugation: Essential Data Series*, J Wiley & Sons, *1994*, ISBN 9780471942719; L.L. Regel and W.R. Wilcox, *Processing by Centrifugation*, Springer, *2001*, ISBN 9780306466546; J.M. Graham and D. Rickwood, *Biological Centrifugation*, Springer, *2001*, 9781859960370; A. Records and K. Sutherland, *Decanter Centrifugation Handbook*, Elsevier, *200I,* ISBN 1856173690].

Purification of Laboratory Chemicals. http://dx.doi.org/10.1016/B978-0-12-382161-4.00007-8

2. *Gel filtration* with polyacrylamide (mol wt exclusion limit from 3000 to 300,000) and agarose gel (mol wt exclusion limit 0.5 to 150 x 10^6) is useful for separating macromolecules. In this technique high-molecular-weight substances are too large to fit into the gel microapertures and pass rapidly through the matrix (with the void volume), whereas low-molecular-weight species enter these apertures and are held there for longer periods of time, being retarded by the column material in the equilibria, relative to the larger molecules. This method is also used for desalting solutions of macromolecules.
   *Dry gel*s and *crushed beads* are also useful in the gel filtration process. Selective retention of water and inorganic salts by the gels or beads (e.g. Sephadex G-25) results in increased concentration and purity of the protein fraction which moves with the void volume. (See also section on "Gel filtration" in Chapter 1.)

3. *Ion-exchange matrices* are microreticular polymers containing carboxylic acid (e.g. Bio-Rad 70) or phosphoric acid (Pharmacia, Amersham Biosciences, Mono-P) exchange functional groups for weak acidic cation exchangers, sulfonic acid groups (Dowex 50W) for strong acidic cation exchangers, diethylaminoethyl (DEAE) groups for weakly basic anion exchangers and quaternary ammonium (QEAE) groups for strong anion exchangers. The old cellulose matrices for ion exchanges have been replaced by Sephadex, Sepharose or Fractogel which have more even particle sizes with faster and more reproducible flow rates. Some can be obtained in fine, medium or coarse grades depending on particle size. These have been used extensively for the fractionation of peptides, proteins and enzymes. The use of *p*H buffers controls the strength with which the large molecules are bound to the support in the chromatographic process. Careful standardisation of experimental conditions and similarly the very uniform size distribution of Mono beads have led to high resolution in the purification of protein solutions. MonoQ is a useful strong anion exchanger, and MonoS is a useful strong cation exchanger, whereas MonoP is a weak cation exchanger (Pharmacia, Amersham Biosciences and alternative sources, see Chapter 1). These have been successful with medium pressure column chromatography (HPLC, see below in 7). Chelex 100 binds strongly and removes metal ions from macromolecules. [See sections on "HPLC", "Ion-exchange Resins" and "Ion-exchange Celluloses and Sephadex" in Chapter 1.]

4. *Hydroxylapatite* is used for the later stages of purification of enzymes. It consists essentially of hydrated calcium phosphate which has been precipitated in a specific manner. It combines the characteristics of gel and ionic chromatography. Crystalline hydroxylapatite is a structurally organised, highly polar material which, in aqueous solution (in buffers), strongly adsorbs macromolecules such as proteins and nucleic acids, permitting their separation by virtue of the interaction with charged phosphate groups and calcium ions, as well as by physical adsorption. The procedure therefore is not entirely ion-exchange in nature. Chromatographic separations of singly and doubly stranded DNA are readily achievable, whereas there is negligible adsorption of low-molecular-weight species.

5. *Affinity chromatography* is a chromatographic technique whereby the adsorbant has a particular and specific affinity for one of the components of the mixture to be purified. For example the adsorbant can be prepared by chemically binding an inhibitor of a specific enzyme (which is present in the crude complex mixture) to a matrix (e.g. Sepharose). When the mixture of impure enzyme is passed through the column containing the adsorbant, only the specific enzyme binds to the column. After adequate washing, the pure enzyme can be released from the column by either increasing the salt concentration (e.g. NaCl) in the eluting buffer or adding the inhibitor to the eluting buffer. The salt or inhibitor can then be removed by dialysis, gel filtration (above) or ultrafiltration (see below). [See W.H. Scouten, *Affinity Chromatography: Bioselective Adsorption on Inert Matrices*, J.Wiley & Sons, NY, *1981*, ISBN 0471026492; H. Schott, *Affinity Chromatography: Template Chromatography of Nucleic Acids and Proteins*, Marcel Dekker, NY, *1984*, ISBN 0824771117; P. Matejtschuk Ed. *Affinity Separations* Oxford University Press 1997 ISBN 0199635501 (paperback); M.A. Vijayalakshmi, *Biochromatography, Theory and Practice*, Taylor & Francis Publ, 2002, ISBN 0415269032; and the section on "Other Types of Chromatography" in Chapter 1.]

6. In the *Isoelectric focusing* of large charged molecules on polyacrylamide or agarose gels, slabs of these are prepared in buffer mixtures (e.g. ampholines) which have various pH ranges along the length of the gel. When a voltage is applied for some time, the buffers arrange themselves on the slabs in respective areas according to their pH ranges (prefocusing). Then the macromolecules are applied near the middle of the slab and allowed to migrate in the electric field until they reach the pH area similar to their isoelectric points and focus at that position. This technique can also be used in a chromatographic mode, *chromatofocusing*, whereby a gel in a column is run (also under HPLC conditions) in the presence of ampholines (narrow or wide pH ranges as required) and the macromolecules are then run through in a buffer. *Capillary electrophoresis* systems in which a current is applied to set the gradient are now available in which the columns are fine capillaries and are used for qualitative and quantitative purposes [See R. Kuhn and S. Hoffstetter-Kuhn, *Capillary Electrophoresis*: Principles and Practice, Springer-Verlag Inc, NY, *1993*; P. Camilleri Ed. *Capillary Electrophoresis-Theory and Practice*, CRC Press, Boca Raton, Florida, *1993*; D.R. Baker, *Capillary Electrophoresis*, J Wiley & Sons, NY, *1995*; P.G. Righetti,

A. Stoyanov and M. Zhukov, *The Proteome Revisited, Isoelectric Focusing; J.Chromatography Library Vol* **63** *2001*, Elsevier, ISBN 0444505261, P. Schmitt-Kopplin, *Capillary Electrophoresis: Methods and Protocols,* Humana, *2007*, ISBN 9781588295392; J.P. Landers, *Handbook of Capillary & Microchip Electrophoresis and Associated Microtechniques*, CRC Press, Boca Raton, Florida, *2007*, ISBN 9780849333293, C. Henry, *Microchip Capillary Electrophoresis*, Humana, *2006*, ISBN 9781588292933.] The bands are eluted according to their isoelectric points. Isoelectric focusing standards are available which can be used in a preliminary run in order to calibrate the effluent from the column, or alternatively the pH of the effluent is recorded using a glass electrode designed for the purpose. Several efficient commercial equipment are available for separating proteins on a preparative and semi-preparative scale.

7. *High performance liquid chromatography* (HPLC) is liquid chromatography in which the eluting liquid is sent through the column containing the packing (materials as in 2-6 above, which can withstand higher than atmospheric pressures) under pressure. On a routine basis this has been found useful for purifying proteins (including enzymes) and polypeptides after enzymic digestion of proteins or chemical cleavage (e.g. with CNBr) prior to sequencing (using reverse-phase columns such as μ-Bondapak C18). Moderate pressures (50-300psi) have been found most satisfactory for large molecules (FPLC). [See Scopes *Anal Biochem* **114** 8 *1981*; *High Performance Liquid Chromatography and Its Application to Protein Chemistry,* Hearn in *Advances in Chromatography,* **20** 7 *1982*; B.A. Bidlingmeyer *Practical HPLC Methodology and Applications*, J Wiley & Sons, NY *1991*; L.R. Snyder, J.L. Glajch and J.J. Kirkland *Practical HPLC Method Development*, J Wiley & Sons, NY *1988*; ISBN 0471627828; R.W.A. Oliver, *HPLC of Macromolecules: A Practical Approach*, 2nd Edn, Oxford University Press, *1998*, T. Hanai, *HPLC: A Practical Guide*, Royal Society of Chemistry (UK), *1999*, ISBN 084045155; P. Millner *High Resolution Chromatography*, Oxford University Press, *1999* ISBN 0199636486; see also Chapter 1, Bibliography.]

8. *Ultrafiltration* (UF) using a filter (e.g. Millipore) can remove water and low-molecular-weight substances without the application of heat. Filters with a variety of molecular-weight exclusion limits not only allow the concentration of a particular macromolecule to be determined, but also the removal (by washing during filtration) of smaller molecular-weight contaminants (e.g. salts, inhibitors or cofactors). This procedure has been useful for changing the buffer in which the macromolecule is present (e.g. from Tris-Cl to ammonium carbonate), and for desalting. Ultrafiltration can be carried out in a stirrer cell (Amicon) in which the buffer containing the macromolecule (particularly protein) is pressed through the filter, with stirring, under argon or nitrogen gas pressure (e.g. 20-60psi). During this filtration process the buffer can be changed. This is rapid (e.g. 2L of solution can be concentrated to a few mls in 1 to 2 hours depending on pressure and filter). A similar application uses a filter in a specially designed tube (Centricon tubes, Amicon) and filtration occurs under centrifugal force in a centrifuge (4-6000rpm at 0^o/40min). The macromolecule (usually DNA) then rests on the filter and can be washed on the filter also by centrifugation. The macromolecule is recovered by inverting the filter, placing a conical receiver tube on the same side where the macromolecule rests, filling the other side of the filter tube with eluting solution (usually a very small volume e.g. 100 μL), and during further centrifugation this solution passes through the filter and collects the macromolecule from the underside into the conical receiver tube. With the development of polymeric and ceramic nanofilters use can be made of nanofiltration (NF) in which particles or molecules of less than 2nm can be held back. This is to be compared with UF where the size limit is between 2nm and 0.1μm (see Chapter 8).

9. *Partial precipitation* of a protein in solution can often be achieved by controlled addition of a strong salt solution, e.g ammonium sulfate. This is commonly the first step in the purification process. Its simplicity is offset by possible denaturation of the desired protein and the (sometimes gross) contamination with other proteins. It should therefore be carried out by careful addition of small aliquots of the powdered salt or concentrated solution (below 4^o, with gentle stirring) and allowing the salt to be evenly distributed in the solution before adding another small aliquot. Under carefully controlled conditions and using almost pure protein, it is sometimes possible to obtain the protein in crystalline form suitable for X-ray analysis (see below).

10. *Dialysis*. This is a process by which small molecules, e.g. ammonium sulfate, sodium chloride, are removed from a solution containing the protein or DNA using a membrane which is porous to small molecules. The solution (e.g. 10ml) is placed in a dialysis bag or tube tied at both ends, and stirred in a large excess of dialysing solution (e.g. 1.5 to 2 L), usually a weak buffer at *ca* 4^o. The dialysing buffer is replaced with fresh buffer several times, e.g. four times in 24 hours. This procedure is similar to ultrafiltration (above) and allows the replacement of buffer in which the protein, or DNA, is dissolved. It is also possible to concentrate the solutions by placing the dialysis tube or bag in Sephadex G25 which allows the passage of water and salts from the inside of the bag thus concentrating the protein (or DNA) solution. Dialysis tubing is available from various distributors, but "Spectra/por" tubing (from Spectrum Medical Industries, Inc, LA) is particularly effective because it retains macromolecules and allows small molecules to dialyse out very rapidly, thus reducing dialysing time considerably. This procedure is used when the buffer has to be changed so as to be compatible with the next purification or storage step, e.g. when the protein (or DNA) needs to be stored frozen in a particular buffer over

extended periods. UF and NF can also serve this purpose whereby the solvent can be completely replaced by washing with an alternative solvent.

11. *Gel Electrophoresis.* This is becoming a more commonly used procedure for purifying proteins, nucleic acids, nucleoproteins, polysaccharides and carbohydrates. The gels can be "electroblotted" onto membranes, and the modern procedures of identifying, sequencing (proteins and nucleic acids) and amplifying (nucleic acids) on sub-micro scales have made this technique of separation a very important one. See below for polyacrylamide gel electrophoresis (PAGE), [D. Patel *Gel Electrophoresis*, J.Wiley-Liss, Inc., *1994*; P. Jones and D. Rickwood, *Gel Electrophoresis: Nucleic Acids*, J. Wiley and Sons, *1999* (paperback) ISBN 0471960438; D.M. Gersten and D. Gersten, *Gel Electrophoresis: Proteins*, J. Wiley and Sons, *1996*, ISBN 0471962651; R. Westermeier *Electrophoresis in Practice*, 4th Edn, Wiley-VCH Publishing, *2004* ISBN 9783527311811].

12. *Crystallisation.* The ultimate in purification of proteins or nucleic acids is crystallisation. This involves very specialised procedures and techniques and is best left to the experts in the field of X-ray crystallography who can provide a complete picture of the structure of these large molecules. [A. Ducruix and R. Giegé Eds, *Crystallisation of Nucleic Acids and Proteins: A Practical Approach*, 2nd Edition, *2000*, Oxford University Press, ISBN 0199636788 (paperback); T.L. Blundell and L.N. Johnson *Protein Crystallisation*, Academic Press, NY, *1976*; A. McPherson *Preparation and Analysis of Protein Crystals*, J.Wiley & Sons, NY, *1982*; A. McPherson, *Crystallisation of Biological Macromolecules*, Cold Spring Harbour Laboratory Press, *2001* ISBN 0879696176, see also Bibliography in Chapter 1.]

Other details of the above can be found in Chapters 1 and 2 which also contain relevant references.

Several illustrations of the usefulness of the above methods are given in the *Methods Enzymol* series (Academic Press) in which 1000-fold purifications or more have been readily achieved. In applying these sensitive methods to macromolecules, reagent purity is essential. It is disconcerting, therefore, to find that some commercial samples of the widely used affinity chromatography ligand Cibacron Blue F3GA contained this dye only as a minor constituent. The major component appeared to be the dichlorotriazinyl precursor of this dye. Commercial samples of Procion Blue and Procion Blue MX-R were also highly heterogeneous [Hanggi and Cadd *Anal Biochem* **149** 91 *1985*]. Variations in composition of sample dyes can well account for differences in results reported by different workers. The purity of substances of biological origin should therefore be checked by one or more of the methods given above. Water of high purity should be used in all operations. Double glass distilled water or water purified by a MilliQ filtration system (see Chapter 2) is most satisfactory.

Brief general procedures for the purification of polypeptides and proteins. Polypeptides of up to *ca* 1-2000 (10-20 amino acid residues) are best purified by reverse phase HPLC. The desired fractions that are collected are either precipitated from solution with EtOH or lyophilised. The purity can be checked by HPLC and identified by microsequencing (1-30 picomoles) to ascertain that the correct polypeptide was in hand. Polypeptides larger than these are sometimes classified as proteins and are purified by one or more of the procedures described above. The purification of enzymes and functional proteins which can be identified by specific interactions is generally easier to follow because enzyme activities or specific protein interactions can be checked (by assaying) after each purification step. The commonly used procedures for purifying soluble proteins involve the isolation of an aqueous extract from homogenised tissues or extracts from ruptured cells from microorganisms or specifically cultured cells, for example, by sonication, freeze shocking or passage through a small orifice under pressure. Contaminating nucleic acids are removed by precipitation with a basic protein, e.g. protamine sulfate. The soluble supernatant is then subjected to fractionation with increasing concentrations of ammonium sulfate. The required fractions are then further purified by the procedures described in sections 2-9 above. If an affinity adsorbant has been identified, then affinity chromatography can provide an almost pure protein in one step sometimes even from the crude extract. The rule of thumb is that a solution with a protein concentration of 1mg/ml has an absorbance A_{1cm} at 280nm of 1.0 units. Membrane-bound proteins are usually insoluble in water or dilute aqueous buffer and are obtained from the insoluble fractions, e.g. the microsomal fractions from the >100,000 x g ultracentrifugation supernatant. These are solubilised in appropriate detergents, e.g. Mega-10 (nonionic), Triton X-100 (ionic) detergents, and purified by methods 2 to 8 (previous section) in the presence of detergent in the buffer used. They are assayed also in the presence of detergent or membrane lipids.

The purity of proteins is best checked by *polyacrylamide gel electrophoresis* (PAGE). The gels are either made or purchased as pre-cast gels and can be with uniform or gradient gel composition. Proteins are applied onto the gels *via* wells set into the gels or by means of a comb, and travel along the gel surface by means of the current applied to the gel. When the buffer used contains sodium dodecylsulfate (SDS), the proteins are denatured and the denatured proteins (e.g. as protein subunits) separate on the gels mainly according to their molecular sizes. These can be identified by running marker proteins, with a range of molecular weights, simultaneously on a track alongside the proteins under study. The protein bands are visualised by fixing the gel (20% acetic acid) and staining with Coomassie blue followed by silver staining if higher sensitivity is required. An Amersham-Pharmacia "Phast Gel Electrophoresis" apparatus, or related equipment, is very useful for rapid analysis of proteins. It uses small pre-cast polyacrylamide gels (two gels can be run simultaneously) with various uniform or gradient polyacrylamide concentrations as well as gels for isoelectric focusing. The gels are usually run for 0.5-1.5 hours and can be stained and developed (1-1.5 hours) in the same apparatus. The equipment can be used to "electroblot" the protein bands onto a membrane from which the proteins can be isolated and sequenced or subjected to antibody or other identification procedures. It should be noted that all purification procedures are almost always carried out at *ca* 4º in order to avoid denaturation or inactivation of the protein being investigated.

There has been considerable necessity for, and interest in, the study of **Proteomics.** This involves the identification, quantitation and isolation of all the proteins produced by a cell or organism at a particular point in time. It provides information on the expression of **all** the proteins produced by particular cells at a desired stage of the cell's development, maturity, activation or condition. A sophisticated apparatus for this purpose is a flat bed polyacrylamide gel which is run electrophoretically in one direction according to the extent of polymerization of the acrylamide and then run at right angles along a pH gradient (isoelectric focusing). Hundreds of polypeptides and proteins are thus separated, collected and identified by various other techniques such as LC-MS-MS, capillary electrophoresis etc (T. Palzkill, *Proteomics*, Springer, *2001*, ISBN 0792375653; T.D. Veenstra and R.D. Smith *Proteome Characterization and Proteomics*, Academic Press, *2003*, ISBN 9780120342655; R. Westermeier, T. Naven and H-R. Höpker, *Proteomics in Practice: A Guide to Successful Experimental Design.* J. Wiley & Sons, *2008*, ISBN 9783527319411; the *Journal of Proteomics (ISSN: 1874-3919)*, which is the official journal of *The European Proteomics Association* published by Elsevier, has been running for several years and is but one of the many journals on Proteomics and Bioinformatics that are avaliable and can be viewed on the internet; see also Bibliography in Chapter 1).
Another rapidly developing field is **metabolomics** where metabolites are screened and identified in the normal and diseased cell at specfic time intervals. These cannot be identified from studies of *genomics*, *transcriptomics* or *proteomics*. The subject is now possible because of the highly improved power of HPLC, GC, MS, NMR and the interfacing of these instruments. Thus *metabolones* can be mapped for various biological systems (plant and animal). Publications that are available include the *Metabolomics Journal* published by SpringerLink and started in 2005, and *Journal of Metabolomics and Systems Biology (JMSB)*, published by Academic Journals which started in 2011. These periodicals publish original papers, reviews and conference reports.

Anyone contemplating the purification of a protein is referred to: Professor R.K. Scopes's monograph *Protein Purification*, 3rd Edn, Springer-Verlag, New York, *1994*, ISBN 0387940723; M.L. Ladisch Ed. *Protein Purification - from Molecular Mechanisms to Large-scale Processes*, American Chemical Society, Washington DC, *1990*; E.L.V. Harris and S. Angal, *Protein Purification Applications - A Practical Approach*, IRL Press, Oxford, *1990*; J.C. Janson and L. Rydén, *Protein Purification - Principles, High Resolution Methods and Applications*, VCH Publ. Inc., *1989*; ISBN 0895731223, Satinder Ahja *Handbook of Bioseparations*, Academic Press, *2000*, ISBN 0120455404; S.M. Wheelwright, *Protein Purification: Design and Scale up of Downstream Processing,* J Wiley & Sons, *1994*, references in the bibliography in Chapter 1, and selected volumes of *Methods Enzymol*, e.g. M.P. Deutscher (Ed), Guide to Protein Purification, *Methods Enzymol*, Academic Press, Vol **182** *1990*, ISBN 0121820831; M.A. Vijayalakshmi, *Biochromatography, Theory and Practice*, Taylor & Francis Publ, *2002*, ISBN 0415269032; J.S. Davies, *Amino Acids, Peptides and Proteins Vol* **32** *2001*, A Specialist Periodical Report, Royal Society of Chemistry, ISBN 0854042326; S. Roe, *Protein Purification Techniques: A Practical Approach*, 2nd Edn, Oxford University Press, *2001*, ISBN 0199636737; J.M. Walker (Ed) *The Protein Protocols Handbook*, 3rd Edn (Springer Protocols Handbooks) Humana Press, 2009, ISBN 978-1-60327-474-6, e-ISBN 978-1-59745-198-7; T. Palmer, *Enzymes, Biochemistry, Biotechnology, Clinical Chemistry,* Horwood Publishing, *2001*, ISBN 1898563780. For a comprehensive treatise of many volumes see *Springer Handbook of*

Enzymes D. Schonburg & I. Schonburg Eds (A. Chang co-Ed) Springer-Verlag, Berlin, Heidelberg, *2003-onwards (with 39 volumes in 2011)* <http://www.springer.de>

Brief general procedures for purifying DNA. Oligo-deoxyribonucleotides (up to *ca* 60-mers) are conveniently purified by HPLC (e.g. using a Bio-Rad MA7Q anion exchange column and a Rainin Instrument Co, Madison, Dynamax-300A C_8 matrix column) and used for a variety of molecular biology experiments. Plasmid and chromosomal DNA can be isolated by centrifugation in cesium chloride buffer (see section 1, Centrifugation above), and then re-precipitated with 70% ethanol at -70^o (18 hours), collected by centrifugation (microfuge) and dried in air before dissolving in TE (10mM TrisHCl, 1mM EDTA pH 8.0). The DNA is identified on an Agarose gel slab (0.5 to 1.0% DNA grade in 45mM Tris-borate + 1mM EDTA or 40mM Tris-acetate + 1mM EDTA pH 8.0 buffers) containing ethidium bromide which binds to the DNA and under UV light causes it to be visualised as pink fluorescent bands. Marker DNA (from λ phage DNA cut with the restriction enzymes Hind III and/or EcoRI) with bands running from 72 to 353 base-pairs (bp) are run in a parallel track in order to estimate the size of the unknown DNA. Various other DNA markers are commercially available such as the step ladder ranging from 50bp to 800bp with bands at 50bp intervals, and the step ladder with bands ranging from 100bp to 4000bp with bands at 200bp intervals. The DNA can be isolated from the band on the gel by transfer onto nitro-acetate paper (e.g. NA 45) electrophoretically, by binding to silica or an ion-exchange resin, extracted from these adsorbents and precipitated with ethanol. The DNA pellet is then dissolved in TE buffer and its concentration determined. A solution of duplex DNA (or RNA) of 50μg/ml gives an absorbance of 1.0unit at 260nm/1cm cuvette (single-stranded DNA or RNA gives a value of 1.3 absorbance units). DNA obtained in this way is suitable for molecular cloning.
Recombinant and chemically synthesised DNA and RNA are now routinely separated and purified by HPLC, and their structures are confirmed by sequencing an aliquot. A variety of commercially available HPLC systems are now available, and the desired system can be selected from them.
Brief mention must be made of the tremendous advances that have been made in recent years in the fields of DNA, RNA gene sequencing and synthesis. The development of instrumentation and analysers by the Illumina Company (www.illumina.com/) and the "*Ion torrent"* semiconductor sequencing of DNA and RNA, using an ion PGM (personal genome machine) sequencer (see; http://lifetech-it.hosted.jivesoftware.com/index.jspa) have made it possible to sequence complete genomes in a matter of weeks or less.

For experimental details on the isolation, purification and manipulation of DNA and RNA the reader is referred to: J. Sambrook, E.F. Fritsch and T. Maniatis, *Molecular Cloning-A Laboratory Manual*, 2nd Edn (3 volumes), Cold Spring Harbor Laboratory Press (CSHL Press) NY, *1989*, ISBN 0879693096 (paperback); P.D. Darbre, *Basic Molecular Biology: Essential Techniques*, J. Wiley and Sons, *1998*, ISBN 0471977055; J. Sambrook and D.W. Russell, *Molecular Cloning-A Laboratory Manual*, 3rd Edn (3 volumes), Cold Spring Harbor Laboratory Press, NY, *2001*, ISBN 0079695773, ISBN 9780879695774 (paperback), ISBN 0079695765 (cloth bound); J. Sambrook and D.W. Russell, *The Condensed Protocols for Molecular Cloning: A Laboratory Manual*, CSHL Press, *2006*, ISBN 9780879697716, also available on line; M.A. Vijayalakshmi, *Biochromatography, Theory and Practice*, Taylor & Francis Publ, *2002*, ISBN 0415269032; A. Travers and M. Buckle, *DNA-Protein Interactions: A Practical Approach,* Oxford University Press, *2000*, ISBN 0199636915 (paperback); R. Rapley and D.L. Manning Eds *RNA: Isolation and Characterisation Protocols,* Humana Press *1998* ISBN 0896034941; R. Rapley, *The Nucleic Acid Protocols Handbook*, Humana Press *2000* ISBN 0896038416 (paperback).

This chapter lists some representative examples of biochemicals and their origins, a brief indication of key techniques used in their purification, and literature references where further details may be found. Simpler low-molecular-weight organic compounds, particularly those that may have been prepared by chemical syntheses, e.g. acetic acid, will be found in Chapter 4. Only a small number of enzymes and proteins are included because of space limitations. The purification of the ones that have been included has been described only briefly. The reader is referred to comprehensive texts such as the *Methods Enzymology* (Academic Press, see below) series which currently runs to volume 489 in 2011, and *The Enzymes* (3rd Edn, Academic Press) which runs to 22 volumes for methods of preparation and purification of proteins and enzymes. Leading references on proteins will be found in *Advances in Protein Chemistry* which was incorporated with *Advances in Structural Biology* (84 volumes (2011), Elsevier Inc) and on enzymes will be found in *Advances in Enzymology* which then became *Advances in Enzymology and Related Areas of Molecular Biology,* J Wiley & Sons (up to volume 77 in 2011). The *Annual Reviews of Biochemistry* (Annual Reviews Inc. Patlo Alto California) is also an excellent source of

key references to the up-to-date information on known and new natural compounds, from small molecules, e.g. enzyme cofactors to proteins and nucleic acids. See also the *Springer Handbook of Enzymes* cited above.

Abbreviations of titles of periodical are defined as in the Chemical Abstracts Service Source Index (CASSI).

Ionisation constants of ionisable compounds are given as **pK** values (published from the literature) and refer to the **pKa** values at room temperature (~15ºC to 25ºC). The values at other temperatures are given as superscripts, e.g. $\mathbf{pK^{25}}$ for 25ºC. Estimated values are entered as $\mathbf{pK_{Est(1)}}$ ~ (see section on "Ionisation Constants" in Chapter 1 for further information).

Benzene, which has been used as a solvent successfully and extensively in the past for reactions and purification by chromatography and crystallisation is now considered a **very dangerous substance**, so it has to be used with extreme care. We emphasise that an alternative solvent to benzene (e.g. toluene, toluene-petroleum ether, or a petroleum ether to name a few) should be used first. However, if benzene has to be used then all operations have to be performed in well-ventilated fumehoods and precautions taken to avoid inhalation and contact with skin and eyes. Whenever benzene is mentioned in the text, an asterisk e.g. *C_6H_6 or *benzene, is inserted to remind the user that special precaution should be adopted.

Selected Amino acids and peptides, Proteins Enzymes DNA and RNA, Carotenoids, Carbohydrates, Steroids, and Miscellaneous Compounds (which include Biochemical reagents, Cofactors, Coenzymes and Vitamins) are collected in the separate respective sections of this chapter.

AMINO ACIDS and PEPTIDES

This section includes amino acid derivatives and related compounds.

***N*-Acetyl-L-alaninamide** *[15962-47-7]* **M 130.2, m 162°.** Crystallise the amide repeatedly from EtOH/diethyl ether. The (±)-*isomer* crystallises from H_2O and has **m** 157-158°. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 1838 *1961*. de Jong *Rec Trav Chim Pays Bas* **19** 288 *1900*, Fischer & Otto *Chem Ber* **36** 2106 *1903*, *Beilstein* **4** H 295.]

***N*-Acetyl-β-alanine** *[3025-95-4]* **M 127.2, m 78.3-80.3°, pK^{25} 4.45.** The **β**-alanine crystallises from acetone. [King & King *J Am Chem Soc* **78** 1089 *1956*, *Beilstein* **4** IV 2526, 2548.]

***N*-Acetyl-L-alanyl-L-alaninamide** *[30802-37-0]* **M 201.2, m 250-251°.** Crystallise the dipeptide derivative repeatedly from EtOH/diethyl ether.

***N*-Acetyl-L-alanyl-L-alanyl-L-alaninamide** *[29428-34-0]* **M 272.3, m 295-300°.** Crystallise the tripeptide derivative from MeOH/diethyl ether.

***N*-Acetyl-L-alanylglycinamide** *[76571-64-7]* **M 187.2, m 148-149°.** Crystallise the dipeptide derivative repeatedly from EtOH/diethyl ether.

Acetyl-α-amino-*n*-butyric acid *[34271-24-4]* **M 145.2**, **pK^{25} 3.72.** Crystallise the acid twice from water (charcoal) and dry it in air [King & King *J Am Chem Soc* **78** 1089 *1956*].

Acetylcarnitine chloride (2-acetoxy-3-carboxy-*N,N,N*-trimethylpropanamine HCl) *[S(*D+*)- 5080-50-2*, *R(*L-*)- 5061-35-8*, *RS 2504-11-2]* **M 239.7, m 181°, 187°(corr, dec), 197°(dec), $[\alpha]_D^{25}$ -28° (c 2, H_2O) for *S*-isomer, pK^{25} 3.6.** Recrystallise the chloride from isopropanol. Dry it over P_2O_5 under high vacuum. The *S-betaine* crystallises from EtOH/Et_2O with **m** 145°(dec) and is hygroscopic; it has $[\alpha]_D^{20}$ -19.5° (c 6, H_2O). [Krimberg & Wittandt *Biochem Z* **251** 231 *1932*, Strack et al. *Z Physiol Chem* **238** 191 *1936*, *Beilstein* **4** III 1630, 1632.]

***R*-(-)-*N*-Acetyl-L-cysteine methyl ester** *[7652-46-2]* **M 177.2, m 71-78°, 80°, $[\alpha]_D^{20}$ -24.0° (c 1, MeOH).** The ester is purified by converting into the cuprous mercaptide which is decomposed by dilute H_2SO_4, extracted into Et_2O, dried (Na_2SO_4), filtered, evaporated and the residue recrystallised from H_2O containing a little AcOH. The crystals are dried in a vacuum. These operations should be carried out in an inert atmosphere (N_2 or argon) to avoid oxidation to the disulfide cystin ester. Note that the cuprous salt is only stable when it is dry, but is readily oxidised when wet. It has been used as a sulfur transfer agent [Gilman & Spero *Tetrahedron Lett* **33** 1751 *1993*]. [Pirie *Biochem J* **25** 618 *1931*, *Beilstein* **4** III 1607.]

***N*-Acetylglutamic acid** *[1188-37-0]* **M 189.2, m 185° (*RS*), 201° (*S*), $[\alpha]_D^{25}$ -16.6° (in H_2O), $[\alpha]_D^{25}$ -5.6° (c 4, MeOH) for *S-enantiomer*, $pK_{Est\ (1)}$ ~3.4, $pK_{Est(2)}$ ~4.3.** A likely impurity is glutamic acid. Crystallise it from boiling water. It inhibits *N*-acetyl-L-glutamate synthase. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 1948 *1961*, Shigesada & Tatibana *Eur J Biochem* **84** 285 *1978*, Coude *Biochem Biophys Res Commun* **102** 1016 *1981*, *Beilstein* **4** IV 3047.]

***N*-Acetylglycinamide** *[2620-63-5]* **M 116.1, m 139-139.5°.** Crystallise the amide repeatedly from EtOH/Et_2O. Dry it in a vacuum desiccator over KOH. [Davis & Levy *J Chem Soc* 3485 *1951*, Fischer & Otto *Chem Ber* **36** 2106 *1903*, *Beilstein* **4** IV 2401.]

***N*-Acetylglycine** *[543-24-8]* **M 117.1, m 206-208°, pK_1^{25} -1.92, pK_2^{25} 3.69.** *N*-Acetylglycine is treated with acid-washed charcoal and recrystallised three times from water or EtOH/Et_2O and is dried *in vacuo* over KOH [King & King *J Am Chem Soc* **78** 1089 *1956*]. [*Beilstein* **4** IV 2399.]

***N*-Acetylglycyl-L-alaninamide** *[34017-20-4]* **M 175.2.** Crystallise the dipeptide derivative repeatedly from EtOH/Et_2O. Dry it in a vacuum desiccator over KOH.

***N*-Acetylglycylglycinamide** *[27440-00-2]* **M 173.2, m 207-208°.** Crystallise the dipeptide derivative repeatedly from EtOH/Et_2O. Dry it in a vacuum desiccator over KOH.

***N*-Acetylglycylglycylglycinamide** *[35455-24-4]* **M 230.2, m 253-255°.** Crystallise the tripeptide derivative repeatedly from EtOH/Et_2O. Dry it in a vacuum desiccator over KOH.

***N*-Acetylhistidine (H_2O)** *[39145-52-3]* **M 171.2, m 148° (*RS*), 169° (*S*), $[\alpha]_D^{25}$ +46.8° (c 1, H_2O) for *S*-*enantiomer*.** A likely impurity is histidine. Crystallise it from water, then 4:1 acetone/water. [Marshall et al. *J Am Chem Soc* **78** 4636 *1956*, Bergmann & Zervas *Biochem Z* **203** 280 *1928*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 1990 *1961*, *Beilstein* **25** IV 4359.]

***N*-Acetyl-*RS*-homocysteine thiolactone (Citiolone)** *[1195-16-0] [17896-21-8 for ±]* **M 159.2, m 110°, 109-111°, 111.5-112.5°.** Dry Citiolone in a vacuum desiccator. It recrystallises from toluene as needles. It is a ninhydrin -ve substance which gives a "slow" nitroprusside test. It has λ_{max} at 238nm (ε 4,400 $M^{-1}cm^{-1}$); and ν_{max} (nujol) 1789*s* and 851*ms* cm^{-1}. [Benesch & Benesch *J Am Chem Soc* **78** 1597 *1956*, cf Laliberté *J Chem Soc* 2756 *1963*.]

***N*-Acetyl-L-leucinamide (2-acetamido-4-methylvaleramide)** *[28529-34-2]* **M 177.2, m 202°.** Recrystallise it from aqueous EtOH or $CHCl_3$/petroleum ether (b 40-60°). [Gränacher *Helv Chim Acta* **8** 216 *1925*, *Beilstein* **4** II 864, for L, and Bergmann et al. *Justus Liebigs Ann Chem* **449** 301 *1926*, *Beilstein* **4** II 877 for DL.]

***N*-Acetyl-L-methionine** *[65-82-7]* **M 191.3, m 103.5-104.5°, 104°, $[\alpha]_{546}$ -24.5° (c 1, in H_2O), pK_{Est} ~3.4.** Crystallise *N*-acetyl-L-methionine from Me_2CO, H_2O or EtOAc. Dry it in a vacuum over P_2O_5. Its solubility at 25° in H_2O is 30.7%, and in Me_2CO it is 29.5%. [Mitzi & Schueter *Biochim Biophys Acta* **27** 168 *1958,* Birnbaum et al. *J Biol Chem* **194** 455 *1952*, *Beilstein* **4** IV 3206.]

Acetylmethionine nitrile *[538-14-7]* **M 172.3, m 44-46°.** Crystallise the nitrile from diethyl ether. [Catch et al. *J Chem Soc* 1611 *1947*, *Beilstein* **4** III 1654.]

***N*-Acetyl-*N′*-methyl-L-alaninamide** *[19701-83-8]* **M 144.2, m 181.2-182° (sealed tube), $[\alpha]_D^{25}$ -51.1° (c 2, EtOH).** Crystallise the amide from EtOAc/Et_2O, then from EtOH and Et_2O. Also recrystallise it twice by dissolving ~2.5g in hot 200ml of toluene and cooling. It sublimes at ~170°, so its **m** is measured in a sealed tube. [Applewhite & Niemann *J Am Chem Soc* **81** 2212 *1959*, *Beilstein* **4** IV 2500.]

***N*-Acetyl-*N′*-methylglycinamide** *[7606-79-3]* **M 130.2**, **m 157.5-158°.** Recrystallise the amide from EtOH/Et_2O mixture. Also recrystallise it twice from EtOAc/EtOH (16:1) and once from EtOAc. [Applewhite & Niemann *J Am Chem Soc* **81** 2212 *1959*.]

***N*-Acetyl-*N′*-methyl-L-leucine amide** *[32483-15-1]* **M 186.3**, **m 165.3-166.8° (sealed tube), $[\alpha]_D^{25}$ -33.9° (c 1, H_2O).** Recrystallise the amide from EtOAc, EtOH/hexane mixture or toluene/hexane mixture. [Applewhite & Niemann *J Am Chem Soc* **81** 2212 *1959*.]

***N*-Acetyl-L-phenylalanine** *[2018-61-3]* **M 207.2, m 170-171°, 174-175°, $[\alpha]_D^{25}$ +47.5° (c 4, EtOH), +52.5° (c 2, EtOH), (DL) m 152.5-153°, pK_{Est} ~3.5.** *N*-Acetyl-L-phenylalanine is recrystallised from H_2O, 20% MeOH/H_2O, or $CHCl_3$; dry and store it at 4°. The *(DL)-isomer* crystallises from H_2O, Me_2CO, EtOAc, or $CHCl_3$ with **m** 152-154° and the solubilities in w% at 25° are 0.73 (H_2O), 4.3 (Me_2CO), 0.79 (EtOAc) and 0.34 ($CHCl_3$) [Kerr & Niemann *J Org Chem* **23** 893 *1958*, Overby & Ingersoll *J Am Chem Soc* **73** 3363 *1951*, L: Fu et al. *J Am Chem Soc* **76** 6057 *1954*, Bender & Glasson *J Am Chem Soc* **81** 1591 *1959*]. [*Beilstein* **14** I 238, **14** IV 1575.]

***N*-Acetyl-L-phenylalanine ethyl ester** *[2361-96-8]* **M 235.3, m 93-94°.** Crystallise the ester from aqueous

EtOH or H_2O. [Izumiya & Fruton *J Biol Chem* **218** 59 *1956*.]

***N*-Acetyltryptophan** *[87-32-1]* **M 246.3, m 206°, 207-208° (*RS*), pK_{Est} ~3.8,** [*1218-34-4*] **m 188°, 189.5-190.5° (*S*), $[\alpha]_D^{25}$ +30.1° (aqueous NaOH), +71.5° (dioxane/aqueous HCl).** A likely impurity is tryptophan. Crystallise it from EtOH by adding water. [Cowgill *Biochim Biophys Acta* **200** 18 *1970,* DL: Berg *J Biol Chem* **100** 79 *1933*, *Beilstein* **22/14** V 40-50.]

***N*-Acetyl-L-valine amide** *[37933-88-3]* **M 158.2, m 275°.** Recrystallise the amide from CH_3OH/Et_2O.

Alamethicin (from *Tricoderma viridae*). *[27061-78-5]* **M 1964.3, m 259-260°, 275-270°, $[\alpha]_D^{22}$ -45° (c 1.2, EtOH), pK^{25} 6.04 (aqueous EtOH).** Recrystallise alamethicin from MeOH. [Panday et al. *J Am Chem Soc* **99** 8469 *1977*.] The *acetate [64918-47-4]* has **m** 195-180° from MeOH/Et_2O, and the *acetate-methyl ester [64936-53-4]* has **m** 145-140° from aqueous MeOH.

α-Alanine (*RS*) *[302-72-7]* **M 89.1, m 295-296°, (*S*)** *[56-41-7]* **m 297°(dec), $[\alpha]_D^{15}$ +14.7° (in 1M HCl), (*R*)** *[338-69-2]* **m 289-291°(dec), $[\alpha]_D^{15}$ -14.1° (c 0.9, 1M HCl), pK_1^{25} 2.34, pK_2^{25} 9.87.** Crystallise alanine from H_2O or aqueous EtOH, i.e. crystallise it from 25% EtOH in water, or recrystallise it from 62.5% EtOH, wash it with EtOH and dry it to constant weight *in vacuo* over P_2O_5. *RS*-α-*alanineamide* [20108-77-4] has **m 62°** (from $CHCl_3$), **pKa 8.02**, the *hydrochloride* [80222-96-4] has **m 173°** (from EtOH) and the *acetate salt* has **m 136-137°**. *S*-α-*alanine methyl ester hydrochloride* [2491-20-5] has **m 109-111°**, $[\alpha]_D^{15}$ +8.0° (c 1.6, MeOH), and *S*-α-*alanine N-methylamide* [7324-05-2] has **m 78°** (hygroscopic, also **m 72°** reported, from $CHCl_3$). [Gutter & Kegeles *J Am Chem Soc* **75** 3893 *1953*, Walsh *J Biol Chem* **264** 2394 *1989*.] 2,2'-Iminodipropionic acid is a likely impurity. [*Beilstein RS*: **4** H 387, **4** I 491, **4** II 814, **4** III 1222, **4** IV 2481; *R*: **4** H 385, **4** I 491, **4** II 812, **4** III 1219, **4** IV 2480; *S*: **4** H 381, **4** I 489, **4** II 809, **4** III 1208, **4** IV 2480.]

β-Alanine *[107-95-9]* **M 89.1, m 197-198°(dec), 205°(dec), 205.5°(dec), 207°(dec, rapid heating), pK_1^{25} 3.55 (3.60, CO_2H), pK_2^{25} 10.24 (10.36, NH_3^+).** Crystallise β-alanine by dissolving it in a hot saturated aqueous solution, filtering, adding four volumes of absolute EtOH and cooling in an ice-bath. Recrystallise it in the same way and then finally, crystallise it from a warm saturated solution in 50% EtOH and adding four volumes of absolute EtOH with cooling in an ice-bath. The crystals are dried in a vacuum desiccator over P_2O_5. It also crystallises from H_2O, and sublimes at 170-180°/0.3mm. The *hydrochloride* [6057-90-5] forms plates with **m 123°**, its *methyl ester* has **b 69°/58mm**, the *methyl ester hydrochloride* [3196-73-4] has **m 107°** (from EtOH/Et_2O), the *amide* has **m 41°** and the *amide hydrochloride* has **m 149°**. *N-Methyl β-alanine* crystallises from EtOH, the monohydrate forms plates with **m 99-100°** and its *hydrochloride* [2679-14-3] has **m 105°**. *N-Methyl β-alanine amide* [4874-17-3] M 102.1 is a liquid with d^{25} 1.052, n_D^{20} **1.458**, and is an antibacterial [Altamura et al. *J Med Chem* **38** 4244 *1955*]. [Donovan & Kegeles *J Am Chem Soc* **83** 255 *1961*, for pKa see Albert *Biochem J* **47** 531 *1950*, *Beilstein* **4** H 401, **4** I 499, **4** II 827, **4** III 1258, **4** IV 2526.]

***S*-Alaninol [*S*-2-aminopropan-1-ol]** *[2749-11-3]* **M 75.1, b 167-169°/760mm, d_4^{20} 0.961, n_D^{20} 1.456, $[\alpha]_{546}$ +26.0° (c 2, EtOH), pK^{25} 9.43.** Purify it as for *S*-2-amino-3-methylbutan-1-ol below. [*Beilstein* **4** IV 1615.]

D-Allothreonine [*2R,3R(-)-isomer*] *[24830-94-2]* **M 119.1, m 272-273°(dec), 276°(dec), $[\alpha]_D^{25}$ -9.1° (c 3.9, H_2O), pK_1^{25} 2.11, pK_2^{25} 9.10.** Recrystallise D-allothreonine from aqueous EtOH or 50% EtOH. [Elliot *J Chem Soc* 62 *1950*, Birnbaum et al. *J Biol Chem* **194** 455 *1952*, IR: Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** *1961*, *Beilstein* **4** IV 3170.]

***RS*-α-Allylglycine (2-aminopent-4-enoic acid).** *[7685-44-1]* **M 115.1, m 250-255°(dec), $pK_{Est(1)}$ ~2.3, $pK_{Est(2)}$ ~9.6.** Dissolve it in absolute EtOH and precipitate it with pyridine, then recrystallise it from aqueous EtOH [R_F on paper in BuOH/EtOH/NH_3/H_2O (4:4:1:1:) is 0.37]. The *hydrobromide* has **m** 136-140° (from EtOAc) and the *phenylureido* derivative has **m** 159-161°. [Schögl *Monatsh Chem* **89** 377 *1958*, *Beilstein* **4** IV 2852.]

Aminoacetic acid (Glycine) *[56-40-6]* **M 75.1, m 262° (dec, goes brown at 226°, sublimes at 200°/0.1mm), pK_1^{25} 2.35, pK_2^{25} 9.78.** Crystallise glycine from distilled water by dissolving at 90-95°, filtering, cooling to

about -5°, and draining the crystals centrifugally. *Alternatively*, crystallise it from distilled water by addition of MeOH or EtOH (e.g. 50g dissolved in 100ml of warm water, and 400ml of MeOH is added). The crystals are washed with MeOH or EtOH, then with diethyl ether. Likely impurities are ammonium glycinate, iminodiacetic acid, nitrilotriacetic acid or/and ammonium chloride. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 1955 *1961*, *Beilstein* **4** IV 2349.]

α-Amino acids. All the α-amino acids with the "natural" configuration [*S* (L), except for cysteine which is *R*(L)] at the α- carbon atom are available commercially in a very high state of purity. Many of the "non-natural" α-amino acids with the [*R*(D)] configuration as well as racemic mixtures are also available, and generally none require further purification before use unless they are of "Technical Grade" or were stored for a very long period. The *R* or *S* enantiomers are optically active except for glycine which has two hydrogen atoms on the α-carbon atom, but these are *pro*-chiral and enzymes or proteins do distinguish between them, e.g. serine hydroxymethyltransferase successfully replaces the *pro*-α-hydrogen atom of glycine with CH_2OH (from formaldehyde) to make *S*-serine. The twenty common natural α-amino acids are: **amino acid**, three-letter abbreviation, **one-letter abbreviation**, pK (-COOH) and pK (-NH_3^+): **Alanine**, Ala, **A**, 2.34, 9.69; **Arginine**, Arg, **R**, 2.17, 9.04; **Asparagine**, Asn, **N**, 2.01, 8.80; **Aspartic acid**, Asp, **D**, 1.89, 9.60; **Cysteine**, Cys, **C**, 1.96, 8.18; **Glutamine**, Gln, **Q**, 2.17, 9.13; **Glutamic acid**, Glu, **E**, 2.19, 9.67; **Glycine**, Gly, **G**, 2.34, 9.60; **Histidine**, His, **H**, 1.8, 9.17; **Isoleucine**, Ile, **I**, 2.35, 9.68; **Leucine**, Leu, **L**, 2.36, 9.60; **Lysine**, Lys, **K**, 2.18, 8.95; **Methionine**, Met, **M**, 2.28, 9.20; **Phenylalanine**, Phe, **F**, 1.83, 9.12; **Proline**, Pro, **P**, 1.99, 10.96; **Serine**, Ser, **S**, 2.21, 9.15; **Threonine**, Thr, **T**, 2.11, 9.62; **Tryptophan**, Trp, **W**, 2.38, 9.39; **Tyrosine**, Tyr, **Y**, 2.2, 9.11, **Valine**, Val, **V**, 2.32, 9.61, respectively. Technical grade amino acids can be purified on ion-exchange resins (e.g. Dowex 50W and eluting with a gradient of HCl or AcOH), and the purity is checked by TLC in two dimensions and stained with ninhydrin. (J.P. Greenstein & M. Winitz, *Chemistry of the Amino Acids* (3 Volumes), J. Wiley & Sons, NY, 1961; C. Cooper, N. Packer and K. Williams, *Amino Acid Analysis Protocols*, Humana Press, 2001, ISBN 0896036561). Recently codons for a further two amino acids have been discovered which are involved in ribosome-mediated protein synthesis giving proteins containing these amino acids. The amino acids are *R*(L)-selenocysteine [Stadtman *Ann Rev Biochem* **65** 83 *1996*] and pyrrolysine [(4*R*, 5*R*)-4-substituted (with Me, NH_2 or OH) pyrroline-5-carboxylic acid] [Krzychi & Chan et al. *Science* **296** 1459 and 1462 *2002*.] They are, however, rare at present and only found in a few microorganisms.

***dl*-α-Aminoadipic acid (hydrate) (2-aminohexane-1,6-dioic acid)** *[542-32-5]* **M 161.2, m 196-198°, 204°, 205-206°, $pK_{Est(1)}$ ~2.0, $pK_{Est(2)}$ ~4.5, $pK_{Est(3)}$ ~9.8.** Crystallise the acid from H_2O. *Alternatively*, purify it by precipitating the Cu salt and decomposing the Cu salt suspended in H_2O by bubbling H_2S, filtering off the CuS, evaporating, and recrystallising the residue from H_2O. Note that prolonged refluxing of an aqueous solution converts the acid to the lactone: *piperid-2-one-6-carboxylic acid* which has **m** 177-178°. [Linstead & Wang *J Chem Soc* 810, 811 *1937*, Waelkes et al. *J Am Chem Soc* **72** 5760 *1950*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p. 2408 *1961*, *Beilstein* **4** III 1555, **4** IV 3070.]

***N*-(*p*-Aminobenzoyl)-L-glutamic acid** *[4271-30-1]* **M 266.3, m 173°, 174-175° (L-form), $[\alpha]_{546}$ -17.5° (c 2, 0.1m HCl); 197° (DL), pK_1^{25} 2.61, pK_2^{25} 3.76, pK_3^{25} 4.83.** Crystallise the acid from H_2O. Also purify it by dissolving 2.7g in H_2O (130ml), adding aqueous NaOH to pH 5.5 and adding portionwise a solution of 0.5M $CuSO_4$ to complete precipitation of the Cu salt. This salt is filtered off, suspended in H_2O and H_2S is bubbled through to precipitate CuS, filter, evaporate and recrystallise the residue from H_2O. It has λ_{max} (H_2O) at 273nm. [Backer & Houtman *Rec Trav Chim Pays Bas* **70** 738, 743 *1951*, *Beilstein* **14** IV 1153.]

***RS*-2-Aminobutyric acid** *[2835-81-6]* **M 103.1, m 287-288°(dec), 303°(dec), 303°(dec, sealed tube), pK_1^{25} 2.29, pK_2^{25} 9.83.** Crystallise the acid from water. [Albertson & McKay *J Am Chem Soc* **81** 505 *1959*, Perrin *J Chem* Soc 3125 *1958*, *Beilstein* **4** IV 2584.]

***S*-2–Aminobutyric acid (Butyrine)** *[1492-24-6]* **M 103.1, m 292°(dec), $[\alpha]_D^{25}$ + 20.6° (c 2, 2.5N HCl), pK_1^{25} 2.55, pK_2^{25} 9.60.** Crystallise butyrine from aqueous EtOH, and the melting point depends on heating rate but has **m** 303° in a sealed tube. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 2399 IR: 2401 *1961*, *Beilstein* **4** III 1294, **4** IV 2584.]

***RS*-3-Aminobutyric acid** *[2835-82-7]* **M 103.1, m 193-194°, $pK_{Est(1)}$ ~3.5, $pK_{Est(2)}$ ~10.3.** Crystallise the acid from aqueous EtOH or MeOH/Et_2O. Also crystallise it by heating a slightly diluted EtOH solution and adding Me_2CO. It gives a purple spot with R_F 0.89 on paper chromatography using 80% aqueous phenol (the α-amino acid has R_F 0.74). [Zilka & Rivlin *J Org Chem* **23** 94 *1958*, Bruylants *Bull Soc Chim Belg* **32** 259 *1923*, *Beilstein* **4** IV 2595.]

***S*-3-Aminobutyric acid** *[3775-72-2]* **M 103.1, m 212°, 210-212°, $[\alpha]_D^{18}$ + 38.8° (c 0.5, H_2O).** Purify the acid from absolute EtOH. It has also been crystallised from MeOH or MeOH/Et_2O and dried in a vacuum. [Balenovic et al. *J Chem Soc* 3316 *1952*, Bruylants *Bull Soc Chim Belg* **32** 259 *1923*, *Beilstein* **4** IV 2595.]

4-Aminobutyric acid (GABA) *[56-12-2]* **M 103.1, m 202°(dec), 203°(dec), pK_1^{25} 4.14, pK_2^{25} 10.55.** Crystallise GABA from aqueous EtOH or MeOH/Et_2O. Also crystallise it by dissolving it in the least volume of H_2O and adding 5-7 volumes of absolute EtOH. [Sherman *Biochemical Preparations* **4** 91 *1955*, de Witt *Org Synth* Coll Vol **II** 25 *1943*, *Beilstein* **4** III 1316, **4** IV 2600.]

1-Amino-1-cyclopentanecarboxylic acid (cycloleucine) *[52-52-8]* **M 129.2, m 328-335°(dec), 328-329°, 330°(dec), pK_1^{20} 2.4, pK_2^{20} 10.3.** Any Cl^- or other anions are removed by stirring with a strong cation exchange resin (Amberlite IR-120), filtering, and washing with distilled H_2O until the filtrate is free from the anion. The resin is then stirred overnight with 6N NH_4OH, filtered, the filtrate is decolourised (charcoal) and evaporated to dryness in a vacuum. The residue is recrystallised from H_2O/EtOH. Also crystallise it from aqueous EtOH. The *hydrochloride* has **m** 222-224°(dec). [Neelakantan & Hartung *J Org Chem* **23** 967 *1958*, Connors & Ross *J Chem Soc* 2119 *1960*. O'Donnell et al. *Synthesis* 127 *1984*, *Beilstein* **14** IV 974.]

***trans*-(1*RS*,4*RS*)-4-Aminoethylcyclohexane-1-carboxylic acid (*t*-AMCHA, Tranexamic acid, Tranex, Transamin, Trasamlon, Ugurol, Frenolyse, Hexapromin, Abvitoff among other names)** *[1197-18-8]* **M 157.2, m 386-392° (dec), and *cis*-(1*RS*,4*SR*)-4-aminoethylcyclohexane-1-carboxylic acid** *[1197-17-7]* **M 157.2, m 236-238° (dec); *cis*- and *trans*- acids have the same pK_1^{25} 4.51 (CO_2H), pK_2^{25} 10.72 (NH_2).** A mixture of *cis*- and *trans*- acids (2:1) is obtained by catalytic reduction of 4-acetamidomethylbenzoic acid (3.9g, 20mmol, from acetylation of 4-aminomethylbenzoic acid see [56-91-7]) in aqueous NaOH (0.8g, 20mmol in 15ml of H_2O) in the presence of Raney Ni (3ml of aqueous suspension) are shaken with H_2 in an bomb (100ml) at 170° and 82atm/cm^2 (1205psi). Reduction is complete after 2 hours, the catalyst is filtered off, the filtrate is acidified with 4N H_2SO_4 and evaporated to dryness *in vacuo*; the residue is extracted with Me_2CO, filtered and evaporated to dryness *in vacuo* to give crude 4-acetamidomethylcyclohexane-1-carboxylic acid (~3.9g). The acid is then refluxed with 20% HCl (20ml) for 3 hours (in an oil bath at 150°), evaporated to dryness *in vacuo*; the residue is dissolved in H_2O (20ml) and freed from HCl by passage throught a column of 'Amberlite IR-4B' (15ml, in OH^- form) and eluted with H_2O. Evaporation of the eluate *in vacuo* and crystallisation of the residue from aqueous Me_2CO gives a **2:1** mixture of ***cis*-and *trans*- 4-aminomethylcyclohexane-1-carboxylic acid** (2.24g, ~71%, **m ~232-236°, dec)**. Both acids are symmetrical, i.e. mirror images are superimposable.
The mixture (10g, 64mmol) is separated by refluxing with $Cu(CO_3)_2$ (9.15g, 38mmol) in H_2O (100ml) for 1 hour (turning deep blue in colour), cooled and the blue precipitate is filtered off, dissolved into 8% aqueous NH_3 (100ml), filtered from a little solid, and passed through a column of "Diaion SK#1 (NH_4^+ form)" and washed with H_2O. The eluted solution is then passed through an "Amberlite IR-4B′ (OH^- form)" column and the effluent is evaporated to dryness. The residue (6.75g, m ~221-223°, dec.) is repeatedly recrystallised from H_2O-Me_2CO to give the pure ***cis*-amino acid** with **m 236-238°, dec**, and IR (KBr) peaks at ν_{max} 2940, 2660, 1639 (*1640*), 1560 (*1563*), 1509 (*1515*), 1408 (*1403*), 1305 (*1308*), 930 and 904 cm^{-1}, value in *italics* are from Meyer (see below). The combined filtrates from the recrystallisation are evaporated, the residue is dissolved in H_2O and similarly de-ionised through the same columns. The final residue is recrystallised from H_2O-Me_2CO to give the pure ***trans*-4-aminoethylcyclohexane-1-carboxylic acid** (3.37g) with **m 286-292°, dec**, and IR (KBr) peaks at ν_{max} 2940, 2610, 1637, 1535 (*1528*), 1383 (*1381*) (*1325*) and 920 cm^{-1}, value in *italics* are from Meyer (see below). On TLC (Silica gel G, eluted with ascending *n*-PrOH/H_2O, 65:35) the R_F of the *cis*-isomer was always 1.2 times larger than that of the *trans*- isomer. [Note that the melting points of the isomers measured in the usual way vary somewhat, and by using a Du Pont Model 900 differential thermal analyzer the *cis*-acid had **m 252°**, and the *trans*-acid had **m 295-300°** as endotherms, Meyer *J Med Chem* **9** 641 *1966*].
The *cis-hydrochloride* has **m 195-197°, dec** (prisms from H_2O-Me_2CO), the *trans-hydrochloride* has **m 238-**

241.5°, dec (needles from H_2O-Me_2CO); the *cis-hydrobromide* has **m 205-208°, dec** (plates from Me_2CO), the *trans-hydrobromide* has **m 227-229°, dec** (plates from H_2O); the *cis-p-toluenesulfonic acid salt* has **m 177-178°** (plates from *n*-PrOH-Et_2O), the *trans-p-toluenesulfonic acid salt* has **m 262-264°** (plates from H_2O), the *cis-HCl-$AuCl_3$ salt* has **m 178-180°, dec** (yellow needles from H_2O), the *trans-HCl-$AuCl_3$ salt* has **m 205-206°, dec** (yellow prisms from H_2O), the *cis-HCl-$PtCl_4$ salt* has **m 233°, dec** (yellow needles from H_2O), the *trans-HCl-$PtCl_4$ salt* has **m 254-255°, dec** (yellow-orange plates from H_2O); the *cis-N-acetamide* has **m 189-190°** (prisms from EtOH), the *trans-N-acetamide* has **m 154-155°** (prisms from Me_2CO); the *cis-N-benzamide* has **m 157-158°** (plates from EtOH/*C_6H_6) and the *trans-N-benzamide* has **m 177-178°** (needles from EtOH/H_2O).
The *cis-* and *trans-* acids are also readily separated from the mixture by recrystallisation of their *p-toluenesulfonic acid salts* which have very different solubility properties. ***Isomerisation:*** When a solution of the *cis-acid* (2g) in 0.5N NaOH (26ml) is heated in a silver vessel in an autoclave at 200° for 6 hours, and the cooled solution is passed through an "Amberlite IR-120" (NH_4^+ form)' column and washed with H_2O, and evaporation of the eluate *in vacuo* and four recrystallisations from aqueous MeOH, the *trans-acid* (0.8g, 40%), **m 384-390° dec**, is obtained [Naito et al. *Chem Pharm Bull Jpn* **16** 728 *1968*, Daiichi Seiyak *Dutch Pat* 6,414,942 *1965*, *Chem Abstr* **64** 3379 *1966*.] The width-at-half height of the peaks from the cyclohexane protons in the ^1H NMR spectra are larger from the *trans*-acid than the corresponding peaks from the *cis*-acid. The structure of the *cis-acid* was confirmed by conversion to a cyclic *lactam* on fusion. It has **m 104°** after recrystallisation from hexane followed by sublimation at 100°/2.5 x 10^{-2}mm. [*Note that this melting point was recorded at the point where, under crossed Nichol prisms, birefringence was lost. The crystal form, however, was only slowly lost thereafter over a wide range of temperatures*]. The lactam has IR (KBr) peaks at ν_{max} 1661 (amide I), 1421, 1325 and 1205 cm^{-1} [Meyer *J Med Chem* **9** 641 *1966*].
These amino acids are haemostatic with antiplasmin activity. The *trans*-acid has potent antiplasmic activity (inhibiting the fibrinolytic enzyme system), being 50 times more active than the *cis*-acid, and 5-7 times more potent than ε-aminocaproic acid [Naito et al. *Chem Pharm Bull Jpn* **16** 357 and 728 *1968*.] The antifibrolytic activity is due to blocking of the lysine binding sites of plasminogen. *t*-AMCHA has been used as a lysine analogue to characterise binding sites in plasminogens. [Hoover at al. *Biochemistry* **32** 10936 *1993*, Marshall et al. *Biochemistry* **33** 3599 *1994*.]

4-Amino hippuric acid (*N-p*-aminobenzoylglycine) *[61-78-9]* **M 194.2, m 198-199°, 200-202°, $pK_{Est(1)}$ ~1.7(NH_2), $pK_{Est(2)}$ ~3.4 (CO_2H).** Crystallise the acid from H_2O. It is soluble in organic solvents. [Cohen & McGilvery *J Biol Chem* **169** 119 *1945*, **171** 121 *1947*, Meunzen et al. *J Biol Chem* **26** 469 *1926*, *Beilstein* **14** III 1069, **14** IV 1152.]

***dl*-4-Amino-3-hydroxybutyric acid** *[924-49-2]* **M 119.1, m 218°(dec), 225°(dec), pK_1^{25} ~3.80 (CO_2H), $pK_{Est(2)}$ ~9.3.** Crystallise the acid from H_2O or aqueous EtOH. Recrystallise it by dissolving it in H_2O and adding MeOH or EtOH. It is not very soluble in $CHCl_3$ or EtOAc. [Renaud & Seebach *Synthesis* 424 *1986*, *Beilstein* **4** IV 3187.]

***R* (L-)-4-Amino-3-hydroxybutyric acid (GABOB)** *[352-21-6]* **M 119.1, m 212°(dec), 213-214°(dec), 216-217°(dec), $[\alpha]_D^{35}$ -20.5° (c 1.75, H_2O).** Purify GABOB through a Dowex 50Wx8 resin, eluting with 1.3N NH_4OH, evaporating and crystallising the residue by dissolving it in H_2O and adding EtOH. It is an anticonvulsant. [Renaud & Seebach *Synthesis* 424 *1986*, Takano et al. *Tetrahedron Lett* **29** 795 *1988*, *Beilstein* **4** IV 3187.]

α-Aminoisobutyric acid (2-amino-2-methylpropionic acid) *[62-57-7]* **M 103.1, m sublimes at 280-281°, 335° (sealed tube), pK_1^{25} 2.36, pK_2^{25} 10.21.** Crystallise the acid from aqueous EtOH and dry it at 110°. [Zelinski & Stadnikoff *Chem Ber* **39** 1726 *1906*, *Beilstein* **4** IV 2616.]

***RS*-β-Aminoisobutyric acid (α-methyl-β-alanine)** *[10569-72-9]* **M 103.1, m 176-178°, 178-180°, 181-182°,** *R-(-)- isomer [144-90-1]* **m 183°, $[\alpha]_D^{25}$ -21° (c 0.43, H_2O), $pK_{Est(1)}$ ~3.7, $pK_{Est(2)}$ ~10.2.** *RS*-β-Amino-isobutyric acid forms colourless prisms by crystallisation from hot H_2O which are powdered and dried *in vacuo*. The purity is checked by paper chromatography (Whatman 1) using ninhydrin spray to visualise the amino acid; R_F values in 95% MeOH and *n*-PrOH/5N HCOOH (8:2) are 0.36 and 0.50 respectively. [Kupiecki & Coon *Biochemical Preparations* **7** 20 *1960*, Pollack *J Am Chem Soc* **65** 1335 *1943*.] The *R-enantiomer*, isolated from

iris bulbs or human urine, crystallises from H_2O and sublimes *in vacuo* [Asen et al. *J Biol Chem* **234** 343 *1959*]. The *RS-hydrochloride* crystallises from EtOH/Et_2O with **m** 128-129° (also 130°) [Böhme et al. *Chem Ber* **92** 1258, 1260, 1261 *1959*]. [*Beilstein* **4** III 1330.]

5-Aminolaevulinic acid hydrochloride (ALA-HCl, δ-aminolaevulinic acid HCl) *[5451-09-2]* **M 167.6, m 148°(dec), 150-151°(dec), 156-158°(dec), pK_1^{22} 4.05, pK_2^{22} 8.90.** Dry ALA-HCl in a vacuum desiccator over P_2O_5 overnight, then crystallise it by dissolving it in cold EtOH and adding dry Et_2O. Also crystallise it by dissolving in the minimum volume of MeOH, and placing in a desiccator containing dry Et_2O (clamp the desiccator). During several days the Et_2O slowly distils into the MeOH causing the hydrochloride to separate as long needles. Filter them off and dry them in a Fischer pistol. [Wynn & Corwin *J Org Chem* **15** 203, 207 *1950*, Neuberger & Scott *J Chem Soc* 1820, 1924 *1954*, *Beilstein* **4** IV 3265.]

4-Aminomethylbenzoic acid (α-amino-*p*-toluic acid) *[56-91-7]* **M 151.2, m 273-274°, 294-295°, >300°, 345°, 347-350° (sealed tube), pK_1^{20} 3.59 (CO_2H), pK_2^{20} 9.64 NH_2).** This acid has been prepared in two different ways from *p*-cyanobenzoic acid [Levine & Sedlecky *J Org Chem* **24** 115 *1959*, Albert & Magrath *J Chem Soc* 678 *1944*], and by reduction of *p*-carboxybenzaldehyde oxime [Nair & Baugh *J Org Chem* **38** 2189 *1973*]. A mixture of *p*-cyanobenzoic acid (14g, 619-65-8), Raney cobalt (2g, W-6 or W-7), 28% aqueous NH_3 (40ml) and H_2O (150ml) are shaken in a Parr hydrogenator at 3 atm (initial pressure) and 25° for ~3 hours when the theoretical volume of H_2 is absorbed. The catalyst is filtered off, the filtrate is boiled to remove NH_3 and the solid that separated is collected, and recrystallised from H_2O (charcoal) to give the amino acid (m 347-350°) in 80% yield. *Alternatively*, the oxime of *p*-carboxybenzaldehyde (1g, 619-66-9) in 95% EtOH (100ml) containing 5% Pd/C (100mg) is shaken with H_2 at 30 psi for 18 hours at 25°. The catalyst is filtered off and washed with hot glacial AcOH (2 x 20ml); the combined washings and filtrate are evaporated to dryness and the residue is recrystallised from H_2O (charcoal) to give the white crystalline amino acid (850mg, m 294-295°). *The melting point appears to vary with heating rate*. UV has λ_{max} at 234nm (H_2O), and the ^1H NMR [TFA] has δ at 4.15 (q, *J* = 6Hz, benzylic H), 7.3 (d, *J* = 8Hz, two protons adjacent to $H_2NCH_2^-$) and 7.9 (d, *J* = 8Hz, two protons adjacent to CO_2H). The *N-acetyl derivative* crystallises from a large volume of xylene and has **m 199-200°** (lit: Levine & Sedlecky state m 199-120°). [For pKa see Goldacre *Nature* **154** 796 *1944, Beilstein* **14** H 487, **14** III 1212, **14** IV 1362.]

***S*-2-Amino-3-methyl-1-butanol (*S*-valinol)** *[2026-48-4]* **M 103.2, m 31-32°, b 88°/11mm, d 0.92, $[\alpha]_{546}$ + 16.5° (c 6.32, *l* = 2 H_2O), $[\alpha]_D$ + 15.6° (EtOH), pK_{Est} ~10.4.** Purify *S*-valinol by vacuum distillation using a short Vigreux column. *Alternatively*, it is purified by steam distillation. The steam distillate is acidified with HCl; the aqueous layer is collected and evaporated. The residue is dissolved in butan-1-ol, filtered and dry Et_2O added to crystallise the hydrochloride salt (*hygroscopic*), **m** 113°. The free base can be obtained by suspending the salt in Et_2O and adding small volumes of saturated aqueous K_2CO_3 until effervescence is complete and the mixture is distinctly alkaline. At this stage the aqueous layer should appear as a white sludge. The mixture is heated to boiling and refluxed for 30 minutes (more Et_2O is added if necessary). The Et_2O layer is decanted off from the white sludge, the sludge is extracted twice with Et_2O (by boiling for a few minutes), the combined organic layers are dried (KOH pellets), evaporated and the residue is distilled in a vacuum. [Nagao et al. *J Org Chem* **55** 1148 *1990*, *Beilstein* **4** III 805.]

***S*-(+)-3-Aminopentanoic acid** *[14389-77-6]* and ***R*-(-)-3-aminopentanoic acid** *[131347-76-7]* **M 115.1, m (175°), 185°, $[\alpha]_D^{20}$ (+) and (-) 43° (c 0.5, H_2O), pK_1^{25} 3.54, pK_2^{25} 10.25.** Crystallise the amino acid from EtOH/Et_2O. [*Beilstein* **4** II 843, **4** III 1342, **4** IV 2635.]

α–Aminothiophene-2-acetic acid [2-(2-thienyl)glycine] *[R(+) 65058-23-3, S(-) 4052-59-9, (-)- 43189-45-3, RS(±) 21124-40-3]* **M 57.2, m 236-237° (*R*), 235-236° (*S*), 208-210°, 223-224° (dec)(*RS*), $[\alpha]_D^{20}$ (+) and (-) 84° (c 1, 1% aqueous HCl), $[\alpha]_D^{25}$ (+) and (-) 71° (c 1 H_2O), $pK_{Est(1)}$~ 1.5, $pK_{Est(2)}$~ 8.0.** Recrystallise 2-(2-thienyl)glycine by dissolving it in H_2O (1g in 3 ml), adjusting the pH to 5.5 with aqueous NH_3, diluting with MeOH (20 ml), stirring, adjusting the pH to 5.5 and cooling to 0°. Also recrystallise it from small volumes of H_2O. [*R*-isomer: Nishimura et al. *Nippon Kagaku Zasshi* **82** 1688 *1961, S*-isomer: Johnson & Panetta *Chem*

Abstr **63** 14869 *1965*, Johnson & Hardcastle *Chem Abstr* **66** 10930 *1967*, *RS*-isomer: LiBassi et al. *Gazz Chim Ital* **107** 253 *1977*.] The *(±) N-acetyl* derivative has **m** 191° (from H_2O) [Schouteenten et al. *Bull Soc Chim Fr* II 248, II 252 *1978*].

5-Amino-*n*-valeric acid (5-aminopentanoic acid) *[660-88-8]* **M 117.2, m 157-158°, pK_1^{25} 4.25, pK_2^{25} 10.66.** Crystallise it from H_2O/EtOH. When heated above its melting point, it is converted to *2-piperidone* with **m** 200°. [Wood & Colver *J Am Chem Soc* **67** 654 *1945*, *Beilstein* **4** IV 2636.]

5-Amino-*n*-valeric acid hydrochloride *[627-95-2]* **M 153.6, m 92-94°, 103-104°.** Crystallise the salt from $CHCl_3$. Otherwise dissolve it in EtOH and add 2 volumes of Et_2O and chill. [Schniepp & Marvel *J Am Chem Soc* **57** 1557 *1935*, Woods & Colver *J Am Chem Soc* **67** 654 *1945*, *Beilstein* **4** III 1343, **4** IV 2636.]

Angiotensinogen (from human blood serum or procine plasma) *[64315-16-8]* **M ~1762.** A tetradecapeptide renin substrate which is purified by chromatography on Blue Sepharose, Phenyl-Sepharose, hydroxylapatite and immobilised 5-hydroxytryptamine [Campbell et al. *Biochem J* **243** 121 *1987*]. [*Beilstein* **25** III/IV 4390 *for angiotensin*.]

Anserine [*N*,β–alanyl-1-methyl-*S*-histidine] *[584-85-0]* **M 240.3, m 238-239°, $[\alpha]_D^{23}$ +12.3° (c 5,H_2O), pK_1^{25} 2.64, pK_2^{25} 7.04, pK_3^{25}9.49.** Crystallise anserine from aqueous EtOH. It is *hygroscopic* and is best stored as the nitrate salt (see below). Purify it by shaking the nitrate salt with Dowex 3 (x4 free base) and washing with H_2O, evaporating the filtrate and removing H_2O by 3 distillations with 10ml of propan-2-ol. Dissolve the crystals in MeOH and add H_2O dropwise until one phase is obtained and cool. Dry the crystals at 60° over P_2O_5 in a vacuum. The *picrate* has **m** 145° (from H_2O). [Rinderknecht et al. *J Org Chem* **29** 1968 *1964*, *Beilstein* **25** II 408, **25** IV 4383.]

***S*-Anserine nitrate** *[5937-77-9]* **M 303.3, m 225°(dec), 226-228°(dec), $[\alpha]_D^{30}$ +12.2°.** Likely impurities are 1-methylimidazole-5-alanine and histidine. Crystallise the nitrate from aqueous MeOH or EtOH (needles). Also dissolve ~20g in 25ml of MeOH, add 2-propanol (150-200ml) and store the mixture at 5° overnight to give shiny needles. Recrystallise it by heating 12g of the nitrate in MeOH (300ml) and adding H_2O (50-60ml) until one phase is obtained and refrigerating overnight. Filter and dry it at 60°/P_2O_5 in a vacuum. [Rinderknecht et al. *J Org Chem* **29** 1968 *1964*, Behrens & duVigneaud *J Biol Chem* **120** 517 *1937*.]

***S*-Arginine** *[74-79-3]* **M 174.2, m 205°(dec, anhydrous), 207°(dec, 2 H_2O), $[\alpha]_D$ +26.5° (c 5, in 5M HCl), $[\alpha]_{546}$ +32° (c 5, in 5M HCl), pK_1^{25} 2.18, pK_2^{25} 9.36, pK_3^{25} 11.5.** *S*-Arginine crystallises from H_2O as the *dihydrate* and as plates from EtOH. It also crystallises from 66% EtOH. Its solubility in H_2O is 15% at 21°. Its isoelectric point is at pH 10.76. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 1841 *1961*, *Beilstein* **4** IV 817.]

***S*-Arginine hydrochloride** *[1119-34-2]* **M 210.7, m 217°(dec), 222°(dec), $[\alpha]_D^{20}$ +26.9° (c 6, M HCl).** A likely impurity is ornithine. Crystallise the salt from H_2O at pH 5-7, by adding EtOH to 80% (v/v). [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 1841 *1961*, *Beilstein* **4** IV 2649.]

***S*-Argininosuccinic acid** *[2387-71-5]* **M 290.3, $[\alpha]_D^{24}$ +16.4° (H_2O).** A likely impurity is fumaric acid. In neutral or alkaline solution it readily undergoes ring closure to the "anhydride" (see below). Crystallise it from water by adding 1.5 volumes of EtOH. The barium salt is stable at 0-5° if dry. [Westfall *Biochem J* **77** 135 *1960*, Ratner & Kunkemueller *Biochemistry* **5** 1821 *1966*.]

***S*-Argininosuccinic anhydride** *[28643-94-9]* **M 272.3, $[\alpha]_D^{23}$ -10° (H_2O for anhydride formed at neutral pH).** Crystallise the anhydride from H_2O by adding two volumes of EtOH. An isomeric anhydride is formed if the free acid is allowed to stand at acid pH. In solution, the mixture of anhydride and free acid is formed [see above entry, Ratner & Kunkemueller *Biochemistry* **5** 1821 *1966*, Kowalsky & Ratner *Biochem J* **8** 899 *1969*].

***S*-Asparagine** *[70-47-3]* **M 150.1, m 234-235° (monohydrate)** *[5794-13-8]* **$[\alpha]_D$ +32.6° (0.1M HCl), pK_1^{25}**

1.98, pK_2^{25} 8.84. Likely impurities are aspartic acid and tyrosine. Crystallise it from H_2O or aqueous EtOH. It slowly effloresces in dry air. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 1856 *1961*, *Beilstein* **4** IV 3005.]

Aspartic acid M 133.1, m 338-339° (*RS*, *[617-45-8]*), m 271° (*S*, requires heating in a sealed tube *[56-84-8]*) **$[\alpha]_D^{25}$ +25.4° (3M HCl), pK_1^{25} 1.99, pK_2^{25} 3.90.** Likely impurities are glutamic acid, cystine and asparagine. Crystallise the acid from water by adding 4 volumes of EtOH and dry it at 110°. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 1856 *1961*, *Beilstein* **4** IV 2998, 3000.]

L-Aspartic acid β-methyl ester hydrochloride *[16856-13-6]* **M 183.6, m 194°, pK^{25} 8.62.** Recrystallise it from MeOH by adding anhydrous Et_2O [Bach et al. *Biochemical Preparations* **13** 20 *1971*].

DL-Aspartic acid dimethyl ester hydrochloride *[14358-33-9]* **M 197.7, 116-117°.** Crystallise it from absolute MeOH. [Kovach et al. *J Am Chem Soc* **107** 7360 *1985*.] The *diethyl ester* has **pK^{25} 6.4.**

Azaserine *[115-02-6]* **M 173.1, m 146-162°(dec), $[\alpha]_D^{27.5}$ -0.5° (c 8.5, H_2O, pH 5.2), $pK_{Est(1)}$ ~4.53, $pK_{Est(2)}$ ~5.40.** Crystallise azaserine from 90% EtOH. Also dissolve it in H_2O, filter it through Supercel and add EtOH to give azaserine as pale yellow crystals. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 1** pp 75-76 *1961*, Curphey & David *J Org Chem* **43** 4666 *1978*, *Beilstein* **4** IV 3124.]

Benzoyl glycine (hippuric acid) *[495-69-2]* **M 179.2, m 188°, pK^{20} 3.81, 3.59. pK^{40} 3.59.** Crystallise the acid from boiling H_2O. Dry it over P_2O_5. Also purify it by dissolving 135-140g in 2L of boiling H_2O, filtering through a steam-heated funnel and allowing to crystallise at ~20° (yield 115-122g first crop, **m** 186-187°). [Ingersoll & Babcock *Org Synth* Coll Vol **II** 328 *1943*, *Beilstein* **9** 225, I 100.]

***N*-Benzyloxycarbonylglycyl-L-alaninamide** *[17331-79-2]* **M 279.3, m dec >200°.** Recrystallise the dipeptide derivative from EtOH/Et_2O.

***N*-Benzyloxycarbonyl-*N'*-methyl-L-alaninamide** *[33628-84-1]* **M 236.3, m dec >200°.** Recrystallise the amide from EtOAc.

Betaine (1-carboxymethyl-*N,N,N*-trimethylammonium zwitterion) *[107-43-7 (anhydrous), 590-47-6, 17146-86-0 (monohydrate)]* **M 117.1, m 294-294°(dec) (monohydrate?) 301-305°(dec) (anhydrous), ~319°(dec), pK^{25} 1.83.** Crystallise betaine from aqueous EtOH or EtOH/Et_2O. The *monohydrate* loses H_2O above 100°. Betaine undergoes internal alkylation to methyl dimethylaminoacetate above its melting point. It is also prepared by treating the hydrochloride (below) with silver oxide and recrystallising from EtOH/Et_2O. [Edsall *J Am Chem Soc* **66** 1767 *1943*, Leifer & Lippincott *J Am Chem Soc* **79** 5098 *1957*, for pK see Grob et al. *Chem and Ind (London)* 1222 *1955*, *Beilstein* **4** III 1127, **4** IV 2369.]

Betaine hydrochloride *[590-46-5]* **M153.6, m 227-228°(dec), 232°(dec), 246-247°(dec).** Recrystallise the salt from EtOH. Its solubility at 25° is 65% in H_2O, and 5% in EtOH. [Edsall *J Am Chem Soc* **66** 1767 *1943*, Kuhn & Ruelius *Chem Ber* **83** 420 *1950*, *Beilstein* **4** III 1127, IV 2369.]

Bis-*N-tert*-butyloxycarbonyl-L-cystine, *[10389-65-8]* **M 440.5, m 144.5-145°, $[\alpha]_D^{20}$ -133.2° (c 1, MeOH), pK_{Est} ~2.9.** Crystallise the cystine derivative from EtOAc by adding hexane [Ferraro *Biochemical Preparations* **13** 39 *1971*].

Bombesin (2-L-glutamine-3,6-L-asparaginealytesin, a tetradecapeptide) *[31362-50-2]* **M 1619.9.** Purify Bombesin by gel filtration on a small column of Sephadex G-10 and elute with 0.01 M AcOH. This procedure removes lower molecular weight contaminants which are retarded on the column. The procedure should be repeated twice, and the material should now be homogeneous on electrophoresis, and on chromatography it gives a single active spot which is negative to ninhydrin but positive to Cl_2 and iodoplatinate reagents. R_F on paper chromatography (*n*-BuOH/pyridine/AcOH/H_2O :: 37.5: 25:7.5:30) is 0.55 for Bombesin and 0.65 for

Alytin. [Bernardi et al. *Experientia* **Part 1 27** 166 *1971,* Anastasi et al. **Part 2 27** 873 *1971*.] The *hydrochloride* has **m** 185°(dec) (from EtOH) $[\alpha]_D^{24}$ -20.6° [c 0.65, $Me_2NCHO/(Me_2N)_3PO$ (8:2)]. [For the stimulation of inositol phosphate see Lloyd et al. *Biochem J* **260** 813 *1989*.]

Bradykinin [ArgProProGlyPheSerProPheArg] *[5979-11-3]* **M_r 1,240.4.** Purify Bradykinin by ion-exchange chromatography on CMC (*O*-carboxymethyl cellulose) and partition chromatography on Sephadex G-25. The purity is checked by paper chromatography using BuOH/AcOH/H_2O (4:1:5) as eluent. [Park et al. *Can J Biochem* **56** 92 1978, ORD and CD: Bodanszky et al. *Experientia* **26** 948 *1970*, activity: Regoli & Barabé *Pharmacol Rev* **32** 1 *1980*, *Beilstein* **22** III/IV 91.]

_S_-Canavanine [2-amino-4-(guanidinooxy)butyric acid] *[543-38-4]* **M 176.2, m 184°, $[\alpha]_D^{17}$ +19.4° (c 2, H_2O), $[\alpha]_D^{20}$ +7.9° (c 3.2, EtOH), pK_1^{25} 2.43, pK_2^{25} 6.60, pK_3^{25} 9.25.** Crystallise *S*-canavanine from absolute EtOH or aqueous EtOH. [Tomiyama *J Biol Chem* **111** 48 *1935* gave pK_1^{25} 9.25 (COOH), pK_2^{25} 7.4 (guanidinium), pK_3^{25} 11.5 (NH_4^+), Gulland & Morris *J Chem Soc* 763 1935*,* (±) Frankel et al. *J Chem Soc* 3127 *1963*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2622-2628 *1961*, *Beilstein* **4** III 1636, **4** IV 3188.]

***S*-Canavanine sulfate (from jackbean, *O*-guanidino-L-homoserine)** *[2219-31-0]* **M 274.3, m 160-165°(dec), 172°(dec), $[\alpha]_D^{18.5}$ +19.8° (c 7, H_2O), pK_1^{25} 7.40 (CO_2H), pK_2^{25} 9.25 (α-NH_2), pK_3^{25} 11.5 (guanidinoxy).** Recrystallise the sulfate by dissolving (~1g) in H_2O (10ml), and adding with stirring 0.5 to 1.0 volumes of 95% EtOH whereby crystals separate. These are collected, washed with Me_2CO/EtOH (1:1) and dried over P_2O_5 in a vacuum. [Hunt & Thompson *Biochemical Preparations* **13** 416 *1971*, Feacon & Bell *Biochem J* **59** 221 *1955*, *Beilstein* **4** III 1636, **4** IV 3188.]

***N*-Carbamoylglycine (hydantoic acid, *N*-carboxymethylurea, ureidoacetic acid)** *[462-60-2]* **M 118.0, m 169-170°(dec), m 173-175°(dec), 178-180°(dec), pKa (H_2O) 3.91 (5°), 3.80 (20.3°), 3.87 (32.1°) and 3.89 (50°).** Hydantoic acid is prepared by reaction of potassium cyanate (KNCO) with glycine in H_2O, and is recrystallised from H_2O or EtOH. [West *J Biol Chem* **34** 187 *1918*, Dakin *J Chem Soc* **107** 434 *1915*, King *J Am Chem Soc* **78** 6020 *1956*, Inouye &Watanabe *J Chem Soc, Perkin Trans I* 1911 *1977*.] It has UV λ_{max} (ε) at 215 (2800) and 240 (165)nm (neutral species: EtOH); 215 (2600) and 240 (105)nm (cation: EtOH + H^+); 215 (2400) and 240 (80)nm (anion: EtOH + OH^-) [Crombie & Hooper *J Chem Soc* 3010 *1955*]. The *ethyl ester* [6293-20-5] **M 146.0,** crystallises from H_2O as needles with **m 135°**; and the *amide* [3530-79-8] **M 117.1,** crystallises from H_2O as prisms with **m 204°** (**180°** has also been reported). [*Beilstein* **4** H 359, **4** I 477, **4** II 792, **4** III 1163, **4** 1V 2411.]

Carnitine (α-hydroxy-β-*N,N,N*-trimethylaminopropionic acid) *[R(+) 541-14-0, S(*L*-) 541-15-1, RS 461-06-3]* **M 161.2, m *R* or *S isomer* 197-198°(dec), 210-212°(dec), *RS isomer* 195-197°, $[\alpha]_{546}^{20}$ (+) and (-) 36° (c 10, H_2O), pK^{25} 3.6.** The *S*(L) isomer is **levocarnitine, Vitamin B_T**. The *R* or *S* isomers crystallise from EtOH/Me_2CO (hygroscopic). The *R* or *S hydrochlorides* crystallise from hot EtOH or EtOH/Et_2O and have **m** 142°(dec). The *RS-isomer* crystallises from hot EtOH (hygroscopic). The *RS hydrochloride* crystallises in needles from hot EtOH and has **m** 196°(dec). [(±) Mazzetti & Lemmon *J Org Chem* **22** 228 *1957*, *Beilstein* **4** H 513, **4** I 548, **4** II 937-8, **4** III 1632-5, **4** IV 3185.]

L-Carnosine (β-alanyl-L-histidine) *[305-84-0]* **M 226.2, m 258-260°(dec), 260°(capillary tube), 262°(dec), $[\alpha]_D^{25}$ +20.5° (c 1.5, H_2O), pK_1^{25} 2.64, pK_2^{25} 6.83, pK_3^{25} 9.51.** Likely impurities are histidine and β-alanine. Crystallise L-carnosine from water by adding EtOH in excess. Recrystallise it from aqueous EtOH by slow addition of EtOH to a strong aqueous solution of the dipeptide. Its solubility in H_2O is 33.3% at 25°. [Vinick & Jung *J Org Chem* **48** 392 *1983*, Turner *J Am Chem Soc* **75** 2388 *1953*, Sifford & du Vigneaud *J Biol Chem* **108** 753 *1935*, *Beilstein* **25** H 516, **25** I 717, **25** II 408.]

***S*-Citrulline (2-amino-5-ureidopentanoic acid)** *[372-75-8]* **M 175.2, m 222°, $[\alpha]_D^{20}$ +24.2° (in 5M HCl), pK_1^{25} 2.43, pK_2^{25} 9.41.** Likely impurities are arginine and ornithine. Crystallise *S*-citrulline from water by adding 5 volumes of EtOH. Also crystallise it from water by addition of MeOH. [Ellenbogen *J Am Chem Soc*

74 5198 *1952*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2491-2494 *1961*, *Beilstein* **4** IV 2647.]

Corticotropin *[92307-52-3]* **polypeptide M_r ~4697**. The extract is purified by ion-exchange on CM-cellulose, desalted, evaporated and lyophilised. Then separate from impurities by gel filtration through Sephadex G-50. [Lande et al. *Biochemical Preparations* **13** 45 *1971*, Esch et al. *Biochem Biophys Res Commun* **122** 899 *1984*].

Creatine (*N*-guanidino-*N*-methylglycine) *[6020-87-7 (monohydrate), 57-00-1 (anhydrous)]* **M 131.1 (anhydrous), 149,1 (hydrate) m 303°, pK_1^{25} 2.63, pK_2^{25} 14.3.** Likely impurities are creatinine and other guanidino compounds. It crystallises from the minimum volume of boiling H_2O as the *monohydrate*. The *hydrate* is also obtained by dissolving in H_2O and adding Me_2CO. Drying under vacuum over P_2O_5 or drying at 100° gives the *anhydrous* base. The *anhydrous base* can be obtained also by dissolving the hydrate in H_2O, seeding with the anhydrous base and cooling in ice. A **m** of **258-268°(dec)** was reported. The *picrate* crystallises from 17 parts of H_2O with **m** of **218-220°(dec)**. [King *J Chem Soc* 2377 *1930*, Hoffmann et al. *J Am Chem Soc* **58** 1730 *1936*, Mendel & Hodgkin *Acta Cryst* **7** 443 *1954*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 2750 *1961*, *Beilstein* **4** III 1170, **4** IV 2425.]

Creatine phosphate di Na, $4H_2O$ salt (phosphocreatine) ***[922-32-7]*** **M 327.1, pK_1^{27} 2.7, pK_2^{27} 4.58, pK_3^{27} ~12.** To 3-4g of the salt in H_2O (220ml) is added 4 volumes of EtOH with thorough stirring and allowed to stand at 20° for 12 hours (this temperature is critical as crystals do not readily form at 23° or 25°). The salt first appears as oily droplets which slowly settle and crystallise. After 12 hours the supernatant is clear. Stirring and scratching the flask containing the filtrate brings out additional crystals (0.3-1g) if the salt is kept at 20° for 12 hours. Filter it off at room temperature, wash with 3 x 5ml of ice-cold 90% EtOH, then 5ml of absolute EtOH and dry it in a vacuum desiccator (Drierite or $CaCl_2$) for 16-30 hours. The *hexahydrate* (plates) is converted to the *tetrahydrate* salt (needles) in a vacuum at -10°. [Ennor & Stocken *Biochemical Preparations* **5** 9 *1957*, *Biochem J* **43** 190 *1958*, *Beilstein* **4** III 1170, **4** IV 2425.]

Creatinine [2-amino-1-methylimidazolidin-4-one, 2-imino-1-methyl-4(3*H*)-oxoimidazolidine] *[60-27-5]* **M 113.1, m ~305°(dec), pK_1^{25} 4.80, pK_2^{25} 9.2.** Likely impurities are creatine and ammonium chloride. Dissolve it in dilute HCl, then neutralise with ammonia. Recrystallise it from H_2O by adding excess of Me_2CO. The *picrate* crystallises from 23 volumes of boiling H_2O and has **m** 220-221°(dec). [King *J Chem Soc* 2377 *1930*, *Beilstein* **25** III/IV 2543.]

D-(*R-natural*) and L-(*S*-non-natural) Cycloserine (2-amino-3-isoxazolidone) *[R- 68-41-7 and S- 339-72-0]* **M 102.1, m 145-150° (dec), 154-155°, 155-156° (dec), 156° (dec), $[\alpha]_D^{25}$ (+) and (-) 137° (c 5, 2N NaOH), pK_1^{10} 4.5, pK_2^{10} 7.74, pK_1^{25} 4.50, pK_2^{25} 7.43, pK_1^{50} 4.44, pK_2^{50} 7.20.** Purify cycloserine by recrystallisation from aqueous EtOH or MeOH or aqueous NH_3/EtOH or isoPrOH. Also recrystallise it from aqueous ammoniacal solution at pH 10.5 (100mg/ml) by diluting with 5 volumes of isopropanol and then adjusting to pH 6 with acetic acid. An aqueous solution, buffered to pH 10 with Na_2CO_3, can be stored in a refrigerator for 1 week without decomposition. Its UV has λ_{max} at 226nm ($A_{1cm}^{1\%}$ 4.02). The *tartrate salt* has **m** 165-166° (dec), 166-168° (dec), and $[\alpha]_D^{24}$ -41° (c 0.7, H_2O). [Stammer et al. *J Am Chem Soc* **79** 3236 *1959*, UV: Kuehl *J Am Chem Soc* **77** 2344 *1955*, *Beilstein* **27** III/IV 5549.]

Cystamine dihydrochloride [2,2'-diaminodiethylene disulfide dihydrochloride, 2,3'-dithio-bis(ethylamine) dihydrochloride] *[56-17-7]* **M 225.2, m 219-220°(dec), pK_1^{30} 8.82, pK_2^{30} 9.58.** Recrystallise the salt by dissolving in EtOH containing a few drops of dry EtOH/HCl, filtering and adding dry Et_2O. The solid is dried in a vacuum and stored in a dry and dark atmosphere. It has been recrystallised from EtOH (solubility: 1g in 60ml of boiling EtOH) or MeOH (plates). The *free base* has **b** 90-100°/0.001mm, 106-108°/5mm and 135-136°/760mm, d_4^{20} 1.1559, n_D^{20} 1.5720. [Verly & Koch *Biochem J* **58** 663 *1954*, Gonick et al. *J Am Chem Soc* **76** 4671 *1954*, Jackson & Block *J Biol Chem* **113** 137 *1936*.] The *dihydrobromide* has **m** 238-239° (from EtOH/Et_2O) [Viscontini *Helv Chim Acta* **36** 835 *1953*]. [*Beilstein* **4** H 287, **4** IV 1578.]

***S,S*-(L,L)-Cystathionine (*S*-2-amino-2-carboxyethyl-L-homocysteine, L-2-amino-4[(2-amino-2-carboxy-ethyl)thio]butyric acid)** *[56-88-2]* **M 222.3, m >300°, dec at 312° with darkening at 270°, $[\alpha]_D^{20}$ +23.9° (c 1, M HCl).** *S,S*-Cystathionine is purified by converting it to the *HCl* salt in 20% HCl and carefully basifying with aqueous NH_3 until separation is complete. Filter it off and dry it in a vacuum. It forms prisms from H_2O. The *dibenzoyl* derivative has **m** 229° (from EtOH). [IR: Greenstein & Winitz *Chemistry of the Amino Acids (J Wiley)* **Vol 3** p2690 *1961* and Tallan et al. *J Biol Chem* **230** 707 *1958*, Synthesis: du Vigneaud et al. *J Biol Chem* **143** 59 *1942*, Anslow et al. *J Biol Chem* **166** 39 *1946*.] [Prepn: Weiss & Stekol *J Am Chem Soc* **73** 2497 *1951*; see also du Vigneaud et al. *J Biol Chem* **143** 60 *1942*, Biological synthesis: Greenberg *Methods Enzymol* **5** 943 *1962*, *Beilstein* **4** IV 3197.]

Cysteamine (2-aminoethanethiol, 2-mercaptoethylamine) *[60-23-1]* **M 77.2, m 97-98.5°, 98-99°, 99-100°, pK_1^0 9.15, pK_2^0 11.93, pK_1^{30} 8.42, pK_2^{30} 10.83.** It is soluble in H_2O giving an alkaline reaction, and it has a disagreeable odour. A likely impurity is the disulfide *cystamine* which is not soluble in alkaline solution. Under a N_2 atmosphere dissolve it in EtOH, evaporate to dryness and wash the white residue with dry petroleum ether, then sublime it at 0.1mm and store it under N_2 at 0-10° in the dark. Its *$HgCl_2$ (2:3) complex* has **m** 181-182° (from H_2O), and its *picrate* has **m** 125-126°. [Mills & Bogert *J Am Chem Soc* **57** 2328 *1935*, **62** 1173 *1940*, Baddiley & Thain *J Chem Soc* 800 1952, Shirley *Preparation of Organic Intermediates (J. Wiley)* **Vol 3** 189 *1951*, Barkowski & Hedberg *J Am Chem Soc* **109** 6989 *1987*, *Beilstein* **4** IV 1570.]

Cysteamine hydrochloride *[156-57-0]* **M 113.6, m 70.2-70.7°, 70-72°.** Purify the salt by recrystallisation from EtOH. It is freely soluble in H_2O and should be stored in a dry atmosphere. [Mills & Bogert *J Am Chem Soc* **62** 1177 *1940*.] The *picrate* has **m** 125-126°; see previous entry for *free base*. [*Beilstein* **4** IV 1570.]

(±)-Cysteic acid (3-sulfoalanine, 1-amino-3-sulfopropionic acid) *[13100-82-8, 3024-83-7]* **M 169.2, m 260°(dec).** Likely impurities are cystine and oxides of cysteine. Crystallise the acid from water by adding 2 volumes of EtOH. It crystallises from H_2O as the *monohydrate*. When recrystallised from aqueous MeOH it has **m** 264-266°, and the *anhydrous* acid has **m** ~260°(dec). [Chapeville & Formageot *Biochim Biophys Acta* **26** 538 *1957*, Gortner & Hoffman *J Biol Chem* **72** 435 *1927*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p1908 *1961*.]

***R*(L)-Cysteic acid (H_2O)** *[23537-25-9]* **M 187.2, m 275-280°(dec), 289°, $[\alpha]_D^{20}$ +8.66° (c 7.4, H_2O, pH 1) and +1.54° (H_2O, pH 13), pK_1^{25} 1.9 (SO_3H), pK_2^{25} 8.7 (CO_2H), pK_3^{25} 12.7 (NH_2).** Likely impurities are cystine and oxides of cysteine. Crystallise it from water by adding 2 volumes of EtOH. When recrystallised from aqueous MeOH it has **m** 264-266°, and the *anhydrous* acid has **m** ~260°(dec). [Chapeville & Formageot *Biochim Biophys Acta* **26** 538 *1957*, Riordan & Giese *Methods Enzymol* **47** 31 *1977*, *Beilstein* **4** IV 3296.]

D-(*S*)- and L-(*R*)- Cysteine (*S*- and *R*-2-amino-3-mercaptopropionoic acid) *[S(+) 921-01-7 , R(-) 52-90-4]* **M 121.2, m 230°, 240° (dec), $[\alpha]_D^{20}$ + and -7.6° (c 2, M HCl), + and -10.1° (c 2, H_2O, pH 10), pK_1^{25} 1.92 (CO_2), pK_2^{25} 8.35 (NH_2), pK_3^{25} 10.46 (SH).** Purify it by recrystallisation from H_2O (free from metal ions) and dry it in a vacuum. It is soluble in H_2O, EtOH, Me_2CO, EtOAc, AcOH, $*C_6H_6$ and CS_2. Acidic solutions can be stored under N_2 for a few days without deterioration. [For synthesis and spectra see Greenstein & Winitz *Chemistry of the Amino Acids (J. Wiley)* **Vol 3** p1879 *1961*, *Beilstein* **4** III 1618, **4** IV 3144.]

L-Cysteine hydrochloride (H_2O) *[52-89-1 (anhydrous), 7048-04-6 (monohydrate)]* **M 175.6, m 175-178° (dec), $[\alpha]_D^{25}$ +6.53° (5M HCl).** Likely impurities are cystine and tyrosine. Crystallise the salt from MeOH by adding diethyl ether, or from hot 20% HCl. Dry it under vacuum over P_2O_5. *Hygroscopic*. [*Beilstein* **4** III 1580, 1600.]

(±)-Cysteine hydrochloride *[10318-18-0 (anhydrous), 116797-51-5 (monohydrate)]* **M 157.6, m 140-141.5° (dec), pK_2^{20} 8.36 (NH_2), pK_2^{20} 10.28 (SH).** Crystallise the salt from hot 20% HCl and dry it under vacuum over P_2O_5. It also crystallises from EtOH with **m** 175° (hydrate?). When crystallised from absolute EtOH or EtOH/Et_2O, it has **m** 140-141.5° (anhydrous?). [Rurner & Voitle *J Am Chem Soc* **72** 628 *1950*, Albert *Biochem J* **50** 690 *1953*, *Beilstein* **4** IV 3145.]

L-Cystine *[56-89-3]* **M 240.3, $[\alpha]_D^{18.5}$ -229° (c 0.92 in M HCl), pK_1^{25} 1.04 (1.65), pK_2^{25} 2.05 (2.76), pK_3^{25} 8.00 (7.85), pK_4^{25} 10.25 (8.7, 9.85).** Cystine disulfoxide impurity is removed by treating an aqueous suspension with H_2S. The cystine is filtered off, washed with distilled water and dried at 100° under a vacuum over P_2O_5. Crystallise it by dissolving in 1.5M HCl, then adjusting to neutral pH with ammonia. Likely impurities are D-cystine, meso-cystine and tyrosine. Also purify it by dissolving it in 10% NH_3 and adding gradually dilute AcOH until the point of precipitation and cooling slowly [Dughton & Harrison *Acta Cryst* **12** 396, 402 *1959*.] Alternatively dissolve it in 6N NH_4OH and evaporate it at room temperature for crystallisation to occur. [Chaney & Steinrauf *Acta Cryst* **30** 711 *1974*, *Beilstein* **4** IV 3155.]

***meso*-2,6-Diaminopimelic acid** *[583-93-7]* **M 190.2, m 313-315°(dec) pK_1^{25} 1.04 (1.65, 1.8), pK_2^{25} 2.05 (2.2, 2.76), pK_3^{25} 8.00 (7.85, 8.8), pK_4^{25} 10.25 (8.7, 9.85, 9.9), pI ~5.5.** Crystallise the acid from H_2O or aqueous EtOH. Also purify it by dissolving it in hot H_2O and adding 5 volumes of EtOH, filter after 12 hours at -10°. The acid has been recrystallised from 35% aqueous EtOH [Wade et al. *J Am Chem Soc* **79** 648, 651 *1957*]. [*Beilstein* **4** IV 3081.]

L(*S*)-2,3-Diaminopropionic acid monohydrochloride (3-amino-L-alanine hydrochloride) *[1482-97-9]* **M 140.6, m 132-133°(dec), 237°(dec), $[\alpha]_D^{25}$ +26.1° (c 5.8, M HCl), pK_1^{25} 1.30, pK_2^{25} 6.79, pK_3^{25} 9.51.** It forms needles from H_2O and can be recrystallised from aqueous EtOH. [Gmelin et al. *Z Physiol Chem.* **314** 28 *1959*, IR: Koegel et al. *J Am Chem Soc* **77** 5708 *1977*, *Beilstein* **4** IV 2501.]

***meso*-2,3-Diaminosuccinic acid** *[23220-52-2]* **M 148.1, m 305-306°(dec, and sublimes), $pK_{Est(1)}$ ~3.6, $pK_{Est(2)}$ ~9.8.** Crystallise the acid from water. Also, dissolve it in dilute NaOH and add AcOH to pH 5-6 and allow it to crystallise (**m** 304° dec). *Alternatively*, dissolve the acid in aqueous NH_3 and boil; when the NH_3 has evaporated, the acid separates, filter it off and dry it at room temperature in a vacuum. In another procedure 1g of acid is dissolved in 10ml of conc HCl + 15ml of H_2O at 80°, filter immediately, dilute with 20ml of H_2O and allow to stand for 24 hours. When the *monohydrochloride* (0.7g, **m** 175-156° dec) crystallises out, filter and dry it. It has also been purified by dissolving it in the minimum volume of 10% HCl, filtering, and diluting with 5 volumes of H_2O when the crystals separate slowly on standing. The acid is filtered off after 24 hours and dried (**m** 306-306° dec). Similar procedures were used for the *dl-isomer*. [Kenner *J Org Chem* **13** 28 *1948*, McKennis & Yard *J Org Chem* **23** 980 *1958*, *Beilstein* **4** III 1528, **4** IV 3025.]

6-Diazo-5-oxo-L-norleucine *[157-03-9]* **M 171.2, m 140-150°(dec), 145-155°(dec), $[\alpha]_D^{20}$ +21° (c 5, EtOH), pK_1 2.1, pK_2 8.95.** Crystallise it from EtOH, H_2O/EtOH, MeOH, 95% aqueous MeOH or H_2O/Me_2CO. [DeWald & Moor *J Am Chem Soc* **80** 3944 *1958*, Dion et al. *J Am Chem Soc* **78** 3075 *1956*, *Beilstein* **4** IV 3278.]

Diglycyl glycine (triglycine) *[556-33-2]* **M 189.2, m 246°(dec), pK_1^{25} 3.30, pK_2^{25} 7.96.** Crystallise triglycine from H_2O or H_2O/EtOH and dry it at 110°. [Yakel & Hughes *Acta Cryst* **5** 847 *1952*, Lenel et al. *Acta Cryst* **3** 313 *1952*, Holley & Holley *J Am Chem Soc* **74** 3072 *1952*, *Beilstein* **4** III 1198, **4** IV 2469.]

***N,N*-Di-(2-hydroxyethyl)glycine (BICINE, *N,N*-bis-(2-hydroxyethyl)glycine)** *[150-25-4]* **M 163.2, m 193°(dec), 193-195°(dec), pK_1^{25} 2.50, pK_2^{25} 8.11.** Dissolve bicine in a small volume of hot water and precipitate it with EtOH, twice. Repeat once more but treat the aqueous solution with charcoal and filter before adding EtOH. Also crystallise it from concentrated aqueous solutions. [Torn & Kolthoff *J Am Chem Soc* **77** 2061 *1955*, Chaberek et al. *J Am Chem Soc* **75** 2185 *1953*, *Beilstein* **4** IV 2390.]

3-(3,4-Dihydroxyphenyl)-L-alanine (DOPA, LEVODOPA, EUODOPA) *[59-92-7, 5796-17-8]* **M 197.2, m 275°(dec), 267-268°(dec), 284-286°(dec), ~295°(dec), $[\alpha]_D^{13}$ -13.1° (c 5.12, N HCl), pK_1^{25} 2.32 (CO_2H), pK_2^{25} 8.72 (NH_2), pK_3^{25} 9.96 (OH), pK_4^{25} 11.79 (OH).** Likely impurities are vanillin, hippuric acid, 3-methoxytyrosine and 3-aminotyrosine. DOPA recrystallises from large volumes of H_2O forming colourless white needles; its solubility in H_2O is 0.165%, but it is insoluble in EtOH, $*C_6H_6$, $CHCl_3$, and EtOAc. Also crystallise it by dissolving it in dilute HCl and adding dilute ammonia to give pH 5, under N_2. *Alternatively*, crystallise it from dilute aqueous EtOH. It is rapidly oxidised in air when moist, and darkens, particularly in

alkaline solution. Dry it *in vacuo* at 70° in the dark, and store it in a dark container preferably under N_2. It has λ_{max} at 220.5nm (log ε 3.79) and 280nm (log ε 3.42) in 0.001N HCl. [Yamada et al. *Chem Pharm Bull Jpn* **10** 693 *1962*, Bretschneider et al. *Helv Chim Acta* **56** 2857 *1973*, NMR: Jardetzky & Jardetzky *J Biol Chem* **233** 383 *1958*, *Beilstein* **4** IV 2492, 2493.]

3-(3,4-Dihydroxyphenyl)-2-methyl-L-alanine [methyldopa, 2-amino-3-(3,4-dihydroxy-phenyl)-2-methylpropionic acid] *[555-30-6, 41372-08-1 (sesquihydrate)]* **M 238.2, m >300°, 300-301°(dec), pK_1^{25} 2.2, pK_2^{25} 9.2, pK_3^{25} 10.6, pK_4^{25} 12.0.** Recrystallise methyldopa from H_2O. [Reinhold et al. *J Org Chem* **33** 1209 *1968*.] The L-*isomer* forms a *sesquihydrate* from H_2O **m** 302-304° (dec), and the *anhydrous* crystals are *hygroscopic*, $[\alpha]_D^{23}$ -4.0° (c 1, 0.1N HCl), $[\alpha]_{546}$ +154.5° (c 5, $CuSO_4$ solution). It has λ_{max} at 281nm (ε 2780). Its solubility in H_2O at 25° is ~10mg/ml and the pH of an aqueous solution is ~5.0. It is insoluble in most organic solvents. [Stein et al. *J Am Chem Soc* **77** 700 *1955*, *Beilstein* **4** IV 2505.]

3,5-Diiodo-L-thyronine (3,5-diiodo-4-[4-hydroxyphenoxy]-1-phenylalanine) *[1041-01-6]* **M 525.1, m 255°(dec), 255-257°(dec), $[\alpha]_D^{22}$ +26° [2N HCl-EtOH (1:2)], pK_1^{20} 3.25, pK_2^{20} 5.32, pK_3^{20} 9.48.** Recrystallise it from EtOH. [Chambers et al. *J Chem Soc* 3424 *1949*, *Beilstein* **14** III 1565, **14** IV 2372.]

3,5-Diiodo-L-tyrosine dihydrate *[300-39-0]* **M 469.0, m 199-210°, 202°(dec), 204°(dec), $[\alpha]_D^{20}$ +2.89° (c 4.9, 4% HCl), pK_1^{25} 2.12, pK_2^{25} 6.48, pK_3^{25} 7.82.** It forms crystals from H_2O [solubility (g/L): 0.204 at 0°, 1.86 at 50°, 5.6 at 75° and 17.0 at 100°]. Also recrystallise it from 50% or 70% EtOH. When boiled in EtOH the crystals swell, and on further boiling a gelatinous precipitate is formed [Harrington *Biochem J* **22** 1434 *1928*, Jurd *J Am Chem Soc* **77** 5747 *1955*]. It also crystallises from cold dilute ammonia on adding acetic acid to pH 6. [*Beilstein* **14** IV 2370.]

***dl*-4-Dimethylamino-2,2-diphenylvaleramide (Dimevamide, Aminopentamide)** *[60-46-8]* **M 296.4, m 183-184°, pK_{Est} ~9.8.** Crystallise dimevamide from aqueous EtOH. The *hydrochloride* forms leaflets from EtOH/Et_2O with **m** 190-191° and is deliquescent. The *picrate* has **m** 210-211°. It is an antispasmotic. [Moffett et al. *J Am Chem Soc* **79** 4451, 4457 *1957*, Beckett *J Pharm Pharmacol* **8** 848 *1956*, *Beilstein* **14** III 1363, **14** IV 1865.]

(-)-L-4-Dimethylamino-2,2-diphenylvaleramide *[6078-64-4]* **M 296.4, m 134.5-135.5°, 136.5-137.5°, $[\alpha]_D^{20}$ -112° (c 0.87, EtOH), -84.1° (c 0.9, 0.04N HCl), $pK_{Est(1)}$ 8.3.** Crystallise the amide from petroleum ether, EtOH or as needles from aqueous EtOH. It is an analgesic. [Beckett et al. *J Chem Soc* 3076 *1957*.]

***N,N*-Dimethylglycinehydrazide hydrochloride** *[539-64-0]* **M 153.6, m 181°.** Crystallise the salt by adding EtOH to a concentrated aqueous solution. [Viscontini & Meier *Helv Chim Acta* **33** 1773 *1950*, *Beilstein* **4** III 1127, **4** IV 2368.]

Djenkolic acid (S,S'-methylene-bis-L-cysteine) *[498-59-9]* **M 254.3, m 300-350°(dec), $[\alpha]_D^{20}$ -65° (c 2, HCl) [See pK of S-methyl-L-cysteine].** Crystallise djenkolic acid from a large volume of water (solubility is 0.5g%). [du Vigneaud & Patterson *J Biol Chem* **114** 533 *1936*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2682, 2687 *1961*, *Beilstein* **4** III 1591.] The *N,N'-dibenzoyl* derivative crystallises with $1H_2O$ from aqueous EtOH with **m** 87.5-89° [*Beilstein* **9** III 1171.]

***S*-Ethionine** *[13073-35-3]* **M 163.2, m 282°(dec), $[\alpha]_D^{25}$ +23.7° (in 5M HCl), pK^{25} 9.02 (for *RS*).** Likely impurities are *N*-acetyl-(*R* and *S*)-ethionine, *S*-methionine, and *R*-ethionine. Crystallise it from water by adding 4 volumes of EtOH or 85% aqueous EtOH. It sublimes at 196-216°/0.3mm with 99.1% recovery and unracemised [Gross & Gradsky *J Am Chem Soc* **77** 1678 *1955*]. [Weiss & Stekol *J Am Chem Soc* **73** 2399 *1951*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2658, 2659 *1961*, *Beilstein* **4** IV 3194.]

Ethylene *N,N'*-bis[(*o*-hydroxyphenyl)glycine] *[1170-02-1]* **M 360.4, m 249°(dec), $pK_{Est(1)}$ ~1.8, $pK_{Est(2)}$ ~4.8, $pK_{Est(3)}$ ~9.0.** Purify it by extensive Soxhlet extraction with acetone. [Bonadies & Carrano *J Am Chem*

Soc **108** 4088 *1986*].

2-Fluorophenylalanine *[R(+) 97731-02-7, S(-) 19883-78-4]* **M 183.2, m 226-232°, 231-234°, $[\alpha]_D^{25}$ (+) and (-) 15° (c 2, H_2O pH 5.5), pK_1^{24} 2.12, pK_2^{24} 9.01.** Recrystallise 2-fluorophenylalanine from aqueous EtOH. The *hydrochloride* has **m** 226-231°(dec), and the *N-acetyl* derivative has **m** 147-149° (aqueous EtOH). [Bennett & Nieman *J Am Chem Soc* **72** 1800 *1950*, *Beilstein* **14** III 1268.]

4-Fluorophenylalanine *[R(+) 18125-46-7, S(-) 1132-68-9]* **M 183.2, m 227-232°, $[\alpha]_D^{25}$ + and -24° (c 2, H_2O), pK_1^{24} 2.13, pK_2^{24} 9.05.** It is recrystallised from aqueous EtOH. The *(R)-N-acetyl* derivative has **m** 142-145°, $[\alpha]_D^{25}$ -38.6° (c 8, EtOH). [Bennett & Nieman *J Am Chem Soc* **72** 1800 *1950*, *Beilstein* **14** III 1268.]

L-5-Fluorotryptophan monohydrate *[16626-02-1; 154-08-5]* **M 240.2, m reported for the L-enantiomer 158-163°(dec), (±)-isomer >250°(dec), 264-265°(also 238-239° dec reported), $[\alpha]_D^{20}$ +5.5° (c 1, 0.1N HCl), $pK_{Est(1)}$~ 2.5 (CO_2H), $pK_{Est(2)}$~ 9.4 (NH_2), $pK_{Est(3)}$~16 (indole-NH).** Recrystallise it from EtOH, aqueous EtOH or AcOH. Also purify it by passage through a Dowex AG1x2 (acetate form) column and recrystallise the L-enantiomer (from enzymic enrichment) from H_2O/EtOH, **m** 158-163°(dec), $[\alpha]_D^{23}$ -8.3° (c 2.5, N NaOH). [Coy et al. *Biochemistry* **13** 3550 *1974*, *Beilstein* **22/14** V 116.]

L-Glutamic acid *[56-86-0]* **M 147.1, m 224-225°(dec), $[\alpha]_D^{25}$ +31.4° (c 5, 5M HCl), pK_1^{20} 2.06, p K_2^{20} 4.35, pK_3^{20} 9.85.** Crystallise L-glutamic acid from H_2O acidified to pH 3.2 by adding 4 volumes of EtOH, and drying at 110°. Likely impurities are aspartic acid and cysteine. It sublimes at 170-175°/10mm. It melts at 160° with cyclisation to L-*pyrrolidone carboxylic acid*. [Dunn & Brophy *J Biol Chem* **99** 224 *1958*, Parikh et al. *J Am Chem Soc* **80** 957*1958*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 1929-1952 *1961*, *Beilstein* **4** III 1530, **4** IV 3028.]

L-Glutamic acid-γ-benzyl ester *[1676-73-9]* **M 237.3, m 179-181°, $[\alpha]_{589}^{20}$ +19.3° (c 1, AcOH), pK_1^{25} 2.17, pK_2^{25} 9.00.** Recrystallise the ester from H_2O and store it at 0°. [Estrin *Biochemical Preparations* **13** 25 *1971*, *Beilstein* **6** IV 2538.]

L-Glutamine *[56-85-9]* **M 146.2, m 184-185°, 187°, $[\alpha]_D^{25}$ +31.8° (M HCl), pK_1^{25} 2.17, pK_2^{25} 9.13.** Likely impurities are glutamic acid, ammonium pyroglutamate, tyrosine, asparagine, isoglutamine, arginine. Crystallise it from water or aqueous EtOH. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 1929-1925 *1961*, *Beilstein* **4** IV 3038.]

L-Glutathione (reduced form, γ-L-glutamyl-L-cysteinyl-glycine) *[70-18-8]* **M 307.3, m 188-190°(dec), 195°(dec), $[\alpha]_D^{20}$ -20.1° (c 1, H_2O), pK_1^{25} 2.12 (CO_2H), pK_2^{25} 3.59 (CO_2H), pK_3^{25} 8.75 (NH_2), pK_4^{25} 9.65 (10.0, SH).** Crystallise L-glutathione from 50% aqueous EtOH, dry it in a vacuum and store it below 5°. *Alternatively*, recrystallise it from aqueous EtOH under N_2, and store it dry in a sealed container below 4°. It is soluble in H_2O. [Weygand & Geiger *Chem Ber* **90** 634 *1957*, Martin & Edsall *Bull Soc Chim Fr* **40** 1763 *1958*, du Vigneaud & Miller *Biochemical Preparations* **2** 87 *1952*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 2** p 1523 *1961*, *Beilstein* **4** IV 3165.]

L-Glutathione (oxidised) *[27025-41-8]* **M 612.6, m 175-195°, 195°, $[\alpha]_D^{20}$ -98° (c 2, H_2O), pK_1 3.15, pK_2 4.03, pK_3 8.75.** Purify it by recrystallisation from 50% aqueous EtOH. Its solubility in H_2O is 5%. Store it at 4°. [Li et al. *J Am Chem Soc* **76** 225 *1954*, Berse et al. *Can J Chem* **37** 1733 *1959*, *Beilstein* **4** IV 3168.]

Glycinamide hydrochloride *[1668-10-6]* **M 110.5, m 186-189°, 203-205°, 207-208°, pK_1^{25} -6.10, pK_2^{25} -1.78, pK_3^{25} 7.95.** Crystallise the salt from EtOH, EtOH/H_2O or MeOH. [Karmas & Spoerri *J Am Chem Soc* **74** 1580 *1952*, *Beilstein* **4** IV 2358.]

Glycine anhydride (2,5-diketopiperazine) *[106-57-0]* **M 114.1, m 309-310°, 311-312°(dec), ~315°(dec), pK_1 -4.45, pK_2 -2.16 (pK_2 -1.94 in AcOH).** Recrystallise glycine anhydride from H_2O (plates) and it can be

sublimed (slowly) at 260° or at 140-170°/0.5mm. The *dihydrochloride* has **m** 129-130° and is prepared by dissolving it in conc HCl and adding EtOH to crystallisation point; dry it in a vacuum. The *bis-1-naphthylurethane* has **m** 232°(dec), and the *diperchlorate* has **m** 117° (*hygroscopic*). [MS: Johnstone *J Chem Soc, Perkin Trans 1* 1297 *1975*, NMR: Blaha & Samek *Col Czech Chem Commun* **32** 3780 *1967*, Sauborn *J Phys Chem* **36** 179 *1932*, Corey *J Am Chem Soc* **60** 1599 *1938*, *Beilstein* **24** IV 1070.]

Glycine ethyl ester hydrochloride *[623-33-6]* **M 136.9, m 145-146°, pK^{25} 7.69.** Crystallise it from absolute EtOH or EtOH/Et_2O. [Marvel *Org Synth* Coll Vol **II** 310 *1943*, *Beilstein* **4** II 780, **4** III 3 75.]

Glycine *tert*-butyl ester (glycine 1,1-methylethyl ester) *[6456-742]* **M 131.1, 65-67°/20mm, d_D^{20} 1.4237, pK_{Est} ~7.6.** The ester, prepared from *tert*-butyl azidoacetate by catalytic reduction (5% Pd/C and H_2), has been purified *via* the phosphite salt. To the ester (23.6g, 0.18mole) in MeOH (150ml) is added phosphorous acid (15g, 0.18mole), the mixture is gently warmed to dissolve the latter and after cooling to 25°, Et_2O (150ml) is added slowly and the stirred mixture is cooled at 0° for 12 hours. The *phosphite salt* is collected, filtered off, washed with Et_2O and dried in an oven at 70° (32g, 82%, **m 144-147° dec.)**. After recrystallisation from MeOH-isopropyl ether, the phosphite salt has **m 154-157° (dec)**. The phosphite salt (32g, 0.15mole) is added with stirring into aqueous 6N-sodium hydroxide solution (50ml) until all the solid has dissolved. The mixture is extracted with Et_2O (2 x 20ml), the extract is dried (Na_2SO_4), filtered, evaporated and the residue is distilled under vacuum to give the *tert*-butyl ester as an oil (14g, 72%). The *tert*-butyl group is versatile and is labile under acidic conditions which do not affect the blocked amino grouping. *Glycine tert-butyl ester hydrochloride* [27532-96-3] **M 167.6**, has **m 143° (**EtOH/Et_2O). [Vollmar & Dunn *J Org Chem* **25** 387 *1960*, More and Rydon *Org Synth* Coll Vol **V** 586 *1973*, *Beilstein* **6** IV 2489.]

Glycine hydrochloride *[6000-43-7]* **M 111.5, m 176-178°, 185°, 187°.** Crystallise the salt from absolute EtOH or 80% EtOH. *Monoglycine hydrochloride* has **m** 176-177°, and *diglycine monohydrochloride* has **m** 187°. [Frost *J Am Chem Soc* **64** 1286 *1942*, *Beilstein* **4** III 1111, **4** IV 2353.]

Glycine methyl ester hydrochloride *[5680-79-5]* **M 125.6, m 174°(dec), 177°(corrected), pK^{25} 7.66.** Crystallise the ester salt from MeOH. [Werbin & Spoerri *J Am Chem Soc* **69** 1682 *1947*, *Beilstein* **4** H 340, **4** III 1116.]

Glycine *p*-nitrophenyl ester hydrobromide. *[7413-60-7]* **M 277.1, m 214° (dec).** Recrystallise the ester salt from MeOH by adding diethyl ether. [Alners et al. *Biochemical Preparations* **13** 22 *1971*].

Glycocyamine (*N*-guanylglycine) *[352-97-6]* **M 117.1, m 280-284°(dec), >300°, pK^{25} 2.86 (NH_3^+).** Recrystallise it from 15 parts of hot H_2O, or by dissolving it in slightly more than the calculated amount of 2N HCl and precipitating it by adding an equivalent of 2N NaOH, filtering, washing with cold H_2O and drying first *in vacuo*, then at 60° *in vacuo*. The *hydrochloride* has **m** 200°(dec) after recrystallisation from aqueous HCl as plates. The *picrate* forms needles from hot H_2O with **m** 210°(dec). [Brand & Brand *Org Synth* Coll Vol **III** 440 *1955*, Failey & Brand *J Biol Chem* **102** 768 *1933*, King *J Chem Soc* 2375 *1930*, *Beilstein* **4** H 359, **4** I 477, **4** II 793, **4** III 1165.]

***N*-Glycylanilide** *[555-48-6]* **M 150.2, m 62°, pK_{Est}~8.0.** *N*-Glycylanilide crystallises from water as needles (*dihydrate*) and is soluble in Et_2O. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp1915-1970 *1961*, *Beilstein* **4** H 343.]

Glycylglycine *[556-50-3]* **M 132.1, m 260-262°(dec), pK^{20} 8.40, pK^{30} 8.04, pK_1^{15} 3.19, pK_2^{15} 8.40.** Crystallise glycylglycine from aqueous 50% EtOH or water at 50-60° by addition of EtOH. Dry it at 110°. It sublimes at 190-200°/0.3mm with 30% recovery [Gross & Gradsky *J Am Chem Soc* **77** 1678 *1955*, King *J Am Chem Soc* **79** 6153 *1957*]. [*Beilstein* **4** IV 2459.]

Glycylglycine hydrochloride *[13059-60-4]* **M 168.6, m 215-220°, 235-236°, 260-262°, pK_1^{25} 3.12, pK_2^{25} 8.17.** Crystallise the salt twice from 95% EtOH. Single crystals are formed by slow evaporation of an aqueous

solution. [Parthasarathy *Acta Cryst (B)* **25** 509 *1969*, Mellon & Hoover *J Am Chem Soc* **73** 3879 *1951*, Garfinkel & Edsall *J Am Chem Soc* **80** 3818 *1958*, *Beilstein* **4** IV 2469.]

Glycyl-L-proline *[704-15-4]* **M 172.2, m 184°(dec), 185°, 204°, pK_1^{25} 2.81, pK_2^{25} 8.65.** Crystallise glycyl-L-proline from water at 50-60° by addition of EtOH. [Saidel *J Am Chem Soc* **77** 3893 *1955*, Bergmann et al. *Z Physiol Chem* **212** 79 *1932*, *Beilstein* **22** IV 49.]

***dl*-Glycylserine** *[687-38-7]* **M 162.2, m 197-199°(dec, sealed tube), 207°(dec), pK_1^{25} 2.92, pK_2^{25} 8.10.** Crystallise it from H_2O (charcoal) by addition of EtOH. [Fölsch *Acta Chem Scand* **12** 561-566 *1958*, NSR: Bovey & Tiers *J Am Chem Soc* **81** 2876 *1959*, *Beilstein* **4** III 1572, **4** IV 3140.]

Gramicidin A (a pentadecapeptide from *Bacillus brevis*) *[11029-61-1]* **m ~229-230°(dec).** Purify gramicidin A by countercurrent distribution from $*C_6H_6/CHCl_3$, $MeOH/H_2O$ (15:15:23:7) with 5000 tubes. Fractions are examined by UV (280nm) of small aliquots. Separation from gramicidin C and other material occurred after 999 transfers. [Gross & Witkop *Biochemistry* **4** 2495 *1965*, Bauer et al. *Biochemistry* **11** 3266 *1972*.] Purify it finally by recrystallisation from $EtOH/H_2O$ and dry it at $100°/10^{-2}$mm over KOH. It forms platelets **m** 229-230°. It is almost insoluble in H_2O (0.6%) but soluble in lower alcohols, dry Me_2CO, dioxane, acetic acid and pyridine. The commercial material is more difficult to crystallise than the synthetic compound. [Sarges & Witkop *J Am Chem Soc* **86** 1861 *1964*, **87** 2011, 2020 *1965*.] It has characteristic $[\alpha]_D^{20}$ +27.3° (c 1.3, MeOH) and UV with λ_{max} at 282nm (ε 22,100). The *N-carbamoyldeformyl gramicidine A* precipitates from EtOAc/petroleum ether (b 40-60°). [*Beilstein* **26** III/IV 4273.]

Gramicidin C (a pentadecapeptide from *Bacillus brevis*) *[9062-61-7]***.** Purify as for Gramicidin A since they are isolated together and separated. [Sarges & Witkop *Biochemistry* **4** 2491 *1965*, Hunter & Schwartz "Gramicidins" in *Antibotics I* (Gotlieb and Shaw Eds) Springer-Verlag, NY, p. 642 *1967,* as well as references above for Gramicidin A.]

Gramicidin S *[113-73-5]* **M 1141.4, m 268-270°, $[\alpha]_D^{25}$ -290° (c 0.5, EtOH + 30mM aqueous HCl {7:3}).** Gramicidin S crystallises from EtOH. The *di-HCl [15207-30-4]* crystallises from EtOH (+ few drops of HCl) with **m** 277-278° (see below). [NMR: Gibbons et al. *Nature* **227** 840 *1970*, *Beilstein* **26** III/IV 4273.]

Gramicidin S 2HCl (from *Bacillus brevis* Nagano) *[15207-30-4]* **M 1214.4, m 277-278°(dec), $[\alpha]_D^{24}$ -289° (c 0.4, 70%H_2O+EtOH).** It crystallises in prisms from EtOH+aqueous HCl.

***N*-Guanyltyramine hydrochloride** *[60-20-8]* **M 215.7, m 218°, pK_1 10.2 (phenolic OH), pK_2 12.4 (guanidino N).** Purify the salt on a phosphocellulose column and elute with a gradient of aqueous NH_3 (0-10%). The second major peak has the characteristic tryptamine spectrum and is collected, and lyophilised to give white crystals of the *dihydrate* which dehydrate at 100°. It has UV with λ_{max} at 274.5nm (ε 1,310) in 0.1N NaOH and 274.5nm (ε 1,330) at pH 7.0. Excitation λ_{max} is at 280nm and emission λ_{max} is at 330nm. [Mekalanos et al. *J Biol Chem* **254** 5849 *1979*.]

_S_-Histidine *[71-00-1]* **M 155.2, m 287°(dec), $[\alpha]_D^{25}$ -39.7° (c 1, H_2O), +13.0° (6M HCl), pK_1^{25} 1.96, pK_2^{25} 6.12, pK_3^{25} 9.17.** A likely impurity is arginine. *S*-Histidine is adsorbed from aqueous solution onto a Dowex 50-H^+ ion-exchange resin, washed with 1.5M HCl (to remove other amino acids), then eluted with 4M HCl as the *dihydrochloride*. This purified *dihydrochloride* (see below) is finally dissolved in water, the pH adjusted to 7.0, and the *free zwitterionic base* crystallises out on addition of EtOH. Its solubility in H_2O is 4.2% at 25°. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 1971-1993 *1961*, *Beilstein* **25** III/IV 4344.]

***S*-Histidine dihydrochloride** *[1007-42-7]* **M 242.1, m 245°, $[\alpha]_D^{20}$ +47.5° (c 2, H_2O).** The dihydrochloride crystallises from water or aqueous EtOH and is washed with acetone, then diethyl ether. *Alternatively*, convert it to the histidine *di-(3,4-dichlorobenzenesulfonate) salt* by dissolving 3,4-dichlorobenzenesulfonic acid (1.5g/10ml) in the aqueous histidine solution with warming, and then the solution is cooled in ice. The resulting crystals (**m** 280° dec) can be recrystallised from 5% aqueous 3,4-dichlorobenzenesulfonic acid, then dried over

$CaCl_2$ under vacuum, and washed with diethyl ether to remove excess reagent. The dihydrochloride can be regenerated by passing the solution through a Dowex-1 (Cl^- form) ion-exchange column. The solid is obtained by evaporation of the solution on a steam bath or better in a vacuum. [Greenstein & Winitz, The Amino Acids **Vol 3** p 1976 *1961*, *Beilstein* **25/16** V 366.]

***S*-Histidine monohydrochloride (H_2O)** *[5934-29-2 (H_2O), 7048-02-4]* **M 209.6, m 80° monohydrate, 254°(dec, anhydrous), $[\alpha]_D^{25}$ +13.0° (6M HCl).** Crystallise the mono-hydrochloride from aqueous EtOH or 60% aqueous EtOH (**m** 259°dec). *Alternatively*, dissolve 10g in 50ml of H_2O, decolourise with Norite, filter, evaporate it in a vacuum to a syrup, cool to room temperature, add 95% EtOH with stirring until slightly turbid, scratch the sides of the vessel until crystals form, then add slowly 40ml of EtOH and keep at 0° overnight, filter the solid off, wash it several times with EtOH and dry it in a vacuum. [Cox *J Biol Chem* **78** 475 *1929*, Cox et al. *J Biol Chem* **81** 73 *1929*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 1972, 2098 *1961*, *Beilstein* **25** II 407, **25** III/IV 4346.]

L-Homocysteine (2-amino-4-mercaptobutyric acid) *[6027-13-0]* **M 135.2, m 232-233°, $[\alpha]_D^{25}$ +153° (c 13, 5N HCl), pK_1^{25} 2.22 (CO_2H), pK_2^{25} 8.87 (NH_3^+), pK_3^{25}10.86 (SH).** Crystallise L-homocysteine from aqueous EtOH. All operations should be carried out under N_2 as the thiol readily oxidizes in air. The acid (3g) is dissolved in freshly boiled H_2O (30ml) under N_2 cooled under N_2 (all operations should be under N_2), add absolute EtOH (100ml), the acid is filterd off, and a second crop is obtained by diluting the filtrate to 500ml with absolute EtOH, kept overnight in a refrigerator, filtering, washing with EtOH and drying in a vacuum. Store it under N_2 or argon.
The S-*benzyl* derivative is repeatedly crystallised from H_2O, or by dissolving it in HCl followed by slow addition of ammonia. It has **m** 240-241°, $[\alpha]_D^{25}$ +27° (c 13, 5N HCl). [Riedel & du Vigneaud *J Biol Chem* **112** 149 *1935*, du Vigneaud & Patterson *J Biol Chem* **109** 101 *1935*, du Vigneaud *J Biol Chem* **126** 217 *1938*, du Vigneaud & Brown *Biochemical Preparations* **5** 93, 95 *1975*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2667-2670 *1961*, *Beilstein* **4** IV 3189, IR: Koegel et al. *J Am Chem Soc* **77** 5708 *1955*.]

***dl*-Homocysteine (2-amino-4-mercaptobutyric acid)** *[454-29-5]* **M 135.2, m 234-235°(corr, dec).** Purify it as for the L-isomer. [Allen & Steinmann *J Am Chem Soc* **74** 3932 *1952*, and references for the L-isomer above, *Beilstein* **4** IV 3189.]

***dl*-Homocystine** *[462-10-2, 870-93-9 (±)]* **M 268.4, m 263-265°(dec), pK_1^{25} 1.59 (CO_2H), pK_2^{25} 2.54 (CO_2H), pK_3^{25} 8.52 (NH_3^+), pK_4^{25} 9.44 (NH_3^+).** *dl*-Homocystine crystallises in platelets from water with $1H_2O$ and **m** 258-260°(dec), all operations should be carried out under N_2. [Sudo *J Chem Soc Jpn (Pure Chem Sect)* **79** 81, 86, 87 *1958*, *Beilstein* **4** IV 3199.]

L(*S,S*)-Homocystine *[626-72-2]* **M 268.4, m 281-284°(dec), $[\alpha]_D^{26}$ +79° (c 1, M HCl), $[\alpha]_D^{21}$ -16° (c 0.06, H_2O), pK (see above).** The acid (3g) is dissolved in freshly boiled H_2O (30ml) under N_2, cooled under N_2 (all operations should be under N_2), absolute EtOH (100ml) is added, the acid is filtered off, and a second crop is obtained by diluting the filtrate to 500ml with absolute EtOH, kept overnight in a refrigerator, filtered, washed with EtOH and dried in a vacuum. The D(*R,R*)-*form* has similar properties but is –ve in M HCl and +ve in H_2O. [du Vigneaud & Patterson *J Biol Chem* **109** 101 *1935*, du Vigneaud & Brown *Biochemical Preparations* **5** 93, 95 *1975*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2667-2670 *1961*, *Beilstein* **4** III 1643, **4** IV 3199, Koegel et al. *J Am Chem Soc* **77** 5708 *1955*.]

L-Homoserine (2-amino-4-hydroxybutyric acid) *[672-15-1]* **M 119.1, m 203°, $[\alpha]_D^{26}$ +18.3° (in 2M HCl), $pK_{Est(1)}$ ~2.1, $pK_{Est(2)}$~9.3.** Likely impurities are *N*-chloroacetyl-L-homoserine, *N*-chloroacetyl-D-homoserine, L-homoserine, homoserine lactone, homoserine anhydride (formed in strong solutions of homoserine if slightly acidic). It cyclises to the lactone in strongly acidic solution. It crystallises from water by adding 9 volumes of EtOH. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2612-2616 *1961*, *Beilstein* **4** IV 3187.]

***erythro*-3-Hydroxy-*RS*-aspartic acid** *[6532-76-9]* **M 149.1, pK_1^{25} 1.91, pK_2^{25} 3.51, pK_3^{25} 9.11.** Likely impurities are 3-chloromalic acid, ammonium chloride, *threo*-3-hydroxyaspartic acid. Crystallise it from water. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 1** p 214, **Vol 3** p 2416 *1961*.]

ß-Hydroxyglutamic acid *[533-62-0]* **M 163.1, m 100°(dec), pK_1^{25} 2.27, pK_2^{25} 4.29, pK_3^{25} 9.66.** Crystallise the acid from water. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 1** pp 211-213, **Vol 3** p 2422 *1961*.]

5-Hydroxy-L-lysine monohydrochloride *[32685-69-1; 13204-98-3]* **M 198.7, m 225°(dec), $[\alpha]_D^{25}$ +17.8° (6M HCl), pK_2^{25} 8.85, pK_3^{25} 9.83.** Likely impurities are 5-*allo*-hydroxy-(D and L)-lysine, histidine, lysine, ornithine. Crystallise the hydrochloride from water by adding 2-9 volumes of EtOH stepwise. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 2000-2009 *1961*.]

DL-*erythro*-3-Hydroxynorvaline (2-amino-3-hydroxypentanoic acid) *[34042-00-7]* **M 133.2, m 257-259°(dec), 263°(dec), pK_1^{20} 2.32, pK_2^{20} 9.12.** Purify it by recrystallisation from aqueous EtOH. The *Cu salt* has **m** 255-256° (dec), the *benzoyl* derivative has **m** 181°, and the *N-phenylcarbamoyl* derivative has **m** 164°. [Buston et al. *J Biol Chem* **204** 665 *1953*, *Beilstein* **4** IV 3220.]

***N*-(*p*-Hydroxyphenyl)glycine** *[22818-40-2]* **M 167.2, m >240°(dec), $[\alpha]_D^{20}$ -156° (c 1, M HCl), $pK_{Est(1)}$~2, $pK_{Est(2)}$~4.5, $pK_{Est(3)}$~10.3.** Crystallise it from water and dry it *in vacuo*. [*Beilstein* **14** I 659.]

***trans*-L-4-Hydroxyproline** *[51-35-4]* **M 131.1, m 274°, $[\alpha]_D^{20}$ -76.0° (c 5, H_2O), pK_1^{25} 1.86, pK_2^{25} 9.79.** Crystallise it from MeOH/EtOH (1:1). Separation from normal *allo*-isomer can be achieved by crystallisation of the copper salts [see Levine *Biochemical Preparations* **8** 114 *1961*]. Separation from proline is achieved *via* the crystalline picrate, $CdCl_2$, or acid ammonium rhodanate salts [see Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 2182 *1961*, Kapfhammer & Mohn *Z Physiol Chem* **306** 76 *1956*]. [*Beilstein* **22/5** V 7.]

5-Hydroxy-L-tryptophan *[4350-09-8]* **M 220.2, m 273°(dec), $[\alpha]_D^{22}$ -32.5°, $[\alpha]_{546}^{20}$ -73.5° (c 1, H_2O), $pK_{Est(1)}$~2.4, $pK_{Est(2)}$~9.0, $pK_{Est(3)}$~9.4, $pK_{Est(4)}$ 16 (NH).** Likely impurities are 5-hydroxy-D-tryptophan and 5-benzyloxytryptophan. Crystallise 5-hydroxy-L-tryptophan under nitrogen from water by adding EtOH. Store it under nitrogen. Also dissolve it in the minimum volume of hot H_2O (~0.7g in 4ml) under nitrogen (charcoal) and allowed it to crystallise at 5°. The *picrolonate* crystallises from H_2O with **m** 184-186°(dec). [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 2732-2737 *1961*, Morris & Armstrong *J Org Chem* **22** 306 *1957*, *Beilstein* **22/14** V 278.]

(±)-Ibotenic acid monohydrate (α-[3-hydroxy-5-isoxazolyl]-glycine, α-amino-3-hydroxy-5-isoxazoleacetic acid) *[2552-55-8]* **M 176.1, m 144-146° (monohydrate), 151-152° (anhydrous), 148-151°, pK_1 2, pK_2 5.1, pK_3 8.2.** It has been converted to the ammonium salt (**m** 121-123° dec) dissolved in H_2O, passed through an Amberlite IR 120 resin (H^+ form) and eluted with H_2O. The acidic fractions are collected, evaporated to dryness and the residue recrystallises from H_2O as the *monohydrate* (**m** 144-146°). The anhydrous acid is obtained by making a slurry with MeOH, decanting and evaporating to dryness, and repeating the process twice more to give the *anhydrous acid* (**m** 151-152°). Recrystallisation from H_2O gives the *monohydrate*. [Nakamura *Chem Pharm Bull Jpn* **19** 46 *1971*.] The *ethyl ester* forms needles when crystallised from a small volume of Et_2O and has **m** 78-79° and IR ($CHCl_3$) with ν_{max} □□ 3500–2300 (OH), 1742 (ester C=O), 1628, 1528cm^{-1}, and UV with λ_{max} □□ (EtOH) at 206nm (ε 7,080). The *hydrazide* has **m** 174-175° (from MeOH) with IR (KBr) 1656 (C=O)cm^{-1}.

Iminodiacetic acid *[142-73-4]* **M 133.1, m 225°(dec), 240°(dec), 247.5°(dec), b 126-127°/14mm, pK_1^{25} 2.50, pK_2^{25} 9.40.** Crystallise the acid several times from water. The *N-Methyl* derivative **m** 215° is purified by dissolving it in an equal weight of warm H_2O and adding 3 volumes of MeOH [Kiematsu et al. *Org Synth* Coll Vol **II** 397 *1943*]. [Laberek & Martell *J Am Chem Soc* **74** 5052 *1952*, *Beilstein* **4** III 2428, **4** IV 1176.]

3-Iodo-L-tyrosine *[70-78-0]* **M 307.1, m 205-208°(dec), $[\alpha]_D^{25}$ -4.4° (c 5, 1M HCl), $pK_{Est(2)}$~2.1, $pK_{Est(3)}$~6.4, pK_4^{25} 8.7.** Likely impurities are tyrosine, diiodotyrosine and iodide. Crystallise it by dissolving it in concentrated ammonia (~200mg in ~20ml), evaporate to ~5ml and NH_4Cl is added to pH4.5—5.0. After a few hours at 0°, the amino acid crystallises in needles. It is filtered off, washed with a little ice-cold H_2O and dried in a vacuum. *Alternatively*, dissolve it in dilute ammonia at room temperature, then add dilute acetic acid to pH 6. Store it at 0°. Recrystallisation of ~250mg from H_2O (~5ml) removes any diiodotyrosine. It is an inhibitor of tyrosine hydroxylase with a Ki of ~500nM. [Harrington & Rivers *Biochem J* **38** 320 *1944*, Rivers *Chem & Ind (London)* 21 *1956*, *Beilstein* **14** III 1562, **14** IV 1562.]

L-Isoleucine *[73-32-5]* **M 131.2, m 285-286°(dec), $[\alpha]_D^{20}$ +40.6° (6M HCl) pK_1^{25} 2.66, pK_2^{25} 9.69.** Crystallise L-isoleucine from H_2O by addition of 4 volumes of EtOH or from aqueous MeOH. It sublimes at 170-181°/0.3mm with 99.7% recovery, unracemised [Gross & Gradsky *J Am Chem Soc* **77** 1678 *1955*]. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 1** p 183-191, **Vol 3** pp 2043-2073 *1961*, Huffman & Ingersoll *J Am Chem Soc* **73** 3366 *1951*, *Beilstein* **4** IV 2775.]

DL-Isoserine (±-3-amino-2-hydroxypropionic acid) *[632-12-2]* **M 105.1, m 235°(dec), 237°(dec), 245°(dec), 250-252°(dec), pK_1^{25} 2.78 (acidic), pK_2^{25} 9.27 (basic).** Recrystallise it from H_2O or 50% aqueous EtOH. It has an isoelectric pH of 6.02. [Rinderknecht & Niemann *J Am Chem Soc* **75** 6322 *1953*, Gundermann & Holtmann *Chem Ber* **91** 160 *1958*, Emerson et al. *J Biol Chem* **92** 451 *1931*.] The *hydrobromide* has **m** 128-130° (from aqueous HBr) [Schöberl & Braun *Justus Liebigs Ann Chem* **542** 288 *1939*]. [*Beilstein* **4** H 503, **4** IV 3116.]

L-Isovaline (2-amino-2-methylbutyric acid) *[595-40-4]* **M 117.2, m** *ca* **300° (sublimes in vac), $[\alpha]_D^{25}$ +113.1° (c 5, H_2O), $[\alpha]_D^{25}$ +10° (5M HCl), $pK_{Est(1)}$~2.4, $pK_{Est(2)}$~9.7.** Crystallise it from aqueous Me_2CO, or better by dissolving in H_2O and adding excess Me_2CO. [Baker et al. *J Am Chem Soc* **74** 4701 *1952*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 2573-2577 *1961*.]

L-Leucine *[61-90-5]* **M 131.2, m 293-295°(dec), $[\alpha]_D^{25}$ +15.6° (5M HCl), pK_1^{25} 2.33, pK_2^{25} 9.74.** Likely impurities are isoleucine, valine, and methionine. Crystallise L-leucine from water by adding 4 volumes of EtOH. It sublimes at 180-188°/0.3mm with 99.1% recovery, and unracemised [Gross & Gradsky *J Am Chem Soc* **77** 1678 *1955*]. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 2075-2094 *1961*, Kameda et al. *J Pharm Soc Jpn* **78** 763 *1958*, *Beilstein* **4** IV 2738.]

L-Lysine *[56-87-1]* **M 146.2,** *[39665-12-8 monohydrate]* **M 164.2, m >210°(dec), $[\alpha]_D^{20}$ +25° (c 2, 6M HCl), pK_1 2.18, pK_2 8.95, pK_3 10.53.** Crystallise L-lysine from aqueous EtOH. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2097-2122 *1961*, Kearley & Ingersoll *J Am Chem Soc* **73** 5783 *1951*, *Beilstein* **4** IV 2717.]

L-Lysine dihydrochloride *[657-26-1]* **M 219.1, m 193°, 199-201°, 203-204°, $[\alpha]_D^{25}$ +25.9° (5M HCl).** Crystallise it from MeOH, in the presence of excess HCl, by adding diethyl ether. [Yoneya *J Biochem (Tokyo)* **38** 343 *1951*, Kearley & Ingersoll *J Am Chem Soc* **73** 5783 *1951*, *Beilstein* **4** IV 2717.]

L-Lysine monohydrochloride *[657-27-2]* **M 182.7, m 256°(dec), $[\alpha]_D^{25}$ +20.5° (c 5, 5M HCl).** Likely impurities are arginine, D-lysine, 2,6-diaminoheptanedioic acid and glutamic acid. Crystallise the mono-hydrochloride from water at pH 4-6 by adding 4 volumes of EtOH. At above 60% relative humidity it forms a *dihydrate*. [Birhbaum et al. *J Biol Chem* **194** 455, 468 *1952*, Kearley & Ingersoll *J Am Chem Soc* **73** 5783 *1951*, *Beilstein* **4** IV 2717.]

α-Melanotropin *[581-05-5]* **(a tridecapeptide, α-MSH, melanocyte stimulating hormone), M 1664.9, $[\alpha]_D^{25}$ -58.5° (c 0.4, 10% aqueous AcOH).** Its solubility in H_2O is 1mg/ml. It is separated from the extract by ion-exchange on carboxymethyl cellulose, desalted, evaporated and lyophilised, then chromatographed on

Sephadex G-25. [Lande et al. *Biochemical Preparations* **13** 45 *1971*.]

ß-Melanotropin *[9034-42-8]* **(octadeca to docosa peptides), amorphous.** An extract of ß-melanotropin is purified by ion-exchange on carboxymethyl cellulose, desalted, evaporated and lyophilised, then chromatographed on Sephadex G-25. [Lande et al. *Biochemical Preparations* **13** 45 *1971*.]

Melphalan (4-[bis-{2-chloroethyl}amino]-L-phenylalanine) *[148-82-3]* **M 305.2, m 182-183° (dec), 183-185°, $[\alpha]_D^{25}$ +7.5° (c 1.33, 1.0 N HCl), $[\alpha]_D^{20}$ -28° (c 0.8, MeOH), pK_{Est} ~6.4.** Purify melphalan by recrystallisation from MeOH, and its solubility is 5% in 95% EtOH containing one drop of 6N HCl. It is soluble in EtOH and propylene glycol but is almost insoluble in H_2O. The *RS-form* has **m** 180-181°, and the *R-form* crystallises from MeOH with **m** 181.5-182° and $[\alpha]_D^{21}$ -7.5° (c 1.26, 1.0 N HCl). [Bergel & Stock *J Chem Soc* 2409 *1954*, *Beilstein* **14** IV 1689.]

***dl*-Methionine (*RS*-2-amino-4-methylthiobutyric acid)** *[59-51-8]* **M 149.2, m 281°(dec), pK_1^{25} 2.28, pK_2^{25} 9.21.** Crystallise it from hot water or EtOH. Also purify it by dissolving it in H_2O and passing through an Amberlite IR-120 resin (NH_4^+ form). The eluate is concentrated and then passed through Amberlite IR-4B resin, and this eluate is evaporated to dryness. The residue is washed with EtOH, then Me_2CO, dried and recrystallised from aqueous EtOH (colourless plates) [Baddiley & Jamieson *J Chem Soc* 4283 *1954*]. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 2125 *1961*, *Beilstein* **4** IV 3190.]

L-Methionine *[63-68-3]* **M 149.2, m 277-279°(dec), 283°(dec), $[\alpha]_D^{25}$ +21.2° (0.2M HCl), pK_1^{25} 2.13, pK_2^{25} 9.73.** Crystallise L-methionine from aqueous EtOH. Also purify it by dissolving ~0.5g of amino acid in ~10ml of hot H_2O, filtering, adjusting the pH to 5.8 with 5N HCl, collecting the solid after addition of ~20ml of EtOH. It is recrystallised by dissolving in H_2O and adding EtOH. It sublimes at 197-208°/0.3mm with 99.8% recovery and unracemised [Gross & Gradsky *J Am Chem Soc* **77** 1678 *1955*]. [Milne & Peng *J Am Chem Soc* **79** 647 *1957*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2125-2152 *1961*, *Beilstein* **4** IV 3189.]

***dl*-Methionine sulfoxide** *[454-41-1, 62697-73-8]* **M 165.2, m >240°(dec), 241-242°(dec).** Likely impurities are *dl*-methionine sulfone and *dl*-methionine. Crystallise the sulfoxide by dissolving it in hot H_2O and adding excess EtOH. [Lepp & Dunn *Biochemical Preparations* **4** 80 *1955*, Micheel & Schmitz *Chem Ber* **72** 518 *1939*, *Beilstein* **4** III 1650, **4** IV 3192.]

S-Methyl-L-cysteine *[1187-84-4]* **M 135.2, m 207-211°, ~240°(dec), 267-270°, $[\alpha]_D^{26}$ -32.0° (-34.5°) (c 5, H_2O), pK_1^{25} 1.94 (COOH), pK_2^{25} 8.73 (NH_2, 8.97).** Likely impurities are cysteine and S-methyl-*dl*-cysteine. Crystallise it from H_2O by adding 4 volumes of EtOH. It also crystallises from MeOH with **m** 234-236°(dec), but after sublimation it has **m** 267-270° and $[\alpha]_D^{27}$ -31.6° (c 1, H_2O). [Rinderknecht et al. *Helv Chim Acta* **41** 1, 10 *1958*, Theodoropoulos *Acta Chem Scand* **13** 383 *1959*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 1904 *1961*, *Beilstein* **4** IV 3145.]

α-Methylmethionine *[562-48-1]* **M 163.0, m 283-284°, $pK_{Est(1)}$ ~ 2.1, pK^{30} 9.45.** Crystallise α-methylmethionine from aqueous EtOH or H_2O. [Pfister et al. *J Am Chem Soc* **77** 697 *1955,* Potts *J Chem Soc* 1623 *1955*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 2566 *1961*.]

S-Methyl-L-methionine chloride See Vitamin U in "Miscellaneous Compounds", this chapter.

***N*-Methyltryptophan (L-abrine)** *[526-31-8]* **M 218.3, m 295°(dec with darkening and sintering), $[\alpha]_D^{21}$ +44.4° (c 2.8, 0.5M HCl), $[\alpha]_D^{20}$ +65° (c 1, 0.5N NaOH), pI 10.10, $pK_{Est(1)}$~2.3, $pK_{Est(2)}$~9.7.** Crystallise L-abrine from H_2O or EtOH/H_2O mixture and dry it for 2 days at 60° in high vacuum; it has **m** 275-290°(dec with browning at 230°) and $[\alpha]_D^{21}$ +47.2° (c 2, 0.5N HCl) [Peter et al. *Helv Chim Acta* **46** 577 *1963*]. [Gregory & Morley *J Chem Soc* 913 *1968*, *Beilstein* **22/14** V 40.]

***dl*-5-Methyltryptophan** *[951-55-3]* **M 218.3, m 275°(dec) [pK see tryptophan].** Crystallise *dl*-5-methyltryptophan from aqueous EtOH after dissolving it in aqueous NaOH, precipitating with AcOH, filtering

the solid off and drying for 24 hours at 50°. [Jackman & Archer *J Am Chem Soc* **68** 2105 *1946*, *Beilstein* **22** IV 6815.] The *picrate* crystallises from MeOH with **m** 202°(dec). The *N-phenylcarbamoyl* derivative crystallises from aqueous MeOH with **m** 202°. [Gordon & Jackson *J Biol Chem* **110** 151, 154 *1935*.]

Nisin *[1414-45-5]* **M 3354.2.** This polypeptide from *S. lactis* is purified by crystallisation from 80% (v/v) EtOH and by countercurrent distribution. The synthetic polypeptide antibiotic can also be purified by preparative HPLC and assayed by HPLC on a Nucleosil 3007C_{18} (6 x 250mm) column using a MeCN—0.01M HCl gradient (30-50%), at 2%/minute, and flow rate of 1.5ml/minute to give a retention time of 8.1 minutes; or MeCN—0.3M guanidine-HCl gradient (30-50%), at 2%/minute, and flow rate of 1.5ml/minute to give a retention time of 10.9 minutes. FAB-MS gave the pseudomolecular ion m/z at 3352.7 $(M + H)^+$. It is soluble in dilute acid and is stable even on boiling. [Berridge et al. *Biochem J* **52** 529 *1952*, synthesis by Fukase et al. *Tetrahedron Lett* **29** 795 *1988*.]

Norleucine (α-amino-*n*-caproic acid) *[R(+) 327-56-0, S(-) 327-57-1]* **M 117.2, m 301°, $[\alpha]_{546}^{20}$ (+) and (-) 28° (c 5, 5M HCl),** *[RS: 616-06-8]* **m 297-300° (sublimes partially at ~280°), pK_1 2.39, pK_2 9.76 (for *RS*).** Crystallise norleucine from water or aqueous MeOH. [Huffman & Ingersoll *J Am Chem Soc* **73** 3366 *1951*, *Beilstein* **4** III 1386, **4** IV 2628.]

Norvaline (*R*-α-amino-*n*-valeric acid) *[R(+) 2031-12-9, S(-) 6600-40-4]* **M 117.2, m 305°(dec), $[\alpha]_{546}^{20}$ (+) and (-) 25° (c 10, 5M HCl), pI 6.04, pK_1^{25} 2.36, pK_2^{25} 9.87 (9.72).** Crystallise norvaline from aqueous EtOH or water. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2390-2399 *1961*, *Beilstein* **4** III 1331-1333, **4** IV 128, 2629.]

L-Ornithine *[70-26-8]* **M 132.2, m 140°, $[\alpha]_D^{25}$ +16° (c 0.5, H_2O), pK_1^{20} 2.11, pK_2^{20} 8.39, pK_3^{25} 10.59.** Crystallise L-ornithine from water containing 1mM EDTA (to remove metal ions). [Perrin *J Chem Soc* 3125 *1958*, Rivard *Biochemical Preparations* **3** 97 *1955*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2477-2491 *1961*, *Beilstein* **4** III 1346, **4** IV 2644.]

L-Ornithine monohydrochloride *[3184-13-2]* **M 168.6, m 230-232°(dec), 233°(dec), 236.5-237.5°(dec), $[\alpha]_D^{25}$ +28.3° (5M HCl).** Likely impurities are citrulline, arginine and D-ornithine. Crystallise the monohydrochloride from water by adding 4 volumes of EtOH and dry it in a vacuum desiccator over fused $CaCl_2$. [Rivard *Biochemical Preparations* **3** 98 *1955*.] The *dihydrochloride* [6211-16-1] has **m** 202-203° and $[\alpha]_D^{20}$ +18.4° (c 2.3, 6N HCl) after recrystallisation from MeOH/Et_2O [Zaoral & Rudinger *Col Czech Chem Commun* **24** 2009 *1959*]. [*Beilstein* **4** IV 2644.]

Oxytocin *[50-56-6]* **M 1007.2, m dec on heating, $[\alpha]_D^{22}$ -26.2° (c 0.53, N AcOH).** It is a cyclic nonapeptide which is purified by countercurrent distribution between solvent and buffer. It is soluble in H_2O, *n*-BuOH and isoBuOH. [Bodanszky & du Vigneaud *J Am Chem Soc* **81** 2504 *1959*, Cash et al. *J Med Pharm Chem* **5** 413 *1962*, Sakakibara et al. *Bull Chem Soc Jpn* **38** 120 *1965*; solid phase synthesis: Bayer & Hagenmyer *Tetrahedron Lett* 2037 *1968*.] It was also synthesised on a solid phase matrix and finally purified as follows: A Sephadex G-25 column is equilibrated with the aqueous phase of a mixture of 3.5% AcOH (containing 1.5% of pyridine)/*n*-BuOH/*C_6H_6 (2:1:1) and then the organic phase of this mixture is run through. A solution of oxytocin (100mg) in H_2O (2ml) is applied to the column which is then eluted with the organic layer of the above mixture. The fractions containing the major peak [as determined by the Folin-Lowry protein assay: Fryer et al. *Anal Biochem* **153** 262 *1986*] are pooled, diluted with twice their volume of H_2O, evaporated to a small volume and lyophilised to give oxytocin as a pure white powder (20mg, 508 U/mg). [Ives *Can J Chem* **46** 2318 *1968*, *Beilstein* **22** III/IV 82.]

***dl*-Phenylalanine** *[150-30-1]* **M 165.2, m 265-266°(capillary, dec), 271-273°(dec), 282-284°(dec), pK_1^{25} 2.58, pK_2^{25} 9.24.** *dl*-Phenylalanine crystallises from H_2O or H_2O/EtOH in large plates and is dried under vacuum over P_2O_5. *S-Phenylalanine ethyl ester hydrochloride* [3182-93-2] has **m** 156-158° and $[\alpha]_D^{20}$ -7.8° (c

2, H_2O) after crystallisation from EtOH/Et_2O [Billimoria & Cook *J Chem Soc* 2328 *1949*, *Beilstein* **14** IV 1556]. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2156-2175 *1961*, *Beilstein* **14** III 1229, **14** IV 1553.]

L-Phenylalanine *[63-91-2]* **M 165.2, m 280°(dec), 281-183°(dec), $[\alpha]_D^{25}$ -34.0° (c 2, H_2O).** Likely impurities are leucine, valine, methionine and tyrosine. Crystallise L-phenylalanine from water by adding 4 volumes of EtOH. Dry it *in vacuo* over P_2O_5. Also crystallise it from saturated refluxing aqueous solutions at neutral pH, or 1:1 (v/v) EtOH/water solution, or conc HCl. It sublimes at 176-184°/0.3mm with 98.7% recovery and unracemised [Gross & Gradsky *J Am Chem Soc* **77** 1678 *1955*]. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2156-2175 *1961*, *Beilstein* **14** IV 1552.]

L-α-Phenylglycine *[2935-35-5]* **M 151.2, m 305-310°, 305-308°(capillary, dec), $[\alpha]_{546}^{25}$ +188° (c 1, M HCl), pK_1^{25} 1.83, pK_2^{25} 4.39 (for *dl*).** Crystallise it from EtOH. [Kaneko *J Chem Soc Jpn* **60** 538 *1939*, Rudman et al. *J Am Chem Soc* **74** 551 *1952*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2694-2697 *1961*, *Beilstein* **14** III 1187, **14** IV 1317.]

Phenylglycine-*o*-carboxylic acid [*N*-(2-carboxyphenyl)glycine] *[612-42-0, 64241-57-2 Me Ester, 67990-19-6 mono-Na Salt, 71807-57-3 di-Na Salt]* **M 195.2, m 206°, 208°, 220°, pK_1^{20} 5.44 (CO_2H), pK_2^{20} 6.96 (CO_2H) (in 50% aqueous dioxane).** Crystallise the acid from hot water (charcoal). It forms complexes with Cu^{2+}, Zn^{2+}, Cd^{2+}, Co^{2+} and Ni^{2+} in aqueous dioxane. [Roileanu et al. *Rev Roumaine Chim* **12** 105 *1967*, *Aldrich library of* ^{13}C, ^1H *FTNMR Spectra*, NMR **2** 1181A, *Beilstein* **14** H 348, **14** I 544, **14** II 225, **14** III 938.]

D-Pipecolinic acid (*R*-piperidine-2-carboxylic acid) *[1723-00-8]* **M 129.2, m 264°(dec), 267°(dec), ~280°(dec), $[\alpha]_D^{19}$ +26.2° (c 2, H_2O), $[\alpha]_D^{25}$ +35.7° (H_2O), pK_1^{20} 2.29 (CO_2H), pK_2^{20} 10.77 (NH^+).** D-Pipecolinic acid recrystallises as platelets from EtOH and is soluble in H_2O. The *hydrochloride* has **m** 256-257°(dec) from H_2O and $[\alpha]_D^{25}$ +10.8° (c 2, H_2O). [*cf* p 422, Lukés et al. *Col Czech Chem Commun* **22** 286 *1957*, Bayerman *Rec Trav Chim Pays Bas* **78** 134 *1959*, Asher et al. *Tetrahedron Lett* **22** 141 *1981*, *Beilstein* **22/1** V 220.]

L-Pipecolinic acid (*S*-piperidine-2-carboxylic acid) *[3105-95-1]* **M 129.2, m 268°(dec), 271°(dec), ~280°(dec), $[\alpha]_D^{20}$ -26° (c 4, H_2O), $[\alpha]_D^{25}$ -34.9° (H_2O).** Recrystallise L-pipecolinic acid from aqueous EtOH, and it sublimes as needles in a vacuum. It is sparingly soluble in absolute EtOH, Me_2CO or $CHCl_3$ but insoluble in Et_2O. The *hydrochloride* has **m** 258-259°(dec, from MeOH) and $[\alpha]_D^{25}$ -10.8° (c 10, H_2O). [Fuji & Myoshi *Bull Chem Soc Jpn* **48** 1241 *1975*, *Beilstein* **22/1** V 220.]

Piperidine-4-carboxylic acid (isonipecotic acid) *[498-94-2]* **M 129.2, m 336°(dec, darkens at ~300°), $pK_{Est(1)}$~ 4.3 (CO_2H), $pK_{Est(2)}$~ 10.6 (NH^+).** It crystallises from H_2O or EtOH as needles. The *hydrochloride* recrystallises from H_2O or aqueous HCl with **m** 293°dec (also 298°dec, 300°dec). [Wibaut *Rec Trav Chim Pays Bas* **63** 141 *1944*, IR: Zacharius et al. *J Am Chem Soc* **76** 2908 *1954*, *Beilstein* **22/1** V 244.]

Polypeptides. These are strings of α-amino acids usually with the natural *S*(L) [L-cysteine is an exception and has the *R* absolute configuration] or sometimes "unnatural" *R*(D) configuration at the α-carbon atom. They generally have less than ~100 amino acid residues. They can be naturally occurring or, because of their small size, can be synthesised chemically from the desired amino acids. Their properties can be very similar to those of small proteins. Many are commercially available, and can be custom made commercially or locally with a peptide synthesiser. They are purified by HPLC and can be used without further purification. Their purity can be checked as described under proteins (Introduction).

L-Proline *[147-85-3]* **M 115.1, m 215-220°(dec)(D-isomer), 220-222°(dec) (L-form), 205°(dec)(DL-isomer), $[\alpha]_D^{20}$ -53° (c 0.6, 0.5N HCl), -93° (c 2.4, 6N KOH) for L-isomer), pI 6.3, pK_1^{25} 1.95, pK_2^{25} 10.64.** A likely impurity is hydroxyproline. Purify L-proline *via* its *picrate* which is crystallised twice from water, then decomposed with 40% H_2SO_4. The picric acid is extracted with diethyl ether, the H_2SO_4 in solution is precipitated with $Ba(OH)_2$, and the filtrate is evaporated. The residue is crystallised from hot absolute EtOH [Mellan & Hoover *J Am Chem Soc* **73** 3879 *1951*] or EtOH/Et_2O. Its solubility in H_2O is >100%. It sublimes

at 182-187°/0.3mm with 99.4% recovery and unracemised [Gross & Gradsky *J Am Chem Soc* **77** 1678 *1955*]. It is *hygroscopic* and is stored in a desiccator. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2178-2199 *1961*, *Beilstein* **22** III/IV 8, **22/1** V 31.]

L-Prolylglycine *[2578-57-6]* **M 172.2, m 236°, $[\alpha]_D^{20}$ +21.1° (c 4, H_2O), pK_1^{25} 3.19, pK_2^{25} 8.97.** Recrystallise L-prolylglycine from water at 50-60° by addition of EtOH. [Appel et al. *Chem Ber* **108** 2680 *1975*, Rydon & Smith *J Chem Soc* 3642 *1956*.]

L-Propargylglycine (*S*-2-aminopent-4-ynoic acid) *[23235-01-0]* **M 113.1, m 230°(dec starting at 210°), $[\alpha]_D^{20}$ -35° (c 1, H_2O), -4° (c 5, 5N HCl), $pK_{Est(1)}$~ 2.3 (CO_2H), $pK_{Est(2)}$~ 9.8 (NH_2).** The acid crystallises readily when ~4g in 50ml H_2O are treated with absolute EtOH at 4°/3 hours, and is collected, washed with cold absolute EtOH and Et_2O and dried in a vacuum. Also, it recrystallises from aqueous Me_2CO, R_F on SiO_2 TLC plates with *n*-BuOH/H_2O/AcOH (4:1:1) is 0.26. The *racemate* has **m** 238-240°. [Leukart et al. *Helv Chim Acta* **59** 2181 *1976*, Eberle & Zeller *Helv Chim Acta* **68** 1880 *1985*, Jansen et al. *Rec Trav Chim Pays-Bas* **88** 819 *1969*.] It is a suicide inhibitor of γ-cystathionase and other enzymes [Washtier & Abeles *Biochemistry* **16** 2485 *1977*, Shinozuka et al. *Eur J Biochem* **124** 377 *1982*].

***R*-Pyroglutamic acid (5-oxo-D-proline, *R*-2-pyrrolidone-5-carboxylic acid)** *[4042-36-8]* **M 129.1, m 156-158°, $[\alpha]_D^{20}$ +11.2° (c 1, H_2O).** Purify *R*-pyroglutamic acid by dissolving it in H_2O, filtering, passing the filtrate through Dowex 50 (H^+ form), washing with H_2O, pooling washings, evaporating, removing H_2O azeotropically with Me_2CO and $*C_6H_6$, washing the residue with Et_2O and recrystallising from EtOH/petroleum ether. [Pradeller et al. *Col Czech Chem Commun* **42** 79, 80 *1977*, *Beilstein* **22/6** V 7.]

***S*-Pyroglutamic acid (5-oxo-L-proline)** *[98-79-3]* **M 129.1, m 156-158°, 162-164°, $[\alpha]_{546}^{20}$ -11° (c 5, H_2O), pK^{25} 12.7 (by electron spin resonance).** Crystallise *S*-pyroglutamic acid by dissolving it in boiling EtOH (20g in 100ml), cooling and after a few minutes adding petroleum ether (b 40-60°, 120ml), then after 5 minutes adding a further 120ml, and cooling to room temperature with 90% recovery. This has **m** 155.5-157.5° and $[\alpha]_D^{20}$ -11.4° (c 4.4, H_2O) [Hardy *Synthesis* 290 *1978*, Pellegata et al. *Synthesis* 614 *1978*]. The *NH_4* salt has **m** 184-186° (from EtOH). [*Beilstein* **22/6** V 7.]

Quisqualic acid (3-[3,5-dioxo-1,2,4-oxadiazolin-2-yl]-L-alanine) *[52809-07-1]* **M 189.1, m 190-191°, $[\alpha]_D^{20}$ +17° (c 2, 6M HCl), $pK_{Est(1)}$~ 2.1 (CO_2H), $pK_{Est(2)}$~ 8.9 (NH_2).** It has been purified by ion-exchange chromatography on Dowex 50W (x 8, H^+ form); the desired fractions are lyophilised and recrystallised from H_2O/EtOH. It has IR (KBr) with ν_{max} at 3400-2750br, 1830s, 1775s, 1745s and 1605s cm^{-1}; and ^1H NMR (NaOD/D_2O, pH 13) δ: 3.55-3.57 (1H m, X of ABX, H-2), 3.72-3.85 (2H, AB of ABX, H-3), ^{13}C NMR (D_2O) δ: 50.1(t), 53.4(d), 154.8(s), 159.7(s) and 171.3(s). [Baldwin et al. *J C S, Chem Commun* 256 *1985*.] It is a quasiqualate receptor agonist [Joels et al. *Proc Natl Acad Sci USA* **86** 3404 *1989*].

Sarcosine (N-methylglycine) *[107-97-1]* **M 89.1, m 2 12-213°(dec), pK_1^{20} 2.12, pK_2^{20} 10.19.** Crystallise sarcosine from absolute EtOH, 95% EtOH or H_2O. It sublimes at 180-185°/0.3mm with 99.1% recovery [Gross & Gradsky *J Am Chem Soc* **77** 1678 *1955*]. [Cocker & Harris *J Chem Soc* 1291 *1940*, Cocker & Lapworth *J Chem Soc* 1897 *1931,* Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** p 2750 *1961*, *Beilstein* **4** III 1121, **4** IV 2363.]

Sarcosine anhydride (1,4-dimethylpiperazin-2,5-dione) *[5076-82-4]* **M 142.2, m 146-147°, 148°, $pK_{Est(1)}$ ~ −4.2, $pK_{Est(2)}$~−1.9.** Crystallise the anhydride from H_2O, EtOH or EtOAc. Dry it in a vacuum at room temperature. [Karrer et al. *Helv Chim Acta* **5** 140 *1922*, *Beilstein* **24** II 144, **24** IV 1072.]

Seleno-DL-methionine (±2-amino-4-methylselanylbutyric acid) *[1464-42-2, 2578-28-1 (±)]* **M 196.1, m 265°(dec), 267-269°(dec), 270° (see pKs of methionine).** It crystallises in hexagonal plates from MeOH and H_2O. [Klosterman & Painter *J Am Chem Soc* **69** 2009 *1949*.] The *L-isomer* [3211-76-5] is purified by dissolving it in H_2O, adjusting the pH to 5.5 with aqueous NH_3, evaporating to near-dryness, and the residue is

washed several times with absolute EtOH till a solid is formed and then recrystallise from Me_2CO. It has **m** 266-268°(dec) [also 275°(dec)], and $[\alpha]_D^{25}$ +18.1°(c 1, N HCl). [Pande et al. *J Org Chem* **35** 1440 *1970*, *Beilstein* **4** IV 3216.]

L-Serine *[56-45-1]* **M 105.1, m 228°(dec), 233-235°(dec), $[\alpha]_D^{25}$ +14.5° (1M HCl), $[\alpha]_{546}^{20}$ +16° (c 5, 5M HCl), pK_1^{25} 2.15, pK_2^{25} 9.21.** A likely impurity is glycine. Crystallise L-serine from H_2O by adding 4 volumes of EtOH. Dry and store it in a desiccator. It sublimes at 160-170°/0.3mm with 99.7% recovery, and unracemised [Gross & Gradsky *J Am Chem Soc* **77** 1678 *1955*]. [Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2202-2235 *1961*, *Beilstein* **4** IV 3118.]

Somatostatin *[38916-34-6]* **M 1637.9, $[\alpha]_D^{25}$ -36° (c 0.57, 1% AcOH).** Somatostatin is a tetradecapeptide which is purified by gel filtration on Sephadex G-25, eluting with 2N AcOH, and then by liquid partition chromatography on Sephadex G-25 using *n*-BuOH/AcOH/H_2O (4:1:5) and has R_F = 0.4. It is a brain growth hormone releasing-inhibiting factor which has also been synthesised. [Burgus et al. *Proc Natl Acad Sci USA* **70** 684 *1973*, Sorantakis & McKinley *Biochem Biophys Res Commun* **54** 234 *1973,* Hartridt et al. *Pharmazie* **37** 403 *1982*.]

L-Threonine *[72-19-5]* **M 119.1, m 251-253°, 254°(dec), 262-263°(dec), $[\alpha]_D^{26}$ -28.4° (H_2O), pK_1^{25} 2.17, pK_2^{25} 9.00.** Likely impurities are *allo*-threonine and glycine. Crystallise L-threonine from H_2O by adding 4 volumes of EtOH. Dry and store it in a desiccator. It also crystallises from 80% EtOH to give hexagonal plates **m** 262-263°(dec). It sublimes at 200-226°/0.3mm with 99.6% recovery and unracemised [Gross & Gradsky *J Am Chem Soc* **77** 1678 *1955*]. [Elliot *J Chem Soc* 62 *1950*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 1** pp 176-183, **Vol 3** pp 2238-2257 *1961*, *Beilstein* **4** IV 3171.]

L-Thyroxine sodium salt ($5H_2O$) *[6106-07-6]* **M 888.9, $[\alpha]_{546}^{20}$ +20° (c 2, 1M HCl + EtOH, 1:4).** Crystallise the sodium salt from absolute EtOH and dry it for 8 hours at 30°/1mm. [Canepa *Acta Cryst* **4** 283 *1951*, *Beilstein* **14** II 378, **14** III 1566, **14** IV 2374.]

D-Thyroxine {*O*-[3,5-diiodo-4-oxyphenyl]-3,5-diiodo-D-(-)-tyrosine, 3,3',5,5'-tetraiodo-D-thyronine} *[51-49-0]* **M 776.9, m 235°(dec), 235-236°(dec), 340°(dec), $[\alpha]_D^{20}$ +4.5° (c 3, aqueous 0.2N NaOH in 70% EtOH), $[\alpha]_D^{20}$ -17° (c 2, aqueous N HCl + EtOH 1:4), pK_1^{25} 2.2 (CO_2H), pK_2^{25} 8.40 (OH), pK_3^{25} 10,1 (NH_2).** Recrystallise D-thyroxine from H_2O (needles) or from an ammonical solution by dilution with H_2O, MeOH or Me_2CO. It has also been purified by dissolving ~6.5 g in a mixture of MeOH (200ml) and 2N HCl (20ml), adding charcoal, filtering then adding NaOAc solution to pH 6. On standing the thyroxine separates, it is filtered off, washed with MeOH then Me_2CO and dried *in vacuo*. *N-Formyl-D-thyroxine* has **m** 210° and $[\alpha]_{546}^{21}$ -26.9° (c 5, EtOH). *(±)-Thyroxine* has **m** 256° and is purified in the same way. [Nahm & Siedel *Chem Ber* **96** 1 *1963*, Salter *Biochem J* **24** 471 *1930*, *Beilstein* **14** I 671, **14** II 384, **14** III 1566, **14** IV 2374.]

L-Thyroxine (*O*-[3,5-diiodo-4-oxyphenyl]-3,5-diiodo-L-(+)-tyrosine, 3,3',5,5'-tetraiodo-L-thyronine) *[51-48-9]* **M 776.9, m 229-230°(dec), ~235°(dec), 237°(dec), $[\alpha]_D^{22}$ -5.1° (c 2, aqueous N NaOH + EtOH 1:2), $[\alpha]_D^{22}$ +15° (c 5, aqueous N HCl in 95% EtOH 1:2), $[\alpha]_D^{22}$ +26° (EtOH/1M aqueous HCl, 1:1) (pK^{25} 6.6).** Purification is the same as for the D-isomer above. Likely impurities are tyrosine, iodotyrosine, iodothyroxines and iodide. Dissolve it in dilute ammonia at room temperature, then crystallise it by adding dilute acetic acid to pH 6. *N-Formyl-L-thyroxine* has **m** 214°(dec) and $[\alpha]_{546}^{21}$ +27.8° (c 5, EtOH). [Harrington et al. *Biochem J* **39** 164 *1945*, Nahm & Siedel *Chem Ber* **96** 1 *1963*, Reineke & Turner *J Biol Chem* **161** 613 *1945*, Chalmers et al. *J Chem Soc* 3424 *1949*, *Beilstein* **14** II 378, **14** III 1566, **14** IV 2373.]

***N*-Tosyl-L-lysine chloromethyl ketone (3*S*-1-chloro-3-tosylamino-7-amino-2-heptanone HCl)** *[4272-74-6]* **M 369.3, m 150-153°(dec), 156-158°(dec), ~165°(dec), $[\alpha]_D^{20}$ -7.3° (c 2, H_2O), pK_{Est} ~ 10.6 (7-NH_2).** The hydrochloride slowly crystallises from a concentrated solution in absolute EtOH, thinned with EtOH/Et_2O for collection and dried *in vacuo*. It is a suicide enzyme inhibitor of serine proteases, e.g. trypsin and clostripain. [Matsuda et al. *Chem Pharm Bull Jpn* **30** 2512 *1982*, Shaw et al. *Biochemistry* **4** 2219 *1965*].

Triglycyl glycine (tetraglycine) *[637-84-3]* **M 246.2, m 270-275°(dec), pK_1^{25} 3.21(CO_2H), pK_2^{25} 7.94(NH_3^+).** Crystallise it from H_2O (optionally, by the addition of EtOH). [Li et al. *J Am Chem Soc* **79** 5859 *1957*, Rising et al. *J Am Chem Soc* **56** 1179 *1934*, *Beilstein* **4** II 807, **4** III 1201, **4** IV 2472.]

Trigonellamide chloride (1-methylnicotinamide chloride) *[1005-24-9]* **M 172.6, m 240°(dec).** It crystallises from MeOH, and is dried *in vacuo*. It is prepared from nicotinamide and MeI in refluxing MeOH then shaking with AgCl [Karrer et al. *Helv Chim Acta* **19** 826 *1936*]. It is soluble in organic solvents but moderately in H_2O. It is a metabolite of nicotinic acid in man, and was isolated from urine [Huff & Perizweig *J Biol Chem* **150** 395 1943]. With ketones in aqueous alkali, it produces a green-blue fluorescence which turns blue on acidification and intensifies on heating. [*Beilstein* **22** III/IV 468, **22/2** V 80.]

3,3',5-Triiodo-*S*-thyronine *[6893-02-3]* **M 651.0, m 236-237°(dec), $[\alpha]_D^{29.5}$ +21.5° (EtOH/1M aqueous HCl, 2:1), pK_1^{25} 6.48, pK_2^{25} 7.62, pK_3^{25} 7.82.** Likely impurities are as in *thyroxine*. Purify it by dissolving in dilute NH_3 at ~20°, then crystallise it by addition of dilute acetic acid to pH 6. *Alternatively*, 35g are purified by dissolving it in a mixture of EtOH (250ml) and 2N NaOH (100ml), then hot 2N HCl is added to the boiling solution until the pH is 4-5. After cooling for a few hours, the solid is filtered off and dried in a vacuum [**m** 233-235°(dec)]. [Chambers et al. *J Chem Soc* 2433 *1949*, *Beilstein* **14** III 1566, **14** IV 2373.]

***N,N,*N-Trimethyl glycinehydrazide chloride (Girard Reagent T, 2-hydrazino-*N,N,N*-trimethyl-2-oxo-ethanaminium chloride)** *[123-46-6]* **M 167.6, m 192°.** It is purified by crystallisation from absolute EtOH (slight decomposition) until it has only a slight odour. Store it in well-stoppered containers because it is very hygroscopic. It is very soluble in H_2O, AcOH and glycerol but slightly soluble in EtOH (0.66%). It forms water-soluble hydrazones with carbonyl compounds. [*Beilstein* **4** III 1133.]

***N*-Tris-(hydroxymethyl)methylglycine (TRICINE)** *[5704-04-1]* **M 179.2, m 186-188°(dec), pK_1^{20} ~2.3, pK_2^{20} 8.15.** Crystallise Tricine from EtOH and water. [Good et al. *Methods Enzymol* **24B** 53 *1968*, McGothlin & Jordan *Analyt Lett* **9** 245 *1976*, *Beilstein* **18** III/IV 3454.]

L-Tryptophan *[73-22-3]* **M 204.3, m 278°, 281-282°, 290°, $[\alpha]_D^{20}$ -33.4° (EtOH), $[\alpha]_{546}^{20}$ -36° (c 1, H_2O), $[\alpha]_D^{28}$ +28° (c 2.1, 10% HCl), pK_1^{25}-6.23 (aqueous H_2SO_4), pK_2^{25} 2.46, pK_3^{25} 9.41, pK_4^{25} 14.82 (acidic NH, in aqueous NaOH).** Crystallise L-tryptophan from H_2O/EtOH, wash it with anhydrous diethyl ether and dry it at room temperature in a vacuum over P_2O_5. It sublimes at 220-230°/0.03mm with 99% recovery and unracemised [Gross & Gradsky *J Am Chem Soc* **77** 1678 *1955*]. [Cox & King *Org Synth* Coll Vol **II** 612 *1943*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2316-2345 *1961*, *Beilstein* **22** IV 6765.]

Tyrocidine A (cyclic decapeptide antibiotic with two D-Phe amino acids) *[1481-70-5]* **M 1268.8, m 240°(dec), $[\alpha]_D^{25}$ -115° (c 0.91, MeOH).** Crystallise tyrocidine A as the *hydrochloride* from MeOH or EtOH/HCl. [Paladin & Craig *J Am Chem Soc* **76** 688 *1954*, King & Craig *J Am Chem Soc* **77** 6624 *1955*, Okamoto et al. *Bull Chem Soc Jpn* **50** 231 *1977*, *Beilstein* **26** III/IV 4280.]

L-Tyrosine *[60-18-4]* **M 181.2, m 290-295°(dec), 294-300°(dec), $[\alpha]_D^{25}$ -10.0° (5M HCl), pK_1^{25} 2.18 (CO_2H), pK_2^{25} 9.21 (OH), pK_3^{25} 10.47 (NH_3^+).** Likely impurities are L-cysteine and the ammonium salt. L-Tyrosine is dissolved in dilute ammonia, then crystallised by adding dilute acetic acid to pH 5. Also, crystallise it from H_2O or EtOH/H_2O, and dry it at room temperature in a vacuum over P_2O_5. It sublimes at 235-240°/0.03mm with 99.2% recovery and unracemised [Gross & Gradsky *J Am Chem Soc* **77** 1678 *1955*]. [Albert *Biochem J* **50** 690 *1952*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2348-2366 *1961*, *Beilstein* **14** IV 2264.]

L-Valine *[72-18-4]* **M 117.2, m 305-308°(dec), 315°, $[\alpha]_D^{17}$ +28.4° (c 2, 5M HCl), pK_1^{20} 2.38 (CO_2H), pK_2^{20} 9.59 (NH_3^+).** Crystallise L-valine from water by addition of EtOH. It sublimes at 178-188°/0.03mm with 99.3% recovery and unracemised [Gross & Gradsky *J Am Chem Soc* **77** 1678 *1955*]. [Perrin *J Chem Soc* 3125 *1958*, Greenstein & Winitz *The Chemistry of the Amino Acids* J. Wiley, **Vol 3** pp 2368-2377*1961*, *Beilstein* **4** IV 2659.]

PROTEINS, ENZYMES, DNA and RNA

Abrin A and C (agglutinins from *Abrus seeds*) *[1393-62-0]* **M_r 63,000-67,000.** These are toxic lectins (proteins) from seeds of *Abras precatorius.* The yellow-white powder is purified by successive chromatography on DEAE-Sephadex A-50, carboxymethylcellulose, and DEAE-cellulose. Abrin A is more positively charged on the DEAE-cellulose column and has been crystallised from $(NH_4)_2SO_4$ by the free interface diffusion technique. Its molecular weight (by sedimentation equilibrium) is 60,000, whereas Abrin C has molecular weight of 63,800. Treatment of A with mercaptoethanol at 100°/2 hours followed by SDSPAGE gave a main band with M_r 32,000 and two very weak bands, whereas C (which is more toxic) gave two intense bands with M_r 28,000 and 33,000. [Wei et al. *J Biol Chem* **249** 3061 *1974*.] Abrin C has been crystallised for X-ray analysis by the free interface diffusion technique described by Salemme [*Arch Biochim Biophys* **151** 533 *1972*]. The crystals were grown at 37° in Pyrex tubes (5 x 30 cm) by layering 50µl of protein solution (22mg/ml) over 100µl of unbuffered 70% saturated $(NH_4)_2SO_4$ [Wei & Einstein *J Biol Chem* **249** 2985 *1974*.] [UV and CD: Herrmann & Behnke *Biochem Biophys Acta* **621** 43 *1980*, for physical and chemical properties see *Biochem Biophys Acta* **667** 397 *1981*, *Beilstein* **22** III/IV 6776.]

Acetoin dehydrogenase [from beef liver, acetoin NAD oxidoreductase] *[9028-49-3]* **M_r 76000 [EC 1.1.1.5].** Purify it *via* the acetone cake, then Ca-phosphate gel filtration (unabsorbed), lyophilised and then fractionated through a DEAE-22 cellulose column. The Km for diacetyl is 40µM, and for NADH it is 100µM in phosphate buffer at pH 6.1. [Burgos & Martin *Biochim Biophys Acta* **268** 261 *1972*, **289** 13 *1972*.]

β-D-*N*-Acetylglucosaminidase [from M sexta insects] *[9012-33-3]* **M_r ~61,000 [EC 3.2.1.52].** Purify it by chromatography on DEAD-Biogel, hydroxylapatite chromatography and gel filtration through Sephacryl S200. Two isoforms: a hexosaminidase EI with Km 177µM (V_{max} 328 sec^{-1}) and EII a chitinase with Km 160µM (V_{max} 103 sec^{-1}) with 4-nitrophenyl-β-acetylglucosamine as substrate. [Dziadil-Turner *Arch Biochem Biophys* **212** 546 *1981*.]

β-D-*N*-Acetylhexosaminidase A and B (from human placenta) *[9012-33-3]* **M_r ~61,000 [EC 3.2.1.52].** Purify it by Sephadex G-200 filtration and DEAE-cellulose column chromatography. The hexosaminidase A is further purified by DEAE-cellulose column chromatography, followed by an ECTEOLA-cellulose column, Sephadex-200 filtration, electrofocusing and Sephadex G-200 filtration. Hexosaminidase B is purified by a CM-cellulose column, electrofocusing and Sephadex G-200 filtration. [Srivastava et al. *J Biol Chem* **249** 2034 *1974*.]

***N*-Acetyl neuraminic acid aldolase [from *Clostridium perfringens, N*-acetylneuraminic acid pyruvate lyase]** *[9027-60-5]* **M_r 32,000 [EC 4.1.3.3].** Purify the aldolase by extraction with H_2O, protamine precipitation, $(NH_4)_2SO_4$ fractionation, Me_2CO precipitation, acid treatment at pH 5.7 and precipitation at pH 4.5. The equilibrium constant for pyruvate + *n*-acetyl-D-mannosamine ⇌ *N*-acetylneuraminidate at 37° is 0.64. The Km for *N*-acetylneuraminic acid is 3.9mM in phosphate at pH 7.2 and 37°. [Comb & Roseman *Methods Enzymol* **5** 391 *1962*.] The enzyme from hog kidney (cortex) has been purified 1700-fold by extraction with H_2O, protamine sulfate precipitation, $(NH_4)_2SO_4$ fractionation, heating between 60-80°, a second $(NH_4)_2SO_4$ fractionation and starch gel electrophoresis. The Km for *N*-acetylneuraminic acid is 1.5mM. [Brunetti et al. *J Biol Chem* **237** 2447 *1962*.]

Acyl-coenzyme A Synthase [from beef liver] *[9013-18-7]* **M_r 57,000 [EC 6.2.1.2].** Purify the synthase by extraction with sucrose/HCO_3 buffer, protamine sulfate precipitation, $(NH_4)_2SO_4$ (66-65%) fractination (pH 4.35) and a second $(NH_4)_2SO_4$ (35-60%) fractionation (pH 4.35). It has Km 0.15mM (V_{rel} 1.0) for octanoate and 0.41mM (V_{rel} 2.37) for heptanoate. The Km for ATP is 0.5mM, all at pH 9.0 in ethylene glycol buffer at 38°. [Jencks et al. *J Biol Chem* **204** 453 *1953, Methods Enzymol* **5** 467 *1962*.]

Acyl-coenzyme A Synthase (from yeast) *[9012-31-1]* **M_r ~151,000 [EC 6.2.1.1].** This enzyme has been purified by extraction into phosphate buffer pH 6.8-7.0 containing 2-mercaptoethanol and EDTA, protamine sulfate precipitation, polyethylene glycol fractionation, Alumina γ gel filtration, concentration by $(NH_4)_2SO_4$

precipitation, Bio-Gel A-0.5m chromatography and DEAE-cellulose gradient chromatography. It has Km (apparent) 0.24mM (for acetate) and 0.035mM (for CoA); 1.2 mM for ATP and Mg^{2+} 4.0mM. [Frenkel & Kitchens *Methods Enzymol* **71** 317 *1981*.]

ADP-Ribosyl transferase (adenylyl transferase, polynucleotide, from human placenta) *[9026-30-6]* **M_r~115,000 [EC 2.4.2.30].** Purify the transferase by making an affinity absorbent for ADP-ribosyltransferase by coupling 3-aminobenzamide to Sepharose 4B. [Burtscher et al. *Anal Biochem* **152** 285 *1986*.]

Agglutinin (from peanuts) [*Arachis hypogaea*] *[1393-62-0]* **M_r 134,900 (tetramer).** Agglutinin is purified by affinity chromatography on Sepharose-ζ-aminocaproyl-ß-D-galactopyranosylamine. [Lotan et al. *J Biol Chem* **250** 8518 *1974*.]

Albumin (bovine and human serum) *[9048-46-8 (bovine), 70024-90-7 (human)]* **M_r ~67,000 (bovine), 69 000 (human), UV: $A^{1\%}_{280nm}$ 6.6 (bovine) and 5.3 (human) in H_2O, $[\alpha]^{25}_{546}$ -78.2° (H_2O).** Albumin is purified by dissolving it in conductivity water and passage at 2-4° through two ion-exchange columns, each containing a 2:1 mixture of anionic and cationic resins (Amberlite IR-120, H-form, Amberlite IRA-400, OH^- form). This treatment removes ions and lipid impurities. Care is taken to exclude CO_2, and the solution is stored at -15°. [Möller et al. *Trans Faraday Soc* **57** 312 *1961*.] More complete lipid removal is achieved by lyophilising the de-ionised solution, covering the dried albumin (human serum) with a mixture of 5% glacial acetic acid (v/v) in iso-octane (previously dried with Na_2SO_4) and allowing it to stand at 0° (without agitation) for upwards of 6 hours before decanting and discarding the extraction mixture, washing with iso-octane, re-extracting, and finally washing twice with iso-octane. The purified albumin is dried under vacuum for several hours, then dialyzed against water for 12-24 hours at room temperature, lyophilised, and stored at -10°C [Goodman *Science* **125** 1296 *1957*]. It has been recrystallised in high (35%) and in low (22%) EtOH solutions from Cohn's Fraction V.

The **high EtOH recrystallisation** is as follows: To 1kg of Fraction V albumin paste at -5° is added 300ml of 0.4 M pH (pH 5.5) acetate buffer in 35% EtOH pre-cooled to -10° and 430 ml of 0.1 M NaOAc in 25% EtOH also at -10°. Best results are obtained by adding all of the buffer and about half of the NaOAc and stirring slowly for 1 hour. The rest of the NaOAc is added when all the lumps have disintegrated. The mixture is set aside at -5° for several days to crystallise. 35% EtOH (1 L) is then added to dilute the crystalline suspension and lower the ionic strength prior to centrifugation at -5° (yield 80%). The crystals are further dissolved in 1.5 volumes of 15% EtOH/0.02M NaCl at -5° and clarified by filtration through washed, calcined diatomaceous earth. This solution may be recrystallised by re-adjusting to the conditions in the first crystallisation, or it may be recrystallised at 22% EtOH with the aid of a very small amount of decanol (enough to give a final concentration of 0.02%). Note that crystallisation from lower EtOH concentration gave better purification (i.e. by removing globulins and carbohydrates) and producing a more stable product.

The **low EtOH recrystallisation** is as follows: To 1kg of Fraction V at -10° to -15° is added 500ml of 15% EtOH at -5°, stirred slowly until a uniform suspension is formed. To the 15% EtOH (500ml) is added sufficient 0.2M $NaHCO_3$ solution (125-150ml) at 0° to bring the pH (1:10 dilution) to 5.3. Some temperature rise occurs, and care must be taken to keep the temperature < -5°. If the albumin is incompletely dissolved a small amount of H_2O is added (100ml at a time at 0°, allowing 15 minutes between additions). Undissolved albumin can be easily distinguished from small amounts of undissolved globulins, or as the last albumin dissolves, the appearance of the solution changes from milky white to hazy grey-green in colour. Keep the solution at -5° for 12 hours and filter by suspending in 15g of washed fine calcined diatomaceous earth, and filtering using a Büchner funnel precoated with coarser diatomaceous earth. The filtrate may require two or more similar filtrations to give a clear solution. To crystallise the filtrate, add through a capillary pipette, and with careful stirring, 1/100volume of a solution containing10% decanol and 60% EtOH (at -10°), and seed with the needle-type albumin crystals. After 2-3 days, crystallisation is complete. The crystals are centrifuged off. These are suspended with gentle mechanical stirring in one-third their weight of 0.005 M NaCl pre-cooled to 0°. With careful stirring, H_2O (at 0°) is added slowly in an amount equal to 1.7 times the weight of the crystals. At this stage there is about 7% EtOH, and the temperature cannot be made lower than -2.5° to -1°. Clarify, and collect as above. [Cohn et al. *J Am Chem Soc* **69** 1753 *1947*.]

Human serum albumin has been purified similarly with 25% EtOH and 0.2% decanol. The isoelectric points of bovine and human serum albumins are 5.1 and 4.9, respectively.

Angiotensin (from rat brain) *[70937-97-2]* **M_r 1524.8.** Angiotensin is purified using extraction, affinity chromatography and HPLC [Hermann et al. *Anal Biochem* **159** 295 *1986*].

Angiotensin-converting enzyme (ACE, peptidyl peptide hydrolase) (from rabbit lung) *[9015-82-1]* **M 129,000 Dal (equilibrium sedimentation), M_r ~140,000 (SDS-PAGE) [EC 3.14.15.1].** Purify ACE by fractionation on DEAE-cellulose, Ca phosphate gel chromatography, elution from Sephadex G-200 and lectin affinity chromatography. The MW varied with glycosidation and is higher by gel filtration. It contains one atom of Zn/mol and has Km values for hydrolysis of hippurylhistidinylleucine and angiotensin I of 2.3 and 0.07 mM, and turnover of 15,430 and 792 mol/min/mol at 37°, respectively. The activity is inhibited by EDTA and increased amounts of Ca ions but required Ca ions. [Das & Soffer *J Biol Chem* **250** 6762 *1975*, Reviewed by Ehlers & Riordan *Biochemistry* **28** 5311 *1989*.]

Angiotensinogen (from porcine plasma) *[64315-16-8]* **M_r 59,400, 60,000, 62,600, 63,600 depending on sialic acid content.** This rennin substrate is purified 390-fold from the serum by chromatography on Blue Sepharose, phenyl sepharose, hydroxyapatite and finally by affinity chromatography on 5-hydroxytryptamine (5-HT) sepharose to which it specifically binds to the 5-HT. It is applied to the latter column in 50mM sodium phosphate at pH 7 and after washing, it is eluted by increasing the ionic strength with 100mM sodium phosphate buffer containing 250mM NaCl. The multiple forms are separated by SDSPAGE and have pI 4.40-4.82. [Campbell et al. *Biochem J* **243** 121 *1987*.]

Avidin (from egg white) *[1405-69-2]* **M_r ~70,000.** Avidin is purified by chromatography of an ammonium acetate solution on CM-cellulose [Green *Biochem J* **101** 774 *1966*]. It is also purified by affinity chromatography on 2-iminobiotin-6-aminohexyl-Sepharose 4B [Orr *J Biol Chem* **256** 761 *1981*]. It is a biotin-binding protein.

Azurin (from *Pseudomonas aeruginosa*) *[12284-43-4]* **M_r 30,000.** Azurin with $A_{625/280}$ = 0.56 is purified by gel chromatography on G-25 Sephadex with 5mM phosphate pH 7 buffer as eluent [Cho et al. *J Phys Chem* **91** 3690 *1987*]. It is a blue Cu protein used in biological electron transport, and its reduced form is obtained by adding a slight excess of $Na_2S_2O_4$. [See *Structure and Bonding* Springer Verlag, Berlin **23** 1 *1975*.]

Bromelain (anti-inflammatory Ananase from pineapple) *[37189-34-7]* **M_r ~33,000 [EC 3.4.33.4].** This protease has been purified *via* the acetone powder, G-75 Sephadex gel filtration and Bio-Rex 70 ion-exchange chromatography, and has $A^{1\%}_{1cm}$ 20.1 at 280nm. The protease from pineapple hydrolyses benzoyl glycine ethyl ester with a Km (app) of 210mM and k_{cat} of 0.36 sec^{-1}. [Murachi *Methods Enzymol* **19** 273 *1970*, Balls et al. *Ind Eng Chem* **33** 950 *1941*.]

Carbonic anhydrase (carbonate hydrolase) *[9001-03-0]* **M_r 31,000 [EC 4.2.1.1].** Purify carbonic anhydrase by hydroxylapatite and DEAE-cellulose chromatography [Tiselius et al. *Arch Biochem Biophys* **65** 132 *1956*, *Biochim Biophys Acta* **39** 218 *1960*], and is then dialysed for crystallisation. A 0.5 to 1% solution of the enzyme in 0.05 M Tris-HCl pH 8.5 is dialysed against 1.75M solution of $(NH_4)_2SO_4$ in the same buffer, and this solution is slowly increased in salt concentration by periodic removal of small amounts of dialysate and replacing with an equal volume of 3.5M $(NH_4)_2SO_4$. The final salt concentration, in which the DEAE-cellulose fractions give beautiful birefringent suspensions of crystals, ranged from 2.4 to 2.7M and appeared first as fine crystals, then underwent transition to thin fragile plates. Carbonic anhydrase is a Zn enzyme which exists as several isoenzymes of varying degrees of activity [*J Biol Chem* **243** 6474 *1968*, crystal structure: *Nature, New Biology* **235** 131 *1972*; see also P.D. Boyer Ed. *The Enzymes* Academic Press NY, pp 587-665 *1971*].

Carboxypeptidase A (from bovine pancreas, peptidyl-L-aminoacid lyase) *[11075-17-5]* **M_r 34,600 [EC 3.4.17.1].** Carboxypeptidase A is purified by DEAE-cellulose chromatography, activation with trypsin and dialysed against 0.1M NaCl, yielding crystals. It is recrystallised by dissolving in 20 ml of M NaCl and dialysed for 24 hours each against the following salts present in 500ml of 0.02M sodium veronal pH 8.0, 0.5M NaCl, 0.2M NaCl and 0.15M NaCl. The last dialysate usually induces crystallisation. If it does not crystallise, then

dialyse the last solution against 0.02M sodium veronal containing 0.10M NaCl. Only 2 or 3 re-crystallisations are required to attain maximum activity. [Cox et al. *Biochemistry* **3** 44 *1964*.] Enzyme activity is measured by hydrolysing hippuryl-L-phenylalanine (or phenylacetic acid) and observing the rate of change of optical density at 254nm (reaction extinction coefficient is ~0.592 cm^2/μmole at pH 7.5) [Bergmyer *Methods in Enzymatic Analysis* (Academic Press) **1** 436 *1974*].

Cathepsin B (from human liver) *[9047-22-7]* **M_r 27,500 [EC 3.4.22.1].** Cathepsin B is purified by affinity chromatography on the semicarbazone of Gly-Phe-glycinal-linked to Sepharose 4B, with elution by 2,2'-dipyridyl disulfide [Rich et al. *Biochem J* **235** 731 *1986*, *Methods Enzymol* **80** 551 *1981*].

Cathepsin D (from bovine spleen) *[9025-26-7]* **M_r 56,000 [EC 3.4.23.5].** Cathepsin D is purified on a CM column after $(NH_4)_2SO_4$ fractionation and dialysis, then starch-gel electrophoresis and by ultracentrifugal analysis. Finally chromatograph on a DEAE column [Press et al. *Biochem J* **74** 501 *1960*].

Ceruloplasmin (from human blood plasma) *[9031-37-2]* **M_r 134,000.** This blue protein is the principal Cu transporter (up to 90% of circulating Cu) and is purified by precipitation with polyethylene glycol 4000, batchwise adsorption and elution from QAE-Sephadex, and gradient elution from DEAE-Sepharose CL-6B. Ceruloplasmin is thus purified 1640-fold and is homogeneous on anionic polyacrylamide gel electrophoresis (PAGE), SDS-PAGE, isoelectric focusing and low-speed equilibrium centrifugation. It has λ_{max} at 280, 260nm ($A^{1\%}_{1cm}$ 1□ □0.68). [Oestnuizen *Anal Biochem* **146** 1 *1985*, Cohn et al. *J Am Chem Soc* **68** 459 *1946*.]

Chemokines. These are small proteins formed from longer precursors and are chemo-attractants for lymphocytes and lymphoid organs. They are characterised by having cysteine groups in specific relative positions. The two largest families are the α and β families that have four cysteine residues arranged (C-X-C) and (C-C) respectively. The mature chemokines have ~70 amino acids with internal cys S-S bonds and attract myeloid type cells *in vitro*. The γ-family (Lymphotactin) has only two cys residues. The δ-family (Neurotactin, Fractalkine) has the C-C-X-X-X-C sequence (*ca* 387 amino acids), binds to membrane and promotes adhesion of lymphocytes. The soluble domain of human Fractalkine "chemo-attracts" monocytes and T cells. Several chemokines are available commercially (some prepared by recombinant DNA techniques), including 6Ckine/exodus/SLC which belongs to the β-family with 6 cysteines (110 amino acids, mature protein), as the name implies (C-C-C-C-X.....X-C-C) and homes lymphocytes to secondary lymphoid organs with lymphocyte adhesion antitumor properties. Other chemokines available are C10 (βCC) and Biotaxin. Several chemokine receptors and antibodies are available commercially and can generally be used without further purification. [Murphy "Molecular biology of lymphocyte chemo-attractant receptors" in *Ann Rev Immunol* **12** 593 *1994*.]

Chirazymes. These are commercially available enzymes, e.g. lipases, esterases, that can be used for the preparation of a variety of optically active carboxylic acids, alcohols and amines. They can cause regio and stereospecific hydrolysis and do not require cofactors. Some can be used also for esterification or trans-esterification in neat organic solvents. The proteases, amidases and oxidases are obtained from bacteria or fungi, whereas esterases are from pig liver and thermophilic bacteria. For preparative work the enzymes are covalently bound to a carrier and do not therefore contaminate the reaction products. Chirazymes are available from Roche Molecular Biochemicals and are used without further purification.

α-Chymotrypsin *[9004-07-3]* **M_r ~25000 [EC 3.4.21.1].** α-Chymotrypsin is crystallised twice from four-tenths saturated ammonium sulfate solution, then dissolved in 1mM HCl and dialysed against 1mM HCl at 2-4°. The solution is stored at 2° [Lang et al. *J Am Chem Soc* **80** 4923 *1958*].

Citric acid cycle components (from rat heart mitochondria). These are resolved by anion-exchange chromatography [LaNoue et al. *J Biol Chem* **245** 102 *1970*].

Clostripain *[9028-00-6]* **M_r ~55,000 [EC 3.4.22.8].** Clostripain is isolated from *Clostridium histolyticum* callogenase by extraction in pH 6.7 buffer, followed by hydroxylapatite chromatography with a 0.1-0.2 M phosphate gradient, then Sephadex G-75 gel filtration with 0.05M phosphate pH 6.7, dialysis and a second

hydroxylapatite chromatography (gradient elution with 0.1M → 0.3M phosphate, pH 6.7) purification. It has proteinase and esterase activity and is assayed by hydrolysing *N*-benzoyl-L-arginine methyl ester. [Mitchell & Harrington *J Biol Chem* **243** 4683 *1968*, *Methods Enzymol* **19** 635 *1970*.]

Colicin E1 (from *E.coli*) *[11032-88-5]***. M_r 56,000, pI 9.5.** Colicin E1 is purified (8.6-fold to Specific Activity of 1.5 x 10^5 units/mg) from *E. coli* JC411 by salt extraction of extracellular-bound colicin followed by $(NH_4)_2SO_4$ (40-60% saturation) fractionation and ion-exchange chromatography on a DEAE-Sephadex A 50 column, and then by CM-Sephadex column chromatography [Schwartz & Helinski *J Biol Chem* **246** 6318 *1971*].

Collagenase (from human polymorphonuclear leukocytes) *[9001-12-1]* **M_r 68,000-125,000 [EC 3.4.24.3].** Collagenase is purified by using *N*-ethylmaleimide to activate the enzyme, and wheat germ agglutinin-agarose affinity chromatography [Callaway et al. *Biochemistry* **25** 4757 *1986*].

Copper-zinc-superoxide dismutase (from blood cell haemolysis) *[9054-89-1]* **M_r ~32,000 [EC 1.15.1.1].** The dismutase is purified by DEAE-Sepharose and copper chelate affinity chromatography. The preparation is homogeneous by SDS-PAGE, by analytical gel filtration chromatography and by isoelectric focusing [Weselake et al. *Anal Biochem* **155** 193 *1986*, Fridovich *J Biol Chem* **244** 6049 *1969*].

Cytochrome c_1 (from horse, beef or fishes' heart, or pigeon breast muscle) *[9007-43-6]* **M_r ~13,000.** Cytochrome c_1 is purified by chromatography on CM-cellulose (CM-52 Whatman) [Brautigan et al. *Methods Enzymol* **53D** 131 *1978*]. It has a high PI (isoelectric point) and has been purified further by adsorption onto an acidic cation exchanger, e.g. Amberlite IRC-50 (polycarboxylic) or in ground form Amberlite XE-40 (100-200 mesh) or Decalso-F (aluminium silicate), where the non-cytochrome protein is not adsorbed and is readily removed. The cytochrome is eluted using a solution containing 0.25g ions/L of a univalent cation at pH 4.7 adsorbed onto the NH_4^+ salt of Amberlite IRC-50 at pH 7, washed with H_2O and then with 0.12M NH_4OAc to remove non-cytochrome protein. When the cytochrome begins to appear in the eluate, then the NH_4OAc concentration is increased to 0.25 M. The fractions with *ca* Fe = 0.465—0.467 are collected, dialysed against H_2O and adsorbed onto a small IRC-50 column and eluted with 0.5M NH_3, then dialysed and lyophilised. (A second fraction II can be eluted from the first resin with 0.5M NH_3 but is discarded). [Keilin & Hartree *Biochemical Preparations* **1** 1 *1952*, Margoliash *Biochemical Preparations* **8** 33 *1957*.]
Cytochrome c has been recrystallised as follows: The above eluate (*ca* 100ml) is dialysed against H_2O (10 vols) at 4° for 24 hours (no more), then passed through an XE-40 column (2 x 1 cm above) which is equilibrated with 0.1M NH_4OAc pH 7.0. The column is washed with 0.1% $(NH_4)_2SO_4$ pH 8.0, and the dark red resin in the upper part of the column is collected and in 0.1% $(NH_4)_2SO_4$ pH 8.0 is transferred to another column (7mm diameter) and the cytochrome c is eluted with 5% $(NH_4)_2SO_4$ pH 8.0. More than 98% of the red colour is collected in a volume of *ca* 4ml in a weighed centrifuge tube. Add a drop of octanol and 0.43g of $(NH_4)_2SO_4$/g of solution. When the salt has dissolved, ascorbic acid (5mg) is added as well as a few drops of 30% aqueous NH_3, and it is kept at 10° for 10 minutes (turns lighter colour due to reduction). Then add finely powdered $(NH_4)_2SO_4$ in small portions (stir with a glass rod) until the solution becomes turbid. Stopper the tube tightly, and set aside at 15-25° for 2 days while the cytochrome c separates as fine needles or rosettes. Further $(NH_4)_2SO_4$ (20mg) are added per ml of suspension and kept in the cold for a few days to complete the crystallisation. The crystals are collected by centrifugation (5000xg), suspended in saturated $(NH_4)_2SO_4$ (pH 8.0 at 10°), then centrifuged again. For recrystallisation the crystals are dissolved in the least volume of H_2O, one drop of ammonia and 1 mg of ascorbic acid are added and the above process is repeated. The yield of twice recrystallised cytochrome c from 2Kg of muscle is *ca* 200 mg, but this varies with the source and freshness of the muscle used. The crystals are stored as a solid after dialysis against 0.08M NaCl or 0.1M sodium buffer and lyophilising, or as a suspension in saturated $(NH_4)_2SO_4$ at 0°. [Hagihara et al. *Biochemical Preparations* **6** 1 *1958*.]
Purity of cytochrome c: This is checked by the ratio of the absorbance at 500nm (reduced form) to 280nm (oxidised form), i.e. $\varepsilon_{500}/\varepsilon_{280}$ should be between 1.1 and 1.28, although values of up to 1.4 have been obtained for pure preparations.
For the preparation of the *reduced form* see Margoliash *Biochemical Preparations* **5** 33 *1957* and Yonetani *Biochemical Preparations* **11** 19 *1966*.
Cytochrome from *Rhodospirillum rubrum* ($\varepsilon_{270}/\varepsilon_{551}$ 0.967) is purified by chromatography on a column of CM-Whatman cellulose [Paleus & Tuppy *Acta Chem Scand* **13** 641 *1959*].

Cytochrome c oxidase (from bovine heart mitochondria). *[9001-16-5]* **M_r 100,000/haeme [EC 1.9.3.1].** The oxidase is purified by selective solubilisation with Triton X-100 and subsequently with lauryl maltoside, finally by sucrose gradient centrifugation [Li et al. *Biochem J* **242** 417 *1978*].
It has also been purified by extraction in 0.02 M phosphate buffer (pH 7.4) containing 2% of cholic acid (an inhibitor which stabilises as well as solubilises the enzyme) and fractionated with $(NH_4)_2SO_4$ collecting the 26-33% saturation cut and refractionating again and collecting the 26-33% saturation fraction. The pellet collected at 10,000x g appears as an oily paste. The cholate needs to be removed to activate the enzyme as follows: The precipitate is dissolved in 10ml of 0.1M phosphate buffer pH 7.4, containing 1% of Tween-80 and dialysed against 1L of 0.01 M PO_4 buffer (pH 7.4) containing 1% of Tween-80 for 10 hours at 0º and aliquoted. The enzyme is stable at 0º for 2 weeks and at -15º for several months. It is assayed for purity (see reference) by oxidation of reduced cytochrome c (Km 10μM). [Yonetani *Biochemical Preparations* **11** 14 *1966*, *J Biol Chem* **236** 1680 *1961*.]

Cytokines See chemokines, interferons, interleukins.

Deoxyribonucleic acid (from plasmids). These are purified by two buoyant density ultracentrifugations using ethidium bromide-CsCl. The ethidium bromide is extracted with Et_2O, and the DNA is dialysed against buffered EDTA and lyophilised. [Marmur & Doty *J Mol Biol* **5** 109 *1962*, Guerry et al. *J Bacteriol* **116** 1064 *1973*.] See "Introduction" in this chapter.

Dermatan sulfate (condroitin sulfate B from pig skin) M_r 20,000-36,000 *[54328-33-5 (Na salt)]***.** Dermatan sulfate is purified by digestion with papain and hyaluronidase, and fractionation using aqueous EtOH. [Gifonelli & Roden *Biochemical Preparations* **12** 1 *1968*.]

Dihydrofolate reductase (from *Mycobacterium phlei*) *[9002-03-3]* **M_r ~18,000 [EC 1.5.1.3].** Dihydrofolate reductase is purified by $(NH_4)_2SO_4$ precipitation, then fractionation on a Sephadex G-75 column, applied to a Blue Sepharose column and eluted with 1mM dihydrofolate. [Al Rubeai & Dole *Biochem J* **235** 301 *1986*.]

Dihydropteridine reductase (from sheep liver) *[9074-11-7]* **M_r 52,000 [EC 1.6.99.7].** Dihydropteridine reductase is purified by fractionation with ammonium sulfate, dialysed against Tris buffer, adsorbed and eluted from hydroxylapatite gel. It is then run through a DEAE-cellulose column and also subjected to Sephadex G-100 filtration. [Craine et al. *J Biol Chem* **247** 6082 *1972*.]

Dihydropteridine reductase (from human liver) *[9074-11-7]* **M_r 52,000 [EC 1.6.99.7].** Dihydropteridine reductase is purified to homogeneity on a naphthoquinone affinity adsorbent, followed by DEAE-Sephadex and CM-Sephadex chromatography. [Firgaira, Cotton and Danks, *Biochem J* **197** 31 *1981*.] [For other dihydropteridine reductases see Armarego et al. *Med Res Rev* **4**(3) 267 *1984*.]

3,4-Dihydroxyphenylalanine-containing proteins. Boronate affinity chromatography is used in the selective binding of proteins containing 3,4-dihydroxyphenylalanine to a *m*-phenylboronate agarose column and eluted with 1M NH_4OAc at pH 10. [Hankus et al. *Anal Biochem* **150** 187 *1986*.]

Dipeptidyl aminopeptidase (dipeptidyl peptidase IV, from rat brain) *[9031-94-1, 54249-88-6]* **M_r 87,500 (monomer SDS-PAGE), (88,107 from nucleotide sequence), up to 4000,000 [EC 3.4.14.5].** The aminopeptidase is purified about 2000-fold by column chromatography on CM-cellulose, hydroxylapatite and Gly-Pro AH-Sepharose. [Imai et al. *J Biochem (Tokyo)* **93** 431 *1983*, Schomburg & Schomburg *Springer Handbook of Enzymes* 2nd Edn **vol 6** p 286 *2002*.]

DNA (deoxyribonucleic acids). The essential structures of chromosomes are DNA and contain the genetic "blueprint" in the form of separate genes. They are made up of the four deoxyribonucleic acids (nucleotides): adenylic acid, guanylic acid, cytidylic acid and thymidylic acid (designated A, G, C, T respectively) linked together by their phosphate groups in ester bonds between the 3' and 5' hydroxy groups of the 2'-deoxy-D-ribose moiety of the nucleotides. The chains form a double-stranded spiral (helix) in which the two identical nucleotide

sequences run antiparallel with the heterocyclic bases hydrogen bonded (A….T, G….C) forming the "ladder" between the strands. Short sequences of DNA are available commercially, are commercially custom made or synthesised in a DNA synthesiser and purified by HPLC. Their purity can be checked by restriction enzyme cleavage followed by gel electophoresis, or directly by gel electrophoresis or analytical HPLC. Commercial DNAs are usually pure enough for direct use but can be further purified using commercially available kits involving binding to silica or other matrices and eluting with Tris buffers. There are now rapid "throughput" techniques for sequencing DNA which are very accurate.

Dopamine-β-hydroxylase (from bovine adrenal medulla) *[9013-38-1]* **M_r ~290,000 [EC 1.14.17.1].** The Cu-containing glycoprotein enzyme has been isolated by two procedures. The first is an elaborate method requiring extraction, two $(NH_4)_2SO_4$ fractionations, calcium phosphate gel filtration, EtOH fractionation, DEAE-cellulose chromatography followed by two Sephadex-G200 gel filtrations giving enzyme with a specific activity of 65 Units/mg. [Friedman & Kaufman *J Biol Chem* **240** 4763 *1965*, Rush et al. *Biochem Biophys Res Commun* **61** 38 *1974*.] The second procedure is much gentler and provides good quality enzyme. Sedimented chromaffin vesicles are lysed in 10 volumes of 5mM K-phosphate buffer pH 6.5 using a loosely fitting Teflon-glass homogeniser. The mixture is centrifuged at 40,000xg/0.5 hours, and the supernatant is diluted with an equal volume of 100mM phosphate buffer (pH 6.5) containing 0.4M NaCl. This lysate is applied to a concanavelin A-Sepharose column (4 x 0.7cm) which had been equilibrated with 50 mM of phosphate buffer (pH 6.5 + 0.2M NaCl) with a flow rate of ~ 0.3 ml/minute. The column is washed thoroughly with the buffer until OD_{280nm} is 0.005. The enzyme is then eluted with the same buffer containing 10% α-methyl-D-mannoside (flow rate 0.1 ml/minute), and the enzyme is collected in 20-column volumes. The pooled eluate is concentrated by ultrafiltration in an Amicon Diaflo stirrer cell using an XM100A membrane. The concentrated enzyme is dialysed against 50mM phosphate buffer (pH 6.5) containing 0.1% NaCl. The enzyme gives one band (+ two very weak bands) on disc gel electrophoresis indicating better than 93% purity (67% fold purification) and has a specific activity of 5.4 Units/mg. [Rush et al. *Biochem Biophys Res Commun* **57** 1301 *1974*, Stewart & Klinman *Ann Rev Biochem* **57** 551 *1988*.]

Exonucleases. Like the endonucleases they are restriction enzymes which act at the 3' or 5' ends of linear DNA by hydrolysing off the nucleotides. Although they are highly specific for hydrolysing nucleotides at the 3' or 5' ends of linear DNA, the number of nucleotides cleaved is time dependent and usually has to be estimated from the time allocated for cleavage. Commercially available exonucleases are used without further purification.

Ferritin (from human placenta) *[9007-73-2]* **M_r ~445,000 (Fe free protein).** The purification of this major iron-binding protein is achieved by homogenisation in water and precipitation with ammonium sulfate, repeating the cycle of ultracentrifugation, and molecular sieve chromatography through a Sephadex 4B column. Isoelectric focusing reveals a broad spectrum of impurities which can be separated by ion-exchange chromatography on Sephadex A-25 and stepwise elution. [Konijn et al. *Anal Biochem* **144** 423 *1985*.]

Fibrinogen (from human plasma) *[9001-32-5]* **M_r 341,000.** This protein is made up of 2Aα,2Bβ and 2γ subunits connected by disulfide bridges. A likely impurity is plasminogen. It is purified by glycine precipitation [Mosesson & Sherry *Biochemistry* ***5*** 2829 *1966*] to obtain fractions 1-2, then further purified [Blombäck & Blombäck *Arkiv Kemi* **10** 415 *1956*] and contaminating plasminogen is removed by passage through a lysine-Sepharose column. Such preparations are at least 95% clottable as determined by Mosesson and Sherry's method (above ref.) in which the OD_{280} is measured before and after clotting with 5 Units/ml of thrombin (>3000U/mg). All fibrinogen preparations are treated with calf intestinal alkaline phosphatase to convert any fibrinogen peptide-AP to fibrinogen peptide-A by removing serine-bound phosphate. Solutions are then lyophilised and stored at -20°. [Higgins & Shafer *J Biol Chem* **256** 12013 *1981*.] It is sparingly soluble in H_2O. Aqueous solutions are viscous with isoelectric point at pH 5.5. It is readily denatured by heating above 56° or by chemical agents, e.g. salicylaldehyde, naphthoquinone sulfonates, ninhydrin or alloxan. [Edsall et al. *J Am Chem Soc* **69** 2731 *1947*, Purification: Cama et al. *Naturwissenschaften* **48** 574 *1961*, Lorand & Middlebrook

Science **118** 515 *1953*, *cf*. Fuller in *Methods Enzymol* **163** 474 *1988*.]
For plasminogen-deficient fibrinogen from blood plasma, the anticoagulated blood is centrifuged and the plasma is frozen and washed with saline solution. It is treated with charcoal, freeze-thawed and dialysed *versus* Tris/NaCl buffer. [Maxwell & Nikel *Biochemical Preparations* **12** 16 *1968*.]

Fibronectin (from human plasma) *[86088-83-7]* **M_r ~220,000.** This glycoprotein contains 5-12% of carbohydrate. It has been purified by glycine fractionation and DEAE-cellulose chromatography. This material is dissolved in 0.25M Tris-phosphate buffer pH 7.0, diluted to 20% and glycine added gradually till 2.1M when the temperature falls to below 15°. The precipitate contains mainly fibrinogen. The supernatant is discarded, and the precipitate is treated with an equal volume of H_2O, cooled (to 0°) and precipitated by adding EtOH to 16% (v/v) at -4°. The precipitate contains some CI (Cold Insoluble) globulin, fibronectin and small quantities of other proteins. To remove these the precipitate is dissolved in 0.25M Tris-phosphate buffer (pH 7.0) *ca* 0.5% and purified by DEAE-cellulose chromatography after diluting the buffer to 0.05M buffer. [Morrison et al. *J Am Chem Soc* **70** 3103 *1948*, Mosesson & Umfleet *J Biol Chem* **245** 5728 *1970*, Mosesson & Amrani *Blood* **56** 145 *1980*, Akiyama & Yamada *Adv Enzymol* **59** 51 *1987*.]

Follicle Stimulating Hormone (FSH, follitropin) *[9002-68-0]* **M_r ~36,000.** FSH is purified by Sephadex G100 gel filtration followed by carboxymethyl-cellulose with NH_4OAc pH 5.5. The latter separates luteinising hormone from FSH. Its solubility in H_2O is 0.5%. It has an isoelectric point of 4.5. A solution of 1mg in saline (100ml) can be kept at 60° for 0.5 hour. Activity is retained in a solution at pH 7-8 for 0.5 hour at 75°. The activity of a 50% aqueous EtOH solution is destroyed at 60° in 15 minutes. [Bloomfield et al. *Biochim Biophys Acta* **533** 371 *1978*, Hartree *Biochem J* **100** 754 *1966*, Pierce & Parsons *Ann Rev Biochem* **50** 465 *1981*.]

ß-Galatosidase (from bovine testes) *[9031-11-2]* **M_r 510,000 [EC 3.2.1.23].** It is purified 600-fold by $(NH_4)_2SO_4$ precipitation, acetone fractionation and affinity chromatography on agarose substituted with terminal thio-ß-galactopyranosyl residues. [Distlern & Jourdian *J Biol Chem* **248** 6772 *1973*.]

Glucose oxidase (from *Aspergillus niger*) *[9001-37-0]* **M_r 186,000, [EC 1.1.3.4].** The oxidase is purified by dialysis against deionized water at 6° for 48 hours and by molecular exclusion chromatography with Sephadex G-25 at room temperature. [Holt & Cotton *J Am Chem Soc* **109** 1841 *1987*.]

Glucose-6-phosphate dehydrogenase *[9001-40-5]* **M_r 128,000 (from Baker's yeast), 63,300 (from rat mammary gland) [EC 1.1.1.49].** The enzyme is useful for measuring pyridine nucleotides in enzyme recycling. The enzyme from Baker's yeast has been purified by $(NH_4)_2SO_4$ fractionation, Me_2CO precipitation, a second $(NH_4)_2SO_4$ fractionation, concentration by DEAE-SF chromatography, a third $(NH_4)_2SO_4$ fractionation and recrystallisation. Crystallisation is induced by addition of its coenzyme NADP, which in its presence causes rapid separation of crystals at $(NH_4)_2SO_4$ concentration much below that required to precipitate the amorphous enzyme. To recrystallise, the crystals are dissolved in 0.01M NADP (pH 7.3) with $(NH_4)_2SO_4$ at 0.55 saturation, and the crystals appear within 10 to 60 minutes. After standing for 2-3 days (at 4°) the $(NH_4)_2SO_4$ is increased to 0.60 of saturation, and more than 80% of the activity in the original crystals is recovered in the fresh crystals. [Noltmann et al. *J Biol Chem* **236** 1255 *1961*]. Large amounts can be obtained from rat livers. The livers are extracted with 0.025M phosphate buffer (pH 7.5) and precipitated with 3M $(NH_4)_2SO_4$ (70% of activity). The precipitate is dissolved in 3 volumes of 0.025M phosphate (pH 7.5), dialysed against this buffer + 0.2mM EDTA at 4° for 5 hours, then diluted to 1% protein and the nucleic acids are precipitated by addition of 0.4 volumes of 1% protamine sulfate. $(NH_4)_2SO_4$ is added to a concentration of 2M (pH adjusted to 7.0 with NH_3), the precipitate is discarded and the supernatant is adjusted to 2.8M $(NH_4)_2SO_4$, dialysed, and the protein is adjusted to 1% and treated with $Ca_3(PO_4)_2$ gel. The gel is added in three steps (1.5ml of 0.4% gel/ml per step), and the gel is removed by centrifugation after each addition. The third gel adsorbed 50% of the activity. The gel is eluted with 0.2M phosphate buffer (pH 7.4, 40ml/g of gel; 60% recovery). The extract is precipitated in 3 volumes of $(NH_4)_2SO_4$ (adjusted to 4M) to give enzyme with an activity of 30µmoles/mg of protein per hour. [Lowry et al. *J Biol Chem* **236** 2746 *1961*.] The Km values for the yeast enzyme are 20µM for G-6P and

2μM for NADP (Tris pH 8.0, 10^{-2} M $MgCl_2$, 38°) [Noltmann & Kuby *The Enzymes* **VII** 223 *1963*].

Glutathione S-transferase (human liver) *[50812-37-8]* **M_r 25,000 [EC 2.5.1.18].** It is purified by affinity chromatography using a column prepared by coupling glutathione to epoxy-saturated Sepharose. After washing contaminating proteins, the pure transferase is eluted with buffer containing reduced glutathione. The solution is then concentrated by ultrafiltration, dialysed against phosphate buffer at pH ~7 and stored in the presence of dithiothreitol (2mM) in aliquots at < −20°. [Simons & Vander Jag *Anal Biochem* **52** 334 *1977*.]

Glyceraldehyde-3-phosphate dehydrogenase *[9001-50-7]* **M_r 144,000 [EC 1.2.1.12].** Purify the dehydrogenase from rabbit muscle by extraction with 0.03N KOH and precipitate it with $(NH_4)_2SO_4$ (0.52 of saturation). The clear supernatant is adjusted to pH 7.5, and NH_3 is added dropwise to pH 8.2-8.4. Crystals appear sometimes even without seeding. The crystals are dissolved in H_2O, filtered to remove suspended material and 2 volumes of saturated $(NH_4)_2SO_4$ at pH 8.2-8.4 is added. After 1 hour the crystals appear. Recrystallise it in the same way. [Cori et al. *J Biol Chem* **173** 605 *1948*, Furfine & Velick *J Biol Chem* **240** 844 *1965, The Enzymes* **7** 243 *1963*, Lui & Huskey *Biochemistry* **31** 6998 *1992*.] The Km values are: NADH (3.3μM) and 1,3-diphosphoglycerate ($8x10^{-7}$M) in pH 7.4 imidazole buffer at 26°, NAD (13μM), glyceraldehyde-3-P (90μM), P_i ($2.9x10^{-4}$M), and arsenate (69μM) in 8.6 M $NaHCO_3$ buffer at 26°C. [Orsi & Cleland *Biochemistry* **11** 102 *1972*.]

Glycerol kinase (from *Candida mycoderma*, *E coli*, rat or pigeon liver glycerokinase) *[9030-66-4]* **M_r 251,000 [EC 2.7.1.30].** Commercial enzyme has been dialysed against 2mM Hepes, 5mM dithiothreitol and 0.3mM EDTA, followed by several changes of 20mM Hepes and 5mM dithiothreitol prior to storage under N_2 at -20°. [Knight & Cleland *Biochemistry* **28** 5728 *1989*.] The enzyme from pigeon liver is purified by acid-precipitation (acetate buffer at pH 5.1), $(NH_4)_2SO_4$ fractionation, heat treatment (60°/ 1 hour), calcium phosphate gel filtration, a second $(NH_4)_2SO_4$ fractionation, dialysis, elution of inert proteins and crystallisation. This is done by repeatedly extracting the precipitate from the last step with 0.05M sodium pyrophosphate (pH 7.5) containing 1mM EDTA and 0.2M $(NH_4)_2SO_4$ is added. Careful addition of solid $(NH_4)_2SO_4$ to this solution leads to crystallisation of the enzyme. Recrystallisation is repeated. The enzyme is activated by Mg^{2+} and Mn^{2+} ions and is most stable in solutions in the pH 4.5-5.5 range. The stability is greatly increased in the presence of glycerol. It has Km for glycerol of 60μM and for ATP 9μM in glycine buffer pH 9.8 and 25°. [Kennedy *Methods Enzymol* **5** 476 *1962*.]

L-Glycerol-3-phosphate dehydrogenase (GDH, from rabbit muscle) *[9075-65-4]* **M_r 78,000 [EC 1.1.1.8].** The dehydrogenase is recrystallised by adding $(NH_4)_2SO_4$ to 0.45 saturation at pH 5.5 at 4°C, and the small amount of precipitate is removed, then a saturated solution of $(NH_4)_2SO_4$ is added dropwise from time to time over several days in the cold room. The crystals are collected and recrystallised until they have maximum activity. The enzyme is stable in half-saturated $(NH_4)_2SO_4$ for several weeks at 4°. The equilibrium [dihydroxyacetone][NADH][H^+]/[G-3-P][NAD] is 1.0 x 10^{-12}M in Tris buffer at 25°. It uses NAD ten times more efficiently than NADP. The Km for G-3-P is 1.1 x 10^{-4}M, for NAD it is 3.8 x 10^{-4}M and for dihydroxyacetone it is 4.6 x 10^{-4}M in phosphate buffer pH 7.0 and at 23.3°. Dihydroxyacetone phosphate and fructose-1,6-diphosphate are inhibitors. [Branowski *J Biol Chem* **180** 515 *1949*, *The Enzymes* **7** 85 *1963*, Young & Pace *Arch Biochem Biophys* **75** 125 *1958*, Walsh & Sallach *Biochemistry* **4** 1076 *1965*.]

Glycogen synthase (from bovine heart) *[9014-56-6]* **M_r 60,000 [EC 2.4.1.11].** Purify the synthase by precipitation in the presence of added glycogen by polyethylene glycol, chromatography on DEAE-Sephacel and high-speed centrifugation through a sucrose-containing buffer. [Dickey-Dunkirk & Kollilea *Anal Biochem* **146** 199 *1985*.]

Haemoglobin A (from normal human blood) *[9008-02-0]* **M_r ~64,500, amorphous.** Purify it from blood using CM-32 cellulose column chromatography. [Matsukawa et al. *J Am Chem Soc* **107** 1108 *1985*.] For the purification of the α and β chains see Hill et al. *Biochemical Preparations* **10** 55 *1963*.

Histones (from S4A mouse lymphoma). The purification of histones uses a macroprocess column, heptafluorobutyric acid as solubilising and ion-pairing agent and an acetonitrile gradient. [McCroskey et al. *Anal Biochem* **163** 427 *1987*.]

Hyaluronidase *[9001-54-1, 37326-33-3]* **M_r 43,000 (bovine testes), 89,000 (bacterial) [EC 3.2.1.35].** Hyaluronidase is purified by chromatography on DEAE-cellulose prior to use. [Distler & Jourdain *J Biol Chem* **248** 6772 *1973*.]

D-Hydantoinase [dihydropyrimidinase, also called 5,6-dihydropyrimidine amidohydrolase, from microorganisms e.g. Pseudomonas, Bacillus, Agrobacterium as well as from mammalian and human tissues) *[9030-74-4]* **M 51,720 (monomer from amino acid sequence, usually dimer or tetramer) [EC 3.5.2.2], pI ~6.5.** This cytosolic enzyme hydrolyses dihydropyrimidines and hydantoins to N-carbamoylamino acids, and with the appropriate substrates are useful for preparing D-amino acids. The enzyme from a recently isolated species of *Agrobacterium* was purified to homogeneity and found to possess hydantoinase activity that was free from dihydropyrimidinase activity. It had an estimated subunit molecular weight of ~66,500 and a theoretical molecular weight of 265,000. The preferred substrates were 5-mono-substituted hydantoins with aromatic groups as shown from the Km values. 5,5-Dimethylhydantoin and thio analogues of 5-*p*-hydroxyphenylhydantoins were competitive inhibitors. [Runser & Meyer *Eur J Biochem* **213** 131 *1993*.]
A commercially available hydantoinase preparation from *Vignia angularis* from aduki bean with a minimum activity of 300U/g is commercially available. These enzymes are generally inhibited by *N*-carbamoylamino acids (reaction products) 8-hydroxyquinoline, EDTA, Sn^{2+} and Zn^{2+}, but are activated by uracil, 2-thiouracil, Co^{2+}, Fe^{2+}, Mg^{2+}, Mn^{2+} and Ni^{2+}, with turnovers of ~27,000min^{-1} for hydantoin. Their pH-range is 6—9.5, and the temperature range is ~4-60°. D-Hydrantoinase genes have been cloned and expressed in *E coli* and the enzymes from several sources have been crystallised.
A **unit** of enzyme activity is defined as the amount that catalyses the formation of 1mmole of *N*-carbamoylglycine from hydantoin per minute at pH 9.0 and 40°. [Morin *Enz Microbiol Technol* **15** 208 *1993*, *Springer Handbook of Enzymes* D. Schonburg & I. Schonburg Eds (A. Chang co-Ed) Springer-Verlag, Berlin, Heidelberg.

3-Hydroxy butyrate dehydrogenase (from *Rhodopseudomonas spheroides*) *[9028-38-0]* **M_r ~85,000 [EC 1.1.1.30], amorphous.** Purify the dehydrogenase by two sequential chromatography steps on two triazine dye-Sepharose matrices. [Scavan et al. *Biochem J* **203** 699 *1982*.]

Interferons [αIFN, βIFN and γIFN]. Interferons are a family of glycosylated proteins and are cytokines which are produced a few hours after cells have been infected with a virus. Interferons protect cells from viral infections and have antiviral activities at very low concentrations (~3 x 10^{-4} M; less than 50 molecules are apparently sufficient to protect a single cell). Double-stranded RNAs are very efficient inducers of IFNs. There are three main types of IFNs. The αIFNs are synthesised in lymphocytes, and the βIFNs are formed in infected fibroblasts. The α and β families are fairly similar, consisting of *ca* 166 to 169 amino acids. Although γIFNs are also small glycosylated proteins (*ca* 146 amino acids), they are different because they are not synthesised after viral infections but are produced by lymphocytes when stimulated by **mitogens** (agents that induced cell division).
Several of these IFNs of mouse and human lymphocytes and fibroblasts are available commercially and have been best prepared in quantity by recombinant DNA procedures because they are produced in very small amounts by the cells. The commercial materials do not generally require further purification for their intended purposes. [Pestkas, Interferons and Interferon standards and general abbreviations, *Methods Enzymol*, Wiley & Sons, **119** *1986,* ISBN 012182019X, Lengyel, Biochemistry of interferons and their actions, *Ann Rev Biochem* **51** 251-282 *1982*, De Maeyer & De Maeyer-Guignard, Interferons in *The Cytokine Handbook*, 3rd Edn, Thomson et al. Eds, pp. 491-516 *1998* Academic Press, San Diego, ISBN 0126896623.]

Interleukin (from human source). Purify these using lyophilisation and desalting on a Bio-Rad P-6DC desalting gel, then two steps of HPLC, first with hydroxylapatite, followed by a TSK-125 size exclusion column. [Kock & Luger *J Chromatogr* **296** 293 *1984*.]

Interleukin-2 (recombinant human) *[94218-72-1]* **M_r ~15,000, amorphous.** Purify it by reverse phase HPLC. [Weir & Sparks *Biochem J* **245** 85 *1987*, Robb et al. *Proc Natl Acad Sci USA* **81** 6486 *1984*.]

Interleukins (IL-1, IL-2 —lL18]. Interleukins are cytokines which cause a variety of effects including stimulation of cell growth and proliferation of specific cells, e.g. stem cells, mast cells, activated T cells, colony stimulating factors etc., as well as stimulating other ILs, prostaglandins release etc. They are small glycosylated proteins (*ca* 15 kD, 130-180 amino acids produced from longer precursors) and are sometimes referred to by other abbreviations, e.g. IL-2 as TCGF (T cell growth factor), IL-3 as multi-CSF (multilineage colony stimulating factor, also as BPA, HCSF, MCSF and PSF). They are produced in very small amounts and are commercially made by recombinant DNA techniques in bacteria or Sf21 insect cells. Interleukins for human (h-IL), mouse (m-IL) and rat (r-IL) are available, and up to IL-18 are available commercially in such purity that they can be used directly without further refinement, particularly those that have been obtained by recombinant DNA procedures which are specific. As well as the interleukins, a variety of antibodies for specific IL reactions are available for research or IL identification. [Symons et al. Lymphokines and Interferons, *A Practical Approach*, Clemens et al. Eds, p.272 *1987*, IRL Press, Oxford, ISBN 1852210354, 1852210362, Thomson et al. Eds, *The Cytokine Handbook,* 3rd Edn, *1998*, Academic Press, San Diego, ISBN 0126896623.]

Lactate dehydrogenase (from dogfish, Beef muscle) *[9001-60-9]* **M_r 140,000 [EC 1.1.1.27].** A forty-fold purification of the dehydrogenase is effected by affinity chromatography using Sepharose 4B coupled to 8-(6-aminohexyl)amino-5'-AMP or -NAD^+. [Lees et al. *Arch Biochem Biophys* **163** 561 *1974*, Pesce et al. *J Biol Chem* **239** 1753 *1964*.]

Lactoferrin (from human whey) *[55599-62-7*, Fe Salt*]* ***M_r* ~90,000.** This iron-binding protein is purified by direct adsorption on cellulose phosphate by batch extraction, then eluted by a stepped salt and pH gradient. The Fe bound protein forms red crystals with λ_{max} at 465nm (pH 8.2). [Foley & Bates *Anal Biochem* **162** 296 *1987*.]

Lectins (proteins and/or glycoproteins of non-immune origin that agglutinate cells, e.g. from seeds of *Robinia pseudoacacia*), M_r~100,000. Lectins are purified by precipitation with $(NH_4)_2SO_4$ and dialysed, then chromatographed on DE-52 DEAE-cellulose anion-exchanger, hydroxylapatite and Sephacryl S-200. [Wantyghem et al. *Biochem J* **237** 483 *1986*.]
Lectins are a group of proteins that are classed as sugar-binding proteins or glycoproteins of non-immune origin and which agglutinate cells and/or precipitate glyco-conjugates. They are present in plants (seeds, roots, leaves or bark) and some invertebrates (snails, clams, crabs) and have M_r values of 10,000-400,000. They may contain Mn^{2+} and/or Ca^{2+}. Mono- or oligo- saccharides of appropriate specificity inhibit lectins. Some lectins are specific to human blood groups and induce mitosis in lymphocytes. [Goldstein *Nature* **286** 66 *1980*.]

Lipoprotein lipase (from bovine skimmed milk) *[9004-02-8]* **M_r ~34,000 and 63,000 (SDSPAGE), 96,900 (sedimentation and diffusion), 100,000-120,000 (gel filtration) [EC 3.1.1.34].** Purify the lipase by affinity chromatography on heparin-Sepharose; Ki 0.026mM for very low density lipoprotein. It is inhibited by 2-mercaptoethanol, Cys, Ca, Hg, Mg and Mn ions. Protamine sulfate, 1mg of bovine serum albumin/ml or in 50% glycerol at -70°, stabilises the lipase for several days. 60% loss of activity occurs at 0°/1hour in the presence of 1% of bovine serum albumin. [Shirai et al. *Biochim Biophys Acta* **665** 504 *1981*.]

Lipoproteins (from human plasma). Individual human plasma lipid peaks are removed from plasma by ultracentrifugation; then they are separated and purified by agarose-column chromatography. Fractions are characterised immunologically, chemically, electrophoretically and by electron microscopy. [Rudel et al. *Biochem J* **13** 89 *1974*.]

Lipoteichoic acids (from gram-positive bacteria) *[56411-57-5]***.** The acids are extracted by hot phenol/water from disrupted cells. Nucleic acids are also extracted and are removed by treatment with nucleases. Nucleic resistant acids, proteins, polysaccharides and teichoic acids are separated from lipoteichoic acids by anion-exchange chromatography on DEAE-Sephacel or by hydrophobic interaction on octyl-Sepharose [Fischer et al. *Eur J Biochem* **133** 523 *1983*].

Lysozyme (Muramidase, *N*-acetylmuramyl hydrolase, *N*-acetylmuramide, peptidoglycan *N*-acetylmuramoyl hydrolase, Globulin G_1) *[human 174883-18-2, from human neutrophils 9001-63-2, from human milk 12671-19-1, from chicken egg white 126050-88-3, chloride from chicken egg white 9066-59-5]* **M 14,400 ±100, E_{280nm} 2.65 (c 1mg/ml) Isoelectric Point (IP) 10.5-11.0 [EC 3.2.1.17].** Lysozymes from human and bird sources are 129 amino acid enzymes that contain four disulfide bonds. Hen lysozyme was isolated in quantity from chicken egg white, crystallised, and its X-ray crystalline structure was determined [Phillips *Proc Natl Acad Sci USA* **57** 484 *1967*]. Lysozyme occurs in many tissues of invertebrate and vertebrate animals. It is found in milk, blood serum and various secretions (saliva, nasal mucus and tears). It also occurs in some moulds and in the latex of certain plants. Lysozyme from human milk was studied in some detail and is very similar to the hen enzyme [Jolles & Jolles *Helv Chim Acta* **52** 2671 *1969* and **54** 2668 *1971*]. Lysozyme is a glycosidase which dissolves various bacterial cell walls [particularly Gram-positive bacteria (which have surface lipoproteins) to give spheroblasts, and various Gram-negative bacteria in the presence of EDTA in hypotonic solutions, or non-ionic detergents]. Bacterial cell walls contain 1,4-β-*N*-acetylglycosaminyl oligosaccharides which are cleaved by the enzyme at the glycosidic C—O bond between the 4th and 5th sugar residues from the non-reducing end of the chain. The mechanism and kinetics of this hydrolysis have been studied extensively [*cf* Fersht *Enzyme Structure and Mechanism, 2nd edn,* W.H. Freeman & Co, Reading *1985,* ISBN 0716716151]. Lysozyme was an extremely useful antibacterial in the pre-antibiotic era. It is a basic protein with 20-22 basic residues and only 3-4 acidic groups (see their isoelectric points); it forms soluble salts and is stable up to 55°.
It is purified from egg white by chromatography through Amberlite IRC50 at pH 7.18 in 0.2M phosphate buffer followed by recrystallisation at pH 9.5 by adding NaCl to a concentration of 5%. *Alternatively*, ~1L of homogenised egg white in the absence of air (from 3 dozen eggs) is added to a 10% suspension of Bentonite [1302-78-9] (150ml, a native hydrated aluminium silicate) in 1% aqueous KCl, and stirred vigorously enough to avoid excessive foaming for ~5 minutes to give a smooth suspension. Separate the clay by centrifugation, wash it twice with 0.5M phosphate buffer (300ml each, pH 7.5) and three times with 5% aqueous pyridine (300ml each) while decanting from the clay and discarding inactive supernatants. From the combined washed clay, lysozyme is extracted out twice with 300ml of 5% aqueous pyridine (adjusted to pH5 with H_2SO_4 using a glass electrode). The combined extracts are dialysed against running tap H_2O (at 12-15°) until free from pyridine odour and dialysed further for 24 hours. Essentially pure amorphous lysozyme is obtained by lyophilising the dialysate below 25°. *Crystalline isoelectric lysozyme* is obtained from the amorphous powder by adding 0.5g of NaCl to a 5% aqueous solution of the enzyme (10ml), adjusting the pH to 9.5-10 (glass electrode) with aqueous NaOH and storing at 4°, whereby it crystallises out. *Crystalline lysozyme carbonate* is obtained from the amorphous powder by adding 0.5g of $NaHCO_3$ to a 5% aqueous solution of the enzyme (10ml), giving a final pH of 8.0-8.5 (glass electrode) with aqueous NaOH and allowing to stand at room temperature, whereby the carbonate crystallises out. *Crystalline lysozyme chloride* is obtained from a 5% solution of amorphous powder by adjusting the pH to 4.5 with hydrochloric acid (glass electrode) followed by solid NaCl to 5%, and storing at 4°, whereby the chloride crystallises out in 4 to 5 days. [Alderton & Fevold *J Biol Chem* **164** 1 *1946*, Fevold & Alderton *Biochemical Preparations* **I** 67 *1949*.] Other salts include the L-*ascorbate* [119189-24-1], the *lactate* [72497-48-4], the *phosphate* [72497-47-3] and the *2,3-dihydroxypropyl dihydrogen phosphate* [119189-23-0].
Dialysis and recrystallisation are simple and yield enzyme of high purity. Several forms of crystals are obtained depending on the pH of the crystallising solution. The activity of lysozyme is measured by the rate of decrease of turbidity (at 570nm) as hydrolysis of acetone-dried cell walls of the Gram-positive bacterium *Micrococcus lysodeikitus* (as substrate) occurs on addition of the enzyme [Hirs *Methods Enzymol* **I** 124 *1968*].
At high concentrations or in the presence of albumin, lysozyme can be lyophilised or desalted without loss of activity. Freezing and thawing does not inactivate it, and Na^+, Mg^{2+}, Ag^+, Ca^{2+}, and Cu^{2+} exert an activating effect. It can be stored for several weeks at -20° without inactivation, and in the presence of 0.1% of bovine serum albumin it can be stored for months at -20° without inactivation. [*Springer Handbook of Enzymes* 2nd edn. Schonburg & Schonburg eds (A. Chang co-ed) Springer-Verlag Berlin, Heidelberg, **Volume 12** *2003* ISBN 3-540-00519-6.]
Agarose-bound lysozyme from hen egg (5,000-10,000 Units/g of solid), a lysozyme Biotin-caproyl solution (20,000 U/mg) and a carboxymethylated-maleylated lysozyme (Lysozyme-RCM, reduced form), and lysozyme of up to 100,000 U/mg protein are commercially available.

A *T_4 bacteriophage lysozyme* (from phage grown on *E.coli* B^1) *[12585-29-4]* was extracted and freed from

DNA, cell debris, intact cells and acidic proteins by precipitation with Rivanol (6,9-diamino-2-ethoxyacridine *dl*-lactate). The filtrate was purified by concentration through an Amberlite IRC50 column which was thoroughly washed with 0.1M phosphate buffer pH 6.5 containing 10^{-3}M $MgSO_4$ and eluted with the phosphate buffer at pH 5.8 containing a 0 to 0.5M NaCl gradient. This was repeated twice, followed by gel filtration through Sephadex G-75 in pH 5.8 phosphate buffer and eluted with 0.5M NaCl. The eluate was dialysed against H_2O and lyophilised to give a 1500-fold purification with 40% recovery. Like the hen lysozyme it is a basic protein but with 164 amino acid residues, and it is unstable >40°. [Tsugita et al. *J Biol Chem* **243** 391 *1968*, Inouye et al. *J Biol Chem* **245** 3439, 3479 *1970*, Matthews *Biochim Biophys Acta* **405** 442 *1975*.]

Metallothionein (from rabbit liver) *[9038-94-2]***.** Purify it by precipitation to give Zn- and Cd-containing protein fractions and running it on a Sephadex G-75 column, then isoelectric focusing to give two protein peaks [Nordberg et al. *Biochem J* **126** 491 *1972*, Comeau et al. *Prep Biochem* **22** 151 *1992*].

Myoglobin (from sperm whale muscle) *[9047-17-0]* **M_r ~17,000.** Myoglobin is purified by CM-cellulose chromatography and Sephadex G-50 followed by chromatography on Amberlite IRC-50 Type III or BioRex 70 (<400mesh). The crystalline product as a paste in saturated $(NH_4)_2SO_4$ at pH 6.5-7.0 may be stored at 4° for at least 4 years unchanged, but must not be kept in a freezer. [Anres & Atassi *Biochemistry* **12** 942 *1980*, Edmundson *Biochemical Preparations* **12** 41 *1968*.]

5'-Nucleotidase (from Electric ray, *Torpedo sp*) *[9027-73-0]* **[EC 3.1.3.5], amorphous.** Purify it by dissolving it in Triton X-100 and deoxycholate, and by affinity chromatography on concanavalin A-Sepharose and AMP-Sepharose [Grondal & Zimmerman *Biochem J* **245** 805 *1987*].

Orosomucoid (glycoprotein α_1 acid, from human plasma) *[66455-27-4]* **M_r 42000-44000, amorphous.** Purify the glycoprotein α_1 acid by passage through a carboxymethyl cellulose column, then through a Sephadex G-25 column. [Aronson et al. *J Biol Chem* **243** 4564 *1968*.]

Papain *[9001-73-4]* **M_r ~21,000 [EC 3.4.22.2], amorphous.** A suspension of 50g of papain (freshly ground in a mortar) in 200ml of cold water is stirred at 4° for 4 hours, then filtered through a Whatman No 1 filter paper. The clear yellow filtrate is cooled in an ice-bath while a rapid stream of H_2S is passed through it for 3 hours, and the suspension is centrifuged at 2000rpm for 20 minutes. Sufficient cold MeOH is added slowly with stirring to the supernatant to give a final MeOH concentration of 70 vol%. The precipitate, collected by centrifugation for 20 minutes at 2000rpm, is then dissolved in 200ml of cold water, the solution is saturated with H_2S, centrifuged, and the enzyme is again precipitated with MeOH. The process is repeated four times. [Bennett & Niemann *J Am Chem Soc* **72** 1798 *1950*.] Papain has also been purified by affinity chromatography on a column of GlyGlyTyrArg-agarose [Stewart et al. *J Am Chem Soc* **109** 3480 *1986*].

Pepsin *[9001-75-6]* **M_r 31,500(human), 6000(hog) [EC 3.4.23.1].** Pepsin is re-chromatographed on a column of Amberlite CG-50 using a pH gradient prior to use. Crystallise it from EtOH. [Richmond et al. *Biochim Biophys Acta* **29** 453 *1958*, Huang & Tang, *J Biol Chem* **244** 1085 *1969*, **245** 2189 *1970*.]

Pertussis toxin (from *Bordetella pertussis*) *[70323-44-3]* **M_r 117,000.** Purify the toxin by stepwise elution from 3 columns comprising Blue Sepharose, Phenyl Sepharose and hydroxylapatite, and the purity is checked by SDS-PAGE. [Svoboda et al. *Anal Biochem* **159** 402 *1986*, *Biochemistry* **21** 5516 *1982*, *Biochem J* **83** 295 *1978*.]

Phosphatase alkaline (alkaline phosphatase) *[9001-78-9]* **M_r ~40,000 (bovine liver), ~140,000 (bovine intestinal mucosa), 80,000 (*E. coli*), [EC 3.1.3.1].** The *E. coli* supernatant in sucrose (20%, 33mM) in Tris-HCl pH 8.0 is purified through a DEAE-cellulose column and recrystallised. To the column eluates in 0.125M NaCl is added $MgCl_2$ (to 0.01M) and brought to 50% saturation in $(NH_4)_2SO_4$ by adding the solid (0.20g/ml). The mixture is centrifuged to remove bubbles and is adjusted to pH 8.0 (with 2N NaOH). Saturated $(NH_4)_2SO_4$ at pH 8.0 is added dropwise until the solution becomes faintly turbid (~61% saturation). It is set aside at ~25°

for 1 hour (turbidity will increase). The mixture is placed in an ice bath for several minutes when turbidity
disappears and a clear solution is obtained. It is then placed in a large ice bath at 0° (~5L) and allowed to warm slowly to room temperature in a dark room whereby crystals are formed appearing as a silky sheen. The crystals are collected by centrifugation at 25° if necessary. The crystalline solutions are stable at ~25° for many months. They can be stored at 0°, but are unstable when frozen. Cysteine at 10^{-3}M and thioglycolic acid at 10^{-4}M are inhibitory. This is reversed on addition of Zn^{2+} ions. Many organic phosphates are good substrates for this phosphatase. [Molamy & Horecker *Methods Enzymol* **9** 639 *1966*, Torriani et al. *Methods Enzymol* **12b** 212 *1968*, Engstrom *Biochim Biophys Acta* **92** 71 *1964*.]
Alkaline phosphatase from rat osteosarcoma has been purified by Me_2CO precipitation and chromatography on DEAE-cellulose, Sephacryl S-200, and hydroxylapatite. [Nair et al. *Arch Biochem Biophys* **254** 18 *1987*.]

Phosphoproteins (various). These are purified by adsorbing onto an iminodiacetic acid substituted agarose column to which are bound ferric ions. This chelate complex acts as a selective immobilised metal affinity adsorbent for phosphoproteins. [Muszyfiska et al. *Biochemistry* **25** 6850 *1986*.]

5'-Phosphoribosyl pyrophosphate synthetase (from human erythrocytes, or pigeon or chicken liver) *[9015-83-2]* **M_r 60,000 [EC 2.7.6.1].** It is purified 5100-fold by elution from DEAE-cellulose, fractionation with $(NH_4)_2SO_4$, filtration on Sepharose 4B and ultrafiltration. [Fox & Kelley *J Biol Chem* **246** 5739 *1971*, Flaks *Methods Enzymol* **6** 158 *1963*, Kornberg et al. *J Biol Chem* **15** 389 *1955*.]

Pituitary Growth Factor (from human pituitary gland) *[336096-71-0]***.** It is purified by heparin and copper affinity chromatography, followed by chromatography on carboxymethyl cellulose (Whatman 52). [Rowe et al. *Biochemistry* **25** 6421 *1986*.]

Plasmids. These are circular lengths of *double-stranded* DNA which invade bacteria or other cells, e.g. insect cells, yeast cells, and have sequences which are necessary for their replication using enzymes and other ingredients, e.g. nucleotides, present in the cells. They contain engineered, or already have, genes which produce enzymes that provide the cells with specific antibiotic resistance and are thus useful for selecting bacteria containing specific plasmids. Plasmids have been extremely useful in molecular biology since they can be very easily identified (from their size or the sizes of the DNA fragments derived from their restriction enzyme digests) and can be readily engineered *in vitro* (outside the cells). Genes coding for specific enzymes or other functional proteins can be inserted into these plasmids which have DNA sequences that allow the expression of large quantities of bacterial or non-bacterial (e.g. human) proteins. They have also been engineered in such a way as to produce "fusion proteins" (in which the desired protein is fused with a specific "reporter, marker or carrier protein" which will facilitate the isolation of the desired protein (e.g. by binding strongly to a nickel support), and then the desired protein can be cleaved from the eluted fusion protein and obtained in very pure form. A large number of plasmids with a variety of sequences for specific purposes are commercially available in very pure form. They can be used to infect cells and can be isolated and purified from cell extracts in large amounts using a number of available procedures. These procedures generally involve lysis of the cells (e.g. with alkaline sodium dodecylsulfate, SDS), separation from nuclear DNA, precipitation of plasmid DNA from the cell debris, adsorbing it on columns which specifically bind DNA, and then eluting the DNA from the column (e.g. with specific Tris buffers as recommended by the suppliers) and precipitating it (e.g. with Tris buffer in 70% EtOH at -70°C). The purity is checked on agarose gels (containing ethidium bromide to visualise the DNA) by electrophoresis. A large number of plasmids are now commercially available (see Clontech GmbH, http://www.clontech.com, Invitrogen http://www.invitrogen.com, among other suppliers) and used as vectors for bacterial, mammalian, yeast and insect cells, and for baculovirus expression.

Protamine kinase (from rainbow trout testes) *[37278-10-7]* **[EC 2.7.1.70].** Partial purification of the kinase is achieved by chromatography through hydroxylapatite followed by biospecific chromatography on nucleotide coupled Sepharose 4B [the nucleotide is 8-(6-aminohexyl)amine coupled cyclic-AMP]. It requires Mg ions specifically but is inactivated by Ca, Mn, Cu, Zn ions and thiol compounds. [Jergil & Dixon *J Biol Chem* **245** 1425 *1970*, Jergil et al. *Biochem J* **139** 441 *1974*.]

Protamine sulfate (from herring sperm) *[9007-31-2]* **$[\alpha]_D^{22}$ -85.5° (saturated H_2O), pK^{25} 7.4-8.0.**

Protamine sulfate is a strongly basic protein (white powder, see pK) used to precipitate nucleic acids from crude protein extracts. It dissolves to the extent of 1.25% in H_2O. It is freely soluble in hot H_2O but separates as an oil on cooling. It has been purified by chromatography on an IRA-400 ion-exchange resin in the SO_4^{2-} form and is washed with dilute H_2SO_4. Eluates are freeze-dried under high vacuum below 20º. This method is used to convert proteamine and protamine hydrochloride to the sulfate. [UV: Rasmussen *Hoppe Seyler's Z Physiol Chem* **224** 97 *1934*, Ando & Sawada *J Biochem (Tokyo)* **49** 252 *1961*, Felix & Hashimoto *Hoppe Seyler's Z Physiol Chem* **330** 205 *1963*.]

Protease nexin (from cultured human fibroblasts) *[148263-58-5]***.** It is purified by affinity binding of protease nexin to dextran sulfate-Sepharose. [Farrell et al. *Biochem J* **237** 707 *1986*.]

Proteins. These are usually naturally occurring (or deliberately synthesised in microorganisms, e.g. bacteria, insect cells, or animal tissues), and are composed of a large number of α-*S* (L)amino acid residues (except for L-cysteine which has the *R* absolute configuration), selected from the 20 or so natural amino acids, in specific sequences and in which the α–amino group forms an amide (peptide) bond with the α–carboxyl group of the neighbouring amino acid. The number of residues is usually upwards of 100. Proteins with less than 100 amino acids are better referred to as **polypeptides**. Aqueous soluble proteins generally fold into ball-like structures mainly with hydrophilic residues on the outside of the "balls" and hydrophobic residues on the inside. Proteins can exist singly or can form dimers, trimers, tetramers etc., consisting of similar or different protein subunits. They are produced by cells for a large variety of functions, e.g. enzymology, reaction mediation as in regulation of DNA synthesis or chaperonins for aiding protein folding, formation of pores in membranes for transport of ions or organic molecules, or for intra or intercellular signalling etc. The purity of proteins can be checked in denaturing (SDS, sodium dodecylsulfate) or non-denaturing polyacrylamide gels using electrophoresis (PAGE), and staining appropriately (e.g. with Coommassie Blue, followed by silver staining for higher sensitivity). If the protein is partly impure, then it should be purified further according to the specific literature procedures for the individual protein (see specific proteins in the *Methods Enzymol*, Wiley series).

Proteoglycans (from cultured human muscle cells). These are separated by ion-exchange HPLC using a Bio-gel TSK-DEAE 5-PW analytical column. [Harper et al. *Anal Biochem* **159** 150 *1986*.]

Prothrombin (Factor II, from equine blood plasma) *[9001-26-7]* **M_r 72,000.** Prothrombin is purified by two absorptions on a barium citrate adsorbent, followed by decomposition of the adsorbents with a weak carboxylic cation-exchanger (Amberlite IRF-97), isoelectric precipitation (pH 4.7-4.9) and further purification by chromatography on Sephadex G-200 or IRC-50. Finally it is recrystallised from a 1% solution adjusted to pH 6.0-7.0 and partial lyophilisation to *ca* 1/5 to 1/10th volume and set aside at 2-5º to crystallise. Occasionally seeding is required. [Miller *Biochemical Preparations* **13** 49 *1971*.]

Prymnesin (toxic protein from phytoflagellate *Pyrymnesium parvum*) *[11025-94-8]***.** Prymnesin is purified by column chromatography, differential dissolution and precipitation in solvent mixtures and differential partition between diphasic mixtures. The product has at least 6 components as observed by TLC. [Ulitzur & Shilo *Biochim Biophys Acta* **301** 350 *1970*.]

Pyruvate kinase isoenzymes (from *Salmonella typhimurium*) *[9001-59-6]* **M_r 64,000 [EC 2.7.1.40], amorphous.** These are purified by $(NH_4)_2SO_4$ fractionation and gel filtration, ion-exchange and affinity chromatography. [Garcia-Olalla & Garrido-Pertierra *Biochem J* **241** 573 *1987*.]

Renal dipeptidase (from porcine kidney cortex) *[9031-96-3]* **M_r 47,000 [EC 3.4.13.11].** The dipeptidase is purified 700-fold by homogenising the tissue, extracting with Triton X-100, elimination of insoluble material, and ion-exchange, size exclusion and affinity chromatography. [Hitchcock et al. *Anal Biochem* **163** 219 *1987*.]

Restriction enzymes (endonucleases). These are enzymes which cleave double-stranded DNA (linear or circular) at specific nucleotide sequences within the DNA strands which are then used for cloning (by ligating bits of DNA sequences together) or for identifying particular DNA materials, e.g. plasmids, genes etc. A very large number of restriction enzymes are now available commercially and are extensively used in molecular biology. They are highly specific for particular nucleotide arrangements and are sensitive to the reaction conditions, e.g. composition of the medium, pH, salt concentration, temperature etc, which have to be strictly adhered to.
Endonucleases are essentially of two types. One type cleaves the DNA producing *blunt ends*, i.e. the nucleotides are paired at each end. The second type cleaves the DNA leaving *hanging ends*, i.e. the nucleotides at the ends of each strand (usually four nucleotides) of the double strands protrude ahead of the paired nucleotides. The latter enzymes particularly allow ligation of the cleaved sequence to occur in a desired direction.
The enzymes do not require further purification, and the reaction conditions are also provided by the suppliers from which the necessary reaction media can also be purchased (see commercial catalogues).

Reverse transcriptase (from avian or murine RNA tumour viruses) *[9068-38-6]* **M_r ~170,000 [EC 2.7.7.49].** This enzyme produces the complementary DNA from the RNA (as template). These are purified by solubilising the virus with non-ionic detergents. Lysed virions are adsorbed on DEAE-cellulose or DEAE-Sephadex columns, and the enzymes are eluted with a salt gradient, then chromatographed on a phosphocellulose column and fractions with enzyme activity are eluted in a salt gradient. They are also purified from other viral proteins by affinity chromatography on a pyran-Sepharose column. [Verna *Biochim Biophys Acta* **473** 1 *1977*, Smith *Methods Enzymol* **65** 560 *1980*; see commercial catalogues for other transcriptases.]

Ribonuclease (from human plasma) *[9001-99-4]* **M_r ~13,700 [EC 3.1.27.5], amorphous.** Purify it by $(NH_4)_2SO_4$ fractionation, followed by PC cellulose chromatography and affinity chromatography (using Sepharose 4B to which $(G)_n$ is covalently bonded). [Schmukler et al. *J Biol Chem* **250** 2206 *1975*.]

Ribozymes. These are ribonucleic acids which act like protein enzyme in catalysing the making and breaking of peptide bonds as well as catalysing reactions and cleavage of DNA and RNA molecules. The short RNAs are being intensively studied (see RNAi below). MicroRNAs (miRNA, see also below) are ubiquitous and are also genetically produced. They are involved in numerous reactions from splicing RNA, e.g. mRNA (messenger RNA) to controlling transcription of DNA to RNA, and translation of RNA to protein. Each miRNA is capable of being involved in a small number to hundreds of interactions with nucleic acids and with proteins.

Ricin (toxin from Castor bean *Ricinus communis*) *[A chain 96638-28-7, B chain 96638-29-8]* **M_r ~30,000, amorphous.** Crude ricin, obtained by aqueous extraction and $(NH_4)_2SO_4$ precipitation, is chromatographed on a galactosyl-Sepharose column with sequential elution of pure ricin. The second peak is due to ricin agglutinin. [Simmons & Russell *Anal Biochem* **146** 206 *1985*.] It is an inhibitor of protein synthesis. **EXTREMELY DANGEROUS, USE EXTREME CARE [instructions accompany product].**

RNA (ribonucleic acids). Ribonucleic acids are like DNA except that the 2'-deoxy-D-ribose moiety is replaced by a D-ribose moiety and the fourth nucleotide thymidylic acid (T) is replaced by uridylic acid (U). RNA does not generally form complete duplex molecules like DNA, i.e. it is generally monomeric, except in certain viruses. The two main classes of RNA are **messenger-RNA** (mRNA) and **transfer-RNA** (tRNA). Pre-mRNAs are transcribed from the DNA genes, and non-coding segments (the introns) are spliced out to give the mRNAs which code for specific proteins. There are many different tRNAs, at least one of which is linked to a specific α-amino acid that binds to the mRNA *via* the ribosome (a set of proteins) to the RNA triplets (three nucleotides) which code for the particular α-amino acids. An enzyme then joins the α-amino acids of two adjacent tRNA-α-amino acid ribosome complexes bound to the mRNA to form a peptide bond. Thus peptide bonds and consequently polypeptides and proteins coded by the DNAs, *via* the respective mRNA, are produced. Martin et al. [*Biochem J* **89** 327 *1963*] purified RNA by dissolving it (5g) in 90ml of 0.1mM EDTA, then homogenised this with 90ml of 90% (w/v) phenol in water using a Teflon pestle. The suspension was stirred vigorously for 1 hour at ~20°, then centrifuged for 1 hour at 0° at 25,000rpm. The lower (phenol) layer was extracted four times with 0.1mM EDTA, and the aqueous layers were combined, then made 2% (w/v) with respect to AcOK and 70% (v/v) with respect to EtOH. After standing overnight at -20°, the precipitate was centrifuged down, dissolved in

50ml of 0.1mM EDTA, made 0.3M in NaCl and kept for 3 days at 0º. The purified RNA was then centrifuged down at 10000x g for 30 minutes, dissolved in 100ml of 0.1mM EDTA, dialysed at 4º against water, and freeze-dried. It was stored at -20º in a desiccator. Michelson [*J Chem Soc* 1371 *1959*] dissolved 10g of RNA in water, added 2M ammonia to adjust the pH to 7, then dialysed in Visking tubing against five volumes of water for 24 hours. The process was repeated three times; then the material after dialysis was treated with 2M HCl and EtOH to precipitate the RNA which was collected, washed with EtOH, ether and dried [see commercial catalogues for further examples]. RNAs are now routinely sequenced.

RNAi (*interfering* RNA). RNAi technology has exploded during the past five years and has become invaluable for exploring gene function, interaction and control. It has considerable potential in therapeutics. This came about from the discovery that a double-stranded RNA (**dsRNA**) complementary to the coding sequence of a muscle protein "turned off" the gene instead of enhancing the effect. It seemed that the dsRNA activated the cellular machinery to degrade the target mRNA. This led to the development and the use of interfering RNA (RNAi) to "silence" specific genes. This silencing of genes comes in various different forms. It can be brought about by *short interfering* RNA (**siRNA**), *micro* RNA (**miRNA**) and *short-hairpin* RNA (**shRNA**). RNA can be notoriously unstable in biological systems, e.g. its half-life in serum is ~6 minutes, but recently methods have been devised (using nanoparticle delivery systems) where they are more stable and can be used to target specific cancer cells.
About 50% of the human genome is apparently transcribed into mRNA and translated into protein or used to produce small RNA fragments. miRNAs are small molecules of about 23 or less ribonucleotides which are cleaved from larger fragments of RNA transcripts encoded from within genes, or large tracts of DNA between the genes. miRNAs are a special group of non-coding RNAs which work by blocking (silencing) gene expression. More than 400 have been discovered in the human genome so far and some appear to regulate many genes, as in embryonic development, e.g, cell growth, apoptosis. A cancer-causing miRNA was identified and called *onco-mi*RNA. miRNA expression in particular cancers can now be quantified.
Single stranded RNAs consisting of 100s of bases fold back on themselves and undergo complementary base-paring to form double-stranded "short-hairpin" RNA (shRNA). The loop of the hair-pin is excised by endonucleases, e.g *Dicer*, to produce multiple functional miRNAs.
Many of the above RNAs for specific purposes are available commercially from several firms in high purity because they are synthetic. These firms will also synthesise particular RNAi's to suit one's requirements.

Subtilisin (from *Bacillus subtilis*) *[9014-01-1]* **M_r 27,000 (sedimentation equilibrium) [EC 3.4.21.62].** This alkaline protease is purified 211-fold by affinity chromatography using 4-(4-aminophenylazo)phenylarsonic acid complex to activated CH-Sepharose 4B. It is inhibited by 2-phenylethane boronic acid, PMSF, 3,4-dichloroisocoumarin, acetone and benzamide. [Chandraskaren & Dhar *Anal Biochem* **150** 141 *1985*, Schomburg & Schomburg *Springer Handbook of Enzymes* 2nd Edn **vol 7** p 286 *2002*.]

Synexin (from bovine liver) M 47,000 Da. This Ca binding protein is purified by $(NH_4)_2SO_4$ precipitation, then by a specific pH step elution from a chromatofocusing medium in the absence of ampholytes. The pI is 7.5. [Scott et al. *Anal Biochem* **149** 163 *1985*.]

Thrombin (from bovine blood plasma) *[9002-04-4]* **M_r 32,600 [EC 3.4.4.13].** Thrombin is purified by chromatography on a DEAE-cellulose column, while eluting with 0.1M NaCl, pH 7.0, followed by chromatography on Sephadex G-200. The final preparation is free from plasminogen and plasmin. [Yin & Wessler *J Biol Chem* **243** 112 *1968*.] Thrombin from bovine blood is also purified by chromatography using *p*-chlorobenzylamino-ε-aminocaproyl agarose, and gel filtration through Sephadex G-25. [Thompson & Davie *Biochim Biophys Acta* **250** 210 *1971*.]
Thrombin from various species was purified initially by precipitation of impurities with Rivanol (see [6402-23-9]). [Miller *Nature* **184** 450 *1959*.]

Tissue inhibitor of metalloproteins (TIMP, from human blood plasma), M_r ~30,000. These are purified by an [anti-human amniotic fluid-TIMP]-Sepharose immuno-affinity column and eluted with 50mM glycine/HCl

pH 3.0 buffer that is 0.5M in NaCl, and followed by gel filtration [Cawston et al. *Biochem J* **238** 677 *1986*].

Transferrin (from human or bovine serum) *[11096-37-0]* **M_r ~80,000.** This transferrin is purified by affinity
chromatography on phenyl-boronate agarose followed by DEAE-Sephacel chromatography. The product is free from haemopexin. [Cook et al. *Anal Biochem* **149** 349 *1985*, Aisen & Listowsky *Ann Rev Biochem* **49** 357 *1980*.]

Trehalase (from kidney cortex, α,α-trehalose glycohydrolase) *[9025-52-9]* **M_r ~80,000 [EC 3.2.1.28].** This trehalase is purified by solubilising in Triton X-100 and sodium deoxycholate, and submitting to gel filtration, ion-exchange chromatography, conA-Sepharose chromatography, phenyl-Sepharose CL-4B hydrophobic interaction chromatography, Tris-Sepharose 6B affinity and hydrolyapatite chromatography. Activity is increased 3000-fold. [Yoneyama *Arch Biochem Biophys* **255** 168 *1987*.]

T4-RNA ligase (from bacteriophage-infected *E. coli*) M_r 43,500, [EC 6.5.1.3 for RNA lyase]**.** This ligase is purified by differential centrifugation and separation on a Sephadex A-25 column, then through hydroxylapatite and DEAE-glycerol using Aff-Gel Blue to remove DNAase activity. (Greater than 90% of the protein in the enzyme preparation migrated as a single band on gradient polyacrylamide gels containing SDS during electrophoresis.) [McCoy et al. *Biochim Biophys Acta* **562** 149 *1979*.]

Ubiquinol-cytochrome c reductase (from beef heart mitochondria) *[9027-03-6]* **[EC 1.10.2.2].** This reductase is purified by solubilising the crude enzyme with Triton X-100, followed by hydroxylapatite and gel chromatography. The minimum unit contains nine polypeptide subunits of **M_r** 6000 – 49,000 kD. [Engel et al. *Biochim Biophys Acta* **592** 211 *1980*.]

Uridine 5'-diphosphoglucose pyrophosphorylase (from rabbit skeletal muscle) *[9029-22-6]* **M_r 350,000 [EC 2.7.7.9].** The pyrophosphorylase is purified by two hydrophobic chromatographic steps and gel filtration. [Bergamini et al. *Anal Biochem* **143** 35 *1984*.] It is also purified from calf liver by $(NH_4)_2SO_4$ (40-58%) precipitation, $Ca_3(PO_4)_2$ gel filtration, DEAE-cellulose chromatography and recrystallisation [by dialysis against concentrations of $(NH_4)_2SO_4$ (from 10%) in 0.02M TEA, at 2.5% increments, until 20% $(NH_4)_2SO_4$ when it crystallises out [Hansen et al. *Methods Enzymol* **8** 248 *1966*].

Urokinase (from human urine) *[9039-53-6]* **M_r 53,000 [EC 3.4.21.31].** Crystallisation of this enzyme is induced at pH 5.0 to 5.3 (4°) by careful addition of NaCl with gentle stirring until the solution becomes turbid (silky sheen). The NaCl concentration is increased gradually (over several days) until 98% of saturation is achieved whereby urokinase crystallises out as colourless thin brittle plates. It can be similarly recrystallised to maximum specific activity [104K CTA units/mg of protein (Sherry et al. *J Lab Clin Med* **64** 145 *1964*)]. [Lesuk et al. *Science* **147** 880 *1965*, NMR: Bogusky et al. *Biochemistry* **28** 6728 *1989*.] It is a plasminogen activator [Gold et al. *Biochem J* **262** *1989*, de Bock & Wang *Med Res Rev* **24**(1) 13 *2004*].

Xylanase (from *Streptomyces lividans*) *[37278-89-0]* **M_r 43,000 [EC 3.2.1.8].** This xylanase is purified by anion-exchange chromatography on an Accell QMA column and finally by HPLC using a ProteinPak DEAE 5PW anion-exchange column. Solutions are stored frozen at -70°. [Morosoli et al. *Biochem J* **239** 587 *1986*, Wong et al. *Microbiol Rev* **52** 305 *1988*.]

CARBOHYDRATES

This section includes natural and synthetic carbohydrates and glycosides.

Z-O-(2-Acetamido-2-deoxy-D-glycopyranosylideneamino)-*N*-phenyl-carbamate

(PUGNAC) *[132063-05-9]* **M 335.3, m 171-174° (dec), 174-180°(dec), $[\alpha]_D^{20}$ +67.5° (c 0.2, MeOH).** Purify PUGNAC by flash chromatography (silica gel and elute with EtOAc/hexane 3:2), evaporate, and the foam is recrystallised from EtOAc/MeOH. The purity is checked by TLC on Merck SiO_2 gel 60 F_{254} and the spots are detected by spraying with 0.025M I_2 in 10% aqueous H_2SO_4 and heating at 200°. It has R_F 0.21. The acetate is hydrolysed with NH_3/MeOH. [*Helv Chim Acta* **68** 2254 *1985*, *Helv Chim Acta* **73** 1918 *1990*.]

Acetobromo-α-D-galactose *[3068-32-4]* **M 411.2, m 87°, $[\alpha]_{546}^{20}$ +255°, $[\alpha]_D^{20}$ +210° (c 3, $CHCl_3$).** Purify acetobromo-α-D-galactose as for the glucose analogue (next entry). If the compound melts lower than 87° or is highly coloured, then dissolve it in $CHCl_3$ (*ca* 3 volumes) and extract with H_2O (2 volumes), 5% aqueous $NaHCO_3$, and again with H_2O and dry it over Na_2SO_4. Filter and evaporate it in a vacuum. The partially crystalline solid or syrup is dissolved in dry Et_2O (must be very dry) and recrystallised by adding petroleum ether (b 40-60°) to give a white product. [McKellan & Horecker *Biochemical Preparations* **11** 111 *1960*, *Beilstein* **17/6** V 369.]

Acetobromo-α-D-glucose (α-acetobromoglucose 2,3,4,6-tetraacetyl-α-D-glucopyranosyl bromide) *[572-09-8]* **M 411.2, m 87-88°, 88-89°, $[\alpha]_{546}^{20}$ +230°, $[\alpha]_D^{20}$ +195° (c 3, $CHCl_3$).** If nicely crystalline, recrystallise it from Et_2O/pentane or petroleum ether (b 40-60°). *Alternatively*, dissolve it in diisopropyl ether (dried over $CaCl_2$ for 24 hours, then over P_2O_5 for 24 hours) by shaking and warming (for as short a period as possible), and filter warm. Cool to *ca* 45°, then slowly to room temperature and finally at 5° for more than 2 hours. Collect the solid, wash it with cold dry diisopropyl ether and dry it in a vacuum over $Ca(OH)_2$ and NaOH. Store it dry in a desiccator in the dark. Solutions can be stabilised with 2% $CaCO_3$. [Redemann & Niemann *Org Synth* **65** 236 *1987*, Coll Vol **III** 11 *1955*, *Beilstein* **17/6** V 368.]

α-Acetyldigitoxin *[1111-39-3]* **M 807.0, m 153-180° (monohydrate, dec), 217-221°, 258°(dec), $[\alpha]_D^{20}$ +5.0° (c 0.7, pyridine), +24.5° (c 1, MeOH).** α-Acetyldigitoxin is obtained from the commercial mixture [α:β (2:1)] *[25395-32-8]*. The α−form is obtained from the β−form by heating in anhydrous or aqueous organic solvent (e.g. aqueous MeOH) at pH 3.5—8. It crystallises from MeOH as plates, $CHCl_3/Et_2O$ or Me_2CO/Et_2O. At 20° 1g dissolves in 16ml of MeOH, 66ml of Me_2CO and ~880ml of EtOAc. [Stoll & Kreis *Helv Chim Acta* **35** 1318, 1322 *1952, Beilstein* **18** III/IV 1479.] It is a cardenolide.

β-Acetyldigitoxin *[1264-51-3]* **M 807.0, m 225°, $[\alpha]_D^{20}$ +18.7° (c 0.7, pyridine), +24.3° (c 0.7, MeOH).** β-Acetyldigitoxin crystallises from MeOH as a methanolate which loses MeOH in a vacuum desiccator. The solubility at room temperature is: H_2O (0.0005%), EtOAc (0.4%), MeOH (0.6%), Me_2CO (1.6%) and $CHCl_3$(12%). [Stoll & Renz *Helv Chim Acta* **35** 1310 *1952*, Kreis US 2776963, 1957 to Sandoz; *Beilstein* **18** III/IV 1479]. It is a cardenolide.

***N*-Acetyl-D-lactosamine [2-acetylamino-*O*-β-D-lactopyranosyl-2-deoxy-D-glucose]** *[32181-59-2]* **M 383.4, m 169-171°, 170-171°, $[\alpha]_D^{18}$ +51.5°→ +28.8° (in 3 hours, c 1, H_2O].** Purify *N*-acetyl-D-lactosamine by recrystallisation from MeOH (with 1 mol of MeOH) or from H_2O. It is available commercially as a solution of 0.5g/ml of H_2O. [Zilliken *J Biol Chem* **271** 181 *1955*, *Beilstein* **17** IV 3452.]

1-*O*-Acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose *[6974-32-9]* **M 504.5, m 128-130°, 130-131°, 131-132°, $[\alpha]_D^{20}$ +44.2° (c 1, $CHCl_3$).** Recrystallise it from EtOH or isoPrOH. [*Helv Chim Acta* **42** 1171 *1959*, NMR: *J Org Chem* **33** 1799 *1968*, IR: *Chem Pharm Bull Jpn* **11** 188 *1963*, *Beilstein* **17/6** V 213.]

***N*-Acetyl muramic acid [NAM]** See "Miscellaneous" in this Chapter.

Alginic acid *[9005-32-7]* **M 48,000-186000.** To 5g of acid in 550ml water containing 2.8g $KHCO_3$ are added 0.3ml of acetic acid and 5g potassium acetate. EtOH is added to make the solution to 25% (v/v) in EtOH, and any insoluble material is discarded. Further addition of EtOH, to 37% (v/v), precipitated alginic acid. Collect the acid and dry it *in vacuo*. [Pal & Schubert *J Am Chem Soc* **84** 4384 *1962*.]

Aloin [10-glucopyranosyl-1,8-dihydroxy-3-(hydroxymethyl)-9(10*H*)anthracenone, Barbaloin] *[8015-61-0, 5133-19-7, 1415-73-2]* **M 418.4, m 148-148.5°, 148-150°.** Aloin forms the *monohydrate* as lemon yellow crystals on crystallisation from H_2O (450g/1.5l) which has a lower **m** ~70-80° than the anhydrous substance. [Cahn & Simonsen *J Chem Soc* 2573 *1932*, Hay & Haynes *J Chem Soc* 3141 *1956*.]

D-Altrose *[1990-29-0]* **M 180.2, m 103-105°, $[\alpha]_{546}$ +35° (c 7.6, H_2O).** Crystallise D-altrose from aqueous EtOH. If it is obtained by the hydrolysis of the acetate, then it may contain sodium and acetate ions. Ions are best removed by dissolving in H_2O, passing through suitable columns of ion-exchange resins, e.g. Amberlite IR-120 and Duolite A, and concentrating in a vacuum to a syrup. This is dissolved in MeOH, filtered and evaporated in a vacuum desiccator over granular $CaCl_2$. The thick syrup is inoculated with seed crystals, stirred, and before it sets to a magma of crystals, transfer the crystals with MeOH to a Büchner funnel. Recrystallise them in the same way. β-D-Altrofuranoside has initial $[\alpha]_D^{20}$ ~−69° (c 4, H_2O) which mutarotates to +33°. [Richtmeyer *Methods in Carbohydrate Chemistry* **I** 107 Academic Press *1962*, *Beilstein* **1** IV 4301, see Angyal *Adv Carbohydrate Chem Biochem* **42** 15 *1984* for ratio of anomers in solution.]

D-Amygdalin (D-mandelonitrile-β-gentiobioside) *[29883-15-6]* **M 457.4, m 214-216°, $[\alpha]_D^{22}$ -38° (c 1.2, H_2O).** D-Amygdalin recrystallises from water as the *trihydrate*, or from EtOH. It is present in bitter almonds. [Smith *Chem Ber* **64** 1115 *1931*, *Beilstein* **17/8** V 188.]

Amylose *[9005-82-7]* **($C_6H_{10}O_5)_n$ (*for use in iodine complex formation*).** Amylopectin is removed from impure amylose by dispersing in aqueous 15% pyridine at 80-90° (concentration 0.6-0.7%) and allowing the solution to stand at 44-45° for 7 days. The precipitate is re-dispersed and recrystallises during 5 days. After a further dispersion in 15% pyridine, it is cooled to 45°, allowed to stand at this temperature for 12 hours, then cooled to 25° and left for a further 10 hours. The combined precipitates are dispersed in warm water, precipitated with EtOH, washed with absolute EtOH, and dried *in vacuo* [Foster & Paschall *J Am Chem Soc* **75** 1181 *1953*.]

1,6-Anhydro-β-D-glucose (levoglucosan, β-glucosan, β-D-pyranose-form) *[498-07-7]* **M 162.1, m 177°, 179-180°, 182-184°, 184°, $[\alpha]_D$ −66.3° (c 2, H_2O).** Levoglucosan is readily formed by pyrolysis (dry distillation) of starch, ash-free amylose, cellulose and β-D-glucose in a vacuum. Best results are obtained when the acidity of the distillate is least. The product is dissolved in MeOH, decolourised with charcoal and cooled to give the glucosan in good yields. Other β-D-glucosides such as Arbutin, Salicin and Phloridzin also yield levoglucosan, and is evidence for the β- linkage configuration because α-glucose and α-glucosides require more drastic conditions for pyrolysis, i.e. longer heating and higher temperatures since the α-orientation at C-1 needs to be inverted to the β-orientation [Karrer *Helv Chim Acta* **3** 258 *1920*, Pictet & Cramer *Helv Chim Acta* **3 640** 1920, Ruchel & Schuerch *J Org Chem* **31** 2233 *1966*, Irvine & Oldham *J Chem Soc* 2903 *1925*, Carvalho et al. *J Am Chem Soc* **81** 4054 *1959*].
Another ready source of levoglucosan is β-phenylglucoside (2.0, see [1464-44-4]) which is dissolved 1.3N aqueous KOH (100ml), heated on boiling water bath for 9 hours, while monitoring the specific optical rotation until it is constant (−64.4°). The clear mixture in cooled, neutralised (to methyl orange, the slight colour of the cooled solution does not interfere) with 3N sulfuric acid, evaporated to dryness *in vacuo*, extracted from the K_2SO_4 residue with warm EtOH, evaporated and the residue is recrystallised from EtOH (10ml) to give *levoglucosan*, m 179-180°, $[\alpha]_D$ −66.3° (c 2, H_2O), in 88% yield. Other β-phenylglyco-*pyrano*-sides give anhydro-glycosans, but the α-linked sugars require much longer heating (~20 hours or weeks) to give the anhydro-sugars. This alkaline reaction has been studied in detail, and similarly β-phenylgalactoside provided a 91% yield of **1,6-anhydro-β-D-galactose (anhydroglactosan)** *[644-76-8]* **M 162.1,** with **m 226°** (plates from 50% aqueous EtOH) and **$[\alpha]_D$ −22.0° (c 2, H_2O)**. [Montgomery et al. *J Am Chem Soc* **65** 3 *1943*.]
Levoglucosan is one of the more important anhydro-sugars as it, and its 2-, 3- and 4-substituted derivatives, are readily hydrolysed by aqueous acid to give glucose and the respective derivatives [Peat *Adv Carbohydrate*

Chem **2** 29 *1946*]. Also at elevated temperature, in the presence of zinc dust, $ZnCl_2$, or platinum black, levoglucosan polymerises to form a variety of oligomers described as ***dextrans***, and these can be commonly 20,000 to 50,000 mers (but 300,000 mers in the extreme); and have found use in chromatographic purification of large molecules, e.g. proteins. The polymerisation process has been studied in detail [Carvalho et al. *J Am Chem Soc* **81** 4054 *1959*, Irvine & Oldham *J Chem Soc* 2903 *1925*, Ruchel & Schuerch *J Org Chem* **31** 2233 *1966*, see also Pictet & Sarasin *Helv Chim Acta* **1** 87 *1918* and later papers]. The 2-, 3- and 4- OH groups are readily derivatised in the usual way, and the *triacetyl* derivative has [13242-55-2] M 288.2, **m 109.5-110.5°**, **$[\alpha]_D^{25}$ –50.8° (CHCl$_3$)**, the *trifluoroacetyl* derivative has M 450.2, **m 63.5-65.0°**, **$[\alpha]_D^{25}$ –39.9° (c 2.1, CHCl$_3$)**, the *tribenzoyl* derivative has [13567-05-7] M 474.4, **m 202-203°**, **$[\alpha]_D^{20}$ –36.4° (CHCl$_3$)**, the *tri-O-methyl* derivative has M 204.2, **m 57.5-58.5°**, **$[\alpha]_D^{25}$ –63.7° (c 2, H$_2$O)**, and the *tri-O-ethyl* derivative has M 246.3, **b 90°/0.60mm**, **d^{28} 1.081**, **$[\alpha]_D^{25}$ –51.5° (c 2.8, CHCl$_3$)**, the *tri-O-benzyl* derivative has M 432.5, **m 89.5-90.5°**, **$[\alpha]_D^{25}$ –30.8° (c 2.7, CHCl$_3$),** and the *tri-O-methylsilyl* derivative has M 378.7, **b 87-87.5°/0.05mm**, **$[\alpha]_D^{30}$ –33.8° (c 3.6, CHCl$_3$)**; all of which have been subjected to the polymerisation process with the "*ether*" derivatives being more successful than the "*ester*" derivatives in producing high polymers. [Ruckel & Scheurch *J Org Chem* **31** 2233 *1966*]. The ^{1}H NMR of levoglucosan and its derivatives in DMSO-d_6 and D_2O have been reported in detail [Woolwage & Seib *J Chem Soc (C)* 3143 *1971*]. [*Beilstein* **19** H 894, **19** I 452, **19** III/V 1181. **19/3** V 498.]

ß-L-(+)-Arabinose (natural) *[87-72-9]* **M 150.1, m 158°**, **$[\alpha]_D$ +104° (c 4, H$_2$O after 24h), pK^{17} 12.4.** ß-L-(+)-Arabinose is recrystallised slowly, twice, from 80% aqueous EtOH, then dried under vacuum over P_2O_5. It can also be purified by heating the arabinose (200g) with glacial acetic acid (300ml) on a boiling water bath for 45 minutes, cooling, filtering, washing with 95% EtOH (500ml) in four portions and drying at 56-60° over P_2O_5. It has been recrystallised from 5 times its weight of 76% EtOH using charcoal (10g) to yield 127g, **m** 155-157°, $[\alpha]_D^{20}$ +190.6° and mutarotating to +104° (c 4, H_2O). [Anderson & Sands *Org Synth* Coll Vol **I** 67 *1941*, Wolfrom & Christian *J Am Chem Soc* **48** 3172 *1926*, *Beilstein* **1** IV 4217.]

D-(-)-Arabinose *[10323-20-3, 28697-53-2 (pyranoside)]* **M 150.1, m 164°**, **$[\alpha]_D^{20}$ -104.5° (c 1, H$_2$O), $[\alpha]_{546}$ -123° (c 10, H$_2$O after 24 hours), pK^{25} 12.54.** Crystallise D-(-)-arabinose three times from EtOH, dry it *in vacuo* at 60° for 24 hours and store it in a vacuum desiccator. It also crystallises from a mixture of H_2O/MeOH/EtOH with **m** 158-160°, or H_2O with **m** 160-161°. [Whistler & Schweiger *J Am Chem Soc* **81** 5190 *1959*, Fletcher et al. *J Am Chem Soc* **72** 4546 *1950*, *Beilstein* **1** IV 4215, see Angyal *Adv Carbohydrate Chem Biochem* **42** 15 *1984* for ratio of anomers in solution.]

D-Arabitol (D-arabinitol) *[488-82-4]* **M 152.2, m 103°**, **$[\alpha]_{546}^{20}$ +13° (c 5, 8% borax solution).** This pentol, which occurs in lichens and fungi, is purified by recrystallisation from 90% EtOH or MeOH. [Ashina & Yamagita *Chem Ber* **67** 801 *1934*, derivarives: Nakagawa et al. *Bull Chem Soc Jpn* **40** 2150 *1967*, Prince & Reichstein *Helv Chim Acta* **20** 101 *1937*, Hough & Theobald *Methods in Carbohydrate Chemistry* **I** 94 *1962*, Academic Press, *Beilstein* **1** IV *2832*.]

L-Arabitol (L-arabinitol) *[7643-75-6]* **M 152.2, m 102°**, **103°**, **$[\alpha]_{546}$ -13° (c 5, 8% borax solution).** This pentol, which occurs in the urine of pentosuric subjects, is purified by recrystallisation from 90% EtOH or MeOH. It has a higher rotation in the presence of molybdate: $[\alpha]_D^{20}$ -130° (c 0.16, acidified molybdate) [Richtmeyer & Hudson *J Am Chem Soc* **73** 2249 *1957*]. [Gätzi & Reichstein *Helv Chim Acta* **21** 197 *1938*, *Beilstein* **1** IV 2832.]

DL-Arabitol (DL-arabinitol) *[2152-56-9]* **M 152.2, m 105-106°.** This synthetic arabitol is purified by recrystallisation from 90% EtOH, MeOH or EtOH/Me_2CO. [Raphael *J Chem Soc, Supplement*, 48 *1949*, Ashina & Yamagita *Chem Ber* **67** 802 *1934*, *Beilstein* **1** IV 2832.]

p-**Arbutin (*p*-hydroquinone-*O*-β-D-glucopyranoside)** *[497-76-7]* **M 272.3, m 195-198°, 199°, 200°(sintering at 163-164°), $[\alpha]_D^{20}$ -65° (c 2, H$_2$O), pK$_{Est}$ ~10.0.** The glycoside from *Protea exima* is purified by recrystallisation from H_2O or moist EtOAc (as *monohydrate*), after chromatography through silica Gel using EtOAc/MeOH. Crystallisation from EtOH/$CHCl_3$ gives crystals **m** 199-200° with intermediate melting at 164° and resolidifying. The *pentaacetate* crystallises from EtOH in fine needles with **m** 145-146°, $[\alpha]_D^{20}$ -28.2°

(c 2, Me_2CO). [Robinson & Waters *J Chem Soc* 2729 *1930*, IR, NMR, MS: Perold et al. *J Chem Soc, Perkin Trans 1* 239 *1979*, *Beilstein* **17/7** V 110.]

L(+)-Ascorbic acid *[50-81-7]* **M 176.1, m 193°(dec), $[\alpha]_{546}$ +23° (c 10, H_2O), pK_1^{25} 4.04, pK_2^{25} 11.34.** Crystallise it from MeOH/Et_2O/petroleum ether [Herbert et al. *J Chem Soc* 1270 *1933*]. [*Beilstein* **18/5** V 26.]

6-Bromo-2-naphthyl-α-D-galactopyranoside *[25997-59-5]* **M 385.2, m 178-180°, 224-226°, 225°, $[\alpha]_D^{28}$ +60° (c 1.2, pyridine).** It is prepared from penta-*O*-acetyl-D-galactoside, 6-bromo-2-naphthol and $ZnCl_2$. The resulting tetra-acetate (2g) is hydrolysed by dissolving in 0.3N KOH (100ml) and heating until the solution is clear, then filtering and cooling to give colourless crystals of the α-isomer which are collected and recrystallised twice from hot MeOH. The high specific rotation is characteristic of the α-isomer. The *tetraacetate* has **m** 155-156°, $[\alpha]_D^{20}$ +60° (c 1, $CHCl_3$) [Dey & Pridham *Biochem J* **115** 47 *1969*] [reported **m** 75-85°, $[\alpha]_D^{24}$ +94° (c 1.3, dioxane), Monis et al. *J Histochem Cytochem* **11** 653 *1963*]. [*Beilstein* **17** IV 2972.]

λ–Carrageenan *[9064-57-7 (κ), 9000-07-1 (κ + little of λ)]*. This D-galactose-anhydro-D or L-galactoside polysaccharide is precipitated from 4g of Carrageenan in 600ml of water containing 12g of KOAc by addition of EtOH. Collect the fraction that precipitates between 30 and 45% (v/v) of EtOH and dry them *in vacuo*. [Pal & Schubert *J Am Chem Soc* **84** 4384 *1962*.]

Colchicoside [7*S*-7*N*-[*3*-(β-D-glucopyranosyloxy)-1,2,10-tetramethoxy-9-oxobenzo[*a*]-heptalen-7-yl-(7*S*)]-acetamide, 7-glucosylcolchicine] *[477-29-2]* **M 547.5, m 216-218° (block), $[\alpha]_D^{15}$ -128.5° (c 1, $CHCl_3$), $[\alpha]_D^{15}$ -231° (c 1, MeOH), $[\alpha]_D^{15}$ -355° (c 1, H_2O).** Purify colchicoside by chromatography through alumina and eluting with $CHCl_3$, then recrystallising from Me_2CO, **m** 275-280° (after releasing solvent at 180°). It also crystallises from EtOH; see colchicine [64-86-8]. The *tetraacetate* has **m** 175-177°, $[\alpha]_D^{15}$ -57° (c 1, $CHCl_3$). [Bellet et al. *Ann Pharm Fr* **10** 241 *1952*, *Chem Abstr* **47** 3323 *1953*, *Beilstein* **14** IV 946 for colchicine.]

Convallatoxin (α-cardenolide mannoside) *[508-75-8]* **M 550.6, m 238-239°, 238-241° (dec), $[\alpha]_D^{20}$ -9.4° (c 0.7, dioxane), $[\alpha]_D^{16}$ -1.0 ±3° (c 0.7, EtOH).** Crystallise convallatoxin from EtOAc, $CHCl_3$/EtOH (9:1) or MeOH/Et_2O. The *tetraacetate* has **m** 238-242° (from MeOH/Et_2O), $[\alpha]_D^{25}$ -5° ($CHCl_3$). [Reyle et al. *Helv Chim Acta* **33** 1541 *1950*, Fieser & Jacobson *J Am Chem Soc* **59** 2335 *1937 Beilstein* **18** III/IV 3142.]

α-Cyclodextrin (H_2O) *[10016-20-3]* **M 972.9, m >280°(dec), $[\alpha]_{546}$ +175° (c 10, H_2O).** Recrystallise α-cyclodextrin from 60% aqueous EtOH, then twice from water, and dry it for 12 hours in a vacuum at 80°. It is also purified by precipitation from water with 1,1,2-trichloroethylene. The precipitate is collected, washed and resuspended in water. This is boiled to steam distil the trichloroethylene. The solution is then freeze-dried to recover the cyclodextrin. [Armstrong et al. *J Am Chem Soc* **108** 1418 *1986*]. [*Beilstein* **19/12** V 789.]

ß-Cyclodextrin (H_2O) *[7585-39-9, 68168-23-0]* **M 1135.0, m >300°(dec), $[\alpha]_{546}$ +170° (c 10, H_2O).** Recrystallise ß-cyclodextrin from water and dry it for 12 hours in a vacuum at 110°, or 24 hours in a vacuum at 70°. The purity is assessed by TLC on cellulose containing a fluorescent indicator. [Taguchi, *J Am Chem Soc* **108** 2705 *1986*, Tabushi et al. *J Am Chem Soc* **108** 4514 *1986*, Orstam & Ross *J Phys Chem* **91** 2739 *1987*.] [*Beilstein* **19** IV 6287, **19/12** V 801.]

***N*-Decanoyl-*N*-methylglucamine (Mega-10, *N*-D-glucidyl-*N*-methyl deconamide)** *[85261-20-7]* **M 349.5, m 91-93°, 92°.** Possible impurities are decanoic acid and *N*-methylglycamine. The former is removed by grinding the solid with Et_2O and then with petroleum ether and drying over P_2O_5. It is twice recrystallised from MeOH/Et_2O by dissolving in the minimum volume of MeOH, adding Et_2O and drying in a vacuum. To remove the glycamine, the solid (800mg) is dissolved in hot H_2O (10ml) and set aside. Mega-10 crystallises as colourless needles. These are filtered off and dried in a vacuum to constant weight. It is a good non-ionic non-hygroscopic detergent with a critical micelle concentration (CMC) of 7.4mM (0.26%) in 0.1M Tris-HCl pH 7.4

at 25°. [Hildreth *Biochem J* **207** 363 *1982*.]

Dehydro-L(+)-ascorbic acid *[490-83-5]* **M 174.1, m 196°(dec), $[\alpha]_{546}^{20}$ +42.5° (c 1, H_2O), pK^{25} 3.90.** Crystallise dehydro-L(+)-ascorbic acid from MeOH. The *anhydrous acid* is formed by heating it in a vacuum at 100°/1 hour to give a crisp glassy product which when shaken with absolute EtOH and then kept at 0° for 2 days gives microcrystals of the anhydrous acid. This is then washed with absolute EtOH and dried in a vacuum. It has **m** 225°(dec) and is stable in acidic solution but decomposes rapidly in alkaline solution. A 1% solution of the anhydrous acid when dissolved in phthalate/HCl buffer pH 3.5 at 60° and cooled to 20° has $[\alpha]_D^{20}$ +56°(0 minutes), +53.5°(2 hours), +19°(3 days), -2°(5 days) and -6°(6 days); then it becomes orange in colour. A freshly prepared 1% solution in H_2O has $[\alpha]_D^{20}$ +50°(0 minutes), +44°(2 hours), +16°(3 days) and 0°(5 days). [Herbert et al. *J Chem Soc* 1270 *1933*, Kenyon et al. *J Chem Soc* 158 *1948*, *Beilstein* **18/5** V 411.]

2-Deoxy-D-allose (2-deoxy-D-*ribo*-hexose] *[6605-21-6]* **M 164.2, m 140-142°, $[\alpha]_D^{24}$ +57.5° (c 1.2, H_2O).** Purify 2-deoxy-D-allose by two recrystallisations from absolute EtOH. The *p-nitrophenylhydrazone* has m 61-62°, $[\alpha]_D^{16.5}$ -55° (MeOH). An equilibrium solution at 31° in D_2O contains 15% α-pyranose, 58% β-pyranose, 12% α-furanose and 15% β-furanose forms as estimated by ^{1}HNMR spectroscopy. [see Angyal *Adv Carbohydrate Chem Biochem* **42** 15 *1984* for ratio of anomers in solution, Zorbach & Ollapally *J Org Chem* **129** 1790 *1964*.] [*Beilstein* **1** IV 4283.]

2-Deoxy-β-D-galactose (2-deoxy-D-*lyxo*-hexose) *[1949-89-9]* **M 164.2, m 110°, 120-121°, (126-128°), $[\alpha]_D^{20}$ +60° (c 2, H_2O, 2 hours).** Crystallise 2-deoxy-β-D-galactose from MeOH or diethyl ether. The *aniline derivative* has **m** 142-143°, $[\alpha]_D^{16.5}$ -149° (c 0.8, pyridine). [Overend et al. *J Chem Soc* 671, 675 *1950* and 992 *1951*.] A 30% equilibrium solution at 31° in D_2O contains 40% α-pyranose, 44% β-pyranose, 8% α-furanose and 8% β-furanose forms as estimated by ^{1}HNMR spectroscopy [Angyal & Pickles *Aust J Chem* **25** 1711 *1972*]. [*Beilstein* **1** IV 4283.]

2-Deoxy-α-D-glucose (2-deoxy-D-*arabino*-hexose) *[154-17-6]* **M 164.2, m 148-151°, $[\alpha]_D^{20}$ +46° (c 0.5, H_2O after 45 hours).** Crystallise 2-deoxy-α-D-glucose from MeOH/Me_2CO, Me_2CO or butanone to give a mixture of α- and β- anomers, **m** 142-144°, $[\alpha]_D^{18}$ +38° (35 minutes) to +46° (c 0.5, H_2O). Recrystallisation from *iso*PrOH gives mainly the α-anomer **m** 134-136° , $[\alpha]_D^{25}$ +156° to +103° (c 0.9, pyridine). ^{1}H NMR studies showed that at 44° in D_2O the solution contained 36% of α-pyranose and 64% of β-pyranose sugar, but furanose structures were undetectable. [Snowden & Fischer *J Am Chem Soc* **69** 1048 *1947*, derivatives: Bollinger & Schmidt *Helv Chim Acta* **34** 989 *1951*; see Angyal & Pickles *Aust J Chem* **25** 1711 *1972* for ratio of isomers in solution, *Beilstein* **1** IV 4282.]

6-Deoxy-D-glucose (D-quinovose) *[7658-08-4]* **M 164.2, m 146°, $[\alpha]_D^{20}$ +73° (after 5 minutes) and +30° (final, after 3 hours) (c 8.3, H_2O).** 6-Deoxy-D-glucose is purified by recrystallisation from EtOAc and is soluble in H_2O, EtOH but insoluble in Et_2O and Me_2CO. [Srivastava & Lerner *Carbohydr Res* **64** 263 *1978*; NMR: Angyal & Pickles *Aust J Chem* **25** 1711 *1972*, *Beilstein* **1** IV 4260.]

2-Deoxy-β-L-ribose *[18546-37-7]* **M 134.1, m 77°, 80°, $[\alpha]_D^{25}$ +91.7° (c 7, pyridine, +40° final).** Crystallise 2-deoxy-β-L-ribose from diethyl ether. It can also be purified by dissolving the ribose (7.3g) in EtOAc (3L) by reflux, decanting from any insoluble material and evaporating at 50°/vacuum to 2.2L, setting aside for 1-2 hours, filtering, and concentrating to 840ml. The ribose separates as compact nodules during 3-5 days at 0° and has **m** 87-93°, and after repeated recrystallisations it has **m** 92-95°. Mutarotation is as follows: $[\alpha]_D^{16.5}$ +80°(0 minutes), +71°(6 minutes), +59°(21 minutes) and +59°(41 minutes) (c 1.14, H_2O); $[\alpha]_D^{20}$ +105°(0 minutes), +71°(9.5 minutes), +67°(12.5 minutes), +49°(81 minutes), +49°(136 minutes) (c 0.9, MeOH). [Deriaz et al. *J Chem Soc* 1879 *1949*, *Beilstein* **1** IV 4181.]

2-Deoxy-β-D-ribose *[533-67-5]* **M 134.1, m 86-87°, 87-90°, $[\alpha]_D^{20}$ -56° (c 1, H_2O after 24 hours).** Dissolve 2-deoxy-β-D-ribose in a little H_2O, evaporate to a syrup (in a vacuum), and seed to crystallise. Triturate the crystals with a little EtOAc containing 5% MeOH, decant and dry in vacuum over P_2O_5. It is best purified *via* the **anilide** which separates from a mixture of the ribose (100-125g) in MeOH (100ml) and redistilled aniline (40ml) in a few minutes. After standing for 20 hours at room temperature, it is cooled to 0°, filtered, washed

with 50% aqueous MeOH and Et_2O followed by recrystallisation from ethylene glycol monomethyl ether. The **anilide** has **m 172-173°, $[\alpha]_D^{25}$ +46° (equilibrium in pyridine).** The anilide (5g), benzaldehyde (5ml) and benzoic acid (0.5g) in H_2O (150ml) are shaken mechanically for 20-24 hours. The aqueous phase is extracted with Et_2O (3x), decolourised with a little charcoal and evaporated in a vacuum to a syrup. This is dried over P_2O_5 in high vacuum. The syrupy sugar weighs 3.1g and crystallises in a few days, but more rapidly on seeding. Triturate it with a little EtOAc containing 5% MeOH, decant and dry it over P_2O_5. At this stage it has **m 78-82°, $[\alpha]_D^{25}$ -57° (c 1, H_2O final).** This is a mixture of α- and β- anomers. Pure **β-anomer** is obtained by recrystallisation from EtOAc The β-anomer when recrystallised from EtOAc and isoPrOH has **m 96-98°, $[\alpha]_D^{25}$ -55° (c 0.5, H_2O final)**. [Sowden *Biochemical Preparations* **5** 75 *1957*.] The mutarotation is as follows: $[\alpha]_D^{20.5}$ +96.3°(0 minutes), -76°(33 minutes), -56° (24 hours) (c 5.8 MeOH). It is moderately hygroscopic and should be kept in a well stoppered bottle. It also crystallises from diethyl ether. [Deriaz et al. *J Chem Soc* 1879 *1949*, *Beilstein* **1** IV 4181, Hauske & Rapoport *J Org Chem* **44** 2472 *1979*.]
The ***1,3,4-tribenzoate (α- and β-mixture)***, obtained by benzoylation, has **m 127°** (after crystallisation from EtOH), **$[\alpha]_D^{23}$ -65° (c 1, $CHCl_3$).** The crude syrupy mixture in $*C_6H_6$ is applied to an acid-washed Alorco Al_2O_3 column. Elution with $*C_6H_6$/hexane (1:1) affords (after crystallisation from MeOH), ***β-1,3,4-tri-O-benzoyl-2-deoxy-D-ribose*, m 159-169°, $[\alpha]_D^{20}$ -196° (c 1, $CHCl_3$).** Further elution with $*C_6H_6$ gives, after recrystallisation from MeOH pure ***α-1,3,4-tri-O-benzoyl-2-deoxy-D-ribose*, m 151-152°, $[\alpha]_D^{20}$ +41.6° (c 083, $CHCl_3$).** [Pedersen et al. *J Am Chem Soc* **82** 3425 *1960*; see Angyal *Adv Carbohydrate Chem Biochem* **42** 15 *1984* for ratio of anomers and ring forms.]

Dextran *[9004-54-0]* **M_r 6,000-220,000.** Solutions of dextran keep indefinitely at room temperature if 0.2ml of Roccal (10% alkyldimethylbenzylammonium chloride) or 2mg phenyl mercuric acetate are added per 100ml solution. This inhibits mould growth. [Scott & Melvin *Anal Biochem* **25** 1656 *1953*.]

Diacetone-D-glucose (1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranoside) *[582-52-5]* **M 260.3, m 107-110°, 110.5°, 111-113°, 112°, $[\alpha]_D^{15}$ -18.4° (c 1, H_2O).** Diacetone-D-glucose crystallises from Et_2O, (needles), petroleum ether or $*C_6H_6$ and sublimes *in vacuo*. It is soluble in 7 volumes of H_2O and 200 volumes of petroleum ether at their boiling points. The solubility in H_2O at 17.5° is 4.3%. It precipitates from aqueous solutions on basification with NaOH. [Schmid & Karrer *Helv Chim Acta* **32** 1371 *1949*, Fischer & Rund *Chem Ber* **49** 90, 93 *1916*, IR: Kuhn *Anal Chem* **22** 276 *1950*, *Beilstein* **19/12** V 318.]

***N,N'*-Diacetylchitobiose (2-acetyl-*O*^{4}-[2-acetylamino-2-deoxy-β-D-glucopyranosyl]-2-deoxy-D-glucose)** *[35061-50-8]* **M 424.4, m 245-247°(dec), 251.5-252.5°, 260-262°, $[\alpha]_D^{25}$ +39.5° (extrapolated) → +18.5° (after 60 minutes, c 1, H_2O).** Recrystallise *N,N'*-Diacetylchitobiose from aqueous MeOH or aqueous EtOH/1,2-dimethoxyethane. [Zilliken et al. *J Chem Soc* **77** 1296 *1955*, *Beilstein* **18/11** V 147.]

1,3,4,6-Di-*O*-benzylidene-D-mannitol *[28224-73-9]* **M 358.4, m 192-195°, 193°, $[\alpha]_D^{20}$ -11.9° (c 0.7, Me_2CO).** 1,3,4,6-Di-*O*-benzylidene-D-mannitol recrystallises from Et_2O in long fine needles with λ_{max} at 256nm (ε 435) in 95% EtOH, and R_F 0.21 (1:1 CCl_4/EtOAc) on TLC Silica Gel G. [Sinclair *Carbohydr Res* **12** 150 *1970*, ORD, CD, NMR, IR, MS: Brecknell et al. *Aust J Chem* **29** 1749 *1976*, *Beilstein* **19/11** V 640.]

Digitonin *[11024-24-1]* **M 1229.3, m >270°(dec), $[\alpha]_{546}^{20}$ -63° (c 3, MeOH).** This digitoxin hexa-glycoside can be recrystallised from aqueous 85% EtOH or MeOH/diethyl ether. It is purified by preparative paper chromatography and developed with the upper phase of a mixture of nBuOH/H_2O/AcOH (4:5:1), and the spot (R_F 0.36) is eluted with 25% CCl_3CO_2H in $CHCl_3$. It has also been purified by countercurrent distribution. It forms an ethanolate, and complexes with cholesterol and other sterols. [Ruhenstroth-Bauer & Breitenfeld *Hoppe Seyler's Z Physiol Chem* **302** 111 *1955*, Grisvold *J Am Pharm Assoc* **23** 664 *1934*, *Beilstein* **19** IV 1243.]

Digitoxin *[71-63-6]* **M 764.9, m 256-257° (anhydrous), $[\alpha]_D^{20}$ +16.7° (c 1, $CHCl_3$), +4.8° (c 1, dioxane).** Digitoxin crystallises from MeOH, aqueous EtOH with 0.5 to 1 H_2O and from H_2O as the *dihydrate*. It also crystallises from $CHCl_3/Et_2O$ as *anhydrous* crystals. The hydrate dehydrates at 120°/vacuum. Its solubility is 2.5% in $CHCl_3$, 1.7% in EtOH, 0.25% in EtOAc, and 0.001% in H_2O; and has $E_{1cm}^{1\%}$ 202.5 at 219-220nm (50% EtOH). [Stoll et al. *Helv Chim Acta* **37** 1134 *1954*, Demoen & Janssen *J Am Pharm Assoc* **42** 635 *1953*, *Beilstein* **18** IV 1478.]

D(+)-Digitoxose (2,6-dideoxy-D-*ribo*-hexose) *[527-52-6]* **M 148.2, m 110°, 112°, $[\alpha]_{546}^{20}$ +57° (c 1, H_2O).** Crystallise D(+)-digitoxose from MeOH/Et_2O, Et_2O, EtOAc, EtOAc/Et_2O/petroleum ether or Me_2CO/Et_2O and dry it over P_2O_5/vacuum. It has $[\alpha]_D^{20}$ +45.2° (6 minutes) mutarotating to +50.2° (16 hours constant) (c 1.65, H_2O). [Gut & Prins *Helv Chim Acta* **20** 1229 *1947*, Bollinger & Ulrich *Helv Chim Acta* **35** 93 *1952*, NMR of derivs: Tsukamoto et al. *J Chem Soc, Perkin Trans 1* 2621 *1988*, *Beilstein* **1** IV 4191.]

Digoxin [5β,20(22)-cardenolide-3β,12β,14β-triol-3-(*O*-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-*O*-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-*O*-2,6-dideoxy-β-D-*ribo*-hexopyrano-syl)-oxy-), 12β-isomer] *[20830-75-5]* **M 781.0, m 265°(dec), $[\alpha]_{546}^{20}$ +14.0° (c 10, pyridine), $[\alpha]_{546}^{25}$ +15.6° (c 0.5, $CHCl_3$/MeOH 1:1).** Crystallise digoxin from aqueous EtOH, aqueous pyridine, EtOH/$CHCl_3$, and dry it in a vacuum at 100°. The melting point depends on heating rate, but when placed in a bath at 260° and heated slowly it decomposes at 265°. In EtOH it has λ_{max} at 220nm (ε 12,800). [Smith *J Chem Soc* 508 *1930*, X-ray: Go et al. *Cryst Struct Commun* **8** 149, 1031 *1979*, *Beilstein* **18/4** V 381.] **HIGHLY TOXIC**.

(-)-2,3:4,6-Di-*O*-isopropylidene-2-keto-L-gulonic acid monohydrate (-DAG) *[18467-77-1]* **M 292.3, m 100-101°, 103°, $[\alpha]_D^{25}$ -21.6° (c 2.3, MeOH).** Dissolve -DAG in Et_2O, filter, dry ($MgSO_4$) it, filter it again and evaporate to give a yellow oil. Addition of one drop of H_2O induces crystallisation to the *monohydrate*, which also forms rhombic crystals on recrystallisation from 95% EtOH/H_2O at room temperature. [Flatt et al. *Synthesis* 815 *1979*, Reichstein & Grussner *Helv Chim Acta* **17** 311 *1934*, Takagi & Jeffrey *Acta Crystallogr Sect B* **34** 2932 *1978*, cf *Org Synth* **55** 80 *1976*, *Beilstein* **19/12** V 520.]

1,2:5,6-Di-*O*-isopropylidene-D-mannitol *[1707-77-3]* **M 262.3, m 121-125°, 122°, $[\alpha]_D^{25}$ +1.2° (c 3, H_2O).** Although quite soluble in H_2O, it gives a purer product when crystallised from this solvent, forming needles [Baer *J Am Chem Soc* **67** 338 *1945*, NMR: Curtis et al. *J Chem Soc, Perkin Trans 1* 1756 *1977*]. [*Beilstein* **19/11** V 589.]

Dulcitol (galactitol) *[608-66-2]* **M 182.2, m 188-189°, b 276-280°/1.1mm, pK^{18} 13.5.** Crystallise dulcitol from water by addition of EtOH. It is optically inactive and is prepared by reduction of D-galactose. Its *hexaacetate* crystallises from EtOH and has **m** 168-169°. [IR: Thompson et al. *Discuss Farad Soc* **9** 222 *1950*, Wolfrom & Thompson *Methods in Carbohydrate Chemistry* **II** 67*1963*, Academic Press, *Beilstein* **1** IV 2844.]

***meso*-Erythritol** *[149-32-6]* **M 122.1, m 122°, b 329-331°, pK^{18} 13.9.** *meso*-Erythritol crystallises from distilled water or absolute EtOH and is dried at 60° in a vacuum oven. It sublimes at 110° in a high vacuum. It is optically inactive. [Jeans & Hudson *J Org Chem* **20** 1565 *1955*, IR: Kuhn *Anal Chem* **22** 276 *1950*, *Beilstein* **1** IV 2807.]

Erythrityl tetranitrate (Cordite) *[7297-25-8]* **M 302.1, m 61°.** Crystallise cordite from EtOH. It explodes on percussion at ~220-460° and is a vasodilator. [*Beilstein* **1** III 2358, **1** IV 2809.]

D(-)-Fructose *[57-48-7]* **M 180.2, m 103-106°, $[\alpha]_{546}^{20}$ -190° (after 1 hour, c 10, H_2O), pK^{25} 12.03.** Dissolve D(-)-fructose in an equal weight of water (charcoal, previously washed with water to remove any soluble material), filter and evaporate under reduced pressure at 45-50° to give a syrup containing 90% of fructose. After cooling to 40°, the syrup is seeded and kept at this temperature for 20-30 hours with occasional stirring. The crystals are removed by centrifugation, washed with a small quantity of water and dried to constant weight under a vacuum over conc H_2SO_4. For higher purity, this material is recrystallised from 50% aqueous ethanol. [Tsuzuki et al. *J Am Chem Soc* **72** 1071 *1950*]. [*Beilstein* **31** H 321, **1** IV 4401.]

D(+)-Fucose (6-deoxy-d-galactose) *[3615-37-0]* **M 164.2, m 144°, $[\alpha]_{546}^{20}$ +89° (after 24 hours, c 10 in H_2O), α-form mutarotates: $[\alpha]_D^{20}$ +124° (10 minutes) to +75.6° (24 hours) (c 9, EtOH).** Crystallise D(+)-fucose from EtOH or 95% EtOH. Its *1,2:3,4-diisopropylidene* derivative has **b** 83-84°/0.45mm and crystallises on seeding with **m** 37° and $[\alpha]_D^{19}$ -52° (melt). [Schmidt *Methods in Carbohydrate Chemistry* **I** 191 *1962*, Academic Press, Haskett et al. *J Am Chem Soc* **61** 1658 *1939*, *Beilstein* **31** H 76, **1** IV 4265.]

D-Galactal (1.5-anhydro-2-deoxy-D-*lyxo*-hex-1-enitol) *[21193-75-9]* **M 146.2, m 100°, 100-102°, 104°, 103-106°, $[\alpha]_D^{20}$ -21.3° (c 1, MeOH).** Recrystallise D-galactal from EtOAc, EtOH or EtOAc/MeOH. [Overend et al. *J Chem Soc* 675 *1950*, Wood & Fletcher *J Am Chem Soc* **79** 3234 *1957*, Distler & Jourdian *J Biol Chem* **248** 6772 *1973*, *Beilstein* **17** III/IV 2332.]

Galactaric acid (mucic acid) *[526-99-6]* **M 210.1, m 212-213°(dec) pK_1^{25} 3.09 (3.29), pK_2^{25} 3.63 (4.41).** Dissolve mucic acid (40g) in the minimum (calculated) volume of N aqueous NaOH (~335ml) without heating, decolorise this with charcoal, filter and precipitate it by adding 5N HCl (~57ml). Cool for 1 hour at 0°, filter off, wash with cold H_2O and dry it *in vacuo*. All temperatures should be kept below 25°. It is optically inactive. [Barker et al. *J Chem Soc* 4128 *1958*, Lewis et al. *Methods in Carbohydrate Chemistry* **II** 39 *1963*, Academic Press, *Beilstein* **3** IV 1292.]

D-Galactonic acid *[576-36-3]* **M 196.2, m 141° (hydrate), 148° (anhydrous) pK_{Est} ~3.5.** Crystallise D-galactonic acid from EtOH or aqueous EtOH. It cyclises to *D-galactono-1,4-lactone*, **m** 134-136°, and mutarotates in 1 hour to $[\alpha]_{546}^{30}$ -92° (c 5, H_2O). It can also be obtained from the Na salt by adding 10 times its weight of acetic acid, warming till just brown, cooling, filtering off the crystals and drying them. It has **m 145-146°, $[\alpha]_D^{25}$ –13.6° (c 1, H_2O, 2 minutes and mutarotates to –57.6°)**. [Blackburn & Upson *J Am Chem Soc* **55** 2514 *1933*, *Beilstein* **3** IV 1257, and for the γ-lactone see below.]

D(-)-Galactono-1,4-lactone *[2782-07-2]* **M 178.1, m 134-135°, 134-137°, $[\alpha]_D^{20}$ -78° (c 5, H_2O, 1 hour).** Crystallise the lactone from EtOH, aqueous EtOH, MeOH or EtOAc. It is also purified by passage through a column of Amberlite IR-120 (H^+ form), and the effluent and washings are then freeze-dried [Wolfrom & Thompson *Methods in Carbohydrate Chemistry* **I** 67 *1963*, Academic Press]. The *5,6-O-isopropylidene-D-galactono-1,4-lactone* is purified by chromatography (EtOAc) and has **m** 165-167° (from EtOH/hexane), and 167.5-168.5° (from Me_2CO/*C_6H_6) [NMR: Copel & Stick *Aust J Chem* **31** 1371 *1978*.] [*Beilstein* **18** III/IV 3026, **18/5** V 18.]

D(+)-Galactosamine hydrochloride *[1772-03-8]* **M 215.6, m 181-185°, $[\alpha]_D^{25}$ +96.4° (after 24 hours, c 3.2 in H_2O), pK_{Est} ~7.7 (free base).** Dissolve the hydrochloride in a small volume of H_2O. Then add three volumes of EtOH, followed by acetone until faintly turbid and keep overnight in a refrigerator. [Roseman & Ludoweig *J Am Chem Soc* **76** 301 *1954*, *Beilstein* **4** IV 2024.]

α-D-Galactose *[59-23-4, 3646-73-9 pyranose]* **M 180.2, m 167-168°, $[\alpha]_D^{20}$ +80.4° (after 24 hours, c 4 in H_2O), pK^{25} 12.48.** α-D-Galactose is crystallised twice from aqueous 80% EtOH at -10°, then dried in a vacuum oven at 90° over P_2O_5 for 10 hours. [Link *Biochemical Preparations* **3** 75 *1953*, Hansen et al. *Biochemical Preparations* **4** 2 *1955*.] Also purify it by recrystallising the dried solid (150g) in hot H_2O (150ml), then adding hot MeOH (250ml) and hot EtOH (500ml), stirring to mix, filtering through a bed of charcoal, and the clear filtrate is stirred to initiate crystallisation. After standing overnight at 10°, the crystals of the α-anomer are filtered off by suction, washed with MeOH, then EtOH, and dried (yield 130g), and more can be obtained by evaporation of the filtrate and washing as before. [Wolfrom & Thompson *Methods in Carbohydrate Chemistry* **I** 120 *1962*, Academic Press, *Beilstein* **1** IV 4336.]

β-D-Galactose *[7296-64-2 (pyranose)]* **M 180.2, m 167°, $[\alpha]_D^{20}$ +52° (initial, c 4 in H_2O).** α-D-Galactose (40g) is dissolved in hot H_2O to establish the equilibrium of α- and β- anomers; then the solution is cooled to 0° and poured into absolute EtOH (500ml). Stir vigorously and crystallisation occurs within a few minutes, and more rapidly if seeded, filter the crystals immediately (7g, $[\alpha]_D^{20}$ +65° initial, c 4 in H_2O). This mixture of α- and β- anomers is further separated by dissolving in an equal weight of cold H_2O, filtering and adding to ice cold absolute EtOH (250ml) and stirring for 1 minute when crystals separate, then filter them off. After two such crystallisations, the initial $[\alpha]_D^{20}$ is +53°. This can be further purified by shaking with 80% EtOH for 2 minutes, filtering, washing with EtOH and Et_2O, and drying in a vacuum desiccator to give β-D-galactose (15g) with **m** 167°, $[\alpha]_D^{20}$ +52° (initial, c 4 in H_2O) mutarotating to +80.4°. Acetylation of D-galactose with hot NaOAc/Ac_2O gives ***β-D-galactopyranoside pentaacetate*** **m 142°, $[\alpha]_D^{25}$ +25 (c 4 in $CHCl_3$)**. [Wolfrom & Thompson *Methods in Carbohydrate Chemistry* **I** 120 *1962*, Academic Press, *Beilstein* **1** IV 4336.]

D(+)-Galacturonic acid *[685-73-4, 91510-62-2 (H_2O)]* **M 194.1, m 159-161°, $[\alpha]_D^{20}$ +36° (c 6, H_2O, 2h), pK_{Est} ~4.8.** Crystallisation of the acid from 95% EtOH and drying it in a vacuum desiccator (12mm) over P_2O_5 gives the *monohydrate* mixture of α- and β- anomers **(mostly α-)** as white micro needles, which sinter at ~100-111° and melt at 159-160°, $[\alpha]_D^{20}$ +107° (initial, c 4 in H_2O mutarotating to +51°). [Link & Sell *Biochemical Preparations* **3** 74, 78 *1953*, *Beilstein* **3** IV 2000.] The **β-anomer** is obtained by warming the α-anomer in EtOH, AcOH or EtOAc and has **m 160° (165°, sinters at 140°),** $[\alpha]_D^{20}$ +27° (initial, c 2 in H_2O mutarotating to +55.3° in 24 hours). The *sodium salt* [14984-39-5] **M** 216.1 has $[\alpha]_D^{20}$ +27° (c 10 in H_2O after 5 hours). The *phenylhydrazone* has **m 141°** (from MeOH). [Ehrlich & Schubert *Chem Ber* ***62*** *1974, 2014* 1929, Anderson & King *J Chem Soc* 5333 *1961*, *Beilstein* **3** IV 2001.]

Genistin (4',5,7-trihydroxyisoflavone-7-D-glucoside) *[529-59-9]* **M 432.4, m 256°, $[\alpha]_D^{22}$ -28° (c 0.6, 0.02N NaOH).** Genistin is repeatedly crystallised from hot 80% EtOH/water and treated with charcoal (Nuchar) until free from saponin. The presence of saponin is detected by adding crystals to conc H_2SO_4 when the citron yellow colour changes to red, then purple. Pure genistin does not change colour. Its UV in 85% EtOH has λ_{max} at 262.5nm. [Walter *J Am Chem Soc* **63** 3273 *1941*, *Beilstein* **18** III/IV 2732.]

α-Gentiobiose (amygdalose, 6-*O*-α-D-glucopyranosyl-D-glucopyranose) *[5995-99-5 (bi-pyranose)]* **M 342.3, m 86° (2MeOH), 189-195°, 195-197° (anhydrous), $[\alpha]_{546}^{20}$ +11° (after 24 hours, c 4, H_2O).** Crystallise α-gentiobiose from MeOH (retains solvent of crystallisation). It is best purified by conversion to the α-*octaacetate*, **m** 191-192° (recrystallise from absolute EtOH or $CHCl_3$ and excess absolute EtOH), $[\alpha]_D^{20}$ +51.6° (c 4.3, $CHCl_3$) [Goldstein & Whelan *Methods in Carbohydrate Chemistry* **I** 313*1962*, Academic Press, Hudson & Johnson *J Am Chem Soc* **39** 1271 *1917*] directly or from the β-*octaacetate* (see below) obtained by acetylation with Ac_2O and $ZnCl_2$, and hydrolysed (see below). It mutarotates from $[\alpha]_D^{22}$ +16° (3 minutes) to +9.5° (c 2, H_2O). [Reynolds & Evans *J Am Chem Soc* **60** 2559 *1938*, NMR of anomers: Bradbury et al. *Carbohydrate Research* **53** 1970 *1957*, *Beilstein* **17/7** V 203.]

β-Gentiobiose (6-*O*-β-D-glucopyranosyl-D-glucopyranose) *[5996-00-9 (bi-pyranose)*, *554-91-6 (one open ring)]* **M 342.3, m 190-195°, $[\alpha]_{546}^{20}$ +8° (after 6 hours, c 3, H_2O).** β-Gentiobiose is best purified *via* the *octaacetate* which is recrystallised from MeOH, EtOH or better from methyl cellosolve by heating at 80°. The octaacetate (15g) is hydrolysed by suspending it in dry 0.05N NaOMe in MeOH (180ml) for 1 hour with occasional shaking at room temperature. Dilute this with H_2O to dissolve suspended matter, pass through Amberlite IR-120 and Duolite A-4 columns and the eluate is evaporated under reduced pressure to a syrup. Residual H_2O is removed by repeated distillation with absolute EtOH under reduced pressure. The syrup is dissolved in methyl cellosolve (~40ml), filtered, nucleated and placed in an oven at 80°. The crystals are filtered off, washed with absolute EtOH (yield 6.7g, 89%), dried and have **m** 187-189°. Further recrystallisation from methyl cellosolve gives **m** 190°, and mutarotates from $[\alpha]_D^{28}$ -1.5° (initial) to +10.6° (final, c 4, H_2O). The β-*octaacetate* has **m** 193° (crystallised from 95% EtOH) and has $[\alpha]_D^{20}$ -5° (c 1.8, $CHCl_3$). [Goldstein & Whelan *Methods in Carbohydrate Chemistry* **I** 313 *1962*, Academic Press, *Beilstein* **17/7** V 203.]

Glucamine (**glycamine, 1-amino-1-deoxy-D-glucitol)** *[488-43-7]* **M 181.2, m 127°, $[\alpha]_D^{20}$ -8° (c 10, H_2O), pK_{Est} ~9.0.** Crystallise glucamine from MeOH or aqueous MeOH and store it in a CO_2-free atmosphere. For the *N-methylglucamine* derivative see below. [Holly et al. *J Am Chem Soc* **72** 5461 *1950*, Karrer et al. *Helv Chim Acta* **20** 83 *1937*.]

D-Gluconamide *[3118-85-2]* **M 197.2, m 142-143°, 144°, $[\alpha]_D^{23}$ +31° (c 2, H_2O).** Crystallise D-gluconamide from EtOH or 1,2-dimethoxyethane. It mutarotates slowly and hydrolytically in aqueous solution from +30.7° to +13.8° in 80 hours to give *ammonium D-gluconate* which recrystallises from 95% EtOH with **m 153-154°** and **$[\alpha]_D^{25}$ +11.8° (c 3, H_2O).** [Wolfrom et al. *J Am Chem Soc* **80** 944 *1958*, *Beilstein* **3** VI 1259.]

D-Glucono-δ-lactone *[90-80-2]* **M 178.1, m 152-153°, $[\alpha]_{546}^{20}$ +76° (c 4, H_2O).** Crystallise D-glucono-δ-lactone from ethylene glycol monomethyl ether and dry for 1 hour at 110°. It can be freed from other sugars *via*

a column of Celite and charcoal (750g of each, 90 x 7.5cm) which is washed with 0.01N formic acid until the pH of the wash is equal to that of the entering acid. The lactone is applied in H_2O and eluted with 0.01N formic acid (7L), then eluted with 7.5% EtOH/0.01N formic acid (8L), then 15% EtOH/0.01N formic acid (8L) which removes pentose and isomaltose (the optical rotation of the eluates are used for sugar detection) and finally elution with aqueous formic acid provides glucolactone which is obtained by evaporating or freeze drying. Its solubility in H_2O is 60% and 1% in EtOH. A solution in H_2O is slightly acidic, and the lactone dissolves in an equivalent of aqueous NaOH to form **sodium D-gluconate** *[527-07-1]* **M 218.1,** has **m 200-206°(dec), $[\alpha]_D^{25}$ +12° (c 10, H_2O), pK^{25} 3.6.** [cf p 553, Smith & Whelan *Biochemical Preparations* **10** 127 *1963*, *Beilstein* **3** IV 1255.]

α- and β- Glucosamine (2-amino-2-deoxy-D-glucose) *[3416-24-8]* **M 179.2, m 110°(dec), $[\alpha]_D^{20}$ +28° to +48° (c 5, H_2O), pK^{24} 7.71.** Crystallise the amines from MeOH. The free base has been obtained from the hydrochloride (21.5g, see below) in a mixture of Et_3N (15ml) and EtOH (125ml) by shaking for 2 days at room temperature, and the solid $Et_3N.HCl$ is filtered off and the process repeated with more Et_3N (3-4 times) until the **α–D-glucosamine** (15g) is free from Cl ions. It has **m 88°**, **$[\alpha]_D^{20}$ +100° mutarotating to +47.5° (c 1, H_2O).** When Et_2NH is used as base, the α- to β- conversion is complete giving **β-D-glucosamine**. The *pentaacetate* is purified by dissolving in $CHCl_3$, treating with charcoal, drying ($MgSO_4$), evaporating the solvent, and adding a little dry Et_2O to induce crystallisation. It has **m** 124-126°, $[\alpha]_D^{20}$ +113° (c 1, $CHCl_3$) after 16 hours in a desiccator. [Leaback *Biochemical Preparations* **10** 118 *1963*.] The *N-acetyl* derivative, **m** 203-205° from MeOH/Et_2O (dry in vacuum P_2O_5) has $[\alpha]_D^{20}$ +75° to +41° (c 2, H_2O); this derivative can also be purified by dissolving in the minimum volume of H_2O to which is added 7-8 volumes of EtOH followed by Et_2O until turbid and keeping at ~20° to crystallise. Wash the crystals with MeOH then Et_2O and dry *in vacuo* over P_2O_5. [Horton *Biochemical Preparations* **11** 1 *1966*.]

D-Glucosamine hydrochloride *[66-84-2]* **M 215.6, m >300°, $[\alpha]_D^{25}$ +71.8° (after 20 hours, c 4, H_2O), pK^{24} 7.71.** Crystallise the hydrochloride from 3M HCl, water, and finally water/EtOH/acetone as for galactosamine hydrochloride. [Purchase & Braun *Org Synth* **26** 36 *1946*, Stacey & Webber *Methods in Carbohydrate Chemistry* **I** 228 *1962*, Academic Press.] The salt has also been purified by dissolving in the minimum volume of boiling H_2O (charcoal), filtering and adding a large excess of 95% EtOH (~4 volumes) and stirring vigorously for several hours. Collect the crystals after 4-6 hours to give **α- anomer** which mutarotates from **$[\alpha]_D^{25}$ +100° to +72° (equilibrium, c 1, H_2O).** A large amount of the **β-anomer** stays in solution. This can be precipitated from the filtrate by adding excess Et_2O. The mixture of α- plus β-anomers has $[\alpha]_D^{25.5}$ +68.8° (c 4.75, H_2O, mutarotating to +70.1°) [Leaback *Biochemical Preparations* **10** 118 *1963*]. *Note that* ***if Et_2NH is used instead of Et_3N, conversion to the* β-anomer** *can be complete* (see above). [Stacey et al. *Methods in Carbohydrate Chemistry* **I** 306*1962*, Academic Press, *Beilstein* **4** IV 2018.]

α-D-Glucose *[492-62-6]* **M 180.2, m 83° (monohydrate), 146° (anhydrous), mutarotates from $[\alpha]_D^{20}$ +112° to +52.5° (after 24 hours, c 4, H_2O), pK^{25} 12.46.** Recrystallise α-D-glucose slowly from aqueous 80% EtOH, then dry it over P_2O_5 *in vacuo*. *Alternatively*, crystallise it from water at 55°, then dry it for 6 hours in a vacuum oven between 60-70°/2mm. Its solubilities are: H_2O (~50%), EtOH (1.7%). [Hendricks et al. *J Am Chem Soc* **56** 99 *1934*, *Beilstein* **1** IV 4302.] [For equilibrium forms see Angyal *Adv Carbohydr Chem* **42** 15 *1984*, Angyal & Pickles *Aust J Chem* **25** 1711 *1972*.]

β-D-Glucose *[50-99-7]* **M 180.2, m 148-150°, mutarotates from $[\alpha]_D^{20}$ +18.7° to +52.5° (after 24 hours, c 4, H_2O).** Crystallise β-D-glucose from hot glacial acetic acid or pyridine. Traces of solvent are removed by drying in a vacuum oven at 75° for >3 hours. [Gottfried *Adv Carbohydr Chem* **5** 127 *1950*, Kjaer & Lindberg *Acta Chem Scand* **13** 1713 *1959,* Whistler & Miller *Methods in Carbohydrate Chemistry* **I** 130*1962*, Academic Press, *Beilstein* **1** IV 4306.] [For equilibrium forms see Angyal *Adv Carbohydr Chem* **42** 15 *1984*, Angyal & Pickles *Aust J Chem* **25** 1711 *1972*.]

α-D-Glucose pentaacetate *[604-68-2]* **M 390.4, m 110-111°, 112-113°, $[\alpha]_{546}^{20}$+119°, $[\alpha]_D^{20}$ +102° (c 5, $CHCl_3$).** Crystallise it from MeOH, EtOH or three recrystallisations from 95% EtOH. [Wolfrom & Thompson *Methods in Carbohydrate Chemistry* **II** 212 *1963*, Academic Press, *Beilstein* **17/7** V 318.]

β-D-Glucose pentaacetate *[604-69-3]* **M 390.4, m 131-132°, $[\alpha]_{546}^{20}$ +5° (c 5, $CHCl_3$).** Crystallise the pentaacetate from MeOH or EtOH. It is best purified by recrystallising 160g from 1L of hot 95% EtOH (charcoal) and filtering hot. It is important that as soon as the temperature of the filtrate cools to ~20° it is filtered off. Note that some α-D-isomer will crystallise out if a prolonged crystallisation period is allowed. Further crystallisation in this manner and drying in a vacuum over $CaCl_2$ will give pure β-D-anomer which has **m** 132°, $[\alpha]_D^{20}$ +4° (c 5, $CHCl_3$). [Wolfrom & Thompson *Methods in Carbohydrate Chemistry* **II** 212 *1963*, Academic Press, Krahl & Cori *Biochemical Preparations* **1** 33 *1955*, *Beilstein* **17/7** V 319.]

D-Glucose phenylhydrazone *[3713-25-5]* **M 358.4, m three forms.** Crystallise the hydrazone from 70% aqueous EtOH or EtOH/Et_2O. Three forms have been described: "α" form **m** 159°, 160° which mutarotates from $[\alpha]_D^{20}$ -87° to -50° (H_2O) [Fischer *Ber* **20** 821 *1887*, Behrends *Justus Liebigs Ann Chem* **353** 106 *1907*], "β" form **m** 140-141°, 142° which mutarotates from $[\alpha]_D^{20}$ -2° to -50° (H_2O) [Behrends & Lohr *Justus Liebigs Ann Chem* **362** 78 *1908*], and Skraup's form **m** 115-116° which mutarotates from $[\alpha]_D^{20}$ -70° to -47° (H_2O) [Skraup *Monatsh Chem* **10** 406 *1889*, Butler & Crechter *J Am Chem Soc* **51** 3161 *1921*]. These mutarotate to the **formazan**. [*Beilstein* **1** IV 4322, Mester & Major *J Am Chem Soc* **77** 4297 *1955*, Stanek et al. The Monosaccharides, Academic Press *1963*, pp 539-541, 543.]

D-Glucuronic acid *[6556-12-3]* **M 194.1, m 159-161°, 165°, $[\alpha]_D^{20}$ +36° (c 6, H_2O, 2 hours, mutarotating from +11.5°), pK_2^{20} 3.18.** Crystallise the acid from EtOH or EtOAc, wash it with MeOH and dry it *in vacuo* to give the "β" form. Heating converts it to the lactone (see below). The *sodium salt monohydrate* [207300-70-7] **M** 234.1 has **m** ~136-138°(dec) $[\alpha]_D^{20}$ +21° (c 2, H_2O after 2hours). [Sutter & Reichstein *Helv Chim Acta* **21** 1210 *1938*, *Beilstein* **3** H 886, **3** IV 1997.]

D-Glucurono-6,3-(δ)-lactone *[32449-92-6]* **M 176.1, m 175-177°, $[\alpha]_{546}^{20}$ +22° (after 24 hours, c 10, H_2O).** Dissolve the lactone or mixture of lactone and acid in H_2O and concentrate on a steam bath until crystallisation begins. Cool rapidly to room temperature wih stirring. After 2 hours the product is filtered off, washed with cold EtOH and dried to **m** 174-175° and $[\alpha]_D^{25}$ +19.8° (c 5.2, H_2O). The amount of free acid can be obtained by titration of an ice-cold aqueous solution with standard alkali. It can be recrystallised from EtOH, EtOH/H_2O or MeOH, and the highest recorded **m** is 180°. [Stacey *J Chem Soc* 1529 *1939*, Mehltretter et al. *J Am Chem Soc* **73** 2424 *1951*, *Beilstein* **18** III/IV 3055, **18/5** V 33.]

D(+)-Glycogen *[9005-79-2]* **M 25,000-100,000, m 270-280°(dec), $[\alpha]_{546}^{20}$ +216° (c 5, H_2O).** A 5% aqueous solution (charcoal) of D(+)-glycogen is filtered, and an equal volume of EtOH is added. After standing overnight at 3° the precipitate is collected by centrifugation, washed with absolute EtOH, then EtOH/diethyl ether (1:1) and diethyl ether, and dried. [Sutherland & Wosilait *J Biol Chem* **218** 459 *1956*.]

Glycyrrhizic acid ammonium salt ($3H_2O$) *[53956-04-0]* **M 823.0, m 210°(dec), 220°(dec, sintering at 170°), $[\alpha]_{546}^{20}$ +60° (c 1, 50% aqueous EtOH), pK_{Est} ~4.0.** Crystallise the ammonium salt from glacial acetic acid, then dissolve it in ethanolic ammonia and evaporate. The *pentahydrate* forms needles from 75% aqueous EtOH, **m** 212-217°. The free acid crystallises from glacial acetic acid. [Karrer et al. *Helv Chim Acta* **4** 100 *1921*, Lithgoe & Tripett *J Chem Soc* 1983, 1987 *1950*, *Beilstein* **18** IV 5156.]

Heparin (from pig intestinal mucosa) *[9005-49-6]* **M_r ~3,000, amorphous, $[\alpha]_D^{20}$ ~+55° (H_2O).** Most likely contaminants are mucopolysaccharides including heparin sulfate and dermatan sulfate. Purify heparin by precipitation with cetylpyridinium chloride from saturated solutions of high ionic strength. [Cifonelli & Roden *Biochemical Preparations* **12** 12 *1968*, Wolfrom et al. *J Org Chem* **29** 540 *1946*, Huggard *Adv Carbohydr Chem* **10** 336-368 *1955*.]

Heparin (sodium salt) *[9041-08-1]* **M_r ~3000 (low Mol Wt, Bovine), amorphous, $[\alpha]_D^{20}$ +47° (c 1.5, H_2O).** Dissolve the salt in 0.1M NaCl (1g/100ml) and precipitate it by additing EtOH (150ml). [Wolfrom et al. *J Org Chem* **29** 540 *1946*, Huggard *Adv Carbohydr Chem* **10** 336-368 *1955*.]

Heptyl-β-D-glucopyranoside *[78617-12-6]* **M 278.4, m 74-77°, 76-77°, $[\alpha]_D^{20}$ -34.2° (c 5, H_2O).** Purify the glucoside by repeated crystallisation from Me_2CO which is a better solvent than EtOAc. The *acetate* has **m** 66-68.5° and $[\alpha]_D^{20}$ -20.5° (c 4, $CHCl_3$) [Pigman & Richtmyer *J Am Chem Soc* **64** 369 *1942*]. [*Beilstein* **17** IV 2936.]

Heptyl-β-D-1-thioglucopyranoside *[85618-20-8]* **M 294.4, m 98-99°.** The *tetraacetyl* derivative is purified by silica gel column chromatography and eluted with a $*C_6H_6/Me_2CO$ gradient (up to 5% of Me_2CO) and recrystallises from *n*-hexane as colourless needles **m** 72-74° (Erbing & Lindberg *Acta Chem Scand* **B30** 611 *1976* gave **m** 69-70°). Hydrolysis with an equivalent of base in methanol gives the desired glucoside. This is a non-ionic detergent for reconstituting membrane proteins and has a critical micelle concentration of 30 mM. [Shimamoto et al. *J Biochem (Tokyo)* ***97*** 1807 *1985*; Saito & Tsuchiya *Chem Pharm Bull Jpn* **33** 503 *1985.*]

D(-)-Isoascorbic acid (araboascorbic acid, 5*R*-[*R*-1,2-dihydroxyethyl-3,4-dihydroxy-5*H*-furan-2-one]) *[89-65-6]* **M 176.1, m 169°, 174°(0.5 H_2O, dec), $[\alpha]_D^{25}$ -16.8° (c 2, H_2O), $[\alpha]_D^{20}$ +77° (c 2, Me_2CO, acetonylidene derivative), pK^{18} 3.99 (4.23).** Crystallise D(-)-isoascorbic acid from H_2O, EtOH or dioxane. λ_{max} is at 245nm with ε 7500 (EtOH). [Reichstein et al. *Helv Chim Acta* **17** 510, 516 *1934*, Heslop et al. *J Chem Soc* 225 *1944*, *Beilstein* **18** III/IV 3037, **18/5** V 26.]

2-Keto-L-gulonic acid (xylo-2-hexulonic acid) *[526-98-7]* **M 194.1, m 159-162°, 171°, $[\alpha]_D^{20}$ -34.8° (c 2, MeOH), $[\alpha]_D^{18}$ -48° (c 1, H_2O), pK_{Est} ~2.2.** Crystallise 2-keto-L-gulonic acid from half its weight of water, wash it with Me_2CO and dry it *in vacuo*. [Reichstein et al. *Helv Chim Acta* **17** 311 *1934,* NMR: Crawford et al. *J Am Chem Soc* **102** 2220 *1980*. *Beilstein* **3** IV 1985.]

Lactobionic acid (4-*O*-β-D-galactopyranosyl-D-gulonic acid) *[96-82-2]* **M 358.3, m 128-130°, mutarotates from $[\alpha]_D^{20}$ +53° to +22.6° (c 3, after 4 hours in H_2O), pK^{25} 3.6.** Crystallise lactobionic acid from water by addition of EtOH. [NMR: Taga et al. *Bull Chem Soc Jpn* **51** 2278 *1978*, *Beilstein* **17** III/IV 3392, **17/7** V 436.]

α-Lactose (H_2O) *[63-42-3]* **M 360.3, m 220°(dec), 253-255° (252.4°), $[\alpha]_D^{20}$ +52.3° (c 4.2, H_2O), pK^{25} 12.2 (OH).** α-Lactose crystallises from water below 93.5° as the *hydrate* which can be dried at 80°/14mm. [Horst *Rec Trav Chim, Bas* **72** 878 *1953*, *Beilstein* **17** III/IV 3066.]

Lactulose (4-*O*-β-D-galactopyranosyl-D-fructose) *[4618-18-2]* **M 342.2, m 168.5-169°(dec), $[\alpha]_{546}^{20}$ -57° (c 1, H_2O).** Crystallise lactulose from MeOH or 50% MeOH. It mutarotates from $[\alpha]_D^{20}$ -11.9° to –50.7° (c 1, H_2O). [Montgomery & Hudson *J Am Chem Soc* **32** 2101, 2104 *1930*, *Beilstein* **17** III/IV 3094, **17/7** V 214.] NMR in Me_2SO at 24° shows 0% α-pyranose, 27% β-pyranose, 20% α-furanose and 52% β-furanose forms [Angyal *Adv Carbohydr Chem* **42** 15 *1984*].

Lanatoside A (digitoxigenin nonoacetyl-tetraglycoside) *[17575-20-1]* **M 969.1, m 245-248°, $[\alpha]_D^{20}$ +32° (EtOH).** Crystallise lanatoside A from MeOH or 95% aqueous EtOH. Its solubility is 1/16000 (H_2O), 1/20 (MeOH), 1/40 (EtOH) and 1/225 ($CHCl_3$). [Stoll et al. *Helv Chim Acta* **16** 1049 *1933*, Kuhn et al. *Helv Chim Acta* **45** 881 *1962*, *Beilstein* **18** III/IV 1480.] It is **cardiotonic**.

Lanatoside B (gitoxigenin nonoacetyl-tetraglycoside) *[17575-21-2]* **M 985.1, m 233°(dec), 245-248°(dec), $[\alpha]_D^{20}$ +35° (MeOH).** Crystallise lanatoside B from MeOH. Its solubility is: 1/20 (MeOH), 1/40 (EtOH), 1/5600 ($CHCl_3$), and is insoluble in H_2O. [Stoll et al. *Helv Chim Acta* **16** 1049 *1933*, Miyatake et al. *Chem Pharm Bull Jpn* **5** 171 *1957*, *Beilstein* **18** III/IV 2465.] It is **cardiotonic**.

Lanatoside C (digoxigenin nonoacetyl-tetraglycoside) *[17575-22-3]* **M 297.1, m 246-248°, $[\alpha]_D^{20}$ +33.5° (c**

1.85, 95% EtOH). Crystallise lanatoside C from MeOH. Its solubility is : 1/17000 (H_2O), 1/45 (EtOH) and 1/1500-2000 ($CHCl_3$). [Stoll et al. *Helv Chim Acta* **16** 1049 *1933,* Stoll & Kreis *Helv Chim Acta* **35** 1318 *1952*, Okada et al. *Chem Pharm Bull Jpn* **23** 2039 *1975*, *Beilstein* **18** III/IV 2455.] It is **cardiotonic**.

α–L(+)-Lyxose *[1949-78-6]* **M 150.1, m 106-108°, $[\alpha]_D^{20}$ +14° after 1 hour (c 6, H_2O).** The α–anomer crystallises from propan-1-ol or EtOH, and the β–anomer crystallises from propan-2-ol. The *2,4-dinitrophenylhydrazone* has **m** 171-172° and $[\alpha]_D^{20}$ -31° (pyridine). In D_2O it has 21% of the α–pyranose form. The *2-methyl ether* has **m** 120-121° and $[\alpha]_D^{20}$ +6° (c 1, H_2O). [Angyal *Adv Carbohydr Chem* **42** 15 *1984*, Bently *J Am Chem Soc* **79** 1720 *1959*, *Beilstein* **1** I 439, **1** IV 4232.]

β-D-Lyxose *[1114-34-7]* **M 150.1, m 118-119°, 120-122°, $[\alpha]_D^{20}$ -14° (c 4, H_2O), α–anomer has m 105-107° mutarotates from $[\alpha]_D^{20}$ +5.6° to –18.8° (c 4, H_2O).** Crystallise β-D-lyxose from EtOH or aqueous 80% EtOH by slow crystallisation. Dry it under vacuum at 60°, and store it in a vacuum desiccator over P_2O_5 or $CaSO_4$. [*Beilstein* **1** IV 4230, Overend et al. *J Chem Soc* 3496 *1961*.] ^{1}H NMR in D_2O has δ: α–H (pyranose) 5.39 (*J* 4.0 Hz), β–H (pyranose) 5.19 (*J* ~0 Hz), α–H (furanose) 5.26 (*J* 4.0 Hz), β–H (furanose) 5.24 (*J* 4.5 Hz), and at 31° in D_2O it consists of 70% α–pyranose, 28% β-pyranose, 1.5% α-furanose and 0.5% β-furanose [Angyal & Pickles *Aust J Chem* **25** 1711 *1972*].

Maltose (H_2O) **(4-*O*-α-D-glucopyranosyl-D-glucose)** *[6363-53-7]* **M 360.3, m 109-110°, 118°, mutarotates from $[\alpha]_D^{20}$ +111.7° to +130.4° (c 4, H_2O).** Purify maltose by chromatography from aqueous solution on to a charcoal/Celite (1:1) column, wash it with water to remove glucose and other monosaccharides, then elute it with aqueous 75% EtOH. Crystallise it from water, aqueous EtOH or EtOH containing 1% nitric acid. Dry it as the *monohydrate* at room temperature under vacuum over H_2SO_4 or P_2O_5. Also purify it by dissolving it in MeOH, evaporating to a syrup which on standing for 12 hours in contact with 1/10th its volume of H_2O gives crystals of the *monohydrate*. Its iodine number is 55.5. The **osazone** has **m** 200°(dec) and $[\alpha]_D^{20}$ +58° (c 1.4, H_2O). [Howarth et al. *J Chem Soc* 793 *1937, Beilstein* **17** III/IV 3057, **17** V 189.]

D-Mannitol *[69-65-8]* **M 182.2, m 166.1°, 168-170°, $[\alpha]_{546}^{20}$ + 29° (c 10, after 1 hour in 8% borax solution), $[\alpha]_D^{22}$ -4.0° (c 0.5, DMF), pK^{18} 13.5.** D-Mannitol is crystallised from EtOH, MeOH or H_2O and dried at 100°. [Thomson *Acta Chem Scand* **6** 270, 279, 280 *1952*, *Beilstein* **1** IV 2841.]

Mannitol hexanitrate *[15825-70-4]* **M 452.2, m 112-113°, $[\alpha]_D^{22}$ +45.8° (c 1.4, EtOH).** The hexanitrate crystallises from EtOH or dilute EtOH as silky white needles. **EXPLOSIVE (on detonation).** [Hayward *J Am Chem Soc* **73** 1974 *1951*, Patterson & Todd *J Chem Soc* 2876 *1929*, *Beilstein* **1** IV 2841.]

α-D(+)-Mannose *[3458-28-4]* **M 180.2, m 132°, $[\alpha]_D^{20}$ mutarotates from +29.9° to +14° (c 4, H_2O).** Crystallise α-D(+)-mannose repeatedly from EtOH, aqueous 80% EtOH, AcOH or MeOH/propan-2-ol and then dry it *in vacuo* over P_2O_5 at 60°. [For ^{1}H NMR and equilibrium forms; Angyal *Adv Carbohydr Chem* **42** 15 *1984*, Angyal & Pickles *Aust J Chem* **25** 1711 *1972*, *Beilstein* **1** IV 4328.]

D(+)-Melezitose (H_2O) (*O*-α-D-glucopyranosyl-(1 → 3)-β-fructofuranosyl-α-D-glucopyranose *[597-12-6]* **M 540.5, m 153-154°(dec), $2H_2O$, 160°(dec), $[\alpha]_D^{20}$ +88° (c 2, H_2O for dihydrate) and $[\alpha]_D^{20}$ +91.7° (c 2, H_2O for anhydrous).** D(+)-Melezitose crystallises from aqueous EtOH as the *monohydrate* and water as the *dihydrate*, and is then dried at 110° (anhydrous). It is also purified by dissolving in an equal volume of H_2O, filtering into a crystallising dish and allowing to stand (loosely covered) for several weeks undisturbed at 20°. The crystals of clear prisms are wiped carefully and dried in air. They effloresce at once losing 3.35% of their weight, and after 3 days in air the loss is for $1H_2O$ from the dihydrate. Drying at 110° for 6 hours *in vacuo* yields the *anhydrous* form which after 2 days in air it absorbs H_2O to give the monohydrate. The monohydrate is also obtained by dissolving it in an equal weight of H_2O at 60° and adding 4 volumes of 95% EtOH and drying in air overnight. [Richtmeyer & Hudson *J Org Chem* **11** 610 *1946*, *Beilstein* **17** III/IV 3815, **17/8** V 414.]

D(+)-Melibiose ($2H_2O$) (6-*O*-α-D-galactopyranosyl-D-glucose) *[585-99-9, monohydrate 66009-10-7]* **M**

360.3, m 84-85°, 178-181°, 184-185°, $[\alpha]_D^{20}$ +135° (c 5, after 10 hours H_2O). D(+)-Melibiose crystallises as a *hydrate* from water or aqueous EtOH. The **α–anomer** is obtained by recrystallising 1g from a mixture of 0.35ml of H_2O and 0.2ml of EtOH. It crystallises easily with **m** 179° and mutarotates from $[\alpha]_D^{20}$ +166° to +142.3° (220 minutes, c 4, H_2O). Crystallisation from MeOH gives the *anhydrous* form which hydrates to the monohydrate in air. The **β-anomer dihydrate m** 85-86° mutarotates from $[\alpha]_D^{20}$ +123.5° to +143.1° (c 4, H_2O for anhydrous). [Fletcher & Diehl *J Am Chem Soc* **74** 5774 *1952*, *Beilstein* **17** III/IV 3075, **17/7** V 206.]

***N*-Methyl-D(-)-glucamine (Meglumine)** *[6284-40-8]* **M 195.2, m 128-129°, $[\alpha]_{546}^{20}$ -19.5°(c 2, H_2O), pK^{28} 9.62.** Crystallise *N*-methyl-D(-)-glucamine from MeOH. Its solubility in H_2O is 10%. [Karrer & Herkenrath *Helv Chim Acta* **20** 83 *1957* also for other N-alkyl derivatives, *Beilstein* **4** IV 1914.]

***N*-Methyl α-L-glucosamine** *[42852-95-9]* **M 193.2, m glass, $[\alpha]_D^{25}$ -65° (c 1, MeOH) pK_{Est} ~9.** The *hydrochloride* crystallises from EtOH as hygroscopic needles with **m** 160-163°, $[\alpha]_D^{25}$ +103° mutarotating to -88° after 24 hours (c 0.6, H_2O), and gives the free base as a glass. The *Pentaacetate* crystallises from $CHCl_3/Et_2O$ with **m** 160.5-161.5°, $[\alpha]_D^{25}$ -100° (c 0.7, $CHCl_3$), and the *N-acetate* crystallises from $CHCl_3$/MeOH with **m** 165-166°, $[\alpha]_D^{25}$ -51° (c 0.4, H_2O). [Kuehl et al. *J Am Chem Soc* **68** 536 *1946*, **69** 3032 *1947*, Lemieux & Wolfrom *Adv Carbohydr Chem* **3** 337 *1948*, *Beilstein* **4** IV 2032.]

Methyl α-D-glucoside (methyl α-D-glucopyranoside) *[97-30-3]* **M 194.2, m 168°, 166-169°, $[\alpha]_D^{20}$ +158.9° (c 10, H_2O), pK_1^{25} 13.71.** Crystallise methyl α-D-glucoside from MeOH or EtOH. Its solubility in H_2O is 10%. [Ferrier et al. *Carbohydr Research* **27** 55, 59 *1973*, *Beilstein* **17/7** V 13.]

Methyl β-D-glucoside (methyl β-D-glucopyranoside *[7000-27-3]* **M 203.2 (0.5 H_2O), m 107-109°, $[\alpha]_D^{20}$ -33° (c 10, H_2O).** Crystallise methyl β-D-glucoside from MeOH or EtOH. Its solubility in H_2O is 10%. [Ferrier et al. *Carbohydr Research* **27** 55, 59 *1973*, *Beilstein* **17/7** V 10.]

4-Methylumbellifer-7-yl-α-D-glucopyranoside *[17833-43-1]* **M 338.3, m 209-210°, 221-222°, $[\alpha]_D^{20}$ +162° (c 0.5, pyridine).** Recrystallise 4-methylumbellifer-7-yl-α-D-glucopyranoside from hot H_2O or EtOH. [Courtin-Duchateau & Veyrière *Carbohydr Research* **65** 23, 29 *1978*, *Beilstein* **18** IV 443.]

4-Methylumbellifer-7-yl-β-D-glucopyranoside *[18997-57-4]* **M 338.3, m 211-213°, 211°, $[\alpha]_D^{20}$ -68° (c 0.5, pyridine), -89.5° (c 0.5, H_2O for half hydrate).** 4-Methylumbellifer-7-yl-β-D-glucopyranoside crystallises as the half hydrate from hot H_2O. [Constantzas & Kocourek *Col Czech Chem Commun* **24** 1099 *1959*, De Re et al. *Ann Chim (Rome)* **49** 2089 *1959*, Courtin-Duchateau & Veyrière *Carbohydr Research* **65** 23, 29 *1978*, *Beilstein* **18** III/IV 5152, **8** IV 433, **18/7** V 616.]

Naringin (4',5,7-trihydroxyflavanone 7-rhamnoglucoside) *[10236-47-2]* **M 580.5, m ~83° ($6H_2O$), 171° ($2H_2O$), $[\alpha]_D^{19}$ -90° (c 1, EtOH), $[\alpha]_{546}^{20}$ -107° (c 1, EtOH).** This bitter principle from grape juice crystallises from water to give the hydrate with 6-8 H_2O which when dried at 110° gives the *dihydrate*. Its solubility in H_2O is 0.1% at 40° and 10% at 75°. The *2,4-dinitrophenylhydrazone* crystallises from aqueous dioxane with **m** 246-247° [Douglass et al. *J Am Chem Soc* **73** 4023 *1951*]. [Pulley & von Loesecke *J Am Chem Soc* **61** 175 *1939*, *Beilstein* **18** III/IV 2637, **18** V 528.]

2-Nitrophenyl-β-D-galactopyranoside *[369-07-3]* **M 301.3, m 185-190°, 193°, 193-194°, $[\alpha]_D^{18}$ -51.9° (c 1, H_2O).** Purify 2-nitrophenyl-β-D-galactopyranoside by recrystallisation from EtOH. [Seidman & Link *J Am Chem Soc* **72** 4324 *1950*, Snyder & Link *J Am Chem Soc* **75** 1758 *1953*]. It is a chromogenic substrate for β-galactosidases [Jagota et al. *J Food Sci* **46** 161 *1981*]. [*Beilstein* **17/7** V 52.]

4-Nitrophenyl-α-D-galactopyranoside *[7493-95-0]* **M 301.3, m 166-169°, 173°, $[\alpha]_D^{25}$ +248° (c 1, H_2O).** Purify 4-nitrophenyl-α-D-galactopyranoside by recrystallisation from H_2O or aqueous EtOH. The *monohydrate* has **m** 85° which resolidifies and melts again at 151-152° (the *hemihydrate*), then resolidifies again and melts at 173° to give the *anhydrous* form. Drying the monohydrate at 60° yields the hemihydrate, and drying at 100°

gives the anhydrous compound. The *tetraacetate* has **m** 147° after drying at 100°. [Jermyn *Aust J Chem* **15** 569 *1962*, Helfreich & Jung *Justus Liebigs Ann Chem* **589** 77 *1954*.] It is a substrate for α-galactosidase [Dangelmaier & Holmsen *Anal Biochem* **104** 182 *1980*]. [*Beilstein* **17/7** V 55.]

4-Nitrophenyl-β-D-galactopyranoside *[3150-24-1]* **M 301.3, m 178°, 178-181°, 181-182°, $[\alpha]_D^{20}$ -83° (c 1, H_2O).** Purify the galactoside by recrystallisation from EtOH. [Horikoshi *J Biochem (Tokyo)* **35** 39 *1042*, Goebel & Avery *J Exptl Medicine* **50** 521 *1929*, Snyder & Link *J Am Chem Soc* **75** 1758.] It is a chromogenic substrate for β-galactosidases [Buoncore et al. *J Appl Biochem* **2** 390 *1980*]. [*Beilstein* **17/7** V 55.]

4-Nitrophenyl-α-D-glucopyranoside *[3767-28-0]* **M 301.3, m 206-212°, 216-217° (sinters at 210°), $[\alpha]_D^{20}$ +215° (c 1, H_2O).** Purify 4-nitrophenyl-α-D-glucopyranoside by recrystallisation from H_2O, MeOH or EtOH. [Jermyn *Aust J Chem* **7** 202 *1954*, Montgomery et al. *J Am Chem Soc* **64** 690 *1942*.] It is a chromogenic substrate from α-glucosidases [Oliviera et al. *Anal Biochem* **113** 188 *1981*], and is a substrate for glucansucrases [Binder & Robyt *Carbohydr Research* **124** 287 *1983*]. [*Beilstein* **17/7** V 53.]

4-Nitrophenyl-β-D-glucopyranoside *[2492-87-7]* **M 301.2, m 164°, 164-165°, 165°, $[\alpha]_D^{20}$ -107° (c 1, H_2O).** Purify 4-nitrophenyl-β-D-glucopyranoside by recrystallisation from EtOH or H_2O. [Montgomery et al. *J Am Chem Soc* **64** 690 *1942*, Snyder & Link *J Am Chem Soc* **75** 1758 *1953*.] It is a chromogenic substrate for β-glucosidases [Weber & Fink *J Biol Chem* **255** 9030 *1980*]. [*Beilstein* **17/7** V 53.]

***N*-Nonanoyl-*n*-methylglucamine (Mega-9)** *[85261-19-4]* **M 335.4, m 87-89°.** It is a non-ionic detergent which is purified as for *n*-decanoyl-*N*-methylglucamine above. [Hildreth *Biochem J* **207** 363 *1982*.]

Nonyl-β-D-glucopyranoside *[69984-73-2]* **M 306.4, m 67.5-70°, 70-71°, $[\alpha]_D^{20}$ -34.4° (c 5, H_2O), $[\alpha]_D^{25}$ -28.8° (c 1, MeOH).** Purify nonyl-β-D-glucopyranoside by recrystallisation from Me_2CO or hexane/Et_2O and store it in well-stoppered containers as it is *hygroscopic*. [Pigman & Richtmyer *J Am Chem Soc* **64** 369 *1942*.] It is a UV transparent non-ionic detergent for solubilising membrane proteins [Schwendener et al. *Biochem Biophys Res Commun* **100** 1055 *1981*]. [*Beilstein* **17** III/IV 2937, **17/7** V 39.]

Octyl-β-D-glucopyranoside *[29836-26-8]* **M 292.4, m 62-65°, 63.8-65°, $[\alpha]_D^{20}$ s-34° (c 4, H_2O).** Purify octyl-β-D-glucopyranoside by recrystallisation from Me_2CO. It is *hygroscopic* and should be stored in a well-stoppered container. [Noller & Rockwell *J Am Chem Soc* **60** 2076 *1938*, Pigman & Richtmyer *J Am Chem Soc* **64** 369 *1942*.] It is a UV transparent non-ionic dialysable detergent for solubilising membrane proteins. The *α–D-isomer* with $[\alpha]_D^{20}$ +118° (c 1, MeOH) has similar solubilising properties. [Lazo & Quinn *Anal Biochem* **102** 68 *1980*, Stubbs et al. *Biochim Biophys Acta* **426** 46 *1976*, *Beilstein* **17/7** V 38.]

Pectic acid *[9046-40-6]* **M_r $(C_6H_8O_6)_n$ ~500,000, amorphous, $[\alpha]_D$ +250° (c 1, 0.1M NaOH).** Citrus pectic acid (500g) is refluxed for 18 hours with 1.5L of 70% EtOH, and the suspension is filtered hot. The residue is washed with hot 70% EtOH and finally with ether. It is dried in a current of air, ground and dried for 18 hours at 80° under vacuum. [Morell & Link *J Biol Chem* **100** 385 *1933*.] It can be further purified by dispersing it in water and adding just enough dilute NaOH to dissolve the pectic acid, then passing the solution through columns of cation- and anion-exchange resins [Williams & Johnson *Ind Eng Chem (Anal Ed)* **16** 23 *1944*], and precipitating with two volumes of 95% EtOH containing 0.01% HCl. The precipitate is worked with 95% EtOH, then Et_2O, dried and ground. [Rees & Walsh *Angew Chem Int Edn* **16** 214 *1977*, Rees *Adv Carbohydr Chem* **24** 267 *1969*.]

Pectin (1-4 linked) *[9000-69-5]* **M_r 30,000-100,000, amorphous.** Dissolve the pectin in hot water to give a 1% solution, then cool, and make it to about 0.05M in HCl by addition of conc HCl, and precipitate it by pouring it slowly, with vigorous stirring into two volumes of 95% EtOH. After standing for several hours, the pectin is filtered through a nylon cloth, then redispersed in 95% EtOH and stood overnight. The precipitate is filtered off, washed with EtOH/Et_2O, then Et_2O and dried in air. [Rees & Walsh *Angew Chem, Int Edn* **16** 214 *1977*, Rees *Adv Carbohydr Chem* **24** 267 *1969*.]

Pentaerythritol (2,2-bis[hydroxymethyl]-1,3-propanediol) *[115-77-5]* **M 136.2, m 260.5°, 268-269°.** Reflux pentaerythritol with an equal volume of MeOH, then cool, and the precipitate is collected and dried at 90°. It can also be crystallised from dilute aqueous HCl. After sublimation under high vacuum at 200° it has **m** 265.5°. Its solubility in H_2O is 10%. [*Beilstein* **18** III 2361, **1** IV 2812.]

Pentaerythritol tetraacetate *[597-71-7]* **M 304.3, m 83-84°, 84-86°.** Crystallise pentaerythritol tetraacetate from hot water, then leach it with cold water until the odour of acetic acid is no longer detectable. It also crystallises from 95% EtOH after dissolving in $CHCl_3$, washing with saturated $NaHCO_3$, then H_2O, drying over anhydrous $CaCl_2$ and evaporating. It has been prepared by acetolysis of the tetranitrate in 95% yield [Wolfrom et al. *J Am Chem Soc* **73** 874 *1951*]. [Breusch & Oguzer *Chem Ber* **88** 1511 *1955*, LeFèvre et. al. *J Chem Soc* 16 *1958*, *Beilstein* **1** IV 1812, **2** IV 264.]

Pentaerythrityl laurate (pentaerythrityl tetra-*n*-dodecanoate) *[13057-50-6]* **M 864.6, m 50°.** Crystallise the laurate from Me_2CO, Et_2O or petroleum ether. [Breusch & Oguzer *Chem Ber* **88** 1511 *1955*.]

Pentaerythritol tetranitrate *[78-11-5]* **M 316.2, m 140.1°.** Crystallise pentaerythritol tetranitrate from acetone or acetone/EtOH. When crystallised from H_2O at 0°, it may have **m** 26-28° (hydrate?). It detonates more easily than TNT on percussion. The *O-acetate*, when crystallised from EtOH, has **m** 87-88°. Although it has been distilled at 60°/2mm, distillation should **NOT** be attempted as it is **VERY EXPLOSIVE.** It is a vasodilator. [Marans et al. *J Am Chem Soc* **76** 1304 *1954*, Camp et al. *J Am Chem Soc* **77** 751 *1955*, *Beilstein* **1** IV 2816, **2** IV 264.]

2-Phenylethyl-β-D-thiogalactoside *[63407-54-5]* **M 300.4, m 108°, $[\alpha]_D^{23}$ -32.2° (c 5, MeOH).** Recrystallise the thiogalactoside from H_2O and dry in air to give the $1.5.H_2O$ which has **m** 80°. The anhydrous surfactant is obtained by drying it at 78° over P_2O_5. [Heilfrich & Türk *Chem Ber* **89** 2215 *1856*.]

Phenyl-β-D-galactopyranoside *[2818-58-8]* **M 256.3, m 153-154°, 146-148°, 155-156°(dried at 105°), $[\alpha]_D^{20}$ -42° (c 1, H_2O).** Recrystallisation of phenyl-β-D-galactopyranoside from H_2O gives the $0.5H_2O$. [Conchie & Hay *Biochem J* **73** 327 *1959*, IR: Whistler & House *Analyt Chem* **25** 1463 *1953*.] It is an acceptor substrate for fucosyltransferase [Chester et al. *Eur J Biochem* **69** 583 *1976*]. [*Beilstein* **17/7** V 46.]

Phenyl-β-D-glucopyranoside *[1464-44-4]* **M 256.3, m 174-175° 174-176°, 176°, 176-178°, $[\alpha]_D^{20}$ -72.2° (c 1 for dihydrate, H_2O).** Phenyl-β-D-glucopyranoside recrystallises from H_2O with $2H_2O$ and can be dried *in vacuo* at 100°/P_2O_5. The dry preparation has $[\alpha]_D^{25}$ -70.7° (c 2, H_2O). [Robertson & Waters *J Chem Soc* 2729 *1930*, IR: Bunton et al. *J Chem Soc* 4419 *1955*, Takahashi *Yakugaku Zasshi (J Pharm Soc Jpn)* **74** 7436 *1954*, Whixtler & House *Anal Chem* **25** 1463 *1953*, UV: Lewis *J Am Chem Soc* **57** 898 *1935*.] It is a substrate for β–D-glucosidase [deBryne *Eur J Biochem* **102** 257 *1979*]. [*Beilstein* **17** III/V 2946, **17/7** V 46.]

Phlorizin ($2H_2O$) [phloretin 2'-*O*-β-D-glucoside] *[60-81-1]* **M 472.5, m 110°, $[\alpha]_{546}^{20}$ -62° (c 3.2, EtOH).** Phlorizin crystallises as the *dihydrate* from water and causes glycosuria. [Brazy & Dennis *Am J Physiol* **234** 1279 *1978*, Zemplen & Bognár *Chem Ber* **17B** 1040 *1943*, *Beilstein* **17/7** V 177.]

D(+)-Raffinose ($5H_2O$) **(Melitose, 6-O-α-D-galactopyranosyl-D-glucopyranosyl-β-D-fructo-furanose** *[17629-30-0 ($5H_2O$), 512-69-6 (anhydrous)]* **M 594.5, m 80°, 80-82°, $[\alpha]_{546}^{20}$ +124° (c 10, H_2O), $[\alpha]_D^{20}$ +105° (c 1 for pentahydrate, H_2O), pK_1^{25} 12.40, pK_2^{25} 13.44, pK_3^{25} 13.52.** D(+)-Raffinose crystallises from H_2O, 90% aqueous EtOH or MeOH as the *pentahydrate*. The *anhydrous* sugar has **m** 132-135°. It has R_F 0.8 on TLC (Silica Gel, and 1:3:3 $CHCl_3$/butanone:/MeOH). The *undecaacetate* has been purified through an alumina column by elution with $CHCl_3$, and recrystallised from EtOH/MeOH/H_2O (3:2:5), with **m** 99-100°, $[\alpha]_D^{20}$ +92.8° (c 5.14, EtOH). [pK : Coccioli & Vicedomini *Ann Chim (Rome)* **66** 269, 275 *1976*, ^{1}H NMR: Suami et al. *Carbohydr Research* **26** 234 *1973*, *Beilstein* **17** III/IV 3801, **17/8** V 403.]

L(+)-α-Rhamnose (H_2O) (6-deoxy-L-mannose) *[10030-85-0 (H_2O), 3615-41-6 (anhydrous)]* **M 182.2, m 90-92°, 101°, 105°, $[\alpha]_D^{18}$ -6.8° mutarotating to +9.1° (c 1, H_2O).** Crystallise the rhamnose from H_2O or

EtOH. It crystallises easily as the *monohydrate* by evaporating a solution in MeOH (90%) and H_2O (10%). It is also purified by dissolving in a small volume of EtOH, adding a few drops of H_2O and cooling. ^1H NMR in D_2O at 44° contains 60% α-pyranose and 40% β-pyranose forms [Angyal *Adv Carbohydr Chem* **42** 15 *1984*.] [Smith *J Chem Soc* 1035 *1940*, McGeachin & Beevers *Acta Cryst* **10** 227,230 *197*, *Beilstein* **1** IV 4261.]

D-(+)-Ribonic acid-γ-lactone *[5336-08-3]* **M 148.12, m 80°, 84-86°, $[\alpha]_D^{20}$ +18.3° (c 5, H_2O).** Purify D-(+)-ribonic acid-γ-lactone by recrystallisation from EtOAc. The *tribenzoate* has **m** 54-56° (from AcOH), $[\alpha]_D^{25}$ +27° (c 2.37, Me_2NCHO), and the *3,5*-O-*benzylidene* derivative has **m** 230-231.5° (needles from Me_2CO-petroleum ether) and $[\alpha]_D^{25}$ -177° ($CHCl_3$). [Chen & Joulié *J Org Chem* **49** 2168 *1984*, Zinner & Voigt *J Carbohydr Research* **7** 38 *1968*.]

α-D(-)-Ribose *[50-69-1]* **M 150.1, m 90°, $[\alpha]_{546}^{20}$ -24° (after 24hours, c 10, H_2O), pK^{25} 12.22.** Crystallise α-D(-)-ribose from aqueous 80% EtOH, dry it under vacuum at 60° over P_2O_5 and store it in a vacuum desiccator. It exhibits a complex mutarotation with : $[\alpha]_D^{10}$ -23.1° (1.5 minutes), -21.3° (5 minutes), -19.5° (10 minutes), -19.1° (30 minutes), -21.2° (60 minutes), -23.1° (120 minutes), -23.7° (300 minutes), (c 4.5, H_2O) [Phelps et al. *J Am Chem Soc* **56** 748 *1934*]. ^1H NMR in D_2O at 44° shows 17% α-pyranose, 59% β-pyranose, 9% α-furanose and 15% β-furanose forms with **furanose** α-H at 5.34ppm (J = 3.0Hz) and β-H at 5.31 (J = 1.7Hz) [Angyal *Adv Carbohydr Chem* **42** 15 *1984*, Angyal & Pickles *Aust J Chem* **25** 1711 *1972*]. The *phenylhydrazone* crystallises from aqueous pyridine in yellow needles, **m** 163-164°, and the *benzylphenylhydrazone* has **m** 127-128° [Snowden *J Am Chem Soc* **72** 808 *1950*]. [*Beilstein* **1** IV 4211.]

(+)-Rutin (quercetin-3-rubinoside) See Vitamin P in "Miscellaneous", this chapter.

Saccharides.

They are separated by anion-exchange chromatography. [Walberg & Kando *Anal Biochem* **37** 320 *1970*.]

D(-)-Salicin [2-(hydroxymethyl)phenyl-β–D-glucopyranoside) *[138-52-3]* **M 286.3, m 204-208°, $[\alpha]_D^{25}$ -63.5° (c *ca* 3, H_2O).** Crystallise D(-)-salicin from EtOAc, EtOH or water and sublime it at 190-195°/12mm. [Armour et al. *J Chem Soc* 412 *1961*, IR: Pearl & Darling *J Org Chem* **24** 731 *1959*, *Beilstein* **17** III/IV 2986, **17/7** V 113.]

Sennoside A (bianthraquinonyl-bis-glucoside *R,R*-enantiomer) *[81-27-6]* **M 862.7, m 220-240°(dec), $[\alpha]_D^{20}$ -164° (c 0.1, Me_2CO/H_2O 6:4), $[\alpha]_D^{20}$ -24° (c 0.2, 70% aqueous dioxane).** Sennoside A forms yellow crystals from aqueous acetone, 2-ethoxyethanol or large volumes of H_2O. [Stoll et al. *Helv Chim Acta* **32** 1896 *1900*, *Beilstein* **17** III/IV 3403.]

Sennoside B (bianthraquinonyl-bis-glucoside *R,S*-enantiomer) *[128-57-4]* **M 862.7, m 209-212°(dec), $[\alpha]_D^{20}$ -100° (c 2, Me_2CO/H_2O 7:1), $[\alpha]_D^{20}$ -67° (c 0.2, 70% aqueous dioxane).** Sennoside B forms yellow crystals from aqueous acetone or large volumes of H_2O. [Stoll et al. *Helv Chim Acta* **32** 1896 *1900*, *Beilstein* **17** III/IV 3402.]

Sinigrin monohydrate (Myronate K, 1-thio-β–D-glucopyranose 1-[N-(sulfooxy)-3-butenimidate] monopotassium salt) *[64550-88-5]* **M 415.5, m 125-127°, 127-129°, 179°(anhydrous), $[\alpha]_D^{20}$ -17° (c 0.2, H_2O), pK_{Est} <0.** Purify sinigrin by recrystallising it three times from EtOH and once from MeOH. The *tetraacetate* has **m** 193-195°, $[\alpha]_D^{20}$ -16° (c 0.14, H_2O). [Benn et al. *J Chem Soc, Chem Commun* 445 *1965*, Kjaer et al. *Acta Chem Scand* **10** 432 *1956*, Marsh et al. *Acta Cryst* (*Sect B*) **26** 1030 *1970*.] It is a β-D-thioglucopyranoside substrate for thiogluconidase [MacLeod & Rossiter *Phytochem* **25** 1047 *1986*]. [*Beilstein* **31** H 476, **17** III/IV 3738.]

α-Solanine (solan-5-en-3β-yl-[O^3-β-D-glucopyranosyl-O^2-α-L-rhamnopyranosyl-β-D-galactopyranoside]) *[20562-02-1]* **M 868.1, m 285°(dec), 286°(dec) (sintering >190°), $[\alpha]_D^{20}$ -58° (c 0.8, pyridine), pK^{15} 6.66.** Recrystallise α-solanine from EtOH, 85% aqueous EtOH, MeOH or aqueous MeOH as *dihydrate* **m** 276-278°.

It solubility in H_2O is 25mg/l and 5% in pyridine, but it is very soluble in Et_2O and $CHCl_3$. The *hydrochloride* is gummy or amorphous but has been crystallised (**m** ~212° dec). It has insecticidal properties. [Kuhn et al. *Chem Ber* **88** 1492 *1955*, *Beilstein* **21** III/IV 1402.]

Solasonine (solasodine-3-*O*-triglycoside) *[19121-58-5]* **M 884.0, m 301-303° (sinters at ~296°), $[\alpha]_D^{20}$ -75° (c 0.5, MeOH), pK_{Est} ~ 7.7.** Solasonine crystallises from aqueous 80% dioxane or MeOH in needles. [Bell & Briggs *J Chem Soc* 1 *1942*, Briggs et al. *J Chem Soc* 4645 *1961*, Briggs et al. *J Chem Soc* 2848 *1963*.] The *picrate* crystallises from 30% aqueous EtOH with **m** 197-198°(dec) [Briggs & Cambie *J Chem Soc* 1422 *1958*]. [*Beilstein* **27** III/IV 2006.]

D(-)-Sorbitol (D-glucitol) *[50-70-4]* **M 182.2, m 89-93° (hemihydrate), 110-111° (anhydrous), $[\alpha]_{546}^{20}$ -1.8° (c 10, H_2O), pK^{60} 13.00.** Crystallise D(-)-sorbitol (as hemihydrate) several times from EtOH/water (1:1), then dry it by fusing and storing over anhydrous $MgSO_4$. [Koch et al. *J Am Chem Soc* **75** 953 *1953*, *Beilstein* **1** IV 2839.]

Starch *[9005-84-9]* **M $(162.1)_n$.** Starch is de-fatted by Soxhlet extraction with Et_2O or 95% EtOH. For fractionation of starch into "amylose" and "amylopectin" fractions, see Lansky et al. [*J Am Chem Soc* **71** 4066 *1949*].

Streptozotocin (*N*-[methylnitrosocarbamoyl]-α-D-glucosamine, streptozocin) *[18883-66-4]* **M 265.2, m 111-114°(dec), 114-115°(dec), 115°(dec with evolution of gas), $[\alpha]_D^{20}$ ~+39° (H_2O, may vary due to mutarotation).** Recrystallise streptozotocin from 95% EtOH. It is soluble in H_2O, MeOH and Me_2CO. It has UV with λ_{max} at 228nm (ε 6360) in EtOH. The *tetraacetate* has **m** 111-114°(dec), and $[\alpha]_D^{25}$ +41° (c 0.78, 95% EtOH) after recrystallisation from EtOAc. [Herr et al. *J Am Chem Soc* **89** 4808 *1967*, NMR: Wiley et al. *J Org Chem* **44** 9 *1979*.] It is a potent methylating agent for DNA [Bennett & Pegg *Cancer Res* **41** 2786 *1981*].

D(+)-Sucrose (β-D-fructofuranosyl-α-D-glucopyranoside) *[57-50-1]* **M 342.3, m 160-186°, 186-188°, $[\alpha]_{546}^{20}$ +78° (c 10, H_2O), $[\alpha]_D^{20}$ + 66° (c 26, H_2O), pK^{25} 12.62.** Crystallise D(+)-sucrose from water (solubility: 1g in 0.5ml H_2O at 20°, 1g in 0.2ml in boiling H_2O). It is soluble in EtOH (0.6%) and MeOH (1%). *Sucrose diacetate hexaisobutyrate* is purified by melting and, while molten, treated with $NaHCO_3$ and charcoal, then filtered. [*Beilstein* **17/8** V 399.]

D(+)-Sucrose octaacetate *[126-14-7]* **M 678.6, m 83-85°, b 260°/1mm, $[\alpha]_{546}^{20}$ +71° (c 2.5, EtOH).** After three recrystallisations from EtOH or 95% EtOH (charcoal), the **m** of the *octaacetate* rises to 88-90°, or Et_2O with **m** 89° and $[\alpha]_D^{25}$ +58.5° (c 2.6, EtOH). It has a bitter taste. [Linstead et al. *J Am Chem Soc* **62** 3260 *1940*, Lemieux & Huber *J Am Chem Soc* **78** 4117 *1956*, *Beilstein* **17/8** V 410.]

D(-)-Tagatose *[87-81-0]* **M 180.2, m 131-132°, 134-135°, $[\alpha]_{546}$ -6.5° (c 1, H_2O).** Crystallise D(-)-tagatose from EtOH/H_2O (6:1). It mutarotates from $[\alpha]_D^{22}$ +2° (2 minutes) to –5.0° (30 minutes) (c 4, H_2O). The *phenylosazone* crystallises from aqueous EtOH with **m** 185-187°(dec), and $[\alpha]_D^{23}$ +47° (c 0.82, 2-methoxyethanol). [Totton & Lardy *J Am Chem Soc* **71** 3076 *1949*, Gorin et al. *Canad J Chem* **33** 1116 *1955*, Reichestein & Bossard *Helv Chem Acta* **17** 753 *1934*, Wolfrom & Bennett *J Org Chem* **30** 1284 *1965*, *Beilstein* **1** IV 4414.] In D_2O at 27° ^1H NMR showed the following ratios: α-pyranose (79), β-pyranose (16), α-furanose (1) and β-furanose (4) [Angyal *Adv Carbohydr Chem* **42** 15 *1984*, Angyal & Pickles *Aust J Chem* **25** 1711 *1972*].

Thevetin A (cardenolide glycoside) *[37933-66-7]* **M 858.9, m softens at 194°, m 208-210°, $[\alpha]_D^{26}$ -72° (c 1.48, MeOH).** Crystallise Thevetin A from H_2O. The *acetyl derivative* crystallises from MeOH/Et_2O at -15° with **m** 145-149°, and $[\alpha]_D^{26}$ -54.2° (c 1.86, $CHCl_3$). [Block et al. *Helv Chim Acta* **43** 652 *1960*, ^{13}C NMR: Tori et al. *Tetrahedron Lett* 717 *1977*, *Beilstein* **18** III/IV 2552, **18/4** V 439.]

Thevetin B (cardenolide glycoside) *[11018-93-2]* **M 858.9, m 197-201°, $[\alpha]_D^{24}$ -61.4° (c 1.5, MeOH).** It crystallises (as *trihydrate*) from isopropanol. Dry it at 100°/0.01mm to give the *hemihydrate* (*very hygroscopic*).

[Block et al. *Helv Chim Acta* **43** 652 *1960*, ^{13}C NMR: Tori et al. *Tetrahedron Lett* 717 *1977*, *Beilstein* **18** III/IV 1493.]

α,α'-D(+)-Trehalose ($2H_2O$) *[6138-23-4]* **M 378.3, m 96.5-97.5°, 94-100° (dihydrate), 214-216° (anhydrous), $[\alpha]_D^{20}$ +180° (dihydrate, c 4, H_2O), $[\alpha]_D^{20}$ +199° (anhydrous, c 4, H_2O).** α,α'-D(+)-Trehalose crystallises (as the *dihydrate*) from aqueous EtOH. Dry it at 13°. For the *anhydrous* compound dissolve 10g in pyridine (200ml) and distil off this solvent at atmospheric pressure, and when the temperature rises to 115.3° all the H_2O is removed and 73ml of distillate is collected. Most of the anhydrous material crystallises out at this stage. The crystals are collected (6.8g), washed with Et_2O to give 6.1g of anhydrous product. Higher yields are obtained by slightly more prolonged distillation. [Birch *J Chem Soc* 3489 *1965*, X-ray cryst: Brown et al. *Acta Cryst* **28** 3145 *1972*, *Beilstein* **17/8** V 3.]

D(+)-Turanose [3-*O*-α–D-glucosido)-D-fructose] *[547-25-1]* **M 342.3, m 168-170°, $[\alpha]_D^{20}$ +88° (c 4, H_2O).** Crystallise D(+)-turanose from H_2O by addition of EtOH (its solubility is 5.3% in 95% EtOH). Form **m** 157° is obtained by crystallisation from hot MeOH, and mutarotates from +27.3° to $[\alpha]_D^{20}$ +88° (c 4, H_2O). The *phenylosazone* crystallises from 15 parts of 95% EtOH with **m** 200-205°, $[\alpha]_D^{20}$ 24.5° mutarotating to +33° [24hours, c 0.82, pyridine/EtOH (4:6)]. [Pascu *Methods in Carbohydrate Chemistry* **I** 353 *1962*, Academic Press, *Beilstein* **17/7** V 213.] In D_2O at 36° ^1H NMR showed the following ratios: α-pyranose (<4), β-pyranose (39), α-furanose (20) and β-furanose (41) [Angyal *Adv Carbohydr Chem* **42** 15 *1984*].

Vicine (2,4-diamino-5-β-D-glucopyranosidoxy-6-hydroxypyrimidine) *[152-93-2]* **M 304.3, m 243-244°, $[\alpha]_D^{20}$ -12° (c 4, 0.2N NaOH).** Crystallise Vicine from water (1%) or aqueous 85% EtOH, and dry it at 135°. [Bendich & Clements *Biochim Biophys Acta* **12** 462 *1953*, *Beilstein* **31** H 163, **25** III/IV 4285.]

Ustilagic acid (Ustizeain B, di-D-glucosyldihydroxyhexadecanoic acid) *[8002-36-6]* **M ~780, m 146-147°, $[\alpha]_D^{23}$ +7° (c 1, pyridine), pK^{25} ~ 4.9.** Ustilagic acid is a mixture of partly acetylated di-D-glucosyldihydroxyhexadecanoic acid which crystallises from diethyl ether. It has also been purified from the culture by dissolving it in hot MeOH, filtering and concentrating by blowing a current of air until the solution becomes turbid, then heating to 50° and adding 4 volumes of H_2O (also at 50°), and cooling very slowly. Filter off the white solid and dry it in air. It crystallises from Et_2O, and is soluble in MeOH, butan-1,2-diol, poorly soluble in EtOH, *n*-BuOH, Me_2CO and insoluble in H_2O, EtOAc and $^*C_6H_6$. [Lemieux et al. *Can J Chem* **29** 409, 415 *1951*, Boothroyd et al. *Can J Biochem Physiol* **33** 289 *1955*.]

Xanthorhamnin (xanthene rhamnoside) *[1324-63-6]* **M 770.7, m 195°, $[\alpha]_D^{20}$ +3.75° (EtOH), pK_1^{24} 8.69, pK_2^{24} 11.28, pK_3^{24} 12.22.** Crystallise xanthorhamnin from a mixture of ethyl and isopropyl alcohols, dry it in air, then dry it further for several hours at 110°. The UV (EtOH) has λ_{max} at 258 and 362nm. [Nystrom et al. *J Org Chem* **22** 1272 *1957*, *Beilstein* **18** III/IV 3498.]

α-D(+)-Xylose *[58-86-6]* **M 150.1, m 146-147°, 153-154°, $[\alpha]_D^{20}$ +92° mutarotating to +18.8° (16 hours, c 10, H_2O), pK^{18} 12.14.** α-D(+)-Xylose forms needles or prisms (which have a very sweet taste) by slow crystallisation from aqueous 80% EtOH or absolute EtOH, which are then dried at 60° *in vacuo* over P_2O_5. Store it in a vacuum desiccator over $CaSO_4$. 1Gram dissolves in 0.8ml H_2O. [Bragg & Hough *J Chem Soc* 4347 *1957*, Hudson & Yanovsky *J Am Chem Soc* **39** 1029 *1917*, Monroe *J Am Chem Soc* **41** 1002 *1919*, *Beilstein* **1** IV 4223.] In D_2O at 31°, ^1H NMR showed the following ratios: α-pyranose (36.5), β-pyranose (63), α-furanose + β-furanose (~1) [Angyal *Adv Carbohydr Chem* **42** 15 *1984*, Angyal & Pickles *Aust J Chem* **25** 1711 *1972*].

CAROTENOIDS

General

Carotenoids are polyene pigments that are mostly naturally occurring in bacteria, plants and animals. They have been isolated from the natural sources and obtained first by extraction with solvents and then purified by column chromatography through Al_2O_3 of various grades, $Ca(OH)_2$ alone or with $CaCO_3$, MgO or Silica Gel and eluted with solvents of various polarities. The progress of separation can be followed visually because the bands of most carotenoids are of various colours. The bands can be collected by elution, or the column can be extruded and the bands cut out and extracted with a polar solvent, e.g. MeOH. This chromatography can be repeated with the separate bands, and finally the carotenoids are recrystallised to analytical purity. The purity can be checked by TLC on Silica Gel or Al_2O_3 plates or paper chromatography and eluted in two dimensions. Gas-liquid or HPLC has been used for preparative work as well as for checking the purity and identifying them using internal standards such as tocopherol acetate (vitamin E acetate) and retinyl acetate.
Carotenoids are generally light sensitive, easily oxidised by air and are affected by traces of acid, e.g. in solvents. These cause the polyenes to bleach or polymerise. The necessary precautions are therefore required to minimise these effects during isolation, purification and storage. They are identified by their UV-VIS spectra, and their molar extinction coefficients at specific wavelengths (λ_{max}) have been used for characterisation and for quantitation. More recently ORD, CD, NMR, IR and mass spectroscopy have been used extensively.

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Antheraxanthin (5,6-epoxy-zeaxanthin) *[68831-78-7]* **M 584.8, m 205°, λ_{max} 460.5, 490.5nm, in $CHCl_3$.** Likely impurities are violaxanthin (see later) and mutatoxanthin (which contains a dihydrofuran ring derived from the epoxy group of antheraxanthin). Purify it by chromatography on columns of $Ca(OH)_2$ and of $ZnCO_3$. It crystallises from *C_6H_6/MeOH as needles or thin plates. Store it in the dark, under N_2 or argon at -20°. In $CHCl_3$/$SbCl_2$ it gives a blue colour with λ_{max} at 587nm and gives a stable blue colour with conc HCl. [Karrer & Oswald *Helv Chim Acta* **18** 1303 *1935*, Karrer & Jucker *Helv Chim Acta* **28** 300 *1945*.]

ß-Apo-4'-carotenal *[12676-20-9]* **M 414.7, m 139°, $A^{1\%}_{1cm}$ 2640 at 461nm.** Recrystallise the carotenal from $CHCl_3$/EtOH mixture or *n*-hexane. The λ_{max} of the absorption spectra of the radical anions and cations of such polyenals formed by pulse radiolysis are linearly dependent on the number of conjugated double bonds [Land et al. *JCS, Faraday Trans 1* **74** 538 *1978*, Bobrowski & Das *J Phys Chem* **91** 1210 *1987*, *Beilstein* **7** IV 1782.]

***trans*-ß-Apo-8'-carotenal** *[1107-26-2]* **M 414.7, m 136-139°.** Recrystallise ß-apo-8'-carotenal from $CHCl_3$/EtOH mixture or *n*-hexane. The absorption spectra of the radical anion of this C_{30} aldehyde in CTAB and Triton X100 micelles suggested an alcohol-like nature of the environment probed by the long-chain polyenal. For effect of conjugation on spectra see preceding entry [Bobrowski & Das *J Phys Chem* **91** 1210 *1987*, Land et al. *JCS, Faraday Trans 1* **74** 538 *1978*, *Beilstein* **7** III 2622, **7** IV 1782.]

ß-Apo-8'-carotenoic acid ethyl ester *[1109-11-1]* **M 526.8, m 134-138°, $A^{1\%}_{1cm}$ 2550 at 449nm.** Recrystallise the ester from petroleum ether or petroleum ether/EtOAc. Store it in the dark under N_2 or argon at -20°. [*Beilstein* **9** IV 2701 for Me ester.]

ß-Apo-8'-carotenoic acid methyl ester *[16266-99-2]* **M 512.7, m 136-137°, $A^{1\%}_{1cm}$ 2575 at 446nm and 2160 at 471nm, in petroleum ether.** Recrystallise the methyl ester from petroleum ether or petroleum ether/EtOAc. Store it in the dark in an inert atmosphere at -20°. [*Beilstein* **9** IV 2701.]

Astacin (β,β-carotene-3,3',4,4'-tetraone, Astacene) *[514-76-1]* **M 592.8, m 228°, 232-233°, 240-243°(evacuated tube), $\varepsilon^{1\%}_{1cm}$ 550,000 at 498nm (pyridine).** Astacin is a red pigment found in marine organisms (protozoa, algae, crustacians, sponges, fish, reptiles) together with astaxanthin (see below) from which it is possibly formed by autoxidation [Kuhn & Lederer *Chem Ber* **66** 488 *1933*]. A probable impurity is astaxanthin (3,3′-dihydroxy-β,β-carotene-4,4′-dione) which may be its precursor. It has been prepared by adding a solution of canthaxanthene (1.0g, see [514-78-3] below) in $*C_6H_6$ (15ml) to *t*-BuOK in *t*-BuOH (1.40N, 130ml) and shaken with O_2 at 20° for 30 hours. Water (200ml) is added, then 0.5N HCl (800ml) and extracted with $CHCl_3$ (300ml). The extract is washed with aqueous $NaHCO_3$ (3 x 300ml), H_2O (2 x 200ml), diluted with $*C_6H_6$ (50ml) and the organic layer is evaporated *in vacuo*. The residue is recrystallised from $CHCl_3$-EtOH (1:5) to give *astacin* (450mg, ~90%) as deep purple leaflets m 232-233° with λ_{max} (pyridine) 498mm (ε 100 x 10^3), (CS_2) 513mm, (hexane) 477mm, (EtOH) 483mm, and (KOH-EtOH) 478mm; the IR ($CHCl_3$) has ν_{max} at 3410br (ε ~90), 1610 (ε 1200), 1550, 1327 and 969 (ε 895) cm^{-1}; the ^1H NMR (60MHz, $CDCl_3$, TMS) has δ at 1.30 (12H, C-1 Me_2 and C-1′ Me_2), 2.10 (6H, C-5 Me and C-5′ Me), 2.02 (6H, C-9 Me and C-9′ Me), 2.02 (6H, C-13 Me and C-13′ Me), and 6.06 (C-2 H and C-2′ H) (14 olefinic H-7,7′, 8,8′, 10,10′, 11,11′, 12,12′, 14,14′, and 15,15′ are not included); and *m/z* 592 $M^{\cdot+}$. [Cooper et al. *J C S Perkin Trans I* 2195 1975.] *Alternatively*, purify astacin by chromatography on alumina/fibrous clay (1:4) or mixed chromatograms on sucrose using $*C_6H_6$/light petroleum 1:4 as eluant; or by partition between petroleum ether and MeOH (alkaline). It crystallises from pyridine/water in purple leaflets or needles with a metallic lustre. Store it in the dark under N_2 at -20°. It is very soluble in pyridine, dioxane, CS_2, $CHCl_3$ and dilute aqueous NaOH, slightly soluble in AcOH, EtOAc and $*C_6H_6$, but almost insoluble in H_2O, Et_2O, petroleum ether and MeOH. Its *diacetate (enol-acetate)*, obtained by Ac_2O/pyridine treatment at 25° for 34 hours has **m 232-233° (dec)** (from $CHCl_3$/EtOH, 1:5) or **235° (dec)** (from pyridine + H_2O), and forms violet/black needles with λ_{max} (pyridine) at 497mm (ε 109 x 10^3) and (EtOH) 474mm; the IR ($CHCl_3$) has ν_{max} at 1756 (ε 530), 1639 (ε 1150), 1555 and 972 cm^{-1}; the ^1H NMR (60MHz, $CDCl_3$, TMS) has δ at 1.35 (12H, C-1 Me_2 and C-1′ Me_2), 2.04 (6H, C-5 Me and C-5′ Me), 2.04 (6H, C-9 Me and C-9′ Me), 2.02 (6H, C-13 Me and C-13′ Me), and 2.29 (2 OAc) (14 olefinic H-7,7′, 8,8′, 10,10′, 11,11′, 12,12′, 14,14′, and 15,15′ are not included); and *m/z* 576 $M^{\cdot+}$. The *dipalmitate (enol-ester, **Astacein**)* has **m 121°**, and forms red square leaflets from petroleum ether. [Davis & Weedon *Proc Chem Soc* 182 *1960*, Widmer et al. *Helv Chim Acta* **65** 671 *1982*, Karrer et al. *Helv Chim Acta* **17** 412,745 *1934*, **18** 96 *1935*, **19** 479 *1936*, *Beilstein* H **30** 102, **7** III 4797.]

Astaxanthin (3,3'-dihydroxy-β,β-carotene-4,4'-dione) *[472-61-7]* **M 596.84, m 182-183°.** It is a potent antioxidant from marine alge, red yeast and other plant and marine animal sources. It was isolated from lobster eggs, is present in salmon, the red feathers of some birds (*Laniarius* spp, and flamingo), and occurs in flower petals of some *Ranunculaceae*. Racemic astaxanthin has been synthesised from astacene (see above) by reduction with KBH_4 to β, β-carotene-3,4,3′,4′-tetraol followed by oxidation with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone and purification by preparative TLC on Kieselgel (20%Me_2CO/light petroleum) to give ***(±)-astaxanthin*** **m 182-183°** as needles, after crystallisation from Me_2CO/light petroleum. It has λ_{max} (MeOH)

472mm, (hexane) 466-467mm, ($CHCl_3$) 485 and (CS_2) 503mm; the IR ($CHCl_3$) has ν_{max} at 3620, 3510, 1660, 1610 and 975 cm^{-1}; the ^1H NMR (60MHz, $CDCl_3$, TMS) has δ at 1.31 (6H, C-1 Me and C-1′ Me), 1.20 (6H, C-1 Me and C-1′ Me), 1.94 (6H, C-5 Me and C-5′ Me), 1.98 (12H, C-9 Me, C-9′ Me, C-13 Me and C-13′ Me), (14 olefinic H-7,7′, 8,8′, 10,10′, 11,11′, 12,12′, 14,14′, and 15,15′ are not included); and *m/z* 592.386 $M^{\cdot+}$. TLC in the above system or Micro-Cel did not separate it from natural (3*S*,3'*S*)-astaxanthin from the common lobster or sea water crayfish. Synthetic ***(±)-astaxanthin*** combined with the appropriate apoprotein to form **α-crustacyanin** with λ_{max} (MeOH) at 630mm. Its *diacetate* has **m 203-205°** (blue-black needles from pyridine/H_2O, **m 189-191°** also reported), λ_{max} ($CHCl_3$) with 482mm, and is also indistinguishable by mixed TLC on Kieselgel, Micro-Cel or alumina from natural **(3*S*,3'*S*)-astaxanthindiacetate, m 187-189°**. All manipulations have to be carried out under argon to avoid their ready oxidation to astacin (see above). [Cooper et al *J C S Perkin Trans I* 2195 1975, Kienzel & Mayer *Acta Chim Acta* **61** 2609 *1978*.]

An efficient synthesis of natural **(3*S*,3′*S*)-astaxanthin** from (4*R*,4′*R*)-4-hydroxy-2,2,6-trimethylcyclohexanone in 67% yield and high optical purity has been described and was purified by recrystallisation from CH_2Cl_2/MeOH to give dark violet crystals, **m 216-218°**, with R_F 0.30 on TLC with kieselgel (CH_2Cl_2/Me_2CO/HCOOH, 95:5:3); its **UV** has λ_{max} nm (ε), ($CHCl_3$) at 492 (1920), 488 (125,000), and (CH_2Cl_2) 324(14,500), 298 (15,500), ~285sh (~14,000), 251 (14,500), ~225 (~15,000); and **IR** (KBr) has ν_{max} at 3486m (OH), 1664s (C=O, conjugated), 1607m, 1557s (C=O, conjugated), 1399w, 1390m, 1366w (gem Me_2), 1076s, 1039m (OH) and 969s (CH=CH, *trans*) cm^{-1}. [Widmer et al. *Helv Chim Acta* **64** 2405 *1981*]. Other high yielding syntheses have been achieved [Becher et al. *Helv Chim Acta* **64** 2419 *1981*, Kienzle & Mayer *Helv Chim Acta* **61** 2609 *1978*], and the absolute configuration of natural *(3S,3′S)-astaxanthin*, **m 219-220°** has been determined by X-ray analysis of a crystalline synthetic intermediate [Widmer et al. *Helv Chim Acta* **64** 2405 *1981*] and comparison of CD spectra [Englert et al. *Helv Chim Acta* **60** 1209 *1977*]. Its **^1H NMR** (270MHz, $CDCl_3$, TMS) has δ for olefinic protons at 6.21 (H-7 and H-7′), 6.43 (H-8 and H-8′), 6.30 (H-10 and H-10′), 6.66 (H-11 and H-11′), 6.45 (H-12 and H-12′), ~6.30 (H-14 and H-14′) and ~6.68 (H-15 and H-15′) with $J_{7,8}$ or $J_{7',8'}$ = 16.3Hz, $J_{10,11}$ or $J_{10',11'}$ = 11.5Hz and $J_{11,12}$ or $J_{11',12'}$ = 14.7Hz; δ for Me groups at 1.21 and 1.32 (6H, C-1 Me and C-1′ Me), 1.95 (6H, C-5 Me and C-5′ Me), 2.00 (6H, C-9 Me and C-9′ Me), 1.99 (6H, C-13 Me and C-13′ Me); and δ for cyclohexenone protons at 1.82 (2H, axial H-2 and H-2′), 2.16 (2H, equatorial H-2 and H-2′), 4.32 (2H, H-3 and H-3′), and 3.70 (2H, 3-OH and 3′-OH, J = 1.8Hz,) with $J_{2,2\ (gem)}$ or $J_{2',2'\ (gem)}$ = 12.7Hz, $J_{2e,3a\ (vic)}$ = 5.7Hz and $J_{2a',3a'\ (vic)}$ = 14.0Hz, $J_{2e',3a'\ (vic)}$ = 5.7Hz and $J_{2a',3a'\ (vic)}$ = 14.0Hz; the **^{13}C NMR** (23MHz, $CDCl_3$, TMS) has δ for methyl group carbons at 12.8 (13,13′), 12.6 (9,9′), 13.9 (5,5′), 26.2 (1 or 1′), 30.8 (1′ or 1); for end group carbons 36.8 (1,1′), 45.6 (2,2′), 69.2 (3,3′), 200.3 (4,4′), 126.9 (5,5′), 162.4 (6,6′); and for olefinic carbons at 123.2 (7,7′), 142.2 (8,8′), 134.7 (9,9′), 135.1 (10,10′), 124.6 (11,11′), 139.7 (12,12′), 136.7 (13,13′), 133.8 (14,14′) and 130.7 (15,15′); and the **CD** spectrum in CH_2Cl_2 has λ_{max} ($\Delta\varepsilon$) at 224 (+12.8), 249 (–14.4), 280 (+ 12.5), 323 (–23.1), 384 (+6.7) and 521 (–3.2, very broad) [Englert et al. *Helv Chim Acta* **60** 1209 *1977*].

It is the prosthetic group in many carotenoproteins, mainly in invertebrates, which vary from colourless to bright blue. It reduces blood glucose and improves some parameters in diabetic metabolism. It ameliorates blood flow and vascular tone in hypertension model and regulates *connexin* 43 in *in vitro* studies, and may be a cancer chemopreventive drug. It is obtained on a large scale from the heterobasidiomycetous yeast *Phaffia rhodozyma* and plays an important role in carotene biosynthesis [Schroeder & Johnson *J Biol Chem* **270** 18374 *1995*].

Bixin (6,6'-diapo-ψ,ψ-carotenedioic acid monomethyl ester) *[6983-79-5]* **M 394.5, m 198°, 217°(dec), λ_{max} ($CHCl_3$) 209, 475 and 443nm, pK_{Est} ~4.3.** Crystallise bixin from Me_2CO (violet prisms) [Pattenden et al. *J Chem Soc (C)* 235 *1970*]. [*Beilstein* **2** III 2020, **2** IV 2455, H **30** 110.]

Canthaxanthin (*trans*) (β, β-carotene-4,4'-dione) *[514-78-3]* **M 564.9, m 211-212°, 213°, ε_{mol} 124,100 (at 466nm, petroleum ether), 118,000 (at 484nm *C_6H_6).** Purify canthaxanthin by chromatography on a column of deactivated alumina or magnesium oxide, or on a thin layer plate of silica gel G (Merck), using dichloromethane/diethyl ether (9:1) to develop the chromatogram. Crystallise it from CH_2Cl_2 or CH_2Cl_2/MeOH. Store in the dark and in an inert atmosphere at -20°. [*Beilstein* **7** III 4364, **7** IV 2680.]

Capsanthin [(3*R*,3′*S*,5′*R*)-3,3′-dihydroxy-β,κ-carotene-6-one) *[465-42-9]* **M 584.9, m 170°, λ_{max} 484 (ε_{mol} 121,000), inflexion at 515 nm, in hexane.** Possible impurities are zeaxanthin and capsorubin (below). Purify

capsanthin by chromatography on a column of alumina (grade IV) and develop with 0.2% EtOH in *C_6H_6. It crystallises from petroleum ether in red needles, IR has ν_{max} at 3600, 1664cm^{-1}, and $\varepsilon_{1033}/\varepsilon_{1664}$ ~ 4.1. [Baker et al. *J Chem Soc* 4019 *1961,* ORD & absolute config: Bartlett et al. *J Chem Soc (C)* 2527 *1969*.] The *di-O-acetate* is purified on an alumina (grade II) column in *C_6H_6 and it is recrystallised from MeOH with **m** 160-162°. [Faigle & Karrer *Helv Chim Acta* **44** 1257 *1961*, *Beilstein* **8** II 415, **8** III 3047, **8** IV 2657.]

Capsorubin (3,3'-dihydroxy-κ,κ-carotene-6,6'dione) *[470-38-2]* **M 604.9, m 218°, λ_{max} 443, 468, 503 nm, in hexane.** Possible impurities are zeaxanthin and capsanthin. Purify capsorubin by chromatography on a column of $CaCO_3$ or MgO. Crystallise it from *benzene/petroleum ether or CS_2. [*Beilstein* **1** III 3327, **8** III 3873, **8** IV 3304.]

α-Carotene (6′*R*-α-carotene) *[7488-99-5]* **M 536.9, m 184-188°, 187.5° (evacuated tube), $[\alpha]_{643}^{20}$ +385° (c 0.08, *C_6H_6), $[\alpha]_D^{25}$ +538°, λ_{max} 422, 446, 474 nm, in hexane, $A_{1cm}^{1\%}$ 2725 (at 446nm), 2490 (at 474nm), ε_{mol} 145,300 (at 455nm, hexane), and 456 (at 485nm, *C_6H_6).** Purify α-carotene by chromatography on columns of calcium hydroxide, alumina or magnesia. Crystallise it from CS_2/MeOH, toluene/MeOH, diethyl ether/petroleum ether, or acetone/petroleum ether. Store it in the dark, under N_2 or Ar at -20°. It gives a blue colour with λ_{max} at 542nm when mixed with $SbCl_3$ in $CHCl_3$. [Karrer & Walker *Helv Chim Acta* **16** 641 *1933*, Eugster et al. *Helv Chim Acta* **52** 1729 *1969*, Eugster & Karrer *Helv Chim Acta* **38** 610 *1955*, Strain *J Biol Chem* **105** 523 *1934*, *Beilstein* **5** III 2457, **5** IV 2620.]

all-*trans*-β-Carotene *[7235-40-7]* **M 536.9, m 178-179°, 179-180°, 180°, 181°, 183° (evacuated capillary), ε_{mol} 138,900 (at 450nm, petroleum ether), 124,300 (at 462nm, *C_6H_6).** It forms purple prisms when crystallised from *C_6H_6/MeOH and red rhombs from petroleum ether. Its solubility in hexane is 0.1% at 0°. It is **oxygen sensitive** and should be stored under N_2 at -20° in the dark. It gives a deep blue colour with λ_{max} at 590nm when mixed with $SbCl_3$ in $CHCl_3$. Its UV (*C_6H_6) has λ_{max} at 429infl, 454 and 484nm. The principal peak at 454nm has $A_{1cm}^{1\%}$ 2000. [Synthesis: Surmatis & Ofner *J Org Chem* **26** 1171 *1961*; Milas et al. *J Am Chem Soc* **72** 4844 *1950*.] β-Carotene is also purified by column chromatography (Al_2O_3 activity I-II). It is dissolved in petroleum ether/*C_6H_6 (10:1), applied to the column and eluted with petroleum ether/EtOH; the desired fraction is evaporated and the residue is recrystallised from *C_6H_6/MeOH (violet-red plates). [UV: Inhoffen et al. *Justus Liebigs Ann Chem* **570** 54, 68 *1950*; Review: Fleming *Selected Organic Synthesis* (J Wiley, Lond) pp. 70-74 *1973*.] *Alternatively*, it can be purified by chromatography on a magnesia column, thin layer of Kieselguhr or magnesia. Crystallise it from CS_2/MeOH, Et_2O/petroleum ether, acetone/petroleum ether or toluene/MeOH. Store it in the dark, under an inert atmosphere, at -20°. Recrystallise it also from 1:1 EtOH/$CHCl_3$. [Bobrowski & Das *J Phys Chem* **89** 5079 *1985*, Johnston & Scaiano *J Am Chem Soc* **108** 2349 *1986*, Strain *J Biol Chem* **105** 523 *1934*, *Meth Biochem Anal* **4** 1 *1957*, *Beilstein* **5** II 638, **5** III 2453, **5** IV 2617.]

δ-Carotene (6*R*-ε,ψ–carotene) *[472-92-4]* **M 536.9, m 140.4°, 142° (evacuated capillary) $[\alpha]_D^{25}$ +352° (c 16 hexane), $[\alpha]_{Cd}$ +317° (CS_2), λ_{max} 430, 456, 486nm (hexane).** δ-Carotene crystallises from CS_2/hexane/EtOH as red needles. The **racemic** carotene is purified through an alumina (Grade II) column by elution with 15% *C_6H_6/petroleum ether (b 60-80°), and the main band eluent is evaporated and the residue is crystallised from MeOH/petroleum ether (b 60-80°) to give δ-carotene with **m** 150-151°. [Porter & Anderson *Arch Biochem* **32** 21 *1951*, Synthesis: Manchand et al. *J Chem Soc* 2019 *1965*, Absolute Config: Buchecher & Eugster *Helv Chim Acta* **54** 327 *1971*, **5** III 2453, **5** IV 2617.]

γ-Carotene (β,ψ–carotene) *[472-93-5, 10593-83-6]* **M 536.9, m 152-153.5° (synthetic), 177.5° (polymorph), $A_{1m}^{1\%}(\lambda_{max})$ 2055 (at 437nm), 3100 (at 462nm), 2720 (at 494nm) in hexane.** Purify γ-carotene by chromatography on alumina [Grade II in petroleum ether (b 60-80°) and elute with *C_6H_6], or magnesia columns. When crystallised from *C_6H_6/MeOH (2:1), it had **m** 177.5°. Store it in the dark, under an inert atmosphere at 0°, or in an evacuated tube at -20°. The purity is verified by TLC on $Ca(OH)_2$/Kieselgel (8:2) using petroleum ether (b 60-80°) as eluant. [Manchand et al. *J Chem Soc* 2019 *1965*, *Beilstein* **5** III 2453, **5** IV 2617.]

ξ-Carotene *[38894-81-4]* **M 536.9, m 38-42°, λ_{max} 378, 400, 425nm, $A_{1m}^{1\%}(\lambda_{max})$ 2270 (400nm), in petroleum ether.** Purify ξ-carotene by chromatography on 50% magnesia-HyfloSupercel, developing with hexane and

eluting with 10% EtOH in hexane. It crystallises from toluene/MeOH. [Gorman et al. *J Am Chem Soc* **107** 4404 *1985*.] Store it in the dark under N_2 or argon at -20°. Also purify it like γ-Carotene. [*Beilstein* **5** IV 2623.]

Citranaxanthin [5,9,14,18-tetramethyl-20-(2,6,6-trimethyl-1-cyclohex-1-enyl)- 3,5,7,9, 11,13,15,17,19-eicosanonen-2-one] *[3604-90-8]* **M 456.7, m 155-156°, $A^{1\%}_{1m}(\lambda_{max})$ 410 (349nm), 275 (466nm) in hexane.** Purify it by chromatography on a column of 1:1 MgO and HyfloSupercel (diatomaceous filter aid). Crystallise it from petroleum ether. Store it in the dark under N_2 or argon at 0°.

Crocetin diethyl ester (8,8'-diapo-ψ,ψ-carotenedioic acid diethyl ester) *[5056-14-4]* **M 384.5, m 218-219°, 222.5°, $A^{1\%}_{1m}(\lambda_{max})$ 2340 (at 400nm), 3820 (at 422nm), 3850 (at 450nm) in petroleum ether.** Purify the diethyl ester by chromatography on a column of silica gel G. Recrystallise it from *benzene. Store it in the dark, under N_2 or argon, at 0°. [*Beilstein* **2** III 2018, H **30** 106.]

α-Cryptoxanthin (all-*trans*-3*R*,6*R'*-β, ε-carotene-3-ol, zeinoxanthin, physoxanthin) *[24480-38-4]* **M 552.9, m 175-176° (racemate 157.5-158.5°), $[\alpha]_D^{25}$ -508° (c 0.4 Me_2CO), CD$_{max}$ Δε -3.6 (218nm), +4.4 (245nm) and –9.0 (283nm), λ_{max} (hexane) 421, 446, 474nm, ε_{mol} 145,500 (at 446nm, hexane), 130,000 (at 459nm, *C_6H_6).** It crystallises from *C_6H_6/MeOH in red needles. The *racemate* is purified through an Al_2O_3 column, eluting with *C_6H_6 and recrystallising from MeOH/Et_2O. It has λmax (ε 10^{-3}) (hexane) at 421, 444, 471nm (90, 133, 122). [Loeber et al. *J Chem Soc (C)* 404 *1971*, Goodfellow et al. *J Chem Soc, Chem Commun* 1578 *1970*, *Beilstein* **6** IV 5113.]

β-Cryptoxanthin (all-*trans*-3*R*-β,β-carotene-3-ol, caricaxanthin) *[472-70-8]* **M 552.9, m 169° (natural), (racemate m 172-173°), ε_{mol} 131,900 (at 449nm, petroleum ether).** Purify it by chromatography on MgO, $CaCO_3$ or deactivated alumina, using EtOH or diethyl ether to develop the column. Crystallise it from *C_6H_6/EtOH (metallic prisms), or needles from *C_6H_6. Store it in the dark under N_2 or argon at -20°. The *acetate* has **m** 117.5°. The *racemate* is purified through a column of alumina (grade IV), eluted with *C_6H_6 then EtOAc/*C_6H_6 (1:9) and recrystallised from petroleum ether (b 60-80°) with **m** 172-173°. [Loeber et al. *J Chem Soc (C)* 404 *1971*, Goodfellow et al. *J Chem Soc Chem Commun* 1578 *1970,* Isler et al. *Helv Chim Acta* **40** 456 *1957*, *Beilstein* **6** III 3772, **6** IV 5111.]

3,30-Diketospirilloxanthin (all-*trans*-2,31-dimethoxy-2,6,10,14,19,23,27,31-octamethyl-4,6,8,10,12,-14,16,18,20,22,24,26,28-dotriacontatridecene-3,30-dione *[24009-17-4]* **M 624.9, m 225-227°, $\varepsilon^{1\%}_{1m}(\lambda_{max})$ 550 (at 349nm), 820 (at 422nm), 2125 (at 488nm), 2725(516nm), 2130(at 551nm) in hexane.** Purify it by chromatography on a column of partially deactivated alumina. Recrystallise it from acetone/petroleum ether. Store it in the dark, in an inert atmosphere at 0°. [cf *Beilstein* **1** III 2297, **1** IV 2750.]

Echinenone (β,β-caroten-4-one) *[432-68-8]* **M 550.8, m 178-179°, $A^{1\%}_{1m}(\lambda_{max})$ 2160 (at 458nm) in petroleum ether.** Purify β,β-caroten-4-one by chromatography on partially deactivated alumina or magnesia, or by using a thin layer plate of silica gel G with 4:1 cyclohexane/diethyl ether as the developing solvent. Recrystallise it from *C_6H_6/MeOH. Store it in the dark at -20°. The *oxime* crystallises from *C_6H_6 with **m** 208°. [*Beilstein* **7** III 2858, **7** IV 1881.]

Ethyl bixin (6,6'-diapo-Ψ,Ψ–carotenedioic acid monomethyl ester monoethyl ester) *[6895-43-8]* **M 436.6, m 138°.** Crystallise the ester from EtOH. [cf. *Beilstein* **2** III 2020, **2** IV 2356.]

Lutein See xanthophyll.

Lycopene (all-*trans*-Ψ,Ψ–carotene) *[502-65-8]* **M 536.9, m 172-173°, 174°, ε_{mol} 184,900 (470nm petroleum ether), 180,600 (at 487nm *C_6H_6).** Crystallise lycopene from CS_2/MeOH, diethyl ether/petroleum ether, or

acetone/petroleum ether. Also purify it by column chromatography on deactivated alumina, $CaCO_3$, calcium hydroxide or magnesia. It is oxygen sensitive and is stored in the dark, in an inert atmosphere. Also purified like γ-Carotene. [*Beilstein* **1** III 1076, **1** IV 1165.]

Lycoxanthin (all*trans*–Ψ,Ψ–carotene-16,16′-ol) *[19891-74-8]* **M 268.3, m 173-174°, $\varepsilon^{1\%}_{1cm}$ 3360 (472.5nm), also λ_{max} 444 and 503nm in petroleum ether.** Crystallise lycoxanthin from diethyl ether/light petroleum, *C_6H_6/petroleum ether or CS_2. Purify it also by chromatography on columns of $CaCO_3$, $Ca(OH)_2$ or deactivated alumina, and washing with *benzene and eluting with 3:1 *C_6H_6/MeOH. Store it in the dark, in an inert atmosphere, at -20°. The *dipalmitate ester* crystallises from *C_6H_6/MeOH and has **m** 76°. [*Beilstein* **1** III 2051, **1** IV 2368.]

Methylbixin (6,6′-diapo-Ψ,Ψ–carotenedioic acid dimethyl ester) *[26585-94-4]* **M 408.5, m stable *trans* form 203°, 205-206° (corr), unstable *cis* form 164°, λ_{max} 405, 425, 450, 484nm in hexane.** Crystallise the dimethyl ester from EtOH/$CHCl_3$, or *benzene. Also purify it by chromatography on alumina (Grade III) and eluting with 9:1 *C_6H_6/petroleum ether (b 60-80°), and recrystallise it from EtOAc. [Pattenden et al. *J Chem Soc (C)* 235 *1970*, *Beilstein* **2** III 2020, **2** IV 2356.]

Physalien (all-*trans* β-carotene-3,3'(*R,R*)-diol dipalmitate) *[144-67-2]* **M 1044, m 98.5-99.5°**, $A^{1\%}_{1m}(\lambda_{max})$ **1410 (at 449nm), 1255 (at 478nm) in hexane.** Purify it by chromatography on water-deactivated alumina, using hexane/diethyl ether (19:1) to develop the column. It crystallises from *benzene/EtOH in red needles. Store in the dark, in an inert atmosphere, at 0°. [See Zeaxanthin dipalmitate.] [*Beilstein* **6** III 5970.]

Phytoene (7,7′,8,8′,11,11′,12,12′-octahydro–ψ,ψ–carotene) *[540-04-5]* **M 544.9,** $A^{1\%}_{1m}(\lambda_{max})$ **850 (at 287nm) in hexane, λ_{max} 275, 287 and 297nm.** Purify phytoene by chromatography on columns of magnesium oxide-Supercel (a diatomaceous filter aid) or alumina [Rabourn et al. *Arch Biochem Biophys* **48** 267 *1954*]. Store it as a solution in petroleum ether under nitrogen at -20°. [*Beilstein* **1** IV 1155.]

Phytofluene (all-*trans*- 5,6,7,8,9,10,10′,9′,8′,7′,6′,5′-dodecahydrolycopene) *[540-05-6]* **M 549.0, b 140-185°(bath temperature)/0.0001mm,** $A^{1\%}_{1m}(\lambda_{max})$ **1350 (at 348nm) in petroleum ether, λ_{max} 331, 348, 267.** Purify it by chromatography on partially deactivated alumina [Goodwin *Biochem J* **53** 538 *1953*, Kushwaha et al. *J Biol Chem* **245** 4708 *1970*]. Store it as a solution in petroleum ether under N_2 at -20°. [*Beilstein* **1** III 1072, **1** IV 1159.]

Prolycopene (all-*cis* [*Z*]-ψ,ψ-carotene or lycopene) *[2361-24-2]* **M 536.5, m 111°, λ_{max} 443.5, 470nm in petroleum ether.** Purify prolycopene by chromatography on deactivated alumina [Kushwaha et al. *J Biol Chem* **245** 4708 *1970*]. Crystallise it from petroleum ether. Store it in the dark, under N_2 or argon at -20°. [*Beilstein* **1** III 1079, **1** IV 1167.]

Proneurosporene (3,4,7′,8′-tetrahydrolycopene) *[10467-46-6]* **M 538.9, λ_{max} 408, 432, 461 nm, $\varepsilon^{1\%}_{1cm}$ 2040 (at 432nm) in hexane.** Purify proneurosporene by chromatography on deactivated alumina [Kushwaha et al. *J Biol Chem* **245** 4708 *1970*]. Store it in the dark, in an inert atmosphere at 0°. [*Beilstein* **1** IV 1156.]

Retinol (vitamin A alcohol), retinoic acid (vitamin A acid), retinyl acetate (vitamin A acetate), retinal (vitamin A aldehyde) and **reinyl palmitate (vitamin A palmitate).** See in "Miscellaneous", this chapter.

Spirilloxanthin (rhodoviolascein) *[34255-08-8]* **M 596.9, m 216-218°, 218°, λ_{max} 463, 493, 528 nm, $\varepsilon^{1\%}_{1cm}$ 2680 (at 493nm) in petroleum ether (b 40-70°).** Spirilloxanthin crystallises from $CHCl_3$/petroleum ether, acetone/petroleum ether, *C_6H_6/petroleum ether or *C_6H_6 as deep red spindle-like crystals. Purify it also by chromatography on a column of $CaCO_3$/$Ca(OH)_2$ mixture, $Ca(OH)_2$ or deactivated alumina and elute it with a

*C_6H_6/MeOH mixture. It gives a blue colour with $SbCl_3$ in $CHCl_3$ with λ_{max} at 642nm. [Polgar et al. *Arch Biochem Biophys* **5** 243 *1944*, Synthesis: Surmatis & Ofner *J Org Chem* **28** 2735 *1963*, Karrer & Koenig *Helv Chim Acta* **23** 460 *1940*.] Store it in the dark in an inert atmosphere at -20°. [*Beilstein* **1** III 2297, **1** IV 2750.]

Squalane (Cosbiol, 2,6,10,15,19,23-hexamethyltetracosane, perhydrosqualene) *[111-01-3]* **M 422.8, m 7-38°, b 176°/0.05mm, 210-215°/1mm, 274°/10mm, ~350°/760mm, d_4^{20} 0.80785, n_D^{20} 1.416.** Purify squalane by fractional distillation *in vacuo* or evaporative distillation. It is soluble in petroleum ether, *C_6H_6, Et_2O and $CHCl_3$, slightly soluble in alcohols, Me_2CO and AcOH but insoluble in H_2O. Small quantities can be purified by TLC as for squalene below. It is used as a marker in GLC and HPLC. [Staudinger & Leupold *Helv Chim Acta* **15** 223 *1932*, Sax & Stross *Anal Chem* **29** 1700 *1951*, Mandai et al. *Tetrahedron Lett* **22** 763 *1981*, *Beilstein* **1** IV 593.]

Squalene (all-*trans*-2,6,10,15,19,23-hexamethyl-2,6,10,14,18,22-tetracosahexaene) *[111-02-4]* **M 410.7, m ~75°, b 203°/0.1mm, 213°/1mm, 285°/25mm, d^{25} 0.8670, n_D^{20} 1.4905.** Crystallise squalene repeatedly from Me_2CO (1.4ml/g) using a Dry-ice bath, wash the crystals with cold acetone, then freeze the squalene under vacuum. Squalene is further purified by passage through a column (or TLC plate) of silica gel or chromatographed on activated alumina, using petroleum ether as eluent and stored in a vacuum in the dark. Dauben et al. [*J Am Chem Soc* **74** 4321 *1952*] purified squalene *via* its *hexachloride* which is bactericidal. It is a key intermediate in sterol biosynthesis. [Capstack et al. *J Biol Chem* **240** 3258 *1965*, Krishna et al. *Arch Biochem Biophys* **114** 200 *1966*, Heilbron & Thompson *J Chem Soc* 883 *1929*, Karrer et al. *Helv Chim Acta* **13** 1084 *1930*, UV: Farmer et al. *J Chem Soc* 544 *1943*, *Beilstein* **1** III 1071.]

Violaxanthin (5*S*,6*S*,5′*S*,6′*S*-diepoxyzeaxanthin) *[126-29-4]* **M 600.9, m 200°, 207-208°, $[\alpha]_{Cd}^{18}$ +35° (c 0.1, $CHCl_3$).** Crystallise violaxanthin from MeOH (orange prisms) by adding a little Et_2O in MeOH, or CS_2 (red brown crystals). Also purify it by column chromatography, and the purity is checked by TLC (see δ-carotene). It has λ_{max} at 415, 440 and 469nm. [Kuhn & Winterstein *Ber* **64** 326 *1931*, Karrer et al. *Helv Chim Acta* **14** 1044 *1931*, Absolute Config: Bartlett et al. *J Chem Soc (C)* 2527 *1969*, *Beilstein* **19** III/IV 1139.]

Xanthophyll (Lutein, 3*R*,3′*R*-α-carotene-3,3′-diol) *[127-40-2]* **M 568.9, m 183°, 193°, 196°, $[\alpha]_{Cd}^{18}$ +165° (c 0.7, *C_6H_6)[NB: Cd I and II have λ 533 & 537 nm], $\varepsilon_{1cm}^{1\%}(\lambda_{max})$ 1750 (423nm), 2560 (446nm), 2340 (477.5nm) and ε_{mol} 144,800 (at 445nm) in EtOH; λ_{max} in CS_2 446, 479 and 511nm, and ε_{mol} 127,000 (at 458nm, *C_6H_6).** Crystallise lutein from MeOH (1g/700ml; copper-coloured prisms) or from diethyl ether by adding MeOH. Also purify it by chromatography on columns of magnesia or calcium hydroxide, and recrystallise it from CS_2/EtOH. It may be purified *via* the *dipalmitate ester* which crystallises from EtOH with **m** 92°. Store it in the dark, in an inert atmosphere, e.g. Ar. [Buchecker et al. *Helv Chim Acta* **57** 631 *1974,* Karrer *Helv Chim Acta* **34** 2060 *1951*, Absolute Config: Goodfellow et al. *J Chem Soc*, *Chem Commun* 1578 *1970*, *Beilstein* **6** II 1026, **6** III 5871, **6** IV 7017.]

Zeaxanthin [all *trans*-β-carotene-3,3'(*R,R′*)-diol] *[144-68-3]* **M 568.9, m 205-206° (natural), 207°, 215.5°, $[\alpha]_{Cd}^{18}$ -44° (c 0.7, $CHCl_3$), [NB: Cd I and II have λ 533 & 537 nm], λ_{max} 275nm (log ε 4.34), 450nm (log ε 5.14), 480nm (log ε 5.07) in EtOH, ε_{mol} 132,900 (at 452nm, Me_2CO).** Zeaxanthin forms yellow plates (with a blue lustre) from MeOH, EtOH and with 0.5 MeOH from *C_6H_6/MeOH. The *diacetate* (from natural) has **m** 154-155° (from CH_2Cl_2/MeOH), the UV has λ_{max} ($\varepsilon_{1cm}^{1\%}$) at 452, 480nm (2210, 1945). The *dipalmitate (Physalein)* (from natural source) has **m** 95-96° (from CH_2Cl_2/MeOH), the UV: λ_{max} ($\varepsilon_{1cm}^{1\%}$) at 452, 480nm (1335, 1190). [Isler et al. *Helv Chim Acta* **31** 2041 *1956*, Hlubeck et al. *J Chem Soc, Perkin Trans 1* 848 *1974*.] The *racemate* is purified by chromatography on an alumina (Grade IV) column by elution with a gradient of petroleum ether (b 60-80°), *C_6H_6 and EtOAc. The red band gives a solid which recrystallises from MeOH with **m** 211°, and the UV has λ_{max} at 439infl, 462, 589nm (ε 10^{-3}: 90, 126, 110 respectively). [Loeber et al. *J Chem Soc (C)* 404 *1971*, *Beilstein* **6** II 1026, **6** III 5865, **6** IV 7017.]

STEROIDS

This section also includes steroidal hormones, steroidal alkaloids and cardenolides.

(-)-3-β-Acetoxy-5-etienic acid [3-β-acetoxy-5-etiocholenic acid, androst-5-ene-17-β-carboxylic acid] *[51424-66-9]* **M 306.5, m 238-240°, 241-242°, 243-245°, 246-247°, $[\alpha]_D^{20}$ -19.9° (c 1, Me_2CO), -36° (c 1, dioxane), -33.5° ($CHCl_3$), pK_{Est} ~ 4.7.** The acid is purified by recrystallisation from Me_2CO, Et_2O/pentane, or AcOH, dried in a vacuum oven (105°/20mm) and sublimed at high vacuum. [Staunton & Eisenbram *Org Synth* **42** 4 *1962*, Steiger & Reichstein *Helv Chim Acta* **20** 1404 *1937*.]

21-Acetoxypregnenolone (3β-21-acetoxypregn-5-en-20-one) *[566-78-9]* **M 374.5, m 184-185°.** Crystallise 21-acetoxypregnenolone from Me_2CO by allowing the solvent to evaporate in a vacuum, then dry it *in vacuo*. The crystals become opaque on standing. [Steiger & Reichstein *Helv Chim Acta* **20** 1164 *1937*.]

Adrenosterone (Reichstein's G, androst-4-ene-3,11,17-trione) *[382-45-6]* **M 300.4, m 214-217°, 220-224°, 224-226°, $[\alpha]_{546}^{20}$ +364° (c 0.18, EtOH).** Dissolve adrenosterone in Me_2CO, decolorise it with charcoal, filter, add H_2O, Me_2CO evaporate and the solid is recrystallised from aqueous EtOH. Also recrystallise it from Et_2O or Et_2O/pentane and dry it at 110°/0.1mm for 2 hours. It can be sublimed under high vacuum. [Reichstein *Helv Chim Acta* **20** 953, 979 *1937*, Mason et al. *J Biol Chem* **116** 267 *1936*, *Beilstein* **7** III 4601.]

Aldosterone (18-aldocorticosterone) *[52-39-1]* **M 360.5, m 108-112°(hydrate), 164°(anhydrous), $[\alpha]_D^{25}$ +161° (c 1, $CHCl_3$).** Crystallise aldosterone from aqueous acetone. It exists in solution as an equilibrium mixture of free aldehyde and its cyclic hemiacetal, favouring the hemiacetal. The *21-acetate* crystallises from Me_2CO/Et_2O or CH_2Cl_2/EtOAc and has **m** 198-199°, $[\alpha]_D^{25}$ +121.7° (c 0.7, $CHCl_3$). [Barton et al. *J Chem Soc Perkin Trans 1* 2243 *1975*, *Beilstein* **8** IV 3491.]

5α-Androstane (etioallocholane) *[5α- 438-22-2, 24887-75-0]* **M 260.5, m 50-50.5°, $[\alpha]_D$ +2° (c 0.12, $CHCl_3$).** Purify 5α-androstane by chromatography through Al_2O_3 (grade III) and elute with petroleum ether and recrystallise from MeOH (2x) and Me_2CO/MeOH. It sublimes at 60°/high vacuum. Also dissolve it in petroleum ether, filter it through silica gel, evaporate and recrystallise it. [Steiger & Reichstein *Helv Chim Acta* **20** 817 *1937*, Prelog et al. *Helv Chim Acta* **27** 66 *1944*, IR, NMR: Halkes & Havinga *Rec Trav Chim, Pays Bas* **84** 889 *1965,* Allinger et al. *Tetrahedron* **27** 5073 *1971*, *Beilstein* **5** III 1110, **5** IV 1211.]

5β-Androstane (etiocholane, testane) *[438-23-3]* **M 260.5, m 78-79°, 78-80°, $[\alpha]_D^{20}$ +2.03°, $[\alpha]_{546}^{18}$ +5° (c 1, $CHCl_3$).** Crystallise etiocholane from acetone. The method of purification for 5α-androstane (above) could be used here. [Shoppee *Helv Chim Acta* **27** 246, 260 *1944*, Butenandt & Dannerbaum *Hoppe Seyler's Z Physiol Chem* **229** 192 *1934*, *Beilstein* **5** III 1110, **5** IV 1211.]

4-Androstene-3,17-dione (androstenedione) *[63-05-8]* **M 286.4, m 170-171°, 173-174°, $[\alpha]_D^{20}$ +196° (c 0.13, EtOH).** Crystallise the dione from hexane. It is soluble in $*C_6H_6$, $CHCl_3$ and EtOH. It has λ_{max} at 239nm. It is a precursor of estrone or testosterone and has androgenic activity. [Ruzicka & Wettstein *Helv Chim Acta* **18** 980 *1935*, *Beilstein* **7** III 3636, **7** IV 2381.]

Androsterone (*Cis*) (3α,5α-3-hydroxyandrostan-17-one) *[53-41-8]* **M 290.4, m 185-185.5°, $[\alpha]_{546}$ +118° (c 1, EtOH), $[\alpha]_D^{20}$ +94.6° (c 0.7, EtOH).** Crystallise androsterone from Me_2CO/Et_2O or Me_2CO and sublime it in high vacuum. The *acetate* [1164-95-0] crystallises from Et_2O, Me_2CO/Et_2O or aqueous EtOH and sublimes in high vacuum with **m** 165-166°, $[\alpha]_D^{25}$ +87° (c 2, EtOH). [Ruzicka *Helv Chim Acta* **17** 1389 *1934*, Marker *J Am Chem Soc* **57** 1755 *1935*, Göndös & Orr *J Chem Soc Chem Commun* 1239 *1982*, *Beilstein* **8** IV 462.]

***epi*-Androsterone (*Trans*)** *[481-29-8]* **M 290.4, m 172-173°, (161-162° *dl*-), $[\alpha]_{546}$ +115° (c 1, MeOH), $[\alpha]_D^{20}$ +44.4° (c 0.27, $CHCl_3$).** Purify *epi*-androsterone *via* the acetate, hydrolyse this and recrystallise it from $CHCl_3$/hexane or aqueous EtOH. The *acetate* [1239-31-2] is purified by chromatography and when crystallised

from petroleum ether has **m** 103-104°, $[\alpha]_D$ +68.5° (c 1, $CHCl_3$). The *oxime* has **m** 194-196° (from MeOH), $[\alpha]_D$ +17.5° (c 6.2, $CHCl_3$). The **racemic ketone** is sublimed at 130°/high vacuum and after two crystallisations from methylcyclohexane it gives prisms with **m** 161-162° (which changed crystal form at 140-145°). [Ruzicka & Wettstein *Helv Chim Acta* **18** 1264 *1935*, Johnson et al. *J Am Chem Soc* **75** 2275 *1953,* **78** 6331 *1956*, Cordwell et al. *J Chem. Soc* 361 *1953*, *Beilstein* **8** IV 462.]

Betamethasone (9α-fluoro-11β,17α,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione) *[378-44-9]* **M 392.5, m 231-136°(dec), 235-237°(dec), $[\alpha]_D^{20}$ +108° (c 1, Me_2CO).** Betamethasone crystallises from ethyl acetate, and has λ_{max} at 238nm (log ε 4.18) in MeOH. The *21-acetate* [287-24-6] crystallises from Me_2CO/Et_2O (charcoal) **m** 196-201° (205-208°) and has $[\alpha]_D^{20}$ +140° ($CHCl_3$). [Taub et al. *J Am Chem Soc* **82** 4012 *1960*, Olivetto et al. *J Am Chem Soc* **80** 6688 *1958*, *Beilstein* **8** IV 3501.]

Bisnorcholanic acid (pregnane-20-carboxylic acid) *[28393-20-6]* **M 332.5, m 214° (α-form), 242° (β-form), 210-211° (γ-form), 184° (δ-form), 181° (ε-form), pK_{Est} ~5.0.** Bisnorcholanic acid crystallises from EtOH (α-form), or acetic acid (all forms). The α-form has $[\alpha]_D^{20}$ -7.5° (c 0.8, EtOH), and its *ethyl ester* has **m** 106-107°; the β-form has $[\alpha]_D^{20}$ +23.3° (c 0.86, EtOH), and its *ethyl ester* is an oil; the γ-form has $[\alpha]_D^{20}$ 0°, and its *ethyl ester* has **m** 82-83°; the δ-form has $[\alpha]_D^{20}$ +31.7° (c 0.76, EtOH), and its *methyl ester* has **m** 99°; the ε-form has $[\alpha]_D^{20}$ +14.3° (c 0.8, EtOH), and its *methyl ester* has **m** 117°. [Wieland et al. *Hoppe Seyler's Z Physiol Chem* **161** 80 *1926*, *Beilstein* **9** III 2650.]

Brassicasterol [24β(*R*)-methylcholesta-5,22*E*-dien-3β-ol, 5,22-cholestadien-24β(*R*)-methyl-3β-ol, 24*R*-Ergosta-5,22*E*-dien-3β-ol] *[474-67-9]* **M 398.7, m 148°, 149-150°, 157-158°, $[\alpha]_D^{20}$ –60°, –66°, (c 1.2, $CHCl_3$).** It is purified from the 7,22*E*-isomer, which is formed during synthesis, by TLC on Silica Gel G-Celite (1:1) with 30% EtOAc/hexane as eluant and recrystallised from MeOH or EtOH [Anastasia et al. *J C S Perkin I* 379 *1983*]. In a different synthesis from enantiomeric 23,24-cyclopropane precursor 3β-acetates, [*22E*,24β(*R*)-3β-*brassicasteryl acetate* **m 152-154°**], is obtained and purified by HPLC [using two *Altex Ultrasphere*™ ODS columns 5µm (10mm id x 25cm) and MeOH mobile phase], has t_R = 118 minutes and crystallises from MeOH. The *acetate* has the ^{1}H NMR (360MHz, $CDCl_3$, TMS) with δ at 5.37 (m, 1H, H-C6), 5.18 (m, 2H, H-C22 and H-C23), 4.60 (m, 1H, H-C3), 2.03 (s, 3H, $OCOCH_3$), 1.02 (s, 3H, H_3C19), 1.01 (d, 3H, *J* = 6.49Hz, H_3C21), 0.91 (d, 3H, *J* = 6.80Hz, H_3C28), 0.83 (d, 3H, *J* = 6.5Hz) and 0.83 (d, 3H, *J* = 6.5Hz, H_3C26), 0.81 (d, 3H, *J* = 6.5Hz, H_3C27), 0.69 (s, 3H, H_3C18); and HRMS *m/z* 380.3452 (100, *M*-HOAc), $C_{28}H_{44}^+$ requires 380.3443. [Lang & Djerassi *Helv Chim Acta* **65** 407 *1982*, Rubinstein et al. *Phytochemistry* **15** 195 *1976*.] The *acetate* (5mg) in dry Et_2O is de-acetylated with LAH (4 fold) at ~25°/30 minutes, excess LAH is decomposed with saturated aqueous Na_2SO_4, H_2O is added and the free sterol is extracted into Et_2O, dried (Mg_2SO_4), evaporated and the residue is recrystallised from MeOH to give pure (22,24*R*)-*brassicasterol* **m 156-158°**, with one peak in HPLC (as above but with an ODS-2 column) at t_R = 55 minutes. Its ^{1}H NMR (360MHz, $CDCl_3$, TMS) has δ at 5.35 (m, 1H, H-C6), 5.181 (m, 2H, H-C22 and H-C23), 3.53 (m, 1H*ax*, H-C3), 1.011 (d, 3H, *J* = 6.34Hz, H_3C21), 1.010 (s, 3H, H_3C19), 0.910 (d, 3H, *J* = 6.84Hz, H_3C28), 0.834 (d, 3H, *J* = 6.10Hz) and 0.817 (d, 3H, *J* = 6.22Hz, H_3C26), 0.815 (d, 3H, *J* = 6.22Hz, H_3C27), 0.693 (s, 3H, H_3C18); and the HRMS has *m/z* at 398.3545 ($M^{\cdot+}$), $C_{28}H_{46}O$ requires 398.3549. [Lang & Djerassi *Helv Chim Acta* **65** 407 *1982*, Rubinstein et al. *Phytochemistry* **15** 195 *1976*, Sheikh & Djerassi *Steroids* **26** 129 *1975*.]
It is a plant sterol (phytosterol) present in canola oils and rape seed but is also found in some marine algae, diatoms and shellfish (oysters). It inhibits the enzyme Δ^{24}-sterol reductase that is involved in mammalian cholesterol biosynthesis [Fernandez et al. *Biochem J* **336** 109 *2002*]. Brassino steroids have plant growth regulating activities [Anastasia et al. *J C S Perkin I* 379 *1983*.]

Crinosterol [24α(*S*)-methylcholesta-5,22*E*-dien-3β-ol, 5,22-cholestadien-24α(*S*)-methyl-3β-ol, 24*S*-Campesta-5,22*E*-dien-3β-ol] *[17472-78-5]* **M 398.7, m 147-148°, 152-154° $[\alpha]_D^{26}$ –47.2° (c 1.2, $CHCl_3$).** Crinosterol occurs in sponges, oysters and in diatoms. It is the 24-**α**–methyl epimer of Brassicasterol (see [474-67-9] above). They sometimes occur together in Nature and sometimes are formed together in synthesis; purification of one invariably requires the removal of the other. ***Crinosteryl acetate* m 148-150°**, when isolated from a synthesis was separated from the 24-**β**-methyl epimer by HPLC (see brassicalsterol above), had t_R = 112 minutes, and was recrystallised from MeOH, or *alternatively*, it is prepared by acetylation of crinosterol, then

purified by TLC (10% w/w $AgNO_3$/silica gel and developed with pure $CHCl_3$) to give homogeneous (by GLC) *acetate* with **m 157-158°** (compare with above). Crinosteryl acetate has IR (Nujol) with ν_{max} at 1720, 970, 955 and 795 cm^{-1}, and the ^1H NMR (360MHz, $CDCl_3$, TMS) with δ at 5.375 (m, 1H, H-C6), 5.160 (m, 2H, H-C22 and H-C23), 4.601 (m, 1H*ax*, H-C3), 2.033 (s, 3H, $OCOCH_3$), 1.019 (s, 3H, H_3C19), 1.002 (d, 3H, *J* = 6.68Hz, H_3C21), 0.909 (d, 3H, *J* = 6.78Hz, H_3C28), 0.835 (d, 3H, *J* = 6.52Hz) and 0.817 (d, 3H, *J* = 6.63Hz, H_3C26), ~0.815 (d, 3H, *J* = 6.6Hz, H_3C27), 0.690 (s, 3H, H_3C18); and HRMS *m/z* 380.3420 (100, *M*-HOAc), $C_{28}H_{44}$ requires 380.3443. [Lang & Djerassi *Helv Chim Acta* **65** 407 *1982*, Anastasia et al. *J Chem Soc, Perkin I* 379 *1983*, Rubinstein et al. *Phytochemistry* **15** 195 *1976*]. Deacetylation with LAH (see brassicasterol above) gives ***crinosterol*** which is purified by TLC (silica gel developed with 2% v/v EtOH/$CHCl_3$) has **m 152-154°** (reported twice, and **147-148°** reported twice, both recrystallised from MeOH or Me_2CO), and has ^1H NMR (360MHz, $CDCl_3$, TMS) has δ at 5.349 (m, 1H, H-C6), 5.162 (m, 2H, H-C22 and H-C23), 3.53 (m, 1H*ax*, H-C3), 1.010 (s, 3H, H_3C19), 1.001 (d, 3H, *J* = 6.21Hz, H_3C21), 0.910 (d, 3H, *J* = 6.86Hz, H_3C28), 0.836 (d, 3H, *J* = 6.45Hz) and 0.817 (d, 3H, *J* = 6.62Hz, H_3C26), 0.815 (d, 3H, *J* = 6.62Hz, H_3C27), 0.693 (s, 3H, H_3C18); and HRMS *m/z* 398.3551 ($M^{\cdot+}$), $C_{28}H_{46}O$ requires 398.3549. [Lang & Djerassi *Helv Chim Acta* **65** 407 *1982*, Anastasia et al. *J Chem Soc. Perkin I* 2365 *1983*, Rubinstein et al. *Phytochemistry* **13** 485 *1974*, Rubinstein et al. *Phytochemistry* **15** 195 *1976*]. Brassino steroids have plant growth regulating activities [Anastasia et al. *J C S Perkin I* 379 *1983*].

Campesterol (24*R*-24-methylcholest-5-en-3β-ol) *[474-62-4]* **M 400.7, m 156-159°, 157-158°, $[\alpha]_D^{24}$ -35.1° (c 1.2, $CHCl_3$).** Campesterol is recrystallised twice from hexane and once from Me_2CO. The *benzoyl* derivative has **m** 158-160° $[\alpha]_D^{23}$ -8.6° ($CHCl_3$), and the *acetyl* derivative has **m** 137-138° (EtOH) and $[\alpha]_D^{23}$ -35.1° (c 2.9, $CHCl_3$) [Fernholz & MacPhillamy *J Am Chem Soc* **63** 1155 *1941*]. [*Beilstein* **6** III 2680.]

CHAPS (3-[(3-cholamidopropyl)dimethylammonio] -1-propanesulfonate betaine) *[75621-03-3 anhydrous], [313223-04-0 hydrate]* **M 614.89, m 157°(dec), $pK_{Est(1)}$ ~<2 (acidic), $pK_{Est(2)}$ ~10 (basic).** Triturate this zwitterionic detergent (~50g) with MeOH (200ml), then triturate it with Me_2CO (500ml), collect it by vacuum filtration and dry it thoroughly at ~20°. Recrystallise it at 0° from absolute MeOH followed by drying *in vacuo* to constant weight. It should give one spot with R_F 0.32 by TLC on silica gel G in 95% MeOH/5% NH_4OH and visualised with iodine vapour; the tertiary amine precursor has R_F 0.40. It has low UV absorption (1% in H_2O: A280nm is 0.029 and A260nm is 0.035), and the CMC (critical micellar concentration) is 8mM. It is soluble in H_2O, MeOH, Me_2SO but insoluble in Me_2CO, MeCN, hexane, toluene and xylene. [Hjelmeland et al. *Anal Biochem* **130** 72 *1983*, Matuo et al. *Methods Enzymol* **198** 155 *1991*.]

CHAPSO (3-[(3-cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate betaine) *[82473-24-3]* **M 630.89, m 184-196°, $[\alpha]_D^{20}$ +19° (c 2, H_2O), $pK_{Est(1)}$ ~<2 (acidic), $pK_{Est(2)}$ ~9 (basic).** Dissolve this zwitterionic detergent (~ 60g) in 40% aqueous MeOH and stir it with the mixed-bed ion-exchange resin RG-501 x 8 (100g, Bio-Rad) until the pH of the supernatant is ~ 7. Filter off the resin and evaporate the filtrate to dryness under reduced pressure. Check for homogeneity by TLC on silica gel G in 95% MeOH/5% NH_4OH and visualize the spot with iodine vapour (see CHAPS above). [Hjelmeland et al. *Anal Biochem* **130** 72 *1983*, Matuo et al. *Methods Enzymol* **198** 155 *1991*.]

Chenodeoxycholic acid (chenodiol, 3α,7α-dihydroxycholan-24-oic acid) *[474-25-9]* **M 392.6, m (119°), 143°, 165-167°, $[\alpha]_{546}^{20}$ +14° (c 2, EtOH), pK_{Est} ~4.9.** This major bile acid in vertebrates (~80mg) is chromatographed on silica gel (5g) and eluted with $CHCl_3$/EtOAc (3:2) and crystallised from EtOAc/hexane. It has IR with ν_{max} at 1705 cm^{-1}($CHCl_3$). It also crystallises from EtOAc, EtOAc/heptane after purifying *via* the poorly soluble Na and K salt if necessary. [Kametani et al. *J Org Chem* **47** 2331 *1982*, *Beilstein* **10** IV 1604.]

5α-Cholanic acid (allocholanic acid) *[546-98-4]* **M 360.6, m 170, $[\alpha]_D^{20}$ +22° ($CHCl_3$), pK_{Est} ~4.9**. Purify 5α-cholanic acid by chromatography on silica gel and eluting with MeOH/EtOAc/hexane (1:5:10) and recrystallising from Et_2O/hexane, MeOH or AcOH. The *methyl ester* has **m** 91° (from MeOH) and ^1H NMR ($CDCl_3$) has δ for C18 & C19 at 0.66 and 0.78 [see 5β-cholanic acid below**,** Mandava et al. *Steroids* **23** 357 *1974*]. [Demir et al. *Org Prepn Proced Int* **19** 197 *1987*, Stoll et al. *Helv Chim Acta* **18** 644 *1935*, *Beilstein* **9** III 2656, **9** IV 1992.]

5β-Cholanic acid (ursocholanic acid) *[546-18-9, 25312-65-6]* **M 360.6, m 164-165°, $[\alpha]_D^{20}$ +21.7° ($CHCl_3$), pK_{Est} ~4.9.** Crystallise 5β-cholanic acid from EtOH, Me_2CO or AcOH. The *ethyl ester* has **m** 93-94° (from 80% EtOH), **b** 273°/12mm, $[\alpha]_D^{20}$ +21° ($CHCl_3$), and the *methyl ester* has **m** 86-87° (from MeOH) after purification through Al_2O_3 and eluting with $*C_6H_6$, and $[\alpha]_D^{20}$ +21.2° ($CHCl_3$). The ^1H NMR ($CDCl_3$) for the C18 & C19 protons has δ at 0.65 and 0.92 [see 5α-cholanic acid above, Mandava et al. *Steroids* **23** 357 *1974*]. [Stoll et al. *Helv Chim Acta* **18** 644 *1935*, Huang-Minlon *J Am Chem Soc* **71** 330 *1949*, *Beilstein* **9** III 2656, **9** IV 1992.]

Cholesta-3,5-diene *[747-90-0]* **M 368.6, m 77-78°, 78°, 78-79°, 79-80°, 79.5-80.5°, 80-81°, $[\alpha]_D^{16}$ –116° (c 1.1, $CHCl_3$).** This diene has been prepared in many ways but several of these are from solvolysis of epicholesteryl toluene-*p*-sulfonate using KOAc/Ac_2O (38 hours at 75°), methanolic KOAc (reflux at 3.5 hours), LAH/Et_2O (20 hours at 20°) in *ca* 60% yield [Schmid & Kägi *Helv Chim Acta* **35** 2194 *1952*], AgOAc/AcOH, KOAc/MeOH or KOAc/AcOH (reflux ~3 hours 92-99% yield), neutralised Al_2O_3 at 20° [Evans & Shoppee *J Chem Soc* 540 *1953*, Shoppee et al. *J Chem Soc* 2876 *1955*], KOAc/aqueous Me_2CO [Becker & Wallis *J Org Chem* **20** 353 *1955*], and diphenylguanidinium salts accelerate solvolysis [Shoppee & Williams *J Chem Soc* 686 *1955*]. After the usual workup involving washing with $NaHCO_3$ and H_2O, the diene is separated from other steroids and impurities by chromatography through Al_2O_3 (various grades, including activity II-III, neutralised, basic or activated at 250-310°) and usually eluted with pentane, pentane/$*C_6H_6$ or Et_2O/MeOH. It is then recrystallised from Me_2CO, Et_2O/MeOH or Et_2O/EtOH, dried *in vacuo* and stored at –20°. The UV has λ_{max} (log ε) at 228.5 (4.308), 235 (4.344) and 243 (4.163) nm.

Cholesta-5,7-dien-3β-ol (7-dehydrocholesterol, 3β-hydroxy-5,7-cholestadiene, Provitamin D_3) *[434-16-2]* **M 384.6, m 150-151° (anhydrous), 148-152°, $[\alpha]_D^{20}$ –113.6° (c 1, $CHCl_3$), $[\alpha]_D^{20}$ –127° ($*C_6H_6$).** It occurs in humans and higher animals, and has been isolated from pig skin or the horned snail (*Buccinum undatum*). It is purified by recrystallisation from MeOH, Et_2O/MeOH or aqueous Et_2O (plates) and holds to H_2O tenaciously. It is insoluble in H_2O but is soluble in most organic solvents. Store it at -20° in the dark and absence of air which oxidises it slowly. Irradiation with UV light produces vitamin D_3 and like all provitamin D have λ_{max} at 260, 270, 281 and 293.5 nm. The *acetate* [1059-86-5] has **m 129-130°, $[\alpha]_D^{20}$ –85.3° (c 1.2, $*C_6H_6$),** crystallises from MeOH, and the *benzoate* has **m 139-140°, $[\alpha]_D^{20}$ –53.2° (c 1.2, $CHCl_3$)**, and crystallises from $CHCl_3$/Me_2CO in plates. [Bernstein et al. *J Org Chem* **14** 443 *1949*, *Beilstein* **6** IV 4153].

Cholesta-5,7-dien-3α-ol, [5765-84-0] **m 125-126°, $[\alpha]_D^{20}$ –70.5° ($CHCl_3$)**, crystallises from MeOH in needles, and its *acetate*, **m 114.5°, $[\alpha]_D^{20}$ –35° ($CHCl_3$)**, also crystallises from MeOH in needles. [Aberhart et al. *J Org Chem* **41** 1067 *1976*]. [for NMR of steroids see Kirk et al. *J Chem Soc Perkin Trans 2* 1567 *1990*, and Anastasia et al. *Steroids* **49** 543 *1987*, and for ORD see Weiss et al. *Tetrahedron* **21** 3105 *1965*].

Cholesta-5,24-dien-3β-ol (Desmosterol, 24-dehydrocholesterol, 3β-hydroxy-5,24-cholestadiene, natural 3β,20*R*-form) *[313-04-2]* **M 384.6, m 117-118°, 119-119.5°, 120.5-121°, 121.5°, 121.5-122.5°, $[\alpha]_D^{20}$ –38.2° (c 1.14, $CHCl_3$).** It occurs in chick embryos, rat skins, red algae, barnacles and *Funtmia latifolia* seeds. This is a useful intermediate for the synthesis of vitamin D metabolites [Koreeda et al. *J Org Chem* **45** 1172 *1980*]. The sterol in hexane can be purifed by chromatography on a $AgNO_3$/silicic acid/Super-Cel column in $*C_6H_6$, then re-chromatographed on Alumina F20, eluting with $*C_6H_6$ followed by $*C_6H_6$/EtOAc (1:1 v/v) and recrystallised from distilled MeOH or from Me_2CO/MeOH. It has IR (KBr) with ν_{max} at 1373, 1056, 1022, 959, 950, 835 and 800 cm^{-1}; and HRMS has *m/z* 384.3421 ($M^{\cdot+}$), $C_{27}H_{44}O$ requires 384.3389 [Apfel *J Org Chem* **43** 2284 *1978*]. The ***acetate*** [2665-04-5] **m 99°, $[\alpha]_D^{28}$ –44.8° (c 1, $CHCl_3$)**, can be obtained by refluxing 3-chlorocholesta-5,24-diene with AcOH/AcOK for 2.5 hours, cooling, adding H_2O, extracting with Et_2O, drying ($MgSO_4$), evaporating the extract, followed by chromatography through silica gel, eluting with $*C_6H_6$, evaporating and the white crystalline residue is recrystallised from Me_2CO/MeOH. The acetate has ^1H NMR (60MHz, CCl_4, TMS) with δ at 0.68 (s, 3H, H_3C18), 0.98 (s, 3H, H_3C19), 1.00 (s, 3H, H_3C21), 1.58 (s, 3H, H_3C26 or H_3C27), 1.65 (s, 3H, H_3C27 or H_3C26), 1.94 (s, 3H, 3-$OCOCH_3$), 4.50 (m, 1H*ax*, H-C3), 5.00 (m, H, H-C24) and 5.35 (m, 1H, H-C5). Hydrolysis of the acetate with MeOH/KOH gave *desmosterol* with **m 119-120°, $[\alpha]_D^{28}$ –41° ($CHCl_3$)**. [Ochi et al. *Steroids* **30** 795 *1977*]. *Desmosterol* has also been obtained from the readily available 3-hydroxy-bisnorcholenic acid in several synthetic steps and finally *via* the 3-tetrahydropyranyl ether which was hydrolysed in THF containing a few drops of concentrated HCl at 40°/5 minutes to give the *sterol* **m 120-122°** in 70% yield

after recrystallisation from MeOH. It has ^{1}H NMR (60MHz, $CDCl_3$, TMS) with δ at 0.41 (s, H_3C18), 0.51 (d, *J* = 6Hz, H_3C21), 0.61 (s, H_3C19), 1.97 and 1.02 (2s, H_3C26, H_3C27), 2.10 (1H*ax*, H-C3), 3.03 (24-H) and 3.20 (6-H). [Dasgupta et al. *J Org Chem* **39** 1658 *1974*.] Store it at –20°.
Cholesta-5,24-dien-3α-ol *[67392-80-7]* **M 384.6,** has **m 137-139°** (from MeOH), **$[\alpha]_D^{28}$ –43.5° ($CHCl_3$)**, and its ***acetate*** *[67383-62-4]* **M 426.6,** has **m 112-115°** (from MeOH), **$[\alpha]_D^{28}$ –47.5° ($CHCl_3$)**.
The **3β,20*S*-form** *[59532-46-6]* **M 384.6,** has **m 125-127°** (from MeOH), obtained by dehydration of 20*S*-3β,25-dihydroxycholest-5-ene with dioxane/H_2SO_4 (50% yield) has IR (KBr) with ν_{max} at 3000 (OH) cm^{-1}, and ^{1}H NMR (60MHz, $CDCl_3$, TMS) with δ at 0.70 (s, H_3C18), 0.84 (d, H_3C21), 1.02 (s, H_3C19), 1.62 and 1.70 (2s, H_3C26, H_3C27). It is an inhibitor of the cholesterol side-chain cleavage enzyme system in bovine adrenocortical preparations. [Bernstein et al. *Steroids* **27** 361 *1976*.]

5α-Cholestane *[481-21-0]* **M 372.7, m 80°, 80-80.5°, $[\alpha]_{546}^{20}$ +29.5°, $[\alpha]_D^{20}$ +24°, $[\alpha]_D^{18}$ +30.2°, (c 2, $CHCl_3$).** 5α-Cholestane is prepared by catalytic reduction of cholestene EtOAc/PtO_2/H_2, and recrystallised from EtOAc or Et_2O/EtOH. Store at room temperature. The ^{1}H NMR (100MHz, $CDCl_3$, TMS) signals of the methyl groups have δ at 0.645 (s, 13-Me), 0.778 (s, 10-Me), 0.898 (, *J* = 6.0Hz, 20-Me) and 0.861 (d, *J* = 6.3Hz, 25-Me_2) [Wittstruck et al. *J Chem Soc, Perkin Trans I* 1403 *1977*], and its CD in hexane has a Δε value of +0.5 at the longest wavelength of 183nm [Kirk et al. *Tetrahedron Lett* 1355 *1973*]. Note that catalytic hydrogenation of cholest-4-ene in acidic medium provides 5-α-cholestane whereas hydrogenation in neutral media results in 5-β-cholestane [Windaus *Chem Ber* **52** 170 *1919*]. [Ruzicka et al. *Helv Chim Acta* **16** 327, 334 *1933, Beilstein* **5** III 1132, **5** IV 1227.]

5β-Cholestane (coprostane, *ψ*-cholestane, pseudocholestane) *[481-20-9, 25269-18-5 + 21 other numbers + 105308-41-6]* **M 372.7, m 70°, 71-72°, $[\alpha]_D^{20}$ +25° (c 2, $CHCl_3$).** Catalytic hydrogenation (Pt_2O/Et_2O) of 3-chlorocholest-4-ene followed by crystallisation from Me_2CO [Young et al. *J Am Chem Soc* **81** 1452 1959], or catalytic reduction (Pt_2O/Et_2O) followed by chromatography through an Al_2O_3 column and eluting with petroleum ether followed by recrystallisation of the residual oil from Et_2O/EtOH give high yields of coprostane [Nickson & Bagli *J Am Chem Soc* **83** 1498 *1961*] (see previous entry). It also recrystallises in needles from EtOH. Store it at room temperature. Its CD in hexane has a Δε value of +1.1 at the longest wavelength of 184nm (see previous entry) [Kirk et al. *Tetrahedron Lett* 1355 *1973*].

5α-Cholestan-3β-ol (β-cholestanol, dihydrocholesterol) *[80-97-7]* **M 388.7, m 142-143°(monohydrate), $[\alpha]_{546}^{20}$ +28° (c 1, $CHCl_3$), $[\alpha]_D$ +27.4° (in $CHCl_3$).** Purify 5-α-cholestan-3ß-ol *via* acetylation, crystallisation and de-acetylation, then recrystallisation from EtOH or slightly aqueous EtOH, or MeOH. Its solubility is: 0.5% (MeOH) and 1% (EtOH) at 25°. [Mizutani & Whitten *J Am Chem Soc* **107** 3621 *1985*.] The *acetate* has **m** 114-115° from EtOAc/MeOH and $[\alpha]_D^{20}$ +13° (c 2, $CHCl_3$). [Bruce & Ralls *Org Synth* Col Vol **II** 191 *1943, Beilstein* **6** IV 3577.]

5β-Cholestan-3α-ol (Epicoprostanol, epi-5β-cholestanol) *[516-88-7]* **M 388.7, m 115-116°, 116-117°, 118°, $[\alpha]_D^{20}$ +32° (c 1.8, $CHCl_3$).** It is the main product from the acetolysis of 3β-chlorocoprostane (KOAc/AcOH, reflux for 6 hours) involving a Walden inversion, and purified as in the following entry [Bridgewater & Shoppee *J Chem Soc* 1709 *1953*]. It has also been obtained by reduction of 5β-coprostan-3-one with LAH to give a 94% yield of epicoprostanol m 115-116°, which did not form a precipitate with digitonin, and the small amount of digitonide formed gave a small quantity of coprostanol m 100° (~4% yield and crystallised from MeOH, see below) [Shoppee & Summers *J Chem Soc* 687 *1950*]. *Alternatively*, the residue is purified as described in the succeeding entry or recrystallised from Me_2CO or Et_2O/*C_6H_6 to give the desired **3α-ol**, after drying *in vacuo* at 80°. Note that crystals from EtOH have **m 115-116°**, and from Me_2CO have **m 117-118°**. Store it at room temperature. The *3α-yl-acetate* (obtained by catalytic reduction of coprostan-3-one, Et_2O/MeOH/PtO_2/H_2, followed by chromatographic separation as below and acetylation) has **m 87-89°**, **89-91°**, **$[\alpha]_D^{18}$ +42° (c 1.42, $CHCl_3$)**. [Shoppee & Summers *J Chem Soc* 687 *1950*, Ruzicka et al. *Helv Chim Acta* **17** 1407 *1934*.]

5β-Cholestan-3β-ol (coprostan-3β-ol) *[360-68-9]* **M 388.7, m 100-101°, 101°, $[\alpha]_D^{20}$ +28° (c 1.8, $CHCl_3$).** It is the main product from the acetolysis of 3α-chlorocoprostane (KOAc/AcOH, reflux for 6 hours) involving a Walden inversion. Unlike epicoprostanol (above), coprostanol is precipitated by a 1.33% solution of digitonin in

95% EtOH, the digitonide can be collected, decomposed by dissolving in pyridine, precipitating the digitonin with excess of Et_2O, filtering off digitonin and the coprostanol is obtained by evaporation of the organic solvent. A possible impurity is the 3α-ol from which it can be separated by chromatography on Al_2O_3 and eluting with Et_2O/*C_6H_6 (1:24) whereby the 3α-ol runs first (**m** 116-117°, see preceding entry) and further elution gives the pure 3β-coprosterol (**m** 99-101°). Crystallise it from MeOH (needles) or aqueous EtOH. Store it at room temperature. The *3β-yl-acetate* from acetylation with Ac_2O (also obtained by catalytic reduction of coprostan-3-one, AcOH/PtO_2/H_2, followed by chromatographic separation as above and acetylation) has **m 91°**, **90- 91°**, **$[\alpha]_D^{18}$ +14.5° (c 1.8, $CHCl_3$)**. Its solubility is 0.79% in H_2O at 25°. [Bridgewater & Shoppee *J Chem Soc* 1709 *1953,* Shoppee & Summers *J Chem Soc* 687 *1950*, see Ruzicka et al. *Helv Chim Acta* **17** 1407 *1934*.]

Cholest-2-ene *[15910-23-3]* **M 370.6, m 75-76°, $[\alpha]_D^{20}$ +66° (c 1.65, $CHCl_3$).** Purify cholest-2-ene by chromatography on Al_2O_3 (Spence H) and elute with petroleum ether (b 40-60°), and recrystallise the residue from EtOAc/MeOH. Also recrystallise it from MeOH or diethyl ether/acetone. [Alt & Barton *J Chem Soc 4284 1954,* Bergbreiter & Chandran *J Am Chem Soc* **109** *174 1987*, *Beilstein* **5** III 1320, **5** IV 1507.]

Cholesterol (cholest-5-en-3ß-ol) *[57-88-5]* **M 386.7, m 148.9-149.4°, $[\alpha]_D^{25}$ -35° (hexane).** Crystallise cholesterol from ethyl acetate, EtOH or isopropyl ether/MeOH. [Hiromitsu & Kevan *J Am Chem Soc* **109** 4501 *1987*.] For extensive details of purification through the dibromide, see Fieser [*J Am Chem Soc* **75** 5421 *1953*] and Schwenk and Werthessen [*Arch Biochem Biophys* **40** 334 *1952*], and by repeated crystallisation from acetic acid; see Fieser [*J Am Chem Soc* **75** 4395 *1953*]. Like many sterols, cholesterol gives colour reactions with conc H_2SO_4: When cholesterol is dissolved in a small volume of $CHCl_3$ and mixed with conc H_2SO_4, the colour of the organic layer becomes crimson, then changes to purple and on further standing in air it turns to blue, then green and finally yellow. The H_2SO_4 layer develops a green fluorescence. [*Beilstein* **6** III 2607, **6** IV 4000.]

Cholesteryl acetate *[604-35-3]* **M 428.7, m 113-115°, 115-116°, $[\alpha]_{546}^{20}$ -51° (c 5, $CHCl_3$).** Crystallise the acetate from *n*-pentanol or Me_2CO. Also purify it by chromatography through silica gel and eluting with MeOH. [*Beilstein* **6** III 2607, **6** IV 4004.]

Cholesteryl myristate *[1989-52-2]* **M 597.0, m 69-71°, $[\alpha]_D^{20}$ -25.4° (c 1, $CHCl_3$).** Crystallise the myristate ester from Me_2CO, EtOH/EtOAc or EtOH/Et_2O or *n*-pentanol. Purify it also by column chromatography on silica gel and eluting with MeOH then evaporating to dryness. Recrystallise it and finally, dry it *in vacuo* over P_2O_5 and store it at -20°. [Labarière et al. *Analyt Chem* **30** 1466 *1958*, Malanik & Malat *Anal Chim Acta* **76** 464 *1975*, *Beilstein* **6** III 2638].

Cholesteryl oleate *[303-43-5]* **M 651.1, m 48.8-49.4°, $[\alpha]_D^{20}$ -24° (c 1, $CHCl_3$).** Purify the oleate ester by chromatography on silica gel and eluting with MeOH. [*Beilstein* **6** III 2642.]

3α-5ß-7α-12α-Cholic acid (3α-7α-12α-trihydroxy-5ß-cholan-24-oic acid, Cholalin) *[81-25-4]* **M 408.6 (anhydrous), 426.6 (hydrate) m 196-198°, 198-200°, $[\alpha]_D^{20}$ +37°, $[\alpha]_{546}$ +41° (c 0.6, EtOH), pK^{20} 4.98.** This bile acid crystallises from H_2O, aqueous AcOH (as hydrate), wet Et_2O (as hydrate) or EtOH (as alcoholate). Dry it under vacuum at 94° to give the *anhydrous acid* **m** 198°. Its solubility (w/v) at 15° is 0.028% in H_2O, 3.06% in EtOH, 0.12% in Et_2O, 0.51% in $CHCl_3$, 0.036% in *C_6H_6, 2.82% in Me_2CO and 15.2% in AcOH. When an alcoholic solution of cholic acid + I_2 is added to aqueous KI, it forms a molecular compound $(C_{24}H_{40}O_5I)_4$ KI. H_2O. The *methyl ester* is dimorphic with **m 155-156°** and **162°** (from 95% aqueous EtOH), and $[\alpha]_D^{20}$ +25° (EtOH), and the *ethyl ester* has **m 155° (162-163°** after recrystallisation from EtOAc/petroleum ether b 30-60° 2:8, Cortese *J Am Chem Soc* **59** 2532 *1937*). [Anderson et al. *Biochem J* **67** 323 *1957*, **85** 236 *1962*, Ekwall et al. *Acta Chem Scand* **11** 50 *1957*.] The acid has been used as a non-denaturing ionic detergent, and for solubilising membrane-bound proteins in their native state [Hooper *Biochem Soc Trans* **14** 586 *1986*]. It has also been used in liposome preparations [Yang & Lundahl *Anal Biochem* **218** 210 *1994*.] [*Beilstein* **10** III 2162, **10** IV 2072.]

4,5-Coprosten-3-ol (cholest-4-ene-3β-ol, allocholesterol) *[517-10-2]* **M 386.7, m 132°, $[\alpha]_D^{24}$ +43.7°, (c 1, *C_6H_6).** Purify 4,5-coprosten-3-ol by dissolving it in Et_2O, adding an equal volume of MeOH and removing the

Et_2O with a stream of CO_2 until crystallisation begins. The sterol crystallises in needles when cooled in an ice-salt bath. Dry it *in vacuo*. The *acetate* crystallises from aqueous MeOH **m** 85°. [Schoenheimer & Evans *J Biol Chem* **114** 567 *1936*, Stoll *Hoppe Seyler's Z Physiol Chem* **246** 10 *1937, Beilstein* **6** IV 3577.]

Corticosterone (11β, 21-dihydroxypregn-4-en-3,20-dione) *[50-22-6]* **M 346.5, m 180-181°, 180-182°, 181-184°, $[\alpha]_D^{15}$ +223° (c 1.1, EtOH), $[\alpha]_D^{23-25}$ +194° (c 0.1, dioxane).** Purify corticosterone by recrystallisation from Me_2CO (trigonal plates), EtOH or isoPrOH. It has UV with λ_{max} at 240nm, and gives an orange-yellow solution with strong fluorescence on treatment with concentrated H_2SO_4. It is insoluble in H_2O but soluble in organic solvents. [Reichstein & Euw *Helv Chim Acta* **21** 1197 *1938*, **27** 1287 *1944*; Mason et al. *J Biol Chem* **114** 613 *1936*; ORD: Foltz et al. *J Am Chem Soc* **77** 4359 *1955*; NMR: Shoolery & Rogers *J Am Chem Soc* **80** 5121 *1958*.] The *21-O-acetyl* derivative [1173-26-8] crystallises from Me_2CO/Et_2O with **m** 152.5-153°, $[\alpha]_D^{20}$ +195° (c 0.6, Me_2CO), and the *21-O-benzoyl* derivative crystallises from $AcOH/Et_2O$ with **m** 201-202° [Reichstein *Helv Chim Acta* **20** 953 *1937*]. [*Beilstein* **8** IV 2907.]

Cortisol See hydrocortisone [50-23-7].

Cortisone *[53-06-5]* **M 360.5, m 230-231°, $[\alpha]_{546}^{20}$ +225° (c 1, EtOH).** Crystallise cortisone from 95% EtOH or acetone. The UV has ε 14,000 $M^{-1}cm^{-1}$ at 237nm (EtOH). [Hems *J Pharm Pharmacol* **5** 409 *1953, Beilstein* **8** IV 3480.]

Cortisone-21-acetate *[50-04-4]* **M 402.5, m 242-243°, $[\alpha]_{546}^{20}$ +227° (c 1, $CHCl_3$).** Crystallise cortisone-21-acetate from acetone or $CHCl_3$. The UV has ε 15,800 $M^{-1}cm^{-1}$ at 238nm in dioxane. [Sarett *J Biol Chem* **162** 601 *1946*, *Beilstein* **8** III 4058, **5** IV 3481.]

Deoxycholic acid *[83-44-3]* **M 392.6, m 171-174°, 176°, 176-178°, $[\alpha]_{546}^{20}$ +64° (c 1, EtOH), $[\alpha]_D^{20}$ +55° (c 2.5, EtOH), pK^{25} 6.58.** Reflux the acid with CCl_4 (50ml/g), filter, evaporate under vacuum at 25°, recrystallise the residue from acetone and dry it under vacuum at 155° [Trenner et al. *J Am Chem Soc* **76** 1196 *1954*]. A solution of (cholic acid-free) material (100ml) in 500ml of hot EtOH is filtered, evaporate it to less than 500ml on a hot plate, and pour it into 1500ml of cold diethyl ether. The precipitate, filtered off by suction, is crystallised twice from 1-2 parts of absolute EtOH, to give an *alcoholate*, **m** 118-120°, which is dissolved in EtOH (100ml for 60g) and poured into boiling water. After boiling until free of the EtOH, the precipitate is filtered off, dried, ground and dried to constant weight *in vacuo* [Sobotka & Goldberg *Biochem J* **26** 555 *1932*]. Deoxycholic acid is also freed from fatty acids and cholic acid by silica gel chromatography and elution with 0.5% acetic acid in ethyl acetate [Tang et al. *J Am Chem Soc* **107** 4058 *1985*]. It can also be recrystallised from butanone. Its solubility in H_2O at 15° is 0.24g/L, but in EtOH it is 22.07g/L. [*Beilstein* **10** IV 1608.]

11-Deoxycorticosterone (21-hydroxyprogesterone) *[64-85-7]* **M 330.5, m 141-142°, $[\alpha]_{546}^{20}$ +178° and $[\alpha]_{546}$ +223° (c 1, EtOH).** Crystallise 11-deoxycorticosterone from diethyl ether. [Schindler et al. *Helv Chim Acta* **24** 360 *1941*, Steiger & Reichstein *Helv Chim Acta* **20** 1164 *1937*.]

11-Deoxycorticosterone acetate (21-acetoxy-4-pregnen-3,20-dione) *[56-47-3]* **M 372.5, m 154-159°, 154-160°, 155-157°, 155-161°, $[\alpha]_D^{20}$ +174° (c 1, dioxane), $[\alpha]_D^{22-24}$ +196° (c 1, $CHCl_3$).** 11-Deoxycorticosterone acetate recrystallises from EtOH as needles or Me_2CO/hexane, and sublimes at high vacuum. It is partly soluble in MeOH, Me_2CO, Et_2O and dioxane but insoluble in H_2O. [Reichstein & Euw *Helv Chim Acta* **23** 136 *1940*, Romo et al. *J Am Chem Soc* **79** 5034 *1957*; NMR: Shoolery & Rogers *J Am Chem Soc* **80** 5121 *1959*, *Beilstein* **8** IV 2195.]

Dexamethasone (9-α–fluoro-16-α-methylprednisolone, prednisolone F) *[50-02-2]* **M 392.5, m 262-264°, 268-271°, $[\alpha]_D^{25}$ +77.5° (c 1, dioxane).** Dexamethasone has been recrystallised from Et_2O or small volumes of EtOAc. Its solubility in H_2O is 10 mg/100ml at 25°; and is freely soluble in Me_2CO, EtOH and $CHCl_3$. Store it below 8°. It is a glucocorticoid steroidal anti-inflammatory agent. A stock solution of 20μg/ml is generally made by adding 1ml of absolute EtOH to 100μg of steroid, stir gently to dissolve then add 49ml of sterile medium while mixing. [Arth et al. *J Am Chem Soc* **80** 3161 *1958*; for the β-methyl isomer see Taub et al. *J Am*

Chem Soc **82** 4025 *1960*, see *Beilstein* **8** IV 3501.]

Dexamethasone 21-acetate (9-α–fluoro-16-α-methylprednisolone-21-acetate, prednisolone F acetate) *[1177-87-3]* **M 434.5, m 215-225°, 229-231°, $[\alpha]_D^{25}$ +77.6° (c 1, dioxane), +73° (c 1, $CHCl_3$).** Dexamethasone 21-acetate is purified on neutral Al_2O_3 using $CHCl_3$ as eluent, the fractions are evaporated, and the residue is recrystallised from $CHCl_3$. Store it below 8°. It has λ_{max} at 239nm (ε 14,900) in EtOH. It is a glucocorticoid steroidal anti-inflammatory agent. [Oliveto et al. *J Am Chem Soc* **80** 4431 *1958*]. [*Beilstein* **8** IV 3501.]

Dexamethasone 21-phosphate disodium salt (Baldex, Colvasone, Dexabene, Desone among many trade names) *[2392-39-4]* **M 516.4, m 233-255°, $[\alpha]_D^{25}$ +74° (for anhydrous salt, c 1, H_2O).** Recrystallise it from EtOH and dry it *in vacuo*. It has λ_{max} at 238-239nm (ε 14,000) in EtOH. Store it below 8°, but ethanolic solutions should be stored at ~0°.
Like the preceding two drugs it is also an anti-inflammatory drug, but is more soluble in H_2O. It is a pro-drug and is converted to dexamethasone *in vivo*; it also stimulates glutamine uptake in the cerebral cortex.

Digitoxigenin (3β,14β-dihydroxy-20(22)-norcholenic acid lactone) *[143-62-4]* **M 374.5, m 253°, 249-255°, $[\alpha]_{546}^{20}$ +17° (c 1, MeOH).** Dissolve digitoxigenin in EtOAc, wash it with H_2O, dry it (Na_2SO_4), evaporate and recrystallise it from 40% aqueous EtOH or aqueous MeOH then EtOAc/Et_2O. The UV has λ_{max} at 218nm (ε 14,500 $M^{-1}cm^{-1}$). The *3-acetate* crystallises from Me_2CO/Et_2O with **m** 222-227°, $[\alpha]_D^{20}$ +21° (c 1, $CHCl_3$). [Wyss et al. *Helv Chim Acta* **43** 644 *1960*, Cruz et al. *J Org Chem* **42** 3580 *1977*, *Beilstein* **18** IV 1468.]

Dihydrotachysterol *[67-96-9]* **M 398.7, m 125-127°, $[\alpha]_D^{20}$ +97° ($CHCl_3$).** Crystallise the sterol from 90% MeOH, and UV with λ_{max} at 242, 251 and 261nm ($E_{1cm}^{1\%}$ 760, 1010 and 650) in EtOH. The *acetate* has **m** 108-110° and $[\alpha]_D^{20}$ +32.8° ($CHCl_3$), and UV with λ_{max} at 242, 251 and 261nm ($E_{1cm}^{1\%}$ 780, 910 and 600) in EtOH. The *propionate* has **m** 97-98° and $[\alpha]_D^{20}$ +37° ($CHCl_3$), and UV with λ_{max} 242, 251 and 261nm ($E_{1cm}^{1\%}$ 750, 860 and 570) in EtOH. [Werder *Hoppe Seyler's Z Physiol Chem* **260** 119 *1939*, Windaus et al. *Justus Liebigs Ann Chem* **499** 1978 *1932*, *Beilstein* **6** III 2833, **6** IV 3994, 4161.]

Diosgenin (25*R*-spirostaen-3β-ol) *[512-04-9]* **M 294.5, m 204-207°, $[\alpha]_D^{25}$ -129° (in Me_2CO).** Crystallise diosgenin from acetone, and chromatograph it on Al_2O_3 and elute with $*C_6H_6/Et_2O$ (9:1), then recrystallise it from MeOH. Its solubility is ~4% in H_2O and 5% in $CHCl_3$. The *acetate* crystallises from AcOH with **m** 198°; and has $[\alpha]_D^{20}$ -119° (pyridine). [Marker et al. *J Am Chem Soc* **65** 1199 *1943*. Mazur et al. *J Am Chem Soc* **82** 5889 *1960*, *Beilstein* **19** IV 862.]

α-Ecdyson *[3604-87-3]* **M 464.7, m 239-242°, 242°, $[\alpha]_D^{20}$ +72° (c 1, EtOH).** Recrystallise α-ecdyson from tetrahydrofuran/petroleum ether and from H_2O as a *hydrate*. It has been purified by chromatogaphy on Al_2O_3 and elution with EtOAc/MeOH. It has λ_{max} at 242nm (ε 12,400). Its *acetate* has **m** 214-216° from EtOAc/petroleum ether, and the *2,4-dinitrophenylhydrazone* has **m** 170-175°(dec) from EtOAc. [Karlson & Hoffmeister *Justus Liebigs Ann Chem* **662** 1 *1963*, Karlson *Pure Appl Chem* **14** 75 *1967*, *Beilstein* **8** IV 3613.]

β-Ecdyson (β-echdysterone, crustecdyson, 20-hydroxyechdyson) *[5289-74-7]* **M 480.7, m 240-242°, 245-247°, $[\alpha]_D^{20}$ +66° (c 1, MeOH).** Crystallise β-ecdyson from water, tetrahydrofuran/petroleum ether, MeOH and EtOAc after chromatographic purification. It has λ_{max} (EtOH) at 240nm (ε 12,670 $M^{-1}cm^{-1}$). [Also IR & NMR: Hüppi & Siddall *J Am Chem Soc* **89** 6799 *1967*, Kametani et al. *Tetrahedron Lett* **21** 4855 *1980*, *Beilstein* **8** IV 343.]

(+)-Equilenin *[517-09-9]* **M 266.3, m 258-259° (vac), $[\alpha]_D^{16}$ +87° (c 0.1, dioxane).** Crystallise (+)-equilenin from EtOH (solubility is 0.63% at 18°, 2.5% at 78°), aqueous EtOH or $*C_6H_6$ (Norite) and dry it in a vacuum. It sublimes on melting and at 170-180°/0.01mm. The *acetate* crystallises from MeOH with **m** 165-167° and $[\alpha]_D^{20}$ +71° (c 1, $CHCl_3$). [Bachmann et al. *J Am Chem Soc* **62** 824 *1940*, *Beilstein* **8** III 1522, 1523, 1525, 8 IV 1420.]

Ergosterol (Provitamin D_2) *[57-87-4]* **M 396.7, m 165-166°, $[\alpha]_{546}^{20}$ -171° (c 1, $CHCl_3$), $[\alpha]_D^{20}$ -135° (c 1, $CHCl_3$).** Crystallise ergosterol from EtOAc, then from ethylene dichloride or EtOH/*C_6H_6 (3:1). It has been purified by conversion to the *isobutyl ester* which crystallises from Et_2O/Me_2CO (1:3) with **m**: turbid at 148°, melts at 159° and becomes clear at 162°, followed by hydrolysis, [Bill & Honeywell *J Biol Chem* **80** 15 *1938*]. When crystallised from EtOH, it forms the *1,5-hydrate* **m** 168°. The water is difficult to remove giving an amorphous solid **m** 166-183°, **b** 250°/high vacuum. It is light sensitive. The *benzoate* has **m** 169-171°, after crystallisation from Me_2CO/*C_6H_6 (4:1) after prolonged standing at 0° and becomes highly charged, with $[\alpha]_D^{20}$ -177° (c 1, $CHCl_3$). [UV of sterols: Hogness et al. *J Biol Chem* **120** 239 *1937*, *Beilstein* **6** IV 4407.]

17α-Estradiol *[57-91-0]* **M 272.3, m 223, $[\alpha]_D^{20}$ +57° (c 1, EtOH).** 17α-Estradiol recrystallises from aqueous EtOH (80%) as the *hemihydrate* and differs from the β-anomer (below) by not precipitating with digitonin in 80% aqueous EtOH. The *diacetate* [1474-52-8] crystallises from aqueous EtOH in needles with **m** 139-140°. The *3-benzoate* crystallises in three forms **m** 158°, 153° and 63°. [See references for 17β-Estradiol below.]

17β-Estradiol (1,3,5-estratrien-3,17β-diol, 17-β-estradiol was incorrectly called α-estradiol) *[50-28-2]* **M 272.4, m 173-179°, 176-178°, $[\alpha]_D^{20}$ +76° to +83° (c 1, dioxane).** 17β-Estradiol (previously known as α-estradiol) is purified by chromatography on SiO_2 (toluene/EtOAc 4:1) and recrystallised from $CHCl_3$/hexane or 80% EtOH. It is stable in air, is insoluble in H_2O, and is precipitated by digitonin. The UV has λ_{max} at 225 and 280 nm. The *diacetate* [3434-88-6] has **m** 97-98° and forms leaflets from aqueous EtOH. The *3-benzoate* [50-50-0] crystallises from aqueous MeOH with **m** 193° and $[\alpha]_D^{25}$ +58° to 63° (c 1, dioxane). [Meischer & Scholz *Helv Chim Acta* **20** 263, 1237 *1937, Biochem J* **32** 1273 *1938*, Oppolzer & Roberts *Helv Chim Acta* **63** 1703 *1980*, Inhoffen & Zühlsdorff *Chem Ber* **74** 1914 *1941*, *Beilstein* **6** IV 6611.]

β-Estradiol-6-one (1,3,5-estratriene-3,17β-diol-6-one) *[571-92-6]* **M 359.4, m 278-280°, 281-283°, $[\alpha]_D^{20}$ +4.2° (c 0.7, EtOH).** β-Estradiol-6-one forms plates from EtOH. The *3,17-diacetate* has **m** 173-175° after recrystallisation from aqueous EtOH. [Longwell & Wintersteiner *J Biol Chem* **133** 219 *1940*.] The UV has λ_{max} at 255 and 326nm in EtOH [Slaunwhite et al. *J Biol Chem* **191** 627 *1951*]. [*Beilstein* **8** IV 2398.]

Estriol (1,3,5-estratrien-3â,16a,17β-triol) *[50-27-1]* **M 288.4, m 278.5-284°, 283°, $[\alpha]_{546}^{20}$ +66° (c 1, dioxane).** Crystallise estriol from EtOH/ethyl acetate. Also purify it by countercurrent distribution with cyclohexane/EtOAc (1:1) and EtOH/H_2O (1:1). The UV (EtOH) has λ_{max} at 280nm (ε 2,090 $M^{-1}cm^{-1}$). [Huffmann & Lott **71** 719 *1949*, Leeds et al. *J Am Chem Soc* **76** 2943 *1954*, *Beilstein* **6** IV 7550.]

Estrone (1,3,5-Estratrien-3β-ol-17-one, Folliculin) *[53-16-7]* **M 270.4, m 260-261°, polymorphs have m 254° and 256°, $[\alpha]_{546}^{20}$ +198° (c 1, dioxane), pK^{25} 0.91.** Purify estrone by chromatography on silica gel, eluting with 2:1 hexane/EtOAc and recrystallising from EtOH or Et_2O/EtOH. [Danishefsky & Cain *J Am Chem Soc* **98** 4975 *1976*.] The *acetate* [901-93-9] crystallises from EtOH with **m** 125-127°. [*Beilstein* **8** III 1171.]

Estrone 3-*O*-sulfamate *[148672-09-7]* **M 349.5.** Estrone 3-*O*-sulfamate is purified by silica gel flash chromatography to give a product with one spot on TLC. It is an active site-directed inhibitor of estrone sulfatase, i.e. a time-dependent enzyme inactivator. [Woo et al. *J Med Chem* **39** 1349 *1996,* Purohit et al. *Biochemistry* **34** 11508 *1995*.]

17-α-Ethynylestradiol *[57-63-6]* **M 296.4, m 141-146°, 145-146°, $[\alpha]_D^{20}$ +4° (c 1, $CHCl_3$).** 17-α-Ethynylestradiol forms a *hemihydrate* on recrystallising from MeOH/H_2O. It dehydrates on melting and re-melts on further heating at **m** 182-184°. The UV has λ_{max} at 281nm (ε 2040) in EtOH. Its solubility is 17% in EtOH, 25% in Et_2O, 20% in Me_2CO, 25% in dioxane and 5% in $CHCl_3$. [Petit & Muller *Bull Soc Chim Fr* 121 *1951*.] The *diacetyl* derivative has **m** 143-144° (from MeOH) and $[\alpha]_D^{20}$ +1° (c 1, $CHCl_3$) [Mills et al. *J Am Chem Soc* **80** 6118 *1958*]. [*Beilstein* **6** IV 6877.]

Etiocholanic acid *[438-08-4]* **M 304.5, m 228-229°, pK_{Est} ~4.7.** Crystallise etiocholanic acid from glacial acetic acid and sublime it at 160°/0.002mm. The *ethyl ester* has **m** 77.5-78.5° (from EtOH) $[\alpha]_{546}^{20}$ +52.5° (c 0.61, pyridine). [Jacobs & Elderfield *J Biol Chem* **108** 497 *1935,* Weiland et al. *Hoppe Seyler's Z Physiol Chem* **161** 80 *1926*, *Beilstein* **9** III 2644.]

Gitoxigenin (3β,14,16β,21-tetrahydroxy-20(22)-norcholenic acid lactone) *[545-26-6]* **M 390.5, m 223-226°, 234°, 239-240° (anhydrous by drying at 60°), $[\alpha]_D^{20}$ +30° (c 1, MeOH).** Recrystallisation of gitoxigenin from aqueous EtOH produces plates of the *sesquihydrate* which dehydrate on drying at 100° *in vacuo*. It also recrystallises from Me_2CO/MeOH and from EtOAc (the crystals contain 1 mol of EtOAc) with $[\alpha]_D^{21}$ +24.8° (c 1, dioxane). It has UV with λ_{max} at 310, 485 and 520nm in 96% H_2SO_4. On heating with ethanolic HCl it yields *digitaligenin* with loss of H_2O. [Smith *J Chem Soc* 23 *1931*, *Beilstein* **8** IV 2456.]

Glycocholic acid (*N*-cholylglycine) *[475-31-0]* **M 465.6, m 130° (hydrate) 154-155°, 165-168°(anhydrous), $[\alpha]_{546}^{20}$ +37° (c 1, EtOH), pK^{25} 4.4.** Glycocholic acid crystallises from hot water as the *sesquihydrate*. Dry it at 110° *in vacuo*. An analytical sample is prepared by suspending the acid (4g) in H_2O (400ml) at ~20°, heating to boiling with slow stirring, filtering hot and allowing to cool to ~20°. The acid is filtered off, washed with H_2O, dried in air, recrystallised from 5% aqueous EtOH, washed well and dried over P_2O_5 in a moderate vacuum to constant weight. Recrystallisation from EtOH/EtOAc, and drying, gave the *anhydrous* acid. [Cortese & Bauman *J Am Chem Soc* **57** 1393 *1935*, Bergstrom & Norman *Acta Chem Scand* **7** 1126 *1953*, *Beilstein* **10** IV 2077.]

Glycodeoxycholic acid monohydrate (*N*-[3α-12α-dihydroxy-5β-cholan-24-oyl]glycine) *[360-65-6]* **M 467.6, m 186-177°(dec), 187-188°, $[\alpha]_D^{23}$ +45.9° (c 1, EtOH), pK_{Est} ~4.4.** Glycodeoxycholic acid recrystallises from H_2O or aqueous EtOH with 1 mol of H_2O and is dried at 100° *in vacuo*. Its solubility in EtOH is ~5%. [UV: Lindstedt & Sjövall *Acta Chem Scand* **11** 421 *1957*.] The *Na salt* recrystallises from EtOH/Et_2O with **m** 245-250° and $[\alpha]_D^{23}$ +41.2° (c 1, H_2O) [Wieland *Hoppe Seyler's Z Physiol Chem* **106** 181 *1919*, Cortese *J Am Chem Soc* **59** 2532 *1937*]. [*Beilstein* **10** IV 1611.]

Hecogenin (25*R*-5α-spirostan-3β-ol-12-one) *[467-55-0]* **M 430.6, m 245-250°, 253°, 264-266°, 268°, $[\alpha]_D^{23}$ +8° (c 1, $CHCl_3$).** The saponin (~35 mg) in EtOAc is chromatographed on Al_2O_3 and eluted with *C_6H_6/Et_2O, and the residue on evaporation is recrystallised from Me_2CO. [Mazur et al. *J Am Chem Soc* **82** 5889 *1960*, Marker et al. *J Am Chem Soc* **69** 2167 *1947*, *Beilstein* **19** III/IV 2581.]

Hecogenin acetate *[915-35-5]* **M 472.7, m 265-268°, $[\alpha]_D^{20}$ -6.0° (c 1, $CHCl_3$).** Crystallise the acetate from MeOH. [*Beilstein* **19** IV 2583.]

Hydrocortisone (Cortisol, 11β,17α,21-trihydroxypregn-4-ene-3,20-dione) *[50-23-7]* **M 362.5, m 212-213°, 214-217°, 218-221°, 220-222°, $[\alpha]_D^{22}$ +167° (c 1, EtOH).** Recrystallise hydrocortisone from EtOH or isoPrOH. It is bitter tasting and has UV with λ_{max} at 242 nm (log ε 4.20). Its solubility at 25° is: H_2O (0.28%), EtOH (1.5%), MeOH (0.62%), Me_2CO (0.93%), $CHCl_3$ (0.16%), propylene glycol (1.3%) and Et_2O (0.35%). It gives an intense green colour with conc H_2SO_4. [Wendler et al. *J Am Chem Soc* **72** 5793 *1950*, *Beilstein* **8** IV 3422.]

Hydrocortisone acetate (21-acetoxy-11β,17α-trihydroxypregn-4-ene-3,20-dione) *[50-03-3]* **M 404.5, m 218-221.5°, 221-223°, 222-225°, $[\alpha]_D^{25}$ +166° (c 0.4, dioxane), +150.7° (c 0.5, Me_2CO).** The acetate recrystallises from Me_2CO/Et_2O or aqueous Me_2CO as *hygroscopic* monoclinic crystals. Its UV has λ_{max} at 242 nm ($A_{1cm}^{1\%}$ 390) in MeOH. Its solubility at 25° is: H_2O (0.001%), EtOH (0.45%), MeOH (0.04%), Me_2CO (1.1%), $CHCl_3$ (0.5%), Et_2O (0.15%), and it is very soluble in Me_2NCHO. [Wendler et al. *J Am Chem Soc* **74** 3630 *1952*; Antonucci et al. *J Org Chem* **18** 7081 *1953*, *Beilstein* **8** IV 3424.]

19-Hydroxy-4-androsten-3,17-dione *[510-64-5]* **M 302.4, m 167-169°, 168-170°, 169-170°, 172-173°, $[\alpha]_D^{20}$ +190° (c 1, $CHCl_3$).** Recrystallise 19-hydroxy-4-androsten-3,17-dione from Me_2CO/hexane or Et_2O/hexane. It has UV with λ_{max} at 242nm in EtOH or MeOH. The *19-acetoxy* derivative has $[\alpha]_D^{26}$ +185° ($CHCl_3$) and λ_{max} with 237.5nm in EtOH. [Ehrenstein & Dünnenberger *J Org Chem* **21** 774 *1956*, *Beilstein* **8** IV2162.]

25-Hydroxycholesterol (cholest-5-en-3β,25-diol) *[2140-46-7]* **M 402.7, m 177-179°, 178-180°, 181.5-182.5°, $[\alpha]_D^{25}$ -39° (c 1.05, $CHCl_3$).** 25-Hydroxycholesterol forms colourless needles from MeOH [Schwartz *Tetrahedron Lett* **22** 4655 *1981*]. The *3β–acetoxy* derivative has **m** 142-142.8° (from Me_2CO) and $[\alpha]_D^{25}$ -40.4°

(c 2, $CHCl_3$). The *3β,25-diacetoxy* derivative has **m** 119-120.5° (from MeOH) and $[\alpha]_D^{25}$ -35.5° ($CHCl_3$). [Dauben & Bradlow *J Am Chem Soc* **72** 4248 *1950*, Ryer et al. *J Am Chem Soc* **72** 4247 *1950*, *Beilstein* **6** IV 6437.]

18-Hydroxy-11-deoxycorticosterone (18,21-dihydroxypregn-4-en-3,20-dione tautomeric with 18,20-epoxy-20,21-dihydroxypregn-4-en-3-one) *[379-68-0]* **M 346.5, m 168-170°, 171-173°, 191-195°, 200-205°, $[\alpha]_D^{20}$ +151° (c 1, $CHCl_3$).** Recrystallise 18-hydroxy-11-deoxycorticosterone from Et_2O/Me_2CO to give crystals **m** 200-205°. When it is recrystallised from M_2CO, it has **m** 191-195°. It has UV with λ_{max} at 240nm. The *21-O-acetoxy-18-hydroxy* derivative has **m** 158-159° (from $Et_2O/*C_6H_6$), and the *21-O-acetoxy-18,20-epoxy* derivative has **m** 149-154° (from Et_2O). [Kahnt et al. *Helv Chim Acta* **38** 1237 *1955*; Pappo *J Am Chem Soc* **81** 1010 *1959*.]

17β-Hydroxy-17α-methyl-3-androsterone (Mestanolone) *[521-11-9]* **M 304.5°, m 192-193°.** Dissolve mestanolone in Et_2O, wash it with N NaOH, H_2O, dry it (Na_2SO_4), evaporate and recrystallise it from EtOAc. The *semicarbazone* has **m** 235-236° (from EtOH). [Ruzicka et al. *Helv Chim Acta* **18** 1487 *1935*.]

17α-Hydroxy-6α-methylprogesterone (Medroxyprogesterone) *[520-85-4]* **M 344.5, m 220°, $[\alpha]_D^{25}$ +75° ($CHCl_3$).** If it contains the *epi*-isomer (TLC), then dissolve it in $CHCl_3$, bubble dry HCl gas to epimerise it, evaporate and recrystallise it from chloroform. The UV has λ_{max} at 241nm (ε 16,150) in EtOH. The *17-acetate* [71-58-9] crystallises from MeOH with **m** 207-208° and $[\alpha]_D^{25}$ +61° ($CHCl_3$). Its UV has λ_{max} at 240nm (ε 15,950) in EtOH. [Babcock et al. *J Am Chem Soc* **80** 2904 *1958*, *Beilstein* **8** IV 2212.]

α-Hyodeoxycholic acid *[83-49-8]* **M 392.6, m 196-197°, $[\alpha]_{546}^{20}$ +8° (c 2, EtOH), pK_{Est} ~4.9.** Crystallise α-hyodeoxycholic acid from EtOAc or Me_2CO. The K salt separates in needles from an alcoholic solution of the acid when an equivalent of KOMe is added (see lithocholic acid [434-13-9]). [Weiland & Gumlish *Hoppe Seyler's Z Physiol Chem* **215** 18 *1933*, Windaus & Bohne *Justus Liebigs Ann Chem* **433** 278 *1923*, *Beilstein* **10** III 1631.]

Lanosterol *[79-63-0]* **M 426.7, m 138-140°, $[\alpha]_D^{20}$ +62.0° (c 1, $CHCl_3$).** If very impure, then it should be acetylated, converted to the *dibromide acetate* [crystallised from EtOAc with slow cooling, **m** 168-170°, $[\alpha]_D^{20}$ +214° ($CHCl_3$)], de-brominated with Zn dust to give the acetate (below) which is recrystallised from 3-4 parts of Me_2CO/MeOH (4:1) and hydrolysed as for stigmasterol (below). Recrystallise it from anhydrous MeOH. Dry it *in vacuo* over P_2O_5 for 3 hours at 90°. The purity is checked by proton magnetic resonance. The *acetate* crystallises from MeOH with **m** 131-133°, $[\alpha]_D^{25}$ +62° (c 1,$CHCl_3$). [Block & Urech *Biochemical Preparations* **6** 32 *1958*. van Tamelen et al. *J Am Chem Soc* **104** 6479, 6480 *1982*, *Beilstein* **6** III 2880, **6** IV 4188.]

Lithocholic acid (3α-hydroxycholanic acid) *[434-13-9]* **M 376.6, m 184-186°, $[\alpha]_D^{23}$ +35° (c 1, EtOH), pK_{Est} ~4.8.** Lithocholic acid can be purified by conversion to the rather insoluble Na or K salt by addition of the equivalent amount of aqueous NaOH or KOH, filtering off the alkali salt, washing it with ice cold H_2O, dissolving it in the least volume of boiling H_2O, acidifying with the dilute HCl (slight excess), filtering off the acid, washing with cold H_2O and drying it thoroughly in a vacuum. Recrystallise it from Me_2CO, EtOH or acetic acid. The *methyl ester* crystallises from MeOH, with 0.5 mol of MeOH, and has **m** 92-93°, $[\alpha]_D^{25}$ +34° (MeOH). It has also been purified by recrystallisation from petroleum ether (b 40-60°) and, after chromatography on Al_2O_3 in petroleum ether, gave a labile form **m** 92-93° which is transformed to the stable form **m** 125-126° after standing for 2 days in a vacuum desiccator. [Hoelm & Mason *J Am Chem Soc* **62** 569 *1940*, Sarel & Yanuka *J Org Chem* **24** 2018 *1959*, *Beilstein* **10** IV 785.]

6-α-Methylprednisolone (Medrol, 11β,17-21-trihydroxy-6α-methylpregna-1,4-dien-3,20-dione) *[83-43-2]* **M 347.5, m 226-237°, 228-237°, 240-242°, $[\alpha]_D^{24}$ +91° (c 0.5, dioxane).** Recrystallise medrol from EtOAc. The UV has λ_{max} at in 95% EtOH 243nm (ε 14,875). The *21-acetoxy* derivative has **m** 205-208° (from EtOAc), and $[\alpha]_D^{24}$ +95° (c 1, $CHCl_3$). [Spero et al. *J Am Chem Soc* **78** 6213 *1956*; Fried et al. *J Am Chem Soc* **81** 1235 *1959*; ^1H NMR: Slomp & McGarvey *J Am Chem Soc* **81** 2200 *1959*, *Beilstein* **8** IV 3498.]

17α-Methyltestosterone (Android, Mesterone) *[58-18-4]* **M 302.5, m 162-168°, 164-165°, $[\alpha]_{546}^{20}$ +87° (c 1, dioxane), $[\alpha]_{D}^{20}$+82.3° (c 1, EtOH) $A_{1cm}^{1\%}$ 241nm is 495-530 (EtOH).** This anabolic steroid is crystallised from hexane or hexane/*benzene. It has $E_{1cm}^{1\%}$ 495-530 at 241nm (EtOH). The colour reaction with 2,4-dinitrophenyl hydrazine is used for assaying it. [Gornall & Macdonald *J Biol Chem* **201** 279 *1953*.] In another colour reaction the sterone (1mg) in acetic acid (0.2ml) + 88% H_3PO_4 (2ml) is allowed to stand for 1 hour when it becomes fluorescent. After 1 hour it is diluted with acetic acid (~3ml) and provides a strong yellow fluorescence with the intensity of 50-100 times that of estrone. [Stuart & Stuckey *J Pharm Pharmacol* **1** 130 *1949*, Openauer *Rec Trav Chim Pays Bas* **56** 137 *137*, *Beilstein* **8** IV 1010.]

Norcholanic acid (5β-24-norcholan-23-oic acid) *[511-18-2]* **M 346.5, m 175.5-176.5°, 186°, $[\alpha]_{D}^{20}$ +32° (EtOH), pK_{Est} ~4.8.** Recrystallise the acid from AcOH. The *methyl ester* has **m** 74° (needles from MeOH), and the *ethyl ester* has **m** 65-66°. [Yanuka et al. *Tetrahedron Lett* 1725 *1968, Beilstein* **9** III 2652, **10** IV 2083.]

α-Oestradiol

See estradiol above [57-91-0].

β-Oestradiol-3-benzoate See estradiol 3-benzoate above [50-50-0].

Ouabain [3-{(6-deoxy-α-L-mannopyranosyl)oxy}-1,5,11a,14,19-pentahydroxycard-20(22)-enolide. G-Strophanthin, Acocantherine] *[630-60-4, 312619-45-7 (hydrate), 11018-89-6 (octahydrate)]* **M 728.8 (8 H_2O), m 190°(dec), 200-202°(dec), $[\alpha]_{546}^{20}$ -30° (c 1, H_2O).** It crystallises from water as the *octahydrate*. Dry it at 130°. It decomposes at 190° when dry. Store it in the dark as it is light sensitive, but it is stable in air. Its solubility (g/100ml) in H_2O is 1.3 (~25°), 20 (~100°), and in EtOH it is 1.0 (~25°) and 12.5 (~78°). It is highly **TOXIC** as it is an inhibitor of cation transport and of Na^+ and K^+ ATPase. [*Beilstein* **18/5** V 625.]

Pancuronium bromide

(2β,16β–dipiperidino-5α-androstan-3α,17β–diol diacetate dimetho-bromide) *[15500-66-0]* **M 732.7, m 212-215°, 215°.** The bromide forms odourless crystals with a bitter taste which are purified through acid-washed Al_2O_3 and eluted with isoPrOH/EtOAc (3:1) to remove impurities (e.g. the monomethobromide) and eluted with isoPrOH to give the pure dibromide which is recrystallised from CH_2Cl_2/Me_2CO or isoPrOH/Me_2CO. It is soluble in H_2O (10%) and $CHCl_3$ (3.3%) at 20°. It is a non-depolarising muscle relaxant. [Buckett et al. *J Med Chem* **16** 1116 *1973*.]

Prednisolone acetate (21-acetoxypregna-1,4-diene-11β-17α-diol-3,20-dione) *[52-21-1]* **M 402.5, m 237-239°, 240-242°, 240-243°, 244°, $[\alpha]_{D}^{20}$ +116° (c 1, dioxane).** Recrystallise prednisolone acetate from EtOH, Me_2CO, Me_2CO/hexane, and it has UV with λ_{max} at 243nm in EtOH. [Joly et al. *Bull Soc Chim Fr* 366 *1958*; Herzog et al. *J Am Chem Soc* **77** 4781 *1955*, *Beilstein* **8** IV 3468.]

Prednisone (17,21-dihydroxypregna-1,4-diene-3,11,20-trione, deltacortisone) *[53-03-2]* **M 358.5, m 238° (dec), $[\alpha]_{D}^{20}$ +172° (c 0.5, dioxane), λ_{max} 238nm (log ε 4.18) in MeOH.** Crystallise prednisone from acetone/hexane, then recrystallise it from Me_2CO. The *monoacetate* crystallises from Me_2CO/hexane with **m** 227-233°(dec), $[\alpha]_{D}^{25}$ +186° (c 1, dioxane), and the *diacetate* crystallises from Me_2CO/hexane with **m** 219-221°(dec), $[\alpha]_{D}^{25}$ +125° (c 1, $CHCl_3$). [Hertzog et al. *Tetrahedron* **18** 581 *1962*, *Beilstein* **8** IV 3531.]

5α-Pregnane (allopregnane) *[641-85-0]* **M 288.5, m 84.5-85°, $[\alpha]_{D}^{20}$ +21.7° (c 1.3, $CHCl_3$).** Recrystallise 5α-pregnane several times from Me_2CO. The melting point is lowered (e.g. to 50-71°) if it is contaminated with the 5β-isomer (see below). [Butenandt et al. *Chem Ber* **64** 2529 *1931*, Steiger & Reichstein *Helv Chim Acta* **21** 161 *1938*, *Beilstein* **5** III 1120, 1121, 1125.]

5β-Pregnane *[481-26-5]* **M 288.5, m 82-83°, 83.5°, $[\alpha]_{D}^{20}$ +21.2° (c 0.75, $CHCl_3$).** Crystallise 5β-pregnane from MeOH or Me_2CO. The mixed melting point with allopregnane (above) is ~50-71°. [Butenandt et al. *Chem*

Ber **64** 2529 *1931*, Steiger & Reichstein *Helv Chim Acta* **21** 161 *1938*.]

5α-Pregnane-3α,20β*R*-diol *[566-57-5]* **M 320.5, m 207-209°, $[\alpha]_D^{26}$ +12° (c 1.1, $CHCl_3$).** Crystallise 5α-pregnane-3α,20α-diol from Me_2CO. Its *diacetate* [6170-22-5] M 404.5, has two melting points 134-140° and 152.4°, and $[\alpha]_D^{26}$ +40.5° (c 0.8, $CHCl_3$). It is a progesterone metabolite in urine during pregnancy. [See references below.]

5α-Pregnane-3α,20α*S*-diol *[566-58-5]* **M 320.5, m 248°, $[\alpha]_D^{20}$ +17° (c 0.15, EtOH).** Crystallise 5α-pregnane-3α,20α-diol from EtOH. Its *diacetate* [6003-18-5] has **m** 142° and $[\alpha]_D^{20}$ +18° (c 0.4, $*C_6H_6$). It is a progesterone metabolite in urine during pregnancy. [See references below.]

5β-Pregnane-3α,20β*R*-diol *[80-91-1]* **M 320.5, m 239°, $[\alpha]_D^{20}$ +10° (c 1, EtOH).** Crystallise pregnane-diol (which is abundant in the urine of pregnant women) from EtOH or Me_2CO and dry it *in vacuo*. It can be oxidised to progesterone (see below) and it is not precipitated by digitonin. Its *diacetate* [6100-28-3] has **m** 112-113° and $[\alpha]_D^{26}$ +60° (c 1, $CHCl_3$). It is a progesterone metabolite in urine during pregnancy. [Marian *Biochem J* **23** 1090 *1929*, Johnson et al. *J Chem Soc*1302 *1954*, Mattox et al. *J Org Chem* **32** 708 *1967*, *Beilstein* **6** III 4778, **6** IV 6111.]

5β-Pregnane-3α,20α *S*-diol *[80-92-2]* **M 320.5, m 243-244°, $[\alpha]_{546}^{20}$ +31° (c 1, EtOH).** Crystallise the diol from acetone. The *diacetate* [1174-69-2] crystallises from petroleum ether with **m** 180° (also 182-183°) and $[\alpha]_D^{20}$ +35° (c 1.1, $CHCl_3$). [Marian *Biochem J* **23** 1090 *1929*, Fish et al. *J Biol Chem* **143** 716 *1942*, Hieschmann *J Biol Chem* **140** 797 *1941,* Johnson et al. *J Chem Soc* 1302 *1954*, Glick et al. *J Org Chem* **27** 3121 *1962*, *Beilstein* **6** III 4778, **6** IV 6111.]

Progesterone *[57-83-0]* **M 314.5, m 128.5°, $[\alpha]_{546}^{20}$ +230° (c 1, EtOH), +214.7° (c 1.3, Me_2CO).** The α–form crystallises from EtOH with **m** 127-131°. The β-form crystallises from petroleum ether or aqueous petroleum ether/aqueous Et_2O with **m** 119-120° or 121°. It also crystallises from Et_2O, Me_2CO/EtOAc, MeOH, aqueous Et_2O, aqueous MeOH, wet petroleum ether, Et_2O/ petroleum ether, petroleum ether/$*C_6H_6$, Et_2O/pentane and isopropyl ether. The UV has λ_{max} is at 240nm with log ε 4.25 (EtOH). [Wintersteiner & Allen *J Biol Chem* **107** 321 *1934*, *Beilstein* **7** III 3648, **7** IV 2395.]

Rubijervine (slanid-5-ene-3β-12α-diol) *[79-58-3]* **M 413.6, m 242-244°, 240-246°, $[\alpha]_D^{20}$ +19° (EtOH), $[\alpha]_D^{27.5}$ +20° (c 1.04, MeOH), pK_{Est} ~7.0.** Rubijervine crystallises from 95% EtOH as colourless rods. It has solvent of crystallisation and is dried at 120°/2mm. It is precipitated by digitonin. The *hydrobromide* crystallises from MeOH/Me_2CO with **m** 265-270°(dec). The *diacetate* crystallises from MeOH with **m** 160-163°. The *3-benzoate* gives colourless prisms from $*C_6H_6$ with **m** 156-159° and $[\alpha]_D^{27.5}$ +22° (c 1.6, $CHCl_3$). [Pelletier & Locke *J Am Chem Soc* **79** 4531 *1957*, Jacobs & Craig *J Biol Chem* **148** 41 *1943*, *Beilstein* **21** III/IV 2310.]

β-Sitosterol (stigmast-5-ene-3β-ol) *[83-46-5]* **M 414.7, m 136.5-137.5°, 140°, $[\alpha]_{546}^{20}$ -42° (c 2, $CHCl_3$).** Crystallise β-sitosterol from EtOH, MeOH, Me_2CO, Me_2CO/EtOH or Me_2CO/MeOH. It has also been purified by zone melting. The *acetate* crystallises from MeOH or EtOH as plates with **m** 127-128° and $[\alpha]_D^{20}$ -41° (c 2, $CHCl_3$). The *benzoate* crystallises from EtOH as needles with **m** 146-147° and $[\alpha]_D^{20}$ –13.8° (c 2, $CHCl_3$). [Fujimoto & Jacobson *J Org Chem* **29** 3377, 3381 *1964*, Shoppee *J Chem Soc* 1043*1948*, Heilbron et al. *J Chem Soc* 344, 347 *1941*, Beilstein **6** III 2696.]

Smilagenin (25*R*-spirostan-3β-ol, isosarsasapogenin) *[126-18-1]* **M 416.6, m 185°, $[\alpha]_D^{25}$ -69°, $[\alpha]_{546}^{25}$ -80° (c 0.3, $CHCl_3$).** Chromatograph smilagenin on active Al_2O_3 and elute with $*C_6H_6$, then recrystallise it from Me_2CO, aqueous EtOH (**m** 187-188°) or MeOH. The *acetate* crystallises from MeOH with **m** 152° and $[\alpha]_D^{25}$ –59.6°, $[\alpha]_{546}^{25}$ –68.9° (c 0.25, $CHCl_3$). [Askew *J Chem Soc* 1399 *1936* and 1402 *1936*, Scheer et al. *J Am Chem Soc* **77** 641*1955*, *Beilstein* **19** III/IV 826.]

Solanidine (solanid-5-en-3β-ol) *[80-78-4]* **M 397.6, m 218-219°(sublimes), $[\alpha]_D^{20}$ -29° (c 0.5, $CHCl_3$), pK^{15}**

6.66. Solanidine crystallises from $CHCl_3$/MeOH, aqueous EtOH or aqueous MeOH as needles. TLC on Al_2O_3 plates using CH_2Cl_2/MeOH (98:2) gives a spot at R_F 0.47. The *hydrochloride* crystallises from aqueous EtOH with **m** 345°(dec). The *acetate* crystallises from EtOH with **m** 208°. [Schreiber & Roensch *Tetrahedron* **21** 645*1965*, Kessar et al. *Tetrahedron* **27** 2153 *1971*, Reichestein & Reich *Ann Rev Biochem* **15** 155 *1946*, *Beilstein* **21** III/IV 1398, **27** III/IV 2000.]

α-Solanine (solan-5-en-3β-yl-[*O*^{3}-β-D-glucopyranosyl-*O*^{2}-α-L-rhamnopyranosyl-β-D-galactopyrano-side]) See "Carbohydrates" in this chapter.

Solasodine (22α,25*R*-spirosol-5-en-3β-ol) *[126-17-0]* **M 413.6, m 202°, $[\alpha]_D^{25}$ -100° (c 2, MeOH), pK^{25} 7.7.** Solasodine crystallises (as *monohydrate*) from MeOH as lustrous plates (on heating, the plates change to needles as they melt and resolidify in needles), or aqueous 80% EtOH, and sublimes at high vacuum. After recrystallisation from H_2O, **m** 198-199°, then from Me_2CO/H_2O, **m** 199-201°, it has $[\alpha]_D^{22}$ -109.3° (c 0.581, $CHCl_3$). On TLC with silica gel G (*C_6H_6/absolute EtOH, 8:2) it has R_F 0.45. The IR (KBr) has ν_{max} at 10.3, 10.4, 11.2, 11.5μ (azaoxaspirane bands). [Schreiber & Rönsch *Tetrahedron* **20** 1939 *1964*, Uhle *J Org Chem* **27** 656 *1962*, Kessar et al. *Tetrahedron* **27** 2153 *1971*, *Beilstein* **27** III/IV 2000.]

Stigmasterol (3β-hydroxy-24-ethylcholesta-5,22-diene) *[83-48-7]* **M 412.7, m 170°, $[\alpha]_D^{22}$ -51° ($CHCl_3$), $[\alpha]_{546}^{20}$ -59° (c 2, $CHCl_3$).** Stigmasterol is best purified *via* the *tetrabromide-acetate*. The impure sterol (3g) is acetylated with Ac_2O (60ml) by refluxing for 1.5 hour. The mixture is cooled at 20° for 1 hour, and the crude acetate is collected. The acetate (3g) in Et_2O (30ml) is then treated with Br_2/AcOH (38ml, from 5g Br_2 in 100ml AcOH), and after cooling at 6° overnight, the tetrabromoacetate is filtered off and washed with Et_2O. After six recrystallisations from $CHCl_3$/MeOH the *tetrabromoacetate* has **m** 194-196°. This product (1g) in AcOH (12ml) and Zn dust (1g) is refluxed for 1.5 hours, filtered hot, diluted with H_2O (30m L) and extracted with Et_2O. The extract is washed with dilute aqueous sodium sulfite, then H_2O, the extract is dried (Na_2SO_4) and the stigmasterol acetate (~550mg) is recrystallised (4x) from EtOH and twice from MeOH/$CHCl_3$ (2:1) to give the *acetate* with **m** 139-148°. This acetate (400mg) is hydrolysed in boiling 10% alcoholic KOH (1ml) for 1hour. Then H_2O (30ml) is added and the mixture is extracted with Et_2O. The extract is washed with aqueous Na_2CO_3, then H_2O, the solvent is distilled off and the residue is recrystallised (3x) from 95% EtOH to give ~110mg of pure stigmasterol. It is dried in a vacuum over P_2O_5 for 3 hours at 90°. The purity is checked by NMR. The *acetate* crystallises from MeOH with **m** 145°, $[\alpha]_D^{25}$ -56° (c 2, $CHCl_3$). [Byerrum & Ball *Biochemical Preparations* **7** 86 *1959*, Thornton et al. *J Am Chem Soc* **62** 2006 *1940*, Colin et al. *Anal Chem* **51** 1661 *1979*, *Beilstein* **6** IV 4170.]

Taurocholic acid (3α, 7α,12α-trihydroxy-5β-cholestan-24-oic acid *N*-(2-sulfoethyl) amide Na salt, *N*-coloyotaurine) *[81-24-3]* **M 515.6, m ~125°(dec), $[\alpha]_D$ +38.8° (c 2, EtOH), pK^{25} 1.4.** The acid is present in bile and is isolated as an amorphous pale yellow powder. Crystallise it from EtOH/EtOAc/Et_2O (amorphous **m** 125°) or EtOH/Et_2O [Josephson *Biochem J* **29** 1484 *1935*]. The anhydrous acid is hygroscopic, freely soluble in H_2O and EtOH but insoluble in H_2O and EtOAc. It is hydrolysed by acids or alkalis to cholic acid and taurine. The *sodium salt (hydrate)* [312693-83-7, 345909-26-4 (xH_2O)] crystallises from aqueous EtOH/Et_2O with **m** 231-232°, $[\alpha]_D^{23}$ +23,6° (c 2.5, H_2O); and has the UV λ_{max} (H_2SO_4) at 303, 389 and 480nm. [cf Cortese *J Am Chem Soc* **59** 2532 *1937*, *Beilstein* **10** III 2177, **10** IV 2078.]

Taurodeoxycholic acid sodium salt monohydrate (3α, 12α-dihydroxy-5β-cholestan-24-oic acid *N*-(2-sulfoethyl) amide Na salt monohydrate, *N*-[desoxycholyl)taurine Na salt H_2O) *[1180-95-6, 207737-97-1 (x H_2O)]* **M 539.7, m 171-175°, $[\alpha]_D^{23}$ +37° (c 1, H_2O), pK^{25} 1.4 (free acid).** The Na salt is dissolved in the smallest volume of H_2O, a saturated solution of aqueous NaCl/Et_2O is added and the mixture is stored at 0° for 24 hours. Then shake the mixture well, keep it in the cold for another day and filter the crystals with gentle shaking, wash them with ice-cold saturated aqueous NaCl saturated with Et_2O, dry them over $CaCl_2$ and extract them with absolute EtOH. Add ~10ml of H_2O to the solid followed by enough Et_2O to incipient cloudiness. Store it overnight at 0°. Add ice-cold Et_2O to make 250ml, collect the crystals, wash them with Et_2O then petroleum ether and dry them in air. The purification can be repeated with NaCl and Et_2O with ~85% recovery. NB: precipitation will not occur unless enough H_2O is present. Its solubility in H_2O is 10%. [Cortese *J Am*

Chem Soc **59** 2532 *1937*.] The *free acid* has **m** 141-144°. [Norman *Ark Kemi* **8** 331 *1956*.] It forms mixed micelles and solubilises some membrane proteins [Hajjar et al. *J Biol Chem* **258** 192 *1983*]. [*Beilstein* **10** IV 1611.]

Testosterone (17-β-hydroxyandrost-4-ene-3-one) *[58-22-0]* **M 288.4, m 155°, $[\alpha]_{546}^{20}$ +130° (c 1, dioxane).** Crystallise testosterone from aqueous acetone, hexane or isoPrOH. The long needles that separated from EtOH/AcOH were used for X-ray crystallography [Roberts et al. *J Chem Soc Perkin Trans II* 1978 *1973*.] The *acetate* [1045-69-8] crystallises from MeOH or aqueous Me_2CO, with **m** 140-141° and $[\alpha]_{D}^{20}$ +87.8° (c 1, EtOH). [Ruzicka et al. *Helv Chim Acta* **18** 1478 *1935* and **19** 99, 842 *1936*, *Beilstein* **8** IV 974.]

Testosterone propionate *[57-85-2]* **M 344.5, m 118-122°, $[\alpha]_{546}^{20}$ +102° (c 2, dioxane).** Crystallise the propionate from aqueous EtOH, or Et_2O/petroleum ether (**m** 121°), and its UV has λ_{max} at 240nm (EtOH), and $[\alpha]_{546}^{20}$ +114° (c 1, $CHCl_3$). Also purify it by HPLC. [Ercol & de Ruggieri *J Am Chem Soc* **75** 650, 652 *1953*, polymorphism: Brandstätter-Kuhnert & Kofler *Microkim Acta* 847, 850 *1959*, *Beilstein* **8** IV 977.]

Ursodiol (ursodeoxycholic acid, 3α,7β-dihydroxy-5β-cholan-24-oic acid, 7β-hydroxylithocholic acid, ursodeoxycholic acid) *[128-13-2]* **M 392.5, m 203°, $[\alpha]_{D}^{20}$ +60° (c 0.2, EtOH), pK_{Est} ~4.8.** Recrystallise ursodiol from wet Et_2O, EtOH or EtOH/MeOH. It is almost insoluble in H_2O, sparingly soluble in Et_2O, very slightly soluble in $CHCl_3$ but freely soluble in AcOH. The *diformate* has **m 170°**, and the *diacetate* has **m 100-102°**. It is an anticholelithogenic drug. [Iwasaki *Hoppe Seyler's Z Physiol Chem* **244** 181, 183 *1936,* Ward et al. *Drugs* **27** 95 *1984*, *Beilstein* **10** III 1635, **10** IV 1604.]

MISCELLANEOUS COMPOUNDS (including biologically useful reagents, low-molecular-weight bioactive substances, antibiotics, coenzymes, vitamins, lipids, phospholipids, nucleosides, nucleotides and polynucleotides)

Acetoacetyl coenzyme A trisodium salt trihydrate *[102029-52-7]* **M 955.6, pK_1 4.0 (NH_2), pK_2 6.4 (PO_4^-).** Purification can be carried out by passage through a DEAE-cellulose formate column, then through a Dowex 50 (H^+) column to remove Na ions, concentrated by lyophilisation and redissolved in H_2O. It is commercially available as a solution of 0.05g/ml of H_2O. The concentration of acetoacetylcoenzyme A is determined by the method of Stern et al. [*J Biol Chem* **221** 15 *1956*]. It is stable at pH 7-7.5 for several hours at 0° (half-life *ca* 1-2 hours). At room temperature it is hydrolysed in *ca* 1-2 hours at pH 7-7.5. At pH 1.0/20° it is more stable than at neutrality. A solution of the trisodium salt (0.05g/ml H_2O) adjusted to pH 5 with 2N NaOH can be stored frozen for several weeks. It is stable at pH 2-3/-17° for at least 6 months. [Hersch & Jencks *J Biol Chem* **242** 3468 *1967*, Clikenbeard et al. *J Biol Chem* **250** 3108 *1975*, Simon & Shemin *J Am Chem Soc* **75** 2520 *1953,* Moffatt & Khorana **81** 1265 *1959*, Salem et al. *Biochem J* **258** 563 *1989*, *Beilstein* **26** III/IV 3668.]

Acetylcholine bromide *[66-23-9]* **M 226.1, m 143°, 146°.** The bromide is a *hygroscopic* solid, but less so than the hydrochloride salt. It crystallises from EtOH as prisms. Some hydrolysis occurs in boiling EtOH, particularly if it contains some H_2O. It can also be recrystallised from EtOH or MeOH by adding dry Et_2O. [Heilbronn *Acta Chem Scand* **12** 1492 *1958*, *Beilstein* **4** IV 1446.]

Acetylcholine chloride *[60-31-1]* **M 181.7, m 148-150°, 151°.** It is very soluble in H_2O (>10%), and is very *hygroscopic*. If pasty, dry it in a vacuum desiccator over H_2SO_4 until a solid residue is obtained. Dissolve this in absolute EtOH, filter it and add dry Et_2O, when the hydrochloride separates. Collect by filtration and store it under very dry conditions. [Jones & Major *J Am Chem Soc* **52** 307 *1930*.] The *chloroplatinate* crystallises from hot H_2O in yellow needles and can be recrystallised from 50% EtOH, **m** 242-244° [Dudley *Biochem J* **23** 1069 *1929*]; other **m** given is 256-257°. The *perchlorate* crystallises from EtOH as prisms **m** 116-117°. [*J Am Pharm Assocn* **36** 272 *1947*, *Beilstein* **4** IV 1446.]

***N^4*-Acetylcytosine** *[14631-20-0]* **M 153.1, m >300°, 326-328°, $pK_{Est(1)}$ ~1.7, $pK_{Est(2)}$ ~10.0.** If TLC or paper chromatography shows that it contains unacetylated cytosine, then reflux it in Ac_2O for 4 hours, cool at 3-4° for a few days, collect the crystals, wash them with cold H_2O, then EtOH and dry at 100°. It is insoluble in EtOH and dissolves in H_2O with difficulty, but crystallises in prisms from hot H_2O. It is hydrolysed by 80% aqueous AcOH at 100°/1 hour. [UV: Brown et al. *J Chem Soc* 2384 *1956*, Codington et al. *J Am Chem Soc* **80** 5164 *1958*.] It forms an Hg salt [Fox et al. *J Am Chem Soc* **79** 5060 *1957*]. [*Beilstein* **25** III/IV 3657.]

***N*-Acetylhistamine [*N*-(2-1{3}*H*-imidazol-4-yl)ethylacetamide]** *[673-49-4]* **M 153.2, m 147-148°, 148-149°, pK^{25} 6.99.** It is purified by recrystallisation from Et_2O/EtOH or EtOAc/EtOH (needles), and dried *in vacuo*. It sublimes at 148°/0.05mm. It is slightly soluble in H_2O and EtOH, soluble in Me_2CO and very soluble in Et_2O. The *nitrate* has **m 170°**, the *picrate* is dimorphic with **m 169-171°** (from EtOH/Et_2O) and **m 181-183°** (from EtOH). [Tabor & Mosettig *J Biol Chem* **80** 703 *1949*, Nagarajan et al. *Indian J Chem, Sect B* **16** 629, 633 *1977*, *Beilstein* **25** II 304, **25** III/IV 2053, **25/9** V 523.]

***O*-Acetyl-β-methylcholine chloride [Methacholine chloride, Amechol, Provocholine, 2-acetoxypropyl-ammonium chloride]** *[62-51-1]* **M 195.7, m 170-173°, 172-173°.** It forms white *hygroscopic* needles from Et_2O and is soluble in H_2O, EtOH and $CHCl_3$. It decomposes readily in alkaline solutions and slowly in H_2O. It should be handled and stored in a dry atmosphere. The *bromide* is less hygroscopic, and the *picrate* has **m** 129.5-131° (from EtOH). [racemate: Annis & Ely *Biochem J* **53** 34 *1953*, IR of iodide: Hansen *Acta Chem Scand* **13** 155 *1959*, *Beilstein* **4** IV 1670.]

***N*-Acetyl neuraminic acid (NANA, *O*-Sialic acid, 5-acetamido-3,5-dideoxy-D-*glycero*-D-*galacto*-2-nonulosonic acid, lactaminic acid)** *[131-48-6]* **M 309.3, m 159°(dec), 181-183°(dec), 185-187°(dec), $[\alpha]_D^{25}$ -33° (c 2, H_2O), pK^{25} 2.6.** A Dowex-1x8 (200-400 mesh) in the formate form is used, and is prepared by

washing with 0.1M NaOH, then 2N sodium formate; excess formate is removed by washing with H_2O. *N*-Acetyl neuraminic acid in H_2O is applied to this column, washed with H_2O, then eluted with 2N formic acid at a flow rate of 1ml/minute. Fractions (20ml) are collected and tested (Bial's orcinol reagent, *cf Biochemical Preparations* **7** 1 *1960*). NANA elutes at a formic acid molarity of 0.38, and the Bial positive fractions are collected and lyophilised. The residue is recrystallised from aqueous AcOH: suspend 1.35g of residue in AcOH, heat rapidly to boiling, add H_2O dropwise until the suspension dissolves (do not add excess H_2O), filter hot and then keep at +5° for several hours until crystallisation is complete. Collect NANA and dry it in a vacuum over P_2O_5. *Alternatively*, dissolve 1.35g of NANA in 14ml of H_2O, filter, add 160ml of MeOH followed by 360ml of Et_2O. Then add petroleum ether (b 40-60°) until heavy turbidity. Cool at 20° overnight. The yield of NANA is *ca* 1.3g. Dry it over P_2O_5 at 100°/1mm to constant weight. It mutarotates in Me_2SO: $[\alpha]_D^{20}$ -115° (after 7 minutes) to -32° (after 24 hours). It is commercially available as an aqueous solution (0.01g/ml). [IR and synthesis: Cornforth et al. *Biochem J* **68** 57 *1958*; Zillikin & O'Brien *Biochemical Preparations* **7** 1 *1960*; ^{13}C NMR and 1-^{13}C synthesis: Nguyen & Perry *J Org Chem* **43** 551 *1978*; Danishefski & DeNinno *J Org Chem* **51** 2615 *1986*; Gottschalk, *The Chemistry and Biology of Sialic Acids and Related Substances,* Cambridge University Press, London, *1960*, *Beilstein* **4** IV 3288.]

***N*-Acetyl penicillamine (*N*-acetyl-3-mercapto-D-valine)** *[*D *-15537-71-0*, DL *-59-53-0]* **M 191.3, m 183°, 186-187° (DL-form), 189-190° (D-form), D-form $[\alpha]_D^{25}$+18° (c 1, 50% EtOH), $pK_{Est(1)}$ ~3.0 (CO_2H), $pK_{Est(2)}$ ~8.0 (SH).** Both forms are recrystallised from hot H_2O. A pure sample of the D-form is obtained after five recrystallisations. [Crooks in *The Chemistry of Penicillin* Clarke, Johnson and Robinson eds, Princeton University Press, 470 *1949*, Review: Chain et al. *Antibiotics* (Oxford University Press) **2** *1949*, *Beilstein* **4** III 1662.]

***p*-Acetylphenyl sulfate potassium salt,** *[38533-41-4]* **M 254.3, m dec on heating, pK_{Est} ~2.1.** Purify the salt by dissolving it in the minimum volume of hot water (60°) and adding EtOH, with stirring, then leave at 0° for 1 hour. The crystals are filtered off and recrystallised from H_2O until free of Cl^- and SO_4^{2-} ions. Dry it in a vacuum over P_2O_5 at room temperature. It is a specific substrate for arylsulfatases which hydrolyse it to *p*-acetylphenol [UV has λ_{max} at 327nm (ε 21700 $M^{-1}cm^{-1}$)] [Milsom et al. *Biochem J* **128** 331 *1972*].

S-Acetylthiocholine bromide *[25025-59-6]* **M 242.2, m 217-223°(dec).** It is a *hygroscopic* solid which can be recrystallised from ligroin/EtOH (1:1), dried and kept in a vacuum desiccator. Crystallisation from *C_6H_6/EtOH gives **m** 227° or from propan-1-ol the **m** is 213°. [Hansen *Acta Chem Scand* **11** 537 *1957*, Heilbronn *Acta Chem Scand* **12** 1481 *1958*, *Beilstein* **4** IV 1585.]

S-Acetylthiocholine chloride *[6050-81-3]* **M 197.7, m 172-173°.** The chloride can be purified in the same way as the bromide, and it can be prepared from the iodide. A few milligrams dissolved in H_2O can be purified by applying onto a Dowex-1 Cl^- resin column (prepared by washing with N HCl followed by CO_3^{2-} -free H_2O until the pH is 5.8). After equilibration for 10 minutes, elution is started with CO_3^{2-} -free distilled H_2O, and 3ml fractions are collected and their OD values at λ 229nm are measured. The fractions with appreciable absorption are pooled and lyophilised at 0-5°. Note that at higher temperatures decomposition of the ester is appreciable; hydrolysis is appreciable at pH >10.5/20°. The residue is dried *in vacuo* over P_2O_5, checked for traces of iodine (add conc H_2SO_4 and heat, violet vapours are released), and recrystallise it from propan-1-ol. [Gal & Roth *Clin Chim Acta* **2** 316 *1957*, *Beilstein* **4** IV 1585.]

S-Acetylthiocholine iodide *[1866-15-5]* **M 289.2, m 203-204°, 204°, 204-205°.** Recrystallise the iodide from propan-1-ol (or *iso*-PrOH, or EtOH/Et_2O) until almost colourless and dry it in a vacuum desiccator over P_2O_5. Its solubility in H_2O is 1% w/v. A 0.075M (21.7mg/ml) solution in 0.1M phosphate buffer pH 8.0 is stable for 10-15 days if kept refrigerated. Store it away from light. It is commercially available as a 1% solution in H_2O. [Ellman et al. *Biochemical Pharmacology* **7**, 88 *1961*, IR: Hansen *Acta Chem Scand* **13** 151 *1959*, **11** 537 *1957*, *Clin Chim Acta* **2** 316 *1957*, Ivin *Zh Obshch Khim* **22** 267 *1952*, *Beilstein* **4** III 726, **4** IV 1585.]

Actinomycin C (Cactinomycin) *[8052-16-2]* **M ~1255.** (A commercial mixture of Actinomycin C_1 ~5%, C_2 ~30% and C_3 ~65% is available). *Actinomycin C_1 (native)* crystallises from EtOAc as red crystals, is soluble in $CHCl_3$, *C_6H_6 and Me_2CO, and has **m** 246-247°(dec), $[\alpha]_D^{20}$ -328° (0.22, MeOH) and λ_{max} 443nm (ε 25,000)

and 240nm (ε 34,000). *Actinomycin C_2 (native)* crystallises as red needles from EtOAc and has **m** 244-246°(dec), $[\alpha]_D^{20}$ -325° (c 0.2, MeOH), λ_{max} 443nm (ε 25,300) and 240nm (ε 33,400). *Actinomycin C_3 (native)* recrystallises from cyclohexane, or *C_6H_6/MeOH/cyclohexane as red needles with **m** 238-241° (dec), $[\alpha]_D^{20}$ -321° (c 0.2, MeOH), λ_{max} 443nm (ε 25,000) and 240nm (ε 33,300). [Brockman & Lackner, *Chem Ber* **101** 1312 *1968*.] It is *light sensitive*. [*Beilstein* **27** III/IV 9642.]

Actinomycin D (Dactinomycin) *[50-76-0]* **M 1255.5, m 241-243°(dec), $[\alpha]_D^{22}$-296° (c 0.22, MeOH).** It crystallises as bright red rhombic crystals from absolute EtOH or from MeOH/EtOH (1:3). It will also crystallise from EtOAc/cyclohexane (**m** 246-247° dec), $CHCl_3$/petroleum ether (**m** 245-246° dec), and EtOAc/MeOH/*C_6H_6 (**m** 241-243° dec). Its solubility in MeCN is 1mg/ml. $[\alpha]_D^{20}$ varies from -296° to -327° (c 0.2, MeOH). λ_{max} (MeOH) 445, 240nm (log ε 4.43, 4.49), λ_{max} (MeOH, 10N HCl, 1:1) 477nm (log ε 4.21) and λ_{max} (MeOH, 0.1N NaOH) 458, 344, 285 (log ε 3.05, 4.28, 4.13). It is **HIGHLY TOXIC,** light sensitive and anti-neoplastic. [Bullock & Johnson, *J Chem Soc* 3280 *1957*, *Beilstein* **27** III/IV 9642.]

Adenosine-5'-diphosphate [adenosine-5'-pyrophosphate, ADP] *[58-64-0]* **M 427.2, $[\alpha]_D^{25}$ -25.7° (c 2, H_2O), pK_1^{25} <2 (PO_4H), pK_2^{25} <2 (PO_4H), pK_3^{25} 3.95 (NH_2), pK_4^{25} 6.26 (PO_4H).** It is characterised by conversion to the *acridine salt* by addition of alcoholic acridine (1.1g in 50ml), filtering off the yellow salt and recrystallising from H_2O. The salt has **m** 215°(dec), UV with λ_{max} at 259nm (ε 15,400) in H_2O. [Baddiley & Todd *J Chem Soc* 648 *1947*, 582 *1949*, *cf* LePage *Biochemical Preparations* **1** 1 *1949*, Martell & Schwarzenbach *Helv Chim Acta* **39** 653 *1956*]. [*Beilstein* **26** III/IV 2369.]

Adenosine-3'-monophosphoric acid hydrate [3'-adenylic acid, 3'-AMP] *[84-21-9]* **M 347.3, m 197°(dec, as $2H_2O$), 210°(dec), m 210°(dec), $[\alpha]_{546}$ -50° (c 0.5, 0.5M Na_2HPO_4), pK_1^{25} 3.65, pK_2^{25} 6.05.** It crystallises from large volumes of H_2O in needles as the *monohydrate*, but is not very soluble in boiling H_2O. Under acidic conditions it forms an equilibrium mixture of 2' and 3' adenylic acids *via* the 2',3'-cyclic phosphate. When heated with 20% HCl, it gives a quantitative yield of furfural after 3 hours, unlike 5'-adenylic acid which only gives traces of furfural. The yellow *monoacridine salt* has **m** 175°(dec), and the *diacridine salt* has **m** 177° (225°)(dec). [Brown & Todd *J Chem Soc* 44 *1952*, Takaku et al. *Chem Pharm Bull Jpn* **21** 1844 *1973*, NMR: Ts'O et al. *Biochemistry* **8** 997 *1969*, *Beilstein* **26** III/IV 3607.]

Adenosine-5'-monophosphoric acid monohydrate [5'-adenylic acid, 5'-AMP] *[18422-05-4]* **M 365.2, m 178°, 196-200°, 200° (sintering at 181°), $[\alpha]_D^{20}$ -47.5°, $[\alpha]_{546}$ -56° (c 2, in 2% NaOH), -26.0° (c 2, 10% HCl), -38° (c 1, 0.5M Na_2HPO_4), pK_1^{25} 3.89, pK_2^{25} 6.14, pK_3^{25} 13.1.** The acid has been recrystallised from H_2O (fine needles) and is freely soluble in boiling H_2O. It crystallises also from H_2O on addition of acetone. *Alternatively*, purify it by chromatography on Dowex 1 (in formate form), eluting with 0.25M formic acid. It is then adsorbed onto charcoal (which had been boiled for 15 minutes with M HCl, washed free of chloride and dried at 100°) and recovered by stirring three times with isoamyl alcohol/H_2O (1:9 v/v). The aqueous layer from the combined extracts is evaporated to dryness under reduced pressure, and the product is crystallised twice from hot H_2O. [Morrison & Doherty *Biochem J* **79** 433 *1961*]. It has UV with λ_{max} at 259nm (ε 15,400) in H_2O at pH 7.0. [Alberty et al. *J Biol Chem* **193** 425 *1951*, Martell & Schwarzenbach *Helv Chim Acta* **39** 653 *1956*]. The *acridinium salt* has **m** 208° [Baddiley & Todd *J Chem Soc* 648 *1947*, Pettit *Synthetic Nucleotides,* van Nostrand-Reinhold, NY, **Vol 1** 252 *1972*, NMR: Sarma et al. *J Am Chem Soc* **96** 7337 *1974*, Norton et al. *J Am Chem Soc* **98** 1007 *1976*, IR of *diNa salt*: Miles *Biochem Biophys Acta* **27** 324 *1958*]. [*Beilstein* **26** III/IV 3615.]

Adenosine 5'-[β-thio]diphosphate tri-lithium salt *[73536-95-5]* **M 461.1.** Purify it by ion-exchange chromatography on DEAE-Sephadex A-25 using gradient elution with 0.1-0.5M triethylammonium bicarbonate. [Goody et al. *Biochem Biophys Acta* **276** 155 *1972*.]

Adenosine 5'-[α-thio]monophosphate di-lithium salt *[19341-57-2]* **M 375.2.** Purify it as for the diNa salt [Murray & Atkinson *Biochemistry* **7** 4023 *1968*]. Dissolve 0.3g in dry MeOH (7ml) and 1M LiI (6ml) in dry Me_2CO containing 1% of mercaptoethanol, and the Li salt is precipitated by adding Me_2CO (75ml). The residue is washed with Me_2CO (4 x 30ml) and dried at 55°/25mm. It has UV with λ_{max} at (HCl, pH 1.2) 257nm (ε 14,800); (0.015M NaOAc, pH 4.8) 259nm (ε 14,800); and (0.015M NH_4OH, pH 10.1) 259nm (ε 15,300).

Adenosine-5'-triphosphate (ATP) *[56-65-5]* **M 507.2, $[\alpha]_{546}$ -35.5 (c 1, 0.5 M Na_2HPO_4), pK_1^{25} 4.00, pK_2^{25} 6.48.** ATP is purified by precipitating it as the barium salt on adding excess barium acetate solution to a 5% solution of ATP in water. The precipitate is filtered off, washed with distilled water, dissolved in 0.2M HNO_3 and again precipitated with barium acetate. The precipitate, after several washings with distilled water, is redissolved in 0.2M HNO_3, and slightly more than an equivalent of 0.2M H_2SO_4 is added to precipitate all the barium as $BaSO_4$ which is filtered off. The ATP is then precipitated by addition of a large excess of 95% ethanol. It is filtered off, washed several times with 100% EtOH and finally with dry diethyl ether. It is dried *in vacuo*. [Kashiwagi & Rabinovitch *J Phys Chem* **59** 498 *1955*, *Beilstein* **26** III/IV 3654.]

S-(5'-Adenosyl)-L-homocysteine *[979-92-0]* **M 384.4, m 202º(dec), 204º(dec), 205-207º(dec), $[\alpha]_D^{25}$ +93º (c 1, 0.2N HCl), $[\alpha]_D^{23}$ +44º (c 0.1, 0.05N HCl), (pK see SAM hydrochloride below).** It has been recrystallised several times from aqueous EtOH or H_2O to give small prisms and the UV has λ_{max} at 260nm in H_2O. The *picrate* has **m** 170º(dec) from H_2O. [Baddiley & Jamieson *J Chem Soc* 1085 *1955*, de la Haba & Cantoni *J Biol Chem* **234** 603 *1959*, Borchardt et al. *J Org Chem* **41** 565 *1976*, NMR: Follmann et al. *Eur J Biochem* **47** 187 *1974*, *Beilstein* **26** III/IV 3676.]

(-)-S-Adenosyl-L-methionine chloride (SAM hydrochloride) *[24346-00-7]* **M 439.9, $pK_{Est(1)}$~ 2.13, $pK_{Est(2)}$~ 4.12, $pK_{Est(3)}$~ 9.28.** Purify it by ion exchange on Amberlite IRC-150 and eluting with 0.1-4M HCl. [Stolowitz & Minch *J Am Chem Soc* **103** 6015 *1981*.] It has been isolated as the tri-reineckate salt by adding 2 volumes of 1% solution of ammonium reineckate in 2% perchloric acid. The reineckate salt separates at once but is kept at 2º overnight. The salt is collected on a sintered glass funnel, washed with 0.5% of ammonium reineckate, dried (all operations at 2º) and stored at 2º. To obtain adenosylmethionine, the reineckate is dissolved in a small volume of methyl ethyl ketone (MEK) and centrifuged at room temperature to remove a small amount of solid. The clear dark red supernatant is extracted (in a separating funnel) with a slight excess of 0.1N H_2SO_4. The aqueous phase is re-extracted with fresh MEK until it is colourless. [Note that reineckates have UV absorption at 305nm (ε 15,000), and the optical density at 305nm is used to detect and estimate reineckate ions.] MEK is removed from the aqueous layer containing adenosylmethionine sulfate; the pH is adjusted to 5.6-6.0 and extracted with two volumes of Et_2O. The *sulfate* is obtained by evaporating the aqueous layer in *vacuo*. The *hydrochloride* can be obtained in the same way but using HCl instead of H_2SO_4. SAM-HCl has a solubility of 10% in H_2O. The salts are stable in the cold at pH 4-6 but decompose in alkaline media. [Cantoni *Biochemical Preparations* **5** 58 *1957*.] The purity of SAM can be determined by paper chromatography [Cantoni *J Biol Chem* **204** 403 *1953*, *Methods Enzymol* **3** 601 *1957*], electrophoretic methods or enzymic analysis [Cantoni & Vignos *J Biol Chem* **209** 647 *1954*]. [*Beilstein* **26** III/IV 3676.]

L-Adrenaline [*R*-(-)-epinephrine, L(-)-(3,4-dihydroxyphenyl)-2-methylaminoethanol] *[51-43-4]* **M 183.2, m 210º(dec), 211º(dec), 211-212º(dec), 215º(dec), $[\alpha]_{546}^{20}$ -61º (c 5, 0.5M HCl), $[\alpha]_D^{20}$ -52º (c 2, 5% HCl), pK_1^{25} 8.88 (8.75), pK_2^{25} 9.90 (9.89), pK_3^{25} 12.0 (~13).** L-Adrenaline has been recrystallised from EtOH/AcOH/NH_3 [Jensen *J Am Chem Soc* **57** 1765 *1935*]. It is sparingly soluble in H_2O, readily in acidic or basic solutions but insoluble in aqueous NH_3, alkali carbonate solutions, EtOH, $CHCl_3$, Et_2O or Me_2CO. It has also been purified by dissolving in dilute aqueous acid, then precipitating it by adding dilute aqueous ammonia or alkali carbonates. It is readily oxidised in air and turns brown on exposure to light and air. (Epinephrine readily oxidises in neutral alkaline solution. This can be diminished if a little sulfite is added). Store it in the dark under N_2. [Lewis *Br J Pharmacol Chemother* **9** 488 *1954*]. The *hydrogen oxalate salt* has **m** 191-192º(dec, evacuated capillary) after recrystallisation from H_2O or EtOH [Pickholz *J Chem Soc* 928 *1945*]. [*Beilstein* **13** H 830, **13** III/IV 2927.]

Adrenolone hydrochloride [3',4'-dihydroxy-2-methylaminoacetophenone hydrochloride] *[62-13-5]* **M 217.7, m 244-249º(dec), 248º(dec), 256º(dec), pK^{25} 5.5.** It is purified by recrystallisation from EtOH or aqueous EtOH. [Gero *J Org Chem* **16** 1222 *1951*, Kindler & Peschke *Arch Pharm* **269** 581, 603 *1931*, *Beilstein* **14** IV 832.]

Amethopterin (Methotrexate, 4-amino-4-deoxy-*N^{10}*-methylpteroyl-L-glutamic acid) *[59-05-2]* **M 454.4, m 185-204º(dec), $[\alpha]_D^{20}$ +19º (c 2, 0.1N aqueous NaOH), pK_1 <0.5 (pyrimidine^{2+}), pK_2 2.5 (N5-Me$^+$), pK_3 3.49 (α-CO_2H), pK_4 4.99 (γ-CO_2H), pK_5 5.50 (pyrimidine$^+$).** Most common impurities are 10-methylpteroyl-

glutamic acid, aminopterin and pteroylglutamic acid. Purify it by chromatography on Dowex-1 acetate, followed by filtration through a mixture of cellulose and charcoal. It has been recrystallised from aqueous HCl or by dissolution in the minimum volume of N NaOH and acidified until precipitation is complete, filter or *better* collect by centrifugation, wash with H_2O (also by centrifugation) and dry at 100°/3mm. It has UV with λ_{max} at 244 and 307nm (ε 17,300 and 19,700) in H_2O at pH 1; 257, 302 and 370nm (ε 23,000, 22,000 and 7100) in H_2O at pH 13. [Momle *Biochemical Preparations* **8** 20 *1961*, Seeger et al. *J Am Chem Soc* **71** 1753 *1949*.] It is a potent inhibitor of dihydrofolate reductase and is used in cancer chemotherapy. [Blakley *The Biochemistry of Folic Acid and Related Pteridines*, North-Holland Publ Co., Amsterdam, NY, pp157-163 *1969*, *Beilstein* **26** IV 3833.] It is **CARCINOGENIC; HANDLE WITH EXTREME CARE.**

Aminopterin (4-amino-4-deoxypteroyl-L-glutamic acid) *[54-62-6]* **M 440.4, m 231-235°(dec), $[\alpha]_D^{20}$ +18° (c 2, 0.1N aqueous NaOH), pK_1 <0.5 (pyrimidine^{2+}), pK_2 2.5 (N5-Me$^+$), pK_3 3.49 (α-CO_2H), pK_4 4.65 (γ-CO_2H), pK_5 5.50 (pyrimidine$^+$).** Purify aminopterin by recrystallisation from H_2O. It has properties similar to those of methotrexate (above). It has UV at λ_{max} 244, 290 and 355nm (ε 18600, 21300 and 12000) in H_2O at pH 1; 260, 284 and 370nm (ε 28500, 26400 and 8600) in H_2O at pH 13. [Seeger et al. *J Am Chem Soc* **71** 1753 *1949*, Angier & Curran *J Am Chem Soc* **81** 2814 *1959*, Blakley *The Biochemistry of Folic Acid and Related Pteridines*, North-Holland Publ Co., Amsterdam, NY, pp 157-163 *1969*.] For small quantities, chromatograph it on DEAE cellulose with a linear gradient of ammonium bicarbonate pH 8 and increase the molarity from 0.1 to 0.4. Monitoring is by following the UV absorption of the fractions. For larger quantities, a near boiling solution of aminopterin (5g) in H_2O (400ml) is slowly treated with small portions of MgO powder (~0.7g, calcined magnesia) with vigorous stirring until a small amount of MgO remained undissolved and the pH rises from 3-4 to 7-8. Charcoal (1g) is added to the hot solution and filtered immediately through a large sintered glass funnel of medium porosity and lined with a hot wet pad of Celite (~2-3 mm thick). The filtrate is cooled in ice, and the crystals of the Mg salt are collected by filtration and recrystallised from boiling H_2O (200ml). The crystals are washed with EtOH and dried *in vacuo*. The Mg salt is redissolved in boiling H_2O (200ml) and carefully acidified with vigorous agitation with AcOH (2ml). Pure aminopterin (3g) separates in fine yellow needles (dihydrate) which are easily filtered. The solid is washed with cold H_2O, then Me_2CO and dried *in vacuo*. If a trace of impurity is still present as shown by DEAE cellulose chromatography or TLC, repetition of the process will remove it; see UV above. [Loo *J Med Chem* **8** 139 *1965*, *Beilstein* **26** IV 3831.] **CARCINOGENIC.**

3-Aminopyridine adenine dinucleotide *[21106-96-7]* **M 635.4 (see NAD for pK).** Purify it by ion-exchange chromatography as described [Fisher et al. *J Biol Chem* **248** 4293 *1973*, Anderson & Fisher *Methods Enzymol* **66** 81 *1980*].

Anion exchange resins. These should be conditioned before use by successive washing with water, EtOH and water, and taken through two OH^-—H^+—OH^- cycles by successive treatment with N NaOH, water, N HCl, water and N NaOH, then washed with water until neutral to give the OH^- form. (See commercial catalogues on ion-exchange resins.)

Aniracetam (1-[4-methoxybenzyl]-2-pyrrolidinone) *[72432-10-1]* **M 219.1, m 121-122°.** Purify aniracetam by recrystallisation from EtOH. It is a nootropic (Alzheimer) drug. [Gouliaev & Senning *Brain Research Rev* **19** 180 *1994*.]

Apocodeine *[641-36-1]* **M 281.3, m 124°, $pK_{Est(1)}$~ 7.0, $pK_{Est(2)}$~ 8.2.** Crystallise apocodeine from absolute EtOH by boiling and allowing to stand at 0° to give the alcoholate, **m** 104.5-106.5°; EtOH is lost slowly at 25°/2mm but readily at 78°/2mm, and the anhydrous base has **m** 122.5-124.5°. It is soluble in Et_2O. [Folkers *J Am Chem Soc* **58** 1814 *1936*.] It has also been crystallised from MeOH or MeOH with a little CH_2Cl_2 as a waxy solid and dried at 80°/2mm. It softens above 100° before melting and is sensitive to air and light. The *hydrochloride*, which is formed from the base in EtOH containing an equivalent amount of HCl followed by addition of Et_2O, is recrystallised from 95% EtOH and adding Et_2O until crystals separate. It melts at 260-263° (dec, with softening at 140°) and has $[\alpha]_D^{20}$ -41.3° to - 43.3° (c 0.81, H_2O). [Neumyer et al. *J Med Chem* **16** 1223 *1973*.]

***R*-Apomorphine** *[58-00-4]* **M 267.3, m 195°(dec), pK_1^{15} 7.20 (NH_2), pK_2^{15} 8.91 (phenolic OH).** Crystallise *R*-apomorphine from $CHCl_3$ and a little petroleum ether, also from Et_2O with 1 mol of Et_2O which it loses at 100°. It sublimes in a high vacuum. It is white but turns green in moist air or in alkaline solution. Its UV has λ_{max} at 336, 399 (98% EtOH). The *di-O-methylether* is an oil **b** 175°/high vacuum, whose *picrate* crystallises from MeOH and has **m** 140° (dec). The *di-O-acetate* crystallises from EtOAc/petroleum ether with **m** 127-128°, $[\alpha]_D^{25}$ -88° (c 1, 0.1 N HCl). The *di-O-benzoyl* derivative has **m** 156-158° (from EtOH) and $[\alpha]_D^{18}$ +43.44° (c 3.3, $CHCl_3$). [Pachorr et al. *Chem* Ber **35** 4377 *1902*, *Beilstein* **21** H 246.] **NARCOTIC.**

***R*-Apomorphine hydrochloride** *[41372-20-7]* **M 312.8, m 285-287°(dec), $[\alpha]_D^{20}$ -48° (c 1, H_2O).** Crystallise the salt from H_2O (*hemihydrate*) and from EtOH. Crystals turn green on exposure to light. (see previous entry). **NARCOTIC.**

Aureomycin (7-chlorotetracycline) *[57-62-5]* **M 478.5, m 172-174°(dec), $[\alpha]_D^{23}$ -275° (MeOH), pK_1 3.3, pK_2 7.44, pK_3 9.27.** Aureomycin is dehydrated by azeotropic distillation of its solution with toluene. On cooling, the anhydrous material crystallises out and is recrystallised from $*C_6H_6$, then dried under vacuum at 100° over paraffin wax. (If it is crystallised from MeOH, it contains MeOH which is not removed on drying.) [Stephens et al. *J Am Chem Soc* **76** 3568 *1954*, Laskin & Chan *Biochem Biophys Res Commun* **14** 137 *1964*]. [*Beilstein* **14** IV 2631.]

Aureomycin hydrochloride (7-chlorotetracycline hydrochloride) *[64-72-2]* **M 514.0, m 234-236°(dec), $[\alpha]_D^{25}$ -23.5° (H_2O).** Purify the salt by dissolving 1g rapidly in 20ml of hot water, cooling rapidly to 40°, treating with 0.1ml of 2M HCl, and chilling in an ice-bath. The process is repeated twice. It is also recrystallised from Me_2NCHO/Me_2CO. [Stephens et al. *J Am Chem Soc* **76** 3568 *1954*, UV: McCormick et al. *J Am Chem Soc* **79** 2849 *1975*, *Beilstein* **14** IV 2631.]

Bacitracin **(Altracin, Topitracin)** *[1405-87-4]* **M 1422.7, $[\alpha]_D^{23}$ +5° (H_2O).** Bacitracin has been purified by carrier displacement using *n*-heptanol, *n*-octanol and *n*-nonanol as carriers and 50% EtOH in 0.1 N HCl. The pure material gives one spot with R_F ~0.5 on paper chromatography using AcOH:*n*-BuOH:H_2O (4:1:5). [Porath *Acta Chem Scand* **6** 1237 *1952*.] It has also been purified by ion-exchange chromatography. It is a white powder soluble in H_2O and EtOH but insoluble in Et_2O, $CHCl_3$ and Me_2CO. It is stable in acidic solution but unstable in base. It is a strong antibacterial. [Abraham & Bewton *Biochem J* **47** 257 *1950*, Synthesis: Munekata et al. *Bull Chem Soc Jpn* **46** 3187, 3835 *1973*, *Beilstein* **27** III/IV 5746.]

***N^6*-Benzyladenosine** *[4294-16-0]* **M 357.4, m 177-179°, 185-187°, $[\alpha]_D^{25}$ -68.6° (c 0.6, EtOH)(see pK of adenosine).** Purify it by recrystallisation from EtOH. It has UV with λ_{max} at 266nm (aqueous EtOH/HCl) and 269 nm (aqueous EtOH/NaOH). [Kissman & Weiss *J Org Chem* **21** 1053 *1956*, *Beilstein* **26** III/IV 3682.]

***N*-Benzylpenicillin sodium salt (penicillin G Na salt)** *[69-57-8]* **M 356.37, m 215° (charring and dec), 225° (dec), $[\alpha]_D^{20}$ +269° (c 0.7, MeOH), $[\alpha]_D^{25}$ +305° (c 1, H_2O), pK^{25} 2.76 (4.84 in 80% aqueous EtOH)(for free acid).** Purify the salt by dissolving it in a small volume of MeOH (in which it is more soluble than EtOH) and treating gradually with ~5 volumes of EtOAc. This gives an almost colourless crystalline solid (rosettes of clear-cut needles) and recrystallising twice more if slightly yellow in colour. The salt has also been conveniently recrystallised from the minimum volume of 90% Me_2CO and adding an excess of absolute Me_2CO. A similar procedure can be used with wet *n*-BuOH. If yellow in colour, then dissolve (~3.8g) in the minimum volume of H_2O (3ml), add *n*-BuOH and filter through a bed of charcoal. The salt forms long white needles on standing in a refrigerator overnight. More crystals can be obtained on concentrating the mother liquors *in vacuo* at 40°. A further recrystallisation (without charcoal) yields practically pure salt. A good preparation has ~600 Units/mg. The presence of H_2O in the solvents increases the solubility considerably. The solubility in mg/100ml at 0° is 6.0 (Me_2CO), 15.0 (Me_2CO/0.5% H_2O), 31.0 (Me_2CO/1.0% H_2O), 2.4 (methyl ethyl ketone), 81.0 (*n*-butanol) and 15.0 (dioxane at 14°). *Alternatively*, it is dissolved in H_2O (solubility is ~10%), filtered if necessary and precipitated by addition of EtOH and dried in a vacuum over P_2O_5. A sample can be kept for 24 hours at 100° without loss of physiological activity. It also crystallises from MeOH/EtOAc. [IR: Barnes et al. *Anal Chem* **19** 620 *1947*, *The Chemistry of Penicillin* (Clarke, Johnson and Robinson eds.) Princeton University Press,

Princeton NJ, Chapter V 85 *1949*, *Beilstein* **27** III/IV 5861.]
Other salts, e.g. the **potassium salt** (M 372.5 [113-58-4]) can be prepared from the Na salt by dissolving it (147mg) ice-cold in H_2O acidified to pH 2, extracting with Et_2O (~50ml), washing once with H_2O, and extracting with 2ml portions of 0.3% $KHCO_3$ until the pH of the extract rises to ~6.5 (~7 extractions). The combined aqueous extracts are lyophilised, and the white residue is dissolved in *n*-BuOH (1ml, absolute) with the addition of enough H_2O to effect solution. Remove insoluble material by centrifugation and add absolute *n*-BuOH to the supernatant. Crystals should separate on scratching, and after 2.5 hours in a refrigerator they are collected, washed with absolute *n*-BuOH and EtOAc and dried (yield 51.4mg). It also crystallises from aqueous Me_2CO. The *potassium salt* has **m** 214-217° (dec) (block preincubated at 200°; heating rate of 3°/min) and $[\alpha]_D^{22}$ +285° (c 0.748, H_2O). [*Beilstein* **27** III/IV 5861.]
The **free acid (penicillin G)** (**M** 334.5, [61-33-6]) has **m** 186-187° (MeOH/Me_2CO), and **m** 190-191° (H_2O) $[\alpha]_D^{25}$ +282°(EtOH). [Review: Sheehan & Henery-Logan *J Am Chem Soc* **84** 2983 *1962*, Chain et al. *Antibiotics* (Oxford University Press) **2** *1949*, and Cook *Quarterly Reviews (Chemical Society)* **2** 46 *1948*.]

Bergapten (5-methoxypsoralen) *[484-20-8]* **M 216.2, m 190-193°, 191-193°.** Crystallise it from EtOH or aqueous MeOH, and it sublimes *in vacuo*. Its properties are similar to those of its 9-methoxy isomer (xanthotoxin, see below). It is slightly soluble in $*C_6H_6$, $CHCl_3$ and AcOH but insoluble in H_2O. Its fluorescence has λ_{ex} at 352nm with λ_{em} at 480nm. It is a DNA intercalator and **possible carcinogen**. [Howell & Robertson *J Chem Soc* 293 *1937*, Boyer et al. *Biochemistry* **27** 3011 *1988*, *Beilstein* **19/6** V 4.]

(+)-Bicuculine [*R*-6(5,6,7,8-tetrahydro-6-methyl-1,3-dioxolo[4,5-*g*]isoquinolin-5-yl)-furo-[3,4-*c*]-1,3-benzo-dioxolo-8(6*H*)-one] *[485-49-4]* **M 367.4, m 177°, 193-195°, 193-197°, 215°, $[\alpha]_D^{20}$ +126° (c 1, $CHCl_3$), $[\alpha]_{546}^{20}$ +159° (c 1, $CHCl_3$), pK^{25} 4.84.** It crystallises from $CHCl_3$/MeOH as plates. The crystals melt at 177°, then solidify and re-melt at 193-195° [Manske *Canad J Research* **21B** 13 *1943*]. It is soluble in $CHCl_3$, $*C_6H_6$, EtOAc but sparingly soluble in EtOH, MeOH and Et_2O. [Stereochem: Blaha et al. *Col Czech Chem Commun* **29** 2328 *1964*, Snatzke et al. *Tetrahedron* **25** 5059 *1969*, Pharmcol: Curtis et al. *Nature* **266** 1222 *1970*, *Beilstein* **27** III/IV 1900].

L-*erythro*-Biopterin (**2-amino-4-hydroxy-6-[{1*R*,2*S*}-1,2-dihydroxypropyl]pteridine)** *[22150-76-1]* **M 237.2, m >300°(dec), $[\alpha]_{546}^{20}$ -80°, $[\alpha]_D^{20}$ -65° (c 2.0, M HCl), pK$_1^{25}$ 2.23(2.45), pK$_2^{25}$ 7.89(8.05).** Purify L-*erythro*-biopterin by chromatography on Florisil, which was washed thoroughly with 2M HCl, and elute with 2M HCl. The fractions with UV-fluorescence are pooled, evaporated *in vacuo* and the residue recrystallised. Biopterin is best recrystallised (90% recovery) by dissolving in 1% aqueous NH_3 (*ca* 100 parts), and adding this solution dropwise to an equal volume of M aqueous formic acid at 100° and allowing to cool at 4° overnight. It is dried at 20° to 50°/0.1mm in the presence of P_2O_5. [Schircks et al. *Helv Chim Acta* **60** 211 *1977*, Armarego et al. *Aust J Chem* **35** 785 *1982*.] It also crystallises from *ca* 50 parts of water or 100 parts of hot 3M aqueous HCl by adding hot 3M aqueous NH_3 and cooling. It has UV with λ_{max} at 212, 248 and 321nm (log ε 4.21, 4.09 and 3.94) in H_2O at pH 0.0; 223infl, 235.5, 274.5 and 345nm (log ε 4.07infl, 4.10, 4.18 and 3.82) in H_2O at pH 5.0; 221.5, 254.5 and 364nm (log ε 3.92, 4.38 and 3.84) in H_2O at pH 10.0. [Sugimoto & Matsuura *Bull Chem Soc Jpn* **48** 3767 *1875*, *Beilstein* **26** III/IV 4032.]

D-(+)-Biotin (vitamin H, hexahydro-2-oxo-1*H*-thieno[3,4-d]imidazole-4-pentanoic acid) *[58-85-5]* **M 244.3, m 229-231°, 230.2°(dec), 230-231°, 232-234°(dec), $[\alpha]_{546}^{20}$ +108°, $[\alpha]_D^{20}$ +91.3° (c 1, 0.1N NaOH), pK$_{Est}$ ~ 4.8.** D-(+)-Biotin crystallises from hot water in fine long needles with a solubility of 22 mg/100ml at 25°. Its solubility in 95% EtOH is 80 mg/100 ml at 25°. Its isoelectric point is at pH 3.5. Store solid and solutions under sterile conditions because it is susceptible to mould growth. [Confalone *J Am Chem Soc* **97** 5936 *1975*, Wolf et al. *J Am Chem Soc* **67** 2100 *1945*, Synthesis: Ohuri & Emoto *Tetrahedron Lett* 2765 *1975*, Harris et al. *J Am Chem Soc* **66** 1756 *1944*.] The *(+)-methyl ester* has **m** 166-167° (from MeOH/Et_2O), $[\alpha]_D^{22}$ +57° (c 1, $CHCl_3$) [du Vigneaud et al. *J Biol Chem* **140** 643, 763 *1941*]; the *(+)-S-oxide* has **m** 200-203°, $[\alpha]_D^{20}$ +130° (c 1.2, 0.1N NaOH) [Melville *J Biol Chem* **208** 495 *1954*]; the *SS-dioxide* has **m** 274-275°(dec, 268-270°), and the *SS-dioxide methyl ester* has **m** 239-241° (from MeOH/Et_2O) [Hofmann et al. *J Biol Chem* **141** 207, 213 *1941*]. [*Beilstein* **27** III/IV 7979.]

D-(+)-Biotin hydrazide *[66640-86-6]* **M 258.4, m 238-240°, 245-247°, $[\alpha]_D^{20}$ +66° (c 1, Me_2NCHO).** Wash the hydrazide with H_2O, dry it, wash it with MeOH then Et_2O, and dry. Recrystallise it from hot H_2O (clusters of prisms) [Hofmann et al. *J Biol Chem* **144** 513 *1942*]. [*Beilstein* **27** III/IV 7980.]

D-(+)-Biotin *N*-hydroxysuccinimide ester (+-biotin *N*-succinimidyl ester) *[35013-72-0]* **M 342.4, m 210°, 212-214°, $[\alpha]_D^{20}$ +53° (c 1, Me_2NCHO).** Recrystallise the ester from refluxing isoPrOH and dry it in a vacuum over P_2O_5 + KOH. [Jasiewicz et al. *Exp Cell Biol* **100** 213 *1976*.]

D-(+)-Biotin 4-nitrophenyl ester *[33755-53-2]* **M 365.4, m 160-163°, 163-165°, $[\alpha]_D^{25}$ +47° (c 2, Me_2NCHO containing 1% AcOH).** The ester has been recrystallised by dissolving 2g in 95% EtOH (30ml), heated to dissolve, then cooled in an ice-water bath. The crystals are collected, washed with ice-cold 95% EtOH (5ml) and dried over P_2O_5. The R_F on silica plates ($CHCl_3$/MeOH 19:1) is 0.19 [Bodanszky & Fagan *J Am Chem Soc* **99** 235 *1977*].

***N*-(+)-Biotinyl-4-aminobenzoic acid** *[6929-40-4]* **M 363.4, m 295-297°, 295-300°, $[\alpha]_D^{23}$ +56.55° (c 0.5, 0.1N NaOH), pK_{Est} ~4.0.** Dissolve the acid in $NaHCO_3$ solution, cool and precipitate it by adding N HCl. Collect the solid, dry it at 100° and recrystallise it from MeOH. Note that it is hydrolysed by aqueous 3M, 1M and 0.2M HCl at 120°, but can be stored in 5% aqueous $NaHCO_3$ at -20° without appreciable hydrolysis [Knappe et al. *Biochem Zeitschrift* **338** 599 *1963*, Wolf et al. *J Am Chem Soc* **73** 4142 *1951*, Bayer & Wilchek *Methods Enzymol* **26** 1 *1980*]. [*Beilstein* **27** III/IV 7984.]

***N*-Biotinyl-6-aminocaproic *N*-succinimidyl ester** *[72040-63-2]* **M 454.5, m 149-152°.** Dissolve ~400mg of the ester in dry propan-2-ol (~25ml) with gentle heating. Reduce the volume to ~10ml by gentle boiling and allow the solution to cool. Decant the supernatant carefully from the white crystals, dry the crystals in a vacuum over P_2O_5 at 60° overnight. This material gives one spot on TLC. [Costello et al. *Clin Chem* **25** 1572 *1979*, Kincaid et al. *Methods Enzymol* **159** 619 *1988*.]

***N*-(+)-Biotinyl-6-aminocaproyl hydrazide (biotin-6-aminohexanoic hydrazide)** *[109276-34-8]* **M 371.5, m 189-191°, 210°, $[\alpha]_D^{20}$ +23° (c 1, Me_2NCHO).** Suspend the hydrazide in ice-water (100mg/ml), stand overnight at 4°, filter and dry the solid in a vacuum. Recrystallise it from isoPrOH. R_F is 0.26 on SiO_2 plate using $CHCl_3$/MeOH (7:3) as eluent. [O'Shannessy et al. *Anal Biochem* **163** 204 *1987*.]

***N*-(+)-Biotinyl-L-lysine (Biocytin)** *[576-19-2]* **M 372.5, m 228.5°, 228-230° (dec), 241-243°, 245-252° (dec, sintering at 227°), $[\alpha]_D^{25}$ +53° (c 1.05, 0.1 N NaOH).** Recrystallise biocytin rapidly from dilute MeOH or Me_2CO. It can also be recrystallised from H_2O by slow evaporation or by dissolving in the minimum volume of H_2O and adding Me_2CO until solid separates. It is freely soluble in H_2O and AcOH but insoluble in Me_2CO. [Wolf et al. *J Am Chem Soc* **74** 2002 *1952*, **72** 1048 *1950*.] It has been purified by chromatography on superfiltrol-Celite, Al_2O_3 and by countercurrent distribution and then recrystallised [IR: Peck et al. *J Am Chem Soc* **74** 1991 *1952*]. The *hydrochloride* recrystallises from aqueous Me_2CO/HCl and has **m** 227° (dec). [*Beilstein* **27** III/IV 7984.]

Brefeldin A [1-*R*-2*c*,15*c*-dihydroxy-7*t*-methyl-(1*r*,13*t*)-6-oxa-bicyclo[11.3.0]hexadeca-3*t*,11*t*-dien-5-one, Decumbin] *[20350-15-6]* **M 280.4, m 200-202°, 204°, 204-205°, $[\alpha]_D^{22}$ +95° (c 0.81, MeOH).** Brefeldin A was isolated from *Penicillium brefeldianum* and recrystallised from aqueous MeOH/EtOAc or MeOH. Its solubility in H_2O is 0.6mg/ml, 10mg/ml in MeOH and 24.9mg/ml in EtOH. The *O-acetate* recrystallises from Et_2O/pentane and has **m** 130-131°, $[\alpha]_D^{22}$ +17° (c 0.95, MeOH). [Sigg *Helv Chim Acta* **47** 1401 *1964*, UV and IR: Härri et al. *Helv Chim Acta* **46** 1235 *1963,* total synthesis: Kitahara et al. *Tetrahedron* 3021 *1979*, X-ray : Weber et al. *Helv Chim Acta* **54** 2763 *1971*, *Beilstein* **18** III/IV 1220.]

5-Bromo-2'-deoxyuridine *[59-14-3]* **M 307.1, m 193-197°(dec), 217-218°, $[\alpha]_D^{25}$ -4.1° (c 0.1, H_2O), pK^{25} ~ 8.1.** Recrystallise the uridine from EtOH or 96% EtOH. It has UV with λ_{max} at 279 nm at pH 7.0, and 279 nm (log ε 3.95) at pH 1.9. Its R_F values are 0.49, 0.46 and 0.53 in *n*-BuOH/AcOH/H_2O (4:1:1), *n*-BuOH/EtOH/H_2O (40:11:19) and *i*-PrOH-25% aqueous NH_3-H_2O (7:1:1), respectively. [*Nature* **209** 230 *1966*, Prystãs & Sorm *Col Czech Chem Comm* **29** 2956 *1964*, *Beilstein* **24** III/IV 1234.]

5-Bromouridine *[957-75-5]* **M 323.1, m 215-217°, 218°, $[\alpha]_D^{22}$ -24.1° (c 2, H_2O), pK^{25} 8.1.** Recrystallise it from 96% EtOH. It has UV with λ_{max} at 279nm (log ε 3.95) in H_2O pH 1.9. R_F in *n*-BuOH/AcOH/H_2O (4:4:1) is 0.49; in *n*-BuOH/EtOH/H_2O (40:11:9) it is 0.46 and in isoPrOH/25%NH_3/H_2O (7:1:2) it is 0.53 using Whatman No 1 paper. [Prystãs & Sorm *Col Czech Chem Commmun* **29** 2956 *1964*, *Beilstein* **31** H 24.]

Brucine *[357-57-3 (anhydrous), 5892-11-5 (4H_2O)]* **M 394.5 (anhydrous), 430.5 (2H_2O), 466.5 (4H_2O), m 178-179°, $[\alpha]_{546}^{20}$ -149.9° (anhydrous; c 1, in $CHCl_3$), $[\alpha]_D^{20}$ -119° (anhydrous; c 2, in $CHCl_3$), pK_1^{15} 2.50, pK_2^{15} 8.16 (pK_2^{25} 8.28).** Crystallise brucine once from water or aqueous Me_2CO (as the *tetrahydrate*), then suspend it in $CHCl_3$ and shake with anhydrous Na_2SO_4 (to dehydrate the brucine, which then dissolves). Precipitate it by pouring the solution into a large bulk of dry petroleum ether (b 40-60°), filter and heat to 120° in a high vacuum [Turner *J Chem Soc* 842 *1951*]. The *tetrahydrate* crystallises from a mixture of EtOH and H_2O as colourless elongated needles [Eeles *Acta Cryst* **6** 809 *1953*, *Beilstein* **27** III/IV 7875.] **VERY POISONOUS.**

Brucine sulfate (hydrate) *[4845-99-2]* **M 887.0, m ~180°(dec), $[\alpha]_{546}^{20}$ -36° (dry; c 1, H_2O).** The *heptahydrate* crystallises from water as colourless laths. [Eeles *Acta Cryst* **6** 809 *1953*, *Beilstein* **27** III/IV 7875.]

Butyryl choline iodide [(2-butyryloxyethyl)trimethyl ammonium iodide] *[2494-56-6]* **M 301.7, m 85-89°, 87°, 93-94°.** Recrystallise the iodide from isoPrOH or Et_2O. [Tammelin *Acta Chem Scand* **10** 145 *1956*.] The *perchlorate* has **m** 72° (from isoPrOH). [Aldridge *Biochem J* **53** 62 *1953*, *Beilstein* **4** IV 1448.]

S-Butyryl thiocholine iodide [(2-butyrylmercaptoethyl)trimethyl ammonium iodide] *[1866-16-6]* **M 317.2, m 173°, 173-176°.** Recrystallise S-butyryl thiocholine iodide from propan-1-ol and dry it *in vacuo*; store it in the dark under N_2. The *bromide* has **m** 150° (from Me_2CO) or **m** 140-143° (from butan-1-ol). [Gillis *Chem Ind (London)* 111 *1957*, Hansen *Acta Chem Scand* **11** 537 *1957*, *Beilstein* **4** IV 1586.]

Carminic acid (7-α-D-glucopyranosyl-9,10-dihydro-3,5,6,8-tetrahydroxy-1-methyl-9,10-dioxo-2-anthracene carboxylic acid, Neutral Red 4: CI 75470) *[1260-17-9]* **M 492.4, m 120°(dec), $[\alpha]_{654}^{15}$ +51.6° (H_2O), (several phenolic pKs).** Carminic acid forms red prisms from EtOH. It gives a red colour in Ac_2O and yellow to violet in acidic solution. Its UV has λ_{max} (H_2O) at 500nm (ε 6,800); (0.02N HCl) 490-500nm (ε 5,800) and (0.0001N NaOH) 540nm (ε 3,450). Its IR has ν_{max} at (Nujol) 1708s, 1693s, 1677m, 1648m, 1632m, 1606s, 1566s, 1509 cm^{-1}. Periodate oxidation is complete after 4 hours at 0° with the consumption of 6.2 mols. The *tetra-O-methyl carminate* has **m** 186-188° (yellow needles from *C_6H_6/petroleum ether). [IR: Ali & Haynes *J Chem Soc* 1033 *1959*, Bhatia & Venkataraman *Indian J Chem* **3** (2) 92 *1965*, Synthesis: Davis & Smith *Biochemical Preparations* **4** 38 *1955*, *Beilstein* **18** III/1V 6697.]

Cation exchange resins. These should be conditioned before use by successive washing with water, EtOH and water, and taken through two H^+-OH^--H^+ cycles by successive treatment with M HCl, water, M NaOH, water and M HCl, then washed with water until neutral to give the H^+ form. (See commercial catalogues on ion exchange resins).

Cephalosporin C potassium salt *[28240-09-7]* **M 453.5, $[\alpha]_D^{20}$ +103° (H_2O), pK_1 <2.6, pK_2 3.1, pK_3 9.8.** Purify the salt by dissolving it in the minimum volume of H_2O (filter) and adding EtOH until separation of solid is complete. A solution is stable in the pH range 2.5-8. It has UV with λ_{max} at 260nm (log ε 3.95) in H_2O. The **Ba salt** has $[\alpha]_D^{20}$ +80° (c 0.57, H_2O) [Woodward et al. *J Am Chem Soc* **88** 852 *1966,* Abraham & Newton *Biochem J* **79** 377 *1961*, Hodgkin & Maslen *Biochem J* **79** 402 *1961*; see also *Quart Reviews Chem Soc* London **21** 231 *1967*]. [*Beilstein* **27** III/IV 5902.]

Chlorambucil [4-{bis(2-chloroethyl)amino)-phenylbutyric acid] *[305-03-3]* **M 304.2, m 64-66°, pK_1 5.8 (6.0 at 66°, 50% aqueous Me_2CO), pK_2 8.0.** Chlorambucil is recrystallised from petroleum ether (flat needles) and has a solubility at 20° of 66% in EtOH, 40% in $CHCl_3$, 50% in Me_2CO but is insoluble in H_2O [Everett et al. *J Chem Soc* 2386 *1953*]. [*Beilstein* **14** IV 1715.] **CARCINOGEN.**

Chloramphenicol [Amphicol, 1*R*,2*R*-(-)-2-{2,2-dichloroacetylamino}-1-{4-nitrophenyl}-propan-1,3-diol]

[56-75-7] **M 323.1, m 149-151°, 150-151°, 151-152°, $[\alpha]_D^{20}$ +20.5° (c 3, EtOH), $[\alpha]_D^{25}$ -25.5° (EtOAc).** Purify chloramphenicol by recrystallisation from H_2O (solubility is 2.5mg/ml at 25°) or ethylene dichloride as needles or long plates, and by sublimation at high vacuum. It has $A_{1cm}^{1\%}$ 298 at λ_{max} 278nm, and it is slightly soluble in H_2O (0.25%) and propylene glycol (1.50%) at 25° but is freely soluble in MeOH, EtOH, BuOH, EtOAc and Me_2CO. [Relstock et al. *J Am Chem Soc* **71** 2458 *1949*, Confroulis et al. *J Am Chem Soc* **71** 2463 *1949*, Long & Troutman *J Am Chem Soc* **71** 2469, 2473 *1949*, Ehrhart et al. *Chem Ber* **90** 2088 *1957*, *Beilstein* **13** IV 2742.]

Chloramphenicol palmitate *[530-43-8]* **M 561.5, m 90°, $[\alpha]_D^{26}$ +24.6° (c 5, EtOH).** The palmitate crystallises from *benzene or xylene with **m** 105-106° and $[\alpha]_D^{21}$ –39.5° (c 2, Et_2O), λ_{max} 267.3nm. [Edgerton et al. *J Am Chem Soc* **77** 27 *1955*, *Beilstein* **13** IV 2753.]

2-Chloroadenosine *[146-77-0]* **M 301.7, m 145-146°(dec), 147-149°(dec), $pK_{Est(1)}$~ 0.5, $pK_{Est(2)}$~ 7.6.** Purify 2-chloroadenosine by recrystallisation from H_2O (~1% in cold), and it has UV with λ_{max} at 264 nm (pH 1 and 7) and 265 nm (pH 13) in H_2O. [Brown & Weliky *J Org Chem* **23** 125 *1958*, Schaeffer & Thomas *J Am Chem Soc* **80** 3738 *1958*, IR: Davoll & Lewy *J Am Chem Soc* **74** 1563 *1952*, *Beilstein* **26** III/IV 3725.]

Chlorophyll *a* *[479-61-8]* **M 983.5, m 117-120°, 150-153°, 178-180° (sinters at ~150°), $[\alpha]_D^{20}$ -262° (Me_2CO).** It forms green crystals from Me_2CO, Et_2O/H_2O, Et_2O/hexane/H_2O or Et_2O/pentane /H_2O. It is sparingly soluble in MeOH and insoluble in petroleum ether. In alkaline solution it gives a blue-green colour with deep red fluorescence. A very crude chlorophyll mixture has been purified by chromatography on low melting polyethylene (MI 0.044; "Dow" melting index MI <2) and developed with 70% aqueous Me_2CO. The order of effluent from the bottom of the column is: xanthophylls, chlorophyll *b*, chlorophyll *a*, phaeophytins and carotenes. A mixture of chlorophylls *a* and *b* is best separated by chromatography on sugar, and the order is chlorophyll *b* elutes first followed by chlorophyll *a*. To an Me_2CO/H_2O solution of chlorophylls 200ml of iso-octane are added, and the mixture shaken in a separating funnel and the H_2O is carefully removed. The iso-octane layer is dried (Na_2SO_4) and applied onto a glass column (5cm diameter) dry packed with 1000ml of powdered sucrose which has been washed with 250ml of iso-octane. Elution with 0.5% of isopropanol in iso-octane gives chlorophyll *a.* Keeping the eluate overnight at 0° yields micro crystals which are collected by filtration or centrifugation (Yield 40mg). The UV_{EtOH} has λ_{max} **660**, 613, 577, 531, 498, **429** and 409 nm. *Note* that anhydrous chlorophylls can be easily enolised, epimerised or allomerised in dry polar organic solvents. [Anderson & Calvin *Nature* **194** 285 *1962*, Stoll & Weidemann *Helv Chim Acta* **16** 739 757 *1933*, NMR: Katz et al. *J Am Chem Soc* **90** 6841 *1968*, **85** 3809 *1963* for *a* and *b*; ORD: Inhoffen et al. *Justus Liebigs Ann Chem* **704** 208 *1967*, Willstätter & Isler *Justus Liebigs Ann Chem* **390** 269, 233 *1912*, *Beilstein* **26** III/IV 3243.]

Chlorophyll *b* *[519-62-0]* **M 907.52, sinters at 86-92°, sinters at 170°, dec at 160-170°, m 183-185°, 190-195°, $[\alpha]_D^{20}$ -267° (Me_2CO/MeOH), $[\alpha]_{720}^{25}$ -133° (MeOH/Pyridine 95:5).** See purification of chlorophyll *a*, and is separated from "*a*" by chromatography on sucrose [UV, IR: Stoll & Weidemann *Helv Chim Acta* **42** 679, 681 *1959*]. It forms red-black hexagonal bipyramids or four-sided plates from dilute EtOH and has been recrystallised from $CHCl_3$/MeOH. It is soluble in MeOH, EtOH, EtOAc and insoluble in petroleum ether. [Dougherty et al. *J Am Chem Soc* **88** 5037 *1966*, *Beilstein* **26** III/IV 3787.]

6-Chloropurine riboside (6-chloro-9-β-D-ribofuranosyl-9*H*-purine) *[2004-06-0]* **M 286.7, m 158-162°(dec), 165-166°(sintering at 155°), 168-170°(dec), $[\alpha]_D^{26}$ -45° (c 0.8, H_2O).** Purify the riboside by suspending the dry solid (~12 g) in hot MeOH (130 ml) and then adding enough hot H_2O (~560ml) to cause solution, filter and set aside at 5° overnight. The colourless crystals of the riboside are filtered off, washed with Me_2CO, Et_2O and dried at 60°/0.1mm. More material can be obtained by evaporating the filtrate to dryness and recrystallisation of the residue from MeOH/H_2O (2:1) (15ml/g). It has UV with λ_{max} at 264nm (ε 9140) in H_2O. [Robins *Biochemical Preparations* **10** 145 *1963*, Baker et al. *J Org Chem* **22** 954 *1957*.]

Chromomycin A_3 *[7059-24-7]* **M 1183.3, m 185°dec, $[\alpha]_D^{23}$ -57° (c 1, EtOH).** Dissolve the antibiotic (10g) in EtOAc and add to a column of Silica Gel (Merck 0.05-0.2microns, 4x70cm) in EtOAc containing 1% oxalic acid. Elute with EtOAc+1% oxalic acid and check fractions by TLC. Pool fractions, wash with H_2O thoroughly, dry and evaporate. Recrystallise the residue from EtOAc. The *heptaacetate* has **m** 214°, $[\alpha]_D^{23}$ -20° (c 1, EtOH). [Miyamoto et al. *Tetrahedron* **23** 421 *1967*, Harada et al. *J Am Chem Soc* **91** 5896 *1969*, *Beilstein* **17/5** V 673.]

8*S*,9*R*-(-)-Cinchonidine *[485-71-2]* **M 294.4, m 210.5°, $[\alpha]_{546}^{20}$ -127.5° (c 0.5, EtOH), $[\alpha]_{D}^{20}$ -109.2° (EtOH), pK_1^{15} 4.17, pK_2^{15} 8.4, pK_1^{20} 5.80, pK_2^{20} 10.03.** Crystallise cinchonidine from aqueous EtOH (prisms or plates). It is a strong base and readily forms a *mono- and di- hydrochloride* and other stable salts. It is slightly soluble in Et_2O, but quite soluble in EtOH and $CHCl_3$. For the *N-benzylcinchonidinium chloride* see [69257-04-1]. [*Beilstein* **23** III/IV 2824, **23/12** IV 406.]

8*R*,9*S*-(+)-Cinchonine *[118-10-5]* **M 294.4, m 265°, $[\alpha]_{546}^{20}$ +268° (c 0.5, EtOH), pK_1^{15} 4.28, pK_2^{15} 8.35, pK_1^{20} 5.85, pK_2^{20} 9.96.** Crystallise cinchonine from EtOH or diethyl ether (needles). Its solubility (w/v) is 1.7% in EtOH, 4% in boiling EtOH, 1% in $CHCl_3$ and is almost insoluble in H_2O. It is a strong base and readily forms a *mono- and di- hydrochloride* and other stable salts. For the *N-benzylcinchoninium chloride* see [69221-14-3]. [Rabe *Justus Liebigs Ann Chem* **365** 366, 371 *1909*, *Beilstein* **23** III/IV 2819, 2832.]

Clonidine hydrochloride [Catapres, 2-(2,6-dichloroanilino)-2-imidazoline hydrochloride] *[4205-91-8]* **M 266.6, m 305°, pK^{25} 5.88 (free base)**. This antihypertensive is recrystallised from EtOH/Et_2O and dried in a vacuum (solubility in H_2O is 5%). The *free base* has **m** 124-125° and is recrystallised from hexane. [Jen et al. *J Med Chem* **18** 90 *1975*, NMR: Jackman & Jen *J Am Chem Soc* **97** 2811 *1975*.]

Cloxacillin sodium salt (sodium 3-*o*-chlorophenyl-5-methyl-4-isoxazolyl penicillin monohydrate) *[642-78-4]* **M 457.9, m 170°, $[\alpha]_{D}^{20}$ +163° (H_2O pH 6.0-7.5), pK_{Est} ~2.8 (COOH).** Purify cloxacillin sodium salt by dissolving it in isoPrOH containing 20% of H_2O, and diluting with isoPrOH to a water content of 5% and chilling. Recrystallise it again in this manner. The sodium salt is collected and dried at 40° in air to give the colourless *monohydrate*. It is soluble in H_2O (5%), MeOH, EtOH, pyridine and ethylene glycol. [Doyle et al. *J Chem Soc* 5838 *1963*, Naylor et al. *Nature* **195** 1264 *1962*.]

(–)-Cocaine {ecogonine methyl ester benzoate, 2β-carbomethoxy-3-β-benzoxytropane, methyl 1*R*-(*exo*,*exo*)]-3-(benzoyloxy)-2-methyl-8-azabicyclo[3.2.1]octane-2-carboxylate} *[50-36-2]* **M 303.4, m 98°, b 187-188°/0.1mm, $[\alpha]_{D}^{20}$ -15.8° (c 4, $CHCl_3$), $[\alpha]_{D}^{20}$ -35° (50% EtOH), pK^{25} 5.59 and 8.61 (8.39).** (–)-Cocaine crystallises from EtOH and sublimes below 90° in a vacuum in an amorphous form. The *hydrochloride* crystallises from MeOH/Et_2O with **m** 195° and $[\alpha]_{D}^{20}$ -72° (c 2 in H_2O, pH 4.5), -78.5° (50% aqueous EtOH). [Sam & Reynolds *J Chem Soc* **97** 1335 *1910*, Tufariello et al. *J Am Chem Soc* **101** 2435 *1979*.] **α-Cocaine** is the (+) enantiomer. [*Beilstein* **22** I 547, **22** II 150.]

Cocarboxylase tetrahydrate (aneurine pyrophosphoric acid tetrahydrate, thiamine pyrophosphoric acid tetrahydrate) *[136-09-4]* **M 496.4, m 220-222°(sinters at 130-140°), 213-214°, $pK_{Est(1)}$~2, $pK_{Est(2)}$~6, $pK_{Est(3)}$~9.** Cocarboxylase tetrahydrate recrystallises from aqueous Me_2CO. [Wenz et al. *Justus Liebigs Ann Chem* **618** 210 *1958*, UV: Melnick *J Biol Chem* **131** 615 *1939*, X-ray: Carlisle & Cook *Acta Cryst (B)* **25** 1359 *1969*.] The *hydrochloride salt* has **m** 242-244°(dec), 241-243°(dec) or 239-240°(dec) and crystallises from aqueous HCl/EtOH, EtOH containing HCl or HCl/Me_2CO. [Weijlard *J Am Chem Soc* **63** 1160 *1941*, Synthesis: Weijlard & Tauber *J Am Chem Soc* **60** 2263 *1938*, *Beilstein* **27** III/IV 1777.]

Codeine *[76-57-3]* **M 299.4, m 151-154°, 154-156°, $[\alpha]_{D}^{20}$ -138° (in EtOH), pK^{15} 6.06(OH), pK^{25} 8.21 (NMe).** Codeine crystallises from water or aqueous EtOH. Dry it at 80°. Evaporation of a $CHCl_3$ extract gives a colourless glass which crystallises on scratching. It crystallises from H_2O as the *monohydrate*, **m** 157-158.5°, and has $[\alpha]_{D}^{25}$ -136° (c 2.8, EtOH). The *hydrobromide* crystallises in needles from H_2O, and effervesces at 151-160°, solidifies and remelts with extensive decomposition at 273-278°. It sublimes at 100°/0.03mm. [Gates *J Am Chem Soc* **75** 4340 *1953*, Dauben et al. *J Org Chem* **44** 1567 *1979*, *Beilstein* **27** II 136, **27** III/IV 2228.]

Coenzyme A trihydrate *[85-61-0]* **M 821.6, pK_1 4.0 (adenine NH_2), pK_2 6.5 (PO_4H), pK_3 9.6 (SH).** The white powder is best stored in an inert atmosphere in the dark in sealed ampoules after drying *in vacuo* over P_2O_5 at 34°. It has UV with λ_{max} at 259 nm (ε 16,800) in H_2O. [Buyske et al. *J Am Chem Soc* **76** 3575 *1954*.] It is soluble in H_2O but insoluble in EtOH, Et_2O and M_2CO. It is readily oxidised in air and is best kept as the more stable *trilithium salt* [Moffat & Khorana *J Am Chem Soc* **83** 663 *1961*; see also Beinert et al. *J Biol Chem* **200** 384 *1953*, De Vries et al. *J Am Chem Soc* **72** 4838 *1950*, Gregory et al. *J Am Chem Soc* **74** 854 *1952* and

Baddiley *Adv Enzymol* **16** 1 *1955*]. [*Beilstein* **26** III/IV 3663.]

Coenzyme Q_0 (2,3-dimethoxy-5-methyl-1,4-benzoquinone, 3,4-dimethoxy-2,5-tolu-quinone, fumigatin methyl ether) *[605-94-7]* **M 182.2, m 56-58°, 58-60°, 59°.** It crystallises in red needles from petroleum ether (b 40-60°) and sublimes at high vacuum at a bath temperature of 46-48° [Ashley et al. *J Chem Soc* 441 *1938*, UV in EtOH: Vischer *J Chem Soc* 815 *1953*, UV in cyclohexane: Morton et al. *Helv Chim Acta* **41** 2343 *1858*, Aghoramurthy et al. *Chem Ind (London)* 1327 *1954*]. [*Beilstein* **8** IV 2721.]

Coenzyme Q_4 (Ubiquinone-4, 2,3-dimethoxy-5-methyl-6-[3,7,11,15-tetramethyl-hexadeca-2*t*,6*t*,10*t*,14-tetraenyl]-1,4-benzoquinone) *[4370-62-1]* **M 454.7, m 30°, 33-45°.** It is a red oil which can be purified by chromatography on SiO_2 plates and eluted with Et_2O/hexane. The purity is checked by HPLC (silica column using 7% Et_2O/hexane). It has UV with λ_{max} at 270 nm (ε 14,800) in petroleum ether. [NMR and MS: Naruta *J Org Chem* **45** 4097 *1980, cf* Morton *Biochemical Spectroscopy* (Adam Hilger, London, 1975) p 491]. It has also been dissolved in MeOH/EtOH (1:1 v/v) and kept at 5° until crystals appear [Lester & Crane *Biochim Biophys Acta* **32** 497 *1958*].

Coenzyme Q_9 (Ubiquinone-9, 2,3-dimethoxy-5-methyl-6-[3,7,11,15,19,23,27,31,35-nonamethyl-hexatriaconta-2*t*,6*t*,10*t*,14*t*,18*t*,22*t*,26*t*,30*t*,34-nonaenyl]-1,4-benzoquinone) *[303-97-9]* **M 795.3, m 40.5-42.5°, 44-45°, 45°.** The yellow crystals are purified by recrystallisation from petroleum ether and by chromatography on SiO_2 plates and eluted with Et_2O/hexane. The purity can be checked by HPLC (silica column using 7% Et_2O/hexane). It has UV with λ_{max} at 270nm (ε 14,850) in petroleum ether. [NMR and MS: Naruta *J Org Chem* **45** 4097 *1980,* Le et al. *Biochem Biophys Acta* **32** 497 *1958*, *cf* Morton *Biochemical Spectroscopy* (Adam Hilger, London, 1975) p 491, IR: Lester et al. *Biochim Biophys Acta* **33** 169 *1959*, UV: Rüegg et al. *Helv Chim Acta* **42** 2616 *1959*, Shunk *J Am Chem Soc* **81** 5000 *1959*, *Beilstein* **8** IV 3313.]

Coenzyme Q_{10} (Ubiquinone-10, 2,3-dimethoxy-5-methyl-6-[3,7,11,15,19,23,27,31,35,-39-decamethyl-tetraconta-2*t*,6*t*,10*t*,14*t*,18*t*,22*t*,26*t*,30*t*,34*t*,38-decaenyl]-1,4-benzoquinone) *[303-98-0]* **M 795.3, m 48-49°,49°, 49.5-50.5°, 50°.** Purify it by recrystallisation from EtOH, EtOH/Me_2CO or Et_2O/EtOH and by chromatography on silica gel using isoPrOH/Et_2O (3:1) to give orange crystals. It has UV with λ_{max} at 270nm (ε 15,170) in petroleum ether. [Terao et al. *J Org Chem* **44** 868 *1979*, NMR and MS: Naruta et al. *J Org Chem* **45** 4097 *1980*, IR: Lester et al. *Biochem Biophys Acta* **42** 1278 *1959*, NMR: Planta et al. *Helv Chim Acta* **42** 1278 *1959*; Morton *Biochemical Spectroscopy* (Adam Hilger, London, 1975) p 491].

Colcemide (Demecocine) *[477-30-5]* **M 371.4, m 182-185°, 183-185°, 186°, $[\alpha]_D^{20}$ -129° (c 1, $CHCl_3$).** Colcemide is purified by chromatography on silica and eluting with $CHCl_3$/MeOH (9:1), and by recrystallisation from EtOAc/Et_2O to form yellow prisms. Its UV in EtOH has λ_{max} at 243nm (ε 30,200) and 350nm (ε 16,300). [Synthesis, IR, NMR, MS: Capraro & Brossi *Helv Chim Acta* **62** 965 *1979*, *Beilstein* **8** IV 3319.]

Colchicine {*N*-[(7*S*)-1,2,3,10-tetramethoxy-5,6,7,9-tetrahydro-9-oxo-benzo[*a*]heptalen-7-yl]-acetamide} *[64-86-8]* **M 399.5, m 150-160° (dec), 155-157°(dec), 156-157°, $[\alpha]_{546}^{20}$ -570° (c 1, H_2O), $[\alpha]_D^{20}$ -443° (c 1.7, H_2O), $[\alpha]_D^{20}$ -120° (c 1, $CHCl_3$), pK^{20} 1.85 and 12.4.** Commercial material contains up to 4% desmethylcolchicine. Purify colchicine by chromatography on alumina and eluting with $CHCl_3$ [Ashley & Harris *J Chem Soc* 677 *1944*]. *Alternatively*, an acetone solution on alkali-free alumina has been used, and eluting with acetone [Nicholls & Tarbell *J Am Chem Soc* **75** 1104 *1953*]. It crystallises as yellow needles from EtOAc or $CHCl_3$ with solvent of crystallisation which can be removed at ~70°. It is soluble in Et_2O (0.5%), *C_6H_6 (1%) and H_2O (4%). It is sold as "**Colgout**" for the treatment of gout and binds to tubulin. [Schreiber et al. *Helv Chim Acta* **44** 540 *1961,* Scott et al. *Tetrahedron* **21** 3605 *1965*, van Tamelen et al. *Tetrahedron* **14** 8 *1961*, *Beilstein* **14** IV 946.]

Compactin (Mevastatin) *[73573-88-3]* **M 390.5, m 151-153°, 152°, $[\alpha]_D^{22}$ +283° (c 0.48, acetone).** Purify compactin by recrystallisation from aqueous EtOH. Its UV (EtOH) has λ_{max} at 230, 237 and 246nm (log ε 4.28, 4.30 and 4.11); and its IR (KBr) has ν_{max} 3520, 1750 (lactone CO) and 1710 (CO ester) cm^{-1}. [Clive et al. *J Am Chem Soc* **110** 6914 *1988*, Review: Rosen & Heathcock *Tetrahedron* **42** 4909 *1986*, IR, NMR, MS: Brown et al.

J Chem Soc Perkin Trans 1 1165 *1976*.] It is a potent inhibitor of 3-hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA reductase), is an enzyme in cholesterol biosynthesis, and lowers cholesterol levels [Brown et al. *J Biol Chem* **253** 1121 *1978*, Nakamura & Ableles *Biochemistry* **24** 1364 *1985*, *Beilstein* **18/3** V 145].

Crotaline (monocrotaline, 12,13-dihydroxy-(13β-14β*H*)-14,19-dihydro-20-norcrotalanan-11,15-dione) *[315-22-0]* **M 325.4, m 196-197°(dec), 197-198°(dec), 203°(dec), $[\alpha]_D^{20}$ -55° (c 1, EtOH).** Crotaline forms prisms from absolute EtOH and recrystallises also from $CHCl_3$. Its UV(96% EtOH) has λ_{max} at 217nm (log ε 3.32). [Adams et al. *J Am Chem Soc* **74** 5612 *1952*, Culvenor & Smith *Aust J Chem* **10** 474 *1957*.] The *hydrochloride* has **m** 212-214° (from MeOH/Et_2O) and $[\alpha]_D^{28}$ -38.4° (c 5, H_2O) [Adams & Gianturco *J Am Chem Soc* **78** 1922 *1956*]. The *picrate* has **m** 230-231.5°(dec) [Adams et al. *J Am Chem Soc* **74** 5614 *1952*]. [*Beilstein* **27** III/IV 6660.]

Curcumin [bis(4-hydroxy-3-methoxycinnamoyl)methane, 1,7-bis(4-hydroxy-3-methoxyphenyl)(1*E*,6*E*)-1,6-heptadiene-3,5-one] *[458-37-7]* **M 368.4, m 182°, 183°, 184-195°, 184-186°, pK^{25} 9.30 (50% v/v aqueous EtOH), pK_1 7.80, pK_2 8.5 and pK_3 9.0 (H_2O).** Purify curcumin by recrystallising it from MeOH, EtOH or acetic acid (yellow, orange-yellow prisms) and drying it *in vacuo*. It is best separated from related compounds by HPLC (see refs below). It is sparingly soluble in H_2O but soluble in AcOH and in alkaline buffer. In solution at pH 1-7 the colour is yellow and at pH 7-9 the colour is brownish-red or deep red. It was commercialised as a pH indicator under the name of "curcuma paper". Curcumin is a phenolic substance which occurs naturally in *Curcuma domestica, C. xanthorrhiza, C. aromatica, C. longa*, and is used in Indian curry cooking as *turmeric*. It has many physiological properties including anti-oxidant, anti-inflammatory, potent anti-tumour, and is an inhibitor of several enzymes (EGFR tyrosine kinase, IkB kinase, nitric oxide synthase, cyclooxygenase, lipoxygenase). It penetrates cell membranes accumulating in plasma membranes, nuclear envelope and endoplasmic reticulum. Its UV-VIS has λ_{max} (logε)(EtOH) at 268 (4.09) and 430nm (4.74), (dioxane) at 265 (4.18) and 420nm (4.37) and (40% aqueous THF) at 429nm (4.780), with fluorescence maxima at λ_{excit} 433nm and λ_{emis} 511nm in 40% aqueous THF. Its IR (KBr) has ν_{max} at 3400 (br), 1625, 1600, 1500, 1275, 1025, 960 cm^{-1}. The ^1H NMR [400MHz, $CDCl_3$] has δ at 6.06 (1H, s, H-4), 16.41 (1H, br s, OH), 7.57 (2H, d, *J* = 16.0Hz, H-2,6), 6.75 (2H, d, *J* = 16.0Hz, H-1,7), 7.32 (2H, d, *J* = 2.0Hz, H-2′,2″), 9.64 (2H, s, OH-4′,4″), 6.85 (2H, d, *J* = 8.1Hz, H-5′,5″), 7.16 (2H, dd, *J* = 2.0, 8.1Hz, H-6′,6″), 3.85 (6H, s, 3′,3″ OMe) (from TMS); and the ^{13}C NMR [100MHz, $CDCl_3$] has δ at 100 (C-4), 183.2 (C-3,5), 121.1 (C-2,6), 140.7 (C-1,7), 126.4 (C-1′,1″), 111.5 (C-2′,2″), 148.0 (C-3′,3″), 149.4 (C-4′,4″), 115.8 (C-5′,5″), 123.0 (C-6′,6″), 55.7 (O***C***H_3) (from TMS). It complexes strongly with boron, iron, copper and nickel, but weakly with calcium and magnesium. As a 0.1% solution in AcOH it is used for the spectrophotometric determination of Boron as a complex with λ_{max} 550nm (ε180,000). [Dyrssen et al. *Analyt Chim Acta* **60** 139 *1972*, Spicer & Strickland *Analyt Chim Acta* **18** 231 *1958*, Roughley & Whiting, *J Chem Soc, Perkin Trans I* 2379 *1973*, Zsila et al. *Tetrahedron Asymm* **14** 2433 *2003*, cf Cooke & Segal *Aust J Chem* **8** 107 *1955*, *Beilstein* **8** H 554, **8** I 757, **8** II 588, **8** III 4312, **8** IV 3697.]
The ***diacetyl*** derivative has **m 171-172°** (from EtOH) and the ***dibenzoyl*** derivative has **m 210°** (from EtOH or C_6H_6*).

The ***dimethyl*** derivative [***1,7-bis(3,4-dimethoxyphenyl)(1E, 6E)-1,6-heptadiene-3,5-one***] has **m 128-130°, M 396.2;** the UV has λ_{max} at 427nm, and the ^1H NMR [200MHz, $CDCl_3$] has δ at 3.92 (6H, s, 2 x CH_3O-Ph), 3.93 (6H, s, 2 x CH_3O-Ph), 5.82 (1H, s, H-4), 6.45 (2H, d, *J* = 13Hz, H-1,2), 6.86 (6H, m, Arom-H), 7.57 (2H, d, *J* = 13Hz, H-6,7) [Nurfina et al. *Eur J Med Chem* **32** 321 *1997*].
5'-Methoxycurcumin [1-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-(1*E*,6*E*)-1,6-heptadiene-3,5-one] **M 398.4**, has **m 145-146°** (from MeOH), and was isolated as a yellow powder from *C. xanthorrhiza* with UV λ_{max} at 429nm in MeOH.
1-Hydroxycurcumin [1-hydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)-(6*E*-6-heptene-3,5-dione] **m 84-88°** was isolated from the same source, had UV λ_{max} at 372nm in MeOH and had a weaker antioxidant activity than the other curcumins towards the autoxidation of linoleic acid in a water-alcohol system [Masuda et al. Phytochemistry **31** 3645 *1992*]. An optically active form, **(1ξ)-1-hydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)-(1E,6E)-1,6-heptadiene-3,5-one**, has **m 92.0-96.0°**, with **$[\alpha]_D$ +12.2° (c 0.06, EtOH, configuration unknown), M 386.4.** Its UV has λ_{max} nm (ε)(MeOH) at 230 (sh), 260 (21000), 283 (18000),

370 (56000); and its IR (CDCl3) has ν_{max} at 965, 1000, 1120, 1260, 1325, 1375, 1460, 1560, 1600, 1620, 1650, 2850, 2900, 3525 cm^{-1}. Its ^1H NMR [270MHz, $CDCl_3$] has δ at 2.65(1H, dd, *J* = 17, 3.5Hz), 2.93 (1H, dd, *J* = 17, 14Hz), 3.93 (3H, s), 3.95 (3H, s), 5.39 (1H. dd, *J* = 14, 3.5Hz), 5.60 (1H, s), 5.80 (1H, br s, disappeared on addition of D_2O), 5.86 (1H, br s, disappeared on addition of D_2O), 6.44 (1H, d, *J* = 16Hz), 6.90 (1H, d, *J* = 8Hz), 7.00 (4H, br s), 7.03 (1H, dd, *J* = 8, 2Hz), 7.30 (1H, d, *J* = 16Hz) and R_F (Silica gel 60 F_{254}, C_6H_6*/EtOAc 1:1) of 0.2. When this *hydroxyheptadiene* was heated at 130°/<15mmHg/10 hours it gave *curcumin* in 79% yield. ***(3S,5S) - 1, 7 - Bis (4 - hydroxy-3-methoxyphenyl) heptane-3, 5-diol*** [colourless needles **m 132-134°**, with **$[\alpha]_D$ -18.5° (c 0.26, EtOH), R_F** 0.1] was also isolated from the rhizomes of *C. xanthorrhizia* (Zingiberaceae) and characterised;and ***(3R,5R)-1-(4-hydroxyphenyl)-7-phenylheptane-3,5-diol*** [colourless needles **m 109-111°**, with **$[\alpha]_D$ +8.3° (c 0.06, $CDCl_3$),** R_F 0.3] was isolated from the rhizomes of *Alpinia officinarum* (Zingiberaceae) and characterised; the absolute configurations were determined from the circular dichroism (CD) spectra of the 3,5-bis-*p*-dimethylaminobenzoate esters of their methylated derivatives, and applying the *exciton chirality rule* [Uehara et al. *Chem Pharm Bull Jpn* **38** 3298 *1987*].

Desmethoxycurcumin *[22608-11-3]* **M 338.3, m 173-175°** (also reported are **168°** and **172°**) is a contaminant of curcumin, isolated from the same source as curcumin, best purified by HPLC and crystallises from EtOH as an orange-yellow powder. Its UV-VIS has λ_{max} (log ε) (MeOH) at 419nm (4.706) and (40% aqueous THF) 425nm (4.806) with fluorescence maxima at λ_{excit} 428nm and λ_{emis} 505nm in 40% aqueous THF. The ^1H NMR [400MHz, $CDCl_3$] has δ at 5.97 (1H, s, H-4), 7.60 (2H, d, *J* = 16.0Hz, H-2,6), 6.69 (1H, d, *J* = 16.0Hz, H-1 or 7), 6.64 (1H, d, *J* = 16.0Hz, H-7 or 1), 7.34 (1H, d, *J* = 1.7Hz, H-2′ or 2″), 6.90 (1H, d, *J* = 8.0Hz, H-2″or 2′), 7.56 (1H, d, *J* = 8.0Hz, H-5′), 6.88 (1H, d, *J* = 8.0Hz, H-5″), 7.27 (1H, dd, *J* = 8,1.7Hz, H-6′), 6.9 (1H, d, *J* = 8Hz, H-6″), 3.92 (3H, s, OCH_3) (from TMS); and the ^{13}C NMR [100MHz, $CDCl_3$] has δ at 101.6 (C-4), 184.4 and 184.5 (C-3,5), 121.1 and 122.3 (C-2,6), 141.4 and 141.0 (C-1,7), 128.2 and 127.7 (C-1′,1″), 111.5 and 130.9 (C-2′,2″), 148.8 and 116.8 (C-3′,3″), 150.0 and 160.5 (C-4′,4″), 116.2 and 116.8 (C-5′,5″), 123.8 and 130.9 (C-6′,6″), 56.3 (O***C***H_3) (from TMS).

Similarly **bis-desmethoxy-curcumin** *[22608-12-4]* **M 308.3, m 224°** (also reported are **216-218°** and **222°**) is a contaminant of curcumin, occurring in the same source, best purified by HPLC and crystallises as the *hydrate* in yellow plates from EtOH. Its UV has λ_{max} (logε)(MeOH) at 414nm (4.675) and (40% aqueous THF) 420nm (4.702) with fluorescence maxima at λ_{excit} 425nm and λ_{emis} 501nm in 40% aqueous THF. The ^1H NMR [400MHz, $CDCl_3$] has □ at 6.03 (1H, s, H-4), 16.4 (1H, br s, 3-OH), 7.56 (2H, d, *J* = 15.9Hz, H-2,6), 7.56 (2H, d, *J* = 15.9Hz, H-1,7), 6.84 (2H, d, *J* = 8.2Hz, H-2′,2″), 7.56 (2H, d, *J* = 8.2Hz, H-3′,3″), 10.03 (2H, s, 4′,4″-OH), 7.56 (2H, d, *J* = 8.2Hz, H-5′,5″), 8.64 (2H, d, *J* = 8.2Hz, H-6′,6″) (from TMS); and the ^{13}C NMR [100MHz, $CDCl_3$] has □ at 100.9 (C-4), 183.2 (C-3,5), 120.8 (C-2,6), 140.3 (C-1,7), 125.8 (C-1′,1″), 130.3 (C-2′,2″), 115.9 (C-3′,3″), 159.8 (C-4′,4″), 115.9 (C-5′,5″), 130.3 (C-6′,6″) (from TMS). [Jayaprakasha et al. *J Agric Food Chem* **50** 3668 *2002*, Inoue et al. *J Agric Food Chem* **56** 9328 *2008*, (HPLC, UV, fluorescence) Rouseff *J Food Sci* **53** 1823 *1988*, (MS) Jiang et al. *Rapid Commun Mass Spectrom* **20** 1001 *2006*, (HPLC, MS) Jiang et al. *J Chromatogr* A **1111** 21 *2006*, (HPLC, MS) Hiserodt et al. *J Chromatogr* A **740** 51 *1996*, (spectroscopy) Tønnesen et al. *Pharmazie* **50** H.10 *1995*, (IR) Tanaka et al. *J Agric Food Chem* **56** 9787 *2008,* (spectroscopy) Péret-Almeida et al. *Food Research International* **38** 1039 *2005*. (cytotoxicity) Ishida et al. *Bioorg Med Chem* **10** 3481 *2002* (anti-inflammatory, antioxidant and anti-amyloid activity) Yang et al. *J Biol Chem* **280** 5892 *2005*.]
The keto-enol tautomerism of curcumin derivatives was shown to be a property that can be employed for amyloid detection in Alzheimer's disease, and may be exploited for the design of amyloid-binding agents for the therapy of the disease [Yanagisawa et al. *Biomaterials* **31** 4179 *2010*]. Over the years, curcumin derivatives have been screened for a variety of diseases (see above) including anti-HIV, and although few have displayed very potent anticancer activity, they are still being considered for development as future anticancer agents. A review on their potential as anticancer agents has been published recently. [Agrawal & Mishra *Med Res Rev* **30** 818 *2010*.] The above information under *Curcumin* was kindly supplied by Prof. Hiroyasu Taguchi, Shiga University of Medical Science, Molecular Neuroscience Research Centre, Japan.

Cytidine *[65-46-3]* **M 243.2**, **m 210-220o(dec), 230° (dec), 251-252° (dec), [α $^{20}_{546}$+37° (c 9, H_2O), $[\alpha]_D^{20}$ +29° (c 9, H2O), pK25 3.85.** Cytidine crystallises from 90% aqueous EtOH. It has also been converted to *sulfate* by dissolving (~200mg) in a solution of EtOH (10ml) containing H_2SO_4 (50mg), whereby the salt crystallises out.

It is collected, washed with EtOH and dried for 5 hours at 120°/0.1mm. The *sulfate* has **m** 225°. The *free base* is obtained by shaking the salt solution with a weak ion-exchange resin, filtering, evaporating and recrystallising the residue from EtOH as before. [Fox & Goodman *J Am Chem Soc* **73** 3256 *1956*, Fox & Shugar *Biochim Biophys Acta* **9** 369 *1952*; see Prytsas & Sorm in *Synthetic Procedures in Nucleic Acid Chemistry* (Zorbach & Tipson Eds) **Vol 1** 404 *1973*.] [*Beilstein* **25** III/IV 3667.]

Cytisine, See entry in "Heterocyclic Compounds", Chapter 4.

Cytochalasin B (from dehydrated mould matter) *[14930-96-2]* **M 479.6, m 218-221°.** Purify it by MeOH extraction, reverse phase C18 silica gel batch extraction by selective elution with 1:1 v/v hexane/tetrahydrofuran, crystallisation, subjected to TLC and recrystallisation [Lipski et al. *Anal Biochem* **161** 332 *1987*]. It is soluble in EtOH (3.6%), Me_2CO (1%), Me_2SO (37%) and Me_2NCHO (49%) at 24°, and can be crystallised from the first two solvents. It interferes with cellular movement [Korm *Physiol Reviews* **62** 672 *1982*].

Cytosine (4-amino-2-hydroxypyrimidine) *[71-30-7]* **M 111.1, m 313° (hydrate, dec), 320-325° (anhydrous, dec), pK_1^{25} 4.6, pK_2^{25} 12.1.** Cytosine crystallises from H_2O as the *monohydrate* which loses water on heating above 100°. Its solubility in H_2O is 0.77%. Its UV has λmax at 267nm (ε 6,100) in H_2O pH 8.8 and 275nm (ε 10,400) in 0.1N HCl. [Hilbert & Johnson *J Am Chem Soc* **52** 1152 *1930*, Hilbert et al. *J Am Chem Soc* **57** 552 *1935*, *Beistein* **25** III/IV 3654.]

Cytosine-1-β-*O*-arabinofuranoside (Cytarabin) *[147-94-4]* **M 243.2, m ~220°(dec), 212-213.5°, $[\alpha]_D^{20}$ +155° (c 1, H_2O), pK^{25} 4.3.** Purify cytarabin by recrystallisation from aqueous EtOH or a large volume of H_2O (it solubility at ~20° is 5%). It has λ_{max} at 212 and 279nm at pH 2 and 272nm at pH 12. It is an acute leukaemic agent. [Walwick et al. *Proc Chem Soc (London)* 84 *1959*, *Beilstein* **25** III/IV 3669.]

Demeclocycline hydrochloride

(7-chloro-6-demethyltetracycline hydrochloride, Clortetrin) *[64-73-3]* **M 501.3, m 174-178°(dec, for sesquihydrate), $[\alpha]_D^{25}$ -258° (c 0.5, 0.1N H_2SO_4), pK^{25} 4.45 [H_2O-Me_2NCHO (1:1)].** Crystallise the salt from EtOH/Et_2O or H_2O and dry it in air [McCormick et al. *J Am Chem Soc* **79** 4561 *1957*, Dobrynin et al. *Tetrahedron Lett* 901 *1962*]. [*Beilstein* **14** IV 2625.]

2'-Deoxyadenosine (adenine 2'-deoxyriboside) *[16373-93-6]* **M 269.3, m 187-189°, 189-191°, $[\alpha]_D^{20}$ -25° (c 0.5, H_2O), $[\alpha]_{589}^{25}$ -26°, $[\alpha]_{310}^{25}$ -206° (c 0.5, H_2O), pK^{20} 3.79.** Purify it by recrystallisation from H_2O (hydrated crystals; solubility of the *monohydrate* is 1.1% in H_2O at 20°). It has UV with λ_{max} at 258nm (pH 1), 260nm (pH 7) and 261nm (pH 13). [Ness & Fletcher *J Am Chem Soc* **81** 4752 *1959*, Walker & Butler *Can J Chem* **34** 1168 *1956*.] The *3',5'-O-diacetyl* derivative has **m** 151-152° (from EtOAc/petroleum ether). [*Beilstein* **26** III/IV 3589.]

3'-Deoxyadenosine (Cordycepin, adenine 3'-deoxyriboside) *[73-03-0]* **M 251.2, m 225-226°, 225-229°, $[\alpha]_D^{20}$ -47° (H_2O), pK_{Est} ~4.8.** 3'-Deoxyadenosine forms needles from EtOH, *n*-BuOH and *n*-PrOH, and a *monohydrate* from H_2O. It has UV with λ_{max} at 260nm (ε 14,600) in EtOH. The *picrate* has **m** 195°(dec, yellow crystals from H_2O). [Kaczka et al. *Biochim Biophys Acta* **14** 456 *1964*, Todd & Ulbricht *J Chem Soc* 3275 *1960*, Lee et al. *J Am Chem Soc* **83** 1906 *1961*, Walton et al. *J Am Chem Soc* **86** 2952 *1964*, *Beilstein* **26** III/IV 3594.]

2'-Deoxycytidine monohydrate *[951-77-9, 652157-52-3 (hydrate), 207121-53-7]* **M 245.2, m 119-200°, 207-209°, 213-215°, $[\alpha]_D^{25}$ +78° (c 0.4, N NaOH), $[\alpha]_D^{23}$ +57.6° (c 2, H_2O), pK^{25} 4.25.** Purify 2'-deoxycytidine by recrystallisation from MeOH/Et_2O or EtOH and dry it in air. [NMR: Miles *J Am Chem Soc* **85** 1007 *1963*, UV: Fox & Shugar *Biochim Biophys Acta* **9** 369 *1952*.] The *hydrochloride* crystallises from H_2O/EtOH and has **m** 174°(dec, 169-173°). [Walker & Butler *Can J Chem* **34** 1168 *1956*.] The *picrate* has **m** 208°(dec). [Fox et al. *J Am Chem Soc* **83** 4066 *1961*, *Beilstein* **25** III/IV 3662.]

2'-Deoxycytidine 5'-monophosphoric acid (deoxycytidylic acid) *[1032-65-1]* **M 307.2, m 170-172°(dec),**

183-184°(dec), 183-187°(dec), $[\alpha]_D^{21}$ +35° (c 0.2, H_2O), pK_1 4.6, pK_2 6.6. Recrystallise the acid from H_2O or aqueous EtOH and dry it in a vacuum. [Volkin et al. *J Am Chem Soc* **73** 1533 *1951*, UV: Fox et al. *J Am Chem Soc* **75** 4315 *1953*, IR: Michelson & Todd *J Chem Soc* 3438 *1954*, *Beilstein* **25** IV 3664.]

2'-Deoxyguanosine monohydrate (9-[2-deoxy-β-D-ribofuranosyl]guanidine) *[961-07-9]* **M 285.3, m *ca* 200°(dec), $[\alpha]_D^{20}$ +37.5° (c 2, H_2O), $[\alpha]_D^{14}$ -47.7° (c 0.9, N NaOH), $pK_{Est(1)}$~ 3.3, $pK_{Est(2)}$~ 9.2.** 2'-Deoxyguanosine recrystallises from H_2O as the monohydrate. [Brown & Lythgoe *J Chem Soc* 1990 *1950*, Levene & London *J Biol Chem* **81** 711 *1929*, **83** 793 *1929*, UV: Hotchkiss *J Biol Chem* **175** 315 *1948*, ORD: Levendahl & James *Biochim Biophys Acta* **26** 89 *1957*.] The *3',5'-di-O-acetyl* derivative crystallises from aqueous EtOH with **m** 222°(dec), and $[\alpha]_D^{18}$ -38° (c 0.3, 10% aqueous EtOH) [Hayes et al. *J Chem Soc* 808, 813 *1955*]. [*Beilstein* **26** III/IV 3897.]

2'-Deoxyinosine *[890-38-0]* **M 252.2, m 206°(dec), 218-220°(dec), $[\alpha]_D^{25}$ -21° (c 2, N NaOH), $[\alpha]_D^{21.5}$ -21° (c 1, H_2O), $pK_{Est(1)}$~8.9, $pK_{Est(2)}$~12.4.** Purify 2'-deoxyinosine by recrystallisation from H_2O. [Brown & Lythgoe *J Chem Soc* 1990 *1950*, UV: MacNutt *Biochem J* **50** 384 *1952*, *Beilstein* **26** III/IV 2086.]

5-Deoxy-5-(methylthio)adenosine *[2457-80-9]* **M 297.3, m 210-213°(dec), 211°, 212°, 213-214°, $[\alpha]_D^{20}$ -23.7° (c 0.02, pyridine), $[\alpha]_D^{20}$ -8° (c 1, 5% aqueous NaOH), $[\alpha]_D^{25}$ +15° (c 0.4-1.0, 0.3N aqueous AcOH), pK_{Est} ~3.5.** Recrystallise it from H_2O and sublime it at 200°/0.004mm. [v.Euler & Myrbäck *Hoppe Seyler's Z physiol Chem* **177** 237 *1928*, Weygand & Trauth *Chem Ber* **84** 633 *1951*, Baddiley et al. *J Chem Soc* 2662 *1953*.] The *hydrochloride* has **m** 161-162° [Kuhn & Henkel *Hoppe Seyler's Z Physiol Chem* **269** 41 *1941*]. The *picrate* has **m** 183°(dec) (from H_2O). [*Beilstein* **26** III/IV 3675.]

Deoxyribonucleic acid (from plasmids). Purify plasmid DNA by two buoyant density ultracentrifugations using ethidium bromide-CsCl. The ethidium bromide is extracted with Et_2O, and the DNA is dialysed against buffered EDTA and lyophilised. [Marmur & Doty *J Mol Biol* **5** 109 *1962*, Guerry et al. *J Bacteriol* **116** 1064 *1973*.] See "Introduction" in this Chapter.

3'-Deoxythymidine {2',3'-dideoxythymidine, 1-[(2*r*)-5*c*-hydroxymethyltetrahydro(2*r*)-furyl]-5-methyl-pyrimidine-2,4-dione} *[3416-05-5]* **M 226.2, m 145°, 149-151°, $[\alpha]_D^{26}$ +18° (c 1, H_2O), pK_{Est} ~ 9.2.** Crystallise it from Me_2CO/MeOH. [Michelson & Todd *J Chem Soc* 816 *1955*, *Beilstein* **24** III/IV 1297.]

2'-Deoxyuridine [1–(β-D-*erythro*-2-deoxypentofuranosyl)-1*H*-pyrimidine-2,4-dione] *[951-78-0]* **M 228.2, m 163°, 163-163.5°, 165-167° 167°, $[\alpha]_D^{26}$ +30° (c 2, H_2O), $[\alpha]_D^{22}$ +50° (c 1, N NaOH), pK^{25} 9.3.** 2'-Deoxyuridine forms needles from absolute EtOH or 95% EtOH. [Dekker & Todd *Nature* **166** 557 *1950*, Brown et al. *J Chem Soc* 3035 *1958*, NMR Jardetzky *J Am Chem Soc* **83** 2919 *1961*, Fox & Shugar *Biochim Biophys Acta* **9** 369 *1952*, UV: MacNutt *Biochem J* **50** 384 *1952*, *Beilstein* **24** III/IV 1200.]

3'-Deoxyuridine {1-[(2*R*)-5*c*-hydroxymethyltetrahydro(2*r*)furyl]-5-methylpyrimidin-2,4-dione, 2'.3'-dide-oxythymidine} *[7057-27-4, 3416-05-5]* **M 226.2, m 149-151°, $[\alpha]_D^{20}$ +18° (c 1, H_2O), pK_{Est} ~ 9.3.** 3'-Deoxyuridine is recrystallised from Me_2CO/MeOH and is dried in a vacuum. [Michelson & Todd *J Chem Soc* 816 *1955*.]

Desthiobiotin (4*R*-*cis*-5-methyl-2-oxo-4-imidazolidinehexanoic acid) *[533-48-2]* **M 214.3, m 156-158°, $[\alpha]_D^{20}$ +10.5° (c 2, H_2O), pK_{Est} ~2.8.** Dissolve desthiobiotin in 0.5% Na_2CO_3, filter, acidify with HCl to Congo Red, concentrate to a small volume (2-3 ml) to give fine needles, filter it off and recrystallise it twice from H_2O, **m** 157-158°. It also crystallises from 95% EtOH. The *methyl ester* crystallises from MeOH and sublimes at 100°/high vacuum, **m** 69-70°, $[\alpha]_D^{27.5}$ +2.6° (c 2, $CHCl_3$). [Melville et al. *Science* **98** 497 *1943*, *J Am Chem Soc* **66** 1422 *1944*, *Beilstein* **25** III/IV 1543.]

Di- and tri-carboxylic acids. These are separated by anion-exchange chromatography. [Bengtsson & Samuelson *Anal Chim Acta* **44** 217b *1969*.]

7,8-Dihydrofolic acid (7,8-dihydropteroyl-L-glutamic acid, DHFA) *[4033-27-6]* **M 443.4, pK_1 2.0 (basic**

10-NH), pK_2 2.89 (2-NH_2), pK_3 3.45 (α-CO_2H), pK_4 4.0 (basic 5N), pK_5 4.8 (γ-CO_2H), pK_6 9.54 (acidic 3NH). DHFA is best purified by suspending (1g mostly dissolved)) in ice-cold sodium ascorbate (300ml of 10% at pH 6.0, prepared by adjusting the pH of 30g of sodium ascorbate in 150ml of H_2O by adding 1N NaOH dropwise using a glass electrode till the pH is 6.0). This gives a clear solution with pH ~5. While stirring at 0°, add N HCl dropwise slowly (0.1ml/min) until the pH drops to 2.8 when white birefringent crystals separate. These are collected by centrifugation (1000xg for 5 minutes), washed 3x with 0.001N HCl also by centrifugation and decantation. The residue is then dried in a vacuum (0.02mm) over P_2O_5 (change the P_2O_5 frequently at first) and KOH at 25° in the dark. After 24 hours the solid reaches constant weight.
For the assay of ***dihydrofolate reductases*** (see [9002-03-3] p 803): suspend ~66.5mg of DHFA in 10ml of 0.001M HCl containing 10mM dithiothreitol (DTT stock made from 154mg in 10ml H_2O making 0.1M), shake well and freeze in 400µl aliquots. Before use, mix 400µl of this suspension with 0.1M DTT (200µl, also made in frozen aliquots), and the mixture is diluted with 200µl of 1.5M Tris-HCl pH 7.0 and 1.2ml of H_2O (making a total volume of ~2ml) to give a clear solution. To estimate the concentration of DHFA in this solution, dilute 20µl of this solution to 1ml with 0.1M Tris-HCl pH 7.0 and read the OD at 282nm in a 1cm path length cuvette. ε at 282nm is 28,000$M^{-1}cm^{-1}$. [Futterman *Methods Enzymol* **6** 801 *1963*, Reyes & Rathod *Methods Enzymol* **122** 360 *1986*, *Beilstein* **26** III/IV 3934.]

DL-*erythro*-Dihydrosphingosine (dl-*erythro*-2-aminooctadecan-1,3-diol) *[3102-56-5]* **M 301.5, m 85-86°, 85-87°, pK_{Est} ~ 8.8.** Purify it by recrystallisation from petroleum ether/EtOAc or $CHCl_3$. The (±)-*N-dichloroacetyl* derivative has **m** 142-144° (from MeOH). [Shapiro et al. *J Am Chem Soc* **80** 2170 *1958*, Shapiro & Sheradsky *J Org Chem* **28** 2157 *1963*.] The D-isomer crystallises from petroleum ether/Et_2O and has **m** 78.5-79°, $[\alpha]_{546}^{28}$ +6° ($CHCl_3$/MeOH, 10:1). [Grob & Jenny *Helv Chim Acta* **35** 2106 *1953*, Jenny & Grob *Helv Chim Acta* **36** 1454 *1953*, *Beilstein* **4** I 448, **4** II 757, **4** III 854, **4** IV 1887.]

Dihydrostreptomycin sesquisulfate *[5490-27-7]* **M 461.4, m 250°(dec), 255-265°(dec), $[\alpha]_D^{20}$ -92.4° (c 1, H_2O), $pK_{Est(1)}$~ 9.5 (NMe), $pK_{Est(2,3)}$~ 13.4 (guanidino).** It crystallises from H_2O, MeOH, *n*-BuOH or methyl ethyl ketone. The crystals are not hygroscopic like the amorphous powder; however, both forms are soluble in H_2O but the amorphous solid is about 10 times more soluble than the crystals. The *free base* also crystallises from H_2O/Me_2CO and has $[\alpha]_D^{26}$ -92° (aqueous solution pH 7.0). [Solomons & Regina *Science* **109** 515 *1949*, Wolf et al. *Science* **109** 515 *1949*, McGilveray & Rinehart *J Am Chem Soc* **87** *4003* 1956]. [*Beilstein* **18** III/IV 7538.]

2,4-Dihydroxyimidazole (hydantoin, imidazolin-2,4-dione) ***[****461-72-3]* **M 100.1, m 215°, 218-220°, 220°, pK^{25} 9.15, pK^{18} 9.16.** Well over the past hundred years many syntheses of hydantoin have been reported involving the reaction of alloxanic acid with HI [Baeyer *Justus Liebigs Ann Chem* **119** 127 *1861* and **130** 159 *1864*], the cyclisation of urea derivatives [Harries & Weiss *Chem Ber* **33** 3418 *1900* and *Justus Liebigs Ann Chem* **327** 366 *1903*], the cyclisation of ethyl *N*-carbamoylglycinate, accomplished with NaOMe in MeOH in 85% yield [Kavalek et al. *Col Czech Chem Commun* **51** 375 *1986*], and more recently by the acid catalysed condensation of glycine with KNCO [El-Deeb et al. *Eur J Med Chem* **45** 2516 *2010*]. In a later patent, glycine (75g, 1 mole) and urea (140g, 2.3 moles) were dissolved in H_2O (120ml) and stirred under reflux for 12 hours. The mixture was acidified by careful addition of concentrated H_2SO_4 while being cooled in an ice bath, then boiled for 1 hour, cooled to 0-5°, and the crystalline solid was filtered off, washed with cold H_2O and dried. A further crop was obtained by evaporating the mother liquor. The combined solids were recrystallised from glacial AcOH (10 parts) to give pure *hydantoin* (71g, 70%) m 220-220°. [Alkaloida US patent 4647694 *1987*.]
It can be purified by dissolving it in at least 2.5 parts of hot H_2O (charcoal), filtering, acidifying to pH ~6, filtering again, collecting the solid, washing it with ice cold H_2O, drying it, and recrystallising it from EtOH (needles) or from 10 parts of AcOH. Its solubility is 39.7g/L in H_2O and 3.24g/L in EtOH at 25°. It has λ_{max} (ε) at 215(400) and 245(60)nm in 0.01N EtOH/NaOH; 215(360) and 245(50)nm in EtOH/H^+; and has ν_{max} at 1697 (2CO) and 1776 (4CO) cm^{-1} in a paraffin mull [West *J Biol Chem* **34** 187 *1918*, Crombie & Hooper *J Chem Soc* 3010 *1955*, *Beilstein* **24** H 242, **24** I 287, **24** II 127, **24** III/IV 1034].

1,2-Dilauroyl-*sn*-glycero-3-phosphoethanolamine (±-dilauroyl-α-cephalin, 3-*sn*-phosphat-idylethanol-amine 1,2-didodecanoyl) *[59752-57-7]* **M 579.8, m 210°, $pK_{Est(1)}$~ 5.8 (PO_4H), $pK_{Est(2)}$~ 10.5 (NH_2).**

Recrystallise it from EtOH or tetrahydrofuran. [Bevan & Malkin *J Chem Soc* 2667 *1951*, IR: Bellamy & Beecher *J Chem Soc* 728 *1953*, *Beilstein* **4** IV 1417.]

1,2-Dimyristoyl-sn-glycero-3-phosphocholine monohydrate (dimyristoyl-L-α-lecithin) *[18194-24-6 ($1H_2O$)]* **M 696.0, $[\alpha]_D^{24}$ +7° (c 8, EtOH-$CHCl_3$ 1:1 for α_1 form), pK_{Est} ~ 5.8 (PO_4).** It has three forms α_1, α_2 and β'. Recrystallise it from aqueous EtOH or EtOH/Et_2O. Its solubility at 22-23° in Et_2O is 0.03%, in Me_2CO it is 0.06% and in pyridine it is 1.3%. [Baer & Kates *J Am Chem Soc* **72** 942 *1950*, Baer & Maurakas *J Am Chem Soc* **74** 158 *1952*, IR: Marinetti & Stotz *J Am Chem Soc* **76** 1347 *1954*.] The *S-isomer* with $1H_2O$ is recrystallised from 2,6-dimethylheptan-4-one and has **m** 226-227° (sintering at 90-95°), and $[\alpha]_D^{20}$ -7° (c 6, MeOH/$CHCl_3$ 1:1). [Baer & Martin *J Biol Chem* **193** 835 *1951*, *Beilstein* **4** IV 1463.]

(±)-1,2-Dimyristoyl-sn-glycero-3-phosphoethanolamine (dimyristoyl-α-kephalin) *[998-07-2]* **M 635-9, m 207°, $pK_{Est(1)}$~ 5.8 (PO_4H), $pK_{Est(2)}$~ 10.5 (NH_2).** Recrystallise the kephalin from EtOH [Bevan & Malkin *J Chem Soc* 2667 *1951*]. The *R-isomer* has **m** 195-196° (sintering at 130-135°) after recrystallisation from $CHCl_3$/MeOH, and $[\alpha]_D^{26}$ +6.7° (c 8.5, $CHCl_3$/AcOH 9:1). [Baer *Can J Biochem Physiol* **35** 239 *1957*, Baer et al. *J Am Chem Soc* **74** 152 *1952*, *Beilstein* **4** IV 1463.]

***S*(-)-1,2-Dipalmitin (*S*-1,2-dipalmitoyl-sn-glycerol)** *[30334-71-5]* **M 568.9, m 68-69° $[\alpha]_D^{20}$ -2.9° (c 8, $CHCl_3$), the *R*(+)-isomer (2,3-dipalmitoyl-sn-glycerol)** *[6076-30-8]* **has m 67.5-68.2°, $[\alpha]_D^{20}$ -2.8° (c 8, $CHCl_3$).** Crystallise *S*(-)-1,2-dipalmitin from chloroform/petroleum ether (b 40-60°) ~1:1.5. [*S*(-)-isomer: Baer & Kates *J Am Chem Soc* **72** 942 *1950*, Hanahan & Vercamer *J Am Chem Soc* **76** 1804 *1954*, *R*(+)-isomer: Tattrie et al. *Arch Biochem* **78** 319 *1958*, *Beilstein* **2** IV 1173.] The *racemate* [40290-32-2] is polymorphic with different IR spectra. When crystallised from hexane, or other solvents, the higher melting form with **m** 71.5-72.5° is obtained. The melt then solidifies to give the lower melting α-form with **m** 49.7-50°. The β-form has **m** 61° (65-66° is also reported). When the lower melting forms are kept at their melting temperatures for a while, they are converted to the higher melting form. [Howe & Malkin *J Chem Soc* 2663 *1951*, Baer & Kates *J Am Chem Soc* **72** 942 *1950*, *Beilstein* **2** IV 1173.]

***R*-Dipalmitoyl-sn-glycero-3-phosphatidic acid** *[7091-44-3]* **M 648.9**, **$[\alpha]_D^{26}$ +4° (c 10, $CHCl_3$), $pK_{Est(1)}$~1.6, $pK_{Est(2)}$~6.1.** Recrystallise the acid from Me_2CO at low temperature. At 21° it is soluble in $*C_6H_6$ (4.2%), petroleum ether (0.01%), MeOH (2%), EtOH (2.5%), AcOH (1.3%), Me_2CO (1.76%), and Et_2O (1.5%). [Baer *J Biol Chem* **189** 235 *1951*.]

***R*-1,2-Dipalmitoyl-sn-glycero-3-phosphocholine monohydrate (dipalmitoyl-α-L-lecithin)** *[63-89-8]* **M 752.1, m sinters at 120°, $[\alpha]_D^{25}$ +7.0° (c 5.6, absolute $CHCl_3$), pK_{Est} ~5.8 (PO_4).** It has three crystalline forms α_1, α_2 and β' which change at 60-70° and at 229°, respectively. In order to obtain a fine powder, ~2 g are dissolved in $CHCl_3$ (15ml) and petroleum ether (b 35-60°) is added; the solution is evaporated to dryness *in vacuo* at <20° and then dried at 0.1mm over $CaCl_2$. [Baer & Maurukas *J Am Chem Soc* **74** 158 *1952*, Baer & Kates *J Biol Chem* **185** 615 *1950*, *Beilstein* **4** IV 1463.]

***d,l*-βγ-Dipalmitoylphosphatidyl choline** *[2797-68-4]* **M 734.1, m 230-233°, pK_{Est} ~5.8 (PO_4).** Recrystallise the choline from chloroform and dry it for 48 hours at 10^{-5} Torr [O'Leary & Levine *J Phys Chem* **88** 1790 *1984*].

1,2-Distearoyl-sn-glycerol *[1429-59-0]* **M 625.0.** The *dl*-form recrystallises from $CHCl_3$/petroleum ether (b 40-60°), **m** 59.5° (α form) and 71.5-72.5° (β form). Recrystallisation from solvents such as EtOH, MeOH, toluene, Et_2O gives the higher melting form, and resolidification gives the lower melting form. [IR: Chapman *J Chem Soc* 4680 *1958*, 2522 *1956*.] The *S-isomer* is recrystallised from $CHCl_3$/petroleum ether and has **m** 76-77°, $[\alpha]_D^{24}$ -2.8° (c 6, $CHCl_3$). [Baer & Kates *J Am Chem Soc* **72** 942 *1950*, *Beilstein* **2** IV 1231.]

1,2-Distearoyl-sn-glycero-3-phosphoethanolamine (distearoyl-α-kephalin) *[1069-79-0]* **M 748.1, m 180-182° (*R*-form, sintering at 130-135°), m 196° (± form), $pK_{Est(1)}$~5.8 (PO_4H), $pK_{Est(2)}$~10.5 (NH_2).** The *R*-form is recrystallised from $CHCl_3$/MeOH, and the ±-form is recrystallised from EtOH. [Bevan & Malkin *J Chem Soc* 2667 *1951*, Baer *Can J Biochem Physiol* **81** 1758 *1959*, *Beilstein* **4** IV 1420.]

Dolichol (from pig liver) *[11029-02-0]* **C_{80}-C_{105} polyprenols.** Crystallise each dolichol 6 times from petroleum ether/EtOH at -20°. The pure individual prenol should run as an entity on a chromatogram on paraffin impregnated paper, with acetone as the mobile phase. [Burgos *Biochem J* **88** 470 *1963*.]

Domoic acid [4-(2-carboxyhexa-3,5-dienyl)-3-carboxymethylproline] *[14277-97-5]* **M 311.3, m 215°, 217°, $[\alpha]_D^{20}$ -108° (c 1, H_2O), pK_1 2.20 (2-CO_2H), pK_2 3.72 (CO_2H), pK_3 4.93 (3-CH_2CO_2H), pK_4 9.82 (NH).** Domoic acid (~300 mg) is purifed on a Dowex1 column (3.5 x 40 mm, 200-400 mesh, acetate form), washed with H_2O until neutral, then eluted with increasing concentrations of AcOH (8L) from 0 to 0.25M. The fraction containing domoic acid (in 50ml) is collected, evaporated to dryness under reduced pressure and recrystallised from aqueous EtOH. It is a glutamate and a Kainate receptor agonist. [Impellizzeri et al. *Phytochemistry* **14** 1549 *1975*, Takemoto & Diago *Arch Pharm* **293** 627 *1960*, *Beilstein* **22/4** V 371.]

Enniatin A *[11113-62-5]* **M 681.9, m 122-122.5°, $[\alpha]_D^{18}$ -92° (c 0.9, $CHCl_3$).** It is a cyclic peptidic ester antibiotic which is recrystallised from EtOH/water but is deactivated in alkaline solution. [Ovchinnikov & Ivanov in *The Proteins* (Neurath and Hill eds) Academic Press, NY, Vol V pp. 365 and 516 *1982, Tomeda et al. J Antibiot* **45** 1626 *1992*.]

(-)-Ephedrine (1*R*,2*S*-2-methylamino-1-phenylpropanol) *[299-42-3]* **M 165.2, m ~34°, 36°, 38.1°, 40°, b 126-129°/7mm, 225-227°/760mm, d^{22} 1.0085, $[\alpha]_{546}^{20}$ -47° and $[\alpha]_D^{26}$ -42° (c 4, 3% HCl), $[\alpha]_D^{22.5}$ +15.1° (c 0.8, H_2O), -9.36° (c 3, MeOH), pK^{22} 9.58 (pK^{25} 8.84 in 80% aqueous methoxyethanol).** Purify (-)-ephedrine by vacuum distillation (dehydrates) and forms waxy crystals or granules, and may pick up 0.5 H_2O. The presence of H_2O raises its melting point to 40°. [Moore & Taber *J Amer Pharm Soc* **24** 211 *1935*.] The *anhydrous base* crystallises from dry ether [Fleming & Saunders *J Chem Soc* 4150 *1955*]. It gradually decomposes on exposure to light and is best stored in an inert atmosphere in the dark (preferably at -20°). Its solubility in H_2O is 5%, in EtOH it is 1% and it is soluble in $CHCl_3$, Et_2O and mineral oils. It has pKa values in H_2O of 10.25 (0°) and 8.69 (60°) [Everett & Hyne *J Chem Soc* 1136 *1958*, Prelog & Häflinger *Helv Chim Acta* **33** 2021 *1950*] and pK_a^{23} 8.84 in 80% aqueous methoxyethanol [Simon *Helv Chim Acta* **41** 1835 *1958*]. The *hydrochloride* has **m** 220° (from EtOH/Et_2O) and $[\alpha]_D^{20}$ -38.8° (c 2, EtOH). [IR: Chatten & Levi *Anal Chem* **31** 1581 *1959*.] The *anhydrous base* crystallises from Et_2O [Fleming & Saunders *J Chem Soc* 4150 *1955*]. [*Beilstein* **13** H 373, **13**, III 1720, **13** IV 1879.]

(+)-Ephedrine hydrochloride (1*S*-2*R*-2-methylamino-1-phenylpropan-1-ol hydrochloride) *[24221-86-1]* **M 201.7, m 216-219°, $[\alpha]_D^{20}$ +34° (c 11.5, H_2O).** Recrystallise the hydrochloride from EtOH/Et_2O. The *free base* crystallises from *C_6H_6 with **m** 40-41° (Skita et al. *Chem Ber* **66** 974 *1933*]. [*Beilstein* **13** H 254, **13** II 375, **13** III 1721, **13** IV 1879.]

(-)Ephedrine hydrochloride *[50-98-6]* **M 201.7, m 218°, $[\alpha]_{546}^{20}$ -48° (c 5, 2M HCl).** It crystallises from water. [*Beilstein* **13** H 254.]

α-Erythroidine (3*R*,5*S*,12*S*) *[466-80-8]* **M 273.3, m 52-55°, 58-60°, $[\alpha]_D^{27}$ +136° (c 0.5, H_2O), $pK_{Est(3)}$~7.4** Recrystallise α-erythroidine from pentane. It is best prepared freshly from the more stable hydrochloride. The hydrochloride (1.3g) in H_2O (20ml) is basified with $NaHCO_3$ to pH ~8 and extracted with *C_6H_6 (6 x 10ml). The combined extracts are evaporated to a small volume and refrigerated. The free base separates as white hygroscopic crystals **m** 52-55°, which are recrystallised from pentane. Although stable in solution, the crystals turn brown on exposure to air.

α-Erythroidine hydrochloride is best purified by dissolving 10g in H_2O (100ml), adjusting the pH to 8 with aqueous $NaHCO_3$, extracting with *C_6H_6 (4 x 20ml), evaporating to 20ml, passing through activated Al_2O_3 and eluting with *C_6H_6. The eluate is evaporated to a small volume and the crystals are collected, dissolved in EtOH and dry HCl gas passed through to give the pure hydrochloride. When recrystallised from EtOH, it has **m 226-228°(dec),** and **$[\alpha]_D^{32}$ +118° (c 0.5, H_2O).** It has λ_{max} at 224nm (ε 35, 500); compare with β-erythroidine hydrochloride below. [Boelkeleide & Grundon *J Am Chem Soc* **75** 2563 *1953*, Boekeleide & Morrison *J Am*

Chem Soc **80** 3905 *1958*, abs config: Hill & Shearer *J Org Chem* **27** 3342 *1955*, *Beilstein* **27** III/IV 3569.]

β-Erythroidine (3*R*,5*S*) *[466-81-9]* **M 273.3, m 97-99°, 99.5-100°, $[\alpha]_D^{25}$ +89° (c 0.5, H_2O).** Purify it like the α-isomer but recrystallise it from EtOH. The *free base* is unstable in air and light, but the hydrochloride is more stable and best stored as such. The *methiodide* has **m** 211° (prisms from EtOH).
β-Erythroidine hydrochloride can be obtained from the α-isomeric salt as follows: The α-hydrochloride (1.2g) in 10% aqueous NaOH (12ml) is refluxed for 3 hours under N_2, cooled in ice and conc HCl added to pH 2. After standing for 3 hours, $NaHCO_3$ is carefully added to pH 7, the solution is extracted with $CHCl_3$ (5x), and the extracts are dried, filtered, and concentrated to give an oil which on seeding gives β-erythroidine **m** 97-99°. When dissolved in EtOH and dry HCl gas is passed through the solution, the pure β-erythroidine hydrochloride crystallises out with **m 230.5-231.5°, $[\alpha]_D^{25}$ +10° (c 0.5, H_2O).** It is a muscle relaxant with a curare-like-action and is more active than the α-isomer. [Koniuszy & Folkers *J Am Chem Soc* **72** 519 *1950*, Boekelheide et al. *J Am Chem Soc* **75** 2550 *1953*, Boekelheide & Morrison *J Am Chem Soc* **80** 3905 *1958*, Wenzinger & Boekelheide *J Org Chem* **29** 1307 *1964*, Berger & Schwartz *J Pharmacol Exp Therap* **93** 362 *1948*, *Beilstein* **4** IV 3568.]

Erythromycin A *[114-07-8]* **M 733.9, m 133-135°(dec), 135-140°, 137-140°, $[\alpha]_D^{20}$ -75° (c 2, EtOH), pK^{25} 8.9.** It recrystallises from H_2O to form hydrated crystals which melt at *ca* 135-140°, resolidifies and melts again at 190-193°. The melting point after drying at 56°/8mm is that of the *anhydrous* material and is at 137-140°. Its solubility in H_2O is ~2mg/ml. The *hydrochloride* has **m** 170°, 173° (from aqueous EtOH, EtOH/Et_2O). [Flynn et al. *J Am Chem Soc* **76** 3121 *1954*, constitution: Wiley et al. *J Am Chem Soc* **79** 6062 *1957*]. [*Beilstein* **18/10** V 398.]

Ethidium bromide *[1239-45-8]* **M 384.3, m 260-262°.** Crystallise it from MeOH or EtOH [Lamos et al. *J Am Chem Soc* **108** 4278 *1986*]. Its solubility in H_2O is 1%. [*Beilstein* **22/11** V 352.] **POSSIBLE CARCINOGEN.**

Ethyl 7-acetoxycoumarin-3-carboxylate *[13207-77-3]* **M 276.3, m 147-148°, 152°, 152-154°, pK^{25} 7.04.** Purify the ester by recrystallisation from EtOH or aqueous EtOH, dry it *in vacuo* and store it at 2-8°. It is a good fluorogenic substrate for esterases that hydrolyse it to the acid, which acts as an indicator. The fluorescence has λ_{ex} 386nm, λ_{em} 445nm in 0.1 M Tris buffer pH 8.0. It has been prepared by refluxing 2-imino-3-ethoxycarbonyl-7-hydroxy-2*H*-chromene with Ac_2O for 1 hour, evaporating and recrystallising the residue from aqueous MeOH [Yasuda & Midorikawa *Bull Chem Soc Jpn* **39** 1754 *1966*]. *Alternatively*, it can be prepared by acetylation of 7-hydroxy-3-carbethoxycoumarin by the Ac_2O/pyridine method, and crystallises from EtOH in plates, m 152°. An attempted Fries rearrangement by heating the ester with anhydrous $AlCl_3$ at 16-170° failed, but gave ***7-hydroxy-3-carboxycoumarin***, **m 271° (dec)** (from H_2O). [Shah & Shah *J Org Chem* **13** 1681 *1954*, see also Boehm *Archiv der Pharmazie (Weinheim)* **271** 490 *1933*.]

Farnesol **(*trans-trans*-3,7,11-trimethyl-2,6,10-dodecatrien-1-ol)** *[106-28-5, 4602-84-0 (trans-trans, E,E)]* **M 222.4, b 111°/0.35mm, 126-127°/0.5mm, 142-143°/2mm, d_4^{20} 0.8871, n_D^{25} 1.4870.** The main impurity is the *cis-trans* isomer. Purify it by gas chromatography using a 4ft x 0.125in 3%OV-1 column at 150°. [Corey et al. *J Am Chem Soc* **92** 6637 *1970*, Popjak et al. *J Biol Chem* **237** 56 *1962*.] It has also been fractionated through a 14-in Podbielniak column at 11°/0.35mm. *Alternatively*, it has been purified by gas chromatography using SF96 silicone on Fluoropak columns or Carbowax 20M on Fluoropak or base-washed 30:60 firebrick (to avoid decomposition, prepared by treating the firebrick with 5N NaOH in MeOH and washed with MeOH to pH 8) at 210° with Helium carrier gas at 60 ml/min flow rate. The *diphenylcarbamoyl* derivative has **m** 61-63° (from MeOH) and has an IR band at 3500 cm^{-1}. [Bates et al. *J Org Chem* **28** 1086 *1963*, *Beilstein* **1** IV 2335.]

Farnesyl acetate **(*trans-trans*-3,7,11-trimethyl-2,6,10-dodecatrien-1-yl acetate)** *[4128-17-0 (trans-trans, E,E); 29548-30-9 (isomeric mixture)]* **M 264.4, b 115-125°/0.3mm, 167-169°/0.3mm, d_4^{20} 0.91, n_D^{20} 1.4870.** Purify farnesyl acetate in the same way as the alcohol above. [*Beilstein* **2** I 66, **2** II 154, **2** III 303.]

Farnesyl pyrophosphate *[13058-04-3, E,E: 372-97-4]* **M 382.3, $pK_{Est(1)}$~<2, $pK_{Est(2)}$~<2, $pK_{Est(3)}$~3.95, $pK_{Est(4)}$~6.26.** Purify the pyrophosphate by chromatography on Whatman No3 MM paper in a system of isopropanol-isobutanol/ammonia/water (40:20:1:30) (v/v). Store it as the Li or NH_4 salt at 0°. See geranyl-

geranyl pyrophosphate below.

Flavin adenine dinucleotide (di-Na, $2H_2O$ salt, FAD) *[146-14-5, 84366-81-4 (anhydrous)]* **M 865.6, $[\alpha]_{546}$ -54° (c 1, H_2O).** Small quantities of FAD are purified by paper chromatography using *tert*-butyl alcohol/water, cutting out the main spot and eluting with water. Larger amounts can be precipitated from water as the uranyl complex by adding a slight excess of uranyl acetate to a solution at pH 6.0, dropwise and with gentle stirring. The solution is set aside overnight in the cold, and the precipitate is centrifuged off, washed with small portions of cold EtOH, then with cold peroxide-free diethyl ether. It is dried in the dark under vacuum over P_2O_5 at 50-60°. The uranyl complex is suspended in water, and, after adding sufficient 0.01M NaOH to adjust the pH to 7, the precipitate of uranyl hydroxide is removed by centrifugation [Huennekens & Felton *Methods Enzymol* **3** 954 *1957*]. It can also be crystallised from water. It should be kept in the dark. More recently it was purified by elution from a DEAE-cellulose (Whatman DE 23) column with 0.1M phosphate buffer pH 7, and the purity was checked by TLC. [Holt & Cotton, *J Am Chem Soc* **109** 1841 *1987*, *Beilstein* **26** III/IV 3632.]

Flavin mononucleotide (Na, $2H_2O$ salt, riboflavin-5'-phosphate [Na salt, $2H_2O$], FMN) *[130-40-5, 6184-17-4 (Na salt)]* **M 514.4, pK_1 2.1 (PO_4H_2), pK_2 6.5 (PO_4H^-), pK_3 10.3 (CONH), fluorescence λ_{max} 530nm (870nm for reduced form).** Purify FMN by paper chromatography using *tert*-butanol/water, cutting out the main spot and eluting it with water. It can also be purified by adsorption onto an apo-flavodoxin column, followed by elution and freeze drying. It crystallises from aqueous acidic solution. [Mayhew & Strating *Eur J Biochem* **59** 539 *1976*, *Beilstein* **26** III/IV 2555.]

5-Fluorouridine (5-fluoro-1-β-D-ribofuranosyl-1*H*-pyrimidine-2,4-dione) *[316-46-1]* **M 262.2, m 180-182°, 182-184°, $[\alpha]_D^{20}$ +18° (c 1, H_2O), $pK_{Est(1)}$~ 8.0, $pK_{Est(2)}$~ 13.** 5-Fluorouridine is recrystallised from EtOH/Et_2O and dried at 100° in a vacuum. It has UV with λ_{max} at 269nm (pH 7.2, H_2O), 270nm (pH 14, H_2O). [Liang et al. *Mol Pharmacol* **21** 224 *1982*, *Beilstein* **24** III/IV 1231.]

Folic acid (FA, pteroyl-S-glutamic acid) *[59-30-3, 75708-92-8 ($2H_2O$)]* **M 441.4, m >250°(dec), $[\alpha]_D^{25}$+23° (c 0.5, 0.1N NaOH), pK_1 2.35 (protonation N10), pK_2 2.75 (protonation N1), pK_3 3.49 (α-CO_2H), pK_4 4.65 (γ-CO_2H), pK_5 8.80 (acidic N3).** If paper chromatography indicates impurities, then recrystallise it from hot H_2O or from dilute acid [Walker et al. *J Am Chem Soc* **70** 19 *1948*]. Impurities may be removed by repeated extraction with *n*-BuOH of a neutral aqueous solution of folic acid (by suspending in H_2O and adding N NaOH dropwise till the solid dissolves, then adjusting the pH to ~7.0-7.5) followed by precipitation with acid, filtration, or *better* collected by centrifugation and recrystallised from hot H_2O. [Blakley *Biochem J* **65** 331 *1975*, Kalifa et al. *Helv Chim Acta* **61** 2739 *1978*.] Chromatography on cellulose followed by filtration through charcoal has also been used to obtain pure acid. [Sakami & Knowles *Science* **129** 274 *1959*.] UV: λ_{max} 247 and 296nm (ε 12,800 and 18,700) in H_2O pH 1.0; 282 and 346nm (ε 27.600 and 7,200) in H_2O pH 7.0; 256, 284 and 366nm (ε 24600, 24,500 and 86,00) in H_2O pH 13 [Rabinowitz in *The Enzymes* (Boyer et al. Eds), **2** 185 *1960*]. [*Beilstein* **26** III/IV 3944.]

3-Formylchromone (4-oxo-4*H*-1-benzopyran-3-carbaldehyde) *[17422-74-1]* **M 174.2, m 151-153°, 152°, 152-153°.** This useful precursor for heterocyclic compounds [Sabitha *Aldrichim Acta* **29** 12 *1996*] is best prepared by a Vilsmeier-Haack reaction. Tetrachloropyrophosphate (80ml) is added dropwise to a solution of *o*-hydroxyacetophenone (25g, 0.184mole) in DMF (80ml) at -20° to 20° during 10 minutes. The mixture is stirred at ~25° for 13 hours, poured into ice-water and the solid is filtered off, washed with H_2O, then EtOH, dried *in vacuo*, and recrystallised from Me_2CO to give white crystals of *3-formylchromone* (19.6g, 61%). *Alternatively*, DMF/$POCl_3$ is used. It has IR bands with ν_{max} at 1605 (CHO), 1650 (C=O) and 1620 (C=C) cm^{-1}, the ^1H NMR [60MHz, DMSO-d_6, TMS) has δ at 10.16 (s, C*H*O), 8.9 (s, H-2) and 8.3-7.4 (m, H-5,6,7 and 8), and the MS *m/z(%)* has peaks at 174(4), 147(10), **146**(100), 121(8), 120(24), 118(3), 105(6), **104**(34). 92(17), 90(13), 89(11), **76**(13), 64(12), 63(18), 53(24), fragments in bold are characteristic of the 4-oxo-4*H*-1-benzopyran-3-carbaldehyde molecule. A large number of substituted derivatives have been prepared in this way and some, particularly the 6-bromoderivative, showed relatively strong anti-anaphylactic activity with low LD_{50}, and decreased gastric acid volume. [Nohara et al *Tetrahedron* **30** 3553 *1974*, Klutchko et al. US Pat 4,098,799 *1978*, *Chem Abs* **90** 22803 *1979*.]

Fructose-1,6-diphosphate (trisodium salt) *[38099-82-0]* **M 406.1, pK_1^{25} 1.48, pK_2^{25} 6.14, pK_3^{25} 6.29, pK_4^{25} 6.93 (free acid).** Fructose-1,6-diphosphate is best purified *via* the acid strychnine salt which is stable for several months. To remove the strychnine, dissolve 5g in H_2O (150ml), and add 5N NaOH (or KOH to obtain the K salt) to pH 8.3 (phenolphthalein) with vigorous stirring. Remove the precipitate by centrifugation, wash with cold H_2O (2x 25ml), extract with $CHCl_3$ until the extract is free of strychnine (*ca* 8 to 10 times, Mandelein spot test). Freeze-dry the aqueous solution to give the Na salt which is hygroscopic. It has been recrystallised from aqueous EtOH as the *octahydrate*, **m** 125°, **$[\alpha]_D^{20}$ +2.6° (c 1, H_2O)**. A neutral solution of the salt keeps well in a frozen state for over several months. [Neuberg et al. *Arch Biochem* **3** 33 *1943*, Sable *Biochemical Preparations* **2** 52 *1952,* Stumpf *J Biol Chem* **182** 261 *1950*]. The *calcium salt* can be partially purified by dissolving in ice-cold N HCl (1g per 10ml) and re-precipitating by dropwise addition of 2N NaOH: the precipitate and supernatant are heated on a boiling water bath for a short time, then filtered, and the precipitate is washed with hot water. The *magnesium salt* can be precipitated from a cold aqueous solution by adding four volumes of EtOH. The *tetramethyl ester* is an oil with **n_D^{10} 1.4648, $[\alpha]_D^{18}$ +20.2 (c 0.4, MeOH)**. [Schulbach & Rauchenberger *Chem Ber* **60** 1178 *1927*, *Beilstein* **1** IV 4424.]

Fructose-6-phosphate *[643-13-0]* **M 260.1, $[\alpha]_D^{21}$ +2.5° (c 3, H_2O), pK_1^{21} 0.97, pK_2^{21} 6.11, (pK_2^{25} 5.84).** Crystallise fructose-6-phosphate as the barium salt from water by adding 4-volumes of EtOH. The barium can be removed by passage through the H^+ form of a cation exchange resin, and the free acid is collected by freeze-drying. *Alternatively*, the Ba salt is dissolved in H_2O, and one equivalent of Na_2SO_4 is added in small portions with stirring, filter off $BaSO_4$ and freeze dry to give the Na salt. The 6-phosphate hydrolyses more slowly than the 1-phosphate and considerably slower than pyrophosphoric acid (10^2 times) and triphosphoric acid (10^3 times). [Neuberg *Biochem Zeitschrift* **88** 432 *1918*, pKa: Meyerhof & Lohmann *Biochem Zeitschrift* **185** 113, 131 *1927,* Neuberg et al. *Arch Biochem* **3** 33, 40 *1944*, Hydrolysis: Friess *J Am Chem Soc* **74** 5521 *1954*, *Beilstein* **1** I 464, **1** IV 4423, H **31** 537.]

Gangcyclovir **[9-{(1,3-dihydroxy-2-propoxy)methyl}guanine; 2-amino-1,9-{(2-hydroxy-1-hydroxymethyl)-ethoxymethyl}-6*H*-purin-6-one; Cytovene; Cymeva(e)n(e)]** *[82410-32-0]* **M 255.2, m >290°(dec), >300°(dec), monohydrate m 248-249°(dec), $pK_{Est(1)}$~1.1, $pK_{Est(2)}$~4.1, $pK_{Est(3)}$~9.7.** Recrystallise gangcyclovir from MeOH. Alternatively, dissolve ~90g of it in 700ml of H_2O, filter and cool (*ca* 94% recovery). It has UV with λ_{max} (MeOH) at 254nm (ε 12,880), 270sh nm (ε 9040); its solubility in H_2O at 25° is 4.3mg/ml at pH 7.0. **ANTIVIRAL.** [Ogilvie et al. *Can J Chem* **60** 3005 *1982*, Ashton et al. *Biochem Biophys Res Commun* **108** 1716 *1982*, Martin et al. *J Med Chem* **26** 759 *1983*.]

Geraniol *[trans, E-form 106-24-1]* **M 145.2, b 114-115°/12mm, 229-230°/757mm, d_4^{20} $_{15}^{15}$ 0.889, n_D^{20} 1.4628.** Purify geraniol by fractional distillation. It has a sweet rose odour when pure, and the UV has λ_{max} at 190-195nm (ε 18,000). [See also p 146, *Beilstein* **1** H 457, **1** IV 2277.]

Geranyl acetate *[trans, E-form 105-87-3; 16409-44-2]* **M 196.3, b 118°/12mm, 138°/25mm, 236-242°/760mm(dec), d_{15}^{15} 0.9174, n_D^{15} 1.4766.** Purify the fragrant smelling geranyl acetate by fractional distillation at as high a vacuum as possible. It is very soluble in EtOH but insoluble in H_2O. [*Beilstein* **2** H 140, **2** I 65, **2** II 153, **2** III 299, **2** IV 204.]

Geranylgeranyl pyrophosphate *[6699-20-3 (NH_4 salt), 64732-91-8]* **M 450.5, $pK_{Est(1)}$~<2, $pK_{Est(2)}$~<2, $pK_{Est(3)}$~3.95, $pK_{Est(4)}$~6.26.** Purify the pyrophosphate by countercurrent distribution between two phases of a butanol/isopropyl ether/ammonia/water mixture (15:5:1:19) (v/v), or by chromatography on DEAE-cellulose (linear gradient of 0.02M KCl in 1mM Tris buffer, pH 8.9). *Alternatively*, purify it through a column of Dowex 1-x8 (formate form previously washed with MeOH) and eluted with a linear gradient of 0.053—0.43M ammonium formate in a total volume of 300ml of MeOH. The purity can be checked by TLC on Silica gel G on buffered plates (pH 6.5), eluted with $CHCl_3$/MeOH/H_2O (60:40:9) and developed with I_2 vapour. Store it as a powder at 0°. [Altman et al. *J Am Chem Soc* **94** 3257 *1972*.] It is more stable as the di(tri-n-butylammonium)hydrogen phosphate salt which can be obtained from the acid by evaporation in a rotary evaporator below 32° [Upper & West *J Biol Chem* **242** 3285 *1967*]. [Gregonis & Rilling *Biochemistry* **13** 1538 *1974*, Gregonis & Rilling

Biochem Biophys Res Commun **54** 449 *1973*.]

Geranyl pyrophosphate *[E-form 763-10-0 tri-(NH_4 salt), Z-form 16751-02-3]* **M 314.2, $pK_{Est(1)}$~<2, $pK_{Est(2)}$~<2, $pK_{Est(3)}$~3.95, $pK_{Est(4)}$~6.26.** Purify the pyrophosphate by paper chromatography on Whatman No 3 MM paper in a system of isopropyl alcohol/isobutyl alcohol/ammonia/water (40:20:1:39), R_F 0.77-0.82. Store it in the dark as the ammonium salt at 0°. The *E*-form crystallises in platelets from aqueous Me_2CO, **m** ~120°. It dissolves in dry MeCN. *Alternatively*, purify it through a column of Dowex AG 1x8(200-400mesh) equilibrated with 50mM NH_4 formate, and elute with MeOH/H_2O/NH_4OH (95:5:05), then freeze-dry. [Dixit et al. *J Org Chem* **46** 1967 *1981*, *Beilstein* **1** IV 3580.]

Gliotoxin (3*R*-6*t*-hydroxy-3-hydroxymethyl-2-methyl-(5*at*)-2,3,6,10-tetrahydro-5*aH*-3,10*ac*-epidisulfido-[1,2-*a*]-indol-1,4-dione) *[67-99-2]* **M 326.4, m 191-218°(dec), 220°(dec), 221°(dec), $[\alpha]_D^{20}$ -254° (c 0.6, $CHCl_3$), $[\alpha]_D^{25}$ -270° (c 1.7, pyridine).** Purify gliotoxin by recrystallisation from MeOH. Its solubility in $CHCl_3$ is 1%. The *dibenzoyl* derivative has **m** 202° (from $CHCl_3$/MeOH). [Glister & Williams *Nature* 153 651 *1944*, Elvidge & Spring *J Chem Soc* Suppl 135 *1949*, Johnson et al. *J Am Chem Soc* **65** 2005 *1943*, Bracken & Raistrick *Biochem J* **41** 569 *1947*.]

Glucose-1-phosphate (G-1-P) *[59-56-3]* **M 260.1, $[\alpha]_D^{25}$ +120° (c 3, H_2O), $[\alpha]_D^{20}$ +78° (c 4, H_2O of di-K salt), pK_1 1.11, pK_2 6.13 [pK^{25} 6.50].** Two litres of a 5% aqueous solution of the phosphate are purified by adjusting the pH to 3.5 with glacial acetic acid (+ 3g of charcoal) and filtering. An equal volume of EtOH is added, the pH is adjusted to 8.0 (glass electrode) and the solution is stored at 3° overnight. The precipitate is filtered off, dissolved in 1.2L of distilled water, filtered and an equal volume of EtOH is added. After standing at 0° overnight, the crystals are collected at the centrifuge and washed with 95% EtOH, then absolute EtOH, ethanol/diethyl ether (1:1), and diethyl ether. [Sutherland & Wosilait, *J Biol Chem* **218** 459 *1956*.] Its barium salt can be crystallised from water and EtOH. Heavy metal impurities are removed by passage of an aqueous solution (*ca* 1%) through an Amberlite IR-120 column (in the appropriate H^+, Na^+ or K^+ forms). *Di-K salt* crystallises as a *dihydrate* from EtOH. [see McGready *Biochemical Preparations* **4** 63 *1955*.] [*Beilstein* **17/8** V 247.]

Glucose-6-phosphate (G-6-P) *[acid 156-73-5; Ba salt 58823-95-3; Na salt 54010-71-8]* **M 260.1, m 205-207°(dec) mono Na salt, $[\alpha]_{546}^{20}$ +41° (c 5, H_2O), pK_1 1.65, pK_2 6.11, pK_3^{25} 11.71 [-C_1(OH)O^-].** It can be freed from metal impurities as described for glucose-1-phosphate. The solubility of the Na salt is 5% in H_2O at 20°. Its *barium* salt can be purified by solution in dilute HCl and precipitation by neutralising the solution. The precipitate is washed with small volumes of cold water and dried in air. *Alternatively*, the barium salt is dissolved in H_2O, 4 volumes of EtOH are added, the precipitate is collected, washed with 90% EtOH, absolute EtOH, 75% EtOH/25% Et_2O, 25% EtOH/75% Et_2O and finally dry Et_2O. The dry Barium salt has $[\alpha]_D^{25}$ +17.9° (c 1, H_2O). [*Beilstein* **1** IV.]
G-6-P is relatively more stable to hydrolysis (12% hydrolysis in N HCl/100° in 4 hours) than G-1-P (45% hydrolysis in N HCl/20° in 20 hours). [Lardy & Fischer *Biochemical Preparations* **2** 39 *1952*.]

L-α-Glycerol phosphocholine (Cadmium Chloride)$_x$ complex *[64681-08-9]* **M 257.2 + (183.3)$_x$, pK_{Est} ~ 5.5.** Glycerol phosphocholine is purified *via* the $CdCl_2$ complex which is recrystallised four times from 99% EtOH by standing at 0° for 1 hour. The white precipitate is collected, washed with EtOH, Et_2O and dried in a vacuum. The amorphous Cd complex can be converted to the crystalline form [$C_8H_{20}O_6NP.CdCl_2.3H_2O$] by dissolving 34.4g in H_2O (410ml), and 99% EtOH (1650ml total) is added slowly with stirring and allowing the clear solution to stand at 25° for 12 hours, then at 5° for 12 hours. The crystalline complex is filtered off, washed with cold 80% EtOH and dried in air. Glycerol phosphocholine can be recovered from the complex by dissolving it in H_2O (2% solution) and passing it through an ion-exchange column (4.9 x 100cm, of 1 volume IRC-50 and 2 volumes of IR-45). The effluent is concentrated to a thick syrup at 45°. It is dried further at 50°/P_2O_5/48 hours. The vitreous product (~8.25g) is then dissolved in 99% EtOH (50ml), and the clear solution is cooled to 5°, whereby crystals begin to appear, and crystallisation is completed at -15° after 16 hours. The crystals are filtered off, washed with 99% EtOH, and Et_2O then dried at 50° *in vacuo* over P_2O_5. It can be recrystallised from 99.5% EtOH (long prisms). It is *hygroscopic* and must be handled in a H_2O-free atmosphere [Tattrie & McArthur *Biochemical Preparations* **6** 16 *1958*, Baer & Kates *J Am Chem Soc* **70** 1394 *1948*, *Acta*

Cryst **21** 79, 87 *1966*].

Hematin (ferrihaeme hydroxide) *[15489-90-4]* **M 633.5, m 200°(dec), pK_{Est} ~ 4.** Crystallise it from pyridine. Dry it at 40° *in vacuo*. [*Beilstein* **26** III/IV 3047.]

Hematoporphyrin IX (8,13-bis(1-hydroxyethyl)-3,7,12,17-tetramethyl-21*H*-23*H*-porphin-2,18-dipropionic acid, **3,3'-[7,12-bis-(1-hydroxyethyl)-3,8,13,17-tetramethyl-porphyrin-2,18-diyl]-dipropionic acid)** *[14459-29-1]* **M 598.7, pK_{Est} ~4.8.** Purify it by dissolving it in EtOH and adding H_2O or Et_2O to give deep red crystals. It has also been recrystallised from MeOH. Its UV has λ_{max} at 615.5, 565, 534.4 and 499.5nm in 0.1N NaOH, and 597, 619, 634, 653, 683 and 701nm in 2N HCl. [Falk *Porphyrins and Metalloporphyrins* Elsevier, NY, p 175 *1964*, LCCCNo 63-19821.] It is used in the affinity chromatographic purification of Heme proteins [Olsen *Methods Enzymol* 123 324 *1986*]. The *O-methyl-dimethyl ester* has **m** 203-206° (from $CHCl_3$/MeOH), and the *O,O'-dimethyl-dimethyl ester* has **m** 145° (from $CHCl_3$/MeOH). [Paul *Acta Chem Scand* **5** 389 *1951*, *Beilstein* **26** III/IV 3157, and 3158 for the HCl.]

Hematoporphyrin dimethyl ester *[33070-12-1]* **M 626.7, m 212°.** It crystallises from $CHCl_3$/MeOH. [*Beilstein* **26** III/IV 3157.]

Hematoxylin (±-11*bc*-7,11*b*-dihydroindeno[2,1-*c*]-chromen-3,4-6*ar*-9,10-pentaol) *[517-28-2]* **M 302.3, m 200°(dec), 210-212°(dec).** Hematoxylin recrystallises from H_2O (as *trihydrate*) in white-yellow crystals which become red on exposure to light and then melt at 100-120°. It has been recrystallised from Me_2CO/*C_6H_6. It has been recrystallised as well from dilute aqueous $NaHSO_3$ until colourless and is soluble in alkali, borax and glycerol. Store it in the dark below 0°. [Morsingh & Robinson *Tetrahedron* **26** 182 *1970*, Dann & Hofmann *Chem Ber* **98** 1498 *1955*, *Beilstein* **17/8** V 469.]

Hemin (ferriproptoporphyrin IX chloride) *[16009-13-5]* **M 652.0, m sinters at 240°, pK_{Est} ~4.8.** Hemin is purified by recrystallisation from AcOH. Also, hemin (5g) is shaken in pyridine (25ml) till it dissolves, then $CHCl_3$ (40ml) is added, the container is stoppered and shaken for 5 minutes (releasing the stopper occasionally). The solution is filtered under slight suction, and the flask and filter are washed with a little $CHCl_3$ (15ml). During this period, AcOH (300ml) is heated to boiling, and saturated aqueous NaCl (5ml) and conc HCl (4ml) are added. The $CHCl_3$ filtrate is poured in a steady stream, with stirring, into the hot AcOH mixture and set aside for 12 hours. The crystals are filtered off, washed with 50% aqueous AcOH (50ml), H_2O (100ml), EtOH (25ml), Et_2O and dried in air. [Fischer *Org Synth* Coll Vol **III** 442 *1955*, *Beilstein* **26** III/IV 3048.]

(+)-Hydroquinidine anhydrous (9*S*-6'-methoxy-10,11-dihydrocinchonan-9-ol) *[1435-55-8]* **M 326.4, m 168-169°, 169°, 169-170°, 171-172°, $[\alpha]_D^{20}$ +231° (c 2, EtOH), +299° (c 0.82, 0.1N H_2SO_4), pK_{Est} ~ 8.8.** (+)-Hydroquinidine forms needles from EtOH and plates from Et_2O. It is slightly soluble in Et_2O and H_2O but readily soluble in hot EtOH. [Heidelberger & Jacobs *J Am Chem Soc* **41** 826 *1919*, King *J Chem Soc* 523 *1946*.] The *hydrochloride* has **m** 273-274°, $[\alpha]_D^{26}$ +184° (c 1.3, MeOH) and is very soluble in MeOH and $CHCl_3$, but less soluble in H_2O, EtOH and still less soluble in dry Me_2CO. [Kyker & Lewis *J Biol Chem* **157** 707 *1945*, Emde *Helv Chim Acta* **15** 557 *1932*, *Beilstein* **23/13** V 340.]

Hydroquinine *[522-66-7]* **M 326.4, m 168-171°, 171.5°, $[\alpha]_D^{16}$-143° (c 1.087, EtOH), pK^{15} 5.33 and 8.87.** Recrystallise hydroquinine from EtOH, Et_2O or *C_6H_6. [Rabe & Schultz *Chem Ber* **66** 120 *1933*, *Beilstein* **23** III/IV 3193, **23/13** V 340.] The *racemate* has **m** 175-175.5° (from EtOH).

5-Hydroxycreatinine (creatol, CTL, 2-amino-5-hydroxy-1-methylimidazolidin-4-one) *[133882-98-1]* **M 129.1, m 190° (191°, dec) for the hydrochloride, pK^{25} 4.2.** Creatol is one of three metabolites of creatinine [60-27-5] which was isolated from inflamed rabbit skin tissues [Ienaga et al. *Tetrahedron Lett* **28** 4587 1987], and the urine of uraemic rats (adenine induced chronic renal failure) and uraemic patients. The other two metabolites are 1-methylhydantoin (1-methylimidazolidine-2,4-dione [616-04-6]) and 5-hydroxy-1-methyl-hydantoin [1-methyl-5-hydroxyimidazolidine-2,4-dione] [84210-26-4]. [Ienaga et al. *J C S, Chem Commun*

509 *1991*.] Urine from uraemic rats (44ml, collected after 24 hours of administration of creatinine) was applied onto a PK216 ion exchange column (H^+ form) that was washed with H_2O, then eluted with aqueous NH_3 (2mol dm^{-3}) and evaporated *in vacuo*. The residue, in H_2O, was applied onto a Biolex-70 ion exchange column (H^+ form) that was washed with H_2O, then eluted with aqueous AcOH (0.1mol dm^{-3}), and the eluate was evaporated *in vacuo* to give *creatol* (0.66mg, 0.11%, purity checked by ODS reverse phase HPLC). [The H_2O wash from the PK216 column gave the other two metabolites (1.5mg, 0.35 and 0.87mg, 0.15% respectively) which were separated on a silica gel column with EtOAc elution.] Creatol has ^{1}H NMR (D_2O, *tert*-BuOH as internal standard) with δ at 3.11 (s, in $N^{12}CH_3$ creatol; but d, in $N^{13}CH_3$ labelled creatol with J = 143 Hz) and 5.11 (s, H-5); and ^{13}C NMR (D_2O, dioxane as internal standard) with δ at 30 (NCH_3), 81 (*C*-5), 160 (*C*-2) and 174 (*C*-4). [Ienaga et al. *J C S, Chem Commun* 509 *1991*.] The natural enantiomer most probably has the ***S*** configuration at C-5 [see Ienaga et al. *J C S, Chem Commun* 509 *1991*]. [Nakamura & Ienaga, Glycocyamidine derivatives, *Japanese Kokai Tokkyo Koho*, JP 2957217 *1989*, US patent 4957936 *1990*.] Data kindly supplied by Dr Kazu Ienaga, Nippon Zoki Pharmaceutical Co Ltd, Osaka, Japan.

***R*-(-)-2-Hydroxy-3,3-dimethyl-γ-butyrolactone (3-hydroxy-4,4-dimethyl-4,5-dihydrofuran-2-one, D-panto-lactone)** *[599-04-2]* **M 130.1, m 89-91°, 90.5-91.5°, 91°, 92-93°, b 120-122°/15mm, $[\alpha]_D^{20}$ -28° (c 5, MeOH), $[\alpha]_D^{20}$ -51° (c 3, H_2O).** Recrystallise the lactone from Et_2O/petroleum ether, diisopropyl ether or $*C_6H_6$/petroleum ether and sublime it at 25°/0.0001mm. It hydrolyses readily to the hydroxy-acid and racemises when heated above 145°. The *Brucine salt* has **m** 211-212° (from EtOH). [Kuhn & Wieland *Chem Ber* **73** 1134 *1940*, and Stiller et al. *J Am Chem Soc* **62** 1779 *1940*, Bental & Tishler *J Am Chem Soc* **68** 1463 *1946*, *Beilstein* **18/1** V 22.]

(±)-5-Hydroxy-1-methyl-imidazolidine-2,4-dione (HMH) *[84210-26-4]* **M 130.1, m 138°, pK 8.64.** The racemic compound was obtained by oxidation of *N*-1-methylhydantoin with $Pb(OAc)_4$ in $*C_6H_6$ (60°, 24 hours), isolation of the 5-acetoxy derivative (*via* a short silica-gel column chromatography; eluting with $*C_6H_6$/hexane), followed by hydrolysis with aqueous 0.3M H_2SO_4 (~25°, 40 minutes). Neutralisation, followed by evaporation, and silica-gel TLC (EtOAc) provided pure racemate m 138°, (64% yield) with the expected ^{1}H NMR spectrum and EI MS and elemental analysis. It is a plant growth regulator affecting the flowering period of cut white chrysanthemums at concentrations as low as 10^{-6} M. [Ienaga et al. *Tetrahedron Lett* **28** 4587 *1987*.]
The natural metabolite *N*-1-methylhydantoin (MH [616-04-6], see below) was isolated from rabbit urine by diluting the urine two-fold with MeOH and evaporating. The residue was extracted with MeOH/EtOAc (1:6), filtered, the filtrate was concentrated, subjected to silica-gel column chromatography and eluted with MeOH/$CHCl_3$ (1:9). The first eluate gave the pure crystalline *5-hydroxy compound* (HMH, 28% of total) that had m 147-150° and $[\alpha]_D^{25}$ -5.1° (c 1.0, MeOH). The expected ^{1}H NMR [Eu(tfc)$_3$] spectrum indicated that its enantiomeric excess was 56% (i.e. a 78:22 mixture). Some racemisation of the 5-hydroxy compound may well have occurred during isolation. The synthetic racemate was resolved by conversion into the diastereoisomeric Bz-L-proline ester (1:1, *R*:*S*) [with 1-(3-diethylaminopropyl)-3-ethylcarbodiimide HCl in the presence of DMAP in MeCN at 0°/2 hours) followed by purification through a silica-gel column and eluting with EtOAc/hexane (7:3)] in 56% yield. Fractional recrystallisation from Me_2CO gave pure 5-(*R*)-(*N*-Bz-L-prolyloxy)-1-methylimidazolidine-2,4-dione (30%), **m 189-192°,** $[\alpha]_D^{25}$ **–**2.1° (c 1.0, MeOH) {^{1}H NMR, DMSOd_6 has δ at 1.8-2.0 (m, 3H), 2.2-2.4 (m, 1 H), [2.52 (s) + 2.75 (s), 3H], 3.4-3.55 (m, 2 H), [4.35 (dd, J = 4, 9 Hz) + 4.46 (dd, J = 4, 9 Hz) 1H], [5.03 (s) + 5.10 (s) 2H] , [6.90 (s) + 6.10 (s) 1H], 7.25-7.45 (m, 5H, aromatic) and 11.21 (br s, NH)}; and when these crystals were subjected to X-ray crystallography they revealed that the absolute configuration at C5 of the *imidazolidine-2,4-dione* part of the molecule was ***R***, and that C5 of the *natural metabolite* was therefore ***S*** when a comparison of the HPLC of the mixture of prolyl-esters from the natural metabolite was made. The residue from evaporation of the mother liquors was recrystallised from EtOAc and gave the diastereoisomeric 5-(*S*)-*N*-Bz-L-prolyl ester (8%) with **m 147-150°,** $[\alpha]_D^{25}$ **–**68.9° (c 1.0, MeOH) {^{1}H NMR, DMSOd_6 has δ at 1.7-2.0 (m, 3H), 2.2-2.4 (m, 1 H), [2.63 (s) +2.73(s), 3H], 3.35-3.55 (m, 2 H), [4.36 (dd, J = 4, 9 Hz) + 4.47 (dd, J = 4, 9 Hz) 1H], [5.04 (d, J = 13Hz) + 5.07 (d, J = 13Hz) 1H], [5.07 (d, J = 13Hz) + 5.13 (d, J = 13Hz) 1H], [6.05 (s) + 6.12 (s) 1H], 7.25-7.45 (m, 5H, aromatic) and 11.25(br s, NH)}. Attempted hydrolysis of these esters gave racemic 5-hydroxyimidazoline-2,4-dione, however, owing to facile racemisation. [Ienaga et al. *J Chem Soc, Perkin Trans I* 1153 *1989*.] The racemate and the optically active form of *5-hydroxy-1-methylhydantoin have* the same ^{1}H NMR (400MHz, Me_2CO-d_6, TMS) with δ at ~5.1 (d, C-5) and ~5.9 (d, 1-NMe). Data kindly supplied by Dr Kazu Ienaga, Nippon Zoki Pharmaceutical Co Ltd, Osaka, Japan.

(-)-Inosine *[58-63-9]* **M 268.2, m 90° (dihydrate), 218° (dec, anhydrous), $[\alpha]_{546}^{20}$ -76° (c 1, 0.1M NaOH), pK_1^{25} 1.06, pK_2^{25} 8.96, pK_3^{25} 11.36.** (-)-Inosine forms *anhydrous* crystals from aqueous 80% EtOH but the *dihydrate* from H_2O. [*Beilstein* **31** H 25, **26** III/IV 2087.]

***myo*-Inositol (cyclohexane[1*r*,2*c*,3*c*,4*t*,5*c*,6*t*]-hexol)** *[87-89-8]* **M 180.2, m 218° (di-hydrate), 225-227°, 226-230°.** Recrystallise *myo*-inositol from aqueous 50% ethanol or H_2O forming a *dihydrate*, or *anhydrous* crystals from AcOH. The dihydrate is efflorescent and becomes anhydrous when heated at 100°. The anhydrous crystals are not hygroscopic. Its solubility in H_2O at 25° is 14%, at 60° it is 28%; it is slightly soluble in EtOH but insoluble in Et_2O. [Ballou & Anderson *J Am Chem Soc* **75** 748 *1953*, Anderson & Wallis *J Am Chem Soc* **70** 2931 *1948*, *Beilstein* **6** II 1157, **6** IV 7919.]

Inositol monophosphate *[15421-51-9]* **M 260.1, m 195-197°(dec).** Crystallise the phosphate from water, and EtOH. Recrystallise 1g by dissolving it in 3ml of H_2O and adding slowly 15ml of commercial EtOH, filter the crystals, wash with a little EtOH then Et_2O and dry it in a vacuum. [McCormick & Carter *Biochemical Preparations* **2** 65 *1952*.]

5-Iodouridine (5-iodo-1-[β-D-ribofuranosyl]-pyrimidine-2,4(1*H*)-dione) *[1024-99-3]* **M 370.1, m 205-208°(dec), 210-215°(dec), $[\alpha]_D^{20}$ -23.5° (c 1, H_2O), pK^{20} 8.5.** Recrystallise 5-iodouridine from H_2O and dry it *in vacuo* at 100°. It UV has λ_{max} at 289nm (0.01N HCl) and 278nm (0.01N NaOH). [Prusoff et al. *Cancer Res* **13** 221 *1953*, *Beilstein* **24** III/IV 1235.]

Isopentenyl pyrophosphate *[358-71-4]* **M 366.2, $pK_{Est(1)}$~<2, $pK_{Est(2)}$~<2, $pK_{Est(3)}$~3.95, $pK_{Est(4)}$~6.26.** Purify the pyrophosphate by chromatography on Whatman No 1 paper using *tert*-butyl alcohol/formic acid/water (20:5:8, R_F 0.60) or 1-propanol/ammonia/water (6:3:1. R_F 0.48). *Alternatively*, purify it by chromatography on a DEAE-cellulose column or a Dowex-1 (formate form) ion-exchanger using formic acid and ammonium formate as eluents. A further purification step is to convert it to the *monocyclohexylammonium salt* by passage through a column of Dowex-50 (cyclohexylammonium form) ion-exchange resin. It can also be converted into its lithium salt. (See geranyl pyrophosphate above.)

Kanamycin B (Bekanamycin, 4-*O*-[2,6-diamino-2,6-dideoxy-α-D-glucopyranosyl]-6-*O*-[3-amino-3-deoxy-α-D-glucopyranosyl]-2-deoxystreptamine) *[4696-76-8, 29701-07-3 (sulfate salt)]* **M 483.5, m 170-179°(dec), 178-182°(dec), $[\alpha]_D^{18}$ +130° (c 0.5, H_2O), pK^{25} 7.2.** A small quantity of kanamycin B (24mg) can be purified on a small Dowex-1 x 2 column (6 x 50mm); the required fraction is evaporated to dryness and the residue crystallised from EtOH containing a small amount of H_2O. [Umezawa et al. *Bull Chem Soc Jpn* **42** 537 *1969*.] It has been crystallised from H_2O by dissolving ~1g in H_2O (3ml), adding Me_2NCHO (3ml) and setting aside at 4° overnight. The needles are collected and dried to constant weight at 130°. It has also been recrystallised from aqueous EtOH. It is slightly soluble in $CHCl_3$ and isoPrOH. [IR: Wakazawa et al. *J Antibiot* **14A** 180, 187 *1961*, Ito et al. *J Antibiot* **17 A** 189 *1964*, *Beilstein* **18** III/IV 7631.]

Lecithin (1,2-diacylphosphatidylcholine mixture) *[8002-43-5]* **M ~600-800, amorphous.** Lecithin from hen egg white is purified by solvent extraction and chromatography on alumina. It is suspended in H_2O and kept frozen until required [Lee & Hunt *J Am Chem Soc* **106** 7411 *1984*, Singleton et al. *J Am Oil Chem Soc* **42** 53 *1965*]. For purification of commercial egg lecithin, see Pangborn [*J Biol Chem* **188** 471 *1951*].

Leucopterin (2-amino-5,8-dihydropteridine-4,6,7(1*H*)-trione) *[492-11-5]* **M 195.1, m >300° (dec), pK_1^{20} -1.66, pK_2^{20} 7.56, pK_3^{20} 9.78, pK_4^{20} 13.6.** Leucopterin is purified by dissolving it in aqueous NaOH, stirring with charcoal, filtering and precipitating by adding aqueous HCl, then drying at 100° in a vacuum. It separates with 0.5 mole of H_2O. Its solubility in H_2O is 1g/750 litres [Albert et al. *J Chem Soc* 4219 *1952*, Albert & Wood *J Appl Chem* (*London*) **2** 591 *1952*, Pfleiderer *Chem Ber* **90** 2631 *1957*]. [*Beilstein* **26** III/IV 4017.]

DL-α-Lipoamide (±-6,8-thioctic acid amide, 5-[1,2]-dithiolan-3-ylvaleric acid amide) *[940-69-2; 3206-73-*

3] **M 205.3, m 124-126°, 126-129°, 130-131°.** DL-α-Lipoamide is recrystallised from EtOH and has UV with λ_{max} at 331nm in MeOH. [Reed et al. *J Biol Chem* **232** 143 *1958*, IR: Wagner et al. *J Am Chem Soc* **78** 5079 *1956*, *Beilstein* **19/7** V 238.]

DL-α-Lipoic acid (±-6,8-thioctic acid, 5-[1,2]-dithiolan-3-ylvaleric acid) *[1077-28-7]* **M 206.3, m 59-61°, 60.5-61.5° and 62-63°, b 90°/10^{-4}mm, 150°/0.1mm, pK^{25} 4.7.** It forms yellow needles from cyclohexane or hexane and has been distilled at high vacuum; and sublimes at ~90° and very high vacuum. It is insoluble in H_2O but dissolves in alkaline solution. [Lewis & Raphael *J Chem Soc* 4263 *1962*, Soper et al. *J Am Chem Soc* **76** 4109, Reed & Niu *J Am Chem Soc* **77** 416 *1955*, Tsuji et al. *J Org Chem* **43** 3606 *1978*, Calvin *Fed Proc USA* **13** 703 *1954*.] The *S-benzylisothiuronium salt* has **m** 153-154° (evacuated capillary, from MeOH), 132-134°, 135-137° (from EtOH). The *d-* and *l-* forms have **m** 45-47.5° and $[\alpha]_D^{23}$ ±113° (c 1.88, $*C_6H_6$) and have UV in MeOH with λ_{max} at 330nm (ε 140). [*Beilstein* **19/7** V 237.] The reduced form, *(±)-6,8-dimercaptooctanoic acid*, [7516-48-5] **M 208.3**, is a light yellow liquid which is sold in sealed ampoules.

D-Luciferin (firefly luciferin, *S*-2[6-hydroxybenzothiazol-2-yl]-4,5-dihydrothiazol-4-carboxylic acid), *[2591-17-5]* **M 280.3, m 189.5-190°(dec), 196°(dec), 201-204°, 205-210°(dec, browning at 170°), $[\alpha]_D^{22}$ -36° (c 1.2, DMF), $pK_{Est(1)}$~ 1.2 (benzothiazole-N), $pK_{Est(2)}$~ 1.6 (thiazolidine-N), $pK_{Est(3)}$~ 6.0 (CO_2H), $pK_{Est(4)}$ 8.5 (6OH).** D-Luciferin crystallises as pale yellow needles from H_2O, or MeOH (83mg/7ml). It has UV with λ_{max} at 263 and 327nm (log ε 3.88 and 4.27) in 95% EtOH. The Na salt has a solubility of 4mg in 1 ml of 0.05M glycine. [White et al. *J Am Chem Soc* **83** 2402 *1961*, **85** 337 *1963*, UV and IR: Bitler & McElroy *Arch Biochem* **72** 358 *1957*, Review: Cormier et al. *Fortschr Chem Org Naturst* **30** 1 *1973*, *Beilstein* **27** III/IV 8934.]

Lumiflavin (7,8,10-trimethylbenzo[*g*]pteridine-2,4(3*H*,10*H*)-dione) *[1088-56-8]* **M 256.3, m 330°(dec), 340°(dec), pK^{25} 10.2.** Lumiflavin forms orange crystals upon recrystallisation from 12% aqueous AcOH, or from formic acid. It sublimes at high vacuum. It is freely soluble in $CHCl_3$, but not very soluble in H_2O and most organic solvents. In H_2O and $CHCl_3$ solution it has a green fluorescence. Its UV has λ_{max} at 269, 355 and 445nm (ε 38,800, 11,700 and 11,800, respectively) in 0.1N NaOH and 264, 373 and 440nm (ε 34,700, 11,400 and 10,400, respectively) in 0.1N HCl, while the UV in $CHCl_3$ has λ_{max} at 270, 312, 341, 360, 420, 445 and 470nm. [Hemmerich et al. *Helv Chim Acta* **39** 1242 *1956*, Holiday & Stern *Chem Ber* **67** 1352 *1834*, Yoneda et al. *Chem Pharm Bull Jpn* **20** 1832 *1972*, Birch & Moye *J Chem Soc* 2622 *1958*, Fluorescence: Kuhn & Moruzzi *Chem Ber* **67** 888 *1934*, *Beilstein* **26** III/IV 2539.]

Magnesium protoporphyrin dimethyl ester *[14724-63-1]* **M 580.7, m 214-217° (others found m 228-230°).** The Mg complex can be prepared from protoporphyrin dimethyl ester (see below) and $Mg(ClO_4)_2$ in boiling pyridine under N_2 for 3-4 hours until the band at 630nm (free porphyrin) is absent. Filter, wash the insolubles with Et_2O until the filtrate is colourless. Evaporate the solvent *in vacuo* at 50-60° to a very small volume, then add excess peroxide free Et_2O in a separating funnel, shake with H_2O (2x), evaporate the Et_2O, and remove the H_2O and pyridine by evaporating (azeotropically) with $*C_6H_6$ (4x). Purify the residue by dissolving the Mg complex in as little hot $*C_6H_6$ (50ml for 800mg) as possible, and add cold petroleum ether (b 30-60°), leave at room temperature until crystallisation begins, then further in a refrigerator to give twinned prisms, **m** >330°. Its IR has ν_{max} at 3080(w CH=CH_2), 1610, 1698, 1740 (s CO_2Me) cm^{-1}, but no NH. Its UV (Et_2O) has λ_{max} (ε) at 588nm (19,000), 550nm (19,300), 417nm (Soret, 252,000). [Ramsey *Biochemical Preparations* **3** 39 *1953*, Fuhrhop & Graniek *Biochemical Preparations* **13** 55 *1971*.]

6-Mercaptopurine-9-β-D-ribofuranoside *[574-25-4]* **M 284.3, m 208-210°(dec), 210-211°(dec), 220-223°(dec), 222-224°(dec), $[\alpha]_D^{25}$ -73° (c 1, 0.1N NaOH), pK^{25} 7.56.** Recrystallise the riboside from H_2O or EtOH. It has UV with λ_{max} (H_2O) at 322nm (pH 1), 320 nm (pH 6.7) and 310nm (pH 13). [IR: Johnson et al. *J Am Chem Soc* **80** 699 *1958*, UV: Fox et al. *J Am Chem Soc* **80** 1669 *1958*, *Beilstein* **26** III/IV 2100.]

***R*-(-)-Methadone (Levomethadone, 6-dimethylamino-4,4-diphenylheptan-3-one)** *[125-58-6]* **M 309.4, m 98-100°, $[\alpha]_D^{20}$ -32° (c 1.8, EtOH), see below for pKa.** This pharmacologically active (against narcotic addiction)

enantiomer was obtained by optical resolution (using D-tartaric acid) of the racemate, and was purified by precipitation of the hydrochloride from aqueous solution at pH >6, dried and recrystallised from propan-2-ol. The *R-hydrochloride* [5967-73-7], when recrystallised from propan-2-ol, has **m** 245-246°, $[\alpha]_D^{20}$ -169° (c 2, EtOH). The *S*-(+)-*enantiomer* [5653-8-5] also recrystallises from propan-2-ol and has recorded **m** of 100-101°, $[\alpha]_D^{25}$ + 26° (c 1.2, H_2O). The *S-hydrochloride* [15284-15-8], when crystallised from propan-2-ol, has **m** 243-244°, $[\alpha]_D^{20}$ +169° (c 2, EtOH). [Larsen et al. *J Am Chem Soc* **70** 4194 *1948*, Brode & Hill *J Org Chem* **13** 191 *1948*, Schultz et al. *J Am Chem Soc* **69** 2454 *1947*, Easton et al. *J Am Chem Soc* **69** 2941 *1947*, Winter & Flataker *J Pharmacol Exp Ther* **98** 305 *1950*, *Beilstein* **14** III 278, **14** III/IV 300.]

(±)-Methadone hydrochloride (6-dimethylamino-4,4-diphenylheptan-3-one HCl) *[1095-90-5]* **M 345.9, m 241-242°, pK_1^{25} 8.94, pK_2^{20} 10.12 (free base).** The salt (see above) crystallises from EtOH, or EtOH/Et_2O. [See methadone references in the above entry.]

Methoxantin coenzyme (PQQ, pyrrolo quinoline quinone, 2,7,9-tricarboxy-1*H*-pyrrolo-[2,3-*f*]-quinoline-4,5-dione, 4,5-dihydro-4,5-dioxo-1*H*-pyrrolo[2,3-*f*]quinoline-2,7,9-tri-carboxylic acid) *[72909-34-3]* **M 330.2, m 220°(dec).** Efflorescent yellow-orange needles of PQQ are formed on recrystallising from H_2O by addition of Me_2CO, or better from a supersaturated aqueous solution, as it forms an acetone adduct. [Forrest et al. *Nature* **280** 843 *1979*.] It has also been purified by passage through a C-18 reverse phase silica cartridge or a silanised silica gel column in aqueous solution whereby methoxantin remains behind as a red-orange band at the origin. This band is collected and washed thoroughly with dilute aqueous HCl (pH 2) and is then eluted with MeOH/H_2O (7:3) and evaporated *in vacuo* to give the coenzyme as a red solid. It has also been purified by dissolving it in aqueous 0.5M K_2CO_3 and acidified to pH 2.5 whereby PQQ precipitates as a deep red solid which is collected and dried *in vacuo*. Methoxantin elutes at 3.55 retention volumes from a C18 μBondapak column using H_2O/MeOH (95:5) + 0.1% AcOH pH 4.5. It has UV with λ_{max} at 247 and 330nm (shoulder at 270nm) in H_2O and with λ_{max} at 250 and 340nm in H_2O at pH 2.5. With excitation at λ_{ex} 365nm it has a λ_{em} at 483nm. The ^{13}C NMR has δ: 113.86, 122.76, 125.97, 127.71, 130.68, 137.60, 144.63, 146.41, 147.62, 161.25, 165.48, 166.45, 173.30 and 180.00.
When a solution in 10% aqueous MeCO is adjusted to pH 9 with aqueous NH_3 and kept at 25° for 30 minutes, the ***acetone adduct*** is formed, which has UV with λ_{max} at 250, 317 and 360nm (H_2O, pH 5.5), and with λ_{ex} at 360nm it fluorescence with λ_{em} at 465nm; and the ^{13}C NMR [$(CD_3)_2SO$, TMS] has δ: 29.77, 51.06, 74.82, 111.96, 120.75, 121.13, 125.59, 126.88, 135.21, 139.19, 144.92, 161.01, 161.47, 165.17, 168.61, 190.16 and 207.03. It also forms a *methanol adduct*.
When it is reacted with Me_2SO_4/K_2CO_3 in dry Me_2NCHO at 80° for 4 hours, it forms the *trimethyl ester* which has **m** 265-267°(dec) [260-263°(dec) also reported] after recrystallisation from hot MeCN it forms orange crystals with UV that has λ_{max} at 252 and 344nm (H_2O) and 251, 321 and 373nm (in MeOH; MeOH adduct ?). [Duine et al. *Eur J Biochem* **108** 187 *1980*, Duine et al. *Adv Enzymology* **59** 169 *1987*, Corey & Tramontano *J Am Chem Soc* **103** 5599 *1981*, Gainor & Weinreb *J Org Chem* **46** 4319 *1981*, Hendrickson & de Vries *J Org Chem* **17** 1148 *1982*, McKenzie et al. *J Chem Soc, Chem Commun* 1372 *1983*.]

Methyl benzylpenicillinate *[653-89-4]* **M 348.3, m 97°, $[\alpha]_D^{20}$ +328° (c 1, MeOH), $[\alpha]_D^{20}$ +286° (c 1, $CHCl_3$).** Crystallise the ester from CCl_4 or EtOAc/hexane. [Sheehan et al. *J Am Chem Soc* **84** 2983 *1962*, Review: Chain et al. *Antibiotics* (Oxford University Press) **2** *1949*.]

1-Methylimidazolidine-2,4-dione (1*N*-methylhydantoin, MH) *[616-04-6]* **M 114.1, m 158°, 155-156°, 157-159°, and 184-185° (dimorphic ?), pK^{25} 9.20.** It is purified by dissolving it in the minimum volume of H_2O, extracting with EtOAc, the extract is dried and evaporated to dryness. The residue, in EtOAc is subjected to column chromatography (silica gel with EtOAc as eluent), or silica gel TLC [MeOH/$CHCl_3$ (1:9)] and recrystallised from EtOH (elongated plates). It is identified by ^1H NMR and MS. The IR has ν_{max} at 1712 (2CO) and 1761 (4CO) cm^{-1}. The *3-acetate* has **m 134-135°**. [Miller & Robson *J Chem Soc* 1910 *1938*, West *J Biol Chem* **34** 187 *1918*, Ienaga et al. *Tetrahedron Lett* **28** 4587 *1987*, Ienaga et al. *J Chem Soc, Perkin Trans I* 1153 *1989*, *Beilstein* **24** H 44.] Data kindly supplied by Dr Kazu Ienaga, Nippon Zoki Pharmaceutical Co Ltd, Osaka, Japan.

(±)-5-Methylimidazoline-2,4-dione (5-methylhydantoin) *[616-03-5]* **M 114.1, m 145°, 148-152°, 149-151°,**

150°, pK^{25} 9.07. Purify it by recrystallisation from H_2O, and dry it *in vacuo*. [Ienaga et al. *Tetrahedron Lett* **28** 4587 *1987*, Ienaga et al. *J Chem Soc, Perkin Trans I* 1153 *1989*, IR: Burland & Christian *Can J Chem* **35** 444 *1957*, *Beilstein* **24** H 279, **24** I 305, **24** II 155, **24** III/IV 1083.] Data supplied by Dr Kazu Ienaga (see above).

5-Methyltetrahydrofolic acid disodium salt (prefolic A) *[68792-52-9]* **M 503.4, pK$_1$ 2.4 (N10 protonation), pK$_2$ 2.7 (pyrimidine N1 protonation), pK$_3$ 3.5 (α-CO$_2$H), pK$_4$ 4.9 (γ-CO$_2$H), pK$_5$ 5.6 (N5-Me) , pK$_6$ 8.5 (3NHCO acidic).** First check the purity by measuring the UV at pH 7.0 (use phosphate buffer), and it should have λ_{max} at 290nm and λ_{min} at 245nm with a ratio of A_{290}/A_{250} of 3.7. This ratio goes down to 1.3 as oxidation to the dihydro derivative occurs. The latter can be reduced back to the tetrahydro compound by reaction with 2-mercaptoethanol at room temperature. If oxidation has occurred, then the compound should be chromatographed on DEAE-cellulose (~0.9 milliequiv/g, in AcO^- form) in $(NH_4)_2CO_3$ (1.5 M) and washed with 1M NH_4OAc containing 0.01M mercaptoethanol till free from UV absorption and then washed with 0.01M mercaptoethanol. All is done in a nitrogen atmosphere. The reduced folate is then eluted with a gradient between 0.01M mercaptoethanol and 1M NH_4OAc containing 0.01M mercaptoethanol, and the fractions with absorption at 290nm are collected. These are evaporated under reduced pressure at 25°, and traces of NH_4OAc and H_2O are removed at high vacuum/25° (~24-48 hours). The residue is dissolved in the minimum volume of 0.01M mercaptoethanol, and an equivalent of NaOH is added to convert the acid to the diNa salt and evaporated to dryness at 25°/high vacuum. The pure product has λ_{max} 290nm (ε 32,000) in pH 7.0 buffer. [Sakami *Biochemical Preparations* **10** 103 *1963*.]

Mevalonic acid lactone *[674-26-0]* **M 130.2, m 28°, b 145-150°/5mm.** Purify the lactone *via* the *dibenzylethylenediammonium salt* (**m** 124-125°) [Hofmann et al. *J Am Chem Soc* **79** 2316 *1957*], or by chromatography on paper or on a Dowex-1 (formate) column. [Bloch et al. *J Biol Chem* **234** 2595 *1959*.] Store it as the *N,N'*-dibenzylethylenediamine (DBED) salt, or as the lactone in a sealed container at 0°. [*Beilstein* **18/1** V 19.]

Mevalonic acid 5-phosphate *[1189-94-2]* **M 228.1, pK$_{Est(1)}$~1.5 (PO_4H_2), pK$_{Est(2)}$~4.4 (CO_2H), pK$_{Est(3)}$~6.31 (PO_4H^-).** Purify the acid by conversion to the *tricyclohexylammonium salt* (**m** 154-156°) by treatment with cyclohexylamine. Recrystallise the salt from water/acetone at -15°. *Alternatively*, the phosphate is chromatographed through an ion-exchange resin or paper (Whatman No 1) in a system of isobutyric acid/ammonia/water (66:3:30; R_F 0.42). Store it as the cyclohexylammonium salt.

Mevalonic acid 5-pyrophosphate *[1492-08-6]* **M 258.1, pK$_{Est(1)}$~<2, pK$_{Est(2)}$~<2, pK$_{Est(3)}$~3.95 (PO_4), pK$_{Est(4)}$ 4.4 (CO_2H), pK$_{Est(5)}$ ~6.26 (PO_4).** Purify the pyrophosphate by ion-exchange chromatography on Dowex-1 formate [Bloch et al. *J Biol Chem* **234** 2595 *1959*], DEAE-cellulose [Skilletar and Kekwick, *Anal Biochem* **20** 171 *1967*], or by paper chromatography [Rogers et al. *Biochem J* **99** 381 *1966*]. Likely impurities are ATP and mevalonic acid phosphate. Store it as a dry powder or in a slightly alkaline (pH 7-9) solution at -20°.

Mithramycin A (Aureolic acid, Plicamycin) *[18378-89-7]* **M 1085.2, m 180-183°, $[\alpha]_D^{20}$ -51° (c 0.3, EtOH), pK$_{Est}$ ~9.2.** Purify mithramycin A by crystallisation from $CHCl_3$. It is soluble in MeOH, EtOH, Me_2CO, EtOAc, Me_2SO and H_2O, and moderately soluble in $CHCl_3$, but is slightly soluble in $*C_6H_6$ and Et_2O. It is a fluorescent antitumour agent used in flow cytometry. [Thiem & Meyer *Tetrahedron* **37** 551 *1981*, NMR: Yu et al. *Nature* **218** 193 *1968*, *Beilstein* **17/1** V 672.]

Mitomycin C *[50-07-7]* **M 334.4, m >360°, pK$_{Est(2)}$~8.0.** Mitomycin C forms blue-violet crystals from $*C_6H_6$/petroleum ether. It is soluble in Me_2CO, MeOH and H_2O, moderately soluble in $*C_6H_6$, CCl_4 and Et_2O but insoluble in petroleum ether. It has UV with λ_{max} at 216, 360 and a weak peak at 560nm in MeOH. [Stevens et al. *J Med Chem* **8** 1 *1965*, Shirahata & Hirayama *J Am Chem Soc* **105** 7199 *1983*, *Beilstein* **25** III/IV 516.]

Muramic acid [*R*-2(2-amino-2-deoxy-D-glucose-3-yloxy)-propionic acid] *[1114-41-6]* **M 251.2, m 145-150°(dec), 152-154°(dec), 155°(dec), $[\alpha]_D^{25}$ +109° (c 2, H_2O), +165.0° (extrapolated to 0 time) → +123° [after 3 hours (c 3, H_2O)], pK$_{Est(1)}$~3.8 (CO_2), pK$_{Est(2)}$~7.7 (NH_2).** Muramic acid crystallises from H_2O or aqueous EtOH as the *monohydrate* which loses H_2O at 80° *in vacuo* over P_2O_5. It sometimes contains some NaCl. It has

been purified by dissolving 3.2g in MeOH (75ml), filtering from some insoluble material, concentrating to ~10ml and refrigerating. The colourless crystals are washed with absolute MeOH. This process does not remove NaCl; to do so, the product is recrystallised from an equal weight of H_2O to give a low recovery yield of very pure acid (0.12g). On paper chromatography 0.26μg give one ninhydrin positive spot after development with 75% phenol (R_F 0.51) or with *sec*-BuOH/HCO_2H/H_2O (7:1:2) (R_F 0.30). [Matsushima & Park *Biochemical Preparations* **10** 109 *1963*, *J Org Chem* **27** 3581 *1962*.] The acid has also been purified by dissolving 990mg in 50% aqueous EtOH (2ml), cooling, collecting the colourless needles on a sintered glass funnel and drying over P_2O_5 at 80°/0.1mm to give the anhydrous acid. [Lambert & Zilliken *Chem Ber* **93** 2915 *1960*.] Alternatively the acid is dissolved in a small volume of H_2O, neutralised to pH 7 with ion-exchange resin beads (IR4B in OH^- form), filtered, evaporated and dried. The residue is recrystallised from 90% EtOH (v/v) and dried as above for 24 hours. [Strange & Kent *Biochem J* **71** 333 *1959*.] The *N-acetyl* derivative **(NAMA, *R*-2-(acetylamino)-3-*O*-(1-carboxyethyl)-2-deoxy-D-glucose, *R*-2(2-acetylamino-2-deoxy-D-glucose-3-yloxy)-propionic acid)** *[10597-89-4]*, M 292.3, has **m** ~125° (dec) and $[\alpha]_D^{20}$ +41.2° after 24 hours (c 1.5, H_2O), pK_{Est} ~ 3.6. [Watanabe & Saito *J Bacteriol* **144** 428 *1980*, *Beilstein* **4** IV 2029.]

Muscimol (pantherine, 5-aminoethyl-3[2*h*]-isoxazolone) *[2763-96-4]* **M 114.1, m 170-172°(dec), 172-174°(dec), 172-175°, 175°, 176-178°(dec), $pK_{Est(1)}$~6 (acidic, ring 2-NH), $pK_{Est(2)}$~8 ($CH_2CH_2NH_2$).** Recrystallise muscimol from MeOH/tetrahydrofuran or EtOH and sublime it at 110-140° (bath) at 10^{-4} mm to give a yellow spot with ninhydrin which slowly turns purple [NMR: Bowden et al. *J Chem Soc (C)* 172 *1968*]. It can also be purified by dissolving in the minimum volume of hot H_2O and adding EtOH dropwise until cloudy, cool, and colourless crystals separate; its IR has ν□□□ at 3445w, 3000-2560w br, 2156w, 1635s and 1475s cm^{-1}. [NMR: Jager & Frey *Justus Liebigs Ann Chem* 817 1982.] *Alternatively*, it has been purified by two successive chromatographic treatments on Dowex-1 x 8, with the first elution with 2M AcOH and a second with a linear gradient between 0—2M AcOH, evaporating the desired fractions and recrystallising the residue from MeOH. [McCarry & Savard *Tetrahedron Lett* **22** 5153 *1981*, Nakamura *Chem Pharm Bull Jpn* **19** 46 *1971*.]

Mycophenolic acid (6-[1,3-dihydro-7-hydroxy-5-methoxy-4-methyl-1-oxoisobenzofuran-6-yl]-4-methylhex-4-enoic acid) *[24280-93-1]* **M 320.3, m 141°, 141-143°, $pK_{Est(1)}$~2.5 (CO_2H), $pK_{Est(2)}$~9.5 (phenolic OH).** Purify the acid by dissolving it in the minimum volume of EtOAc, applying onto a silica gel column (0.05-0.2 mesh) and eluting with a mixture of EtOAc/$CHCl_3$/AcOH (45:55:1) followed by recrystallisation from heptane/EtOAc, from aqueous EtOH or from hot H_2O and drying *in vacuo*. It is a weak dibasic acid, moderately soluble in Et_2O, $CHCl_3$ and hot H_2O but weakly soluble in *C_6H_6 and toluene. [Birch & Wright *Aust J Chem* **22** 2635 *1969*, Canonica et al. *J Chem Soc, Perkin Trans 1* 2639 *1972*, Birkinshaw et al. *Biochem J* **50** 630 *1952*, *Beilstein* **18** II 393, **18** III/IV 6513.]

Myricetin (Cannabiscetin, 3,3',4',5,5',7-hexahydroxyflavone) *[529-44-2]* **M 318.2, m >300°, 357°(dec) (polyphenolic pK_{Est}~8-11).** Recrystallise myricetin from aqueous EtOH (**m** 357° dec, as *monohydrate*) or Me_2CO (**m** 350° dec, with one mol of Me_2CO) as yellow crystals. It is almost insoluble in $CHCl_3$ and AcOH. The *hexaacetate* has **m** 213°. [Hergert *J Org Chem* **21** 534 *1956*, Spada & Cameroni *Gazzetta* **86** 965, 975 *1956*, Kalff & Robinson *J Chem Soc* **127** 181 *1925*, *Beilstein* **18/5** V 670.]

Nalidixic acid

(1-ethyl-7-methyl-1,8-naphthyridin-4-one-3-carboxylic acid) *[389-08-2]* **M 232.3, m 226.8-230.2°, 228-230°, 229-230°, pK^{25} 6.0.** Nalidixic acid crystallises from H_2O or EtOH as a pale buff powder. It is soluble at 23° in $CHCl_3$ (3.5%), toluene (0.16%), MeOH (0.13%), EtOH (0.09%), H_2O (0.01%) and Et_2O (0.01%). It inhibits nucleic acid and protein synthesis in yeast. [Lesher et al. *J Med & Pharm Chem* **5** 1063 *1962*.]

Naloxone hydrochloride hydrate (Narcan, 1-*N*-propenyl-7,8-dihydro-14-hydroxymorphinan-6-one hydrochloride) *[51481-60-8]* **M 399.9, m 200-205°, $[\alpha]_D^{20}$ -164° (c 2.5, H_2O), $pK_{Est(1)}$~6 (N-propenyl), $pK_{Est(2)}$~9.6 (phenolic OH).** This opiate antagonist has been recrystallised from EtOH/Et_2O or H_2O. It is soluble in H_2O (5%) and EtOH but insoluble in Et_2O. The *free base* has **m** 184° (177-178° also reported) after recrystallisation from EtOAc, and $[\alpha]_D^{20}$ -194.5° (c 0.93, $CHCl_3$). [Olofson et al. *Tetrahedron Lett* 1567 *1977*,

Gold et al. *Med Res Rev* **2** 211 *1982*.]

Naltrexone hydrochloride dihydrate (1-*N*-cyclopropylmethyl-7,8-dihydro-14-hydroxy-morphinan-6-one hydrochloride) *[16676-29-2]* **M 413.9, m 274-276°, $[\alpha]_D^{20}$ -173° (c 1, H_2O), $pK_{Est(1)}$~6 (N-cyclopropylmethyl), $pK_{Est(2)}$~9.6 (phenolic OH).** This narcotic antagonist has been purified by recrystallisation from MeOH and dried in air. The *free base* has **m** 168-170° after recrystallisation from Me_2CO. [Cone et al. *J Pharm Sci* **64** 618 *1975*, Gold et al. *Med Res Rev* **2** 211 *1982*.]

1-Naphthyl phosphate disodium salt *[2183-17-7]* **M 268.1, pK_1^{26} 0.97, pK_2^{26} 5.85 (for free acid).** Purify the salt through an acid ion-exchange column (in H^+ form) to give the *free acid* [1136-89-6], M 224.2, which is obtained by freeze drying and recrystallising from Me_2CO/*C_6H_6, or by adding 2.5 volumes of hot $CHCl_3$ (or 20 parts of boiling *C_6H_6) to a hot solution of 1 part acid and 1.2 parts Me_2CO and cooling (**m** 155-157°, 157-158°). The acid is dissolved in the minimum volume of H_2O to which 2 equivalents of NaOH are added and then freeze dried, or by adding the equivalent amount of MeONa in MeOH to a solution of the acid in MeOH and collecting the Na salt, washing with cold MeOH, then Et_2O, and drying in a vacuum. [Friedman & Seligman *J Am Chem Soc* **72** 624 *1950*, Chanley & Feageson *J Am Chem Soc* **77** 4002 *1955*.] The *monosodium salt* [1136-89-6] is similarly prepared but by using 1 equivalent of NaOH. The phosphate group is hydrolysed at pH 1.1-5.85 at 70°. [*Beilstein* **6** IV 4226.] It is a substrate for alkaline phosphatase [Gomori *Methods Enzymol* **4** 381 *1957*, **128** 212 *1968*], and prostatic phosphatase [Babson *Clin Chem* **30** 1418 *1984*]. [See p 519 in "Miscellaneous As, B, P, Si, S, Se and Te Compounds", Chapter 4, *Beilstein* **6** IV 4226.]

2-Naphthyl phosphate monosodium salt *[14463-68-4]* **M 246.2, m 177-178°, 296° (sintering at 228°), pK_1^{26} 1.28, pK_2^{26} 5.53, pK_3^{26} 6.57 (for free acid).** The *free acid* [41845-15-2] is purified as for the preceding 1-isomer and has **m** 176-177° (also 177-178°) after several recrystallisations by adding 2.5 volumes of hot $CHCl_3$ to a hot solution of 1 part of acid in 1.3 volumes of Me_2CO as for the 1-isomer above. It is neutralised with one equivalent of NaOH and freeze dried or prepared as the 1-isomer above. Its solubility in H_2O is ~5%. It also forms a 0.5 Na.1 H_2O salt which has **m** 203-205° (244° also reported). [Friedman & Seligman *J Am Chem Soc* **72** 624 *1950*, Chanley & Fegeason *J Am Chem Soc* **77** 4002 *1955*, See p 520 in "Miscellaneous As, B, P, Si, S, Se and Te Compounds", Chapter 4, *Beilstein* **6** IV 4285.]

D(+)-Neopterin *[2009-64-5]* **M 253.2, m >300°(dec), $[\alpha]_{546}^{20}$ +64.5° (c 0.14, 0.1M HCl), $[\alpha]_D^{25}$ +50.1° (c 0.3, 0.1N HCl), pK_1 2.23 (basic), pK_2 7.89 (acidic).** Purification is as for biopterin. Also purify it on a Dowex-1 x 8 (formate form) column and elute with 0.03M ammonium formate buffer pH 8.0 then pH 7.2. The fluorescent neopterin fraction is evaporated under reduced pressure, leaving neopterin and ammonium formate (the latter sublimes out at high vacuum) behind. Stir the residue for 24 hours with EtOH, collect the solid and recrystallise it from H_2O. [Viscontini et al. *Helv Chim Acta* **53** 1202 *1970*, cf Wachter et al. Eds *Neopterin* W de Gruyter, Berlin *1992*, ISBN 9783110117905, *Beilstein* **26** IV 4038.]

β-Nicotinamide adenine dinucleotide (diphosphopyridine nucleotide, NAD, DPN) *[53-84-9]* **M 663.4, $[\alpha]_D^{23}$ -34.8° (c 1, H_2O), pK_1 2.2 (PO_4H), pK_2 4.0 (adenine NH_2), pK_3 6.1 (PO_4^-).** NAD is purified by paper chromatography or better on a Dowex-1 ion-exchange resin. The column is prepared by washing with 3M HCl until free of material absorbing at 260nm, then with water, 2M sodium formate until free of chloride ions and, finally, with water. NAD, as a 0.2% solution in water, is adjusted with NaOH to pH 8, and adsorbed onto the column, washed with water, and eluted with 0.1M formic acid. Fractions with strong absorption at 360nm are combined, acidified to pH 2.0 with 2M HCl, and cold acetone (*ca* 5L/g of NAD) is added slowly and with constant agitation. It is left overnight in the cold, then the precipitate is collected in a centrifuge, washed with pure acetone and dried under vacuum over $CaCl_2$ and paraffin wax shavings [Kornberg *Methods Enzymol* **3** 876 *1957*]. It has been purified by anion-exchange chromatography [Dalziel & Dickinson *Biochemical Preparations* **11** 84 *1966*.] The purity is checked by reduction to NADH (with EtOH and yeast alcohol dehydrogenase) which has ε_{340mn} 6220 $M^{-1}cm^{-1}$. [Todd et al. *J Chem Soc* 3727, 3733 *1957*.] [pKa, Lamborg et al. *J Biol Chem* **231** 685 *1958*.] The *free acid* crystallises from aqueous Me_2CO with $3H_2O$ and has **m** 140-142°. It is stable in cold neutral aqueous solutions in a desiccator ($CaCl_2$) at 25°, but decomposes at strong acid and alkaline pH. Its purity is checked by reduction with yeast alcohol dehydrogenase and EtOH to NADH and noting the OD at 340nm. Pure NADH (see below) has ε_{340} 6.2 x 10^4 $M^{-1}cm^{-1}$, i.e. 0.1µmole of NADH in 3ml and in a 1cm path

length cell has an OD at 340nm of 0.207. [*Beilstein* **26** IV 3644.]

β-Nicotinamide adenine dinucleotide reduced di-Na salt trihydrate (reduced diphosphopyridine nucleotide sodium salt, NADH) *[606-68-8]* **M 763.5, pKa as for NAD.** This coenzyme is available in high purity, and it is advisable to buy a fresh preparation rather than to purify an old sample as purification will invariably lead to a more impure sample contaminated with the oxidised form (NAD). It has UV with λ_{max} at 340nm (ε 6,200 $M^{-1}cm^{-1}$) at which wavelength the oxidised form NAD has no absorption. At 340nm a 0.161mM solution in a 1cm (pathlength) cell has an absorbance of 1.0 unit. The purity is best checked by the ratio A_{280nm}/A_{340nm} ~2.1, a value which increases as oxidation proceeds. The dry powder is stable indefinitely at -20°. Solutions in aqueous buffers at pH ~7 are stable for extended periods at -20° and for at least 8 hours at 0°, but are oxidised more rapidly at 4° in a cold room (e.g. almost completely oxidised overnight at 4°). [UV: Drabkin *J Biol Chem* **175** 563 *1945*, Fluorescence: Boyer & Thorell *Acta Chem Scand* **10** 447 *1956*, Redox: Rodkey *J Biol Chem* **234** 188 *1959*, Schlenk in *The Enzymes* **2** 250, 268 *1951*, Kaplan in *The Enzymes* **3** 105, 112 *1960*.] Deuterated NADH, i.e. NADD, has been purified through the anion exchange resin AG-1 x 8 (100-200 mesh, formate form) and through a Bio-Gel P-2 column. [Viola et al. *Anal Biochem* **96** 334 *1979*, *Beilstein* **26** III/IV 3639.]

β-Nicotinamide adenine dinucleotide phosphate (NADP, TPN) *[53-59-8]* **M 743.4, pK_1 1.1 (PO_4H_2), pK_2 4.0 (adenine NH_2), pK_3 6.1 (PO_4^-).** Purify it by anion-exchange chromatography in much the same way as for NAD [Dalziel & Dickinson *Biochem J* **95** 311 *1965*, *Biochemical Preparations* **11** 87 *1966*]. Finally it is purified by dissolving in H_2O and precipitating with 4 volumes of Me_2CO and dried *in vacuo* over P_2O_5. It is unchanged by storing *in vacuo* at 2°. [Hughes et al. *J Chem Soc* 3733 *1957*, Schuster & Kaplan *J Biol Chem* **215** 183 *1955*.] Deuterated NADPH, i.e. NADPD, has been purified through the anion exchange resin AG-1 x 8 (100-200 mesh, formate form) and through a Bio-Gel P-2 column. λ_{min} 259nm (ε 18.000) at pH 7.0. [Viola et al. *Anal Biochem* **96** 334 *1979*, *Beilstein* **26** IV 3669, 3672.]

β-Nicotinamide adenine dinucleotide phosphate reduced tetrasodium salt (reduced diphosphopyridine nucleotide phosphate sodium salt, NADPH) *[2646-71-1]* **M 833.4, pKa as for NADP.** Purification is mostly similar to that of NADH above. [*Beilstein* **26** III/IV 3671.]

β-Nicotinamide mononucleotide (NMN) *[1094-61-7]* **M 334.2, $[\alpha]_D^{23}$ -38.3° (c 1, H_2O), pK_{Est} ~6.1 (PO_4^-).** Purify NMN by passage through a column of Dowex-1 (Cl^- form) and washing with H_2O until no absorbance is observed at 260 nm. The tubes containing NMN are pooled, adjusted to pH 5.5-6 and evaporated *in vacuo* to a small volume. This is adjusted to pH 3 with dilute HNO_3 in an ice-bath and treated with 20 volumes of Me_2CO at 0-5°. The heavy white precipitate is collected by centrifugation at 0°. It is best stored wet and frozen or it can be dried to give a gummy residue. It has λ_{max} at 266nm (ε 4,600) and λ_{min} at 249nm (ε 3600) at pH 7.0 (i.e. no absorption at 340nm). It can be estimated by reaction with CN^- or hydrosulfite which form the 4-adducts (equivalent to NADH) which have UV with λ_{max} at 340nm (ε 6,200). Thus after reaction, an OD_{340} of "one" is obtained from a 0.1612mM solution in a 1cm path cuvette. [Plaut & Plaut *Biochemical Preparations* **5** 56 *1957*, Maplan & Stolzenbach *Methods Enzymol* **3** 899 *1957*, Kaplan et al. *J Am Chem Soc* **77** 815 *1955*, *Beilstein* **22/2** V 168.]

(-)-Nicotine ((*2S*)-1-methyl-2[3-pyridyl]-pyrrolidine) *[54-11-5]* **M 162.2, b 123-125°/17mm, 243-248°/760mm (partial dec), d_4^{20} 1.097, n_D^{20} 1.5280, $[\alpha]_D^{20}$ -169° (c 1, Me_2CO), pK_1^{15} 6.16 (pyridine N^+), pK_2^{15} 10.96 (pyrrolidine N^+).** (-)-Nicotine is a very pale yellow *hygroscopic* oil with a characteristic odour (tobacco extract) which turns brown in air on exposure to light. It is purifed by fractional distillation under reduced pressure in an inert atmosphere. A freshly distilled sample should be stored in dark sealed containers under N_2. It is a strong base; a 0.05 M aqueous solution has a pH of 10.2. It is very soluble in organic solvents. It is soluble in H_2O and readily forms salts. [UV: Parvis *J Chem Soc* **97** 1035 *1910*, Dobbie & Fox *J Chem Soc* **103** 1194 *1913*.] The *hydrochlorides* (mono- and di-) form deliquescent crystals soluble in H_2O and EtOH but insoluble in Et_2O. It has also been purified *via* the $ZnCl_2$ double salt. [Ratz *Monatsh Chem* **26** 1241 *1905*, Biosynthesis: Nakan & Hitchinson *J Org Chem* **43** 3922 *1978*.] The *picrate* has **m** 218° (from EtOH). [*Beilstein* **23/6** V 64.] **POISONOUS.**

(±)-Nicotine *[22083-74-5]* **M 162.2, b 113-115°/10mm, 242.3°/atm, d_4^{20} 1.082 (pKa see above).** It is purified

by fractional distillation. Its solubility in EtOH is ~5%. The *picrate* forms yellow needles from hot H_2O and has **m** 219°. The *methiodide* has **m** 219° (from MeOH). [Craig *J Am Chem Soc* **55** 2854 *1933*, Nakane & Hutchinson *J Org Chem* **43** 3922 *1978*, *Beilstein* **23/6** V 64.] **POISONOUS.**

Nonactin *[6833-84-7]* **M 737.0, m 147-148°, $[\alpha]_D^{20}$ 0° (±2°) (c 1.2, $CHCl_3$).** This macrotetrolide antibiotic crystallises from MeOH as colourless needles and is dried at 90°/20 hours/high vacuum. [Cordaz et al. *Helv Chim Acta* **38** 1445 *1955,* crystal structure: Dobler *Helv Chim Acta* **55** 1371 *1972*, Gambos et al. *Tetrahedron Lett* 3391 *1975*, *Beilstein* **19/12** V 751.]

L-Noradrenaline (Adrenor, *R*-2-amino-1-[3,4-dihydroxyphenyl]ethan-1-ol, L-norepi-nephrine) *[51-41-2, 69815-49-2, 636-88-4 (bitartrate salt)]* **M 169.2, m 216.5-218°(dec), ~220-230°(dec), $[\alpha]_D^{20}$ -45° (c 5, N HCl), $[\alpha]_D^{25}$ -37.3° (c 5, 1 equivalent aqueous HCl), pK_1^{25} 5.58 (phenolic OH), pK_2^{25} 8.90 (phenolic OH), pK_3^{25} 9.78 (NH_2).** Recrystallise adrenor from EtOH and store it in the dark under N_2. [pKa, Lewis *Brit J Pharmacol Chemother* **9** 488 *1954*, UV: Bergström et al. *Acta Physiol Scand* **20** 101 *1950*, Fluorescence: Bowman et al. *Science NY* **122** 32 *1955*, Tullar *J Am Chem Soc* **70** 2067 *1948*.] The *L-tartrate salt monohydrate* has **m** 102-104.5°, $[\alpha]_D^{25}$ -11° (c 1.6, H_2O), after recrystallisation from H_2O or EtOH. **[***Beilstein* **13** III 2382.]

L-Noradrenaline hydrochloride (Arterenol) *[329-56-6]* **M 205.6, m 145.2-146.4°, ~150°(dec), $[\alpha]_D^{25}$ -40° (c 6, H_2O), pKa see above.** Recrystallise arterenol from isoPrOH and store it in the dark as it is oxidised under light (see preceding entry). [Tullar *J Am Chem Soc* **70** 2067 *1948*, *Beilstein* **13** III 2382.]

1*R,2S*-(-)-Norephedrine [L(-)-*erythro*-1*R*,2*S*-2-amino-1-phenyl-1-propanol] *[492-41-1]* **M 151.2, m ~49-53°, 50-52°, $[\alpha]_D^{25}$ -14.6° (c 3.4, EtOH), $[\alpha]_D^{20}$ -41° (c 7, M HCl), pK^{25} 8.92.** It crystallises in plates from H_2O or Et_2O/petroleum ether.
The *1R,2S-(-) hydrochloride* **M 187.7**, has **m 174-175°**, crystallises from iso-PrOH, and has **$[\alpha]_D^{20}$ -33.0° (c 5, H_2O)**. [cf Atkins & Cramer *J Am Chem Soc* **52** 4349 *1930*, *Beilstein* **13** II 370, **13** III 1717, **13** IV 1875.]

1*S,2R*-(+)-Norephedrine [D(+)-*erythro*-1*R*,2*S*-2-amino-1-phenyl-1-propanol] *[37577-28-9]* **M 151.2, m ~49-53°, 50-52°, $[\alpha]_D^{27}$ +14.8° (c 4, EtOH), $[\alpha]_D^{20}$ +40° (c 7, M HCl), pK^{25} 8.92.** Purify it by recrystallisation from H_2O (plates), and it is soluble in Et_2O. Lewis [*Brit J Pharmacol Chemother* **9** 488 *1954*] obtained **pK_2^{20} 9.44 (H_2O)**.
The *hydrochloride* [*1S,2R-(+)* 40626-28-7] **M 187.7**, has **m 172-175°** (plates from EtOH) and **$[\alpha]_D^{20}$ +33.4° (c 6, H_2O)**, and the *sulfate* (plates from H_2O) has **m 285-286°** and **$[\alpha]_D^{27}$ +31.5° (H_2O).** [cf Atkins & Cramer *J Am Chem Soc* **52** 4349 *1930*, *Beilstein* **13** II 371, **13** III 1717, **13** IV 1875.]

DL-(±)-Norephedrine hydrochloride [Propadrin, (±)-*erythro*-1*RS*,2*SR*-2-amino-1-phenyl-1-propanol hydrochloride] *[154-41-6]* **m 194-196° (**also **194°** was reported**), pK 8.20.** It crystallises in plates from absolute EtOH or isoPrOH, and the (±)-*oxalate* has **m 245°(dec)** (plates from H_2O). The *2,4-dinitrobenzoate* has **m 86-88°** (from EtOH) and the *3,5-dinitrobenzoate* has **m 78-79°** (from EtOH). It is a mixed anti-sympathomimetic and used as a nasal anticongestant. [cf Atkins & Cramer *J Am Chem Soc* **52** 4349 *1930*, Krantz & Hartung *J Am Pharm Assoc* **19** 461 *1930*, Fischer & Plein *J Am Pharm Assoc* **44** 313 *1955*, *Beilstein* **13** I 252, **13** II 371, **13** III 1717, **13** IV 1875.]

1*R,2R*-(-)-Norpseudoephedrine [L(-)-*threo*-1*R*,2*R*-2-amino-1-phenyl-1-propanol] *[37577-07-4]* **M 151.2, m ~50°, 50-52°, 77°, 77.5-78°, $[\alpha]_D^{20}$ -34° (c 3.5, EtOH), pK^{25} 8.92.** Purify (-)-nor-ψ-ephedrine by recrystallisation from H_2O, MeOH, EtOH, Et_2O/petroleum ether or $*C_6H_6$ (plates). The *mandelate salt* has **m** 163.5° (from EtOH/Et_2O) and $[\alpha]_D^{32}$ -41.3° (c 0.8, H_2O) [Jarowski & Hartung *J Org Chem* **8** 564 566 567 *1943*]. The *hydrochloride* is purified by dissolving 1.44g in 96% EtOH (5ml), adding Et_2O (16ml) and cooling; it has **m** 178-179° (**m**180-181° is also reported) and $[\alpha]_D^{30}$ -42.9° (c 1.8, H_2O) [Fles & Markovac-Prpic *Croat Chem Acta* **29** 186 *1957*]. [*Beilstein* **13** I 252, **13** II 370, **13** III 1716, **13** IV 1874.]

(+)-(1*S*,2*S*)-Norpseudoephedrine [(+)-Cathine, D(+)-*threo*-(1*S*,2*S*)-2-amino-1-phenyl-1-propan-1-ol] ***[****492-39-7]* **M 151.2, m 77.5-78°, $[\alpha]_D^{25}$ +34.0° (c 4, EtOH).** Recrystallise it from $*C_6H_6$ and store away from CO_2 as it is a strong base readily forming a *hydrochloride* [*1S,2S-(+)* 2153-98-2] **M 187.7**, **m 180-181°** (prisms from

EtOH), and is soluble in H_2O with **$[\alpha]_D^{20}$ +42.5°**. It is a stimulant and is an anorexic substance. [Nagaai & Kanao *Justus Liebigs Ann Chem* **470** 157 *1929*, Sicher & Pankova *Col Czech Chem Commun* **20** 1409 *1955*, *Beilstein* **13** I 252, **13** II 370, **13** III 1716, **13** IV 1874.]

Novobiocin (7-[*O*^{3}-carbamoyl-5-*O*^{4}-dimethyl-β-L-*lyso*-6-desoxyhexahydropyranosyloxy]-4-hydroxy-3[4-hydroxy-3-{3-methylbut-2-enyl}-benzylamino]-8-methylcoumarin) *[303-81-1]* **M 612.6, two forms m 152-156° and m 172-174°, 174-178°, λ_{max} at 330nm (acidic EtOH), 305nm (alkaline EtOH), $[\alpha]_D^{25}$ -63° (c 1, EtOH), pK_1 4.03 (4.2), pK_2 9.16.** Crystallise novobiocin from EtOH and store it in the dark. It has also been recrystallised from Me_2CO/H_2O. [Hoeksema et al. *J Am Chem Soc* **77** 6710 *1955*, Kaczka et al. *J Am Chem Soc* **77** 9404 *1955*.]
The **sodium salt** *[1476-53-5]* **M 634.6, m 210-215°, 215-220°(dec), 222-229°, $[\alpha]_D^{25}$ -38° (c 1, H_2O)** has been recrystallised from MeOH, then dried at 60°/0.5mm. [Sensi et al, *Anal Chem* **29** 1611 *1957*, Kaczka et al. *J Am Chem Soc* **78** 4126 *1956*, *Beilstein* **18/8** IV 8125.]

Nucleotide thiophosphate analogues. The preparation and purification of [^{3}H]ATPγS, [^{3}H]GTPγS, S^{6}ITPγS (6-thioinosine), Cl^{6}ITPγS (6-chloroinosine) and [^{3}H]ATPγS were described, and general purification was achieved by chromatography of the nucleotide thiophosphates in the minimum volume of H_2O placed onto a DEAE-Sephadex A25 column and eluted with a linear gradient of triethylammonium bicarbonate (0.1 to 0.6M for G and I nucleotides and 0.2 to 0.5M for A nucleotides). [Googy et al. *Biochim Biophys Acta* **276** 155 *1972*.]

Nystatin dihydrate (Mycostatin, Fungicidin) *[1400-61-9]* **M 962.1, m dec>160° (without melting by 250°), $[\alpha]_D^{25}$ -7° (0.1N HCl in MeOH), -10° (AcOH), +12° (Me_2NCHO), +21° (pyridine).** Nystatin is a light yellow powder with the following solubilities at ~28°: MeOH (1.1%), ethylene glycol (0.9%), H_2O (0.4%), CCl_4 (0.12%), EtOH (0.12%), $CHCl_3$ (0.05%) and *C_6H_6 (0.03%). It has been precipitated from MeOH solution by addition of H_2O. Aqueous suspensions of this macrolide antifungal antibiotic are stable at 100°/10minutes at pH 7.0 but decompose rapidly at pH <2 and >9, and in the presence of light and O_2. [Birch et al. *Tetrahedron Lett* 1491, 1485 *1964*, Weiss et al. *Antibiot Chemother* **7** 374 *1957*.] It may contain a mixture of components A_1, A_2 and A_3. [*Beilstein* **18** III/IV 7480.]

Oxacillin sodium salt (5-methyl-3-phenyl-4-isoxazolylpenicillin sodium salt) *[1173-88-2]* **M 423.4, m 188°(dec), $[\alpha]_D^{20}$ +29° (c 1, H_2O), pK_{Est} ~2.7.** This antibiotic, which is stable to penicillinase, is purified by recrystallisation from isoPrOH and dried *in vacuo*. Its solubility in H_2O at 25° is 5%. [Doyle et al. *Nature* **192** 1183 *1961*, Review: Chain et al. *Antibiotics* (Oxford University Press) **2** *1949*.]

Oxiracetam (4-hydroxy-2-oxo-1-pyrrolidine acetamide) *[62613-82-5 unspecified, 68567-97-5 racemate]* **M 158.2, m 165-168°.** This nootropic (Alzheimer) drug is purified by recrystallisation from MeOH or aqueous Me_2CO and dried *in vacuo*. [NMR, IR: Pifferi & Pinza *Farmaco Ed Sci* **32** 602 *1977*, Banfi et al. *Farmaco Ed Sci* **39** 16 *1984*, Gouilaev & Senning *Brain Research Rev* **19** 180 *1994*.]

***R*-(+)-oxiracetam** *[68252-28-8]* **m 135-136°, $[\alpha]_D^{20}$ +36° (c 1, H_2O),** and ***S*-(-)-oxiracetam** *[88929-35-5]* **m 135-136°, $[\alpha]_D^{20}$ +36.5° (c 1, H_2O),** have been recrystallised from aqueous Me_2CO. [Gouilaev & Senning *Brain Research Rev* **19** 180 *1994*.]

Palmitoyl coenzyme A *[1763-10-6]* **M 1005.9.** Possible impurities are palmitic acid, S-palmitoyl thioglycolic acid and S-palmitoyl glutathione. These are removed by placing *ca* 200mg in a centrifuge tube and extracting with Me_2CO (20ml), followed by two successive extractions with Et_2O (15ml) to remove S-palmitoyl thioglycolic acid and palmitic acid. The residue is dissolved in H_2O (4 x 4 ml), adjusted to pH 5 and centrifuged to remove insoluble S-palmitoyl glutathione and other insoluble impurities. To the clear supernatant is added 5% $HClO_4$ (6ml) whereby S-palmitoyl CoA precipitates. The precipitate is washed with 0.8% $HClO_4$ (10ml) and finally with Me_2CO (3x 5ml) and dried *in vacuo*. It is stable for at least one year in dry form at 0° in a desiccator (dark). Solutions are stable for several months at -15°. Its solubility in H_2O is 4%. The adenine content is used as the basis of purity with λ_{max} at 260 and 232nm (ε 6.4 x 10^6 and 9.4 x 10^6 cm^2/mol, respectively). Higher

absorption at 232nm would indicate other thio ester impurities, e.g. S-palmitoyl glutathione, which absorb highly at this wavelength. Also the phosphate content should be determined, and acid phosphate can be titrated potentiometrically. [Seubert *Biochemical Preparations* **7** 80 *1960*, Srer et al. *Biochim Biophys Acta* **33** 31 *1959*, Kornberg & Pricer *J Biol Chem* **204** 329 , 345 *1953*, *Beilstein* **26** III/IV 3665.]

3-Palmitoyl-*sn*-glycerol (*R*-glycerol-1-palmitate, L-β-palmitin) *[32899-41-5]* **M 330.5, $d^{27.3}$ 0.9014, m 66.5° (α-form), 74° (β'-form) and 77° (β-form).** The stable β-form is obtained by crystallisation from EtOH or Skellysolve B, and recrystallisation from Et_2O provides the β'-form. The α-form is obtained on cooling the melt. [Malkin & el Sharbagy *J Chem Soc* 1631 *1936*, Chapman *J Chem Soc* 58 *1956*, Luton & Jackson *J Am Chem Soc* **70** 2446 *1948*, *Beilstein* **2** III 966.]

D-Panthenol (Provitamin B, *R*-2,4-dihydroxy-3,3-dimethylbutyric acid 3-hydroxy-propylamide) *[81-13-0]* **M 205.3, b 118-120°/0.02mm, d_{20}^{20} 1.2, n_D^{20} 1.4935, $[\alpha]_D^{20}$ +30° (c 5, H_2O).** Purify D-panthenol by distillation *in vacuo*. It is a slightly *hygroscopic* viscous oil and is soluble in H_2O and organic solvents. It is hydrolysed by alkali and strong acid. [Rabin *J Am Pharm Assoc (Sci Ed)* **37** 502 *1948*, Bonati & Pitré *Farmaco Ed Scient* **14** 43 *1959*, *Beilstein* **4** IV 1652.]

***R*-(+)-Pantothenic acid sodium salt (*N*-[2,4-dihydroxy-3,3-dimethylbutyryl] β-alanine Na salt)** *[867-81-2]* **M 241.2, $[\alpha]_D^{25}$ +27.1° (c 2, H_2O), pK^{25} 4.4 (for free acid).** Crystallise the salt from absolute EtOH. It is very *hygroscopic* (keep in sealed ampoules). The *free acid* is a viscous *hygroscopic* oil with $[\alpha]_D^{25}$ +37.5° (c 5, H_2O), easily destroyed by acids and bases. See next entry. [*Beilstein* **4** IV 2569.]

***R*-(+)-Pantothenic acid Ca salt** *[(*D*(+) 137-08-6, 63409-48-3]* **M 476.5, m 195-196°, 200-201°, $[\alpha]_D^{20}$ +28.2° (c 5, H_2O).** The salt crystallises as needles from MeOH, EtOH or isoPrOH (with 0.5mol of isoPrOH). It is moderately *hygroscopic*. The *S-benzylisothiuronium salt* has **m** 151-152° (149° when crystallised from Me_2CO). [Kagan et al. *J Am Chem Soc* **79** 3545 *1957*, Wilson et al. *J Am Chem Soc* **76** 5177 *1954*, Stiller & Wiley *J Am Chem Soc* **63** 1239 *1941*, *Beilstein* **4** IV 2569.]

Paromomycin sulfate {amminosidin, *O*-2,6-diamino-2,6-dideoxy-β-L-idopyranosyl-(1→3)-*O*-β-D-ribo-furanosyl(1→5)-*O*-[2-amino-2-deoxy-α-D-glucopyranosyl-(1→4)]-2-deoxystrepta amine sulfate} *[1263-89-4]* **M 713.7, amorphous, $[\alpha]_D^{25}$ +50° (c 1.5, H_2O pH6), pK_{Est} ~ 9.** Purify it by dissolving it in H_2O (0.5g/10ml) and adding excess EtOH, filter or collect and wash with EtOH, then Et_2O by centrifugation, and dry it *in vacuo*. An aqueous solution is stable at 37° for a week but longer at 0-5°. The *free base* [7542-37-2] is a white amorphous powder which should be stored under N_2 because it is strongly basic and can absorb CO_2 from the atmosphere. It is soluble in MeOH (less soluble in EtOH) and has $[\alpha]_D^{25}$ +65° (c 1.5, MeOH). It is an antimicrobial against Gram +ve and Gram –ve bacteria and is antiamoebic. It inhibits initiation and peptide elongation during protein synthesis. [Haskell et al. *J Am Chem Soc* **81,** 3480, 3482 *1959*, Hichens & Rinehart *J Am Chem Soc* **85** 1547 *1963*, *Beilstein* **18** III/IV 7534.]

D-(-)-Penicillamine (*R*-3-mercapto-D-valine, 3,3-dimethyl-D-cysteine, from natural penicillin) *[52-67-5]* **M 149.2, m 202-206°, 214-217°, $[\alpha]_D^{21}$ -63° (c 1, N NaOH or pyridine).** The melting point of D-(-)-penicillamine depends on the rate of heating (**m** 202-206° is obtained by starting at 195° and heating at 2°/minute). It is soluble in H_2O and alcohols but insoluble in Et_2O, $CHCl_3$, CCl_4 and hydrocarbon solvents. Purify it by dissolving it in MeOH and adding Et_2O slowly. Dry it *in vacuo* and store it under N_2. [Weight et al. *Angew Chem, Int Ed* (English) **14** 330 *1975*, Cornforth in *The Chemistry of Penicillin* (Clarke, Johnson and Robinson eds) Princeton Univ Press, 455 *1949*, Review: Chain et al. *Antibiotics* (Oxford University Press) **2** *1949*, Polymorphism: Vidler *J Pharm Pharmacol* **28** 663 *1976*]. The D-S-*benzyl* derivative has **m** 197-198° (from H_2O), $[\alpha]_D^{17}$ -20° (c 1, N NaOH), -70° (N HCl). [*Beilstein* **4** IV 3228.]

L-(-)-Penicillamine *[1113-41-3]* **M 149.2, m 190-194°, 202-206°, 214-217°, $[\alpha]_D^{21}$ +63° (c 1, N NaOH or pyridine).** Same as the preceding entry for its enantiomer. [*Beilstein* **4** IV 3228.]

D-Penicillamine disulfide hydrate (*S,S'*-di-[D-penicillamine] hydrate) *[20902-45-8]* **M 296.4 + aqueous, m 203-204°(dec), 204-205°(dec), $[\alpha]_D^{23}$ +27° (c 1.5, N HCl), -82° (c 0.8, N NaOH), $pK_{Est(1)}$~ 2.4 (CO_2), $pK_{Est(2)}$**

~ 10.7 (NH_2). Purify it by recrystallisation from EtOH or aqueous EtOH. [Crooks in *The Chemistry of Penicillin* (Clarke, Johnson and Robinson Eds) Princeton University Press, 469 *1949*. Use as a thiol reagent for proteins: Garel *Eur J Biochem* **123** 513 *1982*, Süs *Justus Liebigs Ann Chem* **561** 31 *1948*, *Beilstein* **4** IV 3231.]

Penicillic acid (5-hydroxy-5-isopropenyl-4-methoxy-2(5*H*)furanone) *[90-65-3]* **M 158.2, m 58-64°, 64-65° (monohydrate, acid), 83-84°, 87° (anhydrous, lactone), pK^{25} 5.9.** The lactone (furanone, *anhydrous*) hydrolyses to the acid (3-methoxy-4-oxo-hexa-2,5-dienoic acid, *hydrate*). It crystallises from water as the *monohydrate* (acid), or from petroleum ether as the *anhydrous* (lactone) compound. The free acid is in equilibrium with the lactone. Its UV has λ_{max} at 221nm (ε 12,500) in 0.02M KOH; 228nm (ε 11,500) in 0.02M HCl [Raphael *J Chem Soc* 1508 *1948*]. [*Beilstein* **3** II 519, **3** III 1467.] It is a possible **antineoplastic**.

3-sn-Phosphatidylethanolamine (L-α-cephalin, from Soya bean) *[39382-08-6]* **M_r ~600-800, amorphous, $pK_{Est(1)}$~5.8 (PO_4^-), $pK_{Est(2)}$~10.5 (NH_2).** Purify the cephalin by dissolving it in EtOH, adding $Pb(OAc)_2.3H_3O$ (30g in 100ml H_2O) until excess Pb^{2+} is present. Filter off the solid. Pass CO_2 gas through the solution until precipitation of $PbCO_3$ ceases. Filter the solid off and evaporate (while bubbling CO_2) under vacuum. An equal volume of H_2O is added to the residual oil and extracted with hexane. The hexane extract is washed with H_2O until the aqueous phase is free from Pb [test with dithizone (2 mg in 100 ml CCl_4; Feigel *Spot Tests* Vol I, Elsevier p. 10 *1954*)]. The hexane is dried (Na_2SO_4), filtered and evaporated to give a yellow waxy solid which should be dried to constant weight *in vacuo*. It is practically insoluble in H_2O and Me_2CO, but freely soluble in $CHCl_3$ (5%) and Et_2O, and slightly soluble in EtOH. [Schofield & Dutton *Biochemical Preparations* **5** 5 *1957*.]

***O*-Phosphocolamine (2-aminoethyl dihydrogen phosphate)** *[1071-23-4]* **M 141.1, m 237-240°, 242.3°, 234.5-244.5°, 244-245°(capillary), pK_1^{20} <1.5 (PO_4H_2), pK_2^{20} 5.77 (PO_4H^-), pK_3^{20} 10.26 (NH^+).** Purification by recrystallisation from aqueous EtOH gives a *hydrate* (**m** 140-141°). Its solubility in H_2O is 17% and 0.003% in MeOH or EtOH at 22°. [Fölisch & Österberg *J Biol Chem* **234** 2298 *1959*, Baer & Staucer *Can J Chem* **34** 434 *1956*, Christensen *J Biol Chem* **135** 399 *1940*.] It is a potent inhibitor of ornithine decarboxylase [Gilad & Gilad *Biochem Biophys Res Commun* **122** 277 *1984*]. [*Beilstein* **4** IV 1415.]

Phosphoenolpyruvic acid monopotassium salt (KPEP) *[4265-07-0]* **M 206.1, pK_1^{25} 3.4 (CO_2), pK_2^{25} 6.35 (PO_4H^-) (for free acid).** KPEP is purified *via* the monocyclohexylamine salt (see next entry). The salt (534mg) in H_2O (10ml) is added to Dowex 50Wx4 H^+ form (200-400 mesh, 2ml, H_2O washed) and stirred gently for 30 minutes and filtered. The resin is washed with H_2O (6ml), and the combined solutions are adjusted to pH 7.4 with 3N KOH (~1.4ml) and the volume adjusted to 18.4ml with H_2O to give a solution of 0.1M KPEP which can be lyophilised to a pure powder and is very good for enzyme work. It has been recrystallised from MeOH/Et_2O. [Clark & Kirby *Biochemical Preparations* **11** 103 *1966*, Wold & Ballou *J Biol Chem* **227** 301 *1957*, Cherbuliez & Rabinowitz *Helv Chim Acta* **39** 1461 *1956*, *Beilstein* **3** IV 977.]
The triNa salt *[5541-93-5]* **M 360.0,** is purified as follows: the salt (1g) is dissolved in MeOH (40ml) and dry Et_2O is added in excess. The white crystals are collected and dried over P_2O_5 at 20°. [Cramer & Voges *Chem Ber* **92** 952 *1959*, *Beilstein* **3** IV 977.]

Phosphoenolpyruvic acid tris(cyclohexylamine) salt *[35556-70-8]* **M 465.6, m 155-180°(dec).** Recrystallise it from aqueous Me_2CO and dry it in a vacuum. At 4° it is stable for >2 years and has IR at 1721cm^{-1} (C=O). [Wold & Ballou *J Biol Chem* **227** 301 *1957*, Clark & Kirby *Biochemical Preparations* **11** 103 *1966* for the monocyclohexylamine salt, *Beilstein* **12** IV 8.]

D-3-Phosphoglyceric acid disodium salt (D-glycerate 3-phosphate di-Na salt) *[80731-10-8]* **M 230.0, $[\alpha]_D^{25}$ +7.7° (c 5, H_2O), -735° (in aqueous NH_4^+ molybdate), $pK_{Est(1)}$~1.0 (PO_4H_2), $pK_{Est(2)}$~6.66 (PO_4H^-) (for free acid).** It is best purified by conversion to the **Ba salt** by precipitation with $BaCl_2$, which is recrystallised three times before conversion to the sodium salt. The **Ba salt** (9.5g) is shaken with 200ml of a 1:1 slurry of Dowex 50 (Na^+ form) for 2 hours. The mixture is filtered, and the resin is washed with H_2O (2 x 25ml). The combined filtrates (150ml) are adjusted to pH 7.0 and concentrated *in vacuo* to 30-40ml and filtered if not clear. Absolute EtOH is added to make 100ml, and then *n*-hexane is added whereby a white solid and/or a second phase separates. When set aside at room temperature, complete precipitation of the Na salt as a solid occurs. The salt is

removed by centrifugation, washed with Me_2CO, dried in air then in an oven at 55° to give a stable powder (4.5g). It did not lose weight when dried further over P_2O_5 at 78°/8 hours. The high rotation in the presence of $(NH_4)_6Mo_7O_{24}$ is not very sensitive to the concentration of molybdate or pH as it did not alter appreciably in 1/3 volume between 2.5 to 25% (w/v) of molybdate or at pH values ranging between 4 and 7. [Cowgill *Biochim Biophys Acta* **16** 613 *1955*, Embdan et al. *Hoppe Seyler's Z Physiol Chem* **230** 20 *1934*, *Beilstein* **3** IV 1051.]

Phospholipids. For the removal of ionic contaminants from raw zwitterionic phospholipids, most lipids are purified twice by mixed-bed ionic exchange resins (Amberlite AB-2) of methanolic solutions. (About 1g of lipid in 10ml of MeOH). With both runs the first 1ml of the eluate is discarded. The main fraction of the solution is evaporated at 40°C under dry N_2 and recrystallised three times from *n*-pentane. The resulting white powder is dried for about 4 hours at 50° under reduced pressure and stored at 3°. Some samples are purified by mixed-bed ion exchange of aqueous suspensions of the crystal/liquid crystal phase. [Kaatze et al. *J Phys Chem* **89** 2565 *1985*.]

***O*-Phospho-L-serine** *[407-41-0]* **M 185.1, m 175-176°, $[\alpha]_D^{20}$ +4.3° (c 3.2, H_2O), +16.2° (c 3.2, 2N HCl), pK_1^{25} <1 (PO_4H_2), pK_2^{25} 2.08 (CO_2H), pK_3^{25} 5.65 (PO_4H^-), pK_4^{25} 9.74 (NH_3^+).** Recrystallise the phosphoserine by dissolving 10g in H_2O (150ml) at 25°, stirring for up to 20 minutes. Undissolved material is filtered off (Büchner), and 95% EtOH (85ml) is added dropwise during 4 minutes, and set aside at 25° for 3 hours, then at 3° overnight. The crystals are washed with 95% EtOH (100ml), then dry Et_2O (50ml), and dried in a vacuum (yield 6.5g). A further quantity (1.5g) can be obtained by keeping the mother liquors and washings at -10° for 1 week. The *DL-isomer* has **m** 167-170°(dec) after recrystallisation from H_2O/EtOH or MeOH. [Neuhaus & Korkes *Biochemical Preparations* **6** 75 *1958*, Neuhaus & Byrne *J Biol Chem* **234** 113 *1959*, IR: Fölsch & Mellander *Acta Chem Scand* **11** 1232 *1957*, *Beilstein* **4** IV 3120.]

***O*-Phospho-L-threonine (L-threonine-*O*-phosphate)** *[1114-81-4]* **M 199.1, m 194°(dec), $[\alpha]_D^{24}$ -7.4° (c 2.8, H_2O) (pKa as above).** Dissolve the phosphate in the minimum volume of H_2O, add charcoal, stir for a few minutes, filter and apply onto a column of Dowex 50W (H^+ form), then elute with 2N HCl. Evaporate the eluates under reduced pressure whereby the desired fraction produces crystals of the phosphate which can be recrystallised from H_2O/MeOH mixtures and the crystals are then dried *in vacuo* over P_2O_5 at ~80°. [de Verdier *Acta Chem Scand* **7** 196 *1953*, *Beilstein* **4** IV 3175.]

***O*-Phospho-L-tyrosine (L-tyrosine-*O*-phosphate)** *[21820-51-9]* **M 261.2, m 225°, 227°, 253°, $[\alpha]_D^{20}$ -5.5° (c 1, H_2O), -9.2° (c 1, 2N HCl), $pK_{Est(1)}$~1.6 (PO_4H_2), $pK_{Est(2)}$~2.02 (CO_2H), $pK_{Est(3)}$~5.65 (PO_4H^-), $pK_{Est(4)}$ 9.2 (NH_3^+).** Purify it by recrystallisation from H_2O or H_2O/EtOH. [Levene & Schormüller *J Biol Chem* **100** 583 *1933*, Posternak & Graff *Helv Chim Acta* **28** 1258 *1945*, *Beilstein* **14** III 1510.]

Phytol (*d*-2E-3,7*R*,11*R*,15-tetramethylhexadec-2-en-1-ol) *[150-86-7, 7541-49-93]* **M 296.5, b 145°/0.03mm, 150-151°/0.06mm, 202-204°/10mm, d_4^{25} 0.8497, n_D^{25} 1.437, $[\alpha]_D^{22}$ +0.06° (neat).** It is commercially available as a mixture of isomers. Phytol is purified by distillation under high vacuum. It is almost insoluble in H_2O but soluble in most organic solvents. It has UV with λ_{max} at 212nm (log ε 3.04) in EtOH and IR has ν_{max} at 3300 and 1670cm^{-1}. [Demole & Lederer *Bull Soc Chim Fr* 1128 *1958*, Burrell *J Chem Soc (C)* 2144 *1966*, Bader *Helv Chim Acta* **34** 1632 *1951*, *Beilstein* **1** IV 2208.]

Piracetamide (2-oxo-1-pyrrolidine acetamide) *[7491-74-9]* **M 142.2, m 151.5-152.5°.** This typical nootropic (Alzheimer) drug modulates Na flux in AMPA receptors and is purified by recrystallisation from isoPrOH. [Gouilaev & Senning *Brain Research Rev* **19** 180 *1994*.]

Podophylotoxin *[518-28-5]* **M 414.4, m 181-181°, 183-184°, 188-189°, $[\alpha]_D^{20}$ -132° (c 1, $CHCl_3$).** The toxin recrystallises form $*C_6H_6$ (with $0.5C_6H_6$), EtOH/$*C_6H_6$, aqueous EtOH (with 1-1.5H_2O, **m** 114-115°) and CH_2Cl_2/pentane. When dried at 100°/10mm it has **m** 183-184°. [UV: Stoll et al. *Helv Chim Acta* **37** 1747 *1954*, IR: Schecler et al. *J Org Chem* **21** 288 *1956*.] It is an inhibitor of microtubule assembly [Prasad et al. *Biochemistry* **25** 739 *1986*]. [*Beilstein* **19/10** V 666.]

Polyethylene glycol *[25322-68-3]* **M_r various, from PEG ~200 to ~35,000.** PEG is available commercially as

a powder or as a solution in various degrees of polymerisation depending on the average molecular weight, e.g. PEG 400 and PEG 800 have average molecular weights of 400 and 800, respectively. They may be contaminated with aldehydes and peroxides. Solutions deteriorate in the presence of air due to the formation of these contaminants. Methods available for purification are as follows:
Procedure A: A 40% aqueous solution of PEG 400 (2L, average molecular weight 400) is de-aerated under vacuum and made 10mM in sodium thiosulfate. After standing for 1 hour at 25°, the solution is passed through a column (2.5x20cm) of mixed-bed R-208 resin which has a 5cm layer of Dowex 50-H^+ at the bottom of the column. The column was previously flushed with 30% aqueous MeOH, then thoroughly with H_2O. A flow rate of 1ml/minute is maintained by adjusting the fluid head. The first 200ml are discarded, and the effluent is then collected at an increased flow rate. The concentration of PEG solution is checked by density measurement, and it is stored (preferably anaerobically) at 15°.
Procedure B: A solution of PEG 800 (500g in 805ml H_2O) is made 1mM in H_2SO_4 and stirred overnight at 25° with 10g of treated Dowex 50-H^+ (8% crosslinked, 20-50 mesh). The resin, after settling, is filtered off on a sintered glass funnel. The filtrate is treated at 25° with 1.5g of $NaBH_4$ (added over a period of 1 minute) in a beaker with tight but removable lid through which a propeller-type mechanical stirrer is inserted and continuously flushed with N_2. After 15 minutes, 15g of fresh Dowex 50-H^+ are added, and the rate of stirring is adjusted to maintain the resin suspended. The addition of an equal quantity of Dowex 50-H^+ is repeated and the reaction times are 30 and 40minutes. The pH of a 1 to 10 dilution of the reaction mixture should remain above pH 8 throughout. If it does not, more $NaBH_4$ is added or the addition of Dowex 50-H^+ is curtailed. (Some samples of PEG can be sufficiently acidic, at least after the hydrolysis treatment, to produce a pH that is too low for efficient reduction when the above ratio of $NaBH_4$ to Dowex 50-H^+ is used.) About 30 minutes after the last addition of $NaBH_4$, small amounts of Dowex 50-H^+ (~0.2g) are added at 15 minute intervals until the pH of a 1 to 10 dilution of the solution is less than 8. After stirring for an additional 15 minutes the resin is allowed to settle, and the solution is transferred to a vacuum flask for brief de-gassing under a vacuum. The de-gassed solution is passed through a column of mixed-bed resin as in procedure A. The final PEG concentration would be about 40% w/v.
Assays for aldehydes by the purpural method and of peroxides are given in the reference below.
Treatment of Dowex 50-H^+ (8% crosslinked, 20-50 mesh): The Dowex (500g) is suspended in excess 2N NaOH, and 3ml of liquid Br_2 is stirred into the solution. After the Br_2 has dissolved, the treatment is repeated twice, and then the resin is washed with 1N NaOH on a sintered glass funnel until the filtrate is colourless. The resin is then converted to the acid form (with dilute HCl, H_2SO_4 or AcOH as required) and washed thoroughly with H_2O and sucked dry on the funnel. The treated resin can be converted to the Na salt and stored.
[Ray & Purathingal *Anal Biochem* **146** 307 *1985*.]

Porphobilinogen (5-amino-4-carboxymethyl-1*H*-pyrrole-3-propionic acid) *[487-90-1]* **M 226.2, m 172-175°(dec), 175-180°(dec, darkening at 120-130°), pK_1 3.70 (4-CH_2CO_2H), pK_2 4.95 (3-$CH_2CH_2CO_2H$), pK_3 10.1 (NH^+).** Porphobilinogen recrystallises as the *monohydrate* (pink crystals) from dilute NH_4OAc solutions of pH 4, and is dried *in vacuo*. The *hydrochloride monohydrate* has **m** 165-170°(dec) (from dilute HCl). [Jackson & MacDonald *Can J Chem* **35** 715 *1957*, Westall *Nature* **170** 614 *1952*, Bogarad *J Am Chem Soc* **75** 3610 *1953*, *Beilstein* **22/14** V 210.]

Porphyrin a (from ox heart) *[5162-02-1]* **M 799.0, m dec on heating.** It is purified on a cellulose powder column followed by extraction with 17% HCl and fractionated with HCl. [Morell et al. *Biochem J* **78** 793 *1961*.] It recrystallises from $CHCl_3$/petroleum ether or Et_2O/*C_6H_6 [detailed UV-VIS and NMR data: Caughey et al. *J Biol Chem* **250** 7602 *1975*, Lemberg *Adv Enzymol* **23** 265 *1961*].

Prazosin hydrochloride (2[4-{(2-furoyl)piperazin-1-yl}4-amino-6,7-dimethoxyquinazoline hydrochloride) *[19237-84-4]* **M 419.9, m 278-280°, 280-282°, pK^{25} 6.5.** The salt is recrystallised by dissolving it in hot MeOH, adding a small volume of MeOH/HCl (dry MeOH saturated with dry HCl gas) followed by dry Et_2O until crystallisation is complete. Dry it *in vacuo* over solid KOH till the odour of HCl is absent. It has been recrystallised from hot H_2O, the crystals are washed with H_2O, and the H_2O is removed azeotropically with CH_2Cl_2, and dried in a vacuum. [NMR and IR: Honkanen et al. *J Heterocycl Chem* **17** 797 *1980*, *cf* Armarego & Reece *Aust J Chem* **34** 1561 *1981*.] It is an antihypertensive drug and is an α_1-adrenergic antagonist [Brosman et al. *Proc Natl Acad Sci USA* **82** 5915 *1985*].

Procaine hydrochloride (Novocain, 2-diethylaminoethyl-4-aminobenzoate) *[51-05-8]* **M 272.8, m 153-156°, 154-156°, 156°, $pK_{Est(1)}$~2.52 (NH_2^+) pK_2^{20} 9.0 (Et_2N^+).** Novocain is recrystallised from aqueous EtOH. It is soluble at 25° in H_2O (86.3%), EtOH (2.6%) and Me_2CO (1%), it is slightly soluble in $CHCl_3$, but is almost insoluble in Et_2O. The anhydrous *free base* is recrystallised from ligroin or Et_2O and has **m** 61°. [Einhorn *Justus Liebigs Ann Chem* **371** 125 *1909*, IR: Szymanski & Panzica *J Amer Pharm Assoc* **47** 443 *1958*, *Beilstein* **14** IV 1138.]

***R*-Propranalol hydrochloride (*R*-1-isopropylamino-3-(1-naphthyloxy)-2-propanol HCl)** *[13071-11-9]* **M 295.8, m 192°, 193-195°, $[\alpha]_D^{20}$ -25° (c 1, EtOH), pK^{20} 9.5 (for free base).** The hydrochloride is recrystallised from *n*-PrOH or Me_2CO. It is soluble in H_2O and EtOH but is insoluble in Et_2O, *C_6H_6 or EtOAc. The *racemate* has **m** 163-164°, and the *free base* recrystallises from cyclohexane with **m** 96°. [Howe & Shanks *Nature* **210** 1336 *1966*.] The *S*-isomer (below) is the physiologically active isomer.

***S*-Propranalol hydrochloride (*S*-1-isopropylamino-3-(1-naphthyloxy)-2-propanol HCl)** *[4199-10-4]* **M 295.8, m 192°, 193-195°, $[\alpha]_D^{20}$ +25° (c 1, EtOH) pK^{20} 9.5.** See preceding entry for physical properties and purification. The (+)-salt is the active isomer which blocks isoprenaline tachycardia and is a β-adrenergic blocker. [Leclerc et al. *Trends Pharmacol Sci* **2** 18 *1981*, Howe & Shanks *Nature* **210** 1336 *1966*.]

Protoporphyrin IX (3,18-divinyl-2,7,13,17-tetramethylporphin-8,12-dipropionic acid, ooporphyrin) *[553-12-8]* **M 562.7, pK_{Est} ~4.8.** Protoporphyrin IX is purified by dissolving (4g) in 98-100% HCOOH (85ml), diluting with dry Et_2O (700ml) and keeping at 0° overnight. The precipitate is collected and washed with Et_2O, then H_2O, and dried in a vacuum at 50° over P_2O_5. It crystallises from aqueous pyridine and from Et_2O in monoclinic, brownish-yellow prisms. The UV has λ_{max} at values in 25% HCl are 557.2, 582.2 and 602.4nm. It is freely soluble in ethanolic HCl, AcOH, $CHCl_3$, and Et_2O containing AcOH. It forms sparingly soluble diNa and diK salts. [Ramsey *Biochemical Preparations* **3** 39 *1953*, UV: Holden *Aust J. Exptl Biol and Med Sci* **15** 412 *1937*, Garnick *J Biol Chem* **175** 333 *1948*, IR: Falk & Willis *Aust J Sci Res* [A] **4** 579 *1951*, *Beilstein* **26** IV 3042.]

Protoporphyrin IX dimethylester *[5522-66-7]* **M 590.7, m 228-230°.** The crude dimethyl ester (1g) in $CHCl_3$ (200 ml) is mixed with petroleum ether (b 70-90°, 600ml), and any porphyrin (m > 260°) which is insoluble in this mixture is filtered off. The filtrate is passed through a column of $CaCO_3$ [from $CaCO_3$ (130g) which is kept overnight in a mixture of $CHCl_3$/petroleum ether (b 70-90°, 1:3), and the slurry is poured into a glass tube (2.5 x 26cm) to form the column]. After all the filtrate is applied, the column is eluted with a solution of $CHCl_3$/petroleum ether (b 70-90°, 1:3). All the coloured eluates are collected, evaporated at room temperature in a vacuum to give a residue (0.8g), **m** 208-211°. The residue (0.8g) in $CHCl_3$ (66ml) is heated briefly to its boiling point, then boiling MeOH (198ml) is added immediately to it. The mixture is allowed to cool to room temperature, refrigerated for 2 days and the solid is filtered off. The solid is washed on the filter funnel with $CHCl_3$/MeOH (1:9, 50ml) and dried at 50°/vacuum (yield 0.62-0.66g). It can also be recrystallised by dissolving in as little hot dry *C_6H_6 as possible and left overnight at 20°, and has **m** 228-230°.
It has also been purified by dissolving (0.4g) in $CHCl_3$ (33ml) by boiling for a few minutes, then diluting with boiling MeOH (100ml) and refrigerating for 2 days. The crystals are collected, washed with $CHCl_3$/MeOH (1:9) and dried at 50° in a vacuum (yield 0.3g). Its UV has λ_{max} at 631, 576, 541, 506 and 407nm in $CHCl_3$ and 601, 556 and 406nm in 25% HCl. [Ramsey *Biochemical Preparations* **3** 39 *1953*, *Beilstein* **26** III/IV 3052.]

Pterin-6-carboxylic acid (2-amino-4-oxo-3,4-dihydropteridine-6-carboxylic acid) *[948-60-7]* **M 207.2, m >360°, pK_1^{20} 1.43, pK_2^{20} 2.88, pK_3^{20} 7.72.** The acid gives yellow crystals by repeated dissolution in aqueous NaOH and adding aqueous HCl. It has UV with λ_{max} at 235, 260 and 265nm (ε 11,000, 10,500 and 9,000) in 0.1N HCl and 263 and 365nm (ε 20,500 and 9000) in 0.1N NaOH. [UV: Pfleiderer et al. *Justus Liebigs Ann Chem* **741** 64 *1970*, Stockstad et al. *J Am Chem Soc* **70** 5 *1948*, Fluorescence: Kavanagh & Goodwin *Arch Biochem* **20** 315 *1949*, *Beilstein* **26** III/IV 4053.]

Purine-9-β-ribofuranoside (Nebularin) *[550-33-4]* **M 252.2, m 178-180°, 181-182°, $[\alpha]_D^{25}$ -48.6° (c 1, H_2O), -22° (c 0.8, 0.1N HCl) and -61° (c 0.8, 0.1N NaOH), pK^{25} 2.05.** Nebularin is recrystallised from butanone/Mebutanone/MeOH or EtOH and forms a MeOH photo-adduct. It is a strong inhibitor of adenosine

deaminase [EC 3.5.4.4]. [Nair & Weichert *Bioorg Chem* **9** 423 *1980*, Löfgren et al. *Acta Chem Scand* **7** 225 *1953*, UV: Brown & Weliky *J Biol Chem* **204** 1019 *1953*, *Beilstein* **26** III/IV 1740.]

Puromycin dihydrochloride (*O*-methyl-l-tyrosine[N^6,N^6-dimethylaminoadenosin-3'-yl-amide]) *[58-58-2]* **M 616.5, m 174°, $[\alpha]_D^{25}$ -11° (free base in EtOH), pK_1 6.8, pK_2 7.2.** Puromycin dihydrochloride is purified by recrystallisation from H_2O. The *free base*, [58-60-6] M 294.3, has **m** 175.5-177° (172-173°) (from H_2O). The *sulfate* has **m** 180-187° dec (from H_2O), and the *picrate monohydrate* has **m** 146-149° (from H_2O). [Baker et al. *J Am Chem Soc* **77** 1 *1955*, Fryth et al. *J Am Chem Soc* **80** 3736 *1958*.] It is an inhibitor of aminopeptidase and terminates protein synthesis [Reboud et al. *Biochemistry* **20** 5281 *1981*]. [*Beilstein* **26** III/IV 3704.]

Pyridoxal hydrochloride *[65-22-5]* **M 203.6, m 176-180°(dec), pK_1^{20} 4.23 (3-OH), pK_2^{20} 8.7 (Pyridinium$^+$), pK_3^{20} 13.04 (CH_2OH?).** Dissolve it in water and adjust the pH to 6 with NaOH. Set aside overnight to crystallise. The crystals are washed with cold water, dried in a vacuum desiccator over P_2O_5, and stored in a brown bottle at room temperature. The *free base* is then converted to the hydrochloride with one equivalent of HCl. [Fleck & Alberty *J Phys Chem* **66** 1678 *1962*, *Beilstein* **21/13** V 44.]

Pyridoxal-5'-phosphate monohydrate (PLP, codecarboxylase) *[54-47-7]* **M 265.2, pK_1^{25} <2.5 (PO_4), pK_2^{25} 4.14 (3-OH), pK_3^{25} 6.20 (PO_4), pK_4^{25} 8.69 (pyridinium$^+$).** PLP has been purified by dissolving 2g in H_2O (10-15ml, in a dialysis bag a third full) and dialysing with gentle stirring against 1L of H_2O (+ two drops of toluene) for 15 hours in a cold room. The dialysate is evaporated to 80-100ml, then lyophilised. Lemon yellow microscopic needles of the monohydrate remain when all the ice crystals have been removed. The purity is checked by paper chromatography (in EtOH or *n*-PrOH/NH_3) and the spot(s) visualised under UV light after reaction with a spray of *p*-phenylene diamine, NH_3 and molybdate. Solutions stored in a freezer are 2-3% hydrolysed in 3 weeks. At 25°, only 4-6% hydrolysis occurs even in N NaOH or HCl, and 2% is hydrolysed at 37° in 1 day—but is complete at 100° in 4 hours. It is best stored as a dry solid at -20°. In aqueous acid the solution is colourless but is yellow in alkaline solutions. It has UV with λ_{max} at 305nm (ε 1100) and 380nm (ε 6550) in 0.1 N NaOH; 330nm (ε 2450) and 388nm (ε 4,900) in 0.05M phosphate buffer pH 7.0 and 295nm (ε 6700) in 0.1N HCl. [Peterson et al. *Biochemical Preparations* **3** 34, 119 *1953*.] The *oxime* decomposes at 229-230° and is practically insoluble in H_2O, EtOH and Et_2O. The *O-methyloxime* decomposes at 212-213°. [Heyl et al. *J Am Chem Soc* **73** 3430 *1951*.] It has also been purified by column chromatography through Amberlite IRC-50 (H^+) [Peterson & Sober *J Am Chem Soc* **76** 169 *1954*]. [*Beilstein* **21/13** V 46.]

Pyridoxamine hydrochloride *[5103-96-8, 524-36-7 (free base)]* **M 241.2, m 226-227°(dec), pK_1^{25} 3.54 (3-OH), pK_2^{25} 8.21 (ring N$^+$), pK_3^{25} 10.63 (NH_2).** The amine salt is recrystallised from hot MeOH. The *free base* crystallises from EtOH with **m** 193-193.5° [Harris et al. *J Biol Chem* **154** 315 *1944*, *J Am Chem Soc* **66** 2088 *1944*]. [*Beilstein* **22** IV 6064, **22/12** V 324.]

Quizalofop ethyl {[ethyl 2-[4-(6-chloro-2-quinoxalinyloxy)phenoxy]propionate} *[(±) 76578-14-8*; *R- 100646-51-3*, *100646-52-4*, *100760-08-5*, *100760-10-9]* **M 372.8, m 92-93°, m 220°/0.2mm.** This (±)-herbicide forms white crystals from Me_2CO/EtOH and sublimes *in vacuo*. Large quantities can be distilled at high vacuum. Its solubilities at 20° in g/10ml are 0.09 (EtOH), 1.1 (Me_2CO), 1.2 (xylene), 2.9 (*C_6H_6), and is nearly insoluble in H_2O (0.3mg/l). The (±)-acid has [95977-28-9]. The *R-ester enantiomer* has **m** 76-77° (pale brown crystals from EtOH), **$[\alpha]_D^{20}$ +35.9° (EtOH)**. It is the more active fatty acid synthase inhibitor (designated DPX-Y6202) used to control grassy weeds in broadleaf crops. The *R-acid* has [94051-08-8].

Resorufin (7-hydroxy-3*H*-phenoxazin-3-one Na salt) *[34994-50-8]* **M 252.2, decomposes on heating, pK^{25} 5.8 (H_2O), 6.10 (50% aqueous MeOH).** The free acid is purified by dissolving it in conc H_2SO_4 which on dilution precipitates resorufin and is filtered off, washed well with hot H_2O and dried. [Eichler *J Prakt Chem* **139** 113 *1934*.] Detailed UV and IR studies were reported by Musso & Mattheis *Chem Ber* **90** 1814 *1957*]. [pKa: Musso & Rathjen *Chem Ber* **92** 751 *1959*, *Beilstein* **27** 1V 2263.]
The **monoacetate** *[1152-14-3]* **M 252.2, m 223°** is a fluorogenic substrate used for hydrolytic enzymes, and its fluorescence has E_{em} 593nm (E_{ex} 500nm, in 0.1M phosphate pH 8.0 with lipase) [Kitson & Kitson *Biochem J*

322 701 *1997*]. [*Beilstein* **27** IV 2263.]
The **O7-methylresorufin (7-methoxy-3*H*-phenoxazin-3-one)** *[5735-89-3]* **M 227.2, m >220°** has fluorescence at Eem 585nm (Eext 571 nm in deacylase solution) and is used to differentiate isoenzymes of cytochrome P-450. It is insoluble in H_2O and dilute alkali but is soluble in EtOH and $CHCl_3$ to give an orange yellow colour. [Kehrmann *Justus Liebigs Ann Chem* **372** 352 *1910*, *Beilstein* **27** II 108.]

Riboflavin. See vitamin B_2 or lactoflavin below.

Riboflavin-5'-phosphate (Na salt, $2H_2O$). See flavin mononucleotide (FMN) above.

Rifampicin (Rifampin) *[13292-46-1]* **M 823.0, m 183-185°, pK_1 1.7, pK_2 7.9.** This macrolide antibiotic crystallises form Me_2CO in red-orange plates. It has UV with λ_{max} at 237, 255, 334, and 475nm (ε 33,200, 32,100, 27,000 and 15,400) at pH 7.38. It is stable in Me_2SO and H_2O and is freely soluble in most organic solvents, but slightly soluble in H_2O at pH <6. [Binda et al. *Arzneim.-Forsch* **21** 1907 *1971*.] It inhibits cellular RNA synthesis without affecting DNA [Calvori et al. *Nature* **207** 417 *1965*].

Rifamycin B *[13929-35-6]* **M 755.8, m 300° (darkening at 160-164°), $[\alpha]_D^{20}$ -11° (MeOH), pK_1 2.60, pK_2 7.76.** Rifamycin B forms yellow needles from $*C_6H_6$. Its solubilities are: H_2O (0.027%), MeOH (2.62%) and EtOH (0.44%). It has UV with λ_{max} at 223, 304 and 245nm ($A^{1\%}_{1cm}$ 555, 275 and 220). [Oppolzer & Prelog *Helv Chim Acta* **56** 2287 *1973*, Oppolzer et al. *Experientia* **20** 336 *1964*, X-ray: Brufani et al. *Experientia* **20** 339 *1964*.]

Rifamycin SV *[6998-60-3]* **M 697.8, m 300°(darkening >140°), $[\alpha]_D^{20}$ -4° (MeOH), pK_{Est} ~7.8.** Rifamycin SV gives yellow-orange crystals from Et_2O/petroleum ether or aqueous EtOH, is very soluble in MeOH, EtOH, Me_2CO and EtOAc, and is less soluble in Et_2O and HCO_3^-, but slightly soluble in H_2O and petroleum ether. Its UV has λ_{max} at 223, 314 and 445nm ($A^{1\%}_{1cm}$ 586, 322 and 204) in phosphate buffer pH 7. [NMR: Bergamini & Fowst *Arzneim.-Forsch* **15** 951 *1965*.]

(-)-Scopolamine hydrobromide $3H_2O$ (6β,7β-epoxy-3α-tropanyl *S*(-)-tropate HBr, hyoscine HBr) *[114-49-8]* **M 438.3, m 193-194°, 195°, 195-199°, $[\alpha]_D^{25}$ -25°(c 5, H_2O), pK^{20} 8.15.** The hydrobromide is recrystallised from Me_2CO, H_2O or EtOH/Et_2O and dried. It is soluble in H_2O (60%) and EtOH (5%) but insoluble in Et_2O and slightly in $CHCl_3$. The *hydrochloride* has **m** 300° (from Me_2CO). The *free base* is a viscous liquid which forms a crystalline *hydrate* with **m** 59° and $[\alpha]_D^{20}$ -28° (c 2.7, H_2O). It hydrolyses in dilute acid or base. [Meinwald *J Chem Soc* 712 *1953*, Fodor *Tetrahedron* **1** 86 *1957*, *Beilstein* **6** III 4185.]

Serotonin hydrochloride (5-HT, 3-[2-aminoethyl]-5-hydroxyindole HCl) *[153-98-0]* **M 212.7, m 167-168°, 178-180°, pK_1^{25} 4.9, pK_2^{25} 9.8 (10.0, NH_2), pK_3^{25} 11.1 (5-OH), pK_4^{25} 18.25 (acidic indole NH).** 5-HT is purified by recrystallisation from EtOH/Et_2O or Et_2O to give the *hygroscopic* salt. Store it in the dark as it is light sensitive. The *free base* has **m** 84-86° (from Et_2O). The *5-benzyloxy* derivative has **m** 84-86° (from Et_2O). [Ek & Witkop *J Am Chem Soc* **76** 5579 *1954*, Hamlin & Fischer *J Am Chem Soc* **73** 5007 *1951*.] The *picrate 1H_2O* has **m** 196-197.5° (dec with sintering at 160-165°) after crystallisation from Et_2O. Serotonin is a natural neurotransmitter [Chuang *Life Sci* **41** 1051 *1987*]. [*Beilstein* **22/12** V 16.]

Spectinomycin dihydrochloride pentahydrate (Actinospectacin) *[21736-83-4]* **M 495.3, m 205-207°(dec), $[\alpha]_D^{20}$ +14.8° (c 0.4, H_2O), pK_1 6.95, pK_2 8.70.** The salt is purified by recrystallisation from aqueous Me_2CO and is soluble in H_2O, MeOH and dilute acid and base, but only slightly soluble in Me_2CO, EtOH, $CHCl_3$ and $*C_6H_6$. The *free base* is an amorphous solid, **m** 184-194° with $[\alpha]_D^{20}$ -20° (H_2O). [Wiley et al. *J Am Chem Soc* **93** 2652 *1963*, X-ray: Cochran et al. *J Chem Soc Chem Commun* 494 *1972*.] It is an aminoglycoside antibiotic which interacts with 16S ribosomal RNA [Moazet & Noller *Nature* **327** 389 *1987*] and is used for the treatment of gonorrhea [Rinehart *J Infect Dis* **119** 345 *1969*].

D-Sphingosine (2*S*,3*S*-D-*erythro*-2-aminooctadec-4*t*-ene-1,3-diol from bovine brain) *[123-78-4]* **M 299.5, m 79-82°, 82° 82.5° (softens at ~70°), $[\alpha]_D^{22}$ -3.4° (c 2, $CHCl_3$), pK_{Est} ~ 8.8.** D-Sphingosine is purified by re-

crystallisation from EtOAc, Et_2O or petroleum ether (60-80°). It is insoluble in H_2O but is soluble in Me_2CO, EtOH and MeOH. It has IR bands at 1590 and 875 cm^{-1}, and is characterised as the *tribenzoate* **m** 122-123° (from 95% EtOH). [Tipton *Biochemical Preparations* **9** 127 *1962*.]

Squalene precursor of cholesterol. See "Carotenoids" in this chapter.

Sterigmatocystin (3a,12c-dihydro-8-hydroxy-6-methoxy-3*H*-furo[3',2':4,5]furo[2,3-c]xanthen-7-one) *[10048-13-2]* **M 324.3, m 246°, 247-248°, $[\alpha]_D^{20}$ -398° (c 0.1, $CHCl_3$), pK_{Est} ~ 8.0.** It crystallises from amyl acetate, Me_2CO or EtOH and sublimes *in vacuo*. It has UV with λ_{max} at 208, 235, 249 and 329nm (log ε 4.28, 4.39, 4.44 and 4.12). [UV: Bullock et al. *J Chem Soc* 4179, *1962*, UV, IR: Holker & Mulheirn *J Chem Soc, Chem Commun* 1576, 1576 *1968*, Birkinshaw & Hammady *Biochem J* **65** 162 *1957*.] This mycotoxin induces bone marrow changes in mice [Curry et al. *Mutation Res* **137** 111 *1984*]. [*Beilstein* **19/10** V 575.]

Stigmatellin A (2-[4,6-dimethoxy-3,5,11-trimethyltridecatri-7*t*,9*t*,11*t*-enyl]-8-hydroxy-5,7-dimethoxy-3-methyl-4*H*-1-benzopyran-4-one) *[91682-96-1]* **M 514.6, m 128-130°, $[\alpha]_D^{20}$ +38.5° (c 2.3, MeOH), pK_{Est} ~7 (phenolic OH).** Stigmatellin A is stable in aqueous solution at neutral pH but decomposes at pH <5. It is purified by recrystallisation from toluene/hexane. It has UV with λ_{max} nm (ε) at 248sh (4,100), 258 (59,500), 267 (65,500), 279 (1400) and 335 (5200) in MeOH; 249sh (45,600), 258 (60,000), 268 (72,700), 277 (54,100), 320 (2,500) and 370 (3000) in MeOH + 1 drop of N KOH; 243sh (29,300), 264 (63,200), 274 (64,100), 283sh (45,800), 329 (4800) and 420 (21,000) in MeOH + 6N HCl; and IR ($CHCl_3$) with ν_{max} at 3550m, 1645chs, 1635ss, 1620ss, 1590s, 1510m and 905m cm^{-1}. It gives colour reactions at 110° with vanillin/H_2SO_4 (grey), Ce(IV)/$(NH_4)_2SO_4$ (yellow) and phosphomolybdate (blue-grey). [Höfle et al. *Justus Liebigs Ann Chem* 1882 *1984*.] It inhibits electron transport [Jagow & Link *Methods Enzymol* **126** 253 *1986*, Robertson et al. *Biochemistry* **32** 1310 *1933*], and has antibiotic properties [Kunze et al. *J Antibiot* **37** 454 *1984*]. The **7*t*,9*t*,11*c*-isomer** is ***Stigmatellin B*.**

Streptomycin sulfate *[3810-74-0]* **M 1457.4, $[\alpha]_D^{20}$ -84.3° (c 3, H_2O), $pK_{Est(1)}$~ 9.5 (MeNH), $pK_{Est(2,3)}$~ 13.4 (guanidino).** The sulfate is recrystallised from H_2O/EtOH, washed with a little EtOH, Et_2O and dried in a vacuum. [UV and IR: Grove & Randall *Antibiotics Monographs* **2** 163 *1855*, Heuser et al. *J Am Chem Soc* **75** 4013 *1953*, Kuehl et al. *J Am Chem Soc* **68** 1460 *1946*, Regna et al. *J Biol Chem* **165** 631 *1946*.] During protein synthesis it inhibits initiation and causes misreading of mRNA [Zierhut et al. *Eur J Biochem* **98** 577 *1979*, Chandra & Gray *Methods Enzymol* **184** 70 *1990*]. [*Beilstein* **18/11** V 82.]

Streptonigrin (nigrin, 5-amino-6-[7-amino-5,8-dihydro-6-methoxy-5,8-dioxo-2-quinolinyl]-4-[2-hydroxy-3,4-dimethoxyphenyl]-3-methyl-2-pyridinecarboxylic acid) *[3930-19-6]* **M 506.5, m 262-263°, 275°(dec), pK^{25} 6.3 (1:1 aqueous dioxane).** Streptonigrin is purified by TLC on pH 7-buffered silica gel plates (made from a slurry of Silica Gel 60 and 400ml of 0.05M phosphate buffer pH 7.0) and eluted with 5% MeOH/$CHCl_3$. Material from the extracted band recrystallises from Me_2CO or dioxane as almost black plates or needles. It is soluble in pyridine, Me_2NCHO, aqueous $NaHCO_3$ (some dec), and slightly soluble in MeOH, EtOH, EtOAc and H_2O. It has UV with λ_{max} at 248, 375-380nm (ε 38,400 and 17,400). [Weinreb et al. *J Am Chem Soc* **104** 536 *1982*, Rao et al. *J Am Chem Soc* **85** 2532 *1963*.] It is antineoplastic and causes severe bone marrow depression [Wilson et al. *Antibiot Chemother* **11** 147 *1961*].

Succinyl coenzyme A trisodium salt *[108347-97-3]* **M 933.5.** If it should be purified further, then it should be dissolved in H_2O (0.05g/ml) adjusted to pH 1 with 2M H_2SO_4 and extracted several times with Et_2O. Excess Et_2O is removed from the aqueous layer by bubbling N_2 through it and is stored frozen at pH 1. When required, the pH should be adjusted to 7 with dilute NaOH and used within 2 weeks (samples should be frozen). Succinyl coenzyme A is estimated by the hydroxamic acid method [Hersch & Jencks *J Biol Chem* **242** 3468 *1967*]. It is more stable in acidic than in neutral aqueous solutions, but neutral solutions can be stored at –15° with negligible decomposition. [Jordan & Laghai-Newton *Methods Enzymol* **123** 435 *1986*, *Beilstein* **26** III/IV 3666.]

Terramycin (oxytetracycline) *[79-57-2; 6153-64-6 ($2H_2O$)]* **M 460.4 (anhydrous), 496.5 ($2H_2O$), sinters at 182°, melts at 184-185°(dec), $[\alpha]_D^{20}$ -196.6° (equilibrium in 0.1M HCl), -2.1°(equilibrium in 0.1M NaOH).**

Terramycin crystallises (as dihydrate) from water or aqueous EtOH and is soluble in MeOH, EtOH, Me_2CO and H_2O (0.25mg/ml at 25º) but insoluble in Et_2O and petroleum ether. It is amphoteric, and an aqueous solution has pH 2.0-5.0. It has UV with λ_{max} at 247, 275 and 353nm in 0.1 M phosphate (pH 4.5). [Finlay et al. *Science* **111** 85 *1951*.] The *hydrochloride*, [2058-46-0] M 496.9 [*Beilstein* **14** IV 2630], crystallises from MeOH in needles and from H_2O at 50º it forms plates. Terramycin has also been purified *via* the *hydrochloride* by dissolving it in H_2O, adjusting to pH 6, and the solid is filtered off after 1 hour. The crystals of the *dihydrate* are dried to constant weight in vacuum/$CaCl_2$/25º. Drying at 60º *in vacuo* gives the *anhydrous base* **m** 184.5-185.5º (sintering at 180º). The *dihydrate* has **m** 181-182º. Its optical rotation in MeOH decreases from $[\alpha]_D^{25}$ +26º (c 0.5%) to $[\alpha]_D^{25}$ +11.3º after standing for 16 hours. It forms a *sodium salt* and a *$CaCl_2$ complex*. [Regna et al. *J Am Chem Soc* **73** 4211 *1951*, *Beilstein* **14** IV 2633.]

Tetracycline *[60-54-8]* **M 444.4, m 172-174º(dec), $[\alpha]_{546}^{20}$ -291º (c 1, MeOH), pK_1^{25} 3.30, pK_2^{25} 7.68, pK_3^{25} 9.69.** Tetracycline crystallises from toluene or aqueous MeOH as the *trihydrate*. [Stephen et al. *J Am Chem Soc* **76** 3568 *1954*, *Beilstein* **14** IV 2625.]

Tetracycline hydrochloride *[64-75-5]* **M 480.9, m 214º(dec), 215-220º, $[\alpha]_D^{25}$ -258º (c 0.5, 0.1N HCl), $[\alpha]_D^{20}$ -245º (c 1, MeOH), $[\alpha]_D^{25}$ -257.9º (c 0.5, aqueous HCl), pK_1 1.4 (enolic OH), pK_2 3.30, pK_3 7.68 (phenolic OH), pK_4 9.27 (Me_2N).** The hydrochloride is recrystallised from MeOH/*n*-BuOH or *n*-BuOH/HCl. It is insoluble in Et_2O and petroleum ether. It has UV with λ_{max} at 270 and 366nm in MeOH. [Gottstein et al. *J Am Chem Soc* **81** 1198 *1959*, Conover et al. *J Am Chem Soc* **84** 3222 *1962*, Stephen et al. *J Am Chem Soc* **78** 4155 *1956*, *Beilstein* **14** IV 2627.]

6*R*-Tetrahydro-*erythro*-biopterin dihydrochloride (BH_4.2HCl, 6*R*-2-amino-4-hydroxy-6-[{1*R*,2*S*}-1,2-dihydroxypropyl]-5,6,7,8-tetrahydropteridine 2HCl) *[69056-38-8]* **M 316.2, m 245-246º(dec), $[\alpha]_D^{25}$ -6.8º (c 0.67, 0.1N HCl), pK_1 1.37 (pyrimidine$^+$), pK_2 5.6 (5-NH^+), pK_3 10.6 (acidic, 3NH).** Recrystallisation of BH_4.2HCl from HCl enriches BH_4 in the natural 6*R* isomer. Dissolve the salt (~6g) in conc HCl (15ml) under gentle warming, then add EtOH (30ml) dropwise, chill and collect the colourless needles (67%, up to 99% if the mother liquors are concentrated), and dry it *in vacuo* immediately over P_2O_5 and KOH. It is stable indefinitely at -20º in a dry atmosphere. Better store it in sealed ampoules under dry N_2. It can be recrystallised from 6N aqueous HCl. It has UV with λ_{max} (in 2N HCl) at 264nm (ε 16,770; pH 3.5 phosphate buffer) 265nm (ε 13,900); (in pH 7.6) at 297nm (ε 9500) and 260nm sh (ε 4690). It has been separated from the 6*S*-isomer by HPLC on a Partisil-10SCX column using 30mM ammonium phosphate buffer (pH 3.0) containing 3mM $NaHSO_3$ (2ml/minute flow rate; 275nm detector) with retention times of 5.87 minutes (6*R*) and 8.45 minutes (6*S*). It is stable in acidic solutions and can be stored for extended periods at -20º in 0.04M HCl. Above pH 7 the neutral species are obtained, and these are readily oxidised by the oxygen in the solvent to the *quinonoid species*, and then further oxidation and degradation occurs at room temperature. These changes are slower at 0º. The *sulfate salt* can be obtained by recrystallisation from 2M H_2SO_4 and is less soluble in water than the hydrochloride salt. The *6R-2,5,1',2'-tetraacetylbiopterin* derivative has **m** 292º(dec) after recrystallisation from MeOH (100 parts) and $[\alpha]_{589}^{20}$ -144º (c 0.5, $CHCl_3$), $[\alpha]_{589}^{20}$ +12.8º (c 0.39, Me_2SO). [NMR, UV: Matsuura et al. *Heterocycles* **23** 3115 *1985*, Viscontini et al. *Helv Chim Acta* **62** 2577 *1979*, Armarego et al. *Aust J Chem* **37** 355 *1984*, *Beilstein* **26** III/IV 4032.]

Tetrahydrofolic acid dihydrochloride $2H_2O$ (THFA, 6*S*- or 6*RS*- 5,6,7,8-tetrahydrofolic acid 2HCl $2H_2O$, 5,6,7,8-tetrahydropteroyl-L-glutamic acid 2HCl $2H_2O$) *[135-16-0]* **M 544.4, m >200º(dec), $[\alpha]_D^{27}$ +16.9º (H_2O pH 7.0 + 2-mercaptoethanol), pK_1 1.7 (pyrimidine N$^+$), pK_2 2.4 (10N$^+$), pK_3 3.5 (α-CO_2H), pK_4 4.9 (γ-CO_2H), pK_5 5.6 (5-NH^+), pK_6 10.4 (acidic, 3NH).** Very high quality material is now available commercially, and it should be a white powder. It can be dried over P_2O_5 in a vacuum desiccator and stored in weighed aliquots in sealed ampoules. It is stable at room temperature in sealed ampoules for many months and for much more extended periods at -10º. When moist, it is extremely sensitive to air whereby it oxidises to the yellow *7,8-dihydro* derivative. In solution it turns yellow in colour as it oxidises, and then particularly in the presence of acids it turns dark reddish brown in colour. Hence aqueous solutions should be frozen immediately when not in use. It is always advisable to add 2-mercaptoethanol (if it does not interfere with the procedure for which it is used) which stabilises it by depleting the solution of O_2. The *sulfate salt* is more stable but is much less soluble. The best way to prepare standard solutions of this acid is to dissolve it in the desired buffer and

estimate the concentration by UV absorption in pH 7 buffer at 297nm (ε 22,000 $M^{-1}cm^{-1}$). If a sample is suspect, it is not advisable to purify it because it is likely to deteriorate further as "dry box" conditions are necessary. Either a new sample is purchased or one is freshly prepared from folic acid. It has the above pKa values. [Hafeti et al. *Biochemical Preparations* **7** 89 *1960*, UV: Mathews & Huennekens *J Biol Chem* **235** 3304 *1960*, Osborn & Huennekens *J Biol Chem* **233** 969 *1958*, O'Dell et al. *J Am Chem Soc* **69** 250 *1947*, Blakley *Biochem J* **65** 331 *1957*, Asahi *Yakugaku Zasshi (J Pharm Soc Jpn)* **79** 1548 *1959*, *Beilstein* **26** III/IV 3879.]

5,6,7,8-Tetrahydropterin sulfate (2-amino-5,6,7,8-tetrahydropteridin-4-one H_2SO_4) *[20350-44-1]* **M 265, m >200°(dec), pK_1^{25} 1.3 (pyrimidine$^+$), pK_2^{25} 5.6 (5-NH$^+$), pK_3^{25} 10.6 (acidic, 3NH).** If its colour has become strongly violet, then it will need to be reduced again. It is best to check the UV absorption in N HCl where it has a peak at ~265nm which drops sharply to zero having no absorption at ~340nm. The presence of absorption at 340nm indicates oxidation to quinonoid or 7,8-dihydropterin. If the absorption is weak, then dissolve it in the minimum volume of anhydrous trifluoroacetic acid (fume hood), add charcoal, filter, then add two drops of N H_2SO_4 followed by dry Et_2O at 0°, allow the white tetrahydro salt to settle, collect, and wash it with dry Et_2O, by centrifugation. Dry the residue *in vacuo* over P_2O_5 and KOH. Store it in aliquots in the dark at <0°. It has UV λ_{max} at 265nm (ε 16,980) at pH -1.0 (dication); 219nm (ε 23,440) and 266nm (ε 12,880) at pH 3.5 (monocation); 220nm (ε 18,620), [260nm (ε 4270)sh] and 299nm (ε 9330) at pH 8.0 (neutral species); and 218nm (ε 10,000), [240nm (ε 5500)sh] and 287nm (ε 5500) at pH 13 (anion). [Blakley *Biochem J* **72** 707 *1959*, Asahi *Yakugaku Zasshi (J Pharm Soc Jpn)* **79** 1557 *1959*, Pfleiderer in *Pterins and Folate* (Benkovic and Blakley Eds) J Wiley **Vol 2** p 97 *1985*.]

Thiamine monophosphate chloride $2H_2O$ (Aneurine monophosphate chloride) *[532-40-1]* **M 416.8, m 193°(dec), 200°(dec), 200-203°(dec), pK_1 2.40, pK_2 4.80, pK_3 6.27, pK_4 9.65, pK_5 10.20.** Purify it by recrystallisation from aqueous HCl, EtOH slightly acidified with HCl, EtOH/Me_2CO, H_2O, or H_2O/EtOH/Et_2O. Dissolve it in a small volume of H_2O and mix it with EtOH/Me_2CO (1:1) to give the HCl.H_2O as crystals. Filter it off, wash it with Et_2O and dry it in a vacuum. The *chloride hydrochloride*, **m** 215-217°(dec) is obtained when it is crystallised from aqueous HCl. [Wenz et al. *Justus Liebigs Ann Chem* **618** 2280 *1958*, Viscontini et al. *Helv Chim Acta* **34** 1388 *1951,* Leichssenring & Schmidt *Chem Ber* **95** 767 *1962*, McCormick & Wright *Methods Enzymol* **18A** 141, 147 *1970*, *Beilstein* **27** III/IV 1766.]

Thiamphenicol (Thyocymetin, 1*R*,2*R*-2-[2,2-dichloroacetylamino]-1-[4-methanesulfonyl-phenyl]-propan-1,3-diol) *[15318-45-3 (*D*-threo), 90-91-5]* **M 356.2, m 163-166°, 165.2-165.6°, 165-166°, $[\alpha]_D^{25}$ +15.6° (c 2, EtOH), pK^{25} 7.2.** Recrystallise thiamphenicol from H_2O or $CHCl_3$. The UV has λ_{max} at 224, 266 and 274nm (ε 13,700, 800 and 700) in 95% EtOH. The *1S,2S-isomer [14786-51-7]* has **m** 164.3-166.3° (from H_2O/EtOAc/petroleum ether) and $[\alpha]_D^{25}$ -12.6° (c 1, EtOH); and the *racemate 1RS,2RS*-**Racefenical** *[847-25-6]* has **m** 181-183° (dec) from $CHCl_3$/EtOAc/petroleum ether. [Cutler et al. *J Am Chem Soc* **74** 5475, 5482 *1952*, UV: Nachod & Cutler *J Am Chem Soc* **74** 1291 *1952*, Suter et al. *J Am Chem Soc* **75** 4330 *1953*, Cutler et al. *J Am Pharm Assoc* **43** 687 *1954*, *Beilstein* **13** IV 2957.]

ε-[2-(4-Thiazolidinone)]hexanoic acid (Mycobacidin, Acidomycin, 6[4-oxothiazolidin-2-yl]hexanoic acid) *[539-35-5]* **M 215.3, m 140°, pK^{25} 5.1.** The *dl-form is dimorphic*; it crystallises from $CHCl_3$ with **m** 116-117°, and from H_2O with **m** 123°. The *l(-)-enantiomer* (from Actinomyces) crystallises from H_2O, MeOH (**m** 139-140°), aqueous EtOH (**m** 140-141°) or EtOAc, and has $[\alpha]_D^{20}$ -54° (c 1, MeOH). The *d(+)-enantiomer* (from optical resolution of the brucine salt) has **m** 138-139° (from H_2O) and $[\alpha]_D^{25}$ +57° (c 1, MeOH). The optically active acids racemise in hot alkali. [McLamore et al. *J Am Chem Soc* **75** 105 *1953*, *Beilstein* **27** III/IV 4281.]

6-Thioguanosine (2-amino-6-mercapto-9-β-D-ribofuranosylpurine) *[85-31-4]* **M 299.3, m 224-227°(dec), 230-231°(dec), $[\alpha]_D^{20}$ -64° (c 1.3, 0.1N NaOH), pK^{25} 8.33.** Thioguanosine is crystallised (as *hemihydrate*) from hot H_2O (charcoal) and cooled slowly to give tapered prisms. It also crystallises by dissolving in dilute NH_3 and acidifying with acetic acid, and then recrystallising from H_2O. Its UV (pH 4-6) has λ_{max} at 257nm (ε 8,820) and 342nm (ε 24,800), and at pH 10.4-12.0 it has λ_{max} at 252nm (ε 14,700) and 319.5nm (ε 21,000). [Fox et al. *J Am Chem Soc* **80** 1667 *1958*, *Beilstein* **26** III/IV 3927.]

***dl*-α-Tocopherol (**see **vitamin E)** *[10191-41-0]* **M 430.7, $A_{1cm}^{1\%}$ 74.2 at 292 nm in MeOH.** Dissolve *dl*-α-

tocopherol in anhydrous MeOH (15ml/g) cool to -6° for 1 hour, then chill in a Dry-ice/acetone bath; crystallisation is induced by scratching with a glass rod. The *dl*-α-*acetate* [52225-20-4] (*see DL-vitamin E actetate below*) is a viscous yellow liquid with **m** -7°, **b** 184°/0.01mm, 224°/0.3mm, d_4^{20} 0.953, n_D^{20} 1.496. It is used as a standard for Vitamin E activity where the unit of activity is attained with 1mg of pure *dl*-α-acetate. [Friedrich "Vitamins" Water de Guyter Publ, Berlin 1988, *Beilstein* **17/4** V 168.]

γ-Tocopherol (3,4-dihydro-2,7,8-trimethyl-2-(4,8,12-trimethyltridecyl)-2*H*-benzopyran-6-ol) *[54-28-4]* **M 416.7, m -30°, b 200-210°/0.1mm, d_4^{20} 0.951, n_D^{20} 1.505, $[\alpha]_D^{20}$ -2.4° (EtOH).** γ-Tocopherol is purified by distillation at high vacuum and stored in dark ampoules under N_2. Its UV has λ_{max} at 298nm ($A_{1cm}^{1\%}$ 92.8). It is insoluble in H_2O but soluble in organic solvents. The *allophanate* (used for separating it from its isomers) has **m** 136-138°, $[\alpha]_D^{18}$ +3.4° ($CHCl_3$). [Baxter et al. *J Am Chem Soc* **65** 918 *1943*, Emerson et al. *Science* **83** 421 *1936*, *J Biol Chem* **113** 319 *1936*, *Beilstein* **17/4** V 158.]

Tomatidine (5α,20β,22α,25β,27-azaspirostan-3β-ol) *[77-59-8]* **M 415.7, m 202-206°, $[\alpha]_D^{20}$ +5.9° (c 1, MeOH), $[\alpha]_D^{20}$ +8° ($CHCl_3$).** Tomatidine forms plates from EtOAc. It is also purified by dissolving 80mg in $*C_6H_6$ and applying to an Al_2O_3 column (3.0g) and eluting with $*C_6H_6$, evaporating and recrystallising the residue three times from EtOAc. The *hydrochloride* has **m** 265-270° from EtOH and $[\alpha]_D^{25}$ -5° (MeOH). [IR: Uhle *J Am Chem Soc* **83** 1460 *1961*, Kessar et al. *Tetrahedron* **27** 2869 *1971*, Schreiber & Adams *Experientia* **17** 13 *1961*, *Beilstein* **27** III/IV 1950.]

Tomatine (22*S*,25*S*-3β,β-lycotetraosyloxy-5α-spirosolan) *[17406-45-0]* **M 1034.2, m 263-268°(dec), 290-291°(evacuated capillary), 283.5-287°(dec), 272-277°(dec), 300-305°(dec), $[\alpha]_D^{20}$ -18° to -34° (c 0.55, pyridine).** Tomatine is recrystallised from MeOH, EtOH, aqueous EtOH or dioxane/NH_3. It is almost insoluble in petroleum ether, Et_2O or H_2O. [Reichstein *Angew Chem* **74** 887 *1962*, *Beilstein* **27** III/IV 1954.]

Tubercidin (7-deazaadenosine) *[69-33-0]* **M 266.3, m 247-248°, $[\alpha]_D^{17}$ -67° (50% aqueous AcOH), pK^{10} 5.2-5.3.** 7-Deazaadenosine forms needles from hot H_2O. It is soluble in H_2O (0.33%), MeOH (0.5%) and EtOH (0.05%). It has UV with λ_{max} at 270nm (ε 12,100) in 0.001N NaOH. The *picrate* has **m** 229-231°(dec). [Tolman et al. *J Am Chem Soc* **91** 2102 *1969*, Mizuno et al. *J Org Chem* **28** 3329 *1963*, IR: Anzai et al. *J Antibiot (Japan)* **[9] 10** 201 *1957*, *Beilstein* **26** IV 1117.]

Tunicamycin *[11089-65-9]* **M ~780, m 234-235°(dec), $[\alpha]_D^{20}$ +52° (c 0.5, pyridine), pK_{Est} ~ 9.4.** The components of this nucleotide antibiotic from *Streptomyces sp.* are purified by recrystallising 3 times from hot glass-distilled MeOH, and the white crystals are dissolved in 25% aqueous MeOH and separated on a Partisil ODS-10μ column (9.4 x 25 cm) [Magnum-9 Whatman] using a 260nm detector. The column is eluted with MeOH/H_2O mixture adjusted to 1:4 (v/v) then to 2:4 (v/v). The individual components are recovered and lyophilised. Ten components have been isolated, and all were active (to varying extents) depending on the lengths of the aliphatic side-chains. The mixture has UV with λ_{max} at 205 and 260nm ($A_{1cm}^{1\%}$ 230 and 110). It is stable in H_2O at neutral pH but unstable in acidic solution. It inhibits protein glycosylation. [Mahoney & Duskin *J Biol Chem* **254** 6572 *1979*, Elnein *Trends Biochem Sci* **6** 219 *1981*, Takatsuki *J Antibiot* **24** 215 *1971*.]

Uracil, uridine and uridine nucleotides. These are resolved by ion-exchange chromatography with AG1 (Cl^- form). [Lindsay et al. *Anal Biochem* **24** 506 *1968*.]

Uridine 5'-(1-thio) monophosphate *[15548-52-4, 18875-72-4 (Absolute Stereochemistry specified)]* **and Uridine 5'-(α-thio) diphosphate** *[RS*(α-P*) 27988-67-6*; *R*(α-P) *72120-52-6]* **, $pK_{Est(1)}$~6.4, $pK_{Est(2)}$~9.5.** The Et_3N salts are purified by dissolving ~4g in 500ml of H_2O (adding a drop or two of Et_3N if they do not dissolve) and chromatograph by applying to a column (3 x 30cm) of DEAE-Sephadex A-25 and eluting with 1.4L of a linear gradient of $Et_3NH.HCO_3$ from 0.05 to 0.55M, pH 7.8 and 4°. The product elutes between 0.2-0.3M $Et_3N.HCO_3$. The pooled fractions are evaporated, and the residue is twice taken up in EtOH and evaporated to dryness to remove the last traces of $Et_3NH.HCO_3$. ^{31}P NMR: P_α is a doublet at -40.81 and -40.33, and P_β at 7.02ppm, $J_{\alpha,\beta}$ 32.96Hz. [Sheu et al. *Biochemistry* **18** 5548 *1979*.]

Uridylic acid (di-Na salt) *[27821-45-0]* **M 368.2, m 198.5°, pK $_3^{25}$ 6.63, pK $_4^{20}$ 9.71.** Crystallise it from MeOH. It may contain some Ba salt(s); hence stir it with Amberlite IR-120 cation exchanger (25ml, wet resin, 15-50 mesh in H^+ form) in H_2O (50ml) until the nucleotide dissolves. Filter, wash resin with H_2O until the eluate is neutral. Combine the filtrate and washings, and adjust the pH to 8.0 with 2.0 M aqueous NaOH. Concentrate it *in vacuo* to a small volume (~ 20ml), and add Me_2CO dropwise until crystallisation begins. Cool to 0°, and the shiny plates of di Na uridine-5′-phosphate dihydrate are filtered off and dried over P_2O_5 at 25°/0.1mm for 24 hours (>76% recovery). Its UV has λ_{max} at 262nm (ε 10,000 $M^{-1}cm^{-1}$) in 0.1 M HCl. [Boon et al. *J Chem Soc* 408 *1950*, Smith *Biochemical Preparations* **8** 130 *1960*.] [*Beilstein* **24** IV 1214.]

(+)-Usnic acid (2,6-diacetyl-7,9-dihydroxy-8,9b-dimethyldibenzofuran-1,3(2*H*,9b*H*)-dione) *[7562-61-0, 125-46-2]* **M 344.3, m 201-204°, 203-206°, [α] $_{546}^{20}$ +630° (c 0.7, $CHCl_3$), pK$_1$ 4.4, pK$_2$ 8.8, pK$_3$ 10.7.** This very weak acid is the natural form which is recrystallised from Me_2CO, MeOH or $*C_6H_6$. At 25° it is soluble in H_2O (<0.01%), Me_2CO (0.77%), EtOAc (0.88%), $MeOCH_2CH_2OH$ (0.22%), and furfural (7.32%). [Curd & Robertson *J Chem Soc* 894 *1937*, Barton & Brunn *J Chem Soc* 603 *1953*, resolution: Dean et al. *J Chem Soc* 1250 *1953*, synthesis: Barton et al. *J Chem Soc* 538 *1956*, *Beilstein* **18/5** V 586.]

(-)-Usnic acid (2,6-diacetyl-7,9-dihydroxy-8,9b-dimethyldibenzofuran-1,3(2*H*,9b*H*)-dione) *[6159-66-6, 7562-61-0]* **M 344.3, m 201-204°, 204°, [α] $_D^{20}$ -495° (c 0.9, $CHCl_3$).** Its properties are similar to those of the acid in the preceding entry. [*Beilstein* **18** II 241, **18** III/IV 3522.]

Valinomycin (Potassium ionophore I) *[2001-95-8]* **M 111.3, m 186-187°, 190°, [α] $_D^{20}$ +31.0° (c 1.6, $*C_6H_6$).** Recrystallise valinomycin from dibutyl ether or Et_2O. It is dimorphic: modification A crystallises from *n*-octane, and modification B crystallises from EtOH/H_2O. It is soluble in petroleum ether, $CHCl_3$, AcOH, BuOAc and Me_2CO. [Smith et al. *J Am Chem Soc* **97** 7242 *1975*, UV, IR and NMR see Brocknmann & Schmidt-Kastner *Chem Ber* **88** 57 *1955*, *Beilstein* **27** I 9728. **17** IV 9728.]

(±)-Verapramil hydrochloride (5-[*N*-{3,4-dimethoxyphenylethyl}methylamino]-2-[3,4-dimethoxyphenyl]-2-isopropylvaleronitrile HCl) *[23313-68-0]* **M 491.1, m 138.5-140.5°, 142°(dec), pK$_{Est}$ ~10.6.** The salt is purified by dissolving it in EtOH, filtering (if insoluble particles are present) and adding Et_2O, filtering the salt, washing it with Et_2O and drying it *in vacuo*. It has the following solubilities: hexane (0.001%), CH_2Cl_2 (~10%), MeOH (~10%), EtOH (20%) and H_2O (8.3%). It has UV with λ_{max} at 232 and 278nm. The *free base* is a viscous yellow oil **b** 243-246°/0.01mm (n $_D^{25}$ 1.5448) and is almost insoluble in H_2O but soluble in organic solvents. It is a Ca channel antagonist and is a coronary vasodilator. [Ramuz *Helv Chim Acta* **58** 2050 *1975*, Harvey et al. *Biochem J* **257** 95 *1989*.]

Veratridine (3-veratroylveracevine) *[71-62-5]* **M 673.8, m ~180° (after drying at 130°, pK 9.54 (quinolizidine N), [α] $_D^{20}$ +8.0° (c ~5, EtOH).** It is an alkaloid neurotoxin which prevents inactivation of Na^+ channels. Its solubility in EtOH is ~5%; and it separates as a pale yellow powder from an ethanolic solution on addition of Et_2O. It forms nitrate, sulfate and perchlorate salts. [McKinney et al. *Anal Biochem* **153** 33 *1986*, *Beilstein* **21** V/13 709.]

Vinblastine sulfate (VLB, vincaleucoblastine sulfate) *[143-67-9]* **M 909.5, m 284-285°(dec), 267°(dec), [α] $_D^{26}$ -28° (MeOH), pK$_1$ 5.5, pK$_2$ 7.4.** Crystallise the sulfate from MeOH or EtOH and dry it *in vacuo* over conc H_2SO_4. The *free base* crystallises from EtOH or MeOH **m** 211-216° (+ 2MeOH.1 H_2O) and forms a stable etherate from Et_2O with **m** 201-211°, and [α] $_D^{25}$ +42° ($CHCl_3$), and its UV has λ_{max} at 214 and 259nm (log ε 4.73 and 4.21). The *dihydrochloride* has **m** 244-246°(dec)(MeOH). It is a monoamine oxidase B inhibitor and induces microtubule aggregation. It is an antineoplastic drug for Hodgkin's lymphoma. [Neuss et al. *J Am Chem Soc* **81** 4754 *1959*, Jong-KeunSon et al. *J Med Chem* **33** 1845 *1990*, Warfield & Bouck *Science* **186** 1219 *1974*, *Beilstein* **26** III/IV 3167.]

Vincristine sulfate (22-oxovincaleucoblastine sulfate) *[2068-78-2]* **M 925.1, m 218-220°, [α] $_D^{25}$ +26.2° (CH_2Cl_2), pK$_1$ 5.0, pK$_2$ 7.4 (in 33% Me_2NCHO/H_2O).** The salt is recrystallised from MeOH. It has UV with λ_{max} at 220, 255 and 296nm (log ε 4.65, 4.21 and 4.18). It is a monoamine oxidase inhibitor and is used in

cancer research [Son et al. *J Med Chem* **33** 1845 *1990*, Horio et al. *Proc Natl Acad Sci USA* **85** 3580 *1988*].

Viomycin sulfate (Viocin, Tuberactinomycin B) *[37883-00-4]* **M 685.7, m 266°(dec), $[\alpha]_D^{17}$ -29.5° (c 1, H_2O), pK_1 7.2 (8.2), pK_2 10.3.** Viocin crystallises from H_2O/EtOH and is dried in a vacuum. The dry material is *hygroscopic* and should be stored dry. The UV has λ_{max} at 268 and 285nm (log ε 4.4 and 4.2) in H_2O. [Kitigawa et al. *Chem Pharm Bull Jpn* **20** 2176 *1972*.] The *hydrochloride* forms *hygroscopic* plates with **m** 270°(dec), $[\alpha]_D^{18}$ -16.6° (c 1, H_2O), with λ_{max} at 268nm (log ε 4.5) in H_2O; 268nm (log ε 4.4) in 0.1N HCl and at 285nm (log ε 4.3) in 0.1N NaOH. [*Beilstein* **26** III/IV 4245.]

Vitamin A acetate (retinyl acetate) *[127-47-9]* **M 328.5, m 57°.** The acetate is separated from retinol by column chromatography, then crystallised from MeOH. [Kofler and Rubin *Vitamins and Hormones (NY)* **18** 315 *1960* for purification methods]. Store it in the dark, under N_2 or Ar, at 0°. [*Beilstein* **6** IV 4135.]

Vitamin A acid [Retinoic acid, 3,7-dimethyl-9-(2,6,6-trimethyl-1-cyclohexenyl)-2,4,6,8-nonatetraen-1-oic acid] *[302-79-4]* **M 300.4, m 180-181°, 180-182°, pK_{Est} ~4.2.** Purify the acid by chromatography on silicic acid columns, and eluting it with a small amount of EtOH in hexane. Also dissolve it in Et_2O, wash it with H_2O, dry (Na_2SO_4), evaporate and the solid residue is recrystallised from MeOH (0.53g /3.5ml MeOH to give 0.14g) or EtOH. It also recrystallises from *i*-PrOH, or as the *methyl ester* from MeOH. Its UV(MeOH) has λ_{max} at 351nm (ε 45,000). 9-*Cis*-acid forms yellow needles from EtOH, with **m** 189-190°, and its UV(MeOH) has λ_{max} at 343nm (ε 36,500); the 13-*cis*-acid forms red-orange plates from *i*-PrOH with **m** 174-175°, and its UV has λ_{max} at 345nm (ε 39,800). Store it in the dark, in an inert atmosphere, at 0° [Robeson et al. *J Am Chem Soc* **77** 4111 *1955*]. [*Beilstein* **9** IV 2387.]

Vitamin A alcohol (retinol) *[68-26-8]* **M 286.5, $A_{1cm}^{1\%}$(max) (*all-trans*) 1, 832 (325 nm), (*13-cis*) 1686 (328nm), (*11-cis*) 1230 319 nm), (*9-cis*) 1480 (323 nm), (*9,13-di-cis*) 1379 (324 nm), (*11,13-di-cis*) 908 (311 nm) in EtOH.** Purify retinol by chromatography on columns of water-deactivated alumina and elute with 3-5% acetone in hexane. Separate the isomers by TLC plates on silica gel G, developed with petroleum ether (low boiling)/methyl heptanone (11:2). Store it in the dark, under N_2, at 0°, or in Et_2O, Me_2CO or EtOAc. [See Gunghaly et al. *Arch Biochem Biophys* **38** 75 *1952*, *Beilstein* **6** IV 4133.]

Vitamin A aldehyde [all-*trans*-retinal; 3,7-dimethyl-9-(2,6,6-trimethyl-1-cyclohexenyl)-2,4,6,8-nonatetraen-1-al] *[116-31-4]* **M 284.4, m 61-64°.** The aldehyde is separated from retinol by column chromatography on water-deactivated alumina. Elute with 1-2% acetone in hexane, or on TLC plates of silica gel G and using the same eluting solvent. It crystallises from petroleum ether or *n*-hexane as yellow-orange crystals, and the UV in hexane has λ_{max} at 373nm ($A_{1cm}^{1\%}$ 1548) and 368nm (ε 48,000). It is an **irritant** and is light sensitive. Store it in sealed ampoules under N_2. The *semicarbazone* forms yellow crystals from $CHCl_3$/Et_2O or EtOH, **m** 199-201°(dec). The 9-*cis-isomer [514-85-2]* and the 13-*cis-isomer [472-86-6]* [λ_{max} at 375nm (ε 1,250) in EtOH] are also available commercially. [*Beilstein* **7** III 1742.]

Vitamin A palmitate (retinyl palmitate) *[79-81-2]* **M 524.9, m 28-29°, $\varepsilon_{1cm}^{1\%}$(all – trans)1000 (325 nm) in EtOH.** The palmitate is separated from retinol by column chromatography on water-deactivated alumina with hexane containing a very small percentage of acetone. It is also chromatographed on TLC silica gel G, using petroleum ether/isopropyl ether/acetic acid/water (180:20:2:5) or petroleum ether/acetonitrile/acetic acid/water (190:10:1:15) to develop the chromatogram. It is then recrystallised from propylene at low temperature (below -47°). [*Beilstein* **6** IV 4135.]

Vitamin B_1 Hydrochloride [Aneurine hydrochloride, Thiamine hydrochloride, 3{(4-amino-2-methyl-5-pyrimidinyl)methyl}-4-methylthiazolium chloride monohydrochloride] *[67-03-8]* **M 337.3, m 248°(dec), 249-250°, monohydrate m 135°(dec), pK_1^{25} 4.8, pK_2^{25} 9.2.** The hydrochloride crystallises from 95% EtOH (solubility is *ca* 1%). The *monohydrate* is dehydrated at 100° *in vacuo* over H_2SO_4, but is *hygroscopic* and picks up one molecule of H_2O readily. It can be sterilised at 100° if the pH of the solution is below 5.5. The *nitrate* has **m** 196-200°(dec) and is more stable than the hydrochloride. The *picrolonate* crystallises from H_2O and is *dimorphic*, **m** 164-165° and 228-229°(dec). [Todd & Bergel *J Chem Soc* 364, 367 *1937*, *J Am Chem Soc* **58** 1063, 1504 *1936*, **59** 526 *1937*, *Beilstein* **27** IV 1766.]

Vitamin B_2 [Riboflavin, Lactoflavin, 6,7-dimethyl-9-(D-1'-ribityl)isoalloxazine] *[83-88-5]* **M 376.4, m 278-282°(dec with darkening at 240°), 281-282°, $[\alpha]_D^{25}$ -9.8° (H_2O), $[\alpha]_D^{25}$-112° to -125° (c 2.5, 0.02N NaOH), $[\alpha]_D^{20}$ -59° (c 0.23, AcOH), pK_1 1.7, pK_2 9.69 (10.2, acidic NH).** It crystallises from H_2O as a yellow-orange powder in three different forms with differing amounts of H_2O. It melts if placed in an oil bath at 250°, but decomposes at 280° if heated at a rate of 5°/minute. It is also purified by crystallisation from 2M acetic acid, then extracted with $CHCl_3$ to remove lumichrome impurity. [Smith & Metzler *J Am Chem Soc* **85** 3285 *1963*.] Its solubility in H_2O is 1g in 3-15L depending on the crystal structure. Its solubility in EtOH at 25° is 4.5mg in 100ml. Store it in the dark because it is decomposed to lumichrome by UV light. [Pearson *The Vitamins* **vol V** pp1-96 *1967* and **vol VII** pp 1-96 *1972*, Gyögy and Pearson eds, Academic Press, *Beilstein* **26** IV 2542.]

Vitamin B_3 (vitamin PP, Niacin). See nicotinamide in "Heterocyclic Compounds", Chapter 4.

Vitamin B_6 hydrochloride (adermine, pyridoxine HCl, 3-hydroxy-4,5-bis[hydroxymethyl]-2-methylpyridine HCl) *[58-56-0]* **M 205.6, m 208-208.5°, 208-209°(dec), 209-210°(dec), 205-212° (sublimes), pK_1^{25} 5.0 (3-OH), pK_2^{25} 8.96 (pyridinium$^+$).** Purify the vitamin by recrystallisation from EtOH/Me_2CO, *n*-BuOH or MeOH/Et_2O. Its solubility in H_2O is 22%, and in EtOH it is 1.1%. It is insoluble in Et_2O and $CHCl_3$. Acidic aqueous solutions are stable at 120°/30minute. The *free base* has **m** 159-160° after recrystallisation from Me_2CO and sublimation at 140-145°/0.0001mm. It has UV with λ_{max} at 290nm (ε 84,000), 253 and 325nm (ε 3700 and 7100) in 0.1N aqueous HCl. [Khua & Wendt *Chem Ber* **71** 780 *1938,* **72** 311 *1939,* Harris & Folkers *J Am Chem Soc* **61** 1242 *1939*, Harris et al. *J Am Chem Soc* **62** 3198 *1940*, *Beilstein* **21/5** V 492.] See also **Pyridoxal-5'-phosphate H_2O** above.

Vitamin B_{12} (cyanocobalamine, α-[5,6-dimethylbenzimidazolyl]cyano cobamide) *[68-19-9]* **M 1355.4, m darkens at 210-220° and does not melt below 300°, $[\alpha]_{656}^{23}$ -59° (H_2O).** Vitamin B_{12} crystallises from de-ionized H_2O, with a solubility in H_2O of 1g/80g, and is dried under vacuum over $Mg(ClO_4)_2$. The dry red crystals are *hygroscopic* and can absorb ~12% of H_2O. A solution at pH 4.5-5 can be autoclaved for 20 minutes at 120° without decomposition. Aqueous solutions are stabilised by addition of $(NH_4)_2SO_4$. [Golding *Comprehensive Organic Chem* Vol 5 (Ed. Haslam; Pergamon Press, NY, 1979) pp 549-584.]
Alternatively, an aqueous solution of the coenzyme can be concentrated, if necessary in a vacuum at 25° or less, until the concentration is 0.005 to 0.01M (as estimated by the OD at 522nm of an aliquot diluted with 0.01M K-phosphate buffer pH 7.0). If crystals begin to form on the walls of the container, they should be re-dissolved with a little H_2O. The concentrated solution is placed in a glass stoppered flask and diluted with 5 volumes of Me_2CO. After 2-3 hours at 3° it is centrifuged (10,000xg/10minutes) in Me_2CO-insoluble plastic tubes to remove some amorphous precipitate. The clear supernatant is inoculated with a small crystal of the vitamin and allowed to crystallise overnight at 3°. Crystals are formed on the walls and the bottom of the container. A further 2 volumes of Me_2CO are added and set aside at 3° to further crystallise. Crystallisation is followed by observing the OD_{522} of the supernatant. When the OD falls to 0.27, then *ca* 94% of the crystals have separated. The supernatant is decanted (saved for obtaining a second crop), and the crystals are washed with a little cold 90% aqueous Me_2CO (2x), 100% Me_2CO (2x), Et_2O (2x) at which time the crystals separate from the glass walls. Allow them to settle and remove residual Et_2O with a stream of dry N_2. The process can be repeated if necessary. The crystals can be dried in air or in a vacuum for 2 hours over silica gel at 100° with an 8-9% weight loss. [Barker et al. *Biochemical Preparations* **10** 33 *1963*.] This material gives a single spot on paper chromatography [see Weissbach et al. *J Biol Chem* **235** 1462 *1960*.] The vitamin is soluble in H_2O (16.4mM at 24°, 6.4mM at 1°), in EtOH and PhOH but insoluble in Me_2CO, Et_2O, CH_2Cl_2 and dioxane. Its UV has λ_{max} at 260, 375 and 522nm (ε 34.7 x 10^6, 10.9 x 10^6 and 8.0 x 10^6/mole) in H_2O. The dry crystals are stable for months in the dark, but aqueous solutions decompose on exposure to VIS or UV light or alkaline CN^-, but are stable in the dark at pH 6-7. The vitamin is inactivated by strong acids or alkalies. [Barker et al. *J Biol Chem* **235** 480 *1960*, see also *Vitamin B_{12}* (Zagalak & Friedrich Eds) Walter de Gruyter, Berlin *1979, Beilstein* **26** IV 3117.]

Vitamin C. See ascorbic acid entry in "Carbohydrates" in this chapter.

Vitamin D_2 *[50-14-6]* **M 396.7, m 114-116°, $[\alpha]_{546}^{20}$ +122° (c 4, EtOH).** It is converted into its 3,5-dinitrobenzoyl ester and crystallised repeatedly from acetone. The ester is then saponified and the free vitamin is

isolated. [Laughland & Phillips *Anal Chem* **28** 817 *1956*, *Beilstein* **6** IV 4404.]

Vitamin D_3 (cholecalciferol, Calcitol, activated 7-dehydrocholesterol, (+)-vitamin D_3) *[67-97-0]* **384.6, m 83-85°, $[\alpha]_{546}^{20}$ +126° (c 2, EtOH).** It is converted into its 3,5-dinitrobenzoyl ester and crystallised repeatedly from acetone. The ester is then saponified and the free vitamin is isolated. Store it in sealed ampoules under argon below 8°. It acts through a receptor which modulates differentiation and proliferation of normal and neoplastic cells. [Laughland & Phillips *Anal Chem* **28** 817 *1956*, DeLuca & Schones *Ann Rev Biochem* **52** 411 *1983*, *Beilstein* **6** III 2811, **6** IV 4149.]

Vitamin E (2*R*,4'*R*,8'*R*-α-tocopherol, natural active isomer) *[59-02-9]* **M 430.7, m 2.5-3.5°, b 200-220°/0.1mm, 200°/0.005mm, d_4^{25} 0.950, n_D^{25} 1.5045, $[\alpha]_D^{25}$ +3.58° (c 1, *C_6H_6).** Vitamin E is a viscous yellow oil which is distilled at high vacuum. It has λ_{max} at 294nm ($E_{1cm}^{1\%}$ 71). It is oxygen and light sensitive and is best stored as its stable *D-α-acetate* [58-95-7] which is purified by evaporative distillation at **b** 180-200°(bath temperature)/0.7mm, and has $[\alpha]_D^{25}$ +3.3° (c 5.1, EtOH). It forms needles at -30° and has **m** 26.5-27.5°, $[\alpha]_D^{25}$ +0.25° (c 10, $CHCl_3$). [NMR: Cohen et al. *Helv Chim Acta* **64** 1158 *1981*, Burton & Ingold *Acc Chem Res* **19** 194 *1986*, Karrer et al. *Helv Chim Acta* **21** 520 *1938*, Robeson *J Am Chem Soc,* **64** 1487 *1942*, **65** 1660 *1943*.] Of the eight isomers the D-α-isomer is the most active. [See W. Friedrich "Vitamins" Walter de Guyter Publ, Berlin 1988.] [*Beilstein* **17/4** V 168.]

DL-Vitamin E acetate (DL-α-tocopheryl acetate) *[7695-91-2]* **M 472.8, m -27.5°, b 194-196°/0.01mm, 222-224°/0.3mm, d_4^{20} 0.958, n_D^{20} 1.4958.** It is a viscous liquid which is purified by distillation under high vacuum under N_2 or argon and stored in sealed ampoules in the dark. It is considerably more stable to light and air than the parent unacetylated vitamin. It is insoluble in H_2O but freely soluble in organic solvents. All eight stereoisomers have been synthesised. The commercially pure *d-α–tocopheryl acetate* (2*R*,4'*R*,8'*R*) has **b** 180-200°/0.7mm and $[\alpha]_D^{20}$ +3.9° (c 5, EtOH); see above. [Cohen et al. *Helv Chim Acta* **64** 1158 *1981*, *Beilstein* **17/4** V 169.]

Vitamin K_1 (2-methyl-3-phytyl-1,4-naphthoquinone) *[84-80-0]* **M 450.7, m -20°, b 141-140/0.001mm, b 140-145°/10^{-3} mm, d_{25}^{25} 0.967, n_D^{25} 1.527, $[\alpha]_D^{20}$ -0.4° (c 57.5, *C_6H_6).** Vitamin K_1 is a yellow viscous oil, which can be distilled at high vacuum practically unchanged. It is insoluble in H_2O, but soluble in common organic solvents. Store it in the dark under N_2 as it is oxygen sensitive. It has $A_{1cm}^{1\%}$ 328 at 248nm. [Fieser et al. *J Am Chem Soc* **61** 2557 *1939*, Hirschmann et al. *J Am Chem Soc* **76** 4592 *1954*, Isler & Doebel *Helv Chim Acta* **27** 225 *1954*, *Beilstein* **7** IV 2496.]

Vitamin K_3 (2-methyl-1,4-naphthoquinone, Menadione, Menaphthone) *[58-27-5]* **M 172.2, m 105-106°, 105-107°.** Recrystallise it from 95% EtOH, or MeOH after filtration. It forms bright yellow crystals which are decomposed by light. Its solubility in EtOH is 1.7% and in *C_6H_6 it is 10%. It **IRRITATES** mucous membranes and skin. [Fieser *J Biol Chem* **133** 391 *1940*, *Beilstein* **7** IV 2430.]

Vitamin K_5 (4-Amino-2-methyl-1-naphthol hydrochloride) *[130-24-5]* **M 209.6, m 283°(dec), $pK_{Est(1)}$ ~5.6 (NH_2), $pK_{Est(2)}$ ~10.4 (OH).** Crystallise it from dilute HCl. [Sah *Rec Trav Chim Pays Bas* **59** 458 *1941*, Sah *Rec Trav Chim Pays Bas* **60** 373 *1940*, Veldstra & Wiardi *Rec Trav Chim Pays Bas* **61** 547 *1942*, Veldstra & Wiardi *Rec Trav Chim Pays Bas* **62** 75 *1943*, *Beilstein* **13** III 1921.]

Vitamin P [(+)-Rutin, quercetin-3-rubinoside] *[153-18-4]* **M 610.5, 664.5 (trihydrate), m 188-189°, 195-196°, $[\alpha]_{546}^{20}$ +13° (c 5, EtOH), $[\alpha]_D^{24}$ -37.6° (c 1.24, pyridine), (polyphenolic flavone pKs 7—10).** The vitamin crystallises from MeOH or water/EtOH, dry it in air, then dry it further for several hours at 110° or in high vacuum at 120°. It forms yellow crystals from EtOH/Me_2CO/H_2O (2:1:1). It has also been purified by passing (0.5g) through a Kieselgel column (30 x 5cm) with EtOAc/MeOH/H_2O (100:20:15), and after 750ml have passed through, the yellow fraction of 250ml gives the glycoside (0.3g) on evaporation. [Hörhammer et al. *Chem Ber* **101** 1183 *1968*, Marini-Bettòlo *Gazz Chim Ital* **80** 631 *1950*, *Beilstein* **18/5** V 519.]

Vitamin U (S-Methyl-L-methionine chloride) *[S- 1115-84-0, S-ion- 6708-35-6, RS- 44901-24-8]* **M 199.5, m 135° (dec), 139° (dec), $[\alpha]_D^{23}$ +33° (0.2M HCl), pK_1 1.9, pK_2 7.9.** Likely impurities are methionine, methionine

sulfoxide and methionine sulfone. Crystallise Vitamin U from water by adding a large excess of EtOH. It is *hygroscopic*. It should be stored in a cool, dry place and protected from light. It has also been purified on a column of Dowex 50 H^+ form, washed with H_2O and eluted with 6N ammonia, lyophilised, the residue is dissolved in dilute HCl, lyophilised again and then it is obtained as colourless prisms by vapour diffusion of Et_2O in a 1:1 (v/v) mixture of MeOH/EtOH in which the *hydrochloride* is dissolved [Del Re *Acta Cryst B* **33** 3289 *1977*]. The *iodide salt*, **m** ~150º(dec), is obtained by dissolving it in 50% aqueous EtOH and adding ~3.5 volumes of absolute EtOH. The *bromide salt* has **m** 140º(dec) [Toennies & Kolb *J Amer Chem Soc* **67** 849 *1945*].

***dl*-Warfarin (Coumafene, 4-hydroxy-3-(3-oxo-1-phenylbutyl)-2*H*-1-benzopyran-2-one)** *[81-81-2]* **M 308.3, m 162-164º, pK^{20} 4.85 (the 4-mercapto derivative has pK^{20} 6.60).** *dl*-Warfarin crystallises from EtOH or MeOH. Its UV has λ_{max} at 308nm (ε 13,610) in H_2O. The *acetate* has **m** 117-118º, the *O-triflate* has **m** 90-91º, and the *2,4-dinitrophenylhydrazone* has **m** 215-216º. It is an effective anticoagulant and rodenticide. [West et al. *J Am Chem Soc* **83** 2676 *1961*, HPLC: Banfield & Rowland *J Pharm Sci* **72** 921 *1983*, *Beilstein* **17** III/IV 6794.]

***R*-(+)-Warfarin** has **m 170-171º, $[\alpha]_D^{23}$ +149º (c 1.2, in 0.5N NaOH), +25.5º (c 2, AcOH), +15.5º (c 2, MeCN) and -19º (c 1.1, propan-2-ol),** and ***S*-(-)-Warfarin (*more active enantiomer*)** has **m 172-173º, $[\alpha]_D^{23}$ -148º (c 1.2, in 0.5N NaOH), -25.5º (c 2, AcOH), -15.5º (c 2, MeCN) and +19º (c 1.1, propan-2-ol).** *dl*-Warfarin is resolved *via* recrystallisation of the quinidine salt, and the free acids are recrystallised (70g) from 600ml of 80% aqueous Me_2CO. Large prismatic crystals of the pure enantiomers are obtained by slow crystallisation from Me_2CO or AcOH. The solubilities of the pure enantiomers at 25º are 11.2% in Me_2CO and 2.6% in AcOH, whereas the racemate has solubilities of 6.5% in Me_2CO and 2% in AcOH. The IR spectra are the same with ν_{max} ($CHCl_3$) at 2.78 (w), 5.88, 6.16 and 6.38μ. [West et al. *J Am Chem Soc* **83** 2676 *1961*, Cbz-proline diastereoisomeric esters were used for HPLC analysis: Banfield & Rowland *J Pharm Sci* **72** 921 *1983*.] **Poisonous, anticoagulant and rodenticide.**

Xanthopterin monohydrate (2-amino-4,6-dihydroxypteridine, 2-aminopteridin-4,6(1*H*,5*H*)-dione) *[5979-01-1 (H_2O), 119-48-8 (anhydrous)]* **M 197.2, m <300º, pK_1 1.6 (basic), pK_2 6.59 (acidic), pK_3 9.31 (acidic)(anhydrous species), and pK_1 1.6 (basic), pK_2 8.65 (acidic), pK_3 9.99 (acidic)(7,8-hydrated species).** Purification is as for isoxanthopterin (see [529-69-1] "Heterocyclic Compounds", Chapter 4). It is crystallised by acidifying a hot ammoniacal solution with formic acid, and collecting the crystals by centrifugation followed by washing with EtOH, ether and drying at 100º *in vacuo*. Its R_F values on paper chromatography are 0.15 (*n*-PrOH, 1% aqueous NH_3, 2:1), 0.36 (*n*-BuOH/AcOH/H_2O, 4:1:1) and 0.47 (3% aqueous NH_3). [Inoue & Perrin *J Chem Soc* 260 *1962*, Inoue *Tetrahedron* **20** 243 *1964*, see also Blakley *Biochemistry of Folic Acid and Related Pteridines* North Holland Publ Co, Amsterdam 1969, *Beilstein* **26** II 313, **26** III/IV 4000.]

Xanthotoxin (Methoxalen, 9-methoxypsoralen, Ammoidin, 9-methoxyfuro[3,2-g][1]benzopyran-7-one) *[298-81-7]* **M 216.2, m 146-148º, 148º, 148-149º.** Purify xanthotoxin by recrystallisation from *C_6H_6/petroleum ether (b 60-80º) to give silky needles, or from EtOH/Et_2O to give rhombic prisms or from hot H_2O to give needles. It is soluble in aqueous alkali due to ring opening of the cyclic lactone but recyclises upon acidification. It has UV with λ_{max} (EtOH) at 219, 249 and 300nm (log ε 4.32, 4.35 and 4.06) and ^1H NMR in $CDCl_3$ with δ at 7.76 (d, 1H, *J* = 10Hz), 7.71 (d, 1H, *J* = 2.5Hz), 7.38 (s, 1H), 6.84 (d, 1H, *J* = 2.5Hz), 6.39 (d, 1H, *J* = 10Hz) and 4.28 (s, 3H). [Nore & Honkanen *J Heterocycl Chem* **17** 985 *1980*.] It is a DNA intercalator, is used in the treatment of dermal diseases, and is a **human carcinogen** [Tessman et al. *Biochemistry* **24** 1669 *1985*]. [*Beilstein* **19** I 711, **19/6** V 15.]

Zeatin (*trans*-N^6-[4-hydroxy-3-methylbut-2-en-1-yl]adenine) *[1637-39-4]* **M 219.3, m 207-208, 209-209.5º, pK_1 4.4 (basic), pK_2 9.8 (acidic).** Purify zeatin by recrystallisation from EtOH or H_2O. Its UV has λ_{max} at 207 and 275nm (ε 1400 and 14,650) in 0.1N aqueous HCl; 212 and 270nm (ε 17,050 and 16,150) in aqueous buffer pH 7.2; and 220 and 276nm (ε 15,900 and 14,650) in 0.1N aqueous NaOH. The *picrate* has **m** 192-194º (from H_2O) from which zeatin can be recovered by treatment with Dowex-1 x 8 (200-400 mesh, OH^- form).

[Letham et al. *Aust J Chem* **22** 205 *1969*, *Proc Chem Soc (London)* 230 *1964*, Shaw & Wilson *Proc Chem Soc (London)* 231 *1964*.] It is a cell division factor (plant growth regulator) [Letham & Palni *Ann Rev Plant Physiol* **34** 163 *1983*] and inhibits mitochondrial function [Miller *Plant Physiol* **69** 1274 *1982*]. The commercially available *trans -9-riboside* derivative, [6025-53-2], **M 351.4**, is a cytokine which separates from aqueous AcOH with **m** 177-179º. It solubility in AcOH is ~5%. [McDonald & Morris *Methods Enzymol* **100** 347 *1985*.]

CHAPTER 8

NANOMATERIALS AND NANOTECHNOLOGY

INTRODUCTION

Nanomaterials are substances that are, or have been, reduced in size to the range from 1nm to ~100nm (i.e. 1 to ~100 nanometers, or 1 to ~100 x 10^{-9} meters). ***Nanotechnology*** is the science and applications of nano-materials, and is growing at an ever increasing pace. At this particle size the properties of materials can be altered dramatically. Properties such as solubility, reactivity, spectroscopy, electrical and magnetic, transport through membranes etc. are generally different from those of the same materials with large particle size. The applications of materials of nano size have escalated in the last fifteen or so years and are currently gaining momentum. The technology has broad applications in performance materials, health, consumer products, water, information technology and energy. The discovery of ***fullerenes*** (1996 Nobel Prize for Chemistry to H.W. Kroto, R.E. Smalley and R.F. Curl) and of ***Graphene*** (2010 Nobel Prize for Physics to A. Geim and K Novoselov) are very important factors in the development of nanotechnology. Not very many nanomaterials have so far been included in chemical catalogues of commercially available substances, e.g. as compared with catalysts (although some catalysts are now available as nanoparticles), hence the relatively smaller size of this chapter. Fullerenes and related materials such as carbon nanotubes have found applications in medicine for the transport of drugs and biological materials to targeted sites and some readily available derivatives are described in this chapter, together with other commercially available nanoparticulate substances, e.g. catalysts, magnetic and electrically conducting thin films. General safety aspects of handling nanomaterials have been briefly addressed.

IDENTIFICATION AND MEASUREMENT OF NANOMATERIALS

The 1 to ~ 100nm (10 to ~1000Å) particles are smaller than the wavelength of UV light, and thus the use of appropriate small particles e.g. electrons, or radiation e.g. X-rays is necessary to identify and measure these particles. Instrumentation for these purposes has been developed and the resolutions are continuously being improved. These instruments can measure very accurately, and depending on the physical principles of the machines, they measure different parameters of the nanoparticles, e.g. diameter (if spherical), length (if rod like), width (if bulky) etc, and not necessarily all parameters at the same time with one instrument. The commonly used instruments include the *Transmission Electron Microscope* (TEM) in which the electron beam runs past the particles placed on a transparent surface, and then through the surface giving a 2D image and magnifying one million times. In the *Scanning Electron Microscope* (SEM) and *Scanning Tunneling Microscope* (STM, or *Spectroscopy* STS) the electron beam scans the surface of the particles to provide a 3D picture, e.g. of hairs on a fly. *Dynamic Light Scattering* (DLS) uses light scattering through solutions of nanoparticles. Another technique, *Scattering Probe Microscopy* (SPM), allows scanning with a probe over a surface and includes *Atomic Force Microscopy* (AFM, or *non-contact atomic force microscopy* NC-AFM) where a ceramic or semiconductor tip scans the surface (much like a phonograph needle scans a record), and measures the atomic forces beneath it. The NC-AFM tip is attached to a very small tuning fork that oscillates at amplitudes of 0.2 to 0.5Å, smaller than the diameter of an atom. When the tip is brought very close to a molecule on a surface, this frequency alters slightly thus *detuning* due to the atomic forces between the tip and the molecule to give a complete picture of the molecule on the surface. By placing a CO (carbon monoxide) molecule at the tip, and keeping it there throughout the imaging process, very high resolution can be obtained. Gross and coworkers [Gross et al. *Science* **325** 1110 *2009*] obtained the complete image of pentacene on a copper surface in this way, and succeeded in imaging the amount of charge on a single atom [Gross et al. *Science* **324** 1428 *2011*]. The sensitivity of *Magnetic Resonance Imaging* (MRI) has been considerably increased (with a resolution of ~4nm), by Rugar and coworkers [Degen et al. *Proc Natl Acad Sci* **106** 1313 *2009*, cf H. Birch *MRI on the Nanoscale,* RSC *Chemistry World* **6**(2) 28 *2009*, J. M. Crow *Picture perfect pentacene,*

Purification of Laboratory Chemicals. http://dx.doi.org/10.1016/B978-0-12-382161-4.00008-X

RSC *Chemistry World* **6**(1) 46*2011*] who have developed the *Magnetic Resonance Force Microscopy* (MRFM) technique. Here the sample is placed at the end of a tiny silicon cantilever to which is applied, *via* a magnetic tip, a radio frequency magnetic field. The spin of the nuclei alternate (*up* and *down*) when the frequency reaches their 'wobbling' frequencies making the cantilever vibrate. Photon density 3D images of the specimen (e.g. tobacco mosaic virus, *ca* 18 nanometers across) can be obtained by using a laser to detect the cantilever vibrations. The technique does not affect the sample and gives superior images to those from STM and AFM. [A.I. Kirkland and J. I. Hutchinson (eds) *Nanocharacterisation* RSC Publishing UK, *2007*, ISBN 9781847557926, 1847557929; A. Turley *Sizing it up,* RSC *Chemistry World* **8**(3) 50 *2011*; M. Thompson RSC *The Characterisation of Nanoparticles; Analytical Methods Committee Technical Briefs 48,* December *2010*; ISSN 1757-5958, http://bit.ly/AMCparticle). Other techniques include *Near-Infrared Spectroscopy* (NIR) and solution phase NIR [Iktis et al. *Nano Lett* **3** 309 *2003*], general *Electron Microscopy* (EM), *Field Emission Microscopy* (FEM), *FT-Raman Scattering Spectroscopy*, *Nuclear (proton) Magnetic Resonance Spectroscopy* (NMR for derivatised carbon nanotubes, CNTs), *Thermo Gravimetric Analysis* (TGA), *Energy Dispersive X-ray Spectroscopy* (EDX), as well as other optical techniques (see Bibliography at the end of this chapter).

Preparation of the specimen is very important since the atoms or/and molecules have to be spread over the surface in as close to one atom or molecule thick. Where thicknesses (t) of 7 to ~13nm need to be measured *Grazing Incident X-Ray Reflectometry* (GICRR/XRR) provides an initial measure of particle lengths (l) of 1 to 35nm. *Spectroscopic Elipsometry* (SE, t = ~ 10.5 to 12.3nm, l = 1 to 10.5nm), *Scanning Ion Mass Spectrometry* (SIMS, t ~ 10.4 to 10.8nm, l = ~12 to 13 nm), *Transmission Electron Microscopy* (TEM, t ~ 7.5 to 12.5nm, l = 12.5 to 18.5 nm), *X-Ray Fluorescence Spectroscopy* (XFS, t ~ 7.5 to 9.3nm, l = 16.0 to 19.5 nm), *X-Ray Photoelectron Spectroscopy* (XPS, t ~ 9.2 to 11.7, l = 18.5 to 25.5 nm) and higher resolution *Grazing Incident X-Ray Reflectometry* (GIXRR/XRR, t ~ 9.2 to 11.7, l = 24.0 to 36.0 nm) provide the approximate t and l values stated in the brackets. It must be noted that these values are approximate as they do vary depending on the nature of the materials that are measured.

Average particle size: The accepted method for determining the primary particle size of nanomaterials is by TEM analysis. However, this is expensive and time-consuming. Studies have shown that an average primary particle size for spherical or cubic shaped dry nanoparticles of roughly uniform shape and size can be calculated from the equation:

Average particle size (nanometers) = (6/BET surface area* x density**) x 1000

Where surface area* is in sq. m/g, and density** is in g/cc. *Micrometrics Analytical Services* (MAS) will measure BET surface area by a gas absorption procedure and the real density by gas pycnometry. This gives a good estimate of average primary particle size. For further information see www.micromeritics.com, Micromeritics Analytical Services Downloads.

FULLERENES AND RELATED SUBSTANCES

Fullerenes and related substances are made by heating carbon (e.g. soot, graphite) to form nano-sized carbon 'balls'. These nanoparticles look like 'footballs' in being constructed of five (pentagon) and/or six (hexagon) carbon rings. Their carbon ring sizes make for stable 'ball-like' molecules of 60 or more carbon atoms and have some solubility in organic solvents. These carbon allotropes have a variety of exotic properties including electrochemical [Echegoyen & Echegoyen *Acc Chem Res* **31** 593 *1998*], ferromagnetism [Allemand et al. *Science* **253** 301 *1991*], superconductivity [Hebard et al. *Nature* **350** 600 *1991*], photophysical [Guldi *Chem Commun* 321 *2000*], anti-HIV bioactivity [Friedman et al. *J Am Chem Soc* **115** 6506 *1993*], and their 'aromatic' nature allows them to react accordingly and be functionalised (see below) for further chemical reactions [Kordatos et al. *J Org Chem* **66** 4915 *2001*]. New and useful applications are continually being found in nano science, medicine, pharmaceuticals, and nanotechnology [see references below].

FULLERENES

Fullerene C_{60} (Buckminsterfullerene C_{60}, Footballene, Buckyball 60) *[99685-96-8]* **M 720.66 and Fullerene C_{70}** *[115383-22-7]* **M 840.77.** ***Purification procedures:*** **(a)** This was purified from the soluble toluene extract (400mg) of the soot (Fullerite), formed from resistive heating of graphite, by adsorption on neutral alumina (100g, Brockmann I, 60 x 8cm). Elution with toluene/hexane (5:95 v/v) gives *ca* 250mg of quite pure C_{60}. It has characteristic spectral properties (see below). Further elution with toluene/hexane (20:80

v/v, i.e. increased polarity of solvent) provides 50mg of "pure" C_{70} [Allemand et al. *J Am Chem Soc* **113** 1050 *1991*].
Chromatography on alumina can be improved by using conditions which favour adsorption rather than crystallisation. Thus the residue from toluene extraction (1g) in CS_2 (*ca* 300ml) is adsorbed on alumina (375g, standard grade, neutral *ca* 150 mesh, Brockmann I) and loaded as a slurry in toluene/hexanes (5:95 v/v) to a 50 x 8cm column of alumina (1.5Kg) in the same solvent. To avoid crystallisation of the fullerenes, 10% of toluene in hexane is added quickly followed by 5% of toluene in hexane after the fullerenes had left the loading fraction (2-3 hours). With a flow rate of 15ml/minute the purple C_{60} fraction is eluted during a 3-4 hour period. Evaporation of the eluates gives 550-630mg of product which, after recrystallisation from CS_2/cyclohexane yields 520-600mg of C_{60} which contains adsorbed solvent. On drying at $275^o/10^{-3}$mm for 48 hours a 2% weight loss is observed although the C_{60} still contains traces of solvent. Further elution of the column with 20% of toluene in hexane provides 130mg of C_{70} containing 10-14% of C_{60} (by ^{13}C NMR). This was re-chromatographed as above using a half scale column and adsorbing the 130mg in CS_2 (20ml) on alumina (24g) which gave 105mg of recrystallised C_{70} (containing 2% of C_{60}). The purity of C_{60} can be improved further by washing the crystalline product with Et_2O and Me_2CO followed by recrystallisation from $*C_6H_6$ and vacuum drying at high temperatures.

(b) Carbon soot from resistive heating of a carbon rod in a partial helium atmosphere (0.3bar) under specified conditions is extracted with boiling $*C_6H_6$ or toluene, filtered and the red-brown solution is evaporated to give crystalline material in 14% yield which is mainly a mixture of fullerenes C_{60} and C_{70}. Chromatographic filtration of the 'crude' mixture with $*C_6H_6$ allows no separation of components, but some separation was observed on silica gel TLC with *n*-hexane or *n*-pentane, but not cyclohexane as eluents. Analytical HPLC with hexanes (5µm Econosphere silica) gave satisfactory separation of C_{60} and C_{70} (retention times of 6.64 and 6.93 minutes respectively) at a flow rate of 0.5ml/minute and using a detector at 256nm. HPLC indicated the presence of minor (<1.5% of total mass) unidentified C_n species with retention times of 5.86 and 8.31 minutes. Column chromatography on flash silica gel with hexane gives a few fractions of C_{60} with ≥95% purity, but later fractions contain mixtures of C_{60} and C_{70}. These can be obtained in 99.85 and >99% purity, respectively, by column chromatography on neutral alumina. [Ajie et al. *J Phys Chem* **94** 8630 *1990*.]

(c) Separation of C_{60} and C_{70} can be achieved by HPLC on a dinitroanilinopropyl (DNAP) silica (5µm pore size, 300Å pore diameter) column with a gradient from *n*-hexane to 50% CH_2Cl_2 using a diode array detector at wavelengths 330nm (for C_{60}) and 384nm (for C_{70}). [Cox et al. *J Am Chem Soc* **113**, 2940, *1991*.]
Soxhlet extraction of the "soot" is a good preliminary procedure, or if material of only *ca* 98% purity is required. Soxhlet extraction with toluene is run (20 minutes per cycle) until colourless solvent fills the upper part of the Soxhlet equipment (10 hours). One-third of the toluene remains in the pot. After cooling, the solution is filtered through a glass frit. This solid (purple in toluene) is *ca* 98% C_{60}. This powder is again extracted in a Soxhlet using identical conditions as before, and the C_{60} is recrystallised from toluene to give 99.5% pure C_{60}. C_{70} has greater affinity than C_{60} for toluene. [Coustel et al. *J Chem Soc, Chem Commun* 1402 *1992*.]

(d) Purification of C_{60} from a C_{60}/C_{70} mixture was also achieved by dissolving it in an aqueous solution of γ (but not β) cyclodextrin (0.02M) with refluxing. The rate of dissolution (as can be followed by UV spectroscopy) is quite slow and constant up to 10^{-5}M of C_{60}. The highest concentration of C_{60} in H_2O obtained was 8 x 10^{-5}M and a 2 γ–cyclodextrin:1 C_{60} clathrate is obtained. C_{60} is extracted from this aqueous solution with toluene and C_{60} of >99 purity is obtained by evaporation. With excess of γ–cyclodextrin more C_{60} dissolves and the complex precipitates. The precipitate is insoluble in cold H_2O but soluble in boiling H_2O to give a yellow solution. [Andersson et al. *J Chem Soc, Chem Commun* 604 *1992*.]

(e) C_{60} and C_{70} can also be readily purified by inclusion complexes with *p-tert*-butylcalix[6] and [8]arenes. Fresh carbon-arc soot (7.5g) is stirred with toluene (250ml) for 1 hour and filtered. To the filtrate is added *p-tert*-butylcalix[8]arene, refluxed for 10 minutes and filtered. The filtrate is seeded and set aside overnight at 20^o. The C_{60} complex separates as yellow-brown plates and is recrystallised twice from toluene (1g from 80ml) to give a 90% yield. Addition of $CHCl_3$ (5ml) to the complex (0.85g) releases C_{60} (0.28g, 92% from recrystallised complex).
p-tert-Butylcalix[6]arene-$(C_{60})_2$ complex is prepared by adding *p-tert*-butylcalix[6]arene (4.4mg) to a refluxing solution of C_{60} (5mg) in toluene (5ml). The hot solution is filtered rapidly and cooled overnight to give prisms (5.5mg, 77% yield). Pure C_{60} is obtained by decomposing the complex with $CHCl_3$ as above.

The *p-tert*-butylcalix[6]arene-$(C_{70})_2$ complex is obtained by adding *p-tert*-butylcalix[6]arene (5.8mg) to a refluxing solution of C_{70} (5mg) in toluene (2ml), filtering hot and slowly cooling to give red-brown needles (2.5mg, 31% yield) of the complex. Pure C_{70} is then recovered by decomposing the complex with $CHCl_3$.
Decomposition of these complexes can also be achieved by boiling a toluene solution over KOH pellets for *ca* 10 minutes. The calixarenes form Na salts which do not complex with the fullerenes. These appear to be the most satisfactory means at present for preparing large quantities of relatively pure fullerene C_{60} and C_{70} and is considerably cheaper than previous methods. [Atwood et al. *Nature* **368** 229 *1994*.]

(f) Rapid and economical purification of C_{60} fullerene *[22685-96-8, 99685-96-8]* **M 720.6, m >280º, flash point 94º**. Crude soot enriched in fullerenes with ~5% of soluble fullerenes available from suppliers such as *Texas Fullerene Corporation* (8926 Kirby Drive, Houston, USA) and *Polygon Enterprises* (P.O.Box 5536, Waco) was used. A concentrated slurry of fullerene extract (containing *ca* 2.5g of solid) in toluene was prepared by *Soxhlet* extraction of enriched soot with toluene, and evaporated. It was applied onto a glass filter funnel (*D4* 10cm diameter frit) which was loaded with a slurry of silica gel (125g, 230-400 mesh, ~0.05mm, Merck) and acid washed activated charcoal (63g, *Darco G60*, Fluka) in toluene (800ml), and shaken for 5 minutes to give a 5.5 cm high plug which was not allowed to run dry. The plug is covered with 1cm of washed sea sand. The loading of the plug and washing were performed under low vacuum suction (~ 50mm) applied to the suction flask. The plug was rinsed with toluene (3.5L) and the eluate turned intensely purple on further elution with EtOH (300ml). The total separation took ~15 minutes. The purple solution was evaporated to dryness and the residue was washed with small volumes of Et_2O on a *D4* frit. The yield of C_{60} was ~1.5g (60% of the total 75% present in the fullerene soot). Analysis by HPLC should show absence of C_{70} or higher fullerenes, but depending upon the original sample may show the presence of 1-3% of $C_{60}O$.

(g) A higher purity C_{60} can be obtained by using a glass filter funnel with a *D4* frit (diameter 6.5cm) on a suction flask filled with a slurry of silica gel (~84g, 230-400 mesh) and *Darco G60* charcoal (42g) in toluene to a plug height of 9cm; and covered with sea sand (1cm). A concentrated solution of 1.7g of soot extract in toluene (~500ml) was applied onto the plug which was washed with toluene (2.6L). The first fraction (1.4L) of deep purple eluate gave, after evaporation to dryness and washing with small portions of Et_2O on a *D4* frit, ~690mg of C_{60} (41% of the possible 75% of C_{60} in the soot extract) which contained 99.75% pure C_{60} by HPLC. A further fraction of 1.2L gave, after similar treatment, 143mg (14%) of C_{60} of 99.2% purity plus 0.8% of $C_{60}O$ as the only other product. [For HPLC and NMR see Isaacs et al. *Helv Chim Acta* **76** 1231 *1993*].

(h) Tour and coworkers [Scrivens et al. *J Am Chem Soc* **114** 7917 *1992*] described another ***gram-quantity purification procedure for C_{60} fullerene*** where a slurry of alkaline decolorising carbon Norit-A (36g) and silica gel (72g, flash chromatography grade 60 of 230-240 mesh ASTM, 0.040-0.063mm particle size) in toluene (200ml) was poured into a flash chromatography column (38mm in diameter and 45cm long, tape wrapped in case of cracking due to pressure and should be shielded) with a cotton plug at the bottom to form the stationary phase. The slurry was allowed to settle above the stationary phase and drained under a head of 7.5 psi of N_2 pressure applied at the top of the column which should not be allowed to dry out. A saturated solution of crude fullerenes (1.85g, extracted from carbon arc soot) in toluene (400ml, made homogeneous by sonication for ~30 minutes) was applied slowly at the top of the stationary phase. The pressure applied (7.5—10psi) provides a flow rate of ~16ml/minute. C_{60} elutes as a purple coloured solution after ~37 minutes in a volume of ~600ml. The eluate, after further ~36 minutes, is colourless and after ~3 minutes further it turns to red-brown when the more strongly adsorbed C_{70} fullerene begins to elute out. C_{60} fullerene (1.16g , 63 of the 73% of extractable C_{60} fullerene) is pure as shown by having one signal *only* in the ^{13}C NMR (125MHz, $*C_6H_6$) at δ 143.29 (100%) (compare with the spectrum of C_{70} fullerene below).
Repeated chromatography on neutral alumina yields minor quantities of solid samples of C_{76}, C_{84}, C_{90} and C_{94} believed to be higher fullerenes. A stable oxide $C_{70}O$ has been identified. These have been separated by repeated flash chromatography on alumina with gradient elution using hexane/toluene mixtures (starting from 95:5 and increasing proportions of toluene until the ratio of 50:50 was attained) [Diederich et al. *Science* **252** 548 *1991*].
Physical properties of Fullerene C_{60}*: C_{60} fullerene** *[135105-52-1]* **M 720.64, does not melt below 360º, and starts to sublime at 300º *in vacuo, and is now available commercially in a high state of purity. It is a mustard-coloured solid that appears brown or black with increasing film thickness. It is soluble in common organic solvents, particularly aromatic hydrocarbons which give a beautiful magenta colour. Toluene solutions are

purple in colour. It is soluble in $*C_6H_6$ (5mg/ml), but dissolves slowly. C_{60} crystallises in needles or plates. [Taylor *J Chem Soc, Chem Commun* 1423 *1990*.]
UV-Vis in hexanes: λ_{max} nm(log ε) 211(5.17), 227sh(4.91), 256(5.24), 328(4.71), 357sh(4.08), 368sh(3.91), 376sh(3.75), 390(3.52), 395sh(3.30), 403(3.48), 407(3.78), 492sh(2.72), 540(2.85), 568(2.78), 590(2.86), 598(2.87) and 620(2.60).
IR (KBr): ν_{max} 1429m, 1182m, 724m, 576m and 527s cm^{-1}. ^{13}C NMR: one signal with δ at 142.68.
C_{60} fullerene is a nano-channel organic semiconductor [Newman et al. *Chem Mater* **16** 4436 *2004*].

Purification of [5,6] C_{70} fullerene for derivatisation *[115383-22-7]* **M 840.8, m >280°**. By using a toluene extract (845mg) of Norit A (Aldrich) and a single-column purification using activated charcoal and derivatised polystyrene as stationary phases with toluene/1,2-dichlorobenzene then pure 1,2-dichlorobenzene as eluents, the six fractions obtained (confirmed by HPLC) were: (i) 205mg of pure C_{60}, (ii) 231mg of 38:62 C_{60}/C_{70}, (iii) 101mg of 88% pure C_{70}, (iv) 66mg of 92% pure C_{70}, (v) 131mg of 96% pure C_{70} and (vi) 57mg of 94% pure C_{70}. Fractions with >90% purity were satisfactory for the preparation of fullerene C_{70} derivatives. [Herrmann et al. *Helv Chim Acta* **78** 1673 *1995*; for column used see Tour above and below.] Fullerene C_{70} forms a nano adduct with 4,5-dimethoxy-1,2-quinonedimethane [Smith et al. *J Am Chem Soc* **117** 9359 *1995*, Tour *J Org Chem Perspective* **72** 7477 *2007*].
Tour and coworkers [Scrivens et al. *J Am Chem Soc* **114** 6939 *1994*] described a ***gram-quantity purification procedure for C_{70} fullerene*** where a slurry of alkaline decolourising carbon Norit-A (400g) and silica gel (800g, flash chromatography grade 60 of 230-240 mesh ASTM, 0.040-0.063mm particle size) in 1:1 toluene/ODCB (*o*-dichlorobenzene) was poured into a flash chromatography column (7cm in diameter and 120cm long, tape wrapped in case of cracking due to pressure and should be shielded) with a cotton plug at the bottom to form the stationary phase. The slurry was allowed to settle above the stationary phase and drained under a head of 15 psi of N_2 pressure applied at the top of the column which should not be allowed to dry out. The stationary phase was 75cm long after settling. A solution of carbon arc soot-extracted [Scrivens & Tour *J Org Chem* **57** 6932 *1992*] crude fullerene (10.0g, 36% C_{70} by HPLC analysis) in 1:1 toluene/ODCB (666ml) was applied slowly at the top of the column and eluted with a 15 psi of N_2 head pressure giving a flow rate of ~15ml/minute. Since more solvent was required, the tap at the bottom of the column was closed, the pressure was released, and more solvent was added. After the first colourless fraction (~2516ml), the second purple fraction (1520ml) of C_{60} fullerene was eluted and gave 5.97g of >99.9% pure C_{60} fullerene (by HPLC). Then the eluate became colourless again, but was followed by the red-brown colour of C_{70} fullerene when fraction 3 was collected and the mobile phase was replaced by pure ODCB. Fraction 3 (~750ml) contained a mixture of C_{60}/C_{70} (58:42, 1.3g) and was followed by a change of colour from red-brown to black indicating that pure ODCB had reached the bottom of the column. The black fraction 4 (750ml) was 90% enriched in C_{70} fullerene (0.65g), and the final fraction 5 (total 10L) contained 1.58g of C_{70} of >97% purity. The combined fractions weighed 9.5g (95% mass recovery). Additional column work of impure fractions could give ~3g of >97% pure C_{70} from 10g of crude material. The solubility of C_{70} in ODCB in saturated solutions appears to vary with temperature from 24mg/ml at 25° to >50mg/ml in hot ODCB which on standing overnight give an abundance of C_{70} as long crystals with 99.5% purity (by HPLC). The ^{13}C NMR (125MHz, $*C_6H_6$) of C_{70} has δ (relative peak heights) at 150.73 (4), 148.18 (11), 147.48 (5), 145.44 (9) and 130.94 (3) (compare with one peak at 142.68 for C_{60} fullerene previous entry).
Physical properties of Fullerene C_{70}*: C_{70} (5,6)-fullerene** *[115383-22-7]* **M 840.78, does not melt below 360°, and starts to sublime at 300° *in vacuo, and is now available commercially in a high state of purity. It is a reddish-brown solid but greenish black in thicker films. Solutions are port-wine red in colour. Mixtures of C_{60} and C_{70} are red due to C_{70} being more intensely coloured. It is less soluble than C_{60} in $*C_6H_6$ and also dissolves slowly. C_{70} gives orange-coloured solutions in toluene. Drying at 200-250° is not sufficient to remove all the solvent. Samples need to be sublimed to be free from solvent. [Taylor *J Chem Soc, Chem Commun* 1423 *1990*.]
UV-Vis in hexanes: λ_{max} nm(log ε) 214(5.05), 235(5.06), 249sh(4.95), 268sh(4.78), 313(4.23), 330(4.38), 359(4.29), 377(4.45), 468(4.16), 542(3.78), 590sh(3.47), 599sh(3.38), 609(3.32), 623sh(3.09), 635sh(3.13) and 646sh(2.80).
IR (KBr): ν_{max} 1430 m, 1428m, 1420m, 1413m, 1133mw, 1087w, 795s, 674ms, 642ms, 5778s, 566m, 535ms and 458m cm^{-1}.
^{13}C NMR [run in the presence of $Cr(pentan\text{-}2,4\text{-}dione)_3$ which induces a *ca* 0.12ppm shift in the spectrum]: Five signals with δ at 150.07, 147.52, 146.82, 144.77 and 130.28, which are unaffected by proton decoupling.
C_{70} fullerene is a nano-channel organic semiconductor [Newman et al. *Chem Mater* **16** 4436 *2004*].

C_{76} fullerene *[135113-15-4]* **M 912.85, melts > 350°.** It is now available commercially. After the sequential removal of C_{60} and C_{70} fullerenes from soot extracts (see above) on gel permeation columns (e.g. Buckyclutcher 1 column), C_{76} and higher fullerenes are obtained. These are further separated on a Trident-TriDNP functionalised silica column. After two HPLC runs on a C_{18} reverse phase (Vydac 201 TP C_{18}) column and eluting with 1:1 MeCN/toluene, pure C_{76} fullerene is obtained. The identity is confirmed by HPLC/GPC system with Waters 600E UV/VIS detection, mass and NMR spectroscopy. [Seleque et al. In Kadish and Ruoff (Eds) *Fullerenes: Recent Advances in the Chemistry and Physics of Fullerenes and Related Materials* The Electrochemical Soc. Inc, Pennington, NJ, 1994 ISBN 1566770823, Diederich & Whetten *Acc Chem Res* **25** 119 *1992*, Diederich et al. *Science* **254** 1768 *1991*.]

C_{78} (C_{2v})-fullerene *[136316-32-0]* **M 936.98, melts above 350°.** It is now available commercially. Pure material is obtained as in the previous purification and elutes after C_{76} fullerene, followed by **C_{78} (D_{3h})-fullerene**. The identities are confirmed by an HPLC/GPC system with Waters 600E UV/VIS detection, mass and NMR spectroscopy. [Seleque et al. In Kadish and Ruoff (Eds) *Fullerenes: Recent Advances in the Chemistry and Physics of Fullerenes and Related Materials* The Electrochemical Soc. Inc, Pennington, NJ, 1994 ISBN 1566770823, Diederich & Whetten *Acc Chem Res* **25** 119 *1992*, Diederich et al. *Science* **254** 1768 *1991*, MS and NMR: Taylor et al. *J Chem Soc, Chem Commun* 1043 *1992*.]

C_{84} fullerene *[135113-16-5]* **M 1008.94, melts above 350°.** It is now available commercially. Pure material is obtained as in the previous purification and elutes after C_{78} (D_{3h})-fullerene. It consists of at least two isomers. Common impurities are C_{82} and C_{86} fullerenes. The identities are confirmed by an HPLC/GPC system with Waters 600E UV/VIS detection, mass and NMR spectroscopy. [Seleque et al. In Kadish and Ruoff (Eds) *Fullerenes: Recent Advances in the Chemistry and Physics of Fullerenes and Related Materials* The Electrochemical Soc. Inc, Pennington, NJ, 1994 ISBN 1566770823, Diederich & Whetten *Acc Chem Res* **25** 119 *1992*, Diederich et al. *Science* **254** 1768 *1991*, Manolopoulos & Fowler *J Chem Phys* **96** 7603 *1992*.]

Higher Fullerenes, e.g. **C_{3996} fullerene** *[175833-78-0]* have also been isolated [*Chem Abstr* **124** 299339 *1996*.]

FUNCTIONALISED FULLERENES.
A large number of functionalised fullerenes have been reported. They are synthesised by chemical reactions at the double bonds of the 'ball' to form anchors for further condensation with small or large molecules such as proteins, lipids, DNA etc. They find applications in a variety of industries including drugs and pharmaceutical industries and in medicine. They are of nano size, can circulate in the animal's body and can be used to deliver substances to targeted tissues. A few of these are commercially available in chemical catalogues and some are described here to show how fullerenes can be made to react with reagents.

1,4-Bis(pentafluorobenzyl)[C_{60}]fullerene {7,8-dihydro-7,8-bis[(2,3,4,5,6-pentafluorophenyl)methyl]-[5,6]-fullerene-C60-I_h} *[1260376-31-5]* **M 914.6.** This bifunctional [C_{60}]fullerene was prepared in an argon atmosphere by adding potassium metal (124mg, 3.19mmol) in one portion to a freeze-thawed degassed mixture of fullerene (1.0g, 1.93mmol) and 1-methylnaphthalene (5.93g, 4.1.7 mmol, 30 equivalents, see [90-12-0]) in THF (150ml). This produced a dark red solution after stirring at ~25° for 3 hours under argon. Pentafluorobenzyl bromide (3.63g, 13.9mmol, tenfold excess) is then added, stirring is continued for 8 hours, the reaction is stopped by addition of aqueous NH_4Cl (0.5ml), the mixture is concentrated *in vacuo* down to ~10ml and the crude desired product is precipitated by addition of MeOH. It is purified by chromatography through silica gel and eluting first with CS_2/hexane (1:1) then CS_2 to provide the *bis-perfluorobenzyl fullerene* (830mg, 55%) which is fully characterised by its spectroscopic properties. It is stable in air and in solution (e.g. $CHCl_3$). For further purification preparative HPLC or GPC may be necessary. It is identified by investigations of dynamic light scattering (DLS), X-ray diffraction (XRD), differential scanning calorimetry (DSC), thermogravimetric analysis (TG-DTA), and of its electrochemical (OVP) properties. The data showed that the perfluoroaromatic rings interact in a face-to-face π-π manner with the [C_{60}]fullerene surfaces and exhibit unique aggregation-deaggregation behaviour. These properties allow this fullerene to be used for high-performance organic photovoltaic devices. [see Y. Matsuo and coworkers in Li et al. *Chem Commun* **46** 8582 *2010*, Matsuo et al. *Synfacts* **2** 148 *2011*.] *Note* that the name within the chain brackets above is the name given by the *Chemical Abstract Service*.

tert*-Butyl (1,2-methanofullerene C_{60})-61-carboxylate [*6,6-closed* 1,2-dihydro-1,2-methanofullerene C_{60})-61-carboxylic acid *tert*-butyl ester]** *[150493-29-1]* **M 834.8.** The crude *tert*-butyl ester was prepared as for the ethyl ester below and obtained in 25% yield as a 1:1:3 mixture of 6,6-closed, trans-5,6-open and cis-5,6-open esters. As for the diethyl ester below, the mixture (20mg) was equilibrated in boiling toluene to give pure *6,6-closed-tert*-butyl ester (15mg 75%) which held toluene very strongly. It has UV/VIS with λ_{max} nm(ε) in toluene at 334 (40250), 406 (*sh* 3850), 429 (1800), 503 (1150), 593 (*br* 750); the IR (KBr) has strong bands at ν_{max} 526, 1141, 1733 cm^{-1} as well as 5 other medium-weaker bands; the ^1H NMR (500 MHz, in $*C_6D_6$) has δ at 4.38 (*s* 1 H), 1.51 (*s*, 9 H), and the ^{13}C NMR (125 MHz, $CS_2/(CD_3)_2CO$ 10:1) has δ at 164.33(C***OO), 149.07—71.74 (32 fullerene resonance), 83.28 [COO***C***$(CH_3)_3$], 41.21 (***C***HCOO) and 28.58 [(***C***$H_3)_3$]. The FAB-MS has a peak at 834 (M^+). [Isaacs et al. *Helv Chim Acta* **76** 1231 *1993*, Isaacs & Dieterich *Helv Chim Acta* **76** 2454 *1993*.]

Diethyl (1,2-methanofullerene C_{60})-61,61-carboxylic acid [*6,6-closed*-1,2-dihydro-1,2-methanofullerene C_{60})-61,61-carboxylic acid diethyl ester] *[155679-98-4]* **M 878.8, m >270°**. If the ^1H NMR spectrum indicated the presence of isomeric esters then dissolve it in chlorobenzene (0.2g in 100ml) and heat it under reflux for 24 hours to convert the isomers to the more stable [6,6-closed]-ester. Column chromatography on silica and elution first with toluene/hexane (1:1) then toluene followed by recrystallisation from $CHCl_3$/MeOH and drying (60°/0.1 Torr, 6 hours) provided the desired diester as a dark solid [R_F: SiO_2 toluene is 0.50]. Store it at 2-8°. It has IR (KBr) with ν_{max} bands at 1061w, 1095m, 1186 (C_{60}), 1206m, 1234s, 1266m, 1295m, 1428 (C_{60}), 1745 (C=O) and 2979w cm^{-1}. The ^1H NMR (200MHz; $CDCl_3$) has δ_H at 4.75 (q, *J* = 7Hz) and 1.53 (t, 6H, *J* = 7Hz); and the ^{13}C NMR (125MHz; $CDCl_3$) has δ_C at 163.61, 145.33—139.04 (16 peaks), 71.61, 63.42, 52.21, 14.22. The *di-tert-butyl ester* was similarly purified (see above). [Bingel *Chem Ber* **126** 1957 *1993*, Dieterich et al. *J Chem Soc, Perkin Trans II* 391 *1994*.]

Diethyl (1,2-methanofullerene C_{70})-71,71-carboxylate [*6,6-closed*-1,2-dihydro-1,2-methanofullerene C_{70})-71,71-carboxylic acid diethyl ester] *[153218-95-2]* **M 998.9.** It was prepared by reaction of diethyl bromomalonate with fullerene C_{70} in the presence of DBU in toluene (4 hours, ~25°), filtered and purified by chromatography through Kieselgel (0.063—0.2mm) by eluting with a gradient of toluene/*iso*-hexane (1/1 to 4/1). This gave the *diester* in 60% yield [R_F: SiO_2 toluene is 0.50], with a 40% recovery of the fullerene. Store it at 2-8°. The ^1H NMR (360MHz; $CDCl_3$) has δ_H at 4.75 (q, *J* = 7.1Hz) and 1.46 (t, 6H, *J* = 7.1Hz); and the ^{13}C NMR (100MHz; $CDCl_3$) has δ_C at 163.45, 155.33—130.83 (34 peaks), 66.90, 66.24, 63.47, 37.22, 14.23. [Bingel *Chem Ber* **126** 1957 *1993*.]

1,2-Dihydro-[1,2]fullereneC_{60}[3,4]pyrrolidin-1-ylethoxyethoxyethylammonium bis-trifluoroacetate {2-[2-[2-(2'*H*-[5,6]fullereno-C60-I_h-[1,9-*c*]pyrrol-1'(5'*H*)-yl)ethoxy]ethoxy]ethanamine bis-2,2,2-trifluoro-acetate} [C_{60} =CH)$_2$NH$^+$-$CH_2CH_2OCH_2CH_2OCH_2CH_2NH_3^+$. $2CF_3COO^-$, $C_{70}H_{20}O_6N_2F_6$] *[356066-52-9 for mono(trifluoroacetate)]* **M 1123.0.** *N*-Boc-aminoethoxyethoxyethylaminoacetic acid (423mg, 1.38mmol, see below in SWCNT[=CH)$_2$N-CH_2CH_2O-CH_2CH_2O-$CH_2CH_2NH_3^+$. HCl]$_n$), paraldehyde (456mg, 3.45mmol) and fullerene C_{60} (500mg, 0.69mmol) in toluene (300ml) are refluxed for 1 hour. After cooling to ~25° the mixture is applied onto a column of silica gel (NM Kieselgel 60, 70-320 mesh) and eluted with 9:1 toluene/EtOAc to give the analytically pure (elemental C, H, N) **C_{60}=*N-Boc-pyrrolidinyl*** derivative (212mg, 0.29mmol, 31%). It has IR-DRIFT (KBr) with bands at ν_{max} 545, 794, 1121, 1168, 1457, 1498, 1710, 2853, 2921, 3444 cm^{-1}; the UV-VIS (cyclohexane) has λ_{max} at 254, 309, 429, 466sh, 546sh, 703 nm; the ^1H NMR (200 MHz, $CDCl_3$, TMS) has δ at 5.08 (bs, 1H), 4.50 (s, 4H), 4.05 (t, *J* = 5.5Hz, 2H), 3.77 (m, 4H), 3.60 (t, *J* = 5.3Hz, 2H), 3.36 (m, 4H), 1.44 (s, 9H); the ^{13}C NMR (50 MHz, $CDCl_3$, TMS) has δ at 156.0, 155.1, 147.3, 146.3, 146.1, 145.7, 145.4, 145.3, 144.6, 143.1, 142.7, 142.3, 142.1, 141.9, 140.2, 136.2, 79.3, 70.9, 70.7, 70.6, 70.5, 68.6, 54.4, 28.6; and the ES-MS showed a peak at *m/z* 995 (MH^+).

The *N*-Boc group is removed by treating the pure C_{60}=*N-Boc-pyrrolidinyl* derivative (150mg, 0.14mmol) in CH_2Cl_2 (3ml) with CF_3COOH (3ml), and stirring for 3 hours. The solvent is removed *in vacuo*, the residue is washed with toluene and dried *in vacuo* to give the analytically pure (elemental C, H, N) functionalised title ***fullerene* C_{60}=*N-pyrrolidinyl bis-trifluoroacetate salt*** (168mg, 0.15mmol, ~99%). This has IR-DRIFT (KBr) with bands at ν_{max} 525, 715, 1130, 1190, 1480, 1515, 1680, 2890 cm^{-1}; UV-VIS (cyclohexane) with λ_{max} at 331, 430, 484sh, 684 254, 309, 429, 466sh, 546sh, 703 nm; the ^1H NMR (200 MHz, DMSO-d_6, TMS) has δ at

7.81 (brs, 3H), 4.58 (s, 4H), 3.93 (t, *J* = 5.5Hz, 2H), 3.71-3.43 (m, 6H), 3.32 (m, 2H), 2.95 (m, 2H); the ^{13}C NMR (50 MHz, DMSO-d_6, TMS) has δ at 156.0, 147.4, 146.7, 146.4, 146.2, 146.0, 145.5, 145.4, 144.7, 143.3, 142.8, 142.5, 142.2, 142.0, 140.2, 136.4, 135.4, 71.5, 70.5, 70.1, 68.0, 67.5, 54.1; and the ES-MS showed a peak at *m/*z 896 (MH^+). Related compounds with a two carbon atoms and a thirteen carbon atom chain between the pyrrolidine nitrogen atom and the terminal amino nitrogen atom have also been prepared. The ω-primary amino groups at the end of the chains were derivatised (e.g. with 12-acetylsulfanildodecanoic acid in the presence of EDCI and HOBt for self-assembled monolayers (SAMs) purposes, or various fluorescent indole-2-carboxylic acids) by standard procedures. Useful applications for nano materials science and nano medicinal chemistry (e.g. by linking to DNAs or other biological materials) have been made possible with such fullerene precursors by M. Prato and coworkers. [Kordatos et al. *J Org Chem* **66** 4915 *2001*.]

Ethyl (1,2-methanofullerene C_{60})-61-carboxylate [*6,6-closed* 1,2-dihydro-1,2-methanofullerene C_{60})-61-carboxylic acid ethyl ester] *[50493-27-9]* **M 806.8.** Fullerene C_{60} reacts with an equimolar amount of ethyl diazoacetate in boiling toluene for 7 hours to provide a 30% yield of a 1:1:3 mixture of 6,6-closed : trans-5,6-open : *cis*-5,6-open *tert*-butyl (1,2-methanofullerene C_{60})-61-carboxylate. This mixture was isolated by applying the residual solid from the reaction onto a silica gel column which was first eluted with hexane to remove fullerene C_{60} then with toluene-hexane (1:1) to provide the mixture at R_F *ca* 0.43. The mixture was isomerised almost entirely to the more stable 6,6-close ester by refluxing it (35mg) in toluene (105ml) for 24 hours when the initial purple solution turned pink in colour. Chromatography on silica gel as before provided a pink-red product eluting at the same R_F *ca* 0.43 which was then evaporated to dryness. The black microcrystalline residue was washed with Et_2O and dried at 25°/0.1 Torr (31mg, 89%). It holds residual toluene tenaciously. It has UV/VIS with λ_{max} nm(ε) in toluene at 331 (40250), 395 (*sh* 5250), 404 (*sh* 3300), 417 (1900), 429 (2250), 495 (*br* 1250); the IR (KBr) has strong bands at ν_{max} 527, 1155, 1185, 1742 cm^{-1} as well as 6 other medium to weak bands; the ^1H NMR (400 MHz, in $*C_6D_6$) has δ at 4.31 (*s* 1 H), 4.10 (*q*, *J* = 7.1Hz, 2 H), 1.06 (*t*, *J* = 7.1Hz, 3 H), and the ^{13}C NMR (125 MHz, $CS_2/(CD_3)_2CO$ 10:1) has δ at 165.44 (***C***OOEt), 149.07—71.59 (32 fullerene resonance), 62.70 ($CH_3\boldsymbol{C}H_2$), 40.01 (***C***HCOOEt) and 14.99 ($\boldsymbol{C}H_3CH_2$). The FAB-MS has an *m/z* peak at 807 (M^+), and the elemental analysis is consistent with $C_{62}H_6O_2$. [Isaacs et al. *Helv Chim Acta* **76** 1231 *1993*, Isaacs & Dieterich *Helv Chim Acta* **76** 2454 *1993*.]

Fullerene C_{60}–γ-lactone esters. G-W. Wang and coworkers [Li et al. *Org Lett* **21** 4896 *2010*] have improved the condensation yields of diethyl malonate esters with [C_{60}]fullerene to form the disubstituted fused **γ**-lactone esters by using $Fe(ClO_4)_3$ instead of $Mn(OAc)_3$ for assistance (catalysis). Although the yields are still low, they are however, considerably higher when mediated by the iron perchlorate, and the products are cleaner. The solvent is *o*-dichlorobenzene and the ratios of reagents are 1:2:2:20 for [C_{60}]fullerene:EtOCOCH**R**COOEt: $Fe(ClO_4)_3$:Ac_2O. The following results were obtained: **R** ester (reaction temperature, reaction time, **yield** of γ-lactone ester, consumed fullerene): **Me** (80°, 20 minutes, **34%**, 55%); **Et** (80°, 20 minutes, **37%**, 71%); **PhCH$_2$** (80°, 30 minutes, **27%**, 61%); **Ph*** (0°, 180 minutes, **12%**, 67%); **Br** (80°, 30 minutes, **22%**, 56%); and **EtOCO** (110°, 20 minutes, **16%**, 53%); * reactant ratio was 1:2:2:50. The structures of the lactones are consistent with their HRMS, ^1H NMRs, ^{13}C NMRs, FT-IRs and UVs. It should be possible to convert these lactones into hydrofullerenes, fullerene hemiacetals, fullerene hemiketals and fullerenols. [Li et al. *Synfacts* **1** 38 *2011*.]

Fullerene C_{60}/Poly(bisphenol A)carbonate. C_{60} is a known 'radical sponge' [Morton et al *J Am Chem Soc* **114** 5454 *1992*, McEwen et al. *J Am Chem Soc* **114** 4412 *1992*]. It reacts readily with free radicals and undergoes photolysis to generate C_{60} radical ions. Thus irradiating a mixture of C_{60} and poly(bisphenol A)carbonate polymer (PC, [25037-45-0]) at room temperature with a conventional UV lamp, or warming the mixture at 60° with AIBN (a radical initiator, see [78-61-1]) results in fullerenated-PC. By controlling the ratio of reagents (i.e. 5.4mg C_{60}/500mg PC in 1,1,2,2-tetrachloroethane), a C_{60}/PC can be obtained with a C_{60} content as high as 6.3% (i.e. >2 C_{60} per PC chain) in ~99% yield. Multi-additions of PC did not lead to heavy cross-linking. The fullerenated polymer is a brown powder which is soluble in common organic solvents such as THF and $CHCl_3$. When the polymer is dissolved in THF (a solvent that does not dissolve C_{60}) and the solution is precipitated into hexane through a filter, no particles are left on the filter, and the hexane supernatant is colourless. This shows that all the C_{60} is incorporated into the polymer. The precipitate is then collected and dried under high vacuum to constant weight. The C_{60} content is 1.16 wt%, has M_n ~27,000; the UV (0.3mg/ml in THF) has λ_{max} at 238.9, 259.4, 262.0, 287.2, 329.5sh nm, and the IR (KBr) has ν_{max} at 3040w, 2968s,

1778vs, 1602m, 1506s, 1410m, 1386w, 1364m, 1230vs, 1194s, 1162s, 1080s, 1014s, 888m, 830s, 768m, 556s, 528w cm^{-1}. This fullerenation provides a versatile synthetic tool for making processable fullerene polymers and opens opportunities for exploring fullerene-based speciality materials with properties not found in the unconjugated polymers. [Tang et al. *Macromolecules* **30** 2848 *1997*.]

(1,2-Methanofullerene C_{60})-61-carboxylic acid [*6,6-closed*-1,2-dihydro-1,2-methanofullerene C_{60})-61-carboxylic acid] *[155116-19-1]* **M 778.7.** Attempted hydrolysis of the ethyl ester (see [155679-98-4] above) was unsuccessful, however, treatment of the *6,6-closed*-ethoxycarbonylmethyl ester with BBr_3 in $*C_6H_6$ under N_2 and stirring for 9 hours gave an 82% yield of the acid. Similarly the *tert*-butyl ester (see [150493-29-1] above), but in refluxing toluene for 8 hours, gave a 77% yield of the acid. After hydrolysis, the acid was purified by dissolving it in $CHCl_3/Me_2SO$, re-precipitating with hexane and drying overnight at 25°/0.1 Torr, or at 60°/0.1 Torr for 12 hours. The brown or black solid *6,6-closed-acid* was mostly insoluble in common solvents and slightly soluble in bromobenzene and 1,2-dichlorobenzene. This 6,6-closed acid (i.e. cyclopropane acid) has IR (KBr) with strong bands ν_{max} at 525, 699, 810, 847, 1013, 1426, 1785, 1794 cm^{-1} and twenty other medium to weak bands. The ^1H NMR (300 MHz, in $CHCl_3/Me_2SO$, 1:1) has one signal for the cyclopropane H at 5.13 ppm, the ^{13}C NMR consists of 32 signals between δ 136 and 167, and signals at δ 40.34 and 71.66. Elemental analysis is consistent with the formula $C_{62}H_2O_2$. $0.5Me_2SO$.
With alcohols in the presence of dicyclohexylcarbodiimide, 1-*H*-benzotriazol-1-ol and a base [e.g. 4-$(Me_2N)C_6H_4N$ or Et_3N] in bromobenzene, the corresponding esters were obtained. Similarly peptides with *methyl glycinate* and *methyl*-L-*phenylalaninate* were obtained by using the corresponding amino acid esters. [Isaacs & Diederich *Helv Chim Acta* **76** 2454 *1993*, Diederich et al. *Chem Soc Rev* **23** 243 *1994*.]

6,9,12,15,18-Pentamethyl-1,6,9,12,15,18-hexahydro(C_{60}-I_h)fullerene *[244229-54-7]* **M 796.7.** Preparation of these substituted fullerenes should be carried out in Schlenk-type equipment under an inert atmosphere (N_2 or argon), in dry solvents and reagents (at least in the early stages of the reactions), and any oxygen or air in solvents should be flushed out by bubbling dry inert gas through them. Microcrystalline [C_{60}]fullerene (2.0g, 2.78mmol, [99685-96-8]) in 1,2-dichlorobenzene (90ml), cooled in an ice-water bath, stirred under reduced pressure (1mm) to remove dissolved O_2, and warmed to ~25°, is added during 15 minutes to a stirred mixture of $CuBr.SMe_2$ (6.84g, 33.3mmol, use an efficient fume cupboard) in THF (47ml) at ~25° to which is previously added MeMgBr in THF (3 M, 11.1ml, 33.3mmol) followed by DMI (3.62ml, 33.3mmol, see [80-73-9]) and rapidly warmed to ~35° within 5 minutes. The colour of the white suspension soon turned to dark brown. After stirring at 35° for 40 minutes under a flow of N_2 (note that some liberation of ethane may occur), a degassed saturated aqueous NH_4Cl solution (3.0ml) is added *via* a syringe, the colour of the solution changes from dark brown to red-brown and the mixture is stirred under a vacuum (*ca* 1mm) at ~25° to remove THF and Me_2S and reduce it to half its volume. This is diluted with degassed toluene (200ml) and subjected to silica gel flash chromatography (45 x 200mm size, using 90g of silica gel 230-450 mesh) with toluene as eluent (total volume 100ml). It should be done as rapidly as possible, as care should be taken to avoid oxygen and formation of $C_{60}Me_5O_nH$ (n = 2-3). The vermillion eluate is evaporated at ~40°/10mm then at 80° (to remove 1,2-dichlorobenzene) until solid begins to appear on the sides of the flask. N_2 is allowed to enter the evacuated flask and degassed MeOH is added along the inside wall of the flask, whereby the mixture becomes cloudy, and MeOH (~400ml total) is added until precipitation is complete. The solid is filtered off, washed with MeOH (5 x 10ml) and hexane (3 x 10ml) and dried *in vacuo* (1mm) to give red microcrystals of pentamethylfullerene (2.08g, 94%) of ~91% purity. Purity and/or purification is carried out using a Buckyprep or ODS column (4.6 x 150mm, flow rate 1ml/minute) and eluting with toluene/*i*-PrOH (7:3) or (3:7) respectively. The solid should be stored in an inert atmosphere, as on storage in air it deteriorates slowly over several months, and in solution in the presence of air its purity decreases by 80% in 24 hours. It has IR (neat) with ν_{max} bands at 2973, 2912, 2858, 1572, 1546, 1518, 1459, 1370, 1324, 1286, 1265, 1234, 1169, 1145, 1128, 792, 747, 684 cm^{-1}; the ^1H NMR (500 MHz, $CS_2/(CD_3)_2CO$ 5%) has δ at 2.34 (s, 6H), 2.35 (s, 6H), 2.46 (s. 3H), 4.50 (s, 1H, C_{60}-*H*); and the ^{13}C NMR (100 MHz, $CS_2/(CD_3)_2CO$ 5%) has δ at 27.23 (2C), 27.61 (2C), 33.14 (1C), 51.37 (1C), 51.45 (2C), 53.51 (2C), 59.75 (1C), 143.61 (2C), 144.12 (2C), 144.48 (2C), 144.53 (2C), 144.77 (2C), 144.89 (4C) 145.20 (2C), 145.42 (2C), 145.87 (2C), 145.96 (2C), 146.98 (1C), 147.14 (2C), 147.24 (2C), 148.03 (2C), 148.12 (2C), 148.28 (3C), 148.54 (2C), 148.60 (2C), 148.91 (4C), 149.10 (2C), 150.12 (2C), 154.27 (2C), 154.37 (2C), 154.62 (2C), 157.76 (2C). [Matsuo, Mueamatsu, Tahara, Koide and Nakamura *Org Synth* **83** 80 *2006*, Matsuo et al. *Functional Organic Materials* 58-80 *2007*.]

The procedure described above is unique as all five substituents are symmetrically placed on the bridgehead carbons of five six-membered rings surrounded by a fused five membered cyclopentadiene ring (X-ray evidence). Similar reactions also produce very high yields of fullerenes with *five* C_6H_5*, five 4-*$CF_3C_6H_5$*, five 4-*$MeOC_6H_4$*, five 4-*ClC_6H_5*, five 4-*PhC_6H_5*, five (E)-1-propenyl, five (Z)-1-propenyl* and *five (E)-2-phenylethenyl* groups all symmetrically placed as in the pentamethyl derivative above. [see Matsuo, Mueamatsu, Tahara, Koide and Nakamura *Org Synth* **83** 80 *2006* and references therein.]
The hydrogen atom of the central cyclopentadiene ring can be displaced by potassium with t-BuOK to form the $K(C_{60}Me_5)$ complex in which the potassium atom can then be displaced to form iridium complexes such as $Ir(\eta^5\text{-}C_{60}Me_5)(CO)_2$ [Matsuo, Iwashita and Nakamura *Organometallics* **24** 89 *2005*], and with rhodium to form $Rh(\eta^5\text{-}C_{60}Me_5)(CO)_2$ [Sawamura, Kuninobu and Nakamura *J Am Chem Soc* **122** 12407 *2000*], structures which are supported by X-ray structure analyses. The same cyclopentadiene can complex with Fe and cyclopentadiene (Cp) to form a hybrid of 'buckyferrocene' $Fe(C_{60}Me_5)Cp$ [Sawamura et al. *J Am Chem Soc* **124** 9354 *2002*, Nakamura *Pure Appl Chem* **75** 427 *2003*].

***N*-Tosyl[1,2]-aziridino[C_{60}]fullerene {2*a*[(4-methylphenyl)sulfonyl]-2*a*-aza-1,2(2*a*)-homo[5,6]fullerene-C60-I_h** *[226909-63-3]* **M 889.0.** This useful fullerene precursor is readily prepared. In a dry Schlenk flask with flushing argon is added CuCl (1.2mg, 12μmol), *o*-dichlorobenzene (40ml) and 2,6-toluidine (2.0 μL, 24 μmol), then stirring at ~25° for 30 minutes, followed by adding C_{60} fullerene (432mg, 600μmol) and TsN=IPh (224mg, 600μmol, see synthesis below*). The mixture is stirred ~25° for 12 hours and purified by flash chromatography through silica gel (toluene/hexane 1.2 ~ 1.1) to provide the pure aziridinofullerene (228mg, 43%) as a dark brown solid [and recovered 185mg, 43%, of unreacted C_{60} fullerene]. It has ^{1}H NMR (400 MHz, $CDCl_3/CS_2$ = 1:1, TMS) with δ at 2.56 (s, 3H), 7.50 (d, *J* = 8.3Hz, 2H), 8.19 (d, *J* = 8.3Hz, 2H); the ^{13}C NMR (100 MHz, $CDCl_3$, $CHCl_3$ at δ 77.0 standard) has δ at 21.75, 79.69, 128.44, 129.93, 135.63, 140.75, 141.20, 141.71, 142.02, 142.63, 142.94, 142.99, 143.12, 143.74, 143.81, 144.01, 144.36, 144.83, 144.89, 144.97, 145.14, 145.34; and the HRMS (ESI-TOF; negative) showed a peak at *m/z* 889.0205, and 889.0203 is the calculated value for $C_{67}H_7NO_2S$ (M^-). Note that other Cu catalysts and other pyridine bases resulted in lower yields of this reaction. Itami and coworkers [Nambo et al. *J Am Chem Soc* **133** 2402 *2011*] developed the use of this aziridinofullerene as a versatile platform for preparing a variety of functionalised fullerenes. Thus it reacts with aryl and heteroaryl compounds (5% TfOH, 1,2-$Cl_2C_6H_4$, 100°, 12 hours) to replace the 1,2-aziridine by two aryl or heteroaryl groups to form 1,4-disubstituted fullerenes in over 80% yields; it reacts with bifunctional nucleophiles of the type R-Z(**H**)=Y(X-**H**)-R' (10% TfOH, 1,2-$Cl_2C_6H_4$, 100°, 12 hours) to form 1,2-disubstituted fullerenes (1,2-disubstituted fullerenes fused with a 5-membered ring where the **H's** are replaced by bonds with C1 and C2 of the fullerene), such as 2,3-furano, 2,3-pyrrolo, 2,3-thiazolo-, 1,2-cyclic [1,3,2]-dioxaborolan- fullerenes in over 60% yields; it reacts with 2,2'-bithiophenes in various ways, and undergoes formal [2+2] cycloaddition reactions with 1,2-[bis(*p*-methoxyphenyl]acetylyene (10% TfOH, 1,2-$Cl_2C_6H_4$, 100°, 12 hours) to form a 3,4-adduct (cyclobutene) which retains the 1,2-aziridino moiety in 81% yields. Some of the structures were supported by X-ray crystal structure analysis.

***[*N*-(*p*-Toluenesulfonyl)imino]phenyliodinane (TsN=IPh)** *[55962-05-5]* **M 373.1.** Toluene-*p*-sulfonamide (3.42g, 20mmol) and diacetoxyiodobenzene (6.4g, 20mmol, see [2340-34-4]) are added to a solution of KOH (2.8g, 50mmol) dissolved in MeOH (80ml) at 0°, and then stirred at 25° for 3 hours. The mixture is poured into distilled water at 0°, kept at 4° overnight, the solid is filtered off, drained and recrystallised from hot MeOH (20ml) to give TsN=IPh (2.6g, 35%). It has ^{1}H NMR (200 MHz, DMSO-d_6, TMS) with δ at 7.80-7.73 (m, 2H), 7.56-7.48 (m, 3H), 7.40-7.31 (m, 2H), 7.15-7.10 (m, 2H), 2.34 (s, 3H). [Heuss et al. *Inorg Chim Acta* **342** 301 *2003*.]

2,5,10-Triphenyl-2,5,6,10-tetrahydro(C_{70}-I_h)fullerene [$C_{70}(4\text{-}PhC_6H_4)_3H$] *[244237-40-9]* **M 1073.0.** When a procedure similar to the preparation of $C_{60}Me_5H$ above is applied to fullerene-C_{70} only three substituents are inserted. A suspension of $CuBr.SMe_2$ (374mg, 1.82mmol, 30 equivalents) in THF (23.0ml) is treated with PhMgBr (0.98M, 1.86ml, 1.82mmol, 30 equivalents) and stirred at 28° for 20 minutes. To the resulting yellow suspension is added a degassed solution of C_{70} (49.6mg, 59μmol) in 1,2-dichlorobenzene (25ml) and stirring is continued for 24 hours. The reaction is treated with 5% aqueous HCl, the organic layer is washed with H_2O, brine, dried ($MgSO_4$), evaporated to a small volume and diluted with MeOH to give a dark brown precipitate which is washed thoroughly with MeOH, Et_2O, H_2O again and dried *in vacuo* to give $C_{70}Ph_3H$ (61.2mg, 95%,

96% purity, *cf* $C_{60}Me_5H$ above). The ^1H NMR (400 MHz, $CDCl_3$) has δ at 7.8-7.78 (m, 2H), 7.74-7.70 (m, 2H), 7.61-7.57 (m, 3H), 7.39-7.23 (m, 8H), 4.43 (s, 1H); and the ^{13}C NMR (100 MHz, $CDCl_3$-CS_2) has δ at 160.70, 155.67, 155.07, 153.80, 152.62, 153.14, 152.62, 152.19, 150.16, 149.87, 149.57, 149.42, 149.39, 149.17, 149.08, 148.95, 148.82, 148.68, 148.59, 148.30, 148.21, 148.09, 147.92, 147.88, 147.77, 147.68, 147.18, 147.06, 147.00, 146.65, 146.61, 146.44, 146.23, 146.18, 145.84, 145.64, 145.51, 145.32, 145.06, 145.03, 144.92, 144.88, 144.74, 144.48, 144.15, 143.97, 143.43, 142.99, 142.81, 142.21, 142.18, 140.50, 140.40, 139.54, 139.20, 138.33, 136.87, 133.08, 131.96, 131.93, 131.82, 131.72, 131.59, 131.43, 131 43, 131.41, 130.65, 128.96, 128.88, 128.78, 128.16, 128.04, 127.71, 127.60, 127.47, 127.27, 127.15, 126.70, 126.42, 56.23, 56.19, 55.5; and the APCI-MS has *m/z* 1072 [$(M - H)^-$]. Similarly prepared are $C_{70}Me_3H$, C_{70}(4-$PhC_6H_4)_3H$, C_{70}(4-$ClC_6H_4)_3H$, and C_{70}(1-naphthyl)$_3$H. [Sawamura et al. *J Mater Chem* **12** 2109 *2002*, *cf* Matsuo, Mueamatsu, Tahara, Koide and Nakamura *Org Synth* **83** 80 *2006* and references therein.] C_{70}(4-$CF_3C_6H_4)_3H$ is also prepared similarly and is believed to proceed by formation of [$(4\text{-}CF_3C_6H_4)_2Cu^-$] from the reaction between the arylMgBr and $CuBr.SMe_2$ which attacks successively three six-membered rings around a cyclopentadiene ring to give the intermediate $C_{70}(4\text{-}CF_3C_6H_4)_3Cu^-Ar$ which decomposes on addition of acid or NH_4Cl to provide the desired $C_{70}(4\text{-}CF_3C_6H_4)_3H$. When the latter, in THF-d_8, is treated with 1 equivalent of *t*-BuOK or TlOEt at 25°, the colour changes from reddish-brown to dark red to provide *K*[η^5-$C_{70}(4\text{-}CF_3C_6H_4)_3$] {whose ^1H NMR (400 MHz, THF-d_8) has δ at 8.07-8.05 (m, Ar-H, 6H), 7.57-7.54 (m, ArH, 6H); and the ^{13}C NMR (100 MHz, THF-d_6) has δ at 166.18, 160.50, 153.30, 151.99, 151.04, 150.32, 149.79, 149.77, 149.17, 148.88, 148.82, 148.48, 148.44, 148.26, 147.14, 146.90, 146.81, 146.37, 146.19, 146.07, 145.72, 145.61, 145.43, 144.71, 142.53, 142.28, 137.87, 136.81, 143.54, 134.46, 133.24, 132.92, 132.60, 129.36-129.23 (m), 128.93, 125.80-125.77 (m), 125.6 (q, *J* = 271.19Hz), 121.07, 61.06, 59.11}, or *Tl*[η^5- $C_{70}(4\text{-}CF_3C_6H_4)_3$] {whose ^1H NMR (400 MHz, THF-d_8) has δ at 8.09-8.07 (m, Ar-H, 6H), 7.59-7.53 (m, ArH, 6H)} respectively [Sawamura, Iikura, Hirai and Nakamura *J Am Chem Soc* **120** 8285 *1998*].

1,4,11,15,30-Pentakis(4-hydroxyphenyldimethylsilylmethyl)-2*H*-1,2,4,11,15,30-hexahydro-(60)fullerene {[4-$HOC_6H_4Si(Me)_2CH_2]_5$-2*H*-1,2,4,11,15,30-hexahydro-(C_{60}-I_h)fullerene, 1,7,8,11,24,27-hexahydro-1,7,-11,24,27-pentakis(dimethyl 4-hydroxyphenylsilyl)methyl-[5,6]fullerene-C60-I_h} *[658080-04-7]* **M 1549.1.** This functionalised fullerene can be used as an example of a molecule to which long chains can be coupled for specialised purposes. Typically, using Schlenk equipment under N_2 or argon in strict absence of H_2O, the protected Grignard compound Me_2(4-tetrahydropyranylOC_6H_4)$SiCH_2MgCl$ (0.656M in THF, 13.0ml, 9.84mmol) is added to a purple suspension of a white powder of $CuBr.SMe_2$ (3.00g, 14.6mmol) and microcrystalline [C_{60}]fullerene (400mg, 0.555mmol) in 1,2-dichlorobenzene (80ml), and stirred at 25° for 1 hour. The mixture is treated with saturated aqueous NH_4Cl (0.5ml), concentrated *in vacuo* to *ca* 60ml and diluted with toluene. The brown mixture is applied onto a silica column and washed with toluene (~100ml, i.e. until the effluent becomes yellow), followed by EtOAc/toluene (3:97) and the effluent is collected until its colour is pale yellow. This is evaporated *in vacuo* to a small volume and MeOH is added rapidly to precipitate a brown powder which is collected under N_2, dissolved in MeOH/toluene (1:1, 46ml) and $TsOH.H_2O$ (92mg, 0.48mmol) is added to it. After stirring for 1 hour at 25°, the mixture is neutralised with $NaHCO_3$, the solvent is evaporated, the residue is dissolved in MeOH/toluene (1:9, ~30ml), filtered from some insoluble material and evaporated *in vacuo*. The crude residue is purified by preparative HPLC (Nomura Chemical RPFullerene, with toluene/MeOH 1:9 as eluant) to give on evaporation the desired fullerene as an orange powder (99.5mg, 0.064mmol, 12% yield). Its ^1H NMR (400 MHz, acetone-d_6, TMS) has δ at 7.32-7.28 (m, 8H), 7.23 (d, *J* = 8.0Hz, 2H), 6.69-6.64 (m, 10H), 4.55 (s, 1H), 2.38 (s. 2H), 2.31 (d, *J* = 14.4Hz, 2H), 2.23 (d, *J* = 14.4Hz, 2H), 2.11 (d, *J* = 14.8Hz, 2H), 2.05 (d, *J* = 14.8Hz, 2H), 0.36 (s, 6H), 0.35 (s, 6H), 0.34 (s, 6H), 0.33 (s, 6H), 0.27 (s, 6H); and the ^{13}C NMR (100 MHz, acetone-d_6) has δ at 159.84, 159.81, 158.36, 155.22, 155.18, 154.80, 150.53, 149.13, 149.19, 149.05, 148.74, 148.66, 148.41, 148.18, 148.70, 147.66, 147.30, 146.97, 146.52, 146.22, 145.93, 145.24, 144.07, 143.53, 143.49, 142.76, 136.07 (C_6H_4), 136.03 (C_6H_4), 127.99 (C_6H_4), 127.84 (C_6H_4), 118.89 (C_6H_4), 115.92 (C_6H_4), 115.87 (C_6H_4), 115.82 (C_6H_4), 55.66 (CCH_2SiMe_2), 54.11 (CCH_2SiMe_2), 53.69 (CCH_2SiMe_2), 31.20 ($C_{60}CCH_2Si$), 30.39 ($C_{60}CCH_2Si$), 30.35 ($C_{60}CCH_2Si$), -0.22 ($SiMe_2$), -0.30 ($SiMe_2$), -0.34 ($SiMe_2$), -0.47 ($SiMe_2$); the HRMS (APCI+) has calculated for $C_{105}H_{67}Si_5O_5$ $(M\text{-}2H)^+$ 1547.3835, and the found mass is 1547.3840.

This fullerene now has five phenolic groups for condensation with lipid molecules. When a mixture of it (9.40mg, 6.07μmol) and 4-(dodecan-1yloxy)benzoyl chloride (13.0mg, 9.81μmol) in THF (3.0ml) is treated with Et_3N (5.8 μL, 42mmol) and 4-dimethylaminopyridine (3.5mg, 29μmol), stirred at 25° for 3 hours, evaporated *in vacuo*, and the residue in toluene is filtered through a silica gel pad, and then purified by GPC (JAIGEL 3H, eluting with toluene), precipitated with MeOH/toluene as above and dried *in vacuo* (at 25° for 12 hours), it provided ***1,4,11,15,30-pentakis{4-[4-(dodecan-1-yloxy)benzoyloxy]phenyldimethylsilylmethyl}-2H-1,2,4,11,15,30-hexahydro-(60)fullerene*** (12.9mg, 71% yield). Similarly the ***[4-tetradecan-1-yloxy]*** (75% yield), ***[4-hexadecan-1-yloxy]*** (72% yield), ***[4-octadecan-1-yloxy]*** (61% yield) and ***[3.4-di(octadecan-1-yloxy]*** (37% yield) ***derivatives*** were obtained in high purity and characterised by ^1H NMR, ^{13}C NMR and ACPI MS analysis. These form beautifully coloured liquid crystals and X-ray diffraction studies showed interesting stacking of these fullerene molecules. [Matsuo, Muramatsu, Hamasaki, Mizoshita, Kato and Nakamura *J Am Chem Soc* **126** 432 *2004*.]

[Further reading: H.W. Kroto et al. *Chem Rev* **91** 1213 *1991*; H. Kroto, Fischer and Cox *Fullerenes,* Pergamon Press, Oxford, 1993 ISBN 0080421520; Kadish and Ruoff (Eds) *Fullerenes: Recent Advances in the Chemistry and Physics of Fullerenes and Related Materials,* The Electrochemical Soc. Inc, Pennington, NJ, 1994, ISBN 1566770823; Smalley *Acc Chem Res* **25** 98 *1992*, and following papers; Hammond & Kuck *Fullerenes: Synthesis, Properties and Chemistry of Large Carbon Cluters,* American Chemical Society, Washington, *1992*, ISBN 0-841221820; K. Jinno *Separation of Fullerenes by LC,* RSC Publ.,*1999*, ISBN 9780854045204; S. Nagase & T. Akasaki *Endofullerenes: a new family of carbon clusters,* Springer, *2003*, ISBN 9781402009822; F.J.M. Reitmeijer *Natural Fullerenes and related structures of elemental carbon*, NetLibrary, *2006*, eBook ID 190026, eISBN 9781402041358; P.W. Fowler & D.E. Manopoulos *An Atlas of Fullerenes,* Dover Publications Inc, *2007* ISBN 9780486453620; P. O'Brien, H. Criaghead, H.W. Kroto, F. Langa and J-F. Nierengarten *Fullerenes: principles and applications* RSC Publ., *2007*, ISBN 9780854045518; *Fullerenes, Nanotubes and Carbon Nanostructures,* Marcel Dekker Inc, New York, on line series on *World Wide Web.online*; N. Chaniotakis *Fullerenes-bifunctionalisation (nanostructured for biosensing)* in "Nanomaterials for Biosensors", C. Kumar ed., Wiley-VCH, *2007*, ISBN 9783527313884; C.N. Kramer *Fullerene research advances*, Nova Science Publishers Inc, *2007*, ISBN 9781600218248; M. Lang *Progress in fullerene research,* Nova Science Publishers Inc, *2007*, ISBN 9781600218415; S. Margadonna *Fullerene-related materials: recent advances in their chemistry and physics*, Springer *2007*, ISBN 9781402044588.]

CARBON NANOTUBES (CNTs) AND RELATED MATERIALS

The development of carbon nanotubes (CNTs) since their discovery by Sumio Iijima [*Nature* **354** 56 *1991*] has been explosive, not only because of their mechanical, thermal and electronic properties but because they can be modified physically and chemically in a variety of ways to suit a plethora of applications. Structurally, they are made of rolled up sheets of carbon atoms forming fused hexagonal carbon rings just like a monolayer of graphite. The sides of the sheet are fused to form complete tubes. When one or both ends of a tube come together, like the bottom of a test tube, the round portion is more like half a 'fullerene ball'. The way that the carbon atoms in the half fullerene ball 'finger tip' structure are stable is by forming both hexagonal and pentagonal rings (see Marchand et al. *Nano Lett* **9** 2961 *2009*, FEM imaging below).

Many carbon nanotubes are now available commercially in chemical catalogues, and a selected number are entered here. Their chemical and biochemical applications include diagnostics, novel devices for rapid DNA sequencing, human personalised medicine, bio-labeling for cancer research, novel biomaterials for human implants, and for tissue engineering implants. The non-chemical applications have also been extended to attachments to surfaces with patterned and unpatterned textures to form conductors, and exciting applications as for nano-filters, in LEDs, nanostructured optical fibres, lasers, and solar cells. Carbon nanotubes are very strong materials and could be ~200 stronger than steel. When mixed with building materials, such as cement or aluminium composites, they not only increase their strength but make them much lighter. Carbon sheets such as graphene are conducting surfaces and have found extensive use in touch screens, i-Pods, mobile phones to name a few. [Haddon *Carbon Nanotubes (editorial), Acc Chem Res* **35** 997 *2002*, see also P. Calvert *A recipe for strength, Nature* **399** 210 *1999*].

PREPARATION OF CNTs (NTs)

MWCNTs (multi walled CNTs) were first prepared by the arc discharged evaporation method (as for fullerene synthesis) where the needles (nanotubes) grew at the negative end of the carbon electrode in an argon filled vessel (at 100Torr). TEM micrographs showed tubes of 5 concentric graphic sheets (6.7nm diameter), 2 concentric graphic sheets (5.5nm diameter, DWCNT, double walled CNTs), and 7 concentric sheets (2.2nm diameter MWCNT). Electron diffraction patterns show that the tubes were formed from rolled up graphite sheets of carbon hexagons in helical structures. [Iijima *Nature* **354** 56 *1991*.] In chemical arc deposition, acetylene (at partial pressure ~10^{-2}mbar, 0.0075mm Hg at 0°) is often used as the hydrocarbon gas. J-M Bonard and coworkers prepared CNTs by growing them on 0.3mm diameter wires of Kanthal (Fe-Al-Cr alloy) in the centre of the anode at the rather low temperatures of 700-900°, hence the name *Cold Atmosphere Chemical Vapour Deposition CVD* (CACVD, compare below). The technique produces homogeneous films of well-graphitised NTs allowing control of their length and density. [Croci et al. *Chem Vap Deposition* **8** 89 *2002*, Bonard et al. *Appl Phys Lett* **81** 2836 *2002*]. MWCNTs are generally formed to a smaller or larger extent in the procedures used together with small quantities of buckyballs and amorphous carbon which can be invariably sublimed out, annealed out, or separated by chromatography. Annealing at high temperatures (~2500-2700°) removes volatile carbon, metals (generally bound to the open end of the tubes) and improves the structural order of the tubes.

SWCNTs (single walled CNTs): Among the techniques that have been developed for making SWNTs are EA (electric arc) methods which use a carbon source and catalytic amounts (~ 1 to 6 atom%) of transition metals, commonly Ni/Co, Ni/Y, Rh/Pt or Fe that are allowed to supersaturate the carbon [Kokai et al. *J Phys Chem B* **103** 4346 *1999*, Sen et al. *Chem Phys Lett* **349** 383 *2001*]. The methods have been studied in detail in order to optimise the sizes and yields of CNTs. The technique developed by R.C Haddon and co-workers [Itkis et al. *J Phys Chem B* **108** 12770 *2004]*, and the purity estimated by solution phase NIR [Itkis et al. *Nano Lett* **3** 309 *2003*] adopts the EA method where an electric arc discharge is applied between a graphite cathode and composite anode containing catalytic amounts of metal(s), e.g. 4:1 atom% of Ni/Y, under He buffer gas at ~680Torr, and arc current 90A with a 10mm arc gap. These conditions produce high yields of AP-SWCNT (high purity, As-Prepared nanotubes). The purity can be assessed by Near-Infrared (NIR) spectroscopy.

Large scale production of SWCNTs by the EA technique is achieved by using an arc generated between a graphite rod (16mm diameter, 40mm long) cathode and an anode of graphite (6mm diameter, 100mm long) in which a hole 3.5mm diameter, 40mm deep, is drilled and filled with a mixture of a metallic catalyst (Ni 4.2 atom%/Y1 atom% and graphite) in a He atmosphere (660mbar) formed by a current of 100A/30V and keeping a constant distance (~3mm) between the electrodes. Within ~2 minutes, the total carbon mass was in ~2g quantities consisting of ~70% SWCNTs in highly crystalline bundles. The nature of the product(s) was assessed by SEM, high resolution TEM, Raman spectroscopy and X-ray diffraction. [Journet et al. *Nature* **388** 756 *1997*.]

Another technique developed by R.E. Smalley and coworkers is the laser ablation of carbon targets (*Carbon Vapour Deposition*, CVD), e.g. laser-vaporised carbon-Ni/Co mixture (e.g. 1:1 1.2 atom% in C) at high temperatures (e.g. 1200°C) and vacuum (e.g. 500Torr) and an argon stream. [Thess et al. *Science* **273** 483 *1996*, Sen et al. *Chem Phys Lett* **332** 467 *2000*, Koran et al. *J Vac Sci Technol A* **13** 1171 *1995*]. This CVD produces high yields (~ 70%) of SWCNTs as assessed by X-ray diffraction and electron microscopy (EM) methods at a rate of ~80mg/day. The production of SWCNTs can be increased to ~1g/day by using a 2" tube and dual laser pulses. However, by modifying the apparatus, using up and down scanning of the laser pulses onto a rotating carbon-Ni/Co target in a 4" diameter tube, a lower temperature (1100°C) can be used to generate 20g of 40-50vol% SWCNT material in 48 hours of continuous (largely unattended) operation [Rinzler et al. *Appl Phys A* **67** 29 *1998*]. The high purity was checked by EM, XRD, Raman spectroscopy and TGA. Note that higher temperature operations produce tubes of larger diameters, albeit well within the nanometer scale.

In a more recent, essentially CVD procedure, S.T. Purcell and co-workers [Marchand et al. *Nano Lett* **9** 2961 *2009* which provide an animated supplement, and summarised by H. Birch '*Nanotube growth on camera*', RSC *Chemistry World* **6**(9) 26 *2009*] have demonstrated by *Field Emission Microscopy* (FEM) how the growth of SWCNTs takes place. They used a W-tip connected to the electrodes (at 1200°C) in a chamber at ultra high vacuum (5 x 10^{-10} Torr base pressure). The W-tip (tip radius ~ 60nm) is first covered with a graphite diffusion barrier by heating in acetylene (at $P_{C_2H_2}$ ~1 x 10^{-4} Torr), and Ni nanoparticles are induced to grow directly onto the tip [by dewetting, from a circular Ni wire in the chamber using CVD in C_2H_2 (~1-2 x 10^{-7} Torr during growth) at 800°C] while FEM imaging is performed. The images are collected on camera, and a frame-by-frame analysis of the video showed that the SWCNT grows at one end of the carbon tube at a time. The tube

rotates in discrete steps, ~24 per rotation (half of the number of carbon atoms on the circumference of a common SWCNT) with the CNT turning ~180 times during its 11 minutes growth (as in the 'screw-dislocation-like' model). Growth starts at the Ni atom (of the catalyst), the carbon attaches itself to the metal then it forms carbon rings (as hexagons, because these are the more stable configuration), and the molecule rotates as the tube is being formed. In the end, the tube is sealed by forming a semi-fullerene ball 'finger tip' structure, and produces a 'test-tube like' nano carbon structure with the metal atom at its mouth. The metal can then be removed by heating the SWCNT strongly (annealing).

The ***HiPco*** process for preparing SWCNTs developed by R.E. Smalley and co-workers [Nikolaev et al. *Chem Phys Lett* **313** 91 *1999*] involves formation of the catalysts by *in situ* thermal decomposition of $Fe(CO)_5$ in a heated flow of CO in the gas phase at 1-10atm and 800-1200ºC. By adjusting the processing parameters (best at 1-10atm and 800-1200ºC), SWCNTs were produced in high yields (79 mole%, i.e. 44 wt%) with narrowest tubes (as small as 0.7nm in diameter, same as in C_{60} fullerene) at the rate of 1.24mg/hour. The structures were confirmed by TEM, SEM, EDX and TGA. An important advantage of this procedure is that it is a continuous-flow process which can be used for bulk production of narrow SWCNTs. See below for purification of HiPco tubes.

PURIFICATION OF CNTs (NTs)

***MWCNTs*: ** Raw tubes, as prepared by the EA method, contain about one third of other nanomaterial. This material is best removed by oxidation. Pure tubes can thus be prepared, although the procedure is wasteful. The purest tubes are obtained when 99% is oxidised; but when 95% is oxidised only 10-20% of product contains pure nanotubes. A ground raw sample is placed in an oven and the temperature is raised to 750º in air or oxygen for ~30 minutes until ~1% is left. This consists mostly of pure tubes with length/diameter ratios that exceed 100, and traces of open cylinders with the ratio of 20. [Ebbesen et al. *Nature* **367** 519 *1994*, see also Chen et al. *Adv Mater* **8** 1012 *1996*.]

MWCNTs, prepared by the CVD procedure using ferrocene and xylene (0.75% Fe/C) as catalyst and precursor with argon/H_2 at ~700º [Andrews et al. *Chem Phys Lett* **303** 467 *1999* (a step closer to commercialisation), Rao et al. *Appl Phys Lett* **76** 3813 *2000*], or acetylene as precursor and 2.5wt% Co-2.5wt% Fe/NaY zeolite as catalyst with argon/H_2 at ~700º [Bulusheva et al. *J Phys Chem B* **105** 4853 *2001*], were purified by heating the raw tubes (200mg) in 2.6M aqueous HNO_3 (40ml) for 48 hours. The cooled solution was centrifuged (use PTFE tubes, ~20,000g/30 minutes), the sediment was washed/re-centrifuged with de-ionised H_2O until the supernatant was barely acidic and the MWCNT sediment was dried *in vacuo*. This material was satisfactory for functionalising [Lin et al. *J Phys Chem B* **106** 1294 *2002*]. *Alternatively*, to a dispersed suspension of MWCNTs (100mg), formed by sonication (1 minute), is added an acidic solution of $KMnO_4$ (4g in 120ml of 1N H_2SO_4) dropwise and refluxed for 12 hours, cooled, and centrifuged. The sediment is treated with concentrated HCl (20ml) and refluxed for 24 hours to dissolve the MnO_2, cooled, centrifuged and the sediment is refluxed with 68% (azeotropic) HNO_3 (40ml) for 24 hours, cooled, centrifuged again, and the solids are washed repeatedly (using several centrifugation/washing cycles) with de-ionised H_2O until almost neutral then dried in a vacuum oven. This procedure exposes the CO_2H groups on the CNTs and can be used for conversion to COCl groups, and further reactions to make soluble MWCNTs. [Fu et al. *Nano Lett* **1** 439 *2001*.]

***SWCNTs*: (i)** Mechanically ground cloth-like raw SWCNTs from the electric arc process (EA) can be purified in reproducibly high yields (optimally 25-30wt% and <1wt% of transition metal) in two steps. The first involves thermal annealing in air by rotating the powders at 470ºC for 50 minutes in a quartz tube at 30rpm which burns the carbonaceous particles out, and the second is acid treatment which etches out the metals. The powder is immersed in aqueous 6M HCl for 24 hours, filtered (or centrifuged) several times until the colour of the acid is unaltered, and then washed with de-ionised H_2O. The SWCNTs are then 'unbundled' by boiling in 30% aqueous HNO_3 for 4-6 hours, and the suspension is filtered with a polytetrafluoroethyene (PTFE) membrane in deionised H_2O, rinsed and dried to give a grayish black, thin mat of SWCNTs. The purity at each stage can be observed by SEM, TEM, FT-Raman spectroscopy and TGA which usually show ~96% purity after HCl treatment. The HNO_3 treatment, however, appears to break down the CNTs into small pieces and sometimes forms MWCNTs. [Moon et al. *J Phys Chem B* **105** 5677 *2001*.]

(ii) A gas-phase purification procedure developed by Margrave and co-workers [Zimmerman et al. *Chem Mater* **12** 1361 *2000*] involved purging the CNT sample [prepared by the pulsed laser method (Rinzler et al. *Appl Phys A* **67** 29 *1998*), from Graphite (1-2mm), or from EA] in a quartz tube with a mixture of Cl_2 (7.2ml/min), H_2 (2.7ml/min) and argon (3.0ml/min) for 1 hour at ~25º, which is then lowered into a furnace at 500º while the evolving gases (CO, $COCl_2$, CCl_4 and CO_2) are monitored by IR. Purging is continued until the CO partial

pressure is <0.5Torr. The temperature of the sample is lowered to ~25º, sonicated in DMF/0.6M HCl (1:1) to remove metals, then pure DMF, filtering, and washing with MeOH to form an SWCNT 'paper'. (*Alternatively*, the metals, if present, can be removed by sublimation in HCl gas at higher temperature.) The SWCNT 'paper' is dried at 160º and the purity assessed by SEM, TGA and UV-VIS. Any fullerenes present may be removed by a toluene reflux or by sonication. The yield is ~15wt% to give CNTs that are generally more reactive due to their larger curvature.

(iii) Raw HiPco SWCNTs can be purified in a multi-step process. Low density raw HiPco (~100mg, d ~0.01g/cc) is compressed onto dry filter paper (vacuum), placed in a ceramic boat and inserted into a quartz tube furnace while a gas mixture of 20% O_2 (or air) in argon (wetted by bulbbling through H_2O) is allowed to flow over the sample in the furnace at 100cc/sec. The nanotubes are heated at 225º for 18 hours, sonicated for ~15 minutes (or stirring overnight) in concentrated HCl (yellow colour due to Fe^{3+} ions). The suspension is filtered onto a Teflon membrane (47mm, 1.0μm pore size), washed several times with deionised H_2O, MeOH, and dried in a vacuum oven at 100º for 2 hours (weight loss 33.7%; 0.67% residual metal). This oxidation with wet O_2 (or air) in argon, and extraction cycle is repeated at 325º for 1.5 hours (further weight loss 8.3%, 0.05% residual metal), and again at 425º for 1 hour (further weight loss 22.9%, 0.09% residual metal). After drying *in vacuo*, the HiPco tubes are annealed at 800º in argon for 1 hour (further weight loss 4.2%, 0.03% residual metal). Assessment of purity is by SEM, TEM, TGA, Raman and UV-VIS-NIR spectroscopy. The onset of oxidation of the smaller diameter HiPco SWCNTs is *ca* 100º lower than for the purification of large diameter tubes obtained in the laser-oven process, and is consistent with the greater steric strain present in small diameter SWCNTs. [Chiand et al. *J Phys Chem B* **105** 8297 *2001*.]

(iv) A general purification procedure for raw SWCNTs obtained by the EA process (reaching 2-3g, containing ~70% SWCNTs) [Ebbesen & Ajayan *Nature* **358** 220 *1992*, Journet et al. *Nature* **388** 756 *1996*], or the laser ablation method (reaching ~20g, containing up to 50% SWCNTs) was developed by A. Hirsch and coworkers [Holzinger et al. *Appl Physics A* **70** 599 *2000*]. The process involves three steps. **(a)** Raw material (100mg) was refluxed with 65% HNO_3 (150ml) for 3 hours, and centrifuged. The sediment was washed with H_2O and centrifuged repeatedly until the supernatant (first colourless then darkens, still contains some SWCNTs and was kept for further use) has pH ~1. The sediment is suspended in distilled H_2O, subjected to two and three 0.5 seconds of ultrasonic pulses when the liquid became weakly acidic (pH 3-4), almost free from metal catalyst, and contained ~1mg/ml H_2O of only SWCNTs and nanoparticles. For storage, the pH is adjusted to 8-9 with K_2CO_3 which increased the repulsive interactions between the carboxylate groups of the SWCNTs. **(b)** The suspension is sonicated for 1 minute which reduces the nanoparticles to smaller pieces. The tubes and bundles were also smashed and the difference in size between the SWCNTs and degraded particles increases (as observed by AFM). **(c)** This most important step involved elution of the suspension through a column of potassium polyacrylate which was swollen (the cross-linked polymer particle size swells from <1μm to ~300μm) creating pores large enough to entrap nanoparticles as well as SWCNTs and bundles of comparable size. [Optimum: 15ml of swollen polymer per 1ml of a 1g/L aqueous SWCNTs, and choosing a diameter to give a column height of 6-7cm held by a glass filter pore size 2]. A vacuum is applied at the bottom of the column which squeezes the swollen polymer particles. The SWCNTs are so large that they cannot now be entrapped and elute freely to give large quantities (> 40% of the total mass) in the first fraction. The remaining material contains a large portion of SWCNT fraction of lesser quality which can be recycled. Most of the degraded material and smaller nanoparticles remain in the cavities. The purification can be followed by AFM and the purity can be assessed by Raman spectroscopy. In the Raman spectrum, ***pristine*** SWCNTs have a doublet at 1546 and 1575 cm^{-1} (of about equal intensity — **G**-lines) and a less intense band (**D**-line, *ca* 1/4.75 th of the **G**-lines) at ~1342 cm^{-1}. The relative intensity of the G-lines increase as the purity increases. The broadness of the D-band may originate from disordered or carboxylated carbon formed by oxidation.

PREPARATION AND PURIFICATION OF FULLERENE PIPES (TUBES)

These are short SWCNTs of 100 to 300nm lengths and ~1.2 to 1.4nm in diameter which are most useful for preparing functionalised SWCNTs. They are distinct from the above *fullerenes* which are "bucky balls" and are made up of tubes consisting of a network of hexagonal carbon rings like in CNTs. As prepared, the CNTs are long almost endless single walled highly convoluted, entangled, bundled tubes. R.E. Smalley and coworkers [Rinzler et al. *Appl Phys A* **67** 29 *1998*, Liu et al. *Science* **280** 1253 *1998*] have purified, and cut such material from large batches into small lengths of open-ended tubes, *Fullerene pipes*, which form stable colloidal suspensions in the presence of detergents. These can be made to react like ordinary organic molecules to form any variety of derivatives. In a typical preparation, the raw tubes (10g) in 2.6M HNO_3 were refluxed for 45

hours, cooled, and the black solution was centrifuged in PTFE (Teflon) tubes (20,000g, 20 minutes, Sorvall R5C centrifuge). The supernatant was decanted off, the sediment was resuspended in de-ionised H_2O by vigorous shaking and the centrifuging/washing cycle repeated 3 to 4 times until the supernatant was almost neutral, although black in colour. The acid treatment not only assists in separating the bundles, but also oxidises the material, thus producing carboxylic acid groups at the ends as well as at the sides of the tubes. This makes 'holes' in the sides of the tubes and causes them to be 'cut' [cf K. Kinoshita *Carbon Electrochemical and Physicochemical Properties* Wiley, New York *1988*, ISBN 978047184802-8]. The sediment as examined by SEM and TEM contains carboxylated carbon tubes and other species such as fullerenes, polycyclic aromatic sheets and cross-linked sheets edged with CO_2H groups which, by virtue of de-protonation allow mutual repulsion between the particles. The sediment (using 10g) was dispersed in aqueous NaOH (1.8L, pH 10) containing 0.5vol% of the non-ionic surfactant Triton X 100 by sonication for ~1 hour, and purified by *cross-flow-filtration* (CFF, cellulose ester M22M 600 01N, mini-Kros® Spectrum cartridge: 0.6mm diameter, 200nm pores and 0.56m^2 of surface area) against a buffer of aqueous NaOH (40L, pH 10) containing 0.2vol% of Triton X 100. At a head pressure of 5-6psi and flow rate of ~70ml/min the process was complete in ~10 hours. Salt was removed by washing with de-ionised H_2O (10L). Clogging occasionally occurred and was overcome by momentarily reversing the flow before continuing. Clamping off the buffer line and opening a vent allowed concentration of the SWCNTs down to ~200ml of solution. When a portion of this solution was filtered through a PTFE membrane (Millipore LS 5μ pore) using a vacuum, it deposited a thick pad of SWCNTs on the membrane. After washing with MeOH, the pad can be easily peeled off to give a freestanding mat which was called 'Bucky Paper' and was estimated as typically 10 to 20% yield depending on the initial raw material. TEM images of the SWCNT 'paper' showed that the pipes still contained impurities which were removed by two further oxidising acid treatment which 'cut' (by reacting at the sides of the tubes) and 'polished' the tubes.
In a typical ***cutting***, the purified SWCNT 'Bucky Paper' (10mg) was suspended in a 3:1 mixture of concentrated H_2SO_4/HNO_3 (40ml), sonicated (55kHz) at 35º to 40º for 24 hours. The suspension was diluted with H_2O (200ml), larger tubes were collected onto a 100nm pore filter membrane (Millipore, VCTP type), and washed with 10mM NaOH solution. ***Polishing*** was performed by suspension in a 4:1 mixture of concentrated H_2SO_4/30% H_2O_2, stirring at 70º for 30 minutes, filtering and washing again on a 100nm filter, and re-suspending at 0.1mg/ml of 0.5wt% Triton X100 in H_2O to avoid flocculation. On a larger scale CFF purification was carried out after each oxidation step. Finally, to obtain best purified 'Bucky Paper', annealing *in vacuo* at 1200º was necessary. Note that in 3:1 H_2SO_4/HNO_3 at 70º the average cutting was at a rate of ~130nm/hour, and in 4:1 H_2SO_4/30% H_2O_2 the shortening rate was at ~200nm/hour.
Characterisation of these fullerene tubes was done by electro-deposition [developed by Smalley and coworkers, see above references] which drives the suspended tubes onto the surface of highly oriented pyrolytic graphite surface and are scanned by AFM. The molecular nature of the tubes was demonstrated by converting their CO_2H groups to COCl, followed by reaction with $H_2N(CH_2)_{11}SH$ and exposure to 10nm gold particles. Gold (which reacts with SH) was only found on the carboxylated fullerene tubes.

SOLUBILISATION OF CNTs
CNTs, whether MWCNTs or SWCNTs, readily form bundles, and attempts to separate the bundles by means such as sonication or use of detergents have been uniformly unattractive. The carbon material is 'non-wettable' and quite insoluble in polar and non-polar liquids. Considerable effort has been expended to find means of separating the bundles and much success has been achieved by functionalising the carbon matrices, which destabilise the interaction between the fibres, but also introduce bound groups which afford solubility in organic solvents as well as aqueous solutions. These provide opportunity for purification because the partly purified CNTs are not homogeneous. The non-homogeneity is not only in the length and/or diameter, but also in their nature since during the formation of the tubes, the row of hexagonal rings do not only align to form straight tubes (with parallel hexagonal rows), but can also form spiral tubes in which the row can be out of line by one and/or more than one hexagon while forming the tube. [For the *Dislocation theory of chirality-controlled nanotube growth* see B.I. Yakobsen and coworkers *Proc Natl Acad Sci USA* **106**(8) 2506 *2009*, and for a review see H. Birch RSC *Chemistry World* **6**(3) 25 *2009*.] This provides the opportunity for a variety of chiral CNTs. In his respect M Zheng and coworkers [Zheng & Semke *J Am Chem Soc* **129** 6084 *2007*, Tu et al. *Nature* **460** 250 *2009*, see also P. Broadwith RSC *Chemistry World* **6**(8) 28 *2009*] have selected short strands of DNA [8 to 12 mers, with repeating nucleotides e.g. $(GTC)_2$, $(GTC)_2GT$, $(GTT)_3G$, $(TAT)_4$ etc] which entwine around the SWCNTs (e.g. produced from HiPco, see above) of *ca* 1nm diameter with different selectivities depending on the '*n,m* chirality' of the nanotubes [e.g. (8,6), (9,4), (7,6), (6,5) etc respectively] to form barrels around the

tubes. The mixture is dispersed in appropriate aqueous solutions (e.g. 0.1M NaCl, 0.1M NaCl/10% glycerol) by sonication (~60 minutes), incubated for a period of time, centrifuged (16,000g/90 minutes) and the supernatant is fractionated by Size Exclusion Chromatography (SEC) through an IEX resin (CNT-NS 1500, Biochrom, Terre Haute, IN, USA), and the various DNA-wrapped-SWCNTs are eluted with 2x(0.3M NaCl, 0.03M sodium citrate)/0.5mM EDTA/pH 7.0 and a 0 to 1M sodium benzoate gradient. The fractions are monitored at 300nm and 425nm. The DNA interaction is electrostatic and is easily removed by thermal treatment.
Strong acids solubilise SWCNT and MWCNT bundles by protonating them causing the strands to separate, but chlorosulfonic acid is by far (~1,000 times) the best acid as shown by M. Pasquali and the late R.E. Smalley [Davis et al. *Nature Nanotechnology* **4** 830 2009, summarised by P. Broadwith RSC *Chemistry World* **6**(12) 32 *2009*]. SWCNTs spontaneously dissolve in $ClSO_3H$ at a concentration of as low as 0.5wt%. The Phase Diagram in strong H_2SO_4 exhibited true thermodynamic behaviour forming isotropic (I), liquid crystal (LC), crystal solvate (CS) and solid (S) phases at different concentrations of SWCNTs, $ClSO_3H$ and H_2SO_4. When an 8.5vol% of SWCNTs was coagulated in 96% aqueous H_2SO_4 by extrusion through an orifice while co-flowing with $CHCl_3$ or CH_2Cl_2, the resulting nanotube bundles (10-100nm) combined into larger bundles to form macroscopic fibres which were easily spun into tens of meters of continuous fibres in a matter of minutes. These fibres can yield a strength in excess of 320 MPa. By sandwiching the dope between glass plates, long ribbons of material were produced, and possibly any shapes (e.g. coils) can be made. The technological applications are enormous.
For examples of some currently commercial CNTs and functionalised CNTs see the following paragraphs.

CARBON NANOTUBES (CNTs)
Carbon annealed nanodiscs/nanocones *[7440-44-0]*. These are available as a black powder containing a mixture of 20% cones, 70% discs and 10% of carbon black impurities by weight. The carbon cones have a nearly perfect geometry. The five theoretically possible cones with apical angles of 19.2°, 38.9°, 60°, 84.6° and 112.9° are all present in the mixture with cone lengths of 0.3-0.8μ, maximum base diameter of 1-2μ and wall thickness of 20-50 nanometers. The diameter and thickness of the discs are 0.88-3.5μ and 20-50 nanometers respectively. A product of almost 100% carbon is obtained by annealing at 2500-2700° which increases the structural order and reduces the concentration of impurities particularly of metals (from catalyst). They are similar to multi-walled carbon nanotubes (MWCNTs).

Carbon multi-walled nanotubes (MWCNTs or **MWNTs)** *[1333-86-4]*. These are produced as a black powder by chemical vapour deposition (CVD) and contain >90% of nanotubes which are almost free from metal impurities. The tubes are ~7μ in length and ~140 nanometers in diameter. Multi-walled smaller nanotubes of ~1.5μ in length and ~20-25 nanometers in diameters are similarly prepared. When the multi-walled carbon nanotubes are 'arc-produced' they are even smaller in size with ~2μ in length and ~2-50 nanometers in diameter *[308068-56-6]*. This 'arc process' produces a mixture of 55-65wt% of straight multi-walled nanotubes and 35-45wt% of graphite nanoparticles. They contain almost 100% carbon. By growing the tubes at 3000-4000° using this process they contain less defects than by other procedures, and are purified in this way. They are stable in air up to 700°.
MWCNT arrays for nanoelectronics with nickel-carbide particle tips with same diameters as above are also available. Vertically aligned MWCNTs on a silicon wafer substrate with low resistivity (1-30 ohm-cm), as well as on a copper wafer substrate (1cm x 1cm x 0.05cm high conductivity low-oxygen copper) have been prepared. The latter are produced by plasma-enhanced chemical vapour deposition (PECVD). MWCNTs have also been made in 3-19, 7-13 and 5-15 graphene layers wall thichnesses. See below for breaking up the bundles and graphene.

Carbon double-walled nanotubes (DWCNTs or **DWNTs).** These have been prepared by the *Carbon Vapour Deposition* (CVD) method with >90% carbon content and 50-80% DWCNT. They can be prepared with approximately the following dimension 5nm OD, 1.3-2.0nm ID and 50μm length; and with 0.12-0.14g/ml bulk density and >600m^2/g surface area. The rest (10-40%) consists of amorphous carbon and residual metal catalysts which are deliberately placed in the original carbon in order to synthesise the carbon tubes.

Carbon single-walled nanotubes (SWCNTs or **SWNTs)** *[308068-56-6]* **M 3652-3607**, **d^{25} 1.7-1.9g/ml.** The SWCNTs are of particular use for derivatisation and the applications stated above. They can be prepared in various bundle dimensions, *viz*: d = 1.2-1.5nm, l = 2-5μm (40-60% SWCNT, arc method); d = 1.1-0.5nm, l =

100μm (>50% SWCNT, Carbon Vapour Deposition, CVD, method); *d* = 2-10nm, *l* = 1-5μm (50-70% SWCNT, arc method); individual short tubes *d* = 1-2nm, *l* = 0.5-2μm (90% SWCNT, electric arc, EA, method), and individual long tubes *d* = 1.3-1.5nm, *l* = 1-5μm (40-60% SWCNT, arc method, EA) and the HiPco process (see above).

FUNCTIONALISED CNTs.
MWCNTs and SWCNTs have been successfully functionalised, and the products have found numerous applications. They are conducive to further chemical reactions as they are readily soluble, thus amenable to solution chemistry [see R.C. Haddon and coworkers in *Chemistry of Single-Walled Carbon Nanotubes,* Niyogi et al. *Acc Chem Res* **35** 1105 *2002*; and Sun and coworkers in *Functionalized Carbon Nanotubes: Properties and Chemistry,* Sun et al. *Acc Chem Res* **35** 1096 *2002*]. When purified by the acid and oxidising conditions the tubes invariably are oxidised to form CO_2H or quinone groups, particularly at the ends of the tubes. Depending on the conditions, 'cutting' may occur leaving open-ended tubes (see fullerene tubes above). Annealing at high temperatures *in vacuo* causes some decarboxylation and closing up of the ends which form half fullerene tips (like the end of a glass test tube, see above). Because of the larger curvature at the tips than on the sides of the tubes, the tips are more readily functionalised (due to the easier conversion of sp^2 to sp^3 carbon atoms); but then again they would lose the added function more readily on annealing. The tips are also more easily cleaved by oxidants ($KMnO_4$, OsO_4 and RuO_4) at 100° under acidic conditions [Hwang *Chem Commun* 173 *1995*]. Functionalised SWCNTs dissolve in organic solvents (e.g. THF, CH_2Cl_2) and can be examined by optical spectroscopy. Tubes with CO_2H groups on the sides are commonly formed, are readily converted to COCl groups, and can react with a variety of reagents possessing the appropriate functional group. Also by virtue of the double bonds in the hexagonal rings, the tubes condense with nitrenes (to form aziridino compounds with UV light), react with carbenes (to form cyclopropane derivatives), are reduced (by Birch reduction), form metal derivatives which can be reacted further, react with aryl diazonium compounds (arylation), undergo 1,3-dipolar cycloaddition reactions (e.g. to form pyrrolidine derivatives), undergo nucleophilic reactions, radical reactions, and halogenation. J.L. Musgrave and coworkers [Khabashesku et al. *Acc Chem Res* **35** 1087 *2002*] have prepared 'fluoronanotubes' by direct fluorination of SWCNTs, and the fluoronanotubes dispersed in THF reacted with alkyl-Li reagents, Grignard reagents, alkoxides, hydrazine and ω-diamines to form a variety of useful functionalised tubes. Sun and coworkers [Fu et al. *Nano Lett* **1** 439 *2001*] functionalised SWCNTs with lipophilic and hydrophilic dendra and showed that they can be defunctionalised in homogeneous solutions by base- and acid- catalysed hydrolysis demonstrating the existence of ester linkages. Absorption in the UV/VIS spectra of these functionalised tubes obey Beer's law demonstrating no aggregation effects, and SEM analysis was not successful due to the extent of substitution, whereas the de-functionalised SWCNTs and MWCNTs gave successful SEM imaging. SWCNTs attached to a silicon substrate can be used as very small highly sensitive chemical sensors or memristors for gases. They also adsorb chemicals such as alcohols, aromatics, amines and phosphonates, some of which do not readily desorb and slow the process down unless they are removed by other means such as high temperatures which tend to be time consuming and degrade the sensor. Masel and coworkers [Salehi-Khojin et al. *Science* **329** 1327 *2010*, reviewed by H. Birch, Electric shock resets nanotube sensor, RSC *Chemistry World* **7** (10) *2010*] showed that current induced voltage above the Poole-Frenkel conduction threshold (>12V) desorbed most molecules effectively after 3 hours and the sensors returned rapidly to baseline.

SWCNT—$(CO_2H)_n$, 89-90% SWCNT (carbonaceous purity), bundle dimension: diam 4-5nm x length 0.5-1.5μm. The SWCNTs were produced by EA discharge [Journet et al. *Nature* **388** 756 *1996*, Itkis et al. *J Phys Chem B* **108** 12770 *2004*] or the HiPco procedure (see above). SWCNT-CO_2H is prepared as follows: HiPco SWCNTs (0.2g) are sonicated in a 3:1 mixture of concentrated H_2SO_4/concentrated HNO_3 (80ml) for 4 hours, diluted with deionised H_2O and filtered through a 0.2μm pore acid resistant membrane. The solid is dried at ~25°, then sonicated in a solution of 4:1 concentrated H_2SO_4/30% H_2O_2 for 15 minutes, diluted with excess deionised H_2O, filtered again and dried *in vacuo* at 25° to give 79w/w% of 'shortened' product (85% have length < 600nm, i.e. ~0.6μm). [Zhao et al. *Adv Funct Mater* **14** 71 *2004*.] Solution phase NIR spectroscopy against a standard [see Itkis et al. *Nano Lett* **3** 309 *2003*], gave a carbonaceous purity of 80-90% and 3-6 atom% carboxylic acid. Its solubility is 1mg/ml in DMF, and 0.1mg/ml in H_2O. Metal content is 5-10%. This is suitable for further reactions.

SWCNT—$(COCl)_n$. The preceding shortened SWCNT-acid (100mg) [see also Liu et al. *Science* **280** 1253 *1998*] is stirred in $SOCl_2$ (20ml) containing DMF (1ml) at 70° for 2 hours, centrifuged, the brown coloured supernatant is decanted, the sediment is washed with anhydrous THF, centrifuged again; the pale yellow supernatant is decanted and the sedimented SWCNT-$(COCl)_n$ is dried at ~25° *in vacuo*. This product is reactive and should be used immediately. [Chen et al. *Science* **282** 95 *1998*]. *Alternatively,* the preceding acid (12mg) in dry DMF (20ml) is sonicated for 30 minutes to give a homogeneous suspension, to which is added redistilled oxalyl chloride (0.4ml) dropwise at 0° under N_2. The mixture is stirred at 0° for 2 hours, then at 70° and stirred overnight to remove excess of oxalyl chloride, and dried *in vacuo*. This product is reactive and should be used immediately. [Itkis et al. *Nano Lett* **3** 309 *2003*.]

SWCNT—$(CONH_2)_n$, 89-90% SWCNT (carbonaceous purity), bundle dimension: diam 4-6nm x length 0.7-1.0μm, average diameter of individual SWCNT being 1.4nm ±0.1nm. The preceding cooled SWCNT-$(COCl)_n$ in dry DMF (~0°) is treated with liquid NH_3 (~0.5ml) and stirred while the temperature rose to ~25°, and kept there with stirring for 24 hours. Dry N_2 is bubbled through the mixture to remove excess of NH_3, excess of dry THF is added and the mixture is centrifuged, the supernatant is decanted off, the sediment is washed with dry THF, centrifuged again and the SWCNT-NH_2 residue is dried *in vacuo* at ~25°. The extent of labeling is the same as the original acid, i.e. 3-6 atom % (amide groups) and metals ~6-8%. Their solubilities are 0.5 to 1.0mg/ml, in each of the alcohols, acetone and DMF; and can be functionalised with any reagent that will react with amide groups.

SWCNT-$(ODA)_n$ {SWCNT-$[CONHCH_2(CH_2)_{16}CH_3)]_n$, octadecylamide functionalised}, 89-90% SWCNT (carbonaceous purity), bundle dimension: diam 2-10nm x length 0.5-2.0μm, average diameter of individual SWCNT being 1.4nm ±0.1nm. It is prepared from the above SWCNT-$(COCl)_n$ (obtained from 100mg of the acid) by mixing with octadecylamine (ODA, 2g, m 55-57°) and heating at 90-100° for 96 hours under dry N_2, and cooled. Excess of ODA is removed by washing with EtOH four times (5-10 minutes sonication at 40 KHz) by centrifugation/decantation, the sediment is dissolved in CH_2Cl_2, filtered, the black coloured filtrate is evaporated to dryness in a rotavap and the residue is dried *in vacuo* at ~25° to give >60% yield based on shortened SWCNTs. Note that the reaction of SWCNTS-$(COCl)_n$ and excess of ODA in toluene at ~25° for several days gives only traces of product and the success of the former procedure was attributed to expansion and defoliation of the SWCNTs bundles to give the more reactive individual nanotubes [Chen et al. *Science* **282** 95 *1998*]. The extent of labeling in the commercial sample is 30-40wt% (ODA) and contains 4% of metals. The amide is soluble in $CHCl_3$, CH_2Cl_2, $*C_6H_6$, toluene, and the solubility in CS_2 or THF is >1mg/ml. The solubility of the ODA derivative made it amenable to purification, and R.C. Haddon and coworkers purified it by gel permeation chromatography (SEC) using Styragel HMW7 [Nyogi et al. *J Am Chem Soc* **123** 733 2001] and PLgel MIXED-A [Zhao et al. *J Am Chem Soc* **123** 11673 *2001*], both being polystyrene divinylbenzene resins. The latter proved to be a superior gel (300 x 7.5mm column), and using THF as eluent three bands were separated at a flow rate of 0.5ml/minute. The first band contained 74% of SWCNTs-ODA (as detected by AFM, UV and NIR) [MW range 2000 to 4 x 10^7, particle size 15-20μm, retention time 8 minutes], the second band with retention time of 9 minutes contains mostly nanoparticles with traces of SWCNTs, and the third band with retention time of 19 minutes contained amorphous carbon. IR, Raman and UV spectra confirmed the ODA component, and ^1H NMR (200MHz, $CDCl_3$) demonstrated bands characteristic of CH_2 groups and the terminal CH_3 group. The nature (e.g. such as broadness) of the bands was indicative that both ionic (charge transfer) and covalent interactions were occurring.

SWCNT-{CONH-*p*-$[C_6H_3(m\text{-}SO_3H)$-*p*-$NHC_6H_3(m\text{-}SO_3H)$-$]_m\}_n$ [SWCNT-*n*-poly-*p*-aminobenzene-*m*-sulfonic acid, SWCNT-$(CO\text{-}PABS)_n$], 75-85% SWCNT (carbonaceous purity), average diameter of individual SWCNT being 1.4nm ±0.1nm, average PABS Mw ~400-600g/mol. The PABS polymer was prepared by mixing *m*-aminobenzenesulfonic acid (ABS, 0.865g) and aniline (15-20mol% of ABS, as inhibitor of polymerisation) and 1M HCl with ammonium persulfate as oxidant, stirred at 0° for 6 hours, concentrated at ~25° (*in vacuo*), filtered and the solid was washed with Me_2CO. This was dissolved in H_2O, and the aqueous solution was slowly added to a large excess of Me_2CO. The black solid was filtered off and dried at ~25° (*in vacuo*) to give PABS (340mg, 40%, Av M_W ~400-600 g/mol), which was identified by its UV spectrum that has λ_{max} at 290 and 510nm in aqueous 1N NaOH [Roy et al. *Synth Met* **100** 233 *1999*]. **SWCNT-$(CO\text{-}PABS)_n$** was

obtained from SWCNT-$(COCl)_n$ [prepared as above by the oxalyl method from HiPco SWCNTs (12mg, Carbon Nanotechnologies Inc.)] in dry DMF (~20ml) by mixing with PABS (120mg) in DMF (~50ml) and stirred at 100° for 5 days. After cooling to 25° the solid was filtered through a 0.2mm pore-size membrane and washed thoroughly with DMF and EtOH, and dried *in vacuo*. The black **SWCNT-(CO-PABS)$_n$** (57mg) on the membrane was collected and dried *in vacuo* overnight. Its solubilities are 0.05mg/ml in EtOH, 0.1mg/ml in DMF and 5.0mg/ml in H_2O. The commercial product has 65% (PABS) and 4% metals. The water soluble graft polymer had a much higher conductivity (5.6 x 10^{-3} Scm^{-1}) than PABS (5.4 x 10^{-7} Scm^{-1}), and IR spectrum consistent with an amide bond; the ^1H NMR (300MHz, D_2O) exhibited a very weak broad spectrum compared with the sharp signals of PABS itself, characteristic of the effect of the ring currents in the nanotubes. The UV/VIS/MIR spectrum showed the presence of the interband transitions of the semiconducting SWCNTs and an absorption at 17,750 cm^{-1} due to the PABS moiety. [Zhao et al. *Adv Funct Mater* **14** 71 *2004*.] Solution phase NIR spectroscopy against a standard, provided a carbonaceous purity of 80-90% — a procedure which has an accuracy of ~3% [see Itkis et al. *Nano Lett* **3** 309 *2003*].

SWCNT-$(PEG)_n$ {SWCNT-$[COO(CH_2CH_2\text{-}O\text{-})_m\text{-}H)]_n$, polyethylene glycol functionalised}, 80-90% SWCNT (carbonaceous purity), bundle dimension: diam 4-5nm x length 0.5-0.6μm, average diameter of individual SWCNT being 1.4nm ±0.1nm, PEG Mw ~600g/mol. The above SWCNT-$(COCl)_n$ prepared from 30mg of SWCNT-CO_2H is mixed with PEG (250mg, m 20-25°) and heated under N_2 at 75° with vigorous stirring for 48 hours. The mixture is cooled to 25° extracted with $CHCl_3$ several times, filtered, and the dark coloured solution is repeatedly precipitated with EtOH to give SWCNT-$(PEG)_n$ which is collected (filtration or centrifugation) and dried *in vacuo*. Its solubility in H_2O is high (5.0mg/ml) and has ~30wt% (PEG) and ~6% trace metals. The ester function can be identified by IR (ν_{max} ~1700 cm^{-1}), but the ^1H NMR signals are weak and broad (see above). The ester-free SWCNTs can be recovered by acid- and base- catalysed hydrolysis [see above Fu et al. *Nano Lett* **1** 439 *2001*]. Solution phase NIR spectroscopy against a standard, provides a carbonaceous purity of 80-90% — a procedure which has an accuracy of ~3% [see Itkis et al. *Nano Lett* **3** 309 *2003*].

SWCNT-(*p*-C_6H_4-R; R = F, Cl, Br, I, SO_3H, CO_2H, NO_2, *n*-butyl, *t*-Bu or $CO_2Me)_n$. These were prepared by 'on water' functionalisation of bundled SWCNTs. The term 'on water' refers to the water-based reactions of water-insoluble organic substrates [see K.B. Sharpless and coworkers in Narayan et al. *Angew Chem, Int Ed* **44** 3275 *2005* and Klijn & Engberts *Nature* **435** 746 *2005*]. This technically involves the reaction of *p*-substituted benzene diazonium compounds with the hexagonal rings on the walls of SWCNTs in aqueous medium and represents a "green" or "environmentally friendly" process. The following are optimal conditions for functionalisation. HiPco SWCNTs (10mg) and deionised H_2O (30ml) were homogenised in a flask (100ml) by stirring at medium setting for 30 minutes, then heating at 80° with the substituted aniline (4 equivalents/SWCNT) and isoamyl nitrite (2 equivalents/SWCNT) with vigorous stirring (stirrer bar) under a reflux condenser overnight. The mixture is then cooled, filtered through a 0.45μm Teflon filter, the filter cake is washed with deionised H_2O, and Me_2CO until the filtrate is clear. The cake is collected, sonicated in DMF (25ml) to remove any remaining organic compounds, collected by filtration (0.45μm Teflon filter) and rinsed with Me_2CO to give the desired functionalised SWCNTs as evidenced by 20-30% weight increases. TGA, Raman [elevated D (diamondoid, ν_{max} at 1290 cm^{-1})/G (graphic, ν_{max} 1590 cm^{-1}) band ratios] and UV-VIS-NIR spectroscopy, XPS, AFM and TEM confirmed the structures. It is interesting that TEM images (on a carbon grid) showed that the SWCNT bundles have smooth edges, whereas functionalised SWCNT bundles have 'bumps' all along the edges. These functionalised nanotubes should be useful for further functionalisation reactions [Price & Tour *J Am Chem Soc* **128** 12899 *2006*].

By using the above procedure **SWCNT-(*p*-C_6H_4-CH_2NH_2)** and **MWCNT-(*p*-C_6H_4-CH_2NH_2)** were prepared and successfully coupled, *via* their terminal amino group to the carboxy group of *N*(1)-carboxymethyl-thymine, to form thymine ends. These functionalised CNTs readily form stable *double* hydrogen bonds with other thymine groups of these CNTs. This induces controlled non-covalent self-assembled supramolecular aggregation of the CNTs in solvents that do not break hydrogen bonds such as CH_2Cl_2, and can form good dispersions in polar aprotic solvents such as DMF. All characterisations were performed using spectroscopic, analytical and microscopic techniques. [Quintana & Prato *Chem Commun* 6005 2009, reviewed by K. Davies RSC *Chemistry World* **6**(11) 6005 *2009*.] These properties can be of importance in *nanoelectronics*, or in

biological applications such as making patterned active substrates for neuronal growth [Cellot et al. *Nat Nanotechnol* **4** 126 *2009*].

I-SWCNT, I = {-COOCH$_2$-[3,5-di(hexadecyloxy)phenyl]}$_n$ and I$_{PEG}$-SWCNT, I$_{PEG}$ = {-COOCH$_2$-[3,5-di(methyltriglycoloxy)phenyl]}$_n$. These are respectively hydrophobic and hydrophilic SWCNTs which were prepared as described by Y.-P. Sun and coworkers [Fu et al. *Nano Lett* **1** 439 *2001*] by stirring vigorously SWCNT-(COCl)$_n$ (30mg, see above) and carefully dried **I** (250mg) under N_2 at 75^o/48 hours. The cooled mixture is extracted several times with $CHCl_3$, the combined dark-coloured extracts were repeatedly precipitated with EtOH to give **I-SWCNT** with ^{1}H NMR (500MHz, $CDCl_3$) which had δ at 0.88 (t, *J* = 6.5Hz) and typically weak broad bands at 1.1-1.5, 1.6-1.8, 3.5-3.9, 4.0-4.2 and 6.0-6.5 caused by the effect of the CNT. **I$_{PEG}$-SWCNT** was prepared in a similar manner except that its solubility in H_2O allowed further purification by dialysis for several days against deionised H_2O (dialysis tubing with Mr ~100,000 cut off to remove PEG). Dendron **I** was prepared by reaction of methyl 3,5-dihydroxybenzoate and hexabromodecane followed by reduction with LAH, and Dendron **I$_{PEG}$** was obtained from the same benzoate and triethylene glycol monoethyl ether in the presence of Ph_3P and diethyl azidodicarboxylate in THF, followed LAH reduction. The corresponding hydrophobic **I-MWCNT** and hydrophilic **I$_{PEG}$-MWCNT** dendra were similarly prepared from reacting SWCNT—(COCl)$_n$ with the benzylic OH group in the dendra, and all were characterised by ^{1}H NMR, UV-Vis spectroscopy, TGA and SEM as well by defunctionalisation of homogeneous solutions under acid- and base- catalysed reaction conditions.

MWCNT-(PPEI-EI)$_n$. These functionalised MWCNTs were prepared in two ways. *Firstly*, the MWCNTs (20mg) were refluxed with $SOCl_2$ (5ml) for 24 hours and evaporated *in vacuo*, then the co-polymer PPEI-EI [200mg, poly(propionylethylenimine-*co*-ethylenimine) [as prepared by Y.-P. Sun and coworkers *Macromolecules* **32** 8747 *1999*, *Photochem Photobiol* **66** 301 *1997*, *Chem Commun* 2699 *1996*)] was added and heated at 160-180^o for 12 hours under N_2, cooled, repeatedly extracted with $CHCl_3$ and the dark combined extracts were precipitated with hexane. The isolated solid was dissolved in deionised H_2O and dialysed against fresh H_2O (dialysis tubing with Mr ~100,000 cut off to remove PPEI-EI) for 3 days. Further purification was by re-precipitation from $CHCl_3$ solution into hexane, and drying the dark **MWCNT-(PPEI-EI)$_n$** solid which had ^{1}H NMR (500MHz, $CDCl_3$) with broad weak bands at δ 0.8-1.4, 1.9-2.6, 2.7-2.9, 3.1-4.3. *Secondly*, (without forming the COCl derivative) by directly heating the MWCNTs (20mg) with PPEI-EI (200mg) at 160-180^o for 12 hours under N_2 and worked up as above provided **MWCNT-(PPEI-EI)$_n$** which had ^{1}H NMR (500MHz, $CDCl_3$) with broad weak bands at δ 0.8-1.4, 1.9-2.6, 2.7-2.9, 3.1-4.3. Raman, UV-VIS spectroscopy, SEM, TEM and TGA showed that both procedures were effective in producing functionalised MWCNTs which were readily soluble in common organic solvents and in H_2O. The latter method may have caused amidation as well as ionic interaction between the amino-polymer and the CNT. [Lin et al. *J Phys Chem B* **106** 1294 *2002*.]

SWCNT[=CH)$_2$N-CH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$NH$_3^+$. HCl]$_n$ and **MWCNT[=CH)$_2$N-CH$_2$CH$_2$OCH$_2$CH$_2$-OCH$_2$CH$_2$NH$_3^+$. HCl]$_n$.** These salts are very soluble in H_2O and solutions are stable for more than a month at concentrations of 20mg and 12mg per ml respectively. The free amino terminal group is a useful handle for attachment to physiologically active molecules (see below). They are formed in a 1,3-dipolar cycloaddition reaction between the C=C bonds of the CNTs with the N-glycine **N** atom and formaldehyde. The glycine in this case is BocNHCH$_2$CH$_2$O-CH$_2$CH$_2$OCH$_2$CH$_2$**N**HCH$_2$CO$_2$H and is prepared as follows: BocNHCH$_2$CH$_2$O-CH$_2$CH$_2$OCH$_2$CH$_2$NH$_2$ (30mmol) in dioxane (20ml) at 0^o is treated dropwise with a solution of benzyl bromoacetate (2.3g, 10mmol) in dioxane (30ml) during 1 hour, and the mixture is stirred overnight. The solvent is evaporated off *in vacuo*, the residue is dissolved in H_2O (70ml) and extracted with EtOAc (3 x 50ml), the combined organic phase is dried (Na_2SO_4), evaporated *in vacuo*, and the residue is purified by chromatography on Silica gel [NM Kieselgel 60 (70-230 mesh)] and eluted with 1:1 EtOAc/petroleum ether then pure EtOAc to give ***N-Boc-aminoethoxyethoxyethylaminoacetic*** as an oil. To a solution of this oil (5.05mmol) in MeOH (50ml) is added 10% Pd/C (50mg), the mixture is stirred under H_2 for 24 hours, the catalyst is filtered off (through Celite), the solvent is evaporated and the residue is triturated with dry Et_2O to give ***animoethoxyethoxyethylaminoacetic acid*** as a pure white solid (1.6g, 99%, 5.05mmol), **m 105-106^o** with the expected elemental (C, H and N) analyses. The acid has IR-DRIFT (KBr) with ν_{max} at 3250, 2970, 1706, 1620, 1540, 1365, 1115, 686, 590, 480 cm^{-1}; the ^{1}H NMR (200MHz, $CDCl_3$, TMS) has δ at 1.40 (s, 9H), 3.22 (m, 2H),

3.49 (t, *J* = 5.1 Hz, 2H), 3.64-3.53 (m, 8H), 3.79 (bt, 2H), 5.54 (bt, 1H), 6.23 (bs, 1H), 8.21 (bs, 1H); the ^{13}C NMR (50MHz, $CDCl_3$, TMS) has δ at 170.5, 156.2, 79.1, 70.4, 70.3, 70.1, 66.6, 49.8, 46.8, 40.4, 28.6; EI-MS found *m/z* 306 (M^+). [Kordatos et al. *J Org Chem* **66** 4915 *2001*.].

For **functionalisation**, a suspension of full length SWCNTs or MWCNTs [diameter 20-30nm, from Carbon Nanotechnologies, Inc USA (www.cnanotech.com), and Nanostructured & Amorphous Materials Inc USA, (www.nanoamor.com) respectively] in DMF is treated with the preceding acetic acid and paraformaldehyde, and the mixture is heated at 130º for 96 hours. Unreacted material is removed by filtration, the filtrate is evaporated, the residue is dissolved in $CHCl_3$, washed with H_2O, dried, evaporated, redissolved in $CHCl_3$, precipitated with Et_2O, collected (on a 0.45mm Teflon filter) and washed several times with Et_2O to give the functionalised CNTs in ~10% yields based on the amount of starting CNTs. They are soluble in solvents such as CH_2Cl_2, $CHCl_3$, toluene and Me_2CO. Removal of the *N*-Boc group is achieved by dissolving the previous functionalised SWCNTs or MWCNTs in CH_2Cl_2, dry HCl gas is bubbled through the solution whereby the ***CNT-chloride hydrochloride salts*** (desired materials) separate out. They are collected (or the solvent is evaporated), dissolved in MeOH and precipitated with dry Et_2O. The desired products, as identified by TEM showed that the functionalised SWCNTs and MWCNTs have 10-50nm and 20-30nm mean diameters respectively, their ^1H NMR spectra are similar with the signals from the oligoethylene glycol chains appearing as broad peaks at ~3.6 ppm, and absence of the Boc methyl groups which would have been at 1.2 ppm from TMS. [Georgakilas et al. *Chem Commun* 3050 *2002*.] These functionalised CNTs were successfully coupled *via* their terminal amino group to the carboxy group of *N*(1)-carboxymethyl-thymine to produce thymine ends. The thymine functionalised CNTs readily form stable double hydrogen bonds with other thymine groups of these CNTs. This induces controlled non-covalent self-assembled supramolecular aggregation on the CNTs in solvents that do not break hydrogen bonds such as CH_2Cl_2, and can form good dispersions in polar aprotic solvents such as DMF. All characterisations were performed using spectroscopic, analytical and microscopic techniques. [Quintana & Prato *Chem Commun* 6005 2009, reviewed by K. Davies RSC *Chemistry World* **6**(11) 6005 *2009*.] These properties can be of importance in *nanoelectronics* or in biological applications such as making patterned active substrates for neuronal growth [Cellot et al. *Nat Nanotechnol* **4** 126 *2009*.]

SWCNT[=(CHR')(CH$_2$)N-R"), where R' = H, 4-MeOC$_6$H$_4$- or 2-pyrenyl-, and R" = -(CH$_2$CH$_2$O)$_3$CH$_3$ or -(CH$_2$)$_7$CH$_3$]$_n$ and MWCNT[=(CHR')(CH$_2$)N-R"), where R' = H, 4-MeOC$_6$H$_4$- or 4-pyrenyl-, and R" = -(CH$_2$CH$_2$O)$_3$CH$_3$ or -(CH$_2$)$_7$CH$_3$]$_n$ were prepared by 1,3-dipolar cycloaddition reactions with short oxidised SWCNTs or purified MWSCNTs as in the preceding entry and using paraformaldehyde, 4-methoxybenzaldehyde or 4-formylpyrene to form the substituted pyrrolidines with the double bond(s) of the CNTs. They were characterised by UV-VIS, Raman and ^1H NMR spectroscopy and by TEM. The fluorescence of the pyrene derivatives were of interest, and all provide means for the preparation of nanocomposites. [Georgakilas et al. *J Am Chem Soc* **124** 760 *2002*, Calvert *Nature* **399** 210 *1999*.]

GRAPHENE MATERIALS

Graphene is the name given to a flat monolayer of carbon atoms packed in a two-dimensional (2D) honeycombe lattice of six-membered carbon rings. It is the unit block (2D sheet) of graphitic materials which stack into multilayers to form graphite (3D), rolls to form nanotubes (1D) or wraps to form buckyballs (0D)[see above]. 'Graphenes' are defined as single-, double-, and few (3 to <10) carbon layers (2D), with characteristic electrical properties not found in graphite. *Graphene* is the accepted name for a single, or at most a double carbon thick layer which is ≈ 5Å thick. Single layer 2D crystals have been prepared (see below) that have high crystal quality where charge carriers can travel thousands of atomic distances without scattering. Its electrical behaviour includes a pronounced ambipolar electric field effect in which charged carriers could be tuned continuously between electrons and holes at concentrations *n* as high as 10^{13} cm^{-2}, with mobilities μ greater than 15,000 cm^2 V^{-1} s^{-1} under laboratory conditions. Films of 5 layers would be considered as 'bulk material', and films with more than 100 layers are considered as thin films of 3D graphite (see graphite [7782-42-5] below). [Geim & Novosolov *The Rise of Graphene: Nat Mat* **6** 183 *2007*.]

Graphene films were obtained by mechanical exfoliation (repeated peeling) of highly oriented pyrolytic graphite. The 2D crystallites were collected from a fresh surface of a layered crystal using few-layered graphene, FLG, by rubbing against another surface (any solid is suitable, but an oxidised silicon wafer, i.e. SiO_2 would be also useful later for identification). This allows flakes of graphene to be attached to the surface for characterisation. This approach was very reproducible, has also been used for preparing thicker films (≥ 3nm) which were up to 100μm across, as well as FLGs of up to 10μm in size and visible to the naked eye.

Preliminary identification of single layer films among the resulting flakes was done with an optical microscope. These became visible when they were on top of an oxidised silicon wafer (see above) because even a monomolecular layer adds enough to the optical path of reflected light that the interference colour changes reveal the presence and contours of the film. The process is simple and the 2D crystallites can be identified in about half an hour. Further identification of selected single layers is then done by AFM. It was pointed out that only a small number of single films among the many thicker films were produced by this method, they could not be identified by TEM, but they were transparent to visible light on surfaces other than SiO_2 wafers, and thus require AFM and high resolution AFM imaging for definitive identification and are difficult to find by scanning surfaces at random. These atomically thin sheets, particularly very large 2D molecules, unprotected from the environment are stable in air under laboratory conditions, have high crystal quality and maintain macroscopic continuity. [Novoselov, Geim and coworkers, Electric field effects in atomically thin carbon films, *Science* **306** 666 *2004*, Two dimensional atomic crystals, *Proc Natl Acad Sci USA* **102** 10451 *2005*.]

The sp^2 character of all the C-C bonds of graphene confer remarkable electric conductivity to it due to the delocalisation of electrons, and it is difficult to stop the flowing current at will. Geim and Novoselov and their coworkers [Elias et al. Control of Graphene's properties by reversible hydrogenation: Evidence for Graphane, *Science* **323** 610 *2009*] have succeeded in hydrogenating the double bonds of graphene to make ***graphane*** which now has C-C bonds with sp^3 character. The reduction transforms graphene from the highly conductive zero-overlap semimetal into an insulator. Reduction was achieved with a hydrogen-helium mixture (10% H_2) at low pressure (0.075mm Hg) and the direct current plasma ignited between two aluminium electrodes with the samples 30cm away from the discharge zone to avoid damage by energetic ions. Graphene and graphane have distinctly different Raman properties. The reaction is reversed by annealing graphane at 450º (higher temperatures damage graphene) in an argon atmosphere for 24 hours. Thus the original metallic state, lattice spacing, Raman and TEM properties, and even the quantum 'Hall effect' are restored. Note that when the thin film is on a substrate, reduction takes place on the upper face of the film, and for more effective reduction they used free-standing graphene membranes. If one can imagine a magic pencil which can remove hydrogen from graphane and drawing channels of graphene into it, better control of current flow can be achieved [see review by J. Urquart RSC *Chemistry World* **6** (3) 23 *2009*].

Cutting of single-layer graphene (SLG) by anisotropic etching using thermally activated Ni nanoparticles has been developed by Jarillo-Herrero and coworkers [Campos et al. *Nano Lett* **9** 2600 *2009*, reviewed by L. Brindley, Cutting Graphene to ribbons, RSC *Chemistry World* **9** (8) *2009*]. Unlike previous methods for making graphene nanoribbons and the like, their procedure makes SLG nanoribbons and other SLG structures (e.g. triangles, rectangles) in which all cuts (sub-10nm width) are oriented with the same edge-chirality, i.e. aligned along a single crystallographic directions with no hanging edges. Thus the cuts are straight, and always at an angle of 60º and/or 120º. With graphite and FLGs, etching occurs with chirality changing angles of 30º, 90º, and 150º, as well as 60º and 120º. Their method is described here in some detail as it involves ***purification procedures useful for SLG preparation.*** To ensure reliable cuts in nanoparticle assisted etching, the SiO_2/Si substrates (wafers, see above) have to be cleaned with Me_2CO and *iso*-PrOH, and submitted to UV illumination for 5 minutes to remove organic material and for making the SiO_2/Si surface more hydrophilic to ensure proper wetting during the spin-coating deposition of Ni from solution. Graphene is exfoliated on this clean surface using semiconductor grade tape. The SLG on the clean substrate is identified by optical spectroscopy (see above), AFM (typically SLGs are at a height of 0.8nm) and Raman spectroscopy (graphene's G' 2D peak, see above). The tape residue is removed by heating the SLGs in a quartz tube at 500º for 15 minutes under an argon:H_2 flow (850:150 sccm). After this heat 'cleaning', an aqueous solution of $NiCl_2$ (2.4mg/ml) is centrifuged onto this surface at 1800rpm for 60 seconds, then heated at 90º for 10 minutes on a hot plate to eliminate H_2O. The $NiCl_2$ treated sample in an argon:H_2 flow (850:150 ratio) is firstly annealed at 500º for 20 minutes to convert the salt into Ni nanoparticles, and then the etching is carried out at 1000º for 25 minutes in the same gas flow. The best etching conditions require a slow heating/cooling rate of ~50º/minute. During the etching the Ni nanoparticle (with H_2 adsorbed) furrows through the SLG by catalytically hydrogenating the carbon atoms in its path and converting each atom into a molecule of methane. With SLGs, but not with FLGs or graphite, the cutting paths never cross each other; as soon as the Ni nanoparticle comes within a 10nm distance of a preformed path it changes direction at a 60º or 120º angle. The purification procedure and the Ni concentration stated are very critical if the formation of CNTs are to be avoided. This opens many future directions for studying SLG nanoribbons and other shapes, constrictions and quantum dots with crystallographic edges. H-H. Ahn and B.H Hong and coworkers [Bae, et al, *Nature Nanotechnology* **5** 574 *2010*] have pressed rectangular graphene films (76cm diagonal) with a roller against an adhesive polymer support and the copper

etched away. The graphene is pressed with rollers onto a polyethylene terephthalate substrate and the polymer adhesive is released on heating. In this way further layers of graphene can be added. When treated with HNO_3, the graphene sheet acts as a transparent electrode for touchscreen devices. It is tougher and has better transparency than indium-tin oxide (ITO) electrodes [see below, and review by S. Hadlington RSC *Chemistry World* **7** (8) 22 *2010*].

Stacked Graphene Platelet Nanochips (stacked graphene nanofilms, SGNF heat treated) and Platelet Nanofibres (SGNF acid washed) are commercially avalilable as black powders with 40-50nm mean width, 0.1-10μ length, 0.3g/cm^3 density, and 120m^2 of surface area. The electrical resistivities are 55μWcm and 120μWcm for the chips and fibres respectively. These SGNFs are used in nanotechnology research. [US Patents 6,995,115 and 7,001,586.]

Graphite *[7782-42-5]* **m 3652-3697°, d^{25} 2.09, 2.23.** It is available commercially in various forms such as *flakes* (mesh 75+), *rods* (6mm x 150mm, low density and high density, 3mm x 150mm low density), *powder* (≤20μm, ≤45μm, and 150≤μm), *nanofibres* (I.D. 0.5-10nm x O.D 80-200nm x L. 0.5-20μm, bulk density 0.06-0.08g/ml), *graphitised nanopowder* (particle size <200nm with large mesopores, 10% graphite lattice content, surface area 70m^2/g, average pore ~137Å and d 1.818g/cm^3) and *platelet nanofibres* (prepared by catalytic CVD then demineralised by HCl, with surface area 80m^2/g, particle width ~100nm and particle length ~2.5μm, TEM). [For purification by acid treatment see entry [7782-42-5] in Chapter 5, Inorganic Compounds.] The applications of graphite include the manufacture of 'lead' pencils, lubricants, polishing, pigments, explosives, commutator brushes, carbon anodes, and arc-lamp carbon among many others. **Avoid breathing it** as it can cause coughing, decreased lung function and fibrosis, **use a mouth mask**. [See Holliday et al. in *Comprehensive Inorganic Chemistry* **vol 1**, Bailar Jr et al. Eds, Pergamon Press, Oxford, pp1250-1294 *1973*; ISBN 9780080172750.]

SELF ASSEMBLED MONOLAYERS (SAMs).

SAMs have been of considerable interest for some time [see Chechik, Crooks and Stirling, Reactions and reactivity of self-assembled nanolayers, *Adv Mater* **12** 1161 *2001*] and several useful ones have been prepared using a variety of materials and methods. Only a recent report will be described here, and it is of 2D carbon nanolayers prepared by Mo(IV) and Cu catalysed crosslinking of 1,4-bispropyne- (**1**), 1,4-bisacetylene- **(2),** and 1,4-bis(2,3,4-triacetylenephenyl)propyne- **(3)** benzenes with each benzene ring further substitued with a 3-(triethoxysilyl)propylaminocarbonyloxymethyl— $[(EtO)_3CH_2CH_2CH_2$-NH-$COOCH_2$—] group which acts as a linker in the polymerisation process. These three organic compounds are connected by vacuum-driven Mo(IV) catalysed alkyne metathesis [cf Zhang & Moore *Adv Synth Catal* **349** 93 *2007*], or oxidative Cu catalysed Hay-type coupling [cf Siemen et al. *Angew Chem Int Ed* **39** 2633 2000] which polymerise them to form self-assembled monolayers on SiO_2-, Si_3N_4- coated substrates (wafers) or quartz/glass slides when immersed in monomer solutions.

Preparation and purification of substrates: The freshly cleaned and dried SiO_2-, Si_3N_4- coated substrates or quartz/glass slides are placed in a reaction tube containing a 15mM solution of **(1)** or **(2)**, or **(3)** in toluene and Me_3N (10mM) under N_2, sealed and heated at 95-100° for 24 hours. The liquid is removed, the substrate is rinsed with toluene (1x), CH_2Cl_2 (2x), and sonicated for 5 minutes in toluene. The rinse is repeated, the substrate is sonicated in MeOH for 5 minutes, the rinse is repeated again and the substrate is blown dried under a stream of N_2 ready for monolayer formation.

Preparation and purification of polymerised coated substrate linked monolayers by Cu Coupling: CuCl (20mg) and degassed Me_2CO (3ml) in a reaction vial are treated with TMEDA (61μl), stirred under N_2 at 20° for 30 minutes and the preceding coated substrates are added. The mixture is purged with O_2 from a balloon and stirred under O_2 for 15 hours. The polymerised coated substrate is collected, rinsed with DMF (1x), with a solution of 0.1M sodium diethyldithiocarbamate in DMF (1x), with toluene (1x), with CH_2Cl_2 (2x), sonicated in toluene for 5 minutes, the rinse is repeated, the substrate is finally sonicated for 5 minutes in MeOH, and the *polymerised linked substrate* blown dry with a stream of N_2.

Preparation and purification of polymerised coated substrate linked monolayers by alkyne metathesis: A mixture of trisamidomolybdenum(IV) propylidyne (5.0mg) and *p*-nitrophenol (3.3mg) dissolved in trichlorobenzene (3.3ml, 1,2,4-) are places in a vial, the coated substrate is added, the flask is sealed under a vacuum (5 Torr) for 22 hours. The substrate is collected. Rinsed with DMF (1x), 0.1M sodium diethyldithiocarbamate in DMF (1x), toluene (1x), CH_2Cl_2 (2x), then sonicated in toluene for 5 minutes. The

rinse is repeated, the substrate is sonicated in MeOH for 5 minutes, the rinse repeated again and finally the *polymerised linked substrate* is blown dry in a stream of N_2.

These monolayers (SAMs) are characterised by UV-Vis, fluorescence and Raman spectroscopy. This is made easy because of the presence of benzene cores within the acetylene and linker chains, these being made of poly(1,4-phenylene-1,3-butadiynylene) polymers. AFM then provides the topology, i.e. shapes (contours), thicknesses and aspect ratios (length and width), of the 2D SAMs. This is done at all stages including those described below.

Lift-off and transfer of the SAMs: The 'lifting off' is carried out by simple oxygen-reactive ion etching through a layer of 'photoresist' (e.g. 5μm x 5μm 'aspect ratio') patterned by photolithography. The 'photoresist' is placed on top of the monolayer which lies on top of the silicon substrates (support, i.e. the films of SiO_2, or Si_3N_4, or glass). Selective etching from the support is done with concentrated HF which dissolves the silicon, leaving photoresist/SAM or photoresist/monolayer membrane hybrid which can be transferred onto other substrates and then freed from the 'photoresist' layer by sonication in Me_2CO. Characterisation of the monolayers during these stages showed that very little, if any, changes in structure has occurred. The atomic force micrographs (AFMs) showed that the SAMs derived from **(1)** are monolayers with thicknesses of ≈ 1.5nm (average roughness of 0.18-0.27nm), and those from **(2)** and **(3)**, unlike from **(1),** formed multilayers of 2.8nm and 4.7nm respectively (average roughness of 0.5nm and 0.3nm respectively). These SAMs, with aspect ratios being the same as the 'photoresist' can be transferred by contact onto a variety of surfaces such as films, pleated sheets, spheres, tubes, cones and any other shapes (followed by removal of the 'photoresist' by sonication in Me_2CO). With a free-standing shape, a free standing silicon support can be used which is then removed by etching to give a free standing SAM. The monolayers are quite robust and can be stretched over ~440nm holes without tearing. This approach and these procedures that were developed by J.S. Moore, J.A. Rogers and coworkers [Schultz et al. *Poc Natl Acad Sci USA* **105** 7353 *2008*] have considerable merit for synthesising monolayer carbon networks of varying shapes which can be accessible for analysis and device applications.

DIAMOND NANOMATERIALS

Nanodiamond (ND) *[7782-40-3]* **M 12.01** is commercially available in powder form with particle spherical size <10nm and ≥ 97% trace metal basis, bulk density 0.2-0.7g/ml with BET surface area of 200-450m^2/g, and in powder form with particle spherical size <10nm and ≥ 95% trace metal, bulk density 0.17g/ml with BET surface area of 278-335m^2/g. The diamond powder is made by *explosive detonation procedures* that are performed in stainless steel hermetic tanks (e.g. of 0.17m). Carbon condensed products [the HE (High Explosve) composite explosives] such as cast trotyl/cyclotrimethylene-trinitramine (TNT/RDX) in various proportions from 50/50 and increasing RDX, with various initial inert gas (N_2 or Ar) pressures were used to determine the best conditions to produce diamonds. Thirty minutes after the explosion, the pressure in the tank is slowly released, and the carbon product is washed out with water, allowed to settle (requiring quite a long period), the water is decanted off, and residual water is evaporated at 150°. This yielded solid carbonaceous soots which contain ultradispersed diamond (UDD, 2-15nm), together with amorphous carbon (4-25nm), graphite ribbons (<20nm), and spheres (2-4nm) as investigated by TEM, XRD, SAXS (small angle X-ray scattering) and Auger spectroscopy. Purification was carried out to remove amorphous and graphite-like carbon from the detonation soot by boiling with perchloric acid, and the maximum yield of diamond was identified by X-ray analysis. The best yield was ~7wt% obtained when TNT/RDX was 50/50 and initial pressure in the tank was ~7 atmospheres which optimised the yield of UDD. It was also shown that the UDD was thermally transformed to onion-like carbon (OLC) particles. [Kuznetsov et al. *Carbon* **32** 873 *1994*.] Annealing studies, in the temperature range of 750°—1900°, of detonation diamond (e.g. OLC) in an inert atmosphere (e.g. argon) affected the structure as shown by XRD and HRTEM as well as purified the material further. The IR showed that all the oxygenated groups (mainly OH, COOH and C=O) were removed, and that at the lower temperatures of ~700-800° a higher coverage of the diamond surface with π-bonds resulted. At higher temperatures the powder undergoes a phase transition from cubic diamond to graphite. [Chen et al. *Appl Phys Lett* **74** 3651 *1999*, Okotrub et al. *J Phys Chem A* **105** 9781 *2001*.] Previously, reactions of ND with free radicals lead to diamond alkylation [Nakamura et al. *Chem Commun* 900 *2003*]; and arylation with diazonium salts [Yeap et al. *Langmuir* **25** 185 *2009*, Liang et al. *ACS Nano* **3** 2288 *2009*] resulted in low yields of ***functionalized nanodiamond***. However, with ND annealing at ~800°, the larger coverage of diamond surface with π-bonds allowed A. Kreuger and coworkers [Jarre et al. *Chem Commun* **47** 544 *2011*] to achieve stable covalent C-C bonding of aromatic groups using Diels-Alder reaction onto surface annealed ND. The key reaction involved the addition of *o*-quinodimethane [acting as diene, generated *in situ* from *o*-bis(bromomethyl)benzene and substituted

benzenes] to the π-bonds of ND in the presence of 18-crown-6 and KI in refluxing toluene for 72 hours. The substituent on the benzene ring can be ***functionalised*** further, e.g. an SO_3H group (formed by sulfonation of the benzene ring) can be converted into an SH group (PPh_3, I_2, $*C_6H_6$ reflux, 24 hours) which can be made to react with *N*-dye substituted maleimide to form a condensed sulfide. The dye being fluorescent Oregon Green 488 which provided fluorescent diamond particles. The applications of such functionalisations are similar to those of functionalised fullerenes and CNTs including fluorescence labeling, drug delivery, magnetic sensing, electrochemistry, and composite materials among others.

SOLVENT RESISTANT NANO FILTERS (SRNF)

During the past decade and a half considerable effort has be expended in developing filters for separating mixtures down to the molecular level. An alternative name to SRNF is organic solvent nanofiltration (OSN). This shows promise as an energy- and waste- efficient process. SRNF has been developed particularly for use with organic solvents but it also applies to aqueous media, with the *proviso* that the membranes may be different. The driving force is the pressure applied to the membranes which are classified as UF (ultrafiltration) with pressures of 1 to 5 bar, NF (nanofiltration) with pressures from 5 to 20 bar and RO (reverse osmosis) with pressures >10 bar. In UF substances between 2nm and 0.1μm are rejected, in NF particles or dissolved molecules smaller than 2nm are removed from solution, and in RO only solvents permeate.

SRNFs are essentially of two types, the organic polymer type or the ceramic type. The former are polymers which need to be cross-linked in order to increase their strength. A variety of polymers have been prepared and studied including the composites: PAN (polyacrylonitrile), PVDF [poly(vinylidene fluoride)], PI [polyimide (Matrimide) and (Lenzing P84)], PEI [poly(etherimide)], PA (polyamide), PAH [poly(amide hydrazide)], PSf (polysulfone), PES [poly(ethersulfone)], PEEK (polyether ether ketone), SPEEK (sulfonated PEEK), PPESK [poly(phthalazinone ether sulfone ketone)], SPPESK (sulfonated PPESK), CA (cellulose acetate), and PBI (polybenzimidazole). The polymers are supported by an ultra-thin (submicron) barrier (TFC, thin film composite) on top of a chemically different polymer support. The TFCs are made of a variety of substances including PDMS (polydimethylsiloxane), PEi (polyethyleneimine), PAA (polyacrylic acid), PPz (poly-phosphazene) among others. The TFCs cause the membranes to be quite strong, as the membranes need to be used and reused over again.

Ceramic membranes, which are much stronger than polymer membranes, are commonly made of Al, Si, Ti or Zr oxides and mixed oxides. The top layers of the membrane are prepared by sol-gel synthesis which converts a colloidal or polymeric solution of inorganic precursors (e.g. alkoxides or salts) to a gelatinous product. Viscous binders are usually added prior to layering followed by controlled calcination and finally sintering to form the ceramic membrane. The process can be controlled to provide membranes with specific MWCOs (molecular weight cut-offs) and which can sustain defined solvents, temperatures and pressures.

Unfortunately at present not many of either type of membranes are available commercially, but undoubtedly many more will appear on the market in the near future. Commercially available SRNF include the *SelRO membranes* (Koch Membrane Systems, USA), *Starmem membranes* (Membrane Extraction Technologies, UK), *SolSep membranes* (SolSep, The Netherlands), and *Desal-5 and Desal-5-DK membranes* (GE/Osmomics, USA) designed for aqueous applications, as well as for SRNF.

SRNFs have found applications in food chemistry, catalysis, chiral separations, petrochemical industry and pharmaceutical manufacturing. The preparation, practical considerations, and theoretical transport mechanisms of SRNFs have been critically reviewed by P. Vanezande, L.E.M. Gevers and I.F.J. Vankelecom [*Chem Soc Rev* **37** 365 *2008*].

NANO METALS AND METAL DERIVATIVES

Antimony (III) oxide nanopowder (Sb_2O_3) *[1309-64-4]* **M 291.5, bulk density 0.5-0.6g/ml.** It is available in particle size of <250nm (BET). It is used in paints, pigments, enamels, glasses and flame-proofing canvas. It is toxic and should not be inhaled.

Antimony-tin oxide nanopowder [ATO, $\sim(SnO_2)_{0.9}(Sb_2O_5)_{0.1}$] M 167.0. It is available in particle size of <50nm and has the alloy composition of 89-93% tin(IV) oxide and 7-11% antimony(V) pentoxide. The surface area is 74 m^2/g. It is toxic and should not be inhaled.

Cobalt *[7440-48-4]* **M 58.9, m 1495°, b 2870°, d ^{20} 8.71, resistivity 6.24 μΩcm/20°, Brinell hardness 125.**

Cobalt nanoparticles for use in *magnetic fluids* (MFs) are available commercially with an average particle size of 10-12nm. It is in the form of a black powder and is prepared by a *thermolysis process* using a strict formula. Thus to dicobalt octacarbonyl {$Co_2(CO)_8$, 17.1g, 100mmol, see [10210-68-1]} under flowing argon is added $Al(C_8H_{17})_3$ (4.4ml, 10mmol) [Co:Al = 10.1] dissolved in toluene (300ml) in one portion, and the mixture is stirred and heated at 110° under a reflux condenser for 18 hours. The reaction is carried out in an efficient fume cupboard because **POISONOUS** carbon monoxide evolution occurs. The colour of the solution changes to dark brown and a black precipitate separates from the clear solution. The mixture is cooled to 20°, and still under argon a further amount of $Al(C_8H_{17})_3$ (1.2ml, ~30% of the initial quantity) is added, the temperature is raised to 110° and is heated for 3 hours more. The mixture is cooled to 20°, and stirred further for 16 hours. Smooth oxidation is carried out by bubbling (use a capillary) air through the mixture for 6 hours. The product is stirred overnight and the precipitated Co is allowed to settle during 2 hours. The supernatant is decanted and the solid is isolated in *toluene wet form*, or by drying *in vacuo* to give an air stable *Co nano-powder* (5.2g); both of which can be handled under laboratory conditions. The particle size of the Co, as determined by TEM and HRTEM is ~10±1.1nm (see further, however). The particle size is sensitive to the thermolysis conditions and to the $Al(alkyl)_3$. With alkyl = Me, Et or *n*-octyl (C_8H_{17}) and a Co:Al ratio of 10:1 as above, the nanoparticle sizes are 3-4, 5-8 or ~10nm respectively. However with a $Al(C_8H_{17})_3$ and Co:Al ratio of 1:2 the particle size was always ~5.4nm.

***Peptisation of Co nanoparticles*:** The Co particles are suspended in toluene and peptised by adding 2ml of KorantinSH, oleic acid, LP-4 (a fatty acid condensation polymer, or AOT (sodium dioctylsulfosuccinate) as surfactants and sonicated in an ultrasound bath for 10 minutes to give a clear dark brown Co-MF. After drying a sample *in vacuo* elemental analysis indicated the presence 67.8% of Co and 0.98% of Al. These MFs were found to be stable for more than 5 months [by X-ray absorption near edge structure (XANES) measurements] under air. It should be pointed out that if the $Al(C_8H_{17})_3$ is washed away from the Co particles immediately after the synthesis, the magnetic properties are markedly reduced after exposure to air. The chemical nature of the analysed nanoparticles shows that the stability of the local electronic and geometric structure is significantly affected by the surfactant used. Peptised Co nanoparticles can also be dispersed in kerosene or mineral oil as precursors for MFs.

Cobalt nanoparticles (surface modified with L-cysteine ethyl ester) ethanol wet are available as ~10nm black powder (wet with EtOH) which is best used within 3 months. The material can be easily transferred into stable aqueous suspensions, and can be used as a starting material for surface modifications (e.g. dextran coating) or the preparation of magnetic polymer microspheres.

Copper-zinc alloy, 55-60% Cu *[12682-85-8]* **Cu/Zn, M 64.3.** It has the composition of Cu (60% by wt) and Zn (40% by wt). The **nanopowder, has particle size <150 nm (TEM), 37-41% Zn basis.** It is a macro-agglomeration of ultra-fine particles, with sizes of *ca* 70 nm and is commercially available. It has trace Mn 1.5-2.5%, Sn 1.5-2.0% and Pb 0.5-2.5%.

Copper zinc iron oxide, 98.5% trace metal basis (zinc copper ferrite, copper zinc ferrite) *[66402-68-4]* **M 416.3 ($CuZnFe_4O_4$), d $^{25}_{4}$ 5.5.** It is a nano powder with particle size <100nm (BET). The actual particle size is <50nm (XRD) and is commercially available.

Gold nanoparticles stabilised by gum Arabic (GA-AuNP). AuNPs have been widely used for a variety of purposes and water soluble composites with gum Arabic (GA) are commercially available. Gum Arabic [9000-01-5] from *Acacia* gum is a branched polymer of galactose, rhamnose, arabinose and glucuronic acid as the Ca, Mg and K salts with M ~250,000, and is a non-toxic and physiologically compatible substance. GA-AuNP has been developed by Kannan, Katti and coworkers [Kattumiri et al. *Small* **3** 333 *2007*]. It is prepared simply by mixing $NaAuCl_4$ with an aqueous solution of a non-toxic phosphine amino acid [$P(CH_2NHCHCH_3COOH)_3$ *THPAL, see preparation below] reducing agent in the presence of a 0.2% aqueous solution of gum Arabic. This resulted in an immediate reaction which produced GA-labeled AuNPs in over 98% yield. The aqueous solutions are stable for months. Note that if GA is omitted, the reaction is also instantaneous but the solutions agglomerate within 4-6 hours. TEM images showed that the size of GA-AuNPs thus produced is 15-20nm. It is stable in the presence of cysteine, bovine and human serum albumins and does not agglomerate in 25% NaCl

solution. Formulations of it can be readily administered site specifically (*intravenously*), for diagnostic imaging (*computer tomography* CT), and is biocompatible for therapeutic applications in nanomedicine. GA-AuNPs are also suitable for nanoelectronics which include sensor design, MEMS applications, spin coating, self-assembly and formation of monolayers.

K.V. Katti and coworkers [Raghuraman et al. *J Am Chem Soc* **125** 6955 *2003*] prepared the reducing agent ***tris[N-(R or S)-alaninylmethylene]phosphine*** (*THPAL) by adding tris(hydroxymethyl)phosphine (0.50g, 4.03mmol, see [2767-80-8]) in H_2O (5ml) dropwise to *R*- or *S*- alanine (1.08g, 12mmol) in H_2O (10ml) at 25° with stirring under N_2 for 1 hour. Evaporation *in vacuo* gave a white solid which, after washing with MeOH and drying *in vacuo* was pure product (90% yield). The ^{1}H NMR (300MHz, D_2O) has δ at 1.38 (d, J = 6.0Hz, 9H, NCH(C***H*****$_3$**)COOH), 3.47 (d, 6H, PC***H*****$_2$**), 3.65 (m, 3H, NC***H***(CH_3)COOH); the ^{13}C NMR (75MHz, D_2O) has δ at 14.84 (s, NCH(***C***H_3)COOH), 42.65 (d, $J_{p\text{-}c}$ = 12.82Hz, P***C***H_2), 59.35 (d, $J_{p\text{-}c}$ = 5.77 Hz, N***C***H(CH_3)COOH), 174.10 (s, NCH(CH_3)***C***OOH); and the ^{31}P NMR (121.5MHz, D_2O) has δ at -39.9 (s); and the ESI-MS has calculated for $C_{12}H_{24}N_3O_6P$ 337.3, found *m/z* 337.6. The X-ray crystal structure analysis of the *S*-enantiomer (4 H_2O) revealed that the alanine portions were packed to form two-dimensional bilayers running parallel to (001). [See also Kannan et al. *J Am Chem Soc* **128** 11342 *2006*.]

Gold nanoparticles stabilised by agarose (A-AuNP). K.V. Katti and coworkers [Kattumuri *et al. Appl Phys Lett* **88** 153114 2006] prepared this similarly, but replacing GA by agarose. A-AuNPs were used for surface-enhanced Raman spectroscopic detection of DNA nucleosides as well as the other applications stated above.

Gold (~1%) nanoparticles on titanium oxide extrudates (AURO*lite* Au/TiO_2), on aluminium oxide extrudates (Au/Al_2O_3), on zinc oxide granulates (Au/ZnO), and on manganese oxide and carbon (Au/MnO_x/C). These are available commercially and used to catalyse some reactions. A 1% AuNP(~2nm) preparation on TiO_2 is used for catalytic purposes in 'Green' processes, e.g. in the presence of NaOMe in alcohols as solvents it catalyses the oxidation of aldehydes to esters using air as oxidant at ambient or lower temperatures [Marsden et al. *Green Chem* **10** 168 *2008*]. It also catalyses the oxidation of CO and H_2 using O or NO as oxidants [Walther et al. *J Catal* **260** 86 *2008*]. Au/Al_2O_3, Au/ZnO and Au/Mn_xO/C are active catalysts for low temperature oxidation of CO and/or of CH_4 [Grisel & Nieuwenhuys *Catal Today* **64** 69 *2001*, Ma et al. *J Catal* **252** 119 *2007*, see also Freund *Catal Today* **117** 6 *2006*]. The preparations, properties and identification of these and related 'Gold on support' substances will be found in these references; and in Hugon et al. *Gold Bull* **41** 127 *2008*, Supansomboon et al. *Gold Bull* **41** 296 *2008*, and Steyn et al. *Gold Bull* **41** 318 *2008*.

Indium-tin oxide nanopowder (ITO) *[50926-11-9]* **M 264.9, surface resistivity of 100Ωcm.** Available in particle size <50nm. It is coated on glass for making transparent electrodes for screens (e.g. touch screens). However, graphene electrodes have better transparency and are tougher (see above) [Ahn et al. *Nature Nanotechnol* **5** 574 *2010,* DOI:10.1038/nnano.2010.132]

Pd$^{(0)}$ EnCat™ is obtained by reducing the *EnPd$(OAc)_2$ (0.4g, 0.4mmol/g, see below) in Et_2O (8ml) with formic acid (8ml) at 45° for 2 hours. The mixture is cooled and the solid microcapsules are filtered through a polyethylene frit (20 micron porosity), washed with distilled H_2O (3 x 30ml), Me_2CO (3 x 30ml) and Et_2O (3 x 30ml). The microcapsules are dried (at <0.5mm) at 45° for 5 hours to provide black **Pd$^{(0)}$ EnCat** microcapsules (0.35g, containing Pd nanoparticles of ~2nm size). It is an efficient catalyst for reductive ring-opening of epoxides to the respective alcohols which occurs in ~99% yields. The reaction requires either HCOOH/Et_3N or H_2 as hydrogen donors, and the catalyst can be recycled ~10 times [Ley et al. *Org Lett* **5** 4665 *2003*].

***EnPd$(OAc)_2$ [Pd EnCat™]** is prepared from polymethylene polyphenylene di-isocyanate (SUPRASEC 5025, average functionality of 2.7) and $Pd(OAc)_2$ dissolved in $CHCl_3$ and then dispersed at 800rpm for 1 minute into an aqueous solution of Na lignosulfonate (Reax 100M), polyvinyl alcohol (Gohsenol GL 03) and the polyoxyethylene ether of butanol (Tergitol XD), using a mechanical overhead stirrer with a rotary blade. The resulting emulsion would have a particle size range of 20-250microns and the mixture is then gently shaken for 16 hours. The solid polyurea microcapsules formed are collected on a polyethylene frit (20 micron porosity), washed with de-ionised H_2O (5 x 50ml), Me_2CO (5 x 50ml), Et_2O (3 x 50ml) and dried at room temperature.

Encapsulated Pd catalysts such as **Pd EnCat™** are available commercially. These particles are defined by their matrix content e.g. 30% or 40%, the latter having the smaller pore size. [See also Bremeyer et al. *Synlett* 1843 *2002*, Yu et al. *J C S Chem Commun* 678 *2003*, Vickerstaffe et al. *Org Biomol Chem* **1** 2419 *2003*.]

Platinum nanoparticles on spherical polyelectrolyte brushes (SPB). Pt crystals (2-3nm) were deposited on SPB using the procedure of M. Ballauff and coworkers [Schrinner et al. *Science* **323** 617 *2009*]. The SPB consists of a polystyrene core (~100nm diameter) onto which a cationic polyelectrolyte $(^{+}H_3NCH_2CH_2OOC\text{-})_n$ is attached [Schrinner et al. *Adv Mater* **20** 1928 *2008*]. A mixture of $AuCl_4^-$ and $PtCl_6^{2-}$ was reduced with $NaBH_4$ on the surface of the cationic SPB to form alloy nanoparticles ($Au_{45}Pt_{55}$ ratio) on the surface. The Au was removed with cyanide and O_2. Thus a solution of 1.9 x 10^{-5} M NaCN (4ml) was added dropwise within 25 minutes to a stirred suspension of AuPt-SPB (0.04 weight %) at room temperature under air. The high dilution of the cyanide is crucial for avoiding complete dissolution of the NPs and coagulation. Air was bubbled through the solution to remove completely the Au atoms. After 3 hours the colour of the solution was blue due to the formation of pure Pt NPs. [Schrinner et al. *Macromol Chem Phys* **208** 1542 *2007*.] Detailed examination of the composite particles by cryo-TEM, wide angle XRS and HR-TEM showed that the Pt NPs are well-defined faceted single crystals embedded in the SPB-chain layer. This composite system has excellent colloidal stability, and high catalytic activity with turn over numbers of as high as 1580 ±50 for the reduction of *p*-nitrophenol to *p*-aminophenol using $NaBH_4$, which is among the highest ever observed for this reaction. [For a review see H. Birch RSC *Chemistry World* **6** (3) 29 *2009*.]

Rhodium nanoparticles entrapped in Rh/AlO(OH) matrix (~5wt% Rh loading). The catalyst is prepared from a mixture of $RhCl_3.xH_2O$**,** Al(*sec*BuO)$_3$ and 2-butanol (compare with Ru/AlO(OH) below) at 100^o for 3 hours, aging in air for 1 day, filtering, washing the solid with Me_2CO and drying in air at 25^o. It is estimated by high resolution transmission electron microscopy (HRTEM) and X-ray diffraction that the Rh particle sizes in the matrix are 2.5-3.0nm. It is an efficient catalyst for the hydrogenation of arenes, e.g. benzene, naphthalene, quinoline, at low pressures of H_2 (~1 atmosphere) and room temperature in yields approaching 100% and with high turn over, with *ca* 1 mol% of Rh in the catalyst. [Park et al. *Chem Commun* 5667 *2005*].

Ruthenium (nanoparticles) in aluminium oxide/hydroxide (~2.5wt% Ru loading). In this catalyst, Ru is encapsulated in an aluminium oxy-hydroxide matrix where the metal has been shown by energy dispersive X-ray analysis (EDX) and X-ray photoelectron spectroscopy (XPS) to exists mainly as Rh(0) in the matrix. It is prepared in a one-pot synthesis through nanoparticle generation and gelation. Thus $RuCl_3.xH_2O$ (52mg, 0.25mmol) and Al(*sec*BuO)$_3$ (2.5g, 10mmol) in EtOH (1.2ml, 20mmol) under a reflux condenser are heated, with stirring, at 100^o for 1 hour, forming a black suspension to which H_2O (2.0ml) is rapidly added. The mixture is stirred for a further 30 minutes at 100^o, filtered, the black solid is washed with Me_2CO and dried in air at 25^o to give the catalyst as a grey powder (0.74g, 2.5wt% of Ru). It is used as a recyclable catalyst for the efficient oxidant-free alcohol dehydrogenation see Chapter 6, Catalysts-Part 1. [Kim, Park and Park *Org Lett* **8** 2543 *2006*.]

Ruthenium nanoparticles stabilised in polymer ligands. A general procedure was used for making these colloids (agglomerates) which involved introducing ruthenium (1,5-cyclooctadiene)(1,3,5-cyclooctatetraene) (158mg, 0.5mmol, [Ru(COD)(COT)] see [127382-91-6]) in a Fischer-Parr bottle and left *in vacuo* for 30 minutes, then THF (25ml, degassed by freeze-pump cycles) is added and the yellow solution is cooled to -80^o, after which the ligand (0.1mmol) in THF (~60ml) is introduced to the bottle. The bottle is pressurised under 3 bar of H_2 and allowed to warm to room temperature. After ~20 hours a brown-black suspension was obtained. Complete decomposition of the Ru complex was checked by eliminating the H_2 (e.g. by blowing N_2 through) and taking a 3ml aliquot through a small Al_2O_3 column when the filtrate should be colourless. The volume of the solution was then reduced to *ca* 15ml, pentane (50ml) was added, the resulting mixture was cooled to -80^o at which temperature a brown precipitate was formed. This was filtered off (or centrifuged), washed with pentane and dried *in vacuo*. The ligands used were PVP (poly vinylpyrrolidone), *n*-alkyl (C8, C12 and C16) amines and *n*-alkyl (C8, C12 and C16) thiols in varying amounts (from 0.2 to 1 equivalent) giving Ru percentages of ~55 to 80%. The colloids were characterised by microanalysis, IR after CO absorption, high resolution EM and wide-angle X-ray scattering. In THF and in a polymer matrix (Ru/polymer ~5%) crystalline particles of uniform mean size (1.1nm) and agglomerated particles (1.7nm) were obtained in PVP and cellulose acetate. The reaction with various concentration of alkyl amines and alkyl thiols lead to agglomerate particles or particles dispersed in solution both displaying mean size of 2-3nm. In the case with the amine ligands the particles were generally elongated with the tendency of forming worm or rod like structures at high amine concentrations, whereas ^{13}C NMR studies showed that the stabilised particles were not fluxional, but thiol groups were oxidised to disulfide groups probably by the Ru surface. Because of their chemically reactive groups they are potentially very useful

in nanotechnology. [Pan et al. *J Am Chem Soc* **123** 7584 *2001*]. In a similar synthesis ruthenium nanoparticles were stabilised by organosilane fragments, by using *n*-octylsilane, giving particles of ~2.3nm diameter which is a very narrow distribution of size. They were characterised by TEM, as well as solid state ^{13}C MAS NMR. [Pelzer et al. *Chem Mater* **16** 4937 *2004*.]

Silver acetate *[563-63-3]* see also entry in Chapter 6, "Catalysis—Part I". Among the current intense activities in the synthesis of hybrid materials, where an inorganic phase is present as nanometer-sized particles dispersed throughout an organic matrix, is the preparation of a *ca* 190nm uniform film of exceptionally reflective and surface conductive silver "mirror" on a flexible poly(amic) matrix. The Ag-containing resin solutions are made first by dissolving AgOAc in a small volume of dimethylacetamide (DMAc, [127-19-5]) by adding 1.35 equivalents of 1,1,1-trifluoro-2,4-pentanedione (TFAH). As AgOAc is not very soluble in DMAc, addition of TFAH converts the acetate salt into the much more soluble AgTFAH complex. The poly(amic) matrix is prepared by co-polymerising 3,3',4,4'-benzophenonetetracarboxylic anhydride (BTDA, [2421-28-5]) with 4,4'-oxydianiline (APE, 4,4'-diaminodiphenyl ether, [101-80-4]), and making a 15%w/w solution in DMAc by stirring for 5 hours to give a viscosity of 1.7-1.8 dL/g at 35°. The poly(amic) solution is added to the Ag solution to give the desired Ag to BTDA/APE polymer ratio (10.7 to 13.0% Ag), cast into films (onto soda lime glass plates) to give cured films of 20-25 mm thickness. Air (10% relative humidity) is slowly flowed over the film for 18 hours, then thermally cured in a forced air oven with a cycle involving heating at 135° for 20 minutes, holding for 1 hour, heating at 300° for 4 hours, and holding at 300° for 7 hours. This process reduces Ag(I) to the metal and releases all the volatiles. Uniform nanometer thin films of Ag metal (see above) are thus formed in the polymer matrix. Characterisation by X-ray diffraction, transmission (TEM) and scanning (SEM) microscopy, tapping mode atomic force microscopy, X-ray photoelectron microscopy (XPS), and conductivity, reflectivity, thermal and mechanical measurements showed that the films have excellent properties, and are stable in air below 325°. This 'film-to-film' method minimises the amount of Ag used. The applications for this Ag-copolymer silvered films with exceptional reflectivity, thermal, and surface conductivity are immense, and include the fabrication of lightweight optical mirrors, sunshields (e.g. in space telescopes), radiofrequency antennas for management of electromagnetic signals in space, Ag coated tubing to deter catheter-induced urethritis, elastomeric devices, concentration of solar energy, flexible conductive patterned surfaces and tapes. [Southward et al. *Chem Mater* **11** 501 *1999*.]

Silver nanoparticles on spherical electrolyte brushes (SPB). Compare these with the above Pt NPs on SPB. They were also developed by M. Ballauff and coworkers [Lu et al. *J Phys Chem C* **111** 7676 *2007*]. In this case Ag nanoparticles were synthesised onto the polystyrene (PS) core—poly(acrylic acid) (PAA) SPB particles *in situ* by photoemulsion polymerisation. The PS core with a thin layer of photo initiator {2-[*p*-(2-hydroxy-2-methylpropiophenone)]-ethylene glycol-methacrylate} was made by standard emulsion polymerisation procedures also developed by M. Ballauff and coworkers [Gua et al. *Macromolecules* **32** 6043 *1999*]. The PS-PAA-Ag composite particles were prepared *in situ* by mixing diluted PS core solution (1 wt %) with a defined quantity of functional monomer silver acrylate (30 mol% of the amount of styrene), degassing and refilling with N_2 (5 times). Then the mixture was irradiated under N_2 with UV-VIS radiation at ~25° for 90 minutes while being vigorously stirred to keep the mixture homogeneous. Coagulum was removed by filtration through glass wool and the Ag nanocomposite particles were washed by dialysis against purified H_2O using a cellulose nitrate membrane (100nm pore size). DLS showed that the polyelectrolyte brushes were on the PS core; TEM, Cryo-TEM, and wide-angle XRS revealed that the Ag NPs in the brushes were crystalline with a diameter of 3 ±1.2nm.
This Ag-composite is stable and has very good catalytic activity. Reduction of *p*-nitrophenol using $NaBH_4$ is very fast, albeit slightly slower that with Pt or Pd immobilised on related carriers.

Silver nanoparticles [AgNP], on gum Arabic, gelatin or starch. Available as yellow-brownish liquids. They are water soluble in the form of 5-10nm spheres (10-15nm for starch) and have UV with λ_{max} at 405-410nm. The gum Arabic (GA), gelatin and starch stabilise these particles and can be used for sensor design applications, for *in vitro* as well as *in vivo* antimicrobial and antifungal purposes.

Silver-tin alloy nanoparticles, M 118.3. These particles are available in <150nm in size and contain 3.5% Ag with the formula $Ag_{0.035}Sn_{0.965}$. They have a surface area >5.4 m^2/g.

Stannic oxide nanopowder ($Sn(IV)O_2$) *[18582-10-5]* **M 150.7.** It is available in particle size of <100nm. It is used for polishing metal or glass, used in coloured glass, enamels and as a mordant for colouring fabrics. It is toxic and should not be inhaled.

Zinc nano metallic powder (ZnNP) *[7440-66-6]* **M 65.4.** ZnNP is available as a gray powder of spherical particles of 75-125nm size. It is a very reactive form of the metal as it has a high surface area. The powder is particularly reactive with organo-halides to form organo-Zn compounds and in azo-coupling reactions. Sonication will de-agglomerise the nano Zn into particles of 35nm size. ZnNP with particle size <50nm is also available commercially with BET surface area of 35-50 (m^2/g).

SOME ORGANIC AND METAL-ORGANIC COMPOUNDS USED IN NANOTECHNOLOGY

1-Adamantane thiol (tricyclo[3.3.1.1^{3,7}]decane-1-thiol) *[34301-54-7]* **M 168.3, m 95-97°, 100-102°, 99-106°, pK ~11.2.** This thiol was prepared by various methods namely by formation of 1-adamantylisothiourinium bromide from 1-adamanylbromide followed by alkaline hydrolysis [Geigy A.-G. **Belg. Pat** 629,370 *1963*, *Chem Abstr* **60** 9167 *1963*], by refluxing 1-adamantanol with Lawesson's reagent (see [19172-47-5]) in toluene [Nishio *J Chem Soc, Perkin Trans I* 1113 *1993*], and by photolysis of *N*-(1-adamanylcarbonyloxy)pyridin-2-thione [Barton reaction: Barton et al. *Tetrahedron Lett* **35** 6057 *1994*]. The thiol is generally purified by drying over P_2O_5, dissolving in Skellysolve B (see Aliphatic Compounds, Chapter 4) or *n*-hexane, passing through a column of Alumina in *n*-hexane, and eluting with *n*-hexane/EtOAc (97:3). Store it dry under N_2 or argon. The IR (CCl_4) has ν_{max} at 2190, 2850, 1450 and 2565 (S-H) cm^{-1}, the ^1H NMR (CCl_4) has τ at 8.06 (s, 9, β and γ H), 8.29 (s, 6, δ H) and 8.57 (s, 1 S-H); and the MS has *m/z* (peak height) 168 (14, M^+), 136 (12), 135 (100), 93 (15), 79 (17). The S-*2,4-dinitrophenylsulfenyl derivative* gives yellow needles from MeOH with **m 159-160°**. [Tanner & Brownlee *J Canad Chem* **51** 3366 *1973*]. The *S-CH_2CO_2Et derivative* (from $NaNH_2$/$BrCH_2CO_2Et$) has **b 117-118°/0.001mm**, and on hydrolysis (NaOH/EtOH, 5 hours) gave *α-(adamant-1-ylthio)acetic acid* **m 68-70°** (hexane/pentane). Similarly obtained are *α-(adamant-1-ylthio)propionic acid* **m 142-144°** (cyclohexane), *α-(adamant-1-ylthio)butyric acid* **m 113-114°**, *α-(adamant-1-ylthio)isovaleric acid* **m 134-145°** (cyclohexane), *α-(adamant-1-ylthio)caproic acid* **m 74-76°**, *α-(adamant-1-ylthio)-α-phenylacetic acid* **m 122-124°** (cyclohexane/hexane) as well as other acids that are reported [Geigy A.-G. **Belg. Pat** 629,370 *1963*, *Chem Abstr* **60** 9167 *1963*]. 1-Adamantane-thioether is a good novel sialoside protecting group which is also used for coupling with adequately protected sugars [Critch & Li *J Org Chem* **72** 7794 *2007*].
1-Adamantanethiolate molecules have been used in a new patterning technique (microdisplacement printing) to form self-assembled mono-layers (SAMs) on an Au(111) surface for contact printing. The attached thiolate molecular film hinders lateral surface diffusion of the patterning molecules allowing the use of such molecules which are too mobile to pattern by other methods. It is used for SAMs Cat 659452-5G molecular spacer in nanotechnology [*J Org Chem* **72** 7794 *2007*, Dameron et al. *Nano Lett* **5** 1834 *2005*].

Coronene (hexabenzobenzene, [6]circulene) *[191-07-1]* **M 300.4, m 420°, 425-428°, 428°, 438-440°, 440° (uncorrected), 442° (sealed tube) b 525°/atm.** Purify coronene by passing a solution in $*C_6H_6$ through a short Al_2O_3 column and eluting with $*C_6H_6$, followed by evaporation and recrystallisation from $*C_6H_6$ or xylene (**m 245-248°**), and sublimation at 200-300°/20mm, or 420°/atm requiring ~2 hours. Crystallisation from $*C_6H_6$ yields amber-yellow needles (5—15mm long). *Alternatively*, coronene in $*C_6H_6$ is added to a saturated solution of picric acid in EtOH whereby the *picrate* (**m 310-325° dec**) separates as red needles. The picrate in $*C_6H_6$ is passed through an Al_2O_3 column and eluted with $*C_6H_6$ when picric acid remains strongly adsorbed on the column. The eluate is evaporated and the residue recrystallised from toluene, and sublimed (yellow needles) at 250°/high vacuum. It has been distilled at atmospheric pressure using a naked flame. In concentrated H_2SO_4 a green-yellow solution is obtained. The *picrate* forms bright red needles from $*C_6H_6$ with **m 310-325°**. The *1,3,5-trinitrobenzene adduct* gives orange needles which decompose at high temperature. The UV spectrum in $*C_6H_6$ contains 16 sharp peaks between 290 and 428nm, but in EtOH it has λ_{max} (log ε) at 228 (4.08), 252 (3.88) and 290 (5.10) nm. [Baker et al. *J Chem Soc* 1114 *1951*, Baker et al. *J Chem Soc* 1120 *1951*, Clar & Zander *J Chem Soc* 4616 *1957*, Hopff & Schweizer *Helv Chim Acta* **42** 2315 *1959*, *Beilstein* **5** III 2661, **5** IV 2830.] It is an nano-channel organic semiconductor [Newman et al. *Chem Mater* **16** 4436 *2004*] and is used to synthesise MBE-grown layered superconductors [*Japanese J Appl Phys, Part 1* **34** 3837-3845 *1995*].

6-Mercaptohexylferrocene *[134029-92-8]* **M 302.3, b 321-353°.** This thiol is prepared in four steps from ferrocene. Thus a mixture of 6-bromohexanoyl chloride (3.2g, 15mmol, see [22809-37-6]) and anhydrous $AlCl_3$ (2.0g, 15mmol) in cold (0°) CH_2Cl_2 (40ml), which is stirred (20 minutes) under argon, is added dropwise with stirring to ferrocene (2.79g, 15mmol) in CH_2Cl_2 (40ml) over a period of 20 minutes when the colour of the solution turns purple. After stirring for 2 hours, the stirring rate is increase while H_2O (20ml) is added slowly, and the solvent boils gently. The organic layer is collected after 10 minutes, washed with H_2O until the washings are neutral, dried ($MgSO_4$), filtered, concentrated *in vacuo*, and the residue is subjected to chromatography on silica-gel (230-400 mesh) with hexane/EtOAc (100:1) as eluent. The second orange band (the first is ferrocene) is collected and gives *6-(ferrocenylcarbonyl)pentyl bromide* (4.5g, 85%) on evaporation. A part of it (1.61g, 7.4mmol) and Zn/Hg amalgam (freshly prepared from 7.4g of granulated Zn and 0.5g of $HgCl_2$) in H_2O (25ml), 12M HCl (20ml) and toluene (30ml) are stirred vigorously so that the two liquid phases and the solids are in close contact, and are heated under reflux for 16 hours during which time 12M HCl (2 x 5ml) is added. The mixture is cooled to ~25°, the organic layer is collected washed with H_2O, dried ($MgSO_4$), filtered, concentrated, and the residue is purified through a silica-gel column as before. The yellow-brown band provides the required *6-ferrocenylhexyl bromide* (2.33g, 90%). The bromide (1.11g, 3.2mmol) and thiourea (0.24g, 3.5mmol) in absolute EtOH (20ml) is then boiled under reflux in an atmosphere of argon. After boiling for 18 hours, the solvent is removed *in vacuo*, treated with aqueous KOH (0.20g, 3.5mmol, in 20ml of H_2O) and boiled under reflux in an atmosphere of argon for 2 hours. The orange-yellow oil that settles on cooling is extracted into Et_2O (3 x 50ml), the combined extracts are dried ($MgSO_4$), concentrated, and chromatographed as before. The first yellow band gives the desired ***6-ferrocenylhexanethiol*** (0.68g, 62%) on evaporation. It is identified by its ^{1}H NMR (300 MHz, $CDCl_3$) which has δ at 1.35 (t, 1H, S**H**), 1.39 (br, 4H, $FcCH_2C\mathbf{H}_2\mathbf{CH}_2$), 1.52 (q, 2H, $C\mathbf{H}_2CH_2CH_2SH$), 1.63 (q, 2H, $C\mathbf{H}_2CH_2SH$), 2.34 (t, 2H, $FcC\mathbf{H}_2$), 2.53 (q, 2H, $C\mathbf{H}_2SH$), 4.06 (t, 2H, $C_5\mathbf{H}_4$), 4.07 (t, 2H, $C_5\mathbf{H}_4$), 4.11 (s, 5H, $C_5\mathbf{H}_5$); and EI-MS *m/z* at 302 (M^+). The second yellow band contains the corresponding *disulfide* which can be reduced and used. [Creager & Rowe *J Electroanal Chem (Lausanne Switz)* **370** 203 *1994*, *cf* Yu et al. *J Org Chem* **66** 2937 *2001*.] This and other related ferrocenyl-alkane thiols have been synthesised and characterised electrochemically in solution and in self-assembled monolayer (SAM) films on gold electrodes. The affinities of these on the electrode surface have been described in detail. These red-ox active thiols can be used for selective electrochemical sensing and preparing a new type of thiol self-assembled sensing devices (SAMs). [Creager & Rowe *J Electroanal Chem (Lausanne Switz)* **370** 203 *1994*.]
Gold nanoparticles covered fully with 6-ferrocenylhexanethiolate ligands, with average composition Au_{225}(6-ferrocenylhexanethiolate)$_{42}$, were prepared, and had a unique combination of adsorption properties on Pt electrodes which were studied comprehensively. The adsorbed layers are so robust that sub, mono and multi nanoparticulate layers on the electrodes can be transferred to fresh electrolyte solutions in which they show stable ferrocene voltametry over long time periods. [Stiles et al. *J Am Chem Soc* **130** 1856 *2008*.]

NPs for drug delivery to tissues and particularly to brain, i.e. traverse the blood-brain-barrier, include conjugates of dextran, agarose, chitosan polyacetic acid (PLA), poly(lactic-co-glycolytic acid) (PLGA) and NPs with lipophilic moieties, e.g. polyethylene glycol (PEG) to which drugs can be bound have been explored by Fresta and co-workers [Celia et al. *Med Res Rev* **31** (3) 716-756 *2011*], and shown to be useful devices.

Tetra-*n*-propylammonium perruthenate (TPAP, tetrapropyl tetraoxoruthenate) *[114615-82-6]* **M 351.4, m 160°(dec).** This oxidant (at 5 mol%) acts catalytically in oxidising 2-substituted *N-1, N-3*-dihydroxy-imidazolidines (1mol) in CH_2Cl_2 at room temperature in 1-12 hours in the presence of *N*-methylmorpholine *N*-oxide (1.1mol) to provide the respective 2-substituted imidazoline-1-nitronyl-3-nitroxide radicals (NNRs) in 44-90% yields. NNRs have found applications in Physics, Chemistry and Nanotchnology for the development of organic molecular magnets [Palacio et al. *Phys Rev Lett* **79** 2336 *1997*] and single chain magnets [Caneschi et al. *Angew Chem Int Ed* **40** 1760 *2001*]. Gorini et al. *Synlett* 948 *2006*; for further reading see TPAP entries on p. 656 in Chapter 5, 'Metal-Organic Compounds', and on p. 708 Chapter 6, 'Catalysis-Part 1'.]

SAFETY ISSUES

Materials of nanometer size have been present on earth almost since its formation ~4.6 billion (eon) years ago, as well as in the universe. Recently J. Cami, and coworkers have discovered large clouds in the planetary nebula Tc1 in which C_{60} and C_{70} fullerenes were identified by infra red spectroscopy. [*Science* **329 (Issue 5996)** 1180

2010, reviewed by A. Extance RSC *Chemistry World* **7** (9) 21 *2010*, and L. Howes RSC *Chemistry World* **8** (1) 34 *2011*.] During the past 30 years or so the development of nanomaterials and their wide ranging applications have avalanched, and progress is continuing. The safety aspects of nanomaterials have been of concern for many years, and it is generally accepted that conscious efforts have to be made to protect the individual workers in the field, the general public and the environment. Research on safety aspects is slowly gaining pace, and it has already been shown in mice that carbon nanotubes (CNTs) exhibit asbestos-like pathogenicity when inhaled. [K. Donaldson and coworkers: Poland et al. *Nature Nanotechnol* **3** 423 *2008*, J.C. Bonner and coworkers: Ryman-Rasmussen et al. *Nature Nanotechnology* **4** 747 *2009*, Reviewed by H. Birch RSC *Chemistry World* **6** (12) 24 *2009*.] The movement of nanomaterial from lungs to lymph nodes to the blood stream and clearance through the kydneys has been demonstrated by J.V. Frangioni and A. Tsuda and their coworkers [Choi et al. *Nature Biotechnol* **28** 1300 *2010*, reviewed by L. Howes RSC *Chemistry World* **7** (12) 24 *2010*.] More recently W. Wohlleben and coworkers have subjected two thermoplastic materials and two cement materials infused with different nanoparticles (i.e. nanotubes and nanoparticle in polymers filters and in inorganic matrices) to gentle abrasion, high speed sanding and UV radiation. They did not find significant release of nanopowders into the atmosphere in which the sizes of the nanoparticles were very different from those in control powders. Moreover, rats exposed to the dust fared no worse than those exposed to dust that contained nanocomponents. However, further studies are in progress. [Wohlleben et al. *Small* **7** (16) 2384 *2011*, DOI: 10: 1002/smll.201002054; reported by K. McAlpine *Chemistry World* **8** (8) 28 *2011*.]
Safety was rather slack in the early days, but it is being realised that nanomaterials should be treated differently from hazardous chemicals due to their unknown long-term effects. Nano-enabled hoods and nano-enabled-gear for personnel are being used, but only to a small extent. Safety protocols have been written and updated, but nano-regulation is only slowly creeping in [see special report by V. Gill RSC *Chemistry World* **6** (4) 10 *2009*.] A comprehensive report on nanosafety practices in research laboratories worldwide was compiled by J. Santamaria and coworkers recently, where they detail an up-to-date account of the present situation regarding to safety issues. [Balas et al. *Nature Nanotechnol* **5** 93 *2010*; Reviewed by K. McAlpine RSC *Chemistry World* **7** (3) 15 *2010*.]

Our advice is that in the manipulation and disposal of nanomaterials the same guidelines for asbestos handling should be used. In addition, further precautions should be exercised which should consider the known toxicity and the chemical nature of the nanomaterials in use.

The following is a list of more recent books that were published on legal, personal, industrial, and environmental safety aspects of nanotechnology:

L.L. Bergeson (Ed), *Nanotechnology: Environmental Law, Policy and Business Considerations*, American Bar Association, ABA Publishing USA, *2010*. ISBN 9781604225826.

J-Y. Botero, *Environmental Nanotechnology*, McGraw Hill, *2007*. ISBN 97800714777505, 0071477500.

R.E. Hester and R.M. Harrison (Eds), *Nanotechnology: Consequences for Human Health and the Environment*, RSC Publ. *2009*. ISBN 9781847559562, 1847559565.

C. Kumar (Ed), *Nanomaterials: Toxicity (Health and Environment Issues)*, WILEY-VCH, Weinheim, *2006*. ISBN 9783527313853, 3527313850.

J.R. Lead and E. Smith (Eds), *Environmental and Human Aspects of Nanotechnology*, J. Wiley & Sons, NY, *2009*. ISBN 9781405176347.

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N.A. Montiero-Riviere and C.L. Tran, *Nanotoxicology: Characterisation, Dosing and Health*, Informa Healthcare Publ, *2007*. ISBN 9781420024147, 1420045148.

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V.E. Borisenko, S.V. Gaponenko and V.S. Gurin (Eds), *Physics, chemistry and application of nanostructures*: *reviews and short notes*: *proceedings of the international conference, Nanomeeting 2007*. ISBN 978981275990, 981275996.

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J.L. Feather and M.F. Azner, *Nanotechnology: Education and Workforce Development*, CRC Press, Boca Raton, Fl, *2011*. ISBN 9781420053944.

B.D. Feldman, *Materials Chemistry*, Springer, Dordrecht, *2008*. ISBN 978-1-4020-6119-6, 978-1-4020-6120-2 (e-book).

J.H. Grassian, *Nanoscience and Nanotechnology*, J. Wiley & Sons, *2008*. ISBN 978047081037.

J.A. Helsen and Y. Missirlis, *Biomateriials: Biological and Medical Physics, Biomedical Engineering*, Springer Verlag, *2010*. ISBN 9783642125317, 9783642125324 (e-book).

C. Hess and R. Schlögl (Eds), *Nanostructured Catalysts,* RSC Publ. Nanoscience & Nanotechnology, *2011*. ISBN 9780854041866.

G.L. Hornyak and H.F. Tibbals, *Fundamentals of Nanotechnology*, CRC Press, Boca Raton, Fl, *2009*. ISBN 978140048032, 1420048031.

G.L. Hornyak, H.F. Tibbals and J. Dutta, *Introduction to Nanoscience and Nanotechnology*, CRC Press, Boca Raton, Fl, *2009*. ISBN 9781420047790, 1420047795.

M.S. Johal, *Understanding Nanomaterials*, CRC Press, Boca Raton, Fl, *2011*. ISBN 9781420073102.

C.S.S.R. Kumar, *Nanocomposites*, Wiley-VCH, Weinhein, *2010*. ISBN 9743527321681.

C.S.S.R. Kumar, *Nanostructured Thin Films and Surfaces*, Wiley-VCH, Weinhein, *2010*. ISBN 9783527321551, 3527321551.

D.P. O'Mathuna, *Nanoethics: Big Issues with Small Technology*, Continuum International Publ. Co. London, *2009*. ISBN 9781847063946 (HB), 9781847063953 (PB).

G.A. Ozin, A. Arsenault and L. Cademartiri, *Nanochemistry: A Chemical Approach to Nanomaterials*, RSC Publ., *2009*. ISBN 9781847558954.

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G. Schmid (Ed), *Nanoparticles: From Theory to Application*, 2nd edition, Wiley-VCH, *2010*, ISBN 3527325891 (available from the internet with Babylon Translation Software free download, 538 pp, 12 MB as PDF).

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CAS Registry Numbers Index

HOW TO VALIDATE CHEMICAL ABSTRACTS SERVICE REGISTRY NUMBERS

Almost all chemical and biochemical entries in this book have CAS (Chemical Abstract Service) Registry Numbers to identify them and have been entered for each substance. The registry numbers are an efficient way for identifying substances and are independent of the nomenclature of substances. Unlike chemical names which may have more than one synonymous name, there is only one CAS Registry Number for each substance (with only a few exceptions, e.g. where a substance may have another number before purification, or before determination of absolute configuration).

The registry numbers are made up of three sets of digits separated by two hyphens with the general form: $n\mathrm{N}_n + \ldots\ldots + 4\mathrm{N}_4 + 3\mathrm{N}_3 - 2\mathrm{N}_2 + 1\mathrm{N}_1 - R$ where the Ns are sequential numbers and *R* is the *check digit*. The first set can be up to eight digits (at this point in time, but not less than two), and the second is made of two digits (zeros are included as a digits) and the third is a single digit which *checks* the validity of the sequential numbers, e.g. 379669-72-4 for *but-3-enylboronic acid* or 83-32-9 for *acenaphthene*. The validity of a registry number can be checked by the following formula (computer generated):

$$\frac{n\mathbf{N}_n + \ldots\ldots + 4\mathbf{N}_4 + 3\mathbf{N}_3 + 2\mathbf{N}_2 + 1\mathbf{N}_1}{10} = \mathbf{Q} + \boldsymbol{R}/\mathbf{10}$$

where the **N**s include all numbers except the last *check* digit, **Q** represents an integer (fractions not included) which, although it is disregarded, does give the value of ***R*** equal to the *check digit* in a **valid** Registry Number.

The following three examples demonstrate the application of the formula and the validity of the Registry Number:

1. 1,5-Dihydroxynaphthalene 83-56-7

$$\frac{(4\mathrm{x}\mathbf{8}) + (3\mathrm{x}\mathbf{3}) + (2\mathrm{x}\mathbf{5}) + (1\mathrm{x}\mathbf{6})}{10} = \frac{5\mathbf{7}}{10} = 5 + \frac{\mathbf{7}}{10}$$

[Note: *the last (check) digit of the CAS number 7 is not included*.]

When the value of **Q** is made to equal 5, the *check* digit *R* becomes equal to 7; thus the Registry Number is **valid**. In this case the value of **Q** is in fact the digit(s) (**5**), before the last *check* digit (**7**).

2. 4,5-Diamino-6-hydroxypyrimidine hemisulfate 102783-18-6

$$\frac{(8\mathrm{x}\mathbf{1}) + (7\mathrm{x}\mathbf{0}) + (6\mathrm{x}\mathbf{2}) + (5\mathrm{x}\mathbf{7}) + (4\mathrm{x}\mathbf{8}) + (3\mathrm{x}\mathbf{3}) + (2\mathrm{x}\mathbf{1}) + (1\mathrm{x}\mathbf{8})}{10} = \frac{10\mathbf{6}}{10} = 10 + \frac{\mathbf{6}}{10}$$

When the value of Q is made to 10, the *check* digit *R* becomes equal to 6; thus the Registry Number is **valid**. In this case the value of **Q** is in fact the digit(s) (**10**), before the last *check* digit (**6**).

3. 1,4-Bis(pentafluorobenzyl)[C_{60}]fullerene 1260376-31-5

$$\frac{(9\text{x}\mathbf{1}) + (8\text{x}\mathbf{2}) + (7\text{x}\mathbf{6}) + (6\text{x}\mathbf{0}) + (5\text{x}\mathbf{3}) + (4\text{x}\mathbf{7}) + (3\text{x}\mathbf{6}) + (2\text{x}\mathbf{3}) + (1\text{x}\ \mathbf{1})}{10} = \frac{13\mathbf{5}}{10} = 13 + \frac{\mathbf{5}}{10}$$

When the value of Q is made to 13, the check digit *R* becomes equal to 5; thus the Registry Number is **valid**. In this case the value of **Q** is in fact the digit(s) (**13**), before the last *check* digit (**5**).

The CAS Registry Handbook (Number Section) and supplements should be consulted for obtaining the substance name and elemental formula corresponding to a Registry Number.

To facilitate the method for locating the purification of a substance, a CAS Registry Number Index of the numbers of the entries with their respective page numbers is included here. This will also provide the reader with a rapid way to see if the purification of a particular substance has been reported in the book.