PYRIDINE AND ITS DERIVATIVES

SUPPLEMENT IN FOUR PARTS
PART THREE

This is the fourteenth volume in the series
THE CHEMISTRY OF HETEROCYCLIC COMPOUNDS

THE CHEMISTRY OF HETEROCYCLIC COMPOUNDS

A SERIES OF MONOGRAPHS

ARNOLD WEISSBERGER and EDWARD C. TAYLOR

Editors

PYRIDINE
AND
ITS DERIVATIVES
SUPPLEMENT
PART THREE

Edited by

R. A. Abramovitch

University of Alabama

AN INTERSCIENCE® PUBLICATION

JOHN WILEY & SONS
NEW YORK • LONDON • SYDNEY • TORONTO

An Interscience ® Publication

Library of Congress Cataloging in Publication Data:

Abramovitch, R. A. 1930–
Pyridine supplement.

(The Chemistry of heterocyclic compounds, v. 14)
"An Interscience publication."
Supplement to E. Klingsberg's Pyridine and its derivatives.
Includes bibliographical references.
1. Pyridine. I. Klingsberg, Erwin, ed. Pyridine and its derivatives. II. Title.

QD401.A22 547′.593 73–9800

ISBN 0–471–37915–8

Contributors

C. S. GIAM, *Chemistry Department, Texas A&M University, College Station, Texas*
RENAT H. MIZZONI, *Ciba Pharmaceutical Company, Division of Ciba-Geigy Corporation, Summit, New Jersey*
M. E. NEUBERT, *Department of Chemistry, Kent State University, Kent, Ohio*
PETER I. POLLAK (deceased)
HOWARD TIECKELMANN, *State University of New York, Buffalo, New York*
MARTHA WINDHOLZ, *Merck Sharp & Dohme Research Laboratories, Rahway, New Jersey*

TO THE MEMORY OF

Michael

The Chemistry of Heterocyclic Compounds

The chemistry of heterocyclic compounds is one of the most complex branches of organic chemistry. It is equally interesting for its theoretical implications, for the diversity of its synthetic procedures, and for the physiological and industrial significance of heterocyclic compounds.

A field of such importance and intrinsic difficulty should be made as readily accessible as possible, and the lack of a modern detailed and comprehensive presentation of heterocyclic chemistry is therefore keenly felt. It is the intention of the present series to fill this gap by expert presentations of the various branches of heterocyclic chemistry. The subdivisions have been designed to cover the field in its entirety by monographs which reflect the importance and the interrelations of the various compounds, and accommodate the specific interests of the authors.

In order to continue to make heterocyclic chemistry as readily accessible as possible new editions are planned for those areas where the respective volumes in the first edition have become obsolete by overwhelming progress. If, however, the changes are not too great so that the first editions can be brought up-to-date by supplementary volumes, supplements to the respective volumes will be published in the first edition.

Arnold Weissberger

Research Laboratories
Eastman Kodak Company
Rochester, New York

Edward C. Taylor

Princeton University
Princeton, New Jersey

Preface

Four volumes covering the pyridines were originally published under the editorship of Dr. Erwin Klingsberg over a period of four years, Part I appearing in 1960 and Part IV in 1964. The large growth of research in this specialty is attested to by the fact that a supplement is needed so soon and that the four supplementary volumes are larger than the original ones. Pyridine chemistry is coming of age. The tremendous variations from the properties of benzene achieved by the replacement of an annular carbon atom by a nitrogen atom are being appreciated, understood, and utilized.

Progress has been made in all aspects of the field. New instrumental methods have been applied to the pyridine system at an accelerating pace, and the mechanisms of many of the substitution reactions of pyridine and its derivatives have been studied extensively. This has led to many new reactions being developed and, in particular, to an emphasis on the direct substitution of hydrogen in the parent ring system. Moreover, many new and important pharmaceutical and agricultural chemicals are pyridine derivatives (these are usually ecologically acceptable, whereas benzene derivatives usually are not). The modifications of the properties of heteroaromatic systems by *N*-oxide formation are being exploited extensively.

For the convenience of practitioners in this area of chemistry and of the users of these volumes, essentially the same format and the same order of the supplementary chapters are maintained as in the original. Only a few changes have been made. Chapter I is now divided into two parts, Part A on pyridine derivatives and Part B on reduced pyridine derivatives. A new chapter has been added on pharmacologically active pyridine derivatives. It had been hoped to have a chapter on complexes of pyridine and its derivatives. This chapter was never received and it was felt that Volume IV could not be held back any longer.

The decision to publish these chapters in the original order has required sacrifices on the part of the authors, for while some submitted their chapters on time, others were less prompt. I thank the authors who finished their chapters early for their forebearance and understanding. Coverage of the literature starts as of 1959, though in many cases earlier references are also given to present sufficient background and make the articles more readable. The literature is covered until 1970 and in many cases includes material up to 1972.

I express my gratitude to my co-workers for their patience during the course of this undertaking, and to my family, who saw and talked to me even less than usual during this time. In particular, I acknowledge the inspiration given me by the strength and smiling courage of my son, Michael, who will never know how much the time spent away from him cost me. I hope he understood.

R. A. ABRAMOVITCH

University, Alabama
June 1973

Contents

Part Three

Part One

I. Part A. Properties and Reactions of Pyridines

R. A. ABRAMOVITCH and G. M. SINGER

Part B. Partially Reduced Pyridines

R. E. LYLE

II. Synthetic and Natural Sources of the Pyridine Ring

N. S. BOODMAN, J. O. HAWTHORNE, A. W. SIMON, and P. X. MASCIANTONIO

III. Quaternary Pyridinium Compounds

O. RODIG

Part Two

IV. Pyridine-1-Oxides

R. A. ABRAMOVITCH and ELIZABETH M. SMITH

V. Alkylpyridines and Arylpyridines

RONALD G. MICETICH

VI. Halopyridines

MAX M. BOUDAKIAN

VII. Organometallic Compounds of Pyridines

HARRY L. YALE

Part Four

PYRIDINE AND ITS DERIVATIVES

SUPPLEMENT IN FOUR PARTS
PART THREE

This is the fourteenth volume in the series
THE CHEMISTRY OF HETEROCYCLIC COMPOUNDS

Chemistry of Heterocyclic Compounds, Volume 14
Edited by R. A. Abramovitch

CHAPTER VIII

Nitropyridines and Reduction Products (Except Amines)

RENAT H. MIZZONI

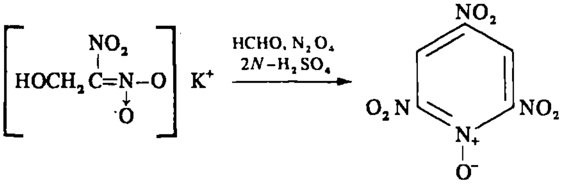
Ciba Pharmaceutical Co.
Division, Ciba-Geigy Corp.
Summit, New Jersey

I. Nitropyridines

1. Preparation

A. *Synthesis from Aliphatic Intermediates*

Gundermann and Alles[1] have studied the stepwise reaction of potassium 2,2-dinitroethanol with formaldehyde, dinitrogen tetroxide, and dilute acid (VIII-1). They concluded that the reaction product was 2,4,6-trinitropyridine-1-oxide on the basis of spectral evidence and mode of formation. The reaction is analogous to one employing potassium nitroacetonitrile to give 2,4,6-tricyano-pyridine-1-oxide.



(VIII-1)

B. *By Nitration of Substituted Pyridines*

The nitration of 2-dimethylaminopyridine-1-oxide under mild conditions gives 2-dimethylamino-5-nitropyridine-1-oxide; significantly, none of the 4-nitro isomer is formed in the reaction.[2]

DeSelms[3] has reinvestigated the nitration of 2-methyl- and 2-chloro-3-pyridinol. The entering nitro group is directed to the 4- and 6- positions in a 4 to 1 ratio. Electrophilic nitration of 3-pyridinol to give 2-nitro-3-pyridinol[4] and 2,6-dinitro-3-pyridinol[3] was confirmed. This seems to be the only example of 4-nitration except for the case of the pyridine-1-oxides.

C. *By Oxidation of Aminopyridines*

The preparation of 3-fluoro-4-nitropyridine can be effected by oxidation of the aminofluoro compound with persulfuric acid.[5] A similar reaction yields 4-nitrotetrafluoropyridine from the corresponding amino precursor.[6,7]

4-Nitrotetrafluoropyridine is a liquid whose boiling point (152 to 154°) is appreciably lower than that of 2-nitropyridine (256°), or of 3-nitropyridine (216°).

In futher examples, 2-aminopyridine and 2-amino-5-bromopyridine give 2-nitropyridine-1-oxide and 5-bromo-2-nitropyridine-1-oxide directly, in low yields, on oxidation with peroxytrifluoroacetic acid.[8]

D. *From Nitropyridine-1-oxides*

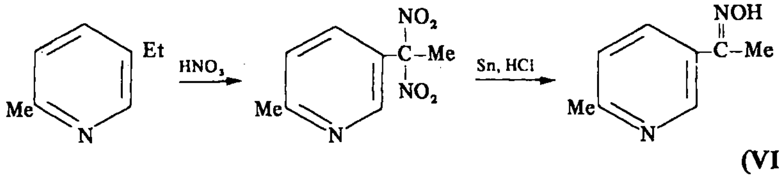
Kroehnke and Schaefer[9] have studied the deoxygenation of 4-nitropyridine-1-oxides by various reagents. Nitrosylsulfuric acid and "nitration acid" give yields of deoxygenated products in excess of 90%; the conventional reagent (PCl_3-CHCl_3) is somewhat less effective and gives up to 71% of products.

Simultaneous nitration-deoxygenation has also been observed by these workers. For example, pyridine-1-oxide undergoes nitration and deoxygenation with concentrated sulfuric acid and fuming nitric acid at 130 to 165° to give 4-nitropyridine in 71% yield. As additional examples, 3-picoline-1-oxide gives 4-nitro-3-picoline (81%), and 3-bromopyridine-1-oxide affords 3-bromo-4-nitropyridine (75%) on treatment with nitric oxide and sulfuric acid at 150 to 200°.

The *N*-oxide function is retained on treatment with nitric and sulfuric acids at somewhat lower temperatures. Thus Talik and Talik[10] prepared 3-chloro-4-nitropyridine-1-oxide (84.5%) and 3-iodo-4-nitropyridine-1-oxide (56.4%) with this reagent at steam-bath temperature.

E. *Side-Chain Nitro Compounds*

Rubinstein, Hazen, and Zerfing[11] noted the occurrence of appreciable side-chain nitration during the oxidation of 5-ethyl-2-picoline with nitric acid (VIII-2). The product of this reaction gives methyl 2-methyl-5-pyridyl ketoxime on reduction with tin and hydrochloric acid.



(VIII-2)

2. Reactions of Nitropyridines

A. *Reduction*

Yamada and Kikugawa[12] reported that 2- and 4-nitropyridines give the hydrazo- and azo- compounds, respectively, on reduction with sodium borohydride in boiling ethanol; nitrobenzene, however, does not react under these conditions. The reduction of picolinonitrile and isonicotinonitrile with this reagent further exemplifies the enhanced reactivity of 2- and 4- substitutents on the pyridine ring.

B. *Reactivity of Nitropyridines and Halonitropyridines*

The relative reactivity of substituents in nitropyridines, halonitropyridines, and halonitropyridine-1-oxides has been studied extensively during recent years.

Johnson[13] investigated the reactivities of 2- and 4-halo- and 2- and 4-nitropyridine-1-oxides toward sodium methoxide and found that the energies of activation were lower for the nitropyridine-1-oxides than for the corresponding halo compounds.

Talik[14, 15] studied the behavior of 3-chloro-4-nitropyridine-1-oxide with various reagents, and showed that sodium methoxide causes replacement of the nitro group, while amines, on the other hand, effect displacement of the halogen.

2-Halo-4-nitropyridine-1-oxides react with two equivalents of sodium methoxide at room temperature to effect replacement of both halogen and nitro groups. One equivalent of sodium methoxide at that temperature, however, causes replacement of the nitro group alone to give 2-chloro-4-methoxypyridine-1-oxide in 84% yield.[16, 17] The use of two equivalents of the base in boiling methanol gives 2,4-dimethoxypyridine-1-oxide.

Boiling aqueous potassium hydroxide converts 2-chloro-4-nitropyridine into 2-chloro-4-pyridone.[18] In general, the reactivity pattern of 2-halo-4-nitropyridines parallels that of the corresponding 1-oxides.[17, 19]

3-Fluoro-4-nitropyridine-1-oxide undergoes facile displacement of the halogen under mild conditions. Alkoxides in general lead to replacement of fluorine at room temperature, and of both substituents at higher temperatures.[20, 22]

Abramovitch and his co-workers[21] have studied the reaction kinetics of variously substituted halopyridines with methoxide ion in methanol. As part of this study, energies of activation were determined for 2-chloro-3-nitro- and 2-chloro-5-nitropyridines; they were found to be 18.7 and 18.1 kcal/mole, respectively.

4-Nitro-3-chloropyridine-1-oxide is reduced with hydrazine to 4-amino-3-chloropyridine-1-oxide.[17] 2-Chloro-4-nitropyridine gives 1,2-bis-(2-chloro-4-pyridyl)hydrazine on treatment with hydrosulfide.[18]

C. *Reactions of Nitroaminopyridines*

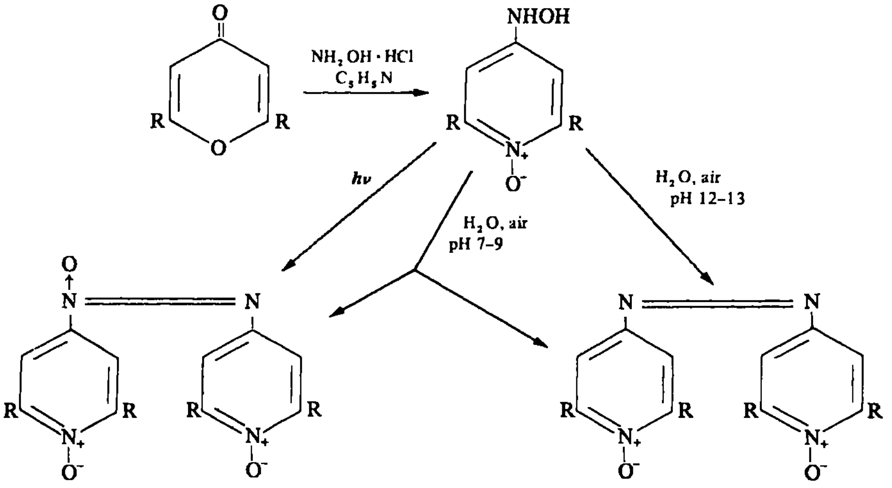
2-, 3-, And 4-nitroaminopyridines react with halogens and red phosphorus in boiling chloroform or carbon tetrachloride to give chloro-, bromo- and iodopyridines.[23]

II. Nitrosopyridines and Hydroxylaminopyridines

4-Nitropyridine-1-oxide undergoes reduction with phenylhydrazine to give 4-hydroxylaminopyridine-1-oxide in nearly quantitative yield.[24] This product is very reactive; it undergoes oxidation in aqueous ammonia to form 4,4′-azopyridine-1,1′-dioxide, and with potassium permanganate in acid solution to give 4-nitrosopyridine-1-oxide.

Photolysis of 4-nitropyridine in ethanol yields 4-hydroxylaminopyridine.[25]

Yates and his co-workers[26] have studied the reactions of 2,6-dialkyl-4-pyrones with hydroxylamine. Thus, 2,6-dimethyl-4-pyrone and 2,6-diethyl-4-pyrone give the corresponding 2,6-dialkyl-4-hydroxylaminopyridine-1-oxides in 17 to 20% yields (VIII-3).



(VIII-3)

The hydroxylaminopyridine-1-oxides are reactive compounds that are oxidized by air in strongly alkaline solutions to azopyridines, and that undergo photochemical conversion to azoxy derivatives. Mixtures of azo and azoxy compounds are produced by atmospheric oxidation under less alkaline conditions (VIII-3).

III. Azopyridines and Azoxypyridines

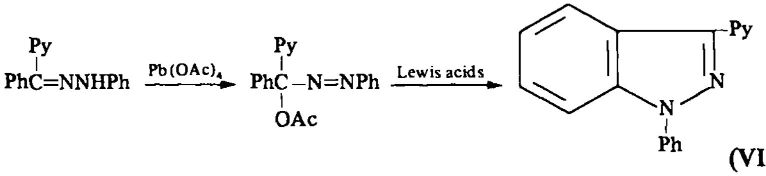
Brown and his collaborators[27] found that 5-amino-2-dimethylaminopyridine does not react with nitrosobenzene to give the expected 2-dimethylamino-5-phenylazopyridine. Instead, the desired compound is obtained by reaction of 2-chloro-5-phenylazopyridine with dimethylamine. In contrast to the biological action of 3-(*p*-dimethylaminophenyl)azopyridine, this substance is not carcinogenic.

Elslager and his co-workers[28] have prepared a variety of pyridylazo compounds for testing as chemotherapeutic agents.

Czuba[29] has investigated the behavior of a large number of substituted 3-nitraminopyridines on treatment with sulfuric acid. The products of the reaction are substituted 3-azopyridines, 3-azoxypyridines, and 3-pyridinol.

The oxidation of 2-(*p*-nitrophenylazo)pyridine with perbenzoic acid gives a mixture of the 1-oxide and the α-azoxy-1-oxide.[4]

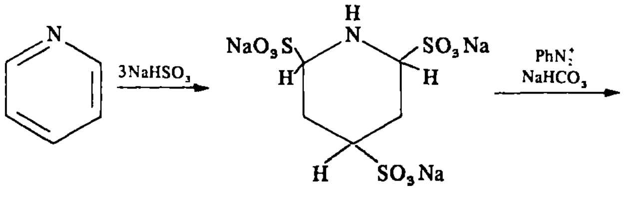
Gladstone and Norman[30] have subjected benzoylpyridine phenylhydrazones to lead tetraacetate oxidation. The intermediate side-chain azo compounds thus formed undergo conversion to 3-pyridylindazoles with Lewis acids (VIII-4).

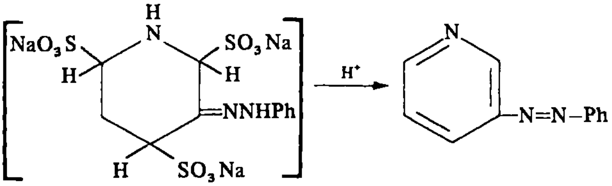


(VIII-4)

2-Substituted-5-aminopyridines react with nitrosobenzene under basic conditions to afford 2-substituted-5-phenylazopyridines in yields of 53 to 84%.[31]

In a significant reaction, pyridine couples with phenyldiazonium salts in the presence of sodium bisulfite to give 3-phenylazopyridine. The pyridine-sodium bisulfite adduct is thought to be the reactive heterocyclic moiety[32] (VIII-6).



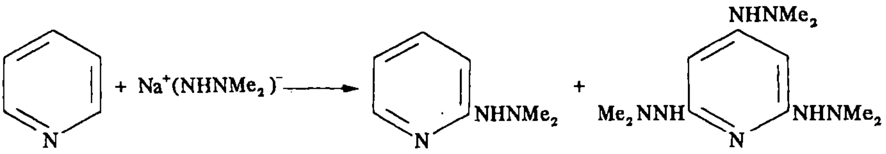


(VIII-6)

IV. Hydrazinopyridines

A number of reactive fluoropyridines have been used to synthesize hydrazinopyridines. Thus 3-fluoropyridine-1-oxide reacts readily with hydrazine to give 3-hydrazinopyridine-1-oxide.[33] Similarly, pentafluoropyridine gives 4-hydrazinotetrafluoropyridine.[34] In like manner, 3,5-difluoro-4-hydrazinopyridine is readily prepared.[35]

Pyridine and some of its homologs have been subjected to direct hydrazination with substituted hydrazines. Reaction occurs almost exclusively at the 2-position, although in one case a trihydrazino compound forms as a by-product (VIII-5).[36]



(VIII-5)

The reaction of 2-chloropyridine with monosubstituted hydrazines in the presence of sodium hydride gives 1,1-disubstituted hydrazines.[37]

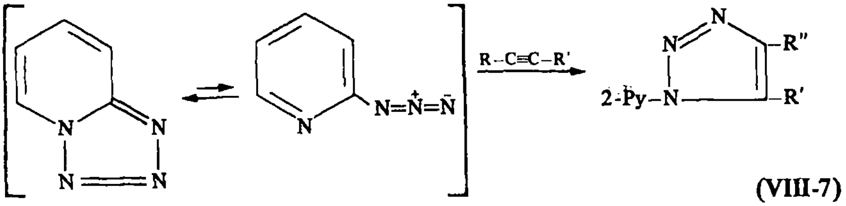
V. Pyridyl Azides

A number of pyridyl azides have been prepared by conventional methods. The reaction of 4-hydrazino-2-picoline with nitrous acid, for example, gives 4-azido-2-picoline. 4-Azidopyridine-1-oxide is obtained in a similar manner. The reaction of 4-chloropyridine with sodium azide is less satisfactory, and gives the product in low yield.[38]

3-Pyridylazide is formed by reaction of 3-pyridyldiazonium chloride with sodium azide.[39] 2-Aminopyridine-1-oxides can be diazotized, and treatment of the salt with azide ion gives rise to the 2-azidopyridine-1-oxide in good yields.[39a]

4-Azido-2-picoline is oxidized with hydrogen peroxide to 4,4′-azoxy-2,2′-dimethylpyridine,[38] which reacts with propargyl alcohol to give the pyridyl-(hydroxymethyl)-1,2,3-triazole. 4-Azidopyridine-1-oxide yields 4,4′-azoxypyridine-1,1′-dioxide on photolysis in acetone.[40]

Huisgen and his co-workers have investigated the reaction of 2-pyridylazide with various acetylenes. Although the equilibrium is largely toward the tetrazole,[40a, 40b] the substance reacts to give 1-(2-pyridyl)-1,2,3-triazoles (VIII-7).[40a] (See Ch. IA for some reactions of 2-azidopyridine-1-oxides.)



(VIII-7)

R′ = H , R″ = CO_2Me
R′, R″ = CO_2Me
R′, R″ = Ph

VI. Tables

TABLE VIII-1. Nitropyridines

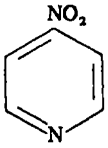
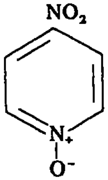
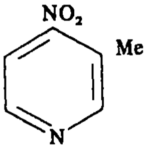
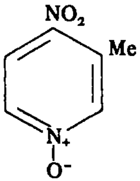
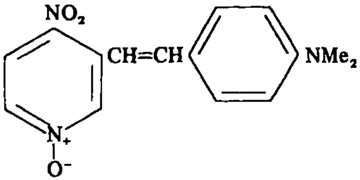
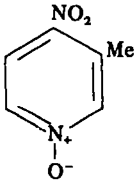
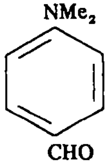
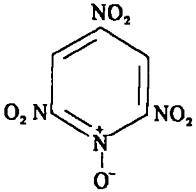
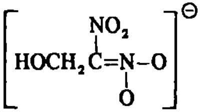
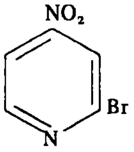
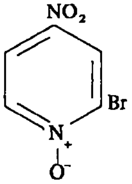
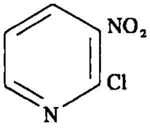
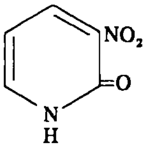
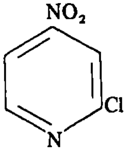
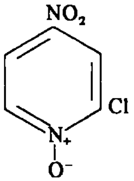
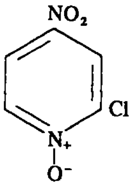
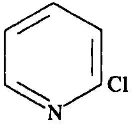
Compound	Method of preparation	Yield (%)	Properties	Ref.
	 + (a) Nitrosylsulfuric acid (b) NO, conc. H_2SO_4 (c) PCl_3–$CHCl_3$	93 91.5 71		9
	 , NO, H_2SO_4	81	m.p. 28°	9
	 ,  , (piperidine)		m.p. 208°	41
	 $\left[HOCH_2\overset{NO_2}{C}=\underset{O}{N}-O\right]^{\ominus}$ $K^{\oplus}$, H_2SO_4, HCHO		m.p. 190° (dec.)	1

TABLE VIII-2. Preparation and Properties of Halonitropyridines and 1-Oxides

Compound	Method of preparation	Yield (%)	Properties	Ref.
	 , PCl_3–$CHCl_3$		m.p. 64°	42
	 , $POCl_3$–$HCONMe_2$	97	m.p. 99°	43
			m.p. 53°	41
	 , HNO_3		m.p. 151–152°	44

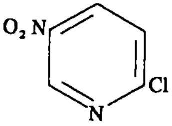
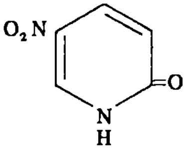
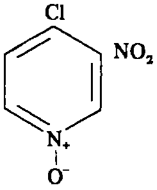
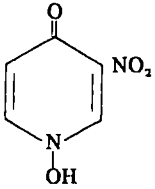
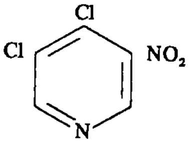
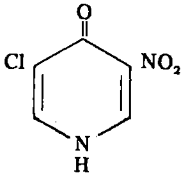
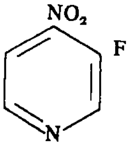
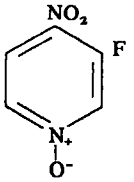
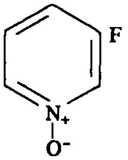
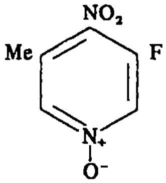
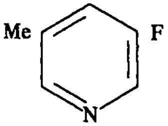
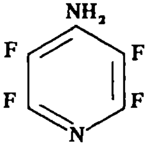
	 , $POCl_3-HCONMe_2$	95	m.p. 108-109° methochloride, m.p. 191-192°	43
	 , $POCl_3-HCONMe_2$	82	m.p. 147-148° m.p. 115°	10,43
	 , $POCl_3-HCONMe_2$		m.p. 43-47°	45
	 , persulfuric acid		b.p. 62-64° (5 mm)	5

TABLE VIII-2. Preparation and Properties of Halonitropyridines and 1-Oxides (Continued)

Compound	Method of preparation	Yield (%)	Properties	Ref.
	 , HNO_3–H_2SO_4		m.p. 128°	20
	 , (i) H_2O_2–Ac_2O (ii) HNO_3–H_2SO_4		m.p. 119°	46
	 , H_2O_2–$(CF_3CO_2)O$	56	b.p. 152–154° n_D^{20} = 1.4459	6,7

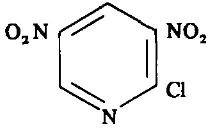
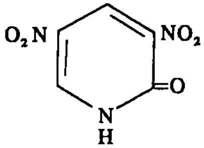
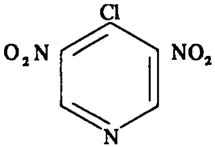
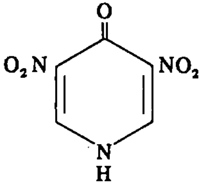
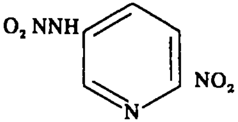
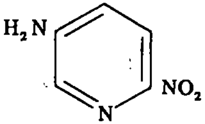
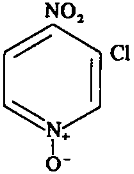
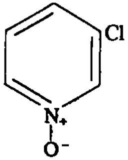
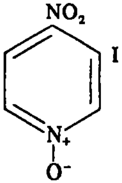
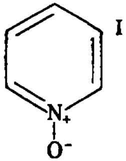
	 , $POCl_3$–$HCONMe_2$	96	m.p. 64°	43
	 , $POCl_3$–$HCONMe_2$	96	m.p. 67-68°	43
	 , HNO_3–H_2SO_4		m.p. 113° (expl.)	47
	 , HNO_3 H_2SO_4	84.5	m.p. 115°	10
	 , HNO_3 H_2SO_4	56.4	m.p. 201°	10

TABLE VIII-3. Side-Chain Nitro Compounds

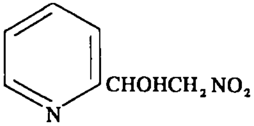
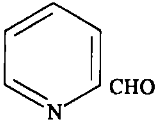
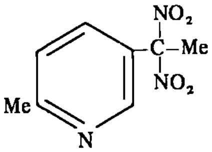
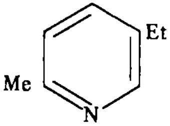
Compound	Method of preparation	Properties	Ref.
	 , $MeNO_2-K_2CO_2$	m.p. 68° HCl salt, m.p. 136-137°	48
	 , HNO_3	b.p. 112°(1 mm); 138°(4 mm)	11

TABLE VIII-4. Pyridylhydrazines

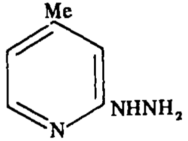
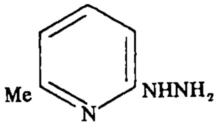
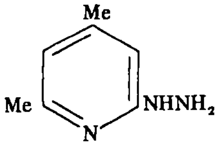
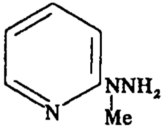
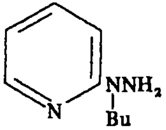
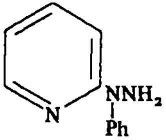
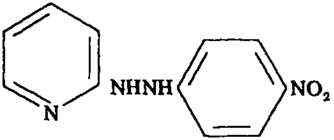
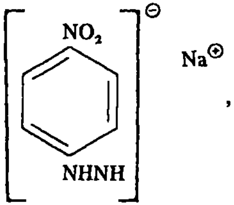
Compound	Method of preparation	Yield	Properties	Ref.
2-PyNHNH$_2$	2-PySO$_3$H, N$_2$H$_4$·H$_2$O, ZnCl$_2$		picrate, m.p. 187–189°	49
	Pyridine, NaNHNH$_2$, Heat		m.p. 46–47° mono-HCl salt, m.p. 183° di-HCl salt, m.p. 214–215°	36
	4-Picoline, NaNHNH$_2$, Heat		m.p. 74-75°	36
	2-Picoline, NaNHNH$_2$, Heat		m.p. 58-59°	36
	2, 4-Lutidine, NaNHNH$_2$, Heat		m.p. 67-68°	36
2-PyNHNHMe	Pyridine, NaNHNHMe, Heat		m.p. 46° picrate, m.p. 145–146°	36
2-PyNHNMe$_2$	Pyridine, NaNHNMe$_2$, Heat		m.p. 95° picrate, m.p. 185°	26
2-PyNHNHPy-2	2-PyNHNH$_2$, Pyridine, NaNH$_2$			36

TABLE VIII-4. Pyridylhydrazines (Continued)

Compound	Method of preparation	Yield	Properties	Ref.
	2-PyCl, NaNHNHMe		b.p. 68°(5 mm)	37
	2-PyCl, NaNHNHBu		b.p. 120°(0.2 mm)	37
	2-PyCl, NaNHNHPh		b.p. 140°(0.2 mm)	37
	2-PyCl, NaNHNHCH$_2$Ph		b.p. 142°(0.3 mm)	37
	2-PyBr,  , 140°		m.p. 158-159° HBr salt, dec. 227-228°	4

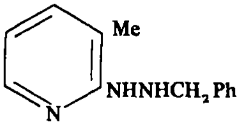
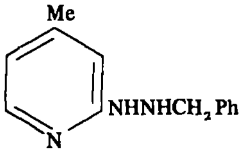
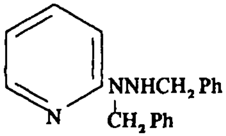
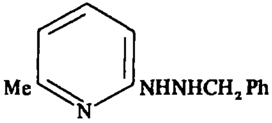
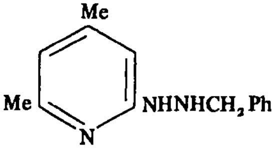
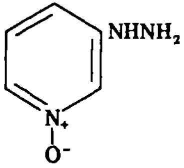
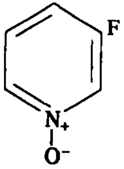
		m.p. 198-200°	50
		m.p. 175-178°	50
		m.p. 165°	50
		m.p. 147-148°	50
		m.p. 172-173°	50
	 , N_2H_4	m.p. 148°	33

TABLE VIII-4. Pyridylhydrazines (Continued)

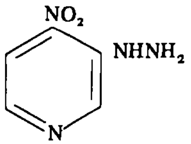
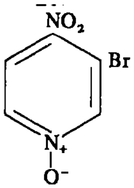
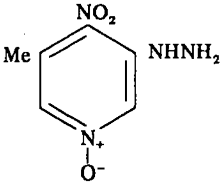
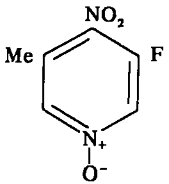
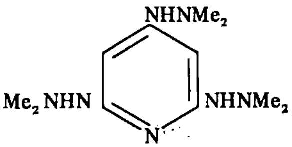
Compound	Method of preparation	Yield	Properties	Ref.
	 , $N_2H_4 \cdot H_2O$(50°)		m.p. 192°	14
	 , $N_2H_4 \cdot H_2O$	84%	m.p. 192°	46
4–PyNHNH$_2$	4-PySO$_3$H, $N_2H_4 \cdot H_2O$, ZnCl$_2$		HCl salt, m.p. 242-244° dibenzoyl deriv. m.p. 234 to 250° deriv. with MeCOCO$_2$Et, m.p. 128 to 130°	49
	Minor product in reaction of pyridine with NaNHNMe$_2$		m.p. 154° Tri-HCl salt, m.p. 214°	36

TABLE VIII-5. Miscellaneous Pyridylhydrazines and Derivatives

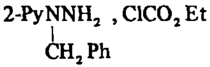
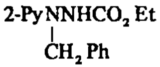
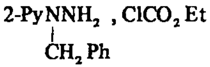
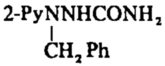
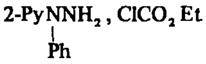
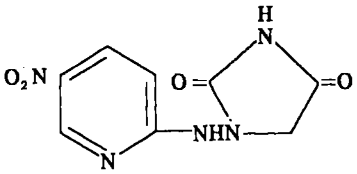
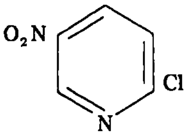
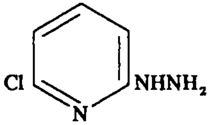
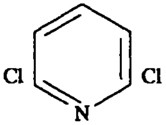
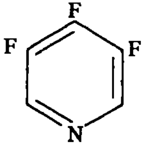
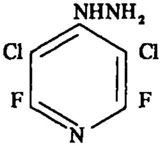
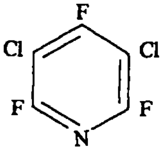
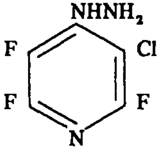
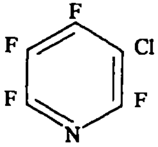
Compound	Method of preparation	Yield	Properties	Ref.
 $2\text{-}Py\underset{\substack{\mid \\ Me}}{N}NHCONH_2$			m.p. 220°	37
 $2\text{-}Py\underset{\substack{\mid \\ Bu}}{N}NHCO_2Et$	 $2\text{-}Py\underset{\substack{\mid \\ CH_2Ph}}{N}NH_2\ ,\ ClCO_2Et$		b.p. 130° (0.2 mm)	37
 $2\text{-}Py\underset{\substack{\mid \\ Bu}}{N}NHCONH_2$			m.p. 190° (dec.)	37
 $2\text{-}Py\underset{\substack{\mid \\ CH_2Ph}}{N}NHCO_2Et$	 $2\text{-}Py\underset{\substack{\mid \\ CH_2Ph}}{N}NH_2\ ,\ ClCO_2Et$		m.p. 50°	37
 $2\text{-}Py\underset{\substack{\mid \\ CH_2Ph}}{N}NHCONH_2$			m.p. 220° (dec.)	37
 $2\text{-}Py\underset{\substack{\mid \\ Ph}}{N}NHCO_2Et$	 $2\text{-}Py\underset{\substack{\mid \\ Ph}}{N}NH_2\ ,\ ClCO_2Et$		m.p. 103–104°	37
 $2\text{-}Py\underset{\substack{\mid \\ Ph}}{N}NHCONH_2$			m.p. 227°	37
	 , 1-Aminohydantoin		m.p. 247-249°	51

TABLE VIII-6. Halopyridylhydrazines

Compound	Method of preparation	Properties	Ref.
	 , $N_2H_4 \cdot H_2O$, Heat	m.p. 118-120°	52
	 , $N_2H_4 \cdot H_2O$	m.p. 134-135° sublimes *in vacuo*	35
	 , N_2H_4, Heat		7
	 , N_2H_4, Heat	m.p. 101-102°	7

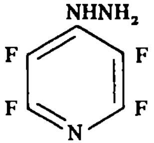
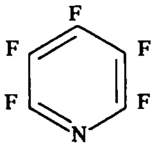
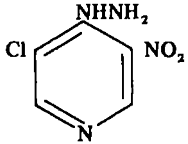
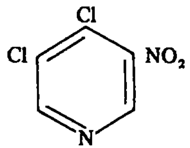
	 , N_2H_4	m.p. 56-57°	7,34
	 , $N_2H_4 \cdot H_2O$	m.p. 199°	45

TABLE VIII-7. Preparation and Properties of Nitroso- and Hydroxylaminopyridines and Derivatives

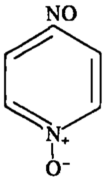
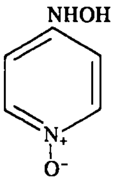
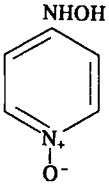
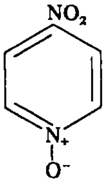
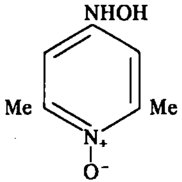
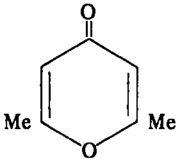
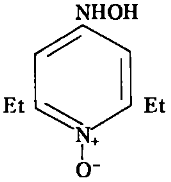
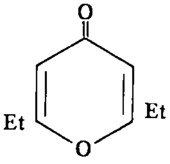
Compound	Method of preparation	Yield (%)	Properties	Ref.
	 , $KMnO_4$, dil. H_2SO_4		m.p. 139°	24
	 , $PhNHNH_2$	100	m.p. 237°	24
	 , $NH_2OH \cdot HCl{-}C_5H_5N$	17	m.p. not sharp	26
	 , $NH_2OH \cdot HCl{-}C_5H_5N$	20	m.p. 170° (dec.)	26

TABLE VIII-8. Preparation and Properties of Azidopyridines and Derivatives

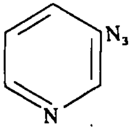
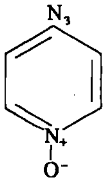
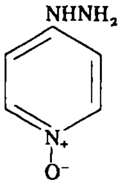
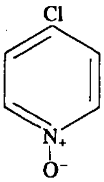
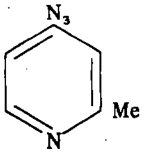
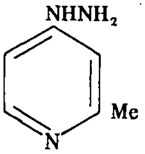
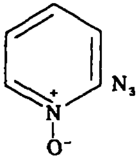
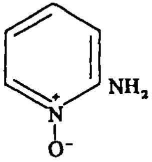
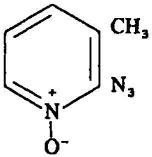
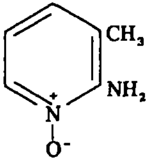
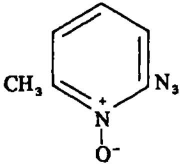
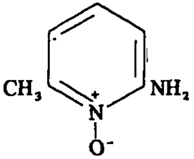
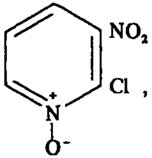
Compound	Method of preparation	Yield (%)	Properties	Ref.
	3-PyN$_2^+$, Cl$^-$, NaN$_3$		b.p. 75°(2 mm) n 1.5752 d_{19} 1.196	39
	 , HNO$_2$	55	m.p. 139-140°(dec.)[a]	38
	 , NaN$_3$	10	m.p. 142-143°[a]	38
	 , HNO$_2$	69	b.p. 74-78°(6 mm) (bath temp.)	38

TABLE VIII-8. Preparation and Properties of Azidopyridines and Derivatives (Continued)

Compound	Method of preparation	Yield (%)	Properties	Ref.
	 (i)HNO_2 (ii)NaN_3		m.p. 84.5-85.5°	39a
	 (i)HNO_2 (ii)NaN_3		m.p. 89-90°	39a
	 (i)HNO_2 (ii)NaN_3		m.p. 43-46°	39a
	 , NaN_3		m.p. 86-88°	39a

[a] Identical IR spectra

TABLE VIII-9. Preparation and Properties of Azopyridines

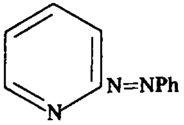
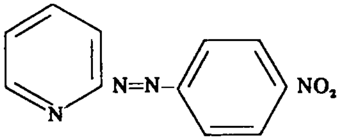
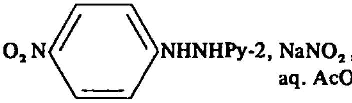
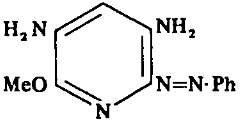
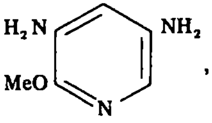
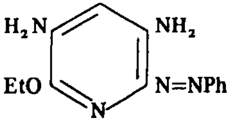
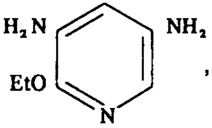
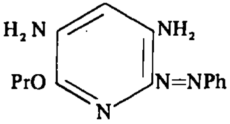
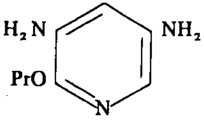
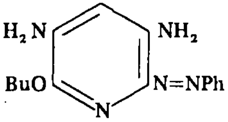
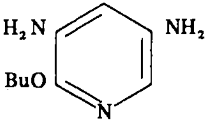
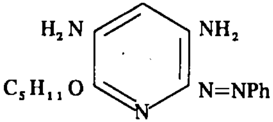
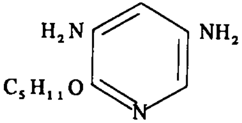
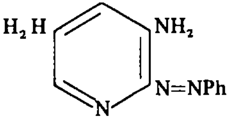
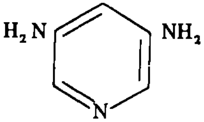
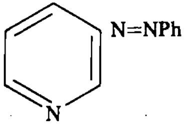
Compound	Method of preparation	Properties	Ref.
	2-PyNH$_2$, PhNO, aq. NaOH	m.p. 32° picrate, m.p. 133–135° 1-oxide, m.p. 137–138° 1-oxide picrate, m.p. 126–128°	53
	 NaNO$_2$, aq. AcOH	m.p. 160–162° 1-oxide, m.p. 214–215°	4
	 , $PhN_2^{\oplus}Cl^{\ominus}$	m.p. 141°	27
	 , $PhN_2^{\oplus}Cl^{\ominus}$	m.p. 119°	27

TABLE VIII-9. Preparation and Properties of Azopyridines (Continued)

Compound	Method of preparation	Properties	Ref.
	 , $PhN_2^{\oplus}Cl^{\ominus}$	m.p. 122°	27
	 , $PhN_2^{\oplus}Cl^{\ominus}$	m.p. 126°	27
	 , $PhN_2^{\oplus}Cl^{\ominus}$	m.p. 96°	27
	 , $PhN_2^{\oplus}Cl^{\ominus}$	m.p. 192°	27
	3-PyNH$_2$, PhNO, aq. NaOH	m.p. 53–54° picrate, m.p. 163–165° 1-oxide, m.p. 85–87° 1-oxide picrate, m.p. 159–161°	53

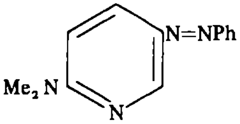
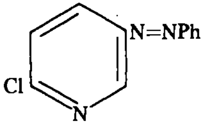
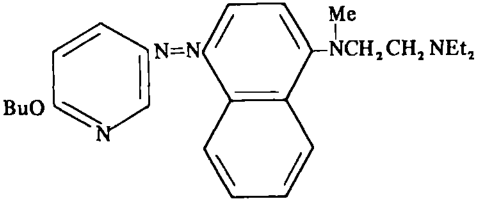
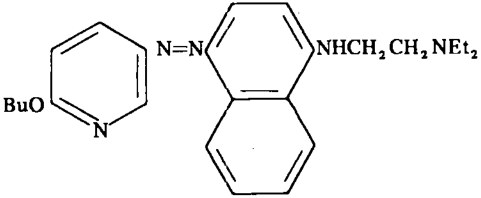
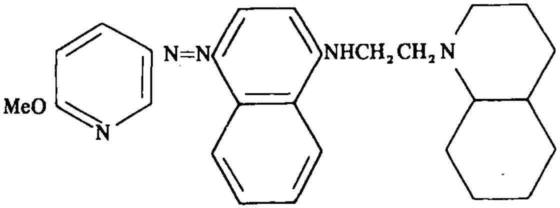
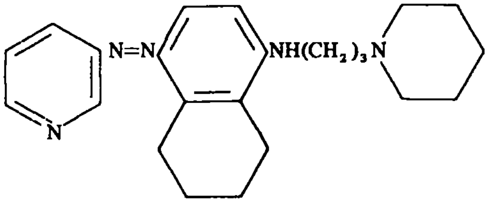
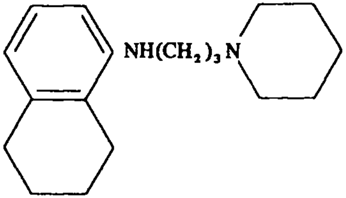
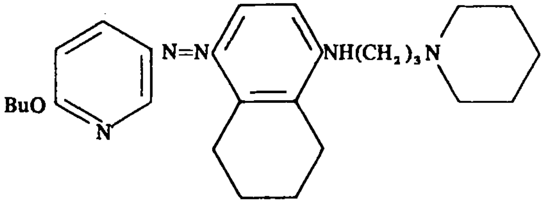
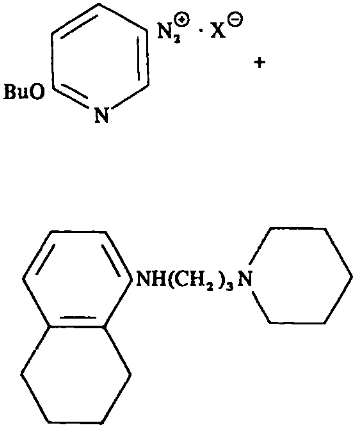
	 , Me_2NH	m.p. 114.5–115.2°	27
		m.p. 90–95°	28
		m.p. 92–94°	28
		m.p. 214–216° (dec.)	28

TABLE VIII-9. Preparation and Properties of Azopyridines (Continued)

Compound	Method of preparation	Properties	Ref.
	 + 3-PyN$_2^{\oplus}$ X$^{\ominus}$	m.p. 117–119°	28
		m.p. 123–124°	54

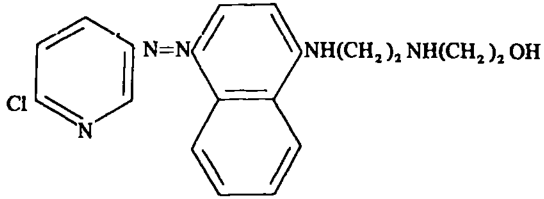
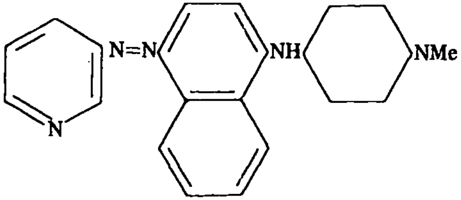
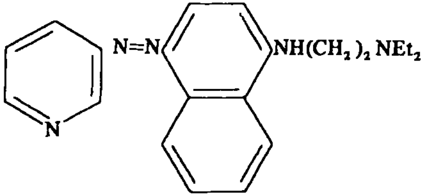
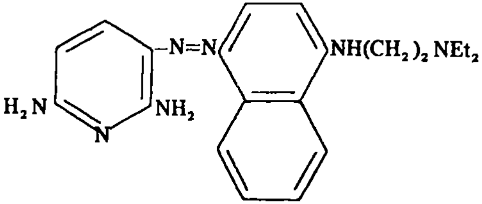
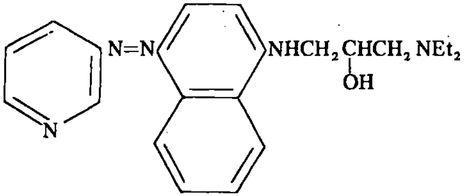
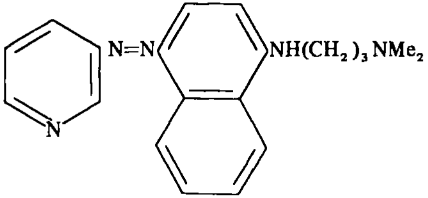
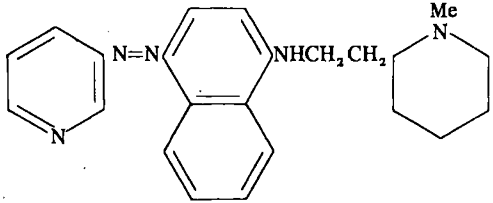
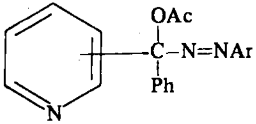
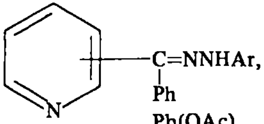
	m.p. 166–167°	28
	m.p. 171–172°	28
	m.p. 139–141°	28
	m.p. 234°(dec.)	28

TABLE VIII-9. Preparation and Properties of Azopyridines (Continued)

Compound	Method of preparation	Properties	Ref.
		m.p. 154–157°	28
		m.p. 130–132°	28
		m.p. 166° (dec.)	28
	 $Pb(OAc)_4$		30

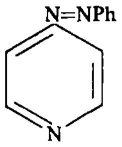
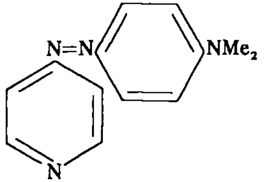
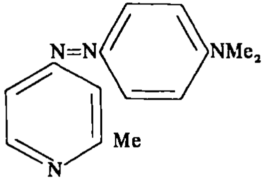
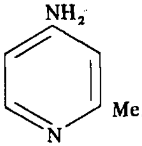
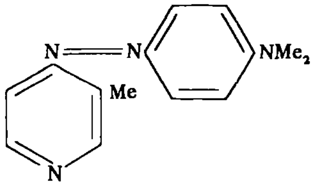
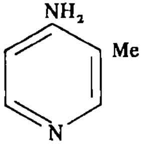
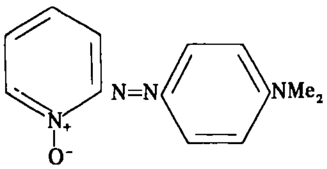
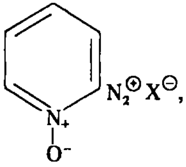
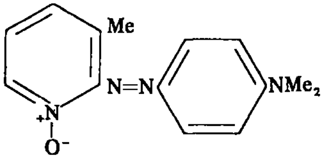
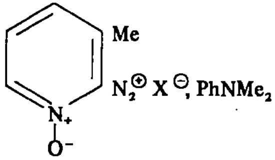
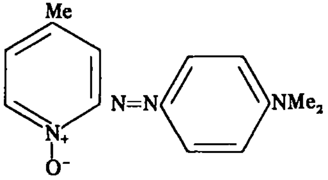
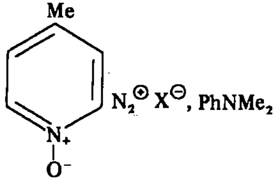
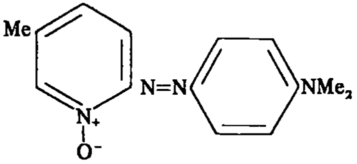
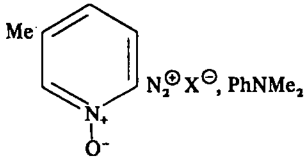
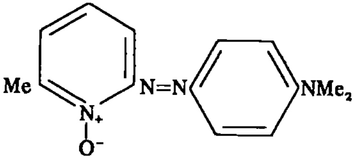
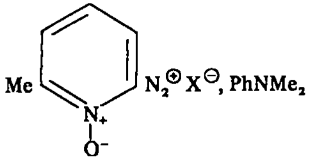
	4-PyNH$_2$, PhNO, aq. NaOH	m.p. 98–99° picrate, m.p. 208–209° 1-oxide, m.p. 150°	53
	4-PyNH$_2$, (i) HNO$_3$–H$_3$PO$_4$ (ii) NaNO$_2$ (O°) (iii) PhNMe$_2$	m.p. 207–209° 1-oxide, m.p. 210–211°	55
	 (i) HNO$_3$–H$_3$PO$_4$ (ii) NaNO$_2$ (O°) , (iii) PhNMe$_2$	m.p. 142–143° 1-oxide, m.p. 191–192°	55
	 (i) HNO$_3$–H$_3$PO$_4$ (ii) NaNO$_2$ (O°) , (iii) PhNMe$_2$	m.p. 186–187° 1-oxide, m.p. 193–194°	55
	 , PhNMe$_2$	m.p. 181–182°	55

TABLE VIII-9. Preparation and Properties of Azopyridines (Continued)

Compound	Method of preparation	Properties	Ref.
		m.p. 193–194°	55
		m.p. 184–185°	55
		m.p. 201–202°	55
		m.p. 170–171°	55

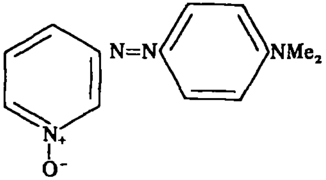
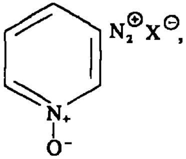
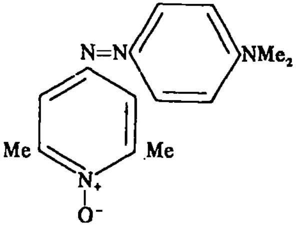
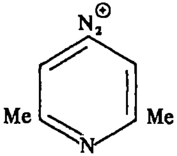
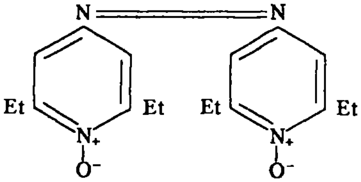
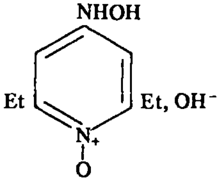
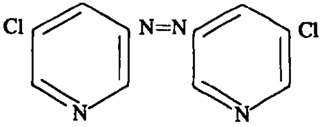
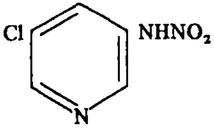
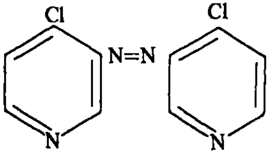
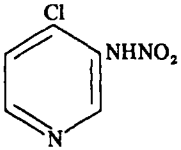
	 , $PhNMe_2$	m.p. 189–191°	55
	 $X^{\ominus}$, $PhNMe_2$	m.p. 197–198°	55
		m.p. 176–177°	26
	 , H_2SO_4 (40–100°)	m.p. 183°	8
	 , H_2SO_4 (40–100°)	m.p. 164°	8

TABLE VIII-9. Preparation and Properties of Azopyridines (Continued)

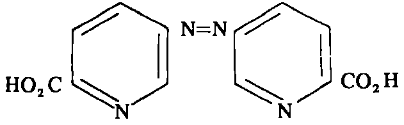
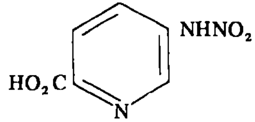
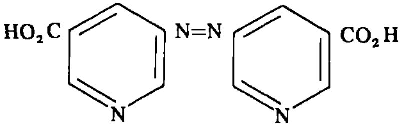
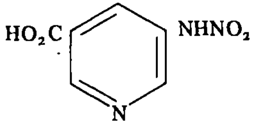
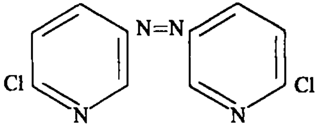
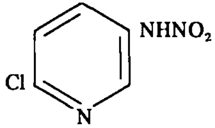
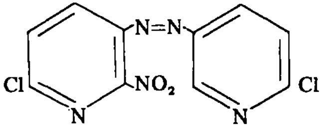
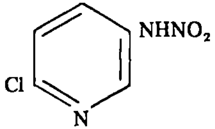
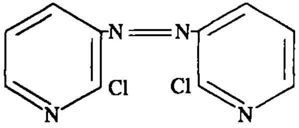
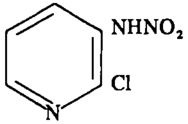
Compound	Method of preparation	Properties	Ref.
	 , H_2SO_4 (40–100°)	m.p. 246°	8
	 , H_2SO_4 (40–100°)	m.p. 298°	8
	 , H_2SO_4 (40–100°)	m.p. 215–217°	8
 (minor product)	 , H_2SO_4 (40–100°)	m.p. 165°	8
	 , H_2SO_4 (40–100°)	m.p. 237–239°	8

TABLE VIII-10. Preparation and Properties of Azoxypyridines and Derivatives

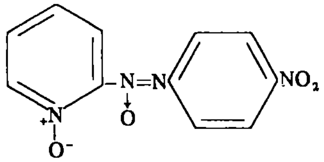
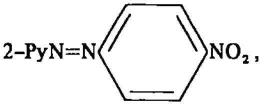
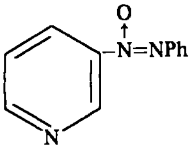
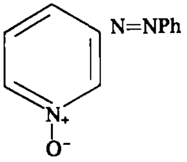
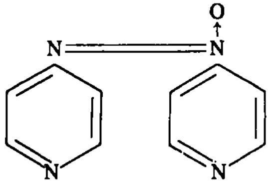
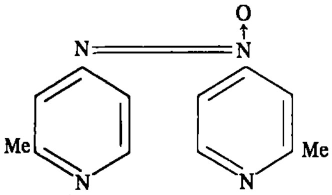
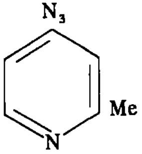
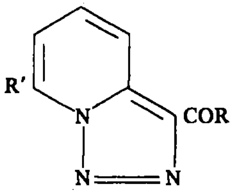
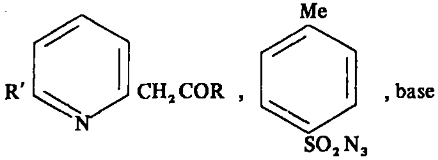
Compound	Method of preparation	Properties	Ref.
	 PhCO$_3$H	m.p. 192–193°	4
	3-PyNH$_2$, PhNO, NaOH  , PCl$_3$–CHCl$_3$	m.p. 61–62° picrate, m.p. 180°	53
	4-PyN$_3$, photolysis in Me$_2$CO	m.p. 235°(dec.)	40
	 , H$_2$O$_2$	m.p. 218°(dec.)	38

TABLE VIII-11. Preparation and Properties of Pyridotriazoles[56]

Compound	Method of Preparation		Yield (%)	Properties
				
	R	*R'*		
	Me	H	50	m.p. 157–158°
	Pr	H	79	m.p. 98°
	t-Bu	H	90	m.p. 95–96°
	2-Furyl	H	94	m.p. 215°
	Ph	H	88	m.p. 111–112°
	2-Py	H	72	m.p. 153°
	3-Py	H	57	m.p. 134–135°
	2-Furyl	Me	77	m.p. 183°
	2-Thienyl	Me	88	m.p. 150°
	3-Py	Me	75	m.p. 160°

VII. Supplement

The following table contains references to the spectral data on the material covered in this chapter. The studies cited are of a more comprehensive nature. In most cases the original literature was consulted; chemical abstract citations are included for all references for the purpose of convenience, however.

Substance	Type of Study	Reference
2-Nitropyridine	UV	61
3-Nitropyridine	ESR	59, 67
	UV	61
4-Nitropyridine	UV	61
	NMR	72, 73, 81
	IR	63
	ESR	65
4-Nitropyridine-1-oxide	UV	71, 77
	NMR	70, 73
	Mass Spec.	58
	ESR	66, 75
2-Nitro-3-picoline	Mass Spec.	74
2-Nitro-4-picoline	Mass Spec.	74
2-Nitro-4-picoline	Mass Spec.	74
2-Nitro-6-picoline	Mass Spec.	74
4-Nitro-2-picoline	IR	79
4-Nitro-3-picoline	IR	60, 69, 79
	UV	60
3-Ethyl-4-nitropyridine	UV, IR	60
4-Nitro-3-propylpyridine	UV, IR	60
2-Chloro-3-nitropyridine	UV	57
3-Bromo-4-nitropyridine-1-oxide	IR	69
3-Methoxy-2-nitropyridine	UV	62
2-Methoxy-3-nitropyridine	UV	62
4-Ethoxy-3-nitropyridine	UV	57
2-Methoxy-5-nitropyridine	UV	62
3,5-Dinitropyridine	ESR	59
4-Nitro-2,6-lutidine	IR	79
4-Nitro-2,6-lutidine-1-oxide	IR	79
4-Nitro-3,5-lutidine	IR, UV	60
2,3,5,6-Tetramethyl-4-nitropyridine	IR, UV	60
4-Nitrosopyridine-1-oxide	ESR	68
Dinitro-(2-pyridyl)methane	IR, UV	78
4-Hydrazinopyridine-1-oxide	IR study of hydrazones from	80
4-Hydrazino-2,3,5,6-tetrafluoro-pyridine	NMR	76
2,2′-Azopyridine	NMR	64
3,3′-Azopyridine	NMR	64

Substance	Type of Study	Reference
4,4'-Azopyridine	NMR	64
3,3'-Dimethyl-4,4'-azopyridine-1,1'-dioxide	IR	69
2,2',6,6'-Tetramethyl-4,4'-azopyridine-1,1'-dioxide	IR	79

References

1. K. D. Gundermann and H. U. Alles, *Angew. Chem. Intern. Ed. Engl.*, **5**, 846 (1966).
2. J. S. Wieczorek and E. Plazek, *Rec. Trav. Chim. Pays-Bas,* **83**, 249 (1964); *Chem. Abstr.*, **60**, 15822b (1964).
3. R. C. De Selms, *J. Org. Chem.*, **33**, 478 (1968).
4. L. Pentimalli, *Gazz. Chim. Ital.*, **93**, 404 (1963); *Chem. Abstr.*, **59**, 5127b (1963).
5. T. Talik and Z. Talik, *Rocz. Chem.*, **40**, 1187 (1966); *Chem. Abstr.*, **66**, 11165u (1967).
6. R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc.*, 5040 (1965).
7. R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, Belg. patent 660,873 (1965).
8. M. D. Coburn, *J. Heterocycl. Chem.*, **7**, 455 (1970).
9. F. Kroehnke and H. Schaefer, *Chem. Ber.*, **95**, 1098 (1962).
10. T. Talik and Z. Talik, *Rocz. Chem.*, **36**, 539 (1962); *Chem. Abstr.*, **57**, 12421a (1962).
11. H. Rubinstein, G. Hazen, and R. Zerfing, *J. Chem. Eng. Data,* **12**, 149 (1967); *Chem. Abstr.*, **66**, 55347m (1967).
12. S. Yamada and Y. Kikugawa, *Chem. Ind.* (London), 1325 (1967).
13. R. M. Johnson, *J. Chem. Soc.*, *B*, 1058 (1966).
14. T. Talik, *Rocz. Chem.*, **36**, 1465 (1962); *Chem. Abstr.*, **59**, 6360b (1963).
15. T. Talik, *Rocz. Chem.*, **36**, 1563 (1962); *Chem. Abstr.*, **59**, 6231d (1963).
16. Z. Talik, *Rocz. Chem.*, **35**, 475 (1961); *Chem. Abstr.*, **57**, 15065h (1962).
17. Z. Talik, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.*, **9**, 561 (1961); *Chem. Abstr.*, **60**, 2884d (1964).
18. Z. Talik, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.*, **9**, 567 (1961); *Chem. Abstr.*, **60**, 2883h (1964).
19. Z. Talik, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.*, **9**, 571 (1961); *Chem. Abstr.*, **60**, 2885b (1964).
20. T. Talik and Z. Talik, *Rocz. Chem.*, **38**, 777 (1964); *Chem. Abstr.*, **61**, 10653e (1964).
21. R. A. Abramovitch, F. Helmer, and M. Liveris, *J. Chem. Soc.*, *B*, 492 (1968).
22. T. Talik and Z. Talik, *Rocz. Chem.*, **40**, 1675 (1966); *Chem. Abstr.*, **66**, 94889j (1967).
23. A. Puszynski and T. Talik, *Rocz. Chem.*, **43**, 1771 (1969).
24. E. Ochiai and H. Mitarashi, *Chem. Pharm. Bull.* (Tokyo), **11**, 1084 (1963); *Chem. Abstr.*, **59**, 12755a (1963).
25. C. Kaniko and S. Yamada, *Tetrahedron Lett.*, 4729 (1966).
26. P. Yates, M. J. Jorgensen, and S. K. Roy, *Can. J. Chem.*, **40**, 2146 (1962).
27. E. V. Brown, A. F. Smetana, and A. A. Hambden, *J. Med. Chem.*, **8**, 252 (1965).
28. E. W. Elslager, D. B. Capps, D. H. Kurtz, L. M. Werbel, and D. R. Worth, *J. Med. Chem.*, **6**, 646 (1963).
29. W. Czuba, *Bull. Acad. Polon. Sci., Ser. Sci. Chem.*, **8**, 281 (1960); *Chem. Abstr.*, **60**, 2883g (1964).
30. W. A. F. Gladstone and R. O. C. Norman, *J. Chem. Soc.*, *C*, 1527 (1966).

31. P. Tomasik, *Rocz. Chem.*, **44**, 509 (1970).
32. Z. J. Allan, J. Podstata, and Z. Vrba, *Tetrahedron Lett.*, 4855 (1969).
33. M. Bellas and H. Suschitsky, *J. Chem. Soc.*, 4007 (1963).
34. R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *Proc. Chem. Soc.*, 83 (1964).
35. M. T. Chaudhry, G. A. Powers, R. Stephens, and J. C. Tatlow, *J. Chem. Soc.*, 874 (1964).
36. T. Kauffman, J. Hansen, C. Hansen, C. Kosel, and W. Schoeneck, *Ann. Chem.*, **656**, 103 (1962).
37. G. Palazzo and L. Baiocci, *Ann. Chim.* (Rome), **55**, 935 (1965); *Chem. Abstr.*, **63**, 16335h (1965).
38. T. Itai and S. Kamiya, *Chem. Pharm. Bull.* (Tokyo), **9**, 87 (1961).
39. V. Ya. Pochinok and L. F. Ayromenko, *Ukr. Chim. Zh.*, **28**, 511 (1962); *Chem. Abstr.*, **58**, 2348g (1963).
39a. R. A. Abramovitch and B. W. Cue, *J. Org. Chem.*, **38**, 173 (1973).
40. S. Kamiya, *Chem. Pharm. Bull.* (Tokyo), **10**, 471 (1962).
40a. R. Huisgen and K. von Frauenberg, *Tetrahedron Lett.*, 2595 (1969).
40b. T. Sasaki, K. Kanematsu, and M. Murata, *Tetrahedron*, **27**, 5121 (1971).
41. L. Pentimalli, *Ann. Chim.* (Rome), **53**, 1123 (1963); *Chem. Abstr.*, **60**, 10645d (1964).
42. Z. Talik and T. Talik, *Rocz. Chem.*, **36**, 417 (1962); *Chem. Abstr.*, **58**, 5627b (1963).
43. A. Signor, E. Scoffone, L. Biondi, and S. Bezzi, *Gazz. Chim. Ital.*, **93**, 65 (1963); *Chem. Abstr.*, **59**, 2811g (1963).
44. P. C. Jain, S. K. Chatterjee, and N. Anand, *Ind. J. Chem.*, **4**, 403 (1966); *Chem. Abstr.*, **66**, 46552x (1967).
45. P. Nantka-Namirski, *Acta Polon. Pharm.*, **18**, 391 (1961); *Chem. Abstr.*, **57**, 16554b (1962).
46. T. Talik and Z. Talik, *Rocz. Chem.*, **40**, 1457 (1966); *Chem. Abstr.*, **66**, 9488h (1967).
47. K. Lewicka and E. Plazek, *Rocz. Chem.*, **39**, 643 (1945); *Chem. Abstr.*, **63**, 8311a (1965).
48. K. W. Merz and H. J. Janssen, *Arch. Pharm.* (Weinheim), **297**, 10 (1964); *Chem. Abstr.*, **60**, 10643f (1964).
49. Y. Suzuki, *Yakugaku Zasshi*, **81**, 1146 (1961); *Chem. Abstr.*, **56**, 3450f (1962).
50. K. T. Potts and H. R. Burton, *J. Org. Chem.*, **31**, 251 (1966).
51. K. M. Ghoneim, M. Khalifa, and Y. M. Abou-Zeid, *J. Pharm. Sci.*, **55**, 349 (1966); *Chem. Abstr.*, **64**, 12637b (1966).
52. J. Buchi, P. Fabiani, H. U. Frey, A. Hofstetter, and A. Schorno, *Helv. Chim. Acta*, **49**, 272 (1966).
53. L. Pentimalli, *Ann. Chim.* (Rome), **55**, 435 (1965); *Chem. Abstr.*, **63**, 6963d (1965).
54. L. M. Werbel, E. W. Elslager, M. W. Fisher, Z. B. Gavrilis, and A. A. Phillips, *J. Med. Chem.*, **11**, 411 (1968).
55. R. W. Faessinger and E. V. Brown, *Trans. Kentucky Acad. Sci.*, **24**, 349 (1966); *Chem. Abstr.*, **60**, 14465a (1964).
56. M. Regitz and A. Liedhegener, *Chem. Ber.*, **99**, 2918 (1966).
57. G. B. Barlin, *J. Chem. Soc.*, 2150 (1964); *Chem. Abstr.*, **61**, 7763d (1964).
58. N. Bild and M. Hesse, *Helv. Chim. Acta*, **50**, 1885 (1967); *Chem. Abstr.*, **67**, 120957x (1967).
59. P. T. Cottrell and P. H. Reger, *Mol. Phys.*, **12**, 149 (1967); *Chem. Abstr.*, **67**, 69314f (1967).
60. J. M. Essery and K. Schofield, *J. Chem. Soc.*, 225 (1963); *Chem. Abstr.*, **58**, 12389f (1963).

61. G. Favini, A. Gamba, and I. R. Bellobono, *Spectrochim. Acta,* **23A,** 89 (1967); *Chem. Abstr.,* **66,** 50516f (1967).
62. G. Favini, M. Raimondi, and G. Gandolfo, *Spectrochim. Acta,* **24A,** 207 (1968); *Chem. Abstr.,* **68,** 118201y (1968).
63. C. R. Frank and L. B. Rogers, *Inorg. Chem.,* **5,** 615 (1966); *Chem. Abstr.,* **64,** 15186g (1966).
64. G. Giacometti and G. Rigatti, *Nucl. Mag. Res. Chem. Proc. Symp. Cagliari, Italy* 173 (1964); *Chem. Abstr.,* **66,** 15277g (1967).
65. A. Ishitani and S. Nagakura, *Bull. Chem. Soc. Jap.,* **38,** 367 (1965); *Chem. Abstr.,* **63,** 5144c (1965).
66. M. Itô, T. Okamoto, and S. Nagakura, *Bull. Chem. Soc. Jap.,* **36,** 1665 (1963); *Chem. Abstr.,* **60,** 7595d (1964).
67. M. Itô and S. Nagakura, *Bull. Chem. Soc. Jap.,* **38,** 825 (1965); *Chem. Abstr.,* **63,** 5497b (1965).
68. M. Itô and T. Okamoto, *Chem. Pharm. Bull.* (Tokyo), **15,** 435 (1967); *Chem. Abstr.,* **67,** 43237h (1967).
69. R. A. Jones and R. P. Rao, *Aust. J. Chem.,* **18,** 583 (1965); *Chem. Abstr.,* **62,** 15593e (1965).
70. C. R. Kanekar and H. V. Venkatasetty, *Current Sci.* (India), **34,** 555 (1965); *Chem. Abstr.,* **64,** 2886a (1966).
71. C. Kaneko, S. Yamada and I. Yokoe, *Tetrahedron Lett.,* 4729 (1966); *Chem. Abstr.,* **66,** 2043v (1967).
72. P. D. Kaplan and M. Orchin, *Inorg. Chem.,* **4,** 1393 (1965); *Chem. Abstr.,* **64,** 14238f (1965).
73. A. R. Katritzky and J. M. Lagowski, *J. Chem. Soc.,* 43 (1961); *Chem. Abstr.,* **56,** 4727a (1962).
74. G. H. Keller, L. Bauer, and C. L. Bell, *J. Heterocycl. Chem.,* **5,** 647 (1968); *Chem. Abstr.,* **69,** 111306y (1968).
75. T. Kubota, K. Nishikida, H. Miyazaki, K. Iwatani, and Y. Oishi, *J. Amer. Chem. Soc.,* **90,** 5080 (1968); *Chem. Abstr.,* **69,** 95819k (1968).
76. J. Lee and K. G. Orrell, *J. Chem. Soc.,* 582 (1965); *Chem. Abstr.,* **62,** 6455h (1965).
77. T. Okano, K. Uekama, Y. Isawa, and K. Tsukuda, *Yakugaku Zasshi,* **87,** 1309 (1967); *Chem. Abstr.,* **68,** 95185e (1968).
78. V. I. Slovetskii, L. I. Khmal'nitskii, O. V. Lebedev, T. S. Novikova, and S. S. Novikov, *Khim. Geterotsikl. Svedin., Akad. Nauk Latv. SSR,* 835 (1965); *Chem. Abstr.,* **64,** 15705f (1966).
79. J. Suszko and M. Szafran, *Bull. Acad. Polon. Sci., Ser. Sci. Chem.,* **10,** 233 (1962); *Chem. Abstr.,* **58,** 7519c (1963).
80. G. Tacconi and S. Pietra, *Ann. Chim.* (Rome), **55,** 810 (1965); *Chem. Abstr.,* **64,** 686f (1966).
81. T. K. Wu and B. P. Dailey, *J. Chem. Phys.,* **41,** 3307 (1964); *Chem. Abstr.,* **62,** 1228d (1965).

Chemistry of Heterocyclic Compounds, Volume 14
Edited by R. A. Abramovitch

CHAPTER IX

Aminopyridines

C. S. GIAM

Chemistry Department,
Texas A & M University
College Station, Texas

I. Nuclear Amines

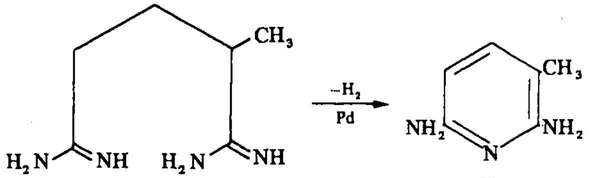
1. Preparation of Primary Amines

A. *From Nonpyridine Starting Materials*

Aminopyridines were detected in the complex mixture of products resulting from the condensation of paraldehyde with excess ammonia at 210° at 100 atm pressure.[1]

Aminohalopyridines are obtained by the action of anhydrous halogen acids (hydrogen bromide or hydrogen iodide) on 3-hydroxyglutaronitriles, glutaconitriles or 1,3-dicyano-2-propanol; thus, a mixture of 1,3-dicyano-2-propanol and anhydrous hydrogen bromide gives (after neutralization of the product) 2-amino-6-bromopyridine.[2,3]

2,6-Diamino-3-picoline (**IX-1**) is obtained in 30% yield by the dehydrogenation of α-methylglutarimidine with a Pd catalyst. 2,6-Diamino-3,5-dimethylpyridine was prepared similarly from α,α-dimethylglutarimidine.[4]

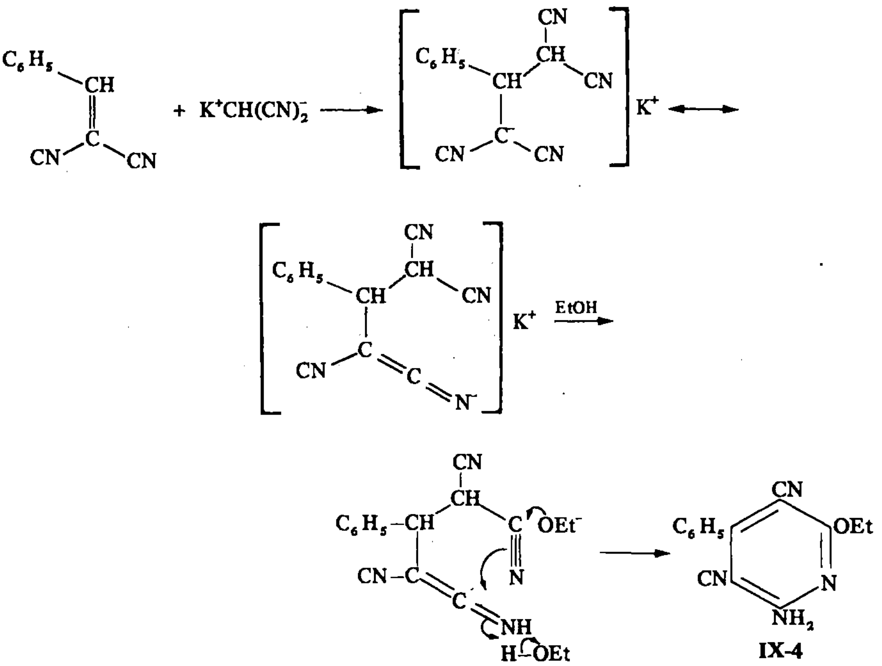


IX-1

The reaction of 3-hydroxyglutaronitrile with aniline hydrobromide yields 2,6-dianilinopyridine;[5] using thiophenol, hydrogen bromide, and acetic acid instead of aniline hydrobromide, 2-amino-6-phenylthiopyridine results.[6]

Interesting cases of ring formation have been reported, for example, the synthesis of 2-amino-3,5-dicyano-6-ethoxy-4-phenylpyridine (**IX-4**) from benzalmalonitrile (**IX-3**) and ethanolic potassium hydroxide.[7] The presence of

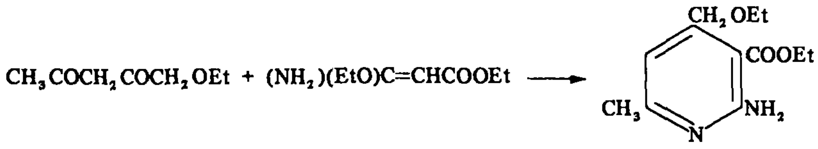
$$\underset{\textbf{IX-3}}{C_6H_5CH{=}C(CN)_2} + KOH \xrightarrow{EtOH} C_6H_5CHO + \underset{\textbf{IX-2}}{K^+CH(CN)_2^-}$$



IX-4

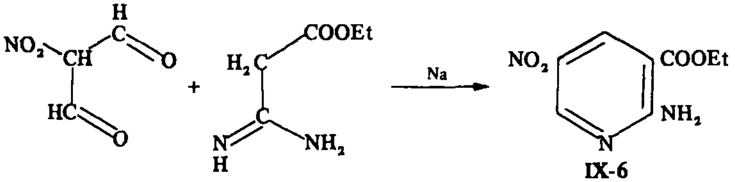
benzaldehyde and the absence of malonitrile in the reaction products suggested a mechanism involving a reverse aldol condensation to form benzaldehyde and the potassium salt of malonitrile (IX-2). IX-2 then condenses with IX-3 to yield the substituted pyridine IX-4. If methanol is used instead of ethanol, the 6-methoxy derivative is formed.

Cyclizations involving activated carbonyl compounds have been reported. 1-Ethoxy-2,4-dioxopentane condenses with β-amino-β-ethoxyacrylate to yield ethyl 2-amino-4-ethoxymethyl-6-methylnicotinate (IX-5).[8] Another condensation



IX-5

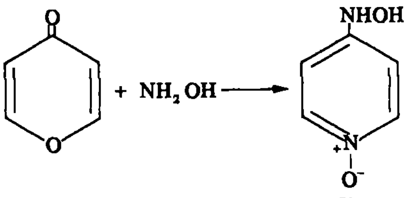
reaction involves nitromalondialdehyde and ethyl amidinoacetate; this results in the formation of ethyl 2-amino-5-nitronicotinate (IX-6):[9]



IX-6

The reaction of acetamidine with 3-(phenylazo)acetylacetone gives 6-amino-2,4-dimethyl-3-phenylazopyridine.[10]

4-Hydroxylaminopyridine-1-oxide (IX-7) was obtained from the reaction of hydroxylamine with γ-pyrone. Its structure was proved by hydrogenation to 4-aminopyridine and also by oxidation to 4-nitropyridine-1-oxide.[11]

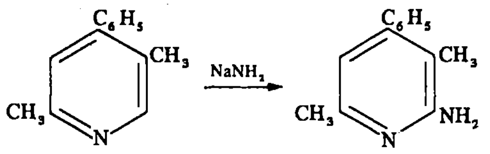


IX-7

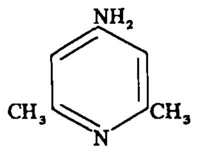
B. *Amination of Pyridines with Alkali Amides (The Tschitschibabin Reaction)*

Direct amination of alkylpyridines with sodium amide generally results in the formation of the 2- or 6-amino-derivatives. 2-Amino-3-picoline and 2-amino-4-picoline were obtained in good yields (70–80%) from the direct amination of the crude picoline fraction of coal tar with sodamide.[12] 4-Alkylpyridines having more than 5 carbon atoms in the alkyl group can be aminated with sodamide in inert solvents, or with sodium in liquid ammonia, to give 2-amino-4-alkylpyridine;[13, 14] for example, 4-isopentylpyridine yields 2-amino-4-isopentylpyridine when boiled under reflux with sodamide in xylene at 130 to 140° for 8 hours.[13] Even with 2-methyl-4-pyridone, direct amination results in the formation of 6-amino-2-methyl-4-pyridone.[15] Amination of 3-substituted pyridines by sodamide gives predominantly the 2-amino-3-substituted derivative rather than the 6-isomer;[16] for example, 3-picoline gives a mixture of 2-amino-3-picoline and 6-amino-3-picoline in the ratio of 10.5:1.[17, 18]

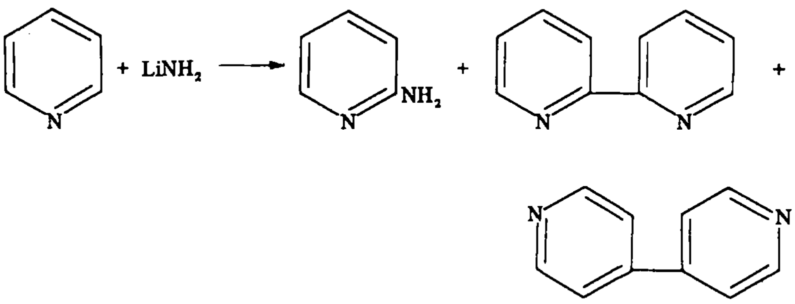
When 2,5-dimethyl-4-phenylpyridine is heated with sodium amide at 180° for 5 hours, 2-amino-3,6-dimethyl-4-phenylpyridine (**IX-8**) is obtained.[19] If the 2- and 6-positions are not available, direct amination takes place at the 4-position; thus, the reaction of 2,6-lutidine with sodium in liquid ammonia yields 4-amino-2,6-lutidine (**IX-9**).[20] The 4-chloro substituent in perchloropyridine is easily replaced by an amino group; for example, perchloropyridine readily reacts with sodium amide to give 4-amino-2,3,5,6-tetrachloropyridine[21] (see Chapter VI).



IX-8



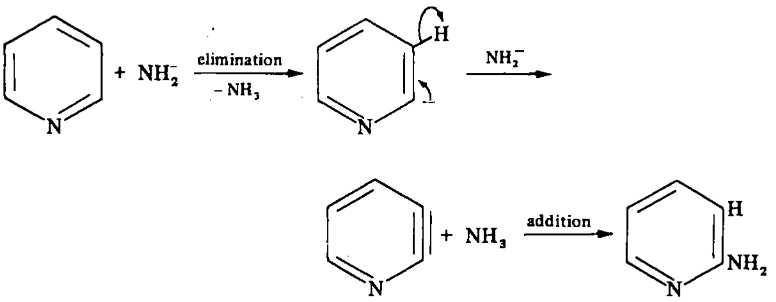
IX-9



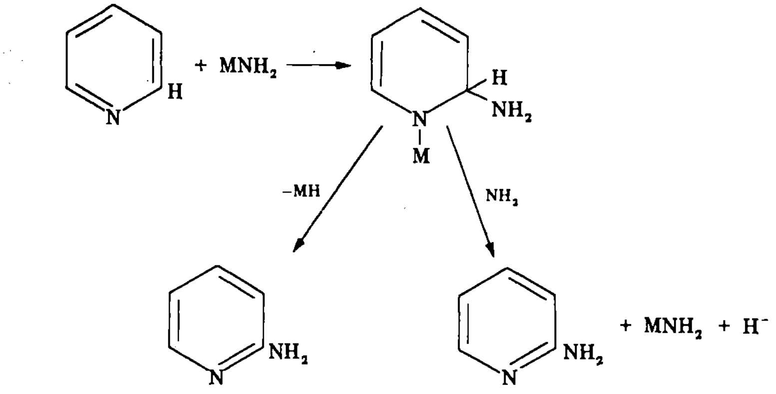
IX-10

The reaction of lithium amide with pyridine has been studied; 2,2′- and 4,4′-dipyridyl, rather than 2-aminopyridine, were the predominant products **(IX-10)**.[22] Whereas the reaction of sodium amide with pyridine in various solvents gave yields of 2-aminopyridine of at least 43%, lithium amide under similar reaction conditions produced less than 1% of 2-aminopyridine.[22] The mechanism of the Tschitschibabin reaction in which a ring hydrogen atom was replaced by an amino group has been the subject of much recent discussion. The "pyridyne" mechanism **(IX-11)** proposed by Levitt and Levitt[23] and supplemented by molecular orbital calculations[24] was proved unacceptable by Abramovitch and by other workers.[17,18,25-27] Instead, convincing evidence indicated that the overall mechanism was an S_NAr2 type addition-elimination pathway **(IX-12)**. The subject has been reviewed by Abramovitch and Saha.[16]

The mechanism of ammonodehalogenation reactions of halopyridines by alkali amides probably involves two mechanistic pathways. The reactions of 3- or 4-halopyridines with potassium amide in liquid ammonia proceed mainly, if not exclusively, *via* 3,4-pyridines to give mixtures of 3- and 4-aminopyridines; in contrast, 2-halopyridines react *via* an addition-elimination pathway, giving only 2-aminopyridines.[28-31]



(IX-11)



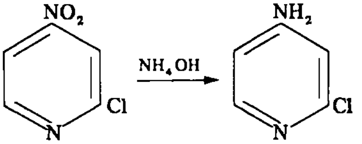
Addition-elimination mechanism **(IX-12)**

The mechanistic pathways of the ammonodehalogenation reactions of aminohalopyridine-1-oxides have been studied[30-32] and are discussed in Chapter IV.6.

The reactions of dibromopyridines and various substituted bromopyridines with alkali amides have been reported;[33-36] aminopyridines were the products in most but not all cases. For example, 2,6-dibromopyridine gives 4-amino-2-methylpyridine when treated with potassium amide in liquid ammonia;[37] under similar conditions but using 2-amino-3-bromopyridine, 3-cyanopyrrole is formed[38] (see Chapter I.A.).

C. *Ammonolysis of Halopyridines*

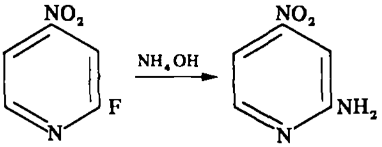
Halopyridines are converted to aminopyridines under a variety of conditions. The conversion of 3-bromopyridine to 3-aminopyridine requires a catalyst (copper sulfate), ammonium hydroxide, and 20 atm pressure.[39-40] When 2-bromo-5-chloro-3-methylaminopyridine was heated with aqueous ammonium hydroxide and copper sulfate in a sealed tube, the bromine atom was preferentially replaced to yield 2-amino-5-chloro-3-methylaminopyridine.[41] Concentrated ammonium hydroxide is used to ammonodehalogenate 4-chloronicotinic acid-1-oxide[42] and 4-chloro-3,5-dimethylpyridine-1-oxide[43] to the corresponding 4-amino derivatives. Nitrohalopyridines undergo amination under milder conditions;[44] for example, 2-chloro-3,5-dinitropyridine[45] and 2,4-dichloro-3-nitropyridine[42] react with ammonia at ambient temperatures to give the corresponding 2-amino derivatives. The reactions of some chloro-, bromo-, or iodonitropyridines with ammonia do not necessarily result in the displacement of the halogen atom. Thus, 2-halo- or 3-halo-4-nitropyridines react with ammonium hydroxide to give 2-halo- and 3-halo-4-aminopyridines, respectively[47, 48] (e.g., **IX-13**).



IX-13

The fluorine atom in 2-fluoro-4-nitropyridine is more labile than the nitro group, and it is readily replaced by ammonium hydroxide to give 2-amino-4-nitropyridine (**IX-14**) rather than 2-fluoro-4-aminopyridine.[49] Similarly, 3-fluoro-4-nitropyridine and its *N*-oxide give the corresponding 3-amino-4-nitro derivatives.[50-52]

The ammonolysis reactions of various polyfluoropyridines have been studied.[53-57] The 4-fluoro substituent in pentafluoropyridine is easily



IX-14

replaced by ammonia (or other amines) to give 4-amino-2,3,5,6-tetrafluoropyridine;[53, 54] similarly, 3-chloro-2,4,5,6-tetrafluoropyridine and 3,5-dichloro-2,4,6-trifluoropyridine yield the corresponding 4-amino derivatives.[56, 58] If the 4-position does not bear a fluorine atom, as in 4-iodo-2,3,5,6-tetrafluoropyridine, the 2-fluoro substituent undergoes ammonolysis preferentially to give 2-amino-4-iodo-3,5,6-trifluoropyridine[59] (see also Chapter VI).

D. *Hofmann, Schmidt, and Curtius Reactions*

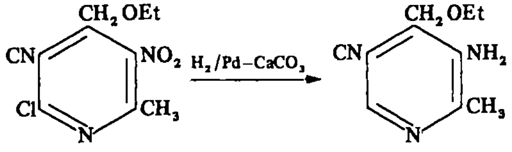
Hofmann degradations were carried out on 5-chloro- and 5-bromonicotinamide and 5-ethyl-2-picolinamide to yield 3-amino-5-chloropyridine,[60] 3-amino-5-bromopyridine,[61] and 2-amino-5-ethylpyridine,[62] respectively. When pyridine carboxylic acids are treated with sodium azide in an oleum medium, a good yield (69%) of 3-aminopyridine and poorer yields (<30%) of 2- and 4-aminopyridine are realized.[63] 3-Amino-5-nitropyridine is similarly prepared by the Schmidt reaction using 5-nitronicotinic and hydrazoic acid.[64, 65]

Several aminofluoropyridines are prepared either by the Hofmann reaction or the Curtius degradation. Thus, 2-amino-6-fluoropyridine is easily obtained from either 6-fluoropicolinamide or 6-fluoropicolinic hydrazide.[66] 3-Amino-2-fluoropyridine and 5-amino-2-fluoropyridine are prepared best from the appropriate 2-fluoropyridine carboxamide rather than from the hydrazide because the α-fluorine atom is easily replaced by hydrazine.

E. *Reduction of Nitro Compounds*

The preparation of aminopyridines through the reduction of nitropyridines and nitropyridine-1-oxides, may be subdivided into catalytic hydrogenation and noncatalytic reducing systems. 3-Ethyl-4-nitropyridine-1-oxide and 4-amino-2,6-lutidine-1-oxide are hydrogenated over platinum oxide to give 3-ethyl-4-aminopyridine and 4-amino-2,6-lutidine,[68] respectively. Palladium on various inert supports[69-77] has been used instead of platinum oxide. If a halogen substituent is present, not only is the nitro group reduced but the halogen atom is removed as well; for example, 6-chloro-5-cyano-4-ethoxymethyl-3-nitro-2-picoline gives

3-amino-5-cyano-4-ethoxymethyl-2-picoline (IX-15) when hydrogenated in absolute ethanol in the presence of palladium on calcium carbonate.[77] Often the

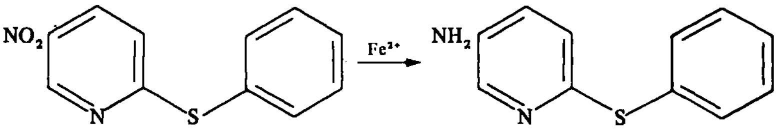


IX-15

halogen substituent may be more effectively removed by treatment of the halopyridine with hydrazine prior to hydrogenation.[69]

Catalytic hydrogenation of 6-chloro-5-cyano-4-ethoxymethyl-3-nitro-2-picoline over nickel formate selectively reduces the nitro function but spares the chloro and cyano groups, giving 3-amino-6-chloro-5-cyano-4-ethoxymethyl-2-picoline.[78] Both nitropyridines and nitropyridine-1-oxides are converted to aminopyridines by catalytic hydrogenation over Raney nickel.[79-88] For example, 4-nitropyridine-1-oxide and 4-nitro-3-picoline-1-oxide are hydrogenated over Raney nickel to give 4-aminopyridine and 4-amino-3-picoline, respectively.[84-86] Similarly, halonitropyridine-1-oxides may be converted to the corresponding aminohalopyridines;[87] the halogen atom is not removed.

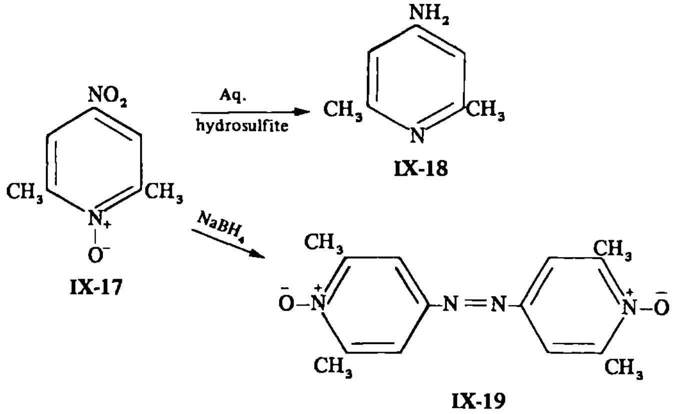
Metal-acid solutions have been employed in the reduction of nitropyridines to aminopyridines. Zinc dust and acetic acid have been used in the preparation of 3-amino-1-benzyl-4-pyridone or 3-amino-1-benzyl-5-iodo-4-pyridone from the corresponding 3-nitro derivatives.[89] Tin or iron in acids is more popular.[74, 90-97] For example, 3-amino-2-(*o*-bromobenzyloxy)-pyridine is obtained by the reduction of 2-(*o*-bromobenzyloxy)-3-nitropyridine using iron and hydrochloric acid.[94] Various ferrous salts have also been effective reducing agents. Several derivatives of phenyl 5-amino-2-pyridyl sulfide (IX-16) (or the sulfone) are



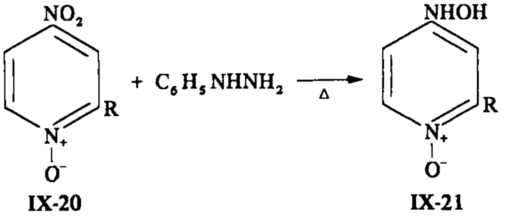
IX-16

obtained by the reduction of phenyl 5-nitro-2-pyridyl sulfide (or the sulfone) with ferrous salts in ammonium chloride solution.[98] These amino derivatives are given in Tables IX-19 and IX-20. Ferrous sulfate successfully reduces 3-nitro-2-picoline-4-carboxaldehyde to the unstable 3-amino-2-picoline-4-carboxaldehyde;[99] ferrous hydroxide converts 3-iodo-4-nitropyridine-1-oxide to 3-iodo-4-aminopyridine.[100]

4-Nitropyridine is reduced to 4-aminopyridine by sulfur dioxide dissolved in dilute sulfuric acid containing hydrogen iodide as a catalyst.[101] Aqueous solutions of sodium sulfide or ammonium sulfide reduce only the 3-nitro substituent in 3,5-dinitropyridine and 3,5-dinitro-2-pyridone.[102-104] 4-Nitro-2,6-lutidine-1-oxide (**IX-17**) reacts with aqueous hydrosulfite to give 4-amino-2,6-lutidine (**IX-18**);[105] however, **IX-17** reacts with sodium borohydride to give 4,4′-azo-2,6-lutidine-1,1′-dioxide (**IX-19**).[106]

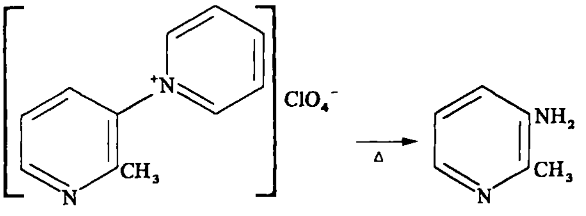


When 2-halo-4-nitropyridine-1-oxides are treated with hydrazine hydrate in ethanol, 4-amino-2-halopyridine-1-oxides result.[107] The reaction of 4-nitropyridine-1-oxide (**IX-20**, R = H) and of 4-nitro-2-picoline-1-oxide (**IX-20**, R = CH_3) with phenylhydrazine gives 4-hydroxylaminopyridine-1-oxide (**IX-21**, R = H) and 4-hydroxylamino-2-picoline-1-oxide (**IX-21**, R = CH_3), respectively, rather than the corresponding 4-amino derivatives[108, 109] (See also Chapter VIII).



F. *From Pyridylpyridinium Halides and* N*-(Pyridyl)-2-pyridones*

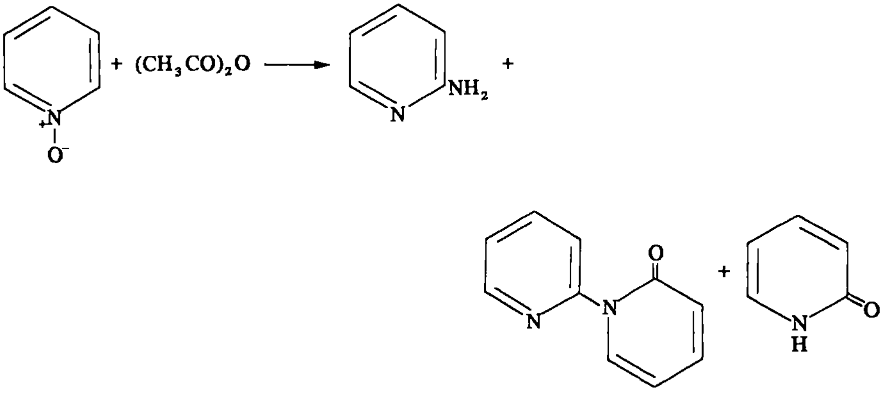
When *N*-(2-methyl-3-pyridyl)pyridinium perchlorate is dissolved in piperidine and ethanol and heated, 3-amino-2-picoline (**IX-22**) is obtained.[110] Similarly, other *N*-(2- and 4-pyridyl)pyridinium salts give the corresponding 2- and 4-aminopyridines.[111]



IX-22

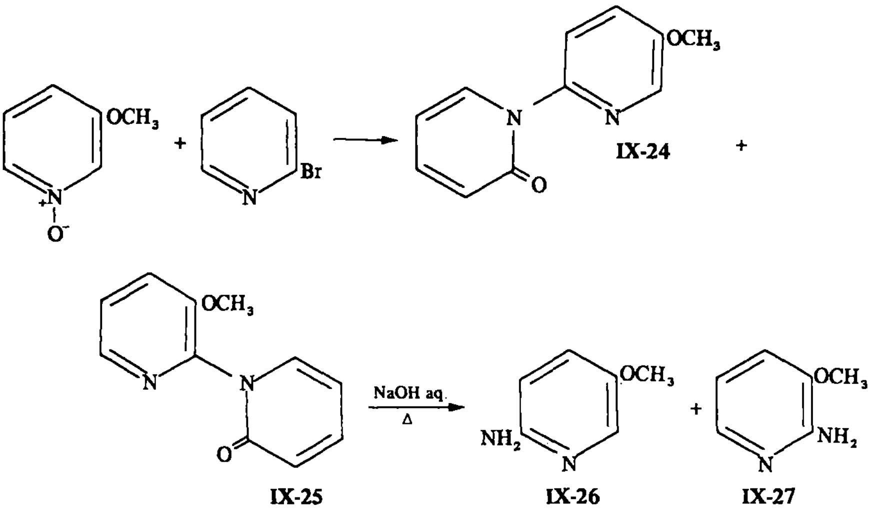
Heating 1-(4-hydroxy-2-pyridyl)pyridinium chloride in aniline and acetic anhydride gives a product that, on hydrogenation over palladium-charcoal, proved to be 2-aminopyridine.[112]

Contrary to a previous report,[113] the reaction of pyridine-1-oxide with acetic anhydride does not give exclusively 2-pyridone; 2-aminopyridine and *N*-(2-pyridyl)-2-pyridone (**IX-23**) are also formed.[114] Similarly, 6-amino-3-picoline and 3-methyl-*N*-(5-methyl-2-pyridyl)-2-pyridone were isolated in the reaction of 3-picoline-1-oxide with acetic anhydride[115] (see also Chapter IV).



IX-23

When 3-methoxypyridine-1-oxide is treated with 2-bromopyridine, 1-(5-methoxy-2-pyridyl)-2-pyridone (**IX-24**), 1-(3-methoxy-2-pyridyl)-2-pyridone (**IX-25**), and some other unidentified products are obtained. Heating **IX-24** and **IX-25** with aqueous sodium hydroxide gives the corresponding aminomethoxypyridines **IX-26** and **IX-27**. Several other aminomethoxypyridines are prepared similarly.[116]

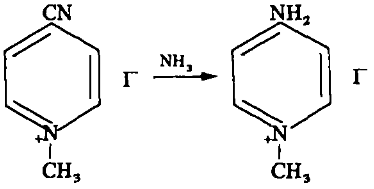


IX-24 IX-25 IX-26 IX-27

G. *Miscellaneous Methods*

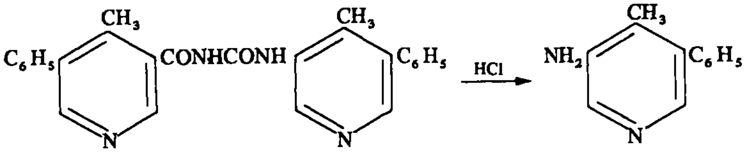
Hydroxylamine reacts with 2,6-dimethylpyrone or with the barium salt of diacetyl acetone to give 4-hydroxylamino-2,6-lutidine-1-oxide, which can be reduced catalytically to 4-amino-2,6-lutidine using hydrogen and platinum oxide.[117]

When pyridine-4-sulfonic acid is heated with ammonium hydroxide or with an alkylamine in the presence of a small amount of zinc chloride it gives 4-aminopyridine and 4-alkylaminopyridine, respectively.[118] 4-Amino-2,6-di-*t*-butylpyridine is obtained on heating 2,6-di-*t*-butylpyridine-4-sulfonic acid with aqueous ammonia in a small sealed tube.[119] The cyano group in the 4-position is also labile; thus 4-cyanopyridinium methiodide reacts with ammonium hydroxide to give 4-aminopyridine methiodide (IX-28).[120]



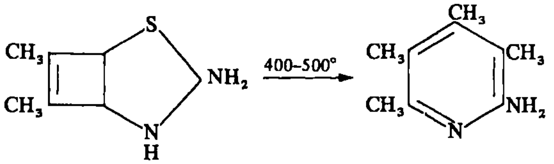
IX-28

2-Amino-6-fluoropyridine is prepared by the hydrolysis of 6-fluoropyridine-2-isocyanate.[121] *N*-(4-Methyl-5-phenylnicotinyl)-*N'*-(4-methyl-5-phenyl-3-pyridyl) urea is hydrolyzed with hydrochloric acid to give 3-amino-4-methyl-5-phenylpyridine (IX-29).[12]



IX-29

When the thiazoline **IX-30** was sublimed at 400 to 500°, small amounts of 2-amino-3,4,5,6-tetramethylpyridine (**IX-31**) were isolated.[122] 4,4-Dimethyl-1-(2-pyridylamino)glutamide is obtained from the pyrolysis of the mono-2-pyridylhydrazide of 3,3-dimethylglutaric acid.[123]



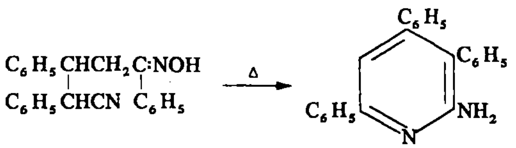
IX-30

IX-31

4-Aminonicotinamide is obtained by the hydrogenation of 4-benzyloxynicotinamide over a Raney nickel catalyst.[124]

2-Aminopyridine-1-oxide can now be converted to 2-aminopyridine by heating it with granulated lead and ferrous oxalate; this procedure is valuable for aminopyridine-1-oxides that cannot be deoxygenated by phosphorous trichloride.[125]

The thermal decomposition of oximes of γ-nitro or γ-cyano ketones results in a complex mixture of products, the major component of which is a substituted 2-aminopyridine (IX-32).[126]



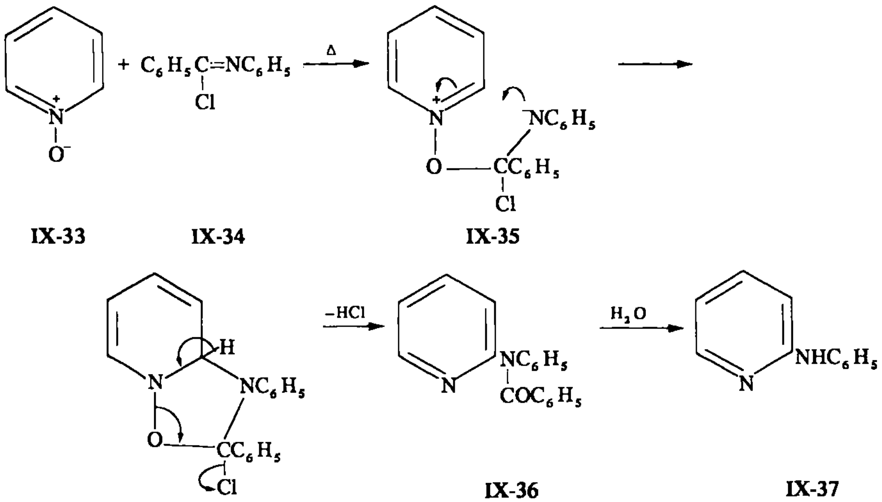
IX-32

A mixture of chloramine and ammonia with pyridine, 4-picoline, 2,4-lutidine, or nicotinic acid is reported to give the corresponding 2-amino derivative. 1-Aminopyridine hydrochloride as well as 2-aminopyridine hydrochloride are detected in aqueous solutions of chloramine and pyridine.[127]

2. Preparation of Secondary and Tertiary Amines

Vajda and Kovacs[128, 129] described three methods labeled A, B, and C, for the direct amination of the pyridine with alkyl amines in the presence of sodium amide or finely divided potassium or sodium metal. An example of method A was the preparation of 2-*n*-butylaminopyridine from a mixture of *n*-butylamine, pyridine, and sodium amide in boiling toluene (60 hours). In method B, powdered sodium (or potassium) metal was used instead of sodium amide and the reflux time was 20 hours. Method C employed sodium metal, a bath temperature of 120°, boiling under reflux with stirring for 3 hours and an additional 7 hours of boiling without stirring. The yields of 2-*n*-butylaminopyridine in the above three methods were 38%, 50%, and 33%, respectively. These authors claimed that the reaction proceeded via a radical rather than an ionic (nucleophilic) pathway because dipyridyls were also formed. When a pyridine is heated with a three- to fourfold excess of a primary aliphatic amine in the presence of finely divided sodium metal, 70 to 80% yields of 2-alkylaminopyridines are obtained.[130, 131]

Another general method of direct alkyl- and aryl- amination of the pyridine ring has recently been reported by Abramovitch and Singer.[132] Pyridine-1-oxide (**IX-33**) and *N*-phenylbenzimidoyl chloride (**IX-34**) in boiling ethylene chloride give *N*-benzoyl-2-anilinopyridine (**IX-36**), which, on hydrolysis, gives 2-anilinopyridine (**IX-37**); the reaction is believed to proceed *via* an intramolecular nucleophilic substitution. Various *N*-oxides (except 4-nitropyridine-1-oxide) and imidoyl chlorides have been successfully employed in this synthesis (see Tables IX-1 and IX-2). Reduction of **IX-36** gives the corresponding tertiary amine.[133]



IX-33 **IX-34** **IX-35**

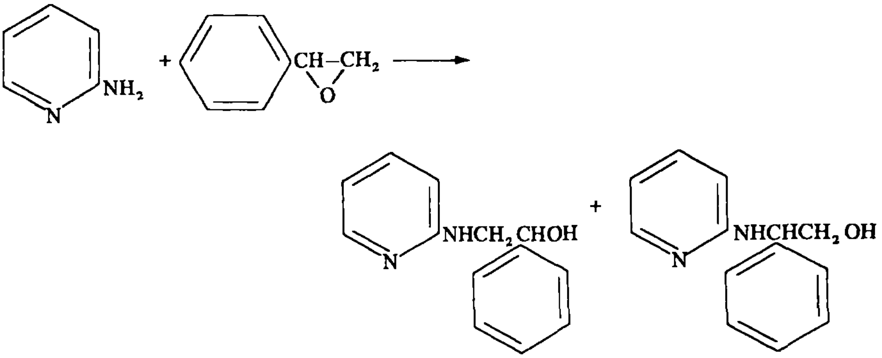
IX-36 **IX-37**

Pyridine-1-oxide also reacts with phenyl isocyanate to give good yields of 2-anilinopyridine.[134]

Secondary amines are also prepared from aminopyridines and alkyl halides.[135-138] For example, sodium amide and 2-aminopyridine are boiled under reflux in ether for 1 hour and then with allyl chloride for 3 hours to give 61% of 2-allylaminopyridine; similarly 2-allylamino-5-bromopyridine and 2-allylamino-3,5-dibromopyridine were prepared.[140, 141]

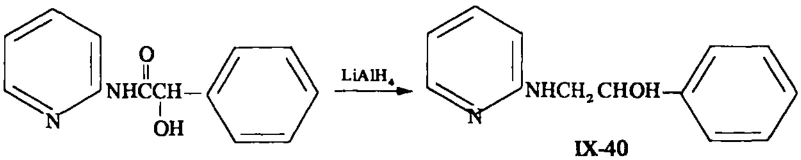
2-Aminopyridine condenses with alcohols to yield 2-alkylaminopyridines.[142-144] 2-Aminopyridine and cyclohexanol are dissolved in 80% sulfuric acid and heated at 60 to 70° for 6 hours; the reaction mixture is then poured over ice and neutralized with ammonia to give 2-(cyclohexylamino)pyridine (70% yield). 2-Isopropylaminopyridine is similarly prepared from isopropyl alcohol.

When 2-aminopyridine is treated with sodium amide and styrene oxide, a mixture of 2-(β-hydroxy-β-phenethylamino)pyridine (**IX-38**) and 2-(β-hydroxy-α-phenethylamino)pyridine (**IX-39**) in the ratio 3:1 is obtained.[145]



IX-38 **IX-39**

2-(β-Hydroxy-β-phenethyl)aminopyridine (**IX-40**) can be prepared by the reduction of 2-mandelaminopyridine with lithium hydride.[146]



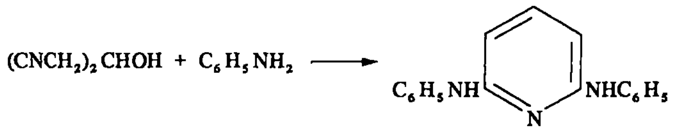
IX-40

Wibaut and Broekman reported that 4-chloropyridine reacted slowly with primary and secondary amines.[147] Tertiary amines do not react with

4-chloropyridine. A mixture of 4-chloropyridine and methylamine in benzene was heated in a sealed tube at 160° for 6 hours to yield 34% of 4-methylaminopyridine. The formation of various secondary aminopyridines from a halopyridine and an alkyl amine include the preparations of 4-isopropylaminopyridine and 4-dodecylaminopyridine.[147-151]

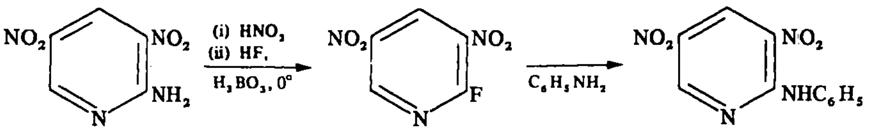
4-Chloropyridine-1-oxide when heated with 30% aqueous methylamine at 140° for 18 hours gives 4-methylaminopyridine-1-oxide. Several substituted 4-methylaminopyridines are similarly prepared.[43] 2-Propylaminopyridine and 2-phenethylaminopyridine are obtained by heating 2-bromopyridine with propylamine[152] and phenethylamine,[153] respectively. 2-Bromopyridine also reacts with 1-aminoindane to give 2-(1-indanylamino)pyridine.[154, 155] 2,6-Dichloropyridine reacts with butylamine to give 2-butylamino-6-chloropyridine.[156] 2-Benzylamino-3-nitropyridine and 2-(chlorobenzylamino)-3-nitropyridine are readily prepared from 2-chloro-3-nitropyridine with benzyl amine and *p*-chlorobenzyl amine, respectively.[157]

Anilinopyridines are prepared by heating aniline and a halopyridine, generally in the presence of an inorganic base.[158-161] For example, 2-nitro-*N*-(3-pyridyl)-aniline is obtained by boiling a mixture of 3-bromopyridine, *o*-nitroaniline, and potassium carbonate in nitrobenzene for 24 hours under reflux.[158] 2-Anilinopyridine is also isolated (14% yield) from a reaction mixture containing aniline, iodobenzene, 2-chloropyridine, methyl salicyate and potassium carbonate, though the main product is diphenylamine.[159] When 2,6-dichloropyridine is heated with aniline, both substituents are replaced and 2,6-dianilinopyridine is obtained.[160] 2,6-Dianilinopyridine (**IX-41**) has also been obtained by the cyclization of 3-hydroxyglutaronitrile with aniline hydrobromide.[6] 2-Amino-



IX-41

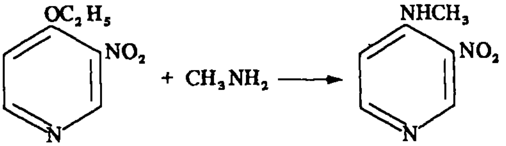
3,5-dinitropyridine can be diazotized and undergoes the Schiemann reaction to give 2-fluoro-3,5-dinitropyridine,[1] which, with aniline, gives the 2-anilino derivative (**IX-42**).[161]



IX-42

4-Chloropyridine reacts with *p*-(2-diethylaminoethoxy)aniline to give 4-[*p*-(2-diethylaminoethoxy)anilino]pyridine; other substituted *p*-dialkylamino-alkoxyanilinopyridines are prepared similarly.[162, 163]

Alkoxy groups in the 2- or 4-positions of alkoxynitropyridines are easily replaced by ammonia, alkylamines, or dialkylamines. Thus, 4-methylamino-3-nitropyridine (**IX-43**) is obtained in near quantitative yield by heating 4-ethoxy-3-nitropyridine hydrochloride in an autoclave with aqueous methylamine.[152]



IX-43

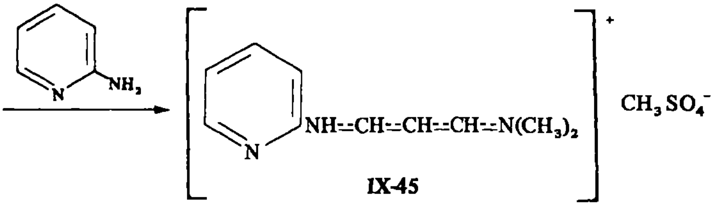
Other methods of preparing secondary aminopyridines have also been reported.

4-(*m*-Hydroxyphenyl)aminopyridine is obtained by heating the sodium salt of *m*-aminophenol with 4-chloropyridine.[164] A number of 4-arylaminopyridines have been prepared similarly (see Table IX-41).

A preparation of the secondary aminopyridine **IX-45** involves the reaction of 2-aminopyridine with the salt **IX-44**.[165]

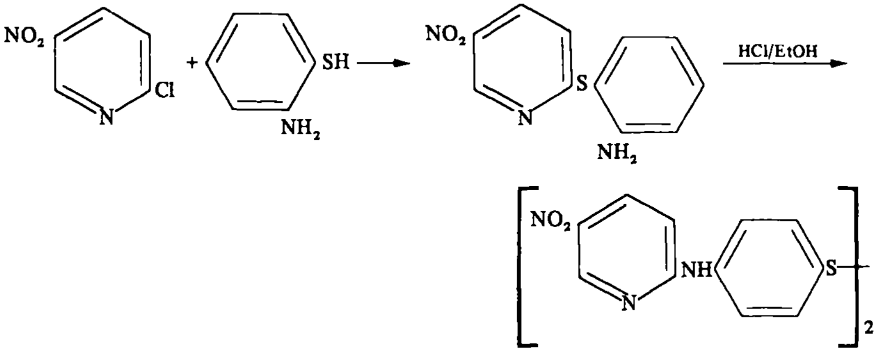
$$(CH_3)_2NCH{=}CHCHO + (CH_3)_2SO_4 \longrightarrow [(CH_3)_2N{=}CH{=}CH{=}CHOCH_3]^+CH_3SO_4^-$$

IX-44



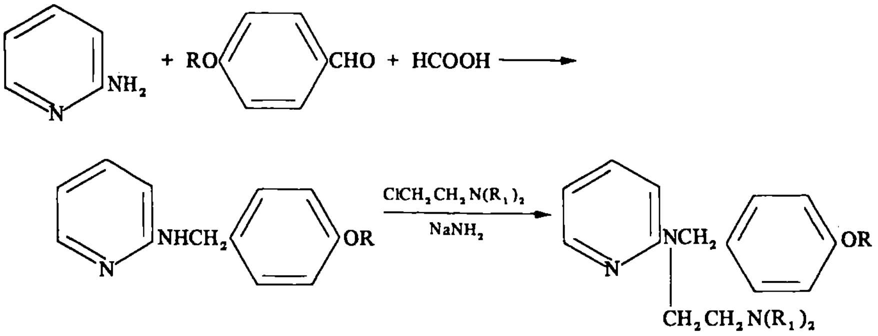
IX-45

2-Chloro-5-nitropyridine condenses with 2-aminobenzenethiol to give 2-(5-nitropyridylthio)aniline, which, when heated in ethanolic solutions of hydrogen chloride, gives **IX-46**.[166] This Smiles rearrangement has been investigated[166-170] (see also Chapter XV).



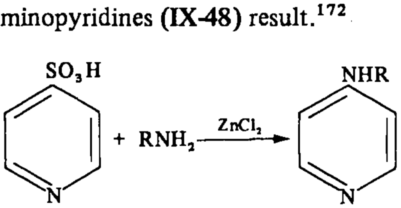
IX-46

Aralkylaminopyridines are prepared by reductive alkylation; for example, when 2-aminopyridine is heated with 4-alkoxybenzaldehyde and formic acid, 2-(4-alkoxybenzylamino)pyridines are formed. The latter compounds, when treated with sodium amide and dialkylaminoethyl chloride, give *N*-4-alkoxybenzyl-*N*-2-pyridyl-*N*′,*N*′-dialkylethylenediamine (**IX-47**).[171]



IX-47

When 4-pyridinesulfonic acid is heated with an alkyl amine in the presence of zinc chloride, 4-alkylaminopyridines (**IX-48**) result.[172]



IX-48

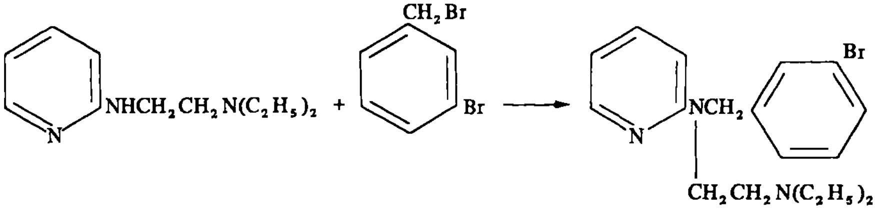
Tertiary aminopyridines are generally prepared either by the amination of halopyridines with secondary alkyl or aryl amines or by the amination of a secondary pyridylamine with an alkyl or aryl halide.[162-167] The reactions of 2-halopyridines and their *N*-oxides with an excess of dimethylamine have been studied. Based on the yields of diethylaminopyridines and dimethylaminopyridine-1-oxides produced, the following is the order of decreasing reactivities of the halopyridines:[174]

2-bromopyridine-1-oxide > 2-chloropyridine-1-oxide >

(2-iodopyridine-1-oxide, 2-iodopyridine, 2-chloropyridine)

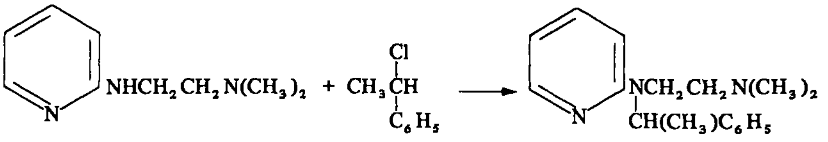
2-Dimethylamino-3,5-dinitropyridine is obtained from 2-chloro-3,5-dinitropyridine with 40% aqueous dimethylamine. 2-Diethylamino-3,5-dinitropyridine is formed from anhydrous diethylamine and 2-(β-chloroethoxy)-3,5-dinitropyridine.[181]

N-(2-Pyridyl)-*N*-bromobenzyl-*N*′,*N*′-dialkylethylenediamines are prepared from 2-(β-dialkylaminoethylamino)pyridine, alkali amide and an alkyl bromide (preferably bromobenzyl bromide; see Table IX-35). Thus, *N*-(2-pyridyl)-*N*-(*m*-bromobenzyl)-*N*′,*N*′-diethylethylene diamine **(IX-49)** is obtained from the condensation of 2-(β-diethylaminethylamino)pyridine with *m*-bromobenzyl bromide in the presence of sodium amide.[181]



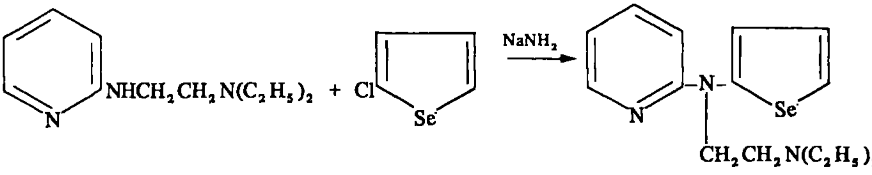
IX-49

2-(2-Dimethylaminoethylamino)pyridine reacts with 1-phenethyl chloride in the presence of sodamide to give *N*-(1-phenethyl)-*N*-(2-pyridyl)-*N*′,*N*′-dimethylaminoethylene diamine **(IX-50)**;[182] other aryl derivatives have been prepared[183] (see Table IX-36).



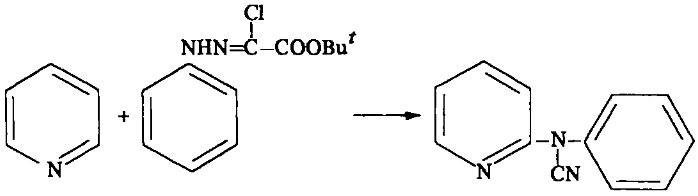
IX-50

Heating *N*,*N*-diethyl-*N*′-2-pyridylethylenediamine with sodium amide in toluene followed by treatment with 2-chloromethylselenophene gives *N*,*N*-diethyl-*N*′-2-pyridyl-*N*′-2-selenylethylene diamine (**IX-51**). Other pyridyl derivatives of selenylethylene diamine were prepared.[184, 185]



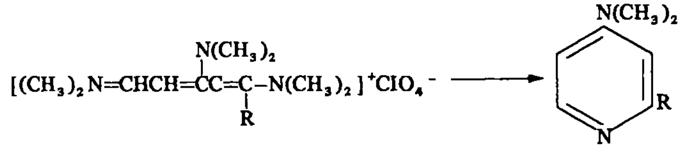
IX-51

An unusual preparation is that of 2-(*N*-cyano-*N*-phenyl)aminopyridine (**IX-52**), which is obtained by heating pyridine with *N*-anilino-*t*-butoxycarbonyl imidoyl chloride at 170° for 15 minutes.[186]



IX-52

When an aqueous solution of ammonium chloride and a polymethinium perchlorate salt (**IX-53**, R = H or C_6H_5) is heated, it gives 4-dimethylaminopyridine (78%) and 4-dimethylamino-2-phenylpyridine (49%), respectively[187]



IX-53

4-Aminopyridine reacts with acrylonitrile to give a quantitative yield of 4-[*N*,*N*-bis(2-cyanoethyl)] aminopyridine.[188]

Aminopyridines also react with aldehydes, ketones, and other carbonyl derivatives to give products that can be converted to secondary or tertiary amines; these reactions are discussed in Section I.4.C.

3. Structures and Properties

Many excellent books, reviews, and reports[189-196] are now available on the investigations of the structure and properties of aminopyridines.

The dipole moments of many aminopyridines in several solvents have been measured.[189, 197, 198] These studies contain many interesting observations. One amino-hydrogen in 2-aminopyridine is reported to be in the same plane as the heterocyclic ring.[199] While the resonance interactions of the methyl and chloro substituents in methyl- and chloropyridine are not very very marked, those of the amino group in 4-aminopyridine are significant.[191] Dioxane forms complexes with 2-, 3-, and 4-aminopyridine through hydrogen bonds to the amino-nitrogen; intermolecular associations by hydrogen bonding with 3- and 4-aminopyridine in benzene have also been reported.[200]

The ultraviolet spectra of various aminopyridines,[190, 201-206] their methoxy derivatives[207] and dipyridyl amines[208] were recorded. The investigation of amino-imino tautomerism continues;[192, 200, 209-212] the amino form generally predominates. 2-, 3-, And 4-acetylamidopyridine exist predominantly in the acylamino form.[213] The ultraviolet spectra of 3-monosubstituted tertiary 4-aminopyridines or 3,5-disubstituted secondary 4-aminopyridines show changes in intensities of bands that were attributed to steric inhibition of resonance. No evidence for such inhibition in the case of the primary 3- and 4-aminopyridines or the 3-monosubstituted 4-methylaminopyridines was observed. The spectra of the monocations of all the above aminopyridines indicated that the ring nitrogen atom was the basic center.[214] Theoretical calculations of transition energies, oscillator strengths, and dipole moments of $\pi \rightarrow \pi^*$ bands agree well with experimental results; these calculations were based on the localized-orbital model,[215] LCAO-MO,[216-218] SCF[219] and CNDO[220] methods.

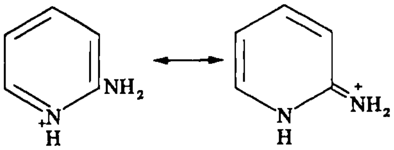
The basicities (pK_a) of a large number of pyridines have been determined.[189, 190, 193, 221-227] The variation of pK_a values with temperature for monovalent and divalent organic cations may be calculated from the following expressions (the entropy change of −4 ± 6 cal/degree was assumed to be a constant):[228]

$$\left(\begin{array}{l} \dfrac{-d(pK_a)}{dT} = (pK_a - 0.9)_T \pm 0.004 \\[2ex] \dfrac{-d(pK_a)}{dT} = \dfrac{pK_a}{T} \end{array} \right)$$

Protonation first occurs at the 2- or 4-amino group in 2,3- and 3,4-diaminopyridines; a second protonation then takes place at the 3-amino group. Replacement of a hydrogen atom by a methyl group on an extranuclear NH_2 gives rise to a small bathochromic shift for the cation of 3,4-diaminopyridine or 4-amino-3-nitropyridine, but not with the neutral species.[225]

The fluorescence properties of 2-, 3-, and 4-aminopyridines in various solvents have been investigated.[229] The 2- and 3-isomers are efficient fluorescers with quantum yields approaching unity in $0.1N$ H_2SO_4. 4-Aminopyridine, however, fluoresces weakly due to an n → π^* (rather than $\pi \rightarrow \pi^*$) lowest excited singlet and a second excited state that has large charge-transfer character. The pK_a values of the excited states of 2- and 3-aminopyridine indicate that the excited states are weaker conjugate acids than the ground states. The fluorescence of biacetyl sensitized by 2-aminopyridine (but not by the 3- or 4-isomer) has been observed.[230] The europium complex of 2-aminopyridine, but not that of the 3-isomer, fluoresces weakly red.[231]

Considerable activity in the study of the infrared spectroscopy of aminopyridines,[189,195,196,205,232-240] methylaminopyridines,[239,241] and aminomethyl pyridines[194,242,243] is noted. In addition, the Raman spectra of aminopicolines were reported.[244,245] In the crystalline state, 2-amino-, 2-amino-5-halo-, and 2-amino-5-nitropyridines were reported to exist in the tautomeric amino form, and the NH_2 group absorbed at 3280, 3400, and 1640 cm^{-1}.[205] Whereas the vibrational spectrum of 3-aminopyridine hardly changes on protonation, the vibrational spectra of the 2- and 4-isomer change distinctly. The hydrochloride of 2-(and of 4-)aminopyridine is best represented as the aminium ion **IX-54**. The fundamental symmetrical and asymmetrical N—H stretching vibrations of 2-, 3-, and 4-aminopyridines were studied in eleven solvents. It was concluded that the excess basicities were due to excess π-charges on the nuclear nitrogen. The hydrogen bonding strength was governed by the charges on the extranuclear nitrogen.[246]



IX-54

Magnetic resonance spectroscopy employing the nuclei ^{1}H,[190,247-251] ^{19}F[252,253] and ^{14}N[254-256] has been used to study the π-electron densities and the various structural and electronic properties of the amino group in aminopyridines. The PMR spectra of various aminopyridines in various solvents give good linear relationships between chemical shifts and electron densities derived from molecular orbital calculations.[248,255,257,258] Inter-, intra-, and solvent hydrogen-bonding studies have also been reported.[259,260] The preferred configuration of amides is related to the magnitudes of the downfield shifts.[261] Proton resonance spectra confirm that aminopyridines protonate at the ring nitrogen.[262]

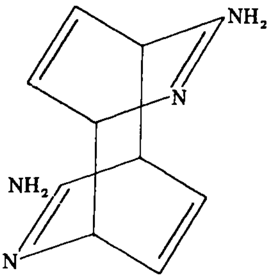
The crystal structures of 2-amino-6-pyridone,[263] 2-amino-5-chloropyridine hydrochloride[264,265] and 3-pyridylmethylamine dihydrochloride[266] were examined. Electron-impact induced fragmentations of aminopicolines showed unexpected loss of ammonia from both 2-amino-3-picoline and 2-amino-6-picoline.[267]

Miscellaneous studies include the use of 2-aminopyridine as a standard for low wave-length spectrofluorimetry,[268] the change-transfer complexes of iodine and aminopyridine,[269, 270] the linear isotherm free-energies of absorption of 2- and 3-aminopyridine on alumina,[271] rotation mobility of an amino group by dielectric relaxation[272] and the free energies, enthalpies and entropies of protonation.[271, 273]

Various rearrangement reactions involving aminopyridines have been studied; the rearrangement of nitraminopyridines will be discussed later. Reversible hydrolytic ring opening of 2-amino-^{15}N-pyridine has been reported, but 3-amino-^{15}N-pyridine yielded no rearrangment of ^{15}N.[274]

Hydrogen-deuterium exchange at the α- and β-positions of 4-aminopyridine and 4-dimethylaminopyridine in $DClO_4$ and NaOD solutions have been studied by NMR spectroscopy.[275] Base-catalyzed H–D exchange occurred at both positions, but acid-catalyzed exchange took place preferentially at the β-position. Mechanisms of exchange were postulated. Hydrogen-deuterium exchange is believed to occur between the $-ND_2$ group and the ring-hydrogen in 2- or 3-aminopyridine.[276]

Photolysis of aminopyridines has been studied by Taylor and his co-workers.[277, 278] Ultraviolet irradiation of 2-aminopyridine (and several substituted 2-aminopyridines) in hydrochloric acid solution results in the formation of the 1,4-dimer having the *anti-trans* configuration **IX-55**.



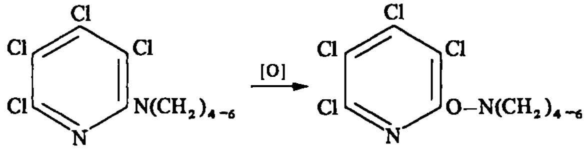
IX-55

4. Reactions

A. *Oxidation*

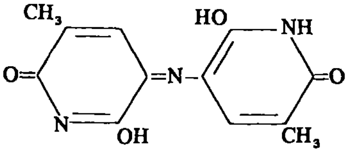
Various studies on the oxidation of aminopyridines have been reported. Taylor and Driscoll[279] suggested that the best way to convert 3-aminopyridine to 3-nitropyridine is by oxidation with persulfuric acid followed by peracetic acid.

The oxidation of 2-aminopyridine, 2-methylaminopyridine, and 2-dimethylaminopyridine with perbenzoic acid at 10° and room temperature gives the pyridine-1-oxide of 2-amino- and 2-methylaminopyridine but the *amine*-N′-*oxide* of 2-dimethylaminopyridine. The difference in behavior is attributed to steric factors.[280] The perbenzoic acid oxidation of 4-methylaminopyridine and 4-dimethylaminopyridine gives the corresponding pyridine-1-oxides;[281] however, the reaction of the cyclic 2-amino-tetrachloropyridines with performic or trifluoroperacetic acid gives the corresponding hydroxylamines (**IX-56**) rather than the 1-oxides.[282]



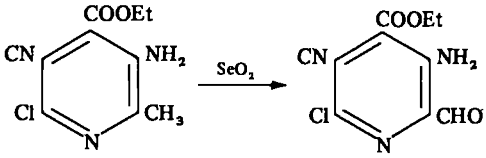
IX-56

Chloro- and bromoaminopyridines are oxidized by persulfuric acid at 0° to their nitro derivatives;[283, 284] thus, 3-chloro-, and 3-bromo-4-aminopyridine are converted to the respective 3-halo-4-nitropyridines. However, 4-amino-3-iodopyridine is *not* oxidized under these conditions.[283] 4-Amino-2,3,5,6-tetrafluoropyridine is difficult to oxidize and requires refluxing peroxytrifluoroacetic acid for 22 hours in order to yield the 4-nitro derivative. Potassium bromate has been used to oxidize 5-amino-3-methyl-2-pyridone, but the product was not a nitro compound; instead 3-hydroxy-6-methyl-2-aza-1,4-benzoquinone-4-(2,6-dihydroxy-5-methyl-3-pyridyl)imine (**IX-57**) was obtained.[284]



IX-57

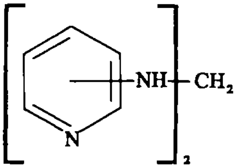
In some cases in which other functional groups (not the amino group) in aminopyridine have to be oxidized, protection of the amino groups and the use of mild oxidizing agents are resorted to. Thus, 6-amino-2-picoline is converted to 6-acetamido-2-picoline, which is then oxidized with aqueous potassium permanganate to 6-acetaminopicolinic acid. The latter, on hydrolysis, gives 6-aminopicolinic acid.[285] In the preparation of intermediates of nor-vitamin B_6, 3-amino-6-chloro-5-cyano-4-ethoxycarbonyl-2-picoline is oxidized by selenium dioxide to 3-amino-6-chloro-5-cyano-4-ethoxycarbonyl-2-formylpyridine (**IX-58**).[286]



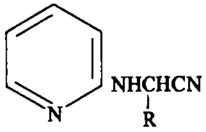
IX-58

B. *Reactions with Aldehydes and Ketones*

When a solution of 2- or 3-aminopyridine in 48% formalin is allowed to stand for 2 days at room temperature, crystals of *N,N′*-di-2- **(IX-59)** and *N,N′*-di-3-pyridylmethylenediamine **(IX-59)**, respectively, are isolated. Under similar reaction conditions, 4-aminopyridine requires 7 days to produce *N,N′*-di-4-pyridylmethylenediamine **(IX-59)**.[287]



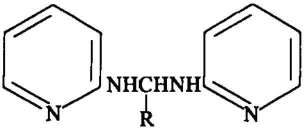
IX-59



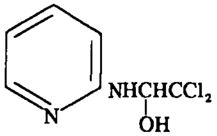
IX-60

With 2-aminopyridine-1-oxide, formaldehyde gives 2-methylolaminopyridine-1-oxide; similarly, 5-bromo-2-methylolaminopyridine-1-oxide is obtained from 5-bromo-2-aminopyridine-1-oxide.[288] When 2-aminopyridine is treated with a hot aqueous solution of sodium bisulfite and formalin followed by sodium cyanide, 2-pyridylaminoacetonitrile **(IX-60**, R = H) is obtained; when benzaldehyde instead of formalin is used, α-(2-pyridylamino)phenylacetonitrile **(IX-60**, R = C_6H_5) is formed.[289]

It has been shown that two moles of 2-aminopyridine condense with one mole of an aliphatic aldehyde (C_1–C_{10}) to give a 2,2′-(alkylidenedimino)dipyridine **(IX-61)**; these are suitable crystalline derivatives for the identification of aldehydes.[290] The reaction of 2-aminopyridine with trichloroacetaldehyde had



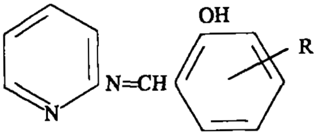
IX-61



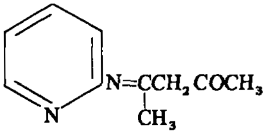
IX-62

been carried out previously,[291-293] but the structure of the product was not established. A patent now claims the structure of the product to be **IX-62**.[294]

Substituted benzylidene-2-aminopyridines (**IX-63**) are obtained by boiling methanolic solutions of equimolar quantities of the appropriate *o*-hydroxybenzaldehyde and 2-aminopyridine for 1 hour.[295] Other azomethines are also formed from aminopyridines with carbonyl compounds. Thus **IX-64** is obtained by boiling 2-aminopyridine with acetyl acetone.[296, 297] 2-Aminopyridine reacts with 1-pyrenecarboxaldehyde to give *N*-(2-pyridyl)-1-pyrenyl methenimine.[298]

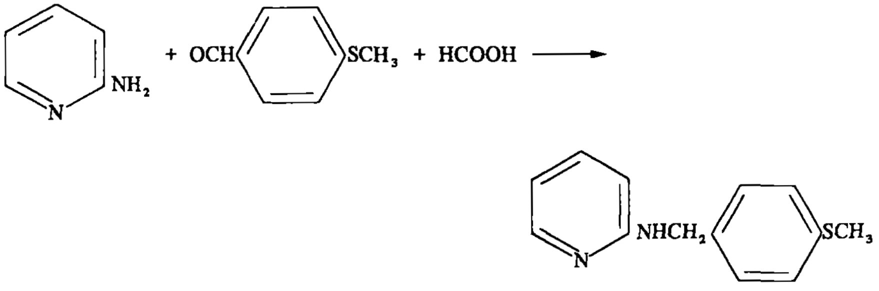


IX-63

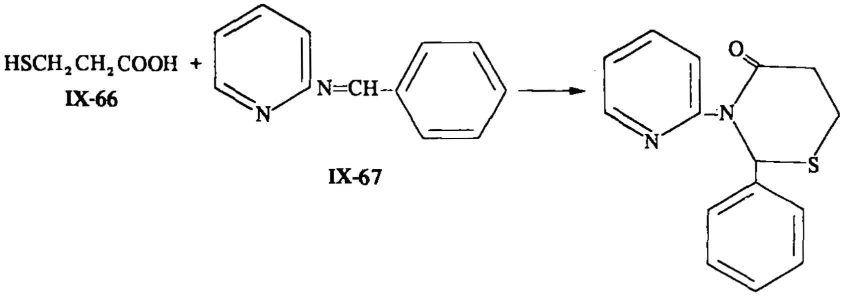


IX-64

The imines formed in the reactions of aminopyridine with aldehydes and ketones may be reduced to the amines either *in situ* in the presence of formic acid, or with sodium borohydride. Thus, 2-(4-methylthiobenzylamino)pyridine (**IX-65**) is obtained from 2-aminopyridine, 4-methylthiobenzaldehyde and formic acid.[299]



IX-65



IX-66

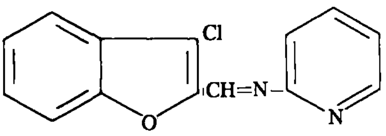
IX-67

IX-68

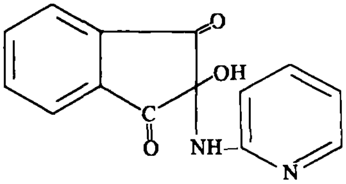
When 3-mercaptoproponic acid (**IX-66**) is added to the Schiff's base **IX-67** (from 2-aminopyridine and benzaldehyde), 2-phenyl-3-(2-pyridyl)-1,3-thiazan-4-one (**IX-68**) is obtained. Similarly, Schiff's bases from 3- and 4-aminopyridine give the corresponding phenylpyridyl-1,3-thiazan-4-one.[299-301]

2-Aminopyridine condenses with cinnamaldehyde in the presence of anhydrous zinc chloride to give a product that, on treatment with sodium borohydride, gives 2-cinnamylaminopyridine; similarly, various 2-(substituted-cinnamyl)aminopyridines are prepared from 2-aminopyridine and substituted cinnamaldehydes.[302, 303] When 2-aminopyridine and formylferrocene are boiled under reflux in toluene containing phosphorus oxychloride, there is isolated a product which, when reduced with sodium borohydride, gives 2-pyridylaminomethyl ferrocene.[304]

2-Aminopyridine condenses with heteroaromatic aldehydes; with furfural or 3-chloro-2-formylbenzofuran it gives the 2-(furfurylideneamino)pyridine and 2-[(3-chloro-2-benzofuranyl)-methylene] aminopyridine (**IX-69**), respectively.[305-308] With ninhydrin and 2-aminopyridine, 2-hydroxy-2-pyridylamino-1,3-indandione (**IX-70**) results.[309]

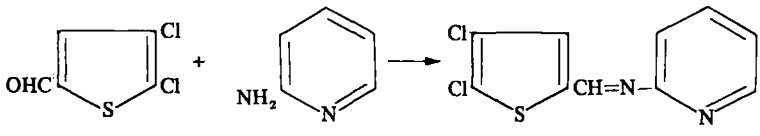


IX-69



IX-70

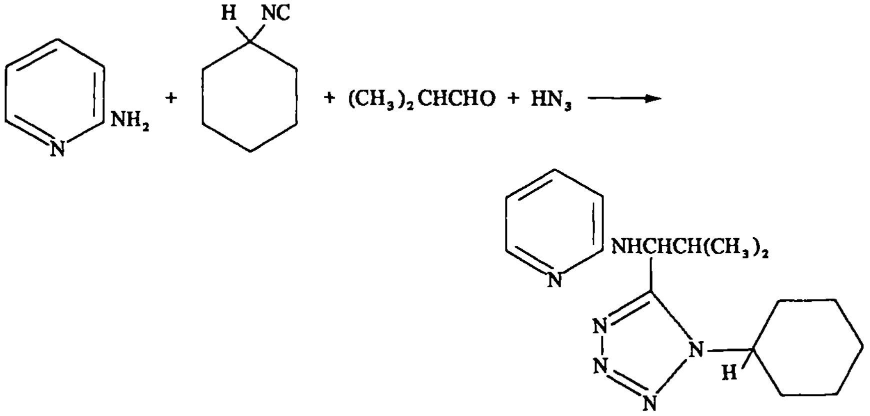
2,3-Dichlorothiophene-5-carboxaldehyde condenses with 2-aminopyridine to yield 2-(4,5-dichloro-2-thienylidene)aminopyridine (IX-71).[310]



IX-71

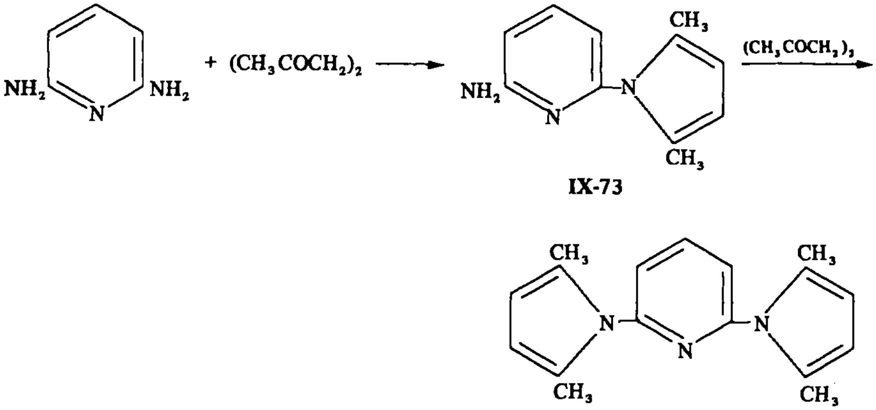
When diketene is added to a benzene solution of 2-aminopyridine and the reaction mixture is heated for 5 minutes, 2-acetoacetamidopyridine (61% yield) is obtained. Diketene reacts with 2-aminopyridine-1-oxide to yield 2-acetoacetamidopyridine-1-oxide (80%). A similar reaction is observed with 3-aminopyridine and with 3-aminopyridine-1-oxide.[311]

The complex reaction of 2-aminopyridine, isobutyraldehyde, cyclohexyl isocyanide, and hydrazoic acid gives 2-[1-(1-cyclohexyl-1*H*-tetrazolyl-5-yl)-2-methylpropyl]aminopyridine (IX-72).[312]



IX-72

The reaction of 2,6-diaminopyridine with acetonylacetone produces 2-amino-6-(2,5-dimethyl-1-pyrrolyl)pyridine (IX-73), which reacts with another mole of acetonylacetone to yield 2,6-bis-(2,5-dimethyl-1-pyrrolyl)-pyridine (IX-74).[313]

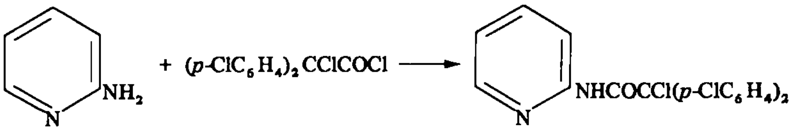


IX-73

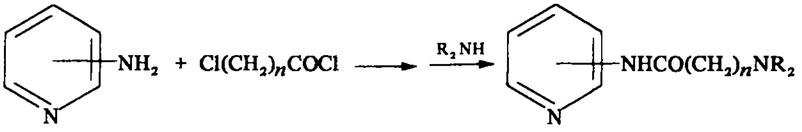
IX-74

C. *Acylation*

a. CARBONYL DERIVATIVES 4-Aminopyridine is formylated with a mixture of formic acid and acetic anhydride. Similarly, 4-amino-3-picoline is converted to 4-formamido-3-picoline.[314] 2-, 3-, And 4-acetamidopyridines are obtained by heating the appropriate aminopyridine either with acetic anhydride or with acetic acid in tetrahydrofuran.[315-317] The benzamido-, phenylacetamido-, and chloroacetamidopyridines are similarly prepared from benzoic, phenyacetic, and monochloracetic acids, respectively.[315] Various 2-(substituted benzamido)pyridines are also prepared from substituted benzyl chlorides and 2-aminopyridine;[318] 2-(2-aminoethyl)pyridine gives 2-(2-benzamidoethyl)pyridine when treated with benzoyl chloride.[319] A quantitative yield of 2-[2-chloro-2,2-bis-(*p*-chlorophenyl)acetamido]pyridine (**IX-75**) was obtained from the reaction of 2-aminopyridine with bis(*p*-chlorophenyl)chloroacetyl chloride.[320] The reaction of 2- and 4-aminopyridines with chloroacetyl chloride or chloropropionyl chloride followed by various amines (R_2NH) gives products having the general structure **IX-76**.[321, 322]



IX-75

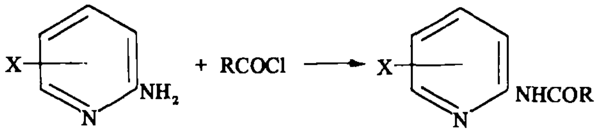


IX-76

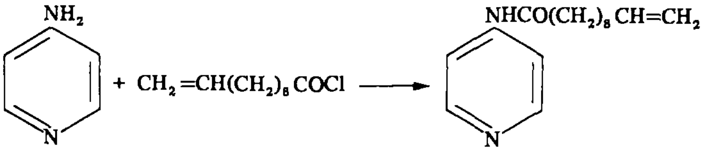
Aminopyridyl derivatives of carbazole, phenoxazine, iminodibenzyl, and phenothiazine have been reported.[323] Thus 3-(10-phenothiazinyl)propionic acid gives the corresponding 2-, 3-, and 4-pyridylpropionamides when boiled with 2-, 3-, or 4-aminopyridine in triethylamine. These pyridylamides are reduced with lithium aluminum hydride to yield the corresponding 2-, 3-, or 4-[3-(10-phenothiazinyl)propylamino] pyridines.

3-Aminopyridine reacts with 2-benzo-1,5-dioxepanylformyl chloride to form *N*-3-pyridyl-2-benzo-1,5-dioxepanylformamide, which, on reduction with lithium aluminum hydride, yields 3-[3,4-dihydro-2*H*-1,5-benzodioxepin-2-yl)-methyl] aminopyridine.[324]

Aminopyridines react with acyl or aroyl chlorides to give the corresponding amides (**IX-77**);[325-329] for example, 4-aminopyridine reacts with 10-undecenoyl chloride to give the amide **IX-78**.[326]

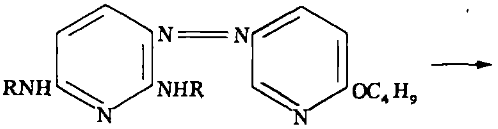


IX-77

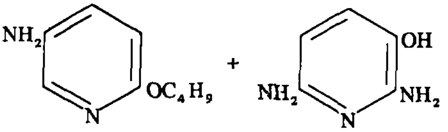


IX-78

Attempts to prepare 2,6-diacyldiamino-3-aminopyridine by means of the reductive cleavage of 2,6-diacyldiamino-2′-butoxy-3,5′-azopyridine did not give the desired product. Thus, heating 2,6-diphthaloydiamino-2′-butoxy-3,5′-azopyridine (**IX-79**) with iron and hydrochloric acid leads to 5-amino-2-butoxypyridine (**IX-80**) and 2,6-diamino-3-hydroxypyridine (**IX-81**).[330]

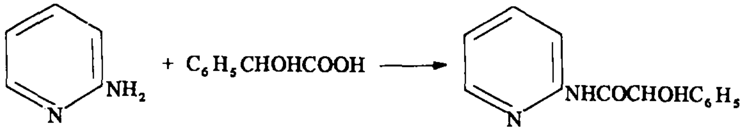


(R = phthaloyl)
IX-79



IX-80 **IX-81**

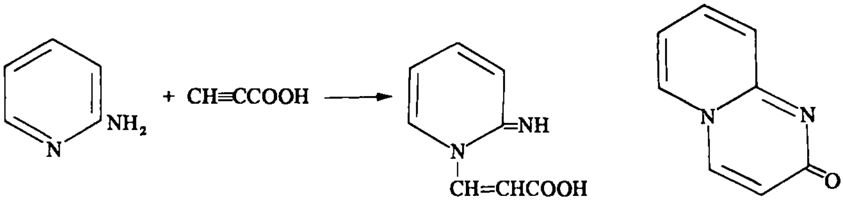
When 2-aminopyridine and mandelic acid are azeotroped for 20 hours in toluene, 2-mandelamidopyridine (**IX-82**) is obtained; several substituted 2-mandelaminopyridines are similarly prepared.[331-333] Generally, acids react



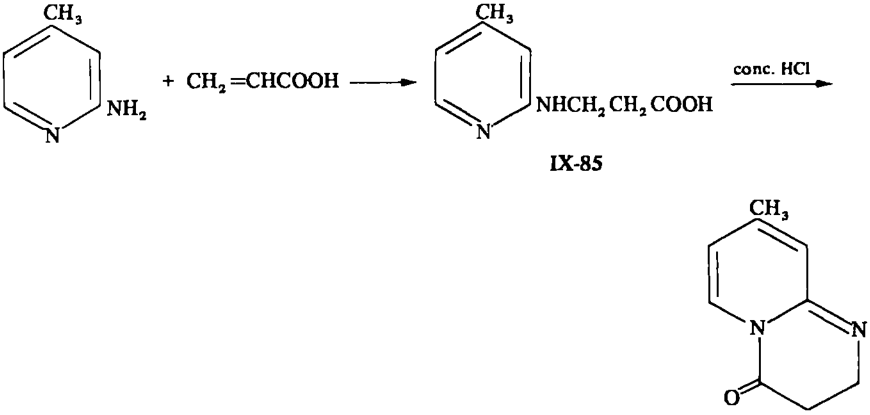
IX-82

with aminopyridines to give salts[334-337] that are often crystalline and are used as derivatives for identification or purification purposes. Thus, the reactions 2-, 3-, or 4-aminopyridines with fatty acids,[334, 338] uric acid,[336] dinitrophthalic acid,[339] and antipyrine-4-sulfonic acid[340] all yield crystalline salts. Phosphoric, perchloric, and nitric acids have also been used.[341-344]

Unsaturated acids react with aminopyridines to form condensation products rather than salts. Thus, 2-aminopyridine reacts with propiolic acid to form *trans*-2-imino-1(2*H*)-pyridineacrylic acid (**IX-83**) and 2*H*-pyrido[1,2-*a*]pyrimidin-2-one (**IX-84**).[345] The reactions of aminopyridines with acrylonitrile and acrylic acid and its derivatives have been investigated.[346, 347, 188] Heating 2-amino-4-picoline with acrylic acid, its nitrile, amide, methyl or ethyl ester in water at 100° gives β-[1-(4-methyl-2-aminopyridyl)]propionic acid (**IX-85**).[346] The latter, on heating with concentrated hydrochloric acid, cyclizes to **IX-86**.



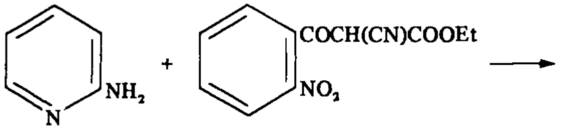
IX-83 **IX-84**



IX-85

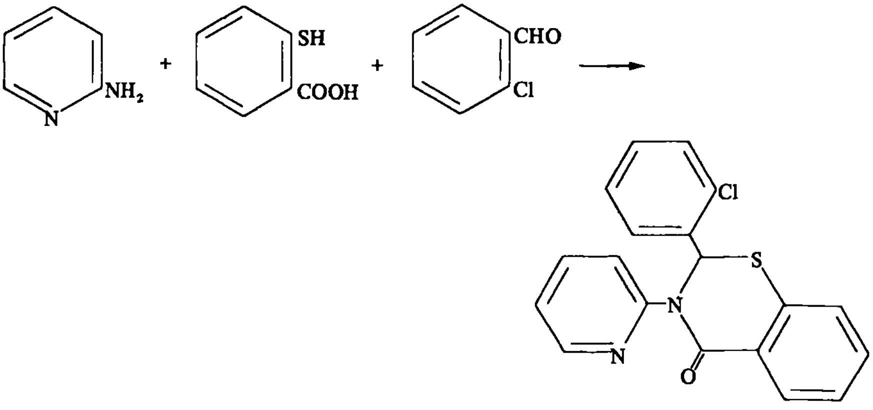
IX-86

2-Aminopyridine reacts with ethyl α-cyano-α-(*o*-nitrobenzoyl)acetate to form a 1:1 adduct (**IX-87**), the structure of which has not been established.[348]



1 : 1 adduct
IX-87

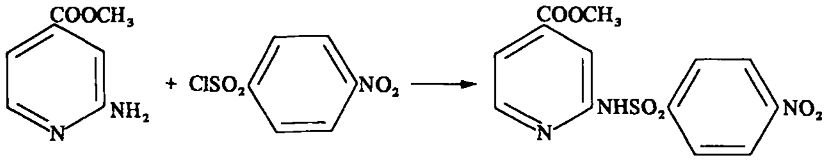
Metathiazanones (IX-88) are prepared by heating a benzene solution of thiosalicylic acid, 2-(or 3-)-aminopyridine, and *o*-chloro-(or *m*-nitro-)benzaldehyde.[357]



IX-88

b. SULFONYL DERIVATIVES Aryl sulfonamidopyridines are formed by the direct reaction of arylsulfonyl chlorides with aminopyridines.[92, 349-352] Thus, 2,6-dimethyl-3-aminopyridine reacts with benzenesulfonyl chloride to give *N*-(2,6-dimethyl-3-pyridyl)benzenesulfonamide.[351]

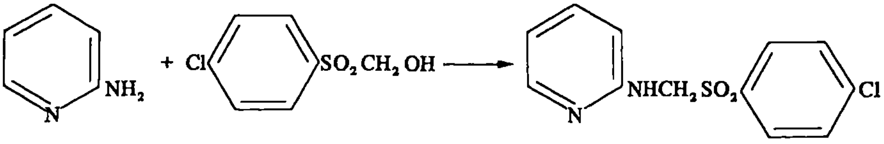
Methyl 2-aminoisonicotinate in anhydrous pyridine reacts with *p*-nitrobenzenesulfonyl chloride to give methyl 2-(*p*-nitrobenzenesulfonamido)isonicotinate (IX-89).[353]



IX-89

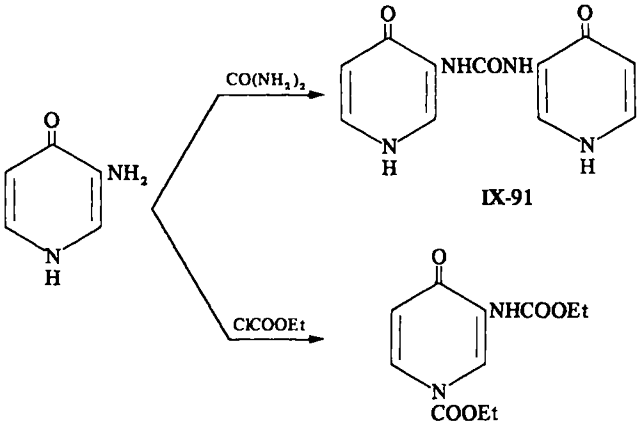
Chloromethanesulfonyl chloride reacts with 2-aminopyridine to give 2-(chloromethylsulfonamido)pyridine.[354] *N*-2-Pyridylalkanesulfonamides are formed from 2-aminopyridine and an alkane sulfonic acid; these sulfonamides are amphoteric.[355]

Miscellaneous reactions of aminopyridines with sulfur derivatives have been observed. *p*-Chlorophenyl hydroxymethylsulfone reacts with 2-aminopyridine to give *p*-chlorophenyl-2-pyridylaminomethyl sulfone (**IX-90**).[356]



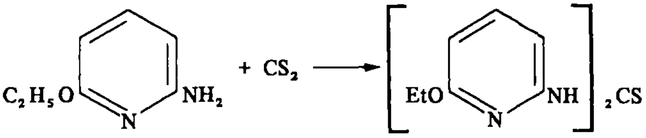
IX-90

c. UREAS, AMIDINES 2-Amino-5-chloropyridine reacts with methyl isocyanate to give 1-methyl-3-(5-chloro-2-pyridyl)urea; 1-methyl-3-(5-iodo-2-pyridyl)urea and 1-methyl-3-(2-methoxy-5-pyridyl)urea are prepared similarly.[358] 3-Amino-4-pyridone condenses with urea to give *N,N′*-bis-(4-hydroxy-3-pyridyl)urea (**IX-91**);[358] with ethyl chloroformate, it gives 1,3-diethoxycarbonylamino-4-pyridone (**IX-92**).



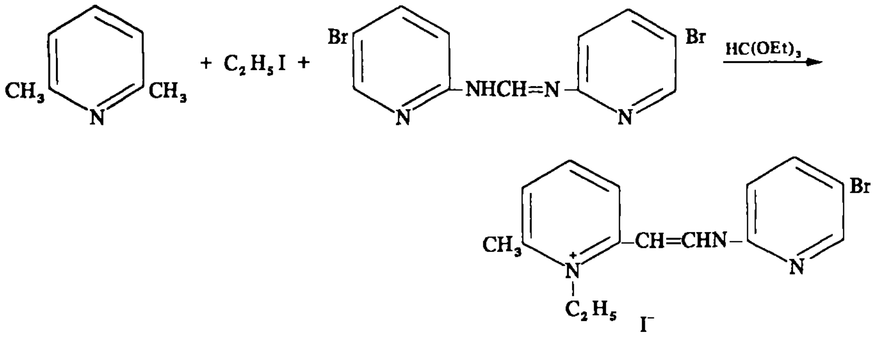
IX-92

When 2-amino-6-ethoxypyridine in ethanol is boiled under reflux with carbon disulfide, *N,N′*-bis-(6-ethoxy-2-pyridyl)thiourea (**IX-93**) is obtained. Similarly, treatment with an aryl isothiocyanate gives the corresponding thiourea.[359]



IX-93

When a mixture of 2,6-lutidine, ethyl iodide, and *N*,*N*′-di-(5-bromo-2-pyridyl)-formamidine is heated with ethyl orthoformate, **IX-94** results.[360]

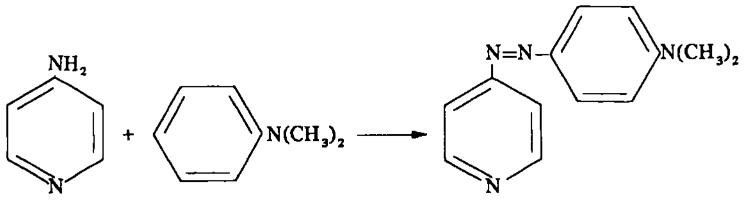


IX-94

D. *Diazotization Reactions*

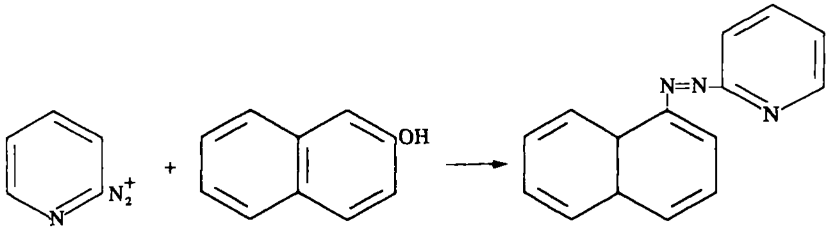
If 2- and 4-aminopyridines are diazotized in dilute mineral acids, diazonium salts are formed; however, the diazonium ions are not stable and they hydrolyze rapidly to the corresponding pyridones.[361-364] For example, the diazotization of 2-amino-4-nitropyridine in sulfuric acid yields 85% of 4-nitro-2-pyridone. Diazonium salts of 2-substituted-4-aminopyridines with electron-withdrawing substituents such as COOH, $CONH_2$ and CN are particularly unstable.[365]

The kinetics of the diazotization of 4-aminopyridine in 0.0025-5.0 *M* perchloric acid were studied,[366] and the reaction was believed to proceed by only one mechanism whose kinetic form is first order with respect to the amine as well as to nitrous acid. The rate of the reaction showed an exponential catalytic dependence on the concentration of added perchloric acid and sodium perchlorate. In solutions of constant ionic strength the rate was directly related to the acidity function (H_0). The 4-diazonium ion was characterized as 4-(2-hydroxy-1-naphthylazo)pyridine.[361] When 4-aminopyridine is diazotized and treated with *N*,*N*-dimethylaniline, 4-(*p*-dimethylaminophenylazo)pyridine (**IX-95**) is obtained.[367] 2-(*p*-Dimethylaminophenyl)pyridine is isolated when 2-aminopyridine is used instead of 4-aminopyridine.[368]



IX-95

When 2-aminopyridine and isoamylnitrite are added to sodium ethoxide and the mixture boiled for 8 hours, good yields of the diazonium salt are obtained. When β-naphthol is added to the diazonium salt, azo coupling to **IX-96** occurs.[369]



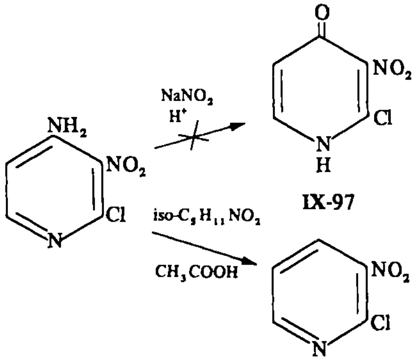
IX-96

2-Aminopyridine-1-oxide and its derivatives are diazotized and coupled with anilines to give azo dyes for acrylic fibers.[370-372]

The amino function in 4-amino-3-halopyridines behaves unexceptionally. Thus 4-amino-3-chloropyridine gives the 3-chloro-4-pyridinediazonium salt when treated with nitrous acid; the diazonium salt decomposes in the presence of potassium iodide to yield 3-chloro-4-iodopyridine.[373]

4-Amino-2,3,5,6-tetrafluoropyridine is a very weak base but it can be diazotized in 80% hydrofluoric acid. The diazonium salt is converted to 4-bromo-2,3,5,6-tetrabromopyridine with cuprous bromide, but its reaction with water or with *N,N*-dimethylaniline are complex.[374]

4-Amino-2-chloro-3-nitropyridine is *not* converted to 2-chloro-3-nitro-4-pyridone (**IX-97**) on diazotization with mineral acids and sodium nitrite or with isoamyl nitrite in glacial acetic acid; with the latter reagent 2-chloro-3-nitropyridine (**IX-98**) is formed.[46] Nitrous acid reacts with 4-amino-2-pyridone to give 4-amino-3-nitroso-2-pyridone instead of the diazonium salt.[375]



IX-98

When 3-aminopyridine is diazotized with hydrochloric acid and sodium nitrite and then treated with acetic acid containing sulfur dioxide and cupric chloride, 3-pyridinesulfonic acid can be isolated.[376] Similarly, 4-aminopyridine-1-oxide gives 4-pyridinesulfonic acid-1-oxide, but the 2-isomer gives very poor yields of the corresponding sulfonic acid. The preparations and reactions of various 3-pyridinediazonium salts have been reported.[52, 377, 378] 3-Amino-2,6-lutidine is diazotized with hydrochloric acid and sodium nitrite and then decomposed in the presence of copper powder to give 3-chloro-2,6-lutidine.[68] The diazonium salt reacts with potassium cyanide and with β-naphthol to give 3-cyano-2,6-lutidine and (2,6-dimethyl-3-pyridyl)-1-azo-2-hydroxynaphthalene, respectively.[379]

3-Amino-5-hydroxypyridine and nitrous acid give 3,5-dihydroxypyridine,[380] but diazotization of 3-amino-5-nitro-2-pyridone yields 3-diazo-5-nitro-2-pyridone.[379]

The Sandmeyer reaction on 1-phenethyl-4(or 5)-amino-2-pyridone has been reported.[381] Thus, 5-chloro-1-phenethyl-2-pyridone is obtained when 5-amino-1-phenethyl-2-pyridone is diazotized and then treated with cuprous chloride.

E. *Nuclear Substitution Reactions*

5-Chloro- and 5-bromo-2-aminopyridine are prepared by the action of hydrogen peroxide on a mixture of 2-aminopyridine and the appropriate hydrogen halide.[382, 383] 2-Amino-5-chloropyridine is also obtained by bubbling chlorine gas into a solution of 2-aminopyridine in sulfuric acid.[384]

When a solution of 2-aminopyridine is treated with bromine, 2-amino-5-bromopyridine is obtained.[385] Bromination of 2-amino-3-nitropyridine and 2-amino-5-nitropyridine gives 2-amino-5-bromo-3-nitropyridine and 2-amino-3-bromo-5-nitropyridine, respectively.[386]

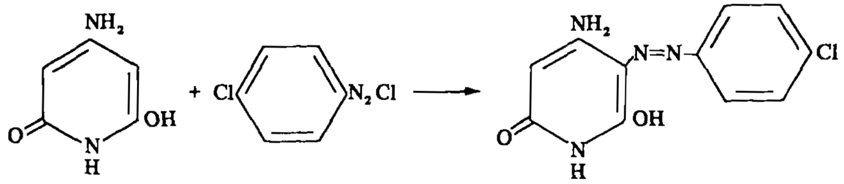
6-Amino-2-bromo-3,4,5-tricyanopyridine reacts with the sodium salt of malonitrile to form 6-amino-α,α,3,4,5-pentacyano-2-picoline.[387]

When 2-amino-4-chloropyridine is added to sodium in absolute methanol containing a little copper powder, and the mixture is heated for 12 hours at 150° in a sealed tube, 2-amino-4-methoxypyridine is obtained. This reaction has been used to prepare a large number of aminomethoxypyridines (see Tables IX-16 to IX-18).[388]

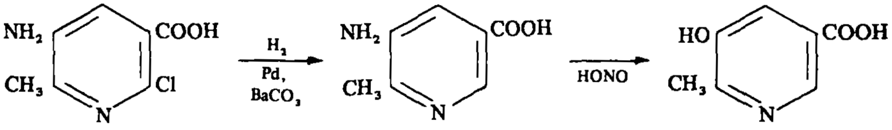
4-Amino-2-methoxypyridine is acetylated to give the acetyl derivative that, when treated with perbenzoic acid in chloroform, gives 4-amino-2-methoxypyridine-1-oxide.[389] Similarly, 4-amino-3-chloropyridine-1-oxide is obtained from 4-amino-2-chloropyridine.

Glutazine (**IX-99**) reacts with *p*-chlorobenzenediazonium chloride to give **IX-100**.[390] 4-Amino-2,6-dichloropyridine is prepared in 60% yield from the reaction of glutazine with phosphorus oxychloride at 150° for 5 hours.[390]

5-Hydroxy-6-methylpyridine-3-carboxylic acid **(IX-102)**, a metabolite of pyridoxamine in *Pseudomonas MA*, has now been synthesized from 5-amino-2-chloro-6-methylpyridine-3-carboxylic acid **(IX-101)** by hydrogenation

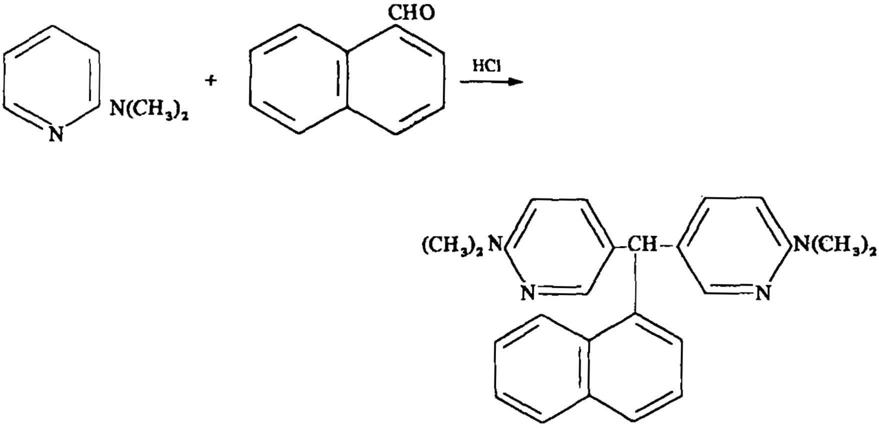


IX-99 IX-100



IX-101 IX-102

of an aqueous suspension using palladium on barium carbonate followed by diazotization with nitrous acid.[378, 391, 392]



IX-103

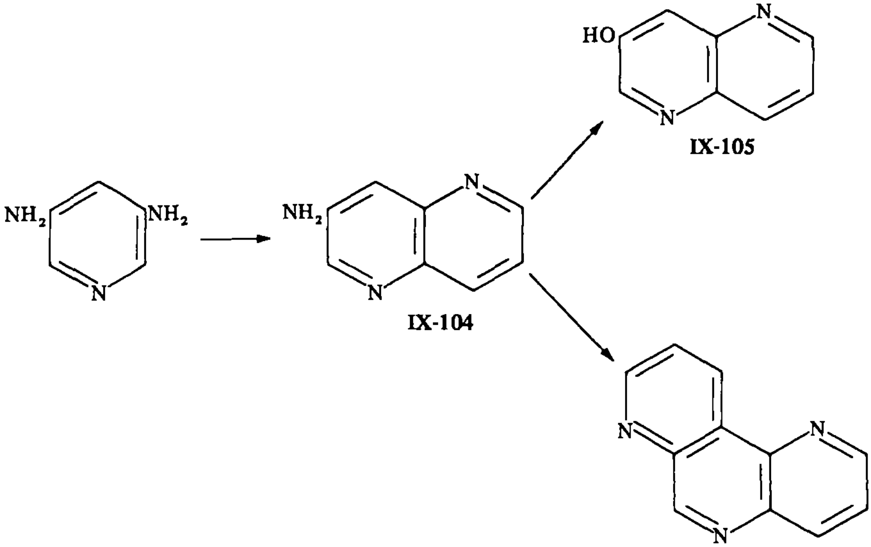
2-Dimethylaminopyridine condenses with α-naphthaldehyde in the presence of concentrated hydrochloric acid to give bis[5-(2-dimethylamino)pyridyl]-1-naphthylmethane **(IX-103)**.[393]

F. *Synthesis of Polycyclic Systems*

The present discussion on the synthesis of condensed-ring systems is limited to aminopyridines in which only one amino group is involved; syntheses involving more than one amino group are discussed in Section I.7., on "Diamino- and Triaminopyridines."

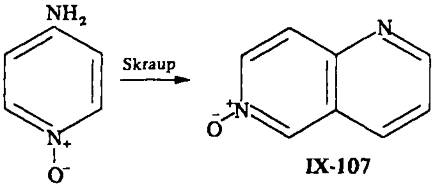
a. NAPHTHYRIDINES An excellent review of the chemistry of naphthyridines has recently appeared.[394] Aminopyridines have been used to prepare 1,5-, 1,6-, 1,7-, and 1,8-naphthyridines.

Various substituted 3-aminopyridines have been cyclized to 1,5-naphthyridines.[394, 395] Three products, **IX-104** to **IX-106**, have been isolated from the Skraup reaction with 3,5-diaminopyridine; Czuba has suggested that 3-amino-1,5-naphthyridine (**IX-104**) was the logical precursor to **IX-105** and **IX-106**.[396] In contrast, 2,5-diaminopyridine afforded only 2-amino-1,5-naphthyridine.[61, 397] When 3-amino-5-bromopyridine was used, 3-bromo-1,5-naphthyridine was produced.[61] Besides glycerol, other reagents were employed (see Table IX-3).



After several failures[398, 399] to prepare 1,6-naphthyridine by means of the Skraup reaction with 4-aminopyridine, it can now be obtained using glycerol and "sulfomix".[400, 401] The Skraup reaction yields 1,6-naphthyridine-6-oxide

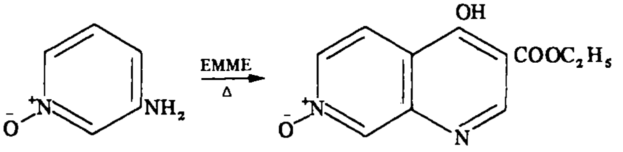
(IX-107) and its derivatives when it is applied to 4-aminopyridine-1-oxide and some of its derivatives.[402, 403]



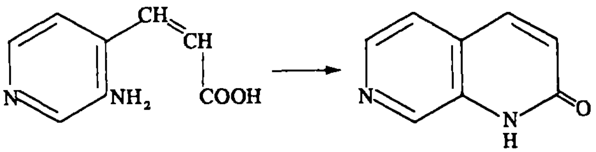
IX-107

The reagents for cyclization are not limited to glycerol; they include crotonaldehyde, methacrolein, and methyl vinyl ketone, which afford 2-methyl-,[404] 3-methyl[405] and 4-methyl-1,6-naphthyridines,[404] respectively.

The cyclization of the condensation product of 3-aminopyridine-1-oxide with diethyl ethoxymethylenemalonate (EMME) yields ethyl 4-hydroxy-1,7-naphthyridine-7-oxide-3-carboxylate **(IX-108)**;[406] the *N*-oxide function need not be present if the α-positions of 3-aminopyridines are blocked.[407] The Skraup reaction with 3-amino-2-pyridone yields 1,7-naphthyridin-8-one.[408] Several 4-substituted-3-aminopyridines are also cyclized to 1,7-naphthyridine derivatives **(IX-109)**;[409, 410] for example, 2-aminopyridine and some of its derivatives are cyclized under Skraup conditions to 1,8-naphthyridines. Table IX-4 summarizes some of these cyclizations.[405, 411] 2-Aminopyridine and diethyl ethoxymethylenemalonate also gives 1,8-naphthyridine in boiling "Dowtherm A".[412]

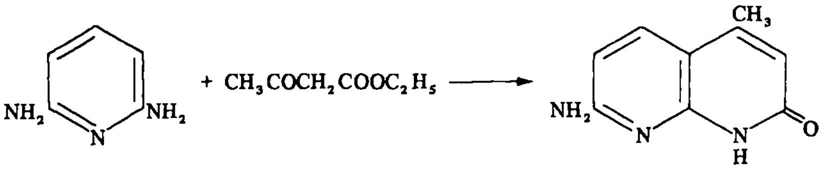


IX-108



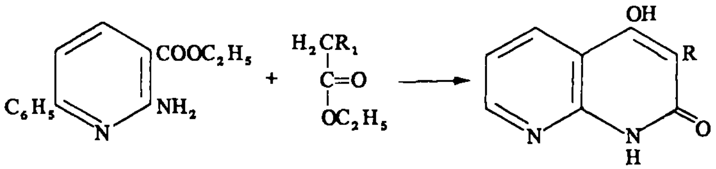
IX-109

The condensation of 2,6-diaminopyridine with ethyl acetoacetate under Conrad-Limpach conditions is now believed to give 7-amino-4-methyl-1,8-naphthyridin-2-one **(IX-110)**[412-414] and not 7-amino-2-methyl-1,8-naphthyridin-4-one as previously claimed.[415] Other 7-amino-1,8-naphthyridines are prepared similarly.[413-421]



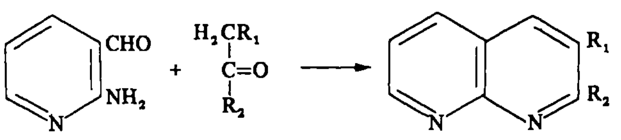
IX-110

1,8-Naphthyridines have been prepared by means of a Niementowski synthesis from ethyl 2-amino-6-phenylnicotinate and by means of Friedlander synthesis from 2-aminonicotinaldehydes.[422, 423] Ethyl 2-amino-6-phenylnicotinate (**IX-111**), which is readily prepared from ethyl α-ethoxycarbonyl acetimidate and benzoylacetaldehyde, condenses with the simple esters (**IX-122**; R = H, CH_3, C_6H_5) in the presence of sodium to give good yields of 1,8-naphthyridinones (**IX-113**).



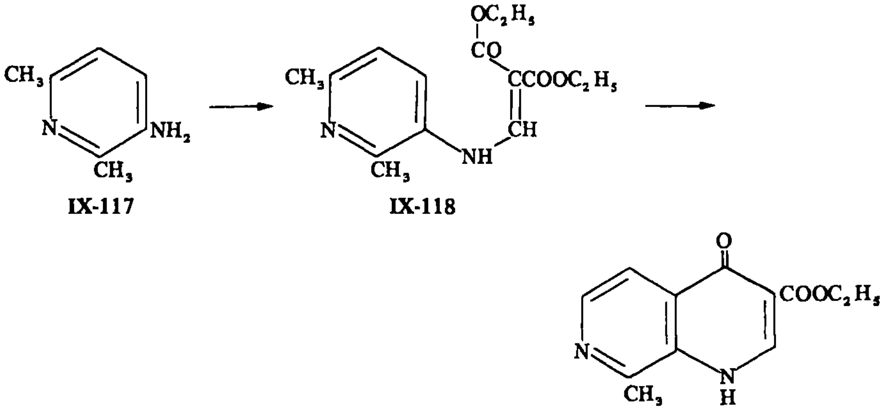
IX-111 **IX-112** **IX-113**

2-Aminonicotinaldehydes (**IX-114**) are potentially more reactive than 2-aminonicotinates. Thus, **IX-114** condenses readily with various ketones or aldehydes (**IX-115**) in the presence of piperidine to give 2,3-disubstituted-1,8-naphthyridines (**IX-116**).[422] Malononitrile and cyanoacetamide may be used in place of **IX–115**.



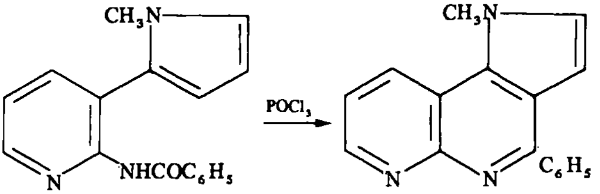
IX-114 **IX-115** **IX-116**

A mixture of 3-amino-2,6-dimethylpyridine (**IX-117**) and diethyl ethoxymethylenemalonate when heated on a steam bath under reduced pressure gives diethyl (2,6-dimethyl-3-pyridyl) methylenemalonate (**IX-118**). The latter yields ethyl 4-hydroxy-6,8-dimethyl-1,7-naphthyridine-3-carboxylate (**IX-119**) when boiled for 4 minutes in diethyl phthalate.



IX-117 **IX-118** **IX-119**

A new heterocyclic ring system, pyrrolo[3,2-3,4]-1,8-naphthyridine (**IX-121**) is obtained from the cyclization of mono- and di-*N*-acyl derivatives of 2-aminonicotyrine (**IX-120**) with phosphorus oxychloride.[424] Thus, 2-dibenzoylaminonicotyrine is dissolved in toluene and phosphorus oxychloride and heated

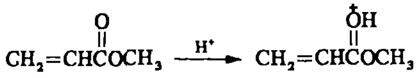


IX-120 **IX-121**

under reflux for 3 hours to yield 1-methyl-2-phenylpyrrolo[3,2-3,4]-1,8-naphthyridine (**IX-121**).

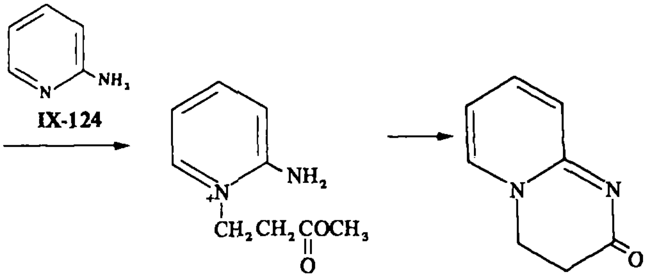
b. PYRIDOPYRIMIDINE The reaction of 2-aminopyridine (**IX-124**) with methyl acrylate (**IX-122**) in the presence of an acid to give 2*H*-pyrido[1,2-*a*]-pyrimidin-2-one (**IX-126**) has been studied. It was suggested that **IX-122** was "activated" by protonation of the carboxyl group **IX-123**, followed by a nucleophilic attack at the β-carbon atom by the ring-nitrogen to form the intermediate **IX-125**, which cyclized to **IX-126**.[425,426] When **IX-124** is heated in water with 1-3 moles of a derivative of acrylic acid (the nitrile, amide, methyl or ethyl ester), good yields (30-83%) of β-[1-(2-aminopyridyl)] propionic acid are obtained. This, on heating with concentrated hydrochloric acid, can be cyclized to the hydrochloride of **IX-126**.[427]

Lappin[428,429] claimed that a cold ethereal solution of 2-aminopyridine and methyl propiolate give **IX-126** as well as a di-adduct, methyl 2-(2-carbomethoxyvinylimino)-1(2*H*)-pyridineacrylate (**IX-127**). Subsequently,



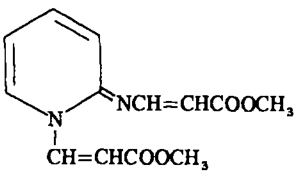
$$CH_2{=}CH\overset{\overset{O}{\|}}{C}OCH_3 \xrightarrow{H^+} CH_2{=}CH\overset{\overset{\overset{+}{O}H}{\|}}{C}OCH_3$$

IX-122 IX-123

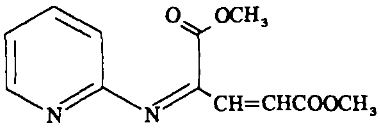


IX-124 IX-125 IX-126

the structure of the di-adduct was proved by Wilson and Bottomley to be **IX-128** and not **IX-127**.[430]

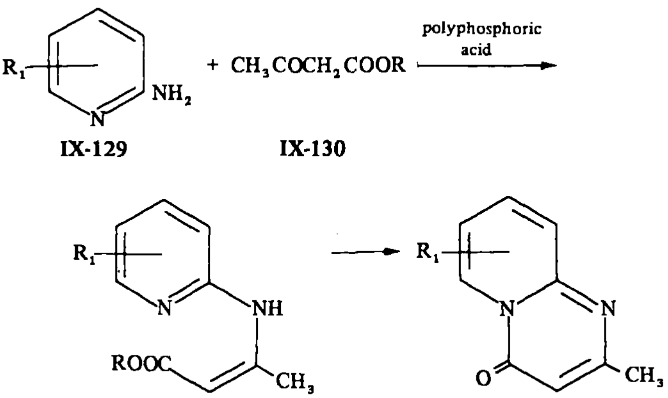


IX-127



IX-128

High yields (80% and better) of 4*H*-pyrido[1,2-*a*]pyrimidin-4-ones **(IX-131)** are obtained in a one-step synthesis involving the condensation of 1 mole of a 2-aminopyridine **(IX-129)** with 1.5 mole of *β*-keto ester **(IX-130)** at 100° for 1 hour in the presence of polyphosphoric acid.[431]



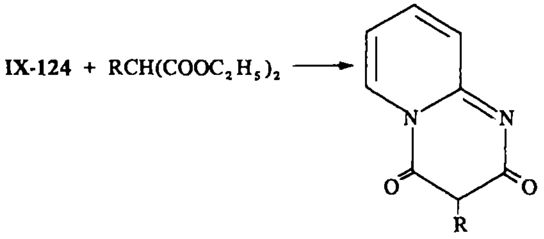
IX-129 IX-130

R = CH_3, C_2H_5

IX-131

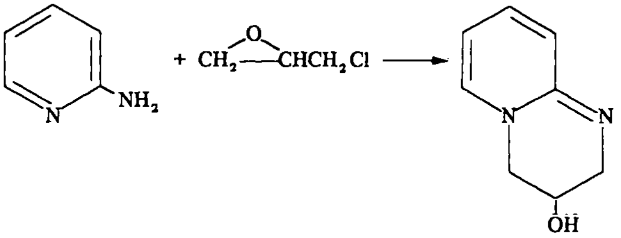
R_1 = 3-CH_3, 5-Cl, 5-Br, 3,5-Br_2

If 2-aminopyridine is boiled with ethyl malonate for 5 minutes, it gives *N,N*-di-(2-pyridyl)malonamide; when the reaction time is extended to 6 hours, the product is pyrido[1,2-*a*]pyrimidine-4,6-dione (**IX-132**, R = H). When alkylmalonyl chloride is used instead of ethyl malonate, the 5-alkyl derivative **IX-132** is obtained in good yield.[432, 433] The chemistry of these cyclized "malonyl-α-aminopyridines" is being investigated.[434, 435]



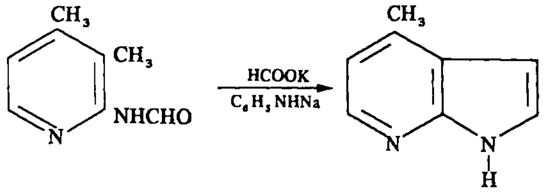
IX-132

The reaction of 2-aminopyridine with epichlorohydrin yields the hydrochloride of 3-hydroxy-3,6-dihydro-2*H*-pyrido[1,2-*a*]pyrimidine (**IX-133**).[436] If chlorohydrin is used instead of epichlorohydrin, no pyridopyrimidine is formed.[437]



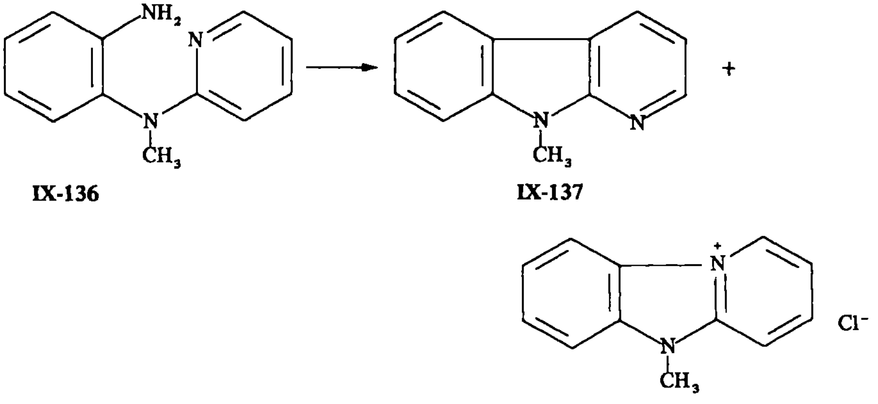
IX-133

c. DIAZAINDENES 4-, 5-, And 6-methyl-1,7-diazaindene are prepared by the Madelung ring closure of the corresponding 2-formamidolutidines, which are obtained by formylation of aminolutidines; for example, 2-formamido-3,4-lutidine (**IX-134**) cyclizes to 4-methyl-1,7-diazaindene (**IX-135**) in the presence of potassium formate and sodium anilide.[438] 3-Formamido-4-picoline gives only 3-amino-4-picoline and no cyclized product when treated with various bases.[439]



IX-134 **IX-135**

d. CARBOLINES The Pschorr-type ring closure for the synthesis of the carboline ring system was first investigated by Abramovitch, Hey, and Mulley.[440] When an aqueous solution of the diazonium salt of 2-amino-*N*-methyl-*N*-2-pyridylaniline (**IX-136**) is heated, a small amount (7%) of *ind*-*N*-methyl-α-carboline (**IX-137**) is formed, though the main product is 5-methylpyrido[1,2-*a*]benzimidazolium chloride (**IX-138**)

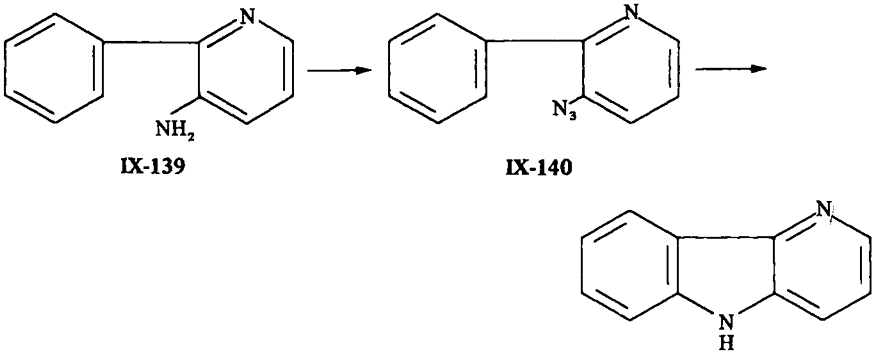


IX-136

IX-137

IX-138

The first synthesis of δ-carboline (**IX-141**) was achieved by the thermal decomposition of 3-azidopyridine (**IX-140**), prepared from 3-amino-2-phenylpyridine (**IX-139**).[441] When the diazonium salt from 2-amino-*N*-methyl-*N*,3′-

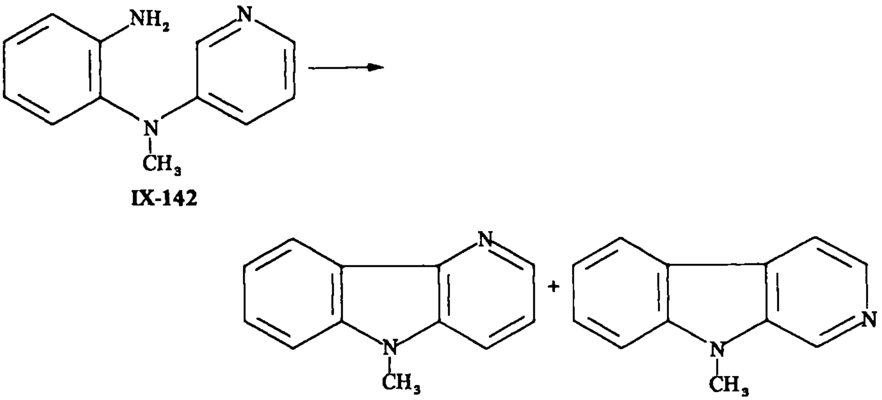


IX-139

IX-140

IX-141

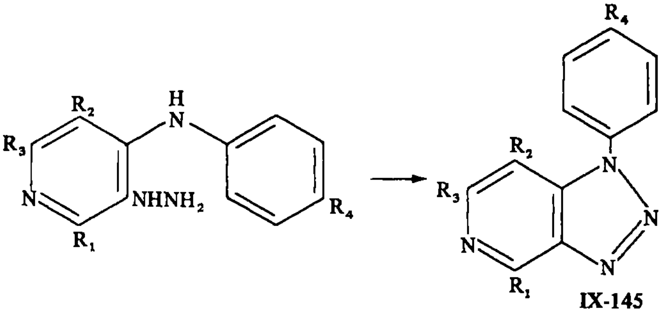
pyridylaniline (**IX-142**) in aqueous acid solution is decomposed in the presence of copper powder, a mixture of *ind*-*N*-methyl-δ-carboline (**IX-143**) and *ind*-*N*-methyl-β-carboline (**IX-144**) is obtained.[442, 443]



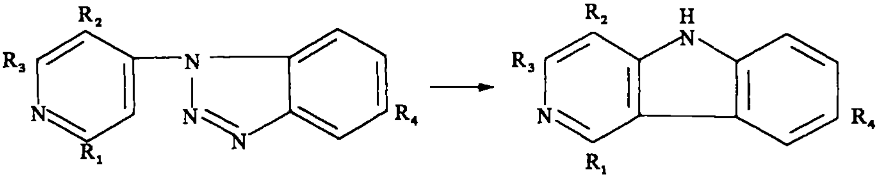
IX-142

IX-143 **IX-144**

Nantka-Namirski[44] has employed the Graebe-Ullmann method to prepare γ-carbolines (**IX-147**) from phenyl-substituted triazolopyridines (**IX-145**) or pyridyl-substituted benzotriazoles (**IX-146**) in pyrophosphoric acid. Various aspects of carboline synthesis have been discussed.[16, 444]

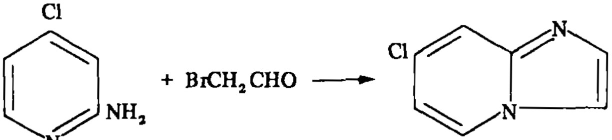


IX-145



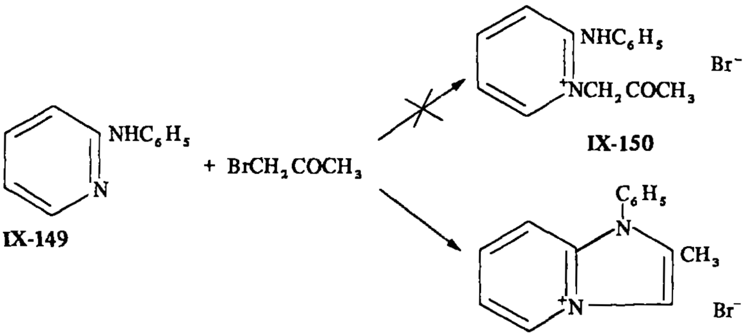
IX-146 **IX-147**

e. IMIDAZOPYRIDINES Improved laboratory procedures for the synthesis of imidazopyridines have been reported.[331, 445] 7-Chloro-, 5-chloro-, 5-amino-, 5-amino-2-methyl and 5-amino-2,3-dimethyl-imidazo[1,2-*a*]pyridines were prepared by condensation of haloaminopyridines with haloaldehydes. Thus, bromoacetaldehyde and 2-amino-4-chloropyridine give 7-chloroimidazo[1,2-*a*]-pyridine (**IX-148**).[445]



IX-148

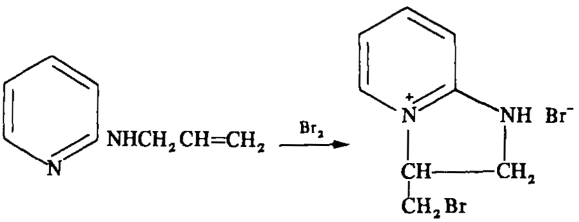
Various imidazopyridinium salts were also prepared. 2-Alkylamino- or arylaminopyridines react with α-bromoketones to give 1-alkyl- or 1-arylimidazo-[1,2-*a*]pyridinium salts substituted at position 2. 2-Anilinopyridine (**IX-149**) and bromoacetone in boiling acetone give the 2-methyl-1-phenylimidazo[1,2-*a*]-pyridinium bromide **IX-151** rather than the 1-acetonyl salt **IX-150**.[446] When 2-(*N*-methylanilino)pyridine was used instead of 2-anilinopyridine, cyclization was not possible. The bromination in benzene of 2-allylaminopyridine gives **IX-152**.[447]



IX-149

IX-150

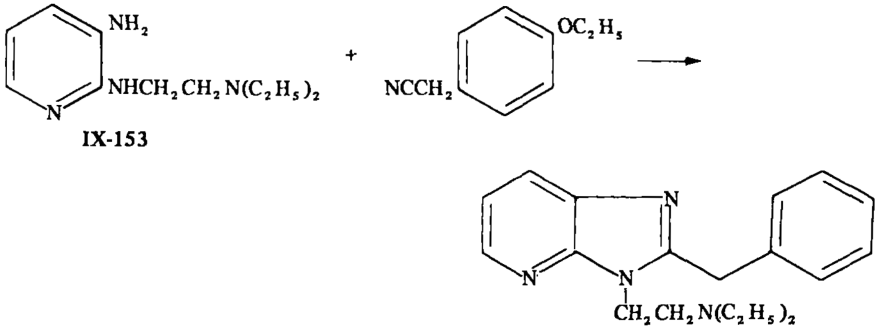
IX-151



IX-152

In the presence of dry hydrochloric acid, 3-amino-2-(β-diethylaminoethyl-amino)pyridine (**IX-153**) condenses with *p*-ethoxyphenylacetonitrile to give

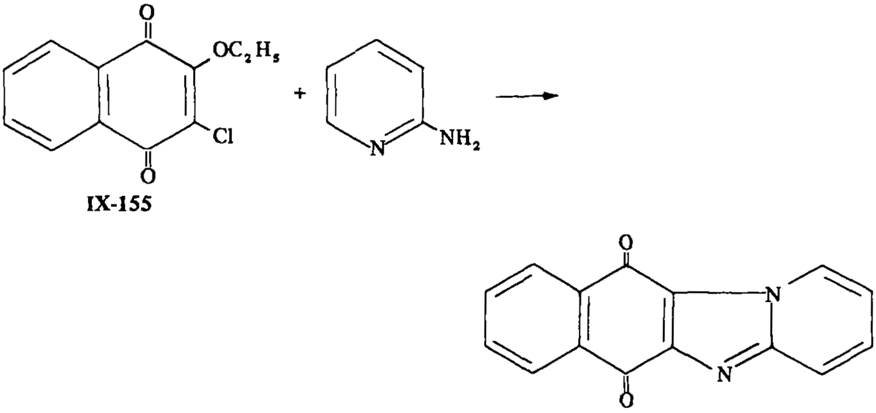
3-(β-diethylaminoethyl)-2-(*p*-ethoxylbenzyl)imidazo[4,5-*c*]pyridine **(IX-154).** Using other arylacetonitriles, various imidazopyridines are prepared.[80]



IX-153

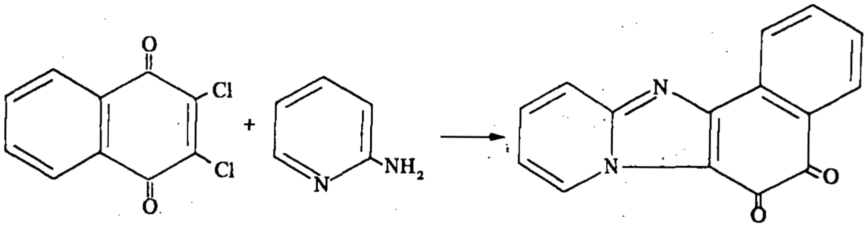
IX-154

f. MISCELLANEOUS CYCLIZATIONS 2-Aminopyridine condenses with 3-chloro-2-ethoxy-1,4-naphthoquinone **(IX-155)** to yield 6*H*,11*H*-benzo(*f*)pyrido-[1,2-*a*]benzimidazole-6,11-dione **(IX-156)**;[448] with 2,3-chloro-1,4-naphthoquinone, it yields 5*H*,6*H*-benzo[*e*]pyrido[1,2-*a*]benzimidazole-5,6-dione **(IX-158)**.[449, 450]



IX-155

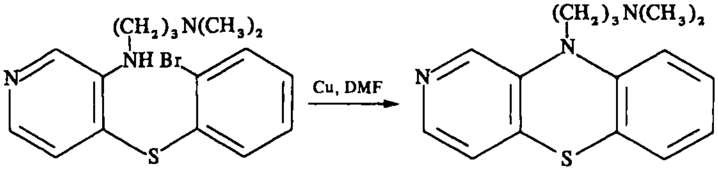
IX-156



IX-157

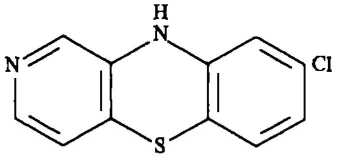
IX-158

10-Substituted aminoalkylazaphenothiazines are obtained by intramolecular cyclization of aminoalkylaminohalophenylthiopyridine. Thus, 10-(3-dimethylaminopropyl)-2-azaphenothiazine (**IX-160**) is obtained by heating 4-(2-bromophenylthio)-3-(3-dimethylaminopropyl)aminopyridine (**IX-159**) in dimethylformamide with sodium and copper powder.[449] Similarly, 3-amino-4-(2-bromo-4-chlorophenythio)pyridine gives 8-chloro-2-azaphenothiazine (**IX-161**).[451]

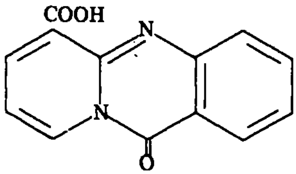


IX-159 **IX-160**

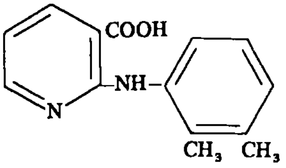
2-Chloronicotinic acid, when heated gradually to 145° with methyl *o*-aminobenzoate and potassium iodide, gives **IX-162**; with 3-amino-*o*-xylene, however, the 2-anilinonicotinic acid derivative (**IX-163**) is obtained.[452] When a mixture of 2-aminopyridine and *N*-acetylanthranilic acid is heated to 120° for 4 hours and the product is then hydrolyzed, 2-methyl-3-(2-pyridyl)-3,4-dihydro-4-oxoquinazoline (**IX-164**) is obtained.[453] The latter can also be prepared by heating *o*-amino-*N*-(2-pyridyl)benzamide (**IX-165**) with acetic anhydride.[453]



IX-161

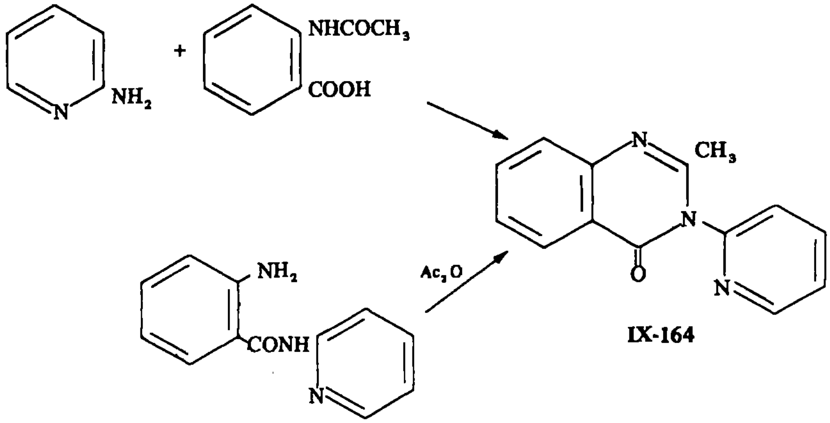


IX-162



IX-163

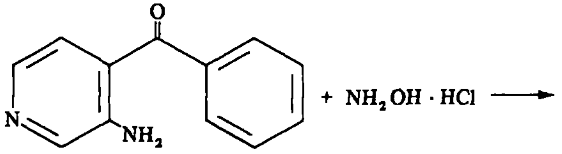
3-Amino-4-benzoylpyridine (**IX-166**) reacts with hydroxylamine hydrochloride (**IX-167**) to give 3-amino-4-benzoylpyridine oxime (**IX-168**). With chloroacetyl chloride (**IX-168**) at room temperature for 72 hours, this gives a



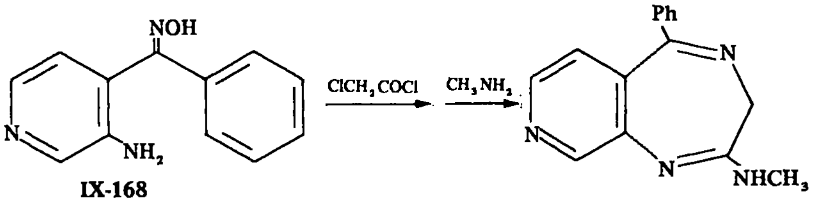
IX-164

IX-165

chloro intermediate that, on treatment with methylamine, cyclizes to give 2-methylamino-5-phenyl-3*H*-pyrido[3,4-*e*]-1,4-diazepine (IX-169).[454]



IX-166 IX-167



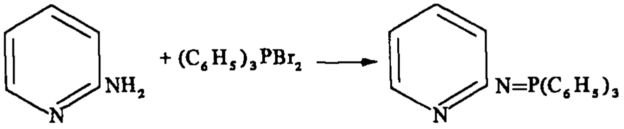
IX-168

IX-169

G. *Miscellaneous Reactions*

Aminopyridines undergo a variety of reactions that have not been discussed in the above sections.

Triphenylphosphine dibromide and 2-aminopyridine give the phosphineimine IX-170.[455]



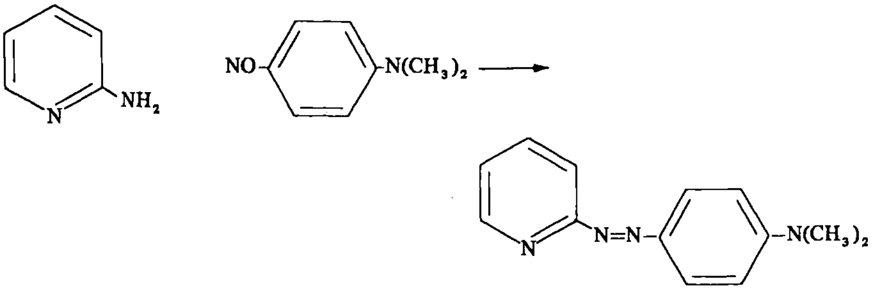
IX-170

The identification and determination of 2,4-, 2,5-, and 2,6-dinitrophenols by their color reactions with 2-aminopyridine have been reported.[456a]

2-Aminopyridine-1-oxide gives a blue color when it is heated with *N,N*-dimethylaniline and concentrated hydrochloric acid.[455] On diazotization and treatment with azide ion it yields 2-azidopyridine-1-oxide.[456b]

If 2-aminopyridine is boiled with methyl iodide in ethanol and the resultant precipitate (2-imino-1-methyl-1,2-dihydropyridine) is heated with sodium hydroxide it gives 2-methylaminopyridine (Dimroth rearrangement).[457]

2-Aminopyridine condenses with *p*-dimethylaminonitrosobenzene to give 2-(*p*-dimethylaminophenylazo) pyridine (**IX-171**).[458] 3-Aminopyridine reacts with nitrosobenzene to yield 3-phenylazopyridine.[459]

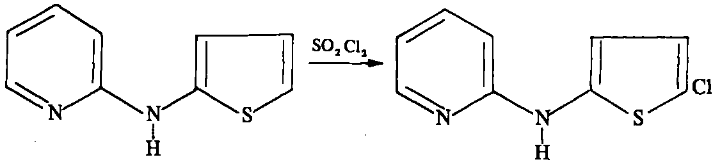


IX-171

2-Aminopyridine and styrene oxide give *N*-(β-hydroxy-β-phenethyl)-2-pyridonimine[460] (see also ref. 145).

2-Amino-5-bromopyridine condenses with acetonitrile in the presence of aluminum chloride to give *N*-(5-bromo-2-pyridyl)acetamidine, which can be hydrolyzed to 2-acetamido-5-bromopyridine.[461]

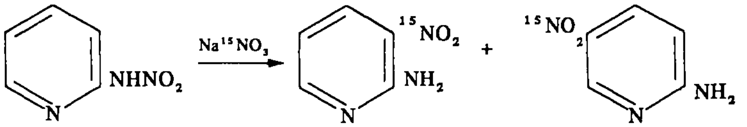
5-Halothienylaminopyridines (**IX-172**) (Table IX-26) are prepared by treating thienylaminopyridines with sulfuryl halides.[462]



IX-172

5. Nitraminopyridines

Geller and Samosvat[463] found that the rearrangement of 2-nitraminopyridine in sulfuric acid in the presence of $Na^{15}NO_3$ resulted in incorporation of ^{15}N into 3- (**IX-173**) and 5-nitro-2-aminopyridines (**IX-174**) to a smaller extent than remained in $NaNO_3$. They claimed that intramolecular rearrangement had occurred.



IX-173 **IX-174**

An improved preparation of 3-nitraminopyridine has been reported.[464] The reaction of nitraminopyridines with phosphorus halides gives the corresponding halopyridine.[464] Thus, 2-, 3-, and 4-nitraminopyridine react with phosphorous trichloride to yield 2-chloro- (38%), 3-chloro (45%), and 4-chloropyridine (65%), respectively.

In the presence of an *ortho*- or a *para*-nitro substituent, a nitramino function in the 2- or 4-position is easily replaced by a hydrazino group. Thus, a solution of 2-nitramino-3-nitropyridine in methanol gives 2-hydrazino-3-nitropyridine when treated with hydrazine hydrate. Various hydrazinonitropyridines are prepared similarly;[465] these are listed in Table IX-51.

Hydrolysis of nitraminopyridines generally gives hydroxypyridines; 5-nitramino-3-picoline and 3-nitramino-4-picoline are hydrolyzed with sulfuric acid to 5-hydroxy-3-picoline and 3-hydroxy-4-picoline, respectively.[466]

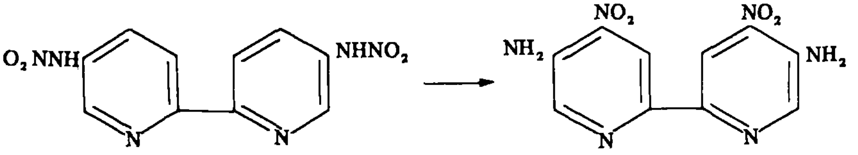
3-Nitramino-2-pyridinesulfonic acid gives 3-hydroxy-2-pyridinesulfonic acid when heated in concentrated sulfuric acid at 60 to 80°; but 3-nitramino-6-pyridinesulfonic acid gives only 3-hydroxypyridine.[467]

Aminopyridinecarboxylic acids are converted into nitramino derivatives by treating a cold solution of the amino compounds in sulfuric acid with nitric acid. Thus 5-aminonicotinic acid and 5-aminopicolinic acid give 5-nitraminonicotinic and 5-nitraminopicolinic acid, respectively.[468]

The nitration of 4-amino-3-picoline yields 3-methyl-4-nitraminopyridine, which, on heating, gives 4-amino-5-nitro-3-picoline. Reduction of this with iron and acetic acid gives 4,5-diamino-3-picoline.[469]

5-Amino-2-nitropyridine gives 2-nitro-5-nitraminopyridine when treated with a mixture of concentrated nitric acid and sulfuric acid below 0°; similarly, 4-amino-2-iodopyridine is nitrated to 2-iodo-4-nitraminopyridine. When the latter is dissolved in concentrated sulfuric acid, it rearranges to 4-amino-2-iodo-3-nitropyridine.[470]

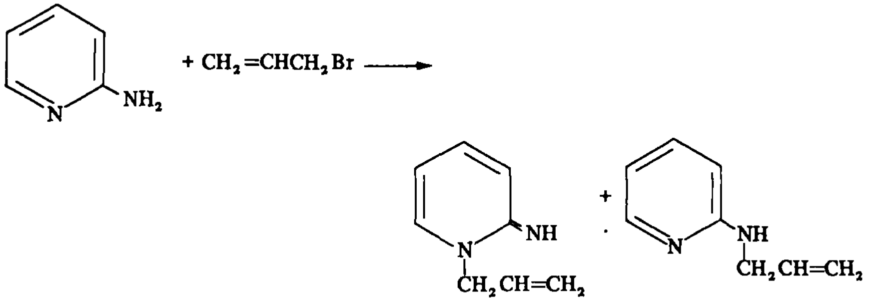
When a mixture of concentrated nitric acid and sulfuric acid is added to a cold solution of 5,5′-diamino-2,2′-dipyridyl and the mixture is allowed to come to room temperature 5,5′-dinitramino-2,2′-dipyridyl (**IX-175**) is formed. At room temperature, **IX-175** decomposes to give 5,5′-diamino-4,4′-dinitro-2,2′-dipyridyl (**IX-176**).[476]



IX-175 **IX-176**

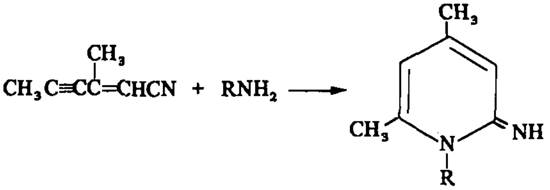
6. Pyridonimines

Pyridonimines are usually prepared by the reaction of aminopyridines with alkyl halides. Thus, 2-aminopyridine and allyl bromide form, predominantly, 1-allyl-2-pyridonimine (**IX-177**) together with *N*-allylaminopyridine (**IX-178**).[472]



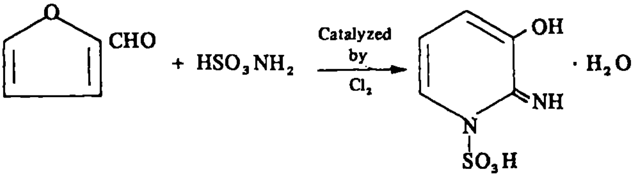
IX-177 **IX-178**

Other methods of preparing pyridonimines have been reported.[473,474] 1-Cyano-2-methylpenta-3-yne-1-ene (**IX-179**) reacts with alkylamines to yield *N*-alkyl-2-pyridonimines; for example, methylamine yields 1,4,6-trimethyl-2-pyridonimine (**IX-180**, R = CH_3).[473]



IX-179 **IX-180**

When furfural is treated with sulfamic acid (preferably in the presence of chlorine and chlorination catalysts) 3-hydroxy-2-imino-1(2*H*)-pyridinesulfonic acid monohydrate (**IX-181**) is isolated.[475]



IX-181

7. Diamino- and Triaminopyridines

A. *Preparation*

Most investigations of the synthesis of diamino- and triaminopyridines are directed toward the substituted rather than the unsubstituted polyaminopyridines. Generally, the procedures are similar to those used for the preparation of monoaminopyridines.

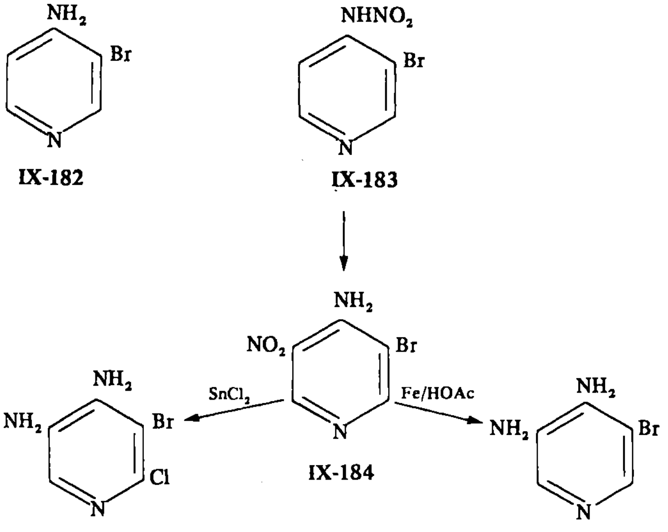
a. REDUCTION OF NITRO GROUPS This may be effected chemically or catalytically. Stannous chloride and hydrochloric acid introduce a chloro substituent into the 2-position of the pyridine ring, in addition to reducing nitro groups. Thus, 4,5-diamino-3-picoline is obtained by the reduction of 4-amino-5-nitro-3-picoline with iron and acetic acid; if stannous chloride and hydrochloric acid are used, the reduction product is 2-chloro-4,5-diamino-3-picoline.[469]

The preparation and reactions of 3-bromo-4,5-diaminopyridine have been studied. The nitration of 4-amino-3-bromopyridine (**IX-182**) and the subsequent rearrangement of the nitramino derivative **IX-183** give 4-amino-3-bromo-5-nitropyridine (**IX-184**). The reduction of **IX-184** with iron and acetic acid produces 5-bromo-3,4-diaminopyridine (**IX-185**), but treatment of **IX-184** with stannous chloride again gives a chloro derivative, 5-bromo-2-chloro-3,4-diaminopyridine (**IX-186**).[476]

Sodium dithionite has been used as a reducing reagent for 2-amino-5-chloro-3-nitropyridine to yield 5-chloro-2,3-diaminopyridine.[477]

2-Amino-3,5-dinitropyridine is selectively reduced with freshly prepared ammonium sulfide to 2,3-diamino-5-nitropyridine; catalytic reduction with palladium and hydrochloric acid gives 2,3,5-triaminopyridine trihydrochloride.[478]

Treatment of 2-bromo-3,5-dinitropyridine with hydrogen bromide and granulated tin gives 3,5-diaminopyridine.[175]

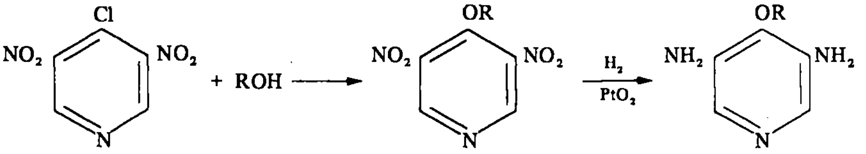


IX-182 IX-183

IX-184

IX-186 IX-185

2-Chloro-3,5-dinitropyridines give 2-alkoxy-3,5-dinitropyridines when heated with various alcohols in a sealed tube at 140° for 3 to 5 hours. Reduction of these compounds over PtO$_2$ gives the corresponding diamino derivatives

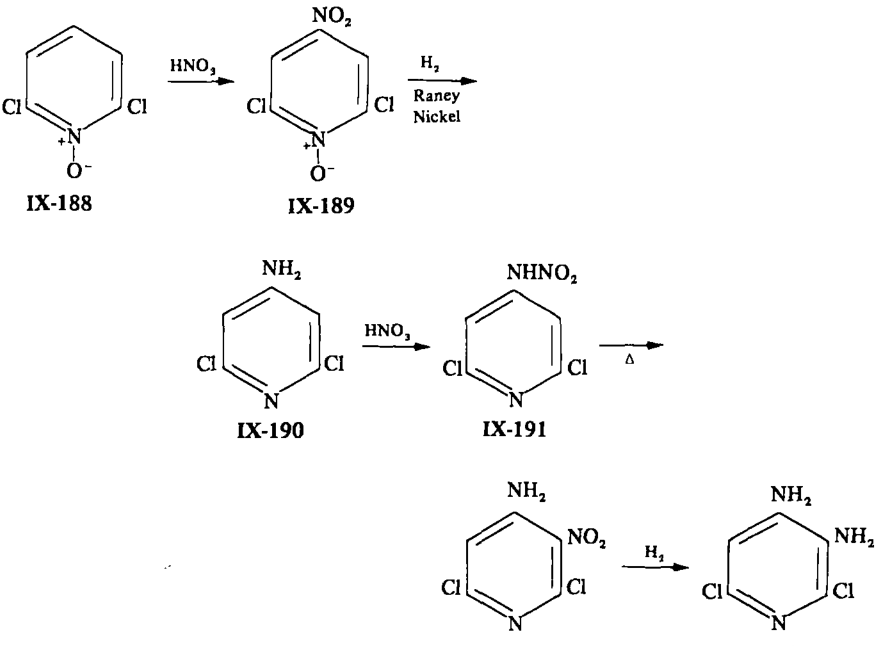


IX-187

(**IX-187**) (see also Table IX-61).[479]

Nitration of 2,6-dichloropyridine-1-oxide (**IX-188**) gives 2,6-dichloro-4-nitropyridine-1-oxide (**IX-189**), which, on catalytic reduction using Raney nickel as the catalyst, gives 4-amino-2,6-dichloropyridine (**IX-190**). From the amino compound, the 2,6-dichloro-4-nitraminopyridine (**IX-191**) is readily formed and rearranges to **IX-192**. Catalytic reduction of **IX-192** gives an almost quantitative yield of 2,6-dichloro-3,4-diaminopyridine (**IX-193**).[87]

2,4-Dichloro-3-nitro-6-*n*-propylpyridine reacts with alcoholic ammonia to give 2,4-diamino-3-nitro-6-propylpyridine, which can be reduced further to 6-propyl-2,3,4-triaminopyridine on catalytic hydrogenation over palladium chloride.[480]

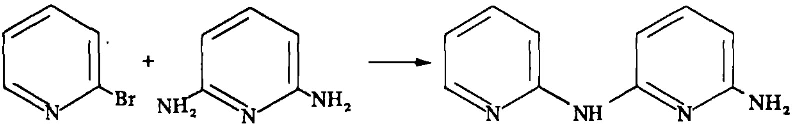


IX-188 IX-189 IX-190 IX-191 IX-192 IX-193

A series of 4-alkoxy-, 4-aralkoxy-, and 4-aryloxy-2,6-diaminopyridines and some of their thio and seleno analogues are prepared by the Curtius reaction, employing the appropriately substituted pyridinecarboxylic acid azides.[481, 482] For example, 4-butoxypyridine-2,6-dicarboxylic acid diazide is heated to give 4-butoxy-2,6-diaminopyridine.[481] Table IX-58 lists the various 4-substituted 2,6-diaminopyridines prepared this way.

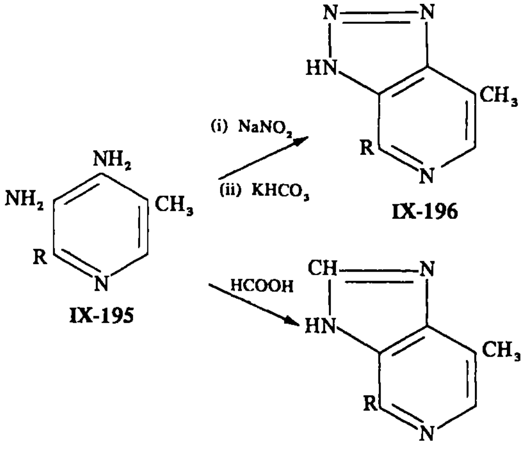
B. *Properties and Reactions*

Tables IX-52 to IX-61 list the physical properties of the diaminopyridines. Miscellaneous reactions, including the oxidation and diazotizations of diaminopyridines, have been reported. 2,6-Diaminopyridine reacts with 2-bromopyridine to give 2-amino-6-(2-pyridylamino)pyridine (**IX-194**).[116]



IX-194

When a solution of 4,5-diamino-3-picoline (**IX-195**, R = H) in sulfuric acid is diazotized with sodium nitrite and then neutralized with potassium bicarbonate, 3-methyl-4,5-pyridotriazole (**IX-196**, R = H) is obtained. When **IX-195** is treated with freshly distilled formic acid, 3-methyl-4,5-pyridoimidazole (**IX-197**, R = H) results.



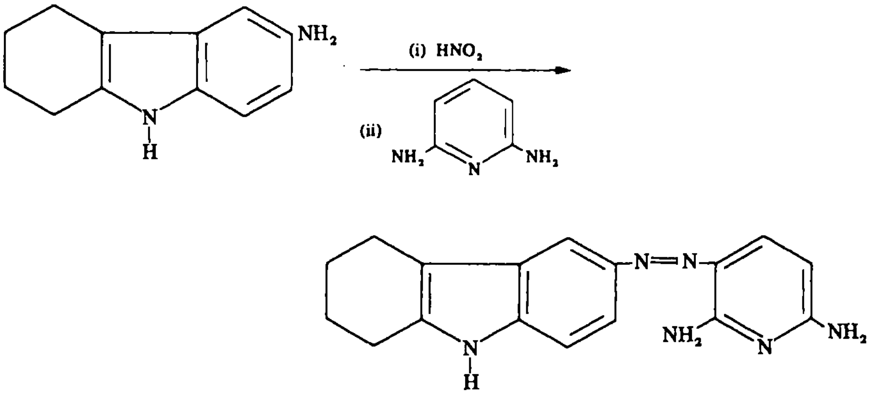
IX-195

IX-196

IX-197

A solution of 6-chloro-4,5-diamino-3-picoline (**IX-195**, R = Cl) and hydrazine hydrate in absolute alcohol is boiled for 3 hours to yield 6-hydrazino-3-methyl-4,5-pyridotriazole (**IX-196**, R = NHNH$_2$). Oxidation of 2,5-diaminopyridines produces dyes of various hues, provided the 5-amino group is unsubstituted.[483]

2,6-Diamino-3-nitrosopyridine is easily oxidized to the 3-nitro compound by a solution of 30% hydrogen peroxide in trifluoroacetic acid—the same procedure used for oxidizing 5-nitrosopyrimidines to 5-nitropyrimidines.[484]

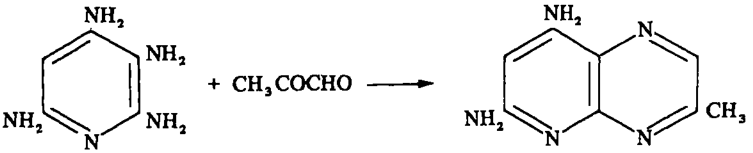


IX-198

3-Amino-2,4,6-triiodobenzoic acid is diazotized and allowed to react with 2,6-diaminopyridine to give 3-(2,6-diamino-3-pyridylazo)-2,4,6-triiodobenzoic acid.[485] Diazotization of 6-amino-1,2,3,4-tetrahydrocarbazole followed by treatment with 2,6-diaminopyridine yields **IX-198**.[486]

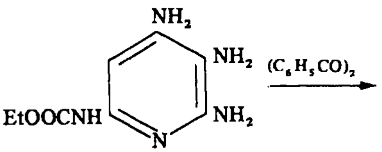
C. *Synthesis of Condensed Heterocyclic Systems*

a. PYRIDOPYRAZINES (AZAQUINOXALINES) *o*-Diaminopyridines condense with α-carbonyl compounds to form pyridopyrazines. The reaction of 2,3,4,6-tetraaminopyridine with pyruvaldehyde under acidic conditions gives mainly 6,8-diamino-3-methylpyrido[2,3-*b*]pyrazine (**IX-199**).[487]

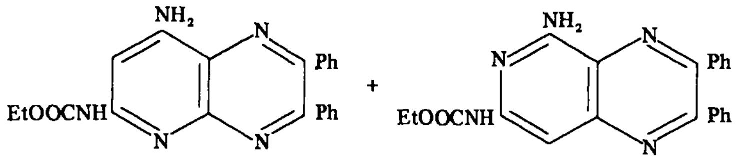


IX-199

The condensation of benzil with ethyl 4,5,6-triamino-2-pyridylcarbamate (**IX-200**) gives a mixture of 8-amino-2,3-diphenylpyrido[2,3-*b*]pyrazines (**IX-201**) and (**IX-202**) under neutral conditions, and mainly IX-202 under acidic conditions.[487]

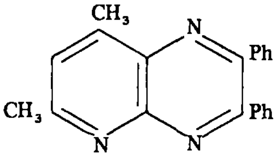


IX-200

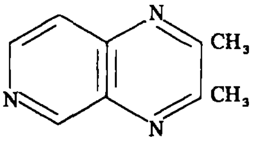


IX-201 **IX-202**

Benzil also condenses with 2,3-diamino-4,6-lutidine to yield 6,8-dimethyl-2,3-diphenylpyrido[2,3-*b*]pyrazine (**IX-203**).[488] The reaction of diacetyl with 3,4-diaminopyridine yields 2,3-dimethylpyrido-[3,4-*b*]pyrazine (**IX-204**).[489]

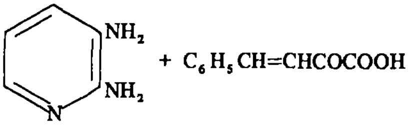


IX-203

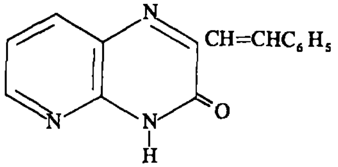


IX-204

Other azaquinoxalines are prepared from 2,3-diaminopyridine and α-dicarbonyl compounds. For example, 2,3-diaminopyridine and **IX-205** in hot acetic acid gives 5-aza-2-styryl-3-quinoxalone (**IX-206**).[490]

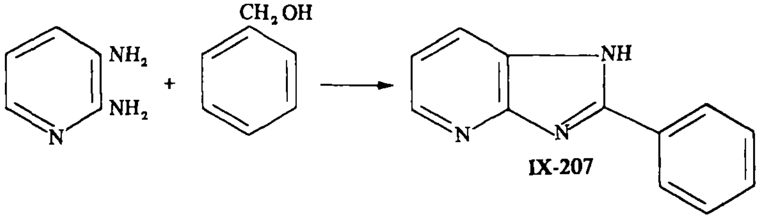


IX-205



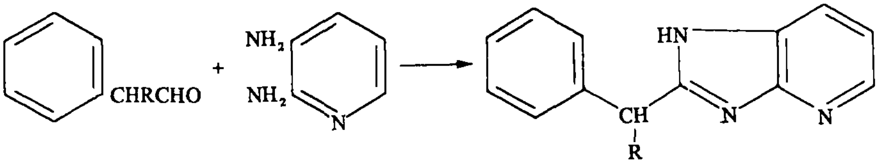
IX-206

b. IMIDAZOPYRIDINES 2,3- and 3,4-diaminopyridines cyclize with a variety of reagents to give imidazopyridines. When benzyl alcohol and 2,3-diaminopyridine are stirred with polyphosphoric acid, 2-phenylimidazo-[4,5-*b*]pyridine (**IX-207**) is formed. Using this procedure, and the appropriate alcohols, 2-thienyl- and 2-pyridylvinylimidazo[4,5-*b*]pyridine can be prepared.[491]



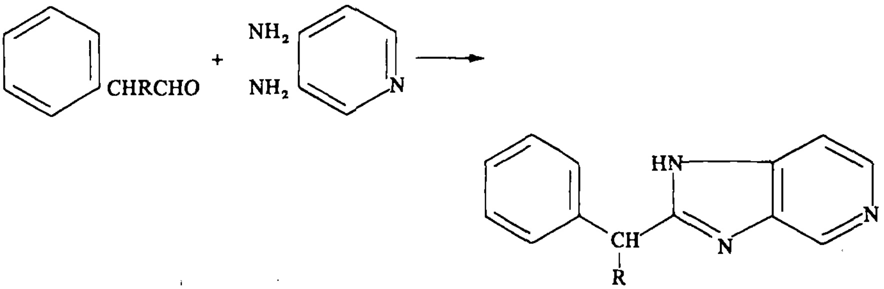
IX-207

2,3- And 3,4-diaminopyridine condense with phenylacetaldehyde to give 2-benzylimidazo[4,5-*b*]pyridine (**IX-208**, R = H) and 2-benzylimidazo[4,5-*c*]-



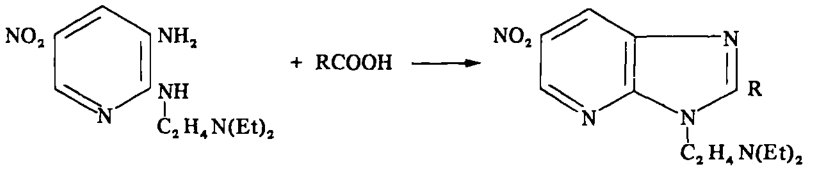
IX-208

pyridine (**IX-209**, R = H), respectively;[492] the iminoether hydrochloride of benzyl cyanide may be used instead of phenyl acetaldehyde. If mandelic acid is used, the products are 2-(α-hydroxybenzyl)imidazo[4,5-*b*]pyridine (**IX-208**, R = OH) and 2-[α-hydroxybenzyl]imidazo[4,5-*c*]pyridine (**IX-209**, R = OH), respectively.[493]



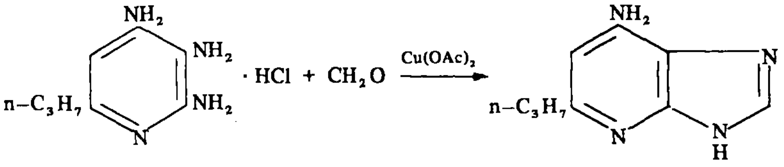
IX-209

A simple procedure for preparing 6-nitroimidazo[4,5-*b*]pyridine involves the action of formic acid on 2,3-diamino-5-nitropyridine.[493] Similarly, when 3-amino-2-(β-diethylaminoethylamino)-5-nitropyridine (**IX-210**) is heated with formic acid (**IX-211**, R = H), the product is 3-(β-diethylaminoethyl)-6-nitroimidazo[4,5-*b*]pyridine (**IX-212**, R = H). Using propionic acid (**IX-211**, R = C_2H_5), **IX-212** (R = C_2H_5) is obtained.[494]

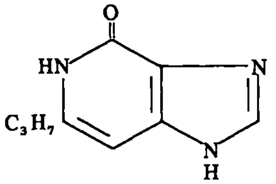


IX-210 **IX-211** **IX-212**

When 6-*n*-propyl-2,3,4-triaminopyridine hydrochloride is heated with formalin in the presence of cupric acetate, 7-amino-5-*n*-propylimidazo[4,5-*b*]pyridine (**IX-213**) is formed.[480] 3,4-Diamino-6-propyl-2-pyridone reacts with formic acid to yield 5-propylimidazo[5,4-*c*]-4-pyridone (**IX-214**).[480]

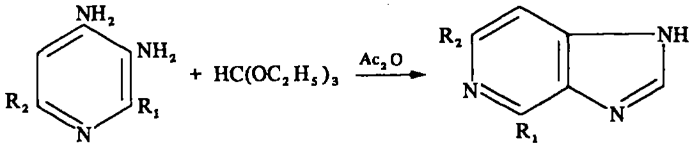


IX-213



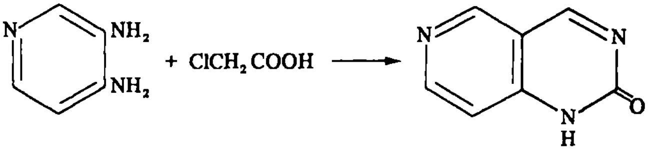
IX-214

The preparation of 6-chloroimidazo[4,5-*c*]pyridine (**IX-216**, R_1 = H, R_2 = Cl) and 4,6-dichloroimidazo[4,5-*c*]pyridine (**IX-216**, R_1 = R_2 = Cl) has been accomplished by the ring closure of the appropriate chloro-3,4-diaminopyridine (**IX-215**) with ethyl orthoformate and acetic anhydride.[87] 6-Aminoimidazo-[4,5-*c*]pyridine (**IX-215**, R_1 = H, R_2 = NH_2) was obtained similarly.



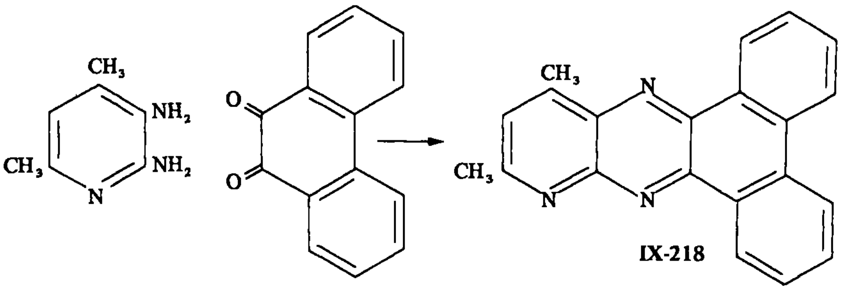
IX-215 IX-216

Heating 3,4-diaminopyridine with chloroacetic acid gives 6-aza-2-quinazolone (IX-217). However, if glycollic acid or acetic anhydride is used instead of chloroacetic acid, 2-hydroxymethylimidazo[4,5-*c*]pyridine and 2-methyl-imidazo[4,5-*c*]pyridine are obtained, respectively.[495]



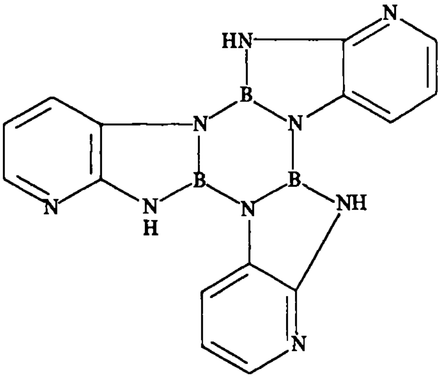
IX-217

c. MISCELLANEOUS CYCLIZATIONS Miscellaneous cyclizations include the reactions of diaminopyridines with phenanthraquinone or with triphenyl borate. Thus, 2,4-dimethyl-5,6-diaminopyridine condenses with 9,10-phenanthraquinone to yield **IX-218**.[488]



IX-218

2,3-Diaminopyridine is reported to react with triphenyl borate to give phenol and tris[1*H* (or 3*H*)-pyridino[2,3-*d*]-1,3,2-diazaborolo]borazine (**IX-219**).[496]



IX-219

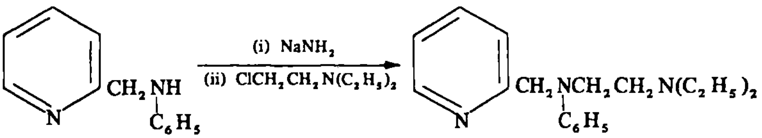
II. Side-Chain Amines

1. Preparation

A. *Aminolysis of Side-Chain Halides*

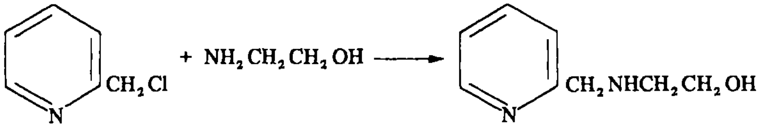
Side-chain aminopyridines are easily prepared by the action of ammonia or of an amine on haloalkylpyridines.[497]

2-Chloromethylpyridine reacts with aniline in the presence of potassium carbonate to yield 2-(phenylaminomethyl)pyridine. When the latter is treated with sodium amide followed by 2-chloroethyl-*N*,*N*-diethylamine, 2-[*N*-phenyl-*N*-(2-*N*,*N*-diethylaminoethyl)]picolylamine (**IX-220**) is formed.[498] Other 2-, 3-, and 4-(pyridylmethyl)-*N*,*N*′-diethylethylenediamines (Table IX-62) have been prepared similarly.[499, 500]



IX-220

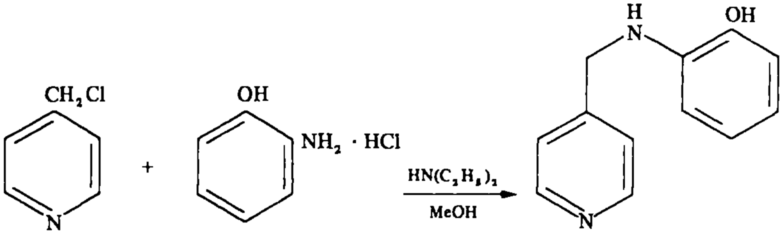
When 2-chloromethylpyridine is treated with ethanolamine, *N*-2-hydroxyethyl-*N*-2-picolylamine (**IX-221**) is isolated.[501] A mixture of 2-chloromethylpyridine and *N*-(4-hydroxybutyl)aminoethanol is heated for 2 hours to yield *N*-(4-hydroxybutyl)-*N*-(2-hydroxyethyl)-2-pyridylmethylamine.[502]



IX-221

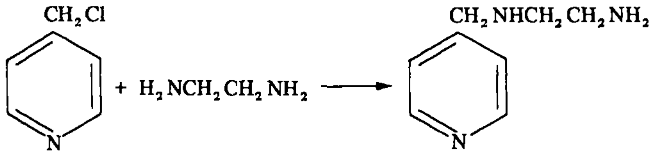
2-Pyridylmethyl chloride and potassium phthalimide give a solid that is decomposed by hydrogen bromide to give 2-pyridylmethylamine hydrobromide.[503]

o-(4-Pyridylmethylamino)phenol (**IX-222**) is obtained from the reaction of 4-chloromethylpyridine with the hydrochloride of *o*-aminophenol, diethylamine, and methanol.[504]



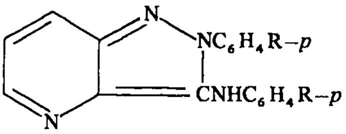
IX-222

2-, 3-, And 4-pyridylmethyl chloride condense with 1,2-diaminoethane to give the corresponding *N*-(pyridylmethyl)-1,2-diaminoethanes. For example, 4-pyridylmethyl chloride and 1,2-diaminoethane give *N*-(4-pyridylmethyl)-1,2-diaminoethane (**IX-223**).[505]



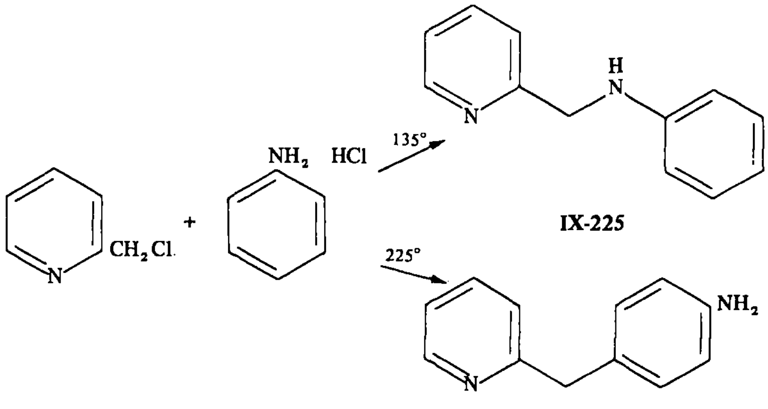
IX-223

Substituted side-chain amines may also be prepared by aminolysis of substituted haloalkyl pyridines.[506-508] Thus, 2-bromomethyl-3-nitropyridine yields the expected 2-arylaminomethyl-3-nitropyridines when treated with aromatic amines at room temperature. At higher reaction temperatures, however, 2*H*-pyrazolo[4,3-*b*]pyridines (**IX-224**) result.[506]



IX-224

When a mixture of aniline hydrochloride and 2-chloromethylpyridine is heated at 135 to 140° for 2 hours and then made alkaline with sodium carbonate, *N*-(2-picolyl)aniline (**IX-225**) results. If the reaction temperature is raised to 225 to 230°, rearrangement occurs and 4-(2-picolyl)aniline (**IX-226**) is obtained instead.[506]



IX-225

IX-226

B. *Reduction of Nitriles*

Cyanopyridines have been reduced to aminoethylpyridines by a variety of methods, 2- And 4-cyanopyridine are reduced with sodium borohydride to 2- and 4-aminomethylpyridine, respectively.[509] In acidic solutions, the polarographic reduction of 4-cyanopyridine yields 4-aminomethylpyridine.[510]

Hydrogenation of 6-chloro-5-cyano-4-methoxymethyl-3-nitro-2-picoline over palladium-charcoal in aqueous hydrochloric acid gives 3-amino-5-aminomethyl-4-methoxymethyl-2-picoline hydrochloride.[511, 512]

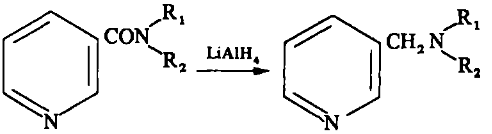
3-Amino-5-aminomethyl-2,4-lutidine is prepared in good yield by the catalytic reduction (Pd—C in methanol) of 6-chloro-3-cyano-2,4-dimethyl-3-nitropyridine.[513] The hydrogenation of 3-(β-pyridylmethoxy)propionitrile over Raney Nickel yields 3-[(3-aminopropoxy)methyl] pyridine.[514]

3-Aminomethyl-4-picoline is obtained by the catalytic reduction of 3-cyano-2,6-dichloro-4-picoline using 30% Pd—$CaCO_3$ as the catalyst.[515]

Pyridoxamine dihydrochloride may be prepared by the reduction of 4-cyano-3-hydroxy-5-hydroxymethy-2-picoline hydrochloride in methanol over a palladium-on-carbon catalyst.[516]

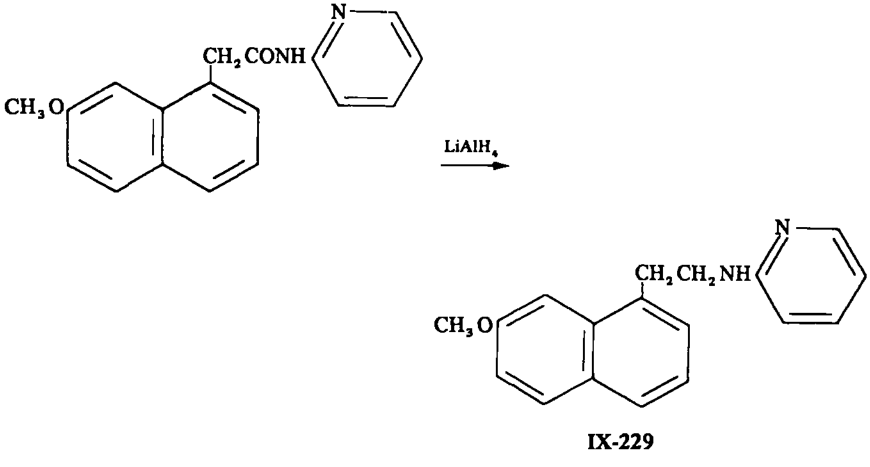
C. *Reduction of Amides*

The use of lithium aluminum hydride for the reduction of pyridinecarboxylic acid amides (**IX-227**) to side-chain aminopyridines (**IX-228**) has been reported; thus, *N,N*-dibenzylnicotinamide (**IX-227**, $R_1 = R_2 = C_6H_5CH_2$) is reduced to



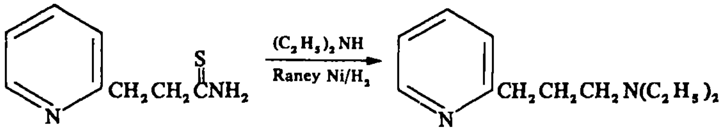
IX-227 **IX-228**

N-(3-pyridylmethyl)dibenzylamine (**IX-228**, $R_1 = R_2 = C_6H_5CH_2$).[517] Diisobutyl aluminum hydride has also been used, as in the preparation of 3-diethylaminomethylpyridine (**IX-227**, $R_1 = R_2 = C_2H_5$) from *N,N*-diethylnicotinamide (**IX-228**, $R_1 = R_2 = C_2H_5$).[518] 7-Methoxy-1-naphthylacetyl chloride reacts with 2-aminopyridine to give the corresponding amide, which is reduced by lithium aluminum hydride to **IX-229**.[519]



IX-229

Aminoalkylpyridines have been prepared by heating thioamides with an alkyl amine and Raney Nickel in an autoclave under 10 atm of hydrogen at 70° for several hours. Under these conditions, β-(2-pyridyl)propionic thioamide reacts with diethylamine to give 2-(3-diethylaminopropyl)pyridine (**IX-230**).[520]

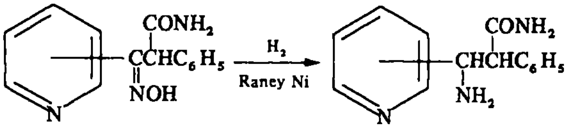


IX-230

D. *Reduction of Oximes*

Aldoximes and ketoximes have been reduced to aminoalkyl pyridines; reduction methods include polarographic, catalytic and chemical means. 2-, 3-, And 4-aminomethylpyridine have been prepared by the polarographic reduction of the corresponding pyridinealdoximes.[521]

The oximes of 1-(2-pyridylcarbonyl)-, 1-(3-pyridylcarbonyl)-, and 1-(4-pyridylcarbonyl)-1-phenylacetamide (**IX-231**) are hydrogenated over Raney Nickel at 50° and 55 atm to give **IX-232**.[522]

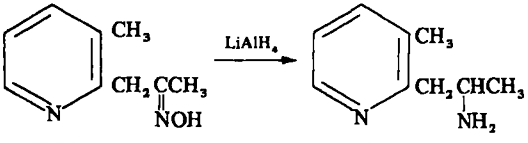


IX-231 IX-232

4-Amino-3-hydroxy-5-hydroxymethylpyridine dihydrochloride is prepared by hydrogenation of the oxime of 4-formyl-3-hydroxyl-5-hydroxymethylpyridine in aqueous hydrochloric acid over palladium-charcoal.[523]

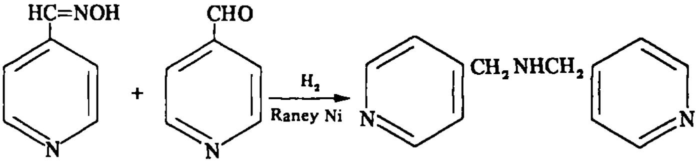
2-(α-Aminobenzyl)pyridine is obtained by the reduction of phenyl 2-pyridyl ketone oxime with zinc dust and acetic acid.[524]

Lithium aluminum hydride is used to reduce the oxime of (3-methyl-2-pyridyl)acetone (**IX-233**) to 2-amino-1-(3-methyl-2-pyridyl)propane (**IX-234**) Oximes of other 2-pyridylacetones can be used similarly.



IX-233 IX-234

If a mixture of 4-pyridinecarboxaldehyde and its oxime are hydrogenated in methanol in the presence of Raney Nickel, bis(4-pyridylmethyl)amine (**IX-235**) is formed.[525]

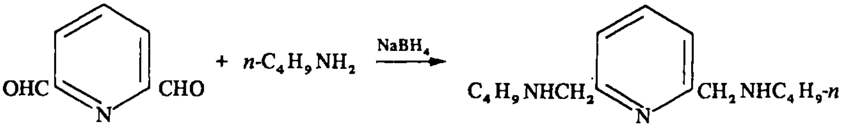


IX-235

E. *Reduction of Schiff Bases*

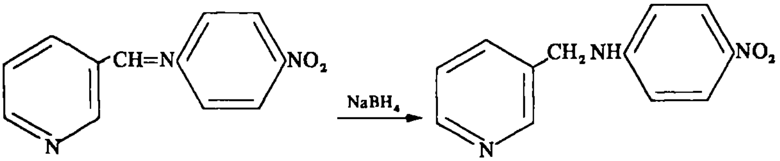
Schiff bases that are obtained from pyridine aldehydes and amines are reduced to aminoalkylpyridines by various reagents.

The Schiff bases obtained by condensing 2,6-pyridinedicarboxylaldehyde with aliphatic amines are reduced by sodium borohydride to bis(alkylaminomethyl)-pyridines. For example, the product obtained from 2,6-pyridinedicarboxaldehyde and *n*-butylamine gives 2,6-bis(*n*-butylaminomethyl)pyridine (**IX-236**) on reduction.[526]



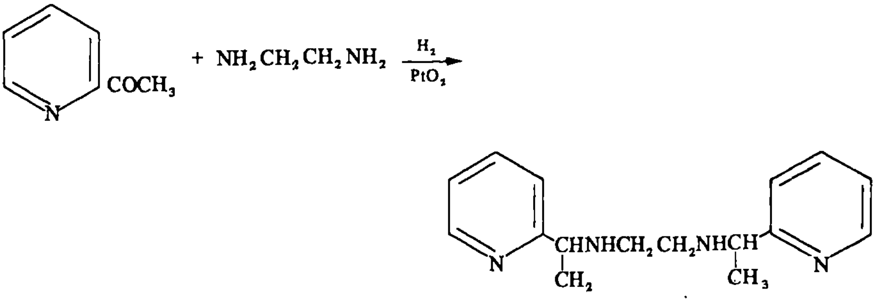
IX-236

Various secondary pyridylamines have been prepared by the sodium borohydride reduction of the corresponding arylidene-amines.[527, 528] For example, pyridine-3-aldehyde condenses with *p*-nitroaniline to give **IX-237**, which, on reduction, gives the secondary amine **IX-238**.[527]



IX-237 **IX-238**

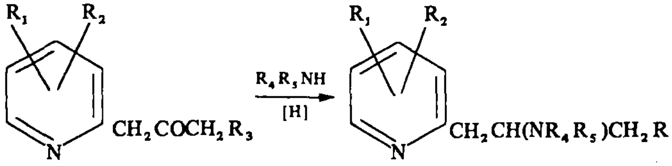
Catalytic reduction of Schiff bases has also been used to produce side-chain aminopyridines.[529-532] 2-Acetylpyridine condenses with ethylene diamine to give an imine which is reduced with hydrogen in the presence of platinum oxide to give *N,N*-bis[α-(2-pyridyl)ethyl]ethylenediamine (**IX-239**). Table IX-65 lists



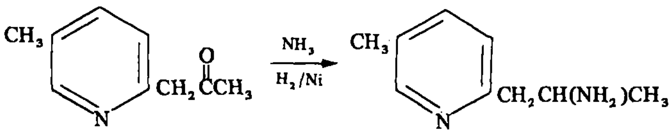
IX-239

compounds so obtained.

Compounds of the general structure **IX-241** are prepared from the appropriate ketone (**IX-240**) and amines (R_4R_5NH) by reductive amination; thus 1-(5-methyl-2-pyridyl)-2-aminopropane (**IX-243**) is obtained by autoclaving (5-methyl-2-pyridyl)acetone (**IX-242**) in the presence of ammonia, hydrogen, and Raney Nickel.[533]

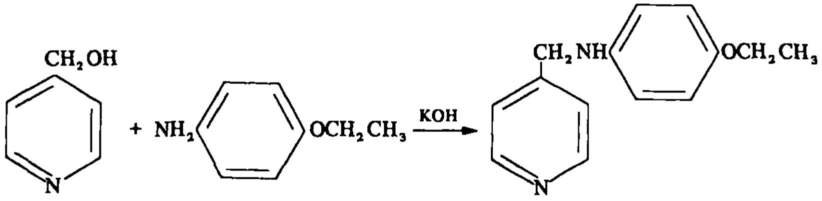


IX-240 IX-241



IX-242 IX-243

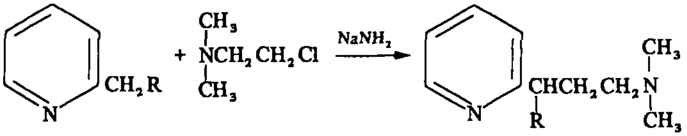
A good source of *N*-(2-pyridylmethyl)anilines and *N*-(4-pyridylmethyl)anilines is the reaction of 2- and 4-pyridinemethanol with anilines in the presence of potassium hydroxide at high temperature. Thus, a mixture of 4-pyridinemethanol, *p*-ethoxyaniline, potassium hydroxide, and a trace of amyl nitrite gives *N*-(4-pyridylmethyl)-*p*-ethoxyaniline (**IX-244**).[534] Amyl nitrite is not a necessary reagent.[535]



IX-244

F. *Side-Chain Alkylation with Aminoalkyl Halides*

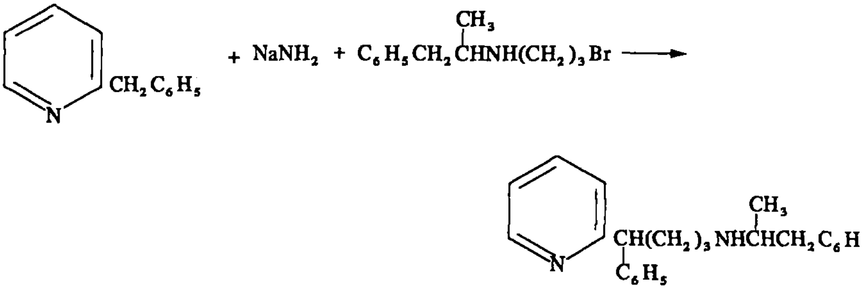
In the presence of sodamide, 2-picoline or 2-benzylpyridine condenses with 2-dimethylaminoethyl chloride to give 1-(2-pyridyl)-3-dimethylaminopropane (**IX-245**, R = H) and 1-phenyl-1-(2-pyridyl)-3-dimethylaminopropane (**IX-245**, R = C_6H_5), respectively.[536, 537]



IX-245

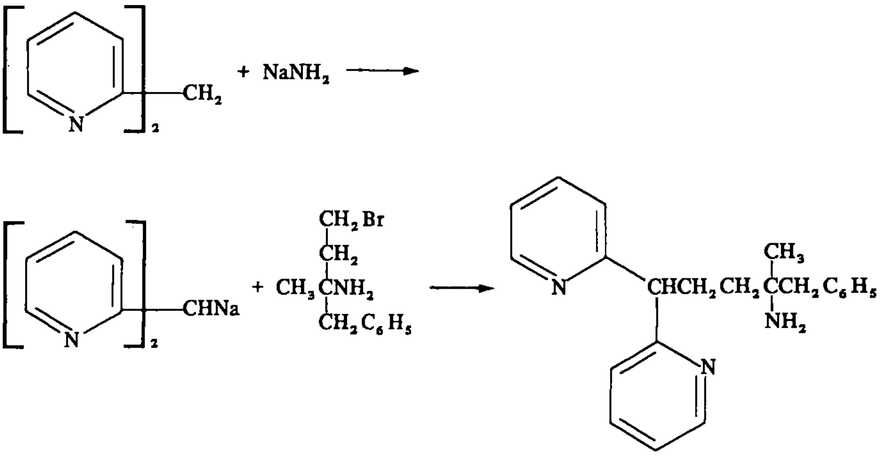
2-Benzylpyridine is boiled with sodium amide and then treated with *N*-(3-bromopropyl)-3-phenyl-2-propylamine to yield 3-phenyl-*N*-[4-(phenyl)-4-(2-pyridyl)]butyl-2-propylamine (**IX-246**).[538]

Other 3-substituted-2-propylamines have been prepared in an analogous manner.



IX-246

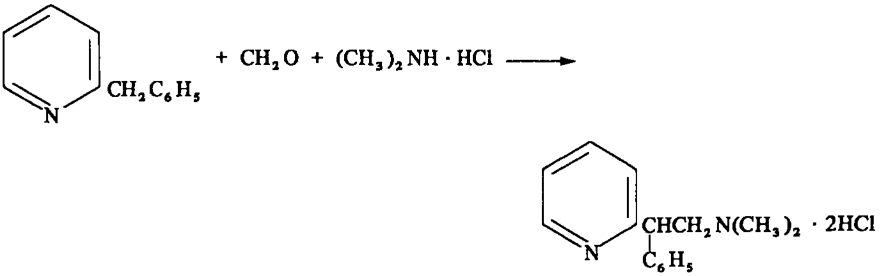
The reaction of di-(2-pyridyl)methane with 2-(2-bromoethyl)-1-phenylamino-propane in the presence of sodamide produces 2-amino-2-benzyl-1,1-(2,2-dipyridyl)pentane (**IX-247**).[539]



IX-247

G. *Mannich Reactions*

When 2-benzylpyridine, paraformaldehyde, and dimethylamine hydrochloride are heated in water for 24 hours, 2-(2-dimethylaminoethyl-1-phenyl)pyridine dihydrochloride (**IX-248**) results.[540]

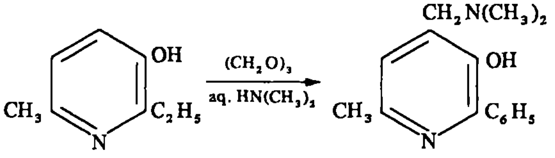


IX-248

Heating 3-hydroxypyridine in water with secondary amines and formaldehyde gives various 2-aminoalkyl-3-hydroxypyridines; for example, with dimethylaminoethylamine, 2-(dimethylaminomethyl)-3-hydroxypyridine is obtained in 73% yield.[541]

A mixture of 3-hydroxy-6-nitro-2-picoline, dimethylamine, and 30% formalin gives 2-[2-(dimethylamino)ethyl]-3-hydroxy-6-nitropyridine.[542] 2-Aminomethyl-5-hydroxy-6-nitropyridine is prepared similarly from 3-hydroxy-2-nitropyridine.[543]

The 4-position can also be aminomethylated. Thus, 4-dimethylaminomethyl-6-ethyl-3-hydroxy-2-picoline (**IX-249**) is obtained from condensation of formalin, dimethylamine, and 6-ethyl-3-hydroxy-2-picoline.[544]



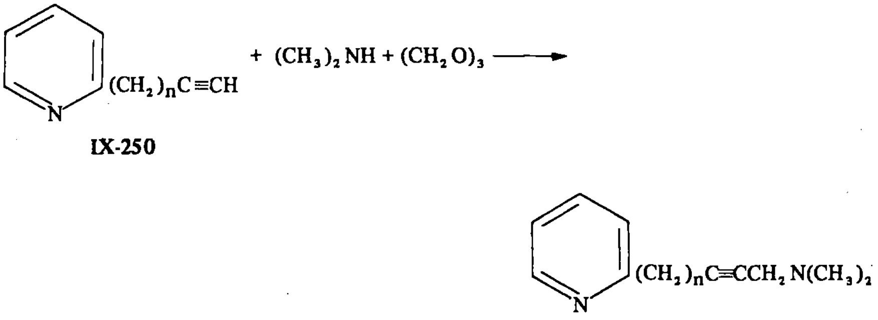
IX-249

A study by NMR and chemical methods shows that aminomethylation of 2-alkyl-3-hydroxypyridines under the above conditions produces 6-aminomethyl and 4,6-diaminomethyl-2-alkyl-3-hydroxypyridines; the 6-position is the site of initial aminomethylation.[545, 546]

H. *From Alkynes*

Side-chain pyridineamines, particularly those containing an alkyne function, are prepared from pyridylalkynes or by the action of alkynes on pyridyl ketones.

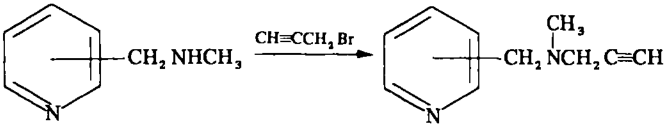
Miocque has prepared various *N,N*-dimethylaminopyridylalkynes of the type **IX-251** by aminomethylation of **IX-250** with dimethylamine and trioxane;[546, 548] for example, 1-dimethylamino-5-(2-pyridyl)-2-pentyne (**IX-251**, n = 1) is obtained by heating 4-(2-pyridyl)-1-butyne (**IX-250**, n = 1), trioxane, and dimethyl amine. Furthermore, this and other aminoalkynylpyridines may be reduced to the corresponding aminoalkylpyridines by catalytic hydrogenation.[547]



IX-250

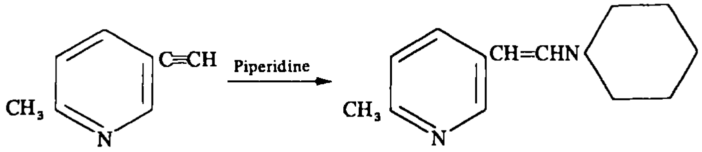
IX-251

N-substituted derivatives of aminoalkynyl pyridines are readily prepared when propargyl bromide is heated with a 2-, 3-, or 4-picolylamine in acetone to give the corresponding *N*-methyl-*N*-picolyl-2- propynylamine (**IX-252**).[549, 550]



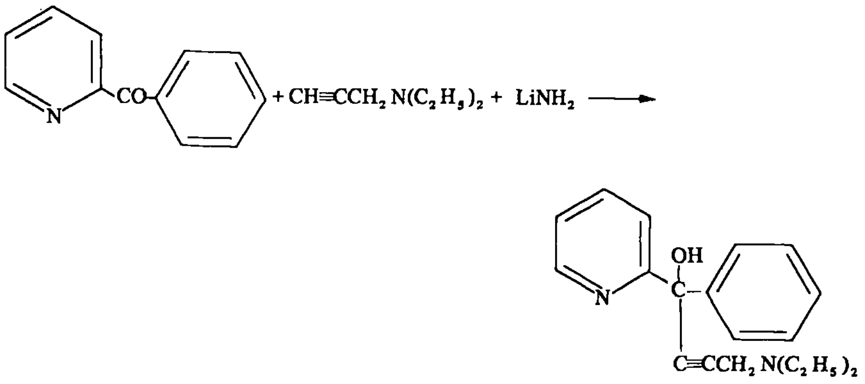
IX-252

5-Ethynyl-2-methylpyridine heated with piperidine gives a 70% yield of 2-methyl-5-(2-piperidinoethenyl)pyridine (**IX-253**). Similarly, 2-methyl-5-(2-morpholinoethenyl)pyridine is obtained with morpholine.[551]



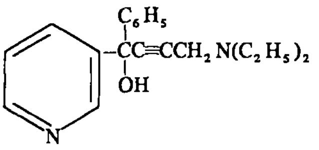
IX-253

Another method of preparing aminoalkynylpyridines involves the reaction of lithium alkynes with pyridyl ketones. Thus, 4-diethylamino-1-phenyl-1-(2-pyridyl)-2-butyn-1-ol (**IX-254**) is obtained by the reaction of lithium amide with diethylamino-2-propyne followed by 2-benzoylpyridine. Similarly, the use of 3-

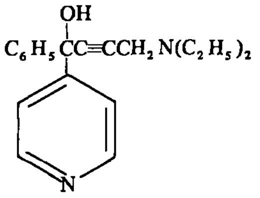


IX-254

and 4-benzoylpyridine yields **IX-255** and **IX-256**, respectively.[552]



IX-255

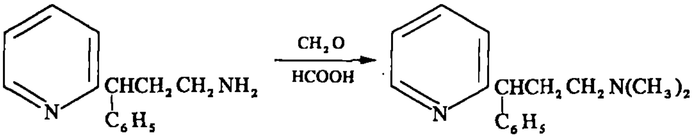


IX-256

I. *Leuckart, Clarke-Eschweiler, and Hofmann Reactions*

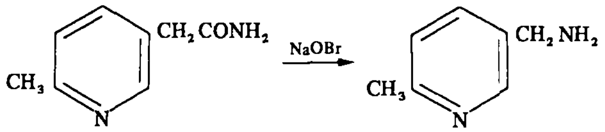
The Leuckart reaction has been used for the preparation of 4-(α-aminobenzyl)-pyridine, which was obtained by heating a mixture of concentrated ammonia, formic acid, and 4-benzoylpyridine.[553]

The related Clarke-Eschweiler reaction in which the reductive alkylation of an amine is carried out with formaldehyde and formic acid was used to prepare 3-dimethylamino-1-phenyl-1-(2-pyridyl)propane (**IX-258**) from 3-phenyl-3-(2-pyridyl)propylamine (**IX-257**).[554]



IX-257 IX-258

The Hofmann rearrangement has not been used often for the preparation of aminoalkylpyridines; it has been reported in the synthesis of 5-aminomethyl-2-picoline (**IX-260**), which is isolated from the reaction of sodium hypobromide with **IX-259**.[555]

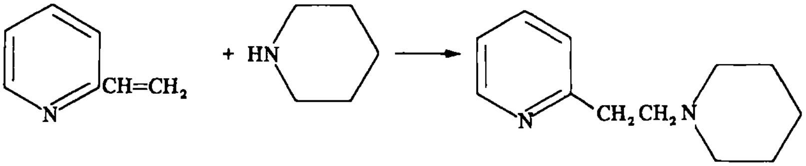


IX-259 IX-260

J. *Addition of Amines to Vinylpyridines*

The addition of amines to vinylpyridines has been the source of a large variety of side-chain aminopyridines. For example, the reactions of 2-vinylpyridine with four aliphatic diamines ethylene-, tetramethylene-, hexamethylene-, and octamethylenediamine—and the mono-, di-, tri-, and tetra-addition compounds obtained were studied.[556, 557] Mono- and di-addition compounds are best prepared in benzene with acetic or propionic acid as a catalyst; tri- and tetra-addition compounds require the same catalyst but higher temperatures and longer reaction times. Some examples are given below.

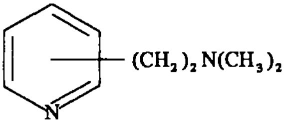
Pyridylethylation resulting from the addition of monoamines to 2-vinylpyridine was shown to be strongly catalyzed by organic and inorganic acids and by ammonium salts of inorganic acids, for example, the alkanoic (C_1–C_5) acids, stearic acid, phenol, and piperidine hydrochloride. Protic solvents affect the reactions slightly; aprotic solvents have no influence. Thus, heating 2-vinylpyridine in piperidine for 8 hours gives 63% 2-(β-piperidinoethyl)pyridine (**IX-261**); in the presence of the above catalysts yields of up to 92% are obtained.[558]



IX-261

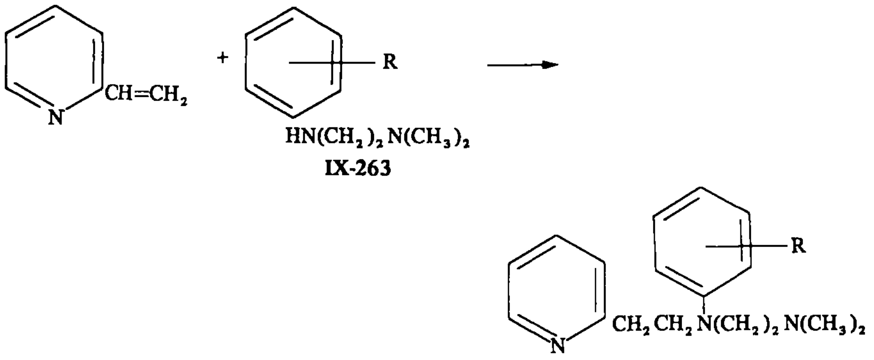
The reactions of 2- and 4-vinylpyridines with various amines include the following: 2-vinylpyridine reacts with ammonium chloride to yield 2-(2-aminoethyl)pyridine (35%);[559] when treated with methylamine it yields 2-(2-methylaminoethylpyridine).[540]

2- And 4-vinylpyridine when heated for 5 hours with dimethylamine give 2- and 4-(2-dimethylaminoethyl)pyridine (**IX-262**), respectively.[540, 560]



IX-262

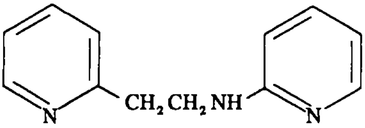
Secondary aromatic amines such as **IX-263** add to 2-vinylpyridine to give *N*-dimethylaminoalkyl-*N*-(pyridylethyl)anilines (**IX-264**)[561-563] (see Table IX-76).



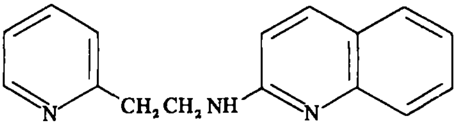
IX-263

IX-264

Heterocyclic amines also add to vinylpyridines. 2-Aminopyridine and 2-aminoquinoline react with 2-vinylpyridine in the presence of sodium metal to give **IX-265** and **IX-266**, respectively.[564, 565]

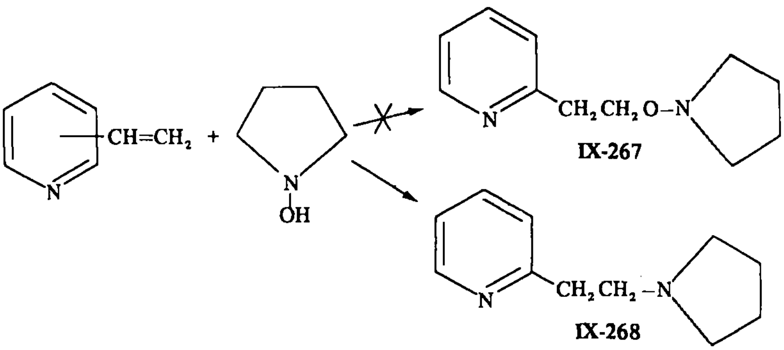


IX-265



IX-266

The reaction of 2-vinyl- or 4-vinylpyridine with *N*-hydroxypyrrolidine give the oxygen-free product **IX-268** rather than the expected **IX-267**. A variety of such



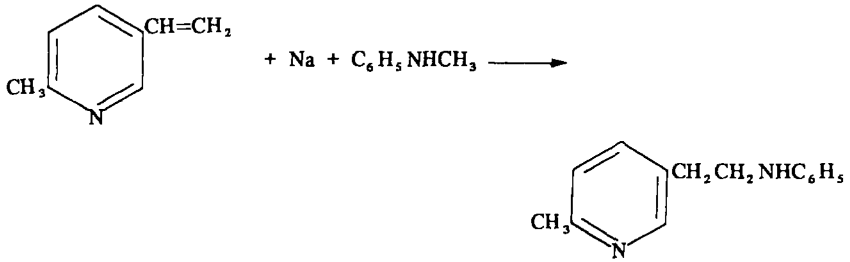
IX-267

IX-268

pyridylethylamines rather than the oxygenated products have been obtained in this way.[566]

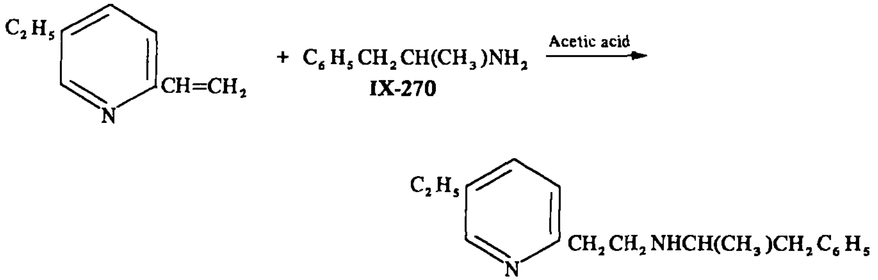
Ethylenimine condenses with 2-vinylpyridine in the presence of metallic sodium to give 2-ethyleniminoethylpyridine.[567]

The reactions of substituted vinylpyridines have not been intensively studied. *N*-Methylaniline and 5-vinyl-2-picoline condense in the presence of sodium metal to give 5-(*N*-methyl-2-phenylaminoethyl)pyridine (**IX-269**).[568]



IX-269

When *d*-α-methylphenethylamine (**IX-270**) and 5-ethyl-2-vinylpyridine are heated in acetic acid and methanol, *N*-(*d*-α-methylphenethyl)-2-(5-ethyl-2-pyridyl)ethylamine (**IX-271**) is formed.[569, 570]



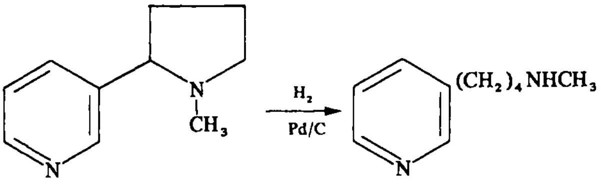
IX-271

2-[β-Alkyl- or arylaminoethyl]-5-vinylpyridines were prepared by treating 2,5-divinylpyridine with an amine in protic solvents in the presence of an acid catalyst at 90 to 120°.[571]

K. *Miscellaneous Reactions*

The reduction of pyridine derivatives also provides a source of side-chain amines. Nicotine and its analogues are reduced to side-chain aminopyridines;

thus, hydrogenation of nicotine over palladium-charcoal at 54° until one mole of hydrogen is consumed gives 3-(4-methylaminobutyl)pyridine (**IX-272**).[572] If the latter is treated with formic acid and formaldehyde, 3-(4-dimethylaminobutyl)-

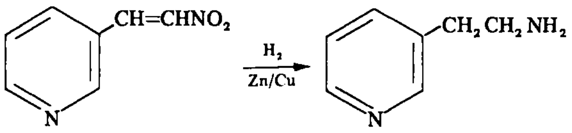


IX-272

pyridine results.

At a cathode potential of −0.75 volts, isonicotinanilide is reduced to 4-anilinomethylpyridine and 4-pyridylcarbinol.[573]

1-Nitro-2-(3-pyridyl)ethylene is reduced by copper coated with zinc dust to β-(3-pyridyl)ethylamine (**IX-273**), which can also be obtained from the reduction of 3-pyridylacetaldoxime.[574]

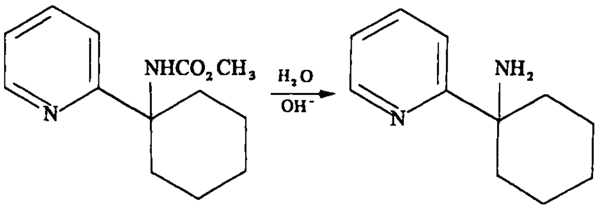


IX-267

L. *Miscellaneous Preparations*

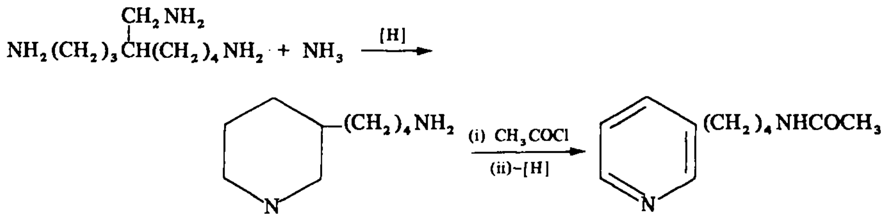
The preparations discussed here did not fit in previous sections. They include side-chain amines obtained from hydrolysis or condensation reactions. The preparation of aminoethers and aminothioethers have also been included.

Several aminocyclohexylpyridines are prepared by the hydrolysis of pyridylcyclohexyl carbamates. Thus 2-(1-aminocyclohexyl)pyridine (**IX-274**) is obtained by the alkaline hydrolysis of methyl *N*-[1-(2-pyridyl)cyclohexyl] carbamate.[575] Other aminocyclohexyl pyridines have been reported.[576]



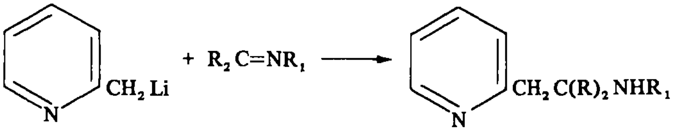
IX-274

It has been reported[577] that 3-(4-aminobutyl)piperidine is obtained by the hydrogenation of 1,8-diamino-4-aminomethyloctane in the presence of ammonia. Acetylation of this piperidine, followed by dehydrogenation at 200° over palladium-charcoal gives 3-(4-acetylaminobutyl)pyridine (**IX-275**).



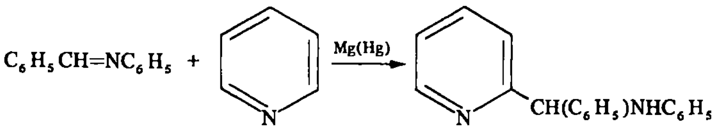
IX-275

When 2-picolyllithium is added to an azomethine linkage, various substituted 2-(2-pyridyl)ethylamines (**IX-276**) are formed in good yield.[578, 579]

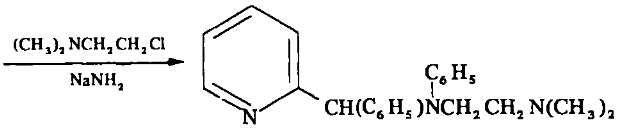


IX-276

Heating *N*-benzylidine aniline with a mixture of magnesium turnings (or aluminum), mercuric chloride, and pyridine, gives 1,*N*-diphenyl-1-(2-pyridyl)-methylamine (**IX-277**). Several such picolylamines are prepared by this modification of the Emmert-Asendorf reaction.[580] When **IX-277** is heated with



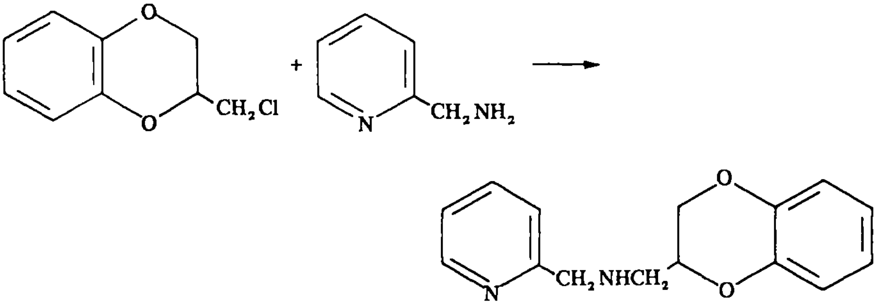
IX-277



IX-278

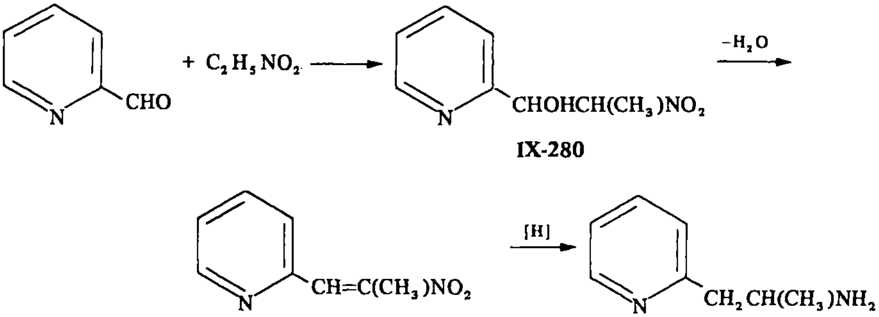
sodium amide and β-dimethylaminoethyl chloride, it yields 2-[α-(*N*-2-dimethylaminoethyl-*N*-phenylamino)benzyl] pyridine (**IX-278**).

2-Chloromethyl-1,4-benzodioxan reacts with picolylamine to give 2-picolylaminomethyl-1,4-benzodioxan (**IX-279**).[581] Table IX-64 lists the 1,4-benzodioxans thus prepared.



IX-279

When 2-pyridinecarboxaldehyde is added to a cooled solution of nitroethane and diethylamine in ethanol, 2-nitro-1-(2-pyridyl)propanol (**IX-280**) is obtained.[582] Dehydration of **IX-280** followed by hydrogenation gives

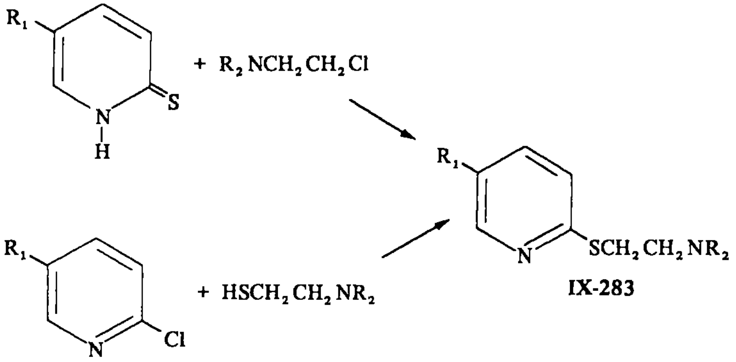


IX-281 **IX-282**

3-amino-1-(2-pyridyl)propane (**IX-282**).[582, 583] The 3- and 4-pyridyl analogs are prepared similarly.

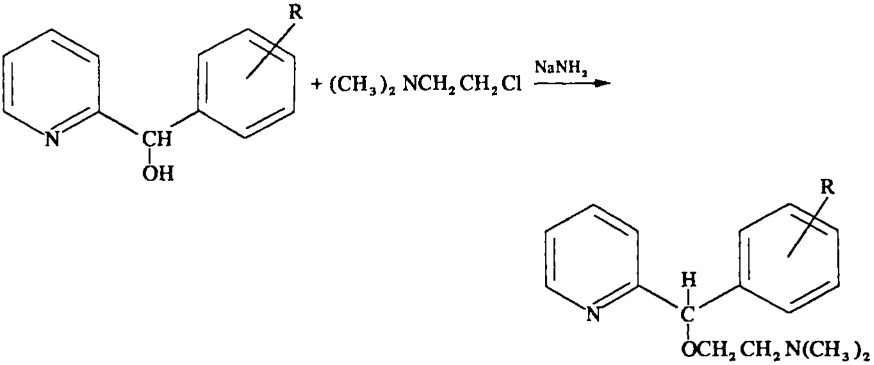
The preparation of aminoethers and aminothioethers of pyridine have been reported. 4-Chloropyridine-1-oxide reacts with ethanolamine to give 4-(β-aminoethoxy)pyridine-1-oxide.[584]

β-Dialkylaminoethyl chlorides have been used to prepare β-aminoalkyl 2-pyridyl sulfides (**IX-283**).[585, 586] The preparation involves heating 2-pyridinethiones and β-dialkylaminoethyl chlorides in ethanol. Compounds **IX-283** are also obtained from the reaction of chloropyridines with β-dialkylaminoethyl mercaptans (see also Chapter XV).



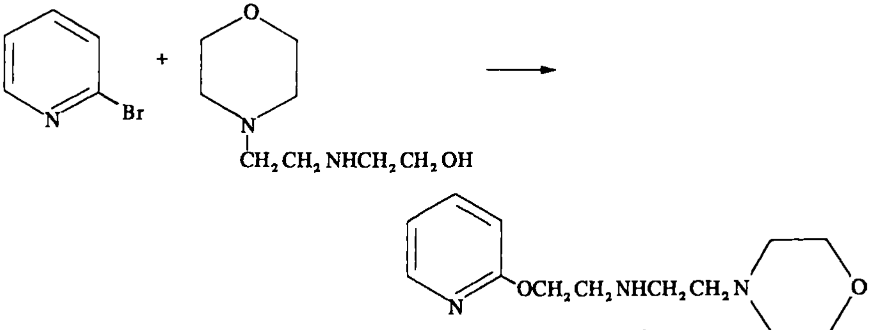
IX-283

Dimethylaminoethyl ethers (**IX-284**) are obtained when aryl 2-pyridyl carbinols are treated with (β-dimethylamino)ethyl chloride. For example,



IX-284

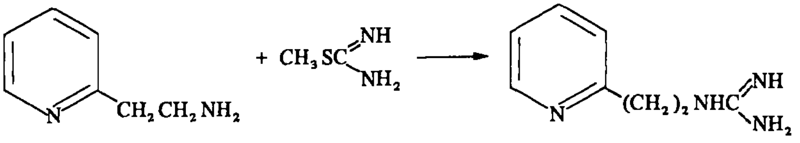
pyridine-2-aldehyde reacts with phenylmagnesium bromide to give phenyl 2-pyridyl carbinol, which, when treated with sodium amide and 2-dimethylaminoethyl chloride hydrochloride, gives dimethylaminoethyl α-2-pyridylbenzyl



IX-285

ether (**IX-284**, R = H).[587,588] When 2-bromopyridine is added to a suspension of 2-(2-*N*-morpholinoethylamino)ethanol and sodamide in boiling toluene, 2-[2-(2-*N*-morpholinoethylamino)]ethoxypyridine (**IX-285**) results.[589]

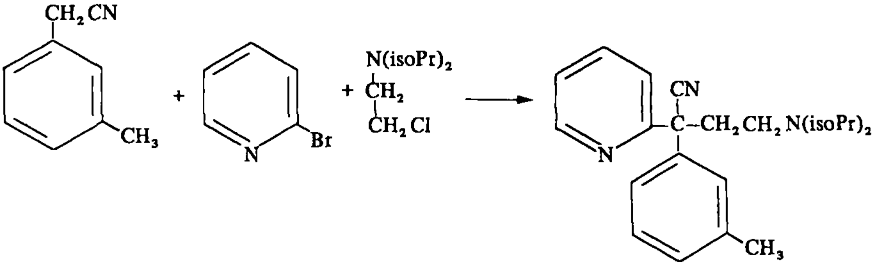
2-Pyridylalkylguanidines (**IX-286**) are obtained by the reaction of 2-pyridylalkylamine with 2-methyl-2-thiopseudourea.[590]



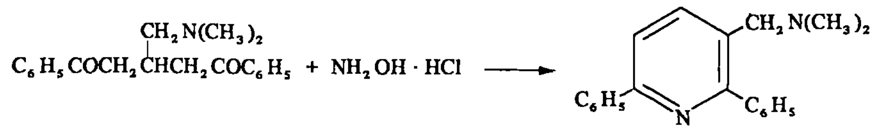
IX-286

Various 5-aminoethyl-2-picolines are prepared by nitrosation of the corresponding 5-(2-phenylaminoethyl)-2-picolines, with subsequent cleavage of the resulting nitrosyl derivatives by heating them with alkali hydroxide; no further details are reported in this patent.[591]

Nitrile derivatives of dialkylaminoalkylpyridines have been synthesized.[592,593] Thus, in the presence of sodamide, *m*-tolylacetonitrile condenses with 2-bromopyridine and β-diisopropylaminoethyl chloride to give 4-diisopropylamino-2-(2-pyridyl)-2-(3-tolyl)butyronitrile (**IX-287**). 3-[(Dimethylamino)methyl]-2,6-diphenylpyridine (**IX-288**) is obtained by heating 1,3-dibenzoyl-2-dimethylaminomethylpropane hydrochloride with hydroxylamine hydrochloride.[594]



IX-287

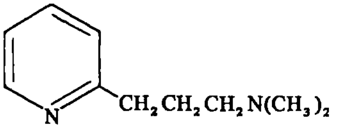


IX-288

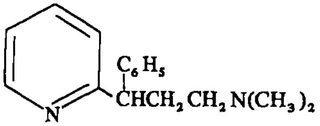
2. Properties and Reactions

The physical properties of side-chain aminopyridines are listed in Tables IX-63 to IX-80. Their chemical reactions are reported below.

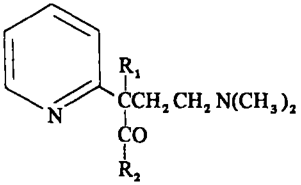
The acylation of 3-dimethylamino-1-(2-pyridyl)propane (**IX-289**) and 3-dimethylamino-1-phenyl-1-(2-pyridyl)propane (**IX-290**) with various esters using phenyllithium or phenylsodium as the base to produce the carbanion yields the ketones **IX-291**. For example, when the ester is ethyl benzoate, the ketone **IX-291**, (R_1 = H, R_2 = C_6H_5) is obtained.[537]



IX-289

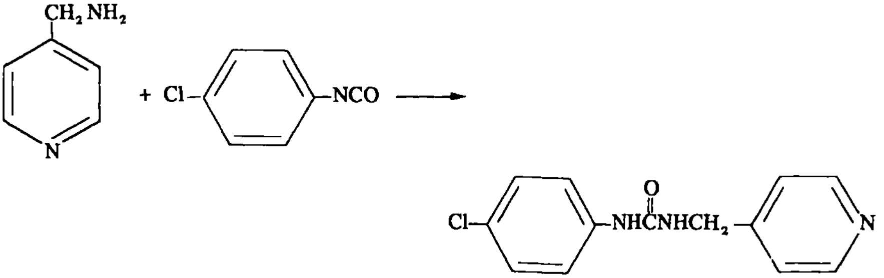


IX-290



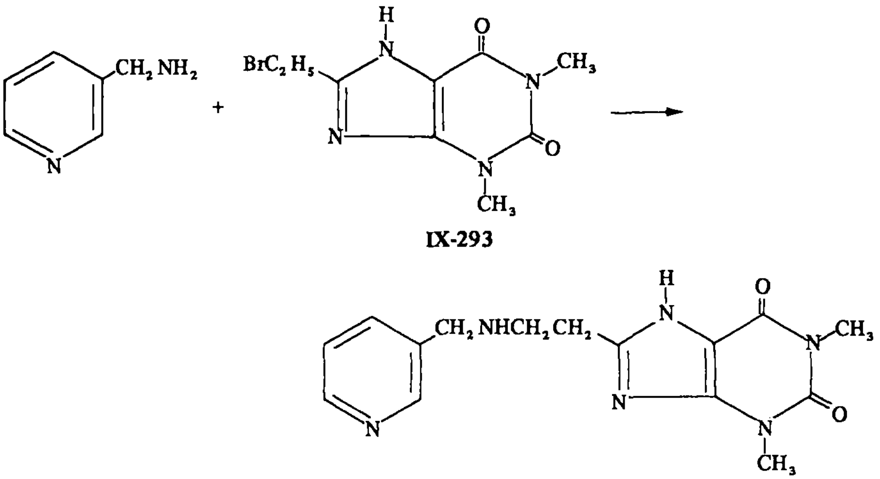
IX-291

When treated with hydrochloric acid and an aqueous solution of sodium nitrite, *N*-methyl-2-picolylamine gives 2-(*N*-methyl-*N*-nitroso)picolylamine.[594] 1-(*p*-Chlorophenyl)-3-(4-picolyl)urea (**IX-292**) results from the action of 4-aminomethylpyridine on *p*-chlorophenylisocyanate.[596] Other ureas are similarly prepared (Table IX-88).



IX-292

3-Picolylamine is alkylated with 7-β-bromoethyltheophylline (**IX-293**) to give **IX-294**.[596]



IX-293

IX-294

III. List of Tables

IV. Acknowledgments

For their help and cooperation, I wish to thank the secretaries of the Chemistry Department and several of my colleagues, especially, Mr. Emil Krochmal, Mr. Kirby Lowery, Dr. Klaus Adam, Dr. James L. Lyle, and Dr. A. E. Martell. I am especially grateful to the Robert A. Welch Foundation whose grant

permitted me to continue my research projects during the writing of this chapter, and to the many helpful comments of our untiring editor.

V. Guide to Locating Compounds in Tables

The reader should first consult the list of tables (Section III), which summarizes the general classes of aminopyridines compiled; generally, derivatives are listed in the same tables as the parent compounds.

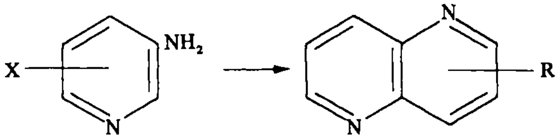
Compounds in a particular table are arranged in alphabetical order except when abbreviations (e.g., Me, Et, *n*-Pr, Ph, etc.) for alkyl or aryl substituents are used. In this case, groups with fewer carbon atoms have priority over those with more carbon atoms (thus Me before Et). When several columns of substituents are present in a table, the column on the left is first filled, then the next column, and the last to be filled is that on the right. Monosubstituted compounds are listed before di- or trisubstituted aminopyridines.

VI. TABLES

TABLE IX-1. Reaction of 3-Substituted Pyridine-1-oxides with *N*-Phenylbenzimidoylchlorides (See Chapter IV)

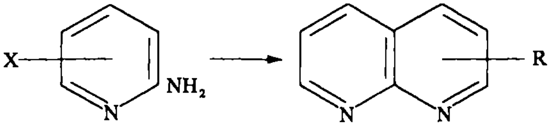
TABLE IX-2. Reaction of Pyridine-1-oxides with *N*-Arylbenzimidoyl Chlorides (See Chapter IV)

TABLE IX-3. Preparation of 1,5-Naphthyridines from 3-Aminopyridines



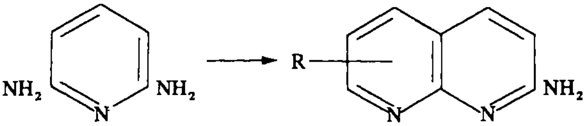
X	Reagent	R				% Yield	Ref.
		2	3	4	6		
H	Glycerol	H	H	H	H	31	394, 598
H	Crotonaldehyde	Me	H	H	H	8	394, 598
H	Methacrolein	H	Me	H	H	30	394, 598
H	Methylvinylketone	H	H	Me	H	11	394, 598
H	Ethylacrolein	H	Et	H	H	4	394, 598
H	Acetaldehyde and acetone	Me	H	Me	H	–	394, 398
2-OH	Glycerol	OH	H	H	H	15	394, 599
6-OH	Acetaldehyde	OH	H	H	Me	27	394, 599
6-Cl	Acetaldehyde	Me	H	H	Cl	–	394, 600
4-OH	Glycerol	H	H	OH	H	37	394, 601
1-Me-5-NH_2-2-pyridone	Acetaldehyde	1,6-Me_2-1,5-naphthyridine-2-one				30	394, 599

TABLE IX-4. Preparation of 1,8-Naphthyridines from 2-Aminopyridines



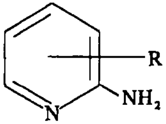
		R							
X	Reagent	2	3	4	5	6	7	% Yield	Ref.
H	Glycerol	H	H	H	H	H	H	30	411
4-Me	Glycerol	H	H	Me	H	H	H	17	411
4-Me	Crotonaldehyde	Me	H	H	Me	H	H	17	405
4-Me	Methylvinylketone	H	H	Me	Me	H	H	3	405
5-Me	Glycerol	H	Me	H	H	H	H	18	405
5-Me	Crotonaldehyde	Me	H	H	H	Me	H	15	405
5-Me	Methylvinylketone	H	Me	H	Me	H	H	3	405
5-Me	Methacrolein	H	Me	H	H	Me	H	1	405
6-Me	Glycerol	Me	H	H	H	H	H	10	411
6-Me	Crotonaldehyde	Me	H	H	H	H	Me	15	405
4,6-Me_2	Glycerol	Me	H	Me	H	H	H	10	411
4,6-Me_2	Crotonaldehyde	Me	H	Me	H	H	Me	16	405

TABLE IX-5. Preparation of 7-Amino-1,8-naphthyridines from 2,6-Diaminopyridine



	R				
Reagent	2	3	4	7	Ref.
Ethyl 2-oxalylpropionate	OH	Me	COOH	NH_2	413
Ethyl oxalacetate	OH	COOEt	–	NH_2	416
Malic acid	OH	–	–	NH_2	417
Ethyl β-methylmalate	OH	Me	–	NH_2	417
Citric acid	OH	–	CH_2COOH	NH_2	417
Acetone dicarboxylic acid	OH	–	CH_2COOH	NH_2	417
Ethyl oxalate	OH	–	COOH	NH_2	421
Ethyl acetoacetate	OH	–	Me	NH_2	414

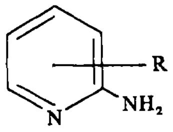
TABLE IX-6. Alkyl- and Aryl-2-aminopyridines



Substituents					
3	4	5	6	Physical properties	Refs.
H	H	H	H	m.p. 57–8°; picrate, m.p. 223–5°; 1-oxide, HCl, m.p. 154–6°	112 111 280
Me	H	H	H	acetyl, m.p. 204–5°; *N,N*-dibenzoyl, m.p. 124–5°	367 367
t-Bu	H	H	H	m.p. 128–9°; picrate, m.p. 242°	41 41
H	1,2,4-Trimethylpentyl	H	H	b.p. 152–4°/4 mm; picrate, m.p. 134°	13 13
(1-Me-2-pyrrolidinyl)	H	H	H		602, 609
(1-Me-pyrrol-2yl	H	H	H	m.p. 76–8°	424
H	H	(1'-Me-3'-nitro-2'-pyrrolidinyl)	H	m.p. 171–2°	602
H	Me	H	H	m.p. 182° (dec.); picrate, m.p. 162.5–3.5°; HCl, m.p. 194.5–5.5°; perchlorate, m.p. 143.5–4.5°	436

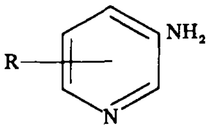
H	Et	H	H		606
H	*n*-Pentyl	H	H	b.p. 161°/20 mm;	13
				b.p. 150–60°/6 mm;	13, 14
				m.p. 54–5°;	13
				m.p. 50–8.5°	14
H	2-Pentyl	H	H	b.p. 145–50°/10 mm; m.p. 31–2° picrate, m.p. 150°	13
H	Isopentyl	H	H	b.p. 150–60°/10 mm	13
H	*n*-Hexyl	H	H	b.p. 180–200°/20 mm; m.p. 58–60°	13
H	Isohexyl	H	H	b.p. 175–80°/10 mm; m.p. 74°; picrate, m.p. 161–2°	13
H	*n*-Heptyl	H	H	b.p. 155–65°/7 mm; m.p. 59°; picrate, m.p. 136°	13
H	*n*-Octyl	H	H	b.p. 230–40°/35 mm; m.p. 64°	13
H	2-Octyl	H	H	b.p. 152–5°; m.p. 54°; picrate, m.p. 134–6°	13
H	5-Nonyl	H	H	b.p. 170–80°/20 mm; m.p. 56°; picrate, m.p. 112°	13
H	Benzyl	H	H	m.p. 103.5–4°	14
H	H	Me	H	picrate, m.p. 247.5–9.5°	115, 436
H	H	Et	H	b.p. 90–2°/3 mm	27, 62
H	H	(1-Me-2-pyrrolidinyl)	H		602, 609
H	H	(1-Me-2-pyrrol-2-yl)	H	m.p. 90–2°	424
H	H	H	Et	picrate, m.p. 191–3°	603

TABLE IX-6. Alkyl- and Aryl-2-aminopyridines (Continued)



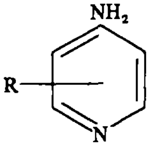
Substituents					
3	4	5	6	Physical properties	Refs.
H	H	H	*n*-Heptyl		604
H	H	H	(2,5-Me_2-pyrrol-l-yl)	b.p. 142°/0.15 mm; m.p. 121.5°	313
Me	Me	H	H	b.p. 124/10 mm; HCl, m.p. 239–40°	438
Me	H	Me	H	HCl, m.p. 203–5°	438
Me	H	H	Me	m.p. 50–2°	605
				HCl, m.p. 243–4°	438
Et	H	H	Me		26
H	Ph	H	Ph	picrate, m.p. 198–200°	607
H	*p*-Nitrophenyl	H	Ph	m.p. 245–50°	607
H	H	Et	Pr	b.p. 67°/0.15 mm	480
H	H	Me	Me	m.p. 54–5°	603, 608
Ph	Ph	H	Ph	m.p. 156–7°	126
Me	Me	Me	Me	m.p. 113–14°	122, 214

TABLE IX-7. Alkyl- and Aryl-3-aminopyridines



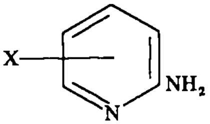
Substituents					
2	4	5	6	Physical properties	Ref.
Me	H	H	H	m.p. 114–15°	40, 110
Ph	H	H	H	b.p. 119–21°/0.35 mm	110, 392
				m.p. 65–7°	441
				m.p. 62–4°; picrate, m.p. 204–6°	110, 392, 441
p-BrC$_6$H$_4$	H	H	H	m.p. 99–101°	110
				m.p. 134.5–7°; picrate, m.p. 177–9°	610
H	Me	H	H	m.p. 106–7°, 104–6°	40, 468
				picrate, m.p. 177–8°	95
H	H	Me	H	m.p. 61–3°, 58°; picrate, m.p. 225° (dec.)	40, 468
H	H	H	Me	m.p. 95–6°; acetyl, m.p. 158–60°	40, 555
Me	Me	H	H	b.p. 246–56° m.p. 70–4°	91, 92, 352
					611
				picrate, m.p. 227–8°	91
				sulfonyl, m.p. 54°	92
Me	H	Me	H		379
Me	H	H	Me	m.p. 123°; picrate, m.p. 180–1°; 1-oxide, m.p. 155–8°	68
H	Me	Ph	H	m.p. 136–6.5°	612
H	Me	H	Me	b.p. 255–7°; m.p. 62–3°, m.p. 68–71°; picrate, m.p. 186–7°; sulfonyl, m.p. 62–3°	91, 92, 352
Me	Me	H	Me	1-oxide HCl, m.p. 211°	351

TABLE IX-8. Alkyl-4-aminopyridines



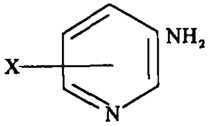
Substituents					
2	3	5	6	Physical properties	Ref.
H	H	H	H	m.p. 152–5°; picrate, m.p. 215–17°; 1-oxide, HCl, m.p. 181–3°	119
Me	H	H	H	m.p. 94–5°;	86, 118
				1-oxide, m.p. 190°	71
				1-oxide-HCl, m.p. 191–2°	75
Et	H	H	H	b.p. 128–30°/4–5 mm; 117–20°/2.5 mm	88, 614
H	Me	H	H	m.p. 108–9°;	86, 118
				1-oxide, m.p. 120–5°;	71
				1-oxide HCl, m.p. 219–20°	75
H	Et	H	H	m.p. 42–3°; picrate, m.p. 202–3°	41, 67, 615
				HCl, m.p. 209–10°	62
				hemihydrate, m.p. 52–3°	214
				hemihydrate, picrate, m.p. 196–7°	41, 214
H	isoPr	H	H	hemihydrate, m.p. 69–70° hemihydrate, picrate, m.p. 156–7°	41, 214
H	Styryl	H	H	1-oxide, m.p. 179°	616
H	H	Et	H	m.p. 91–2°	97, 617, 618
Me	H	COOCH$_3$	H	m.p. 125–6°	97
Me	H	CH$_2$OH	H	m.p. 132–4°	97
Me	H	Et	H	1-oxide HCl, m.p. 181–3°; picrate, m.p. 181–2°	75
Me	H	H	Me	m.p. 192–3°; 190–1°	74, 118
				m.p. 188–90°, 192°	20, 105
				1-oxide, m.p. 265°	74, 619
				1-oxide HCl, m.p. 257°	74
t-Bu	H	H	*t*-Bu	chloroaurate, m.p. 193–5°;	119
				picrate, m.p. 146–50°	119, 620
H	Me	Me	H	1-oxide, m.p. 227–9°; 1-oxide, picrate, m.p. 221–3°	41, 214
Me	Me	Me	Me	hemihydrate, m.p. 196–7°; picrate, m.p. 225–6°	41

TABLE IX-9. Halo-2-aminopyridines



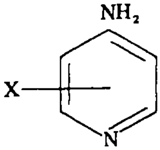
Substituents					
3	4	5	6	Physical properties	Ref.
H	Cl	H	H		445
H	H	Br	H		382, 385
H	H	Cl	H	m.p. 135–6°	278, 382, 384
H	H	H	Br	m.p. 89–90°	2
H	H	H	F	m.p. 53–4.5°, 58–9°	66, 121
H	H	H	I	m.p. 109–10°	2, 3
Br	Br	H	H		34
H	Br	H	Br		34
F	H	F	F	m.p. 94.5–5.5°	53, 374
F	Br	F	F	m.p. 116–17°	53, 374
F	I	F	F	m.p. 114–5°	59

TABLE IX-10. Halo-3-aminopyridines



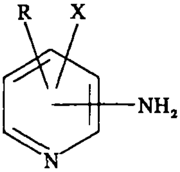
Substituents					
2	4	5	6	Physical properties	Ref.
Cl	H	H	H	2-nitrobenzoyl, m.p. 158–61.5° 2-aminobenzoyl, m.p. 168–72° 4-Cl-2-NO_2-benzoyl, m.p. 205° 2-NH_2-4-Cl-benzoyl, m.p. 202° 5-Me-2-NO_2-benzoyl, m.p. 154–5° 2-NH_2-5-Me-benzoyl, m.p. 186–8°	621
F	H	H	H	b.p. 116–17°/24 mm; HCl, m.p. 187–8°	66
H	I	H	H	m.p. 75–6°; picrate, m.p. 253° (dec.)	373
H	H	Br	H		386
H	H	H	F	m.p. 87–7.5°	66
SH		Cl		m.p. 204–5°	168
H	Cl	Br	H	m.p. 108.5°; nitrate, m.p. 176°	44
H	Cl	Cl	H	m.p. 108°; nitrate, m.p. 169°	44, 622
H	Cl	I	H	m.p. 102°	623
H	Cl	H	Cl	m.p. 84–5°	223, 225, 624
H	$NHNH_2$	H	Cl	m.p. 167–9°	624
Me	CH_2Br	CH_2Br	H	HBr, m.p. 220°	625

TABLE IX-11. Halo-4-aminopyridines



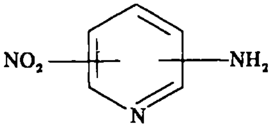
Substituents					
2	3	5	6	Physical properties	Ref.
Br	H	H	H	m.p. 95–6°	47
Cl	H	H	H	m.p. 92°; 1-oxide HCl, m.p. 152–3.5°	47, 87, 96, 389
I	H	H	H	m.p. 99°, 1-oxide m.p. 110° (dec.)	47, 107, 177, 470
H	Br	H	H	m.p. 110° 1-oxide, m.p. 67°	373 47, 107, 177
H	Cl	H	H	m.p. 59°; 60°	48, 373
H	F	H	H	m.p. 77°	51
H	I	H	H	m.p. 71°; 75–6°; picrate, m.p. 253° (dec.) 1-oxide, picrate, m.p. 189°	48, 100 47, 177, 107
H	H	H	F	m.p. 89°; picrate, m.p. 223°	49
Cl	H	H	Cl	m.p. 172–3°, 170°	87, 390
CCl_3	Cl	Cl	H	m.p. 136–8°	56
Cl	Cl	H	CCl_3	m.p. 81–4°	56
Cl	Cl	Cl	Cl	m.p. 220–1°	21
Cl	Cl	Cl	CCl_3	m.p. 113–18°	56
F	Cl	Cl	F	m.p. 112–13°	53, 58
F	Cl	F	F	m.p. 117–18°	53, 58, 374
F	F	F	F	m.p. 85–6°	53, 54, 57, 252, 626
F	F	F	MeO	m.p. 92.5–3°	252

TABLE IX-12. Alkylhalo-(2,3, or 4)-aminopyridines



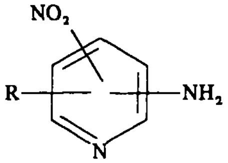
Substituents						
2	3	4	5	6	Physical properties	Ref.
NH_2	Me	H	Br	H	m.p. 90–2°	40
NH_2	Me	H	H	Br	m.p. 114–14.5°	3
NH_2	H	Me	H	Br	m.p. 115–16°	2, 3
NH_2	H	Et	H	Br	m.p. 113–13.5°	3
NH_2	H	Et	H	I	m.p. 112–13°	3
NH_2	H	Cl	H	Me	m.p. 108–9°	388
NH_2	H	Ph	H	Br	m.p. 141–3°	3
NH_2	H	Ph	H	I	m.p. 154–5.5°	3
NH_2	H	H	Me	Br	m.p. 97.5–8°	3
Me	NH_2	H	Cl	H		627
NH_2	Br	Me	Br	H	m.p. 123–4°	40
Me	NH_2	H	H	COOH	m.p. 262–3°	391
Me	NH_2	COOH	H	Cl	m.p. 218–19° (dec.)	391
Me	COOH	H	NH_2	Cl	m.p. 227–8°	391
Me	NH_2	CH_2Br	CH_2Br	H	HBr, m.p. 220°	625
Me	NH_2	$EtOCH_2$	CN	Cl	m.p. 146°	78
Me	H	NH_2	H	Cl	m.p. 155–7°	388
Me	F	NH_2	H	Me	m.p. 92°; picrate m.p. 235°	52
F	F	NH_2	F	MeO	m.p. 92.5–3°	252

TABLE IX-13. Aminonitropyridines



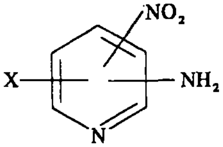
Substituents						
2	3	4	5	6	Physical properties	Ref.
NH_2	NO_2	H	H	H		386
NH_2	H	NO_2	H	H	m.p. 96°; *N*-acetyl, m.p. 211°	628
					1-oxide, m.p. 245–6°; acetyl, m.p. 206°	371, 628
NH_2	H	H	NO_2	H	m.p. 188°	9
					N-acetyl, m.p. 194–6°; 1-oxide, m.p. 196–7°	371, 386
NH_2	NO_2	H	NO_2	H	m.p. 188° (190–2°), 188°	45, 176, 367, 478
NH_2	H	NO_2	NO_2	H	m.p. 217°	628
OH	NH_2	H	NO_2	H	m.p. 199–201°; *N*-acetyl, m.p. 281°	102
H	NH_2	NO_2	H	H	b.p. 62–4°/0.5 mm	50
					m.p. 138°	51
					1-oxide, m.p. 237°	178
H	NH_2	H	NO_2	H	m.p. 141°; acetyl, m.p. 146–8°	64, 68
					benzoyl, m.p. 170–2°	103
H	NO_2	NH_2	H	H	m.p. 204°; HCl, m.p. 260–1°; picrate, m.p. 197–8°	152

TABLE IX-14. Alkylnitro-(2,3, or 4)-aminopyridines



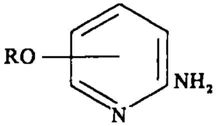
Substituents						
2	3	4	5	6	Physical properties	Ref.
NH_2	NO_2	H	H	Pr	m.p. 150°; picrate, m.p. 165–6°	480
NH_2	NO_2	Me	H	Me	m.p. 164°	488
NH_2	NO_2	H	Me	Me	m.p. 165–6°	608
NH_2	H	Me	NO_2	Me	m.p. 188–9°, 184°	10, 488
Me	NH_2	NO_2	H	Me	m.p. 112°; 1-oxide, m.p. 189–90°	52
Me	NO_2	NH_2	H	Me	m.p. 126°	469
Pr	H	NH_2	NO_2	H	m.p. 193°	480
H	Me	NH_2	NO_2	H	m.p. 193°	469

TABLE IX-15. Haloaminonitropyridines



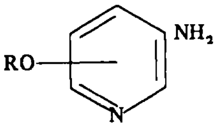
Substituents						
2	3	4	5	6	Physical properties	Ref.
NH_2	NO_2	Cl	H	H	m.p. 176°	46
NH_2	Br	H	NO_2	H	m.p. 213°, 222°	9, 386
NH_2	NO_2	H	Br	H	m.p. 205°	386
NH_2	NO_2	H	Cl	H		477
NH_2	NO_2	H	NO_2	H	m.p. 205°	386
NH_2	NO_2	Me	Br	H		477
NH_2	F	NO_2	F	F		252
NH_2	NO_2	Me	Br	Me	m.p. 169–70°	630
F	NH_2	NO_2	F	F	m.p. 84–4.5°	252
Br	NO_2	NH_2	H	H	m.p. 197°	375
Cl	NO_2	NH_2	H	H	m.p. 209–10°	87, 96, 375, 629
I	NO_2	NH_2	H	H	m.p. 269–71° (dec.)	470
Cl	H	NH_2	NO_2	H	m.p. 190–1°, 206°	87, 96
H	Cl	NH_2	NO_2	H	m.p. 181°	44
Cl	NO_2	NH_2	H	Cl	m.p. 142–3°	87

TABLE IX-16. Alkoxy-2-aminopyridines



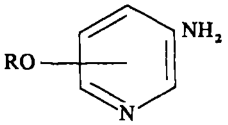
Substituents					
3	4	5	6	Physical properties	Ref.
CH_3O	H	H	H		116
C_2H_5O	H	H	H	m.p. 79–82°	33, 35, 38
H	CH_3O	H	H	m.p. 115–16°	116, 388
H	C_2H_5O	H	H		34, 35
H	n–C_3H_7O	H	H	m.p. 143–5°	482
H	isoC_3H_7O	H	H	m.p. 150–2°	482
H	n–$C_5H_{11}O$	H	H	m.p. 135–7°	482
H	iso$C_5H_{11}O$	H	H	m.p. 129–31°	482
H	n–$C_6H_{13}O$	H	H	m.p. 132–4°	482
H	H	H	C_2H_5O	b.p. 120–2°/ 16 mm	359
H	H	H	iso$C_5H_{11}O$	b.p. 162–4°/23 mm	359
Br	C_2H_5O	H	H	m.p. 147–8°	34
H	CH_3O	H	CH_3	m.p. 141–2°	388
H	C_2H_5O	Br	H	m.p. 149–50°	34, 35
H	C_2H_5O	H	C_2H_5O	m.p. 35–6°; picrate, m.p. 176–7°	34
Br	C_2H_5O	Br	H	m.p. 100–1°	34

TABLE IX-17. Alkoxy- and Aryloxy-3-aminopyridines



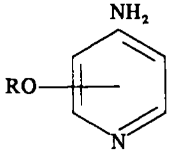
Substituents					
2	4	5	6	Physical properties	Ref.
o-BrC_6H_4O	H	H	H	–	94
Ethoxy	H	H	H	b.p. 105–6°/10 mm; m.p. 31–2°	468
1-β-*D*-Glucopyranosyloxy	H	H	H	m.p. 147–53°	81
tetra-*O*-acetyl-1-β-*D*-glucopyranosyloxy	H	H	H	m.p. 147–8°; acetyl, m.p. 129–31°	81
H	C_2H_5O	H	H	m.p. 83°	83
				HCl, m.p. 216°	152
					35, 30, 359
H	H	CH_3O	H	b.p. 166–8°/15 mm; m.p. 64–5°	388
H	H	C_2H_5O	H	picrate, m.p. 189–91°	28, 35, 468
H	H	H	CH_3O	b.p. 141°/25 mm	313
H	H	H	C_2H_5O		28
H	H	H	C_4H_9O		330
H	H	H	4-NH_2-2-ClC_6H_3O	m.p. 174–5°	98
H	H	H	4-NH_2-2-ClC_6H_3O	m.p. 145–6° di-*N*-acetyl, m.p. 195–6°	98 631

TABLE IX-17. Alkoxy- and Aryloxy-3-aminopyridines (Continued)



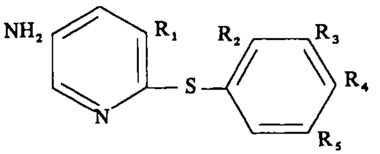
Substituents					
2	4	5	6	Physical properties	Ref.
H	H	H	4-NH_2-2,6-$Cl_2C_6H_2O$	m.p. 147–8° di-*N*-acetyl, m.p. 226–7°	98 631
H	H	H	tetra-*O*-acetyl-1-β-*D*-glucopyranosyloxy	m.p. 59–63°; acetyl, m.p. 176–7° benzoyl, m.p. 253–5°	82
Me	MeO	H	H	m.p. 102–4.5°	632
MeO	H	H	Br	m.p. 78–9°	388
MeO	H	H	CH_3	m.p. 74–5°	388
MeO	H	H	CH_3O	b.p. 116–17°/10 mm; m.p. 43–5°; acetyl, m.p. 85–7°	388
H	H	Br	C_2H_5O	m.p. 142–4°	61
H	H	Cl	4-NH_2-2-ClC_6H_3O	m.p. 164–5° di-*N*-acetyl, m.p. 171–2°	98 631
H	H	Cl	4-NH_2-2,6-$Cl_2C_6H_2O$	m.p. 215–16° di-*N*-acetyl, m.p. 252–3°	98
Me	EtO	H	Me	m.p. 62–3°	105
H	MeO	MeO	Me	b.p. 140–1°/15 mm; HCl, m.p. 163–4°	388

TABLE IX-18. Alkoxy- and Aryloxy-4-aminopyridines



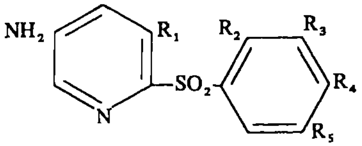
Substituents					
2	3	5	6	Physical properties	Ref.
MeO	H	H	H	m.p. 88–9°; 1-oxide	388, 389, 633
				acetyl, m.p. 93°	389
EtO	H	H	H	m.p. 87–9°	28, 33, 35
H	EtO	H	H	–	35
MeO	H	H	Me	m.p. 98–9°	388
MeO	H	H	MeO	m.p. 82–3°	388

TABLE IX-19. 5-Amino-2-arylthiopyridines and Other Thioaminopyridines



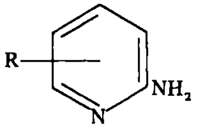
R_1	R_2	R_3	R_4	R_5	m.p.	Acetate m.p.	Ref.
H	H	H	OH	H	169–70°	168–9°	98
Cl	H	H	OH	H	217–18°	192–3°	98
H	Cl	H	Cl	H	84–5°	125–6°	98
H	Cl	H	OH	H	205–8°	159–60°	98
H	H	Cl	OH	H	148–9°	169–70°	98
H	H	Cl	H	Cl	87–8°	–	98
Cl	Cl	H	Cl	H	114–15°	121–2°	98
Cl	Cl	H	OH	H	172–4°	217–18°	98
Cl	H	Cl	Cl	H	103–4°	118–19°	98
Cl	H	Cl	OH	H	171–2°	137–8°	98
Cl	H	Cl	H	Cl	129–30°	148–9°	98
H	Cl	H	OH	Cl	213–14°	–	98
H	H	Cl	OH	Cl	222–3°	172–3°	98
Cl	Cl	H	OH	Cl	178–9°	137–8°	98
Cl	H	Cl	OH	Cl	223–4°	167–8°	634
4-(2′-Bromophenylthio)					–	–	449
2-Methylthio-3-(2,4-dinitrophenyl)amino-5-chloropyridine					223–24°	–	168

TABLE IX-20. 5-Amino-2-pyridyl aryl sulfones



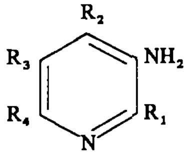
R_1	R_2	R_3	R_4	R_5	m.p.	Acetate m.p.	Ref.
H	H	H	H	H	–	–	98
H	H	H	OH	H	219–20°	97–8°	98
Cl	H	H	OH	H	214–15°	–	98
H	Cl	H	Cl	H	166–7°	195–6°	98
H	Cl	H	OH	H	216–7°	–	98
H	H	Cl	Cl	H	242–3°	153–4°	98
H	H	Cl	OH	H	232–3°	107–8°	98
H	H	Cl	H	Cl	104–5°	138–9°	98
Cl	Cl	H	Cl	H	185–6°	–	98
Cl	Cl	H	OH	H	276–7°	–	98
Cl	H	Cl	Cl	H	212–13°	183–4°	98
Cl	H	Cl	OH	H	211–13°	263–4°	98
Cl	H	Cl	H	Cl	184–5°	–	98
H	Cl	H	OH	Cl	230–1°	157–8°	98
H	H	Cl	OH	Cl	232–3°	227–8°	98
Cl	H	Cl	OH	Cl	238–9°	213–14°	98

TABLE IX-21. Miscellaneous 2-Aminopyridines



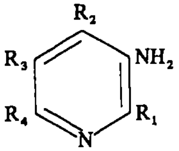
Substituents					
3	4	5	6	Physical properties	Ref.
CHO	H	H	H	m.p. 86–8°	422
CHO	H	H	Ph	m.p. 124–5°	422
H	H	H	COOH	m.p. 317–19° acetyl, m.p. 227–9°	285
H	H	H	COOMe	m.p. 88° acetyl, m.p. 180°	285
H	H	H	COOEt	m.p. 56°	285
H	H	H	$CONH_2$	–	285
H	H	H	$(-N{=}\underset{\underset{Me}{\mid}}{C}-CH_2-COOEt)$	m.p. 68–70°	414
H	H	H	C_6H_5S	m.p. 117–7.5°	6
H	H	H	β-(o–$NH_2C_6H_4Et$)	m.p. 96–7°	635
H	H	H	(2-ethoxalyl-propylamido)	m.p. 245°	415
NO_2	–S–	H	H	m.p. 98°	38
COOEt	H	2-naphthylazo	H	m.p. 25°	9
H	OH	H	Me	nitrate, m.p. 250–1°; picrate, m.p. 182–3°	15

TABLE IX-22. 3-Aminopyridinecarboxylic Acids and Esters



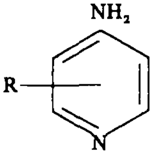
R_1	R_2	R_3	R_4	Physical properties	Ref.
COOH	H	H	H	m.p. 210°	62
Me	H	COOH	H	m.p. 217°	95
				$0.5\ H_2SO_4$,	378, 391
				m.p. 262–3°	392
H	COOH	COOH	H	H_2O, m.p. 240–5°	286
Me	H	COOH	OH	m.p. 319–20°	391
Me	H	COOH	Cl	m.p. 227–8°	378, 391, 392
COOH	COOEt	CN	H	m.p. 160–2°	286
Me	COOH	COOH	H	H_2O, m.p. 233–5° (dec.)	641
COOH	COOH	COOH	H	H_2O, m.p. 205–10°	286
Me	COOH	COOH	Cl	m.p. 218–20°	636
H	COOEt	CN	H	m.p. 129–31°	286
H	COOMe	COOMe	H	m.p. 74–6°	286
Me	COOEt	CN	H	m.p. 130–1°	77
CHO	COOEt	CN	H	m.p. 85–8°	286
OH	COOEt	CN	H	m.p. 235–40°	286
Me	CO_2Me	CN	Cl		391
CHO	COOEt	CN	Cl	m.p. 131–2°	286
Me	COOMe	COOMe	Cl	m.p. 121–2°	636

TABLE IX-23. Miscellaneous 3-Aminopyridines



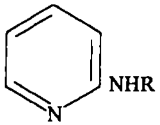
R_1	R_2	R_3	R_4	Physical properties	Ref.
H	OH	H	H	*N*-benzyl, m.p. 161–2°	89
OH	H	H	Pr	m.p. 167–8°	480
H	OH	I	H	*N*-benzyl, m.p. 232–3°	89
Me	CH_2CHO	H	H	phenylhydrazone	99
Me	CH_2OH	CH_2OH	H	m.p. 150–60°; picrate, m.p. 214.5–16.5°; HCl, m.p. 160–70°	636
Me	Me	NH_2CH_2	H	di-HCl, m.p. 310° dipicrate, m.p. 225°	513 78, 314
Me	CF_3	NH_2CH_2	H	tri-HCl, m.p. 276–8°	639
Me	CH_2OMe	NH_2CH_2	H	di-HCl, m.p. 230–1°; dipicrate, m.p. 214–15°	78
Me	CH_2OEt	NH_2CH_2	H	di-HCl, m.p. 127°	78
Me	CH_2OEt	CN	H	m.p. 80°	77
Me	CH_2OEt	CN	Cl	m.p. 146°	78
1-(2-Pyridone)	H	H	H	acetyl, m.p. 243–4°	116
H	H	H	1-(2-Pyridone)	acetyl, m.p. 210–11°	116
2'-Pyridyl	H	H	H	m.p. 105–8°	169
(3'-Nitro-2'-pyridyl)	H	H	H	m.p. 167–8°	169, 170
(5'-Nitro-2'-pyridyl)	H	H	H	m.p. 176–7°	169
(5'-Methyl-3'-nitro-2'-pyridyl)	H	H	H	m.p. 145–6°	169
(3'-Methyl-5'-nitro-2'-pyridyl)	H	H	H	m.p. 159–60°	169
(1-Pyrrolidinyl)	H	H	H	m.p. 70°; picrate, m.p. 184°	637, 638
H	(1-Pyrrolidinyl)	H	H	b.p. 150°/1.1 mm; picrate, m.p. 170°	637, 638
2,4-Dinitrophenyl	H	Cl	H	m.p. 183–4°; picrate, m.p. 170°; acetyl, m.p. 162–4°	168

TABLE IX-24. Miscellaneous 4-Aminopyridines



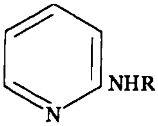
Substituents					
2	3	5	6	Physical properties	Ref.
COOH	H	H	H	m.p. 319°; amide, m.p. 169°	365
H	COOH	H	H	1-oxide, m.p. 270.5°	42
CN	H	H	H	m.p. 145°	365
Me	SO_3H	H	Me	m.p. 293–5°	106
OH	H	H	OH	–	390
OH	p-$ClC_6H_4N{=}N-$	H	OH	m.p. 315° (dec.)	390
OH	NO	H	H	m.p. 330° (dec.)	375
2-[(5-Nitro-2-furyl)vinyl]	H	H	H	m.p. 203°; acetyl, m.p. 223–5°	316
1-(2-Pyridone)	H	H	H	m.p. 169.5–70°; picrate, m.p. 256–8° (dec.)	116
H	HgCl	H	H	m.p. 293–5°	642
H	HgSCN	H	H	m.p. 195°	642
H	HgCl	Cl	H	m.p. 283–5°	642

TABLE IX-25. 2-Alkylaminopyridines



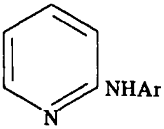
R	Physical properties	Ref.
β-Acetoxy-β-phenylethyl		146
Allyl	b.p. 108°/12 mm	447
	b.p. 56–8°/1 mm; picrate, m.p. 151–2°	141
2-Aminoethyl		643
1-(3-Amino)propyl		643
n-Butyl	b.p. 100–5°/0.4 mm; b.p. 90–100°/0.6 mm	128
	dipicrate, m.p. 181–3°	60
β-(*N*-Butylcarbamoyloxy)-β-phenylethyl	m.p. 95–8°	146
3-(9-Carbazoyl)propyl	m.p. 98.9°	323
Carboxymethyl	HCl, m.p. 206°; picrate, m.p. 199°	289
β-[β-Chloro)phenethyl]	picrate, m.p. 170°	137
(5-Chloro-1-indanyl)	b.p. 160–70°/0.5 mm; m.p. 117°	155
1-Cyanoethyl	m.p. 133–5°	289
Cyanomethyl	m.p. 126°	289
Cyclohexyl	m.p. 124–5°; picrate, m.p. 184–5°	60, 142
2-(Diethylamino)ethyl	b.p. 110–15°/0.6 mm; dipicrate, m.p. 197–8° n_D^{20} 1.5270	60
Dihydro-β-ionyl	b.p. 180°/0.5 mm	644, 645
2-(Dimethylamino)ethyl	b.p. 96–102°/0.4 mm n_D^{20} 1.5412 di-HCl, m.p. 221–3°	60
Dimethylaminovinyl	m.p. 113–15°	165
Dodecyl	b.p. 160–85°/0.6 mm m.p. 57–9° dipicrate, m.p. 134–5°	60, 129

TABLE IX-25. 2-Alkylaminopyridines (Continued)



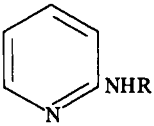
R	Physical properties	Ref.
Ethyl	HCl, m.p. 138–40°	60
β-Hydroxy-β-cyclohexylethyl	m.p. 86–8°; HCl, m.p. 143–4°	146
β-Hydroxy-β, β-diphenylethyl	m.p. 167–9° HCl, m.p. 201–2°	146
6-β-Hydroxy-β-phenylethyl	m.p. 83–5°; HCl, m.p. 140–2°	146
β-[(β-Hydroxyl)phenethyl]	m.p. 84°; picrate, m.p. 151–2°	137
2-Hydroxypropyl	HCl, m.p. 164–5°	331
1-Indanyl	b.p. 140–50°/0.2 mm; m.p. 126°	155
Isopropyl	b.p. 84–6°/4–5 mm	142, 144
(2-Isopropyl-2-propynylamino)ethyl	tri-HCl, m.p. 209–10°	135
2-(7-Methoxy-1-naphthyl)ethyl	HCl, m.p. 168.5–9.5°	519
Methyl	b.p. 84–5°/15 mm;	509
	1-oxide, m.p. 67–8°; picrate, m.p. 156–8°	280, 434
Methylcyclohexyl	m.p. 163°	176
1-Methyl-3-(2,6,6-trimethyl-1-cyclohexen-1-yl)propyl		644
1-Methyl-3-(2,6,6-trimethyl-1-cyclohexyl)propyl		644
3-(10-Phenothiazinyl)propyl	m.p. 98–9°; HCl, m.p. 172°	323
Propyl	b.p. 110–11°/15 mm; picrate, m.p. 149–50.5°	434
	b.p. 66–7°/1.5 mm; picrate, m.p. 148.5–9.5°	141
Tetrahydro-β-ionyl	b.p. 132–4°/0.03 mm	644

TABLE IX-26. 2-Arylaminopyridines



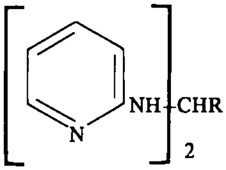
R	Physical properties	Ref.
5-Chloroindol-1-yl	m.p. 117° b.p. 170°/0.5 mm;	154
4-(7-Chloroquinolyl)	m.p. 171°	138
5-Chloro-2-thienyl	b.p. 163–8°/1.9 mm m.p. 87–90°;	462
3-Cyano-2-pyridyl	m.p. 350°	151
1-(1'-Cyclohexyl-5'-tetrazolyl)-2-methyl-2-propyl	m.p. 166–8°	312
5-(5'-Nitro-2'-furyl)-1,3,4-thiadiazol-2-yl	m.p. 330–40°	646–649
1-Indolyl	b.p. 140–50°/0.2 mm; m.p. 126°	154

TABLE IX-27. 2-Aralkylaminopyridines



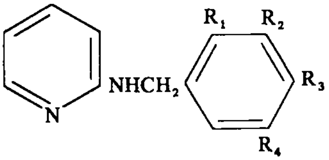
R	Physical properties	Ref.
1,4-Benzodioxan-2-ylmethyl	HCl, m.p. 265–7°	581
Benzyl	b.p. 116–31°/0.6 mm; m.p. 94–5°	131
α-Cyanobenzyl	m.p. 210–11°	289
α-[*p*-(β-Diethylaminoethoxy)-phenyl]-β-phenylethyl	m.p. 75–6°	579
2-Diphenylmethyl	m.p. 100–1°; HCl, 197–8°	331
α-Hydroxybenzyl	m.p. 123–4°	146
(2-Ethyl-3-benzofuranyl)methyl	b.p. 118–25°/0.001 mm	650
(4-Methylthiobenzyl)	m.p. 128°	299
m-Nitrobenzylidene		300
p-Nitrobenzylidene	0.5 H_2O, m.p. 147°	652
Phenethyl	m.p. 112–13°	137
(2-Phenyl-1,3-dioxolan-2-yl-methyl)	b.p. 140–65°/0.3 mm; m.p. 29°; picrate, m.p. 143–4°	153, 651
1-Pyrenylmethylene	m.p. 158–60°	298, 653

TABLE IX-28. 2,2′-(Alkylidenediamino)dipyridines[290]



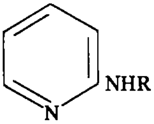
R	m.p.	R	m.p.
Amyl	100°	Hexyl	92°
Butyl	122°	Methyl	122°
Isobutyl	108°	Nonyl	72°
Decyl	66°	Octyl	76°
Ethyl	154°	Propyl	110°
Heptyl	81°	Isopropyl	146°

TABLE IX-29. 2-(Alkoxybenzyl)aminopyridines



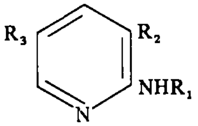
R_1	R_2	R_3	R_4	b.p./10 mm	m.p.	Ref.
MeO	H	H	H	181–4°	120–1°	171
EtO	H	H	H	184–7°	90–1°	171
n-PrO	H	H	H	190–3°	87–8°	171
IsoPrO	H	H	H	186–9°	105–6°	171
n-BuO	H	H	H	202–5°	86–7°	171
IsoBuO	H	H	H	188–91°	109–10°	171
n-Pentyloxy	H	H	H	206–9°	80–1°	171
isoPentyloxy	H	H	H	207–10°	87–8°	171
MeO	H	H	F	–	77°	654
EtO	H	H	F	–	77.5°	654
n-PrO	H	H	F	–	70°	654
n-BuO	H	H	F	–	58°	654
H	F	MeO	H	–	113°	654
H	F	EtO	H	–	88.5°	654
H	F	*n*-PrO	H	–	75°	654
H	MeO	MeO	H	–	–	72
H	MeO	MeO	MeO	–	167–8°	72

TABLE IX-30. Halo-2-alkylaminopyridines



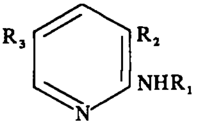
Substituents						
R	3	4	5	6	Physical properties	Ref.
Pr	H	H	Br	H	m.p. 40.3–41°; picrate, m.p. 146–7°	141
Pr	H	H	Cl	H	m.p. 31.5–32°; picrate, m.p. 138–9°	140
Pr	Br	H	Br	H	b.p. 95–6°/2 mm; picrate, m.p. 119.5–20.5°	141
Pr	Cl	H	Cl	H	b.p. 100–2°/2 mm; picrate, m.p. 199–201° (dec.)	140

TABLE IX-31. Nitro Secondary 2-Aminopyridines



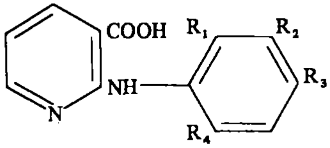
R_1	R_2	R_3	m.p.	Ref.
Benzyl	NO_2	H	80°	157
p-Chlorobenzyl	NO_2	H	105°	157
3,4-Dimethoxy-β-phenethyl	NO_2	H	110°	655
4-Dimethylamino-β-phenethyl	NO_2	H	110°	655
3,4-Dimethyl-β-phenethyl	NH_2	H	98–9°	655
Dodecyl	NO_2	H	102°	655
β-Hydroxy-β-phenethyl	NO_2	H	90–2°	655
2-(3-Indolyl)ethyl	NO_2	H	161°	655
Phenethyl	NO_2	H	85–6°	655
Benzyl	H	NO_2	131–4°	656
4-Dimethylaminophenyl	H	NO_2	187–9°	656
β-Hydroxy-β-phenethyl	H	NO_2	137–8°	655
Morpholino	H	NO_2	142–3°	656
Methyl	H	NO_2	180–1°	457, 656

TABLE IX-31. Nitro Secondary 2-Aminopyridines (Continued)



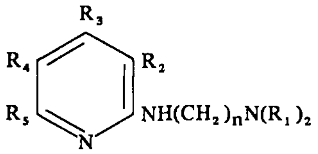
R$_1$	R$_2$	R$_3$	m.p.	Ref.
2,2′-(*p,p*′-Methylenedianilino)-bis	H	NO$_2$	203–7°	656
Phenyl	H	NO$_2$	136°	723
			110°	166
Piperazino	H	NO$_2$	84–5°	656
p-Tolyl	H	NO$_2$	136–7°	656
p-Acetamidophenyl	NO$_2$	NO$_2$	276°	176
p-Acetophenyl	NO$_2$	NO$_2$	186°	180
o-Anisyl	NO$_2$	NO$_2$	200°	176
Benzyl	NO$_2$	NO$_2$	112°	176
p-Chlorophenyl	NO$_2$	NO$_2$	178°	176
Cyclohexyl	NO$_2$	NO$_2$	117°, 116–7°	176, 180
Ethyl			103–4°	180
β-Hydroxyethyl	NO$_2$	NO$_2$	104°	176
Methyl	NO$_2$	NO$_2$	163°	176
			148°	493
			142–3°	180
α-Naphthyl	NO$_2$	NO$_2$	234°	176
β-Naphthyl	NO$_2$	NO$_2$	229°	176
o-Nitrophenyl	NO$_2$	NO$_2$	167°	176
m-Nitrophenyl	NO$_2$	NO$_2$	158°	176
p-Nitrophenyl	NO$_2$	NO$_2$	200°	176
1-Piperidinyl	NO$_2$	NO$_2$	138–9°	180
Phenyl	NO$_2$	NO$_2$	149°	176
p-$NH_2SO_2C_6H_4$	NO$_2$	NO$_2$	249°	176
p-$H_2O_3AsC_6H_4$	NO$_2$	NO$_2$	>300°	176
o-$HO_2CC_6H_4$	NO$_2$	NO$_2$	239°	176
p-$HO_2CC_6H_4$	NO$_2$	NO$_2$	298°	176
o-$CH_3O_2CC_6H_4$	NO$_2$	NO$_2$	163°	176
p-$C_2H_5O_2CC_6H_4$	NO$_2$	NO$_2$	160°	176
[(2-C_5H_4N)CONH–]	NO$_2$	NO$_2$	229°	176
o-Tolyl	NO$_2$	NO$_2$	170°	176, 180
p-Tolyl	NO$_2$	NO$_2$	162°	176, 180

TABLE IX-32. 2-Anilinonicotinic Acids



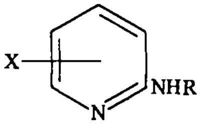
R_1	R_2	R_3	R_4	m.p.	Ref.
Me	H	H	H	107–8°	151
OH	H	H	H	234–5°	452
H	CF_3	H	H	204°	452
H	H	MeO	H	208°	452
H	H	EtO	H	202°	452
Me	Me	H	H	248°	452
				acetyl deriv.	452
				m.p. 195°	452
Me	H	Cl	H	208–9°	452
OH	H	Cl	H	276°	452
Me	H	H	Me	219–20°	452
H	OH	CO_2Me	H	218°	452
Me	H	Me	H	245–50°	151

TABLE IX-33. 2-Dialkylaminoalkylaminopyridines



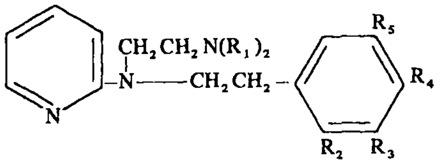
n	R_1	R_2	R_3	R_4	R_5	Physical properties	Ref.
2	Me	H	H	H	Me	b.p. 105–15°/0.6 mm di-HCl, m.p. 226–8°	131 128
2	Me	H	H	H	Cl	b.p. 124–6°/0.16 mm; picrate, m.p. 151–2°	156
2	Me	H	H	H	BuO	b.p. 127–9°/.05 mm; HCl, m.p. 104–5°	156
2	Et	NH_2	H	H	H	b.p. 140°/0.05 mm	80
2	Et	H	H	H	Cl	b.p. 150–2°/0.18 mm; picrate, m.p. 118–19°	156
2	Et	H	H	H	BuO	b.p. 163–5°/0.2 mm; HCl, m.p. 76–7°	156
2	Et	NO_2	H	H	H	b.p. 120°/0.05 mm m.p. 58–9°	80, 149 494
2	Me	NH_2	NO_2	H	H	m.p. 137–8°	494
2	Me	NO_2	NO_2	H	H	HCl, m.p. 268–70°	494
2	Et	NH_2	NO_2	H	H	m.p. 83° HCl, m.p. 200–5°	80 494
2	Et	NO_2	NO_2	H	H	m.p. 66°; HCl, m.p. 179–80°	80, 149, 494
2	Et	NO_2	H	NO_2	H	m.p. 66°	181
3	Me	H	H	H	Cl	b.p. 176–82°/11 mm	657
3	Me	H	H	NO_2	H	m.p. 64°	143
3	Et	H	H	NO_2	H	m.p. 78–80°	143
3	Morpholino	H	H	NO_2	H	m.p. 102°; picrate,	143
3	Piperidino	H	H	NO_2	H	m.p. 112° m.p. 80–2°; picrate, m.p. 195°	143
3	CH_2CH_2Cl	H	H	H	H	m.p. 144–6°	658

TABLE IX-34. Nuclear Substituted Secondary 2-Aminopyridines



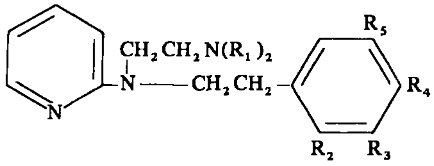
R	Substituents				Physical properties	Ref.
	3	4	5	6		
Allyl	H	H	H	H	b.p. 56–8°/1 mm; picrate, m.p. 151–2°	141
Allyl	H	H	Cl	H	b.p. 98–9°/2 mm; picrate, m.p. 150–1°	140
Allyl	H	H	Br	H	m.p. 50°–50.7°; picrate, m.p. 170–70.5°	141
Allyl	Cl	H	Cl	H	b.p. 111–13°/6 mm; picrate, m.p. 201–3°	140
Allyl	Br	H	Br	H	b.p. 108–10°/1.5 mm picrate, m.p. 125.5–6.5°	141
Pr	H	H	Br	H	m.p. 40.3–41°; picrate, m.p. 146–7°	141
Bu	H	H	H	Cl	b.p. 99–105°/0.02 mm; benzoate, m.p. 91–2°	156
Bu	NO_2	H	Me	Me	b.p. 26°	608
Benzyl	H	Isopentyl	H	H	b.p. 24°–50°/20 mm	13
Benzyl	H	Pentyl	H	H	b.p. 25°/23 mm	13
Benzyl	H	5-Nonyl	H	H	b.p. 220–30°/10 mm	13
Benzyl	NO_2	H	Me	Me	m.p. 104–5°	608
5-Chloro-2-pyridyl	Me	H	H	H		170
6-(β-Hydroxy-β-phenylethyl-)	H	H	Me	H	m.p. 97–9°; HCl, m.p. 116–17°	146
2-(β-Hydroxy-β-phenylethyl-)	H	H	Cl	H	m.p. 102–3°; HCl, m.p. 177–8°	146
2-(β-Hydroxyl-β-phenylethyl-)	H	H	Br	H	m.p. 110–11°; HCl, m.p. 187–9°	146
6-(β-Hydroxy-β-phenylethyl-)	Me	H	Me	H	m.p. 77–8°; HCl, m.p. 132–3°	146
2-MeS-3-pyridyl	Me	H	NO_2	H		170
2-MeS-3-pyridyl	NO_2	H	Me	H		170
p-Methoxybenzyl	H	Heptyl	H	H	b.p. 225–30°/2 mm	13
3-Me-2-pyridyl	H	H	Cl	H	m.p. 68–9°	723
Phenethyl	NO_2	H	Me	Me	m.p. 93°	608
Phenyl	Cl	H	H	H	m.p. 49–50°	723
4-Pyridylmethyl	H	Me	H	H		659
$CH_2CH_2N(CH_3)_2$ $C_6H_4OCH_3$-*p*	H	H	H	BuO	b.p. 195–200°/0.4 mm HCl, m.p. 129–30°	156

TABLE IX-35. 2-[(*N*-Benzyl-*N*-(β-dialkylaminoethyl)]aminopyridines



R_1	R_2	R_3	R_4	R_5	b.p./mm	HCl m.p.	di-HCl m.p.	Ref.
Et	Br	H	H	H	210°/1	145°	–	181, 660
Et	EtO	H	H	F	169°/0.5	118°	–	654
Et	MeO	H	H	F	166°/0.1	138.5°	121°	654
Et	H	Br	H	H	210°/1	–	–	181, 660
					perchlorate, m.p. 88°			181
					maleate, m.p. 110°			
Et	H	F	EtO	H	180°/0.1	127°	115°	654
Et	H	F	MeO	H	178°/0.09	128°	110°	654
Et	H	H	Br	H	210°/1	–	–	181, 660
					perchlorate, m.p. 123°			181
					maleate, m.p. 115°			
					citrate, m.p. 127°			
Et	H	H	BuO	H	217–20°/1	–	–	171
Et	H	H	isoBuO	H	214–17°/1	–	–	171
Et	H	H	EtO	H	200–3°/1	–	–	171
Et	H	H	MeO	H	195–8°/1	–	–	171
Et	H	H	$C_5H_{11}O$	H	221–4°/1	–	–	171
Et	H	H	iso$C_5H_{11}O$	H	217–20°/1	–	–	171
Et	H	H	PrO	H	208–11°/1	–	–	171
Et	H	H	isoPrO	H	202–5°/1	–	–	171

TABLE IX-35. 2-[*N*-Benzyl-*N*-(β-dialkylaminoethyl)]aminopyridines (Continued)



R_1	R_2	R_3	R_4	R_5	b.p./mm	HCl m.p.	di-HCl m.p.	Ref.
Me	BuO	H	H	F	171°/0.5	105°	–	654
Me	EtO	H	H	F	159°/0.6	152°	116°	654
MeO	MeO	H	H	F	163°/0.1	174°	143°	654
Me	PrO	H	H	F	164°/0.6	114°	–	654
Me	H	F	BuO	H	182°/0.5	108°	–	654
Me	H	F	EtO	H	161°/0.4	144°	108°	654
Me	H	F	PrO	H	170°/0.5	116.5°	76°	654
Me	H	H	n-BuO	H	221–4°/1	–	–	171
Me	H	H	isoBuO	H	218–21°/1	–	–	171
Me	H	H	EtO	H	202–5°/1	–	–	171
Me	H	H	MeO	H	198–210°/1	–	–	171
Me	H	H	n-$C_5H_{11}O$	H	226–9°/1	–	–	171
Me	H	H	isoC_5H_{11}	H	223–6°/1	–	–	171
Me	H	H	PrO	H	208–11°/1	–	–	171
Me	H	H	isoPr	H	204–7°/1	–	–	171
Me	Me	H	Me	H	160°/0.5	–	222°	154
Morpholino	MeO	H	H	F	200°/0.6	171°	138°	654
Morpholino	H	F	MeO	H	208°/0.2	158.5°	139°	654
Piperidino	MeO	H	H	F	182°/0.4	179°	126.5°	654
Piperidino	H	F	MeO	H	202°/0.2	165°	124°	654

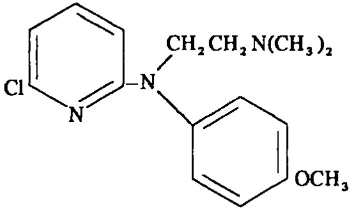
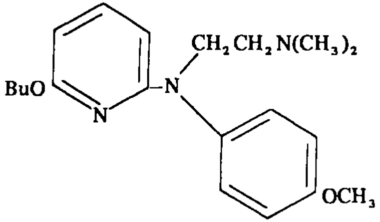
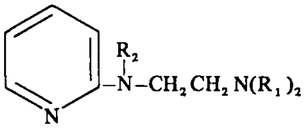
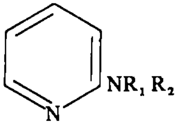
isoPr	MeO	H	H	F	171°/0.5	143°	122°	654
isoPr	H	F	MeO	H	188°/0.2	140°	117°	654
					170–4°/0.2; (picrate, m.p. 101–2°)				156
					195–200°/0.4; (HCl, m.p. 129–30°)				156

TABLE IX-36. Other 2-*N*-Substituted-*N*-(β-dialkylaminoethyl)aminopyridines



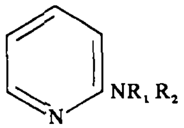
R_1	R_2	Physical properties	Ref.
Et	*p*-AnisylCOCH$_2$	b.p. 189–92°	661
Et	β-Hydroxy-β-Phenethyl	–	183
Me	4-Bromophenethyl	b.p. 160–5°/0.1 mm; HCl, m.p. 178°	154
Me	5-Bromo-2-selenophenyl	b.p. 194°/4 mm;	185
Me	4-Chlorophenethyl	b.p. 145–50°/0.1 mm; HCl, m.p. 171°	154, 182
Me	5-Chloro-1-indanyl	b.p. 160–70°/0.2 mm; HCl, m.p. 191°	154, 155
Me	5-Chloro-2-selenophenyl	b.p. 199–200°/4.5 mm	185
Me	5-Chloro-2-thienyl	b.p. 162–6°/0.75 mm; n_D^{25} 1.5860; citrate, m.p. 114–16°	462
Me	4-Fluorophenethyl	b.p. 190–200°/10 mm,	154
		b.p. 122°/0.1 mm; di-HCl, m.p. 156°	182
Me	1-Indanyl	b.p. 156°/0.2 mm; HCl, m.p. 186°	154, 155
Me	α-Phenethyl	b.p. 140°/0.15 mm; HCl, m.p. 160°	182
Me	2-Thienyl	–	462
Me	α-(*p*-Tolyl)ethyl	b.p. 160°/0.5 mm; di-HCl, m.p. 222°	182

TABLE IX-37. Other Tertiary 2-Aminopyridines



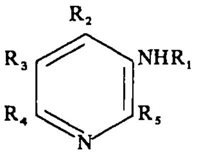
		Substituents					
R_1	R_2	3	4	5	6	Physical properties	Ref.
Me	Me	H	NO_2	H	H	m.p. 99°, 98–9°; 1-oxide, m.p. 126°	107, 177
Me	Me	H	H	NO_2	H	m.p. 154–5° m.p. 150–1°	656, 179 180
Me	Me	H	H	H	2-Amino-propyl	b.p. 94–6°/1.3 mm	662
Me	Me	H	H	H	Me	–	662
Me	Me	Me	H	NO_2	H	m.p. 181–91°	656
Me	Me	NO_2	H	NO_2	H	m.p. 124–5°, 119°, m.p. 118–19°	175, 176 180
Me	Me	Me	H	NO_2	H	m.p. 181–91°	656
Me	Me	H	H	H	H	2-*N*-oxide; m.p. 59–60°; picrate, m.p. 132–4°	280
Me	Ph	NO_2	H	NO_2	H	m.p. 134–35°	180
Me	Ph	H	H	NO_2	H	m.p. 102–4°	656
Me	2-Amino-3,5-dibromobenzyl	H	H	H	H	HCl, m.p. 198.5–201° HBr, m.p. 208–11°	664
Me	β-Hydroxyl-β-phenethyl	H	H	H	H	b.p. 147–57°	146
Me	1-Pyrenylmethyl	H	H	H	H	m.p. 165–7°; m.p. 158–60°	298, 653
Et	Et	NH_2	H	H	H	m.p. 260°; diazonium salt, m.p. 165°	656

TABLE IX-37. Other Tertiary 2-Aminopyridines (Continued)



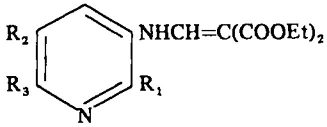
		Substituents					
R_1	R_2	3	4	5	6	Physical properties	Ref.
Et	Et	NO_2	H	H	H	m.p. 154–5°	656
Et	Et	H	NO_2	H	H	m.p. 33°; 1-oxide, m.p. 90°	107
Et	Et	NO_2	H	NO_2	H	m.p. 62°, 59°	181, 176
Et	Ph	NO_2	H	NO_2	H	m.p. 135°	176
Bu	Bu	2-Chloroethyl	Me	H	Cl	b.p. 175°	663
Bu	Bu	Et	Me	H	H	b.p. 132–4°/4 mm; picrate, m.p. 139–40°	150
Bu	Bu	H	Me	2-Chloro-ethyl	H	b.p. 138–40°/13 mm; HCl, m.p. 133–4°	150
Bu	Bu	H	Me	Et	H	picrate, m.p. 143–4°	150
Bu	Bu	H	Me	Vinyl	Cl	b.p. 168°/6 mm	150
Ph	$(CH_2)_2-$ $-N[CH(CH_3)-$ $-CH_2Ph]$	H	H	H	H	maleate, m.p. 136–8°	322
Ph	Ph	Vinyl	Me	H	Cl	b.p. 220–1°/0.5 mm m.p. 182–3°	663
Me	Ph	NO_2	H	NO_2	H	m.p. 134–5°	180
CN	Ph	H	Ph	H	H	m.p. 92°	186
CN	Ph	H	Me	H	Me	b.p. 120°/0.1 mm	186
CN	Ph	H	H	H	H	m.p. 52°	186
CN	o-ClC_6H_4	H	H	H	H	m.p. 116°	186
CN	p-ClC_6H_4	H	H	H	H	m.p. 105°	186
CN	2,4-$Me_2C_6H_3$	H	H	H	H	m.p. 58°	186

TABLE IX-38. Secondary 3-Aminopyridines



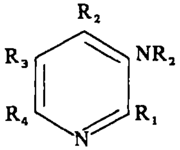
R_1	R_2	R_3	R_4	R_5	Physical properties	Ref.
Benzyl	NO_2	H	H	H	1-oxide, m.p. 189°	178
[2-(1,4-Benzodioxan-2-yl)ethyl] –	H	H	H	H	HCl, m.p. 104–5°	666
Cetyloxypropyl	H	H	H	H	b.p. 210–13°/10 mm; m.p. 30°	514
Cyclohexyl	NO_2	H	H	H	1-oxide, m.p. 197–9°	178
2-Dimethylaminopropyl	2-bromo-4-chlorophenylthio	H	H	H	b.p. 208–11°/0.3 mm	449
2-Dimethylaminopropyl	2-bromophenylthio	H	H	H	b.p. 198–202°/0.3 mm	448
3-Dimethylaminopropyl	2-bromo-4-chlorophenylthio	H	H	H	b.p. 210–15°/0.3 mm	449
2,4-Dinitrophenyl	H	Cl	H	H	methyl sulfonyl, m.p. 211–13°	168
Et	H	NO_2	H	H	m.p. 96°	50
Et	H	H	H	Me	b.p. 104–5°; picrate, m.p. 207–8°	555
α-Hydroxyethyl	H	NO_2	H	H	m.p. 129°	50
Me	Me	H	H	H	b.p. 116°/10 mm; picrate, 230°; HCl, m.p. 278–9°	515, 665
Me	NO_2	H	H	H	1-oxide m.p. 227°	152
Me	H	H	H	Me	m.p. 61–2°; picrate, m.p. 209°	555
Me	H	Cl	H	Br	m.p. 43–4°	41
Ph	H	NO_2	Me	Me	1-oxide, m.p. 146°	52
Ph	H	H	Me	H	m.p. 126–6.5°	158
Ph	H	H	H	Me	m.p. 102–3°	158
Ph	H	H	H	H	m.p. 125.5–6°	158
3,4,5-Trimethoxybenzyl	H	H	H	H	m.p. 109–10°	72
Veratryl	H	H	H	H		72

TABLE IX-39. Diethyl (2,6-Disubstituted-3-pyridylamino)-methylene Malonates[407]



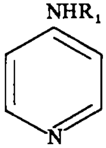
R_1	R_2	R_3	m.p.
Me	H	H	100–100.8°
MeO	H	H	81–3°
H	H	Me	83.6–7.6°
Me	H	Et	85.8–6.2°
Me	H	CH_3CONH	151.6–2.8°
Et	H	Et	81.0–3.6°
CH_3CONH	H	CH_3CONH	217–18°
Me	Me	Me	108–9°

TABLE IX-40. Tertiary 3-Aminopyridines[178]



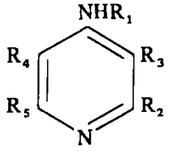
R	R_1	R_2	R_3	R_4	Physical properties
Me	H	NO_2	H	H	1-oxide, m.p. 146°
Et	H	NO_2	H	H	1-oxide, m.p. 73–4°

TABLE IX-41. Secondary 4-Aminopyridines



R_1	Physical properties	Ref.
n-Butyl	1-oxide, picrate, m.p. 189–90°	43
4-Carbethoxyphenyl	m.p. 197–8°	164
4-Carboxyphenyl	m.p. above 250°	164
4-Chlorophenyl	m.p. 245–7°	164
2-(3,4-Dihydroxyphenyl)ethyl	HBr, m.p. 140°	655
2-(3,4-Dimethoxyphenyl)ethyl	oil	655
Dodecyl	m.p. 83–4°; picrate, m.p. 94.2–5.4°	147
Ethyl	1-oxide, m.p. 117–18°; picrate, m.p. 182–3°	43
Hydroxy	1-oxide, m.p. 237°	43
3-Hydroxyphenyl	m.p. 210–12°	164
4-Methoxyphenyl	m.p. 178–9°	164
Methyl	b.p. 87–90°/6 mm; di-HCl, m.p. 271–2°;	509, 510, 525
	picrate, m.p. 122–4°	118
	1-oxide, m.p. 192–4°	118, 509, 510, 525
β-Phenethyl	m.p. 39°	655
isoPr	m.p. 82–2.5°; picrate, m.p. 118–19°	147
p-$NH_2SO_2C_6H_4$	m.p. 210–212°	164
$C_6H_5CH_2CO$	oil	655
C_6H_3-3,4-$(OCH_3)_2CH_2CO$	HCl, m.p. 203–5°	655

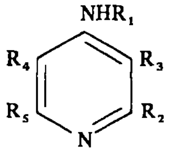
TABLE IX-42. Nuclear Substituted Secondary 4-Aminopyridines



	Substituents					
R_1	R_2	R_3	R_4	R_5	Physical properties	Ref.
Allyl	CCl_3	Cl	Cl	H	m.p. 93–4°	56
2-Aminoethyl	CCl_3	Cl	Cl	H	m.p. 119–20°	56
2-(2-Aminoethyl)-aminoethyl	CCl_3	Cl	Cl	H	HCl, m.p. 170–200°	56
6-Aminohexyl	CCl_3	H	Cl	Cl	–	56
o-Aminophenyl	Me	H	H	Me	m.p. 180–1°	105
o-Aminophenyl	H	NO_2	H	H	m.p. 169–74°	667
3-(3-Aminopropyl)-aminopropyl	CCl_3	Cl	Cl	H	–	56
Amyl	Cl	Cl	H	CCl_3	–	56
p-Aminophenyl	Me	NO_2	H	Me	m.p. 109–10°	105
Benzyl	CCl_3	Cl	Cl	H	m.p. 63.5–4.5°	56
Bis(2-hydroxypropyl)	Cl	Cl	H	CCl_3	–	56
Bu	CCl_3	Cl	Cl	H	m.p. 36–8°	56
3-Carboxyphenyl	H	NO_2	H	H	m.p. 266°	669
Cyclohexyl	CCl_3	Cl	Cl	H	m.p. 72–3°	56
2-Diethylaminoethyl	H	NH_2	H	H	b.p. 155–60°/0.07 mm	80
2-Diethylaminoethyl	H	NO_2	H	H	b.p. 141–3°/0.05 mm	80, 494

2-Diethylaminoethyl	H	Phenyl-acetamide	H	H	m.p. 135–7°	80
2-Diethylaminoethyl	Cl	Cl	H	CCl_3		56
2-Dimethylaminoethyl	H	NH_2	H	H	b.p. 144–8°/0.05 mm	494
2-Dimethylaminoethyl	H	NO_2	H	H	m.p. 97–8.5°	494
2-Dimethylaminoethyl	H	NH_2	NO_2	H	m.p. 98–100°	494
Dodecyl	Cl	Cl	H	CCl_3		56
Et	CCl_3	Cl	Cl	H		56
OH	Me	H	H	H	1-oxide, m.p. 212–14°	109
OH	H	COOH	H	H		42
OH	Me	H	H	Me		73
OH	C_6H_5	H	H	C_6H_5	1-oxide, m.p. 152°	670
OH	CH_3	H	H	NH_2	nitrate, m.p. 250–1°; picrate, m.p.182–3°	43
OH	H	H	H	H	1-oxide, m.p. 237°	108
2-Hydroxycyclo-hexyl	CCl_3	Cl	Cl	H		56
Hydroxyethyl	CCl_3	Cl	Cl	H	m.p. 88–90°	56
2-Hydroxypropyl	Cl	Cl	H	CCl_3		56
β-Hydroxy-β-phenethyl	H	NO_2	H	H	m.p. 174°	655
Hexadecyl	Cl	Cl	Cl	CCl_3	–	56
p-Iodophenyl	H	NO_2	I	H	m.p. 149°	669
Me	H	Br	H	H	m.p. 92°	43
Me	H	NO_2	H	H	m.p. 160°	118, 152, 509, 510, 525
Me	H	CH_3	H	H	m.p. 125–6°; picrate, m.p. 199–200°; 1-oxide, m.p. 94.5–5.5°	43
Me	H	Et	H	H	m.p. 117–18°	214
Me	H	isoPr	H	H	m.p. 95–6°	43

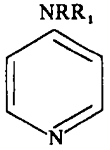
TABLE IX-42. Nuclear Substituted Secondary 4-Aminopyridines (Continued)



Substituents						
R$_1$	R$_2$	R$_3$	R$_4$	R$_5$	Physical properties	Ref.
Me	H	Me	Me	H	m.p. 94.5–5.5°; picrate, m.p. 172–3°	43, 158
Me	CCl_3	Cl	Cl	H	m.p. 140–2°	56
Me	Me	Me	Me	Me	m.p. 118–19°; picrate, m.p. 160–1°; 1-oxide picrate, m.p. 140–1°	43
Me	CCl_3	Cl	Cl	Cl	81–7°	56
6-Me-2-pyridyl	CCl_3	Cl	Cl	H		56
Morpholino	CCl_3	Cl	Cl	H	m.p. 108.5–12°	56
Octadecyl	CCl_3	Cl	Cl	H	m.p. 30–2°	56
Octyl	CCl_3	Cl	Cl	H		56
Octyl	CCl_3	Cl	H	Cl		56
Ph	H	Br	NO_2	H	m.p. 153.5–4°	44
Ph	H	Cl	NO_2	H	m.p. 148–8.5°	44
Ph	H	NO_2	I	H	m.p. 148.5–49°	669
Ph	Me	NO_2	H	Me	m.p. 109–10°	105
Ph	Me	NO_2	Cl	Me	m.p. 114–15°	105
3-Phenylpropyl	H	NO_2	H	H	HCl, m.p. 170–2°	655
Phenylpropylamino	CCl_3	Cl	Cl	H		56
Piperazino	CCl_3	Cl	Cl	H	HCl, m.p. 192–5° (dec.)	56

Propargyl	CCl_3	Cl	Cl	H	m.p. 137–8°	56
2-Pyridyl	Cl	H	Cl	CCl_3		56
2-Pyrimidinyl	Cl	Cl	H	CCl_3		56
Pyrrolidino	Cl	Cl	Cl	CCl_3	m.p. 98–103°	56
CH_2-CH_2R R =						
m-Anisyl	H	NO_2	H	H	HCl, m.p. 223° (dec.)	655
p-Anisyl	H	NO_2	H	H	m.p. 99°	655
3-Benzyloxy-4-methoxyphenyl	H	NO_2	H	H	m.p. 123°	655
3,4-Dichlorophenyl	H	NO_2	H	H	m.p. 189–90°	655
3-Indolyl	H	NO_2	H	H	m.p. 193°	655
α-Naphthyl	H	NO_2	H	H	m.p. 180°	655
β-Naphthyl	H	NO_2	H	H	m.p. 114°	655
N-Phenyl-*N*-piperazinyl	H	NO_2	H	H	m.p. 115–17°	655

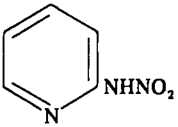
TABLE IX-43. Tertiary 4-Aminopyridines



R	R_1	2	3	5	6	Physical properties	Ref.
n-Bu	*n*-Bu	H	H	H	H	b.p. 124–32°/1.3 mm; picrate, m.p. 124°	147
CH_2CN	CH_2CN	H	H	H	H	m.p. 208–9°	188
Me	Me	Ph	H	H	H	m.p. 83–4°	187
Me	Me	H	Br	H	H	b.p. 82–4°/0.5 mm; picrate, m.p. 182–3°; 1-oxide picrate, m.p. 160–1°	43
Me	Me	H	Et	H	H	b.p. 82–3°/0.8 mm; picrate, m.p. 118–19°; 1-oxide, b.p. 178–80°/1 mm; m.p. 139–40°	43
Me	Me	H	isoPr	H	H	b.p. 79–80°/0.45 mm; picrate, m.p. 138–9°; 1-oxide picrate, m.p. 151–2°	43
Me	Me	H	Me	H	H	b.p. 73–5°/1 mm; picrate, m.p. 172–3°; 1-oxide, b.p. 142–4°/0.15 mm; 1-oxide picrate, m.p. 130–1°	43, 214 43
Me	Me	H	Me	Me	H	b.p. 69–70°; picrate, m.p. 172–73°	43, 214
Me	Me	CCl_3	Cl	Cl	H	m.p. 72–3°	56

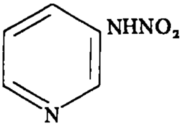
Me	Me	Cl	Cl	Cl	CCl_3	m.p. 52.5–4.5°	56
Me	Me	H	H	H	H	m.p. 110–12°	147
						m.p. 112–13°	118
						m.p. 114°	187
						1-oxide, m.p. 97–9°	281
						picrate, m.p. 204°	118
						picrate, m.p. 206–8°	147

TABLE IX-44. 2-Nitraminopyridines



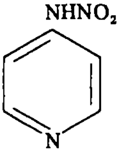
Substituents					
3	4	5	6	Physical properties	Ref.
Br	H	H	H	m.p. 181°	465
NO_2	H	H	H	m.p. 137°	465
H	NO_2	H	H	m.p. 154°	465
H	H	NO_2	H	m.p. 161°	465
H	H	H	Pr	m.p. 97°	480
Me	H	NO_2	H	m.p. 165°	465
H	Me	H	Me	m.p. 154° (dec.)	488
H	H	Me	Me	m.p. 141–2°	608
1-Me-2-pyrrolidinyl	H	1-Me-2-pyrrolydinyl	H		602
NO_2	H	Me	H	m.p. 62°	465
NO_2	Me	H	H	m.p. 162°	465
H	Me	NO_2	H	m.p. 163°	465
H	NO_2	NO_2	H	m.p. 105°	465
H	H	NO_2	Me	m.p. 116°	465
H	Me	Br	Me	m.p. 159–60°	630

TABLE IX-45. 3-Nitraminopyridines



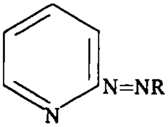
Substituents					
2	4	5	6	Physical properties	Ref.
H	Me	H	H	m.p. 184°	466, 468
H	H	Me	H	m.p. 172°	466
H	NO_2	H	H	m.p. 104°; 1-oxide, m.p. 108°	465
H	H	H	NO_2	m.p. 113° (explosive dec.)	470
H	H	H	Cl	m.p. 179°	60
H	H	EtO	H	m.p. 160°	468
COOH	H	H	H	m.p. 186°	468
H	H	COOH	H	m.p. 201°	468
SO_3H	H	H	H	m.p. 184° (dec.)	467
H	H	H	SO_3H	m.p. 217–20° (dec.)	467
Me	H	H	Me	m.p. 162°	351
Me	Me	H	Me	m.p. 162°	351

TABLE IX-46. 4-Nitraminopyridines



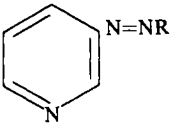
Substituents					
2	3	5	6	m.p.	Ref.
Br	H	H	H	181°	375
Cl	H	H	H	148°	465
I	H	H	H	195°	465
H	Br	H	H	203°	465
H	Cl	H	H	206°	465
H	I	H	H	204°	465
H	Me	H	H	212°	469
H	NO_2	H	H	204°	465
Me	NO_2	H	H	187°	465
Cl	H	H	Cl		87

TABLE IX-47. 2-Azopyridines



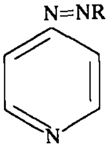
Substituents					
R	3	5	6	Physical properties	Ref.
4-Amino-1-naphthyl	H	H	H	1-oxide, m.p. 192–3°	673
p-Anilino	H	H	H	1-oxide	370, 671, 672
p-Dimethylaminophenyl	H	H	H	m.p. 142–3°	367
2-Hydroxy-1-naphthyl	H	H	H		369
Ph	NH_2	NH_2	MeO	di-HCl, m.p. 141°	674
Ph	NH_2	NH_2	EtO	di-HCl, m.p. 119°	674
Ph	NH_2	NH_2	PrO	di-HCl, m.p. 122°	674
Ph	NH_2	NH_2	BuO	di-HCl, m.p. 126°	674
Ph	NH_2	NH_2	$C_5H_{11}O$	di-HCl, m.p. 96°	674

TABLE IX-48. 3-Azopyridines



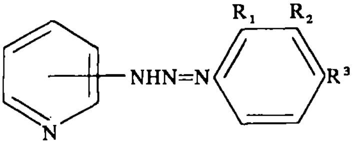
	Substituents					
R	2	4	5	6	Physical properties	Ref.
R_1 = Naphthyl						
4-NH$_2$-1-R$_1$	H	H	H	H	m.p. 185–7°	675
4-NH$_2$-1-R$_1$	H	H	H	Cl	–	673
4-NH$_2$-8-Cl 2-Me-1-R$_1$	H	H	H	H	–	673
Phenyl						
4-Chlorophenyl	NH$_2$	H	H	H	–	676, 677
4-Chlorophenyl	NH$_2$	H	H	NH$_2$	–	676, 677
4(2-Diethylaminoethylamino)phenyl	OH	NH$_2$	H	OH	m.p. 315° (dec.)	390
	NH$_2$	H	H	NH$_2$	m.p. 234°	675
4-(2-Diethylaminoethoxy)phenyl	NH$_2$	H	H	NH$_2$	HCl, m.p. 243°	679
4-Iodophenyl	NH$_2$	H	H	NH$_2$	m.p. 204.5–5°	623 485
2,4,6-Tri-iodophenyl	NH$_2$	H	H	NH$_2$	–	485
Ph	NH$_2$	H	H	NH$_2$	–	678
Ph	Me	Me	H	NH$_2$	m.p. 131–2°	10
R_2 =Pyridyl						
2′-BuO-3′-R$_2$	NH$_2$	H	H	NH$_2$	–	680, 681
6′-BuO-3′-R$_2$	NH$_2$	H	H	NH$_2$	–	330
4′-Cl-5′-I-3′-R$_2$	NH$_2$	H	H	NH$_2$	m.p. 270°	623
4′-Cl-3′-R$_2$	H	Cl	H	H	–	60
5′-Cl-3′-R$_2$	H	H	Cl	H	m.p. 183°	60

TABLE IX-49. 4-Azopyridines



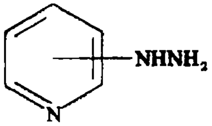
Substituents						
R	2	3	5	6	Physical properties	Ref.
4-Amino-1-naphthyl	H	H	H	H	m.p. 164–6°	673
4-Dimethylaminophenyl	H	H	H	H	m.p. 207–9°	367
2',6'-Me_2-4'-pyridyl	Me	H	H	H	m.p. 124–6°	74
3'-Me-4'-pyridyl	H	Me	H	H	m.p. 150°	86
4'-Pyridyl	H	H	H	H	m.p. 106–7.5°	509

TABLE IX-50. 2-, 3-, and 4-Arylazoaminopyridines



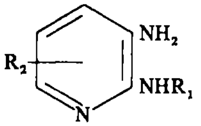
Substituted pyridine	R_1	R_2	R_3	Physical properties	Ref.
2-Pyridyl	H	H	H	–	652
2-Pyridyl	NO_2	H	H	m.p. 185–6°	652
2-Pyridyl	H	NO_2	H	m.p. 212°	652
2-Pyridyl	H	H	NO_2	m.p. 246°, 249°	652
3-Me-2-pyridyl	H	H	$(CH_3)_2N$	m.p. 193–4°	367
4-Me-2-pyridyl	H	H	$(CH_3)_2N$	m.p. 184–5°	367
5-Me-2-pyridyl	H	H	$(CH_3)_2N$	m.p. 201–2°	367
6-Me-2-pyridyl	H	H	$(CH_3)_2N$	m.p. 170–1°	367
3-Pyridyl	NO_2	H	H	m.p. 128°	652
3-Pyridyl	H	NO_2	H	m.p. 205°, 212°	652
3-Pyridyl	H	H	NO_2	m.p. 226°	652
3-Pyridyl	H	H	$(CH_3)_2N$	m.p. 189–91°	367
4-Pyridyl	H	H	$(CH_3)_2N$	m.p. 210–11°	367
2-Me-4-pyridyl	H	H	$(CH_3)_2N$	m.p. 191–2°	367
3-Me-4-pyridyl	H	H	$(CH_3)_2N$	m.p. 193–4°	367
2,6-Me_2-4-pyridyl	H	H	$(CH_3)_2N$	m.p. 197–8°	367

TABLE IX-51. 2- and 4-Hydrazinopyridines



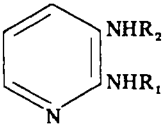
Hydrazino	Substituents 2	3	4	5	6	Physical properties	Ref.
2	–	H	H	NO_2	H	m.p. 204°	465
2	–	Br	H	NO_2	H	m.p. 170°	386
2	–	NO_2	H	Br	H	m.p. 138° acetyl deriv., m.p. 172°	386 386
2	–	NO_2	H	Me	H	m.p. 166°	465
2	–	Me	H	NO_2	H	m.p. 177°	465
2	–	H	Me	NO_2	H	m.p. 192°	465
2	–	H	$NHNO_2$	NO_2	H	m.p. 218°	465
2	–	H	H	NO_2	Me	m.p. 122°	465
2	–	NO_2	Me	H	Me	m.p. 153°	488
2	–	H	Me	NO_2	Me	m.p. 145–6°	488
2	–	H	H	H	H	picrate, m.p. 162–3°	118
4	H	NO_2	–	H	H	m.p. 207°	465
4	Br	H	–	NO_2	H	m.p. 152° (dec.)	628
4	H	Cl	–	NO_2	H	m.p. 199°	44
4	CCl_3	Cl	–	Cl	H	m.p. 171–2°	56
4	Me	NO_2	–	H	Me	m.p. 117–8°	105
4	F	F	–	F	F	m.p. 56–7°	53
4	Me	NO_2	–	Cl	Me	m.p. 171–3°	105
4	H	H	–	H	H	HCl, m.p. 242–4°	118

TABLE IX-52. Alkyl 2,3-Diaminopyridines



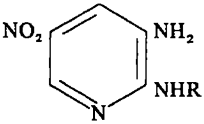
Substituents					
	R_2				
R_1	4	5	6	Physical properties	Ref.
Benzyl	H	Me	Me	m.p. 58–9°	608
n-Bu	H	Me	Me	m.p. 183–4°	608
2-(Diethylamino)-ethyl	H	NO_2	H	m.p. 83°; HCl, m.p. 200–5°	149
2-(Diethylamino)-ethyl	H	H	H	b.p. 140°/0.05 mm	149
3,4-Difluorophenyl	H	Me	Me	m.p. 123–4°	608
p-Fluorophenyl	H	Me	Me	m.p. 90–1°	608
β-Hydroxy-β-phenethyl	H	H	H	di-HCl, m.p. 157–8°	655
Phenethyl	H	Me	Me	m.p. 96–7°	608
Phenethyl	H	H	H	HCl, m.p. 144°	682
Ph	H	H	MeO	m.p. 210° (dec.)	723
Ph	H	Me	Me	m.p. 69–70°	608
H	H	H	Pr	picrate, m.p. 193.5–195°	480
H	Me	H	Me	m.p. 183°	488
H	H	Me	Me	m.p. 179–81°	608
$CH_2CH_2R_3$ R_3 =					
3,4-Dihydroxyphenyl	H	H	H	di-HBr, 174°	655
3,4-Dimethoxyphenyl	H	H	H	$HCl.H_2O$, m.p. 162–4°	655
4-Dimethylamino-phenyl	H	carboxy-methyl	H	m.p. 134–5°	655
3-Indolyl	H	H	H	di-HCl, m.p. 240°	655
α-Naphthyl	H	H	H	HCl, m.p. 175°	655
3,4-Xylyl	H	H	H	HCl, m.p. 168°	655

TABLE IX-53. Halo 2,3-Diaminopyridines



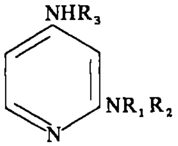
Substituents					Physical properties	Ref.
R_1	R_2	4	5	6		
Benzyl	H	H	Cl	H	m.p. 113°	683
Diethylaminoethyl	H	H	Br	H	b.p. 70°/1 mm	684
2-Dimethylamino-ethyl	H	H	Cl	H	picrate, m.p. 202°	683
Et	H	H	Cl	H	m.p. 107–8°	683
Me	H	H	Br	H	m.p. 126°	684
Me	H	H	Cl	H	m.p. 132°	683
Ph	H	H	Cl	H	m.p. 144–5°	723
Ph	H	H	H	Cl	m.p. 232–3°	723
H	Me	H	Cl	H	m.p. 122–4°	41
H	H	H	Br	H	m.p. 158–60°	41
H	H	H	Cl	H	–	477
H	H	H	Cl	Cl	m.p. 167°	477
H	H	Me	Br	Me	m.p. 186°; picrate, m.p. 217°	630

TABLE IX-54. Nitro 2,3-Diaminopyridines



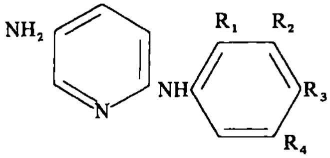
R	Physical properties	Ref.
H	m.p. 260°	45, 478, 685
	m.p. 256°	493
2-Diethylaminoethyl	m.p. 83°; HCl, m.p. 200–5°	80
3,4-Dimethoxyphenethyl	m.p. 174–6°	685
2-Dimethylaminoethyl	m.p. 137–8°	494
Me	m.p. 222–4°	493
2-Methylphenethyl	HCl, m.p. 208–11°	685
Phenethyl	m.p. 136°	682

TABLE IX-55. 2,4-Diaminopyridines



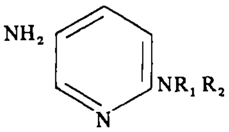
			Substituents				
R$_1$	R$_2$	R$_3$	3	5	6	Physical properties	Ref.
H	H	H	H	H	NO$_2$	m.p. 197.5–98°	87, 628
H	H	H	H	H	OH	m.p. 178°	390
H	H	H	NO$_2$	H	H	m.p. 212°	375
Me	Me	H	H	H	H	m.p. 151°; picrate, m.p. 216°	107, 177
Et	Et	H	H	H	H	m.p. 117°; picrate, m.p. 172°	107, 177
H	H	Me	H	Cl	H	m.p. 122–4°	41
H	H	H	NO$_2$	H	Pr	m.p. 145.5°	480
H	H	H	F	F	F	m.p. 111–12°	252

TABLE IX-56. 5-Amino-2-anilinopyridines



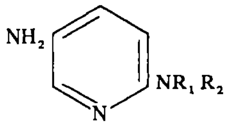
R$_1$	R$_2$	R$_3$	R$_4$	Physical properties	Ref.
H	H	H	H	HCl, m.p. 219–23°	656, 686, 723
H	H	F	H	m.p. 141°	723
H	H	Me	H	HCl, m.p. 237–42°	656
H	H	NMe$_2$	H	HCl, m.p. 245°	656
H	H	C$_5$H$_{11}$O	H	b.p. 225–35°/ 0.5 mm	723
H	CF$_3$	H	H	m.p. 115°	723
Me	H	H	H	b.p. 178–85°/ 0.2 mm	723
MeO	H	H	Cl	b.p. 190–5°	723
Me	Me	H	H	b.p. 200–5°/0.7 mm	723
				m.p. 105°	723

TABLE IX-57. Other 2,5-Diaminopyridines



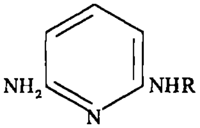
Substituents						
R$_1$	R$_2$	3	4	6	Physical properties	Ref.
H	H	Carboxy	H	H	m.p. 302°	9
H	H	H	Me	H	–	483
H	H	H	H	Me	–	483
H	H	H	Me	Me	m.p. 175–7°	10
H	Benzoyl	H	H	H	m.p. 141–2°	687
H	Benzoyl	H	H	H	HCl, m.p. 210–20°	656
H	Cyclohexyl	H	H	H	–	483
H	3-Dimethyl-aminopropyl	H	H	H	–	483
H	β-Hydroxy-β-phenethyl	H	H	H	m.p. 179–80°	655
H	Me	H	H	H	HCl, m.p. 239–41°	656
H	MeO	H	H	Me	m.p. 126–8°	669
H	2-Methoxy-propyl	H	H	H	–	483
H	3-Methoxy-propyl	H	H	H	–	483
H	Morpholino	H	H	H	HCl, m.p. 250°	656
H	Piperazino	H	H	H	HCl, m.p. 240–5°	656

TABLE IX-57. Other 2,5-Diaminopyridines (Continued)



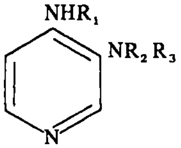
Substituents						
R_1	R_2	3	4	6	Physical properties	Ref.
H	2,2'-(*p,p'*-Methylenedianilino)bis	H	H	H	HCl, m.p. 235°	656
H	2-[(2-nitro-2-furyl)vinyl]-	H	H	H	m.p. 255–8°; HCl, m.p. 235–45°	317
Me	Me	H	H	H	di-HCl, m.p. 244–7°;	179, 656
					picrate, m.p. 246–8°;	483, 686
					HCl, m.p. 260°	179, 656, 686
Me	Me	Me	H	H	HCl, m.p. 221–4°	656

TABLE IX-58. 2,6-Diaminopyridines



Substituents					
R	3	4	5	Physical properties	Ref.
H	Me	H	H	m.p. 156–7°	4
H	NO_2	H	H	–	484
H	Ph	H	H	–	688
H	PhN=N	H	H	acetyl, m.p. 208°	181
H	H	EtO	H	–	482, 689, 690
H	H	MeO	H	–	482, 689, 690
H	H	PrO	H	–	482
H	H	IsoPro	H	m.p. 150–2°	482
H	H	BuO	H	m.p. 146.5–7°	481, 482
H	H	Hexyloxy	H	m.p. 132–4°	482
H	H	$C_5H_{11}O$	H	m.p. 135–7°	482
H	H	iso$C_5H_{11}O$	H	m.p. 129–31°	482
H	H	$CH_2{=}CHCH_2O$	H	m.p. 114.5–16°	691
H	H	$CH_3OCH_2CH_2O$	H	m.p. 97–9°	691
H	H	C_6H_5O	H	m.p. 195°	691
H	H	$C_6H_5CH_2O$	H	m.p. 166–68.5°	691
H	H	$C_6H_5CH_2CH_2O$	H	m.p. 133–5°	691
H	H	$C_6H_5CH_2CH_2CH_2O$	H	m.p. 138°	691
H	H	$C_6H_5CH{=}CHCH_2O$	H	m.p. 146–7°	691
H	H	EtS	H	m.p. 165°	691
H	H	*n*-C_4H_2S	H	m.p. 157–9°	691
H	H	PhS	H	m.p. 108–10°	691
H	H	*p*-ClC_6H_4S	H	m.p. 133–5°	691
H	H	$C_6H_5CH_2S$	H	m.p. 202–3°	691
H	H	C_6H_5Se	H	m.p. 99–100°	691
H	H	$EtSO_2$	H	m.p. 170–71.5°	691
H	H	*n*-$BuSO_2$	H	m.p. 161–3°	691
H	H	$PhSO_2$	H	m.p. 285°	691
H	I	H	I	–	485
H	Me	H	Me	m.p. 186–7°	4
H	NO_2	Ph_2CH	H	m.p. 260°	692
Ph	Phenyl-aminoethyl	Bu_2N	H	b.p. 202–4°/0.5 mm	150

TABLE IX-59. Alkyl and Aryl 3,4-Diaminopyridines



			Substituents				
R_1	R_2	R_3	2	5	6	Physical properties	Ref.
o-Aminophenyl	H	H	H	H	H	m.p. 141–2°	667
p-Anisyl	H	H	H	H	H	m.p. 175–6°	667
p-Chlorophenyl	H	H	H	H	H	m.p. 172–3°	667
3,4-Dimethoxyphenethyl	H	H	H	H	H	di-HCl, m.p. 202°	682, 693
2-Dimethylaminoethyl	H	H	H	H	H	b.p. 144–8°/0.05 mm	494
Methyl	H	H	H	H	H	m.p. 169–70°; picrate, m.p. 185°; di-HCl, m.p. 227–8°	152
α-Methylphenethyl	H	H	H	H	H	b.p. 210–20°/0.001 mm	682, 693
Phenethyl	H	H	H	H	H	HCl, m.p. 174–5°	682, 693
Ph	H	H	Me	H	Me	m.p. 174°	44
Ph	H	H	Me	Cl	Me	m.p. 199–200°	44
3-Phenylpropyl	H	H	H	H	H	di-HCl, m.p. 189–92°	655
H	H	Cyclohexyl	H	H	H	m.p. 164°; picrate, m.p. 199°	178
H	H	2-Diethylaminoethyl	H	H	H	m.p. 103°	682
H	H	Me	H	H	H	m.p. 114°; picrate, m.p. 233°	152, 225, 238
H	H	Phenethyl	H	H	H	HCl, m.p. 174–5°	682, 693
H	H	Ph	H	H	H	m.p. 132°	178

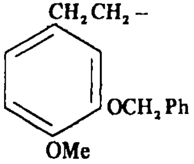
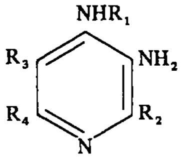
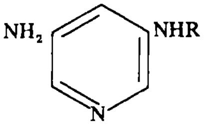
2-Diethylaminoethyl	H	Phenylacetamido	H	H	H	m.p. 135–7°	80
H	Me	Me	H	H	H	m.p. 79–80°; picrate, m.p. 185°	178
H	H	H	H	Me	H	m.p. 149°; picrate, m.p. 198°	469
H	H	H	Me	H	Me	m.p. 181°; picrate, m.p. 215°	52, 109, 469
H	H	H	Cl	Me	H	–	469
CH_2CH_2R							
R =							
m-Anisyl	H	H	H	H	H	di-HCl, m.p. 185°	655
p-Anisyl	H	H	H	H	H	di-HCl, m.p. 188–9°	655
3,4-Dichlorophenyl	H	H	H	H	H	m.p. 135–6°; di-HCl, m.p. 274°	655
p-Hydroxyphenyl	H	H	H	H	H	di-HBr, m.p. 217–8°	655
3-Hydroxy-4-methoxyphenyl	H	H	H	H	H	$HCl \cdot H_2O$, m.p. 170°	655
β-Hydroxy-β-phenethyl	H	H	H	H	H	di-HCl, m.p. 178–9° (dec.)	655
3-Indolyl	H	H	H	H	H	di-HCl, m.p. 198°	655
α-Naphthyl	H	H	H	H	H	di-HCl, m.p. 218°	655
β-Naphthyl	H	H	H	H	H	$HCl \cdot H_2O$, m.p. 243°	655
N-Phenyl-*N*-piperazinyl	H	H	H	H	H	tri-HCl, m.p. 250–2°	655
	H	H	H	H	H	di-HCl, m.p. 177°	655
H	H	3,4-Dimethoxyphenyl	H	H	H	oil	655
H	H	3,4-Dihydroxyphenyl	H	H	H		655

TABLE IX-60. Other 3,4-Diaminopyridines



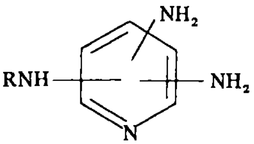
R_1	R_2	R_3	R_4	Physical properties	Ref.
H	Cl	H	H	HCl, m.p. 209–10°; di-HCl, m.p. 175–7°	87
H	H	Br	H	m.p. 140–1°; picrate, m.p. 220–1°	476
H	H	H	Cl	m.p. 146°	624
				HCl, m.p. 238–9°	87
H	H	NO_2	H	–	682
H	Cl	Br	H	m.p. 206–8°	476
H	Cl	Me	H	m.p. 157°	469
H	Cl	H	Cl	HCl, m.p. 205–7°	87
H	OH	H	Pr	m.p. 198°	480
H	Me	H	Me	1-oxide HCl, m.p. 211°	351
H	H	Br	Cl	m.p. 206–8°	476
H	F	F	F	m.p. 117.5–18.5°	252
H	H	H	H	m.p. 220°; picrate, m.p. 234–6°	152
p-Anisyl	H	Br	H	m.p. 134–5°	667
p-Chlorophenyl	H	Br	H	m.p. 157–8°	667
2-Diethylaminoethyl	H	Br	H	HCl, m.p. 208–9°	682
2-Diethylaminoethyl	H	NO_2	H	m.p. 82–3°	682
2-Dimethylaminoethyl	H	NO_2	H	–	494
p-Iodophenyl	H	I	H	m.p. 202–5.5°	624
Me	H	H	H	m.p. 169–70°; picrate, m.p. 185°; di-HCl, m.p. 227–8°	152
Phenethyl	H	Br	H	HCl, m.p. 203–4°	682
Phenethyl	H	NO_2	H	m.p. 112°	682
Ph	H	Br	H	m.p. 144.5°	44
Ph	H	Cl	H	H_2O, m.p. 149.5°	44
Ph	H	I	H	m.p. 187.5–8.5°	624
Ph	Me	H	Me	m.p. 174°	105
Ph	Me	Br	Me	m.p. 177–9°	44
Ph	Me	Cl	Me	m.p. 199–200°	105

TABLE IX-61. 3,5-Diaminopyridines



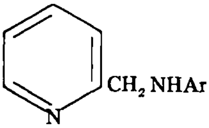
	Substituents				
R	2	4	6	Physical properties	Ref.
H	H	H	H	m.p. 107–8°; acetyl, m.p. 246–8°	102, 175 75, 102
H	H	H	H	1-oxide, m.p. 229–30°	694
H	H	H	PhN=N–	m.p. 192°	674
H	Cl	H	H	m.p. 101–3°; picrate, m.p. 213–4° diacetyl, m.p. 210–12°	102
H	Me_2N	H	H	–	695
H	OH	H	H	di-HCl, m.p. 205°, acetyl, m.p. 267–9°	102
H	MeO	H	H	di-HCl, m.p. 190°	674
H	EtO	H	H	di-HCl, m.p. 168°	674
H	PrO	H	H	di-HCl, m.p. 192°	674
H	BuO	H	H	di-HCl, m.p. 175°	674
H	$C_5H_{11}O$	H	H	di-HCl, m.p. 150°	674
H	2-Hydroxyethoxy	H	H	di-HCl, m.p. 210°	181
H	2-Acetoxyethoxy	H	H	acetyl, m.p. 203°	181
H	MeO	H	PhN=N–	m.p. 141°	674
H	EtO	H	PhN=N–	m.p. 119°	674
H	EtO	H	PhN=N–	acetyl, m.p. 173°	181
H	PrO	H	PhN=N–	m.p. 122°	674
H	BuO	H	PhN=N–	m.p. 126°	674
H	AmO	H	PhN=N–	m.p. 96°	674
H	Me	Cl	Me	m.p. 283–5°	696, 697
OH	Me	Cl	Me	m.p. 97.5–8°	696

TABLE IX-62. Triaminopyridines



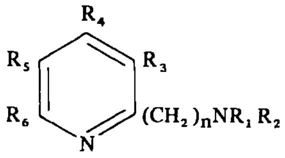
R	Position of NHR	Position of NH$_2$	Position of NH$_2$	Physical properties	Ref.
NH$_2$	2	3	5	tetra-HCl, m.p. 140°	478
2-Diethylaminoethyl	4	3	5	picrate, m.p. 164–7°	682
Ph	6	2	3	m.p. 144°	723
Ph	4	3	5	–	619
m-$CF_3C_6H_4$	6	2	3	m.p. 300°	723
H	2	3	4	m.p. 298° (dec.); di-HCl, m.p. 260°	87
H	2	3	5	tri-HCl, m.p. 160° (dec.)	478
(2,3,4-Triamino-6-propylpyridine)				picrate, m.p. 155–6°	478

TABLE IX-63. *N*-Aryl-2-picolylamines



Ar	Physical properties	Ref.
o-Anisyl	b.p. 173–6°/7 mm	534
	picrate, m.p. 144° (dec.)	534
N,N'-Bis(2-pyridylmethyl)-*O*-phenylenediamine	b.p. 235–43°/7 mm	534
p-Carboxyphenyl	m.p. 207–9°	527
1-(3,4-Methylenedioxyphenyl)-2-propyl	m.p. 210°	527
o-Ethoxyphenyl	m.p. 102–4°	534
β-Hydroxy-β-(3,4-dimethoxyphenethyl)	m.p. 145°	527
β-Hydroxy-β-(4-methoxyphenethyl)	m.p. 78°	527
β-Hydroxy-β-(4-methylphenethyl)	m.p. 115°	527
β-Hydroxy-β-phenethyl	m.p. 166°	527
p-Hydroxyphenyl	m.p. 164–6°	527
1-(4-Hydroxyphenyl)-2-propyl	m.p. 221°	527
1-Hydroxy-1-phenyl-2-propyl	m.p. 218°	527
1-(4-Methoxyphenyl)-2-propyl	m.p. 197° (dec.)	527
α-Naphthyl	b.p. 211–13°/6 mm; picrate, m.p. 172° (dec.)	534
α-Phenethyl	m.p. 224°	527
β-Phenethyl	m.p. 170°	527
Ph	m.p. 50–3°	698
	m.p. 50–4°	534
1-Phenyl-2-propyl	m.p. 203°	527
o-Tolyl	b.p. 153–8°/4 mm; picrate, m.p. 147°	534

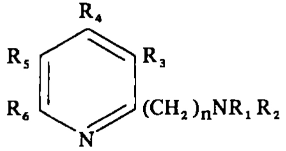
TABLE IX-64. Simple 2-Aminoalkylpyridines



n	R_1	R_2	R_3	R_4	R_5	R_6	Physical properties	Ref.
1	2-Aminoethyl	H	H	H	H	H	b.p. 77°/0.01 mm. tri-HCl, m.p. 174–5°	224, 556, 699 505
1	*p*-Anisyl	H	H	H	H	H	m.p. 74–5°	535
1	1,4-Benzodioxan-2-ylmethyl	H	H	H	H	Me	di-HCl, m.p. 142–5°	581
1	1,4-Benzodioxan-2-ylmethyl	H	H	H	H	H	di-HCl, m.p. 165–70°	581
1	Benzyl	H	H	H	H	H	b.p. 156–9°/3 mm; picrate, m.p. 162–2.5°	524
1	Benzyl	H	H	H	Me	H	b.p. 143–52°/9.3 mm; di-HCl, m.p. 178–9°	533
1	2-Diethylaminoethyl	H	H	H	H	H	b.p. 109–10°/0.9 mm; tri-picrate, m.p. 185–6°	499
1	Diphenylmethyl	Me	H	H	H	H	m.p. 56–8°	528
1	*p*-Ethoxyphenyl	H	H	H	H	H	m.p. 72–3°	535
1	Et	Et	H	H	H	H	b.p. 109–10°/0.9 mm	499
1	Et	Et	H	H	Acetoxy	Me	b.p. 110–5°/1–2 mm	545
1	Et	Et	H	H	OH	Me	m.p. 137.5–8.5°, di-HCl, m.p. 205–6° tripicrate, m.p. m.p. 185–6°	545 545 499
1	2-Hydroxyethyl	H	H	H	H	H	b.p. 150–5°/6.5 mm; picrate sesquihydrate, m.p. 152–4°	501

1	2-Hydroxyethyl	2-Hydroxyethyl	H	H	H	H	b.p. 187–90°/3.5 mm; di-HCl, m.p. 164–6°	501
1	4-Hydroxybutyl	2-Hydroxyethyl	H	H	H	H	b.p. 195–205°/3 mm	501
1	Me	2-NH_2-5-Br-benzyl	H	H	H	H	–	664
1	Me	2-NH_2-3,5-Br_2-benzyl	H	H	H	H	HCl, m.p. 198.5–201°	664
1	Me	4-NH_2-3,5-Br_2-benzyl	H	H	H	H	HCl, m.p. 208–11°	664, 700, 702
1	Me	Me	H	H	OH	NO_2	m.p. 181–1.5°	542
1	Me	Me	OH	H	H	H	m.p. 59–60°	541
1	Me	Me	OH	H	H	Me	b.p. 100–2°/1 mm	541
1	Me	Me	H	H	OH	Me	m.p. 159–60°; di-HCl, m.p. 210–11°	545
1	Me	Me	OH	*n*-Bu	H	IsoAm	m.p. 113–14°	546
1	Me	Me	OH	IsoBu	H	IsoAm	m.p. 118–19°	546
1	Me	H	H	H	Et	H	b.p. 135–7°/12 mm; di-HCl, m.p. 178–9°	533
1	Me	H	H	H	H	Me	*N*-nitroso, m.p. 49°	594
1	Me	H	H	H	H	H	*N*-nitroso, b.p. 100–1°/0.2 mm	594
1	α-[3,4-Methylenedioxy]-phenethyl	H	H	H	H	H	HCl, b.p. 150–2°	577
1	β-Naphthyl	H	H	H	H	H	m.p. 82–3° (sealed capillary)	535
1	β-Phenethyl	H	H	H	H	H	HCl, m.p. 183–5° di-HCl, m.p. 186–8°	530
1	Piperidino	–	OH	*n*-Pr	H	IsoAm	m.p. 165–6°	546
1	Piperidino	–	OH	IsoPr	H	IsoAm	m.p. 155–6°	546
1	Piperidino	–	OH	*n*-Bu	H	IsoAm	m.p. 168–9°	546
1	Piperidino	–	OH	IsoBu	H	IsoAm	m.p. 192–3°	546
1	Piperidino	–	OH	IsoAm	H	IsoAm	m.p. 170–1°	546

TABLE IX-64. Simple 2-Aminoalkylpyridines (Continued)



n	R$_1$	R$_2$	R$_3$	R$_4$	R$_5$	R$_6$	Physical properties	Ref.
1	Ph	H	H	H	H	Me	m.p. 61–2°	698
1	Ph	H	H	H	H	H	m.p. 54–5°, 47–9°; b.p. 105–10°/0.04 mm b.p. 137–40°/3 mm; picrate, m.p. 154–5° (dec.); dipicrate, m.p. 151–2°; di-HCl, m.p. 190–2°	498, 535 498 535
1	2-Pyridyl	H	H	H	H	H	b.p. 152–3°/3 mm; m.p. 53–4°; picrate, m.p. 202–4°	535
1	*p*-Tolyl	H	H	H	H	H	b.p. 150–2°/3 mm; m.p. 41–3°	535
1	H	H	H	H	Me	H	b.p. 121–4°/13 mm; di-HBr, m.p. 200–3°	533
1	H	H	H	H	Et	H	b.p. 130–2°/13 mm; di-HCl, m.p. 208–9°	533
1	H	H	H	H	OH	NO$_2$	m.p. 128–9°	542
1	Benzoyl	Benzoyl	H	H	H	H	b.p. 183°/0.25 mm; methiodide, m.p. 140–1°	499

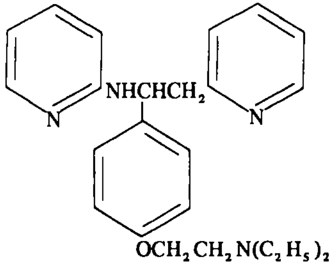
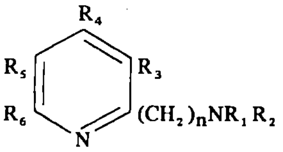
1	2-Benzyloxyethyl	2-Benzyloxy-ethyl	H	H	H	H	di-HCl, m.p. 165.5°; dipicrate, m.p. 150–1°	501
1	4-Chlorobutyl	2-Chloroethyl	H	H	H	H	picrate, m.p. 122–3°	501
1	Diphenylacetyl	Diphenylacetyl	H	H	H	H	b.p. 190°/0.15 mm; m.p. 65–6°	499
1	Et	Et	OH	H	H	Me	b.p. 79–80°/1 mm	541
1	Et	Et	OH	H	H	H	b.p. 85–6°/1 mm; di-HCl, m.p. 201–2°	541
1	Me	2-Propynyl	H	H	H	H	b.p. 97°/4 mm; HCl, m.p. 177°	549, 550
1	Ph	Diethylamino-ethyl	H	H	H	H	b.p. 128–30°/0.04 mm; dipicrate, m.p. 164–6°	498
1	2-Picolyl	Ph	H	H	H	Me	m.p. 81–83°	698
1	2-Picolyl	Ph	H	H	H	H	m.p. 152–3°	535
2	4-Aminobutyl	H	H	H	H	H	b.p. 69°/0.001 mm	556
2	2-Aminoethyl	H	H	H	H	H	b.p. 77°/0.01 mm	556
2	6-Aminohexyl	H	H	H	H	H	b.p. 91–3°/0.002 mm	556
2	8-Aminooctyl	H	H	H	H	H	b.p. 113°/0.002 mm	556
2	Butyl	H	H	H	H	H	b.p. 117–18°/8 mm picrate, m.p. 144.5–5.5°; HCl, m.p. 117–18°	558
2	Hexamethylenimino	H	H	H	H	H	b.p. 150–2°/10 mm; MeI, m.p. 113–14.5°; picrate, m.p. 120–20.5°	558
							m.p. 75–6°	578

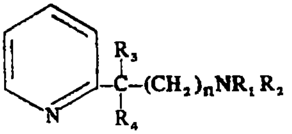
TABLE IX-64. Simple 2-Aminoalkylpyridines (Continued)



n	R$_1$	R$_2$	R$_3$	R$_4$	R$_5$	R$_6$	Physical properties	Ref.
2	Diphenylmethyl	H	H	H	H	H	m.p. 69–71°	528
2	Benzyl	Benzyl	H	H	H	H	b.p. 179°/0.1 mm	559
2	Et	Et	NO_2	H	H	H	b.p. 170°/0.05 mm	80
2	Et	Et	OH	H	H	NO_2	m.p. 113–14°	542
2	Et	Me	H	H	H	H	HCl, m.p. 178–90°	540
2	Me	Me	OH	H	H	NO_2	m.p. 143–4°	542
2	Me	Me	H	H	H	H	b.p. 120–3°/0.4 mm; 51–3°/0.1 mm, di-HCl, m.p. 195–7°	128, 540
2	Me	2-Propynyl	H	H	H	H	b.p. 150°/ 30 mm	550
2	IsoPr	IsoPr	H	H	H	H	b.p. 91–2°/7 mm	559
2	H	H	H	H	Et	H	b.p. 69–71°/0.7 mm; di-HCl, m.p. 205°;	532
							b.p. 105°/10 mm; picrate, m.p. 194°; chloroplatinate, m.p. 211°	547, 703
2	H	H	OH	H	H	NO_2	di-HCl, m.p. 125–7°	542
2	H	H	H	H	H	H	b.p. 87°/10 mm; b.p. 88–90°/8 mm	559, 703
							picrate, m.p. 164°; chloroplatinate, m.p. 230°;	703
							dipicrate, m.p. 95.5°	547

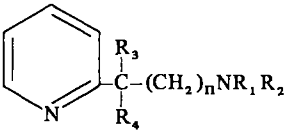
2	α-Methylphenethyl	H	H	H	Et	H	b.p. 148–50°/0.4 mm	570
2	Piperidino	–	OH	H	H	NO_2	m.p. 210°	542
2	Piperidino	–	H	H	OH	NO_2	m.p. 160°; m.p. 172–3°	542, 543
2	β-Piperidino		H	H	H	H	b.p. 136–6.5°/10 mm; picrate, m.p. 126.5°; HCl, m.p. 173–4°	563
2	1-Ph	H	H	H	H	H	acetyl, b.p. 170–90°/ /0.16 mm; methiodide, m.p. 151–2°	569
2	1-Phenyl-2-propyl	H	H	H	H	H	4-methoxyphenylcarboxamide, b.p. 238–4°/0.03 mm	569
2	1-Phenyl-2-propyl	H	H	H	H	H	b.p. 120°/0.05 mm	569
2	*p*-Anisyl	2-Dimethylaminoethyl	H	H	H	H	b.p. 152–4°/0.07 mm; dipicrate, m.p. 179–80°	561, 562
2	*m*-Chlorophenyl	2-Dimethylaminoethyl	H	H	H	H	b.p. 140–8°/0.03 mm; dipicrate, m.p. 180–3°	561, 562
2	*p*-Chlorophenyl	2-Dimethylaminoethyl	H	H	H	H	b.p. 152–4°/0.09 mm; dipicrate, m.p. 142–5°	561, 562
2	*m*-Chlorophenyl	3-Dimethylaminopropyl	H	H	H	H	b.p. 138°/0.02 mm	561, 562
2	*p*-Chlorophenyl	3-Dimethylaminopropyl	H	H	H	H	b.p. 166–70°/0.05 mm; dipicrate, m.p. 160–3°	561, 562
2	α-Methylphenethyl	H	H	H	Et	H	b.p. 148–50°/0.4 mm	570
3	Me	Me	OH	H	H	NO_2	–	542
5	Me	Et	H	H	H	H	b.p. 100–8°/2 mm; methobromide m.p. 199–200°	508
7	H	H	H	H	H	H	dipicrate, m.p. 103°	547
8	H	H	H	H	H	H	b.p. 183°/15 mm	547
13	H	H	H	H	H	H	b.p. 202°/1.5 mm	547

TABLE IX-65. 2-(α-Alkyl-branched)aminoalkylpyridines



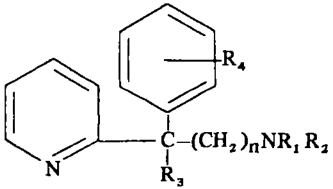
	Substituents					
n	R_1	R_2	R_3	R_4	Physical properties	Ref.
0	EtNH	H	Me	H	b.p. 74–5°/0.07 mm; fumarate, m.p. 159–61°	529
0	*t*-Bu	H	Me	H	b.p. 63–9°/0.03 mm; maleate, m.p. 124–5°	529
0	Me	Me	Me	H	methobromide, m.p. 189–91°	529
0	Ph	H	Me	IsoBu	b.p. 145°/0.08 mm; picrate, m.p. 145–6°	580
0	Ph	H	Me	Hexyl	b.p. 141°/0.03 mm	580
2	Me	Me	H	H	b.p. 67–9°/0.6 mm	537
2	Me	Me	H	Acetyl	b.p. 86–7°/0.33 mm; dipicrate, m.p. 179.7–80.4°	537
2	Me	Me	H	Benzoyl	b.p. 132–3°/0.28 mm; dipicrate, m.p. 179.2–9.8°	537
2	Me	Me	H	Butyroyl	b.p. 95–6°/0.26 mm; dipicrate, m.p. 149.6–50.6°	537
2	Me	Me	H	Isobutyroyl	b.p. 89–90°/0.28 mm; dipicrate, m.p. 155.8–6.7°	537
2	Me	Me	H	Propionyl	b.p. 90–1°/0.29 mm; dipicrate, m.p. 169–70°	537

TABLE IX-65. 2-(α-Alkyl-branched)aminoalkylpyridines (Continued)



	Substituents					
n	R_1	R_2	R_3	R_4	Physical properties	Ref.
2	Me	Me	H	Trimethyl-acetyl	b.p. 90–1°/0.29 mm; dipicrate, m.p. 171.3–2.5°	537
2	Me	Me	Ph	Acetyl	b.p. 151–2°/0.62 mm; dipicrate, m.p. 159.2–60.4°	537
2	Me	Me	Ph	Benzoyl	b.p. 200–5°/1 mm; m.p. 86–7.4°; tripicrate, m.p. 199–200.5°	537
2	Me	Me	Ph	Butyroyl	b.p. 152–3°/0.29 mm; dipicrate, m.p. 150.5–1.4°	537
2	Me	Me	Ph	Isobutyroyl	b.p. 145–6°/0.29 mm; dipicrate, m.p. 159–60°	537
2	Me	Me	Ph	2-Ethyl-hexanoyl	b.p. 176–7°/9.28 mm	537
2	Me	Me	Ph	Propionyl	b.p. 144.5°/0.27 mm; maleate, m.p. 144.2–5.3°	537
2	Me	Me	Ph	Trimethyl-acetyl	b.p. 156–8°/0.25 mm; m.p. 65–70°; dipicrate, m.p. 156.6–7.4°	537

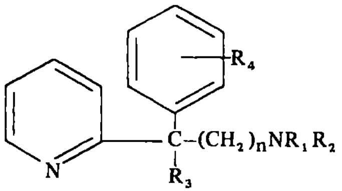
TABLE IX-66. 2-(α-Aryl-branched)aminoalkylpyridines



n	R$_1$	R$_2$	R$_3$	R$_4$	R$_5$	b.p./mm	m.p.	Picrate, m.p.	Ref.
0	*o*-Anisyl	H	H	H	H	176°/0.02	–	146°	580
0	*p*-Anisyl	H	H	H	H	185°/0.03	91°	131°	580
0	Benzyl	H	H	H	H	184°/0.03	–	131°	580
0	*o*-ClC$_6$H$_4$	H	H	H	H	168°/0.05	100°	154°	580
0	*p*-ClC$_6$H$_4$	H	H	H	H	171°/0.08	113°	158°	580
0	Et	H	H	H	H	106°/0.50	–	150°	580
0	*o*-MeOC$_6$H$_4$	H	H	H	H	136–41°/1	–	130–1°	580
0	Me	H	H	H	H	122°/0.50	–	–	580
0	Ph	H	H	H	H	158°/0.01 155–62°/0.1	78°	175°	580
0	Ph	H	H	2-Cl	H	–	–	165–6°	580
0	Ph	H	H	3-Cl	H	183°/0.09	96°	163°	580
0	Ph	H	H	4-Cl	H	163°/0.03	86°	169°	580
0	Ph	H	H	4-Me	H	167°/0.02	–	163°	580
0	*o*-Tolyl	H	H	H	H	161°/0.01	–	156°	580
0	*p*-Tolyl	H	H	H	H	166°/0.03	81°	128°	580
0	Ph	H	Ph	H	H	156°/0.08	53°	195°	580
1	H	H	H	4-Br	H	160–3°/1	–	–	497
1	H	H	H	4-Cl	H	160–4°/1	–	–	497
1	H	H	H	4-Me	H	148–50°/1	–	–	497
1	H	H	H	H	H	130–5°/2	–	–	497

2	1-(4′-Anisyl)-2-propyl	H	H	H	H	200°/0.01	(1:1 maleate, m.p. 126°)		538
2	Bu	H	H	4-Br	IsoBu	175–6°/0.01	–	–	704
2	Et	H	H	4-Br	IsoBu	167–70°/0.05	–	dipicrate, 167–70°	704
2	Me	H	H	4-Br	IsoBu	160–1°/0.05	–	dipicrate 140–2°	704
2	2-[2-Methyl-3-(4-chlorophenyl)]-propyl	H	H	H	H	210–23°/0.3	(1:1 maleate, m.p. 137–8°)		538
2	1-Phenyl-3-butyl	H	H	H	H	210–12°/0.4	(1:5 fumaric m.p. 157–8°)		538
2	IsoPr	H	H	4-Br	IsoBu	165–7°/0.01	–	84–9°	704
2	Cl	Me	H	4-Cl	IsoBu	148–50°/0.1	–	185–7°	704
2	Et	Et	H	4-Br	IsoBu	158–62°/0.1	–	149–50°	704
2	Et	Et	H	4-Cl	IsoBu	155–8°/0.01	–	157–60°	704
2	Me	Me	H	4-Cl	H	136–8°/0.3	–	–	554
						155–60°/3.0	(maleate, m.p. 132–3°) dipicrate, m.p. 194–6°		705
2	Me	Me	H	4-Br	IsoBu	137–40°/0.01	–	–	704
2	Me	Me	H	H	H	132–6°/0.4	–	–	554
						128–9°/0.85	–	201–2°	537
2	Me	IsoPr	H	4-Br	IsoBu	–	–	150–6°	704
2	*N*-Pyrrolidino		H	H	H	136–8°	–	dipicrate 170–1°	537
2	Pr	Pr	Amido	H	H	–	63–4°	–	592
2	IsoPr	IsoPr	Amido	4-Cl	H	–	–	–	592
2	IsoPr	IsoPr	Amido	3,4-Dimethoxy	H	–	102–3°	–	592
2	IsoPr	IsoPr	Amido	3,5–Me_2	H	–	152–5°	–	592
2	IsoPr	IsoPr	Amido	2-F	H	–	77–8°	–	592

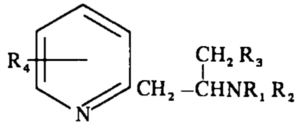
TABLE IX-66. 2-(α-Aryl-branched)aminoalkylpyridines (Continued)



n	R_1	R_2	R_3	R_4	R_5	b.p./mm	m.p.	Picrate, m.p.	Ref.
2	IsoPr	IsoPr	Amido	4-MeO	H	–	–	–	592
2	IsoPr	IsoPr	Amido	3-Me	H	–	113–14°	–	592
2	IsoPr	IsoPr	Amido	H	Cl	–	–	–	592
2	IsoPr	IsoPr	Amido	H	H	–	94.5–5°	–	592
2	IsoPr	IsoPr	Amido	2-Naphthyl	H	–	152–5°	–	592
2	Pr	Pr	CN	H	H	164.5°/0.1	–	–	592
2	IsoPr	IsoPr	CN	4-Cl	H	176–9°/0.4	–	–	592
2	IsoPr	IsoPr	CN	3,4–$(MeO)_2$	H	185–90°/0.1	–	–	592
2	IsoPr	IsoPr	CN	3,5-Me_2	H	–	–	–	592
2	IsoPr	IsoPr	CN	2-F	H	–	–	–	592
2	IsoPr	IsoPr	CN	4-F	H	154°/0.4	–	–	592
2	IsoPr	IsoPr	CN	4-MeO	H	–	–	–	592
2	IsoPr	IsoPr	CN	3-Me	H	164–8°/0.2	–	–	592
2	IsoPr	IsoPr	CN	H	Cl	165–72°/0.25	–	–	592
2	IsoPr	IsoPr	CN	H	H	145–60°/0.3	–	–	592
2	H	H	H	4-Cl	H	138–40°/0.13	–	–	554
2	H	H	H	H	H	128–32°/0.25	–	–	554

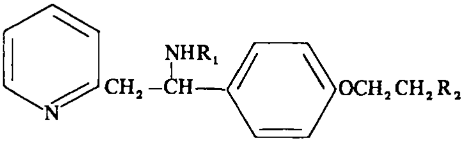
3	2-[1-Methyl-3-(4-chlorophenyl)]-propyl	H	H	H	H	216–20°/0.2	(1:1 maleate, m.p. 129–30°)	538
3	1-Phenyl-3-butyl	H	H	H	H	207–12°/0.1	(1:1 maleate, m.p. 129–30°)	538
3	1-Phenyl-2-propyl	H	H	H	H	215–17°/0.8	(1:1 maleate, m.p. 127–8°)	538

TABLE IX-67. 2-(β-Alkyl-branched)aminoalkylpyridines[533]



R_1	R_2	R_3	R_4 4	5	6	Physical properties
Benzyl	H	H	H	Et	H	b.p. 143–52°/0.3 mm; di-HCl, m.p. 178–9°
2-Chloroethyl	H	H	H	Me	H	m.p. 179–80°
2-Hydroxyethyl	H	H	H	Me	H	b.p. 162–5°/12 mm
2-Hydroxyethyl	H	H	Me	H	Me	b.p. 161–4°
Me	H	H	H	Me	H	b.p. 112–16°/12 mm; di-HCl, m.p. 175–6°
Me	H	H	Me	H	Me	b.p. 109–10°
H	H	Me	H	Et	H	b.p. 130–2°/13 mm; di-HCl, m.p. 208–9°
2-Chloroethyl	Me	H	H	Me	H	di-HCl, m.p. 171–2°
2-Chloroethyl	Me	H	Me	H	Me	di-HCl, m.p. 175–6°
2-Hydroxyethyl	Me	H	H	Me	H	b.p. 163–6°/13 mm
2-Hydroxyethyl	Me	H	Me	H	Me	b.p. 152–5°
Me	Me	H	H	Me	H	b.p. 123–4°/15 mm; di-HCl, m.p. 181–2°
Me	Me	H	H	H	Me	b.p. 101–3°/14 mm
Me	Me	H	Me	H	Me	b.p. 123–6°/17 mm; dipicrate, m.p. 155–60°; methiodide, m.p. 170°
2-Chloroethyl	H	Me	H	Et	H	–
2-Hydroxyethyl	H	Me	H	Et	H	b.p. 175–80°/10 mm; di-HCl, m.p. 129–30°
Me	H	Me	H	Et	H	b.p. 135–7°/12 mm; di-HCl, m.p. 173–5°
2-Chloroethyl	Me	Me	H	Et	H	di-HCl, m.p. 152–3°
2-Hydroxyethyl	Me	Me	H	Et	H	b.p. 148–51°/0.18 mm
H	H	H	Me	H	H	b.p. 127–32°/15 mm
H	H	H	H	Et	H	b.p. 121–4°/13 mm
H	H	H	Me	H	Me	b.p. 111–40°; di-HCl, m.p. 209–10°

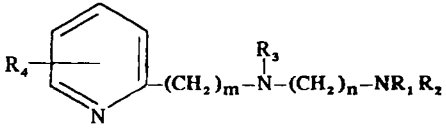
TABLE IX-68. 2-(β-Aryl-branched)aminoalkylpyridines



R_1	R_2	m.p.	Ref.
p-Anisyl	Diethylamino	66–8°	579
m-ClC_6H_4	Diethylamino	62–4°	579
p-ClC_6H_4	Diethylamino	76–7°	579
p-FC_6H_4	Diethylamino	–	579
p-$MeOC_6H_4$	Pyrrolidino	93–5°	579
p-Tolyl	Morpholino	103–5°	579
p-Tolyl	Piperidino	93–5°	579
Ph	Diethylamino	61–3°	579
Ph	Piperidinomethyl	88–91°	579
p-Tolyl	Diethylamino	77–9°	579
2-Pyridyl	(Phenyl[a])	84–5° (b.p. 182–7°/0.1 mm)	578

[a] This is a β-phenyl substituent and not an alkoxyphenyl group.

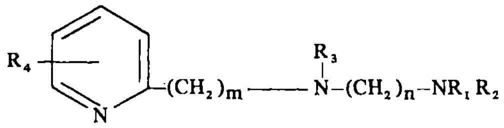
TABLE IX-69. Longer Chain 2-Aminoalkylpyridines



m	n	R_1	R_2	R_3	R_4	Physical properties	Ref.
2	2	Acetyl	H	Acetyl	H	b.p. 136°/0.003 mm	556
2	2	Acetyl	H	2-(2-Pyridyl)ethyl	H	b.p. 138–40°/0.003 mm	556
2	2	2-Benzoyloxyethyl	H	2-(2-Pyridyl)ethyl	H	m.p. 172°	556
2	2	Bu	H	H	H	b.p. 69°/0.001 mm	556
2	2	Carbanilido	H	Carbanilido	H	m.p. 138°	556
2	2	Ethoxymethyl	H	2-(2-Pyridyl)-3-hydroxypropyl	H	b.p. 168°/0.001 mm	556
2	2	2-Hydroxyethyl	H	H	H	b.p. 110°/0.003 mm	556
2	2	Octylsulfonyl	H	Octylsulfonyl	H	m.p. 77°	556
2	2	2-(2-Pyridyl)ethyl	H	2-(2-Pyridyl)ethyl	H	b.p. 148°/0.1 mm	556
2	2	Acetyl	Acetyl	2-(2-Pyridyl)ethyl	H	b.p. 156°/0.003 mm	556
2	2	Acetyl	2-(Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	b.p. 180°/0.01 mm	556
2	2	Benzyl	*p*-Chlorophenyl	Ethyl	H	dimaleate, m.p. 103–5°	563
2	2	Benzyl	*p*-Chlorophenyl	Me	H	methiodide, m.p. 130–1°	563
2	2	Benzyl	Ph	Me	H	methiodide, m.p. 125° ; dimaleate, m.p. 114–16°	563
2	2	Benzyl	Ph	H	H	tri-HCl, m.p. 151–2°	563
2	2	Butylsulfonyl	Butylsulfonyl	Butylsulfonyl	H	m.p. 270° (dec.)	556
2	2	4-Chlorobenzyl	Ph	Me	H	dimaleate, m.p. 106.5–7°	563
2	2	Dichloroacetoxyethyl	Dichloroacetoxyethyl	Dichloroacetyl	H	m.p. 170°	556
2	2	Ethoxymethyl	2-(2-Pyridyl)allyl	2-(2-Pyridyl)allyl	H	–	556
2	2	Ethoxymethyl	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	b.p. 90–5°/0.02 mm	556
2	2	2-Hydroxyethyl	2-Hydroxyethyl	2-Hydroxyethyl	H	b.p. 172°/0.01 mm	556

2	2	2-Hydroxyethyl	2-Hydroxyethyl	H	H	b.p. 138°/0.01 mm	556
2	2	Me	Me	*m*-Chlorophenyl	5-Et	b.p. 172–4°/0.02 mm	561, 562
2	2	Me	Me	*m*-Chlorophenyl	H	b.p. 140–8°/0.03 mm	561, 562
2	2	Me	Me	*p*-Chlorophenyl	H	b.p. 152–4°/0.09 mm; dipicrate, m.p. 142–5°	561, 562
2	2	Me	Me	*p*-Methoxyphenyl	H	b.p. 152–4°/0.07 mm; dipicrate, m.p. 179–80°	561, 562
2	2	Morpholino	H	H	H	b.p. 75–80°/15 mm	556
2	2	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	b.p. 183°/0.01 mm	556
2	2	H	H	Acetyl	H	b.p. 108°/0.003 mm	556
2	2	H	H	Benzoyloxy	H	m.p. 152°	556
2	2	H	H	2-(2-Pyridyl)ethyl	H	b.p. 120°/0.004 mm	556
2	2	H	H	H	H	b.p. 77°/0.01 mm	556
2	3	Benzyl	Ph	H	H	maleate, m.p. 117.5–18.5°	563
2	3	Benzyl	Ph	Me	H	di-HCl, m.p. 133.5–4.5°	563
2	3	Me	Me	*m*-Chlorophenyl	5-Et	b.p. 158–60°/0.03 mm	561, 562
2	3	Me	Me	*p*-Chlorophenyl	5-Et	b.p. 170–2°/0.02 mm	561, 562
2	3	Me	Me	*m*-Chlorophenyl	H	b.p. 138°/0.02 mm	561, 562
2	3	Me	Me	*p*-Chlorophenyl	H	b.p. 166–70°/0.05 mm dipicrate, m.p. 160–3°	561, 562
2	4	Acetyl	H	H	H	b.p. 108°/0.001 mm	556
2	4	Acetyl	H	Acetyl	H	b.p. 138°/0.001 mm	556
2	4	Carbanilido	H	Carbanilido	H	m.p. 156°	556
2	4	2-Hydroxyethyl	H	H	H	b.p. 120°/0.001 mm	556
2	4	2-Hydroxyethyl	H	2-Hydroxyethyl	H	b.p. 150°/0.01 mm	556
2	4	2-(2-Pyridyl)ethyl	H	2-(2-Pyridyl)ethyl	H	b.p. 156°/0.001 mm	556
2	4	Acetyl	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	b.p. 175°/0.005 mm	556
2	4	2-Cyanoethyl	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	b.p. 158°/0.02 mm	556
2	4	2-Hydroxyethyl	2-Hydroxyethyl	2-Hydroxyethyl	H	b.p. 175°/[a]	556
2	4		(Morpholino)	H	H	b.p. 100°/1 mm	556
2	4	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	b.p. 183–5°/0.001 mm	556
2	4	H	H	2-(2-Pyridyl)ethyl	H	b.p. 128°/0.001 mm	556

TABLE IX-69. Longer Chain 2-Aminoalkylpyridines (Continued)



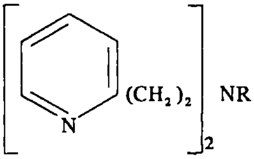
m	n	R_1	R_2	R_3	R_4	Physical properties	Ref.
2	4	H	H	H	H	b.p. 83°/0.01 mm	556
2	6	Acetyl	H	H	H	b.p. 118°/0.002 mm	556
2	6	Acetyl	H	Acetyl	H	b.p. 143°/0.002 mm	556
2	6	Acetyl	H	2-(2-Pyridyl)ethyl	H	b.p. 143°/0.001 mm	556
2	6	2-Hydroxyethyl	H	H	H	b.p. 125°/0.01 mm	556
2	6	2-(2-Pyridyl)ethyl	H	2-(2-Pyridyl)ethyl	H	b.p. 163°/0.001 mm	556
2	6	Acetyl	Acetyl	Acetyl	H	b.p. 205°/0.02 mm	556
2	6	Acetyl	Acetyl	2-(2-Pyridyl)ethyl	H	b.p. 163°/0.002 mm	556
2	6	Acetyl	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	b.p. 175°/0.005 mm	556
2	6	3-Aminopropyl	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	b.p. 152°/0.002 mm	556
2	6	2-Carbamoylethyl	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	m.p. 342°	556
2	6	Carbanilido	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	m.p. 134°	556
2	6	Cyanoethyl	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	b.p. 193°/0.08 mm	556
2	6	2-Hydroxyethyl	2-Hydroxyethyl	H	H	b.p. 166–8°/0.004 mm	556
2	6	2-Hydroxyethyl	2-Hydroxyethyl	2-Hydroxyethyl	H	b.p. 186°/0.01 mm	556
2	6	2-Hydroxyethyl	2-Hydroxyethyl	2-(2-Pyridyl)ethyl	H	b.p. 160°/0.005 mm	556
2	6	2-Hydroxyethyl	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	b.p. 139°/0.001 mm	556
2	6	(Morpholino)		H	H	b.p. 110°/1 mm	556
2	6	Propen-2-yl	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	b.p. 95–100°/0.001 mm	556
2	6	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	b.p. 220°/0.02 mm	556
2	6	Thiocarbanilido	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	m.p. 85°	556
2	6	H	H	2-(2-Pyridyl)ethyl	H	b.p. 136°/0.002 mm	556

2	6	H	H	H	H	b.p. 91–3°/0.002 mm	556
2	8	Acetyl	H	H	H	b.p. 125°/0.001 mm	556
2	8	Acetyl	H	Acetyl	H	b.p. 165°/0.002 mm	556
2	8	2-Hydroxyethyl	H	H	H	b.p. 126°/0.001 mm	556
2	8	2-Hydroxyethyl	H	2-Hydroxyethyl	H	b.p. 172°/0.02 mm	556
2	8	2-(2-Pyridyl)ethyl	H	2-(2-Pyridyl)ethyl	H	b.p. 185°/0.001 mm	556
2	8	Acetyl	Acetyl	Acetyl	H	b.p. 208°/0.001 mm	556
2	8	Acetyl	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	b.p. 193°/0.001 mm	556
2	8	2-Cyanoethyl	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	b.p. 162°/0.02 mm	556
2	8	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	2-(2-Pyridyl)ethyl	H	b.p. 225°/0.001 mm	556
2	8	H	H	2-(2-Pyridyl)ethyl	H	b.p. 148°/0.001 mm	556
2	8	H	H	H	H	b.p. 113°/0.002 mm	556
3	2	Benzyl	*p*-Bromophenyl	Me	H	maleate, m.p. 133–4°; dipicrate, m.p. 155–60°	563
3	2	Benzyl	*p*-Chlorophenyl	H	H	di-HCl, m.p. 171–1.5°	563

---

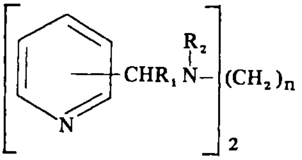
[a] Pressure not reported.

TABLE IX-70. 2,2′-{[(Aminoalkyl)imino]diethylene}dipyridines[556]



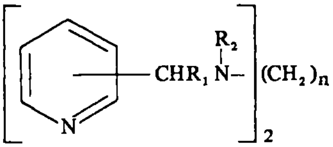
R	Physical properties
2-Aminoethyl	
4-Aminobutyl	b.p. 128°/0.001 mm
6-Aminohexyl	b.p. 136°/0.002 mm
8-Aminooctyl	b.p. 148°/0.001 mm

TABLE IX-71. *N,N*-Bis[2-, 3-, 4-(pyridylalkyl)amino]alkylenediamine



Pyridine ring position	R_1	R_2	n	Physical properties	Ref.
2	H	H	2	b.p. 151–8°/0.8 mm dimaleate, m.p. 174–5°	530 529
2	Me	H	2	b.p. 154–6°/0.25 mm; dimaleate, m.p. 162–3°	530
2	Me	H	2	b.p. 153–6°/0.25 mm; difumarate, m.p. 197–8°	529
2	Me	CHO	2	b.p. 165–8°/0.01–.03 mm; dimaleate, m.p. 145–7°	530 529
2	Me	Me	2	b.p. 168–72°/0.08 mm tetra-HCl, salt, m.p. 170°	530
2	Me	H	$-\mathrm{CH_2}\underset{\mathrm{CH_3}}{\mathrm{C}}\mathrm{H}-$	b.p. 140–5°/0.04 mm; difumarate, m.p. 151–3°	530 529, 544
2	Me	H	$(CH_3CH)_2$	b.p. 160–3°/0.75 mm; difumarate, m.p. 172–4°	529
2	Me	H	3	b.p. 148–52°/0.2 mm	530
2	Me	H	5	b.p. 167–8°/0.04 mm; dimaleate, m.p. 148–50°	530
2	CH_3	H	(*trans*-1,2-Cyclohexenyl)	b.p. 153–5°/0.005 mm; tetra-HCl, m.p. 244–6°	529

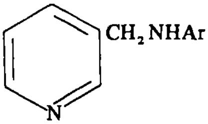
TABLE IX-71. *N,N*-Bis[2-, 3-, 4-(pyridylalkyl)amino]alkylenediamine (Continued)



Pyridine ring position	R_1	R_2	n	Physical properties	Ref.
3	Me	H	2	b.p. 176–80°/0.1 mm; dimaleate, m.p. 151–3°	529
4	Me	H	2	b.p. 170–4°[a] dimaleate, m.p. 145–7°	529

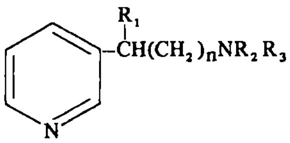
[a] Pressure not reported.

TABLE IX-72. *N*-Aryl-3-picolylamines



Ar	m.p.	Ref.
Bis(3-chloro-2-methyl-4-picolyl)amine	114–14.5°; tri-HCl, m.p. 292–5° (dec.)	640
m-Carboxyphenyl	190–2°	527
p-Carboxyphenyl	220–2°	527
1-(3,4-Dimethoxyphenyl-2-propyl)	202°	527
β-(3,4-Dimethoxyphenethyl)	226°	527
o-Hydroxyphenyl	177–8°	527
β-Hydroxy-β-(3,4-dimethoxyphenethyl)	197°	527
β-Hydroxy-β-(4-methylphenethyl)	198°	527
β-Hydroxy-β-(4-methoxyphenethyl)	153°	527
1-Hydroxy-1-phenyl-2-propyl	227°	527
1-(4-Hydroxyphenyl)-2-propyl	228° (dec.)	527
β-Hydroxy-β-phenethyl	179°	527
4-Hydroxyphenyl	145–6°	527
1-(3,4-Methylenedioxyphenyl)-2-propyl	232°	527
1-(4-Methoxyphenyl)-2-phenyl	216°	527
p-Nitrophenyl	114–15°	527
α-Phenethyl	199°	527
β-Phenethyl	205°	527
1-Phenyl-2-propyl	203° (dec.)	527

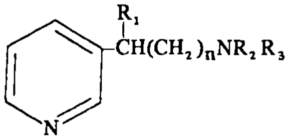
TABLE IX-73. 3-Aminoalkylpyridines



n	R_1	R_2	R_3	Substituents 2	4	5	6	Physical properties	Ref.
0	Benzyl	H	H	H	H	H	H	–	422
0	Et	H	H	H	H	H	H	b.p. 105–8°/12 mm; phenylthiourea, m.p. 164–5°	572
0	Me	H	H	H	H	H	H	b.p. 100–2°/12 mm; dipicrate, m.p. 204–5°	572
0	*n*-Pr	H	H	H	H	H	H	b.p. 109–11°/12 mm; dipicrate, m.p. 237–8°	572
0	H	6-Chloro-1,4-benzodioxan-2-ylmethyl	H	H	H	H	H	di-HCl, m.p. 144–50°	581
0	H	Diethylaminoethyl	H	H	H	H	H	b.p. 120–2°/1 mm; tripicrate, m.p. 185–6°	499
0	H	Me	H	H	H	H	H	*N*-nitroso, b.p. 115–6°/0.2 mm	594
0	H	Methylaminoethyl	H	H	H	H	H	–	224
0	H	Methylaminoethyl	H	H	H	H	H	–	224
0	H	Methylaminopropyl	H	H	H	H	H	–	707
0	H	6-Methyl-1,4-benzodioxan-2-ylmethyl	H	H	H	H	H	di-HCl, m.p. 137–42°	581

0	H	Methyleneamino	H	H	H	H	H	b.p. 100.5°/0.04 mm; n_D 1.5450; d_{20} 1.0604; tri-HCl, m.p. 184–6°	505 706
0	H	3,4-Methylenedioxyphenethyl	H	H	H	H	H	HCl, m.p. 229–31°	583
0	H	5-Methyl-8-isopropyl-1,4-benzodioxan-2-ylmethyl	H	H	H	H	H	di-HCl, m.p. 142–51°	581
0	H	Ph	H	H	H	H	H	m.p. 92–3° b.p. 130–5°/0.06 mm; di-HCl, m.p. 194–5°; dipicrate, m.p. 137–9°	498
0	H	Ph	H	H	H	H	H	m.p. 92–3°; b.p. 130–5°/0.06 mm; di-HCl, m.p. 194–5°; dipicrate, m.p. 137–9°	498
0	H	Phenethyl	H	H	H	H	H	HCl, m.p. 216–18°	531
0	H	*n*-Pr	H	H	H	H	H	b.p. 100–100.5°/0.04 mm	505
0	H	3,4,5-Trimethoxybenzyl	H	H	H	H	H	m.p. 205–7°	72
0	Ph	2-Dimethylaminoethyl	H	H	H	H	H	b.p. 160–3°/0.03 mm	580
0	*n*-Pr	Me	H	H	H	H	H	b.p. 112°/10 mm; dipicrate,	572
0	H	Benzoyl	2-Diethylaminoethyl	H	H	H	H	m.p. 234–5° b.p. 190°/0.5 mm;	499, 505
0	H	Benzyl	Benzyl	H	H	H	H	dipicrate,	
0	H	Cinnamoyl	2-Diethylaminoethyl	H	H	H	H	m.p. 138–9° m.p. 62–3° b.p. 220°/0.5 mm; HCl·H_2O, 102–4°	517 499, 505
0	H	α-Cyanobenzyl	Benzyl	H	H	H	H	m.p. 80–1°	517

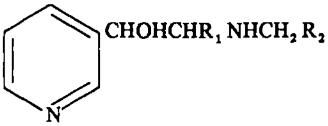
TABLE IX-73. 3-Aminoalkylpyridines (Continued)



				Substituents					
n	R_1	R_2	R_3	2	4	5	6	Physical properties	Ref.
0	H	Diphenylacetyl	2-Diethylaminoethyl	H	H	H	H	b.p. 235°/0.75 mm; m.p. 66–7°, dipicrate, m.p. 159–61°	499, 505
0	H	Et	Et	H	H	H	H	b.p. 106–8°/12 mm; b.p. 96–7°/13 mm	572 708
0	H	Me	2-Propynyl	H	H	H	H	b.p. 100°/3 mm	550
0	H	3-Methylpyridyl	Benzyl	H	H	H	H	b.p. 225°/5 mm	517
0	H	4-Methoxybenzyl	Benzyl	H	H	H	H	b.p. 230°/3–4 mm	517
0	H	Me	Et	H	H	H	H	b.p. 96–8°/12 mm; dipicrate, m.p. 172–3°	572
0	H	Me	Me	H	H	H	H	b.p. 72–5°/3 mm	708
0	H	Me	Me	Ph	H	H	Ph	b.p. 164–8°/0.1 mm	593
0	H	Ph	2-Diethylaminoethyl	H	H	H	H	b.p. 129–30°/0.03 mm	498
0	H	H	H	H	Me	Ph	H	b.p. 120–3°/5 mm; dipicrate, m.p. 218–21°	612
1	Benzyl	H	H	H	H	H	H	–	709
1	Et	H	H	H	H	H	Me	b.p. 132–6°/10 mm	568
1	Me	H	H	H	H	H	Me	b.p. 109–10°/7 mm	568
1	OH	Benzyl	H	H	H	H	H	b.p. 189°/0.2 mm; m.p. 81°; di-HCl, m.p. 189°	538

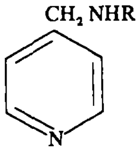
1	OH	Et	H	H	H	H	H	b.p. 114°/0.2 mm; di-HCl, m.p. 190–5°	538
1	OH	Me	H	H	H	H	H	b.p. 115–18°/0.4 mm; dibenzyl, m.p. 139–41°	538
1	OH	Pr	H	H	H	H	H	b.p. 126–8°/0.2 mm; di-HCl, m.p. 136°	538
1	Ph	Bu	H	H	H	H	Me	b.p. 180–3°/3 mm; picrate, m.p. 205–7°	568
1	Ph	Me	H	H	H	H	Me	b.p. 175–7°/3 mm	568
1	H	Et	Et	H	Me	H	H	b.p. 104°/4 mm; dipicrate, m.p. 202–3°; HCl, m.p. 153–4°	507
1	H	H	H	H	H	H	Me	b.p. 118°/8 mm; dipicrate, m.p. 210–11°	568
2	Ph	H	H	H	H	H	H	b.p. 180–90°/0.3 mm	592
4	H	*n*-BuO	H	H	H	H	H	–	
3	H	Et	Et	H	H	H	H	b.p. 133°/15 mm	710

TABLE IX-74. 3-Amino-α-hydroxyalkylpyridines[532]



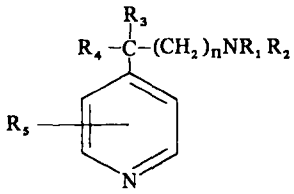
R_1	R_2	Properties
Me	H	b.p. 115–18°/0.2 mm; di-HCl, m.p. 222–4°
H	CH_2OH	b.p. 180–5°/0.54 mm; m.p. 90° dipicrate, m.p. 172°
Me	Me	b.p. 107–10°/0.14 mm; di-HCl, m.p. 232–4°
Me	Et	b.p. 119–23°/0.34 mm; di-HCl, m.p. 208–12°
Me	Ph	b.p. 163°/0.19 mm; di-HCl, m.p. 210–11°
Et	CH_2OH	b.p. 184–8°/0.01 mm

TABLE IX-75. 4-Picolylamines



R	m.p.	Ref.
Anilino	tri-HCl, 228–30°	525
p-Anisyl	78–80°; b.p. 184–6°/4 mm	534
p-Carboxyphenyl	244–7°	527
β-(3,4-Dimethoxyphenethyl)	210°	527
1-(3,4-Dimethoxyphenyl)-2-propyl	153°	527
β-Hydroxy-β-(3,4-dimethoxyphenethyl)	203°	527
β-Hydroxy-β-(4-methylphenethyl)	201°	527
β-Hydroxy-β-(4-methoxyphenethyl)	161°	527
1-(4-Hydroxyphenyl)-2-propyl	230° (dec.)	527
1-Hydroxy-1-phenyl-2-propyl	228°	527
β-Hydroxy-β-phenethyl	143°	527
o-Hydroxyphenyl	176–8°	504, 527
1-(3,4-Methylenedioxyphenyl)-2-propyl	168°	527
1-(4-Methoxyphenyl)-2-phenyl	190°	527
α-Phenethyl	232°	527
β-Phenethyl	198° (dec.)	527
Ph	101–3°, 103–4°; b.p. 125–50°/0.04 mm di-HCl, m.p. 197–9°; picrate, m.p. 147–8°	534, 698 498
1-Phenyl-2-propyl	185°	527
2-Pyridyl	109–11°; b.p. 166–7°/4 mm	534
3,4,5-Trimethoxyphenethyl	210° (dec.)	527
o-Tolyl	75–6°; b.p. 165–7°/3 mm	534
p-Tolyl	74°; b.p. 162–6°/4 mm	534

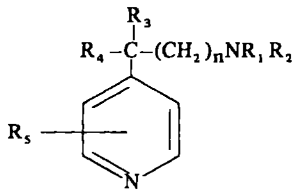
TABLE IX-76. 4-(Aminoalkyl)pyridines



					R_5					
n	R_1	R_2	R_3	R_4	2	3	5	6	Physical properties	Ref.
0	Diethylaminoethyl	H	H	H	H	H	H	H	b.p. 110–12°/0.4 mm; tripicrate, m.p. 176–7°	499
0	Ethylamino	H	H	H	H	H	H	H	b.p. 108.5°/0.1 mm; n_D^{20} 1.5454	505
									d_{20} 1.0580 tri-HCl, m.p. 247°	
0	3,4-(Methylenedioxy)phenethyl	H	H	H	H	H	H	H	HCl, m.p. 216–18°	583
0	Piperidino	–	H	H	IsoBu	OH	H	Me	HCl, m.p. 209–10°	546
0	Aminomethyl	H	H	Ph	H	H	H	H	m.p. 178–81°	591
0	Me	H	H	Ph	H	H	H	H	m.p. 178–81°	591
0	H	H	H	Ph	H	H	H	H	b.p. 143–7°	595
0	H	H	H	H	H	OH	Hydroxymethylene	H	di-HCl, m.p. 165–9° (dec.)	523
0	Benzyl	Benzyl	H	H	H	H	H	H	m.p. 85-6°	517
0	Benzoyl	Diethylaminoethyl	H	H	H	H	H	H	b.p. 170°/0.04 mm; dipicrate, m.p. 159–61°	499

0	Cinnamoyl	Diethylaminoethyl	H	H	H	H	H	H	b.p. 195°/0.04 mm; dipicrate, m.p. 151–3°	499
0	Diethylaminoethyl	Diphenylacetyl	H	H	H	H	H	H	b.p. 215°/0.09 mm; m.p. 93–4°; dipicrate, m.p. 165–6°	499
0	Diphenylmethyl	Me	H	H	H	H	H	H	m.p. 135–7°	528
0	Diethylaminoethyl	Ph	H	H	H	H	H	H	b.p. 135–40°/0.04 mm; tripicrate, m.p. 292–3°	498
0	Et	Et	H	H	H	H	H	H	b.p. 101–3°/5 mm	708
0	Me	2-Propynyl	H	H	H	H	H	H	b.p. 79°/1.2 mm; HCl, m.p. 183–5°	549, 550
0	2-Phenylpropyl	3,4,5-Trimethoxyphenyl	H	H	H	H	H	H	m.p. 214–16°	72
0	Me	Me	H	H	Me	OH	H	Me	b.p. 110–12°/2–3 mm; di-HCl, m.p. 255–6°	544
0	Me	Me	H	H	Et	OH	H	Me	b.p. 115–20°/2–3 mm; di-HCl, m.p. 190.5–1.5°	544 544
1	H	H	H	H	H	H	H	H	b.p. 104°/9 mm; picrate, m.p. 152°	564
1	Benzoyl	H	H	H	H	H	H	H	1-oxide, di-HCl, m.p. 177–8°	574
1	H	H	OH	H	H	H	H	H	b.p. 138°/0.7 mm	574
1	*o*-Chlorophenyl	Dimethylaminoethyl	H	H	H	H	H	H	m.p. 99–100°; dipicrate, m.p. 138–42°	561, 562
1	*o*-Chlorophenyl	Dimethylaminoethyl	H	H	H	H	H	H	b.p. 156°/0.09 mm	561, 562
1	*m*-Chlorophenyl	Dimethylaminoethyl	H	H	H	H	H	H	b.p. 164–8°/0.02 mm	561, 562
1	*m*-Chlorophenyl	Dimethylaminopropyl	H	H	H	H	H	H	b.p. 178–80°/0.02 mm	561, 562
1	*p*-Chlorophenyl	Dimethylaminoethyl	H	H	H	H	H	H	b.p. 168–70°/0.02 mm; dipicrate, m.p. 165–6°	561, 562

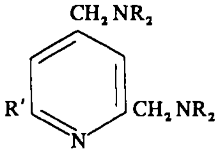
TABLE IX-76. 4-(Aminoalkyl)pyridines (Continued)



n	R₁	R₂	R₃	R₄	R₅ 2	R₅ 3	R₅ 5	R₅ 6	Physical properties	Ref.
1	*p*-Chlorophenyl	Dimethylaminopropyl	H	H	H	H	H	H	b.p. 168–70°/0.05 mm	561, 562
1	Dimethylaminoethyl	*m*-Methylphenyl	H	H	H	H	H	H	b.p. 158–60°/0.05 mm; dipicrate, m.p. 178–9°	561, 562
1	Dimethylaminoethyl	Ph	H	H	H	H	H	H	b.p. 154–6°/0.02 mm; dipicrate, m.p. 176–7°	561, 562
1	2-Ethoxybenzoyl	2-Phenylpropyl	H	H	H	H	H	H	m.p. 103–6°	569
1	Me	Me	H	H	H	H	H	H	b.p. 70°/2 mm	508
1	Me	2-Propynyl	H	H	H	H	H	H	b.p. 153°/20 mm	550
1	2-Phenylpropyl	H	H	H	H	H	H	H	b.p. 138–40°/0.08 mm	569
2	H	H	H	H	H	H	H	H	b.p. 90–2°/3 mm	508
2	3-Pyrrolidino	H	H	H	H	H	H	H	b.p. 132–5°/5 mm; methobromide, m.p. 191–3°	508 508
2	Me	Me	H	H	H	H	H	H	b.p. 90–2°/3 mm; methobromide, m.p. 253–4°	508 508
2	Me	Me	H	Ph	H	H	H	H	b.p. 133–5°/5 mm	508

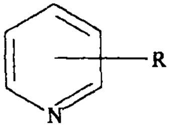
2	IsoPr	IsoPr	Amido	Ph	H	H	H	H	m.p. 138.5–9°	592
2	IsoPr	IsoPr	CN	Ph	H	H	H	H	b.p. 164–8°/0.7 mm	592
3	Me	Me	H	H	H	H	H	H	b.p. 95–105°/2 mm; methobromide, m.p. 209–10°	508
4	H	H	H	H	H	H	H	H	dipicrate, m.p. 134–5°	547
7	H	H	H	H	H	H	H	H	dipicrate, m.p. 108°	547
12	H	H	H	H	H	H	H	H	dipicrate, m.p. 110°	547

TABLE IX-77. 6-Substituted-2,4-bis(alkylaminomethyl)-pyridines[546]



R_2N	R_1	Physical properties
Me_2N	*n*-Bu	b.p. 180–2°/1 mm
Me_2N	IsoAm	b.p. 150–1°/1 mm
Piperidino	*n*-Bu	tri-HCl, m.p. 224–5.5°
Piperidino	*n*-Pr	b.p. 98–100°/1–2 mm; tri-HCl, m.p. 213–4°
Piperidino	IsoPr	m.p. 76–7°; tri-HCl, m.p. 198–9°

TABLE IX-78. Miscellaneous Aminopyridines



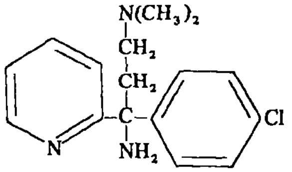
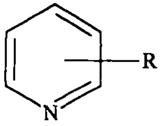
	Physical properties	Ref.
3-Amino-5-aminomethyl-4-methoxymethyl-2-methylpyridine	di-HCl, m.p. 230–1°; dipicrate, m.p. 214–15°	511
3-Amino-5-aminomethyl-2-methylpyridine	di-HCl, m.p. 295–7°	711
3-Amino-4,5-bis(aminomethyl)-2-methylpyridine	tri-HCl	378
3-Amino-4,5-bis(carbethoxyaminomethyl)-2-methylpyridine	m.p. 195–6°	378
2-[1-(2-Aminoethyl)amino]ethylpyridine	b.p. 74–5°/0.07 mm	529
4,5-Bis(aminomethyl)-3-chloro-2-methylpyridine	tri-HCl	378
2,2′-{3-[(*p*-Chloro-α-methyl)amino]propylidene}dipyridine	b.p. 201–10°/0.5 mm	539
1-Methylamino-2-pyridylcyclohexane	b.p. 72–4°/0.08 mm	575
	b.p. 155–60°/3 mm; maleate, m.p. 132–3°; dipicrate, m.p. 194–6°	705
	m.p. 146°	351

TABLE IX-78. Miscellaneous Aminopyridines (Continued)



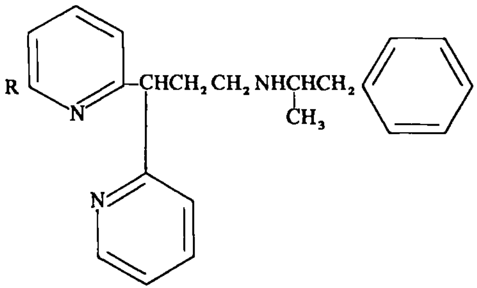
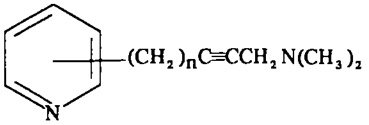
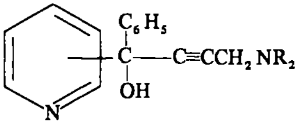
		Physical properties	Ref.
	R = H	b.p. 210–18°/1.5 mm m.p. 69–70° HCl, m.p. 130–1°	539
	R = CH_3	b.p. 204–8°/0.5 mm; HCl, m.p. 146–7°	539
1-(2-Pyridyl)-1-aminocyclohexane		di-HCl, m.p. 241–2°; acetamide, m.p. 141–2°	575
1-(2-Pyridyl)-1-ethylaminocyclohexane		m.p. 63.5–64°	575
1-(2-Pyridyl)-1-ethylmethlaminocyclohexane		b.p. 90–100°/0.1 mm	575
1-(2-Pyridyl)-1-*N*-piperidinocyclohexane		b.p. 105–8°/0.03 mm	575
2-(2-Pyridylthio)-1-aminoethane		di-HCl, m.p. 201°	

TABLE IX-79. 2-, 3-, and 4-Dimethylamino-2-alkynylpyridines



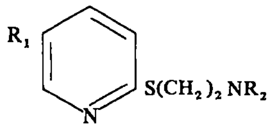
Ring position	n	b.p./mm	Dipicrate, m.p.	Ref.
2	2	142–3°/13	159°	547
2	3	159–60°/14	–	547
2	4	177°/17	157–8°	547
2	5	187°/14	134°	547
2	10	182°/0.7	70° monopicrate, m.p. 88°	547
3	3	151–2°/2	–	548
3	4	147–8°/0.8	–	548
4	3	142–3°/1.4	–	548
		162°/14	135°	547
4	5	166°/1.5	158.5°	547
4	10	213–14°/1.6	75°	547

TABLE IX-80. Other 2-, 3-, or 4-Dialkylamino-2-butynylpyridines[552]



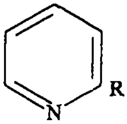
Ring position	R	Properties
2	Et	m.p. 70–2°; methobromide, m.p. 151–2°
2	Me	m.p. 116–7°; methobromide, m.p. 154–5°
3	Et	m.p. 81.2°
4	Et	m.p. 72–4°

TABLE IX-81. β-Dialkylaminoethyl Pyridyl Sulfides



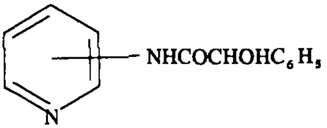
Ring position	R_1	R	Physical properties	m.p. of derivatives: Picrate	HCl	MeI	EtI	Ref.
2	NO_2	Me	m.p. 40–2°	167–70°	182–3°	190–2°	218–20°	585
2	NO_2	Et	m.p. 50–2°	–	173–4°	172–4°	206–8°	585
2	H	Me	b.p. 91–3°/3 mm	30–2°	194–6°	183–4°	150–2°	585
2	H	Et	b.p. 130–2°/4 mm	103–5°	–	130–2°	182–4°	585
2	H	H	(di-HCl, m.p. 201°; (acetyl, m.p. 70°) (diacetamide, m.p. 102°) (diacetamide sulfone, m.p. 120°)					586
4	H	H	(di-HCl, m.p. 236°) (acetyl, m.p. 75°) (diacetamide sulfone, m.p. 124°)					586

TABLE IX-82. 2-Aminoethoxypyridines[589]



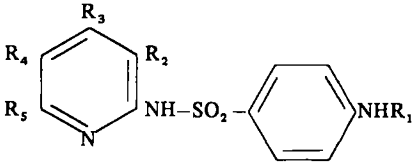
R	Physical properties
[2-(2-Morpholinoethylamino)ethoxy]-	b.p. 170–8°/1 mm
[2-(3-Morpholinopropylamino)ethoxy]-	di-HCl, m.p. 189–90°
[2-(*N*-methyl-2-morpholinoethylamino)-ethoxy]-	di-HCl, m.p. 180–2°
[2-(*N*-methyl-2-piperidinoethylamino)-ethoxy]-	di-HCl, m.p. 208–10°

TABLE IX-83. Mandelamidopyridines



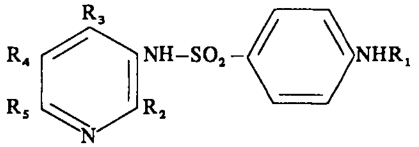
Compound	m.p.	HCl, m.p.	Ref.
2-(*O*-Acetylmandelamido)pyridine	–	–	331
4-(*O*-Acetylmandelamido)pyridine			331
2-(4-Bromomandelamido)pyridine	146–7°	197–8°	331
5-Bromo-2-mandelamidopyridine	155–6°	175° (dec.)	331
2-[β-(*N*-Butylcarbamyloxy)phenethylamino] pyridine	95–8°		332
5-Chloro-2-mandelamidopyridine	146–8°	169°	332
2-[β-(*N*-Ethylcarbamoyloxy)phenethylamino] pyridine	132–4°	75–8°	332
2-(Hexahydromandelamido)pyridine	118–20°	–	331
2-(β-Hydroxy-4-bromophenethylamino)pyridine	105–6°	135–6°	332
2-(β-Hydroxy-4-chlorophenethylamino)pyridine	91–8°	112–23°	332
2-(β-Hydroxy-β-cyclohexylethylamino)pyridine	86–8°	143–4°	322
2-(β-Hydroxyphenethylamino)-5-bromopyridine	110–11°	187–9°	322
2-(β-Hydroxyphenethylamino)-5-chloropyridine	102–3°	177–8°	332
6-(β-Hydroxyphenethylamino)-2,4-lutidine	77–8°	132–3°	322
2-[*N*-(β-Hydroxyphenethyl)methylamino] pyridine	b.p. 147–57°/0.3 mm	170–3°	332
6-(β-Hydroxyphenethylamino)-3-picoline	97–9°	116–17°	332
2-(β-Hydroxy-β-phenethylamino)-4-picoline	90–1°	135–6°	332
2-(β-Hydroxyphenethylamino)pyridine	102–5°	124–6°	332
3-(β-Hydroxyphenethylamino)pyridine	b.p. 195–202°/0.3 mm	–	322
2-(γ-Hydroxy-γ-phenylpropylamino)pyridine	123–4°	138–60°	332
2-Mandelamido-4-picoline	143–6°	188–9°	332
6-Mandelamido-2,4-lutidine	167–9°	195–6°	332
6-Mandelamido-3-picoline	141–2°	203°	332

TABLE IX-84. 2-Sulfanilamidopyridines[388]



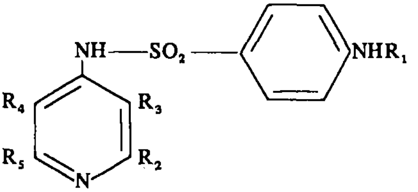
R_1	R_2	R_3	R_4	R_5	m.p.
Acetyl	OMe	H	H	H	212°
Acetyl	H	OMe	H	H	262–3°
Acetyl	H	H	OMe	H	228–30°
Acetyl	H	OMe	H	OMe	201–3°
Acetyl	H	OMe	H	Me	236–8°
H	OMe	H	H	H	214–15°
H	H	OMe	H	H	237–9°
H	H	H	OMe	H	200–1°
H	H	OMe	H	OMe	158–9°
H	H	OMe	H	Me	184–5°

TABLE IX-85. 3-Sulfanilamidopyridines[388]



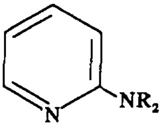
R_1	R_2	R_3	R_4	R_5	m.p.
Acetyl	H	H	Br	H	250–1°
Acetyl	H	H	Cl	H	255–6°
Acetyl	OMe	H	H	H	194–5°
Acetyl	H	OMe	H	H	257–8°
Acetyl	H	H	OMe	H	263–4°
Acetyl	OMe	H	H	OMe	193–5°
Acetyl	OMe	H	H	Br	210–11°
Acetyl	H	OMe	H	Me	228–9°
Acetyl	OMe	OMe	H	Me	236–7°
H	H	H	Br	H	208–10°
H	H	H	Cl	H	208–9°
H	OMe	H	H	H	134–6°
H	H	OMe	H	H	222–3°
H	H	H	OMe	H	220–1°
H	OMe	H	H	Br	172–3°
H	OMe	H	H	OMe	165–7°
H	H	OMe	H	Me	210–11°
H	OMe	OMe	H	Me	225–7°

TABLE IX-86. 4-Sulfanilamidopyridines[388]



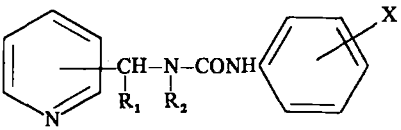
R_1	R_2	R_3	R_4	R_5	m.p.
Acetyl	OMe	H	H	H	218–19°
Acetyl	H	OMe	H	H	232–3°
Acetyl	OMe	H	OMe	H	230–1°
Acetyl	OMe	H	Me	H	204–5°
H	OMe	H	H	H	151–2°
H	H	OMe	H	H	173–4°
H	OMe	H	OMe	H	181–2°
H	OMe	H	Me	H	69–71°

TABLE IX-87. 1-(2-Pyridylamino)glutarimides[123]



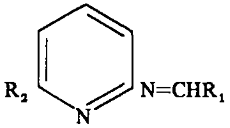
R_2	m.p.
4,4-Dimethylglutarimide	196°
4-Ethyl-4-methylglutarimide	137–8°
4,4-Tetramethyleneglutarimide	172–3°
4-Phenylglutarimide	201–3°

TABLE IX-88. *N*-Aryl-*N*′-(Pyridylalkyl)ureas[595]



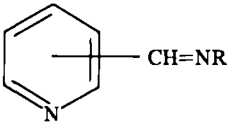
Pyridine ring position	R_1	R_2	X	Physical properties
2	Me	H	2-Cl	HBr, m.p. 134–5°
2	Me	H	4-OEt	–
2	H	H	2-Cl	m.p. 148–50°; HCl, m.p. 173–5°
3	Me	H	2-Cl	–
3	Me	H	4-OEt	m.p. 118–19°
3	H	H	4-Cl	m.p. 171–3°
3	H	H	3,4,5-$(OMe)_3$	m.p. 164–6°; HCl, m.p. 169–70°
4	Me	H	4-Br	m.p. 159–60°
4	Me	H	2-Cl	HCl, m.p. 145–6°
4	Me	H	3-Cl	HCl, m.p. 143–7°
4	Me	H	4-Cl	m.p. 136–7°
4	Me	H	2,5-Cl_2	m.p. 95–7°
4	Me	H	3-F	–
4	Me	H	4-I	–
4	Ph	H	2-Cl	m.p. 192–5°
4	H	H	4-Cl	HCl, m.p. 235–6°
4	H	H	2-OEt	–
4	H	H	3,4,5-$(OMe)_3$	m.p. 170.5–2.5°; HCl, m.p. 222–4°

TABLE IX-89. Arylmethylene-2-aminopyridines



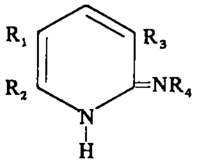
R_1	R_2	Physical properties	Ref.
2-Furanyl	Me	b.p. 138-9°/0.3 mm	305
o-Aminobenzylidene	H	m.p. 125°	297
o-Anilino	H	m.p. 125°	296, 297
Benzyl	H	b.p. 123–5°/1 mm	578
(3-Chloro-2-benzyfuranyl)methyl	H	m.p. 107–9°	307
Dibenzoylmethylene	H	m.p. 70°	297
4,5-Dichloro-2-thienyl	H	m.p. 98.5°	310
p-(2-Diethylaminoethoxy)phenyl	H	b.p. 160–5°/0.1 mm	578
2-Et-3-benzofuranyl	H	b.p. 105–15°/0.001 mm	650
2-Furanyl	H	m.p. 88–9°	305
Isopropylidene	H	Acetyl, m.p. 36°	297
p-Nitrobenzyl	H	m.p. 147–8°	712

TABLE IX-90. Aldimines



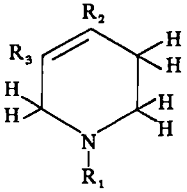
Ring position	R	m.p.	Ref.
2	*p*-Carboxyphenyl	235–7°	527
2	*p*-Hydroxyphenyl	186°	527
2	β-Phenethyl	39–41°; b.p. 147–8°	531
3	*p*-Aminophenyl	144°	527
3	*o*-Carboxyphenyl	87–8°	527
3	*m*-Carboxyphenyl	219–21°	527
3	*p*-Carboxyphenyl	241–3°	527
?	Diphenylmethyl	105–7°	528
3	*p*-Hydroxyphenyl	212–13°	527
3	*m*-Nitrophenyl	109–11°	527
3	β-Phenethyl	46–7°	531
4	*p*-Carboxyphenyl	288–90°	527
4	*o*-Hydroxyphenyl	166–8°	527
4	*p*-Hydroxyphenyl	201–2°	527
4	β-Phenethyl	b.p. 150–1°	531

TABLE IX-91. Amino-2-imino-1,2-dihydropyridines



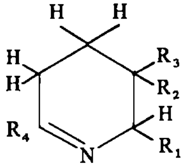
R_1	R_2	R_3	R_4	Physical properties	Ref.
NH_2	H	H	2-Pyridyl		656
H	NH_2	H	2-Pyridyl	m.p. 132.5–4°	116
NH_2	NH_2	H	2-Pyridyl	m.p. > 300°	723
2-Amino-3,3,4,4,5,5-hexafluoro-6-imino-piperidine				m.p. 162–73°	713

TABLE IX-92. 1,2,3,6-Tetrahydroaminopyridines



R_1	R_2	R_3	Physical properties	Ref.
Me	*p*-Aminobenzamido	Me	m.p. 168–70°	718
Me	*p*-Aminobenzylamino	Me	m.p. 126–7°	718
2-Aminoethyl	Et	H	b.p. 102–4°/10 mm	717
2-Aminoethyl	Ph	H	–	329
4-Aminobutyl	Ph	H	b.p. 135–6°/0.2 mm	329
Me	$NH_2C_6H_4CH_2CH_2CONH$	Me	m.p. 153–4°	719, 720

TABLE IX-93. 1,2,3,4-Tetrahydroaminopyridines



R_1	R_2	R_3	R_4	Physical properties	Ref.
2-Dimethylamino	H	H	H	–	383
2-Diethylamino	H	H	H	–	383
Me	3-Aminopropyl	Me	H	b.p. 92°;[a] picrate, m.p. 162–3°	722
H	H	H	4-Aminobutyl	–	721

[a]Pressure not reported.

References

1. M. I. Farberov, A. M. Kut'in, B. F. Ustaushchikov, and N. K. Shemyakina, *Zh. Prikl. Khim.*, **37**, 661 (1964); *Chem. Abstr.*, **60**, 14467 (1964).
2. F. Johnson, U.S. patent, 3,096,377 (1963); *Chem. Abstr.*, **59**, 12768 (1963).
3. F. Johnson, J. P. Panella, A. A. Carlson, and D. H. Hummeman, *J. Org. Chem.*, **27**, 2473 (1962).
4. T. Takata, *Bull. Chem. Soc. Jap.*, **35**, 1438 (1962); *Chem. Abstr.*, **58**, 2451 (1963).
5. F. Johnson, U.S. patent, 3,255,041 (1965); *Chem. Abstr.*, **64**, 6623 (1966).
6. F. Johnson, U.S. patent, 3,247,214 (1966); *Chem. Abstr.*, **64**, 19570 (1966).
7. M. R. S. Weir, K. E. Helmer, and J. B. Hyne, *Can. J. Chem.*, **41**, 1042 (1963).
8. Daiichi Seiyaku Co., Ltd., Jap. patent, 26,386 (1963); *Chem. Abstr.*, **60**, 1199 (1964).
9. D. J. Collins, *J. Chem. Soc.*, 1337 (1963).
10. R. Urban, L. H. Chopard-dit-Jean, and O. Schnider, *Gazz. Chim. Ital.*, **93**, 163 (1963); *Chem. Abstr.*, **59**, 1582 (1963).
11. F. Parisi, P. Bovina, and A. Quilico, *Gazz. Chim. Ital.*, **90**, 903 (1969); *Chem. Abstr.*, **55**, 21116 (1961).
12. P. Nantka-Namirski, Pol. patent, 43,117 (1960); *Chem. Abstr.*, **55**, 13451 (1961).
13. W. Mathes and A. Wolf, Ger. patent, 1,119,274 (1961); *Chem. Abstr.*, **56**, 14247 (1962).
14. F. H. Case and W. A. Butte, *J. Org. Chem.*, **26**, 4415 (1961).
15. H. Bojarska-Dahlig and I. Gruda, *Rocz. Chem.*, **33**, 505 (1959); *Chem. Abstr.*, **54**, 522 (1960).
16. R. A. Abramovitch and J. G. Saha, in "Advances in Heterocyclic Chemistry," A. R. Katritzky and A. J. Boulton, Eds., Vol. 6, Academic Press, New York, 1966, p. 295.
17. R. A. Abramovitch, F. Helmer, and J. G. Saha, *Chem. Ind.*, (London) 659 (1964).
18. R. A. Abramovitch, F. Helmer, and J. G. Saha, *Can. J. Chem.*, **43**, 725 (1965).

19. N. S. Prostakov, N. N. Mikheeva, and D. Pkhal'gumani, *Khim. Geterotsikl. Soedin.*, 671 (1967); *Chem. Abstr.*, **68**, 104915X (1968).
20. R. F. Evans and H. C. Brown, *J. Org. Chem.*, **27**, 1329 (1962).
21. A. Roedig and K. Grohe, *Chem. Ber.*, **98**, 923 (1965).
22. Presented by C. S. Giam, First International Congress of Heterocyclic Chemistry, June 15, 1967, Albuquerque, N. Mex. Abstr. No. 92.
23. L. S. Levitt and B. W. Levitt, *Chem. Ind.* (London), 1621 (1963).
24. H. L. Jones and D. L. Beveridge, *Tetrahedron Lett.*, 1577 (1964).
25. G. C. Barrett and K. Schofield, *Chem. Ind.* (London), 1980 (1963).
26. R. F. Childs and A. W. Johnson, *Chem. Ind.* (London), 542 (1964).
27. Y. Ban and T. Wakamatsu, *Chem. Ind.* (London), 710 (1964).
28. M. J. Pieterse and H. J. den Hertog, *Rec. Trav. Chim. Pays-Bas*, **80**, 1376 (1961); *Chem. Abstr.*, **58**, 5625 (1963).
29. R. J. Martens, H. J. den Hertog, and M. Van Ammers, *Tetrahedron Lett.*, 3207 (1964).
30. R. J. Martens and H. J. den Hertog, *Rec. Trav. Chim. Pays-Bas*, **83**, 621 (1964); *Chem. Abstr.*, **61**, 9460 (1964).
31. T. Kato, T. Niitsuma, and N. Kusaka, *Yakugaku Zasshi*, **84**, 432 (1964); *Chem. Abstr.*, **61**, 4171 (1964).
32. R. J. Martens and H. J. den Hertog, *Rec. Trav. Chim. Pays-Bas*, **86**, 655 (1967).
33. M. J. Pieterse and H. J. den Hertog, *J. S. African Chem. Inst.*, **17**, 41 (1964); *Chem. Abstr.*, **61**, 5604 (1964).
34. M. J. Pieterse and J. H. den Hertog, *Rec. Trav. Chim. Pays-Bas*, **81**, 855 (1962); *Chem. Abstr.*, **58**, 11325 (1963).
35. H. J. den Hertog, M. J. Pieterse, and D. J. Buurman, *Rec. Trav. Chim. Pays-Bas*, **82**, 1173 (1963).
36. J. W. Streef and H. J. den Hertog, *Rec. Trav. Chim. Pays-Bas*, **85**, 803 (1966); *Chem. Abstr.*, **66**, 75975t (1967).
37. H. J. den Hertog, H. C. Van der Plas, M. J. Pieterse, and J. W. Streef, *Rec. Trav. Chim. Pays-Bas*, **84**, 1569 (1965); *Chem. Abstr.*, **64**, 12670 (1966).
38. H. J. den Hertog, R. J. Martens, H. C. Van der Plas, and J. Bon, *Tetrahedron Lett.*, 4325 (1966).
39. Yu. I. Chumakov, *Metody Polucheniya Khim. Reaktivov i Preparatov, Gos. Kom. Sov. Min. SSSR po Khim.*, **11**, 77, (1964); *Chem. Abstr.*, **64**, 15832 (1966).
40. L. van der Does and H. J. den Hertog, *Rec. Trav. Chim. Pays-Bas*, **84**, 951 (1965); *Chem. Abstr.*, **63**, 14805 (1965).
41. T. Takahasi, K. Kanematsu, R. Ohishi, and T. Mizutani, *Chem. Pharm. Bull.* (Tokyo), **8**, 539 (1960); *Chem. Abstr.*, **55**, 13429 (1961).
42. E. C. Taylor and J. S. Driscoll, *J. Amer. Chem. Soc.*, **82**, 3141 (1960).
43. J. M. Essery and K. Schofield, *J. Chem. Soc.*, 4953 (1960).
44. P. Nantka-Namirski, *Acta Polon. Pharm.*, **18**, 391 (1961); *Chem. Abstr.*, **57**, 16554 (1962).
45. A. Hunger, H. Keberle, A. Rossi, and K. Hoffman, Swiss patent 386,442 (1965); *Chem. Abstr.*, **63**, 14876 (1965).
46. J. A. Montgomery and K. Hewson, *J. Med. Chem.*, **9**, 354 (1966).
47. Z. Talik, *Rocz. Chem.*, **36**, 1313 (1962); *Chem. Abstr.*, **59**, 6358 (1963).
48. T. Talik, *Rocz. Chem.*, **37**, 69 (1963); *Chem. Abstr.*, **59**, 8698 (1963).
49. T. Talik and Z. Talik, *Rocz. Chem.*, **41**, 1721 (1967); *Chem. Abstr.*, **69**, 2823u (1968).
50. T. Talik and Z. Talik, *Rocz. Chem.*, **40**, 1187 (1966); *Chem. Abstr.*, **66**, 11165u (1967).

51. T. Talik and Z. Talik, *Rocz. Chem.*, **38**, 777 (1964); *Chem. Abstr.*, **61**, 10653 (1964).
52. Z. Talik, T. Talik, and A. Puszynski, *Rocz. Chem.*, **39**, 601 (1965); *Chem. Abstr.*, **63**, 16298 (1965).
53. R. D. Chambers, J. Hutchinson, W. K. R. Musgrave, Belg. patent, 660,873 (1965); *Chem. Abstr.*, **65**, 7152 (1966).
54. R. E. Banks, J. E. Burgess, W. M. Cheng, and R. N. Hazeldine, *J. Chem. Soc.*, 575 (1965).
55. R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc.*, 3573 (1964).
56. C. T. Redemann, Belg. patent, 628,486 (1963); *Chem. Abstr.*, **60**, 15840 (1964).
57. R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *Proc. Chem. Soc.*, **83**, (1964).
58. R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc., Suppl.*, **1**, 5634 (1964).
59. R. E. Banks, R. N. Haszeldine, E. Phillips, and I. M. Young, *J. Chem. Soc., C*, 2091 (1967).
60. W. Czuba, *Rocz. Chem.*, **34**, 905 (1960).
61. W. Czuba, *Rec. Trav. Chim. Pays-Bas*, **82**, 988 (1963); *Chem. Abstr.*, **60**, 1723 (1964).
62. L. N. Yakhontov, E. I. Lapan, and M. V. Rubtsov, *Khim. Geterotsikl. Soedin.*, 1063 (1967); *Chem. Abstr.*, **69**, 86786v (1968).
63. V. L. Zbarskii, G. M. Shutov, V. F. Zhilin, and E. Yu. Orlova, *Khim. Geterotsikl. Soedin.*, **1**, 178 (1967); *Chem. Abstr.*, **67**, 73500f (1967).
64. M. Nakadate, Y. Takano, T. Hirayama, S. Sakizawa, T. Hirano, K. Okamoto, K. Hirao, T. Kawamura, and M. Kimura, *Chem. Pharm. Bull.* (Tokyo), **13**, 113 (1965); *Chem. Abstr.*, **62**, 14620 (1965).
65. V. L. Zbarskii, L. M. Glazunova, G. M. Shutov, V. F. Zhilin, and E. Yu. Orlova, U.S.S.R. patent, 195,455 (1967); *Chem. Abstr.*, **68**, 104990t (1968).
66. G. C. Finger, L. D. Starr, A. Roe, and W. J. Link, *J. Org. Chem.*, **27**, 3965 (1962).
67. B. M. Ferrier and N. Campbell, *Proc. Roy. Soc. Edinburgh*, **A65**, 231 (1959).
68. T. Kato and T. Niitsuma, *Chem. Pharm. Bull.* (Tokyo), **13**, 963 (1965); *Chem. Abstr.*, **63**, 14804 (1965).
69. W. L. Mosby, *Chem. Ind.* (London), 1348 (1959).
70. S. Pietra and G. Tacconi, *Farmaco, Ed. Sci.*, **19**, 741 (1964); *Chem. Abstr.*, **62**, 1637 (1965).
71. J. DeLarge, *Farmaco., Ed. Sci.*, **22**, 99 (1967); *Chem. Abstr.*, **66**, 94891d (1967).
72. G. N. Walker, M. A. Moore, and B. N. Weaver, *J. Org. Chem.*, **26**, 2740 (1961).
73. P. Yates, M. J. Jorgenson, and S. K. Roy, *Can. J. Chem.*, **40**, 2146 (1962).
74. J. Suszko and M. Szafran, *Rocz. Chem.*, **39**, 709 (1965); *Chem. Abstr.*, **64**, 3466 (1966).
75. G. Tocconi and S. Pietra, *Ann. Chim.* (Rome), **55**, 810 (1965); *Chem. Abstr.*, **64**, 686 (1966).
76. E. V. Brown, A. F. Smetana, and A. A. Hamdan, *J. Med. Chem.*, **8**, 252 (1965); *Chem. Abstr.*, **62**, 12279 (1965).
77. B. Benke, S. Joger, L. Szabo, I. Koczka, G. Losonczi, and I. Hoffmann, Hung. patent, 150,277, (1963); *Chem. Abstr.*, **60**, 2909 (1964).
78. V. A. Kon'kova and L. A. Petrova, *Trudy Vsesoyuz, Nauch.-Issledovatel, Vitamin Inst.*, **6**, 10 (1959); *Chem. Abstr.*, **55**, 12399 (1961).
79. P. Krumholz, *Inorg. Chem.*, **4**, 609 (1965).
80. K. Hoffmann, A. Hunger, J. Kerbrle, and A. Ross, U.S. patent, 2,987,518 (1961); *Chem. Abstr.*, **55**, 24795 (1961).
81. G. Wagner and E. Fickweiler, *Arch. Pharm.* (Weinheim), **298**, 297 (1965); *Chem. Abstr.*, **63**, 5728 (1965).

82. G. Wagner and E. Fickweiler, *Arch. Pharm.* (Weinheim), **298**, 62 (1965); *Chem. Abstr.*, **63**, 1847 (1965).
83. T. Wieland, C. Fest, and G. Pfleiderer, *Ann. Chem.*, **642**, 163 (1961)
84. E. Hayashi and H. Yamanaka, Jap. patent, 15,616 (1961); *Chem. Abstr.*, **56**, 12863 (1962).
85. H. J. Knackmuss, *Chem. Ber.*, **101**, 1148 (1968).
86. R. P. Rao, *Austr. J. Chem.*, **17**, 1434 (1964).
87. R. J. Rousseau and R. K. Robins, *J. Heterocycl. Chem.*, **2**, 196 (1965).
88. J. Dadrowski, W. Jasiobedzki, T. Jaworski, M. Midon, and J. Terpinski, Pol. patent, 45,711, (1962); *Chem. Abstr.*, **58**, 9033 (1963).
89. A. Raczka, A. Swirska, and H. Bojarska-Dahling, *Acta Polon. Pharm.*, **20**, 155 (1963); *Chem. Abstr.*, **62**, 1630 (1965).
90. Z. Skrowaczewska and H. Ban, *Bull. Acad. Polon. Sci., Ser. Chem.*, **9**, 213 (1961); *Chem. Abstr.*, **59**, 7474 (1963).
91. L. Archremowicz, T. Batkowski, and Z. Skrowaczewska, *Rocz. Chem.*, **38**, 1317 (1964); *Chem. Abstr.*, **62**, 1630 (1965).
92. W. Sliwa and E. Plazek, *Acta Polon. Pharm.*, **23**, 105 (1966); *Chem. Abstr.*, **65**, 10559 (1966).
93. L. Achremowicz and Z. Skrowaczewska, *Rocz. Chem.*, **39**, 1417 (1965); *Chem. Abstr.*, **64**, 17530 (1966).
94. H. L. Yale, F. A. Sowinski, and J. Bernstein, U.S. patent, 3,123,614 (1964); *Chem. Abstr.*, **61**, 4385 (1964).
95. E. V. Brown and R. H. Neil, *J. Org. Chem.*, **26**, 3546 (1961).
96. P. C. Jain, S. K. Chatterjee, and N. Anand, *Indian J. Chem.*, **4**, 403 (1966); *Chem. Abstr.*, **66**, 46522x (1967).
97. T. Nakashima and M. Endo, *Nippon Kagaku Zasshi*, **81**, 816 (1960); *Chem. Abstr.*, **56**, 5923 (1962).
98. S. P. Acharya and K. S. Nargund, *J. Sci. Res.*, **21B**, 483 (1962); *Chem. Abstr.*, **58**, 5623 (1963).
99. L. Achremowicz and Z. Skrowaczewska, *Rocz. Chem.*, **41**, 1555 (1967); *Chem. Abstr.*, **69**, 10335b (1969).
100. Z. Talik and T. Talik, *Rocz. Chem.*, **36**, 417 (1962); *Chem. Abstr.*, **58**, 5627 (1963).
101. C. Koenig, H. Pelster, and H. Puetter, Ger. patent, 1,270,563 (1968); *Chem. Abstr.*, **69**, 96341k (1968).
102. P. Tomasik and E. Plazek, *Rocz. Chem.*, **39**, 1671 (1965); *Chem. Abstr.*, **64**, 19549 (1966).
103. P. Tomasik and E. Plazek, *Rocz. Chem.*, **38**, 709 (1964); *Chem. Abstr.*, **62**, 4003 (1965).
104. B. Glowiak and R. Kulik, *Rocz. Chem.*, **36**, 959 (1962); *Chem. Abstr.*, **58**, 5631 (1963).
105. P. Nantka-Namirski, *Acta Polon. Pharm.*, **18**, 391, 449 (1961); *Chem. Abstr.*, **58**, 3424 (1963).
106. R. F. Evans and H. C. Brown, *J. Org. Chem.*, **27**, 1665 (1962).
107. Z. Talik, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.*, **9**, 561 (1961); *Chem. Abstr.*, **60**, 2884 (1964).
108. E. Ochiai and H. Miarashi, *Chem. Pharm. Bull.* (Tokyo), **11**, 1586 (1963); *Chem. Abstr.*, **60**, 5446 (1964).
109. P. Nantka-Namirski, C. Kaczmarczyk, and L. Toba, *Acta Pol. Pharm.*, **24**, 231 (1967); *Chem. Abstr.*, **69**, 2827y (1968).
110. K. Dickoré and R. Kröhnke, *Chem. Ber.*, **93**, 2479 (1960)

111. M. Hamana and K. Funakoshi, *Yakugaku Zasshi*, 82, 518 (1962); *Chem. Abstr.*, 58, 4513 (1963).
112. M. Hamana and K. Funakoshi, *Yakugaku Zasshi*, 84, 23 (1964); *Chem. Abstr.*, 61, 3068 (1964).
113. M. Katada, *J. Pharm. Soc. Jap.*, 67, 51 (1947); *Chem. Abstr.*, 45, 9536 (1951).
114. D. M. Pretorius and P. A. de Villiers, *J. S. African Chem. Inst.*, 18, 48 (1965); *Chem. Abstr.*, 63, 14807 (1965).
115. G. F. van Rooyen, C. V. D. M. Brink, and P. A. de Villiers, *Tydskr. Naturwetenskappe*, 4, 182 (1964); *Chem. Abstr.*, 63, 13202 (1965).
116. S. Kajihara, *Nippon Kagaku Zasshi*, 86, 839 (1965); *Chem. Abstr.*, 65, 16935 (1966).
117. F. Parisi, P. Bovina, and A. Quilico, *Gazz. Chim. Ital.*, 92, 1138 (1962); *Chem. Abstr.*, 58, 13908 (1963).
118. Y. Suzuki, *Yakugaku Zasshi*, 81, 1146 (1961); *Chem. Abstr.*, 56, 3450 (1962).
119. H. C. van der Plas and H. J. den Hertog, *Rec. Trav. Chim. Pays-Bas*, 81, 841 (1962); *Chem. Abstr.*, 59, 1579 (1963).
120. E. J. Poziomek, *J. Org. Chem.*, 28, 590 (1963).
121. G. C. Finger and L. D. Starr, *Nature*, 191, 595 (1961).
122. R. Criegee and M. Krieger, *Chem. Ber.*, 98, 387 (1965).
123. J. Beuchi, H. Muehle, H. Braunschweiger, and P. Fabiani, *Helv. Chim. Acta*, 45, 449 (1962); *Chem. Abstr.*, 57, 776 (1962).
124. T. Weiland and H. Biener, *Chem. Ber.*, 96, 266 (1963).
125. R. A. Abramovitch and K. A. H. Adams, *Can. J. Chem.*, 39, 2134 (1961).
126. C. F. H. Allen, *Can. J. Chem.*, 43, 2486 (1965).
127. B. Rudner, U.S. patent, 2,982,841 (1959); *Chem. Abstr.*, 54, 1558 (1960).
128. T. Vajda and K. Kovacs, *Rec. Trav. Chim. Pays-Bas*, 80, 47 (1961); *Chem. Abstr.*, 55, 16547 (1961).
129. K. Kovacs and T. Vajda, *Acta Chim. Acad. Sci. Hung.*, 21, 445 (1959); *Chem. Abstr.*, 55, 1608 (1961).
130. K. Kovacs and T. Vajda, *Acta Pharm. Hung.*, 31, Suppl. 72 (1961); *Chem. Abstr.*, 56, 5922 (1962).
131. K. Kovacs and T. Vajda, *Acta Chim. Acad. Sci. Hung.*, 29, 245 (1961); *Chem. Abstr.*, 57, 5892 (1962).
132. R. A. Abramovitch and G. M. Singer, *J. Amer. Chem. Soc.*, 91, 5672 (1969).
133. R. A. Abramovitch, Private Communication.
134. R. Huisgen, *Angew. Chem.*, 75, 604 (1963).
135. N. D. Dawson, U.S. patent, 3,106,553 (1963); *Chem. Abstr.*, 60, 2959 (1964).
136. C. E. Frost and Co., Nether. patent, 6,401,902 (1965); *Chem. Abstr.*, 8200 (1966).
137. R. Delaby, J. Mandereau, and P. Reynaud, *Bull. Soc. Chim. Fr.*, 2065 (1961).
138. Industrial Iberica Quimico-Farmaceutica, S. A., Span. patent, 299,510 (1964); *Chem. Abstr.*, 61, 14646 (1964).
139. S. M. Roberts and H. Suschitzky, *Chem. Commun.*, 893 (1967).
140. B. I. Mikhant'ev and E. I. Fedorov, *Zh. Obshch. Khim.*, 33, 865 (1963); *Chem. Abstr.*, 54, 24714 (1960).
141. B. I. Mikhant'ev and E. I. Fedorov, *Zh. Obshch. Khim.*, 30, 568 (1960); *Chem. Abstr.*, 54, 24714 (1960).
142. S. I. Burnistov and V. A. Krasovskii, *Khim. Geterotsikl. Soedin*, 1, 173 (1967); *Chem. Abstr.*, 67, 64214p (1967).
143. A. B. Sen and S. K. Gupta, *J. Indian Chem. Soc.*, 39, 129 (1962); *Chem. Abstr.*, 57, 4662 (1962).
144. S. I. Burmistrov and Y. A. Krasovskii, USSR patent, 159,843 (1964); *Chem. Abstr.*, 60, 11991 (1964).

145. L. Halski, Pol. patent, 48,154 (1963); *Chem. Abstr.*, **62**, 1633 (1965).
146. Irwin, Neisler and Co., Brit. patent, 901,311 (1962); *Chem. Abstr.*, **58**, 7915 (1963).
147. J. P. Wibaut and F. W. Broekman, *Rec. Trav. Chim. Pays-Bas*, **80**, 309 (1961); *Chem. Abstr.*, **56**, 24745 (1961).
148. W. G. Duncan and D. W. Henry, *J. Med. Chem.*, **11**, 909 (1968); *Chem. Abstr.*, **69**, 51953v (1968).
149. K. Hoffmann, A. Hunger, J. Kebrle, and A. Rossi, Ger. patent 1,120,454 (1959); *Chem. Abstr.*, **57**, 836 (1962).
150. L. N. Yakhontov and M. V. Rubtsov, *Zh. Obshch. Khim.*, **34**, 1129 (1964); *Chem. Abstr.*, **61**, 3066 (1964).
151. E. Kretzschmar, H. Barth, H. Goldhahn, and E. Carstens, Ger. (East) patent, 52,138 (1966); *Chem. Abstr.*, **68**, 49457x (1968).
152. J. W. Clark-Lewis and R. P. Singh, *J. Chem. Soc.*, 2379 (1962).
153. S. Biniecki and W. Modrzejewska, *Acta Polon. Pharm.*, **19**, 103 (1962); *Chem. Abstr.*, **59**, 1613 (1963).
154. L. Novak and M. Protiva, Czech. patent, 106,406 (1963); *Chem. Abstr.*, **60**, 1716 (1964).
155. L. Novak and M. Protiva, *Collect. Czech. Chem. Commun.*, **27**, 2413 (1962); *Chem. Abstr.*, **58**, 12477 (1963).
156. J. Beuchi, S. Allisson, and W. Vetsch, *Helv. Chim. Acta*, **48**, 1216 (1965); *Chem. Abstr.*, **63**, 11488 (1965).
157. F. Yoneda and T. Kato, Jap. patent, 15,194 (1965); *Chem. Abstr.*, **63**, 14826 (1965).
158. T. V. Tsaranova, *Khim. Geterotsikl. Soedin., Akad. Nauk. Latv. SSSR*, 909 (1965); *Chem. Abstr.*, **64**, 12637 (1966).
159. W. T. Dent, Brit. patent, 850,870 (1960); *Chem. Abstr.*, **55**, 22237 (1961).
160. M. Hamana and M. Yamasaki, *Yakugaku Zasshi*, **81**, 612 (1961); *Chem. Abstr.*, **55**, 24742 (1961).
161. T. Talik and Z. Talik, *Rocz. Chem.*, **41**, 1507 (1967); *Chem. Abstr.*, **69**, 10337d (1969).
162. J. P. English, F. L. Bach, Jr., and S. Gordon, Brit. patent, 1,034,538 (1966); *Chem. Abstr.*, **65**, 15397 (1966).
163. J. P. English, F. L. Bach, Jr., and S. Gordon, U.S. patent, 3,330,832 (1967); *Chem. Abstr.*, **68**, 49453t (1968).
164. N. N. Vereshchagina and I. Ya. Postovski, *Trudy Ural. Politekh. Inst. im. S. M. Kirova*, 24 (1960); *Chem. Abstr.*, **56**, 8681 (1962).
165. H. Bredereck, F. Effenberger, and D. Zeyfang, *Angew. Chem.*, **77**, 219 (1965); *Chem. Abstr.*, **62**, 14494 (1965).
166. Y. Maki, K. Kawasaki, and K. Sato, *Gitu Yakka Daigaku Kiyo*, **13**, 34 (1963); *Chem. Abstr.*, **60**, 13220 (1964).
167. Y. Maki, K. Yamane, and M. Sato, *Yakugaku Zasshi*, **86**, 50 (1966); *Chem. Abstr.*, **64**, 11165 (1966).
168. Y. Maki, Y. Okada, Y. Yoshida, and K. Obata, *Gifu Yakka Daigaku Kiyo*, (12), 54 (1962); *Chem. Abstr.*, **59**, 11479 (1963).
169. O. R. Rodig, R. E. Collier, and R. K. Schlatzer, *J. Org. Chem.*, **29**, 2652 (1964).
170. O. R. Rodig, R. E. Collier, and R. K. Schlatzer, *J. Med. Chem.*, **9**, 116 (1966).
171. A. A. Aroyan and M. A. Iradyan, *Arm. Khim. Zh.*, **20**, 915 (1967); *Chem. Abstr.*, **69**, 77083m (1969).
172. Y. Sazuki, *Yakugaku Zasshi*, **81**, 1146 (1961); *Chem. Abstr.*, **56**, 3450 (1962).
173. J. B. Petersen, J. Lei, N. Clauson-Kaas, and K. Norris, *Kg. Dan. Vidensk, Selsk., Mat.-Fys. Medd.*, **36**, 23 (1967); *Chem. Abstr.*, **69**, 59063a (1968).

174. Z. Talik, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.*, **9**, 571 (1961); *Chem. Abstr.*, **60**, 2885 (1964).
175. P. Tomasik and Z. Skrowaczewska, *Rocz. Chem.*, **41**, 275 (1967); *Chem. Abstr.*, **67**, 11404u (1967).
176. Z. Talik and E. Plazek, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.*, **8**, 219 (1960); *Chem. Abstr.*, **60**, 9241 (1964).
177. Z. Talik, *Rocz. Chem.*, **35**, 475 (1961); *Chem. Abstr.*, **57**, 15065 (1962).
178. T. Talik, *Rocz. Chem.*, **36**, 1465 (1962); *Chem. Abstr.*, **59**, 6360 (1963).
179. J. S. Wieczorek and E. Plazek, *Rec. Trav. Chim. Pays-Bas*, **83**, 249 (1964); *Chem. Abstr.*, **60**, 15822 (1964).
180. Z. Talik, *Rocz. Chem.*, **34**, 465 (1960); *Chem. Abstr.*, **54**, 24705a (1960).
181. J. Barycki and E. Plazek, *Rocz. Chem.*, **39**, 1811 (1965); *Chem. Abstr.*, **64**, 15831 (1966).
182. M. Protiva, L. Novak, and Z. Sedivy, *Collect. Czech. Chem. Commun.*, **27**, 2102 (1962); *Chem. Abstr.*, **59**, 483 (1963).
183. H. Zellner, Austrian patent 229,312 (1963); *Chem. Abstr.*, **60**, 507 (1964).
184. Y. K. Yur'ev and M. A. Gal'bershtam, *Zh. Obshch. Khim.*, **32**, 1301 (1962); *Chem. Abstr.*, **58**, 13909 (1963).
185. Y. K. Yur'ev and M. A. Gal'bershtam, *Zh. Obshch. Khim.*, **33**, 1789 (1963); *Chem. Abstr.*, **59**, 9956 (1963).
186. R. Fusco, C. P. Dalla, and A. Salvi, *Gazz. Chim. Ital.*, **98**, 511 (1968); *Chem. Abstr.*, **69**, 96598z (1968).
187. Z. Arnold and A. Holy, *Collect. Czech. Chem. Commun.*, **28**, 2040 (1963); *Chem. Abstr.*, **59**, 13802 (1963).
188. P. Buckus and A. Buckiene, *Zh. Obshch. Khim.*, **33**, 3112 (1963); *Chem. Abstr.*, **60**, 1687 (1964).
189. A. Albert, in "Physical Methods in Heterocyclic Chemistry," (A. R. Katritzky, ed.), Vol. I, Academic Press, N. Y., 1963, p. 1.
190. F. Mason, in "Physical Methods in Heterocyclic Chemistry," (A. R. Katritzky, ed.), Vol. II, Academic Press, New York, 1963, p. 1.
191. K. Schofield, "Hetero-aromatic Nitrogen Compounds," Plenum Press, New York, 1967, p. 120.
192. A. R. Katritzky and J. M. Lagowski, in "Advances in Heterocyclic Chemistry," Vol. 1, Academic Press, New York, 1963, p. 341.
193. A. Albert, "Heterocyclic Chemistry," Oxford University Press, New York, 1968, p. 67.
194. E. D. Schmid and R. Goeckle, *Spectrochim. Acta*, **22**, 1645 (1966); *Chem. Abstr.*, **65**, 16247 (1966).
195. R. Joeckle, E. D. Schmid, and R. Mecke, *Z. Naturforsch.*, **21**, 1906 (1966); *Chem. Abstr.*, **67**, 16291q (1967).
196. R. Isaac, F. F. Bentley, H. Sternglanz, W. C. Coburn, Jr., C. V. Stephenson, and W. S. Wilcox, *Appl. Spectr.*, **17**, 90 (1963).
197. C. W. N. Cumper, R. F. A. Ginman, D. G. Redford, and A. I. Vogel, *J. Chem. Soc.*, 1731 (1963).
198. I. R. Bellobono and A. Gamba, *Gazz. Chim. Ital.*, **96**, 935 (1966); *Chem. Abstr.*, **65**, 16192 (1966).
199. H. Lumbroso and J. Barassin, *Bull. Soc. Chim. Fr.*, 3143 (1965); *Chem. Abstr.*, **64**, 6466 (1966).
200. J. Barassin and H. Lumbroso, *Bull. Soc. Chim. Fr.*, 492 (1961); *Chem. Abstr.*, **56**, 4204 (1962).

201. C. W. N. Cumper and A. Singleton, *J. Chem. Soc., B,* 649 (1968).
202. N. Mataga and S. Mataga, *Bull. Soc. Chem. Jap.,* 32, 600 (1969); *Chem. Abstr.,* 54, 6303 (1960).
203. V. I. Bliznyukou and V. A. Grin, *Trudy Kar'kov. Farm. Inst.,* 26 (1957); *Chem. Abstr.,* 55, 12031 (1961).
204. T. N. Misra, *Indian J. Phys.,* 35, 420 (1961); *Chem. Abstr.,* 56, 5540 (1962).
205. S. G. Bogomolov, M. G. Bystritskaya, and M. M. Kirillova, *Izvest. Akad. Nauk S.S.S.R., Ser. Fiz.,* 23, 1199 (1959); *Chem. Abstr.,* 54, 7337 (1960).
206. S. F. Mason, *J. Chem. Soc.,* 219 (1960).
207. G. Favini, M. Raimondi, and C. Gandolfo, *Spectrochim. Acta,* 207 (1968).
208. L. Sobczyk and A. Koll, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.,* 13, 97 (1965); *Chem. Abstr.,* 63, 6483 (1965).
209. Y. N. Sheinker and E. M. Peresleni, *Zh. Fiz. Khim.,* 35, 2623 (1961); *Chem. Abstr.,* 59, 1454 (1963).
210. E. M. Peresleni, L. N. Yakhontov, D. M. Krasnolutskaya, and Yu. N. Sheinker, *Dokl. Akad. Nauk SSSR,* 177, 592 (1967); *Chem. Abstr.,* 68, 95634a (1968).
211. Yu. N. Sheinker and E. M. Peresleni, *Stroenie Veschestva i Spektroskopiya, Akad. Nauk. S.S.S.R.,* 28 (1960); *Chem. Abstr.,* 55, 10067 (1961).
212. H. Sterk and H. Junek, *Monatsh.,* 98, 1763 (1967); *Chem. Abstr.,* 67, 116432e (1967).
213. R. A. Y. Jones and A. R. Katritzky, *J. Chem. Soc.,* 1317 (1959).
214. J. M. Essery and K. Schofield, *J. Chem. Soc.,* 3939 (1961).
215. G. Favini, A. Gamba, and I. R. Bellobono, *Spectrochim. Acta,* 23A, 89 (1967); *Chem. Abstr.,* 66, 50516f (1967).
216. J. Sandstrom, *Acta Chem. Scand.,* 18, 871 (1964).
217. O. E. Polansky and M. A. Grassberger, *Monatsh.,* 94, 662 (1963); *Chem. Abstr.,* 59, 13367 (1963).
218. G. Tsoucaris, *J. Chim. Phys.,* 58, 613 (1961).
219. J. S. Kwiatowski, *Acta Phys. Pol.,* 30, 963 (1966); *Chem. Abstr.,* 68, 29164w (1968).
220. J. Del Bene and H. H. Jaffe, *J. Chem. Phys.,* 49, 1221 (1968).
221. H. Deelstra, W. Vanderleen, and F. Verbeek, *Bull. Soc. Chim. Belg.,* 72, 632 (1963); *Chem. Abstr.,* 60, 54 (1964).
222. F. Peradejordi, *C. R. Acad. Sci., Paris, Ser. C,* 258, 1241 (1964); *Chem. Abstr.,* 60, 10518 (1964).
223. G. B. Barlin, *J. Chem. Soc., B,* 285 (1966).
224. D. Wagler and E. Hoyer, *Z. Anorg. Allgem. Chem.,* 337, 169 (1965); *Chem. Abstr.,* 63, 9421 (1965).
225. G. B. Barlin, *J. Chem. Soc.,* 2150 (1964).
226. M. Paabo, R. A. Robinson, and R. C. Bates, *Anal. Chem.,* 38, 1573 (1966).
227. R. Nasanen, I. Virtamo, and P. Merilainen, *Suomen Kemist,* 37B, 67 (1964); *Chem. Abstr.,* 63, 12399 (1965).
228. D. D. Perrin, *Austr. J. Chem.,* 17, 484 (1964).
229. A. Weisstuch and A. C. Testa, *J. Phys. Chem.,* 72, 1982 (1968).
230. J. Hennessy and A. C. Testa, *J. Chem. Phys.,* 49, 956 (1968).
231. G. Kallistratos, A. Pfau, and B. Ossowski, *Naturwissenshaften,* 47, 468 (1960); *Chem. Abstr.,* 55, 7036 (1961).
232. M. R. Yagudaev and Y. N. Sheinker, *Dokl. Akad. Nauk. SSSR,* 144, 177 (1962); *Chem. Abstr.,* 57, 6759 (1962).
233. B. Glowiak. *Bull. Acad. Polon. Sci., Ser. Sci. Chim.,* 10, 9 (1962); *Chem. Abstr.,* 58, 501 (1963).

234. J. Suszko and M. Szafran, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.*, **10**, 233 (1962); *Chem. Abstr.*, **58**, 7519 (1963).
235. M. R. Yagudaev, E. M. Popov, I. P. Yakovlev, and Yu. N. Sheinker, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1189 (1964); *Chem. Abstr.*, **64**, 18706 (1966).
236. W. E. Thompson, R. J. Warren, I. B. Eisdorfer, and J. E. Zarembo, *J. Pharm. Sci.*, **51**, 1819 (1965); *Chem. Abstr.*, **64**, 4906 (1966).
237. M. L. Josien, *Proc. Int. Conf. Spectrosc.* (Bombay), **2**, 282 (1967); *Chem. Abstr.*, **69**, 47819n (1968).
238. R. A. Jones and R. P. Rao, *Austr. J. Chem.*, **18**, 583 (1965).
239. A. R. Katritzky and R. A. Jones, *J. Chem. Soc.*, 3674 (1959).
240. M. R. Yagudaev and Y. N. Sheinker, *Uzbeksk. Khim. Zh.*, **8**, 86 (1964); *Chem. Abstr.*, **62**, 11303 (1965).
241. G. C. Kulasingam, W. R. McWhinnie, and R. R. Thomas, *Spectrochim. Acta*, **22**, 1365 (1966); *Chem. Abstr.*, **65**, 4849 (1966).
242. P. G. Puranik and K. V. Ramiah, *Proc. Indian Acad. Sci.*, **54A**, 121 (1961); *Chem. Abstr.*, **56**, 8183 (1962).
243. P. S. Puranik and K. V. Ramiah, *Proc. Indian Acad. Sci.*, **54A**, 146 (1964).
244. K. V. Ramiah and V. V. Chalapathi, *Current Sci.*, **34**, 687 (1965).
245. E. Spinner, *J. Chem. Soc.*, 3119 (1962).
246. K. C. Medhi and G. S. Kastha, *Indian J. Phys.*, **38**, 483 (1964); *Chem. Abstr.*, **62**, 6368 (1965).
247. W. Bruegel, *Z. Elektrochem.*, **66**, 159 (1962).
248. T. K. Wu and B. P. Dailey, *J. Chem. Phys.*, **41**, 3307 (1964).
249. N. Das, N. Chatterjee, and M. Bose, *Proc. Int. Conf. Spectros.* (Bombay), **2**, 478 (1967); *Chem. Abstr.*, **69**, 23498g (1968).
250. W. W. Paudler and H. L. Blewitt, *J. Org. Chem.*, **31**, 1295 (1966).
251. G. R. Bedford, H. Dorn, G. Hilgetag, and A. R. Katritzky, *Rec. Trav. Chim. Pays-Bas*, **83**, 189 (1964).
252. R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc., C*, 220 (1966).
253. C. S. Giam and J. L. Lyle, *J. Chem. Soc., B*, 1516 (1970).
254. D. H. Evans and R. E. Richards, *Mol. Phys.*, **8**, 19 (1964).
255. M. L. Martin, J. P. Dorie, and F. Peradejordi, *J. Chim. Phys.*, **64**, 1193 (1967).
256. L. Guibe, *Ann. Phys.*, **7**, 177 (1962); *Chem. Abstr.*, **58**, 6352 (1963).
257. B. M. Lynch, B. C. Macdonald, and J. G. K. Webb, *Tetrahedron*, **24**, 3595 (1968).
258. A. Veilland and B. Pullman, *C. R. Acad. Sci., Paris, Ser. C*, **253**, 2418 (1961).
259. F. Genet, *Bull. Soc. Fr., Mineral Crist.*, 88, 463 (1965); *Chem. Abstr.*, **64**, 4375 (1966).
260. C. Giessner-Prettre, *Ann. Phys.*, **9**, 557 (1964).
261. R. F. C. Brown, L. Radom, S. Sternhell, and I. D. Rae, *Can. J. Chem.*, **46**, 2577 (1968).
262. A. R. Katritzky and R. E. Reavill, *J. Chem. Soc.*, 3825 (1965).
263. B. D. Sharma, *Acta Cryst.*, **20**, 921 (1966).
264. B. T. Gorres, Univ. Microfilms (Ann Arbor, Mich.), Order No. 64-12,125; **25**(7), 3857 (1965); *Chem. Abstr.*, **62**, 13963 (1965).
265. B. T. Gorres and R. A. Jocobson, *Acta Cryst.*, **17**, 1599 (1964).
266. F. Genet, *C. R. Acad. Sci., Paris, Ser. C*, **251**, 1397 (1960); *Chem. Abstr.*, **55**, 5082 (1961).
267. G. H. Keller, L. Bauer, and C. L. Bell, *J. Heterocycl. Chem.*, **5**, 647 (1968).
268. R. Rusakowicz and A. C. Testa, *J. Phys. Chem.*, **72**, 2680, (1968).
269. G. Aloisi, G. Cauzzo, and U. Mazzucato, *Trans. Faraday Soc.*, **63**, 1858 (1967).

270. K. R. Bhaskar and S. Singh, *Spectrochim. Acta,* **33A,** 1155 (1967).
271. C. D. Ritchie and P. D. Heffley, *J. Amer. Chem. Soc.,* **87,** 5402 (1965).
272. P. Knobloch, *Z. Naturforsch.,* **20a,** 854 (1965); *Chem. Abstr.,* **63,** 10810 (1965).
273. O. Chalvet, R. Daudel and F. Peradejordi, *C. R. Acad. Sci., Paris, Ser. C,* **254,** 1283 (1962).
274. M. Wahren, *Z. Chem.,* **6,** 181 (1966); *Chem. Abstr.,* **65,** 7005 (1966).
275. J. A. Zoltewicz and J. D. Meyer, *Tetrahedron Lett.,* 421 (1968).
276. I. F. Tupitsyn and V. I. Komarov, *Tr. Gos. Inst. Prikl. Khim.,* **52,** 160 (1964); *Chem. Abstr.,* **63,** 13005 (1965).
277. E. C. Taylor, R. O. Kan, and W. W. Paudler, *J. Amer. Chem. Soc.,* **83,** 4484 (1961).
278. E. C. Taylor and R. O. Kan, *J. Amer. Chem. Soc.,* **85,** 776 (1963).
279. E. C. Taylor and J. S. Driscoll, *J. Org. Chem.,* **25,** 1716 (1960).
280. L. Pentimalli, *Gazz. Chim. Ital.,* **94,** 458 (1964); *Chem. Abstr.,* **61,** 11963 (1964).
281. L. Pentimalli, *Gazz. Chim. Ital.,* **94,** 902 (1964); *Chem. Abstr.,* **62,** 1628 (1965).
282. S. M. Roberts and H. Suschitzky, *J. Chem. Soc., C,* 1537 (1968).
283. Z. Talik and T. Talik, *Rocz. Chem.,* **36,** 545 (1962); *Chem. Abstr.,* **57,** 12420 (1962).
284. T. Talik and Z. Talik, *Rocz. Chem.,* **36,** 539 (1962); *Chem. Abstr.,* **57,** 12421 (1962).
285. G. Ferrari and E. Marcon, *Farmaco, Ed. Sci.,* **14,** 594 (1959); *Chem. Abstr.,* **54,** 6709 (1959).
286. B. van der Wal, Th. J. de Boer, and H. O. Huisman, *Rec. Trav. Chim. Pays-Bas,* **80,** 203 (1961); *Chem. Abstr.,* **55,** 21116 (1961).
287. M. Marzona and R. Carpignano, *Ann. Chim.,* **55,** 1007 (1965); *Chem. Abstr.,* **64,** 6607 (1966).
288. D. V. Maier, U.S. patent, 3,163,655 (1964); *Chem. Abstr.,* **62,** 10419 (1962).
289. M. Ohta and M. Masaki, *Bull. Chem. Soc. Jap.,* **33,** 1392 (1960); *Chem. Abstr.,* **55,** 14457 (1961).
290. R. Tiollais, G. Bouget, and H. Bouget, *C. R. Acad. Sci., Paris, Ser. C,* **254,** 2597 (1962); *Chem. Abstr.,* **57,** 651 (1962).
291. L. Schmidt and B. Becker, *Monatsh.,* **46,** 674 (1926); *Chem. Abstr.,* **21,** 94 (1927).
292. K. Feist, W. Awe, J. Schultz, and F. Klatt, *Arch. Pharm.* (Weinheim), **272,** 100 (1934); *Chem. Abstr.,* **28,** 3407 (1934).
293. E. Steinhäuser and E. Diepolder, *J. Prakt. Chem.,* **93,** 387 (1916).
294. CIBA Ltd., Fr. patent, 1,363,599 (1964); *Chem. Abstr.,* **61,** 1388 (1965).
295. O. A. Osipov, V. I. Minkin, D. Sh. Verkhovodova, and M. I. Knyazhanskii, *Zh. Neorg. Khim.,* **12,** 1549 (1967); *Chem. Abstr.,* **68,** 87107r (1968).
296. A. S. Kudryavtsev and I. A. Savich, *Zh. Obshch. Khim.,* **33,** 1351 (1963); *Chem. Abstr.,* **59,** 12952 (1963).
297. A. S. Kudryavtsev, and I. A. Savich, *Vestn. Mosk. Univ., Ser. II, Khim.,* **17,** no. 2, 57 (1962); *Chem. Abstr.,* **58,** 4512 (1963).
298. E. Marcus and J. T. Fitzpatrick, *J. Org. Chem.,* **25,** 199 (1960).
299. L. Novak, Czech. patent, 110,210 (1964); *Chem. Abstr.,* **61,** 9475 (1964).
300. G. Fenech and M. Basile, *Gazz. Chim. Ital.,* **91,** 145 (1961); *Chem. Abstr.,* **56,** 12898 (1962).
301. G. Fenech and M. Basile, *Gazz. Chim. Ital.,* **91,** 163 (1961); *Chem. Abstr.,* **56,** 12898 (1962).
302. M. Protiva and K. Petz, Czech. patent, 111,880 (1964); *Chem. Abstr.,* **62,** 1463 (1965).
303. K. Pelz and M. Protiva, *Collect. Czech. Chem. Commun.,* **30,** 2231 (1965); *Chem. Abstr.,* **63,** 8235 (1965).
304. I. K. Barben, *J. Chem. Soc.,* 1827 (1961).

305. I. P. Tsukervanik and S. A. Israilova, *Dokl. Akad. Nauk. Uz. SSSR*, **20**, 25 (1963); *Chem. Abstr.*, **59**, 11392 (1963).
306. Z. M. Rodionova, *Tr. po Khim. i Khim. Tekhnol.*, **2**, 262 (1964); *Chem. Abstr.*, **63**, 9899 (1965).
307. Taisho Pharmaceutical Co. Ltd., Jap. patent 1430 (1964); *Chem. Abstr.*, **60**, 11986 (1964).
308. Y. Anmo, Y. Tsuruta, S. Ito and K. Noda, *Yakugaku Zasshi*, **83**, 807 (1963); *Chem. Abstr.*, **59**, 15239 (1963).
309. M. Friedman, *Can. J. Chem.*, **45**, 2275 (1967).
310. E. Profft and H. Mitternacht, *J. Prakt. Chem.*, **16**, 13 (1962); *Chem. Abstr.*, **57**, 16528 (1962).
311. T. Kato, H. Yamanaka, T. Niitsuma, K. Wagatsuma, and M. Oizumi, *Chem. Pharm. Bull.* (Tokyo), **12**, 910 (1964); *Chem. Abstr.*, **63**, 2949 (1965).
312. I. Ugi, *Agnew. Chem.*, **74**, 9 (1962).
313. N. P. Buu-Hoi, R. Rips, and C. Derappe, *Bull. Soc. Chim. Fr.*, 3456 (1965).
314. S. Okuda and M. M. Robison, *J. Org. Chem.*, **24**, 1008 (1959).
315. A. Buzas, F. Canac, C. Egnell, and P. Freon, *C. R. Acad. Sci., Paris, Ser. C*, **262**, 658 (1966); *Chem. Abstr.*, **64**, 15831 (1966).
316. E. Haach, H. Berger, and W. Vomel, Brit. patent, 1,014,050 (1965); *Chem. Abstr.*, **64**, 6624 (1966).
317. C. F. Boehringer and G. Soehne, m.b.H., Neth. Appl., 6,402,960 (1964); *Chem. Abstr.*, **62**, 7732 (1965).
318. R. F. Coles and R. A. Miller, U.S. patent, 3,149,990 (1964); *Chem. Abstr.*, **61**,16217 (1964).
319. H. O. Hankovszky and K. Hideg, *J. Med. Chem.*, **9**, 151 (1966).
320. C. R. McArthur, Belg. patent, 665,984 (1965); *Chem. Abstr.*, **65**, 659 (1966).
321. K. N. Gaind and S. D. Popli, *Indian J. Chem.*, **5**, 524 (1967); *Chem. Abstr.*, **69**, 10336c (1969).
322. Deutsch Gold-und Silber-Scheideanstalt vorm. Roessler, Belg. patent, 626,079 (1963); *Chem. Abstr.*, **59**, 1000 (1963).
323. M. Thiel and K. Stach, *Monatsh.*, **93**, 1080 (1962); *Chem. Abstr.*, **59**, 6389 (1963).
324. F. Leonard and J. Koo, Belg. patent, 613,212 (1962); *Chem. Abstr.*, **57**, 16639 (1962).
325. J. R. Geigy A.-G., Neth. patent, 6,509,930 (1966); *Chem. Abstr.*, **64**, 19571 (1966).
326. G. N. Pershin, N. S. Bogdanova, S. N. Milovanova, E. G. Popova, and M. G. Karaseva, *Farmakol. i Toksikol.*, **27**, 716 (1964); *Chem. Abstr.*, **63**, 2950 (1965).
327. M. Hooper, D. A. Patterson, and D. G. Wibberley, *J. Pharm. Pharmacol.*, **17**, 734 (1965); *Chem. Abstr.*, **64**, 17535 (1966).
328. J. Mirek, *Rocz. Chem.*, **40**, 205 (1966); *Chem. Abstr.*, **65**, 7137 (1966).
329. G. E. Bonvicino, U.S. patent, 3,072,649 (1963); *Chem. Abstr.*, **58**, 13924 (1963).
330. M. Melandri, G. Vittorina, and A. Buttini, *Ann. Chim.* (Rome), **50**, 125 (1960); *Chem. Abstr.*, **55**, 27306 (1961).
331. A. P. Gray and D. E. Heitmeier, *J. Amer. Chem. Soc.*, **81**, 4347 (1959).
332. A. P. Gray, U.S. patent, 3,165,527 (1965); *Chem. Abstr.*, **62**, 11787 (1965).
333. Irwin, Neisler and Co., Brit. patent, 901,312 (1962); *Chem. Abstr.*, **58**, 7914 (1963).
334. E. L. Skau, R. R. Mod, and F. C. Magne, U.S. patent, 2,951,849 (1958); *Chem. Abstr.*, **57**, 3418 (1962).
335. P. Papini and G. Auzzi, *Gazz. Chim. Ital.*, **96**, 125 (1966); *Chem. Abstr.*, **64**, 19592 (1966).
336. L. P. Kulev and A. V. Boldyreva, *Izv. Tomsk. Politekhm. Inst.*, **102**, 41 (1959); *Chem. Abstr.*, **59**, 2812 (1963).

337. E. V. Vladzimirskaya, *Biol. Aktivn. Soedin., Akad. Nauk. SSSR*, 262 (1965); *Chem. Abstr.*, **63**, 18019 (1965).

338. R. R. Mod, F. C. Magne, and E. L. Shau, *J. Amer. Oil Chemists Soc.*, **36**, 616 (1959).

339. T. Momose and M. Nakamura, *Chem. Pharm. Bull.* (Tokyo), **10**, 544 (1962); *Chem. Abstr.*, **59**, 5242 (1963).

340. B. Janik, B. Lucka, and I. Zagala, *Dissertationes Pharm.*, **14**, 165 (1962); *Chem. Abstr.*, **59**, 1618 (1963).

341. B. A. Arbuzov, V. M. Zoroastrova, and S. P. Achesbak, *Zh. Obshch. Khim.*, **1**, 2190 (1966); *Chem. Abstr.*, **66**, 94896j (1967).

342. B. A. Arbuzov, V. M. Zorastrova, and M. P. Osipova, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk.*, 2163 (1961); *Chem. Abstr.*, **57**, 8536 (1962).

343. C. J. Barnes and A. J. Matuszko, *U.S. Dept. Com., Office Tech. Sew., A. D.* 415, 706, 11 pp. (1963); *Chem. Abstr.*, **60**, 10642 (1964).

344. C. J. Barnes and A. J. Matuszko, *J. Org. Chem.*, **27**, 2239 (1962).

345. I. R. Pachter, *J. Org. Chem.*, **26**, 4157 (1961).

346. P. Buckus, N. Raguotiene, and B. Buckiene, *Zh. Obshch. Khim.*, **34**, 3847 (1964); *Chem. Abstr.*, **62**, 9128 (1965).

347. H. Zimmer and J. P. Bercz, *Ann. Chem.*, **686**, 107 (1965); *Chem. Abstr.*, **63**, 14731 (1965).

348. R. T. Coutts and D. G. Wibberley, *J. Chem. Soc.*, 2518 (1962).

349. H. Dorn, *Monatsber. Deut. Akad. Wiss. Berlin*, **3**, No. 1, 51 (1961); *Chem. Abstr.*, **58**, 2439d (1963).

350. A. Puszyniski and T. Talik, *Rocz. Chem.*, **41**, 1625 (1967); *Chem. Abstr.*, **68**, 114379q (1968).

351. T. Batkowski and E. Plazek, *Rocz. Chem.*, 37, 273 (1963); *Chem. Abstr.*, **59**, 74786 (1963).

352. W. Sliwa and E. Plazek, *Acta Polon. Pharm.*, **20**, 253 (1963); *Chem. Abstr.*, **62**, 514 (1965).

353. C. Casagrande, M. Canova, and G. Ferrari, *Boll. Chim. Farm.*, **104**, 424 (1965); *Chem. Abstr.*, **64**, 5037 (1966).

354. A. G. Kostsova, *Trudy Voronezh. Gosudarst. Univ.*, **49**, 15 (1958); *Chem. Abstr.*, **56**, 2358b (1962).

355. A. G. Kostsova, E. P. Kosheleva, *Zh. Obshch. Khim.*, **32**, 1009 (1962); *Chem. Abstr.*, **58**, 5630 (1963).

356. I. K. Fel'dman, Z. E. Ovsyanaya, and E. S. Kozlov, *Tr. Leninyr. Khim. Farmatsevt. Inst.*, (11), 34 (1960); *Chem. Abstr.*, **59**, 11311 (1963).

357. G. Fenech, M. Basile, and G. Vigorita, *Ann. Chim.* (Rome), **54**, 607 (1964); *Chem. Abstr.*, **62**, 2772 (1965).

358. Mobil Oil Corp., Brit. patent, 1,078,288 (1967); *Chem. Abstr.*, **68**, 78139a (1968).

359. N. P. Buu-Hoï, M. Gauthier, and N. Dat Xuong, *Bull. Soc. Chim. Fr.*, 52 (1965).

360. T. Takahashi, Jap. patent, 4,216 (1965); *Chem. Abstr.*, **62**, 16202 (1965).

361. E. Kalatzis, *J. Chem. Soc., B*, 273 (1967).

362. E. Meuller and H. Huber-Enden, *Ann. Chem.*, **649**, 70 (1961).

363. C. R. Kolder and H. G. den Hertog, *Rec. Trav. Chim., Pays-Bas*, 79, 474 (1960).

364. J. Kozlowska and E. Plazek, *Rocz. Chem.*, **33**, 831 (1959).

365. T. Talik and E. Plazek, *Rocz. Chem.*, **35**, 463 (1961); *Chem. Abstr.*, **53**, 18954 (1959).

366. E. Kalatzis, *J. Chem. Soc., B*, 277 (1967).

367. R. W. Faessinger and E. V. Brown, *Trans. Kentucky Acad. Sci.*, **24** (3–4) 106 (1963); *Chem. Abstr.*, **60**, 14465 (1964).

368. L. Pentimali, *Gazz. Chim. Ital.*, **89**, 1843 (1959); *Chem. Abstr.*, **55**, 4505 (1961).

369. G. S. Petrova and V. A. Platonova, *Metody Poluch. Khim. Reaktivov Prep.*, No. 15, 120 (1967); *Chem. Abstr.*, **68**, 14381j (1968).
370. C. E. Lewis, A. P. Paul, Sien-Moo Tsang, and J. J. Leavitt, U.S. patent, 3,051,697 (1962); *Chem. Abstr.*, **59**, 5291 (1964).
371. J. W. Dehn, Jr. and A. J. Salina, U.S. patent, 3,249,597; *Chem. Abstr.*, **65**, 9061 (1966).
372. Sien-Moo Tsang, C. E. Lewis, and A. P. Paul, U.S. patent, 2,893,816 (1959); *Chem. Abstr.*, **54**, 1868 (1961).
373. T. Talik, *Rocz. Chem.*, **36**, 1049 (1962); *Chem. Abstr.*, **59**, 7480 (1964).
374. R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc.*, 5040 (1965).
375. T. Talik and Z. Talik, *Rocz. Chem.*, **37**, 75 (1963); *Chem. Abstr.*, **59**, 8698 (1963).
376. L. Thunus and J. Delange, *J. Pharm. Belg.*, **21**, 485 (1966); *Chem. Abstr.*, **66**, 37736 (1966).
377. L. O. Shnaidman, M. I. Siling, I. N. Kushchinskava, T. N. Eremiva, O. N. Shevyreva, V. P. Shishkov, N. A. Kosolapova, L. G. Kazakevich, and T. P. Timofeeva, *Tr. Inst. Ekspevim. Klinich. Med. Akad. Nauk. Latv. SSSR*, **27**, 1 (1962); *Chem. Abstr.*, **58**, 4508 (1963).
378. M. Gadekar, J. L. Frederick, and E. C. DeRenzo, *J. Med. Pharm. Chem.*, **5**, 531 (1962).
379. T. Batkowski and E. Plazek, *Rocz. Chem.*, **36**, 51 (1962); *Chem. Abstr.*, **57**, 15066 (1962).
380. P. Tomasik and T. Plazek, *Rocz. Chem.*, **39**, 365 (1965); *Chem. Abstr.*, **63**, 16298 (1965).
381. H. Tomisawa, *Yakugaku Zasshi*, **79**, 1167 (1959); *Chem. Abstr.*, **54**, 3416 (1960).
382. F. Friedrich and R. Pohloudek-Fabini, *Pharmazie*, **19**, 677 (1964); *Chem. Abstr.*, **62**, 7720 (1965).
383. F. Freifelder, R. W. Matton, and Y. H. Ng, *J. Org. Chem.*, **9**, 3730 (1964).
384. P. A. Van Zwieten, J. A. Valthuijsen, and H. O. Huisman, *Rec. Trav. Chim. Pays-Bas*, **80**, 1066 (1961); *Chem. Abstr.*, **56**, 3448 (1962).
385. S. N. Godovikova, USSR patent, 1,611,756 (1964); *Chem. Abstr.*, **61**, 3078 (1964).
386. T. Batkowski, *Rocz. Chem.*, **41**, 729 (1967); *Chem. Abstr.*, **67**, 82061r (1967).
387. W. J. Middleton, U.S. Patent, 2,914,534 (1959); *Chem. Abstr.*, **54**, 9962 (1960).
388. R. Urban and O. Schnider, *Helv. Chim. Acta*, **47**, 363 (1964).
389. C. S. Mizukami, E. Hirai, and M. Morimoto, *Schionogi Kenkyusho Nempo*, **16**, 29 (1966); *Chem. Abstr.*, **66**, 10827g (1967).
390. H. N. Rydon and K. Undheim, *J. Chem. Soc.*, 4676 (1962).
391. C. J. Argoudelis and F. A. Kummerow, *J. Org. Chem.*, **26**, 3420 (1961).
392. R. A. Abramovitch and A. D. Notation, *Can. J. Chem.*, **38**, 1445 (1960).
393. B. N. Dashkevich and Yu. Yu. Tsmur, *Invest. Vysshikh, Ucheb. Zavedenil, Khim. i Khim. Teknol.*, **3**, 754 (1960); *Chem. Abstr.*, **55**, 2636 (1961).
394. W. W. Paudler and T. J. Kress, in "Advances in Heterocyclic Chem.," (A.R. Katritzky, ed.), Vol. II, 1961, p. 123
395. E. Ziegler and E. Noelken, *Monatsh.*, **92**, 1184 (1961).
396. W. Czuba, *Rocz. Chem.*, **41**, 289 (1967).
397. K. Miyaki, *J. Pharm. Soc. Jap.*, **62**, 257 (1942); *Chem. Abstr.*, **45**, 2950 (1951).
398. B. Bobranski and E. Sacharda, *Chem. Ber.*, **60**, 1081 (1926).
399. B. Bobranski and E. Sucharda, *Rocz. Chem.*, **7**, 192 (1927).
400. T. J. Kress and W. W. Paudler, *Chem. Commun.*, **3**, (1967).
401. W. P. Utermohlen, Jr., *J. Org. Chem.*, **8**, 544 (1943).
402. T. Kato, F. Hamaguchi, and T. Oiwa, *Chem. Pharm. Bull.* (Tokyo), **4**, 178 (1956); *Chem. Abstr.*, **51**, 7367 (1957).

403. S. Tamura, T. Kudo, and Y. Yanagihara, *Yakugaku Zasshi*, 80, 562 (1960); *Chem. Abstr.*, 54, 22650 (1960).
404. W. W. Paudler and T. J. Kress, *J. Org. Chem.*, 31, 3055 (1966).
405. W. W. Paudler and T. J. Kress, *J. Heterocycl. Chem.*, 4, 284 (1967).
406. J. G. Murray and C. R. Hauser, *J. Org. Chem.*, 19, 2008 (1954).
407. Sterling Drug Inc., Brit. patent, 1,022,214 (1966); *Chem. Abstr.*, 64, 19618 (1966).
408. W. W. Paudler and T. J. Kress, *J. Org. Chem.*, 33, 1384 (1968).
409. H. E. Baumgarten and K. C. Cook, *J. Org. Chem.*, 22, 138 (1957).
410. H. E. Baumgarten and A. L. Krieger, *J. Amer. Chem. Soc.*, 77, 2438 (1955).
411. W. W. Paudler and T. J. Kress, *J. Org. Chem.*, 32, 832 (1967).
412. E. V. Brown, *J. Org. Chem.*, 30, 1607 (1965).
413. S. Carboni, A. DaSettimo, and G. Pirisino, *Ann. Chim.* (Rome), 54, 677 (1964); *Chem. Abstr.*, 61, 11980 (1964).
414. S. Carboni, S. DaSettimo, G. Pirisino, and D. Segnini, *Gazz. Chim. Ital.*, 96, 103 (1966).
415. S. Carboni and G. Pirisino, *Ann. Chim.* (Rome), 52, 340 (1962); *Chem. Abstr.*, 57, 9825 (1962).
416. S. Carboni and G. Pirisino, *Ann. Chim.* (Rome), 52, 279 (1962); *Chem. Abstr.*, 57, 791 (1962).
417. S. Carboni, A. DaSettimo, and G. Pirisino, *Ann. Chim.* (Rome), 54, 883 (1964); *Chem. Abstr.*, 63, 5620 (1965).
418. S. Carboni, A. DaSettimo, D. Segnini, and I. Tennetti, *Gazz. Chim. Ital.*, 96, 1443 (1966).
419. S. Carboni, A. DeSettimo, and P. L. Ferrarini, *Gazz. Chim. Ital.*, 97, 1961 (1967).
420. S. Carboni, A. DaSettimo, P. I. Ferrarini, and G. Pirisino, *Gazz. Chim. Ital.*, 96, 1456 (1966); *Chem. Abstr.*, 67, 100084g (1967).
421. V. Burckhardt, H. Suter, and W. Kundig, Ger. patent, 829,894 (1954); *Chem. Abstr.*, 52, 11,127 (1958).
422. E. M. Hawes and D. B. Wibberley, *J. Chem. Soc., C,* 315 (1966).
423. E. M. Hawes and D. G. Wibberley, *J. Chem. Soc., C,* 1564 (1966).
424. A. W. Johnson, T. J. King, and J. R. Turner, *J. Chem. Soc.*, 1509 (1960).
425. R. Baltrusis and A. Maciulus, *Lietuvos TSR Mokslu Akad, Darbai Ser.*, B, 163 (1964); *Chem. Abstr.*, 61, 4165 (1964).
426. R. Baltrusis, A. Maciulis, and A. Purenas, *Lietuvos TSR Mokslu Akad. Darbai, Ser. B.*, No. 2, 125 (1962); *Chem. Abstr.*, 58, 6827 (1963).
427. P. Buckus, G. Denis, and N. Raquotiene, *Zh. Obshch. Khim.*, 33, 1236 (1963); *Chem. Abstr.*, 59, 10036 (1963).
428. G. R. Lappin, *J. Org. Chem.*, 26, 2350 (1961).
429. G. R. Lappin, *Org. Chem. Bull.*, 33, No. 1, 6 (1961); *Chem. Abstr.*, 55, 14453 (1961).
430. J. G. Wilson and W. Bottomley, *J. Heterocycl. Chem.*, 4, 360 (1967).
431. M. Shur and S. S. Israelstam, *J. Org. Chem.*, 33, 3015 (1968).
432. M. Khalifa, *Bull. Fac. Pharm.*, 1, 149 (1961); *Chem. Abstr.*, 61, 5643 (1964).
433. M. Khalifa and Y. M. Abou-Zeid, *Bull. Fac. Pharm.*, 1, 159 (1961); *Chem. Abstr.*, 61, 5643 (1964).
434. A. R. Katritzky and A. J. Waring, *J. Chem. Soc.*, 1540 (1962).
435. E. A. Ingalls and F. D. Popp, *J. Heterocycl. Chem.*, 4, 523 (1967).
436. V. Klusis and S. Kutkevicius, *Lietuvos TSR Aukstuju Mokykly Mokslo Dorhai, Chem. ir Chem. Technol.*, 6, 51 (1965); *Chem. Abstr.*, 64, 19607 (1966).
437. V. Klusis and S. Kutkevicius, *Lietuvos TSR Audstuju Mokylu Mokslo Darbai, Chem. ir Chem. Technol.*, 7, 67 (1965); *Chem. Abstr.*, 64, 19607 (1966).

438. A. Albert and R. E. Willette, *J. Chem. Soc.*, 4063 (1964).
439. W. Herz and D. R. K. Murty, *J. Org. Chem.*, **25**, 2242 (1960).
440. R. A. Abramovitch, D. H. Hey, and R. D. Mulley, *J. Chem. Soc.*, 4623 (1954).
441. R. A. Abramovitch, K. A. H. Adams, and A. D. Notation, *Can. J. Chem.*, **38**, 2152 (1960).
442. R. A. Abramovitch, *Can. J. Chem.*, **38**, 2273 (1960).
443. T. V. Tsaranova and Tr. Kishinev, *Politekh. Inst.*, No. 5, 65 (1966); *Chem. Abstr.*, **67**, 32612a (1967).
444. R. A. Abramovitch and I. D. Spenser, in "Advances in Heterocylic Chemistry," (A. R. Katritzky, ed.), Vol. 3, Academic Press, New York, 1964, p. 79.
445. J. P. Paolini and R. K. Robins, *J. Heterocycl. Chem.*, **2**, 53 (1965).
446. C. K. Bradsher, E. F. Litzinger, and M. F. Zinn, *J. Heterocycl. Chem.*, **2**, 331 (1965).
447. V. I. Staninets and E. A. Shilov, *Ukr. Khim. Zh.*, **31**, 1286 (1965); *Chem. Abstr.*, **64**, 12626 (1966).
448. W. L. Mosby, *J. Org. Chem.*, **26**, 1316 (1961).
449. Société des usines chimiques Rhône-Poulenc, Fr. patent, 1,167,657 (1958); *Chem. Abstr.*, **55**, 9436 (1961).
450. W. L. Mosby and R. J. Boyle, *J. Org. Chem.*, **24**, 374 (1959).
451. Société des usines chimiques Rhône-Poulenc, Fr. patent, 1,170,119 (1959); *Chem. Abstr.*, **55**, 9437 (1961).
452. Laboratoires U.P.S.A., Neth. patent, 6,414,717 (1965); *Chem. Abstr.*, **64**, 712 (1966).
453. W. Kaupmann and S. Funke, Ger. patent, 1,168,435 (1964); *Chem. Abstr.*, **61**, 3123 (1965).
454. R. Littell and D. S. Allen, U.S. patent, 3,314,941 (1967); *Chem. Abstr.*, **67**, 64453r (1967).
455. L. Homer and H. Oediger, *Ann. Chem.*, **627**, 142 (1959); *Chem. Abstr.*, **55**, 1492 (1961).
456. (a) I. M. Bortovoi, *Dokl. 2-oi Vtoroi Mezhvuz. Konf. po Khim. Organ. Kompleksn. Soedin.*, 94 (1963); *Chem. Abstr.*, **61**, 13876 (1964).
(b) R. A. Abramovitch and B. W. Cue, Jr., *J. Org. Chem.*, **38**, 173 (1973).
457. T. Goerdeler and W. Roth, *Chem. Ber.*, **96**, 534 (1963); *Chem. Abstr.*, **58**, 12557 (1963).
458. A. Spiliadis, M. Hilsenrath, V. Cornea-Ivan, and E. Balta, *Bull. Soc. Chim. Fr.*, 921 (1966); *Chem. Abstr.*, **65**, 10700 (1966).
459. L. Pentimalli, *Ann. Chim.* (Rome), **55**, 435 (1965); *Chem. Abstr.*, **63**, 6963 (1965).
460. J. Klosa, *J. Prakt. Chem.*, **8**, 168 (1959); *Chem. Abstr.*, **54**, 5640 (1961).
461. T. Okamoto, M. Hirobe, and E. Yabe, *Chem. Pharm. Bull.* (Tokyo), **14**, 523 (1966); *Chem. Abstr.*, **65**, 8897 (1966).
462. F. C. Meyer and H. C. Godt, U.S. patent Appl., 2,983,729 (1958); *Chem. Abstr.*, **56**, 1430 (1962).
463. B. A. Geller and L. S. Samosvat, *Zh. Obshch. Khim.*, **34**, 613 (1964); *Chem. Abstr.*, **60**, 13112 (1964).
464. A. Puszynski and T. Talik, *Rocz. Chem.*, **41**, 917 (1967); *Chem. Abstr.*, **67**, 82062s (1967).
465. T. Talik and Z. Talik, *Rocz. Chem.*, **41**, 483 (1967); *Chem. Abstr.*, **67**, 64192e (1967).
466. W. Czuba, *Rocz. Chem.*, **56**, 1647 (1962); *Chem. Abstr.*, **56**, 3445 (1962).
467. W. Czuba, *Rocz. Chem.*, **35**, 1347 (1961); *Chem. Abstr.*, **57**, 8543 (1962).
468. W. Czuba, *Rocz. Chem.*, **34**, 1639 (1960); *Chem. Abstr.*, **56**, 3445 (1962).
469. B. Brekiesz-Lewandowska and Z. Talik, *Rocz. Chem.*, **41**, 1887 (1967); *Chem. Abstr.*, **69**, 2199w (1968).

470. K. Lewicka and E. Plazek, *Rocz. Chem.*, **39**, 643 (1965); *Chem. Abstr.*, **63**, 8310 (1965).
471. M. Balme and M. Gruffaz, Fr. patent, 1,477,734 (1967); *Chem. Abstr.*, **68**, 68889t (1968).
472. E. I. Fedorov and B. I. Mikhant'ev, *Tr. Pobl. Lab. Khim. Vysokoml. Soedin., Voronezh Gos. Univ.*, (4), 48 (1966); *Chem. Abstr.*, **69**, 18986k (1968).
473. F. Ya. Perveev and N. V. Koshmina, *Zh. Org. Khim.*, **4**, 177 (1968); *Chem. Abstr.*, **68**, 78086f (1968).
474. T. Okamoto, M. Hirobe, Y. Tamai, and E. Yabe, *Chem. Pharm. Bull.* (Tokyo), **14**, 506 (1966); *Chem. Abstr.*, **65**,8896 (1966).
475. J. R. Geigy, Brit. patent, 1,108,975 (1968); *Chem. Abstr.*, **69**, 67226w (1968).
476. J. S. Wieczorek and T. Talik, *Rocz. Chem.*, **36**, 967 (1962); *Chem. Abstr.*, **58**, 5675 (1963).
477. M. Israel and A. R. Day, *J. Org. Chem.*, **24**, 1455 (1959).
478. P. Tomasik and Z. Skrowaczewska, *Rocz. Chem.*, **40**, 637 (1966); *Chem. Abstr.*, **56**, 3826 (1966).
479. J. Barycki and E. Plazek, *Rocz. Chem.*, **37**, 1443 (1963); *Chem. Abstr.*, **60**, 7987 (1964).
480. C. A. Salemink, *Rec. Trav. Chim. Pays-Bas*, **80**, 545 (1961).
481. Smith, Kline & French Laboratories, Brit. patent, 1,020,060 (1966); *Chem. Abstr.*, **64**, 11181 (1966).
482. D. G. Markees, V. C. Dewey, and X. Y. Kidder, *Arch. Biochem. Biophys.*, **86**, 179 (1960).
483. F. W. Lange, *Seifen-Oele-Fette-Wachse*, **91**, 593 (1965); *Chem. Abstr.*, **64**, 11349 (1966).
484. E. C. Taylor and A. McKillop, *J. Org. Chem.*, **30**, 3153 (1965).
485. H. Bojarska-Dahlig and P. Nantka-Namirski, *Pharm. Acta Helv.*, **35**, 423 (1960); *Chem. Abstr.*, **55**, 1607 (1961).
486. J. Kotler-Brajtburg, *Acta Polon. Pharm.*, **20**, 169 (1963); *Chem. Abstr.*, **62**, 1623 (1965).
487. R. D. Elliot, C. Temple, Jr., and J. A. Montgomery, *J. Org. Chem.*, **33**, 2393 (1968).
488. T. Batkowski, *Rocz. Chem.*, **37**, 385 (1963); *Chem. Abstr.*, **59**, 11486 (1963).
489. R. C. De Selms and H. S. Mosher, *J. Amer. Chem. Soc.*, **82**, 3762 (1960).
490. S. Bodforss, *Ann. Chem.*, **676**, 136 (1964); *Chem. Abstr.*, **62**, 560 (1965).
491. D. L. Garmaise and J. Kombossy, *J. Org. Chem.*, **29**, 3404 (1964).
492. S. K. Chatterjee, P. C. Jain, and N. Anand, *Indian J. Chem.*, **3**, 138 (1965); *Chem. Abstr.*, **63**, 5628 (1965).
493. P. C. Jain and N. Anand, *Indian J. Chem.*, **6**, 123 (1968); *Chem. Abstr.*, **69**, 67294s (1968).
494. A. Hunger, J. Kabrle, A. Rossi, and K. N. Hoffman, U.S. patent, 3,004,978 (1960); *Chem. Abstr.*, **56**, 4771 (1962).
495. W. Knoblock and H. Kuehne, *J. Prakt. Chem.*, **17**, 199 (1962); *Chem. Abstr.*, **58**, 3431 (1963).
496. K. Pilgrim and F. Korte, *Tetrahedron*, **19**, 137 (1963).
497. F. J. Villani, U.S. patent, 2,898,338 (1959); *Chem. Abstr.*, **54**, 580 (1961).
498. V. Carelli, M. Cardellini, and F. Liberatore, *Ann. Chim.* (Rome), **48**, 1342 (1958); *Chem. Abstr.*, **58**, 1428 (1963).
499. V. Carelli, M. Cardellini, and F. Liberatore, *Farmaco, Ed. Sci.*, **15**, 803 (1960); *Chem. Abstr.*, **55**, 21109 (1961).
500. V. Carelli, M. Cardellini, and F. Liberatore, *Farmaco, Ed. Sci.*, **16**, 375 (1961); *Chem. Abstr.*, **56**, 5921 (1962).

501. B. K. Varma and A. B. Lal, *J. Indian Chem. Soc.*, **43**, 416 (1966); *Chem. Abstr.*, **65**, 18556 (1966).
502. Yoshitomi Pharmaceutical Industries Ltd., Jap. patent, 26,852 (1964); *Chem. Abstr.*, **62**, 10418 (1965).
503. S. Kuwata, *Bull. Chem. Soc. Jap.*, **33**, 1668 (1960).
504. H. Kakimoto, I. Sekigawa, and K. Yamamoto, Jap. patent, 20,716 (1965); *Chem. Abstr.*, **64**, 2065 (1966).
505. E. Hoyer, *Chem. Ber.*, **93**, 2475 (1960).
506. J. Hurst and D. G. Wibberly, *J. Chem. Soc.*, *C*, 1487 (1968).
507. L. N. Yakhontov and M. V. Rubtsov, *Zhur. Obshch. Khim.*, **30**, 1507 (1960); *Chem. Abstr.*, **55**, 1606 (1961).
508. J. Krapcho and W. A. Lott, U.S. patent, 2,918,470 (1959); *Chem. Abstr.*, **54**, 6761 (1960).
509. S. Yamada and Y. Kikugawa, *Chem. Ind.* (London), 1325 (1967).
510. J. Volke and J. Holubek, *Collect. Czech. Chem. Commun.*, **28**, 1597 (1963); *Chem. Abstr.*, **59**, 8361 (1963).
511. B. V. Balyakina, E. S. Zhanovich, and N. A. Preobrazhenskii, *Zhur. Obshch. Khim.*, **31**, 542 (1961); *Chem. Abstr.*, **55**, 22308 (1961).
512. J. Rus, V. Loeffelmann, V. Prokes, and A. Kana, Czech. patent 101,790 (1961); *Chem. Abstr.*, **59**, 1013 (1963).
513. J. P. Wibaut, J. H. Uhlenbroek, E. C. Kooijman, and D. K. Kettenes, *Rec. Trav. Chim. Pays-Bas*, **79**, 481 (1960); *Chem. Abstr.*, **55**, 1609 (1961).
514. G. Erlemann, W. Guea, and O. Schnider, Fr. patent, M3398 (1965); *Chem. Abstr.*, **64**, 716 (1966).
515. Y. Sawa and R. Maeda, Jap. patent, 2147 (1965); *Chem. Abstr.*, **62**, 14635 (1965).
516. T. Maruyama, M. Yasumatsu, and K. Kurisono, Jap. patent, 4074 (1965); *Chem. Abstr.*, **62**, 16211 (1965).
517. T. S. Gardner, E. Wenis, and J. Lee, *J. Med. Pharm. Chem.*, **3**, 461 (1961).
518. L. I. Zakharkin and I. M. Khorlina, *Izvest. Akad. Nauk. SSSR, Otdel. Khim. Nauk.*, 2146 (1959); *Chem. Abstr.*, **54**, 10932 (1960).
519. J. Ankrieux, D. Anker, and C. Mentzer, *Chim. Therap.*, **2**, 57 (1966); *Chem. Abstr.*, **65**, 8837 (1966).
520. M. Nakanishi and T. Numakata, Jap. patent, 14,366 (1960); *Chem. Abstr.*, **55**, 15518 (1961).
521. J. Volke, R. Kubicek, and F. Santavy, *Collect. Czech. Chem. Commun.*, **25**, 871 (1960); *Chem. Abstr.*, **58**, 13448 (1963).
522. L. Karzynski, J. Nowak, and H. Witek, *Diss. Pharm. Pharmacol.*, **20**, 169 (1968); *Chem. Abstr.*, **69**, 43648s (1968).
523. V. L. Florent'ev, N. A. Drobinskaya, L. V. Ionova, M. Y. Karpeiskii, and K. F. Turchin, *Dokl. Akad. Nauk. SSSR*, **177**, 617 (1967); *Chem. Abstr.*, **69**, 27198g (1968).
524. S. O. Winthrop and G. Gavin, *J. Org. Chem.*, **24**, 1936 (1959).
525. S. Binieck, and B. Kabzinska, Pol. patent, 51,864 (1966); *Chem. Abstr.*, **68**, 95700u (1968).
526. R. H. Mizzoni, U.S. patent, 2,963,486 (1960); *Chem. Abstr.*, **55**, 10475 (1961).
527. G. N. Walker and M. A. Klett, *J. Med. Chem.*, **9**, 624 (1966); *Chem. Abstr.*, **65**, 7001 (1966).
528. R. I. Meltzer, U.S. patent, 3,313,822 (1967); *Chem. Abstr.*, **67**, 5403w (1967).
529. J. E. Robertson, J. H. Biel, T. F. Mitchell, Jr., W. K. Hoya, and H. A. Leiser, *J. Med. Chem.*, **6**, 805 (1963); *Chem. Abstr.*, **60**, 1692 (1964).

530. J. H. Biel and W. K. Hoya, U.S. patent, 3,205,133 (1965); *Chem. Abstr.*, **65**, 3496 (1966).
531. S. Biniecki and W. Zlakowska, *Acta Polon. Pharm.*, **23**, 89 (1966); *Chem. Abstr.*, **65**, 3813 (1966).
532. F. Zymalkowski and F. Koppe, *Arch. Pharm.* (Weinheim), **294**, 453 (1961); *Chem. Abstr.*, **56**, 2415 (1962).
533. F. Hoffman-La Roche & Co., Belg. patent, 615,478 (1962); *Chem. Abstr.*, 7496 (1963).
534. S. Miyano and N. Abe, *Chem. Pharm. Bull.* (Tokyo), **15**, 511 (1967); *Chem. Abstr.*, **67**, 73494g (1967).
535. S. Miyano, *Chem. Pharm. Bull.* (Tokyo), **13**, 1135 (1965); *Chem. Abstr.*, **64**, 688 (1966).
536. W. A. Shuler and A. Gross, U.S. patent, 2,953,562 (1960); *Chem. Abstr.*, **55**, 4552 (1961).
537. S. Raynolds and R. Levine, *J. Amer. Chem. Soc.*, **82**, 1152 (1960).
538. Deutsche Gold-und Silber-Scheideanstalt vorm. Roessler, Fr. patent, 1,380,771 (1964); *Chem. Abstr.*, **63**, 584 (1965).
539. K. Thiele, U.S. patent, 3,042,680 (1962); *Chem. Abstr.*, **57**, 13736 (1962).
540. F. F. Blicke and J. L. Hughes, *J. Org. Chem.*, **26**, 3257 (1961).
541. L. D. Smirnov, V. P. Lezina, V. F. Bystrov, and K. M. Dyumaer, *Izv. Akad, Nauk. SSSR, Ser. Khim,* (1), 198 (1965); *Chem. Abstr.*, **62**, 11774 (1965).
542. L. D. Smirnov, V. P. Lezina, T. P. Kartasheva, and K. M. Dyumaev, *Isv. Akad. Nauk. SSSR, Ser. Khim.*, 199 (1968); *Chem. Abstr.*, **69**, 77086g (1968).
543. L. D. Smirnov, T. P. Kartasheva, V. P. Lezina, and K. M. Dyumaev, *Izv. Akad. Nauk. SSSR, Ser. Khim.*, 2742 (1967); *Chem. Abstr.*, **69**, 67191f (1968).
544. K. M. Dyumaev, L. D. Smirnov, and V. F. Bystrov, *Izv. Akad. Nauk. SSSR. Otd. Khim. Nauk.*, 883, (1962); *Chem. Abstr.*, **57**, 12424 (1962).
545. L. D. Smirnov, V. P. Lezina, V. F. Bystrov, and K. M. Dyumaev, *Izv. Akad. Nauk. SSSR, Ser. Khim.*, **10**, 1836 (1965); *Chem. Abstr.*, **64**, 5038 (1966).
546. L. D. Smirnov, S. L. Orlova, V. P. Lezina and K. M. Dymaev, *Izv. Akad. Nauk. SSSR, Ser. Khim.*, 1816 (1967); *Chem. Abstr.*, **68**, 87111n (1968).
547. M. Miocque, *Bull. Soc. Chim. Fr.*, **2**, 330 (1960).
548. M. Mioque and J. A. Gautier, *C. R. Acad. Sci., Paris, Ser. C,* **252**, 2416 (1961); *Chem. Abstr.*, **56**, 14232 (1962).
549. Abbott Laboratories, Fr. patent, M2474 (1964); *Chem. Abstr.*, **61**, 13290 (1964).
550. Abbott Laboratories, Span. patent, 281,171 (1962); *Chem. Abstr.*, **60**, 2904 (1964).
551. A. N. Kost, P. B. Terent'ev, and T. Zavada, *Dokl. Akad. Nauk. SSSR,* **130**, 326 (1960); *Chem. Abstr.*, **54**, 11015 (1961).
552. R. Dahlbom, B. Karlen, S. Ramsey, I. Kraft, and R. Mollberg, *Acta Pharm. Suecica,* **1**, 237 (1964); *Chem. Abstr.*, **63**, 5595 (1965).
553. C. Lovell and K. J. Rorig, U.S. patent, 3,025,302 (1962); *Chem. Abstr.*, **57**, 11173 (1962).
554. G. Ehrhart, H. Ruschig, and K. Schmitt, Ger. patent, 1,116,226 (1961); *Chem. Abstr.*, **57**, 2199 (1962).
555. M. Masamichi, K. Isagawa, T. Kuki, and Y. Fushizaki, *Nippon Kagaku Zasshi,* **83**, 212 (1962); *Chem. Abstr.*, **59**, 3879 (1963).
556. E. Profft and S. Lojack, *Rev. Chim., Acad. Rep. Populaire Roumaine,* **7**, 405 (1962); *Chem. Abstr.*, **59**, 8696 (1963).
557. D. Wagler and E. Hoyer, *Chem. Ber.*, **98**, 1073 (1965); *Chem. Abstr.*, **63**, 14352 (1965).

558. S. I. Suminov and A. N. Kost, *Zh. Obshch. Khim.*, **34**, 2421 (1964); *Chem. Abstr.*, **61**, 11966 (1964).
559. L. E. Brady, M. Freifelder, and G. H. Stone, *J. Org. Chem.*, **26**, 4757 (1961).
560. N. F. Kazarinova, N. V. Dzhigirei, and N. A. Shabaeva, *Metody Poluch. Khim. Reaktivov Prep.*, No. 14, 38 (1966); *Chem. Abstr.*, **67**, 64187g (1967).
561. S. L. Shapiro, L. Freedman, H. Soloway, U.S. patent, 2,993,905 (1959); *Chem. Abstr.*, **56**, 2429 (1962).
562. S. L. Shapiro, H. Soloway, E. Chodos, and L. Freedman, *J. Pharm. Sci.*, **50**, 1035 (1961).
563. N. V. Organon, Belg. patent, 627,240 (1964); *Chem. Abstr.*, **60**, 9284 (1964).
564. G. N. Shibanova and R. G. Kulikova, USSR patent, 195,454 (1967); *Chem. Abstr.*, **68**, 104989z (1968).
565. G. N. Shibanova and R. G. Kulikova, USSR patent 195,456 (1967); *Chem. Abstr.*, **68**, 104991u (1968).
566. L. A. Paquette, *J. Org. Chem.*, **27**, 2870 (1962).
567. N. F. Kazarinova and A. O. Grinberg, USSR patent, 178,378 (1966); *Chem. Abstr.*, **64**, 19570 (1966).
568. A. N. Kost, E. V. Vinogradova, and V. Kozler, *Zh. Obshch. Khim.*, **33**, 3602 (1963); *Chem. Abstr.*, **60**, 9239 (1963).
569. S. L. Shapiro, I. M. Rose, F. C. Testa, and L. Freedman, *J. Org. Chem.*, **26**, 1323 (1961).
570. S. L. Shapiro and L. Freedman, U.S. patent, 3,055,906 (1962); *Chem. Abstr.*, **58**, 6808 (1963).
571. M. I. Druzin, A. K. Val'kova, A. B. Pashkov, I. V. Zaitseva, N. V. Bogdanova, L. D. Pertsov, S. F. Kalinkin, and B. M. Kuindzhi, USSR patent, 215,997 (1968); *Chem. Abstr.*, **69**, 52016d (1968).
572. H. Erdtman, F. Haglid, I. Wellings, and U.S. v. Euler, *Acta Chem. Scand.*, **17**, (6) 1717 (1963).
573. H. Lund, *Acta Chem. Scand.*, **17**, 2325 (1963).
574. K. W. Merz and H. Stolte, *Arch. Pharm.* (Weinheim), **292**, 496 (1959); *Chem. Abstr.*, **54**, 8809 (1961).
575. Parke, Davis & Co., Brit. patent, 851,577 (1960); *Chem. Abstr.*, **55**, 12428 (1961).
576. CIBA, Neth. patent, 6,513,784 (1966); *Chem. Abstr.*, **65**, 15342 (1966).
577. M. M. Baizer, U.S. patent, 3,426,000 (1966); *Chem. Abstr.*, **64**, 19568 (1966).
578. R. F. Shuman and E. D. Amstutz, *Rec. Trav. Chim. Pays-Bas*, **84**, 441 (1965); *Chem. Abstr.*, **63**, 5596 (1965).
579. E. D. Amstutz, F. P. Papopoli, C. H. Tilford, and R. F. Shyman, Brit. patent, 990,340 (1965); *Chem. Abstr.*, **63**, 6978 (1965).
580. G. B. Bachman and M. Karickhoff, U.S. patent, 3,217,012 (1965); *Chem. Abstr.*, **64**, 2062 (1966).
581. C. E. Frosst & Co., Belg. patent, 645,217 (1964); *Chem. Abstr.*, **63**, 11576 (1965).
582. S. Biniecki and S. Emiljan, *Acta Polon. Pharm.*, **24**, 345 (1967); *Chem. Abstr.*, **68**, 114387r (1968).
583. S. Biniecki and W. Zladkowska, *Acta Polon. Pharm.*, **21**, 521 (1964); *Chem. Abstr.*, **63**, 2948 (1965).
584. E. Profft and G. Shulz, *Arch. Pharm.* (Weinheim), **294**, 292 (1961); *Chem. Abstr.*, **55**, 18725 (1961).
585. A. V. Voropaeva and I. Kh. Feldman, *Khim. Ceterotsikl. Soedin., Akad. Nauk. Latv. SSSR*, 271 (1965); *Chem. Abstr.*, **63**, 6967 (1965).
586. Kh. Feldman and A. V. Voropaeva, *Tr. Leningr. Khim.-Farmatsuet. Inst.*, (16), 21, (1962); *Chem. Abstr.*, **61**, 639 (1964).

587. P. A. Roukema, *Sci. Commun.*, **10**, No. 162, 1 (1960–61); *Chem. Abstr.*, **58**, 4513 (1963).
588. N. V. Koninklijke Pharmaceutische Fabrieken Voorheen Bracades-Sfeeman & Pharmacia, Fr. patent, M1801 (1963); *Chem. Abstr.*, **59**, 12769 (1963).
589. N. V. Nederlands Conbinatie Voor Chemische Industrie, Belg. patent, 624,975 (1963); *Chem. Abstr.*, **60**, 13257 (1964).
590. CIBA Ltd., Brit. patent, 890,602 (1962); *Chem. Abstr.*, **56**, 15489 (1962).
591. A. N. Kost, E. V. Vinogradova, and W. Kozler, USSR patent, 161,758 (1964); *Chem. Abstr.*, **61**, 3075 (1964).
592. Smith, Kline & French Laboratories, Neth. patent, 6,512,616 (1966); *Chem. Abstr.*, **65**, 7095 (1966).
593. J. W. Cusic and H. W. Sause, U.S. patent, 3,255,054 (1965); *Chem. Abstr.*, **64**, 6625 (1966).
594. M. N. Tilichenko and G. V. Pavel, *Zh. Organ. Khim.*, 1, 1992 (1965); *Chem. Abstr.*, **64**, 8132 (1966).
595. F. Bergel, S. S. Brown, C. L. Leese, C. M. Timmis, and R. Wade, *J. Chem. Soc.*, 846 (1963).
596. K. J. Rorig, U.S. patent, 3,128,280 (1964); *Chem. Abstr.*, **60**, 14481 (1964).
597. Eprova Ltd., Neth. patent, 6,600,250 (1966); *Chem. Abstr.*, **65**, 18600 (1966).
598. H. Rapoport and A. D. Batcho, *J. Org. Chem.*, **28**, 1753 (1963).
599. V. Petrow and B. Sturgeon, *J. Chem. Soc.*, 1157 (1949).
600. T. Takahashi, T. Yatsuka, and S. Senda, *J. Pharm. Soc. Jap.*, **64**, 9 (1944); *Chem. Abstr.*, **46**, 110 (1952).
601. E. P. Hart, *J. Chem. Soc.*, 212 (1956).
602. Ya. L. Gol'dfarb, L. V. Antik, and V. A. Petukhov, *Izvest. Akad. Nauk. SSSR., Otdel Khim. Nauk.*, 887 (1961); *Chem. Abstr.*, **55**, 22307 (1961).
603. G. Y. Lesher and D. Gruett, Belg. patent, 612,258 (1962); *Chem. Abstr.*, **58**, 7954 (1963).
604. D. E. Orr and K. Weisner, *Chem. Ind.* (London), 672 (1959).
605. A. M. Roe, *J. Chem. Soc.*, 2195 (1963).
606. E. A. Mistryukov, N. I. Aronova, and V. F. Kucherov, *Izv. Akad. Nauk. SSSR, Ser. Khim.*, 512 (1964).
607. W. Zecher and F. Krohnke, *Chem. Ber.*, **94**, 698 (1961).
608. A. Dornow and E. H. Rohe, *Chem. Ber.*, **93**, 1093 (1960); *Chem. Abstr.*, **54**, 18519 (1960).
609. A. N. Hambly and B. V. O'Grady, *Austr. J. Chem.*, **17**, 860 (1964).
610. W. Herz and D. R. K. Murty, *J. Org. Chem.*, **26**, 418 (1961).
611. B. M. Bain and J. E. Saxton, *J. Chem. Soc.*, 5216 (1961).
612. J. A. Moore and H. H. Puschner, *J. Amer. Chem. Soc.*, **81**, 6041 (1959).
613. E. Profft and F. Melichar, *J. Prakt. Chem.*, **2**, 87 (1955); *Chem. Abstr.*, **54**, 1514 (1960).
614. N. F. Kucherova, R. M. Khomutov, E. I. Budovskii, V. P. Evdakov, and N. K. Kotchekov, *Zhur. Obshch. Khim.*, **29**, 915 (1959); *Chem. Abstr.*, **54**, 1515 (1959).
615. V. A. Zasosov, E. I. Metel'kova, and V. S. Onoprienko, *Med. Prom. SSSR*, **15**, No. 3, 35 (1961); *Chem. Abstr.*, **55**, 24748 (1961).
616. L. Pentimalli, *Ann. Chim.* (Rome), **53**, 1123 (1963); *Chem. Abstr.*, **60**, 10645 (1964).
617. T. Sakuragi, C. Argoudelis, and F. A. Kummerow, *Arch. Biochem. Biophys.*, **89**, 160 (1960); *Chem. Abstr.*, **54**, 25201 (1960).
618. A. N. Kost, L. A. Golovleva, P. B. Terent'ev, and M. Islam, *Zh. Analit. Khim.*, **21**, 859 (1966); *Chem. Abstr.*, **65**, 19290 (1966).

619. L. D. Goodhue, A. J. Reinert, and R. P. Williams, U.S. patent, 3,150,041 (1964); *Chem. Abstr.*, **61**, 15289 (1964).

620. H. C. Van der Plas and H. J. den Hertog, *Tetrahedron Lett.*, 13 (1960).

621. G. Schmidt, Ger. patent, 1,179,943 (1964); *Chem. Abstr.*, **62**, 1677 (1965).

622. P. Nantka-Namirski, S. Kurzepa, J. Kazimierczyh, H. Kierylowicz, and M. Kobylinska, *Acta Physiol. Polon*, **17**, 145 (1966); *Chem. Abstr.*, **64**, 17936 (1966).

623. H. Bojarska-Dhalig and P. Nantka-Namirski, *Rocz. Chem.*, **34**, 189 (1960); *Chem. Abstr.*, **54**, 19674 (1960).

624. A. Albert and G. B. Barlin, *J. Chem. Soc.*, 5156 (1963).

625. G. E. McCasland, L. K. Gottwald, and A. Furst, *J. Org. Chem.*, **26**, 3541 (1961).

626. R. C. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc.*, 3736 (1964).

627. C. A. I. Goring, U.S. patent, 3,050,382 (1962); *Chem. Abstr.*, **57**, 14218 (1962).

628. T. Talik and Z. Talik, *Nitro Compds., Proc. Intern. Symp. Warsaw*, 81 (1963); *Chem. Abstr.*, **64**, 2046 (1966).

629. J. A. Montgomery and K. Hewson, *J. Med. Chem.*, **9**, 105 (1966).

630. T. Batkowski and M. Tuszynska, *Rocz. Chem.*, **38**, 585 (1964); *Chem. Abstr.*, **61**, 10654 (1964).

631. S. P. Acharya and K. S. Nargund, *J. Sci. Ind. Res.*, **21B**, 452 (1962); *Chem. Abstr.*, **58**, 2429 (1963).

632. B. E. Fisher and J. E. Hodge, *J. Org. Chem.*, **29**, 776 (1964).

633. T. Talik and E. Plazek, *Rocz. Chem.*, **33**, 1343 (1959); *Chem. Abstr.*, **54**, 13123 (1960).

634. I. Kh. Fel'dman and A. V. Voropaeva, *Tr. Leningr. Khim.-Farmatsevt. Inst.*, 17 (1962); *Chem. Abstr.*, **61**, 638 (1964).

635. F. J. Villani and T. A. Mann, *J. Med. Chem.*, **11**, 894 (1968); *Chem. Abstr.*, **69**, 42647w (1968).

636. B. Van der Wal, Th. J. de Boer, and H. O. Huisman, *Rec. Trav. Chim. Pays-Bas*, **80**, 228 (1961).

637. O. Meth-Cohn, R. K. Smalley, and H. Suschitzky, *J. Chem. Soc.*, 1666 (1963).

638. R. K. Smalley, *J. Chem. Soc., C*, 82 (1966).

639. J. L. Greene and J. A. Montgomery, *J. Med. Chem.*, **6**, 294 (1963); *Chem. Abstr.*, **58**, 12507 (1963).

640. S. M. Gadehar, U.S. patent, 3,206,464 (1965); *Chem. Abstr.*, **64**, 711 (1966).

641. C. H. Huang and G. Ya Kondrat'eva, *Izv. Akad. Nauk. SSSR, Otd. Khim. Nauk.*, 525 (1962); *Chem. Abstr.*, **57**, 15064 (1962).

642. E. Profft and K. H. Otto, *J. Prakt. Chem.*, **8**, 156 (1959).

643. E. Neuzil, J. C. Breton, and H. Plagnol, *Bull. Mem. Ecole Natl. Med. Phar. Dakar*, **7**, 157, 159 (1959); *Chem. Abstr.*, **57**, 4993 (1962).

644. T. Kralt and J. Van Dijk, U.S. patent, 3,046,280 (1963); *Chem. Abstr.*, **58**, 4606 (1963).

645. N. V. Philips' Gloeilampenfobrieken, Brit. patent, 848,690 (1960); *Chem. Abstr.*, **57**, 875 (1962).

646. Aktiebolaget Pharmacia, Brit. patent, 852,795 (1960); *Chem. Abstr.*, **55**, 13446 (1961).

647. E. N. Ifversen, K. Rubinstein, and K. T. J. Skagius, Ger. patent, 1,077,220 (1960); *Chem. Abstr.*, **55**, 22343 (1961).

648. K. T. J. Skagius, Swed. patent, 174,845 (1959); *Chem. Abstr.*, **56**, 7339 (1962).

649. K. Shagius, K. Rubinstein, and E. Ifversen, *Acta Chem. Scand.*, **14**, 1054 (1960); *Chem. Abstr.*, **56**, 12904 (1962).

650. R. Landi-Vittory, F. Gatta, F. Toffler, S. Chiavarelli, and G. L. Gatta, *Farmaco, Ed. Sci.*, **18**, 465 (1963); *Chem. Abstr.*, **59**, 9941 (1963).

651. A. P. Gray, D. E. Heitmeier, and E. E. Spinner; *J. Amer. Chem. Soc.*, **81**, 4351 (1959).
652. P. Grammaticakis, *Bull. Soc. Chim. Fr.*, 480 (1959).
653. E. Marcus, J. T. Fitzpatrick and F. C. Frostick, Jr., U.S. patent, 2,993,894 (1961); *Chem. Abstr.*, **56**, 1416 (1962).
654. B. Maziere and N. Dat-Xuong, *Chim. Ther.*, **3** (1), 1 (1968); *Chem. Abstr.*, **69**, 43880d (1968).
655. P. C. Jain, V. Kapoor, N. Anand, G. K. Patnaik, A. Ahmad, and M. M. Vohra, *J. Med. Chem.*, **11**, 87 (1968).
656. R. G. D. Moore and R. J. Cox, Brit. patent, 870,027 (1961); *Chem. Abstr.*, **55**, 23134 (1961).
657. W. A. Schuler and H. Beschke, Belg. patent, 630,125 (1963); *Chem. Abstr.*, **60**, 14515 (1964).
658. R. M. Peck, R. K. Preston, and H. J. Creech, *J. Org. Chem.*, **26**, 3409 (1961).
659. A. Wolf and E. V. Haxthausen, *Arzneimittel-Forsch.*, **10**, 50 (1969); *Chem. Abstr.*, **54**, 11289 (1960).
660. K. Credner, G. Renwanz, and H. Engelhard, Ger. patent, 1,049,863 (1959); *Chem. Abstr.*, **55**, 4541 (1961).
661. H. Zellner, Austrian patent, 226,703 (1963); *Chem. Abstr.*, **59**, 10,000 (1963).
662. A. Burger and H. Hu Ong, *J. Med. Chem.*, **6**, 205 (1963).
663. L. N. Yakhontov and M. V. Rubtsov, *Zhur. Obshch. Khim.*, **30**, 3300 (1960); *Chem. Abstr.*, **55**, 18721 (1961).
664. J. Keck, *Ann. Chem.*, **662**, 171 (1963).
665. E. T. Holmes and H. R. Synder, *J. Org. Chem.*, **29**, 2155 (1964).
666. F. Leonard and J. Koo, Belg. patent, 613,213 (1962); *Chem. Abstr.*, **57**, 16629 (1962).
667. P. Nantka-Namirski, *Acta Polon. Pharm.*, **19**, 299 (1962); *Chem. Abstr.*, **59**, 15260 (1963).
668. N. Kinoshita, M. Hamana, and T. Kawasahi, *Chem. Pharm. Bull.* (Tokyo), **10**, 753 (1962); *Chem. Abstr.*, **58**, 6785 (1963).
669. H. Bojarska-Dahlig and P. Nantka-Namirski, *Congr. Sci. Farm., Conf. Comun., Pisa*, **21**, 203 (1961); *Chem. Abstr.*, **59**, 6408 (1963).
670. I. E. El-Kholy, F. K. Rafla, and G. Soliman, *J. Chem. Soc.*, 1857 (1962).
671. F. Brody and W. J. Sydor, U.S. patent, 3,118,871 (1964); *Chem. Abstr.*, **60**, 16021 (1964).
672. Sien-Moo Tsang and C. E. Lewis, U.S. patent, 3,151,106 (1964); *Chem. Abstr.*, **61**, 1619 (1964).
673. E. F. Elslager and D. F. Worth, *J. Med. Chem.*, **6**, 444 (1963).
674. J. Barycki and E. Plazek, *Rocz. Chem.*, **38**, 553 (1964); *Chem. Abstr.*, **61**, 10654 (1964).
675. E. F. Elslager, D. F. Worth, D. B. Copps and L. M. Werbel, U.S. patent, 3,139,421 (1964); *Chem. Abstr.*, **61**, 6973 (1964).
676. E. Jeney and T. Zsolnai, *Zentr. Bakteriol, Parasitenk*, **180**, 84 (1960); *Chem. Abstr.*, **55**, 5657 (1961).
677. T. Zsolnai, *Biochem. Pharmacol.*, **11**, 995 (1962); *Chem. Abstr.*, **58**, 837 (1963).
678. American Cyanamid Co., Brit. patent, 871,624 (1961); *Chem. Abstr.*, **56**, 14437 (1962).
679. H. Martin and E. Habicht, Swiss patent, 337,098 (1959); *Chem. Abstr.*, **54**, 19720 (1960).
680. G. Nabert-Bock, *Arzneimittel-Forsch.*, **10**, 125 (1960); *Chem. Abstr.*, **54**, 13264 (1960).
681. J. Matzke, Austr. patent, 242,701 (1965); *Chem. Abstr.*, **63**, 18112 (1965).

682. M. Vohra, S. Pradhan, P. Jain, S. Chatterjee, and N. Anand, *J. Med. Chem.*, **8**, 296 (1965).
683. T. Takahashi, F. Yoneda, and R. Oishi, *Chem. Pharm. Bull.* (Tokyo), **7**, 602 (1959); *Chem. Abstr.*, **54**, 14246 (1960).
684. T. Kurihara and T. Chiba, *Tohoku Uakka Diagaku Kenyu Nempo*, **10**, 65 (1963); *Chem. Abstr.*, **61**, 651 (1964).
685. L. A. Elson, *Proc. Intern. Congr. Intem. Soc. Hematol.*, (7th Rome), **3**, 647 (1958); *Chem. Abstr.*, **55**, 4772 (1961).
686. I. Tanaka, *Kagaku To Kogyo*, **17**, 961 (1964); *Chem. Abstr.*, **61**, 11349 (1964).
687. J. A. Moore and F. J. Marascia, *J. Amer. Chem. Soc.*, **81**, 6049 (1959).
688. M. Balassa, *Orvosi Hetilap*, **101**, No. 8, 259 (1960); *Chem. Abstr.*, **55**, 1767 (1961).
689. H. Schwarzkopf, Belg. patent, 615,394 (1962); *Chem. Abstr.*, **58**, 8850 (1963).
690. F. W. Lange, Ger. patent, 1,142,045 (1963); *Chem. Abstr.*, **58**, 13708 (1963).
691. D. G. Markees, V. C. Dewey, and W. George, *J. Med. Chem.*, **11**, 126 (1968).
692. R. D. Elliot, C. Temple, Jr., and J. A. Montgomery, *J. Org. Chem.*, **31**, 1890 (1966).
693. A. Ahmad, C. K. Patnaik, and M. M. Vohra, *Indian J. Exptl. Biol.*, **4**, 154 (1966); *Chem. Abstr.*, **65**, 15969 (1966).
694. W. Sliwa, *Acta Polon. Pharm.*, **24**, 359 (1967); *Chem. Abstr.*, **68**, 39420r (1968).
695. Firma Hans Schwarzkopf, Fr. patent, 1,397,551 (1965); *Chem. Abstr.*, **63**, 11246 (1965).
696. M. Fujimoto, Jap. patent, 3370 (1959); *Chem. Abstr.*, **54**, 14275 (1960).
697. M. Fujimoto, Jap. patent, 2169 (1959); *Chem. Abstr.*, **54**, 11055 (1960).
698. M. Hamana and K. Funakoshi, *Yakugaku Zasshi*, **82**, 523 (1962); *Chem. Abstr.*, **58**, 3385 (1963).
699. R. G. Lacoste and A. E. Martell, *Inorg. Chem.*, **3**, 881 (1964); *Chem. Abstr.*, **61**, 2531 (1964).
700. G. J. Sutton, *Austr. J. Chem.*, **16**, 371 (1963).
701. G. J. Sutton, *Austr. J. Chem.*, **16**, 1137 (1963).
702. G. J. Sutton, *Austr. J. Chem.*, **16**, 1134 (1963).
703. K. Nakajima, *Nippon Kagaku Zasshi*, **81**, 1746 (1960); *Chem. Abstr.*, **56**, 4667 (1962).
704. K. Schulte, U.S. patent, 2,991,289 (1961); *Chem. Abstr.*, **56**, 3465 (1962).
705. M. Susai and S. Miyamoto, Jap. patent, 11,829 (1962); *Chem. Abstr.*, **59**, 10005 (1963).
706. R. P. Mull and W. E. Barrett, U.S. patent, 3,252,860 (1966); *Chem. Abstr.*, **65**, 5309 (1966).
707. F. Kuffner and T. Kirchenmayer, *Monatsh.*, **92**, 701 (1961); *Chem. Abstr.*, **56**, 1424 (1962).
708. H. Kamimura, A. Matsumoto, Y. Miyazaki, and I. Yamamoto, *Agr. Biol. Chem.* (Tokyo), **27**, 684 (1963); *Chem. Abstr.*, **60**, 6160 (1964).
709. C. H. Krauch and W. Metzner, *Chem. Ber.*, **99**, 88 (1966).
710. T. Kisaki and E. Tamaki, *Nippon Nogei Kagaku Kaishi*, **38**, 549 (1964); *Chem. Abstr.*, **63**, 7059 (1965).
711. T. Naito, T. Yoshikawa, F. Ishikawa, S. Isoda, Y. Omura, and I. Takamura, *Chem. Pharm. Bull.* (Tokyo), **13**, 869 (1965); *Chem. Abstr.*, **63**, 11488 (1965).
712. Yu. A. Zhdanov, I. D. Sadekov, A. D. Garnovskii, and V. I. Minkin, *Izv. Vysshikh Uchebn. Zavedenii, Khim. i Khim. Teckhnol.*, **8**, 954 (1965); *Chem. Abstr.*, **64**, 17574 (1966).
713. E. H. Kober, R. F. W. Raetz, and H. Ulrich, U.S. patent, 3,041,346 (1962); *Chem. Abstr.*, **57**, 13731 (1962).

714. H. Ubrich, E. Kober, H. Schroeder, R. Raetz, and C. Grundmann, *J. Org. Chem.*, **27**, 2585 (1962).
715. H. Brown and P. Schuman, *J. Org. Chem.*, **28**, 1122 (1963).
716. H. Brown, *J. Polymer Sci.*, **44**, 9 (1960); *Chem. Abstr.*, **55**, 4039 (1961).
717. Farbenfabriken Bayer A.-G., Brit. patent, 985,354 (1965); *Chem. Abstr.*, **63**, 586 (1965).
718. F. Hoffmann-La Roche & Co., A.-G., Neth. Appl. 6,407,413 (1965); *Chem. Abstr.*, **63**, 1774 (1965).
719. L. Berger, A. J. Corraz, and J. Lee, Fr. patent, M3502 (1965); *Chem. Abstr.*, **64**, 2104 (1966).
720. F. Hoffmann-La Roche & Co., Neth. Appl., 6,407,463 (1965); *Chem. Abstr.*, **62**, 16207 (1965).
721. Kanegafuchi Spinning Co., Ltd., Belg. patent, 652,893 (1964); *Chem. Abstr.*, **64**, 11084 (1966).
722. T. Takata, K. Sayama, and M. Takigawa, *Nippon Kagaku Zasshi*, **85**, 237 (1964); *Chem. Abstr.*, **63**, 2950 (1965).
723. Deutshe Gold-und Silber-Scheideanstalt vorm. Roessler, Neth. patent, 6,511,104 (1966); *Chem. Abstr.*, **65**, P2231 (1966).

Chemistry of Heterocyclic Compounds, Volume 14
Edited by R. A. Abramovitch

CHAPTER X

Pyridinecarboxylic Acids

PETER I. POLLAK* AND MARTHA WINDHOLZ

Merck Sharp & Dohme Research Laboratories
Rahway, New Jersey

I. Preparation

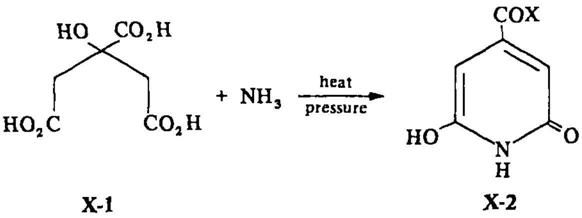
1. From Nonpyridine Starting Materials

Additional syntheses of pyridine ring systems from 1,5-dicarbonyl precursors have been described (see also Chapter II).

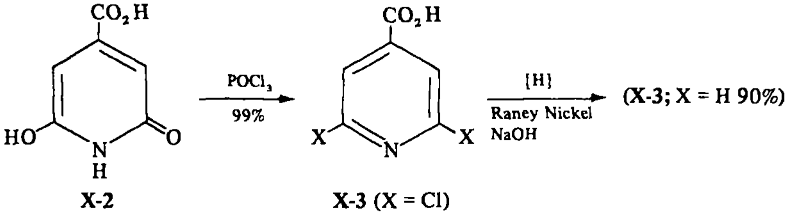
---

*Deceased, 1971.

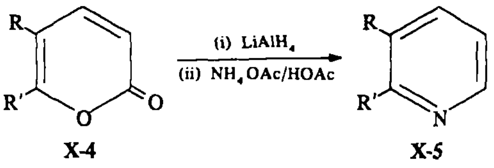
Citric acid (X-1) when treated with ammonia or urea at 130 to 200°[1] or with *p*-toluenesulfonic acid under autoclaving conditions[2] affords citrazinic acid (X-2, X = OH) or its amide (X-2, X = NH_2) in yields exceeding 60% of theory.†



Citrazinic acid can be converted in high yield to 2,6-dichloroisonicotinic acid (X-3, X = Cl) with $POCl_3$. The latter is easily reduced catalytically to isonicotinic acid (X-3, X = H).[2]



2-Pyrone (X-4, R = R′ = H) and its 5- (X-4; R = CO_2H, R′ = H) and 6-carboxylic acid (X-4; R = H, R′ = CO_2H) or its 5,6-dicarboxylic acid (X-4, R = R′ = CO_2H) were converted to the corresponding pyridine carboxylic acids (X-5) by treatment with $LiAlH_4$ followed by aminolysis.[3] The intermediate

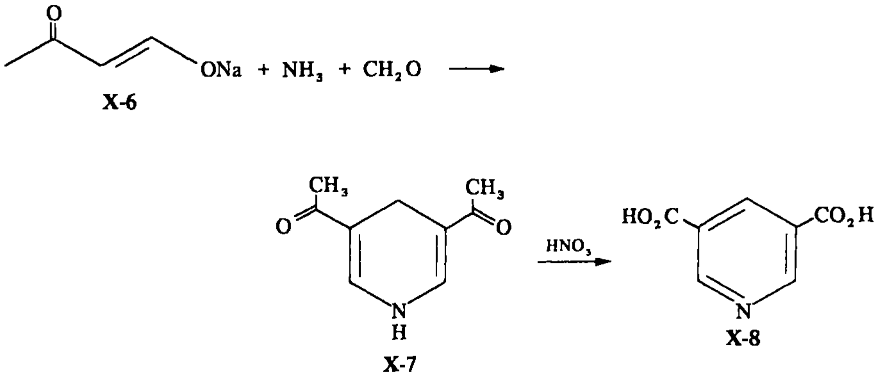


cis,trans-muconic acid semialdehydes could be isolated.

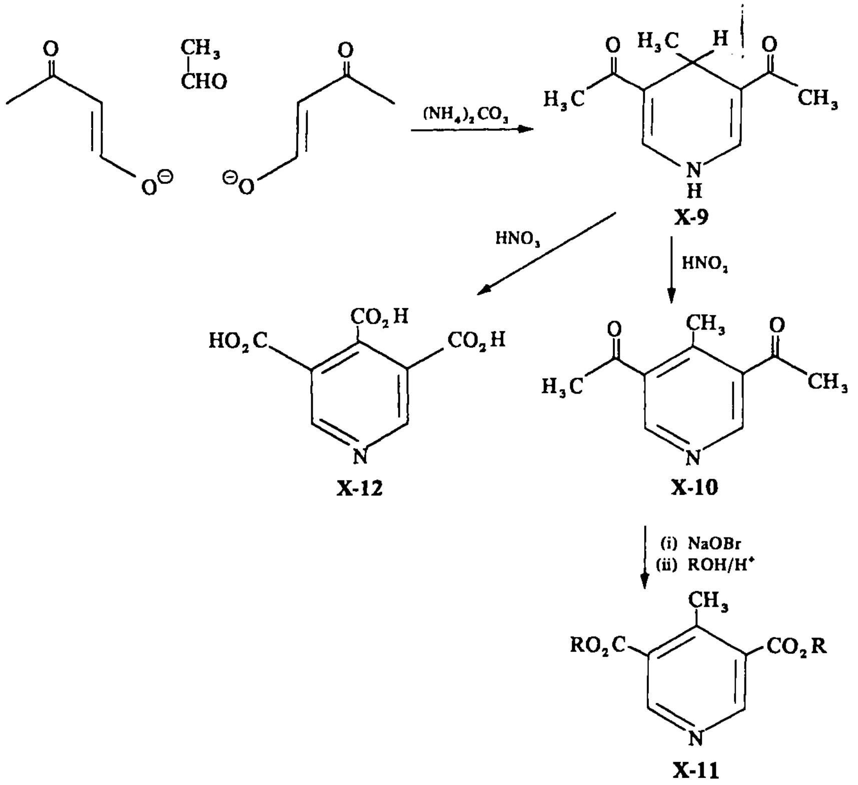
The sodium enolate of acetoacetaldehyde (X-6) could be condensed with formaldehyde and ammonolyzed to yield the dihydropyridine (X-7). Subsequent nitric acid oxidation gave pyridine-3,5-dicarboxylic acid (X-8).[4] When this

---

†In this chapter all 2- or 4-oxipyridine derivatives will be formulated as pyridones rather than as hydroxypyridines in keeping with modern structural evidence (A. R. Katritzky, *Principles of Heterocyclic Chemistry*, Academic Press, New York, 1968).



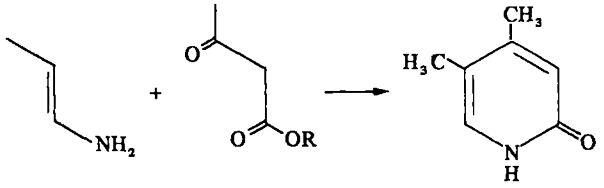
reaction was carried out with acetaldehyde and ammonium carbonate, the product was 4-methyl-3,5-diacetyl-1,4-dihydropyridine (**X-9**), which is readily oxidized with nitrous acid to the pyridine (**X-10**). Sodium hypobromite



oxidation followed by esterification in methanol or ethanol gave the corresponding dialkyl 4-methylpyridine-3,5-dicarboxylates (**X-11**, R = CH_3 or C_2H_5). Oxidation of the dihydropyridine (**X-9**) with nitric acid afforded pyridine-3,4,5-tricarboxylic acid (**X-12**), which could be esterified with diazomethane.[5]

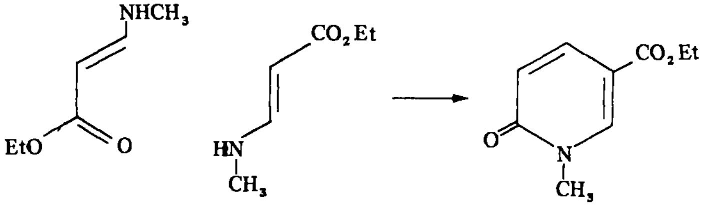
Related bimolecular condensations of enamines derived from *β*-diketones with an aldehyde have also been described.[6]

Similar reaction systems in which the aldehyde has been replaced by a suitable malonic acid or malononitrile precursor, undergo similar condensations to pyridones.[7-14] With appropriately substituted precursors, the synthesis is suitable



for the preparation of pyridonecarboxylic acids.

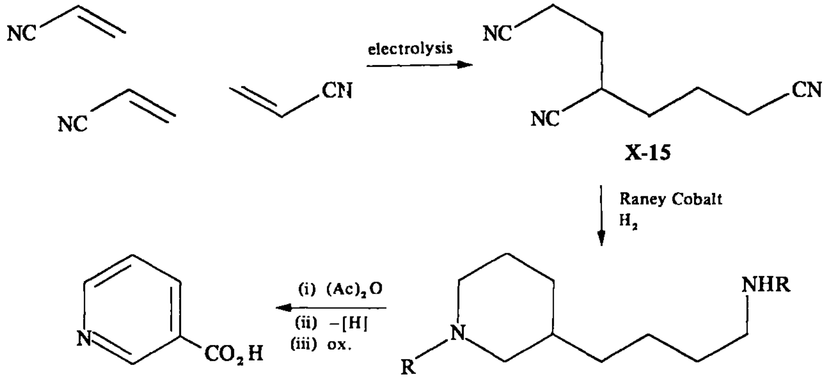
A related reaction is the bimolecular self-condensation of ethyl *β*-methylaminoacrylate (**X-13**) to *N*-methyl-5-carbethoxy-2-pyridone (**IX-14**).[15]



X-13 **X-14**

Nicotinic acid (**X-17**) can be obtained by an interesting electrolytic trimerisation of acrylonitrile to 1,3,6-tricyanohexane (**X-15**). The latter is reduced with Raney Cobalt to the corresponding triamine, which, in turn, is catalytically cyclized to 3-(ω-amino-*n*-butyl)piperidine (**X-16**, R = H). The acetylated piperidine (**X-16**, R = OAc) is dehydrogenated and oxidized to the vitamin (**X-17**).[16]

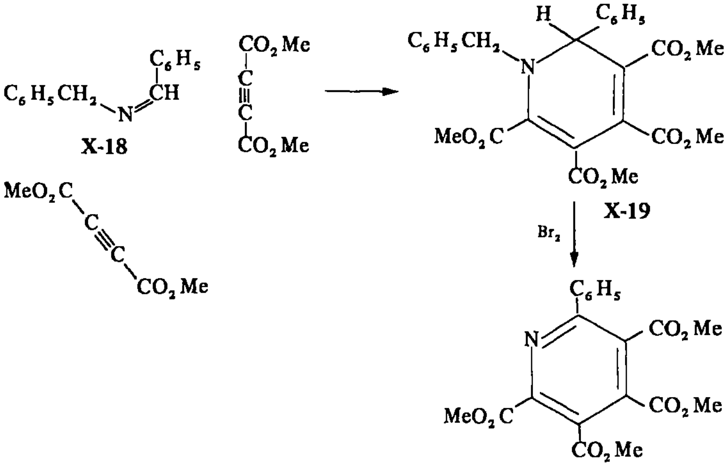
Huisgen and Herbig[17] condensed *N*-benzylphenylazomethine (**X-18**) with two moles of dimethyl acetylenedicarboxylate to obtain the corresponding 1,2-dihydropyridinetetracarboxylic acid ester (**X-19**). Oxidation with bromine afforded tetramethyl 2-phenylpyridine 3,4,5,6-tetracarboxylate (**X-20**).



X-15

X-16

X-17

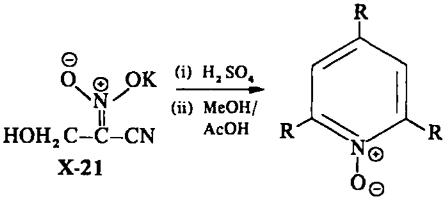


X-18

X-19

X-20

The acid-catalyzed trimerization of potassium β-hydroxy-α-nitropropionitrile (X-21) yields 2,4,6-tricyanopyridine-1-oxide (X-22, R = CN). The latter could be

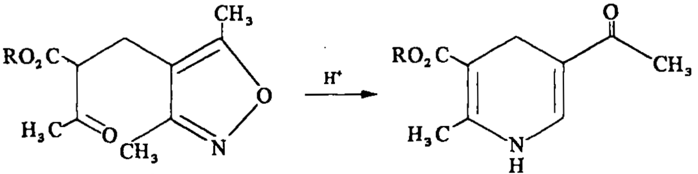


X-21

X-22

converted to the trimethyl ester (**X-22**, R = CO_2Me) by methanolysis in acetic acid.[18]

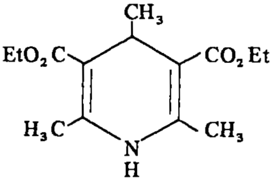
Isoxazoles (**X-23**) have been used to protect β-iminocarbonyl systems in the manipulation of complex starting materials. Thus they yield dihydro-β-acetylpyridine-β′-carboxylic acids (**X-24**).[19]



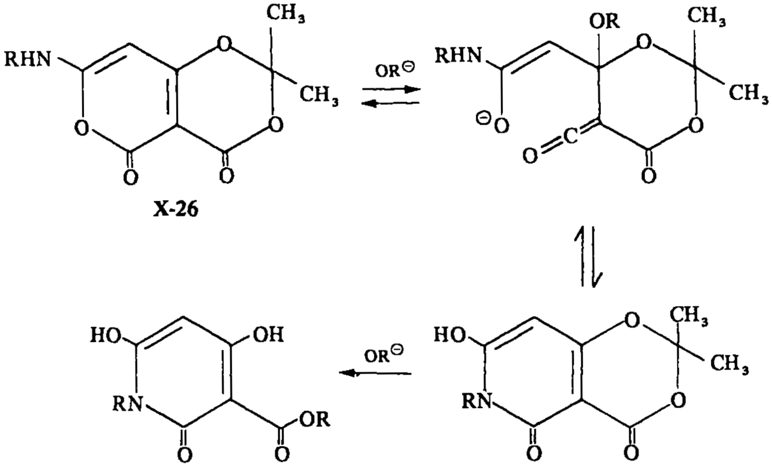
X-23 **X-24**

A number of miscellaneous condensations have been recorded in the last ten years. Thus, the Hantzsch synthesis has been reexamined and a 53% yield of **X-25** was obtained.[20]

Treatment of aminopyranodioxins (**X-26**) and aminopyranooxazines (**X-27**) with alkoxides or hydroxides afforded 4,6-dihydroxy-2-oxopyridine-3-carboxylates (**X-28**) or carboxanilides (**X-29**) *via* the following mechanism:[21]

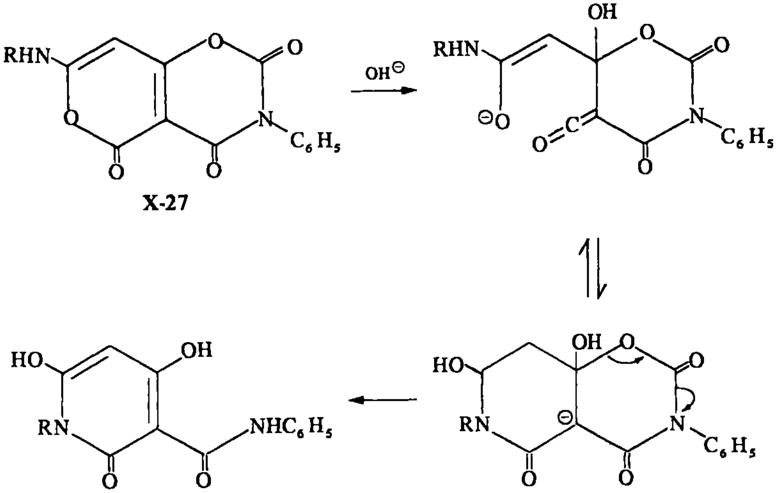


X-25



X-26

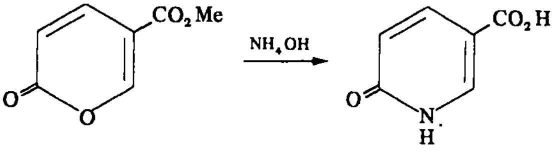
X-28



X-27

X-29

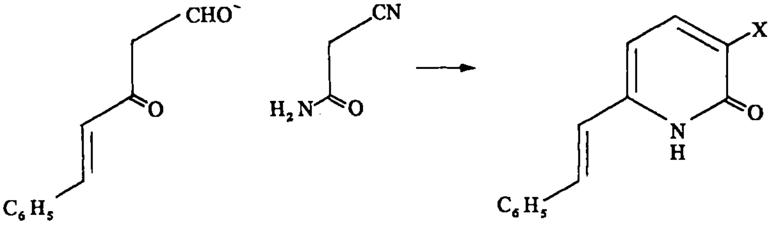
Maleic acid, when treated with sulfuric acid containing oleum and methanol, gave a 50% yield of methyl coumalate (**X-30**). Ammonolysis afforded a 75% yield of 2-pyridone-5-carboxylic acid (**X-31**).[22] Cinnamoylacetaldehyde (**X-32**)



X-30

X-31

and cyanoacetamide were condensed to 3-cyano-6-styryl-2-pyridone (**X-33**, X = CN), which was hydrolyzed to the carboxylic acid **X-34** (X = CO_2H).

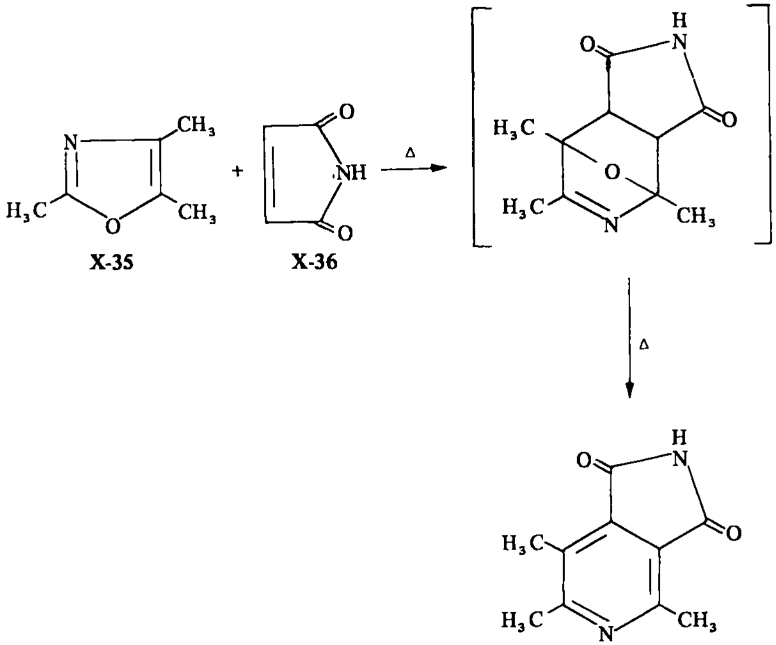


X-32

X-33 (X = CN)
X-34 (X = CO_2H)

2. By Electrocyclic Reactions

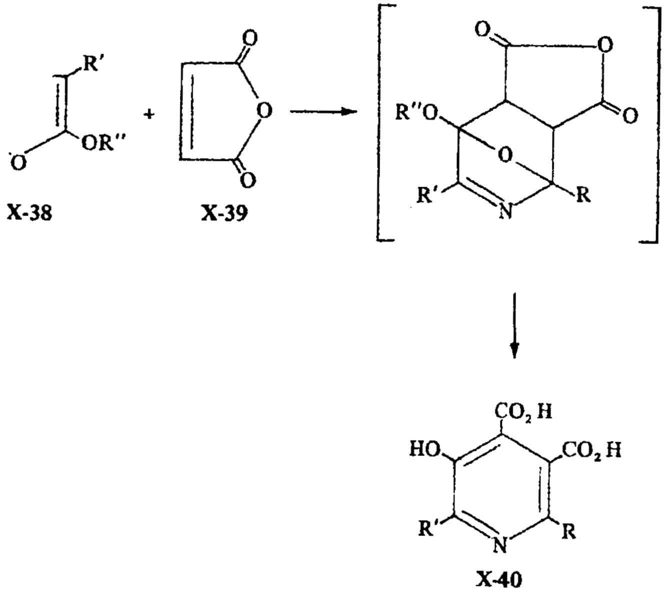
A new class of pyridine syntheses is based on the proclivity of some heteroazoles to add dienophiles with the intermediate formation of hetero-2,2,1-bicycloazaheptenes. Thus, substituted oxazoles (**X-35**) react with a typical dienophile such as maleimide (**X-36**) at elevated temperatures to yield substituted pyridines (**X-37**).[24] The same type of reaction utilizing substituted 5-alkoxyoxazoles (**X-38**) and maleic anhydride (**X-39**) affords 4,5-dicarboxy-3-pyridinols (**X-40**).[25] (See also Chapter XII.)

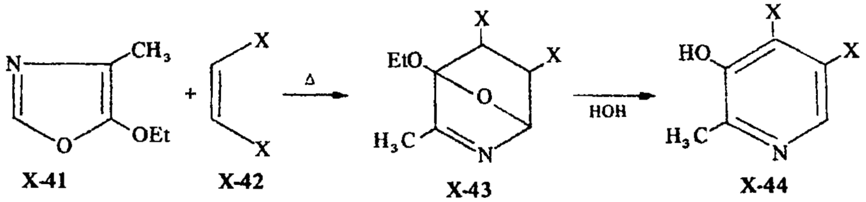


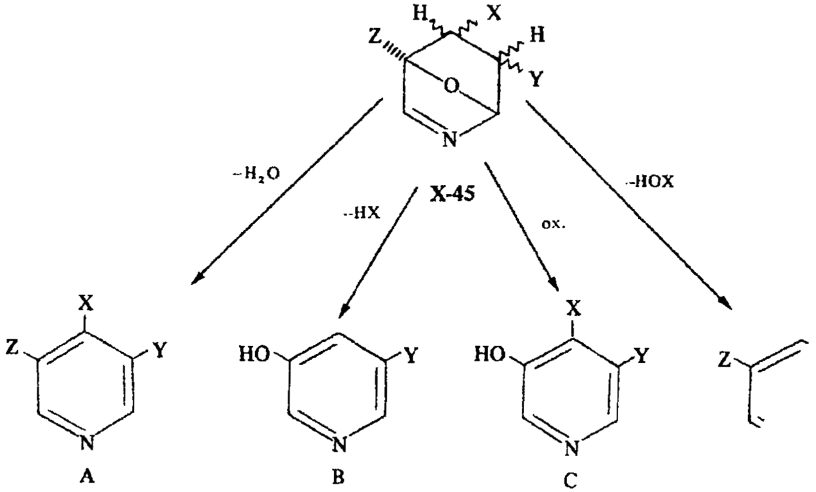
X-35 **X-36**

X-37

It was immediately recognized that this system offers a new route to pyridoxol (vitamin B_6): 4-methyl-5-ethoxyoxazole (**X-41**), on treatment with diethyl maleate (**X-42**, X = CO_2Et) or maleonitrile (**X-42**, X = CN), gave the expected bicyclic adducts (**X-43**, X = CO_2Et or CN) which were readily solvolyzed to 2-methyl-4,5-dicarbethoxy-3-pyridinol (**X-44**, X = CO_2Et) or the corresponding nitrile (**X-44**, X = CN). The latter are easily converted to pyridoxol (**X-44**, X = CH_2OH).[26-28]

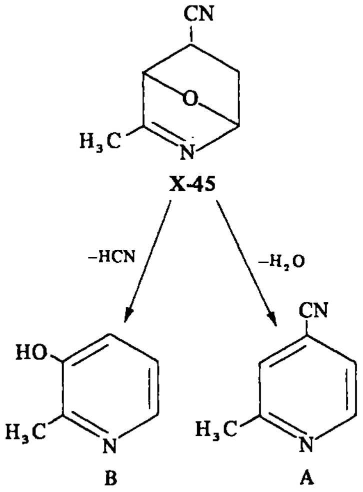

R′
OR″
X-38
X-39
R″O
R′
N
R
CO₂H
HO
CO₂H
R′
N
R
X-40

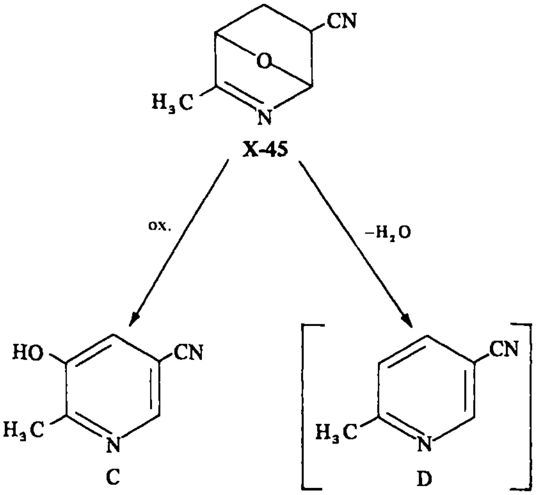

N
CH₃
OEt
X-41
X
X
X-42
Δ
EtO
X
X
H₃C
N
X-43
HOH
X
HO
X
H₃C
N
X-44


H
X
Z
H
Y
O
N
X-45
–H₂O
–HX
ox.
–HOX
X
Z
Y
N
A
HO
Y
N
B
X
HO
Y
N
C
Z

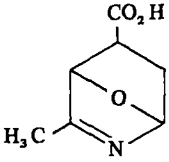
Investigation of the mechanism and stereochemistry of this Diels-Alder reaction showed that the intermediate **X-45** could lead to four different product types depending on the electronic nature of X, Y, and Z, on the stereochemical relationship of the 4-proton to the oxide bridge, and on whether or not the medium contains an oxidant.[29]

The use of unsymmetrical dienophiles such as acrylonitrile fits well into this scheme in that the two possible intermediates (**X-45**; X = CN, Y = Z = H) and (**X-45**; X = Z = H, Y = CN), formed from 4-methyloxazole, are transformed to the expected product mixture.[30, 31]



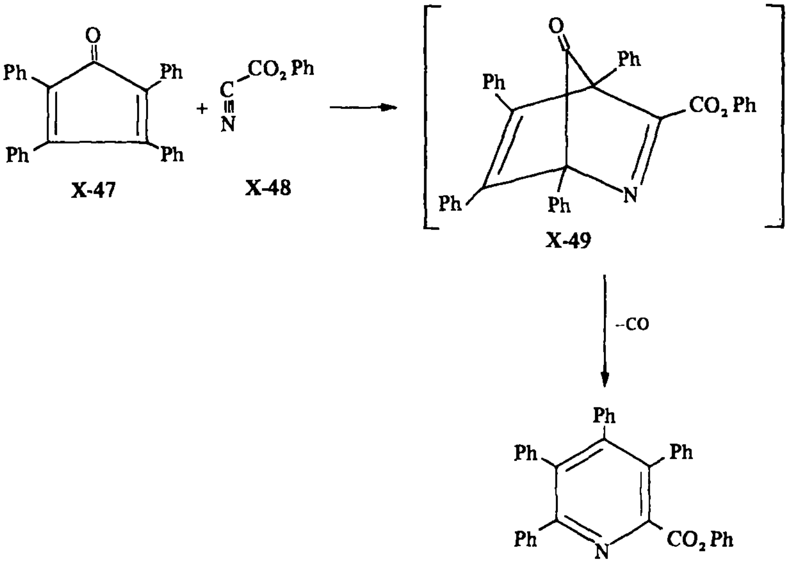


Results similar, but less complete, than those reported for the above dienophile were reported for acrylic acid. The products isolated correspond to only one (**X-46**) of the two possible isomeric adducts that could be formed. Thermolysis to pyridinecarboxylic acid occurred as expected in about 50% overall yield.[32]



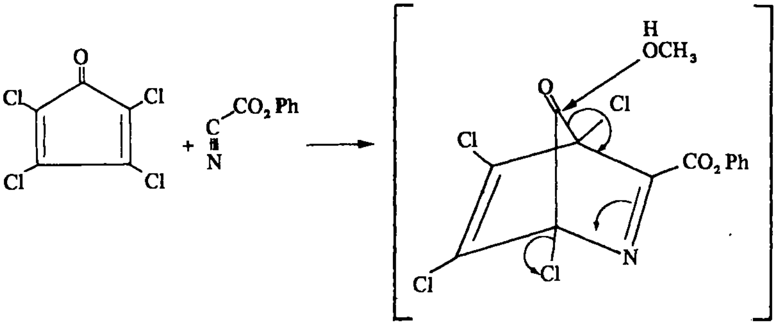
X-46

Tetraphenylcyclopentadienone (**X-47**) added phenyl cyanoformate (**X-48**) at 186° to yield phenyl 3,4,5,6-tetraphenylpyridine-2-carboxylate (**X-50**). An intermediate, [2.2.1]-azabicycloheptadienone (**X-49**), is postulated.[33] The

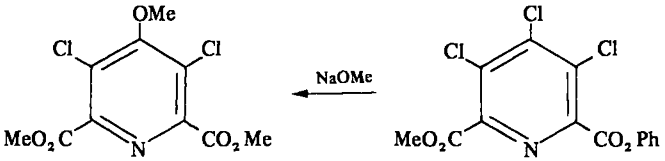


X-47 X-48 X-49 X-50

phenyl ester was hydrolyzed to give the free acid. The same reaction was run with tetrachlorocyclopentadienone. Continuous extraction with methanol afforded methyl phenyl 3,4,5-trichloropyridine-2,6-dicarboxylate (**X-52**), which may have arisen from the solvolytic ring-opening of the intermediate **X-51**.



X-51



X-53 X-52

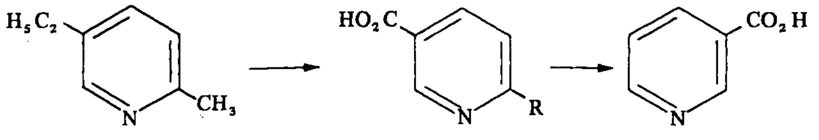
Treatment of the mixed ester (X-50) with sodium methoxide led to dimethyl 3,5-dichloro-4-methoxypyridine-2,6-dicarboxylate (X-53).

3. By Oxidation of Alkylpyridines, Quinolines, and Isoquinolines

The oxidation of appropriate alkylpyridines and quinolines continues to represent the most important process for the manufacture of nicotinic acid. All aspects of the field have seen continuing development, and a Czech review is available.[34] A general developmental study comparing seven oxidizing agents on a quantitative basis has also appeared.[35]

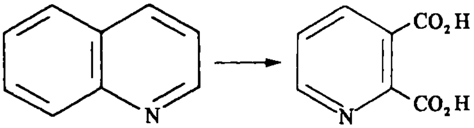
The oxidation of alkylpyridines in general, and 5-ethyl-2-methylpyridine (X-54) in particular, by dilute nitric acid at elevated pressures and temperatures has been the subject of many publications.[36-47]

The use of cupric nitrate as a catalyst in these systems has also been described.[48,49] The reaction usually proceeds to isocinchomeronic acid (X-55, $R = CO_2H$), which is decarboxylated to nicotinic acid (X-56) either *in situ* or in a subsequent operation. Under specific conditions of temperature and pressure, the reaction can be stopped at the 6-methylnicotinic acid (X-55, $R = CH_3$) stage.[50] It thus seems clear that under those conditions the 5-alkyl group is more prone to oxidative attack. The same nitric acid reaction system, with or without



X-54 X-55 X-56

Cu^{+2} or MoO_4^{-2} catalysis, converts quinoline (X-57) to quinolinic acid (X-58).[51-54] If quinoline is first converted to the 8-sulfonic acid with 65%



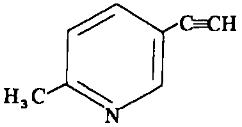
X-57 X-58

oleum, oxidation with nitric acid yields an improved direct yield of nicotinic acid.[55]

Picolines and 5-ethyl-2-methylpyridine (X-54)[1] can also be converted to the corresponding acids in basic media containing lead dioxide[56] or iron-aluminum oxide catalysts.[57] Again elevated pressures and temperatures are required.

A number of publications also describe the air oxidation of the same pyridine substrates in the presence of cupric nitrate.[58-62] Extensive work has also been reported on the fixed or fluidized bed vapor phase of alkylpyridines using vanadium catalysts.[63-67] The intermediate aldehydes can be isolated,[68] but usually the conditions are set to minimize this side reaction. Vanadates, molybdates, and tin salts of these two oxyacids are also described as effective catalysts in the high temperature oxidation of quinolines and isoquinolines.[69-71]

In the laboratory, selenium dioxide in organic solvents is a good reagent for the oxidation of alkylpyridines to carboxylic acids.[72-74] The intermediate aldehydes can be obtained depending on the position of the alkyl side-chain and the substrate/SeO_2 ratio. The reaction is selective in the case of 5-ethynyl-2-methylpyridine (X-59) yielding 5-ethynyl-2-picolinic acid in 40% yield.[75]

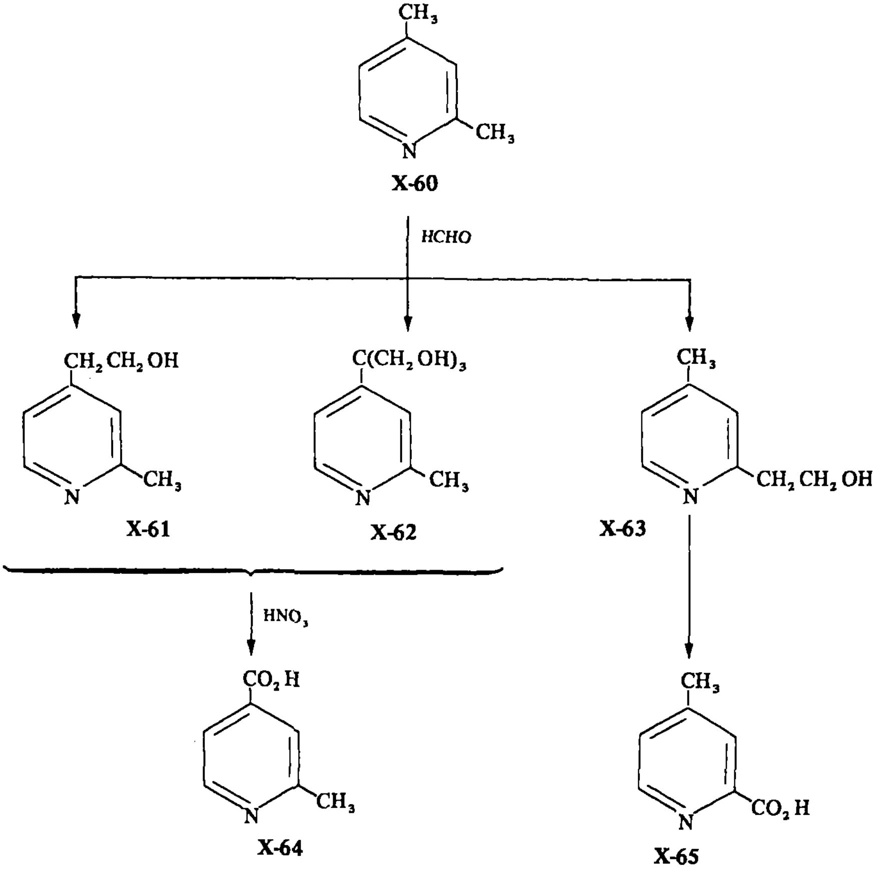


X-59

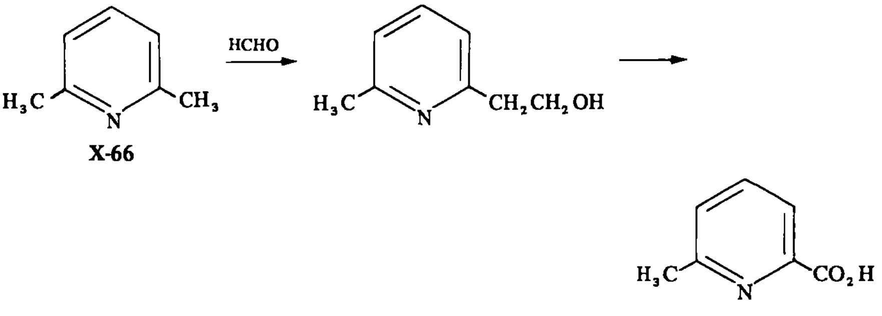
A number of industrially important systems have been described that use SeO_2 formed *in situ* from Se metal and nitric or sulfuric acid containing SO_3.[76-78]

The same oxidants can be used with quinoline or isoquinoline as substrates.[79-82] *In most of these reactions Se metal is used in catalytic amounts and is* continuously regenerated by the other oxidants present.

Ozone has been used to convert 8-hydroxyquinoline to nicotinic acid.[83,84] In the case of alkylquinolines, acridine, and phenanthridine, ozonolysis leads to alkylpyridine carboxylic acids, their *N*-oxides, and more extensive degradation products derived from the subsequent C—N bond cleavage in the *N*-oxides.[85] 5-Fluoronicotinic acid was obtained from 3-fluoroquinoline using a Cu(II) acetate/hydrogen peroxide couple.[86] Manganese dioxide[87,88] and permanganate[89,90] are also effective, even in the case of acetamidopicolines.[91] The use of chromic acid seems an obvious extension.[92-94] An interesting mechanistic study concerning the air oxidation of alkylpyridines in strongly basic media shows that the reaction proceeds through direct electrophilic attack of oxygen on the alkylpyridine carbanions concerned.[95]



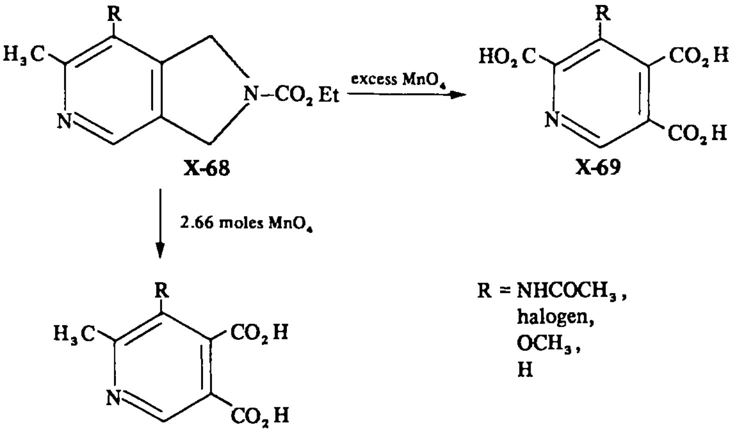
An interesting variant on this scheme to form alkylpyridinecarboxylic acids by nitric acid oxidation has been described by Czech workers: starting with 2,4- or 2,6-lutidine these bases are condensed with formaldehyde to yield unsymmetrical β-(hydroxyethyl)methylpyridines. Nitric acid oxidation now occurs preferentially at the hydroxylated side chain yielding the corresponding methylpicolinic acids.[96-99] Thus, 2,4-lutidine (**X-60**) is converted to a separable mixture of 4-(β-hydroxyethyl)-2-methylpyridine (**X-61**), 4-[tris(hydroxymethyl)methyl]-2-methylpyridine (**X-62**), and 2-(β-hydroxymethyl)-4-methylpyridine (**X-63**). Nitric acid oxidation yields 2-methylpyridine-4-carboxylic acid (**X-64**) from **X-61** and **X-62**, and 4-methylpyridine-2-carboxylic acid (**X-65**) from **X-63**. A similar reaction sequence carried out with 2,6-lutidine (**X-66**) affords ultimately 6-methylpyridine-2-carboxylic acid (**X-67**).



X-66

X-67

Vigorous oxidation conditions of course vitiate any selectivity adduced by functionalizing one of the side-chains: complete oxidation of all alkyl substituents is the result.[100]



X-68

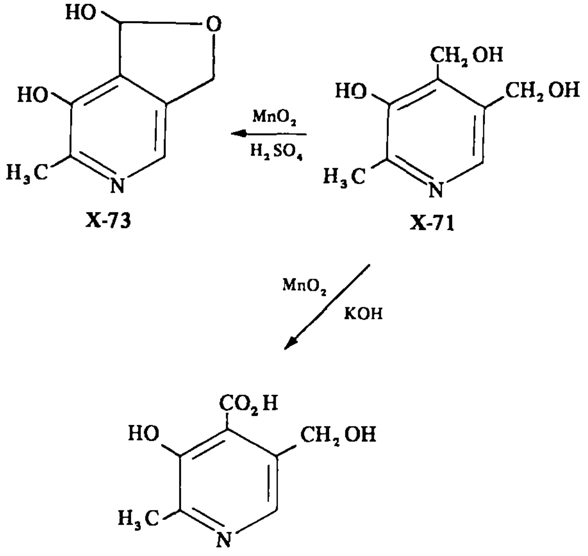
X-69

X-70

R = NHCOCH₃,
halogen,
OCH₃,
H

Substituted merimines (X-68) yield tricarboxylic acids (X-69) on vigorous oxidation with excess permanganate. With exactly 2.66 moles of permanganate, selective oxidation can be accomplished to a number of substituted 6-methylcinchomeronic acids (X-70).[101]

A nice example of a selective oxidation with manganese dioxide has been reported in the pyridoxine series:[102] in ethanolic KOH pyridoxine (X-71) yields 3-hydroxy-5-hydroxymethyl-2-methylpyridine-4-carboxylic acid (X-72). The same reagent in dilute sulfuric acid yields the hemiacetal X-73.

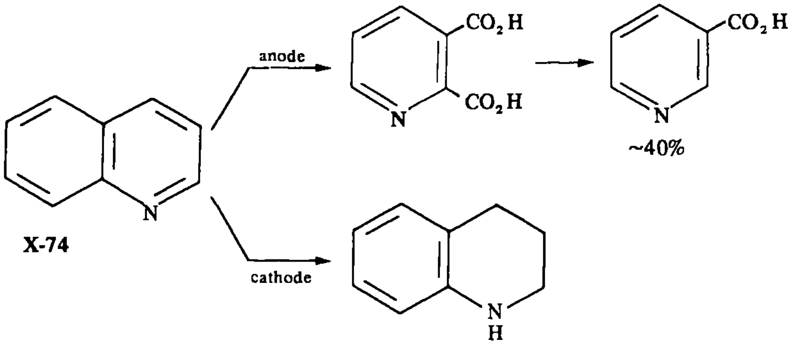


X-73 X-71

X-72

4. Electrolytic Oxidation

In efforts to develop industrial processes for the manufacture of nicotinic acid, Russian workers have studied the electrolytic oxidation of alkylpyridines and quinolines (X-74) using neutral or acidic media and platinum and lead anodes.[103-110] Reactions occurred at 40 to 100° with high current efficiencies, but reported yields are low (<50%). Desired products appeared, of course, in the anolyte compartment. In the catholyte compartment, on the other hand, quinoline substrate was, *inter alia*, reduced to 1,2,3,4-tetrahydroquinoline (X-75), isolated as the *N*-acetyl derivative.

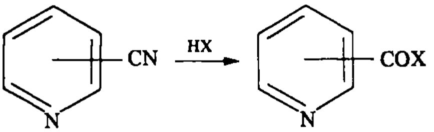


X-74

X-75

5. Synthesis via Nitriles

The solvolysis of pyridine nitriles (X-76) is an important route to pyridinecarboxylic acids (X-77, X = OH) or their derivatives (X-77).[111] In this section, only those new syntheses that proceed through nitriles that are not derived in the first place from precursor carboxylic acids[112-118] will be described.



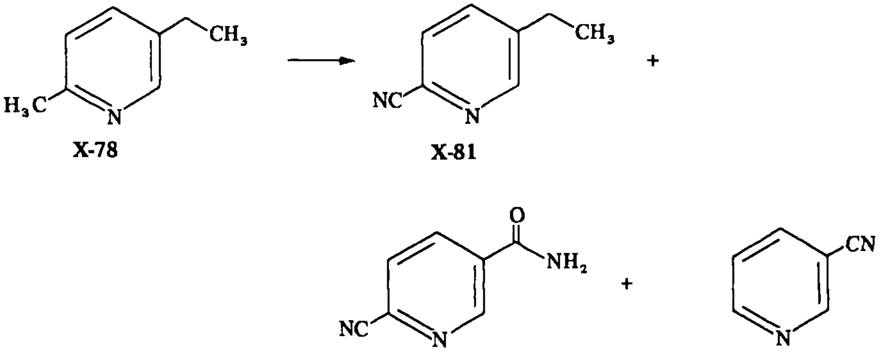
X-76

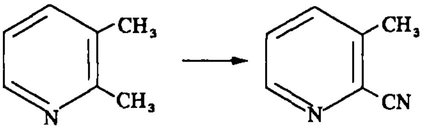
X-77

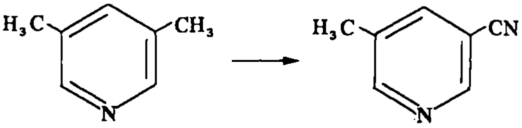
X = OH, NH_2, OR

Much progress has been made in the catalytic air ammoxidation of alkylpyridines to cyanopyridines (X-76). Yields are generally high. The catalysts employed are oxides of B, Al, P, Bi, Mo and V.[119-128] In the case of 5-ethyl-2-methylpyridine (X-78) the principal products observed were nicotinonitrile (X-79), 6-cyanonicotinamide (X-80), and 5-ethylpicolinonitrile (X-81). These products indicate that initial oxidative attack in X-78 may occur at the 2-methyl position, and that initial oxidative attack to the alcohol equivalent is the slow step in the reaction sequence.[129]

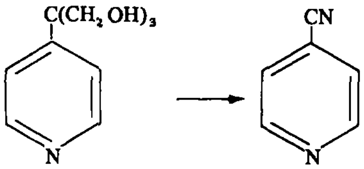
Additional support for this interpretation comes from work on isomeric lutidines: 2,3-lutidine (X-82) is converted to 2-cyano-3-methylpyridine (X-83) and 3,5-lutidine (X-84) affords 5-methylnicotinonitrile (X-85).[130]


X-78 X-81 X-80 X-79

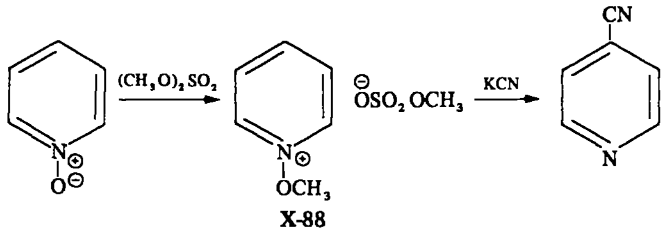

X-82 X-83

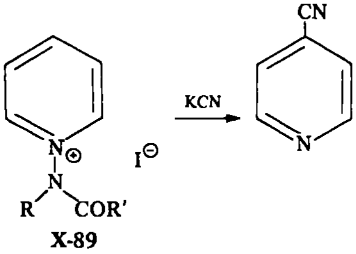

X-84 X-85

A related reaction is the oxidative ammonolysis of 1,1,1-trihydroxymethyl-4-picoline (**X-86**) to isonicotinonitrile (**X-87**).[131]

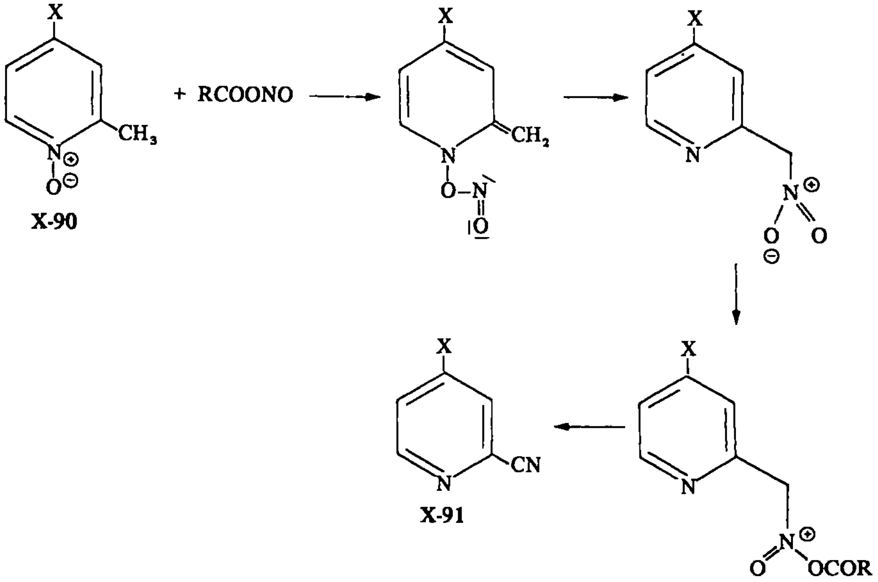

X-86 X-87

The cyanation of alkylated pyridine-1-oxides (**X-88**) leads to 2- or 4-cyanopyridines[132-134] (see also Chapter IV). The intermediate quaternary salts (**X-88**) can be isolated. Related acylated pyridinum-1-imines (**X-89**) undergo a similar reaction.[135]



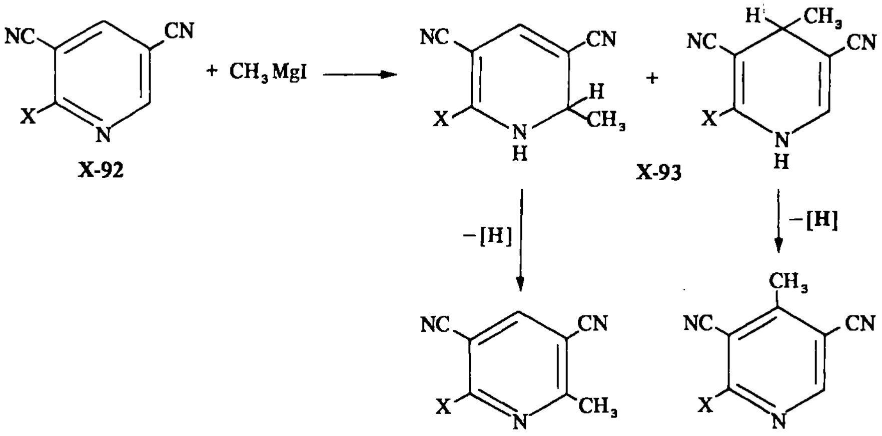


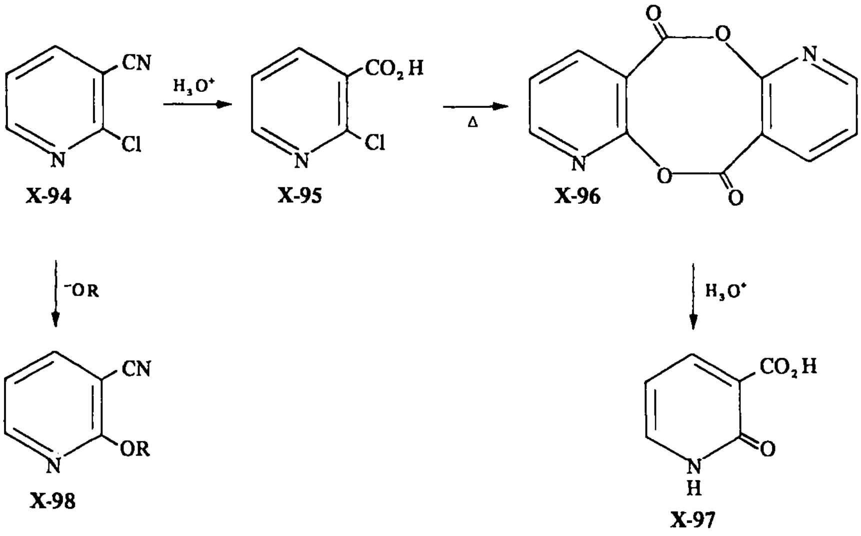
An internal redox reaction of 2-picoline-1-oxide (**X-90**, X = H) and its alkyl derivatives with nitrite ion and an acylating agent yields 2-cyanopyridines (**X-91**, X = H).[136] The following mechanism is proposed:



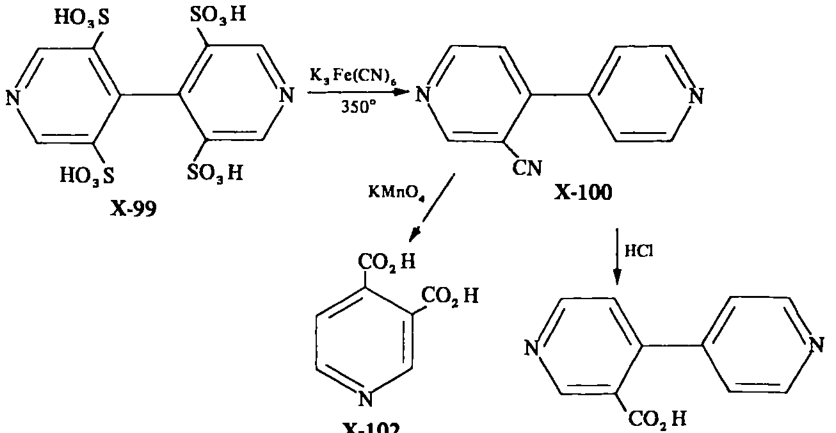
This reaction can also be achieved with an intramolecular source of nitrite ion: 4-nitro-2-picoline-1-oxide (**X-90**, X = NO_2), on treatment with acetyl chloride under cooling, yields a 68% yield of 4-chloro-2-picoline-1-oxide (**X-90**, X = Cl). If this reaction is carried out with warming, some 4-chloro-2-cyanopyridine (**X-91**, X = Cl), and a large yield (57%) of 4-chloro-2-cyanopyridine-1-oxide is claimed.[137]

2- or 4-Methylcyanopyridines, convertible to 2- or 4-methylpyridinecarboxylic acids, can be obtained by the action of methylmagnesium iodide on 2,5-dicyanopyridines (**X-92**, X = H or CH_3). The intermediate 1,2- or 1,4-dihydropyridines (**X-93**, X = H or CH_3) are isolable yellow solids. They can be dehydrogenated catalytically (Pd/C) or with silver oxide.[138, 139]


X-92
X-93


X-94
X-95
X-96
X-98
X-97

In the acid-catalyzed hydrolysis of halocyanopyridines such as 2-chloro-3-cyanopyridine (**X-94**), an intermediate 2-chloronicotinic acid (**X-95**) is formed which, on heating, undergoes a bimolecular condensation to the bis-ester (**X-96**). Further hydrolysis leads to 2-pyridone-3-carboxylic acid (**X-97**). Treatment of **X-94** with alkoxides leads to the 2-alkoxy-3-cyanopyridine (**X-98**).[140]

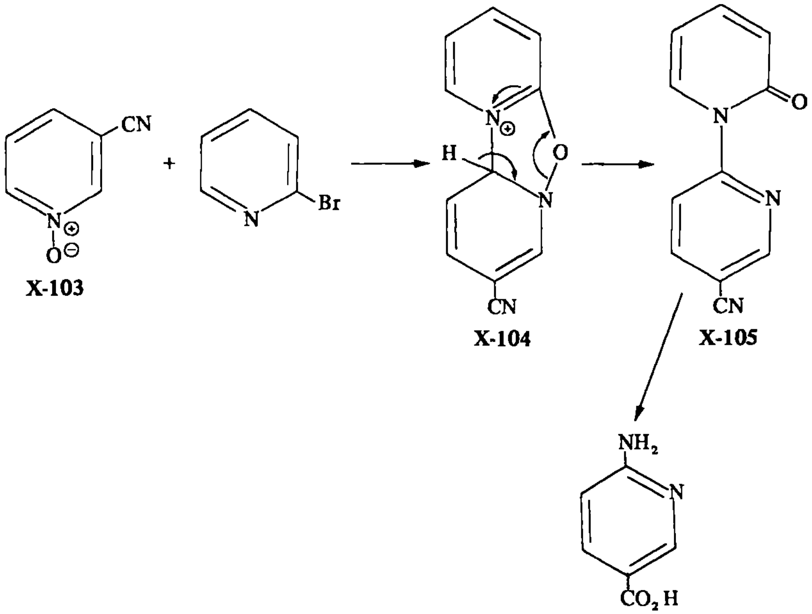


X-99

X-100

X-102

X-101



X-103

X-104

X-105

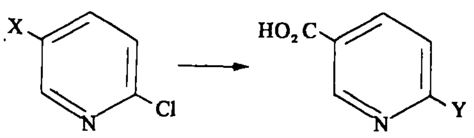
X-106

Treatment of (4,4′-bipyridyl)-3,3′,5,5′-tetrasulfonic acid (**X-99**) with potassium ferricyanide at 350° affords 3-cyano-4,4′-bipyridyl (**X-100**) as the distillate. The latter could be hydrolyzed with concentrated hydrochloric acid to (4,4′-bipyridyl)-3-carboxylic acid (**X-101**). Oxidation of **X-100** with neutral permanganate yielded cinchomeronic acid (**X-102**).[141]

Nicotinonitrile-1-oxide (**X-103**) on treatment with 2-bromopyridine afforded 1-(3-cyano-6-pyridyl)-2-pyridone (**X-105**), which could be hydrolyzed to 6-aminonicotinic acid (**X-106**). It is proposed that the reaction proceeds through the intermediate 2,4-oxadiazoline (**X-104**).[142] (See also Chapter IV.)

6. Synthesis of Pyridinecarboxylic Acids Containing Sulfur Substituents

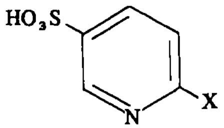
5-Amino-2-chloropyridine (**X-107**, X = NH_2), obtained by reduction of the 5-nitro precursor (**X-107**, X = NO_2), was converted by a Sandmeyer reaction to the 5-cyano-compound (**X-107**, X = CN). Saponification afforded 5-carboxylic acid (**X-107**, X = CO_2H), which, on treatment with potassium hydrogen sulfide, yielded 2-mercaptopyridine-5-carboxylic acid (**X-108**, Y = SH). The latter was oxidized with alkaline permanganate to the 2-sulfonic acid (**X-108**, Y = SO_3H).



X-107
X = NO_2, NH_2, CN, CO_2H

X-108
Y = SH, SO_3H

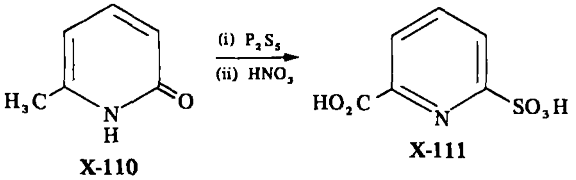
A second Sandmeyer reaction on 5-amino-2-chloropyridine (**X-107**, X = NH_2) and copper-catalyzed coupling with SO_2-saturated acetic acid gave the 2-chloropyridine-5-sulfonic acid (**X-109**, X = Cl). This substance was converted



X-109
X = Cl, SH, SO_3H

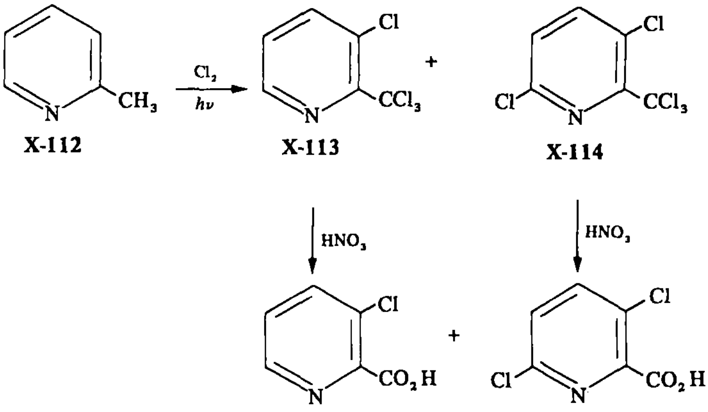
to the pyridine-2,5-disulfonic acid (**X-109**, X = SO_3H) by treatment with KHS and permanganate.[143, 144]

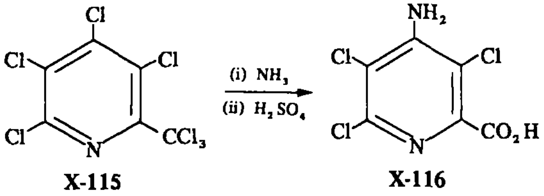
A second excellent method of introducing a mercapto substituent consists of treating 6-methyl-2-pyridone (**X-110**) with P_2S_5. Oxidation with concentrated nitric acid leads directly to the 6-carboxypyridine-2-sulfonic acid (**X-111**).[144, 145] The same sequence can be carried out with 4-methyl-2-pyridone.



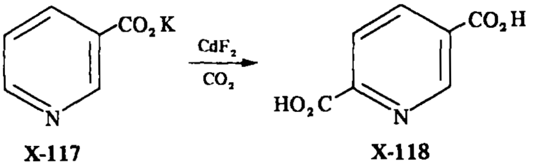
7. Miscellaneous Syntheses

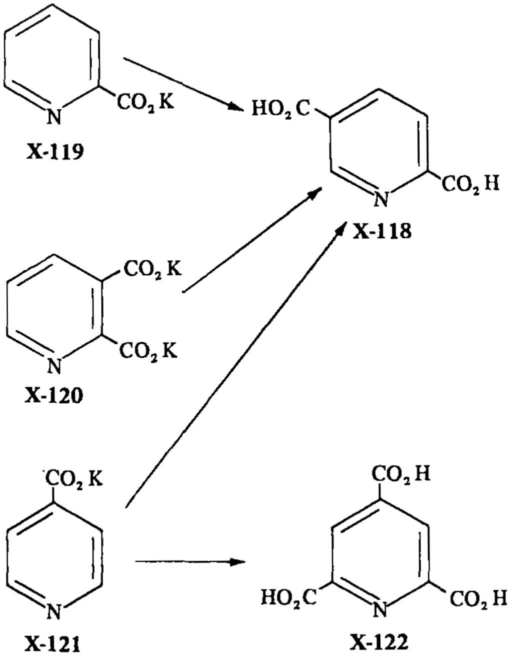
Photochlorination of 2-picoline (**X-112**) at 50 to 150° produces 3-chloro-2-trichloromethylpyridine (**X-113**) and 3,6-dichloro-2-trichloromethylpyridine (**X-114**). Hydrolysis with concentrated nitric acid gave a 95% yield of the corresponding 2-carboxylic acids.[146] Continued photochlorination affords a perchlorinated trichloromethylpyridine (**X-115**), which, after ammonolysis and boiling in sulfuric acid, afforded picloram (**X-116**).[147, 148]



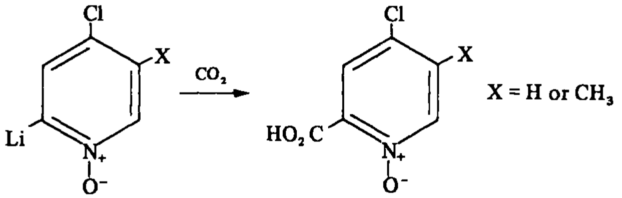


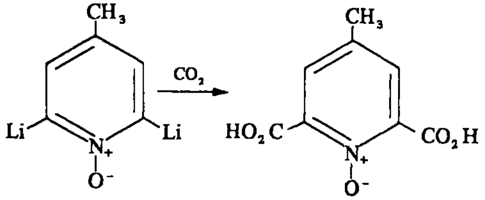
Potassium nicotinate (**X-117**) when autoclaved with CdF_2 under CO_2 pressure yields isocinchomeronic acid (**X-118**). The same product is obtained when potassium picolinate (**X-119**) or potassium quinolinate (**X-120**) is exposed to the same reaction conditions. Potassium isonicotinate (**X-121**) affords **X-118** and pyridine-2,4,6-tricarboxylic acid (**X-122**).[149]





Preparation of substituted pyridinecarboxylic acid 1-oxides by means of H-abstraction is reported by Abramovitch and others.[150] Thus, treatment of the lithium derivative of 4-chloropyridine-1-oxide or 4-chloro-3-methylpyridine-1-oxide with CO_2 gave the corresponding 4-chloro- and 4-chloro-5-methylpicolinic acid-1-oxides. Under the same conditions, 4-picoline-1-oxide gave the 2,6-dicarboxylic acid.





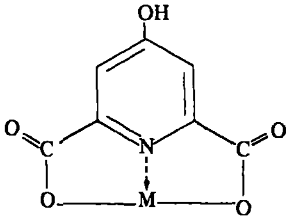
II. Physical Properties

The apparent ionization constants and ultraviolet absorption spectra of the three isomeric pyridine monocarboxylic acids were determined at 25° in aqueous KCl. As expected, it was confirmed that these acids exist in aqueous isoelectric solutions mainly in the dipolar ion form.[151] Similar data for monocarboxylic and monosulfonic acids[152] and polyvalent acids[153] were obtained more recently. The dissociation constants and electrophoretic mobilities of fifteen substituted alkyl-, nitro-, and chloropyridine carboxylic acids were also determined.[154] The ultraviolet absorption spectra of a series of dihydropyridine-3,5-dicarboxylic acids were correlated with electronic and steric factors.[155]

Intermolecular hydrogen bonding has been observed by infrared spectroscopy for nicotinic and isonicotinic acid, while the expected intramolecular phenomenon was observed with picolinic acid.[156] Spectral abnormalities of the carboxylate ion absorption at 1640 cm^{-1} and 1380 cm^{-1} have been recorded.[157] The infrared spectra of isomeric pyridinecarboxylic acid-1-oxides have been reported and Hammett σ values determined for the 4- ($\sigma = 0.25$) and 3- ($\sigma = 1.18$) positions.[158]

The NMR spectra of 154 pyridine derivatives were examined neat or in DMSO solution. With the exception of strong electron withdrawing substituents in the 3-position, the coupling constants are normal.[159]

The acid dissociation constants of chelidamic acid chelates [2,6-dicarboxy-4-hydroxypyridine (**X-123**)] as a function of the metal M were determined.[160, 161] The pK_a of the hydroxyl group in these chelates increased in the order: Cu(II) < Co(II) < Zn(II) < Ni(II) < Mn(II).



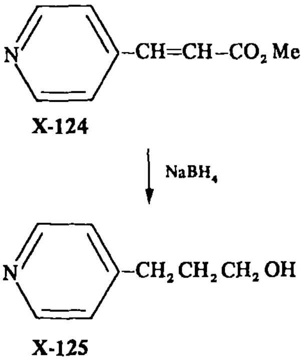
X-123

Separation schemes for pyridinecarboxylic acids[162] and nicotinic and isonicotinic acids[163] are reported. Paper chromatography[164] and gas chromatography[165] of pyridinecarboxylic acids have been discussed, and the crystal structures of picolinic acid hydrochloride[166] and picolinamide[167] have been described.

III. Reactions

1. Chemical Reduction

Reduction of pyridinecarboxylic acid methyl esters with a large excess of sodium borohydride in methanol is reported to give the corresponding alcohol.[168] Thus, using a twentyfold excess of hydride, nicotinic acid gave high yields of 3-hydroxymethylpyridine. Similar reductions of unsaturated pyridinecarboxylic acid esters such as **X-124** gave predominantly the saturated alcohols (**X-125**).

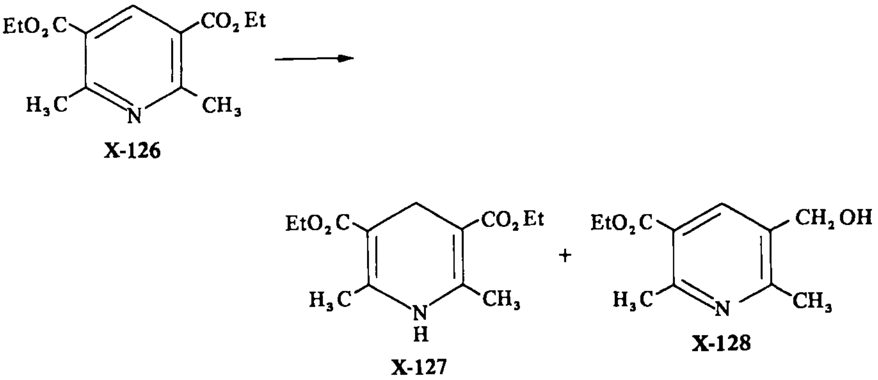


X-124

X-125

Similar reductions in ethanol gave the same result for methyl nicotinate, but diethyl 2,6-dimethyl-3,5-pyridine dicarboxylate (**X-126**) gave the dihydropyridine (**X-127**) and the partially reduced ethyl 5-hydroxymethyl-2,6-dimethylnicotinate (**X-128**).[169]

Reduction of isomeric methyl pyridine dicarboxylates (2,5-; 2,3-; 3,4-) with lithium aluminum hydride at −80° afforded good yields of the corresponding dialdehydes.[170]



X-126

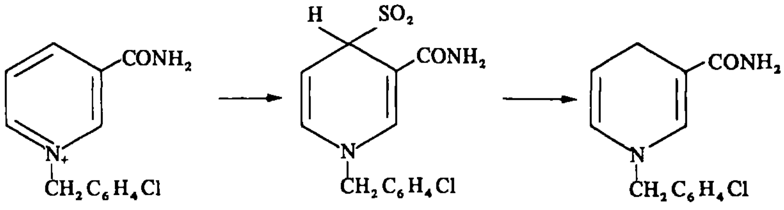
X-127

X-128

Electrolytic reductions of isonicotinic acid and isonicotinamide in acid solutions were investigated.[171-172] The main reduction product was the aldehyde. Its stability to further reduction is explained by hydrate formation. In an acetate buffer the reduction of the amide proceeds to the carbinol. If the amide is *N*-phenylsubstituted the *N*-phenylaminomethyl compound is obtained.

Reduction of 2,6-dichloroisonicotinic acid with hydrazine hydrate in presence of palladium on charcoal is claimed to yield isonicotinic acid.[173]

Intermediates in the sodium dithionite reduction of pyridinium salts have been isolated.[174] Thus 1-(*p*-chlorobenzyl)nicotinamide (**X-129**) yielded the dihydrosulfinate **X-130**, which is desulfinated in alkaline media to 1-(*p*-chlorobenzyl)-1,4-dihydronicotinamide (**X-131**). The desulfination of **X-130** was confirmed by deuterium exchange experiments.



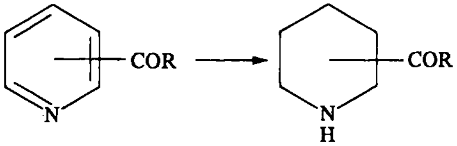
X-129

X-130

X-131

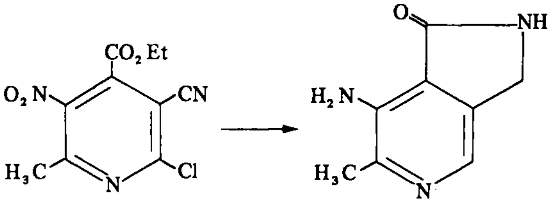
2. Catalytic Reduction

Rhodium (5%) on carbon is a better catalyst for the reduction of the isomeric pyridinecarboxylic acids, their esters, and amides to the corresponding piperidine analogues than is rhodium on alumina.[175] Reductions are generally slow, but yields are very satisfactory. Catalytic reductions of pyridylalkane carboxylic acids using rhodium catalysts and ammonia are also successful.[176] Good results have also been claimed with a nickel, copper, chromic oxide, and alumina catalyst system.[177]



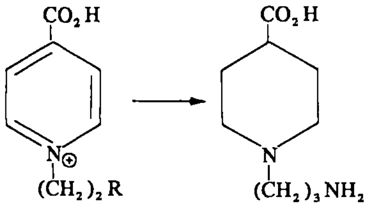
R = OH, OMe, OEt, NH_2, NEt_2

Catalytic reductions of substituted pyridinecarboxylic acids continue to play an important role in some syntheses of pyridoxol. Thus 4-carbethoxy-6-chloro-5-cyano-2-methyl-3-nitropyridine (**X-132**) is reduced over Raney Nickel in water to 3-amino-5-aminomethyl-4-carboxy-2-methylpyridine-4,5-lactam (**X-133**).[178-180]



X-132 X-133

Raney Nickel catalyzed reductions of pyridinium salts (**X-134**) afforded the corresponding *N*-(aminoalkyl)piperidinecarboxylic acid (**X-135**).[181]



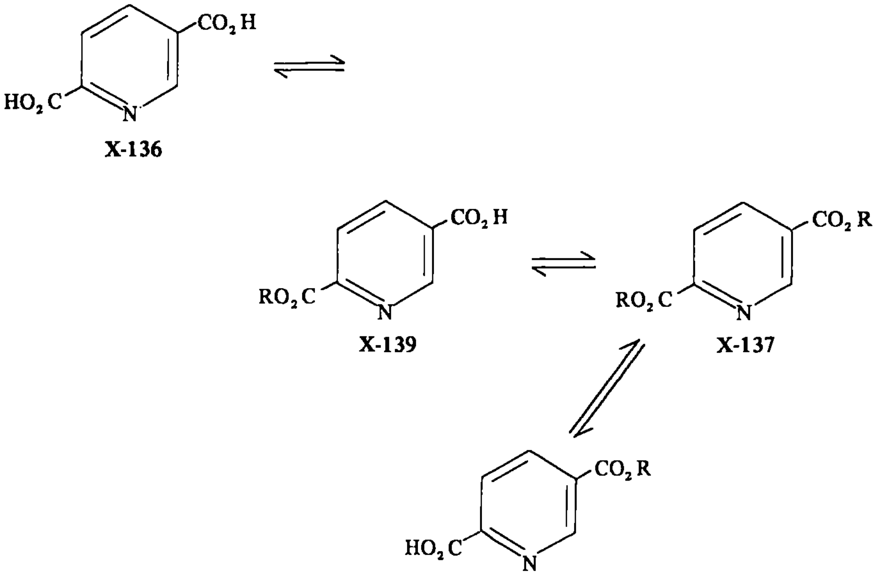
X-134 X-135

R = CN, CH_2NH_2

3. Esterification

The selective esterification of isocinchomeronic acid continues to be of obvious interest in the large-scale preparation of nicotinic acid. Selectivity is attempted by hydrolysis of the diesters as well as by selective monoesterification.[182-184]

Alcoholic KOH hydrolyzed the diester **X-137** predominantly to the 5-monoester **X-138**. The 2-monoester **X-139** was isolated from the mother liquors. Esterification of **X-136** with large amounts of H_2SO_4 and alcohol afforded the diester **X-137**, but reduced amounts of solvent and acid led to the 2-monoester **X-139**.



X-136

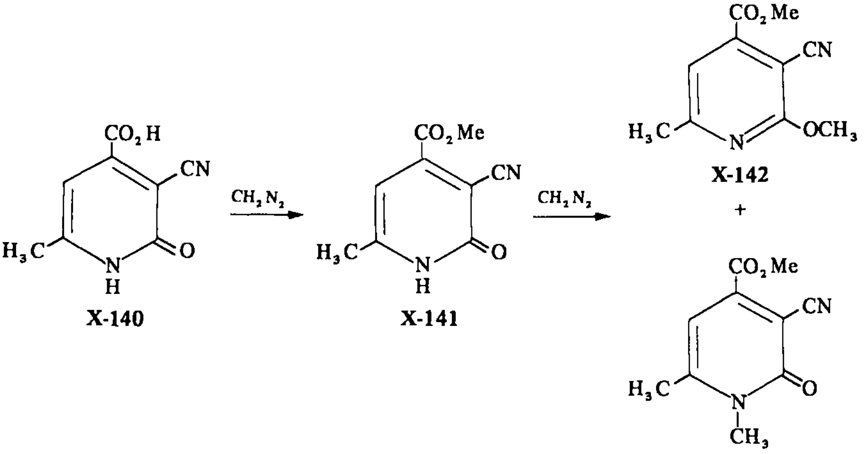
X-139

X-137

X-138

The second order rate constants *k* of the esterification of the three isomeric pyridinecarboxylic acids with diphenyldiazomethane in absolute ethanol were determined to be 0.108 for picolinic acid, 0.096 for nicotinic acid, and 0.182 for isonicotinic acid (temperature not specified in *Chemical Abstracts*). The reactivity ratios agree with theoretical expectations.[185]

Diazomethane reacted with 4-carboxy-3-cyano-6-methyl-2-pyridone (**X-140**) in the expected manner to form the methyl ester (**X-141**). Further treatment of **X-141** with diazomethane led to a mixture of *O*- (**X-142**) and *N*-methyl (**X-143**) derivatives. Treatment of **X-141** with methyl iodide in sodium methoxide yielded **X-143** exclusively.[186]

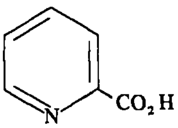


X-140 **X-141** **X-142** **X-143**

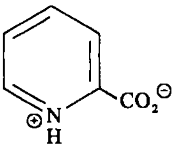
Vinyl esters of pyridine-2,5- and 2,6-dicarboxylic acids were prepared from the diacid chlorides and mercuriacetaldehyde. The allyl and propargylic esters of pyridine 2,4- and 2,6-diacids were prepared similarly from the alcohols.[187]

4. Decarboxylation

An extensive study of the decarboxylation of picolinic acid in twelve polar solvents has been concluded.[188] Thirty-two sets of activation parameters were obtained. The data favor the uncharged molecule (**X-144**) over the zwitterion (**X-145**) as the entity involved in the formation of the transition state.



X-144



X-145

The decarboxylation of 2-substituted pyridinecarboxylic acids was studied in ethylene glycol at constant pressure[189] and in sulfuric acid and in ammonium bisulfate.[190, 191] The reactions obeyed apparent first order kinetics. The determined parameters of activation are given in Table X-1. The data were again

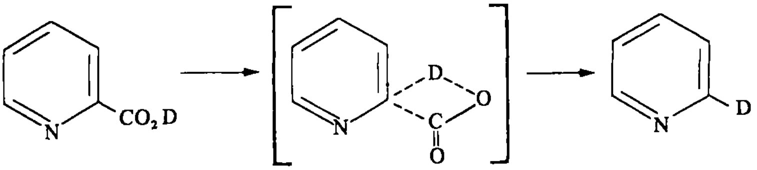
TABLE X-1. Activation Energies (E), Activation Enthalpies (ΔH*), and Activation Entropies (ΔS*) in the Decarboxylation Process

Pyridine carboxylic acid	ethylene glycol[189]			H_2SO_4			NH_4HSO_4 [190, 191]		
	E kcal/mole	ΔH* kcal/mole	ΔS* e.u.	E	ΔH*	ΔS*	E	ΔH*	ΔS*
2-	44.03	43.1	20.84						
2,6-	38.97	38.1	8.71						
2,5-	47.64	46.1	30.01				53.6	52.6	31.3
2,3-	31.63	30.9	6.04	36.0	35.1	-5.1	31.8	31.0	-2.5
2,4-							55.8	54.9	36.6

interpreted as favoring the neutral molecule **(X-144)** as the reactive species. The 3-carboxyl group was not lost over the temperature ranges studied (up to 164° in NH_4HSO_4 and 233° in H_2SO_4). Its effect as a neighboring group in the decarboxylation of the 2,3-dicarboxylic acid (quinolinic acid) is apparent.

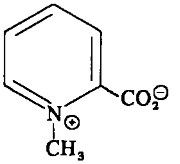
The ^{14}C kinetic isotope effect in the decarboxylation of picolinic acid **(X-144)** was measured in a variety of solvents. The observed effects are related to hydrogen bonding.[192]

The deutero-decarboxylation of isomeric pyridinecarboxylic acids is a good way of introducing deuterium into the pyridine nucleus.[193] The 2- and 6-positions are especially favorable. The role of the hypothetical intermediate **(X-146)** is reviewed.

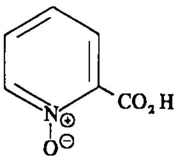


X-146

The relative rates of decarboxylation of picolinic acid **(X-144)**, its *N*-methyl homologue, homarine **(X-147)**, and its *N*-oxide **(X-148)** in ethylene glycol at 134° are 1:720:160. Homarine decarboxylates 10^3 times faster than the 3-position isomer, trigonelline, and *N*-methylisonicotinic acid.[194] The



X-147



X-148

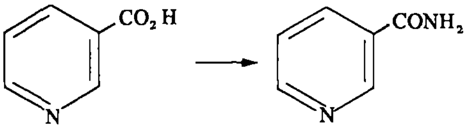
decarboxylations of **X-144** and **X-148** are inhibited by divalent metal ions such as Cu(II), Mg(II), and Mn(II).[194] The rapid decarboxylation of betaine **X-147** has biological significance.

The decarboxylation of 2,3- or 3,4-substituted pyridinedicarboxylic acids is still of importance in technical syntheses of nicotinic acid[195] and pyridoxol.[196]

The photodecarboxylation of isomeric pyridinedicarboxylic acids has been studied.[197] Monocarboxylic acids are photostable in aqueous solution. Dicarboxylic acids with 1,3-related carboxyl groups decarboxylate. Other dicarboxylic acids are photostable. Dissolved oxygen has no effect, which suggests that the photodecarboxylations are related to a $\pi \rightarrow \pi^*$ singlet excited state. In contrast to its thermal stability the photolability of the 3-carboxyl group is remarkable.

5. Pyridinecarboxylic Acid Amides

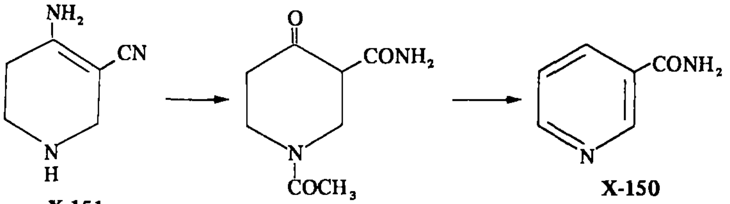
The conversion of nicotinic acid (**X-149**) to its amide (**X-150**) continues to be examined.



X-149 **X-150**

The use of urea at 150 to 250° is described for this reaction and for the analogous conversion of isonicotinic acid.[198] Urea has also been used to amidate quinolinic acid and substituted pyridine-3,4-dicarboxylic acids.[199] Sulfamic acid and its ammonium salt at 165° in the presence of ammonia also converts **X-149** to **X-150** and amidates isonicotinic acid.[200]

More exotic procedures are the Raney Nickel-catalyzed hydrogenation of the nicotinic hydroxamic acid to **X-150**,[201] and a sequence of reactions starting with 4-amino-3-cyano-1,2,3,6-tetrahydropyridine (**X-151**). This compound is hydrolyzed to 1-acetyl-4-oxohexahydronicotinamide (**X-152**), which is reduced and



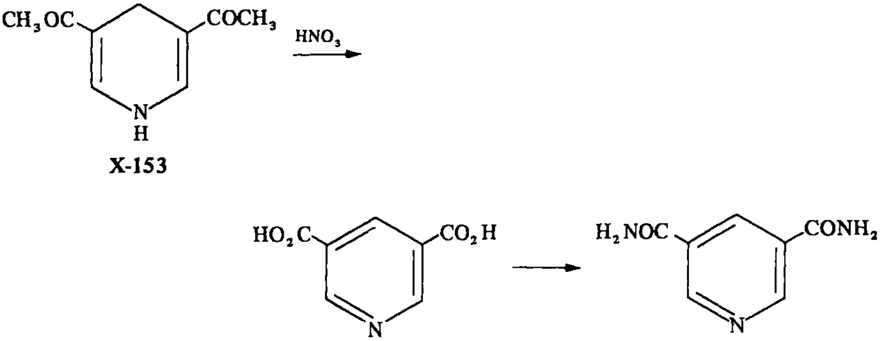
X-151 **X-152** **X-150**

then hydrogenated, deacetylated and dehydrated to **X-150** in 60 to 75% overall yield.[202-204]

Some new work in very classical procedures is also reported such as the ion-exchange catalyzed hydration of nicotinonitrile,[205,206] the ammonolysis of esters of nicotinic acid,[207,208] as well as of the free acid.[209]

Substituted nicotinamides have been prepared by the reaction of the acid (**X-149**) with phosphorus oxychloride and diethylamine.[210] The Bodroux reaction using a dibutylaminomagnesium salt has been applied to ethyl picolinate.[211]

The diamide of pyridine-3,5-dicarboxylic acid (**X-154**) was prepared by oxidizing 3,5-diacetyl-1,4-dihydropyridine (**X-153**) with dilute nitric acid followed by treatment with thionyl chloride and dimethylformamide.[212]



X-153

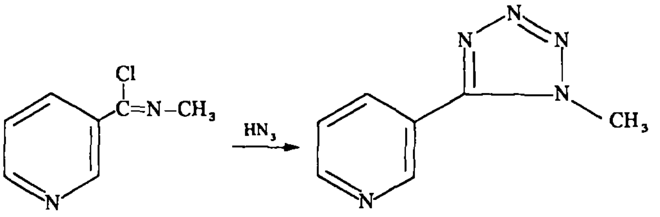
X-154

The alkali- and acid-catalyzed hydrolysis of the isomeric pyridine monocarboxamides was examined. In the second order alkaline process, the calculated Hammett σ-values agreed well with constants obtained by molecular orbital calculations. The methods were extended to the acid-catalyzed process where Hammett constants are not available for comparison.[213] The rate of acid-catalyzed hydrolysis of picolinamide and *N*-methylpicolinamide is somewhat decreased by Cu(II) ions.[214]

Picolinamide and isonicotinamide can be N^1-alkylated by treatment with alkyl bromides or iodides. These can be converted to the chlorides by treatment with freshly precipitated silver chloride.[215]

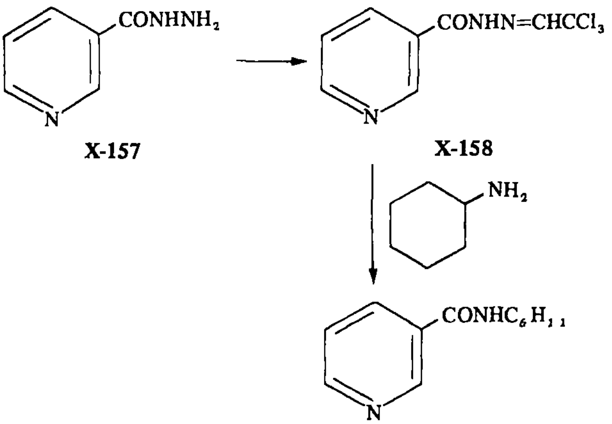
Pyridine carboxamides are readily converted to the corresponding aldehydes by treatment with lithium aluminum hydride in tetrahydrofuran.[216]

Nicotinamide and quinolinamide are readily converted to nitriles by treatment with phosphorus pentoxide[217] or thionyl chloride in dimethylformamide.[218] The methylamide of nicotinic acids is converted to the *N*-methylimidochloride (**X-155**) by treatment with phosphorus pentachloride. Reaction of **X-155** with hydrazoic acid yields the tetrazole (**X-156**).[219]



X-155 X-156

An interesting amidation procedure utilizes the condensation of nicotinic acid hydrazide (**X-157**) with chloral. The resulting Schiff's base (**X-158**) is smoothly converted to the *N*-cyclohexylamide (**X-159**) on treatment with cyclohexylamine.[220] The reaction has general utility.

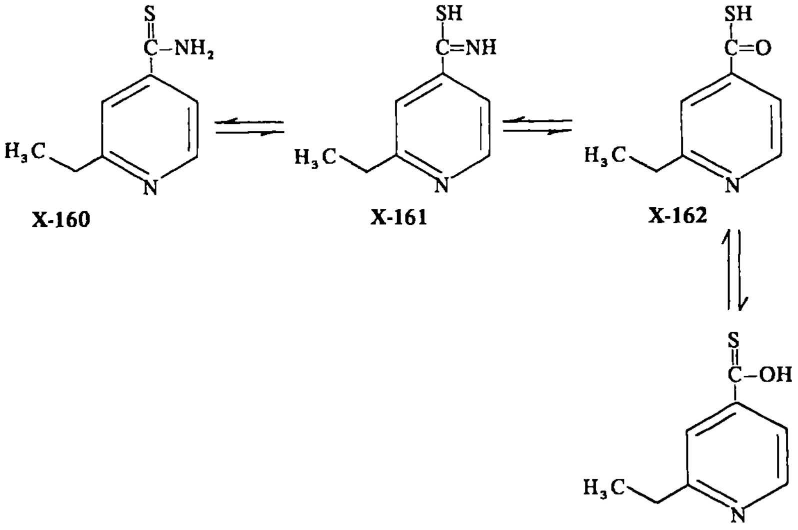


X-157 X-158 X-159

Hydrolysis of the isomeric pyridinecarboxylic acid azides has been examined.[221] The rate-determining step involves hydroxide ion attack on carbonyl carbon. The rates fall in the order: isonicotinic > picolinic > nicotinic. Azides are relatively easily hydrolyzed.

6. Pyridinethiocarboxylic Acids

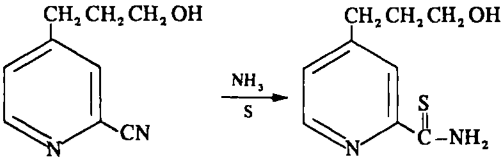
Mild alkaline hydrolysis of 2-ethylpyridine-4-thioamide (**X-160**) leads to the corresponding thiocarboxylic acid (**X-163**) through the iminothiol (**X-161**) and the carbonylthiol (**X-162**).[222] The carboxamide and the free acid are side products.



X-160 X-161 X-162

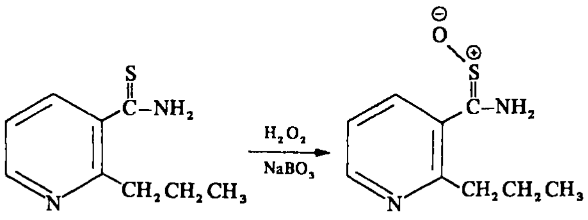
X-163

4-(3-Hydroxypropyl)picolinonitrile (**X-164**) is converted to the thioamide (**X-165**) by treatment with alcoholic ammonia and sulfur.[223]



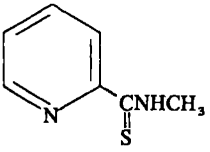
X-164 X-165

2-*n*-Propylnicotinothioamide (**X-166**) yields the *S*-oxide derivative (**X-167**) on reaction with the hydrogen peroxide-sodium perborate couple.[224]



X-166 X-167

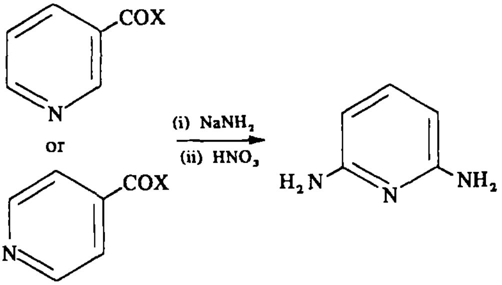
Treatment of 2-picoline with methylformamide and sulfur leads to thiopicolinic acid methylamide (**X-168**).[225]



X-168

7. Miscellaneous Reactions

Treatment of nicotinic acid and isonicotinic acid, or their corresponding amides, with sodamide followed by oxidation with concentrated nitric acid affords 2,6-diaminopyridine.[226]

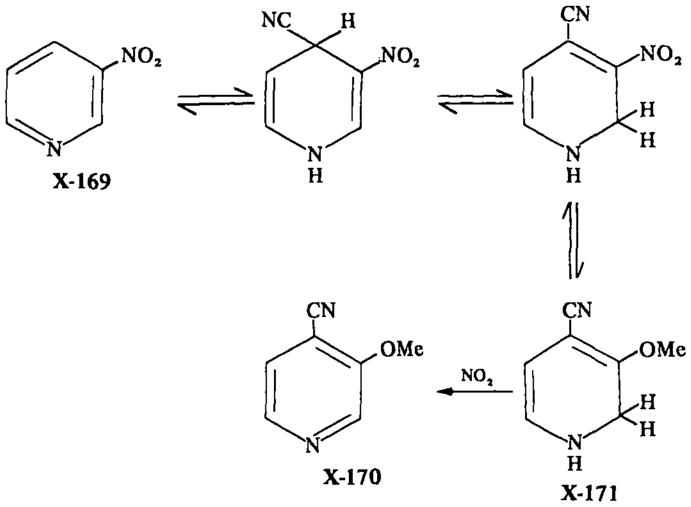


Cyanopyridines are prepared by passage of nicotinic or isonicotinic acid, their ammonium salts, or amides over a dehydration catalyst at 350° in the presence of ammonia. Boron phosphate and aluminum phosphate are mentioned specifically as catalysts.[227]

2- And 4-cyano-3-methoxypyridines (X-170) are prepared from the corresponding 3-nitropyridines (X-169) by the action of methanol and cyanide ion.[228] The mechanism might involve a series of addition-elimination steps as indicated. The final dehydrogenation of the hypothetical dihydropyridine intermediate (X-171) must be accomplished by the expelled nitrite ion. The reaction is general and yields are reported to exceed 50% of theory.

Isocinchomeronic acid (X-172, X = OH) when treated with PCl_5 at 100° afforded the corresponding diacid chloride (X-172, X = Cl). Ammonolysis of the latter followed by dehydration with $POCl_3$ gave 2,5-dicyanopyridine (X-173).[229]

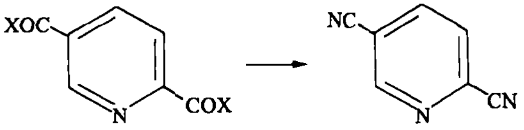
Nicotinic or isonicotinic acids when heated to 200° with *p*-toluenesulfonamide yield the corresponding nitriles. Carboxyl groups in the 2-position are eliminated in this reaction.[230]



X-169

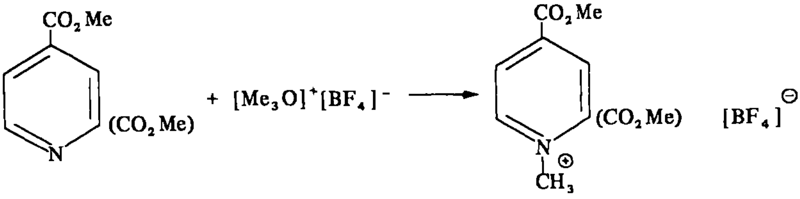
X-170

X-171



X-172

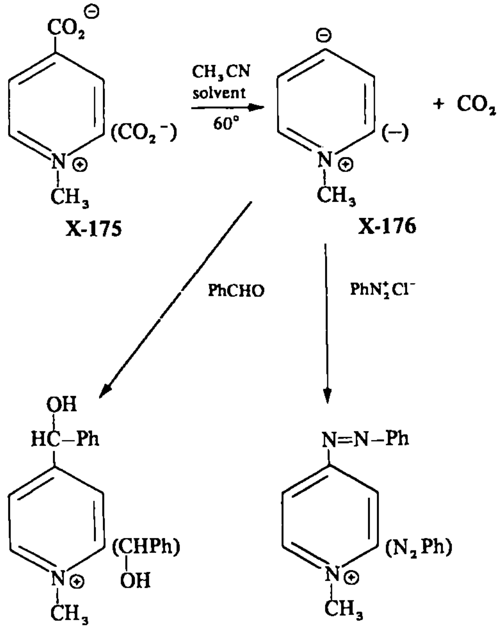
X-173

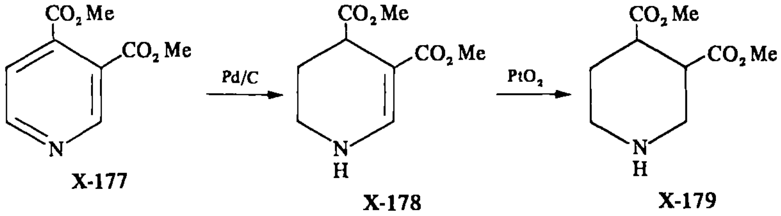


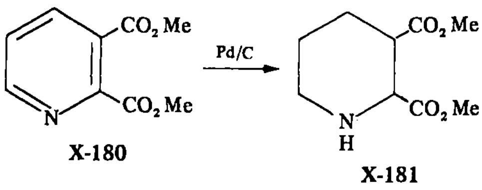
X-174

Methyl 2- or 4-pyridinecarboxylates gave high yields of *N*-methylated pyridinium salts (**X-174**) when treated with the Meerwein reagent. Mild hydrolysis of **X-174** gave the corresponding betaines (**X-175**), which were readily decarboxylated under mild conditions in dipolar aprotic solvents. The intermediate betaines (**X-176**) could be trapped with electrophiles such as benzaldehyde or diazonium salts.[232]

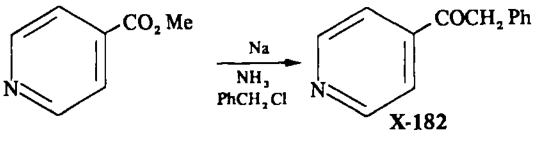
Hydrogenation of dimethyl pyridine-3,4-dicarboxylate (**X-177**) over palladium-on-charcoal affords the 1,4,5,6-tetrahydro derivative (**X-178**), which, on further reduction over platinum oxide, yields the piperidine derivative (**X-179**). On the other hand, dimethyl pyridine-2,3-dicarboxylate (**X-180**) is reduced over palladium-on-charcoal directly to the piperidine (**X-181**).[233]



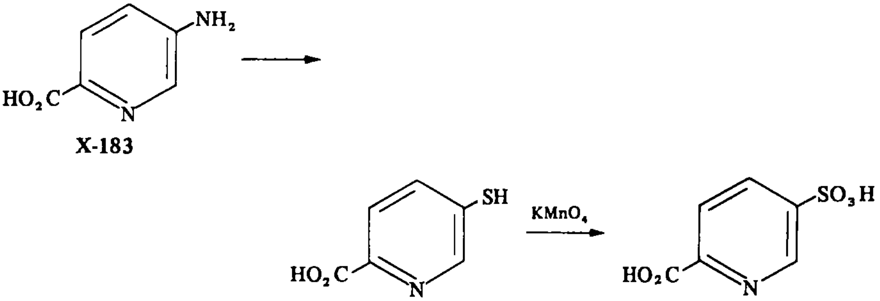




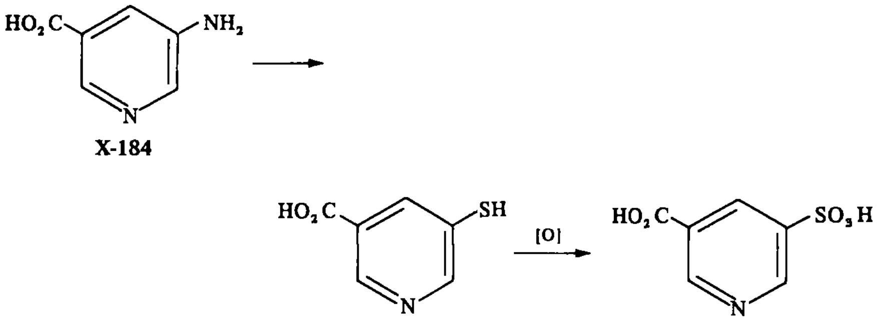
Reductive alkylation of methyl isonicotinate with benzyl chloride yields 4-pyridyl benzyl ketone (X-182).[234]



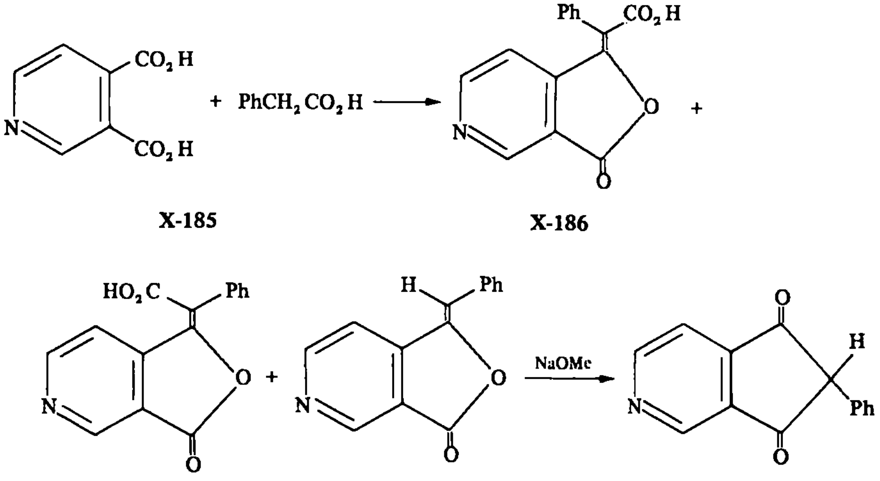
Mercapto derivatives derived from 5-amino-2-picolinic acid (**X-183**) and 5-aminonicotinic acid (**X-184**) are obtained by diazotization in the presence of sulfur and sodium sulfide. The thiols can be converted to the corresponding sulfonic acids with permanganate.[235]



X-183



X-184

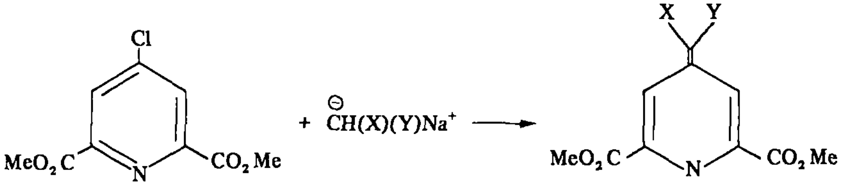


X-185 **X-186**

X-187 **X-188** **X-189**

Cinchomeronic acid (**X-185**) condenses with phenylacetic acid in the presence of acetic anhydride and triethylamine to yield 1-benzylidene-3-oxo-1,5-dihydrofuro[3,4-*c*]pyridine (**X-188**) and a mixture of the isomeric acids (**X-186**) and (**X-187**).[236] The lactone (**X-188**) was converted to the dione (**X-189**) with sodium methoxide.

Dimethyl 4-chloropyridine-2-6-dicarboxylate (**X-190**) on treatment with sodium salts of cyanoacetic esters, or malononitrile, yields dihydropyridine derivatives (**X-191**).[237]

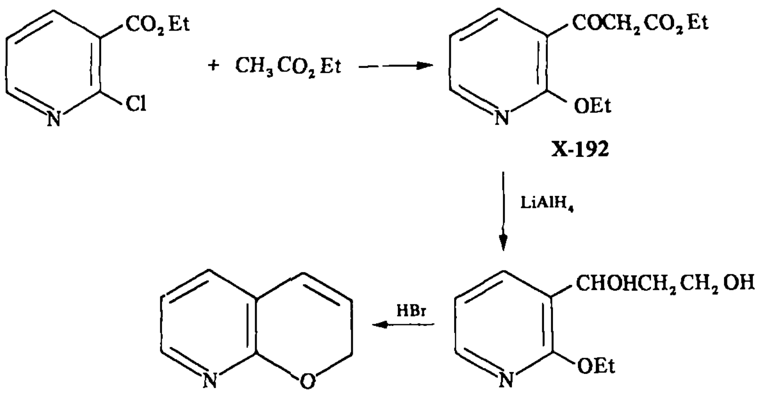


X-190

X-191

$X = CN \quad Y = CO_2Bu\text{-}t$
$X = CN \quad Y = CO_2Et$
$X = Y = CN$

Ethyl 2-chloronicotinate reacts with ethyl acetate and sodium ethoxide to form ethyl α-(2-ethoxynicotinoyl)acetate (**X-192**). Reduction of the latter to the diol (**X-193**) followed by treatment with hydrobromic acid affords 2*H*-pyrano[2,3-*b*]pyridine · HBr (**X-194**) (R.I. 1701).[238]

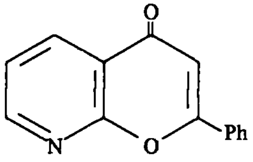


X-192

X-194

X-193

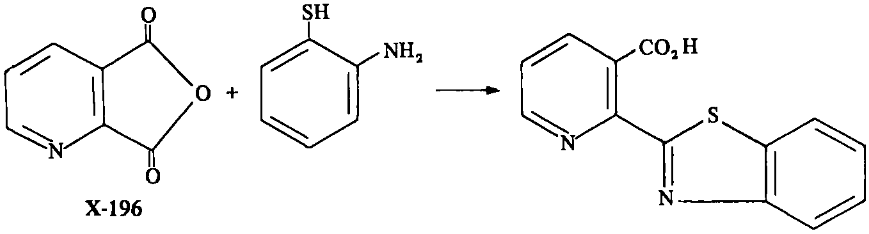
A similar reaction sequence with acetophenone but omitting the reduction step yields azaflavone (2-phenyl-4*H*-pyrano[2,3-*b*]pyridin-4-one) (**X-195**).



X-195

Cinchomeronic acid, on treatment with ammonium molybdate, urea, and cupric chloride at elevated temperatures affords copper tetra-3,4-pyridinoporphyrazine, the nitrogen analogue of copper phthalocyanine.[239]

Quinolinic anhydride (**X-196**) reacts with *o*-aminothiophenol in dimethylformamide to yield 2-(2-benzothiazolyl)pyridine-3-carboxylic acid (**X-197**), which could be decarboxylated to the known 2-(2-pyridyl)benzothiazole.[240]



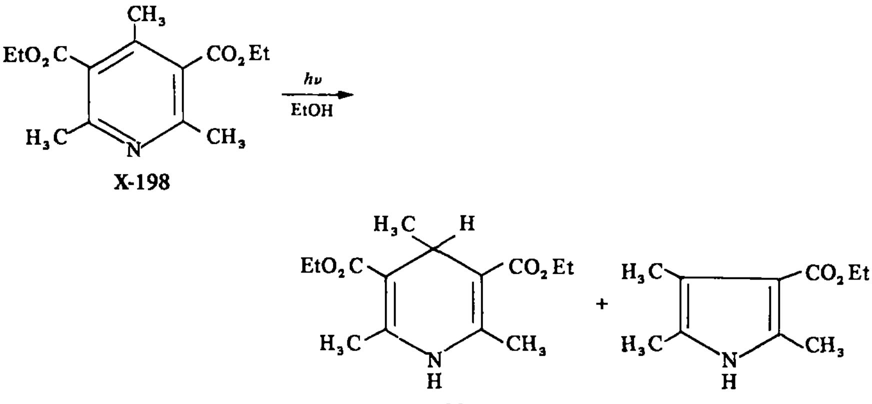
Cinchomeronic anhydride yielded a mixture of analogous 4-(2-benzothiazolyl)-pyridine-3- and 3-(2-benzothiazolyl)pyridine-4-carboxylic acids.

Another example of the Schmidt reaction was reported: isomeric pyridinecarboxylic acids were treated with sodium azide in sulfuric acid at elevated temperatures to give 3-aminopyridine (69% yield) and 2- and 4-aminopyridines in less than 30% yield.[241]

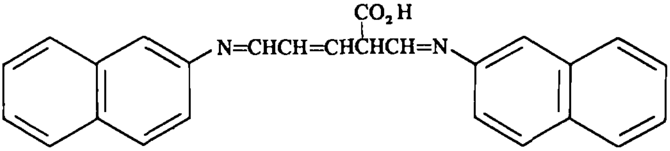
Wynberg described the photolysis of some pyridinecarboxylic acid derivatives.[242] 3,5-Dicarbethoxy-2,4,6-trimethylpyridine (**X-198**) gave 3,5-dicarbethoxy-2,4,6-trimethyl-1,4-dihydropyridine (**X-199**) and 3-carbethoxy-2,4,5-trimethylpyrrole (**X-200**) upon irradiation in ethanol. Irradiation of the 4-desmethyl derivative of **X-198** in methanol afforded only reduction products or those of addition of solvent at the 2- or 4-positions.

The characteristic color reaction of nicotinic acid with cyanogen bromide and β-naphthylamine has been studied. The product is believed to be **X-201**.[243]

Argentic picolinate is a powerful oxidizing agent.[244] Thus, toluene is oxidized to benzyl alcohol, benzaldehyde, and benzoic acid in a stepwise, controllable manner. Primary alcohols were converted to aldehydes, secondary alcohols to ketones. Amines were oxidized to aldehydes or ketones in dimethylsulfoxide.



X-198 X-199 X-200



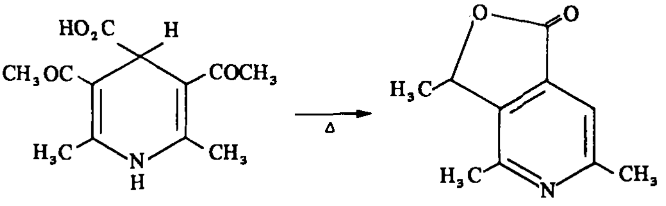
X-201

Cyclohexanol was converted to cyclohexanone, cyclohexanediol and the vicinal diketone. Activated methylenes reacted readily to yield mixtures of products. The method has potential utility in carbohydrate chemistry.

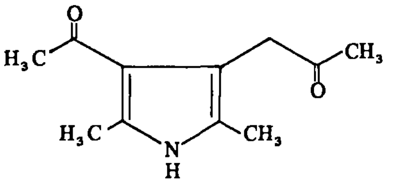
Quinolinic acid anhydride undergoes fragmentation under electron impact analogously to phthalic anhydride.[245]

Pyridine-2,6-dicarboxylic acid and pyridine-2,4,6-tricarboxylic acid are valuable reagents for the precise photometric determination of iron.[246, 247]

Pyrolysis of the 1,4-dihydropyridine (**X-202**) gave mainly the lactone (**X-203**), but some ring contraction to **X-204** was observed.[248]



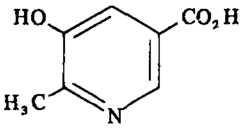
X-202 X-203



X-204

Treatment of alkyl isonicotinates or 4-cyanopyridine with alkyl free radicals (generated from diacyl peroxides) afforded 2-alkyl-substituted molecules.[249]

An improved synthesis of pyridoxol has appeared[250] and 5-hydroxy-6-methylnicotinic acid (**X-205**), a metabolite of pyridoxal in *Pseudomonas* MA has been prepared.[251]

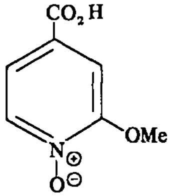


X-205

IV. Pyridinecarboxylic Acid-1-oxides

N-Oxides of pyridinecarboxylic acids are prepared by oxidation of their potassium salts in hydrogen peroxide/acetic acid.[252] (See also Chapter IV.) The *N*-oxides, particularly those derived from isocinchomeronic acid, are reputed to inhibit the decomposition of peracids.[253]

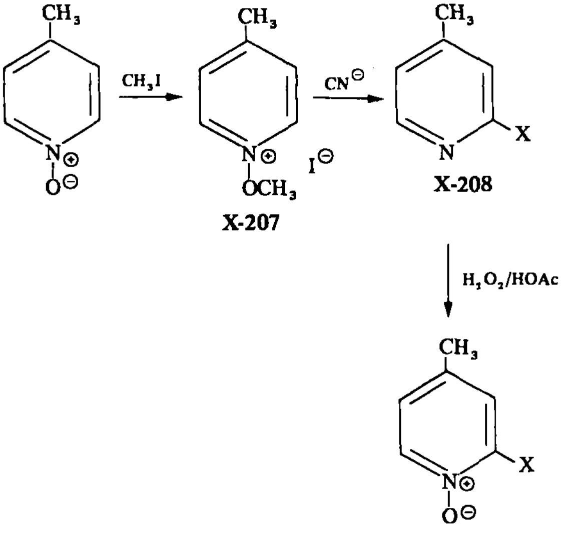
The reaction has been applied to substituted pyridinecarboxylic acids such as 2-methoxyisonicotinic acid (**X-206**),[254] or to the parent 2-pyridone. These acid *N*-oxides form amides and nitriles *via* the esters.



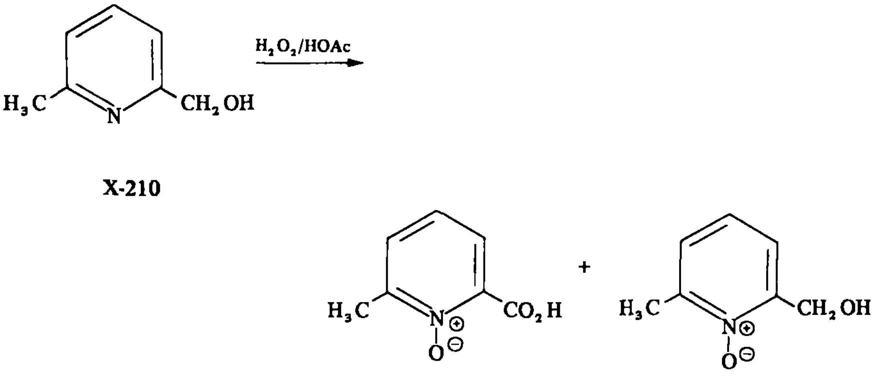
X-206

Picolinic acid amide undergoes oxidation to the *N*-oxide with the H_2O_2/HOAc. The latter undergoes a normal Hoffman degradation with potassium hypobromite to form 2-aminopyridine-1-oxide.[255] The amine *N*-oxide can also be obtained directly by the oxidation of 2-aminopyridine with or without the intermediate formation of the acetylated *N*-oxide.

4-Picoline-1-oxide was converted to the *N*-methoxy-4-picolinium iodide (**X-207**) by treatment with methyl iodide. The latter was treated with cyanide to yield 2-cyano-4-picoline (**X-208**, X = CN) which was hydrolyzed to the acid (**X-208**, X = CO_2H) with dilute hydrochloric acid. The nitrile (**X-208**, X = CN) was converted to the 1-oxide (**X-209**, X = CN), which could also be hydrolyzed to the corresponding acid (**X-209**, X = CO_2H). The same *N*-oxide acid (**X-209**, X = CO_2H) could be obtained directly by *N*-oxidation of the acid (**X-208**, X = CO_2H).[256]

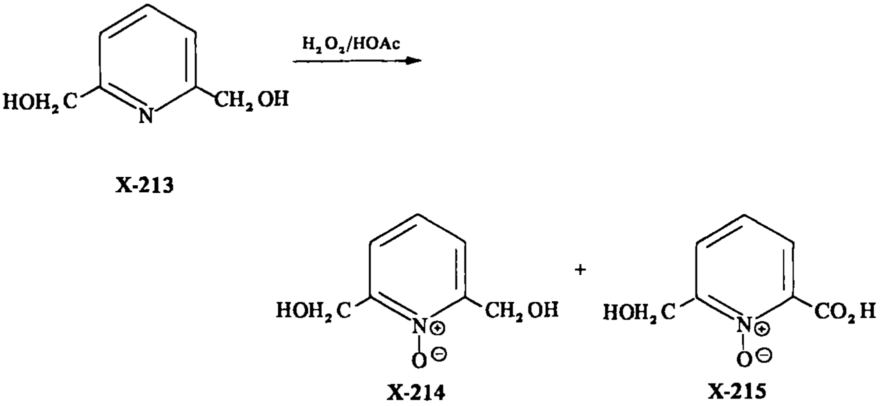


X-207 **X-208** **X-209**



X-210 **X-211** **X-212**

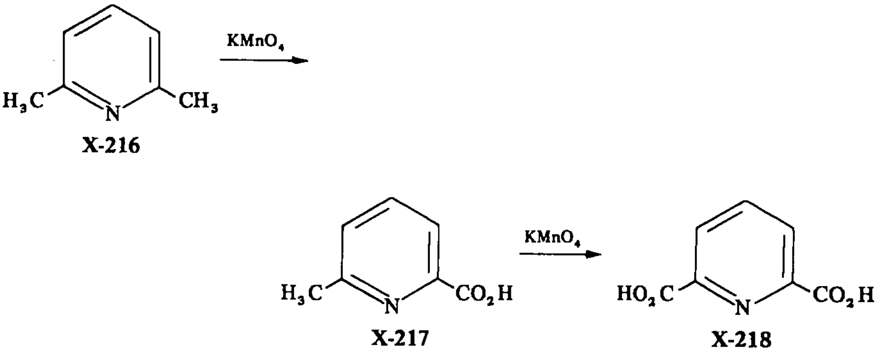
Oxidation of hydroxymethyl alkylpyridines with the H_2O_2/HOAc affords *N*- and *C*-oxidation products: 2-hydroxymethyl-6-methylpyridine (**X-210**) yielded 6-methylpicolinic acid-1-oxide (**X-211**) and 2-hydroxymethyl-6-methylpyridine-1-oxide (**X-212**). Similarly, 2,6-bis(hydroxymethyl)pyridine (**X-213**) yielded the expected pyridine-1-oxide (**X-214**) and a small amount of 6-hydroxymethylpicolinic acid-1-oxide (**X-215**). On the other hand, permanganate oxidations lead exclusively to *C*-oxidation even with appropriate *N*-oxides: thus lutidine (**X-216**) afforded pyridine-2,6-dicarboxylic acid (**X-218**) and the intermediate 6-methylpicolinic acid (**X-217**). Lutidine-1-oxide (**X-219**) was oxidized to **X-220** and **X-221** with permanganate.[257]



X-213

X-214

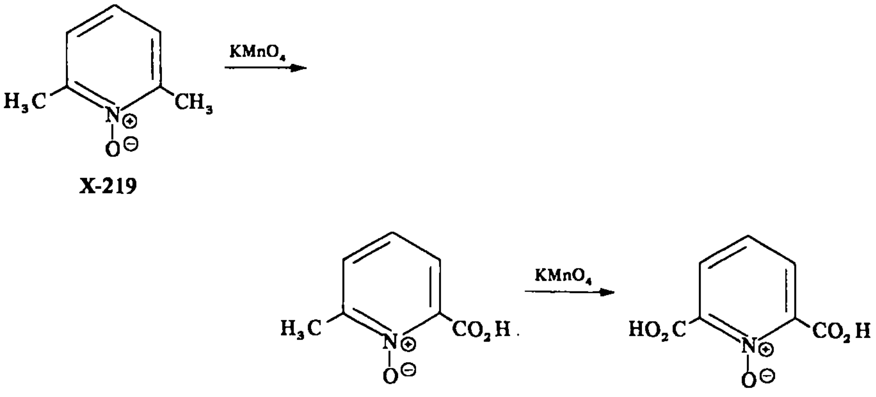
X-215



X-216

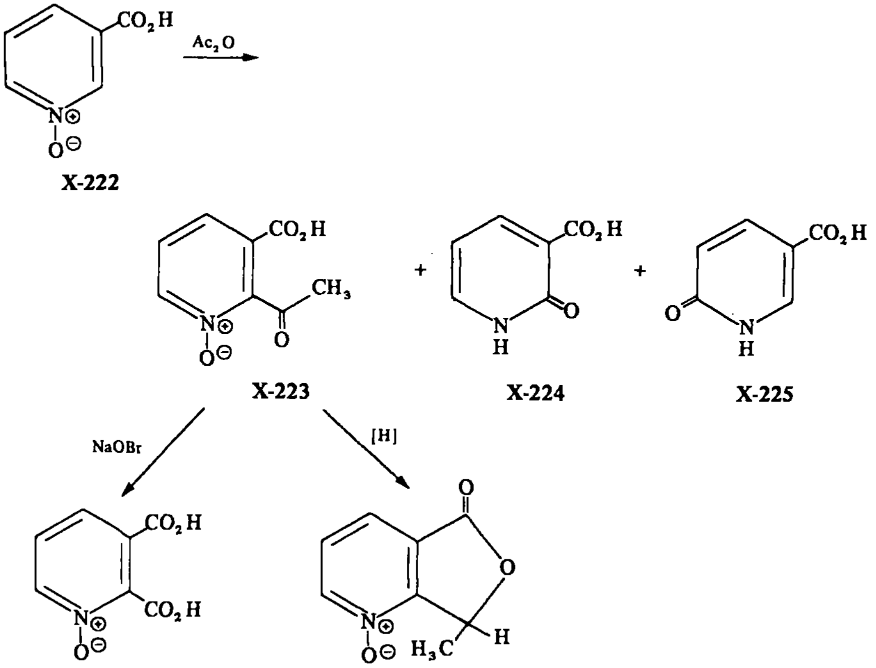
X-217

X-218

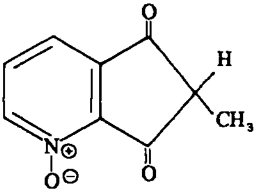


X-219 **X-220** **X-221**

Nicotinic acid-1-oxide (**X-222**) on treatment with acetic anhydride is converted to 2-acetylnicotinic acid-1-oxide (**X-223**) and 3-carboxy- (**X-224**) and 5-carboxy-2-pyridone (**X-225**).[258] The structure of **X-223** was proved by derivatization, oxidation, and reduction. Reaction of **X-222** with propionic anhydride yielded **X-224**, **X-225**, and the diketone-1-oxide (**X-226**). Treatment of

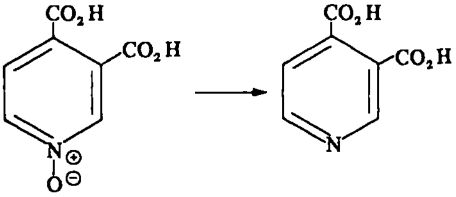


X-222 **X-223** **X-224** **X-225**



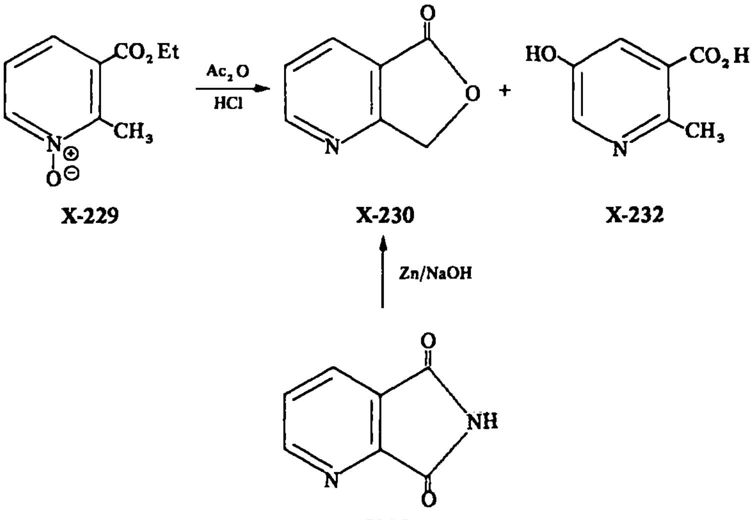
X-226

isonicotinic acid-1-oxide with acetic anhydride afforded 4-carboxy-2-pyridone and an unidentified material. Cinchomeronic acid-1-oxide (X-227) is claimed to yield cinchomeronic acid (X-228) in boiling acetic acid.[259]



X-227 X-228

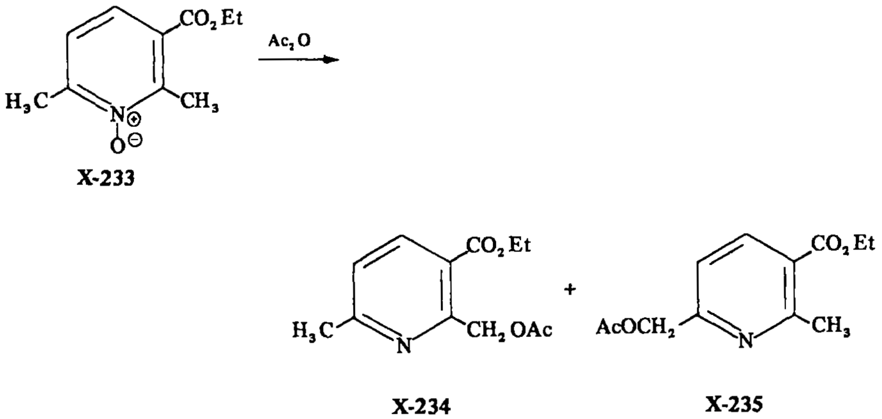
A rearrangement of alkylpyridine-1-oxides that is related was also investigated.[259] Ethyl 2-methylnicotinate-1-oxide (X-229) afforded an oil on treatment with acetic anhydride, which, after acid hydrolysis, yielded the

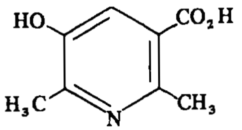


X-229 X-230 X-232

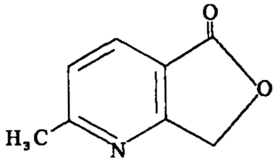
X-231

lactone (**X-230**) [synthesized independently from quinolinimide (**X-231**) by reduction with zinc and alkali], and 5-hydroxy-2-methylnicotinic acid (**X-232**). Under the same conditions ethyl 2,6-dimethylnicotinate-1-oxide (**X-233**) yielded ethyl 2-acetoxymethyl- (**X-234**) and 6-acetoxymethylnicotinate (**X-235**). Hydrolysis of crude **X-234** afforded 2,6-dimethyl-5-hydroxynicotinic acid (**X-236**), 5-methyl-4-azaphthalide (**X-237**), and 6-hydroxymethyl-2-methylnicotinic acid (**X-238**).

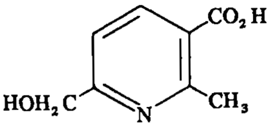




X-236

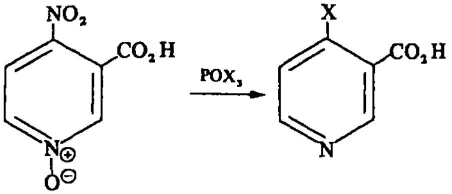


X-237



X-238

A reaction deals with the preparation of 4-halogenated pyridinecarboxylic acids (**X-240**) from 4-nitronicotinic acid-1-oxide (**X-239**) by explosive interaction with phosphorous trichloride or tribromide.[260] The requisite formation of nitrosyl chloride is not recorded. The 4-iodoacid (**X-240**, X = I) was prepared from the chloro-acid with hydrogen iodide. The authors also report



X-239 X-240

the formation of 5-iodonicotinic acid from 3-iodo-5-methylpyridine by oxidation with permanganate.

Picolinic acid-1-oxide is readily converted to the 4-nitro derivative. The nitro group is easily replaced by nucleophiles such as alkoxide, hydroxide, hydrogen sulfide, ammonia, chloride, and phenoxide.[261,262] Derivatization of the acid function and other reactions remain as expected.

The rate constants for the esterification of the *N*-oxides of picolinic, nicotinic, isonicotinic, and dipicolinic acids with diphenyldiazomethane were determined. The rates reflect the decrease in electron availability at the various nuclear positions as $2 < 4 < 3$. The 2,6-diacid had the highest rate constant indicating that the slow rate for picolinic acid is not due to steric effects.[263]

V. Tables

TABLE X-2. Pyridine Monocarboxylic Acids and Their Derivatives

Substituent and position							
2	3	4	5	6	m.p.	Derivatives	Ref.
CH_3	CH_3	CO_2H			224–6°		32
CH_3	CH_3	CO_2H		CH_3	270–1°		32
CH_3	OH	CO_2H		CH_3	290–1°		32
C_6H_5	CH_3	CO_2H			272–3°		32
CO_2H	Ph	Ph	Ph	Ph	106–8°	Ph ester, m.p. 206–8°	33
CO_2H			$C\equiv CH$		160°	Et ester, m.p. 110-12°	75
CO_2H			$C\equiv CC(OH)(CH_3)_2$		171–2°		75
CO_2H			$C\equiv CC(OH)(Me)(t\text{-}Bu)$		153–4°		75
CO_2H			$C\equiv CC(OH)(CH_2)_5$		166–8°		75
CH_3		CO_2H			263°	thioamide, m.p. 187°	115
CH_3		CO_2H		CH_3	283–4°	Et ester, m.p. 164°	
						thioamide, m.p. 205–7°	115
	CH_3	CO_2H				thioamide, m.p. 185–7°	115
	CO_2H	4'-Pyridyl			65°		141
CH_3	CO_2H		CH_2OH	CH_3		Et ester, m.p. 104°	169
CO_2H						*N*-cyclohexyl amide, m.p. 57–8°	220
						anilide, m.p. 75–6°	220
	CO_2H					*N*-butyl amide, b.p. 186–8°/11 mm	220
						N-cyclohexyl amide, m.p. 138°	220
						anilide, m.p. 123°	220
			CO_2H			*N*-butyl amide, b.p. 140°/15 mm	220
						N-cyclohexyl amide, m.p. 138–9°	220
						anilide, m.p. 170°	220
2-Benzothiazolyl		CO_2H			206–7°	Me ester, m.p. 61–2°	240

2-Benzothiazolyl	CO_2H				214°	Me ester, m.p. 115°, amide, m.p. 117°	240
	2-Benzothiazolyl	CO_2H			245°	Me ester, m.p. 124°	240
$-\underset{\substack{\vert \\ OH}}{C}HCH_3$	CO_2H					lactone, m.p. 77–9°	258
CO_2H						*N*-methylthioamide, m.p. 74–8°	225
						N,*N*-dimethylthioamide, b.p. 129–33°/0.55 mm	225
		CO_2H				*N*-methylthioamide, m.p. 94–7°	225
						N,*N*-dimethylthioamide, m.p. 64–5°	225
						N-butylthioamide, m.p. 75–8°	225
C_2H_2		CSOH			146°		222
	Ac	CO_2H	Ac		205°	Et ester, m.p. 86°	6
n-C_3H_7		CO_2H				thioamide *S*-oxide, m.p. 117–18°	224
n-C_4H_9		CO_2H				thioamide, *S*-oxide, m.p. 92–3°	224
C_2H_5		CO_2H				Me ester, b.p. 91°/3 mm	249
C_3H_7		CO_2H				Et ester, b.p. 108–10°/4 mm	249
$AcOCH_2$	CO_2H			CH_3		Et ester, m.p. 52–4°	259
CH_3	CO_2H			CH_2OH		Et ester, m.p. 58–62°	259

TABLE X-3. Pyridine Polycarboxylic Acids

Substituent and position					Physical Properties	Derivatives	Ref.
2	3	4	5	6			
	CO_2H		CO_2H			bis(ethylamide), m.p. 161–2.5°	4
						bis(diethylamide), m.p. 81–2.5°	4
						bis(piperidide), m.p. 125–6°	4
						diamide .½H_2O, m.p. 318–19°	4
	CO_2H	CO_2H	CO_2H			tri-Me ester, m.p. 87–8°	5
CH_3	CO_2H	CO_2H	OH	CH_3		di-Et ester HCl, m.p. 145–7°	29
CH_3	CO_2H		CO_2H			di-Et ester, m.p. 60–4°	29
Cl	CO_2H		CO_2H	CH_3		di-Et ester, m.p. 52–5°	29
CO_2H	Cl	Cl	Cl	CO_2H		di-Me ester, m.p. 73–5°	33
CO_2H	Cl	CH_3O	Cl	CO_2H		di-Me ester, m.p. 141–3°	33
CO_2H	CO_2H		F		m.p. 147°		86
CO_2H			CO_2H			divinyl ester, m.p. 68°	187
						dipropynyl, m.p. 92°	187
CO_2H				CO_2H		divinyl ester, m.p. 68°	187
						diallyl ester, b.p. 164–6°/3 mm	187
						dipropynyl ester, m.p. 124°	187
CO_2H		CO_2H			b.p. 130°/3 mm	diallyl ester, b.p. 171–3°/4.5 mm	187
						dipropynyl, m.p. 78–9°	187

CH_3	CO_2H	CO_2H		CH_3	imide, m.p. 225–6°	199
CH_3	CO_2H	CO_2H	CH_3		imide, m.p. 271–2°	199
	CO_2H	CO_2H	CH_3	CH_3	imide, m.p. 273–4°	199
CH_3	CO_2H	CO_2H	CH_3	CH_3	imide, m.p. 220–1°	199
CH_3	CO_2H	CO_2H	$-(CH_2)_4-$		imide, m.p. 246–7°	199
CO_2H		CO_2H			bis(dimethylthioamide), m.p. 169–71°	225
					bis(methylthioamide), m.p. 158–62°	225
CO_2H		CH_3			*N*-methylthioamide, b.p. 174–6°/13 mm	225
CO_2H				CO_2H	bis(dimethylthioamide), m.p. 194–7°	225
					bis(methylthioamide), m.p. 168-70°	225
CO_2H		CO_2H		CO_2H	tris(dimethylthioamide), m.p. 239–42°	225
CO_2H			CO_2H		bis(*N*-methylthioamide), m.p. 163–6°	225

TABLE X-4. Polyalkyl or Aryl Polycarboxylic Acids

Substituent and position							
2	3	4	5	6	m.p.	Derivatives	Ref.
	CO_2H	CO_2H	CH_3	CH_3		imide, m.p. 268–70°	24
CH_3	CO_2H	CO_2H	CH_3			imide, m.p. 271–2°	24
CH_3	CO_2H	CO_2H	CH_3	CH_3		imide, m.p. 220–1°	24
						3-monoamide, m.p. 183–5.5°	
			$-(CH_2)_4-$			3-monoamide, m.p. 246–7°	24
	CO_2H	CO_2H	$t\text{-}C_4H_9$			3-monoamide, m.p. 176°	24
CH_3	CO_2H	CO_2H	OH		239°	imide, m.p. 308°	24, 25
C_2H_5	CO_2H	CO_2H	OH		240°	imide, m.p. 258°	24, 25
C_3H_7	CO_2H	CO_2H	OH		216–17°	imide, m.p. 251°	24, 25
C_4H_9	CO_2H	CO_2H	OH		198–99°	imide, m.p. 234–5°	24, 25
C_5H_{11}	CO_2H	CO_2H	OH		181–3°	imide, m.p. 234°	24, 25
C_6H_5	CO_2H	CO_2H	OH		286–7°		24
CH_3	CO_2H	CO_2H	OH	CH_3	269–70°	imide, m.p. 275–7°	24, 25
CH_3	CO_2H	CO_2H	OH	C_2H_5	255–7°		24
C_2H_5	CO_2H	CO_2H	OH	CH_3	233–4°		25
C_5H_{11}	CO_2H	CO_2H	OH	CH_3	213–14°		25
	CO_2H	CO_2H	OH	$C_2H_5OCOCH_2$		diethyl ester, m.p. 124–5°	28
	CO_2H	CO_2H		CH_3	252°	imide, m.p. 266–8°	30
		CO_2H	CO_2H	CH_3		5-Et ester, m.p. 201°	32

TABLE X-5. Hydroxypyridine (or Pyridone) Carboxylic Acids

Substituent and position								
1	2	3	4	5	6	m.p.	Derivatives	Ref.
	OH		$CONH_2$		OH	> 270° with charring		1
	OH		CO_2H		OH			1
Ph	OH		OH	CO_2H	Me		Et ester, m.p. 175°	7
2,4-$(Me)_2C_6H_3$	OH		OH	CO_2H	Me		Et ester, m.p. 198–9°	7
p-$CH_3OC_6H_4$	OH		OH	CO_2H	Me		Et ester, m.p. 207–8°	7
	OH	CN	CO_2H		Et		Me ester, m.p. 205°	8
	OH	CN	CO_2H		Me		Me ester, m.p. 228°	8
	OH	CN	CO_2H		Me		Et ester, m.p. 217°	8
	OH	CN	CO_2H		Et		Et ester, m.p. 211°	8
	OH	CN	CO_2H		Me		amide, m.p. 300°	8
	OH	CO_2H		CN	OH	no data given		9
	OH	CN	CO_2H		Et	316–18°	Et ester, m.p. 218°	12
	OH	CN	CO_2H		Pr		Et ester, m.p. 150–1°	12
	OH	CN	CO_2H		$PhCH_2$		Et ester, m.p. 168–72°	12
	OH	CN	CO_2H		$C_6H_{11}CH_2$		Et ester, m.p. 168–70°	12
	OH		CO_2H		Et	308–10°	Et ester, m.p. 103–5°	12
	OH		CO_2H		Pr	276–8°		12
	OH		CO_2H		$C_6H_{11}CH_2$		Me ester, m.p. 162–4°	12
Ph	OH	CO_2H	OH		OH		PhNHCO, m.p. 234°	21
		CO_2H		OH	CH_3	201°	amide, m.p. 305°, hydrazide, m.p. 330°, thioamide, m.p. 259-60°, diethyl ester HCl, m.p. 143–4°	30
	OH		CO_2H			270° (decomp.)	Me ester, m.p. 208–10°	115
	OH		CO_2H		CO_2H	318°		23
	OH	CO_2H					benzyl ether, m.p. 135°	140
	OH		CO_2H		CH_3	300°	Me ester, m.p. 224–5°	186

TABLE X-5. Hydroxypyridine (or Pyridone) Carboxylic Acids (continued)

Substituent and position								
1	2	3	4	5	6	m.p.	Derivatives	Ref.
CH_3	OH	CN	CO_2H		CH_3		Et ester, m.p. 134°	186
	CH_3	OH	CO_2H	CO_2H			acetate, m.p. 207–11° acetate di-Me ester, m.p. 60–1°	250
	CH_3	CH_3O	CO_2H	CO_2H			di-Me ester, b.p. 145–50°/1–3 mm	250
	CH_3	$C_6H_5CH_2O$	CO_2H	CO_2H			bisbenzyl ester HCl, m.p. 110°	250
		CO_2H		OH	CH_3		Me ester, m.p. 243–4°	251
	CH_3	CO_2H		OH	CH_3	300°	Et ester, m.p. 179–80°	259
		CO_2H	OH				amide, benzyl ether, m.p. 178°	262
	OH	CN			Styryl	304°	2-Me ether, m.p. 122°	23
	OH	CN			α-methylstyryl	238°	*N*-Me, m.p. 124°	23
	OH	CN			Ac	213°		23
	OH	CN			α-Phenylstyryl	257°		23
	OH	CN			Benzoyl	253°		23
	OH	CO_2H	CO_2H		CO_2H	262°	tri-Me ester, Me ether, m.p. 132°	23
	OH		CO_2H		α-Methylstyryl	314°	Me ester, Me ether, m.p. 128°	23
	OH	CO_2H	CO_2H		Ac	254°	oxime, m.p. 350°, di-Me ester, Me ether, m.p. 80°	23
	CO_2H	OH	CO_2H	CO_2H			acid, dihydrate, m.p. 198–9°	101
	OH	CO_2H			Styryl	256°	methyl ether, m.p. 63°	23
	OH	CN			CO_2H	275°	Me ether, Me ester, m.p. 124°	23
	OH	CO_2H			CO_2H	304°		23
	OH	CO_2H			α-Methylstyryl		Me ether, Me ester, m.p. 73°	23
	OH	CO_2H			Ac	271°	Me ester, Me ether, m.p. 80°	23
	OH	CO_2H			Benzoyl	257°		23
	OH		CO_2H		Styryl	343°	Me ether, Me ester, m.p. 98°	23

TABLE X-6. Halopyridinecarboxylic Acids

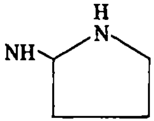
Substituent and position							
2	3	4	5	6	m.p.	Derivatives	Ref.
Cl		CO_2H		Cl	209–10°		2
	CO_2H		F				86
Cl		CO_2H			251°		
Br		CO_2H			229°		115
	CO_2H	CO_2H	Br	CH_3	247–8° (decomp.)	monoamide, m.p. 230–1°	101
	CO_2H	CO_2H	Cl	CH_3	248–50° (decomp.)	monoamide, m.p. 275–7° (decomp.)	101
	CO_2H	CO_2H	I	CH_3		acid, monohydrate, m.p. 241–6° (decomp.)	101
CO_2H		Cl			183–4°		137
	CO_2H		Br			Et ester, HBr, m.p. 147–8°	138
Cl			CO_2H		199°		143
SH			CO_2H		273°		143
SO_3H			CO_2H		310°		143
Cl				CO_2H	190°		144
Cl		CO_2H			245°		144
SH		CO_2H			304°		144
SO_3H				CO_2H	260–2°		144
SO_3H		CO_2H			296–7°		144
	CO_2H	SH			234–7°		145
CO_2H		SH			188–90°		145
	SH	CO_2H			259–60°		145
CO_2H	Cl			Cl	150–2°	Me ester, m.p. 53°; amide m.p. 188°	146
CO_2H	Cl	NH_2	Cl	Cl	218–19°	Me ester, m.p. 116–18°	148
CO_2H	Cl	$NHCH_3$	Cl	Cl	134–7°		148
CO_2H	Cl		Cl	Cl	146–8°		148

TABLE X-6. Halopyridinecarboxylic Acids (continued)[a]

Substituent and positions							
2	3	4	5	6	m.p.	Derivatives	Ref.
CO_2H	Cl	$N(CH_3)_2$	Cl	Cl	122–4°		148
	CO_2H		SH		162–5°		235
CO_2H			SH		205–8°		235
	CO_2H		SO_3H		333–5°		235
CO_2H			SO_3H		285°		235
CO_2H		Cl		CO_2H		dimethyl ester, m.p. 142°	237
CH_3	NH_2	CO_2H	CN	Cl		Et ester, m.p. 171–2°	250
Cl	CO_2H	CO_2H	NH_2	CH_3	218–19°		251
	CO_2H	Br			165–6°		260
	CO_2H	I			138–40°		260
	CO_2H		I		224–5°		260
	CO_2H	Cl				amide, m.p. 100°	262
	CO_2H	Br				amide, m.p. 140°	262
	CO_2H	SH				amide, m.p. 250°	262

[a]See also Table X-8

TABLE X-7. Nitropyridinecarboxylic Acids

Substituent and position							
2	3	4	5	6	m.p.	Derivatives	Ref.
Cl	CN	CO_2H	NO_2	Et		Et ester, m.p. 70–1.5°	11
CH_3	NO_2			CO_2H	126°		90
CO_2H	NO_2				122–3°		90
CH_3	NO_2	CH_3		CO_2H	138°		90
CH_3	NO_2	CO_2H		CH_3	238°		90
CO_2H	NO_2	CH_3			138°		90
CH_3	NO_2	CO_2H			250–2°		90
CH_3	NO_2	CO_2H	CN	=O		Et ester, m.p. 196–8°	250
CH_3	NO_2	CO_2H	CN	Cl		Et ester, m.p. 56–8°	250

TABLE X-8. Aminopyridinecarboxylic Acids[a]

Substituent and position							
2	3	4	5	6	m.p.	Derivatives	Ref.
CO_2H	NH_2	CO_2H	CO_2H		215–17°		11
CO_2H	NH_2				217°		90
NH_2		CO_2H			> 360°	Me ester, m.p. 148° Et ester, m.p. 118° amide, m.p. 258°	91
$NHCOCH_3$		CO_2H			286°	Me ester, m.p. 198° amide, m.p. 258–60°	91
NH_2		CO_2H				*N*-methylthioamide, m.p. 134–7°	225
CH_3	NH_2	CO_2H	CN	Cl		Et ester, m.p. 171–2°	250
CH_3	NH_2	CO_2H	CN			Et ester, m.p. 127°	250
CH_3	NH_2	CO_2H	CO_2H			monohydrate, m.p. 240–5°	250
	CO_2H		NH_2	CH_3	262–3°		251
Cl	CO_2H	CO_2H	NH_2	CH_3	218–19°		251
	CO_2H	NH_2				amide, m.p. 233–4°	262

[a] See also table X-6.

TABLE X-9. Cyanopyridines and Cyanopyridinecarboxylic Acids

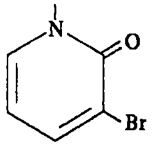
Substituent and position								
1	2	3	4	5	6	m.p.	Derivatives	Ref.
	CH_3	OH	CN	CN		189-91°		26
	CH_3		CN			43°	picrate, m.p. 163-4°	30
	CH_3		CN	NH_2		174°		30
	CH_3	OH		CN		190-1°		30
	CH_3	CN		OH	CH_3	249-51°		29
	Cl		CN			67-8°		115
	CN	OH				211-12°		118
	CN	CH_3				85°		130
	CN				CH_3	71°		130
		CO_2H		CN			Et ester, m.p. 89-90°; amide, m.p. 220-1°	130 138
		CN		CN		113-14°		138
	Cl	CN		CN	CH_3	143-4°		138
	CH_3	CN		CN		76°		138
		CN	CH_3	CN		84-5°		138
	CH_3	CN		CN	CH_3	118-19°		138
	CH_3	CN	CH_3	CN		115°		138
	CH_3	CN	C_2H_5	CN		68°		139
	C_2H_5O	CN				35°		140
	C_6H_5O	CN				109°		140
		CN	4′-Pyridyl			152°		141
				CN		264°		142

TABLE X-9. Cyanopyridines and Cyanopyridinecarboxylic Acids (Continued)

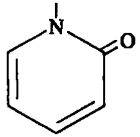
Substituent and position								
1	2	3	4	5	6	m.p.	Derivatives	Ref.
				CN		204–5°		142
	CN	Cl	NH_2	Cl	Cl	240–1°		148
	OCH_3	CN	CO_2H		CH_3		Et ester, m.p. 70°	186
							Me ester, m.p. 114°	186
CH_3	OCH_3	CN	CO_2H		CH_3		Et ester, m.p. 174°	186
		CH_3O	CN			61–2°		228
	CH_3	CH_3O	CN	C_2H_5		87–9°		228
	CN			CN		112–13°		229
	C_2H_2		CN			b.p. 82–5°		249
	CN		CH_3			89°		256

TABLE X-10. Dihydropyridinecarboxylic Acids and Nitriles

Substituent and position								
1	2	3	4	5	6	m.p.	Derivatives	Ref.
H		Ac	H_2	Ac		195°		6
	OH	H_2	H_2	CO_2H	Me		amide	13
H	Me	CO_2H	H_2	Et			Et ester	14
CH_3		CO_2H			=O	241–3°	Et ester, m.p. 78–80° amide, m.p. 211°	15
CH_3		CO_2H	=O			245–7°	amide, m.p. 183–4°	15
CH_3	CO_2H	CO_2H	CO_2H	CO_2H	Ph; H		tetra-Me ester, m.p. 165–7°	17
CH_2Ph	CO_2H	CO_2H	CO_2H	CO_2H	Ph; H		tetra-Me ester, m.p. 128–30°	
CH_2CH_2Ph	CO_2H	CO_2H	CO_2H	CO_2H	Ph; H	150–2°		
H	Me	CO_2H	H_2	Ac			Et ester	19
	OH	CN; H	H; OH		Styryl	315°	4-acetate, m.p. 289	23
CH_3NAc			H; CN			98–9°		135
H	CH_3; H	CN		CN		114–15°		138
H	CH_3	CN	H_2	CN		180–1°		138
H	CH_3; H	CN		CN	CH_3	152–3°		138
H	CH_3	CN	H; CH_3	CN		129–30°		138
H		CN	H_2	CN		205–6°		139
H	H_2	CN		CN		188–90°		139
H	H_2	CN	CH_3	CN		214–15°		139
H	H; CH_3	CN	C_2H_5	CN	CH_3	101–2°		139
H	CH_3	CN	H_2	CN	CH_3	215–20°		169
H	CH_3	CO_2H	H_2	CO_2H	CH_3		di-Et ester, m.p. 175–8°	169
Ac	H	CO_2H					amide, m.p. 175–80°	203
H	CO_2H		$(CN)_2C=$		CO_2H		di-Me ester, m.p. 218–19°	237
H	CO_2H		(*t*-Butyl-OOC)(CN)C=		CO_2H		di-Me ester, m.p. 175°	237
H	CO_2H		$(C_2H_5OOC)(CN)C=$		CO_2H		di-Me ester, m.p. 149°	
H	H, $CH(OH)CH_3$	CO_2H		CO_2H			di-Me ester, m.p. 160–6° (2 isomers) (2 isomers) 150–8°	242
H		CO_2H	H, $CH(OH)CH_3$	CO_2H			di-Me ester, m.p. 135–6°	242

TABLE X-11. Cyano- and Carboxypyridine-1-oxides

Substituent and position							
2	3	4	5	6	m.p.	Derivatives	Ref.
CN		CN		CN	222°		18
CO_2H		CO_2H		CO_2H		tri-Me ester	18
		CO_2H				amide	115
CH_3		CO_2H				thioamide, m.p. 188°	115
	CH_3	CO_2H				thioamide, m.p. 191-3°	115
CH_3		CO_2H		CH_3		thioamide, m.p. 215-16°	
CH_3	CO_2H	CO_2H			235-40° (decomp.)		85
CH_3		CO_2H	CO_2H		205-10° (decomp.)		
CN		Cl			130.5-31°		137
CN		NO_2			178-9°		137
CH_3	CH_3O	CN			175-6°		229
CO_2H					162°		253
CO_2H				CO_2H	155-7°		253
CO_2H			CO_2H		241-4°		253
CH_3O		CO_2H			186-8°	Me ester, m.p. 129-30°	254
OH		CO_2H				Et ester, m.p. 147-8°; amide, m.p. 270-2°	254
OH		CO_2H	NO_2		185°		254
CO_2H						amide, m.p. 161-2°	
CO_2H		CH_3			169°		256
CO_2H		CH_3		CO_2H	160°		150
CO_2H		CO_2H			262°		256
CO_2H				CH_2OH	195°		257
C_2H_5CO	CO_2H				195-6°		258
CH_3	CO_2H				50-2°		259
CH_3	CO_2H			CH_3		di-Et ester, m.p. 35-45°	259
CO_2H					162-5°		261
CO_2H		NO_2			148°	amide, m.p. 156°	261

CO_2H		CH_3O		154°	amide, m.p. 179°	261
CO_2H		C_2H_5O		144°	amide, m.p. 169°	261
CO_2H		C_3H_7O		107°	amide, m.p. 126°	261
CO_2H		IsoC_3H_7O		147°		261
CO_2H		OH		213°, 243°		261
CO_2H		OCH_2CH_2OH		152°		261
CO_2H		*p*-Cresyloxy		145°		261
CO_2H		Cl		144°	Me ester, m.p. 102°	261
				135–6°		150
	CH_3	Cl	CO_2H	160°		150
CO_2H		NH_2		217°	Me ether, m.p. 139°	261
CO_2H		SO_3H			Na salt monohydrate, m.p. 317°	261
CO_2H		SH		155°	benzyl ether, m.p. 157°	261
	CO_2H	NO_2			amide, m.p. 204°	262
	CO_2H	$C_6H_5CH_2O$		147°		262
	CO_2H	CH_3O		200°		262
	CO_2H	Cl		173–5°		262
	CO_2H	Br		155°		262
	CO_2H	NH_2		300°		262
	CO_2H	SH		165–7°		262

References

1. M. DeMaldè and E. Alneri, *Chim. Ind.* (Milan) **38,** 473 (1956).
2. M. M. Baizer, M. Dub, S. Gister, and N. G. Steinberg, *J. Amer. Pharm. Assoc.*, **45,** 478 (1956).
3. L. R. Morgan, Jr., *J. Org. Chem.*, **27,** 343 (1962).
4. J. Kuthan and J. Palecek, *Collect. Czech. Chem. Commun.*, **31,** 2618 (1966).
5. J. Palecek and J. Kuthan, *Collect. Czech. Chem. Commun.*, **34,** 3336 (1969).
6. F. Micheel and H. Dralle, *Ann. Chem.*, **670,** 57 (1963).
7. E. Ziegler, F. Hradetzky, and K. Belegratis, *Monatsh. Chem.*, **96,** 1347 (1965).
8. F. Cuiban, S. Cilianu-Bibian, S. Popescu, and I. Rogozea, Fr. patent, 1,366,064 (1964) to Ministry of Petroleum and Chemical Industry, Romania; *Chem. Abstr.*, **61,** 14643c (1964).
9. H. Hellmann and K. Seegmuller, *Angew. Chem.*, **70,** 271 (1958).
10. H. Junek, *Monatsh. Chem.*, **96,** 2046 (1965).
11. S. M. Gadekas, J. L. Frederick, J. Semb, and J. R. Vaughan, *J. Org. Chem.*, **26,** 468 (1961).
12. O. Fuchs, V. Senkariuk, A. Nemes, G. Zolyomi, T. Somogyi, and A. Lazar, Hung. patent, 157,008 (1970); *Chem. Abstr.*, **72,** 100533f (1970).
13. T. Kato, H. Yamanaka, and J. Kawamata, *Chem. Pharm. Bull.* (Tokyo), **17,** 2411 (1969).
14. H. D. Eilhauer and I. Kaempfer, *Z. Chem.*, **9,** 188 (1969).
15. S. Tanaka and J. M. Price, *J. Org. Chem.*, **32,** 2351 (1967).
16. M. Baizer, U.S. patent, 3,246,000 (1966); *Chem. Abstr.*, **64,** 19568h (1966).
17. R. Huisgen and K. Herbig, *Ann. Chem.*, **688,** 98 (1965).
18. K. D. Gundermann and H. U. Alles, *Angew. Chem.*, **78,** 906 (1966); *Angew. Chem. Intern. Ed. Engl.*, **5,** 846 (1966).
19. M. Ohashi, H. Kamachi, H. Kakisawa, and G. Stork, *J. Amer. Chem. Soc.*, **89,** 5460 (1967).
20. I. Ehsan and Karimullah, *Pakistan J. Sci. Ind. Res.*, **11,** 5 (1968).
21. A. Butt, I. A. Akhter, and M. Akhter, *Tetrahedron*, **23,** 199 (1967).
22. H. Gault, J. Gilbert, and D. Briancourt, *C. R. Acad. Sci., Paris, Ser. C,* **266,** 131 (1968).
23. L. Rateb, G. A. Mina, and G. Soliman, *J. Chem. Soc., C,* 2140 (1968).
24. G. Ya. Kondrat'eva and C. -H. Huang, *Dokl. Akad. Nauk SSSR*, **141,** 628 (1961).
25. G. Ya. Kondrat'eva and C. -H. Huang, *Dokl. Akad. Nauk SSSR*, **141,** 961 (1961).
26. E. E. Harris, R. A. Firestone, K. Pfister, III, R. R. Boettcher, F. J. Cross, R. B. Currie, M. Monaco, E. R. Peterson, and W. Reuter, *J. Org. Chem.*, **27,** 2705 (1962).
27. K. Pfister, III, E. E. Harris, and R. A. Firestone, U.S. patent, 3,227,721 (1966); *Chem. Abstr.*, **64,** 9690d (1966).
28. M. Kawazu, Jap. patent, 18627 (1967); *Chem. Abstr.*, **69,** 10366n (1968).
29. T. Naito and T. Yoshikawa, *Chem. Pharm. Bull.* (Tokyo), **14,** 918 (1966).
30. T. Naito, T. Yoshikawa, F. Ishikawa, S. Isoda, Y. Omura, and I. Takamura, *Chem. Pharm. Bull.* (Tokyo), **13,** 869 (1965).
31. P. Colin, Fr. patent, 1,550,352, (1968); *Chem. Abstr.*, **72,** 31629c (1970).
32. G. Ya. Kondrat'eva and C. -H. Huang, *Dokl. Akad. Nauk SSSR*, **164,** 816 (1965).
33. T. Jaworski and B. Korybut-Daszkiewicz, *Rocz. Chem.*, **41,** 1521 (1967).
34. N. Kucharczyk, *Chem. Listy*, **55,** 1199 (1961).

35. L. O. Shnaidman and M. I. Siling, *Tr. Vses. Nauchn.-Issled. Vitamin. Inst.*, **7**, 18 (1961); *Chem. Abstr.*, **60**, 7988h (1964).
36. Swiss patent, 339,625 (1955), to Lonza Elektrizitaetswerke & Chemische Fabriken A.-G.; *Chem. Abstr.*, **56**, 2430e (1962).
37. E. Bartholome, H. Nienburg, and K. Scherf, Ger. patent, 1,119,842 (1961); *Chem. Abstr.*, **57**, 786b (1962).
38. Ya. N. Ivashchenko, *Pererabotka Vydelenie, i Analizy Koksokhim. Produktov Sb.*, 45 (1961); *Chem. Abstr.*, **60**, 4102d (1964).
39. Yu. I. Chumakov, L. A. Rusakova, A. I. Mednikov, and R. I Virnik, *Metody Polucheniya Khim. Reaktivov i Preparatov, Gos. Kom Sov. Min. SSSR po Khim.*, **7**, 79 (1963); *Chem. Abstr.*, **61**, 5604f (1964).
40. V. Kudlacek and V. Stverka, *Sb. Ved. Praci, Vysoka Skola Chem.-Technol., Pardubice* (1), 33 (1965); *Chem. Abstr.*, **65**, 681b (1966).
41. B. F. Ustavshchikov, T. S. Titova, E. V. Degtyarev, and M. I. Farberov, *Zh. Prikl. Khim.*, **39**, 1388 (1966); *Chem. Abstr.*, **65**, 10557g (1966).
42. El Mutafchieva, N. Gospodinov, and Ya. Todorova, *Farmatsiya* (Sofia), **17**, 20 (1967); *Chem. Abstr.*, **68**, 87110m (1968).
43. W. Swietoslawski, J. Bialek, and A. Bylicki, Polish patent, 47,460 (1963); *Chem. Abstr.*, **61**, 5614d (1964).
44. J. Zundel, Fr. patent, 1,509,120 (1968); *Chem. Abstr.*, **70**, 68170f (1969).
45. R. Aries, Fr. patent, 1,509,049 (1968); *Chem. Abstr.*, **70**, 37657r (1969).
46. T. S. Titova, B. F. Ustavshchikov, M. Farberov, and E. V. Degtyarev, *Zh. Prikl. Khim.*, **42**, 910 (1969); *Chem. Abstr.*, **71**, 38750y (1969).
47. W. Hoefling, H. D. Eilhauer, G. Krautschik, and R. Mohrhauer, East Ger. patent, 58,090 (1967); *Chem. Abstr.*, **70**, 3842g (1969).
48. B. F. Ustavshchikov, M. I. Farberov, A. M. Kut'in, and G. S. Levskaya, *Uch. Zap. Yaroslavsk. Tekhnol. Inst.*, **5**, 71 (1960); *Chem. Abstr.*, **57**, 11153h (1962).
49. M. I. Farberov, B. F. Ustavshchikov, A. M. Kut'in, and I. T. Baranova, *Metody Polucheniya Khim. Reaktivov i Preparatov, Gos. Kom. Sov. Min. SSSR po Khim.* (11), 60 (1964); *Chem. Abstr.*, **65**, 758b (1966).
50. J. E. Mahan and R. P. Williams, U.S. patent, 2,993,904 (1957); *Chem. Abstr.*, **56**, 1434a (1962).
51. E. B. Bengtsson, Ger. patent, 1,161,563 (1964); *Chem. Abstr.*, **60**, 10654g (1964).
52. E. S. Zhdanovich, I. B. Chekmareva, L. I. Kaplina, and N. A. Preobrazhenskii, USSR patent, 148,411 (1962); *Chem. Abstr.*, **58**, 9031e (1963).
53. W. L. F. Armarego and R. F. Evans, *J. Appl. Chem.* (London), **12**, 45 (1962).
54. I. B. Chekmareva, E. S. Zhdanovich, and N. A. Preobrazhenskii, *Zh. Prikl. Khim.*, **38**, 220 (1965); *Chem. Abstr.*, **62**, 13119g (1965).
55. J. O'Brochta, U.S. patent, 2,999,094 (1959); *Chem. Abstr.*, **56**, 2432b (1962).
56. W. Schwarze, Ger. patent, 1,071,085 (1959); *Chem. Abstr.*, **57**, 11172g (1962).
57. A. Matsuura, Y. Suzuki, and K. Matsuki, Jap. patent, 17,340 (1963); *Chem. Abstr.*, **60**, 2904c (1964).
58. T. Kato, *Bull. Chem. Soc. Jap.*, **34**, 636 (1961).
59. H. Sobue, A. Tomita, Y. Sumita, T. Kato, and S. Hasegawa, Jap. patent 13,081 (1963); *Chem. Abstr.*, **60**, 507f (1964).
60. T. I. Baranova, A. M. Kut'in, M. I. Farberov, and B. F. Ustavshchikov, USSR patent, 161,755 (1964); *Chem. Abstr.*, **61**, 4325d (1964).
61. K. Uda, A. Sakurai, and K. Sakakibara, Jap. patent, 23,792 (1965); *Chem. Abstr.*, **64**, 3502g (1966).

62. T. I. Baranova, L. F. Titova, and A. M. Kut'in, *Khim. Prom.*, **43**, 204 (1967); *Chem. Abstr.*, **67**, 21792h (1967).
63. S. K. Bhattacharyya, V. Shankar, and A. K. Kar, *Ind. Eng. Chem., Prod. Res. Develop.*, **5**, 65 (1966).
64. S. K. Bhattacharyya and A. K. Kar, *Indian J. Appl. Chem.*, **30**, 35 (1967).
65. S. K. Bhattacharyya and A. K. Kar, *Indian J. Appl. Chem.*, **30**, 42 (1967).
66. T. A. Afanas'eva, A. D. Kagarlitskii, and B. V. Surorov, *Khim. Geterotsikl. Soedin.* (1), 142 (1968); *Chem. Abstr.*, **70**, 3791q (1969).
67. B. V. Suvorov, A. D. Kagarlitskii, T. A. Afanas'eva, and I. I. Kan, *Khim. Geterotsikl. Soedin.* (6), 1129 (1969); *Chem. Abstr.*, **72**, 121320z (1970).
68. L. Leitis and M. V. Shimanskaya, *Khim. Geterotsikl. Soedin.* (3), 507 (1967); *Chem. Abstr.*, **68**, 29553x (1968).
69. F. Komatsu, *Muroran Kogyô Daigaku Kenkyû Hôkoku*, **3**, 61 (1958); *Chem. Abstr.*, **53**, 13149e (1959).
70. F. Komatsu, Y. Ozono, K. Sakurei, and H. Komori, *Koru Taru* **12**, 420 (1960); *Chem. Abstr.*, **61**, 4309h (1964).
71. A. B. Sanz, Span. patent, 272,411 (1962); *Chem. Abstr.*, **60**, 2905h (1964).
72. (a) D. Jerchel, J. Heider, and H. Wagner, *Ann. Chem.*, **613**, 153 (1958); (b) *Ibid.*, 180.
73. B. Marcot and R. Palland, *C. R. Acad. Sci., Paris, Ser. C.*, **248**, 252 (1959).
74. T. Slebodzinski, H. Kielczewka, and W. Biernacki, *Przem. Chem.*, **48**, 90 (1969); *Chem. Abstr.*, **71**, 38751z (1969).
75. A. N. Kost, P. B. Terent'ev, and L. V. Moshentseva, *Khim.-Farm. Zh.*, **1**, 12 (1967); *Chem. Abstr.*, **68**, 68846q (1968).
76. S. de Groot and J. Strating, *Rec. Trav. Chim. Pays-Bas*, **80**, 944 (1961).
77. C. R. Adams, *J. Heterocycl. Chem.*, **4**, 137 (1967).
78. K.-M. Wu, *Hua Hsueh* (4), 147 (1966); *Chem. Abstr.*, **67**, 116802a (1967).
79. Brit. patent, 979,761 (1965) to Instytut Chemii Ogolnej; *Chem. Abstr.*, **62**, 16208f (1965).
80. A. Kotarski, *Chim. Ind.* (Paris) **94**, 366 (1965).
81. W. Swietoslawski, J. Bialek, A. Bylicki, and A. Kotarski, U.S. patent, 3,261,843 (1966); *Chem. Abstr.*, **65**, 12177b (1966).
82. J. Dialek and J. Malczynski, *Chim. Ind.* (Paris) **95**, 69 (1966).
83. I. B. Chekmareva, E. S. Zhdanovich, A. I. .Reznik, and N. A. Preobrashenskii, *Zh. Prikl. Khim.*, **38**, 707 (1965); *Chem. Abstr.*, **62**, 16186a (1965).
84. N. D. Rus'yanova, N. V. Malysheva, and L. P. Yurkina, *Khim. Prod. Koksovaniya Uglei Vostoka SSSR, Poluch., Obrab., Ispol'z, Metody Anal., Vost. Nauch. -Issled. Uglekhim. Inst., Sb. Statei*, **4**, 231 (1967); *Chem. Abstr.*, **69**, 2825w (1968).
85. E. J. Moriconi and F. A. Spano, *J. Amer. Chem. Soc.*, **86**, 38 (1964).
86. N. J. Leonard and L. R. Peters, U.S. patent, 3,027,380 (1962); *Chem. Abstr.*, **57**, 5896e (1962).
87. M. Levi and Sh. Levi, *Farmatsiya* (Sofia), **8**, No. 4, 20 (1958); *Chem. Abstr.*, **53**, 18951h (1959).
88. M. Levi and Ch. Ivanov, *Farmatsiya* (Sofia), **15**(2), 85 (1965); *Chem. Abstr.*, **63**, 11492d (1965).
89. M. I. Farberov, B. F. Ustavshchikov, and T. T. Titov, *Metody Polucheniya Khim. Reaktivov i Preparatov, Gos. Kom. Sov. Min. SSSR po Khim.* (11), 58 (1964); *Chem. Abstr.*, **64**, 15832d (1966).
90. E. V. Brown and R. H. Neil, *J. Org. Chem.*, **26**, 3546 (1961).
91. G. Ferrari and E. Marcon, *Farmaco, Ed. sci.*, **13**, 485 (1958); *Chem. Abstr.*, **53**, 7162c (1959).

92. R. D. Lekberg, R. A. Jensen, and W. Buiter, U.S. patent, 3,313,821 (1967); *Chem. Abstr.*, **67**, 90685n (1967).

93. L. H. Beck, U.S. patent, 3,154,549 (1964); *Chem. Abstr.*, **62**, 1673e (1965).

94. J. Kuthan and J. Palecek, Czech. patent, 124,047 (1967); *Chem. Abstr.*, **69**, 35953q (1968).

95. W. Bartok, D. D. Rosenfeld, and A. Schriesheim, *J. Org. Chem.*, **28**, 410 (1963).

96. R. Lukes, V. Galik, and J. Jizba, *Collect. Czech. Chem. Commun.*, **26**, 2727 (1961).

97. R. Lukes, J. Jizba, and V. Galik, *Collect. Czech. Chem. Commun.*, **26**, 3044 (1961).

98. R. Bodalski, J. Michalski, and K. Studniarski, *Rocz. Chem.* **38**, 1337 (1964).

99. T. A. Afanas'eva, A. D. Kagarlitskii, and B. V. Surorov, *Khim. Geterotsikl. Soedin.* (1), 142 (1968); *Chem. Abstr.*, **70**, 3791q (1969).

100. E. Kobayashi and K. Matsumoto, Jap. patent, 7481 (1962); *Chem. Abstr.*, **59**, 1604a (1963).

101. S. M. Gadekas and J. L. Frederick, *J. Heterocycl. Chem.*, **5**, 125 (1968).

102. H. Ahrens and W. Korytnyl, *J. Heterocycl. Chem.*, **4**, 625 (1967).

103. T. Mutavchiev and A. Marinov, *Godishnik Khim.-Tekhnol. Inst.*, **2**, 193 (1956); *Chem. Abstr.*, **52**, 11631e (1958).

104. V. G. Khomyakov, S. S. Kruglikov, and L. I. Kazakova, *Tr. Mosk. Khim.-Tekhnol. Inst.*, No. 32, 189 (1961); *Chem. Abstr.*, **57**, 15065e (1962).

105. S. S. Kruglikov and V. G. Khomyakov, *Tr. Mosk. Khim.-Tekhnol. Inst.*, No. 32, 194 (1961); *Chem. Abstr.*, 57, 16542i (1962).

106. L. D. Borkhi and V. G. Khomyakov, USSR patent, 187,024 (1966); *Chem. Abstr.*, **67**, 17395p (1967).

107. V. G. Khomyakov, N. A. Dzbanovskii, and L. D. Borkhi, *Tr., Vses. Nauch. Issled. Inst. Khim. Reaktivov Osobo Chist. Khim. Veshchestv.*, **29**, 304 (1966); *Chem. Abstr.*, **67**, 116796b (1967).

108. V. V. Tsodikov, L. D. Borkhi, V. G. Brudz, N. E. Khomutov, and V. G. Khomyakov, *Khim. Geterotsikl. Soedin.* (1), 112 (1967); *Chem. Abstr.*, **67**, 17256u (1967).

109. L. D. Borkhi and V. G. Khomyakov, *Khim. Geterotsikl. Soedin.* (1), 167 (1967); *Chem. Abstr.*, **67**, 64209r (1967).

110. N. A. Dzbanovskii and L. D. Borkhi, USSR patent, 166,654 (1964); *Chem. Abstr.*, **62**, 11789h (1965).

111. B. Lipka and E. Treszczanowicz, Polish patent, 50,077 (1965); *Chem. Abstr.*, **65**, 5446a (1966).

112. I. B. Chekmareva, E. S. Zhdanovich, G. I. Sazonova, and N. A. Preobrazhenskii, USSR patent, 164,601 (1964); *Chem. Abstr.*, **62**, 9115d (1965).

113. I. B. Chekmareva, E. S. Zhdanovich, and N. A. Preobrazhenskii, *Med. Prom. SSSR*, **19**(7), 11 (1965); *Chem. Abstr.*, **63**, 11488a (1965).

114. I. B. Chekmareva, E. S. Zhdanovich, and N. A. Preobrazhenskii, *Zh. Prikl. Khim.*, **38**, 2387 (1965); *Chem. Abstr.*, **64**, 689d (1966).

115. Y. Suzuki, *Yakugaku Zasshi*, **81**, 1204 (1961); *Chem. Abstr.*, 56, 3445d (1962).

116. I. A. Arkhipova, S. R. Rafikov, and B. V. Suvorov, *Zh. Prikl. Khim.*, **35**, 389 (1962); *Chem. Abstr.*, **57**, 9808d (1962).

117. J. Pennington and B. Yeomans, Fr. patent, 1,327,679 (1963); *Chem. Abstr.*, **59**, 12768g (1963).

118. F. W. Broekman, A. van Veldhuizen, and H. Jansen, *Rec. Trav. Chim. Pays-Bas*, **81**, 792 (1962).

119. B. Scherhag, S. Hartung, A. Hausweiler, and H. Gruenewald, Belg. patent, 636,800 (1963); *Chem. Abstr.*, **61**, 14643f (1964).

120. R. S. Aries, U.S. patent, 3,029,245 (1962); *Chem. Abstr.*, **57**, 11115i (1962).

121. Japan Catalytic Chemical Industry Co., Ltd., Fr. patent 1,368,494 (1964); *Chem. Abstr.*, **62**, 1606b (1965).
122. E. S. Zhdanovich, I. B. Chekmareva, and N. A. Preobrazhenskii, *Zh. Obshch. Khim.*, **31**, 3272 (1961).
123. V. I. Trubnikov, E. S. Zhdanovich, and N. A. Preobrazhenskii, *Khim.-Farm. Zh.*, **3**, 42 (1969); *Chem. Abstr.*, **72**, 111241k (1970).
124. B. Lipka, B. Buszynska, and E. Treszczanowicz, *Przem. Chem.*, **49**, 34 (1970); *Chem. Abstr.*, **72**, 111231g (1970).
125. T. A. Afanas'eva, A. D. Kagarlitskii, V. A. Serazetdinova, L. S. Saltybaeva, and B. V. Suvorov, *Khim. Geterotsikl. Soedin.* (4), 672 (1969); *Chem. Abstr.*, **72**, 43365b (1970).
126. T. A. Afanas'eva, A. D. Kagarlitskii, I. I. Kan, and B. V. Suvorov, *Khim. Geterotsikl. Soedin.* (4), 675 (1969); *Chem. Abstr.*, **72**, 43366c (1970).
127. B. V. Suvorov, A. D. Kagarlitskii, T. A. Afanas'eva, O. B. Lebedeva, A. I. Loika, and V. A. Serazetdinova, *Khim. Geterotsikl. Soedin.* (6), 1024 (1969); *Chem. Abstr.*, **72**, 132456x (1970).
128. V. I. Trubnikov, V. V. Petrov, E. S. Zhdanovich, and N. A. Preobrazhenskii, *Khim.-Farm. Zh.*, 3(9), 49 (1969); *Chem. Abstr.*, **72**, 12498t (1970).
129. E. A. Pavlov and B. V. Suvorov, *Tr. Kaz. Sel'skokhoz. Inst.*, **10**, 229 (1965); *Chem. Abstr.*, **66**, 85676k (1967).
130. N. Kucharczyk and A. Zvakova, *Collect. Czech. Chem. Commun.*, **28**, 55 (1963).
131. B. V. Suvorov, A. D. Kagarlitskii, and T. A. Afanas'eva, USSR patent, 197,591 (1967); *Chem. Abstr.*, **69**, 27267d (1968).
132. W. E. Feely, U.S. patent, 2,991,285 (1961); *Chem. Abstr.*, **56**, 7282 (1962).
133. W. E. Feely, G. Evanega, and E. M. Beavers, *Org. Synth.*, **42**, 30 (1962).
134. T. Okamoto and H. Tani, Jap. patent, 9089 (1962); *Chem. Abstr.*, **59**, 5140g (1963).
135. T. Okamoto, M. Hirobe, C. Mizushima, and A. Osawa, *Chem. Pharm. Bull.* (Tokyo), **11**, 780 (1963).
136. F. E. Cislak, U.S. patent, 2,989,534 (1961); *Chem. Abstr.*, **56**, 3466f (1962).
137. T. Kato and H. Hayashi, *Yakugaku Zasshi*, **83**, 352 (1963); *Chem. Abstr.*, **59**, 7473b (1963).
138. J. Kuthan, E. Janeckova, and M. Havel, *Collect. Czech. Chem. Commun.*, **29**, 143 (1964).
139. J. Kuthan and E. Janeckova, *Collect. Czech. Chem. Commun.*, **29**, 1654 (1964).
140. P. Nantka-Namirski, *Acta Pol. Pharm.*, **23**, 403 (1966); *Chem. Abstr.*, **66**, 85678n (1967).
141. A. A. Ziyaev, O. S. Otroshchenko, and A. S. Sadykov, *Zh. Obshch. Khim.*, **34**, 351 (1964).
142. S. Kajihari, *Nippon Kagaku Zasshi*, **86**, 839 (1965); *Chem. Abstr.*, **65**, 16935b (1966).
143. J. Delarge, D. Fernandez, and C. L. Lapiere, *J. Pharm. Belg.*, **22**, 213 (1967); *Chem. Abstr.*, **68**, 59406u (1968).
144. J. Delarge, *Farmaco, Ed. Sci.*, **22**, 1069 (1967; *Chem. Abstr.*, **69**, 2830u (1968).
145. J. Delarge, *J. Pharm. Belg.*, **22**, 257 (1967); *Chem. Abstr.*, **68**, 104913v (1968).
146. H. Johnston, U.S. patent, 3,317,549 (1967); *Chem. Abstr.*, **68**, 29611q (1968).
147. Yu. V. Shcheglov, M. S. Sokolov, A. N. Kasikhin, N. P. Zhukov, Yu. V. Boronin, M. L. Kirmalova, and V. P. Litvinov, *Agrokhimiya* (5), 105 (1967); *Chem. Abstr.*, **68**, 21795g (1968).
148. H. Johnston and M. S. Tomita, Belg. patent, 628,487 (1963); *Chem. Abstr.*, **61**, 1838d (1964).

149. B. Raecke, B. Blaser, W. Stein, H. Shirp, and H. Schuett, Ger. patent, 1,095,281 (1955); *Chem. Abstr.*, **56**, 2425e (1962).

150. R. A. Abramovitch, M. Saha, E. M. Smith, and R. T. Coutts, *J. Amer. Chem. Soc.*, **89**, 1537 (1967).

150a. R. A. Abramovitch, E. M. Smith, and R. T. Coutts, *J. Org. Chem.*, **37**, 3584 (1972).

151. P. O. Lumme, *Suomen Kemistilehti*, **30B**, 168 (1957); *Chem. Abstr.*, **52**, 3514c (1958).

152. V. M. Reznikov and V. I. Bliznyukov, *Nekotorye Vopr. Emission. i Molekulyarh. Spektroskopii, Krasnoyarsk, Sb.*, 193 (1960); *Chem. Abstr*, **58**, 9768c (1963). L. Thunus, *J. Pharm. Belg.*, **21**, 491 (1966); *Chem. Abstr.*, **66**, 32415t (1967).

153. K. C. Ong, B. Douglas, and R. A. Robinson, *J. Chem. Eng. Data*, **11**, 574 (1966).

154. A. N. Kost, P. B. Terent'ev, L. A. Golovleva, and A. A. Stolyarchuk, *Khim.-Farm. Zh.*, 1(5), 3 (1967); *Chem. Abstr.*, **68**, 29556a (1968).

155. P. J. Brignell, U. Eisner, and P. G. Farrell, *J. Chem. Soc., B*, 1083 (1966).

156. R. F. Evans and W. Kynaston, *J. Chem. Soc.*, 1005 (1961).

157. L. D. Taylor, *J. Org. Chem.*, **27**, 4064 (1962).

158. H. Shindo, *Chem. Pharm. Bull.* (Tokyo) **6**, 117 (1958); *Chem. Abstr.*, **53**, 19457c (1958).

159. W. Bruegel, *Z. Elektrochem.*, **66**, 159 (1962).

160. S. P. Bag, Q. Fernando, and H. Freiser, *Inorg. Chem.*, **1**, 887 (1962).

161. G. Anderegg and E. Bottari, *Helv. Chim. Acta*, **48**, 887 (1965).

162. J. Bialek, A. Bylicki, A. Chwistek, A. Galazka, and J. Szaton, Polish patent, 50,079 (1965); *Chem Abstr.*, **65**, 540a (1966).

163. E. Katscher and W. Moroz, U.S. patent, 3,147,269 (1964); *Chem. Abstr.*, **62**, 4013h (1965).

164. F. Schindler and F. Kuffner, *Monatsh. Chem.*, **94**, 252 (1963).

165. H. Liliedahl, *Acta Chem. Scand.*, **20**, 95 (1966).

166. A. Laurent, *C. R. Acad. Sci., Paris, Ser. C*, **256**, 916 (1963).

167. T. Takano, Y. Sasada, and M. Kakudo, *Acta Cryst.*, **21**, 514 (1966).

168. M. S. Brown and H. Rapoport, *J. Org. Chem.*, **28**, 3261 (1963).

169. S. Yamada and Y. Kikugawa, *Chem. Ind.* (London), 2169 (1966).

170. G. Queguiner and P. Pastour, *C. R. Acad. Sci., Paris, Ser. C*, **258**, 5903 (1964).

171. H. Lund, *Acta Chem. Scand.*, **17**, 972 (1963).

172. H. Lund, *Acta Chem. Scand.*, **17**, 2325 (1963).

173. S. L. Mukherjee and G. M. Shah, Indian patent, 72,814 (1963); *Chem. Abstr.*, **60**, 2890d (1964).

174. J. F. Bjellmann and H. Callot, *Bull. Soc. Chim. Fr.*, 1154 (1968).

175. M. Freifelder, R. M. Robinson, and G. R. Stone, *J. Org. Chem.*, **27**, 284 (1962).

176. M. Freifelder, U.S. patent, 3,159,639 (1964); *Chem. Abstr.*, **62**, 7732c (1965).

177. G. von Schuckmann and O. Weissel, Ger. patent, 1,233,870 (1967); *Chem. Abstr.*, **67**, 43682z (1967).

178. H. Fukawa and H. Kurihara, Jap. patent, 9091 (1962); *Chem. Abstr.*, **59**, 5140b (1963).

179. B. Benke, S. Jager, L. Szabo, I. Koczka, G. Losonczi, and I. Hoffmann, Hung. patent, 150,277 (1963); *Chem. Abstr.*, **60**, 2909c (1964).

180. R. Schliessel, L. Szabo, S. Jager, and M. Pogany, Hung. patent, 150,349 (1963); *Chem. Abstr.*, **60**, 2909b (1964).

181. F. E. Cislak and W. H. Rieger, Fr. patent, 1,390,118, (1965); *Chem. Abstr.*, **62**, 16208b (1965).

182. Z. D. Tadic and M. D. Muskatirovic, *Glasnik Hem. Drustva, Beograd*, **25-26**, 491 (1960-1961); *Chem. Abstr.*, **59**, 6358b (1963).

183. K. Isagawa, M. Kawai, and Y. Fushizaki, *Nippon Kagaku Zasshi,* **88,** 553 (1967); *Chem. Abstr.,* **68,** 68840h (1968).

184. L. Thunus and M. Dejardin-Duchene, *J. Pharm. Belg.,* **24,** 3 (1969); *Chem. Abstr.,* **71,** 81100y (1969).

185. D. M. Dimitrijevic, Z. D. Tadic, and M. D. Muskatirovic, *Glasnik Hem. Drustva, Beograd,* **28,** 83 (1963); *Chem. Abstr.,* **60,** 14346g (1964).

186. C. Musante and S. Fatutta, *Ann. Chim.* (Rome), **47,** 385 (1957).

187. V. E. Blokhin, Z. Yu. Kokoshko, L. V. Kireeva, and S. Kirova, *Khim. Geterotsikl. Soedin.* (4), 744 (1969); *Chem. Abstr.,* **72,** 90227t (1970).

188. L. W. Clark, *J. Phys. Chem.,* **69,** 2277 (1965).

189. A. Kaneda and T. Hara, *Doshisha Daigaku Rikogaku Kenkyu Hokoku,* **7,** 161 (1967); *Chem. Abstr.,* **67,** 90244t (1967).

190. J. Biakel, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.,* **10,** 621 (1962).

191. J. Bialek, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.,* **10,** 625 (1962).

192. M. Zelinskii, *Tr. po. Khim. i Khim. Tekhnol.,* No. 4, 707 (1961); *Chem. Abstr.,* **58,** 9670d (1963).

193. J. A. Zoltewicz, C. L. Smith, and J. D. Meyer, *Tetrahedron,* **24,** 2269 (1968).

194. P. Haake and J. Mantecon, *J. Amer. Chem. Soc.,* **86,** 5230 (1964).

195. K. Uda, A. Sakurai, and K. Sakabibara, Jap. patent, 20,555 (1965); *Chem. Abstr.,* **64,** 2069c (1966).

196. D. Palm, A. A. Smucker, and E. E. Snell, *J. Org. Chem.,* **32,** 826 (1967).

197. C. Azuma and A. Sugimori, *Kogyo Kagaku Zasshi,* **72,** 239 (1969); *Chem. Abstr.,* **70,** 96575k (1969).

198. W. Hoefling, D. Eilhauer, and G. Reckling, Ger. patent, 1,189,995 (1965); *Chem. Abstr.,* **63,** 583b (1965).

199. G. Ya. Kondrat'eva and C. -H. Huang, *Zhur. Priklad. Khim.,* **35,** 199 (1962); *Chem. Abstr.,* **56,** 14230b (1962).

200. P. Mueller and R. Trefzer, U.S. patent, 3,026,324 (1962); *Chem. Abstr.,* **57,** 11172f (1962).

201. R. M. Gipson, F. H. Pettit, C. G. Skinner, and W. Shive, *J. Org. Chem.,* **28,** 1425 (1963).

202. D. Taub, C. H. Kuo, and N. L. Wendler, *J. Chem. Soc., C,* 1558 (1967).

203. N. L. Wendler, D. Taub, and C. H. Kuo, U.S. patent, 3,441,568 (1969); *Chem. Abstr.,* 71, 81191d (1969).

204. N. L. Wendler, D. Taub, and C. H. Kuo, U.S. patent, 3,435,044 (1969); *Chem. Abstr.,* **71,** 38820w (1969).

205. Z. Blaszkowska and H. Grochowska, *Przemysl. Chem.,* **45,** 145 (1966); *Chem. Abstr.,* **64,** 19547f (1966).

206. E. F. Kozlova, M. I. Kustanovich, M. M. Yanina, and I. B. Chekmareva, *Khim. Farm. Zh.,* 2(7), 28 (1968); *Chem. Abstr.,* **70,** 3772j (1969).

207. I. B. Chekmareva, E. S. Zhdanovich, T. S. Novopokrovskaya, and N. A. Preobrazhenskii, *Zh. Prikl. Khim.,* **35,** 1157 (1962); *Chem. Abstr.,* **57,** 8546c (1962).

208. N. V. Dormidontova, B. F. Ustavshchikov, M. I. Farberov, and L. M. Malinnikova, *Zh. Prikl. Khim.,* **42,** 666 (1969); *Chem. Abstr.,* **71,** 38746b (1969).

209. E. S. Zhdanovich, E. B. Chekmareva, T. S. Novopokrovskaya, and N. A. Preobrazhenskii, *Zh. Obshch. Khim.,* **32,** 2828 (1962).

210. A. Pelka, L. Grabowski, S. Poradowski, and T. Kosinski, Polish patent, 43,588 (1960); *Chem. Abstr.,* **57,** 13736g (1962).

211. R. P. Houghton and C. S. Williams, *Tetrahedron Lett.,* 3929 (1967).

212. (a) J. Palecek and J. Kuthan, Czech. patent, 125,165 (1967); *Chem. Abstr.*, **69**, 96476h (1968); (b) *Ibid.*, Czech. patent, 125,164 (1967); *Chem. Abstr.*, **69**, 96475g (1968).

213. G. Favini, *Rend. Ist. Lombardo Sci.*, Pt. I, **91**, 162 (1957); *Chem. Abstr.*, **52**, 11539e (1958).

214. A. Agren, G. Ekenved, S. O. Nilsson, and E. Svensjo, *Acta Pharm. Suecica*, **2**, 421 (1965); *Chem. Abstr.*, **64**, 9532c (1966).

215. H. Hjedo, *Acta Chem. Scand.*, **17**, 2351 (1963).

216. W. Ried and G. Neidhardt, *Ann. Chem.*, **666**, 148 (1963).

217. W. Kirsten and H. Schulz, East Ger. patent, 30,872 (1965); *Chem. Abstr.*, **64**, 8152g (1966).

218. M. G. Gal'pern and E. A. Luk'yanets, *Zh. Vses. Khim. Obshchest.*, **12**, 474 (1967); *Chem. Abstr.*, **68**, 2789s (1968).

219. G. F. Holland and J. N. Pereira, *J. Med. Chem.*, **10**, 149 (1967).

220. T. Kametani, S. Takano, O. Umezawa, H. Agui, K. Kanno, Y. Konno, F. Sato, H. Nemoto, K. Yamaki, and H. Ueno, *Yakugaku Zasshi*, **86**, 823 (1966); *Chem. Abstr.*, **65**, 20093h (1966).

221. R. Camain-Giabicani and A. Broche, *Bull. Soc. Chim. Fr.*, 1254 (1964).

222. J. Syedel, *Tetrahedron Lett.*, 1145 (1966).

223. F. E. Cislak, U.S. patent, 3,045,024 (1962); *Chem. Abstr.*, **57**, 15080e (1962).

224. Rhône-Poulenc S.A., Fr. patent, M1861 (1963); *Chem. Abstr.*, **60**, 2904h (1964).

225. W. Schaeffer and R. Wegler, Ger. patent, 1,149,356 (1963); *Chem. Abstr.*, **59**, 11441f (1963).

226. H. Bojarska-Dahlig and P. Nantka-Namirski, *Rocz. Chem.*, **30**, 621 (1956).

227. W. Hoefling, D. Eilhauer, and H. Reckling, East Ger. patent, 33,621 (1964); *Chem. Abstr.*, **63**, 11518g (1965).

228. T. Okamoto and H. Takahashi, Jap. patent, 70 03,380 (1970); *Chem. Abstr.*, **72**, 111308n (1970).

229. E. A. Pavlov, V. A. Serazetdinova, A. D. Kagarlitskii, and B. V. Surorov, *Khim. Geterotsikl. Soedin.*, **4**, 665 (1968); *Chem. Abstr.*, **70**, 28778d (1969).

230. T. Hirakata, S. Kubota, and T. Akita, *Yakugaku Zasshi*, **77**, 219 (1957); *Chem. Abstr.*, **51**, 11341i (1957).

231. H. Quast and E. Schmitt, *Ann. Chem.*, **732**, 64 (1970).

232. H. Quast and E. Schmitt, *Ann. Chem.*, **732**, 43 (1970).

233. E. Wenkert and G. D. Reynolds, *Aust. J. Chem.*, **22**, 1325 (1969).

234. M. Winn, D. A. Dunningan, and H. E. Zaugg, *J. Org. Chem.*, **33**, 2388 (1968).

235. J. Delarge, *Pharm. Acta Helv.*, **44**, 637 (1969); *Chem. Abstr.*, **71**, 112761w (1969).

236. L. Neilands and G. Vanags, *Latvijas PSR Zinatnu Akad. Vestis, Kim. Ser.* (2), 203 (1964); *Chem. Abstr.*, **61**, 6999d (1964).

237. Y. Omote, K.-T. Kuo, and N. Sugiyama, *Bull. Chem. Soc. Jap.*, **40**, 1695 (1967).

238. H. Sliwa, *C. R. Acad. Sci., Paris, Ser. C*, **264**, 1893 (1967).

239. M. Yokote, F. Shibamiya, and S. Tokairin, *Kogyo Kagaku Zasshi* 67, 166 (1964); *Chem. Abstr.*, **61**, 3235f (1964).

240. F. S. Babichev, L. A. Kirpianova, and T. A. Dashevskaya, *Ukr. Khim. Zh.*, **32**, 706 (1966); *Chem. Abstr.*, **65**, 13681f (1966).

241. V. L. Sbarskii, G. M. Shutov, V. Zhilin, and E. Yu. Orlova, *Khim. Geterotsikl. Soedin.* (1), 178 (1967); *Chem. Abstr.*, **67**, 73500f (1967).

242. R. M. Kellogg, T. J. Van Bergen, and H. Wynberg, *Tetrahedron Lett.*, 5211 (1969).

243. A. M. Aliev and M. A. Salimov, *Aptechn. Delo*, **13**, 36 (1964).

244. J. B. Lee and T. G. Clarke, *Tetrahedron Lett.*, 415 (1967).

245. M. P. Cava, M. J. Mitchell, D. C. DeJongh, and R. Y. Van Fossen, *Tetrahedron Lett.*, 2947 (1966).
246. H. Hartkamp, *Z. Anal. Chem.*, **190**, 66 (1962).
247. I. Morimoto and S. Tanaka, *Nippon Kagaku Zasshi*, **83**, 357 (1962); *Chem Abstr.*, **58**, 5033f (1963).
248. J. F. Biellmann, R. J. Highet, and M. P. Goeldner, *J. Chem. Soc., D*, 295 (1970).
249. Fr. patent, 1,393,092 (1965); *Chem. Abstr.*, **63**, 1774e (1965).
250. H. M. Wuest, J. A. Bigot, Th. J. de Boer, B. van der Wal, and J. P. Wibaut, *Rec. Trav. Chim. Pays-Bas*, **78**, 226 (1959).
251. C. J. Argoudelis and F. A. Kummerow, *J. Org. Chem.*, **26**, 3420 (1961).
252. W. Steinke, East Ger. patent, 23,754 (1962); *Chem. Abstr.*, **59**, 8713b (1963).
253. J. T. Dunn and D. L. Heywood, U.S. patent, 3,048,624 (1962); *Chem. Abstr.*, **59**, 6369f (1963).
254. S. Mizukami, E. Hirai, and M. Morimoto, *Shionogi Kenkyusho Nempo*, **16**, 29 (1966); *Chem. Abstr.*, **66**, 10827q (1967).
255. J. Delarge and L. Thunus, *Farmaco, Ed. Sci.*, **21**, 846 (1966); *Chem. Abstr.*, **66**, 75889t (1967).
256. M. Szafran and Z. Sarbak, *Rocz. Chem.*, **43**, 309 (1969).
257. M. Szafran and B. Brezinski, *Rocz, Chem.*, **43**, 653 (1969).
258. B. M. Bain and J. E. Saxton, *J. Chem. Soc.*, 5216 (1961).
259. H. J. Rimek, *Ann. Chem.*, **670**, 69 (1963).
260. M. Celadnik, L. Novacek, and K. Palat, *Chem. Zvesti*, **21**, 109 (1967); *Chem. Abstr.*, **67**, 64196j (1967).
261. E. Profft and W. Steinke, *J. Prakt. Chem.*, **13**, 58 (1961).
262. T. Wieland and H. Biener, *Chem. Ber.*, **96**, 266 (1963).
263. Z. D. Tadic, M. M. Misic, and D. M. Dimitrijevic, *Glasnik Hem. Drustva, Beograd*, **27**, 407 (1962); *Chem. Abstr.*, **60**, 15698f (1964).

Chemistry of Heterocyclic Compounds, Volume 14
Edited by R. A. Abramovitch

CHAPTER XI

Pyridine Side-Chain Carboxylic Acids

MARY E. NEUBERT

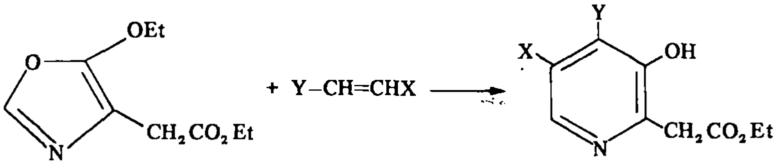
Liquid Crystal Institute
Kent State University
Kent, Ohio

The area of pyridine side-chain carboxylic acids continues to be a rapidly expanding segment of pyridine chemistry. In addition to the general chemical interests in these compounds, which are discussed throughout this chapter, many have been investigated for a wide variety of practical applications. They have been employed in the synthesis of natural products such as hydroxycotinine;[1] nicotine;[2] a variety of isoquinoline,[3-8] lupine,[9] and indole[10-13] alkaloids; *des DL*-castoramins;[14] porphobilinogen;[15] and flavonoids.[16] Structural determination studies of dioscorine,[17] retamine,[18,19] and evonine[20] involved the use of pyridine side-chain acids. Wilfordic and hydroxywilfordic acids have been shown to be pyridine side-chain acids.[21] Pyridine side-chain acids are also formed in the metabolism of nicotine[22,23] and have been employed in metabolic studies performed with cotinine.[24] Many have been investigated as therapeutic agents such as antibacterial and antifungal,[25-35] antiviral,[36] anti-inflammatory,[37-40] antifertility,[41] hypoglycemic,[42] hypocholesterolemic,[41-43] and eurhythmic[44,45] agents. Additionally, they have been examined as CNS depressants[46-49] and stimulants,[50] analgesics,[51] antispasmodics,[52-55] analeptics and hypotensors,[56,57] monoamine oxidase inhibitors,[58] and corticosuprarenal inhibitors.[59] A few have been studied as bactericides and fungicides,[60-63] pesticides,[64] insecticides,[65] solubilizing agents,[66] and sensitizers[67] and desensitizers in photographic emulsions.[68]

I. Preparations

1. From Nonpyridine Starting Materials (Table XI-1)

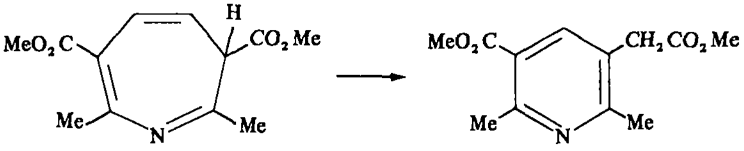
Several esters (**XI-3**) were obtained from a Diels-Alder cycloaddition between the oxazole **XI-1** and the activated olefins **XI-2**.[69]



XI-1 **XI-2** **XI-3**

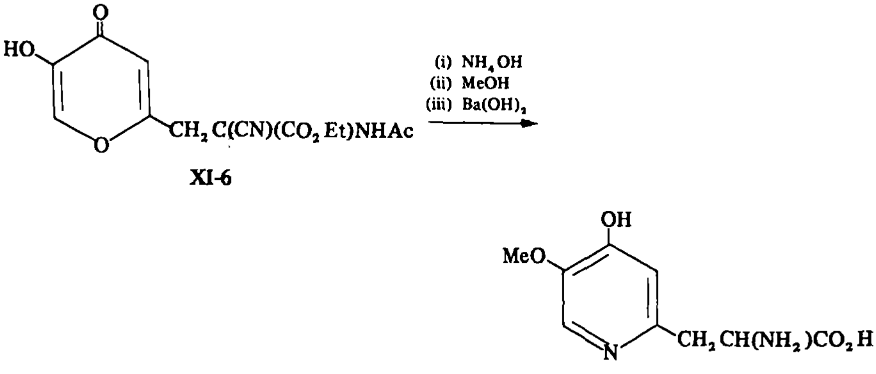
$X = Y = CO_2Et$
$X = Y = CN$
$X = Y = CH_2OMe$
$X = CN$, $Y = CH_2OAc$

When the proper conditions were employed, the 3*H*-azepine (**XI-4**) was converted to the pyridine ester **XI-5** in good yields.[70]



XI-4 **XI-5**

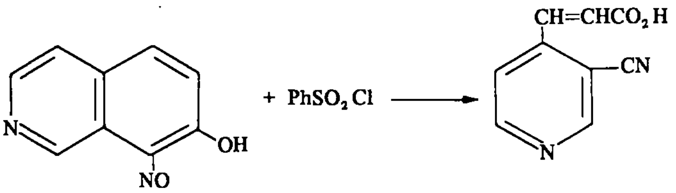
The 2-pyridylalanine (**XI-7**) was synthesized from the pyrone (**XI-6**)[71] and



XI-6

XI-7

treatment of the isoquinoline **XI-8** with benzenesulfonyl chloride produced the 4-pyridylacrylic acid **XI-9**.[72]



XI-8 **XI-9**

The remaining syntheses of pyridine side-chain acids from nonpyridine precursors involves typical condensation reactions. The preparations of acids containing a partially reduced pyridine nucleus were performed either through condensation reactions or by the treatment of pyrones with amines.

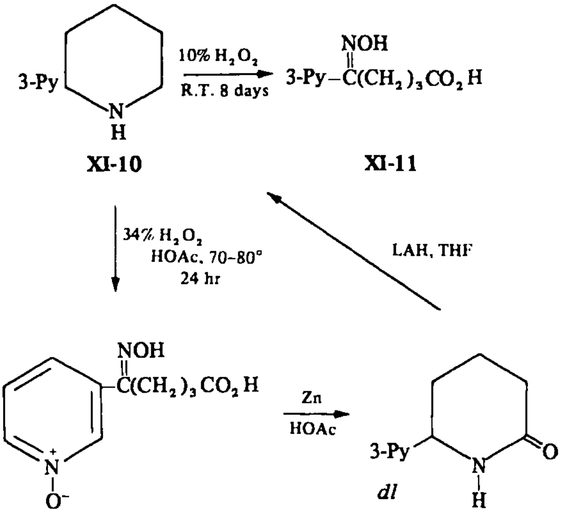
2. From Pyridine Starting Materials

A. *Side-Chain Oxidation* (Table XI-2)

Side-chain acids have been obtained by employing the following oxidizing agents on a variety of functional groups:

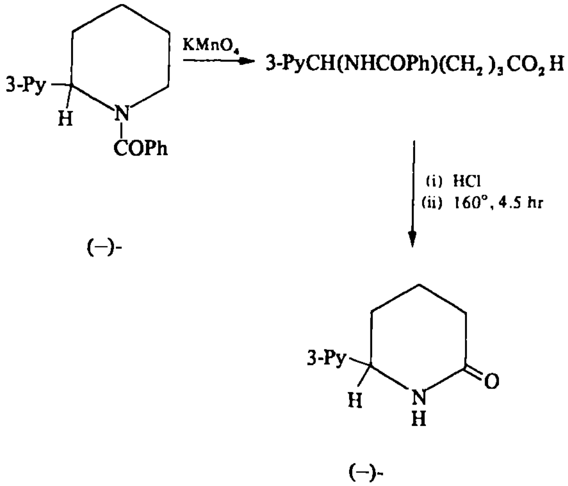
(i)	Chromic Acid	$-CH_2OH$	$\longrightarrow -CO_2R$
(ii)	$AgNO_3$	$-CHO$	$\longrightarrow -CO_2H$
(iii)	SeO_2	$-COMe$	$\longrightarrow -COCO_2H$
(iv)	$KMnO_4$	$-CH{=}CH_2$	$\longrightarrow -CO_2H$
(v)	MnO_2	$-COCO_2Et$	$\longrightarrow -CO_2H$

In three instances, enzymes were used as the oxidizing agents.[73, 74] Oxidation of *l*-anabasine (**XI-10**) with 10% hydrogen peroxide under mild conditions caused cleavage of the piperidine ring to form the acid **XI-11**.[75] When 34% hydrogen peroxide in acetic acid was employed at a higher temperature, however, oxidation of the pyridine nitrogen atom occurred to form the *N*-oxide acid (**XI-12**). This latter acid yielded the *dl*-lactam (**XI-13**) on reduction with zinc in acetic acid. The *dl*-lactam was then converted to *dl*-anabasine by reduction with



XI-10 **XI-11** **XI-12** **XI-13**

lithium aluminum hydride in tetrahydrofuran. The *l*-isomer of the lactam (**XI-13**) was synthesized by using the following reaction scheme:



In one instance,[76] a dihydropyridine acetic acid was oxidized by oxygen to the pyridylacetic acid.

B. *Carbonation of Organometallic Compounds* (Table XI-3)

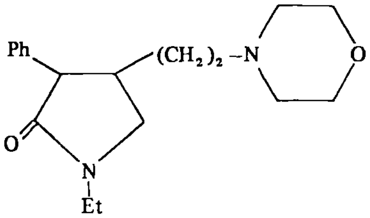
The carbonation of side-chain metallated lutidines has been investigated.[77, 78] As expected, the lithium derivatives of 2,3- and 2,5-lutidine were carbonated only at the C-2 methyl group. The addition of carbon dioxide to the side-chain lithium or sodium derivatives of 2,4- and 2,6-lutidine yielded primarily the C-2 acetic acids. In one instance,[77] the 2,6-diacetic acid was also isolated. The sodium salts of pyridylacetylenes were converted to the corresponding acids in good yields when treated with carbon dioxide.[79-81]

C. *Increase of Chain Length by the Arndt-Eistert Method* (Table XI-4)

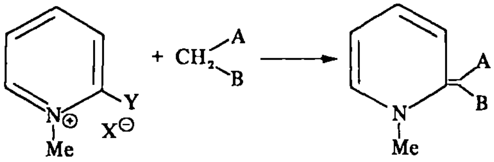
Only two examples employing this method were found.

D. *Condensations of Halogenated Pyridines with Active Methylene Compounds* (Table XI-5)

Although many phenylacetamides were successfully alkylated with 2-bromopyridine, the corresponding thioamides were not.[82] The pyrrolidone **XI-14** was employed as the active methylene compound in a condensation with 2-bromopyridines.[50] Treatment of quaternary salts of halo- or alkoxy-pyridines (**XI-15** and **XI-17**) with an active methylene compound gave the anhydro bases **XI-16** and **XI-18**. The electron-attracting substituents stabilized the anhydro bases.

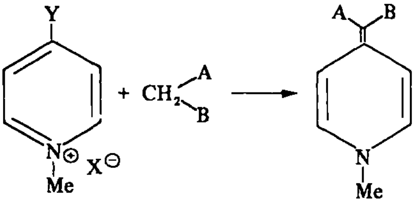


XI-14



XI-15 **XI-16**

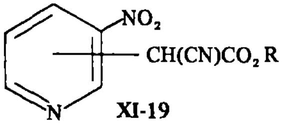
Y = Br, Cl, or OPh



XI-17 **XI-18**

Y = OMe, OPh

Attempts to hydrolyze the ester group in the *o*-nitro-2- and 4-pyridyl acetates **XI-19**, synthesized by treating the corresponding pyridyl halide with a malonic acid derivative, were unsuccessful using either basic or acidic conditions.^{84} The



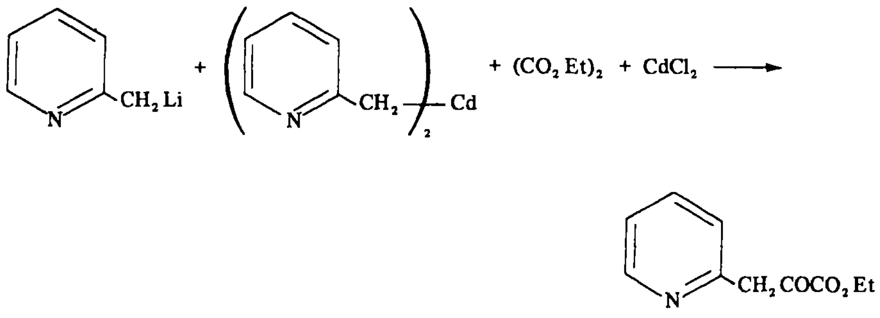
XI-19

benzyl esters (**XI-19**, R = CH_2Ph) also did not undergo hydrogenolysis when 10% Pd-C, 30% Pd-C, Ra-Ni, or PtO_2 were employed as catalysts. Only reduction of the nitro group to the amine occurred.

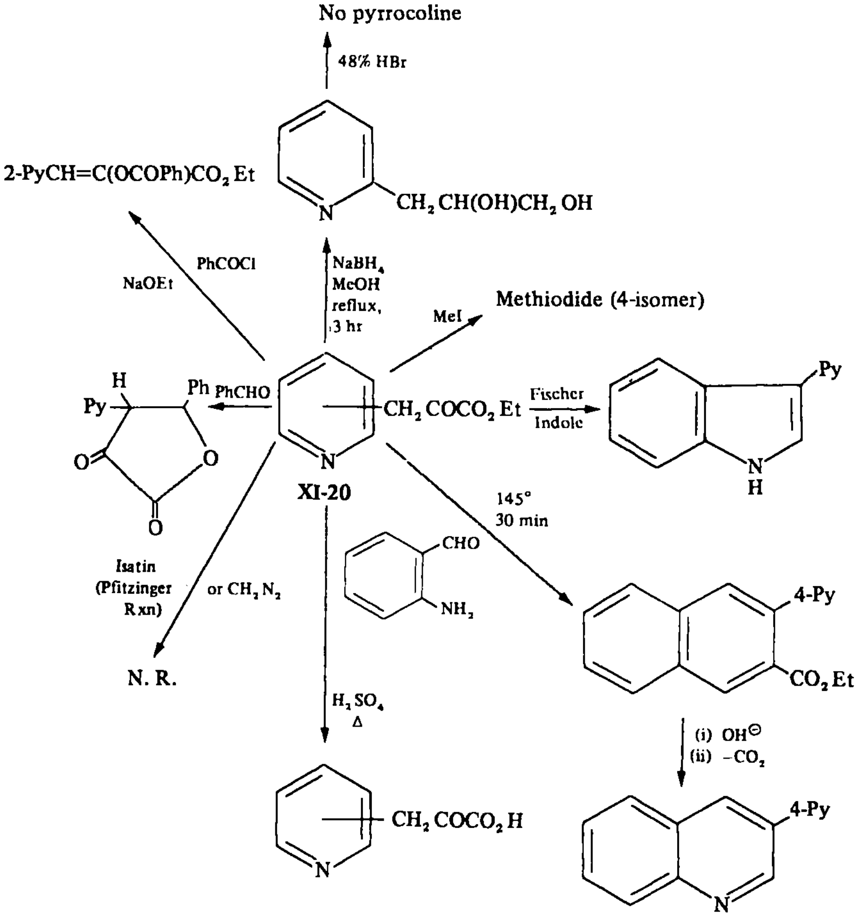
E. *Condensations of Picolines and Related Compounds*

a. *Condensation of Chloral with Picolines (Table XI-6) and Hydrolysis of the Products (Table XI-7)*

b. *Condensations with Picolines to Give Side-Chain Acids and Esters (Table XI-8) (see also Chapter IV, Section V.1.)* The previously unknown ethyl 2- and 4-pyridyl pyruvates (**XI-20**) have been synthesized, although only in 10% yields.$^{85, 86}$ The C-2 isomer was prepared by treating the lithium derivative of 2-picoline with diethyl oxalate in the presence of a mixture of the cadmium salts, $(2\text{-}PyCH_2)_2Cd$ and $CdCl_2$ (in Chapter XI of the 1964 edition, attempts to



CH₂Li
+
CH₂
Cd
2
+ (CO₂Et)₂ + CdCl₂
N
CH₂COCO₂Et

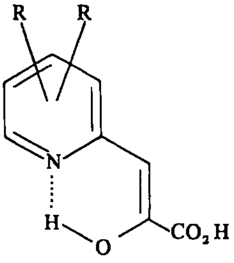


No pyrrocoline
48% HBr
CH₂CH(OH)CH₂OH
2-PyCH=C(OCOPh)CO₂Et
PhCOCl
NaOEt
NaBH₄
MeOH
reflux,
3 hr
MeI
Methiodide (4-isomer)
H
Py
Ph
PhCHO
O
O
O
CH₂COCO₂Et
Fischer
Indole
Py
N
H
XI-20
145°
30 min
CHO
NH₂
Isatin
(Pfitzinger
Rxn)
or CH₂N₂
N. R.
4-Py
CO₂Et
H₂SO₄
Δ
(i) OH⊖
(ii) -CO₂
CH₂COCO₂H
4-Py
N

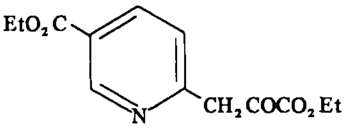
Scheme XI-1

synthesize these pyruvates using diethyl oxalate and base were reported to give disubstitution). In the synthesis of the 4-isomer, the mercury salts, $(4\text{-PyCH}_2)_2\text{Hg}$ and $HgCl_2$ had to be employed. These pyruvates were reported to undergo the reactions illustrated in Scheme XI-1.

Pyridylpyruvic acids have been synthesized in good yields by treating several picolines containing electron withdrawing substituents with oxalyl chloride in the presence of phosphoryl chloride.[87] These pyruvates exist primarily in the enol form with hydrogen bonding between the enol hydroxyl group and the pyridine nitrogen atom (**XI-21**). This probably explains the reluctance of the pyruvate **XI-21** to undergo decarbonylation to the acetate.[17] Pyruvates also have



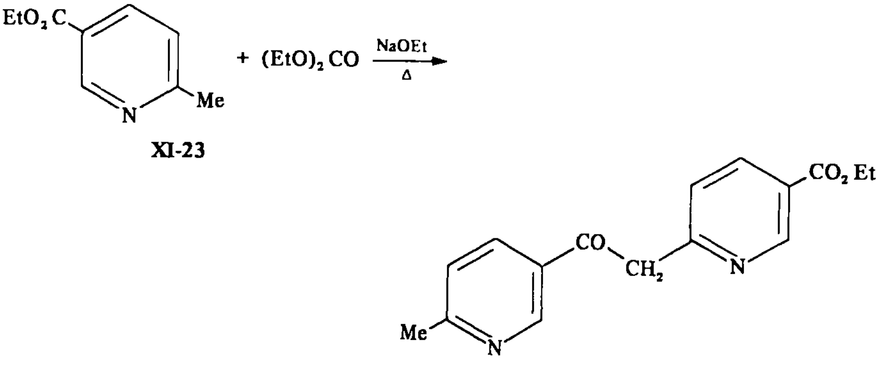
XI-21



XI-22

been reported to be formed by treatment of 2-picoline-1-oxides with diethyl oxalate in the presence of base.[135, 139]

Although a picoline was usually converted to a pyridine acetate when treated with ethyl carbonate under basic conditions, ethyl 6-methylnicotinate (**XI-23**) gave the ketone **XI-24** instead.[17]

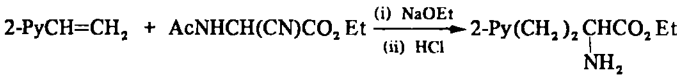


XI-23

XI-24

F. *Condensations of Vinylpyridines with Esters* (Table XI-9)

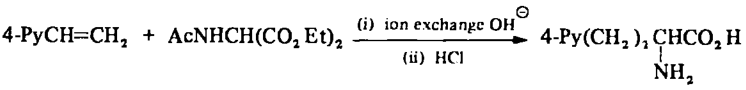
Two syntheses of α-amino-γ-(2- and 4-pyridyl)butyric acids employing the Michael addition have been reported. In the one instance, 2-vinylpyridine was allowed to react with the activated ester **XI-25** and the resulting product was hydrolyzed to give the amino acid ester (**XI-26**).[89] The second synthesis involved



$$\text{2-PyCH=CH}_2 + \text{AcNHCH(CN)CO}_2\text{Et} \xrightarrow[\text{(ii) HCl}]{\text{(i) NaOEt}} \text{2-Py(CH}_2\text{)}_2\underset{\underset{\text{NH}_2}{|}}{\text{C}}\text{HCO}_2\text{Et}$$

XI-25 **X-26**

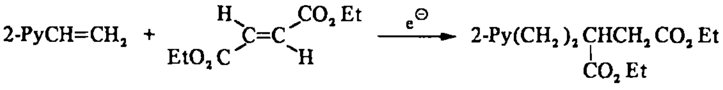
the condensation of 4-vinylpyridine with the malonic ester (**XI-27**) on a basic ion-exchange resin. Acid treatment of the product yielded the amino acid **XI-28** isolated as the hydrochloride.[30]



$$\text{4-PyCH=CH}_2 + \text{AcNHCH(CO}_2\text{Et)}_2 \xrightarrow[\text{(ii) HCl}]{\text{(i) ion exchange OH}^{\ominus}} \text{4-Py(CH}_2\text{)}_2\underset{\underset{\text{NH}_2}{|}}{\text{C}}\text{HCO}_2\text{H}$$

XI-27 **XI-28**

An electrolytic condensation of 2-vinylpyridine with the activated olefin diethyl fumarate (**XI-29**) produced the diester **XI-30**.[90] The Michael addition of

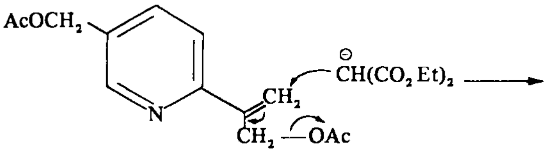


$$\text{2-PyCH=CH}_2 + \begin{array}{c}\text{H}\diagdown\quad\diagup\text{CO}_2\text{Et}\\ \text{C=C}\\ \text{EtO}_2\text{C}\diagup\quad\diagdown\text{H}\end{array} \xrightarrow{e^{\ominus}} \text{2-Py(CH}_2\text{)}_2\underset{\underset{\text{CO}_2\text{Et}}{|}}{\text{C}}\text{HCH}_2\text{CO}_2\text{Et}$$

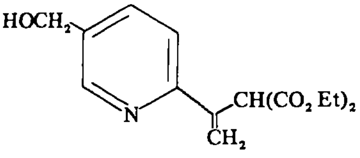
XI-29 **XI-30**

diethylmalonate to compound **XI-31** occurred in the normal manner, except that the α-acetate group was lost to yield the olefin **XI-32**, probably by the mechanism shown.[14] Hydrolysis of the acetate function also occurred.

Barbituric acids have been employed as the active methylene compounds in the Michael addition to 4-vinylpyridine to yield the barbiturates **XI-33**.[91] A variety of 3-vinylpyridyl ketones of the type **XI-34** were treated with esters containing active methylene groups to form the δ-keto esters (**XI-35**).[208]

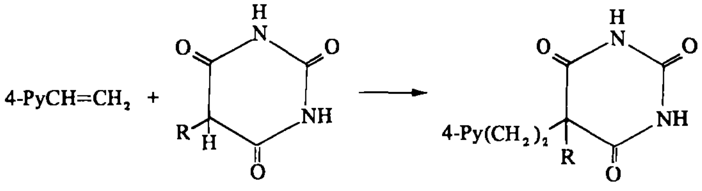


XI-31



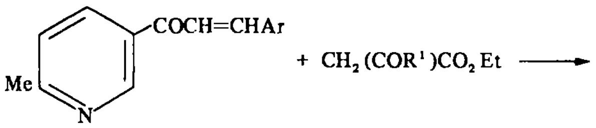
36%

XI-32

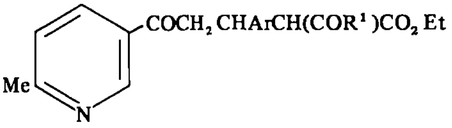


R = Et, Ph

XI-33



XI-34

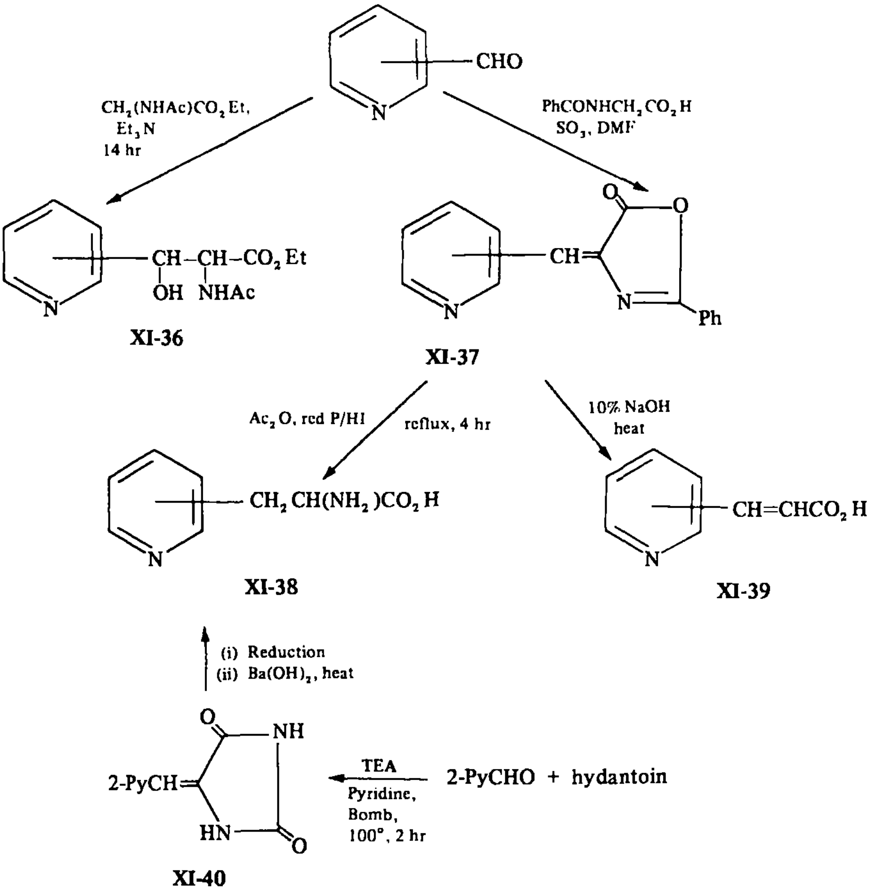


XI-35

G. *Condensations of Pyridinealdehydes and Ketones*

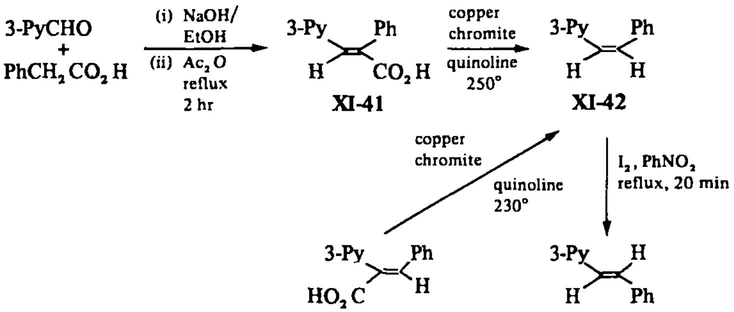
(Table XI-10)

The use of acylaminoacetates as the active methylene compounds in condensations with pyridinealdehydes and -ketones has produced a variety of pyridineacetic acids. When monoethylacetamidomalonate was employed in the presence of base, *N*-acetyl-β-pyridylserines **(XI-36)** were formed.[93] Hippuric acid, when allowed to react with these aldehydes in the presence of sulfur trioxide yielded azlactones **(XI-37)** that were converted either to α-aminopropionic acids **(XI-38)** or to acrylic acids **(XI-39)**.[94] In these instances, the acetals of the pyridinealdehydes had to be used to avoid the formation of tars. α-Amino-β-(2-pyridyl)propionic acid **(XI-38**, 2-isomer) was also synthesized from the hydantoin **(XI-40)**.[95] Nitrosoamino esters[96] and alkynes[79, 97] have also

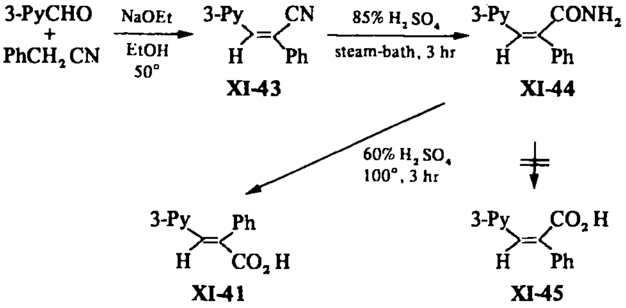


been employed as the active methylene compounds.

The stereochemistry of the β-carboxystilbazoles formed in a Perkin condensation of pyridinealdehydes with arylacetic acids has been shown to be *cis* (**XI-41**)[98-100] rather than *trans* as reported earlier.[10] The *cis* stereochemistry was shown to be correct by the following transformations:



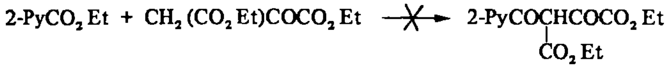
This stereochemistry is the opposite of that found in the β-cyanostibazoles (**XI-43**) obtained from a Knoevenagel condensation of arylacetonitriles with pyridinealdehydes (see Table XI-25). Unfortunately, these results do not provide syntheses for both the *cis*- (**XI-41**) and the *trans*- (**XI-45**) carboxystilbazoles because, although the nitriles can be hydrolyzed to the *trans* amides (**XI-44**), these amides isomerize when hydrolyzed further to yield the *cis* acids.[98]



H. *Condensations of Pyridinecarboxylic Esters*
(Table XI-11)

Some of the keto esters, obtained from condensation reactions with pyridinecarboxylic esters as listed in Table XI-11, have been hydrolyzed and decarboxylated,[11, 23, 75, 101-104] condensed with aldehydes in Aldol condensations,[105, 106] and converted to barbiturates,[91] azomethine dyes,[107, 108] arylhydrazones,[176] and acylpyridines.[109]

Ethyl picolinate failed to undergo condensation with diethyl oxaloacetate (**XI-46**) (using Claisen conditions) to give the desired product **XI-47**.[110]

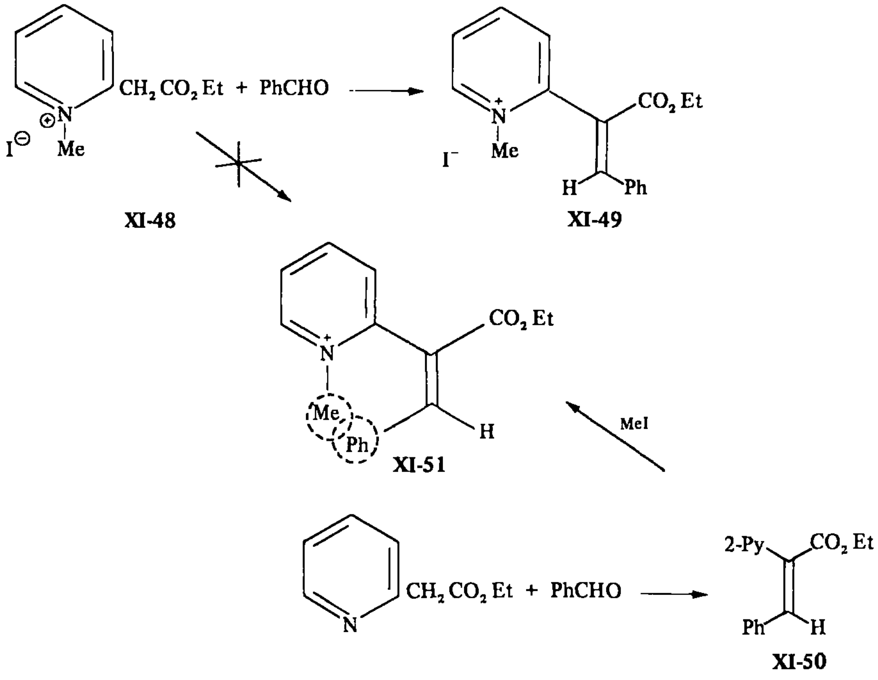


$$\text{2-PyCO}_2\text{Et} + \text{CH}_2(\text{CO}_2\text{Et})\text{COCO}_2\text{Et} \nrightarrow \text{2-PyCO}\underset{\text{CO}_2\text{Et}}{\underset{|}{\text{CH}}}\text{COCO}_2\text{Et}$$

XI-46 **XI-47**

I. *Condensations of Pyridineacetic Esters* (Table XI-12)

Usually the condensation of ethyl pyridylacetates with aromatic aldehydes requires the presence of a base to form the required anion. When, however, the methiodide of the pyridine ester is employed no added base is needed.[111] Quaternization of the pyridine nitrogen atom facilitates proton removal. The stereochemistry of the cinnamate isolated from the condensation of ethyl 2-pyridylacetate methiodide (**XI-48**) with benzaldehyde has been shown to be *cis* (**XI-49**) whereas the product obtained by using the free base has the *trans* configuration (**XI-50**).[111] On the other hand, the 4-isomer yielded only the *trans*-cinnamate in both instances. Apparently the steric crowding between the phenyl group and the quaternary nitrogen atom in the 2-pyridyl-*trans*-cinnamate methiodide (**XI-51**) is too great to allow its formation, whereas in the 4-isomer this crowding is absent.



When the aromatic aldehyde contained an *ortho* hydroxyl or amino group, cyclization to the coumarins or quinolines, respectively, occurred.[111] Attempts to condense ethyl 2- and 4-pyridylacetate (either as the free base or as the methiodide) with phenyl methyl ketone or with *o*-hydroxyphenyl methyl ketone were unsuccessful. However, the methiodide of the 4-isomer yielded a quinoline when treated with *o*-aminophenyl methyl ketone.

The condensation of ethyl 2-pyridylacetate with benzoyl chloride in the presence of base gave only the disubstituted product **(XI-52)** rather than the monosubstituted derivative.[112] Acetyl chloride did not produce the corresponding diacetyl ester.

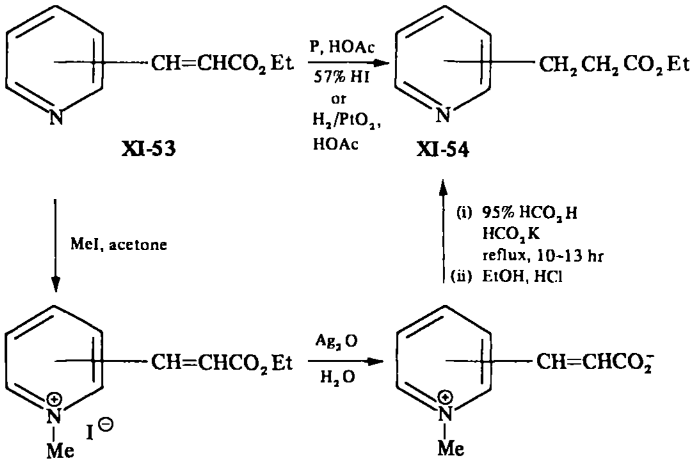
$$2\text{-PyC(PhCO)}_2\text{CO}_2\text{Et}$$

XI-52

Several Mannich-type reactions have been performed using 3- and 4-pyridylacetates to form the expected products in fair yields.[113]

J. *Reduction of Side-Chain Functions* (Table XI-13)

Reduction of the double bond of β-(2-pyridyl)acrylates **(XI-53)** without reducing the ester group in order to obtain 2-pyridylpropionates **(XI-54)** was accomplished in good yields by using either a mixture of phosphorus with 57% hydriodic acid in acetic acid[114] or by hydrogenation over platinum oxide[114] or 10% palladium-on-carbon[34] in acetic acid. Treatment of the betaine of either the 2- or 4-pyridineacrylate **(XI-55)** with fused potassium formate in formic acid also



XI-55

gave the propionates, but in poor yields, and accompanied by the corresponding piperidine propionates.[114]

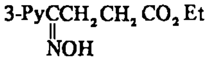
The use of sodium borohydride in the reduction of the acrylate **XI-56** caused the formation of a mixture of products resulting from the reduction of both the ester and the double bond functions.[115] As expected, the composition of this mixture was dependent on the amount of sodium borohydride employed.

$$\underset{\textbf{XI-56}}{\text{4-PyCH=CHCO}_2\text{Me}} + \text{NaBH}_4 \xrightarrow[\text{reflux}\atop 1\text{–}2\text{ hr}]{\text{MeOH}} \underset{\textbf{XI-57}}{\text{4-Py(CH}_2)_2\text{CO}_2\text{Me}} +$$

$$\underset{\textbf{XI-58}}{\text{4-PyCH=CHCO}_2\text{Me}} + \underset{\textbf{XI-59}}{\text{4-Py(CH}_2)_3\text{OH}} + \underset{\textbf{XI-60}}{\text{4-PyCH=CHCH}_2\text{OH}}$$

Molar Ratio		% Product in Mixture			
XI-56	$NaBH_4$	**XI-57**	**XI-58**	**XI-59**	**XI-60**
1	2	34	36	8	22
1	5	10	0	54	36
1	10	1	0	91	8

Sodium borohydride has also been used to reduce the carbonyl group to a hydroxyl group in some pyridine keto acids[23] and esters[19, 116] without reducing the acid function. Reduction of the oxime of ethyl 4-oxo-4-(3-pyridyl)butyrate in the presence of a lead catalyst yielded the amino acid **XI-61**.[2] Attempts to reduce the carbonyl groups of the diketo ester **XI-62** failed in the presence of Raney Nickel.[110]



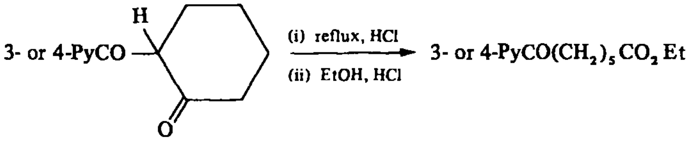
$$\text{3-Py}\underset{\text{NOH}}{\underset{\|}{\text{C}}}\text{CH}_2\text{CH}_2\text{CO}_2\text{Et} \longrightarrow \underset{\textbf{XI-61}}{\text{3-PyCH(NH}_2)\text{CH}_2\text{CH}_2\text{CO}_2\text{Et}} \qquad \underset{\textbf{XI-62}}{\text{2-PyCOCH}_2\text{COCO}_2\text{Et}}$$

K. *Willgerodt Reaction* (Table XI-14)

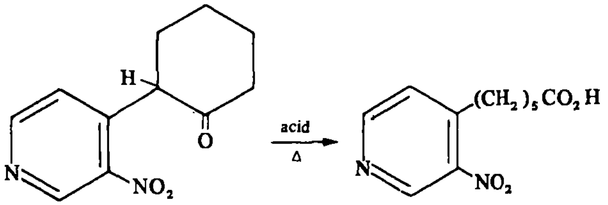
Only a few examples of the use of this reaction to synthesize pyridine side-chain acids were found. 4-Pyridyl propyl ketone was converted to the methyl ester of 4-pyridylbutyric acid.[117]

3. Miscellaneous Methods (Table XI-14-1)

Several methods that employ the opening of a variety of side-chain or fused pyridine ring systems have been developed for the synthesis of side-chain acids and derivatives.[95, 102, 117–122] An interesting example is the ring opening of cyclohexanones **XI-63** and **XI-64**.[117, 119]



XI-63



XI-64

The α-keto ester **XI-65** was synthesized in good yields by treating 3-nicotinoyl chloride with a Wittig reagent.[123, 124] Treatment of the oxime of 3-oxo-4-(3-pyridyl)butyric acid **(XI-66)** with phosphorus oxychloride yielded 3-pyridylacetic acid.[22]

$$\begin{tikzcd} \begin{array}{c} 3\text{-PyCOCl} + \mathrm{Ph_3\overset{\oplus}{P}CH_2OMe\ Br^{\ominus}} \\ \text{or} \\ \mathrm{Ph_3P{=}CHOMe} \end{array} \arrow[r, "\mathrm{PhLi}", "\mathrm{Et_2O}"'] & 3\text{-PyCOC(OMe)=PPh}_3 \arrow[d, "\mathrm{PhI(OAc)_2}"] \\ & 3\text{-PyCOCO}_2\text{Me} \end{tikzcd}$$

XI-65

$$3\text{-PyCH}_2\text{C(=NOH)CH}_2\text{CO}_2\text{H} \xrightarrow{\mathrm{POCl_3}} 3\text{-PyCH}_2\text{CO}_2\text{H}$$

XI-66

II. Properties and Reactions

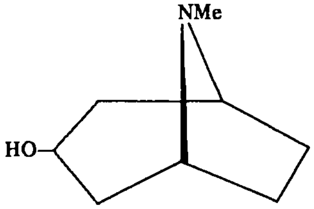
1. Esterification and Ester Hydrolysis

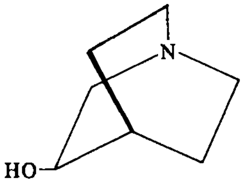
Several methyl esters were synthesized by the treatment of pyridine acetic acids with diazomethane.[3, 102, 114, 125] A variety of C-21 steroidal alcohols[37-40, 126] and the following alcohols have been employed in esterification reactions with pyridine side-chain acids.[53, 127]

$HOCH_2CH_2NEt_2$

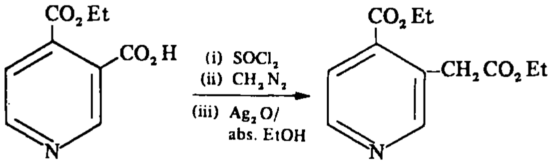
$HOCH_2CH_2\overset{\oplus}{N}Me_3\ Br^{\ominus}$

$HOCH_2CH_2Br$





In one instance, a pyridinecarboxylic acid **XI-67** was converted to a pyridine acetic acid **XI-68** through the Arndt-Eistert reaction.[128]

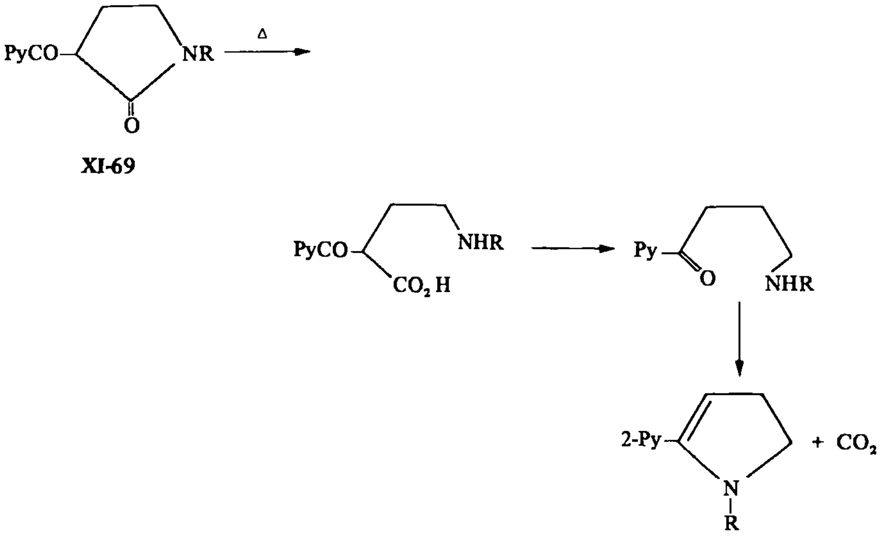


XI-67 **XI-68**

2. Decarboxylation (Tables XI-16 and XI-17)

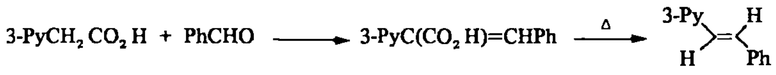
Heating the pyrrolidones **(XI-69)** caused cleavage of the lactam bond, which was then followed by decarboxylation and enamine formation to yield the pyrrolines **(XI-70)**.[129]

The decarboxylation of α-pyridylcinnamic acids yielded a variety of stilbazoles. Beard and Katritzky reported that they obtained the *trans*-stilbazole **(XI-72)** (as shown by i.r.) by the decarboxylation of the α-3-pyridylcinnamic acid **(XI-71)** which itself was obtained by the condensation of benzaldehyde with 3-pyridylacetic acid.[101] Clarke and co-workers found, however, that the



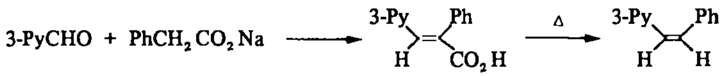
XI-69

XI-70



XI-71 **XI-72**

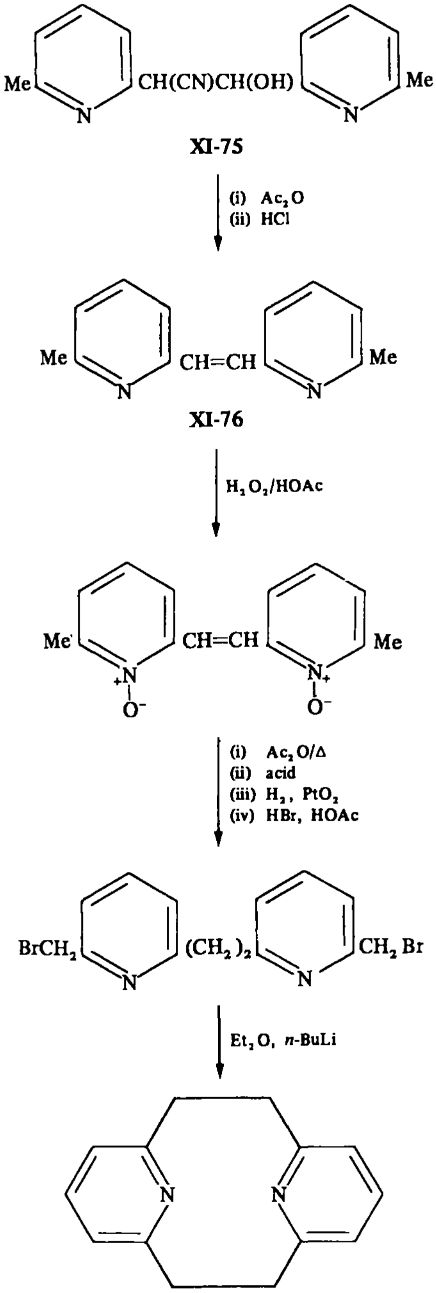
cis-stilbazole (**XI-74**) was formed when they repeated this work as well as when the *trans*-cinnamic acid (**XI-73**) (formed by the condensation of 3-pyridinealdehyde with sodium phenylacetate) was decarboxylated.[98] This latter reaction has



XI-73 **XI-74**

been discussed earlier under pyridinealdehyde condensations. Although the *trans*-stilbazoles are apparently not formed by the condensation of a pyridylacetic acid with an aldehyde, they have been synthesized by irradiation of the *cis*-isomer with a tungsten lamp.[100] Although the base **XI-73** underwent decarboxylation readily on heating, the corresponding pyridine-1-oxide did not.[101]

Hydrolysis, decarboxylation followed by dehydration of the nitrile **XI-75** gave the olefin **XI-76**, which was converted to the di-(pyridine-2,6-dimethylene) (XI-77) (RIS–8671).[130]

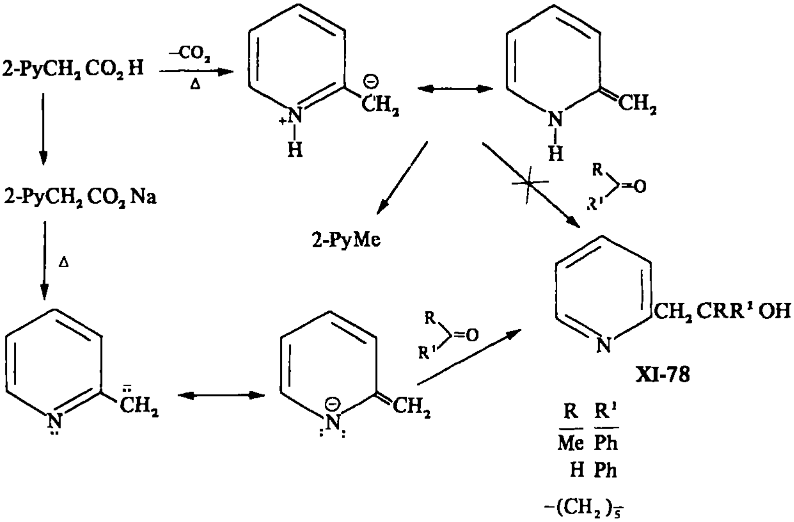


XI-75

XI-76

XI-77

An attempt to perform a Hammick reaction on 2-pyridylacetic acid to obtain a variety of alcohols gave only 2-picoline.[131] However, the sodium salt of this acid was successfully converted to a variety of alcohols (**XI-78**). Apparently, the free acid provides the proton necessary to form 2-picoline, whereas the sodium salt does not.



XI-78

R	R'
Me	Ph
H	Ph
$-(CH_2)_5-$	

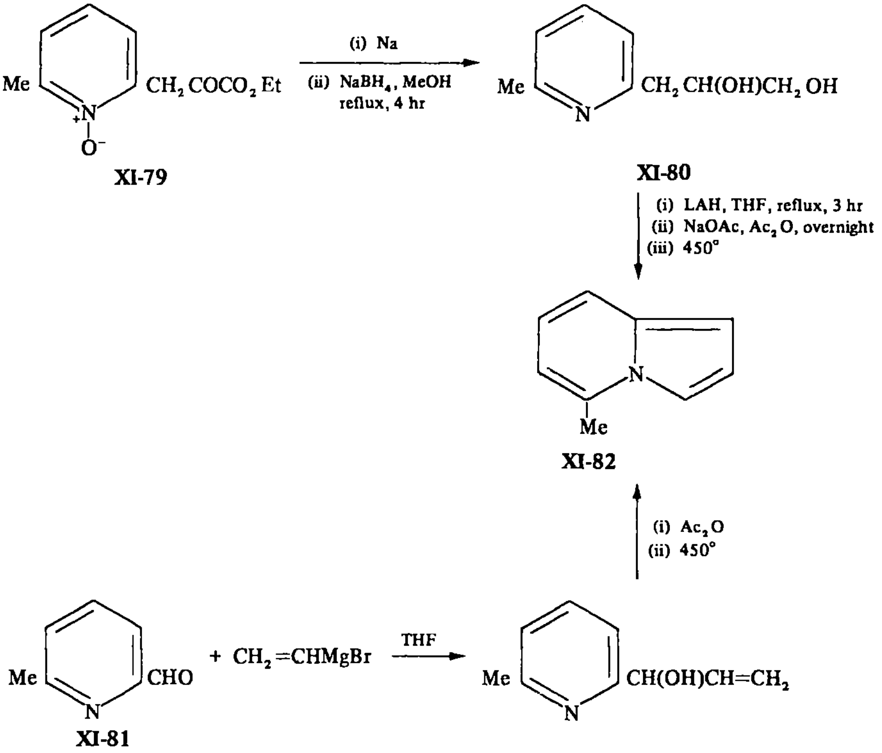
3. Active Methylene Reactions

No new examples of this type of reaction were found.

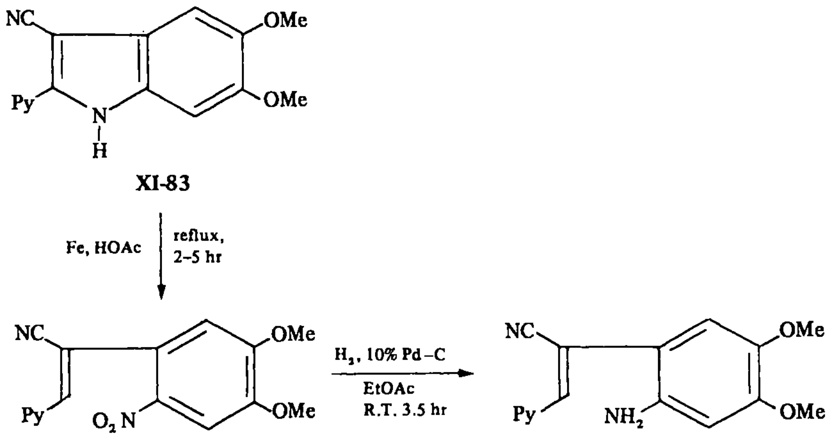
4. Reduction (Table XI-18)

In general the reduction of a pyridine side-chain acid or ester using platinum oxide, Raney Nickel, rhodium-on-carbon, rhodium-on-alumina, or ruthenium oxide as the catalyst gives the piperidine acid or ester. Partial reduction of the pyridine ring to a tetrahydropyridine usually occurred when palladium-on-carbon was employed as the catalyst, although two exceptions were reported.[132, 133] Either a mixture of the piperidine and the tetrahydropyridine ester[133] or the tetrahydropyridine ester alone[134] was formed when sodium borohydride was used at room temperature in the reduction of pyridine side-chain ester salts. When the free bases were employed, reduction of the ester group occurred instead of nuclear reduction.[46, 47, 115, 177] The use of lithium aluminum hydride gave the same results (see Table XI-18). Many acetamides were reduced to tetrahydropyridylacetamides with sodium borohydride at room temperature.[367]

The diol **XI-80**, obtained by the side-chain reduction of the keto ester (**XI-79**) with sodium borohydride, served as a precursor to 5-methylindolizine (**XI-82**).[135] However, the yield was low in this synthesis and the indolizine could be prepared by a more favorable route from the aldehyde **XI-81**.



Catalytic reduction of the α-(*o*-nitroaryl)acrylonitriles (**XI-84**) over a palladium catalyst at room temperature gave the amine (**XI-85**).[10] Reduction with iron in boiling acetic acid yielded the indole **XI-83**, however.[10] In an earlier work by Walker,[136] catalytic (palladium, 80°) reduction of the corresponding β-phenylacrylonitriles (**XI-86**) caused reductive cyclization of the nitrile to give the indole **XI-87**. An attempt was made to apply Walker's method to the 2-pyridyl isomer of **XI-84** but the expected indole was not isolated.[137] The mechanism proposed for the cyclization of **XI-84** to the indole (**XI-83**; Py = 2-Pyridyl) involves an intramolecular Michael addition of a hydroxylamino group to the double bond rather than attack by an amino group. Support for this mechanism was shown by the lack of cyclization of the amino compound **XI-88**.

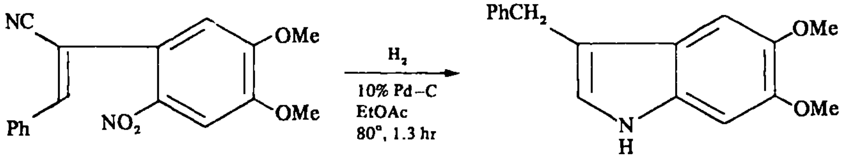


XI-83

XI-84

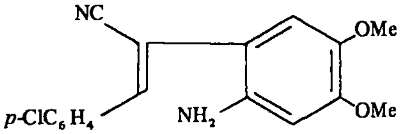
XI-85

Py = 3- or Pyridyl



XI-86

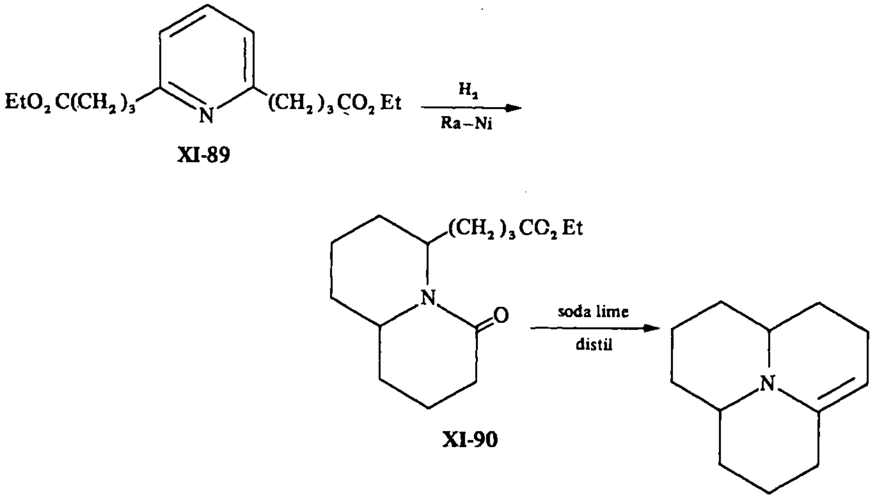
XI-87



XI-88

5. Synthesis of Condensed Heterocycles—Quinolizines and Quinolizidines (Table XI-19)

The quinolizidine **XI-90** obtained by reduction of the diester **XI-89** was converted to the azaphenalene **XI-91**.[138] The diester **XI-93** (R = H) failed to

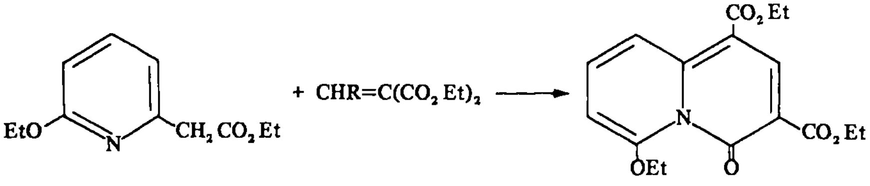


XI-89

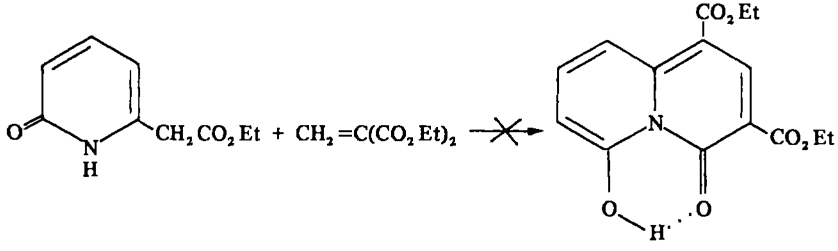
XI-90

XI-91

condense with either compound **XI-92** or **XI-95** to yield the corresponding quinolizines **XI-94** and **XI-96**, respectively.[139] However, when R = OEt, condensation did take place.

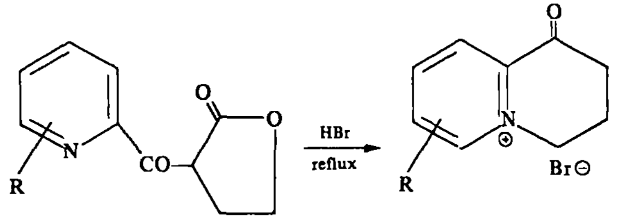


XI-92 **XI-93** **XI-94**



XI-95 **XI-96**

Several quinolizines were synthesized by heating 2-pyridyl 3-butyrolactonyl ketones (XI-97) in acid.[140]



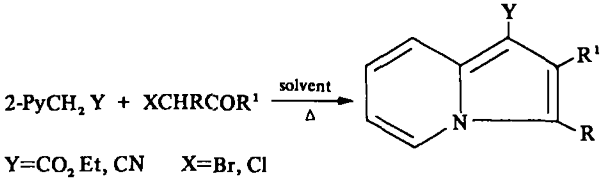
XI-97

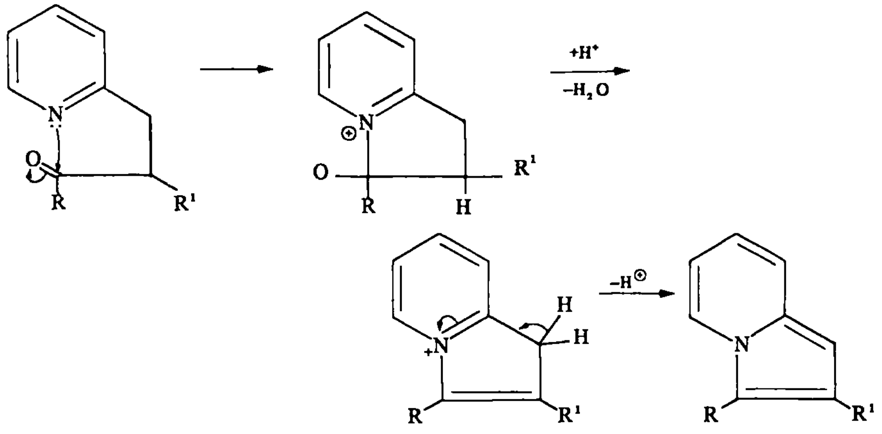
6. Synthesis of Condensed Heterocycles Other Than Quinolizines
(Table XI-20)

A great deal of research has been performed in this area since the earlier review, especially in the synthesis of indolizines, chromones, and naphthyridines.

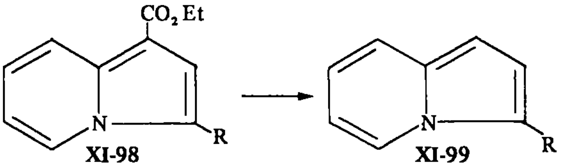
A. *Indolizines*

The most common procedure employed for the synthesis of indolizines is the condensation of a 2-pyridylacetate or acetonitrile with an α-halo activated methylene compound.[141-145] The yields were often good but decreased when R was a large alkyl residue or when X was a chlorine, instead of a bromine, atom. Since the indolizine was formed without employing a base, the earlier belief of Stepanov and Grineva that a base is required for cyclization to occur[136] is not justified. A mechanism for this cyclization has been proposed as shown in Scheme XI-2.[143] In a few instances, the 1-carbethoxyindolizines (XI-98) that occasionally formed were hydrolyzed and decarboxylated to yield the C-1 unsubstituted indolizines (XI-99).[142]

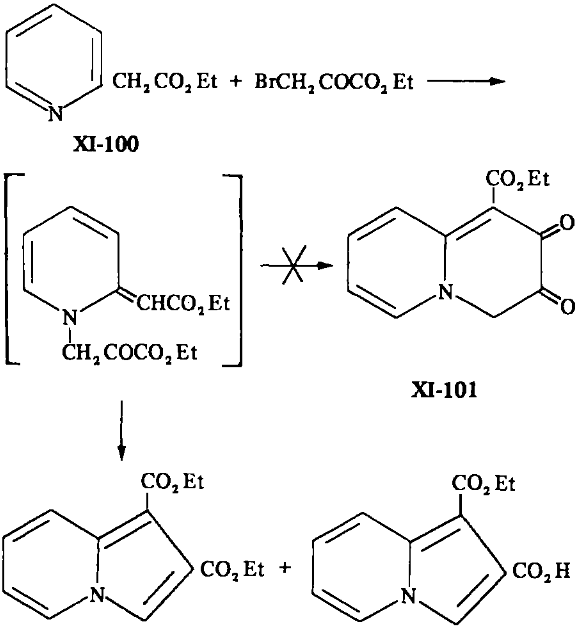




Scheme XI-2



XI-98 **XI-99**



XI-100

XI-101

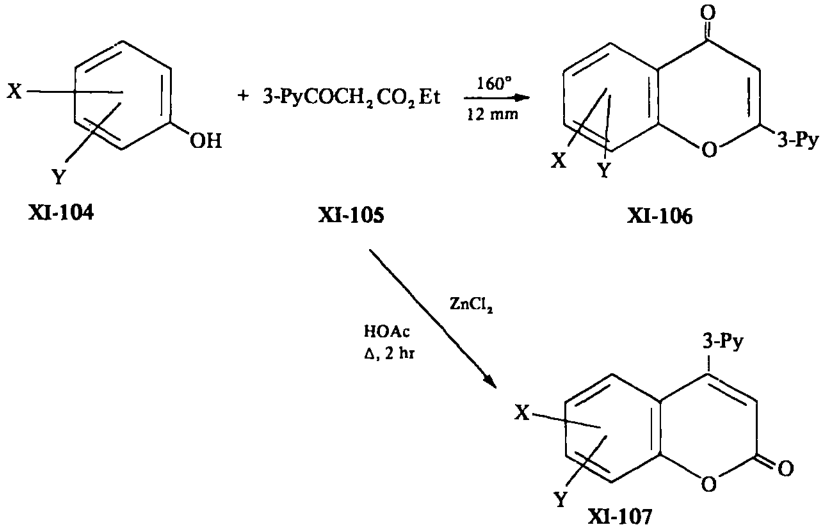
XI-102 + **XI-103**

Initially the quinolizine **XI-101** was thought to be formed in the reaction of ethyl 2-pyridylacetate (**XI-100**) with ethyl bromopyruvate,[146] but it was later shown that indolizines **XI-102** and **XI-103** were actually produced.[144, 147]

Several indolizines were synthesized by cyclizing pyridine side-chain acid derivatives or nitriles in boiling acetic anhydride.[143, 145] Only two indolizidines have been prepared from pyridine side-chain acids.[132, 148]

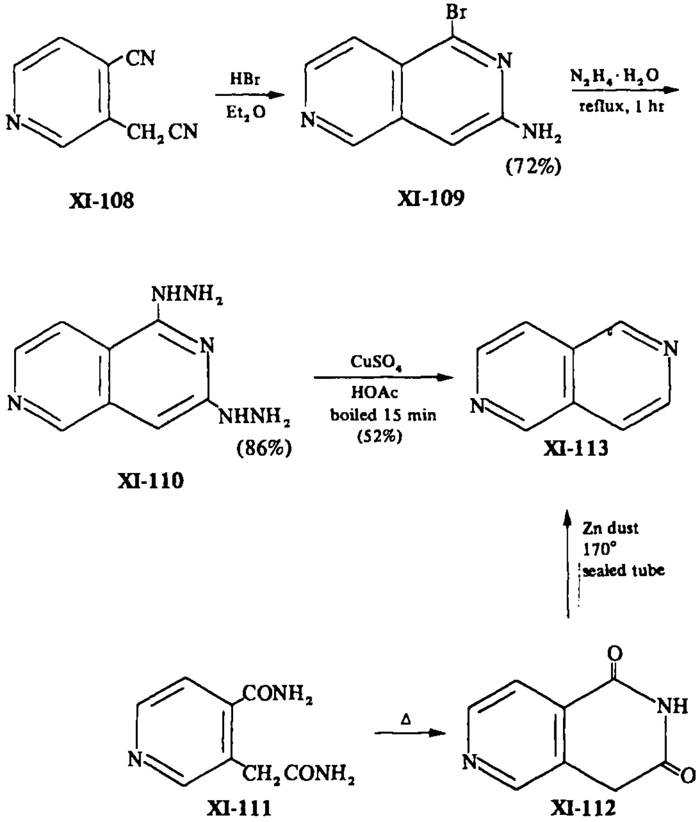
B. *Coumarins and Chromones*

Coumarins and chromones containing pyridine substituents were synthesized from pyridine side-chain acids by employing the Knoevenagel,[48, 49, 149] Pechmann,[16, 149] and Simonis[149] reactions. The chromones **XI-106** were obtained from a Simonis condensation of ethyl nicotinoylacetate (**XI-105**) with a variety of phenols (**XI-104**), whereas a Pechmann condensation yielded the coumarins (**XI-107**).



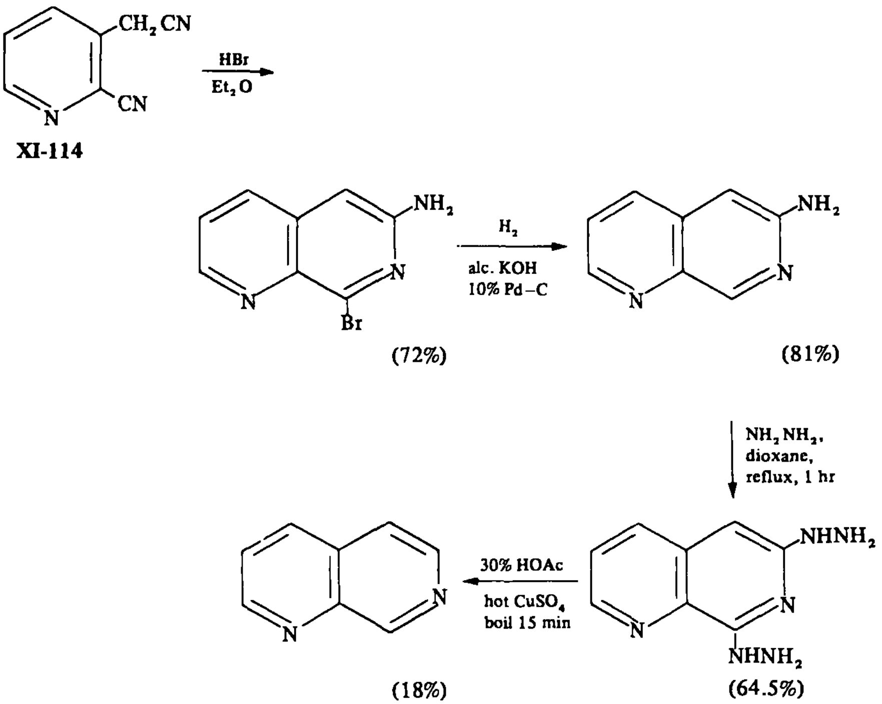
C. *Naphthyridines*

2,6-Naphthyridine (**XI-113**) has been synthesized from pyridine side-chain acids *via* two different routes. Treatment of the dinitrile **XI-108** with anhydrous hydrogen bromide yielded the naphthyridine (**XI-107**). Boiling **XI-109** with hydrazine gave the dihydrazino naphthyridine **XI-110**. The hydrazino groups were removed by treating **XI-110** with copper sulfate in boiling acetic acid to yield 2,6-naphthyridine (**XI-113**).[150] The yields were good and the dinitrile **XI-108** could be obtained by a four-step synthesis from ethyl 3-pyridylacetate. The other route involved cyclizing the diamide **XI-111** to the imide (**XI-112**), which was then reduced to 2,6-naphthyridine (**XI-113**).[128] No yields were reported in this synthesis. The diamide **XI-111** was synthesized in four steps



from 4-carbethoxynicotinic acid. Similarly, 1,7-naphthyridine (**XI-115**) was prepared from the dinitrile (**XI-114**).[92]

Syntheses of 1,5-[151] and 1,6-[152, 153] naphthyridine from pyridine side-chain acids have also been reported.



XI-114

XI-115

III. Functional Derivatives

1. Esters

The esterification of side-chain acids has already been discussed under esterification (Section II.1.).

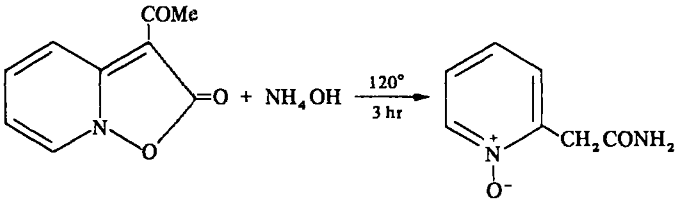
2. Acid Chlorides and Anhydrides

Several acid chlorides have been prepared, usually as intermediates (Table XI-21). Two of these have been characterized, one through its boiling point[128] and one through its hydrochloride salt.[298, 299] As in the earlier review, no anhydrides have been reported.

3. Amides

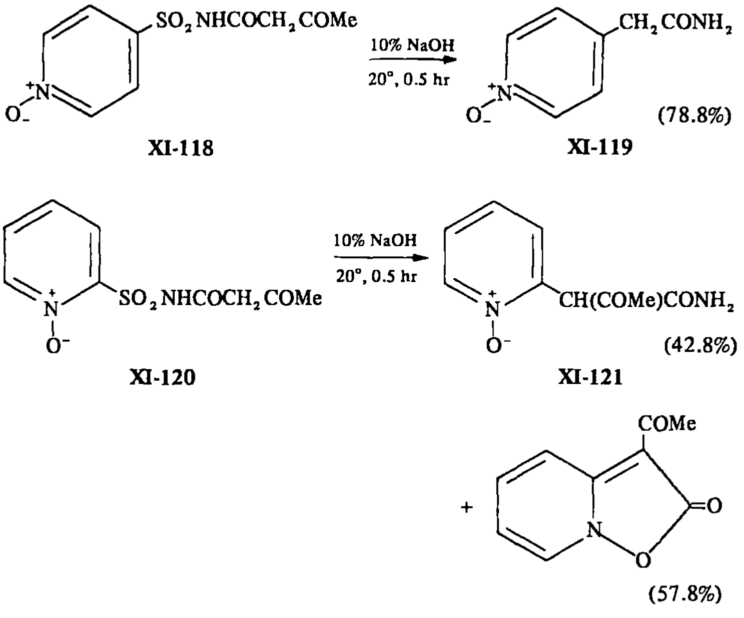
Amides prepared by conventional methods are listed in Tables XI-14 and XI-27.

The pyridine-1-oxide **XI-117** was synthesized by treating compound **XI-116** with ammonium hydroxide.[154] Reaction of the sulfonamide **XI-118** with



XI-116 **XI-117**

sodium hydroxide gave the amide **XI-119**, whereas the 2-isomer **(XI-120)** formed a mixture of the amide **(XI-121)** and **XI-122**.[154] The proposed mechanism for



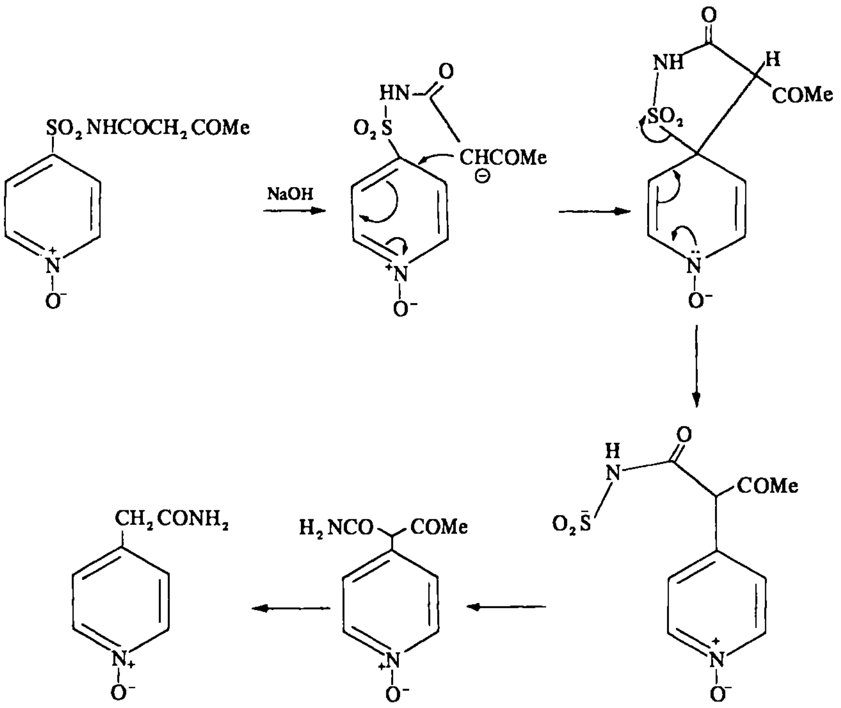
XI-118 **XI-119**

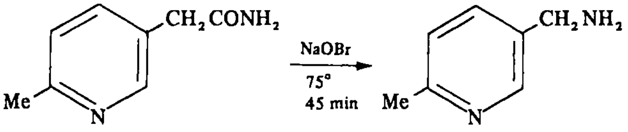
XI-120 **XI-121**

XI-122

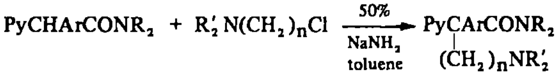
this reaction is the same as that proposed for the rearrangement of nitrophenyl sulfonamides.[155] A few acids have also been prepared by this method.

6-Methyl-3-pyridylacetamide **(XI-123)** was converted to the 3-aminomethylpyridine **(XI-124)** by the Hofmann reaction.[156] Alkylation of the amides **XI-125** with aminoalkyl halides yielded amides containing substituted amino groups **(XI-126)**[157, 158]





XI-123 **XI-124**



$$PyCHArCONR_2 + R'_2N(CH_2)_nCl \xrightarrow[\text{NaNH}_2\ \text{toluene}]{50\%} Py\underset{(CH_2)_nNR'_2}{\underset{|}{C}}ArCONR_2$$

XI-125 XI-126

4. Hydrazides, Hydroxamic Acids, and Amidines

A few hydrazides have been treated with ketones and the resulting acylhydrazones **XI-127** were reduced to yield substituted hydrazides (**XI-128**).[58,159,160] The properties of these hydrazides are listed in Table XI-33.

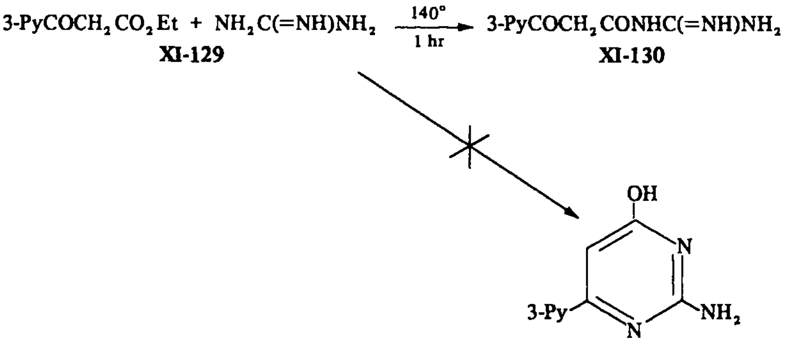
$$\mathrm{Py(CH_2)_nCONHNH_2 + RR'CO \longrightarrow \underset{\textbf{XI-127}}{Py(CH_2)_nCONHN{=}CRR'}}$$

$$\Big\downarrow \mathrm{H_2}$$

$$\mathrm{\underset{\textbf{XI-128}}{Py(CH_2)_nCONHNHCHRR'}}$$

Two examples of the conversion of a hydrazide to an amide through the Curtius reaction have been reported.[8, 291]

The guanidine **XI-130** and not 2-amino-4-hydroxy-6-(3-pyridyl)pyrimidine (**XI-131**) was reportedly formed when the ester **XI-129** was treated with guanidine carbonate at 140°.[161] Treatment of the ester **XI-132** with guanidine gave the substituted guanidine **XI-133** in 85% yield.[162]



XI-129 **XI-130** **XI-131**

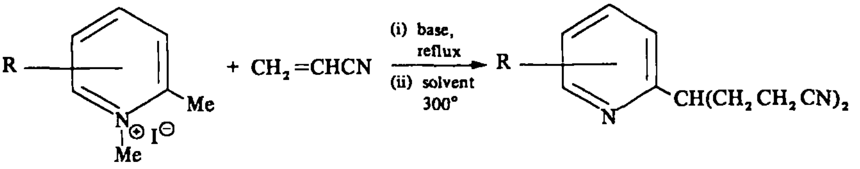
$$\mathrm{\underset{\textbf{XI-132}}{3\text{-}PyCOC({=}NH)CO_2Et} + NH_2C({=}NH)NH_2 \longrightarrow \underset{\textbf{XI-133}}{3\ PyCOC({=}NH)CONHC({=}NH)NH_2}}$$

5. Nitriles

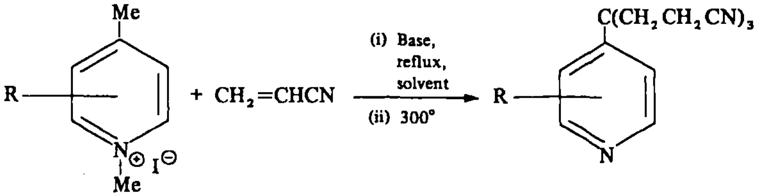
A. *Synthesis*

As reported in the earlier edition, side-chain nitriles have been synthesized by pyridylation of nitriles (Table XI-22), alkylation of pyridylacetonitriles (Table XI-23), employing the Michael addition (Table XI-24), and the Knoevenagel (Table XI-25) and Strecker (Table XI-26) reactions, by the dehydration of amides (Table XI-26), and the nucleophilic displacement of halogens or alkoxyl groups by cyanide (Table XI-26).

In the Michael addition of acrylonitrile to the methiodides of a variety of picolines **(XI-134)** and **(XI-135)**, two molecules of the nitrile added to a C-2 methyl group whereas three molecules added to a C-4 methyl group.[312]

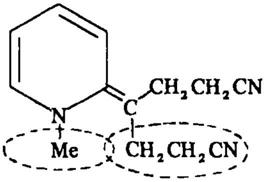


XI-134



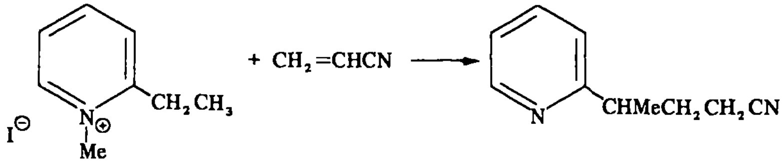
XI-135

Apparently steric hindrance between the C-1 methyl and the cyanoethyl groups in the anhydro base intermediate of the C-2 isomer **XI-136** prevented its formation and therefore the addition of a third molecule of acrylonitrile. No such steric hindrance is present in the C-4 isomer. The same reasoning was



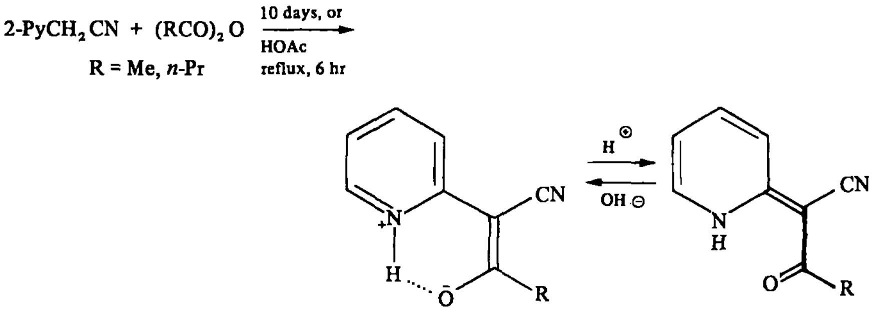
XI-136

employed to explain the addition of only one molecule of acrylonitrile to a C-2 ethyl group in compound **XI-137**.



XI-137

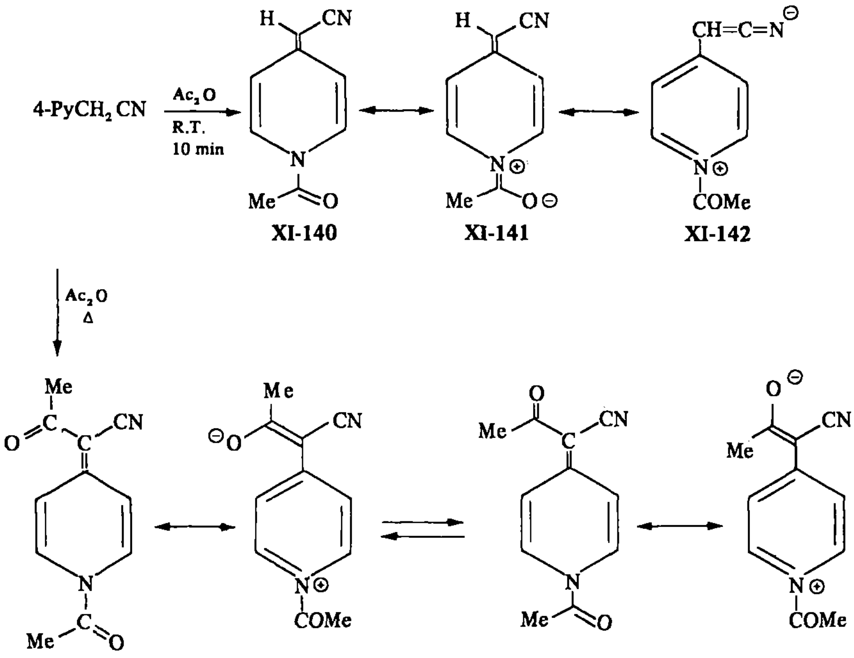
Investigation of the reaction of 2-pyridylacetonitrile with acid anhydrides showed that the α-acylpyridyl acetonitriles formed exist in two pH dependent tautomeric forms **XI-138** and **XI-139**, as determined by uv and nmr spectroscopy.[163] When 4-pyridylacetonitrile was treated with acetic anhydride



$$\underset{R\,=\,Me,\ n\text{-}Pr}{2\text{-}PyCH_2CN + (RCO)_2O} \xrightarrow[\text{HOAc reflux, 6 hr}]{\text{10 days, or}}$$

XI-138 **XI-139**

at room temperature, acylation occurred on the nitrogen rather than on the α-carbon atom to give a compound that appeared to be a resonance hybrid of

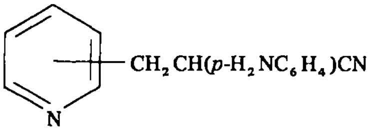


XI-143 **XI-144**

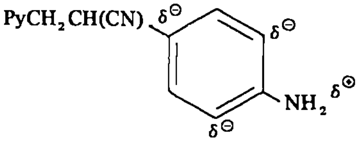
structures **XI-140 - XI-142**. Acylation occurred on both the nitrogen and the α-carbon atoms to give a mixture of tautomers **XI-143** and **XI-144** when the reation mixture was heated.

B. *Solvolysis and Aminolysis* (Table XI-27)

The α-(*p*-aminophenyl)-β-pyridylpropionitriles (**XI-145**) proved difficult to hydrolyze to the corresponding acids.[164] This lack of reactivity is probably caused by the effect of the polarizability of the amino group on the methine hydrogen atom alpha to the nitrile group, which would allow charged complex formation with polar reagents. Also, there is the tendency for the *p*-amino group to localize partial negative charges at the C-1, C-3, and C-5 positions of the aromatic ring (see **XI-146**), which would reduce the usual charge distribution over the arylacetonitrile group. The C-3 and C-4 isomers of **XI-145** were successfully hydrolyzed by first forming the esters in the presence of hydrogen chloride (through the imino ether dihydrochloride) and then hydrolyzing the ester with base. An attempt to hydrolyze nitrile **XI-147** failed. Nitrile **XI-148** could be hydrolyzed and dehydrated by acid to give the amide **XI-149** but this could not be further hydrolyzed to the acid **XI-150**.[99]



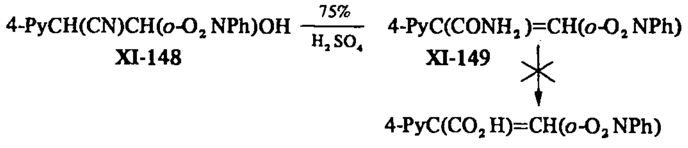
XI-145



XI-146

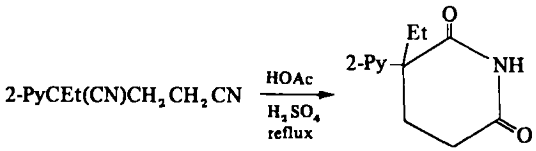
$4\text{-}PyCH(CN)CO(CH_2)_3CO_2Et$

XI-147

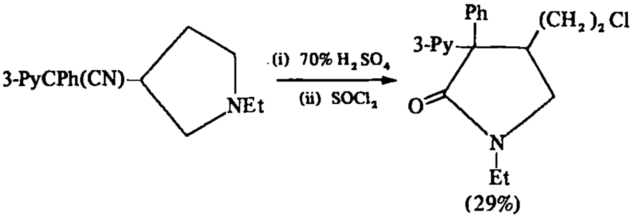


$$\begin{array}{ccc} 4\text{-}PyCH(CN)CH(o\text{-}O_2NPh)OH & \xrightarrow[H_2SO_4]{75\%} & 4\text{-}PyC(CONH_2)\text{=}CH(o\text{-}O_2NPh) \\ \textbf{XI-148} & & \textbf{XI-149} \\ & & \not\downarrow \\ & & 4\text{-}PyC(CO_2H)\text{=}CH(o\text{-}O_2NPh) \\ & & \textbf{XI-150} \end{array}$$

Acid hydrolysis of 1,3-dicyano-3-(2-pyridyl)hexane (**XI-151**) resulted in cyclization to the imide **XI-152**.[178] Lactam **XI-154** was isolated from the hydrolysis of nitrile **XI-153** followed by treatment with thionyl chloride.[57] The

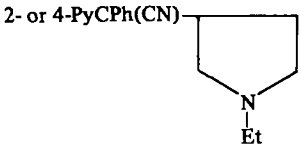


XI-151 **XI-152**



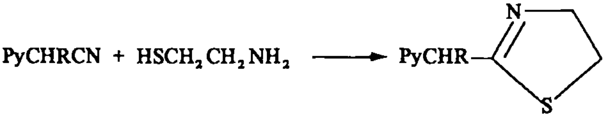
XI-153 **XI-154**

acids obtained from nitriles **XI-155** were found to decarboxylate readily during the hydrolyses.[50]

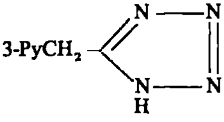


XI-155

Several thioamides have been prepared by treating nitriles with hydrogen sulfide.[166-168] A few Δ^2-thiazoline derivatives (**XI-156**) have been isolated from the reaction of pyridylacetonitriles with 2-aminoethyl thiol.[168] 3-Pyridylacetonitrile was converted to the tetrazole **XI-157** by treatment with boiling butanol-acetic acid followed by sodium azide.[169]



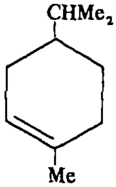
XI-156



XI-157

C. *Reduction* (Table XI-28)

The reduction of 3-pyridylacetonitrile and 3-pyridylacrylonitrile using Δ^1-*p*-menthene (**XI-158**) as the hydrogen source and 10% palladium-on-carbon as the catalyst yielded 3-ethylpyridine and 3-propylpyridine, respectively (yields 85–95%).[170]



XI-158

D. *Reactions with Organometallic Compounds*

These reactions and the products obtained are summarized in Table XI-29.

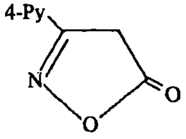
IV. Derivatives with Side-Chains of Mixed Function

1. Carbonyl Derivatives (Table XI-30)

Treatment of the keto ester **XI-159** with hydroxylamine yielded 3-(4-pyridyl)isoxazol-5-one (**XI-160**) rather than the expected oxime.[105]

$(4\text{-}PyCOCHCO_2Et)_2CHPh + NH_2OH$

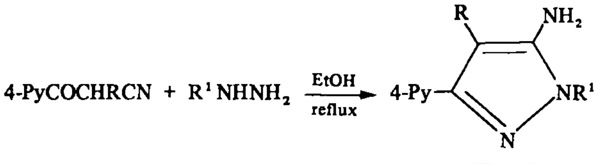
XI-159



XI-160

3-(γ-Pyridyl)-5-aminopyrazoles (**XI-162**) were synthesized by treating the 4-pyridyl-β-ketonitriles (**XI-161**) with substituted hydrazines.[171] No yields were reported.

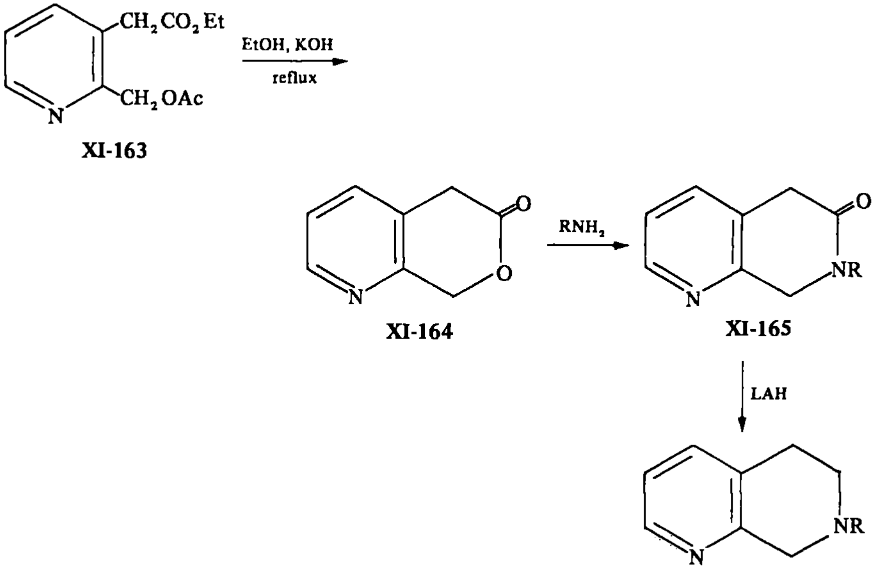
Keto esters have also been employed in the synthesis of a wide variety of condensed heterocycles. These reactions have already been discussed under Section II.6. and recorded in Table XI-20.



XI-161 **XI-162**

2. Hydroxyl Derivatives

Hydroxyl derivatives have been employed to synthesize indenones[172] and quinolines[87, 173] (Table XI-20). The lactone **XI-164**, obtained from ester **XI-163**, was converted to a variety of *N*-substituted lactams (**XI-165**), which were then reduced to the tetrahydronaphthyridines (**XI-166**)[174] (Table XI-20).



XI-163 **XI-164** **XI-165** **XI-166**

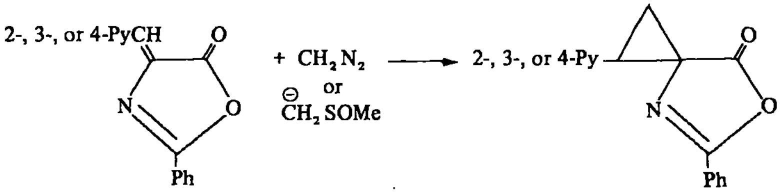
3. Ethylenic Derivatives

A. *Syntheses*

These are summarized in Table XI-31.

B. *Reactions* (Table XI-32)

The cyclopropanes **XI-168** were obtained when the unsaturated side-chain lactones **XI-167** were treated either with diazomethane or with the dimsyl anion.[94]



XI-167 **XI-168**

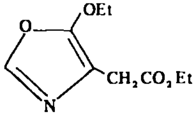
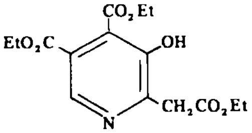
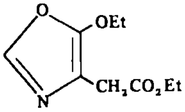
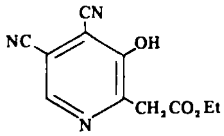
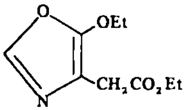
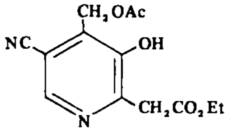
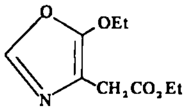
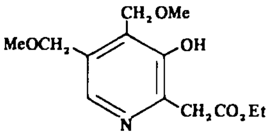
4. Displacement of Side-Chain Substituents

The chlorine atoms of a mixture of compounds **XI-169** and **XI-170** were displaced by amines to yield the enamines **XI-171**.[175]

$$\underset{\textbf{XI-169}}{3\text{-PyCCl=CHCO}_2\text{Et}} + \underset{\textbf{XI-170}}{3\text{-PyCCl}_2\text{CH}_2\text{CO}_2\text{Et}} \xrightarrow{R_2NH} \underset{\textbf{XI-171}}{3\text{-PyC(NR}_2\text{)=CHCO}_2\text{Et}}$$

V. Tables

TABLE XI-1. Preparation of Side-Chain Acids From Nonpyridine Starting Materials

Starting materials	Conditions	Product	Yield	Properties	Ref.
$EtO_2CCH{=}CHCO_2Et$ + 	3 hr, 30°, N_2; anhyd HCl, EtOH			hydrochloride, m.p. 124-125°	69
$NCCH{=}CHCN$ + 	same as above			m.p. 164-166°	69
$AcOCH_2CH{=}CHCN$ + 	same as above			m.p. 118-120°	69
$MeOCH_2CH{=}CHCH_2OMe$ + 	same as above			m.p. 139-142°	69

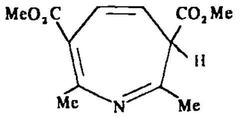
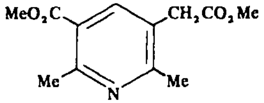
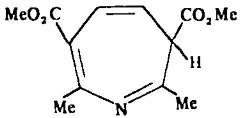
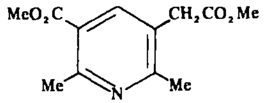
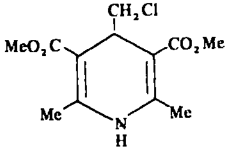
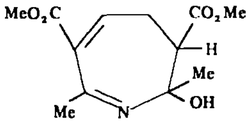
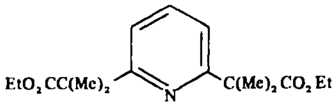
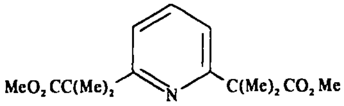
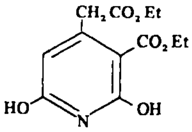
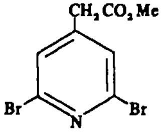
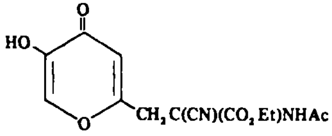
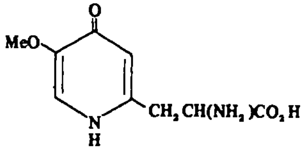
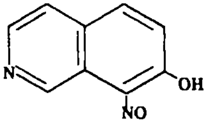
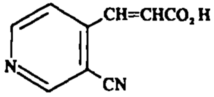
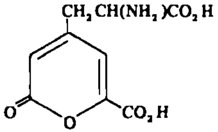
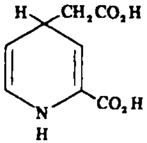
	Conc H_2SO_4, 15 min, steam-bath *or* NaOH, MeOH, reflux 2 hr		72% 78%	m.p. 57.5–58.5°; ir, uv, NMR	70
	MeOH, HCl, R.T., 19 hr	 +  + 			70
2 $EtO_2CC(Me)_2Br + NC(CH_2)_3CO_2Et$ or $NC(CH_2)_3CO_2Me$	Zn			b.p. 174–175°/15 mm; m.p. 58–60°	179, 180
2 $MeO_2CC(Me)_2Br + NC(CH_2)_3CO_2Et$	Zn			b.p. 171–172°/15 mm; m.p. 63–65°	179

TABLE XI-1. Preparation of Side-Chain Acids From Nonpyridine Starting Materials (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
$EtO_2CCH_2COCH_2CO_2Et + NCCH_2CO_2Et$	$EtNH_2$, EtOH, 7 days; overnight. conc. H_2SO_4		2.5 g (nitrile) ↓ 1.4 g		181
$NCCH_2C(OH)(CH_2CN)_2$	30% HBr, HOAc, 1.5 hr; $NaHCO_3$; MeOH, R.T., 1.5 hr; reflux 1 hr				182
	NH_4OH, sealed bomb, 85-90°, 2.5 hr; $Ba(OH)_2$, H_2O, reflux several hr		29 g ↓ 14 g	m.p. 252-255° (decomp.) uv	71
 + $PhSO_2Cl$	NaOH, acetone-H_2O, 55-60°, 10 min		40%	m.p. 232.4-232.8° (decomp.)	72
 Stizolobic Acid	conc. HCl, reflux			uv	76

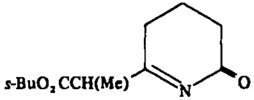
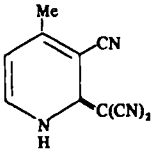
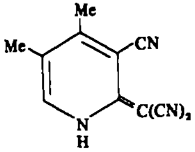
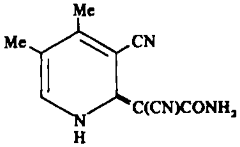
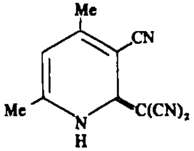
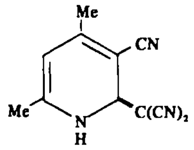
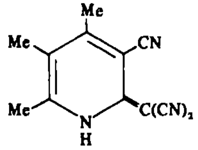
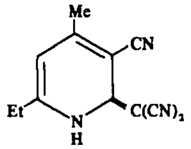
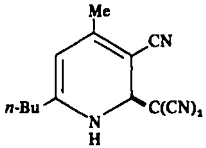
$MeCH(Br)CO_2$ s-Bu + $NC(CH_2)_3CO_2Me$	Zn				180
$MeNHCH{=}CHAc + NCCH_2C(NH_2){=}C(CN)_2$	boil 15 min, EtOH, pyridine		1 g (ketone) ↓ 1.3 g	m.p. 225° (decomp.)	183
$NH_2CH{=}C(Me)Ac + NCCH_2C(NH_2){=}C(CN)_2$	boil 15 min, HOAc		0.7 g (ketone) ↓ 0.3 g	m.p. 238° (decomp.)	183
$MeNHCH{=}C(Me)Ac + NCCH_2C(NH_2){=}C(CN)_2$	HOAc				153
$MeCOCH_2COMe + NCCH_2C(NH_2){=}C(CN)_2$	10% aq. NaOH, 10 min or Na, EtOH, reflux 2 min		0.5 g (nitrile) ↓ 1 g		184

TABLE XI-1. Preparation of Side-Chain Acids From Nonpyridine Starting Materials (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
$NH_2COC(Me)=CHCOMe + NCCH_2C(NH_2)=C(CN)_2$	24 hr, H_2O, or reflux 10 min, HOAc		0.6 g (nitrile) ↓ 0.5 g	m.p. 255°	183
$NH_2COC(Me)=C(Me)COMe$ + $NCCH_2C(NH_2)=C(CN)_2$	same as above			m.p. 246° (decomp)	184
$NH_2COC(Et)=CHCOMe + NCCH_2C(NH_2)=C(CN)_2$	same as above			m.p. 224–225°	184
$NH_2COC(n\text{-}Bu)=CHCOMe + NCCH_2C(NH_2)=C(CN)_2$	same as above			m.p. 224°	184

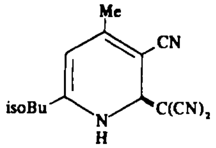
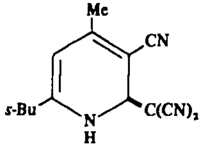
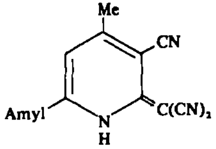
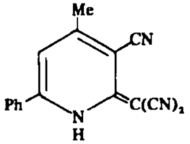
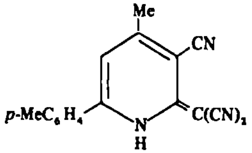
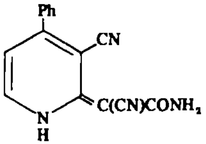
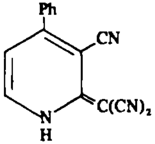
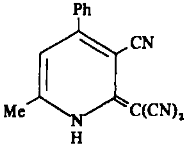
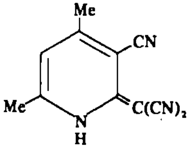
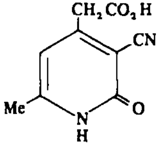
$NH_2COC(isoBu)=CHCOMe$ + $NCCH_2C(NH_2)=C(CN)_2$	same as above		m.p. 226°	184
$NH_2COC(s\text{-}Bu)=CHCOMe$ + $NCCH_2C(NH_2)=C(CN)_2$	same as above		m.p. 205°	184
$NH_2COC(Amyl)=CHCOMe$ + $NCCH_2C(NH_2)=C(CN)_2$	same as above		m.p.192°	184
$NH_2COC(Ph)=CHCOMe$ + $NCCH_2C(NH_2)=C(CN)_2$	same as above		m.p. 227° (decomp)	184
$NH_2COC(p\text{-}MeC_6H_4)=CHCOMe$ + $NCCH_2C(NH_2)=C(CN)_2$	same as above		m.p. 227° (decomp)	184

TABLE XI-1. Preparation of Side-Chain Acids From Nonpyridine Starting Materials (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
$MeNHCH{=}CHCOPh + NCCH_2C(NH_2){=}C(CN)_2$	HOAc			m.p. 330° (decomp)	153
$MeNHCH{=}CHCOPh + NCCH_2C(NH_2){=}C(CN)_2$	boil 15 min, EtOH, pyridine		1 g (ketone) ↓ 0.4 g	m.p. 238°	183
$MeNHC(Me){=}CHCOPh + NCCH_2C(NH_2){=}C(CN)_2$	same as above		0.9 g (ketone) ↓ 0.3 g	m.p. 230° (decomp)	183
$PhCH_2NHC(Me){=}CHAc + NCCH_2C(NH_2){=}C(CN)_2$	same as above			m.p. 255°	183
$Me_2CO + (CO_2Et)_2 + NH_2COCH_2CN$	Na, MeOH, PhMe; 20% H_2SO_4			m.p. 228°	185

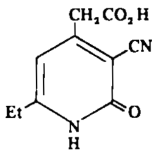
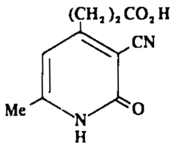
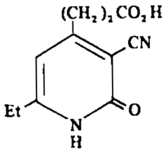
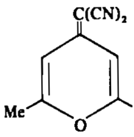
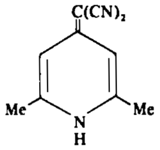
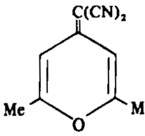
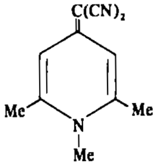
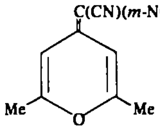
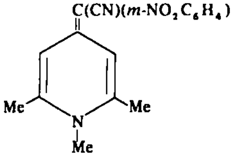
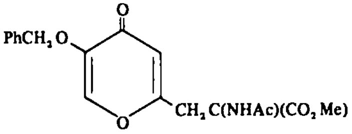
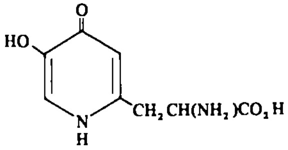
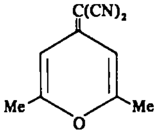
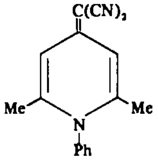
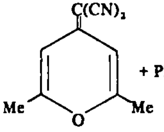
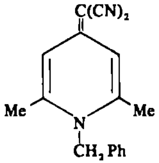
EtCOMe + $(CO_2Et)_2$ + NH_2COCH_2CN	same as above		58%	m.p. 205°	185
Me_2CO + $CH_2(CO_2Et)_2$ + NH_2COCH_2CN	same as above			m.p. 217°	185
EtCOMe + $CH_2(CO_2Et)_2$ + NH_2COCH_2CN	same as above			m.p. 211°	185
 + $HCONH_2$	1 hr, 150°		5 g ↓ 1.7 g	m.p. 330–331°	186
 + $MeNH_2$	EtOH, reflux 30 min			m.p. 225–228°	361

TABLE XI-1. Preparation of Side-Chain Acids From Nonpyridine Starting Materials (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
 + $MeNH_2$	same as above				361
	NH_3, 100° sealed tube, 2 hr; 4 *N* H_2SO_4, reflux 8 hr	 *DL*-	41.6%		187
 + $PhNH_2$			20%	m.p. 314-315°	186, 188
 + $PhCH_2NH_2$			34%	m.p. 242-245°	186, 188

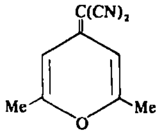
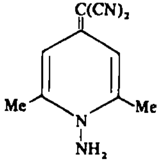
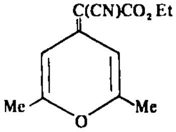
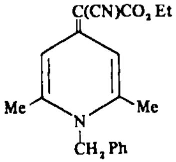
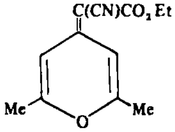
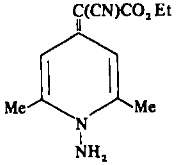
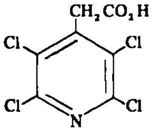
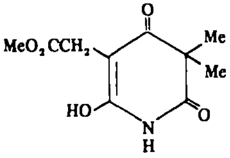
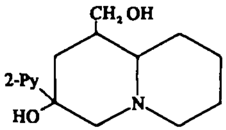
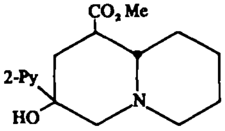
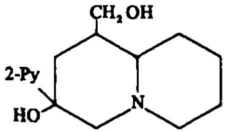
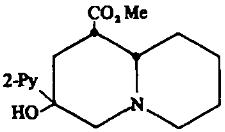
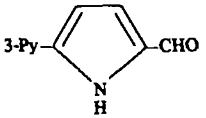
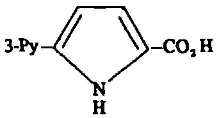
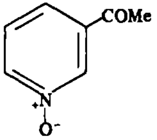
 + $NH_2NH_2 \cdot H_2O$			40%	m.p. 291-292°	186, 188
 + $PhCH_2NH_2$			80%	m.p. 183-184°	186, 188
 + $NH_2NH_2 \cdot H_2O$			71%	m.p. 217-218°	186, 188
$NH_2COC(Cl)=C(Cl)C(Cl)=CCl_2$	PCl_5, C_6H_6, boil 3-4 hr; 160-180°, 6 hr; Na, $CH_2(CO_2Et)_2$, EtOH, boil 20 hr		20 g ↓ 12 g	m.p. 178-180° (decomp)	366
$EtO_2CCH(CO_2Et)COCMe_2CN$	HOAc, 80% H_2SO_4, 90°, 2.3 hr; Na, $BrCH_2CO_2Me$, MeOH, boil 10 hr		3.8 g ↓ 2.4 g	m.p. 130-131°	347

TABLE XI-2. Preparation of Side-Chain Acids by Oxidation

Starting material	Oxidant	Conditions	Product	Yield	Properties	Ref.
2-Py$(CH_2)_2CH{=}CH_2$	$KMnO_4$	acetone, < 35°	2-Py$(CH_2)_2CO_2H$	52%	m.p. 140–141°	189
2-Py$(CH_2)_4CH{=}CH_2$	$KMnO_4$	acetone, < 35°	2-Py$(CH_2)_4CO_2H$	53.5%	m.p. 96.5°	189
	Chromic acid	3 hr, 100°; MeOH, HCl, reflux 1 hr		50%	b.p. 140–190°/0.05 mm	19
	Chromic acid	3 hr, 100°; MeOH, HCl, reflux 4 hr		0.5 g ↓ 0.4 g	b.p. 160–165°/0.02 mm	19
	$AgNO_3$	NaOH, 50% EtOH, 60–65°, H_2O, 4 hr		60%	m.p. 200–201° (decomp)	102
2-Py$(CH_2)_2CHO$			2-Py$(CH_2)_2CO_2H$			189
2-Py$(CH_2)_4CHO$			2-Py$(CH_2)_4CO_2H$			189
	SeO_2	Py, 80°, 105 min	3-Py$COCO_2H$	44%	m.p. 178–179°; phenylhydrazone, m.p. 173–174°; 2,4-DNP, m.p. 255–256°	218

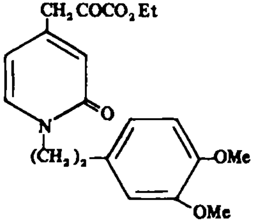
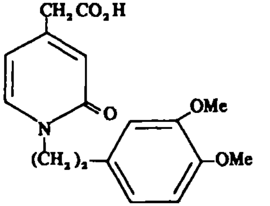
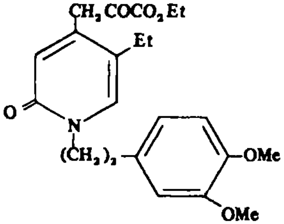
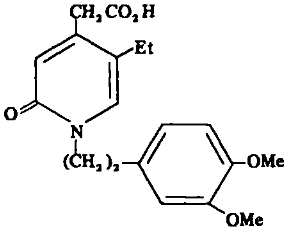
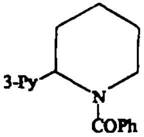
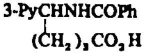
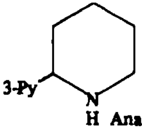
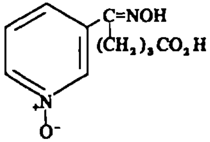
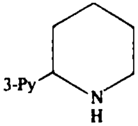
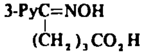
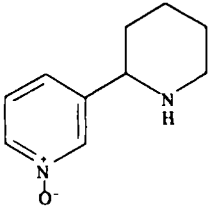
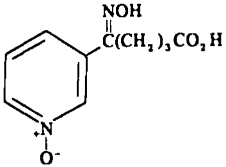
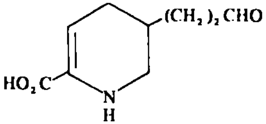
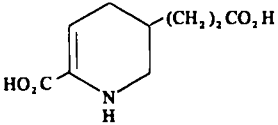
3-PyCOMe	SeO_2	Py, 80°, 120 min	3-PyCOCO$_2$H	69%		218
	MnO_2, H_2O_2	dil. alkali, 0°; oxidant, 16 hr, 0°		78%	m.p. 156.5-157° (decomp.)	3
	MnO_2	10% aq. NaOH		76.5%	hydrochloride, m.p. 160.5-162.5°	4
	$KMnO_4$		 $\underset{(CH_2)_3CO_2H}{\text{3-PyCHNHCOPh}}$	22%	m.p. 145-146°; $[\alpha]_D^{21}$ 9.5°	75
 Anabasine	34% H_2O_2	HOAc, 70-80°, 24 hr			m.p. 229-231° (decomp.)	75

TABLE XI-2. Preparation of Side-Chain Acids by Oxidation (Continued)

Starting material	Oxidant	Conditions	Product	Yield	Properties	Ref.
	10% H_2O_2	R.T., 8 days	 $\text{3-PyC}(=\text{NOH})(CH_2)_3CO_2H$		m.p. 161-163°	75
	H_2O_2	HOAc, 65-80°, 11 hr			m.p. 229-231° (decomp)	190
	*Pseudomonas fluorescens* dehydrogenase					73

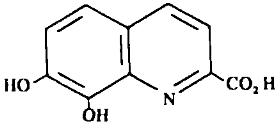
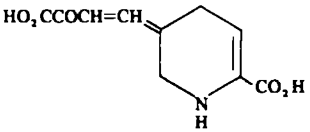
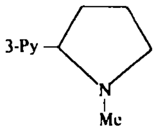
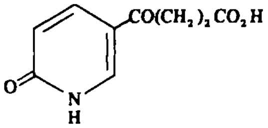
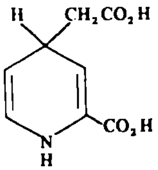
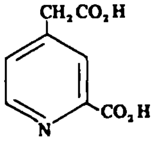
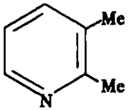
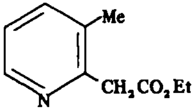
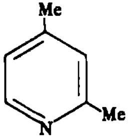
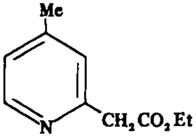
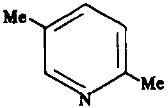
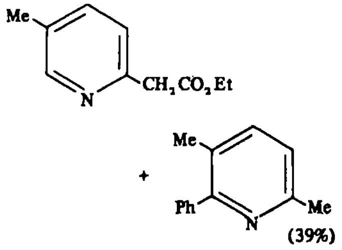
	oxygenase				73
 nicotine	mature resting cell enzyme in *A nicotinophagum*				74
4-$PyCH_2CO_2Me$	SeO_2	HOAc, benzene, reflux 30 min	4-$PyC(OH)_2CO_2Me$	b.p. 150°/3 mm, m.p. 114-118°	31 32
	O_2	acid, boil			76

TABLE XI-3. Carbonation of Organometallic Compounds

Starting materials	Conditions	Product	Yield	Properties	Ref.
2-PyMe	PhNa, PhMe, 1 hr, 35°; CO_2, Et_2O; EtOH, H_2SO_4, reflux 3 hr or	2-PyCH_2CO_2Et	46.5 g ↓ 41.5 g	b.p. 119-122°/12 mm; picrate, m.p. 139°	77
	PhBr, Li, reflux Et_2O, 30 min, dry ice; EtOH, HCl		139.7 g ↓ 83.1 g	b.p. 109-112°/6 mm	66
	PhLi, dry ice; $Br(CH_2)_2OH$, R.T., 4.5 days	$2\text{-PyCH}_2CO_2(CH_2)_2Br$		picrate, m.p. 126-128°	191
	PhLi, Et_2O, 30 min; CO_2; EtOH, HCl, 24 hr, R.T.		33-34%	b.p. 141-145°/18 mm; picrate, m.p. 125.5-126.5°	78
	same as above			b.p. 142-146°/17 mm; m.p. 130-131°; picrolonate, m.p. 165-166°	78
	same as above		56%	b.p. 100-105°/2 mm; picrate, m.p. 136-137°	78

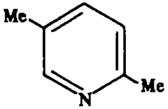
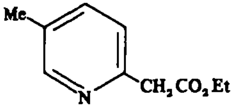
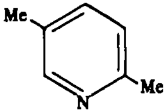
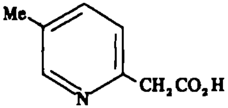
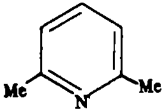
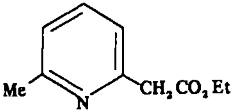
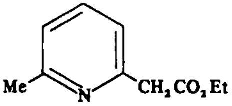
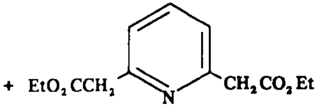
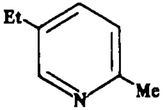
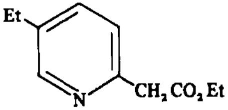
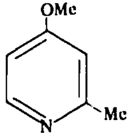
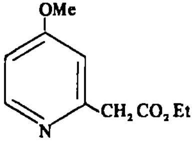
	PhLi, Et_2NH, Et_2O; CO_2; EtOH, HCl		53.5 g ↓ 5 g		78
	PhLi, CO_2				192
	PhLi, Et_2O, 30 min; CO_2; EtOH, HCl, 24 hr, R.T.			b.p. 130–132°/15 mm; picrate, m.p. 105–107°	78
	PhNa, PhMe, 1 hr, 35°; CO_2, Et_2O; EtOH, H_2SO_4, reflux 3 hr	 (1) 58.5 g → 37 g  (2) 1.9 g		(1) b.p. 98–102°/5 mm; picrate, m.p. 80–81° (2) b.p. 158–160°/5 mm; picrate, m.p. 82°	77
	same as above		121 g ↓ 122 g	b.p. 140–142°/0.9 mm; picrate, m.p. 143–144°	77

TABLE XI-3. Carbonation of Organometallic Compounds (Continued)

Starting material	Conditions	Product	Yield	Properties	Ref.
	PhLi, PhBr, Et_2O, dry ice, overnight; EtOH; HCl, 10 hr, R.T.		44 g ↓ 20.8 g	b.p. 94.0–94.5°/0.5 mm; n_D^{21} 1.5038; picrate, m.p. 156–158°; ir	193
2-PyEt	PhLi, Et_2O, 30 min; CO_2; EtOH, HCl, 24 hr, R.T.	2-PyCH(Me)CO_2Et		b.p. 124-127°/13 mm	78
2-Py$(CH_2)_4$C≡CH	$NaNH_2$, Et_2O, N_2, overnight; CO_2, 3 hr, R.T.	2-Py$(CH_2)_4$C≡CCO_2H	55.6%	m.p. 95°, 130°; hydrochloride, m.p. 109–110°, 107–109°; picrate, m.p. 97°; ir	80, 81
2-Py$(CH_2)_5$C≡CH	same as above	2-Py$(CH_2)_5$C≡CCO_2H	72%	m.p. 95°, hydrochloride, m.p. 109–110°; ir	80
2-Py$(CH_2)_{10}$C≡CH	$NaNH_2$, NH_3, Et_2O, reflux 7 hr; CO_2, R.T., overnight; Et_2O, reflux several hr	2-Py$(CH_2)_{10}$C≡CCO_2H	80%	m.p. 87°; hydrochloride, m.p. 97–98°; picrate, m.p. 68°; ir	80, 81
2-PyC(Me)(OH)C≡CH	$NaNH_2$, CO_2; MeOH	2-PyC(Me)(OH)C≡CCO_2Me		m.p. 102–104°	79

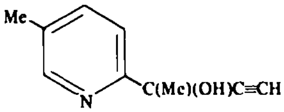
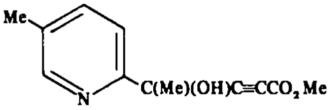
	same as above			m.p. 115–117°	79
3-PyCH(Ph)$_2$	[Ph$_2$Li]Na, CO$_2$, Et$_2$O, N$_2$	3-PyC(CO$_2$H)(Ph)$_2$		m.p. 113–114° (decomp)	194
(3-Py)$_2$CHPh	same as above	(3-Py)$_2$C(Ph)CO$_2$H	40%	unstable	194
4-PyMe	PhNa, PhMe, 1 hr, 35°; CO$_2$, Et$_2$O; EtOH, H$_2$SO$_4$, reflux 3 hr	4-PyCH$_2$CO$_2$Et	46.5 g ↓ 33.5 g	b.p. 129–132°/12 mm; picrate, m.p. 122°	77
4-Py(CH$_2$)$_4$C≡CH	NaNH$_2$, NH$_3$, Et$_2$O; reflux 7 hr; CO$_2$, R.T. overnight; Et$_2$O, reflux several hr	4-Py(CH$_2$)$_4$C≡CCO$_2$H	70%	m.p. 235°; hydrochloride, m.p. 187°; picrate, m.p. 100–101°; ir	80, 81
4-Py(CH$_2$)$_5$C≡CH	same as above	4-Py(CH$_2$)$_5$C≡CCO$_2$H	71%	m.p. 139–140°; picrate, m.p. 103–104°; ir	80

TABLE XI-4. Arndt-Eistert Synthesis

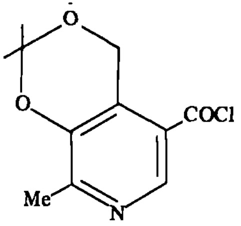
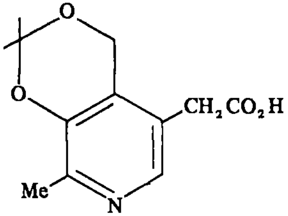
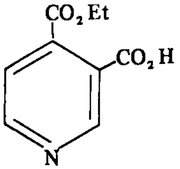
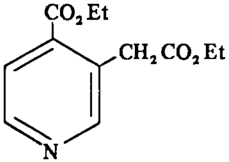
Starting materials	Conditions	Product	Yield	Properties	Ref.
	CH_2N_2, conc. HCl, Et_2O, R.T., overnight; Ag_2O, Na_2CO_3, 50–60°, aq. sodium thiosulfate		22%	m.p. 186–187° (decomp.); ir, nmr	195
	$SOCl_2$; CH_2N_2; Ag_2O abs. EtOH			b.p. 116–117°/0.05 mm; picrate, m.p. 104–106°	128

TABLE XI-5. Condensation of Halopyridines with Active Methylene Compounds

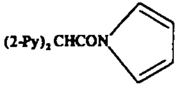
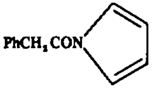
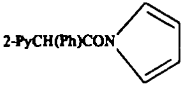
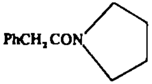
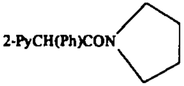
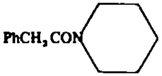
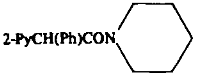
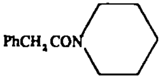
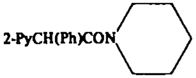
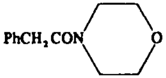
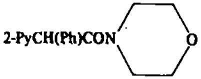
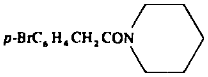
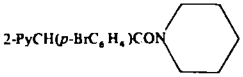
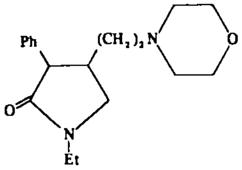
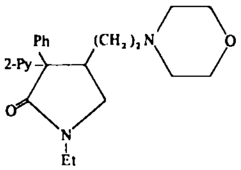
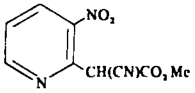
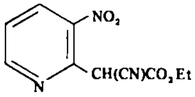
Halide	Active methylene compound	Conditions	Product	Yield	Properties	Ref.
2-PyBr	$PhCH_2CONMe_2$	$NaNH_2$, PhMe, reflux 2 hr	2-PyCH(Ph)$CONMe_2$	57%	m.p. 92–93.5°	82, 158
2-PyBr		same as above			b.p. 220–225°/3 mm; m.p. 103–104°	158
2-PyBr		same as above			m.p. 107–109°	158
2-PyBr	$PhCH_2CONEt_2$	same as above	2-PyCH(Ph)$CONEt_2$	50%	b.p. 185–190°/1.0 mm; m.p. 63–64.5°	82
2-PyBr	$PhCH_2CON(isoPr)_2$	same as above	2-PyCH(Ph)CON$(isoPr)_2$	45%	m.p. 104–106°	82
2-PyBr		same as above		55%	m.p. 108.5–110°	82
2-PyBr		same as above		71%	b.p. 195–197°/0.4 mm; m.p. 72.5–73.5°	82
2-PyCl		same as above		66%		82
2-PyBr		same as above		51%	b.p. 195–198°/0.4 mm; m.p. 84–85.5°	82

TABLE XI-5. Condensation of Halopyridines with Active Methylene Compounds (Continued)

Halide	Active methylene compound	Conditions	Product	Yield	Properties	Ref.
2-PyBr	$PhCH_2CON(Me)Ph$	same as above	2-PyCH(Ph)CON(Me)Ph	41%	m.p. 97–98.5°	82
2-PyBr	p-$ClC_6H_4CH_2CONMe_2$	same as above	2-PyCH(p-ClC_6H_4)$CONMe_2$	80%	b.p. 180–205°/0.2 mm; m.p. 75–76.5°	82
2-PyBr	p-$ClC_6H_4CH_2CONEt_2$	same as above	2-PyCH(p-ClC_6H_4)$CONEt_2$	70%	m.p. 69.5–70°	82
2-PyBr	p-$BrC_6H_4CH_2CONEt_2$	same as above	2-PyCH(p-BrC_6H_4)$CONEt_2$		b.p. 190–200°/1.0 mm	82
2-PyBr	p-$BrC_6H_4CH_2CON$ 	same as above	2-PyCH(p-BrC_6H_4)CON 		b.p. 210–220°/1.0 mm	82
2-PyBr	p-$MeC_6H_4CH_2CONMe_2$	same as above	2-PyCH(p-MeC_6H_4)$CONMe_2$		b.p. 180–185°/1.0 mm	82
2-PyBr	(α-naphthyl)CH_2CONEt_2	same as above	2-PyCH(α-naphthyl)$CONEt_2$	59%	m.p. 165.5–166°	82
2-PyBr		$NaNH_2$, PhMe		27%	m.p. 91–92°; hydrochloride hydrate, m.p. 230°	50
2-Cl-3-NO_2Py	$NCCH_2CO_2Me$	$Me_3CO^{\ominus}K^{\oplus}$, Me_3COH, reflux 5–12 hr		82%	m.p. 186–188°	84
2-Cl-3-NO_2Py	$NCCH_2CO_2Et$	same as above		87%	m.p. 136–137°	84

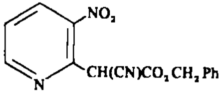
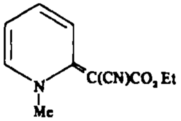
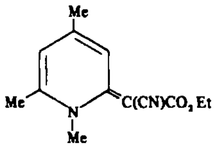
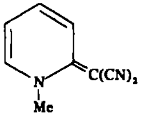
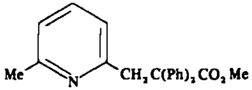
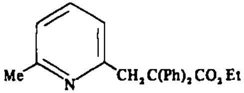
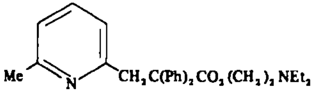
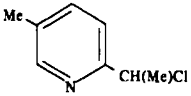
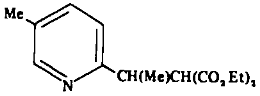
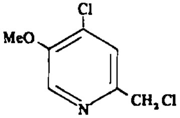
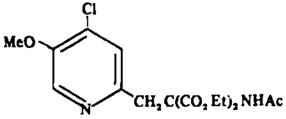
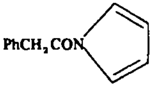
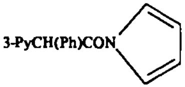
2-Cl-3-NO_2Py	$NCCH_2CO_2CH_2Ph$	same as above		52%	m.p. 141–142°	84
2-Bromo-1-methylpyridinium perchlorate	$CH_2(CN)CO_2Et$	NaOEt, EtOH, reflux 30 min–1 hr		24.5%	m.p. 127.5–128°; uv	83
2-chloro-1,4,6-trimethyl-pyridinium perchlorate	$CH_2(CN)CO_2Et$	same as above		43.5%	m.p. 120–121°; uv	83
1-methyl-2-phenoxy-pyridinium iodide	$CH_2(CN)_2$	same as above		66%	m.p. 203.5–204.5°; uv	83
2-$PyCH_2Cl$	$(Ph)_2CHCO_2Me$	xylene	2-$PyCH_2C(Ph)_2CO_2Me$		m.p. 71–73°; hydrochloride, m.p. 165–168°	51
	$(Ph)_2CHCO_2Et$	xylene	2-$PyCH_2C(Ph)_2CO_2Et$		hydrochloride, m.p. 210–213° (decomp.)	51
2-$PyCH_2Br$	$CH_2(CO_2Et)_2$	reflux 1 hr	2-$PyCH_2CH(CO_2Et)_2$	80.5%	b.p. 132–133°/2.5 mm	143
	$CH_2(Ac)CO_2Et$	reflux 1 hr	2-$PyCH_2CH(Ac)CO_2Et$	43.5%	b.p. 97–99°/0.2 mm	143
	$CH_2(Ac)CO_2Me$	reflux 1 hr	2-$PyCH_2CH(Ac)CO_2Me$			143
	$PhCH_2CN$	$NaNH_2$, PhMe, R.T. 18 hr	(a) 2-$PyCH_2CH(Ph)CN$ + (b) (2-$PyCH_2)_2C(Ph)CN$		(a) m.p. 53° (b) b.p. 220–223°/0.6 mm; m.p. 80–81°	143

TABLE XI-5. Condensation of Halopyridines with Active Methylene Compounds (Continued)

Halide	Active methylene compound	Conditions	Product	Yield	Properties	Ref.
2-chloromethyl-6-methylpyridine	$(Ph)_2CHCO_2Me$	xylene			m.p. 88-90°; hydrochloride, m.p. 170-172° (decomp.)	51
2-chloromethyl-6-methylpyridine	$(Ph)_2CHCO_2Et$	xylene			hydrochloride, m.p. 194-197° (decomp)	51
2-chloromethyl-6-methylpyridine	$(Ph)_2CHCO_2(CH_2)_2NEt_2$	xylene			dihydrochloride, m.p. 144-147°	51
	$CH_2(CO_2Et)_2$	PhMe, Na, reflux 15 hr		4.3 g ↓ 4 g	b.p. 163-164°	196
	$AcNHCH(CO_2Et)_2$	Na, EtOH, reflux 24 hr		32 g ↓ 38.4 g	m.p. 150-151°	95
3-PyCl		$NaNH_2$, PhMe reflux 2 hr			m.p. 149°; hydrochloride, m.p. 223-224°	158

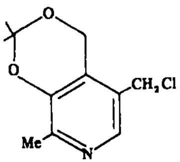
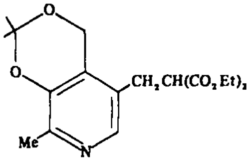
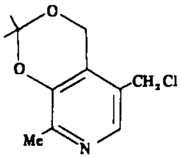
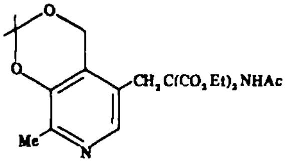
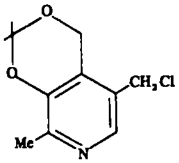
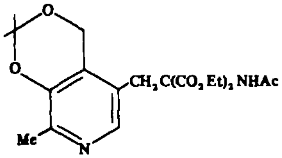
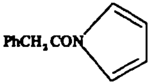
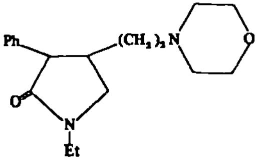
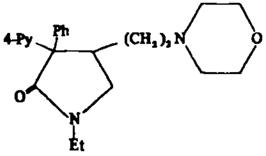
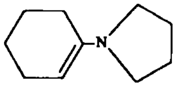
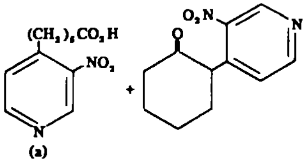
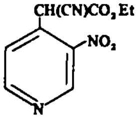
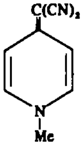
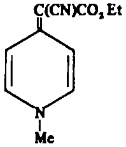
	$CH_2(CO_2Et)_2$	Na, KI, EtOH, R.T. 48 hr		34%	hydrochloride, m.p. 148–149°	195
	$AcNHCH(CO_2Et)_2$	same as above		65%	m.p. 122–123°	195
 · HCl	$AcNHCH(CO_2Et)_2$	Na, EtOH, R.T., 48 hr		95.7%	m.p. 118°	125
4-PyCl		same as above			m.p. 131°	158
4-PyBr		$NaNH_2$, PhMe		20%	m.p. 134–136°	50

TABLE XI-5. Condensation of Halopyridines with Active Methylene Compounds (Continued)

Halide	Active methylene compound	Conditions	Product	Yield	Properties	Ref.
4-chloro-3-nitropyridine		CH_2Cl_2, Et_3N, N_2, 4 days			(a) m.p. 112–114°	119
4-methoxy-3-nitropyridine	$NCCH_2CO_2Et$	$Me_3CO^{\ominus}K^{\oplus}$, Me_3COH, reflux 5–12 hr		52%	m.p. 177–178°	84
4-methoxy-3-nitropyridine	$NCCH_2CO_2CH_2Ph$	same as above		60%	m.p. 204° (decomp)	84
1-methyl-4-phenoxy-pyridinium iodine	$CH_2(CN)_2$	same as above		63%	m.p. 237–239°	83
1-methyl-4-phenoxy-pyridinium iodide	$CH_2(CN)CO_2Et$	same as above		37%	m.p. 179–179.5° ; uv	83

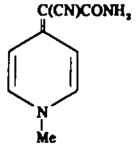
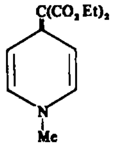
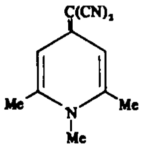
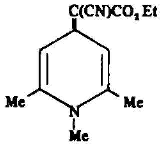
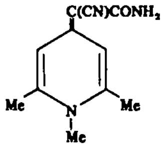
1-methyl-4-phenoxy-pyridinium iodide	$CH_2(CN)CONH_2$	same as above		56%	m.p. 222–223° (decomp); uv	83
1-methyl-4-phenoxy-pyridinium iodide	$CH_2(CO_2Et)_2$	same as above		24%	m.p. 96.5–97°; uv	83
1,2,6-trimethyl-4-methoxy-pyridinium perchlorate	$CH_2(CN)_2$	same as above		71%	m.p. 320–324°	83
	$CH_2(CN)CO_2Et$	same as above		76%	m.p. 215–217°; uv	83
	$CH_2(CN)CONH_2$	same as above		39.5%	m.p. 277–278° (decomp.); uv	83
$4\text{-}PyCH_2Cl$	$(Ph)_2CHCO_2Me$	xylene	$4\text{-}PyCH_2C(Ph)_2CO_2Me$		m.p. 146–149°; hydrochloride, m.p. 180–183° (decomp.)	51

TABLE XI-6. Condensation of Chloral with Picolines

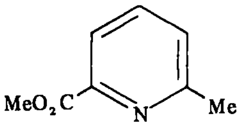
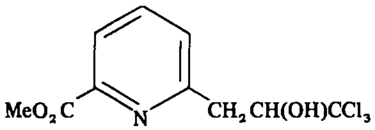
Picoline	Conditions	Product	Yield	Ref.
2-PyMe	HOAc, piperidine, xylene, 12 hr, 150°	2-PyCH$_2$CH(OH)CCl$_3$	28.5%	114
	100°, 100 hr		45 g ↓ 35 g	197
4-PyMe	HOAc, piperidine, xylene, 12 hr, 150°	4-PyCH$_2$CH(OH)CCl$_3$		114
	AmOAc	4-PyCH$_2$CH(OH)CCl$_3$		29
4-PyCOCH$_2$CO$_2$Et	3 hr, HOAc, steam-bath	4-PyCOCH(CO$_2$Et)CH(OH)CCl$_3$		105

TABLE XI-7. Hydrolysis of $PyCH_2CH(OH)CCl_3$

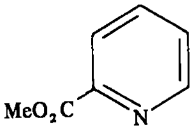
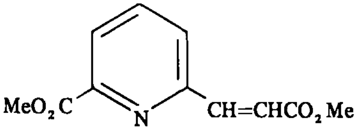
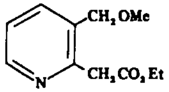
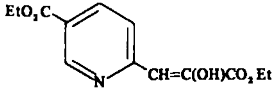
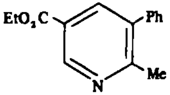
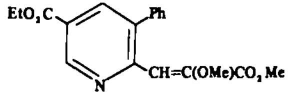
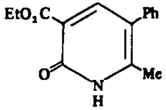
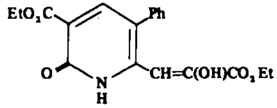
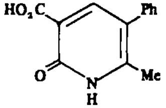
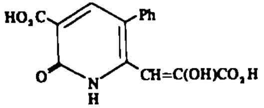
Py isomer	Conditions	Product	Yield	Properties	Ref.
	KOH, EtOH, R.T., reflux 2 hr; dry HCl, 0°		30 g ↓ 15 g	m.p. 107–109°; ir	197
2-Py	KOH, EtOH; EtOH, H_2SO_4, 4 hr, steam-bath	$2\text{-}PyCH{=}CHCO_2Et$	85%	b.p. 118–120°/6 mm; methiodide, m.p. 157–159°	114
		$2\text{-}PyCH{=}CHCO_2H$		m.p. 200.1–200.6°	198
4-Py	KOH, EtOH	$4\text{-}PyCH{=}CHCO_2H$			29
	KOH, EtOH	$4\text{-}PyCH{=}CHCO_2H$	36%	ethyl ester, m.p. 64°; methiodide, m.p. 170–171°	114

TABLE XI-8. Condensation with Picolines to Give Side-Chain Acids and Esters

Picoline	Condensed with	Conditions	Product	Yield	Properties	Ref.
2-PyMe	$Br(CH_2)_{10}CONH_2$	$NaNH_2$, THF	$2\text{-}Py(CH_2)_{11}CONH_2$		m.p. 92–94°	199
$2\text{-}PyCH_2Li$	$(CO_2Et)_2$	$(2\text{-}PyCH_2)_2Cd$, $CdCl_2$, Et_2O, –70°	$2\text{-}PyCH_2COCO_2Et$	10%	m.p. 82.5–83.5°; picrate, m.p. 150–151°; 2,4-DNP, m.p. 141–142°; 2,4-DNP·H_2SO_4, m.p. 168–169°; oxime, m.p. 120–121°	85, 8
3-Methoxymethyl-2-picoline	$(EtO)_2CO$	KNH_2, Et_2O, reflux 2 hr		6 g → 2 g	b.p. 150–152°	9
5-Carbethoxy-2-picoline	$(CO_2Et)_2$	NaOEt, Et_2O, 16 hr		3.3 g ↓ 4.4 g	m.p. 102°; copper complex, m.p. 220°	17
	$(CO_2Et)_2$	NaOMe, MeOH, reflux 0.5 hr			m.p. 173–174°; ir; uv	87
	$(COCl)_2$	$POCl_3$, reflux 40 min; EtOH		good	m.p. 168–170°; ir; uv	87
	$(COCl)_2$	$POCl_3$, reflux 40 min; H_2O		85%	m.p. 190° (decomp); ir; uv	87 173

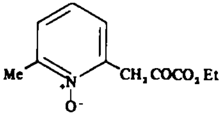
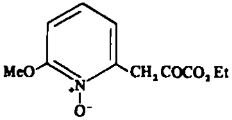
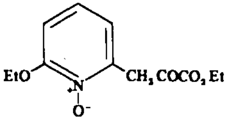
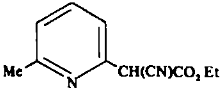
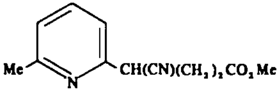
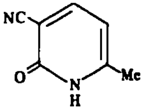
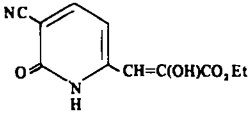
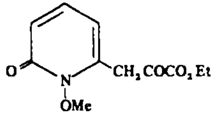
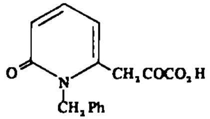
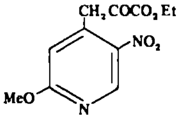
2,6-Lutidine-1-oxide	$(CO_2Et)_2$	NaH, PhH		91%	m.p. 56.5–58.5°	135
2-Methoxy-6-methylpyridine-1-oxide	$(CO_2Et)_2$	not stated			m.p. 132°	139
2-Ethoxy-6-methylpyridine-1-oxide	$(CO_2Et)_2$	KOEt, EtOH, R.T. overnight		75.6%	m.p. 116°	139
2-PyCH(Ph)CN	$CH_2{=}CHCO_2Et$	Na, MeOH, reflux 16 hr	2-PyC(Ph)(CN)$(CH_2)_2CO_2Et$	63%	b.p. 185°/0.01 mm; ir	200
(6-Methyl-2-pyridyl)acetonitrile	$(EtO)_2CO$	$NaNH_2$, Et_2O			m.p. 154–155°	201
	$Cl(CH_2)_2CO_2Me$	K, C_6H_6		86%	b.p. 105°/0.01 mm	200
	$(CO_2Et)_2$	KNH_2, liq. NH_3, 1 hr; Et_2O, reflux 8 hr		46%	m.p. 237–238°; ir; uv	202

TABLE XI-8. Condensation with Picolines to Give Side-Chain Acids and Esters (Continued)

Picoline	Condensed with	Conditions	Product	Yield	Properties	Ref.
1-Methoxy-6-methyl-2-pyridone	$(CO_2Et)_2$	KOEt, EtOH			m.p. 153°	139
1-Benzyl-6-methyl-2-pyridone	$(CO_2Et)_2$	KOEt; 6% H_2SO_4, reflux		99.5%	m.p. 211°	139
3-PyMe	$Br(CH_2)_{10}CONH_2$	$NaNH_2$, THF	3-Py$(CH_2)_{11}CONH_2$		m.p. 93–96°	199
3-PyCOCH$_2$Br	NaC(NHAc)$(CO_2Et)_2$	C_6H_6, reflux 48 hr	3-PyCOCH$_2$C(NHAc)$(CO_2Et)_2$	145 g ↓ 105 g	m.p. 139.5–141.5°	1
3-PyCH$_2$CN	$(EtO)_2CO$	$NaNH_2$, Et_2O	2-PyCH(CN)CO_2Et		m.p. 107–108°	201
4-PyMe	$Br(CH_2)_{10}CONH_2$	$NaNH_2$, THF	4-Py$(CH_2)_{11}CONH_2$	10 g → 4.1 g	m.p. 135.5°	199
4-PyCH$_2$Li	$(CO_2Et)_2$	(4-PyCH$_2$)$_2$Hg, Et_2O, -70°, $HgCl_2$	4-PyCH$_2$COCO$_2$Et	10%	m.p. 138–139°; picrate, m.p. 164–165° (decomp); 2, 4-DNP, m.p. 139–140° (decomp); methiodide, m.p. 199–200°	85, 86
4-PyCH$_2$Li	ClCO$(CH_2)_4CO_2Et$	Et_2O, 25 min; 10% HCl, reflux 5 hr	4-PyCH$_2$CO$(CH_2)_4CO_2H$	76 g → 29 g	m.p. 221–222°	117
2-Methoxy-4-methyl-5-nitropyridine	$(CO_2Et)_2$	KOEt; pH 3		93%	m.p. 97–98°; ir; uv nmr	15

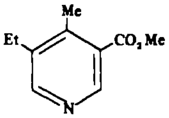
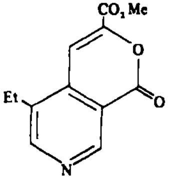
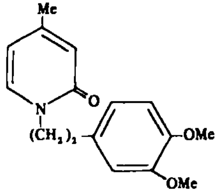
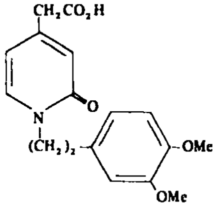
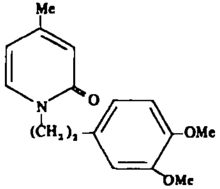
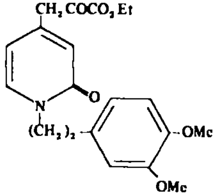
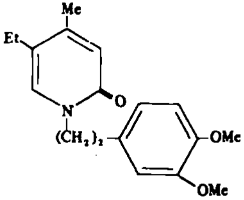
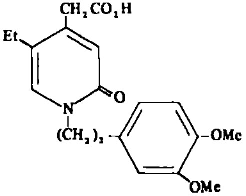
	$(CO_2Me)_2$	Me_3COK, C_6H_6, R.T.			m.p. 123-124°; ir	122
4-$PyCH_2CN$	$EtO_2C(CH_2)_3CO_2Et$	Na, EtOH, reflux 2 hr; R.T., overnight	4-$PyCH(CN)CO(CH_2)_3CO_2Et$	19%	m.p. 142°	165
	$(CO_2Et)_2$	KOEt; NaOH, H_2O_2, 0°			m.p. 159-160° (decomp)	88
	$(CO_2Et)_2$	KOEt, EtOH or KOEt; dil. H_2SO_4		91.2%	m.p. 157-158.5°; oxime, m.p. 186.5-189.5°	3, 88
	$(CO_2Et)_2$	NaOEt; NaOH, H_2O_2, 0°			m.p. 154°	6, 88

TABLE XI-8. Condensation with Picolines to Give Side-Chain Acids and Esters (Continued)

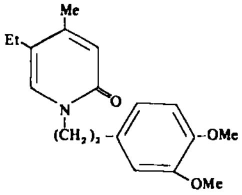
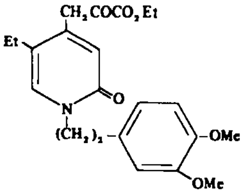
Picoline	Condensed with	Conditions	Product	Yield	Properties	Ref.
	$(CO_2Et)_2$	KOEt; dil. H_2SO_4 or K, abs. EtOH, 0°; reflux 24 hr; 2N H_2SO_4			m.p. 141.5-142.5°	6. 4, 88

TABLE XI-9. Condensations of Vinylpyridines with Esters

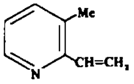
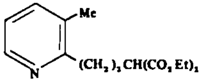
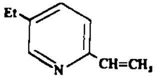
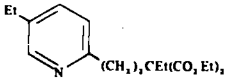
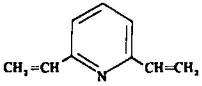
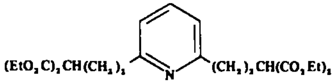
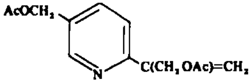
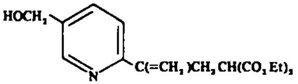
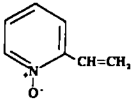
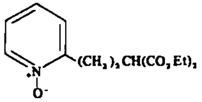
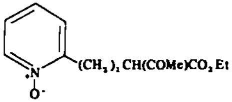
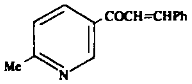
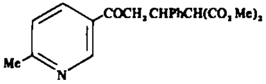
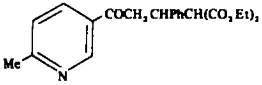
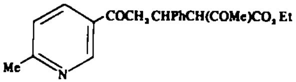
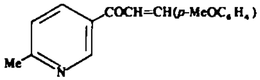
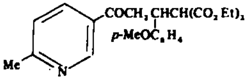
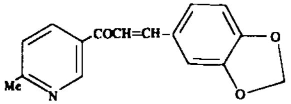
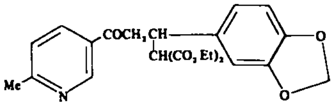
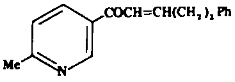
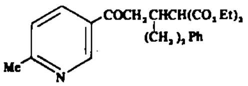
Vinylpyridine	Condensed with	Conditions	Product	Yield	Properties	Ref.
2-PyCH=CH_2	$CH_2(CO_2Et)_2$	hydroquinone, reflux 6 hr	2-Py$(CH_2)_2CH(CO_2Et)_2$	26%	b.p. 130–134°/0.1 mm	91
	$MeCH(CO_2Et)_2$	Na, EtOH, reflux 2 hr	2-Py$(CH_2)_2CMe(CO_2Et)_2$	75%	b.p. 140°; hydrochloride, m.p. 124–126°	200
	$EtCH(CO_2Et)_2$	hydroquinone, reflux 6 hr	2-Py$(CH_2)_2CEt(CO_2Et)_2$	65%	b.p. 150–160°/0.15 mm	91
	n-BuCH$(CO_2Et)_2$	Na, EtOH, reflux 7 hr	2-Py$(CH_2)_2CBu(CO_2Et)_2$		b.p. 150°/0.05 mm; picrate, m.p., 102°	203
	$PhCH(CO_2Et)_2$	hydroquinone, reflux 6 hr	2-Py$(CH_2)_2CPh(CO_2Et)_2$	16%	b.p 150–152°/0.6 mm	91
	$CH_2(CN)CO_2Et$	Na, 100°; 110°, 5 hr	2-Py$(CH_2)_2CH(CN)CO_2Et$		b.p. 148–151°/0.8 mm	204
	AcNHCH(CN)CO_2Et	NaOEt, C_6H_6, reflux 7 hr; conc. HCl, 7 hr, 120–130°	2-Py$(CH_2)_2CH(NH_2)CO_2Et$	3.1 g ↓ 2.1 g	b.p. 138–140°/4 mm; picrolonate, m.p. 222° (decomp); picrate, m.p. 186°	89
	2-Py$(CH_2)_2CH(CO_2Et)_2$	Na, hydroquinone	(2-Py$CH_2CH_2)_2C(CO_2Et)_2$		dipicrate, m.p. 150–152°	205
	$EtO_2CCH=CHCO_2Et$	$MeSO_3^{\ominus}$ $NEt_4^{\oplus}$, Me_2NNO, electrolysis at -1.3 to -1.35V reference calomel electrode for 1.88 amp. hr, Mercury Cathode	2-Py$(CH_2)_2CH(CO_2Et)CH_2CO_2Et$		b.p. 141–143°/25 mm	90
	$(CH_3CO_2Et)_2$	Na, abs. EtOH		34 g ↓ 31 g	b.p. 160°/0.001 mm; picrate, m.p. 104–105.5°	206
	$EtCH(CO_2Et)_2$	hydroquinone, reflux 6 hr		41%	b.p. 160–168°/0.3 mm	91
	$CH_2(CO_2Et)_2$	Me_3COK, DMF, 8 hr		32-33%	b.p. 186–192°/0.03 mm	138
		Na, EtOH		32%	b.p. 200°/0.001 mm; ir	14

TABLE XI-9. Condensations of Vinylpyridines with Esters (Continued)

Vinylpyridine	Condensed with	Conditions	Product	Yield	Properties	Ref.
	$CH_2(CO_2Et)_2$	Na, reflux 6 hr		42%	b.p. 140–170°/0.1 mm n_D^{25} 1.5040	207
	$CH_2(COMe)CO_2Et$	Na, reflux 6 hr		80%	b.p. 180–200°/0.1 mm n_D^{25} 1.5120	207
	$CH_2(CO_2Me)_2$	Et_2NH, NaOMe *or* Triton B, solvent		88%	m.p. 94°; picrate, m.p. 134°	208
	$CH_2(CO_2Et)_2$	same as above		59%	m.p. 96–97°; picrate, m.p. 111°	208
	$MeCOCH_2CO_2Et$	same as above		82.3%	m.p. 105–106°; picrate, m.p. 166–167°	208
	$CH_2(CO_2Et)_2$	same as above		79.8%	m.p. 75–75.5°; picrate, m.p. 169°	208
	$CH_2(CO_2Et)_2$	same as above		92%	m.p. 150°; picrate, m.p. 203–205°	208
	$CH_2(CO_2Et)_2$	same as above		24.4%	m.p. 236°	208

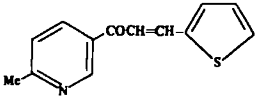
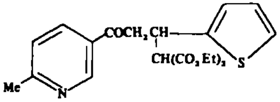
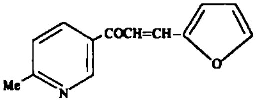
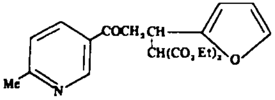
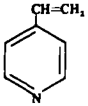
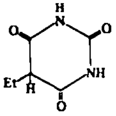
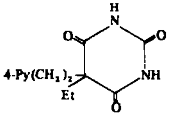
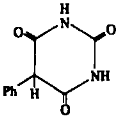
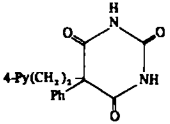
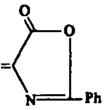
	$(CH_2CO_2Et)_2$	same as above		47%	m.p. 75°; picrate, m.p. 138°	208
	$CH_2(CO_2Et)_2$	same as above		41%	m.p. 74–75°; picrate, m.p. 144°	208
	$MeCOCH_2CO_2Et$	Na, 5 hr, reflux	$4\text{-}Py(CH_2)_2CH(COMe)CO_2Et$		b.p. 150°/0.3 mm; picrate, m.p. 83°	209
	$CH_2(CO_2Et)_2$	NaOEt, EtOH, reflux 3 hr	$4\text{-}Py(CH_2)_2CH(CO_2Et)_2$	76%	b.p. 150–152°/0.7 mm; n_D^{20}, 1.4850; hydrochloride, m.p. 111–113°	210
		or hydroquinone, 6 hr reflux		5%	b.p. 140–142°/0.3 mm	91
	$MeCH(CO_2Et)_2$	hydroquinone, 6 hr reflux	$4\text{-}Py(CH_2)_2CMe(CO_2Et)_2$	37%	b.p. 140–150°/0.1 mm	91
	$EtCH(CO_2Et)_2$	same as above	$4\text{-}Py(CH_2)_2CEt(CO_2Et)_2$	50%	b.p. 150–158°/0.45 mm; picrate, m.p. 113–114°	91
	$PhCH(CO_2Et)_2$	same as above	$4\text{-}Py(CH_2)_2CPh(CO_2Et)_2$		b.p. 176–178°/0.2 mm	91
	$AcNHCH(CO_2Et)_2$	Amberlite ir 400 (OH$^{\ominus}$), EtOH, 60–70°, 20 hr; 6*N* HCl, reflux 12 hr	$4\text{-}Py(CH_2)_2CH(NH_2)CO_2H$, HCl	49.4%	hydrochloride, m.p. 223–224°	30
		EtOH		40%	m.p. 224–226°	91
		EtOH		47%	m.p. 248–249°	91

TABLE XI-10. Condensation of Pyridinealdehydes and Ketones Yielding Side-Chain Acid Derivatives

Aldehyde	Condensed with	Conditions	Product	Yield	Properties	Ref.
2-PyCHO	$CH_2(CN)CO_2Et$	EtOH or	2-PyCH=C(CN)CO$_2$Et	87.6%	m.p. 94–95°	211
		EtOH, piperidine, reflux 1–5 hr		64%	m.p. 94.5–96°	137
	$CH_2(COMe)CO_2Et$	Et_2NH	2-PyCH=C(COMe)CO$_2$Et	80%	m.p. 85–87°	211
	$PhCOCH_2CO_2Et$	piperidine, overnight	2-PyCH=C(COPh)CO$_2$Et	58%	m.p. 98–99°	211
	$EtO_2CCOCHFCO_2Et$	reflux 45 min	2-PyCH=CFCO$_2$Et	35%	b.p. 118–120°/4 mm	212
	p-ClC$_6$H$_4$CH$_2$CO$_2$H	Et$_3$N, Ac$_2$O, stir 0.5 hr; 100° within 0.5 hr; 100°, 5 hr	2-PyCH=C(*p*-ClC$_6$H$_4$)CO$_2$H			53
	$CH_2(NHAc)CO_2Et$	Et$_3$N, 14 hr	2-PyCH(OH)CH(NHAc)CO$_2$Et	56%	m.p. 124–126°	93
2-PyCH(OEt)$_2$	$PhCONHCH_2CO_2H$	SO$_3$, DMF, heat, 1 hr, R.T. overnight	2-PhCH= 	22%		94
	$PhCONHCH_2CO_2H$	SO$_3$, DMF, heat, 1 hr, R.T. overnight; red P, Ac$_2$O, HI, reflux 4 hr	2-PyCh$_2$CH(NH$_2$)CO$_2$H	62%	m.p. 209–212°; ir	94
	$PhCONHCH_2CO_2H$	SO$_3$, DMF, heat, 1 hr, R.T., overnight; 10% NaOH, steam bath, 4 hr; HCl-HOAc (1:1), reflux 20 hr	2-PyCH=CHCO$_2$H	83%	m.p. 206°	94
2-PyCHO	ONNH(CH$_2$)$_2$CO$_2$Me		2-PyCO(CH$_2$)$_2$CO$_2$Me	65%	b.p. 104–106°/0.3 mm; m.p. 46–47°; 2,4-DNP, m.p. 174°	96
	ONNH(CH$_2$)$_3$CO$_2$Me		2-PyCO(CH$_2$)$_3$CO$_2$Me	63%	b.p. 114°/0.3 mm; 2,4-DNP, m.p. 174°	96

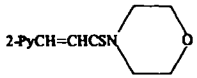
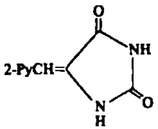
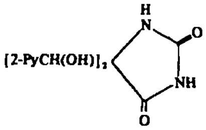
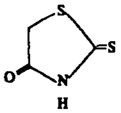
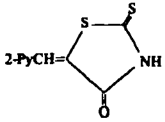
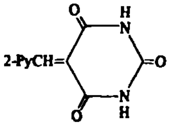
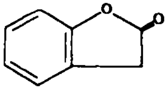
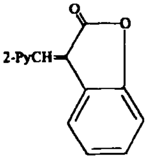
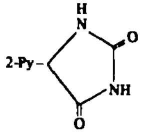
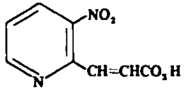
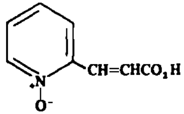
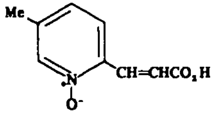
	$ONNH(CH_2)_4CO_2Me$		$2\text{-}PyCO(CH_2)_4CO_2Me$	68%	b.p. 125–127°/0.4 mm; 2,4-DNP, m.p. 187°	96
	$ONNH(CH_2)_8CO_2Me$		$2\text{-}PyCO(CH_2)_8CO_2Me$	70%	b.p. 132–134°/0.4 mm, m.p. 36–38°; 2,4-DNP, m.p. 185°	96
	$MeCOCO_2H$	20% KOH, aq. MeOH, stand 1–2 hr; pH 2	$2\text{-}PyCH{=}CHCOCO_2H$	16%	m.p. 136° (decomp)	213
	$MeCSNH_2$	Na, EtOH, 0–5°, 40 hr	$2\text{-}PyCH{=}CHCSNH_2$	20–25%	m.p. 145°	214
		Na, EtOH, 0–5°, 40 hr		20–25%	m.p. 93–94°	214
	Hydantoin	Et_2NH, pyridine, bomb, 100°, 20 hr			m.p. 228–229°	95
2-PyCHO (2 equiv.)	Hydantoin	80°		55%	m.p. 275–280°	211
2-PyCHO		HOAc, boil				215
	Barbituric acid	heat, H_2O		90%	m.p. 275–280°	211

TABLE XI-10. Condensation of Pyridinealdehydes and Ketones Yielding Side-Chain Acid Derivatives (Continued)

Aldehyde	Condensed with	Conditions	Product	Yield	Properties	Ref.
		Et_3N		69%		216
	KCN, $(NH_4)_2CO_3$	H_2O, EtOH, 50–55°, 4 hr; HOAc, 24 hr			m.p. 301–302° (decomp); ir	217
	KCN,$(NH_4)_2CO_3$	H_2O, EtOH, 50–55°, 4 hr; $Ba(OH)_2$, 40 hr, reflux	2-PyCH$(NH_2)CO_2H$		m.p. 130–132°	217
3-NO_2-2-PyCHO	$CH_2(CO_2H)_2$	pyridine, piperidine, steam-bath, 2 hr			m.p. 192.5–194°	151
2-PyCHO-1-oxide	$CH_2(CO_2H)_2$	pyridine, 60 min, steam-bath		70%	m.p. 257–258°	218
3-Me-2-PyCHO-1-oxide	$CH_2(CO_2H)_2$	pyridine, 60 min, steam-bath		55%	m.p. 245° (decomp)	218

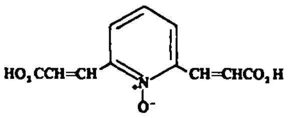
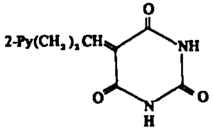
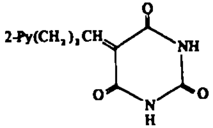
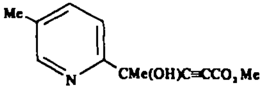
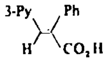
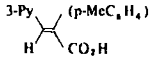
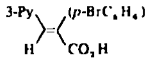
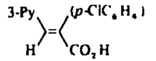
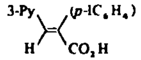
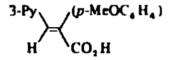
2,6-Py(CHO)$_2$-1-oxide	CH$_2$(CO$_2$H)$_2$	pyridine, 60 min, steam-bath		72%	m.p. 281–282° (decomp)	218
2-Py(CH$_2$)$_2$CHO	CH$_2$(CO$_2$Et)$_2$		2-Py(CH$_2$)$_2$CH=CHCO$_2$H	45%	m.p. 102–104°	219
	Barbituric acid			89%	m.p. 265–267°	219
2-Py(CH$_2$)$_3$CHO	Barbituric acid			73%	m.p. 200–202°	219
2-PyCOMe	(CO$_2$Et)$_2$	Na, EtOH, 25°, 15 hr; 80°, 0.5 hr	2-PyCOCH$_2$COCO$_2$Et	50%	m.p. 171–172°	220
	CH$_2$CO$_2$Et COCO$_2$Et	abs. EtOH, Na, 0°, overnight	2-PyCOCH$_2$COCO$_2$Et		m.p. 68–69.5°	110
	CH≡CCO$_2$Me	NaNH$_2$, NH$_3$	2-PyCMe(OH)C≡CCO$_2$Me	46%	m.p. 102–104°	79, 97
2-Acetyl-5-MePy	CH≡CCO$_2$Me	NaNH$_2$, NH$_3$, Fe$_2$(NO$_3$)$_3$, Et$_2$O, 2.5 hr		44%	m.p. 115–117°	79, 97
2-PyCOPh	ClCH$_2$CO$_2$Et	NaOEt, C$_6$H$_6$, 0–7°, 12 hr; Et$_2$O, HCl, 48 hr; Pd on CaCO$_3$, EtOH	2-PyCPh(OH)CH$_2$CO$_2$Et	25%	m.p. 64–66°	221
	Cl$_2$CHCO$_2$Et	NaOEt, C$_6$H$_6$, 0–7°, 12 hr; Et$_2$O, HCl, 48 hr; Pd on CaCO$_3$, EtOH	2-PyCPh(OH)CHClCO$_2$Et	31%	m.p. 105–107°	221

TABLE XI-10. Condensation of Pyridinealdehydes and Ketones Yielding Side-Chain Acid Derivatives (Continued)

Aldehyde	Condensed with	Conditions	Product	Yield	Properties	Ref.
	$BrCH_2CO_2Et$	Zn	$2\text{-PyCPh(OH)CH}_2CO_2Et$	55%	m.p. 59–61°	132
					m.p. 63–64°; b.p. 160–170°/2 mm	54
					m.p. 65–67°	222
	$BrCHMeCO_2Et$	Zn	$2\text{-PyCPh(OH)CHMeCO}_2Et$		m.p. 51–53°	222
	$PhCH(MgBr)CO_2H$	C_6H_6, reflux 4 hr	$2\text{-PyC(OH)PhCHPhCO}_2H$		m.p. 162.5° (decomp)	172
	$MeCONMe_2$	$NaNH_2$, Et_2O, 1.5 hr	$2\text{-PyC(OH)PhCH}_2CONMe_2$		m.p. 105°	223
3-PyCHO	$CH_2(CO_2H)_2$	pyridine, piperidine	3-PyCH=CHCO_2H	78%	m.p. 235–235.5°	224
	$CH_2(CN)CO_2Et$	piperidine, EtOH, reflux 1–5 hr	$3\text{-PyCH=C(CN)CO}_2Et$	83%	m.p. 87.5–88.5°	137
	$PhCH_2CO_2H$ *or* $PhCH_2CO_2Na$	NaOH, EtOH; Ac_2O, reflux 2 hr *or* Ac_2O, reflux 2 hr		12 g → 35 g 55%	m.p. 197–200°	98, 100
	$p\text{-MeC}_6H_4CH_2CO_2H$	NaOH, EtOH; Ac_2O reflux 2 hr			m.p. 198°	100
	$p\text{-BrC}_6H_4CH_2CO_2H$	same as above			m.p. 183°	100
	$p\text{-ClC}_6H_4CH_2CO_2H$	same as above			m.p. 220°	100
	$p\text{-IC}_6H_4CH_2CO_2H$	same as above			m.p. 189–195°	100
	$p\text{-MeOC}_6H_4CH_2CO_2H$	same as above			m.p. 230°	100

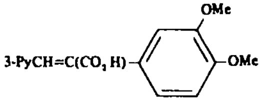
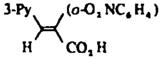
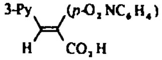
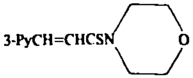
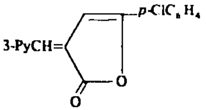
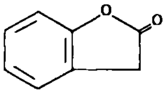
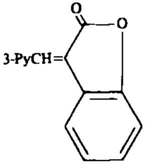
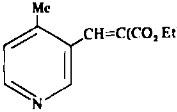
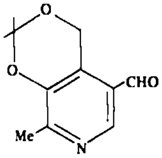
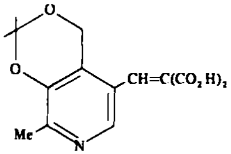
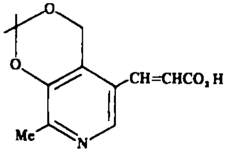
	Sodium homoveratric acid	Ac_2O, reflux 18 hr				225
	o-$NO_2C_6H_4CH_2CO_2Na$	Ac_2O, fused $ZnCl_2$, steam bath, 20 hr		43%	m.p. 203–204°	99
	p-$O_2NC_6H_4CH_2CO_2H$	NaOH, EtOH; Ac_2O, reflux 2 hr			m.p. 155°	100
	$EtO_2CCOCHFCO_2Et$	reflux 45 min	3-PyCH=$CFCO_2Et$	40%	b.p. 120–122°/4 mm	212
	$Me_2NCH_2CO_2Et$	Na, EtOH	3-PyCH=$C(NMe_2)CO_2Et$	71%	b.p. 97–98°/0.05 mm; ir	226
	$CH_2(NHAc)CO_2Et$	Et_3N, 10 hr	3-PyCH(OH)CH(NHAc)CO_2Et	65%	m.p. 154–157°	93
3-PyCH$(OMe)_2$	$PhCONHCH_2CO_2H$	SO_3, DMF, heat, 1 hr; R.T., overnight; red P, Ac_2O, HI, reflux 4 hr	3-$PyCH_2CH(NH_2)CO_2H$	72%	m.p. 278–280°; ir	94
	$PhCONHCH_2CO_2H$	SO_3, DMF, heat, 1 hr; R.T., overnight; 10% NaOH, steam-bath, 4 hr; HCl-HOAc(1:1), reflux 20 hr	3-PyCH=$CHCO_2H$	76%	m.p. 236–241°	94
3-PyCHO	$MeCOCO_2H$	20% KOH, aq. MeOH, 1-2 hr; pH 2	3-PyCH=$CHCOCO_2H$	51%	m.p. 169° (decomp); oxime, m.p. 176° (decomp)	213
	$MeCSNH_2$	Na, EtOH, 0–5°, 40 hr	3-PyCH=$CHCSNH_2$	20–25%	m.p. 184°	214
		same as above		20–25%	m.p. 115°	214

TABLE XI-10. Condensation of Pyridinealdehydes and Ketones Yielding Side-Chain Acid Derivatives (Continued)

Aldehyde	Condensed with	Conditions	Product	Yield	Properties	Ref.
	p-ClC$_6$H$_4$CO(CH$_2$)$_2$CO$_2$H	Ac$_2$O, NaOAc		73%	m.p. 242-243°	227
		Et$_3$N		34.5%	m.p. 147°	216
4-Me-3-PyCHO	CH$_2$(CO$_2$Et)$_2$	piperidine, C$_6$H$_6$, reflux		69%	b.p. 139-143°/0.5 mm; picrate, m.p. 107-110.5°	5
	CH$_2$(CO$_2$H)$_2$	pyridine, 95% EtOH, reflux 45 min		56%	m.p. 200-201° (decomp)	228
	CH$_2$(CO$_2$H)$_2$	pyridine, piperidine, 2 hr, steam-bath; 5°, overnight		82%	m.p. 220-221°	228

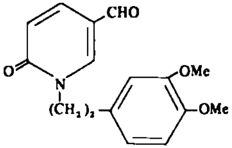
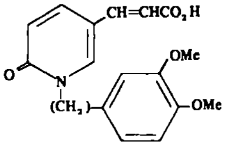
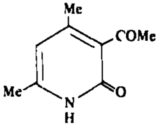
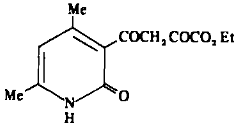
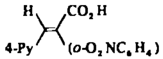
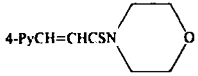
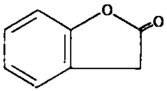
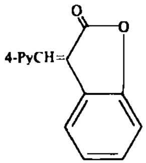
	$CH_2(CO_2H)_2$	piperidine, pyridine, steam-bath, 2 hr		81%	two forms, m.p. 155–157°, m.p. 178–181°	7
3-PyCOMe	$(CO_2Et)_2$	Na, EtOH, 25°, 15 hr; 80°, 0.5 hr	3-PyCOCH$_2$COCO$_2$Et	10%	m.p. 185–187°	220
	NaCH$(CO_2Et)_2$	32% HBr, HOAc, Py. HBr; $CH_2(CO_2Et)_2$, 12 hr, ice; 25°, 12 hr	3-PyCO$(CH_2)_2CO_2H$	60%		229
	BrCHMeCO$_2$Me	Zn, $HgCl_2$, C_6H_6, reflux 1 hr	3-PyC(OH)MeCHMeCO$_2$Me 37% *threo*, 63% *erythro*	50%	NMR	230
	$(CO_2Et)_2$	Na, EtOH, 90–100% 3 hr		2 g ↓ 2.1 g	m.p. 175–176°; ir	231
3-PyCOPh	BrCH$_2$CO$_2$Et	Zn	3-PyC(OH)PhCH$_2$CO$_2$Et	56%	m.p. 77–78°	54
4-PyCHO	o-$O_2NC_6H_4CH_2CO_2Na$	Ac_2O, fused $ZnCl_2$, steam-bath, 20 hr		11.5 g ↓ 5.5 g	picrate, m.p. 203–204°	99
	$CH_2(NHAc)CO_2Et$	Et_3N, 10 days	4-PyCH(OH)CH(NHAc)CO$_2$Et	60%	m.p. 120–122°	93
	AcNHCH$(CO_2H)CO_2Me$	Et_3N, EtOH, R.T., 6 days	4-PyCH(OH)CH(NHAc)CO$_2$Me	75%	m.p. 130°	232
4-PyCH(OMe)$_2$	PhCONHCH$_2$CO$_2$H	SO_3, DMF, heat, 1 hr; R.T., overnight; red P, Ac_2O, HI, reflux 4 hr	4-PyCH$_2$CH$(NH_2)CO_2H$	65%	m.p. 265–270°; ir	94

TABLE XI-10. Condensation of Pyridinealdehydes and Ketones Yielding Side-Chain Acid Derivatives (Continued)

Aldehyde	Condensed with	Conditions	Product	Yield	Properties	Ref.
	$PhCONHCH_2CO_2H$	SO_3, DMF, heat, 1 hr; R.T., overnight; 10% NaOH, steam-bath, 4 hr; HCl-HOAc (1:1), reflux 20 hr	$4\text{-}PyCH{=}CHCO_2H$	80%	m.p. 230°	94
4-PyCHO	$MeCOCO_2H$	20% KOH, MeOH, stand 1-2 hr; pH 2	$4\text{-}PyCH{=}CHCOCO_2H$	24%	m.p. 290–291° (decomp)	213
	$MeCSNH_2$	Na, EtOH, 0–5°, 40 hr	$4\text{-}PyCH{=}CHCSNH_2$	20–25%	m.p. 163–164°	214
		Na, EtOH, 0–5°, 40 hr		20–25%	m.p. 98°	214
		Et_3N		100%	m.p. 148°	216
4-PyCOMe	$(CO_2Et)_2$	NaOAc,	$4\text{-}PyCOCH_2COCO_2Et$		m.p. 96°	233
		or Na, EtOH, 25°, 15 hr; 80°, 0.5 hr		5%	m.p. 98–100°	220
		or Na, Et_2O, 0°, 2hr; several hr, R.T.; reflux, steam-bath			m.p. 75°	234

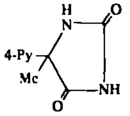
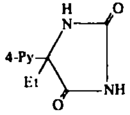
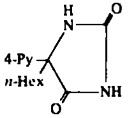
	KCN, $(NH_4)_2CO_3$			88%	m.p. 234.5–235.5°	235
4-PyCOEt	KCN, $(NH_4)_2CO_3$			82.5%	m.p. 181.5–183°	235
4-PyCOHex-*n*	KCN, $(NH_4)_2CO_3$			86%	m.p. 146–147°	235
4-PyCOPh	$ClCH_2CO_2Et$	NaOEt, C_6H_6, 0–7°, 12 hr; Et_2O, HCl, 48 hr; Pd on $CaCO_3$, EtOH	4-PyC(OH)PhCH_2CO_2Et	48%	m.p. 99–100°	221
	Cl_2CHCO_2Et	NaOEt, C_6H_6, 0–7° 12 hr; Et_2O, HCl, 48 hr; Pd on $CaCO_3$, EtOH	4-PyC(OH)PhCHClCO_2Et	56%	m.p. 135–140°	221
	$BrCH_2CO_2Et$	Zn	4-PyC(OH)PhCH_2CO_2Et	49%	m.p. 99–100° m.p. 99–100° m.p. 82–84°	222 54 132
	$BrCH_2CO_2Et$	activated Zn, C_6H_6, reflux 4 hr; 2*N* H_2SO_4	4-PyC(OH)PhCH_2CO_2Et	50 g ↓ 25 g	m.p. 99–100°	236
	$BrCHMeCO_2Et$	Zn	4-PyC(OH)PhCHMeCO_2Et		m.p. 121–122°	222

TABLE XI-10. Condensation of Pyridinealdehydes and Ketones Yielding Side-Chain Acid Derivatives (Continued)

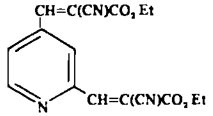
Aldehyde	Condensed with	Conditions	Product	Yield	Properties	Ref.
	$PhCH(MgBr)CO_2H$	C_6H_6, reflux 4 hr	$4\text{-}PyC(OH)PhCHPhCO_2H$			172
$2,4\text{-}Py(CHO)_2$	$CH_2(CN)CO_2Et$	pyridine, piperidine, steam-bath 2 hr				237

TABLE XI-11. Condensations of Pyridinecarboxylic Esters Yielding Side-Chain Acid Derivatives

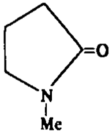
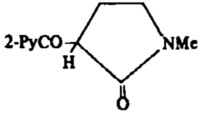
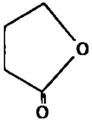
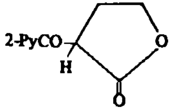
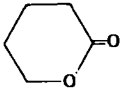
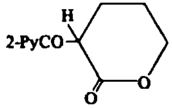
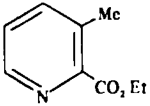
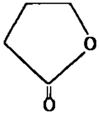
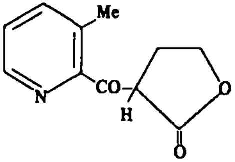
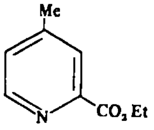
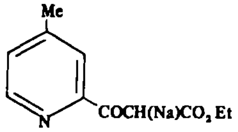
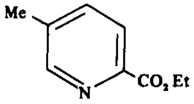
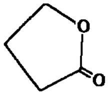
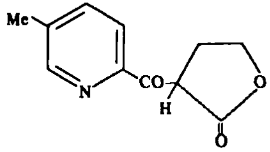
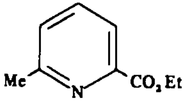
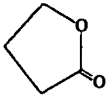
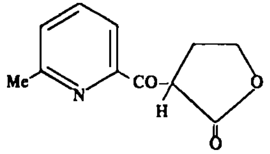
Pyridine ester	Condensed with	Conditions	Product	Yield	Properties	Ref.
2-PyCO$_2$Et	MeCO$_2$Et	6.5 hr 115°, NaOEt	2-PyCOCH$_2$CO$_2$Et	84.3%	b.p. 92–97°/0.1 mm	104
	EtO$_2$C(CH$_2$)$_3$CO$_2$Et	Na, NaNH$_2$, Et$_2$O, N$_2$, 45°, 13 hr	2-PyCOCH(CO$_2$Et)(CH$_2$)$_2$CO$_2$Et	42%	b.p. 160–170°/0.7 mm; n^{20}_D 1.5011	102
		K, C$_6$H$_6$		41%	b.p. 123°/0.05 mm; m.p. 92°	129
		NaH, PhMe, reflux 8 hr; HOAc		45 g ↓ 39.7 g	b.p. 130°/3 × 10^{-6} mm; m.p. 53.5–54.5°; ir; uv	140
		K, C$_6$H$_6$, reflux 5 hr			b.p. 122–124°/3 × 10^{-4} mm; ir; uv	140
2-PyCOCl · HCl	EtCH(CO$_2$Et)$_2$	Na, EtOH, reflux 2.5 hr	2-PyCOCEt(CO$_2$Et)$_2$	18%	b.p. 122–128°/0.05 mm	91
		NaH, PhMe, reflux 8 hr; HOAc		17.8 g ↓ 6.6 g	b.p. 145°/5× 10^{-4} mm; ir; uv	140

TABLE XI-11. Condensations of Pyridinecarboxylic Esters Yielding Side-Chain Acid Derivatives (Continued)

Pyridine ester	Condensed with	Conditions	Product	Yield	Properties	Ref.
	$MeCO_2Et$	Na, Et_2O, reflux 3 hr; kept over night		10 g ↓ 13 g		109
		NaH, PhMe, reflux 8 hr; HOAc			b.p. 136-137°/5 × 10^{-4} mm; m.p. 73-74°; ir; uv	140
		NaH, PhMe, reflux 8 hr; HOAc			b.p. 127-130°/3 × 10^{-5} mm; m.p. 91-93°; ir; uv	140
					b.p. 144-149°/3 mm	238
$3\text{-}PyCO_2Et$	$MeCO_2Et$	NaOEt, 115°, 6.5 hr	$3\text{-}PyCOCH_2CO_2Et$	84%	b.p. 122-132°/0.35 mm	104
		or NaOEt, C_6H_6, 10 hr 80°; aq. HCl		65%	b.p. 165-168°/5 mm	107
	$MeCO_2Et$	Na, PhMe	$3\text{-}PyC(ONa){=}CHCO_2Et$	95%		176
	$(CH_2CO_2Et)_2$	NaH, reflux in C_6H_6, EtOH; 5*N* HCl	$3\text{-}PyCOCH(CO_2Et)CH_2CO_2Et$	58.8%		23
$3\text{-}Py'{}^4CO_2Et$	$(CH_2CO_2Et)_2$	NaH, C_6H_6, EtOH	$3\text{-}Py'{}^4COCH(CO_2Et)CH_2CO_2Et$	33%		24

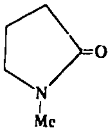
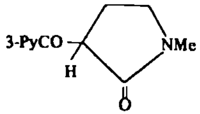
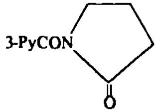
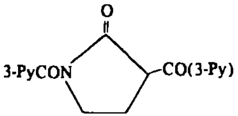
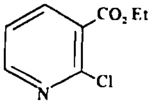
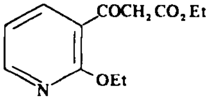
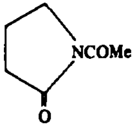
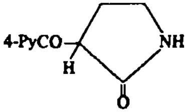
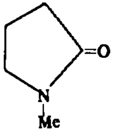
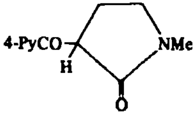
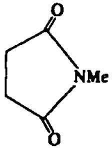
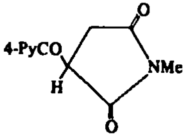
3-PyCO$_2$Et	EtO$_2$C(CH$_2$)$_3$CO$_2$Et	NaOEt, EtOH, heat, 1.5 hr	3-PyCOCH(CO$_2$Et)(CH$_2$)$_3$CO$_2$Et		b.p. 147–147.5°/0.1 mm; n_D^{20} 1.4995	75
	PhCH$_2$CONEt$_2$	NaOEt, PhMe or Xylene	3-PyCOCHPhCONEt$_2$	68.5%	m.p. 136–138°	82
		K, C$_6$H$_6$		52%	m.p. 44–45°; ir; uv	129
		NaH, 40–50°, 2–3 days		45%		129
3-PyCOCl · HCl	NaCH(CN)CO$_2$Et	C$_6$H$_6$, heat, 2 hr; alc. HCl, 20–30 min	3-PyCOCH(CN)CO$_2$Et	3.2 g ↓ 0.15 g	m.p. 201–202.5°	103
3-PyCOCl · HCl	EtCH(CO$_2$Et)$_2$	Na, EtOH, reflux 2.5 hr	3-PyCOCEt(CO$_2$Et)$_2$	5%	b.p. 132°/0.35 mm	91
	MeCO$_2$Et	Claisen conditions			b.p. 122°/1.0 mm; $n_D^{26.5}$ 1.5170	239
4-PyCO$_2$Et	MeCO$_2$Et	NaOEt, 115°, 6.5 hr *or*	4-PyCOCH$_2$CO$_2$Et	86.2%	m.p. 58–61.5°	104
		NaOEt, reflux 10 hr		62%	b.p. 163–169°/4 mm	108
4-PyCO$_2$Me	EtCO$_2$Me	NaH, Claisen conditions	4-PyCOCHMeCO$_2$Me	65%	b.p. 128–130°/1.5 mm	11

TABLE XI-11. Condensations of Pyridinecarboxylic Esters Yielding Side-Chain Acid Derivatives (Continued)

Pyridine ester	Condensed with	Conditions	Product	Yield	Properties	Ref.
4-PyCOCl·HCl	$EtCH(CO_2Et)_2$	Na, EtOH, reflux 2.5 hr	$4\text{-}PyCOCEt(CO_2Et)_2$	14%	b.p. 138–142°/0.3 mm	91
$4\text{-}PyCO_2Et$ (1 equiv)	$EtO_2C(CH_2)_4CO_2Et$	NaH, 130–140°, 4 hr; 20% HCl; Na_2CO_3; 20% H_2SO_4, reflux 8 hr, $-CO_2$	$4\text{-}PyCO(CH_2)_4CO_2H$	15.6%	m.p. 163–164°	117
$4\text{-}PyCO_2Et$ (2 equiv.)	$EtO_2C(CH_2)_4CO_2Et$	NaOEt, 12 hr, 130–140°; 20% HCl	$4\text{-}PyCOCH(CO_2Et)(CH_2)_4CH(CO_2Et)$ $CO(4\text{-}Py)$		m.p. 75°	117
	$EtO_2C(CH_2)_6CO_2Et$	NaOEt, 12 hr, 130–140°; 20% HCl	$4\text{-}PyCOCH(CO_2Et)(CH_2)_6CH(CO_2Et)$ $CO(4\text{-}Py)$	14.5%	m.p. 94–95°	117
$4\text{-}PyCO_2Et$		K, C_6H_6; hydrolysis		32%	m.p. 115°; ir	129
		K, C_6H_6		42%	m.p. 85°; ir	129
		Na, C_6H_6; 120–130°, 12 hr			m.p. 136–137°	117

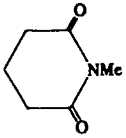
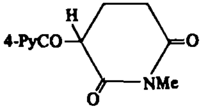
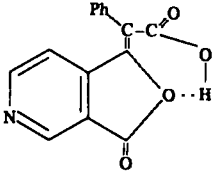
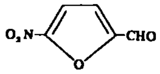
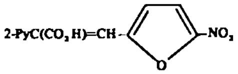
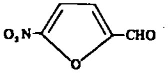
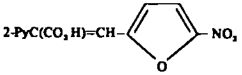
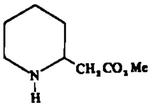
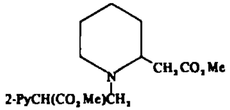
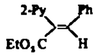
		Na, C_6H_6; 120–130°, 12 hr		87%	m.p. 109–111°	117
3, 4-Py$(CO_2H)_2$		Ac_2O, 2 hr, 120–125°; $PhCH_2CO_2H$, 70°; TEA, R.T., 48 hr; HCl, R.T., 36 hr		0.7 g ↓ 1.0 g	m.p. 221–222°	240

TABLE XI-12. Condensations of Pyridineacetic Acids, Esters, and Amides to give Longer-Chain Acid Derivatives

Pyridine	Condensed with	Conditions	Product	Yield	Properties	Ref.
2-PyCH$_2$CO$_2$H		Ac$_2$O, 20–30°, 4 hr			m.p. 126–128°	28
2-PyCH$_2$CO$_2$K		same as above			m.p. 240–242° (decomp.)	61
2-PyCH$_2$CO$_2$Me	BrCH$_2$CO$_2$Me	(i) K, C$_6$H$_6$, 4 hr; (ii) overnight with halide	2-PyCH(CO$_2$Me)CH$_2$CO$_2$Me	89.3 g ↓ 52.7 g	b.p. 130–140°/0.5 mm	19
		40% HCHO, H$_2$O, 2 hr, steam-bath		42%	b.p. 130–150°/0.05 mm; ir	19
	n-BuBr	(i) NaOEt, EtOH or Na, C$_6$H$_6$, 50°, 6 hr; (ii) reflux 12 hr with halide	2-PyCH(*n*-Bu)CO$_2$Et	50%	b.p. 117–121°/25 mm; n_D^{25} 1.4906	112
	n-HexBr	same as above	2-PyCH(*n*-Hex)CO$_2$Et	50%	b.p. 181–184°/21 mm; n_D^{25} 1.4855	112
	PhCH$_2$Cl	same as above	2-PyCH(CH$_2$Ph)CO$_2$Et	52%	b.p. 204–209°/18 mm; n_D^{20} 1.5451	112
	CH$_2$=CHCH$_2$Br	same as above	2-PyCH(CH$_2$CH=CH$_2$)CO$_2$Et	27%	b.p. 163–168°/18 mm	112
	n-HexCHO	Piperidine, C$_6$H$_6$, HOAc	2-PyC(=CH–Hex)CO$_2$Et	35%	b.p. 194–196°/25 mm	112
	PhCHO	Piperidine, C$_6$H$_6$, HOAc	2-PyC(=CHPh)CO$_2$Et	41%	b.p. 145°/0.3 mm; n_D^{25} 1.5965	112
	PhCHO	piperidine, EtOH, reflux, 17–18 hr		46%	b.p. 160–161°/1.0 mm; methiodide, m.p. 200–201° (decomp.); uv	111

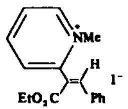
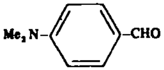
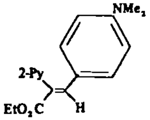
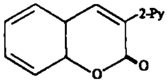
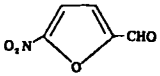
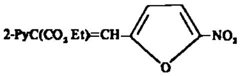
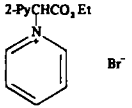
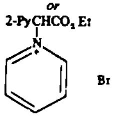
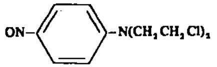
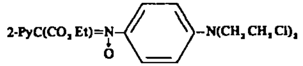
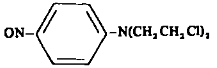
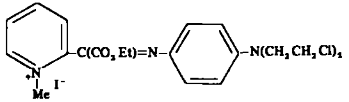
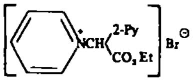
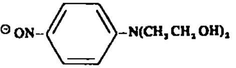
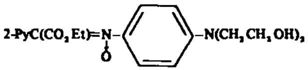
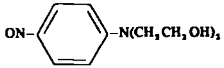
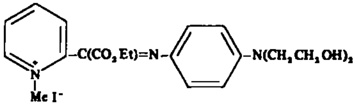
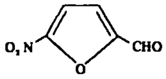
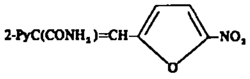
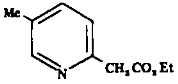
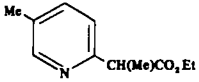
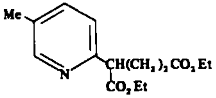
2-PyCH$_2$CO$_2$Et MeI	PhCHO	reflux 2 hr		35%	methiodide, m.p. 227–228° (decomp.); uv	111
2-PyCH$_2$CO$_2$Et		piperidine, EtOH, reflux, 17–18 hr		76%	m.p. 127–128°	111
	p-HOC$_6$H$_4$CHO	same as above		75%	m.p. 141–142°	111
		Ac$_2$O, 3 hr, 130–140°			m.p. 82–84° m.p. 79–81°, 122–124° (two isomers)	28 241
	CH$_2$=CHCO$_2$Et	Na	2-PyCH(CO$_2$Et)CH$_2$CH$_2$CO$_2$Et	82%		242
	MeCH=CHCO$_2$Me	NaOMe, C$_6$H$_6$, reflux 24 hr	2-PyCH(CO$_2$Et)CHMeCH$_2$CO$_2$Me	67%	b.p. 120°	200
	PhCH=CHCO$_2$Et	NaOMe, C$_6$H$_6$, reflux 3 hr	2-PyCH(CO$_2$Et)CHPhCH$_2$CO$_2$Et	84%	b.p. 170–180°/0.001 mm; ir	200
	CH$_2$=CHCHO	(i) Na, EtOH, 0°, 3 hr; (ii) reflux 12 hr	2-PyCH(CH$_2$CH$_2$CHO)CO$_2$Et	24%	b.p. 115–116°/0.3 mm; n_D^{23} 1.5073	112
	 $\underset{O}{CH_2{=}CHP(OEt)_2}$	NaOEt, EtOH, 60°	 $2\text{-}PyCH(CO_2Et)CH_2CH_2\underset{O}{P}(OEt)_2$		b.p. 122–123°/0.01 mm; n_D^{19} 1.4891	243
	Pyridine	Br$_2$, CCl$_4$		38%		244
	PhCOCl	(i) NaOEt, EtOH or Na C$_6$H$_6$, 50°, 6 hr; (ii) reflux 12 hr with halide	2-PyC(PhCO)$_2$CO$_2$Et	53%	b.p. 120–122°	112

TABLE XI-12. Condensations of Pyridineacetic Acids, Esters, and Amides to Give Longer-Chain Acid Derivatives (Continued)

Pyridine	Condensed with	Conditions	Product	Yield	Properties	Ref.
2-PyCH$_2$CO$_2$Et or 		Py·HBr, KOH, EtOH			m.p. 139–140°	244
2-PyCH$_2$CO$_2$Et · MeI					m.p. 151–152°	244
		K$_2$CO$_3$, EtOH, 0.5–1 hr			m.p. 150–153° (decomp.)	244
2-PyCH$_2$CO$_2$Et · MeI					m.p. 161–163° (decomp.)	244
2-PyCH$_2$CONH$_2$		Ac$_2$O, 3 hr, 130–140°			m.p. 180–182°, 180–181.5° (two isomers) m.p. 180–182°	241 28
	MeI	(i) K, C$_6$H$_6$, reflux 15 hr; (ii) halide 2–6 hr		62%	b.p. 132–136°/14 mm; picrate, m.p. 170°	206 192
	ICH$_2$CH$_2$CO$_2$Et	(i) K, C$_6$H$_6$, reflux, 15 hr; (ii) halide, reflux 2 hr		50%	b.p. 140–150°/0.01 mm	206

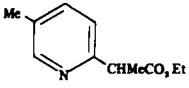
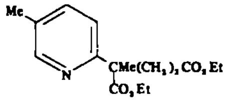
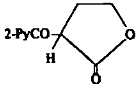
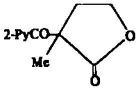
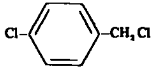
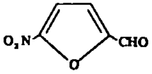
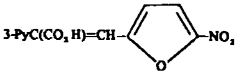
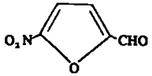
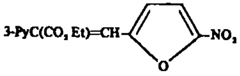
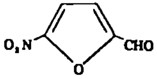
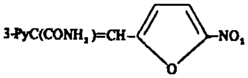
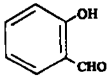
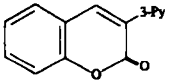
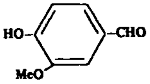
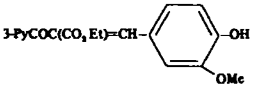
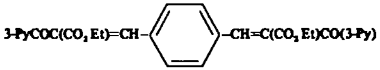
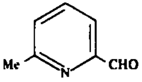
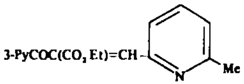
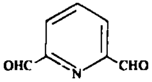
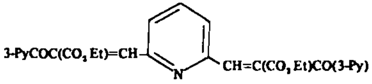
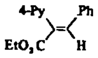
	$ICH_2CH_2CO_2Et$	same as above		50%	b.p. 140–150°/0.01 mm	206
	MeI	(i) Na, C_6H_6; (ii) MeI, R.T. 3 weeks			m.p. 65–66°	140
$2\text{-}Py(CH_2)_2CH(CO_2Et)_2$		(i) NaH, PhMe, reflux 1 hr; (ii) halide, 42 hr; (iii) 20% HCl	$2\text{-}Py(CH_2)_2CH(CO_2H)CH_2(p\text{-}ClC_6H_4)$	57.7%	m.p. 112–113°; ir	245
$3\text{-}PyCH_2CO_2H$	PhCHO	piperidine, pyridine, 120°, 72 hr	$3\text{-}PyC(CO_2H){=}CHPh$	6.3 g ↓ 5.9 g	m.p. 235–236° m.p. 235–238°	101 98
		Ac_2O, 3 hr, 130–140°			m.p. 247–248° (decomp.)	28
$3\text{-}PyCH_2CO_2Et$	MeI	(i) Na, C_6H_6, 23 hr; (ii) MeI, 60°, 16 hr	$3\text{-}PyCH(Me)CO_2Et$		b.p. 63.8–64.6°/0.1 mm	27
		Ac_2O, 3 hr, 130–140°			m.p. 100–102°	28
	HCO_2Et	dry NaOEt, 105° 25 hr	$3\text{-}PyC(CO_2Et){=}CHOH$	55%	m.p. 124–125° (decomp.)	168
	$AcNHCH(CO_2Me)_2 + HCHO$	4 hr, PhMe, reflux *or* 110°, 3.5 hr, DMF	 $3\text{-}PyCH(CO_2Et)CH_2C(NHAc)(CO_2Me)_2$	72% 60–70%	m.p. 111–112°	113
$3\text{-}PyCH_2CONH_2$		Ac_2O, 3 hr, 130–140°			m.p. 175–176°	28
$3\text{-}PyCOCH_2CO_2Et$	$BrCH_2CO_2Et$	K, DMF	$3\text{-}PyCOCH(CO_2Et)CH_2CO_2Et$			2
	PhCHO	piperidine, HOAc 5:2	$3\text{-}PyCOC(CO_2Et){=}CHPh$	51.2%	m.p. 85.5–86°; ir	246

TABLE XI-12. Condensations of Pyridineacetic Acids, Esters, and Amides to Give Longer-Chain Acid Derivatives (Continued)

Pyridine	Condensed with	Conditions	Product	Yield	Properties	Ref.
		same as above		38.5%	m.p. 158–159°; hydrochloride, m.p. 236–237°	246
		same as above		61.3%	m.p. 145–146°	246
	p-$Me_2NC_6H_4CHO$	same as above	3-PyCOC(CO_2Et)=CH(p-$Me_2NC_6H_4$)	46%	m.p. 121°	246
	o-$O_2NC_6H_4CHO$	same as above	3-PyCOC(CO_2Et)=CH(o-$O_2NC_6H_4$)	40.4%	m.p. 103–104°	246
	p-$O_2NC_6H_4CHO$	same as above	3-PyCOC(CO_2Et)=CH(p-$O_2NC_6H_4$)	86.5%	m.p. 110–111°	246
	p-$C_6H_4(CHO)_2$	same as above		50%	m.p. 179; ir	246
	2-FurylCHO	same as above	3-PyCOC(CO_2Et)=CH(2-furyl)	77.9%	m.p. 114–115°	246
	2-PyCHO	same as above	3-PyCOC(CO_2Et)=CH(2-Py)	85%	m.p. 119–120°	246
	3-PyCHO	same as above	3-PyCOC(CO_2Et)=CH(3-Py)	34%	m.p. 84°; ir	246
		same as above		87.8%	m.p. 123.5–124.5°	246
		same as above		89%	m.p. 135°	246
4-$PyCH_2CO_2Et$	PhCHO	Ac_2O, 5 hr, 150–160°; 2N MeOH, KOH	4-PyC(=CHPh)CO_2H	1.8 g → 1 g	m.p. 203° (decomp.)	29
	PhCHO	piperidine, EtOH, reflux 17–18 hr		75%	b.p. 175–176°/2.3 mm; methiodide, m.p. 197–198° (decomp); uv	111

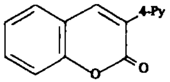
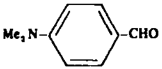
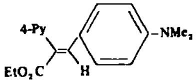
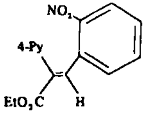
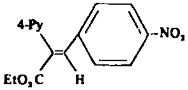
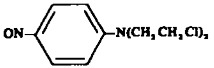
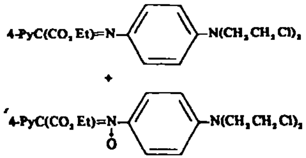
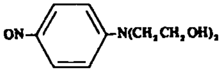
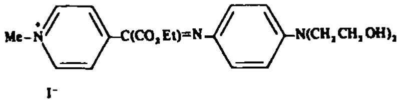
	o-HOC_6H_4CHO	same as above		75%	m.p. 228–229°	111
		same as above		89%	m.p. 101–102°	111
	o-$NO_2C_6H_4CHO$	same as above		4.2%	hydrochloride, m.p. 183–184° (decomp.)	111
	p-$O_2NC_6H_4CHO$	same as above		13%	hydrochloride, m.p. 147–149° (decomp.)	111
	HCO_2Et	NaOEt, 105°, 25 hr	4-$PyC(CO_2Et)$=$CHOH$	34%	m.p. 164–165°	168
	$AcNHCH(CO_2Me)_2$ + CH_2O	piperidine, PhMe, reflux 2.5–3 hr *or* no piperidine, reflux 2 hr, PhMe *or* no piperidine, PhMe, reflux 4 hr *or* DMF, 110°, 3.5 hr	4-$PyCH(CO_2Et)CH_2C(CO_2Me)_2$ $NHAc$	84–86% 60% 70% 76%	m.p. 175–176°	113
4-$PyCH_2CO_2Et$ free base		piperidine, EtOH, 1 hr			m.p. 172–174° (decomp.)	244
4-$PyCH_2CO_2Et$ ·MeI					m.p. 147–148° (decomp.)	244

TABLE XI-12. Condensations of Pyridineacetic Acids, Esters, and Amides to Give Longer-Chain Derivatives (Continued)

Pyridine	Condensed with	Conditions	Product	Yield	Properties	Ref.
4-PyCOCH$_2$CO$_2$Et	BrCH$_2$CH$_2$CO$_2$Et	Na, EtOH; 70°, 2 hr	4-PyCOCH(CO$_2$Et)CH$_2$CH$_2$CO$_2$Et		b.p. 155–160°/0.1 mm	117
	PhCHO	piperidine, 3 hr, steam-bath	(4-PyCOCHCO$_2$Et)$_2$CHPh		m.p. 102–103°	105
	CH$_2$(COPh)$_2$ + CH$_2$O	PhMe, reflux 4 hr	4-PyCOCH(CO$_2$Et)CH$_2$CH(COPh)$_2$	50%	m.p. 112–113°	113
	AcNHCH(CO$_2$Et)$_2$ + CH$_2$O	same as above	4-PyCOCH(CO$_2$Et)CH$_2$C(NHAc)(CO$_2$Et)$_2$	52%	m.p. 160–161°	113
	AcNHCH(Ac)CO$_2$Me + CH$_2$O	same as above	4-PyCOCH(CO$_2$Et)CH$_2$C(NHAc)(Ac)CO$_2$Me	47%	m.p. 122–123°	113
4-PyC(CO$_2$Et)=S(O)Me$_2$	MeI	CHCl$_3$	4-PyC(I)(Me)CO$_2$Et		m.p. 63°	247

TABLE XI-13. Preparation of Acids and Derivatives by Reduction of Side-Chain Functions

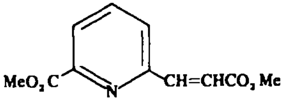
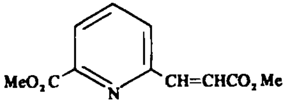
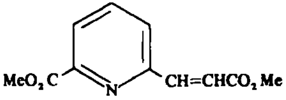
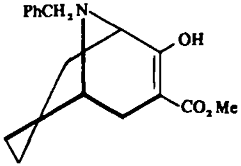
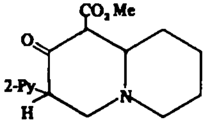
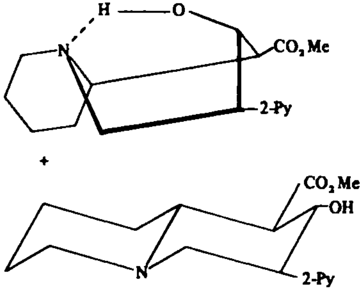
Starting material	Conditions	Product	Yield	Properties	Ref.
2-PyCH=CHCO$_2$H	P, HOAc, 57% HI, 14 hr; Na$_2$HPO$_4$, heat, *n*-BuOH	2-Py(CH$_2$)$_2$CO$_2$H		m.p. 143-144°	114
2-PyCH=CHCO$_2$Et	MeI, acetone; H$_2$O, Ag$_2$O; HCO$_2$H	2-Py(CH$_2$)$_2$CO$_2$H			114
	H$_2$, PtO$_2$ HOAc *or* H$_2$, 10% Pd-C, HOAc	2-Py(CH$_2$)$_2$CO$_2$Et	50%	m.p. 96-97°/3 mm; methiode, m.p. 81-82°	114 34
	or MeI, acetone; Ag$_2$O, H$_2$O; 95% HCO$_2$H, HCO$_2$K, 13 hr, 143-148°; EtOH, HCl, reflux 4 hr		9.5%		114
	H$_2$, PtO$_2$		1.0 g → 0.5 g	m.p. 53-54°; ir	197
	H$_2$, PtO$_2$, 5 atm, 6 hr, MeOH, 5 *N* HCl; PhCOCl, Pyridine; NaH, THF, 2 days, EtOH, N$_2$, 36 hr, R.T.; reflux 4 hr				197
2-PyC(=CH$_2$)CO$_2$H	H$_2$, 5% Pd-C, aq. NaOH, 2 atm, < 2 hr	2-PyCHMeCO$_2$H	67.4%	m.p. 144.5-145°	248
2-Py(CH$_2$)$_4$C≡CCO$_2$H	H$_2$, 0.5% Pd on alumina R.T., pressure	2-Py(CH$_2$)$_4$CH=CHCO$_2$H		m.p. 93-94°; ir	80

TABLE XI-13. Preparation of Acids and Derivatives by Reduction of Side-Chain Functions (Continued)

Starting material	Conditions	Product	Yield	Properties	Ref.
	H_2, Ni or PtO_2, R.T., aq. EtOH	2-Py$(CH_2)_6CO_2H$		m.p. 60°; ir	80
2-Py$(CH_2)_5C{\equiv}CCO_2H$	H_2, 0.5% Pd on alumina R.T., pressure	2-Py$(CH_2)_5CH{=}CHCO_2H$		m.p. 43–44°	80 81
	H_2, Ni or PtO_2, R.T., aq. EtOH	2-Py$(CH_2)_7CO_2H$		m.p. 45°	80
2-Py$(CH_2)_{10}C{\equiv}CCO_2H$	H_2, 0.5% Pd on alumina, R.T., pressure	2-Py$(CH_2)_{10}CH{=}CHCO_2H$		m.p. 75°	80
	H_2, Ni or PtO_2, aq. EtOH, R.T., pressure	2-Py$(CH_2)_{12}CO_2H$		m.p. 77°	80 81
2-PyCOCH_2CO_2Et	H_2, PtO_2, 2 hr, 3 atm, EtOH	2-PyCH(OH)CH_2CO_2Et		b.p. 89–90°/0.1 mm; picrate, m.p. 99–100°; hydrochloride, m.p. 129–130°	249
2-PyCOCHPhCO_2Me	$NaBH_4$, MeOH	2-PyCH(OH)CHPhCO_2Me	75%	m.p. 105–106°; hydrochloride, m.p. 108–110°	116
	$NaBH_4$, MeOH, 20°, 2 hr		82%	m.p. 135–137°; ir m.p. 149°	19

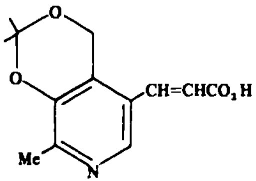
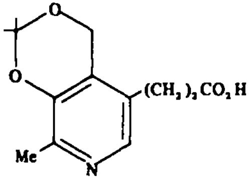
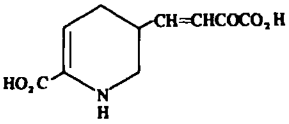
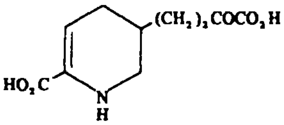
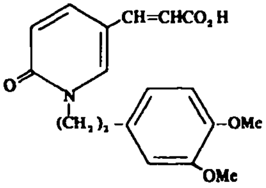
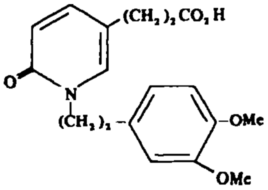
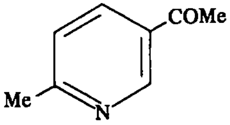
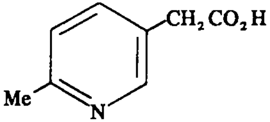
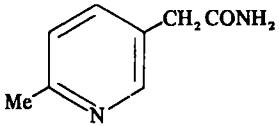
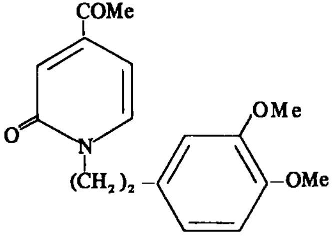
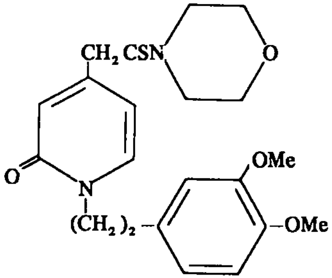
3-PyCH=CHCO$_2$H	H$_2$, PtO$_2$, H$_2$O, 30 min and then repeat	3-Py(CH$_2$)$_2$CO$_2$H	4.5 g → 2.9 g	m.p. 161–162°	152
3-PyCCl=CHCO$_2$Et + 3-PyCCl$_2$CH$_2$CO$_2$Et	H$_2$, 5% Pd-C, EtOH, Py, R.T.	3-PyCH$_2$CH$_2$CO$_2$H		n_D^{20} 1.5140; picrate, m.p. 103°	175
3-PyCPh=CHCO$_2$Na	H$_2$, Ni	3-PyCHPhCH$_2$CO$_2$H	90%	m.p. 171–172°	54
	H$_2$, Pd, EtOH, 4 hr		97.5%	m.p. 188–190°; ir; uv	228
	enzyme reduction				73
	H$_2$, PtO$_2$, EtOH, 40–45°		3 g → 3 g	m.p. 58–59°	7
3-PyC(=CH$_2$)CO$_2$H	H$_2$, 5% Pd-C, aq. NaOH, 2 atm, < 2 hr	3-PyCHMeCO$_2$H	63%	m.p. 163–165°	248
3-PyCOCHPhCONH$_2$	NaBH$_4$, MeOH-H$_2$O	3-PyCH(OH)CHPhCONH$_2$	80%	m.p. 193–194°	116
3-PyCH$_2$COCH$_2$CONHMe	Wolff-Kishner; KOH, 4 hr, 195°	3-Py(CH$_2$)$_3$CO$_2$H		m.p. 121–122°	22

TABLE XI-13. Preparation of Acids and Derivatives by Reduction of Side-Chain Functions (Continued)

Starting material	Conditions	Product	Yield		Ref.
3-PyCO$(CH_2)_2CO_2H$	$NaBH_4$, KOH, H_2O, 2 hr	3-PyCH(OH)$(CH_2)_2CO_2H$			23
3-PyCO$(CH_2)_5CO_2Et$	Wolff-Kishner	3-Py$(CH_2)_6CO_2H$	2.5 → 0.7 g	m.p. 92–93°	117
3-PyC(=NOH)$(CH_2)_2CO_2Et$	Pb-$BaSO_4$, H_2 1 atm	3-PyCH$(NH_2)(CH_2)_2CO_2Et$ *d,l*			2
4-PyCH=CHCO$_2$H	H_2	4-Py$(CH_2)_2CO_2H$			115
4-PyCH=CHCO$_2$Me	$NaBH_4$, MeOH, reflux 1-2 hr	4-Py$(CH_2)_2CO_2Me$			115
4-PyCH=CHCO$_2$Et	MeI, acetone; Ag_2O, H_2O; HCO_2H	4-Py$(CH_2)_2CO_2H$			114
	MeI, acetone; Ag_2O, H_2O; 95% HCO_2H, HCO_2K, 10 hr, 156–157°; HCl, EtOH, reflux 4 hr	4-Py$(CH_2)_2CO_2Et$	30 → 49 g	b.p. 113°/4 mm; picrate, m.p. 119–120°; methiodide, m.p. 88–89°	114
4-PyCH=CHCONHNH$_2$	H_2, PtO_2, EtOH, R.T., 1 atm	4-Py$(CH_2)_2CONHNH_2$	0.3 → 0.15 g	m.p. 84°; hydrate, m.p. 64°	166
4-PyC(=CH_2)CO_2H	H_2, 5% Pd-C, aq. NaOH, 2 atm, < 2 hr	4-PyCHMeCO$_2$H	80%	m.p. 225–227°	248
4-PyC(=CHPh)CONHNH$_2$	H_2, PtO_2, EtOH, R.T., 1 atm	4-PyCH(CH_2Ph)CONHNH$_2$		m.p. 138°	166
4-Py$(CH_2)_4C{\equiv}CCO_2H$	H_2, 0.5% Pd on alumina, R.T., pressure	4-Py$(CH_2)_4CH{=}CHCO_2H$		m.p. 120°	80
	H_2, Ni or PtO_2, aq. EtOH, R.T., pressure	4-Py$(CH_2)_6CO_2H$		m.p. 165–166°	80 81
4-Py$(CH_2)_5C{\equiv}CCO_2H$	H_2, 0.5% Pd on alumina, R.T., pressure	4-Py$(CH_2)_5CH{=}CHCO_2H$		m.p. 98°	80

	H_2, Ra-Ni *or* PtO_2, aq. EtOH, R.T., pressure	4-Py$(CH_2)_7CO_2H$		m.p. 121–122°	80 81
4-PyCOCHPhCONH$_2$	$NaBH_4$, MeOH-H_2O	4-PyCH(OH)CHPhCONH$_2$	82.8%	m.p. 144–145°	116
4-PyCO$(CH_2)_5CO_2$Et	Na, 65% NH_2NH_2, $O(CH_2CH_2OH)_2$; EtOH, 2 hr, 115°; 200°, 3 hr	4-Py$(CH_2)_6CO_2H$	39%	m.p. 163–164°	117

TABLE XI-14. The Willgerodt Reaction

Starting material	Conditions	Product	Yield	Properties	Ref.
2-PyCH=CH$_2$	S, DMF, 30 hr, 140–160°	2-PyCH$_2$CSNMe$_2$		b.p. 153–157°/1.2 mm;	250
	S, morpholine, reflux 6 hr; 95% EtOH, 60% NaOH, reflux 16 hr			hydrochloride, m.p. 170–172°	251
	NH$_4$SH, dioxane, heat 6 hr		27 g ↓ 26 g	m.p. 158–160°; picrate, m.p. 168–169°	156
4-PyEt	S, DMF, 30 hr, 140–160°	4-PyCH$_2$CSNMe$_2$		m.p. 108–112°	250
	S, MeNHCHO, 30 hr, 140–160°	4-PyCH$_2$CSNHMe		m.p. 136–141°	250
	S, morpholine, 150–160°, reflux 5 hr		52%		8

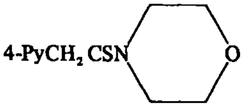
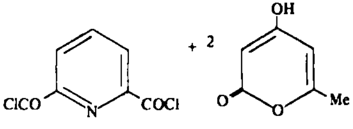
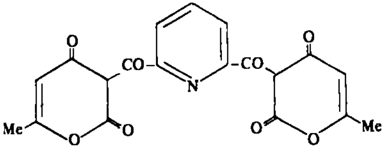
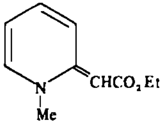
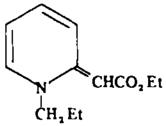
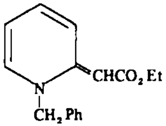
4-PyCOPr	S, morpholine; 50% MeOH, reflux 11 hr, 50% NaOH; HCl, 5 hr, boiled in MeOH	4-Py$(CH_2)_3CO_2Me$	4.4 g ↓ 1.4 g	b.p. 85–87°/2 mm	117
4-PyCH=CH$_2$	S, morpholine, reflux 16 hr		53%	m.p. 105–107°	3

TABLE XI-14-1. Preparation of Acids and Derivatives by Miscellaneous Methods

Reactants	Conditions	Product	Yield	Properties	Ref.
2-PyMgCl + $BrCH_2CO_2Et$		$2\text{-}PyCH_2CO_2Et$			252
	Py, C_6H_6, R.T., 4-5 hr		79%	m.p. 196°	253
$2\text{-}PyCH_2CO_2Et$	$NaNO_2$, HOAc, 15-25° 30 min	2-PyC(=NOH)CO_2Et		m.p. 149-150°; ir	112
$2\text{-}PyCH_2CO_2Et$	MeI, EtOH; 1*N* NaOH			m.p. 52-54°	254
$2\text{-}PyCH_2CN$ + $EtCH_2I$	6 hr steam-bath; NaOH				145
$2\text{-}PyCH_2CO_2Et$ + $PhCH_2Br$	3 hr, steam-bath; NaOH			m.p. 94-95°; ir	145

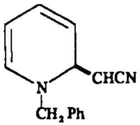
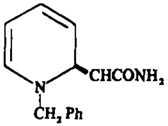
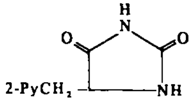
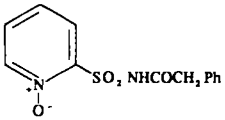
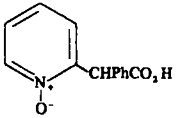
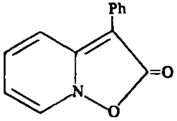
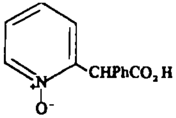
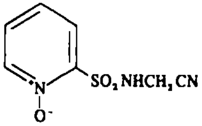
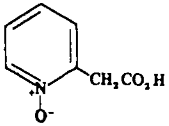
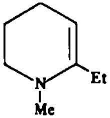
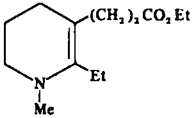
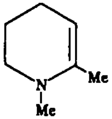
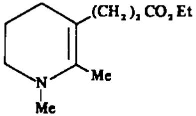
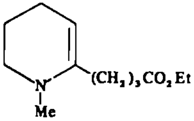
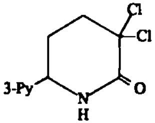
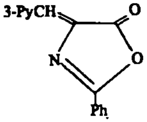
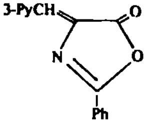
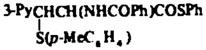
2-PyCH$_2$CN + PhCH$_2$Br	1 hr, steam-bath; NaOH			m.p. 128–129°; ir	145
2-PyCH$_2$CONH$_2$ + PhCH$_2$Br	6 hr, steam-bath; NaOH			m.p. 153–154° (decomp.); ir	145
	Ba(OH)$_2$, H$_2$O, heat	2-PyCH$_2$CH(NH$_2$)CO$_2$H		m.p. 209–210°	95
	10% NaOH, 24°, 1 hr	 (77.8%) +  (6.7%)		m.p. 100–102° (decomp.)	154
	10% NaOH, 95°, 96 min		80%	m.p. 100–102° (decomp.)	255, 256, 257
	10% NaOH, 90–95°, 1 hr			m.p. 126–127° (decomp.)	154

TABLE XI-14-1. Preparation of Acids and Derivatives by Miscellaneous Methods (Continued)

Reactants	Conditions	Product	Yield	Properties	Ref.
 + CH_2=$CHCO_2Et$	dioxane		42%	b.p. 112-114°/2 mm	258
 + CH_2=$CHCO_2Et$	anhyd. dioxane, R.T., 4 days	 + 			259
	HCl, reflux 4 hr; dry HCl	3-PyCH(NH_2)$CH_2CH_2C(CO_2H)Cl_2$	90%	m.p.181-182° (decomp.)	102
 + PhSH	steam-bath, 2 hr	3-PyCH(SPh)CH(NHCOPh)COSPh	82%	m.p. 139°	120
 + p-MeC_6H_4SH	same as above	 $3\text{-Py}\underset{\substack{\vert \\ S(p\text{-}MeC_6H_4)}}{C}HCH(NHCOPh)COSPh$	83%	m.p. 165°	120

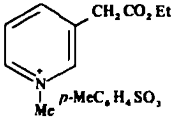
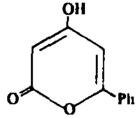
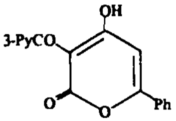
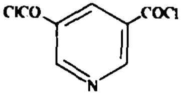
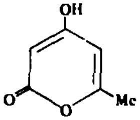
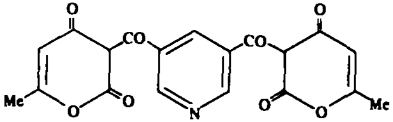
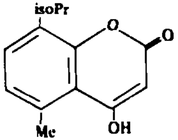
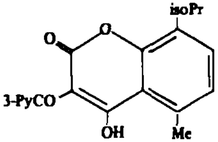
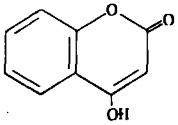
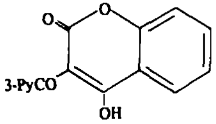
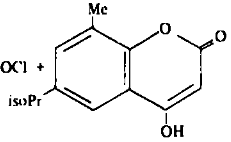
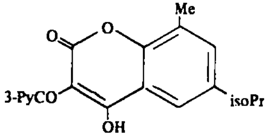
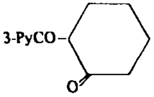
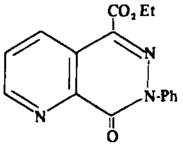
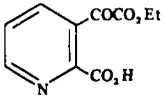
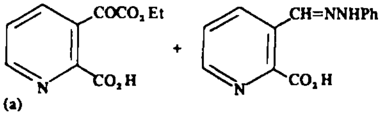
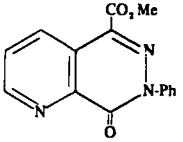
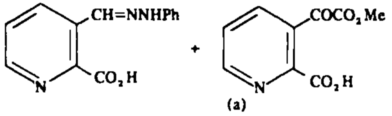
3-PyCH$_2$C(=NOH)CH$_2$CO$_2$H	POCl$_3$	3-PyCH$_2$CO$_2$H		m.p. 167–169°;	22
3-PyCH$_2$CO$_2$Et + p-MeC$_6$H$_4$SO$_3$Me	120°, 6 hr			m.p. 143–144°	254
3-PyCOCl + Ph$_3$P$^{\oplus}$CH$_2$OMe Br$^{\ominus}$ or Ph$_3$P=CHOMe	PhLi, Et$_2$O	3-PyCOC(OMe)=PPh$_3$	31.6% 51.5%	m.p. 212–216° (decomp.) m.p. 220–222°	123 124
3-PyCOC(OMe)=PPh$_3$	PhI(OAc)$_2$	3-PyCOCO$_2$Me	35.2%	b.p. 70–90°/0.001 mm	123, 124
3-PyCOCl + 2 	Py, C$_6$H$_6$, R.T., 4–5 hr			m.p. 139°	253
 + 2 	Py, C$_6$H$_6$, R.T., 4–5 hr		76%	m.p. 197°; ir	253
3-PyCOCl + 	Py, C$_6$H$_6$; R.T., 4–5 hr		78%	m.p. 143°	253
3-PyCOCl + 	Py, C$_6$H$_6$, R.T., 4–5 hr		78%	m.p. 126°	253

TABLE XI-14-1. Preparation of Acids and Derivatives by Miscellaneous Methods (Continued)

Reactants	Conditions	Product	Yield	Properties	Ref.
3-PyCOCl + 	Py, C_6H_6, R.T., 4–5 hr		76%	m.p. 85°	253
	HCl, reflux 1.5 hr; EtOH, reflux; HCl	3-PyCO$(CH_2)_5CO_2Et$	27.4 g ↓ 13.3 g	b.p. 155–158°/0.4 mm	117
	aq. NaOH, cold			m.p. 223° (decomp.)	260
	aq. NaOH, warm			(a) m.p. 223° (decomp.)	260
	aq. NaOH, warm			(a) m.p. 227–229° (decomp.)	260

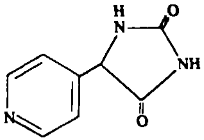
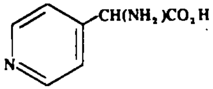
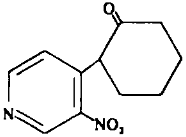
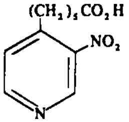
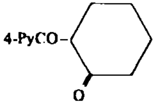
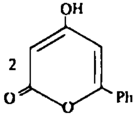
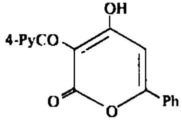
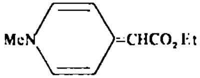
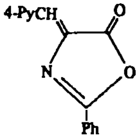
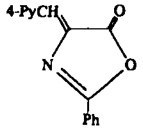
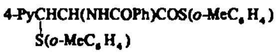
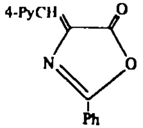
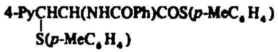
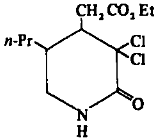
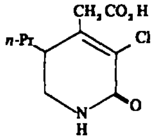
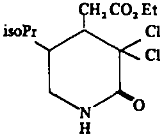
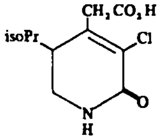
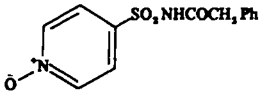
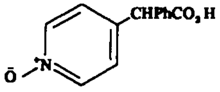
	Ba(OH)$_2$, H$_2$O, reflux 3 days		5.6 g ↓ 1.2 g	m.p. 163-167° (decomp.)	118
	acid, heat			m.p. 112-114°	119
	HCl, reflux 1.5 hr; EtOH, reflux; HCl	4-PyCO(CH$_2$)$_5$CO$_2$Et	31.4%	b.p. 158°/0.4 mm	117
4-PyCOCl + 2 	Py, C$_6$H$_6$, R.T., 4-5 hr			m.p. 154°	253
4-PyCH$_2$CO$_2$Et	MeI, EtOH, 1*N* NaOH			m.p. 110-111°	254
 + PhSh	same as above	4-PyCH(SPh)CH(NHCOPh)COSPh	76%	m.p. 163°	120

TABLE XI-14-1. Preparation of Acids and Derivatives by Miscellaneous Methods (Continued)

Reactants	Conditions	Product	Yield	Properties	Ref.
 + o-MeC$_6$H$_4$SH	same as above	 $\underset{\text{S}(o\text{-MeC}_6\text{H}_4)}{\text{4-PyCH}}\text{CH(NHCOPh)COS}(o\text{-MeC}_6\text{H}_4)$	78%	m.p. 149°	120
 + p-MeC$_6$H$_4$SH	same as above	 $\underset{\text{S}(p\text{-MeC}_6\text{H}_4)}{\text{4-PyCH}}\text{CH(NHCOPh)COS}(p\text{-MeC}_6\text{H}_4)$	72%	m.p. 146°	120
	Ba(OH)$_2$ · 8H$_2$O, H$_2$O, reflux 3 hr			m.p. 200°	261
	same as above			m.p. 203°	261
	10% NaOH, 27°, 17 hr *or* 10% NaOH, 95°, 96 min		84.4% 81.7%	m.p. 144–145° (decomp.)	154 255, 256, 257

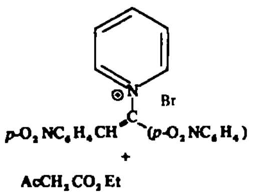
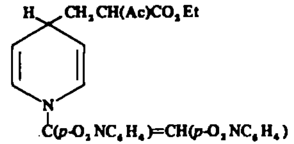
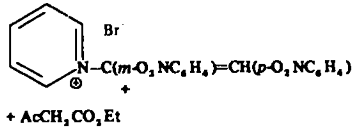
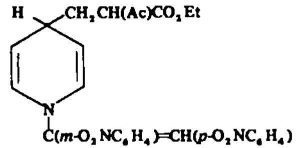
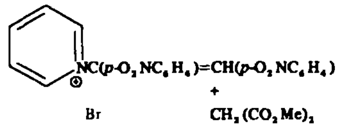
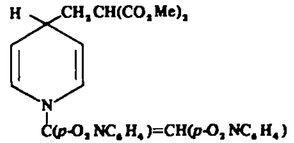
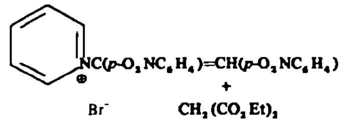
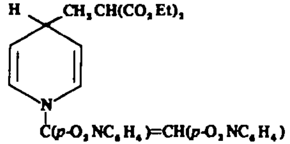
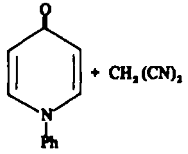
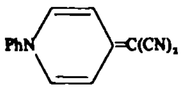
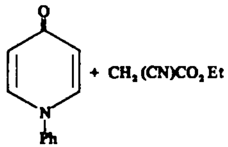
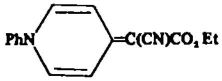
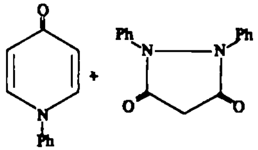
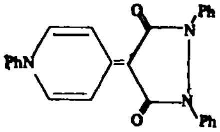
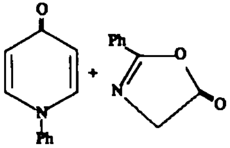
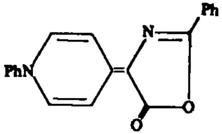
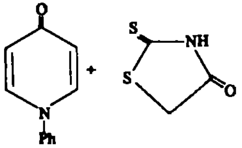
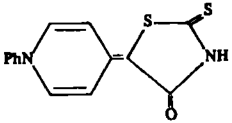
	Et$_3$N, EtOH, H$_2$O, 30 min		95%	m.p. 137-139°	262
	same as above		80%		262
	same as above		74%	m.p. 125-126°; ir	262
	same as above		89%	m.p. 136-137° (decomp.)	262
	same as above		64%	m.p. 310°; uv	263

TABLE XI-14-1. Preparation of Acids and Derivatives by Miscellaneous Methods (Continued)

Reactants	Conditions	Product	Yield	Properties	Ref.
	same as above			m.p. 182°; uv	263
	same as above		79%	m.p. 279°; uv	263
	same as above		63%	m.p. 195°; uv	263
	same as above		49%	m.p. 294°; uv	263

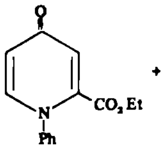
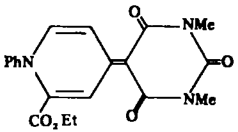
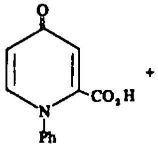
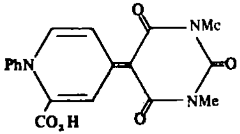
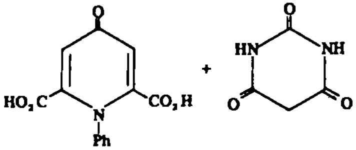
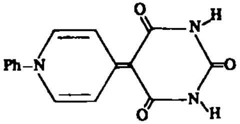
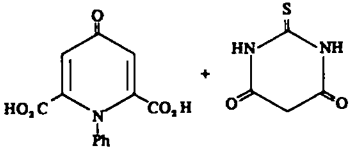
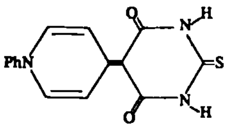
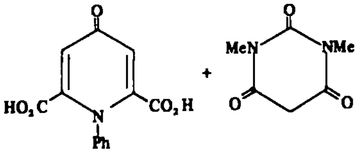
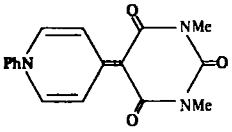
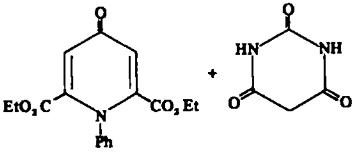
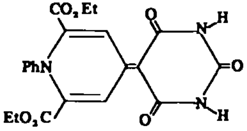
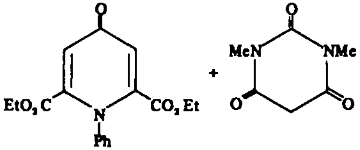
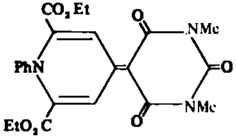
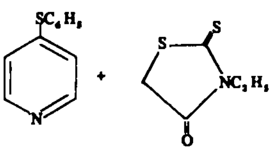
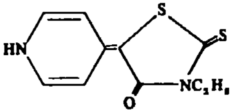
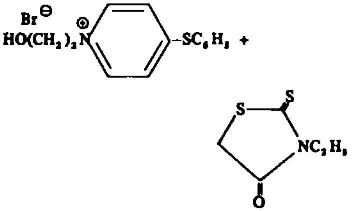
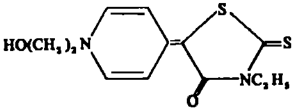
	same as above			m.p. 257°; uv	263
	same as above			m.p. 252°; uv	263
	Ac_2O, HOAc, heat		85%	m.p. 325°; uv	263
	same as above		50%	m.p. 330°; uv	263
	same as above		80%	m.p. 310°; uv	263

TABLE XI-14-1. Preparation of Acids and Derivatives by Miscellaneous Methods (Continued)

Reactants	Conditions	Product	Yield	Properties	Ref.
	same as above			m.p. 247°; uv	263
				m.p. 157–158°; uv	263
	EtOH, Et_3N, boil, 20 min		23%	m.p. 270–271° (decomp.)	67
	same as above		48%	m.p. 249–251° (decomp.)	67

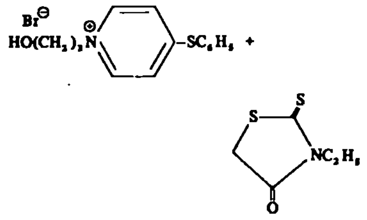
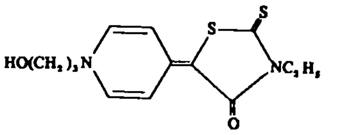
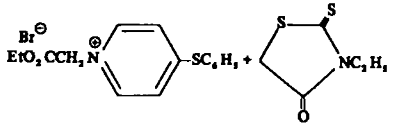
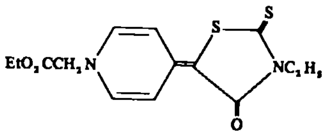
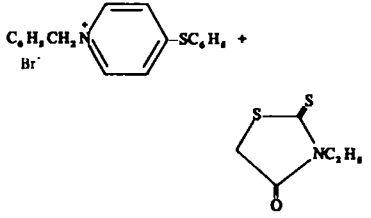
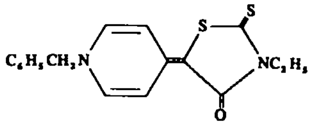
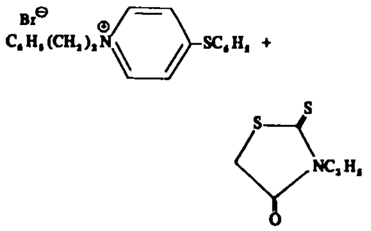
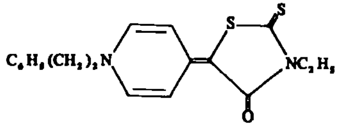
	same as above		m.p. 189–191° (decomp.)	67
	same as above		m.p. 237–238° (decomp.)	67
	same as above		m.p. 246–248° (decomp.)	67
	same as above		m.p. 232–234° (decomp.)	67

TABLE XI-14-1. Preparation of Acids and Derivatives by Miscellaneous Methods (Continued)

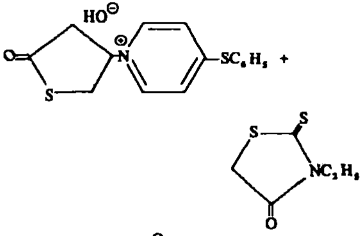
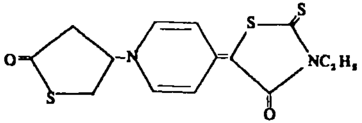
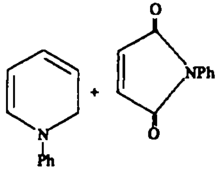
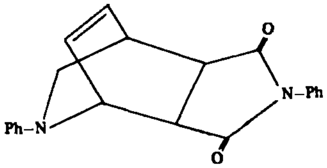
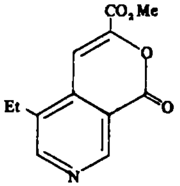
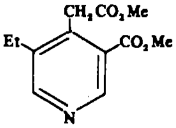
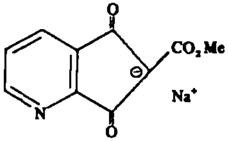
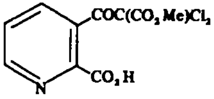
Reactants	Conditions	Product	Yield	Properties	Ref.
	same as above		69%	sodium salt, m.p. > 300°	67
	Et_2O, vac., 6 hr		71%	m.p. 215-216°; ir; nmr	353
	aq. KOH, R.T., 0.5 hr; 30% H_2O_2, 5°, 4 hr			b.p. 135-145°/0.5 mm; m.p. 39-40°	122
	Cl_2, H_2O			m.p. 127° (decomp.)	121

TABLE XI-15. Solvolysis of Amides

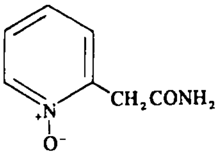
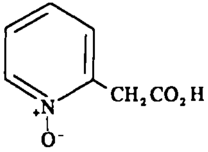
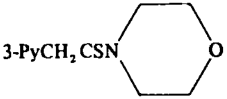
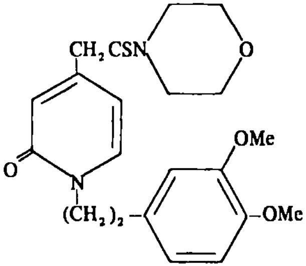
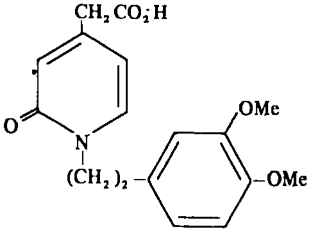
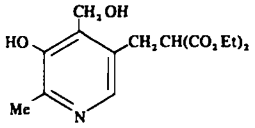
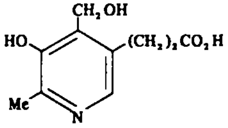
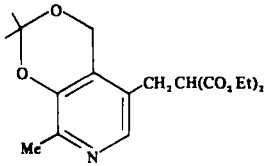
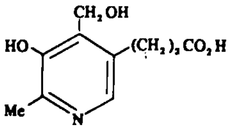
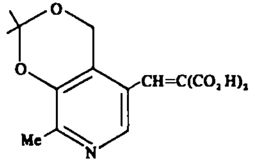
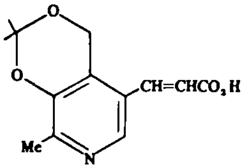
Amide	Conditions	Product	Yield	Properties	Ref.
	10% NaOH, 0.5 hr, 20°			m.p. 126–127° (decomp.)	154
	conc. HCl, reflux 2.5 hr; conc. H_2SO_4, EtOH, reflux 1 hr	3-$PyCH_2CO_2Et$	64%	b.p. 65°/0.1 mm; n_D^{20} 1.5000; $BrCH_2CO_2$ salt, m.p. 81–82°	265
3-$PyCH_2COCH_2CONHMe$	5 *N* HCl, reflux 8 hr *or* 20% KOH, 200°, 20 hr; reflux 36 hr	3-$PyCH_2COCH_2CO_2H$	200 mg ↓ 145 mg	m.p. 159–16.1°; oxime, m.p. 167.5–169° (decomp.)	22
2-$PyCO(CH_2)_2CONHMe$		3-$PyCO(CH_2)_2CO_2H$		m.p. 161–163°	266
4-$Py(CH_2)_{11}CONH_2$	reflux 10 hr, aq. KOH, $MeO(CH_2)_2OH$	4-$Py(CH_2)_{11}CO_2H$		m.p. 130–131.5°	199
	HgO, heat; 10% KOH, steam-bath, 10 hr		94%	m.p. 159–160° (decomp.)	8

TABLE XI-16. Decarboxylation Reactions Yielding Acidic Products

Starting material	Conditions	Product	Yield	Properties	Ref.
2-PyCH$(CO_2Et)CHMeCH_2CO_2Me$	MeOH, H_2O, KOH, reflux 14 hr	2-Py$CH_2CHMeCH_2CO_2Me$	65%	b.p. 120°/0.01 mm; picrate, m.p. 118°	200
2-PyCH$(CO_2Et)CHPhCH_2CO_2Et$	10% NaOH, 3 hr, 80°; HCl; residue, 140°	2-Py$CH_2CHPhCH_2CO_2Et$		b.p. 180–190°/0.05 mm; picrolonate, m.p. 168–169°	200
2-Py$(CH_2)_2CBu(CO_2H)_2$	140°, reduced pressure	2-Py$(CH_2)_2CHBuCO_2H$	86%		203
(2-Py$CH_2CH_2)_2C(CO_2Et)_2$	20% HCl, 120–123°, 3 hr	(2-Py$CH_2CH_2)_2CHCO_2Et$		dipicrate, m.p. 171–172°	205
	conc. HCl, reflux 4.5 hr		68%	m.p. 213–215° (decomp.); ir; nmr; hydrochloride, m.p. 214–215° (decomp.)	195
					195
	95% EtOH, pyridine, reflux, 7 hr			m.p. 220–221°; ir; uv	228

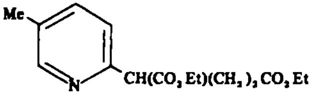
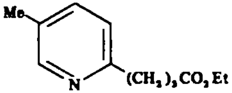
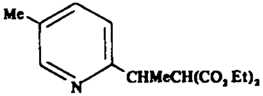
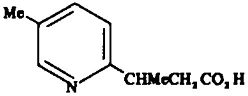
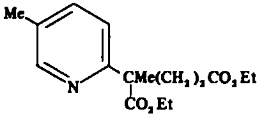
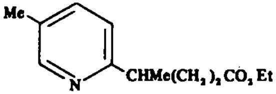
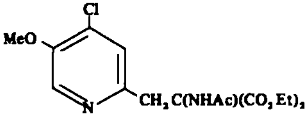
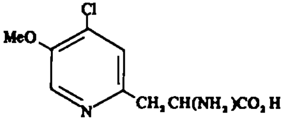
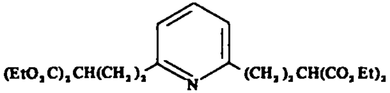
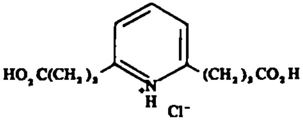
	KOH, MeOH, reflux; 150°, 10 min				206
	10% HCl, reflux 2 hr; 140°, 1 hr			picrate, m.p. 140–141°	196
	HCl, $-CO_2$; MeOH, acid			ir	206
	48% HBr, reflux 7 hr		30 g → 20 g	m.p. 180–182° (decomp.)	95
	20% HCl, 5 hr			m.p. 156–158°	138
3-PyCOCH$(CO_2Et)CH_2CO_2Et$	5 *N* H_2SO_4, reflux 36 hr	3-PyCO$(CH_2)_2CO_2H$	79%	m.p. 162.5–163.5°; uv; picrate, m.p. 139–142° (decomp.)	23
	KBr, reflux; 10% HCl 15 hr	3-PyCO$(CH_2)_2CO_2H$, HCl			2
3-Py^{14}COCH$(CO_2Et)CH_2CO_2Et$		3-Py^{14}CO$(CH_2)_2CO_2H$	63%	m.p. 160–163°	24
3-PyCOCH$(CO_2Et)(CH_2)_2CO_2Et$	10% H_2SO_4, reflux 21 hr	3-PyCO$(CH_2)_3CO_2H$		hydrate, m.p. 165–170°	75
3-PyCOCH$_2$C(NHAc)$(CO_2Et)_2$	1 *N* NaOH, boiled 20 min	3-PyCOCH$_2$CH(NHAc)CO$_2$H	210 g → 110 g	m.p. 181–182°	1
3-PyCOCH$(CO_2Et)(CH_2)_2CO_2Et$	1 *N* H_2SO_4, reflux 24 hr	3-PyCO$(CH_2)_3CO_2H$	95%	m.p. 126–127°	102

TABLE XI-16. Decarboxylation Reactions Yielding Acidic Products (Continued)

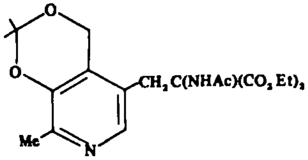
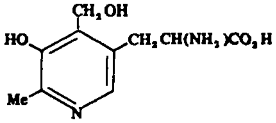
Starting material	Conditions	Product	Yield	Properties	Ref.
	conc. HCl, 2 hr, R.T.; reflux 2 hr		61.5%	m.p. 248–249° (decomp.)	125
4-Py$(CH_2)_2CH(CO_2Et)_2$	conc. HCl, reflux 18 hr	4-Py$(CH_2)_3CO_2H \cdot HCl$		m.p. 199–202°	210
4-Py$(CH_2)_2CPh(CO_2Et)_2$	aq. NaOH, reflux 2 hr	4-Py$(CH_2)_2CHPhCO_2H$	7%	m.p. 125–127°	91

TABLE XI-17. Decarboxylation Reactions Yielding Nonacidic Products

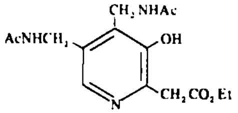
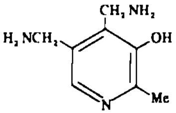
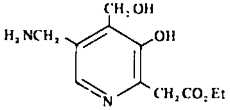
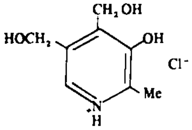
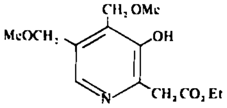
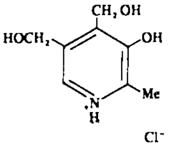
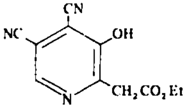
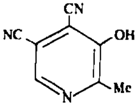
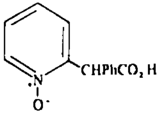
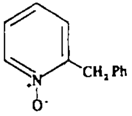
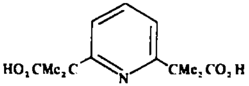
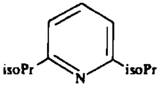
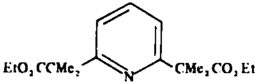
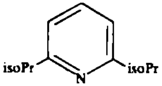
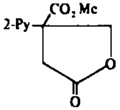
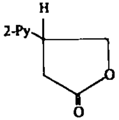
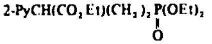
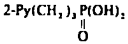
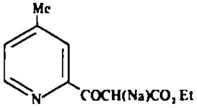
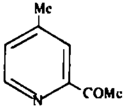
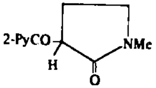
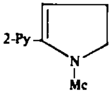
Starting material	Conditions	Product	Yield	Properties	Ref.
		A. Side-chain acid derivatives			
	20% HCl, N_2, reflux 3 hr				69
	HCl, reflux; $NaNO_2$				69
	conc. HCl, 3 hr; sealed tube, 130°				69
	10% KOH, MeOH, reflux 1 hr				267
	EtOH, 1 hr, 70–80°		93.4%		257

TABLE XI-17. Decarboxylation Reactions Yielding Nonacidic Products (Continued)

Starting material	Conditions	Product	Yield	Properties	Ref.
	102–103°				179
	base, fusion				180
	conc. HCl, reflux 13 hr; K_2CO_3, $CHCl_3$, H_2O, 2 hr		80%		19
2-Py$(CH_2)_3$CH(CN)CO_2Et	base; heat	2-Py$(CH_2)_4$CN		b.p. 95–97°/1.0 mm	204
 2-PyCH(CO_2Et)$(CH_2)_2\underset{\overset{\parallel}{O}}{P}(OEt)_2$	30% HCl, reflux 6 hr; base	 2-Py$(CH_2)_3\underset{\overset{\parallel}{O}}{P}(OH)_2$	50%		243
2-PyCOCH_2CO_2Et	0°, HBr; Br_2, 5–10°; 35°, $-CO_2$; 1.5 hr, 40–45°	2-PyCOCH_2Br · HBr	89%		104
	20% HCl, reflux 4 hr		42%		109
	heat, sealed tube				129

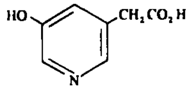
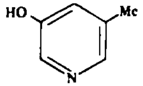
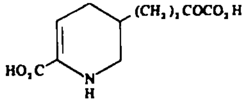
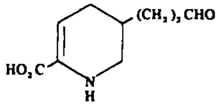
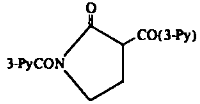
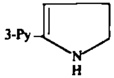
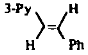
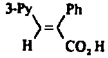
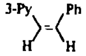
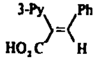
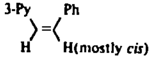
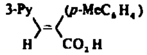
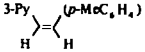
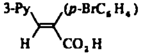
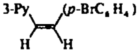
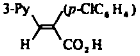
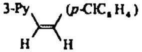
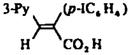
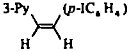
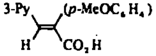
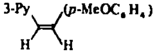
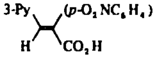
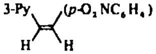
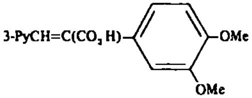
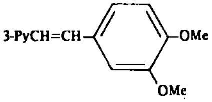
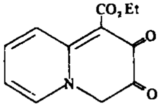
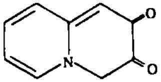
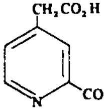
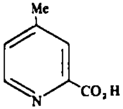
	230°, N_2, 15 min				268
	*Pseudomonas fluorescens* anaerobic decarboxylation				73
3-$PyCOCH_2CO_2Et$	0°, HBr; Br_2, 5–10°; 35°, $-CO_2$; 1.5 hr, 40–45°	3-$PyCOCH_2Br \cdot HBr$	90.1%		104
3-$PyCOC(CO_2K){=}NNH(p\text{-}ClC_6H_4)$		3-$PyCOCH{=}NNH(p\text{-}ClC_6H_4)$	26%		176
3-$PyCOCH(CN)CO_2Et$	7% NaOH, 40°, 2 hr	3-$PyCOCH_2CN$		m.p. 182–184°	103
3-$PyCOC(Na)(CN)CO_2Et$ *or* 3-$PyCOCH(CN)CO_2Et$	10% NaOH, 3–4 hr, concentrated at pH 8; alc. HCl	3-$PyCOCH_2CN$		m.p. 180–183°	269
	conc. HCl, 3 hr				129
3-$PyCH{=}C(CN)CO_2H$	Cu powder, 175–180°, 20 min	3-$PyCH{=}CHCN$ mixture of geometrical isomers		one isomer, b.p. 161–165°/11–12 mm, m.p. 106–107°; other isomer, b.p. 142–143°/11.5 mm, m.p. 30–31°; picrate, m.p. 168°	213
3-$PyC({=}CHPh)CO_2H$	25°, 1 hr		0.5 g → .05 g		101
	Cu chromite, quinoline, reflux 20 min, 230°				100 98
	same as above				98

TABLE XI-17. Decarboxylation Reactions Yielding Nonacidic Products (Continued)

Starting material	Conditions	Product	Yield	Properties	Ref.
	same as above				100
	same as above				100
	same as above				100
	same as above		59%		100
	same as above				100
	same as above				100
	210–220°, quinoline, copper chromite, 4 hr 220–230°				225
	25% HCl, reflux 5 hr		15%		148
					76

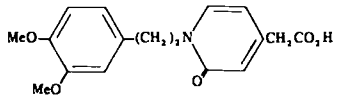
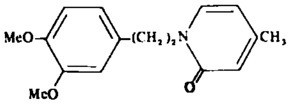
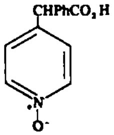
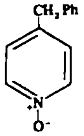
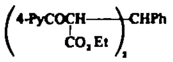
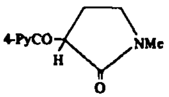
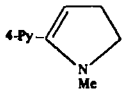
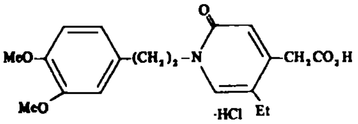
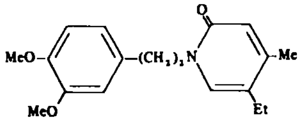
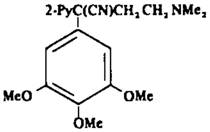
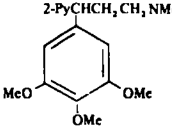
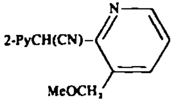
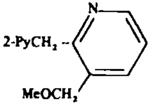
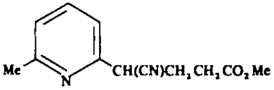
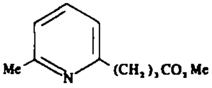
	heat				3
	EtOH, 70–80°, 1 hr		93.4%		257
4-Py(CH$_2$)$_2$ CH(COMe)CO$_2$Et	Na$_2$CO$_3$, reflux 5 hr	4-Py(CH$_2$)$_3$COMe			209
4-PyCOCH$_2$CO$_2$Et	0°, HBr; Br$_2$, 5–10°; 35°, –CO$_2$; 40–45°, 1.5 hr	4-PyCOCH$_2$Br · HBr			104
4-PyCOCHMeCO$_2$Me	HOAc, H$_2$SO$_4$	4-PyCOEt	80%		11
4-PyCOCH(CO$_2$Et)CH(OH)CCl$_3$	20% HCl	4-PyCOCH$_2$CH(OH)CCl$_3$			105
 $\left(\underset{\displaystyle CO_2Et}{4\text{-PyCOCH}}\right)_2CHPh$	20% HCl	(4-PyCOCH$_2$)$_2$CHPh			105
	conc. HCl, reflux		48%		129
4-PyCH=C(CN)CO$_2$H	copper powder, 175–180°, 20 min	4-PyCH=CHCN (mixture of isomers)		b.p. 151–152°/10.5 mm; one isomer, m.p. 70–71°, other isomer, m.p. 22–23°	213
	heat				4

TABLE XI-17. Decarboxylation Reactions Yielding Nonacidic Products (Continued)

Starting material	Conditions	Product	Yield	Properties	Ref.
		B. *Hydrolysis and decarboxylation of pyridine acetonitriles*			
2-Py(CH$_2$)$_2$C(CN)(NHAc)CO$_2$Et	conc. HCl, 120–130°, 7 hr; EtOH	2-Py(CH$_2$)$_2$CH(NH$_2$)CO$_2$Et	5 g → 2.1 g	b.p. 138–140°/4 mm; picrolonate, m.p.222° (decomp), picrate, m.p. 186°	89
2-PyCPh(CN)CH$_2$CO$_2$Et	48% HBr, HOAc, 175°, 24 hr; EtOH, HCl	2-PyCHPh(CH$_2$)$_2$CO$_2$Et		b.p. 164°/0.01 mm	200
2-PyCH(CN)CH(2-Py)CH$_2$COPh	50% H$_2$SO$_4$, reflux 1 hr	2-PyCH$_2$CH(2-Py)CH$_2$COPh	1.7 g → 9 g		270
2-Py(p-ClC$_6$H$_4$)(CH$_2$CH$_2$NMe$_2$)CN	KOH, xylene, reflux 20-24 hr	2-PyCH(p-ClC$_6$H$_4$)CH$_2$CH$_2$NMe$_2$			271
2-PyC(p-MeOC$_6$H$_4$)$_2$CN *or* 2-PyC(p-HOC$_6$H$_4$)$_2$CN	48% HBr. reflux; aq. KOH. reflux	2-PyCH(p-HOC$_6$H$_4$)$_2$			272, 273, 274
2-PyCOCHPhCN	75% H$_2$SO$_4$	2-PyCOCH$_2$Ph	74.5%		275
	LiNH$_2$, xylene, reflux 32 hr		89.9%		276
	70% H$_2$SO$_4$, boiled 4 hr				9
	heat, 14 hr, HCl; MeOH, H$_2$SO$_4$		91%	b.p. 115°/0.7 mm	200

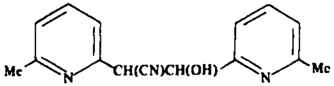
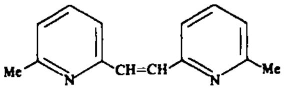
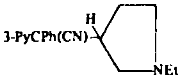
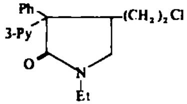
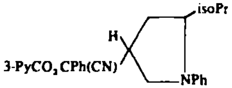
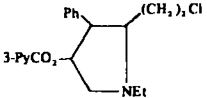
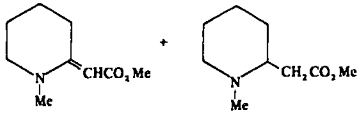
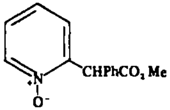
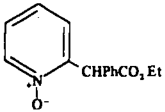
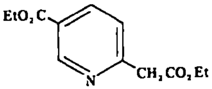
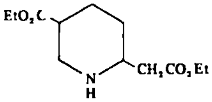
	Ac_2O; HCl				130
3-PyC(p-FC_6H_4)PhCN	H_2SO_4	3-PyCH(p-FC_6H_4)Ph			277
3-PyCOCHPhCN	75% H_2SO_4 *or*	$3\text{-PyCOCH}_2\text{Ph}$	87.7%		275
	conc. HBr, 16 hr				225
3-PyCOCH(CN)CO_2Et	H_2O, boiled	$3\text{-PyCOCH}_2\text{CO}_2\text{H}$			269
4-PyCH(CN)CH(o-$O_2NC_6H_4$)OH	75% H_2SO_4	4-PyC($CONH_2$)=CH(o-$O_2NC_6H_4$)		m.p. 208–209°	99
[4-PyCOCH(CO_2Et)CH_2CH_2]$_2$	20% HCl, reflux 3 hr	[4-PyCO(CH_2)$_3$]$_2$	14.8%		117
	70% H_2SO_4, 130–140°, 48 hr; HCl, $SOCl_2$, 3 hr				56
	same as above				56

TABLE XI-18. Reduction of Side-Chain Acids

Starting material	Conditions	Product (pip = piperidine)	Yield	Properties	Ref.
		Nuclear reduction			
2-PyCH$_2$CO$_2$Me	TsOMe, N$_2$, 65°, 24 hr; NaOMe, 10% Pd-C, H$_2$, MeOH, 45 psi				133
2-PyCHMeCO$_2$H	H$_2$, 5% Rh-C, H$_2$O, 29% NH$_4$OH, 3 hr	2-PipCHMeCO$_2$H	96.4%		248
	H$_2$, PtO$_2$, 10% HCl, EtOH, 1 atm	2-PipCHPhCO$_2$Me · HCl	75.6%		257 256
	same as above	2-PipCHPhCO$_2$Et · HCl			257
	H$_2$, Rh-Al$_2$O$_3$, HOAc, R.T., 10 hr	 *trans* (predominates) + *cis*			17
2-Py(CH$_2$)$_2$CO$_2$Et	H$_2$, PtO$_2$, HOAc, 24 hr	2-Pip(CH$_2$)$_2$CO$_2$Et	82%		148
2-PyCH(OH)CH$_2$CO$_2$Et	H$_2$	2-PipCH(OH)CH$_2$CO$_2$Et			249
2-PyCH(OH)CHPhCO$_2$Me	H$_2$, PtO$_2$, MeOH, 60–65°, 50 atm	2-PipCH(OH)CHPhCO$_2$Me·HCl	78%		116

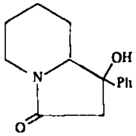
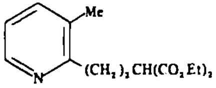
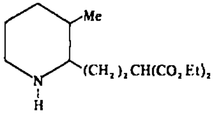
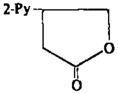
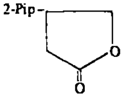
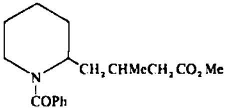
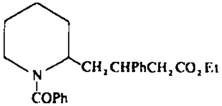
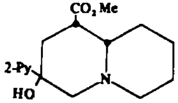
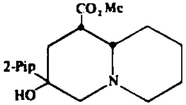
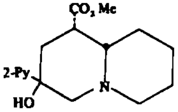
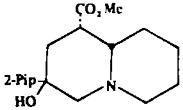
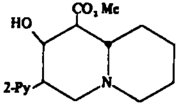
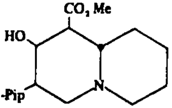
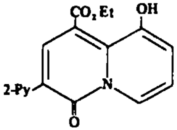
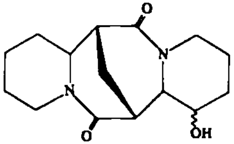
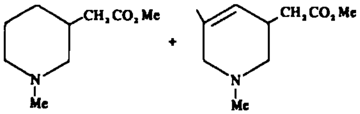
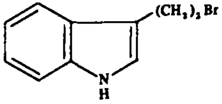
2-PyCPh(OH)CH$_2$CO$_2$Et	H$_2$, PtO$_2$, HCl, 3 hr	 + 2-PipC(OH)PhCH$_2$CO$_2$H 16.5% 78.1%		54
	H$_2$, PtO$_2$, HOAc-EtOH(1:1)			206
	H$_2$, PtO$_2$, HOAc, 70% HClO$_4$		52.5 g ↓ 51.2 g	19
2-PyCH$_2$CHMeCH$_2$CO$_2$Me	H$_2$, PtO$_2$, HOAc; PhCOCl		95%	200
2-PyCH$_2$CHPhCH$_2$CO$_2$Et	same as above		83%	200
2-Py(CH$_2$)$_2$CMe(CO$_2$Et)$_2$	HCl, heat; H$_2$, PtO$_2$, HOAc	2-Pip(CH$_2$)$_2$CHMeCO$_2$H		200
2-Py(CH$_2$)$_2$CHBuCO$_2$Et	H$_2$, PtO$_2$, HCl, EtOH	2-Pip(CH$_2$)$_2$CHBuCO$_2$Et		203
2-PyCH(CO$_2$Et)CH$_2$CH$_2$CN	H$_2$, PtO$_2$, HCl, EtOH, 5 atm	2-PipCH(CO$_2$Et)CH$_2$CH$_2$CN		242
2-PyCOCH$_2$CO$_2$Et	H$_2$, HOAc, 6 hr	2-PipCH(OH)CH$_2$CO$_2$Et	10 g ↓ 9.5 g	249

TABLE XI-18. Reduction of Side-Chain Acids (Continued)

Starting material	Conditions	Product (pip = piperidine)	Yield	Properties	Ref.
	H_2, PtO_2, HOAc				19
	H_2, PtO_2, HOAc				19
 (mixture of isomers)	H_2, PtO_2, HOAc		92%		19
	H_2, Ra-Ni, dioxane, 170–180°; 200°, vac., 4 hr				18
3-$PyCH_2CO_2Me$	MeI, N_2, 15 hr; $NaBH_4$, MeOH, N_2, R.T., 15 hr			nmr; picrate, m.p. 114–117.5°; ir,  salt, ir, NMR	133

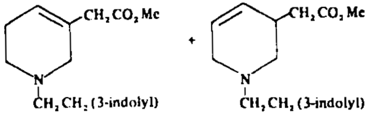
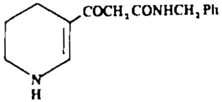
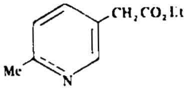
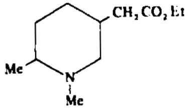
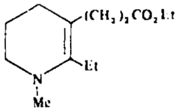
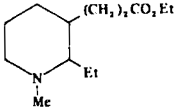
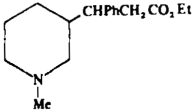
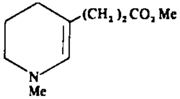
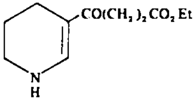
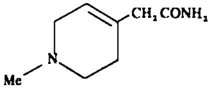
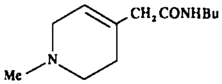
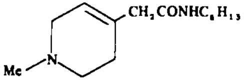
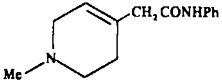
3-PyCH$_2$CO$_2$Me	Tryptophyl bromide, N$_2$, 80°, 45 hr; NaBH$_4$, MeOH, Na, R.T., 15 min				133
3-PyCH$_2$CO$_2$H	H$_2$, PtO$_2$, H$_2$O, 12 hr, 2.5 atm *or* 5% Rh-Al$_2$O$_3$ *or* 5% Rh-C as the catalyst for 10 hr or less	3-PipCH$_2$CO$_2$H	95%		248
3-PyCOCH$_2$CO$_2$Et	PhCH$_2$NH$_2$, TsOH, C$_6$H$_6$, reflux 15 hr; H$_2$, 10% Pd-C		27%	m.p. 151–153°, uv	278
3-PyCHMeCO$_2$H	H$_2$, 5% Rh-C, H$_2$O, 29% NH$_4$OH, 3 hr or less	3-PipCHMeCO$_2$H	94%		248
	TsOMe, 95°, 1 hr; H$_2$, PtO$_2$, EtOH, 4 atm		87%		251
	95% HCO$_2$H, fused HCO$_2$K, 8 hr, 165–170° *or* H$_2$, PtO$_2$, EtOH		68.9%		258
3-PyCH(OH)CHPhCO$_2$Me · HCl	H$_2$, PtO$_2$, 60–65°, 50 atm, 6 hr	3-PipCH(OH)CHPhCO$_2$Me	71%		116
3-PyCPh(OH)CH$_2$CO$_2$Et *or* Me$_2$SO$_4$ salt	Me$_2$SO$_4$; H$_2$, PtO$_2$, EtOH, 1 hr				54

TABLE XI-18. Reduction of Side-Chain Acids (Continued)

Starting material	Conditions	Product (pip = piperidine)	Yield	Properties	Ref.
3-PyCPh(OH)CH$_2$CO$_2$Et	H$_2$, PtO$_2$, HCl, EtOH, 24 hr	3-PipCHPhCH$_2$CO$_2$Et			54
3-PyCOCH$_2$CO$_2$Me	TsOMe C$_6$H$_6$, reflux 3 hr; H$_2$, 10% Pd-C, Et$_3$N, MeOH		2.2 g ↓ 0.9 g	ir; nmr	133
3-PyCO(CH$_2$)$_2$CO$_2$Et	H$_2$, Pd-C, 95% EtOH, 7 hr		50%	m.p. 81-83°	278
3-PyCH=CHCO$_2$H	H$_2$, RuO$_2$, H$_2$O or H$_2$, PtO$_2$, H$_2$O	3-Pip(CH$_2$)$_2$CO$_2$H	82.6%		224 152
4-PyCH$_2$CO$_2$H · HCl	5% Rh-C, NH$_4$OH	4-PipCH$_2$CO$_2$H			248
4-PyCH$_2$CONH$_2$	MeI, MeOH, 3 hr reflux; NaBH$_4$, NaOH, H$_2$O, R.T., 3.5 hr			citrate, m.p. 152-153°	367
4-PyCH$_2$CONHBu	same as above			maleate, m.p. 120°	367
4-PyCH$_2$CONHC$_6$H$_{13}$	same as above			b.p. 180-190°/0.01 mm	367
4-PyCH$_2$CONHPh	same as above			citrate, m.p. 90-92°	367

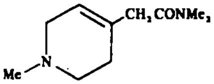
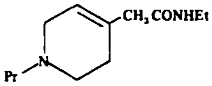
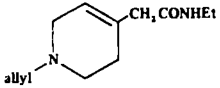
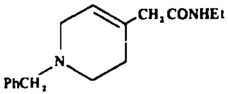
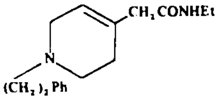
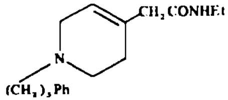
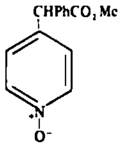
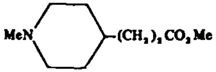
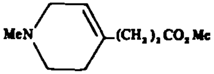
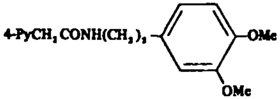
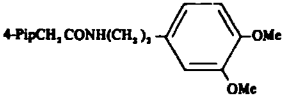
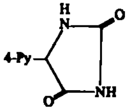
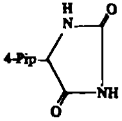
4-PyCH$_2$CONMe$_2$	same as above			b.p. 105-110°/0.02 mm; maleate, m.p. 117°; citrate, m.p. 117-118°	367
4-PyCH$_2$CONHEt	PrI, MeOH, 3 hr, reflux; NaBH$_4$, NaOH, H$_2$O, R.T., 3.5 hr			hydrochloride, m.p. 112°	367
4-PyCH$_2$CONHEt	allyl iodide, MeOH, 3 hr, reflux; NaBH$_4$, NaOH, H$_2$O, R.T., 3.5 hr			citrate, m.p. 78-80°	367
4-PyCH$_2$CONHEt	PhCH$_2$I, MeOH, 3 hr, reflux; NaBH$_4$, NaOH, H$_2$O, R.T., 3.5 hr			hydrochloride, m.p. 110°	367
4-PyCH$_2$CONHEt	Ph(CH$_2$)$_2$I, MeOH, reflux 3 hr; NaBH$_4$ NaOH, H$_2$O, R.T., 3.5 hr			hydrochloride, m.p. 136°	367
4-PyCH$_2$CONHEt	Ph(CH$_2$)$_3$I, MeOH reflux 3 hr; NaBH$_4$, NaOH, H$_2$O, R.T., 3.5 hr			hydrochloride, m.p. 110-113°	367
4-PyCHMeCO$_2$H	5% Rh-C, H$_2$O, 29% NH$_4$OH, 3 hr or less	4-PipCHMeCO$_2$H	89%		248
4-PyCH(NH$_2$)CO$_2$H	H$_2$, Pt, 5% HCl, 50 p.s.i.	4-PipCH(NH$_2$)CO$_2$H	1.2 g → 1.5 g		118
	H$_2$, PtO$_2$, EtOH, conc. HCl, 20°	4-PipCHPhCO$_2$Me			256

TABLE XI-18. Reduction of Side-Chain Acids (Continued)

Starting material	Conditions	Product (pip = piperidine)	Yield	Properties	Ref.
4-Py(CH$_2$)$_2$CO$_2$Me · MeI	H$_2$, PtO$_2$, MeOH				114
	NaBH$_4$, MeOH				114
4-PyCPh(OH)CH$_2$CO$_2$Et	H$_2$, 10% Pd-C, HOAc, 25%, 3-4 atm	4-PipCPh(OH)CH$_2$CO$_2$Et			132
4-PyCH(OH)CHPhCO$_2$Me ·HCl	H$_2$, PtO$_2$, 60-65°, 50 atm, 6 hr	4-PipCH(OH)CHPhCO$_2$Me			116
4-PyCPh(OH)CH$_2$CO$_2$Et	H$_2$, PtO$_2$, HCl, EtOH, 1.5 hr	4-PipCPh(OH)CH$_2$CO$_2$Et			54
4-Py(CH$_2$)$_2$CH(CO$_2$Et)$_2$	H$_2$, Pt, EtOH	4-Pip(CH$_2$)$_2$CH(CO$_2$Et)$_2$ ·HCl			210
	H$_2$, Ra-Ni, EtOH, 1.5 hr; H$_2$, PtO$_2$, HOAc		3 g ↓ 1.7 g		3
	H$_2$, Pt, 5% HCl, 50 p.s.i., 3 hr				118

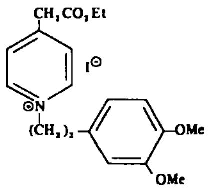
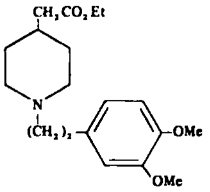
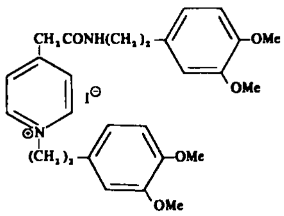
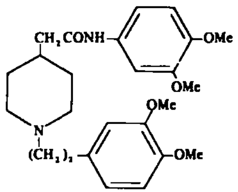
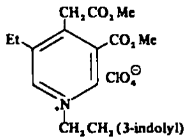
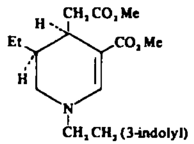
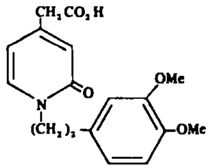
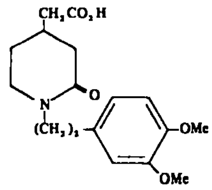
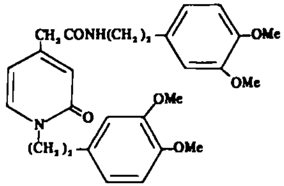
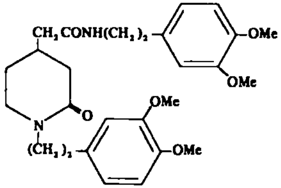
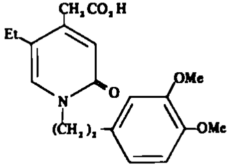
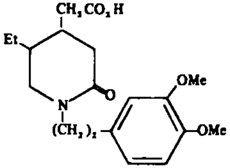
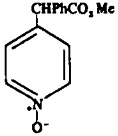
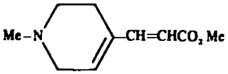
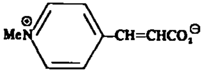
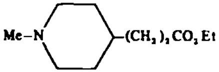
	H_2, Ra-Ni, 144–145°, Et_3N, EtOH, 3 hr		1.6 g ↓ 1.2 g		3
	H_2, PtO_2, R.T.		88%		3
	H_2, Pd-C, Et_3N, abs. MeOH			unstable in air	12
	H_2				88
	H_2, PtO_2, R.T., MeOH	same as above	86%		3

TABLE XI-18. Reduction of Side-Chain Acids (Continued)

Starting material	Conditions	Product (pip = piperidine)	Yield	Properties	Ref.
	H_2, PtO_2, EtOH 40-50°, 3 hr				8
	no details given		84%		6
	H_2, PtO_2, MeOH, R.T., 1 atm, 2-3 days	same as above	*trans*-(70%) *cis*-(15%)		4
	H_2, PtO_2, 10% HCl, EtOH, 1 atm	4-PipCHPhCO$_2$Me · HCl	45%		257
4-PyCH=CHCO$_2$Me · MeI	$NaBH_4$, MeOH, 90 min			b.p. 188.5°/2.5 mm; picrate, m.p. 175-176°	134
	H_2, PtO_2, H_2O, 26 hr; HCl, EtOH, reflux 1 hr				134 279

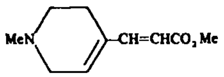
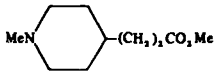
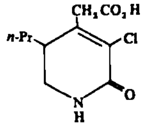
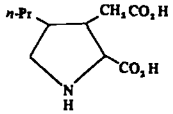
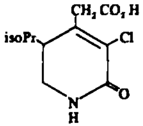
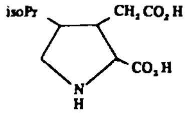
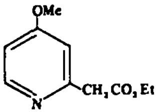
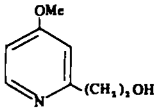
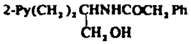
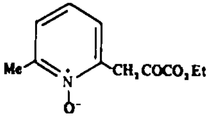
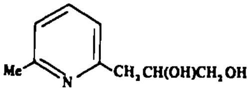
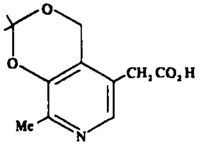
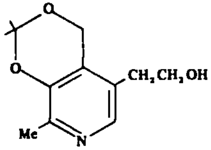
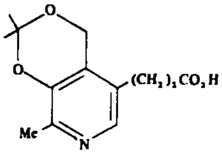
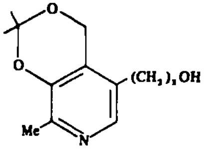
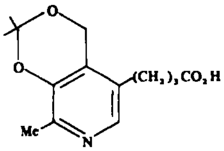
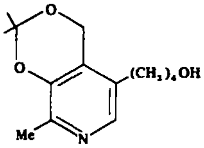
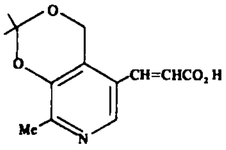
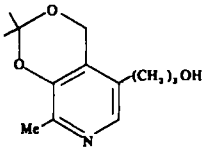
	H_2, PtO_2, MeOH, 30 min			134
	H_2, PtO_2, 8 hr; $Cu(OAc)_2$, 22 days; H_2S			261
	same as above			261
		Reduction of Carboxyl function		
	LAH, Et_2O		37 g → 27 g	193
$2\text{-}Py(CH_2)_2CH(CO_2H)CH_2(p\text{-}ClC_6H_4)$	LAH, THF, reflux 5 hr	$2\text{-}Py(CH_2)_2CH(CH_2OH)CH_2(p\text{-}ClC_6H_4)$	70.4%	245
$2\text{-}Py(CH_2)_2CH(CO_2Me)CH_2(p\text{-}ClC_6H_4)$	LAH, THF, reflux 5 hr	$2\text{-}Py(CH_2)_2CH(CH_2OH)CH_2(p\text{-}ClC_6H_4)$	58.2%	245
$2\text{-}Py(CH_2)_2CH(NHAc)CO_2Et$	LAH, Et_2O, reflux 3 hr	$2\text{-}Py(CH_2)_2CH(NH_2)CH_2OH$		89
$2\text{-}Py(CH_2)_2CH(CO_2Et)NHCOCH_2Ph$	LAH, THF-Et_2O, reflux 10 hr	 $2\text{-}Py(CH_2)_2\underset{CH_2OH}{CH}NHCOCH_2Ph$		89
$(2\text{-}PyCH_2CH_2)_2C(CO_2Et)_2$	LAH, Et_2O, reflux 1.5 hr	$(2\text{-}PyCH_2CH_2)_2C(CH_2OH)_2$		205
$2\text{-}Py(CH_2)_2C(OEt)_2CO_2Et$	LAH, Et_2O, boil	$2\text{-}Py(CH_2)_2C(OEt)_2CH_2OH$		280
	Na; $NaBH_4$, MeOH, reflux 4 hr			135

TABLE XI-18. Reduction of Side-Chain Acids (Continued)

Starting material	Conditions	Product (pip = piperidine)	Yield	Properties	Ref.
2-PyCH=C(CN)CO$_2$Et	NaBH$_4$, isoPrOH, 8 hr	2-PyCH$_2$CH(CN)CH$_2$OH			46 47
	LAH, THF, N$_2$, 2.5 hr				125
	LAH, THF, R.T., 1 hr				228
	LAH, THF, R.T., N$_2$, 2 hr				125
	LAH, THF		71%		228

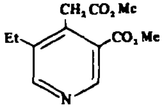
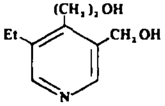
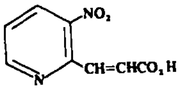
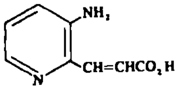
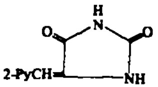
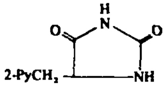
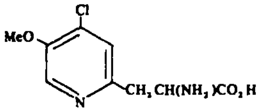
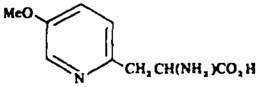
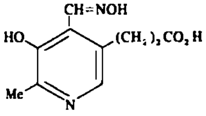
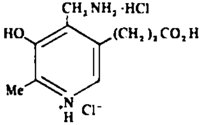
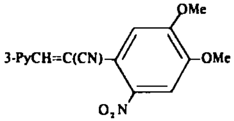
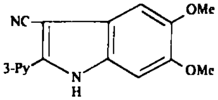
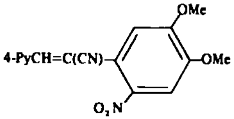
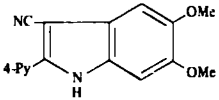
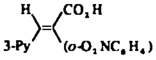
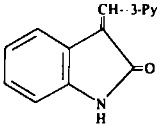
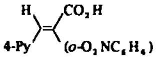
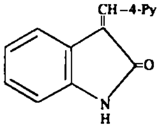
	LAH, Et_2O, reflux 4 hr		2.2 g → 1.9 g		122
4-$PyCH=CHCO_2Me$ *or* 4-$PyCH=CHCO_2Et$	$NaBH_4$, MeOH, reflux 1–2 hr	4-$Py(CH_2)_3OH$			115
4-$PyCH=C(CN)CO_2Et$	$NaBH_4$, isoPrOH, 8 hr *or* in diglyme, R.T., 3 hr	4-$PyCH_2CH(CN)CH_2OH$	68%	m.p. 68–69°	46, 47, 177
		Reduction of Other Substituents			
	$FeSO_4$, NH_3		57%	m.p. 207–208°	151
	H_2, Pd-C, 95% EtOH, 3 atm, 12 hr		5 g → 4 g	m.p. 171–172°	95
	H_2, Pd, 3 atm, 3 hr		1.4 g → 0.7 g	m.p. 224–227° (decomp.)	95
2-$PyC(=NOH)CO_2Et$	5% Pd-C, abs. EtOH	2-$PyCH(NH_2)CO_2Et$	75%	b.p. 103°/0.3 mm; n_D^{25} 1.5163	112
2-$PyC(CN)=CHMe$	H_2, 1 atm, 10% Pd-C, EtOH, R.T.	2-PyCHEtCN	88%	b.p. 73–76°/0.5 mm; ir; nmr	163
3-$PyCH=C(p\text{-}ClC_6H_4)CN$	H_2, 3–4 atm, 10% Pd-C, EtOAc, 70°	3-$PyCH_2CH(p\text{-}ClC_6H_4)CN$	15%	m.p. 76–80°; ir	164
3-$PyCH=C(p\text{-}O_2NC_6H_4)CN$	H_2, 3–4 atm, 10% Pd-C, EtOAc, heat	3-$PyCH_2CH(p\text{-}H_2NC_6H_4)CN$		m.p. 99–100°; ir	164

TABLE XI-18. Reduction of Side-Chain Acids (Continued)

Starting material	Conditions	Product (pip = piperidine)	Yield	Properties	Ref.
	H_2, 10% Pd-C, conc. HCl, R.T., 1 atm, 1 hr		59%	ir; uv	279
4-PyCH=C(p-$O_2NC_6H_4$)CN	H_2, 3-4 atm, 10% Pd-C, EtOAc, heat	4-PyCH$_2$CH(p-$H_2NC_6H_4$)CN		m.p. 80-84°; ir	164
		Miscellaneous			
	Fe, HOAc, reflux 2-5 hr		39%	m.p. 238-239°	10
	Fe, HOAc, reflux 2-5 hr		72.5%	m.p. 321°; ir; uv; nmr	10
	$FeSO_4$, NH_4OH, H_2O, 80-90°, 20 min	 *trans*		m.p. 187-188°	99
	$FeSO_4$, NH_4OH, H_2O, 80-90°, 20 min	 *trans*		m.p. 225°	99

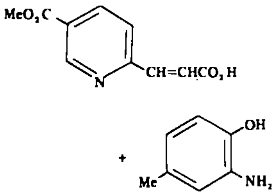
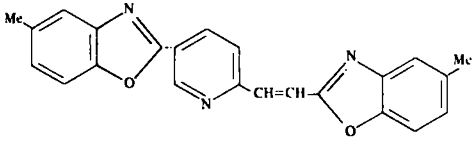
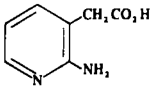
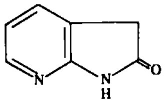
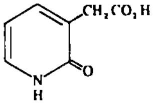
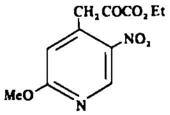
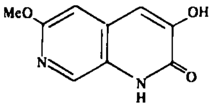
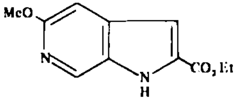
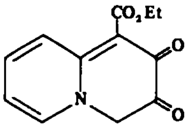
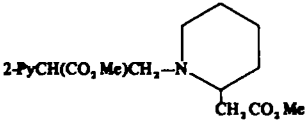
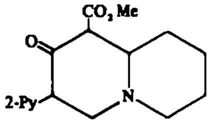
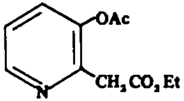
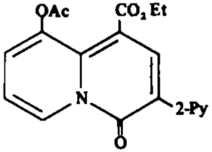
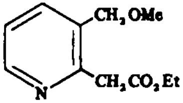
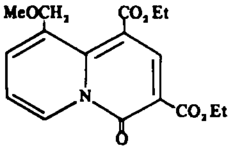
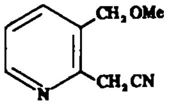
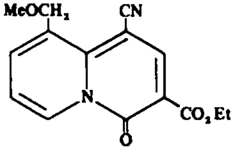
	1, 2-dichlorobenzene, H_3BO_3, 120°, 8 hr, N_2			281
	225°	 (67%) +  (4.6%)	m.p. 240–241° (decomp.)	268
	H_2, PtO_2, EtOH	 + 	m.p. 103–106°; sublimes 90°/0.1 mm; uv; nmr	15

TABLE XI-19. Synthesis of Quinolizidines and Quinolizines

Starting materials	Conditions	Product	Yield	Properties	Ref.
2-PyCH$_2$CO$_2$Et + BrCH$_2$COCO$_2$Et	acetone, 2 hr				148
			28%	m.p. 119–120°	19
 + 2-PyC(CO$_2$Et)=CHOH	Ac$_2$O, reflux 3 hr		10 g → 4 g	b.p. 176°; ir	18
 + EtOCH=C(CO$_2$Et)$_2$	reflux 8 hr		2 → 0.4 g	m.p. 75–77°	9
 + EtOCH=C(CO$_2$Et)$_2$	reflux 2 hr		40%		9

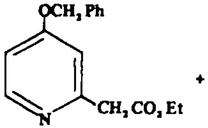
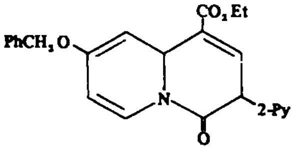
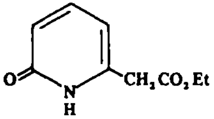
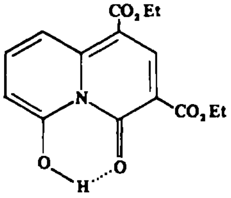
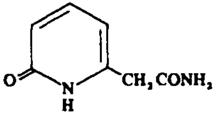
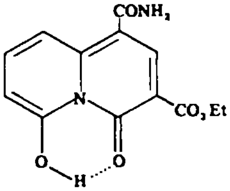
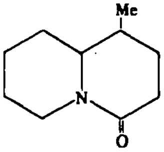
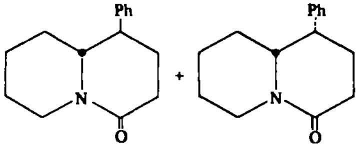
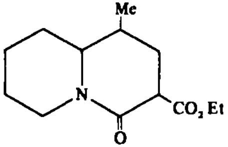
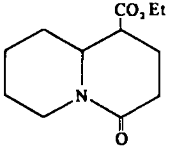
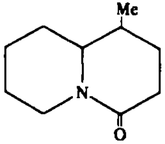
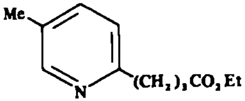
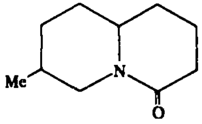
 + 2-PyC(CO$_2$Et)=CHCO$_2$H	Ac$_2$O, reflux 2 hr		25 g → 10 g	282
 + EtOCH=C(CO$_2$Et)$_2$	Na, EtOH		72.1%	139
 + EtOCH=C(CO$_2$Et)$_2$	Na, EtOH		80.8%	139
2-PyCHMe(CH$_2$)$_2$CO$_2$Et	H$_2$, PtO$_2$, HCl, EtOH; 200°, 2 hr		4.6 g → 2.2 g	283

TABLE XI-19. Synthesis of Quinolizidines and Quinolizines (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
2-PyCHPh$(CH_2)_2CO_2Et$	H_2, PtO_2, HOAc, 200°, 4 hr				200
2-PyC(=CH_2)$CH_2CH(CO_2Et)_2$	H_2, PtO_2, HOAc		80%		206
2-PyCH(CO_2Et)$CH_2CH_2CO_2Et$	H_2, Ra-Ni, 175°, 100 atm		95%		242
2-PyCMe(OH)C≡C CO_2Me	H_2, PtO_2, HCl; $SOCl_2$; H_2, PtO_2; 200°, 2 hr				79, 97
	H_2, PtO_2, HCl, EtOH; 200°, 2 hr				283

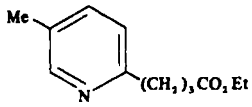
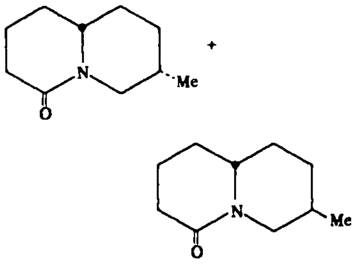
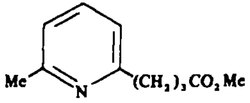
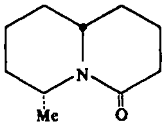
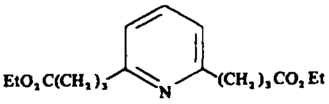
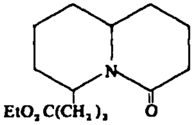
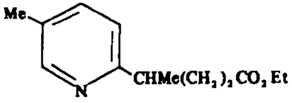
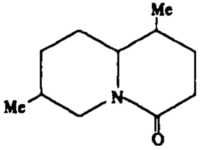
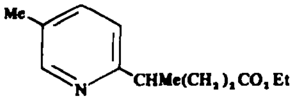
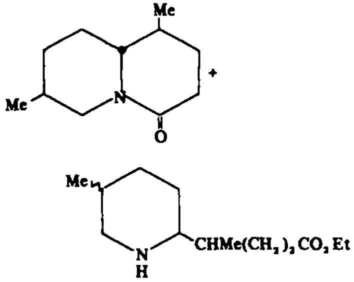
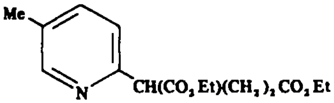
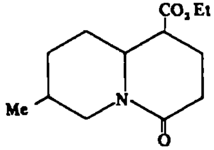
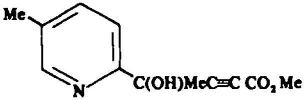
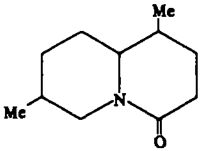
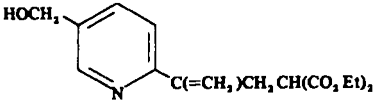
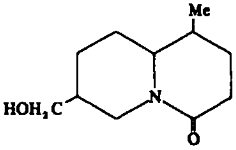
	H_2, PtO_2, HOAc; 200°, 1 hr			206
	H_2, PtO_2, HOAc, 200°, 5 hr			200
	H_2, Ra-Ni, 150–160°, 150 atm		85–90%	138
	H_2, PtO_2, HCl, EtOH; 200°, 2 hr			283

TABLE XI-19. Synthesis of Quinolizidines and Quinolizines (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
	H$_2$PtO$_2$, HOAc; 200°, 1 hr				206
	H$_2$, PtO$_2$, HOAc; 200°, 1 hr				206
	H$_2$, PtO$_2$, HCl; SOCl$_2$; H$_2$, PtO$_2$; 200°, 2 hr				79, 97
	H$_2$, PtO$_2$, HOAc, 24 hr; HCl, reflux; EtOH, HCl		77%		14

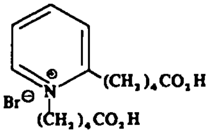
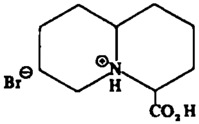
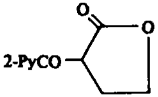
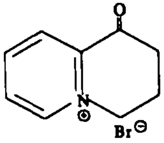
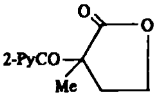
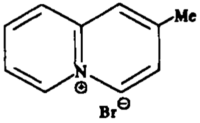
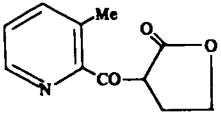
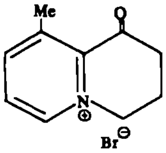
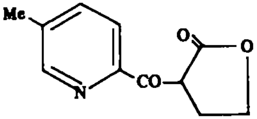
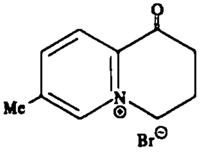
	H_2, PtO_2		21 g → 20 g	284
	48% HBr, 110°, 1.5 hr		82.5%	140
	HBr, heat; Ac_2O, heat			140
	48% HBr, 110°, reflux 1.5 hr; heat 2.5 hr		8 g → 6.8 g	140
	same as above		19 g → 21 g	140

TABLE XI-19. Synthesis of Quinolizidines and Quinolizines (Continued)

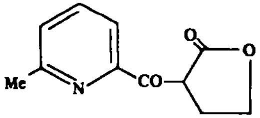
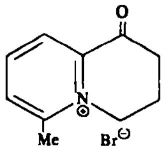
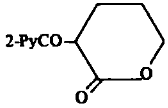
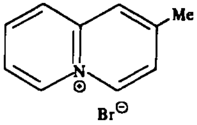
Starting materials	Conditions	Product	Yield	Properties	Ref.
	same as above		49 g → 49 g		140
	6*N*, H_2SO_4, $-CO_2$; PBr_3, steam-bath; Ac_2O, heat				140

TABLE XI-20. Synthesis of Condensed Heterocycles Other Than Quinolizidines

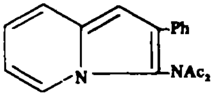
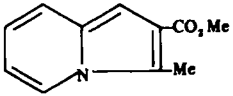
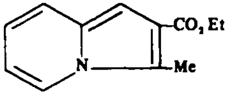
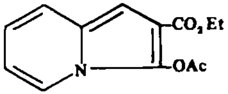
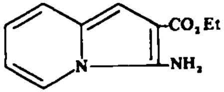
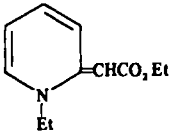
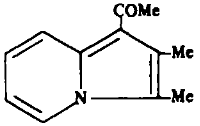
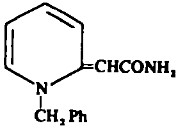
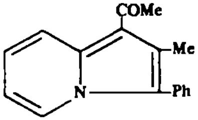
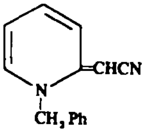
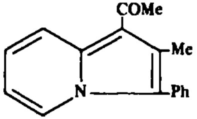
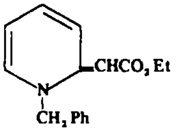
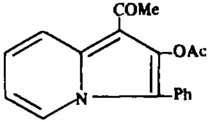
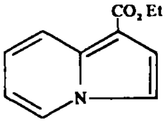
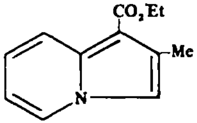
Starting materials	Conditions	Product	Yield	Properties	Ref.
		Indolizines			
2-PyCH$_2$CHPhCN	Ac$_2$O, reflux 2 hr		18%	ir	143
2-PyCH$_2$CH(COMe)CO$_2$Me	Ac$_2$O, reflux 1-2 hr		9%	m.p. 87–88°	143
2-PyCH$_2$CH(COMe)CO$_2$Et	same as above		19%	m.p. 49–50°	143
2-PyCH$_2$CH(CO$_2$Et)$_2$	same as above		36%	m.p. 73–74°	143
2-PyCH$_2$Br + NCCH$_2$CO$_2$Et	R.T. 1 hr			m.p. 71–72°; b.p. 170–200°/2 mm; ir	143
	Ac$_2$O, reflux 4 hr		25%		145

TABLE XI-20. Synthesis of Condensed Heterocycles Other Than Quinolizidines (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
	Ac_2O, reflux 1 hr		96%		145
	Ac_2O, reflux 12 hr		11%		145
	Ac_2O, reflux 2 hr		83%		145
2-$PyCH_2CO_2Et$ + $BrCH_2CHO$	heat, steam-bath, 2 hr		18%	b.p. 124°/3 mm	142
2-$PyCH_2CO_2Et$ + $ClCH_2COMe$	EtOH, reflux 14 hr		36%	m.p. 43–44°	142

Indolizines

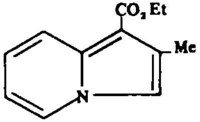
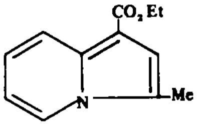
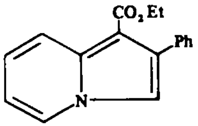
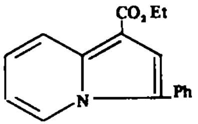
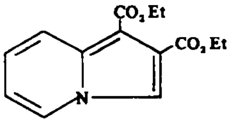
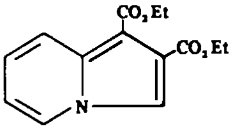
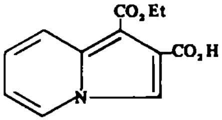
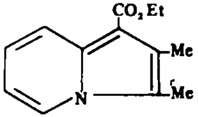
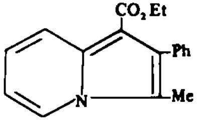
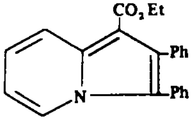
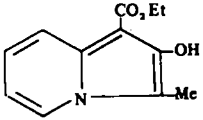
2-PyCH$_2$CO$_2$Et + BrCH$_2$COMe	acetone, reflux 17 hr		91%	m.p. 43–44°	141
2-PyCH$_2$CO$_2$Et + BrCHMeCHO	acetone, reflux 16 hr		76%	b.p. 138°/3 mm	142
2-PyCH$_2$CO$_2$Et + BrCH$_2$COPh	acetone, reflux 7 hr		85%	m.p. 106–107°	141
2-PyCH$_2$CO$_2$Et + BrCHPhCHO	acetone, reflux 22 hr		78%	m.p. 63–64°	142
2-PyCH$_2$CO$_2$Et + BrCH$_2$COCO$_2$Et	acetone, cold, 2 hr			m.p. 86°	144
	80°, 10 min *or* acetone, R.T., 4 hr; 0°, overnight	 +	95%	m.p. 83–84°	142 147

TABLE XI-20. Synthesis of Condensed Heterocycles Other Than Quinolizidines (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
			2%	m.p. 228–229°	
2-PyCH$_2$CO$_2$Et + BrCHMeCOMe	acetone, reflux 17 hr		45%	m.p. 62–63°	141
2-PyCH$_2$CO$_2$Et + BrCHMeCOPh	same as above		38%	m.p. 101–102°	141
2-PyCH$_2$CO$_2$Et + BrCHPhCOPh	same as above		24%	m.p. 151–152°	141
2-PyCH$_2$CO$_2$Et + BrCHMeCO$_2$Et	acetone, heat on steam-bath 24 hr		48%	m.p. 51–52°; acetate, m.p. 128–129°	142

Indolizines

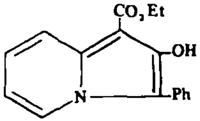
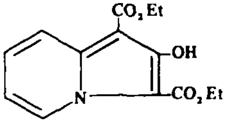
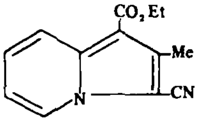
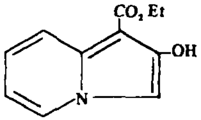
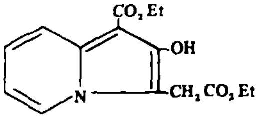
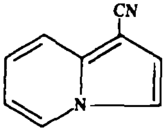
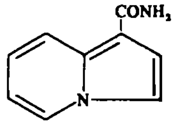
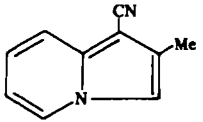
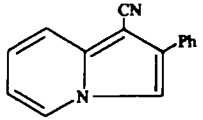
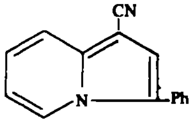
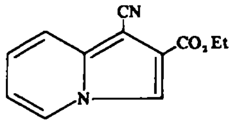
2-PyCH$_2$CO$_2$Et + BrCHPhCO$_2$Et	acetone, steam-bath 17 hr		90%	m.p. 75–76°; acetate, m.p. 131–132°	142
2-PyCH$_2$CO$_2$Et + BrCH(CO$_2$Et)$_2$	acetone, steam-bath, 12 hr		30%	m.p. 124–125°; acetate, m.p. 132–133°	142
2-PyCH$_2$CO$_2$Et + BrCH(CN)COMe	steam-bath, 1 hr		15%	m.p. 101–102°	142
2-PyCH$_2$CO$_2$Et + BrCH$_2$CO$_2$Et	Et$_2$O, reflux 48 hr; dil. HCl; 20% NaOH; CO$_2$	 +	14%	m.p. 131–132°; hydrochloride, m.p. 174–175°	142
			25%	m.p. 106–107°	
2-PyCH$_2$CN + BrCH$_2$CHO	steam-bath, 22 hr		45%	sublimes 50°/1.0 mm; m.p. 52–53°; ir	143

TABLE XI-20. Synthesis of Condensed Heterocycles Other Than Quinolizidines (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
		Indolizines			
	KOH, EtOH, reflux 6 hr		82%	sublimes 130°/0.5 mm; m.p. 148–149°; ir	145
2-$PyCH_2CN$ + $BrCH_2COMe$	reflux 17 hr		69%	sublimes 90°/1.0 mm; m.p. 100–101°; ir	143
2-$PyCH_2CN$ + $BrCH_2COPh$	Me_2CO, reflux 14 hr		48%	m.p. 101–102°	142
2-$PyCH_2CN$ + BrCHPhCHO	reflux 6 hr		50%	sublimes 90°/1.0 mm; m.p. 95–96°; ir	143
2-$PyCH_2CN$ + $BrCH_2COCO_2Et$	reflux 1 hr		77%	m.p. 125–126°; ir	143

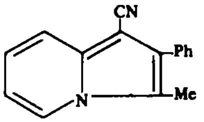
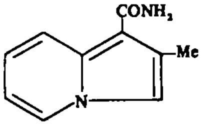
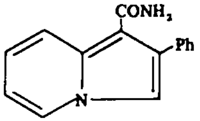
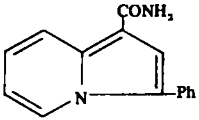
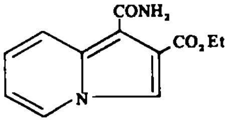
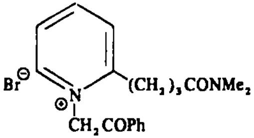
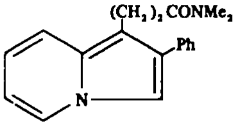
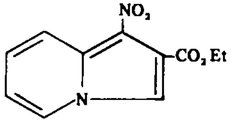
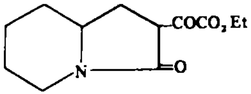
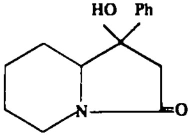
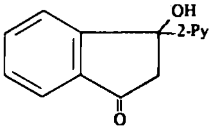
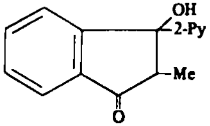
2-PyCH$_2$CN + Br(CH$_2$)$_2$COPh	reflux 17 hr			sublimes 160°/1.0 mm; b.p. 173–174°	143
2-PyCH$_2$CONH$_2$ • BrCH$_2$COMe	acetone, reflux 17 hr		59%	sublimes 160°/0.5 mm; m.p. 196–197° (decomp.); ir	145
or					
2-PyCH$_2$CN • BrCH$_2$COMe	KOH, EtOH, reflux 6 hr		88%		
2-PyCH$_2$CONH$_2$ + BrCH$_2$COPh	acetone, reflux 17 hr		52%	sublimes 140°/0.5 mm; m.p. 169–170°; ir	145
2-PyCH$_2$CN • BrCHPhCHO	KOH, EtOH, reflux 6 hr		89%	sublimes 160°/0.5 mm; m.p. 191–192°; ir	145
2-PyCH$_2$CONH$_2$ • BrCH$_2$COCO$_2$Et	acetone, reflux 1 hr		52%	sublimes 160°/0.1 mm; m.p. 213–214°; ir	145
	aq. NaHCO$_3$, steam-bath			m.p. 93–95°	285

TABLE XI-20. Synthesis of Condensed Heterocycles Other Than Quinolizidines (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
2-PyCH$_2$NO$_2$ + BrCH$_2$COCO$_2$Et	reflux 1 hr		78%	m.p. 117–118°	143
2-Py(CH$_2$)$_2$CO$_2$Et + (CO$_2$Et)$_2$	Na, EtOH, Et$_2$O				148
2-PyCPh(OH)CH$_2$CO$_2$Et	H$_2$, 10% Pd-C, HOAc; 25°, 3–4 atm				132
		Indenes and naphthalenes			
2-PyCPh(OH)CHCO$_2$Et	conc. H$_2$SO$_4$, 100° briefly				172
2-PyCPh(OH)CMeCO$_2$Et	same as above				172

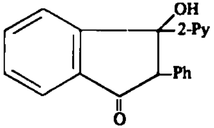
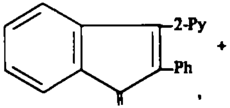
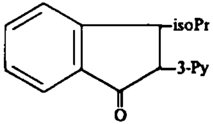
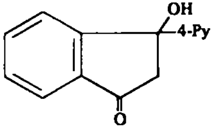
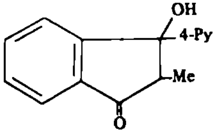
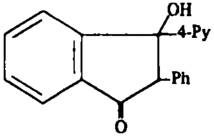
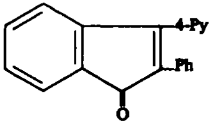
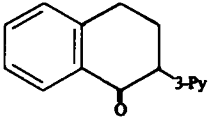
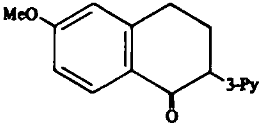
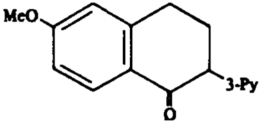
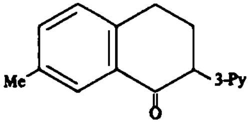
2-PyCPh(OH)CHPhCO$_2$Et	conc. H$_2$SO$_4$, R.T.			172
2-PyCPh(OH)CHPhCO$_2$H	98% H$_2$SO$_4$, 1 hr	 2-PyCPh=CPhCO$_2$H		172
3-PyCH(CN)CHPh-isoPr	PPA, 105-110°		73%	286
4-PyCPh(OH)CHCO$_2$Et	conc. H$_2$SO$_4$, 100° briefly			172
4-PyCPh(OH)CHMeCO$_2$Et	conc. H$_2$SO$_4$, 100° briefly			172
4-PyCPh(OH)CHPhCO$_2$Et	conc. H$_2$SO$_4$, R.T.			172

TABLE XI-20. Synthesis of Condensed Heterocycles Other Than Quinolizidines (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
		Indenes and naphthalenes			
4-PyCPh(OH)CHPhCO$_2$H	98% H$_2$SO$_4$, 1 hr	 + 4-PyCPh=CPhCO$_2$H		m.p. 248–255°	172
3-PyCH(CO$_2$H)(CH$_2$)$_2$Ph	PPA, 105–110°		87%		286–288
3-PyCH(CO$_2$H)CH$_2$CH$_2$(*m*-MeOC$_6$H$_4$)	PPA, 105–110°		55%		286, 289
3-PyCH(CONH$_2$)CH$_2$CH$_2$(*m*-MeOC$_6$H$_4$)	PPA, 125–130°				290
3-PyCH(CO$_2$H)CH$_2$CH$_2$(*p*-tolyl)	PPA, 90–110°				288

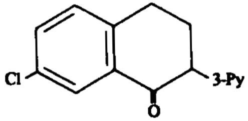
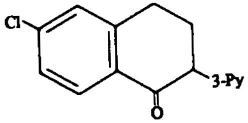
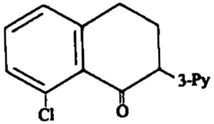
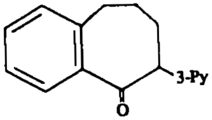
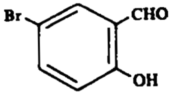
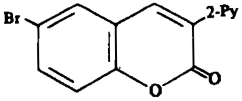
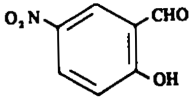
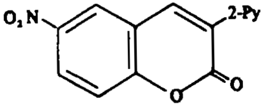
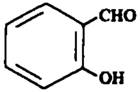
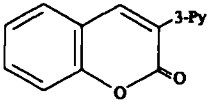
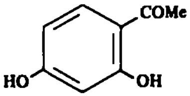
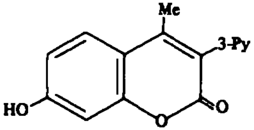
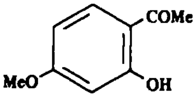
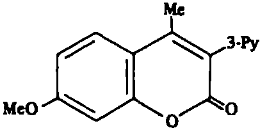
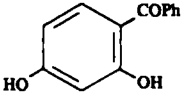
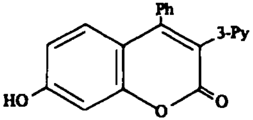
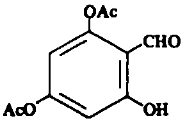
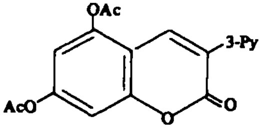
3-PyCH(CO$_2$H)CH$_2$CH$_2$(p-ClC$_6$H$_4$)	PPA, 105–110°		86%		286–289
3-PyCH(CO$_2$H)CH$_2$CH$_2$(m-ClC$_6$H$_4$)	same as above	 +	51%		288, 289
			65%		286
3-PyCH(CO$_2$H)(CH$_2$)$_3$Ph	same as above				288
		Coumarins and chromones			
2-PyCH$_2$CO$_2$H + 	Ac$_2$O, Et$_3$N		24%	m.p. 187.5–188.5°	48 49
2-PyCH$_2$CO$_2$Me + 	piperidine		64%	m.p. 215–216.5°	48 49

TABLE XI-20. Synthesis of Condensed Heterocycles Other Than Quinolizidines (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
		Coumarins and chromones			
3-PyCH$_2$CO$_2$H + 	Ac$_2$O, Et$_3$N		74%	m.p. 167.5–169°	48, 49
3-PyCH$_2$CO$_2$H + 	Ac$_2$O, Et$_3$N		28%	m.p. 257–258.5°; hydrochloride, m.p. 313–315° (decomp.)	48, 49
3-PyCH$_2$CO$_2$H + 	Ac$_2$O, Et$_3$N		51%	m.p. 138–141°	48, 49
3-PyCH$_2$CO$_2$H • 	Ac$_2$O, Et$_3$N		40%	m.p. 288–290.5°	48, 49
3-PyCH$_2$CO$_2$H + 	Ac$_2$O, Et$_3$N		44%	m.p. 182–183°	48, 49

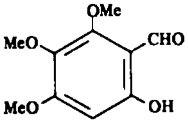
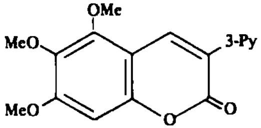
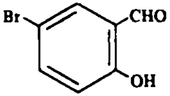
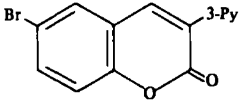
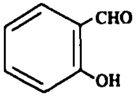
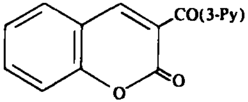
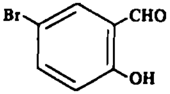
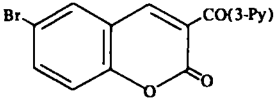
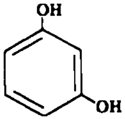
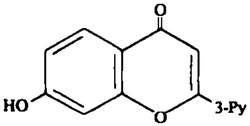
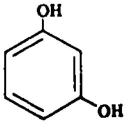
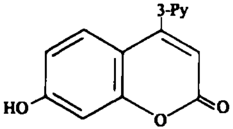
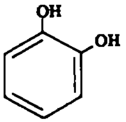
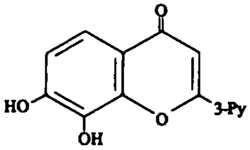
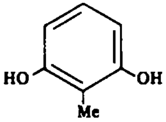
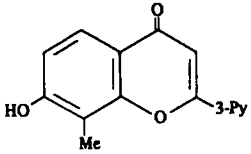
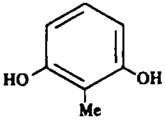
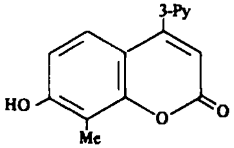
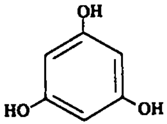
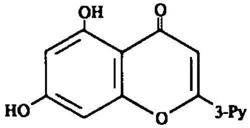
$3\text{-PyCH}_2\text{CO}_2\text{H}$ +		$\text{Ac}_2\text{O}, \text{Et}_3\text{N}$		10%	m.p. 150.5–153.5°	48, 49
$3\text{-PyCH}_2\text{CO}_2\text{Me}$ ●		piperidine		89%	m.p. 230–231°	48, 49
$3\text{-PyCH}_2\text{CO}_2\text{Et}$ +		piperidine, R.T., 24 hr			m.p. 158°	149
$3\text{-PyCOCH}_2\text{CO}_2\text{Et}$ +		piperidine, R.T., 24 hr			m.p. 188°	149
$3\text{-PyCOCH}_2\text{CO}_2\text{Et}$ +		160°, 12 mm			m.p. 248°	149
$3\text{-PyCOCH}_2\text{CO}_2\text{Et}$ +		ZnCl_2, HOAc, steam-bath, 2 hr			m.p. 265°	149

TABLE XI-20. Synthesis of Condensed Heterocycles Other Than Quinolizidines (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
		Coumarins and chromones			
3-PyCOCH$_2$CO$_2$Et + 	160°, 12 mm			m.p. 313°	149
3-PyCOCH$_2$CO$_2$Et + 	160°, 12 mm			m.p. 232°	149
3-PyCOCH$_2$CO$_2$Et + 	ZnCl$_2$, HOAc, steam-bath, 2 hr			m.p. 250°	149
3-PyCOCH$_2$CO$_2$Et • 	160°, 12 mm			m.p. 323°	149

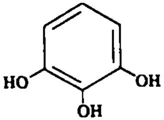
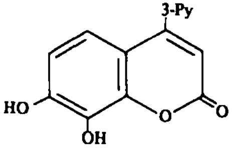
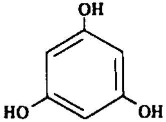
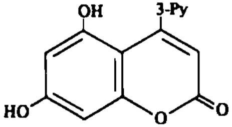
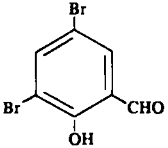
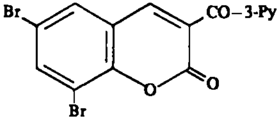
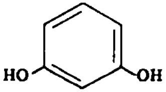
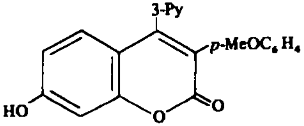
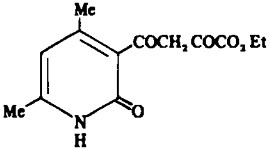
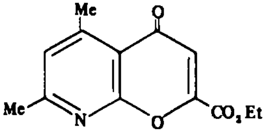
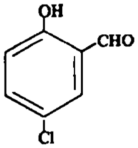
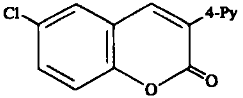
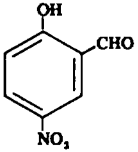
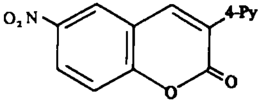
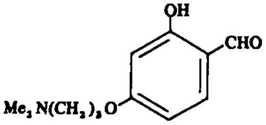
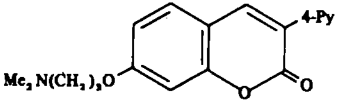
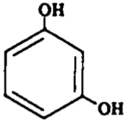
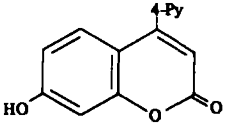
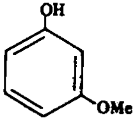
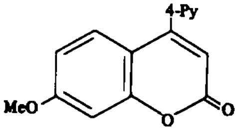
3-PyCOCH$_2$CO$_2$Et + 	ZnCl$_2$, HOAc, steam-bath, 2 hr			m.p. 300°	149
3-PyCOCH$_2$CO$_2$Et + 	ZnCl$_2$, HOAc steam-bath, 2 hr			m.p. 360°	149
3-PyCOCH$_2$CO$_2$Et + 	piperidine, R.T., 24 hr			m.p. 210°	149
3-PyCOCH(*p*-MeOC$_6$H$_4$)CO$_2$Et + 	PPA, 80–85°, 0.5 hr, R.T.		81%	m.p. 201–202°	16
	HCl, 10% EtOH, reflux 1 hr		0.5 g ↓ 0.3 g	m.p. 170–171°; ir; uv; nmr	231

TABLE XI-20. Synthesis of Condensed Heterocycles Other Than Quinolizidines (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
4-$PyCH_2CO_2Me$ + 	piperidine		91%	m.p. 271–272.5°	48 49
4-$PyCH_2CO_2Me$ + 	piperidine		75%	m.p. 270–271°	48, 49
4-$PyCH_2CO_2Me$ +  ·HCl	piperidine		35%	hydrochloride, m.p. 136-138°	48, 49
4-$PyCH_2COCO_2Me$ + 	PPA, 8 hr, 2 days		57%	m.p. 307–312° (decomp.)	48, 49
4-$PyCH_2COCO_2Me$ + 	same as above		31%	m.p. 212–214.5°	48, 49

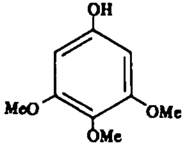
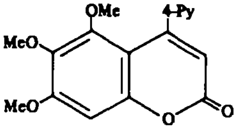
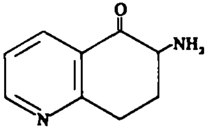
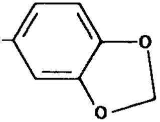
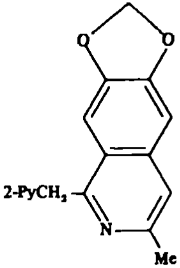
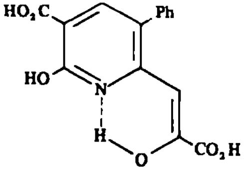
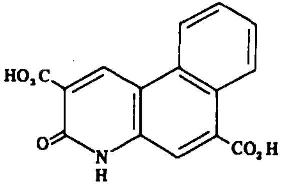
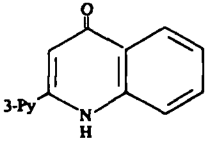
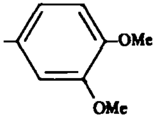
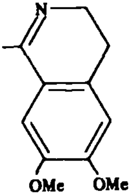
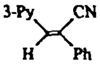
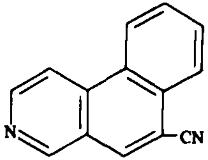
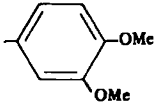
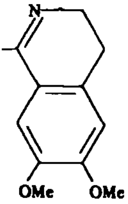
4-PyCH$_2$COCO$_2$Me + 	H$_2$SO$_4$, 8 hr, 2 days		80%	m.p. 183–186°	48, 49
		Quinolines			
2-PyCH$_2$CH$_2$CH(NHAc)CO$_2$Et	H$_2$, PtO$_2$, 5 atm, EtOH, HCl; 20% HCl, 110–120°, 3 hr				89
2-PyCH$_2$CONHCHMeCH(OMe)– 	POCl$_3$, reflux 40 min				291
	conc H$_2$SO$_4$, 3–4 hr; R.T., 2 days		74%	green FeCl$_3$ test; m.p. > 360°; ir; uv; diethyl ester, m.p. 211°	87, 173

TABLE XI-20. Synthesis of Condensed Heterocycles Other Than Quinolizidines (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
3-PyC(NHPh)=CHCONHPh	PPA, 120–130°, 20 min		72%		292
3-Py(CH$_2$)$_3$CONH(CH$_2$)$_2$– 	POCl$_3$, reflux 2 hr, N$_2$	3-Py(CH$_2$)$_2$– 			293
	cyclohexane, light, (40 w Hanovia medium pressure mercury vapor lamp) 3.5 hr		41%	b.p. 180°/10 mm; m.p. 196–196.5°	294
4-Py(CH$_2$)$_3$CONH(CH$_2$)$_2$– 	POCl$_3$, N$_2$, reflux 2 hr	4-Py(CH$_2$)$_2$– 			293

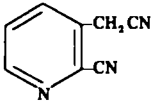
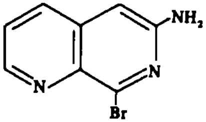
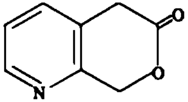
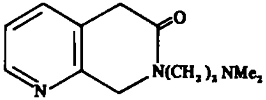
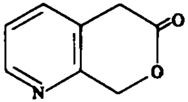
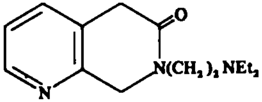
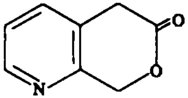
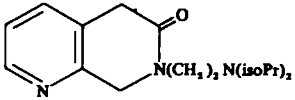
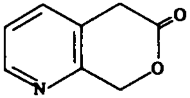
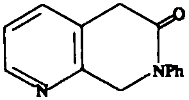
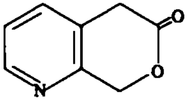
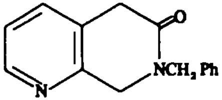
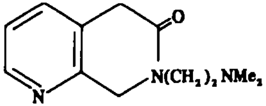
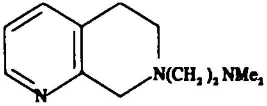
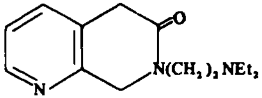
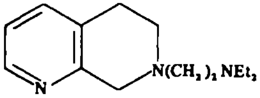
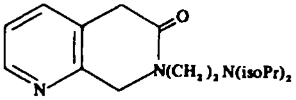
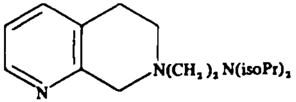
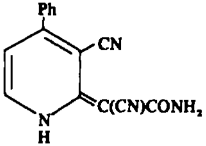
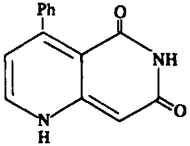
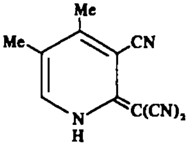
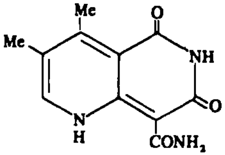
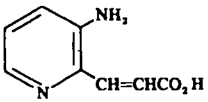
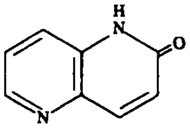
		anhyd. HBr, Et_2O		72%		92
	$+ 2Me_2N(CH_2)_2NH_2$	200°		68%	m.p. 140–150°	174
	$+ 2Et_2N(CH_2)_2NH_2$	200°		62%	m.p. 145–155°	174
	$+ 2(isoPr)_2N(CH_2)_2NH_2$	200°		50%	m.p. 165–170°	174
	$+ 2PhNH_2$	200°		53%	m.p. 131–132°	174
	$+ 2PhCH_2NH_2$	200°		61%	m.p. 117–118°	174
		LAH, Et_2O		60%		174

TABLE XI-20. Synthesis of Condensed Heterocycles Other Than Quinolizidines (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
		Naphthyridines			
	LAH, Et_2O		63%		174
	LAH, Et_2O		45%		174
	50% H_2SO_4			m.p. 227°	153
	50% H_2SO_4			m.p. >300° (decomp.)	153
	NaOMe, NH_4OH			m.p. 260–261°	151

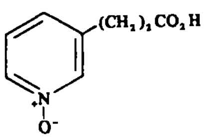
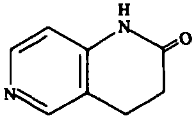
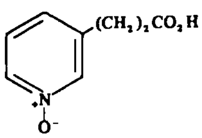
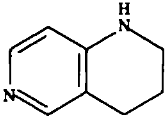
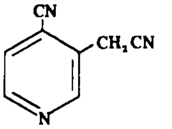
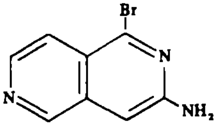
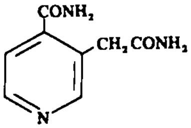
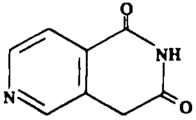
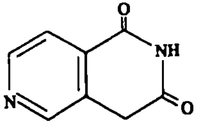
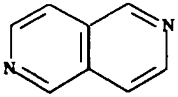
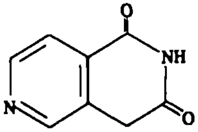
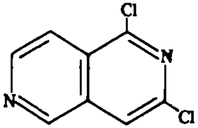
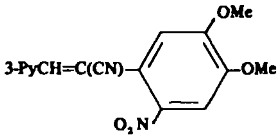
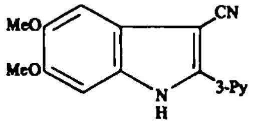
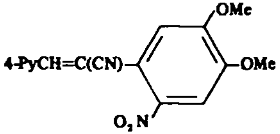
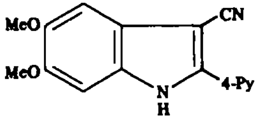
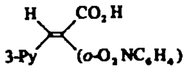
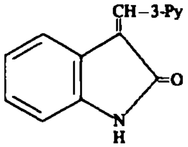
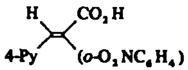
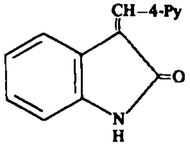
	fuming HNO_3, H_2SO_4; reduced Fe powder, HOAc			m.p. 208°	152
	Zn, HCl, NH_4OH				152
	anhyd. HBr, Et_2O; aq. $NaHCO_3$		80.3%		150
	heat			m.p. 229–230°	128
	Zn dust, 170°, sealed tube				128
	$POCl_3$, 120°, sealed tube, several days				128

TABLE XI-20. Synthesis of Condensed Heterocycles Other Than Quinolizidines (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
		Miscellaneous			
	Fe, HOAc, reflux 2-5 hr		39%	m.p. 238-239°; ir; uv; nmr	10
	same as above		72.5%	m.p. 321°; ir; uv; nmr	10
	$FeSO_4$, NH_4OH, H_2O, 80-90°, 20 min			m.p. 187-188°	99
	same as above			m.p. 225°	99

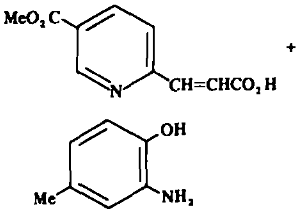
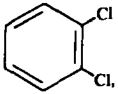
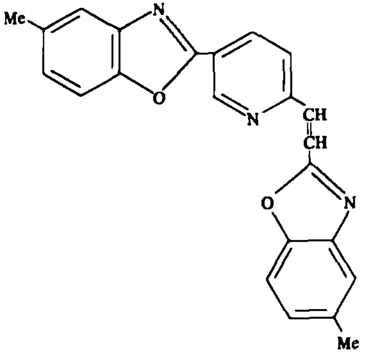
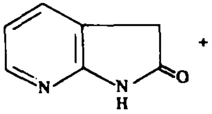
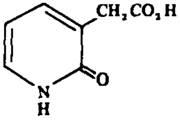
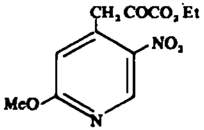
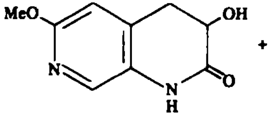
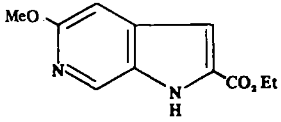
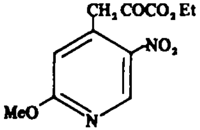
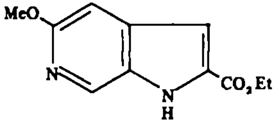
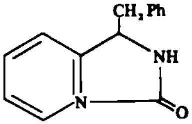
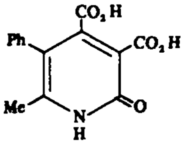
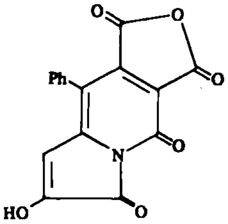
	 Cl, H_3BO_3, 120°, N_2, 8 hr			281
	225°	 (67%) (a)  (4.6%) (b)	(a) m.p. 175° (b) m.p. 240–241° (decomp.)	268

TABLE XI-20. Synthesis of Condensed Heterocycles Other Than Quinolizidines (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
		Miscellaneous			
	H_2, PtO_2, EtOH	 + 			15
	H_2, Pd-C, EtOH		85%	sublimes 90%/0.1 mm; m.p. 103-106°; u.v; nmr	15
2-PyCH(CH_2Ph)CO_2Me	$N_2H_4 \cdot H_2O$, MeOH, heat, 6 hr; $NaNO_2$, 3% HCl			m.p. 161-163°	305
 + $(COCl_2)_2$	$POCl_3$		13 g ↓ 10 g		87

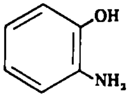
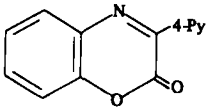
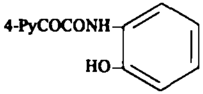
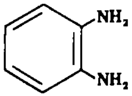
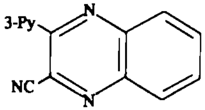
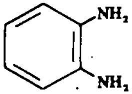
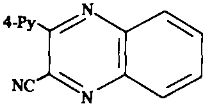
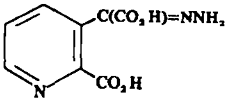
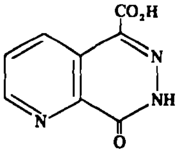
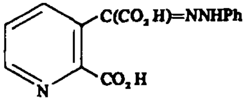
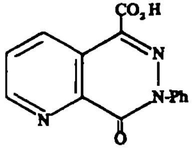
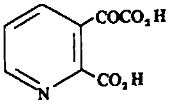
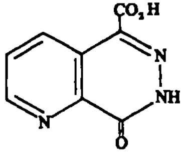
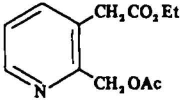
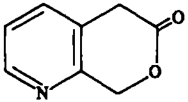
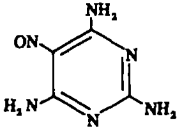
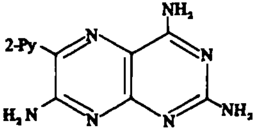
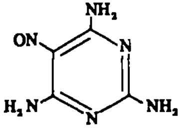
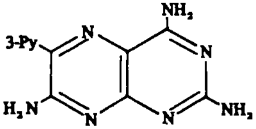
4-PyC(OH)$_2$CO$_2$Me + 	MeOH, 35–50°, 5 hr; steam-bath 20 min		38%	sublimes 162°/0.002 mm; m.p. 168–169°	31
		+ 	11.4%	m.p. 221.5–222.5° (decomp.)	32
3-PyCOC(CN)=N(p-Me$_2$NC$_6$H$_4$) + 			86%	m.p. 193–194°	295
4-PyCOC(CN)=N(p-Me$_2$NC$_6$H$_4$) + 			90%	m.p. 228–229°	295
				m.p. 300–301° (decomp.); methyl ester, m.p. 227–229° (decomp.)	260

TABLE XI-20. Synthesis of Condensed Heterocycles Other Than Quinolizidines (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
		Miscellaneous			
	DMF			m.p. 257° (decomp.); methyl ester, m.p. 178–179°; ethyl ester, m.p. 138–139°	260
	$N_2H_4 \cdot H_2SO_4$, H_2O, 100°, 1 hr		80%	m.p. 300–301° (decomp.)	260
	KOH, EtOH, reflux 9 hr		5.9 g ↓ 1.3 g	m.p. 118–119°	174
2-$PyCH_2CN$ + 	Na, $HOCH_2CH_2OEt$				296
3-$PyCH_2CN$ + 	Na, $HOCH_2CH_2OEt$				296

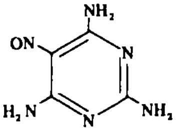
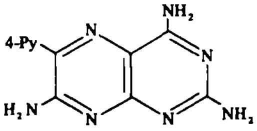
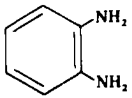
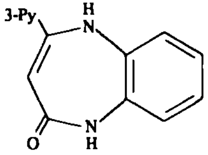
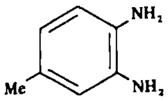
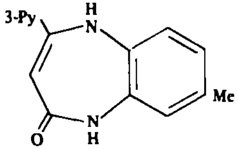
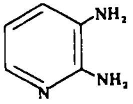
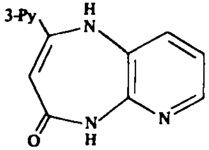
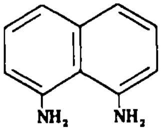
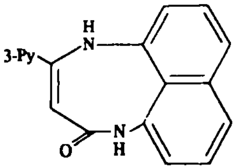
4-PyCH$_2$CN + 	Na, HOCH$_2$CH$_2$OEt			296
3-PyCOCH$_2$CO$_2$H + 	inert solvent, 180° *or* 120° without solvent		m.p. 219–220°; ir; uv	297
3-PyCOCH$_2$CO$_2$H + 	same as above		m.p. 213–217°; ir; uv	297
3-PyCOCH$_2$CO$_2$H + 	same as above		m.p. 249–252°	297
3-PyCOCH$_2$CO$_2$H + 	same as above		m.p. 271–272°	297

TABLE XI-20. Synthesis of Condensed Heterocycles Other Than Quinolizidines (Continued)

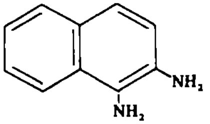
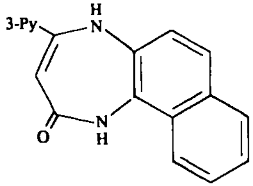
Starting materials	Conditions	Product	Yield	Properties	Ref.
		Miscellaneous			
3-PyCOCH$_2$CO$_2$H + 	same as above			m.p. 209–230°; ir; uv	297

TABLE XI-21. Side-Chain Acid Chlorides

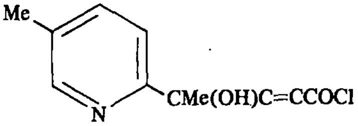
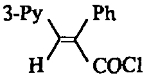
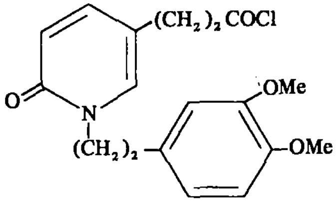
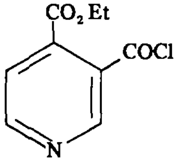
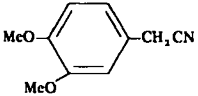
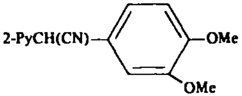
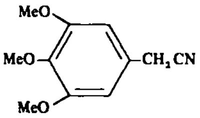
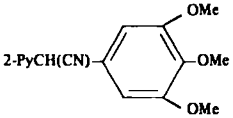
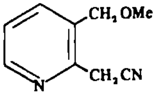
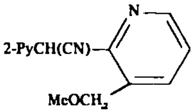
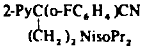
Acid chloride	Properties	Ref.
2-PyCMe(OH)C=CCOCl		79, 97
		79, 97
3-PyCH$_2$COCl		37–40
3-PyCOCOCl		37
3-PyCH=CHCOCl·HCl	m.p. 196° (decomp.)	298, 299, 343
		98
		7
	b.p. 102°/0.1 mm	128
4-PyCPh=CHCOCl		172

Table XI-22. Pyridylation of Nitriles

Halide	Condensed with	Conditions	Product	Yield	Properties	Ref.
2-PyBr	$PhCH_2CN$	$NaNH_2$, PhMe, 45 min; 100°, 2 hr	2-PyCHPhCN		m.p. 87–88°	45, 200, 339
	p-$FC_6H_4CH_2CN$	same as above	2-PyCH(p-FC_6H_4)CN		b.p. 125–129°/0.5 mm	45
	p-$ClC_6H_4CH_2CN$	same as above	2-PyCH(p-ClC_6H_4)CN		m.p. 67.5–68°	45
		same as above			b.p. 175–178°/0.1 mm	45
		Na, NH_3, Et_2O, stir 1 hr; reflux 1 or 15 hr		38.4%		45, 276
	(p-$MeOC_6H_4$)$_2$CHCN *or* p-$MeOC_6H_4CH_2CN$ + p-$MeOC_6H_4Br$	$NaNH_2$, PhMe, reflux until NH_3 evolution ceases	2-PyC(p-MeOPh)$_2$CN			272–274, 300
		$NaNH_2$		15.9%	m.p. 79–80°; picrate, m.p. 132–134°	9
	$PhCH_2CN$ + $Pr_2N(CH_2)_2Cl$	$NaNH_2$, PhMe, 105°, 1 hr; amine added; 108–110°, 3.5 hr; R.T., 12 hr	2-PyCPh(CN)$CH_2CH_2NPr_2$		b.p. 164–165°/0.1 mm	45
	$PhCH_2CN$ + $isoPr_2N(CH_2)_2Cl$	same as above	2-PyCPh(CN)$CH_2CH_2NisoPr_2$		b.p. 145–160°/0.3 mm	45
	o-$FC_6H_4CH_2CN$ + $isoPr_2N(CH_2)_2Cl$	same as above	 $\underset{(CH_2)_2NisoPr_2}{2\text{-}PyC}(o\text{-}FC_6H_4)CN$			45

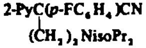
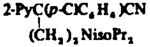
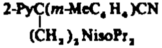
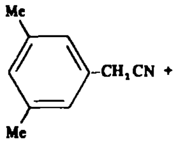
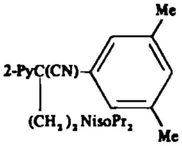
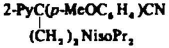
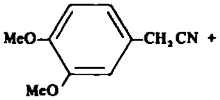
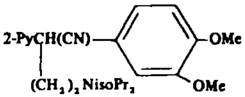
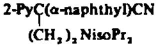
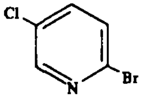
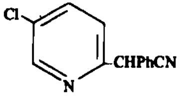
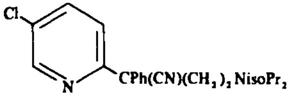
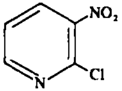
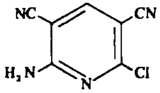
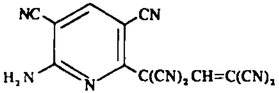
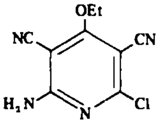
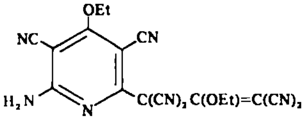
	p-$FC_6H_4CH_2CN$ + $isoPr_2N(CH_2)_2Cl$	same as above	 $2\text{-}PyC(p\text{-}FC_6H_4)CN$ with $(CH_2)_2NisoPr_2$ below	b.p. 154°/0.4 mm	45
	p-$ClC_6H_4CH_2CN$ + $isoPr_2N(CH_2)_2Cl$	same as above	 $2\text{-}PyC(p\text{-}ClC_6H_4)CN$ with $(CH_2)_2NisoPr_2$ below	b.p. 176–179°/0.4 mm	45
	m-$MeC_6H_4CH_2CN$ + $isoPr_2N(CH_2)_2Cl$	same as above	 $2\text{-}PyC(m\text{-}MeC_6H_4)CN$ with $(CH_2)_2NisoPr_2$ below	b.p. 164–168°/0.2 mm	45
	 $isoPr_2N(CH_2)_2Cl$	same as above			45
	p-$MeOC_6H_4CH_2CN$ + $isoPr_2N(CH_2)_2Cl$	same as above	 $2\text{-}PyC(p\text{-}MeOC_6H_4)CN$ with $(CH_2)_2NisoPr_2$ below		45
	 $isoPr_2N(CH_2)_2Cl$	same as above		b.p. 185–190°/0.1 mm	45
	α-naphthyl-CH_2CN + $isoPr_2N(CH_2)_2Cl$	same as above	 $2\text{-}PyC(\alpha\text{-naphthyl})CN$ with $(CH_2)_2NisoPr_2$ below	b.p. 196–202°/0.2 mm	45
	$PhCH_2CN$	$NaNH_2$, PhMe, 45 min; 100°, 2 hr		b.p. 150°/0.5 mm	45
	$PhCH_2CN$ + $isoPr_2N(CH_2)_2Cl$	$NaNH_2$, PhMe, 105°, 1 hr; amine added, 108–110°, 3.5 hr; R.T., 12 hr		b.p. 165–172°/0.25 mm	45

Table XI-22. Pyridylation of Nitriles (Continued)

Halide	Condensed with	Conditions	Product	Yield	Properties	Ref.
	$NCCH_2CO_2Me$	$Me_3CO^{\ominus}K^{\oplus}$, Me_3COH, reflux 5-12 hr		82%	m.p. 186-188°	84
	$NCCH_2CO_2Et$	same as above		87%	m.p. 136-137°	84
	$NCCH_2CO_2CH_2Ph$	same as above		52%	m.p. 139-140°	84
2-$PyCH_2Cl$	$(Ph)_2CH_2CN$	xylene	2-$PyCH_2C(Ph)_2CN$		m.p. 116-118°; hydrochloride, m.p. 208-212° (decomp)	51
	$NaC(CN)_2CH{=}C(CN)_2$	R.T., 1 hr; ion exchange resin (sulfonic acid H^+)			sublimes 200°	301
	$NaC(CN)_2C(OEt){=}C(CN)_2$	same as above			m.p. 264-265°	301

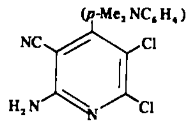
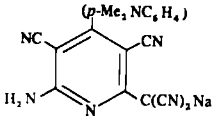
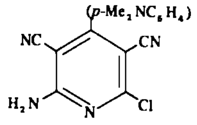
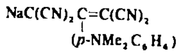
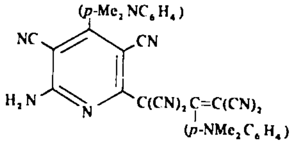
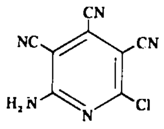
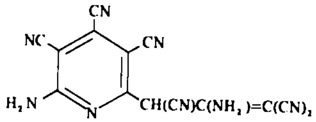
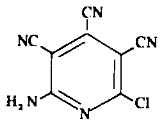
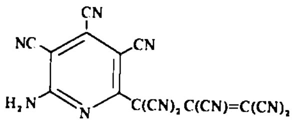
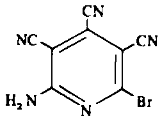
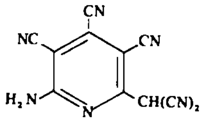
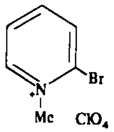
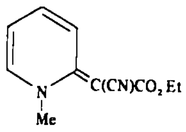
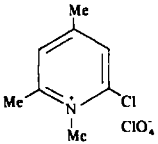
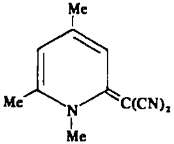
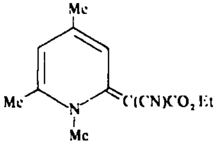
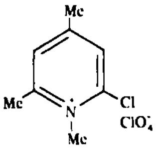
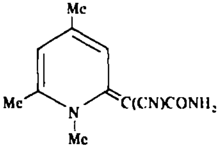
	$NaCH(CN)_2$	R.T., 1 hr			Me_4N^+ salt, m.p. > 300°	301
	 $NaC(CN)_2\underset{(p\text{-}NMe_2C_6H_4)}{C}=C(CN)_2$	R.T., 1 hr; ion exchange resin (sulfonic acid H⁺)			m.p. >320°	301
	$NaCH(CN)C(NH_2)=C(CN)_2$	same as above			m.p. 170–173°; sodium salt, m.p. > 300°	301
	$NaC(CN)_2C(CN)=C(CN)_2$	same as above			m.p. 228–229°	301
	$NaCH(CN)_2$	same as above			$Me_4\overset{+}{N}$ salt, m.p. >300°; $Et_4\overset{+}{N}$ salt, m.p. 190–191°; $Me_3\overset{+}{S}$ salt, m.p. >260°	301
	$CH_2(CN)CO_2Et$	NaOEt, EtOH, reflux 30 min–1 hr		24.5%	m.p. 127.5–128°	83

Table XI-22. Pyridylation of Nitriles (Continued)

Halide	Condensed with	Conditions	Product	Yield	Properties	Ref.
	$CH_2(CN)_2$	NaOEt, EtOH, reflux 30 min–1 hr		34%	m.p. 201–202°; uv	83
	$CH_2(CN)CO_2Et$	same as above		43.5%	m.p. 120–121°	83
	$CH_2(CN)CONH_2$	NaOEt, EtOH, reflux 30 min–1 hr		44%	m.p. 162–164	83
3-PyBr	$PhCH_2CN$	$NaNH_2$, PhMe, 45 min; 100°, 2 hr	3-PyCHPhCN		b.p. 150°/0.5 mm b.p. 155–170°/0.5 mm	45 277
	$PhCH(p\text{-}FC_6H_4)CN$	$Me_3CO^{\ominus}K^{\oplus}$	$3\text{-}PyCPh(p\text{-}FC_6H_4)CN$		b.p. 170–182°/0.4 mm	277
	$PhCH_2CN$ + $isoPr_2N(CH_2)_2Cl$	$NaNH_2$, PhMe, 105° 1 hr; amine added, 108–110°, 3.5 hr; R.T., 12 hr	$3\text{-}PyCPh(CN)(CH_2)_2NisoPr_2$		b.p. 180–190°/0.3 mm	45

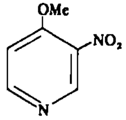
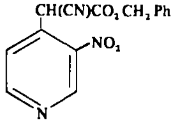
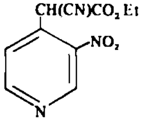
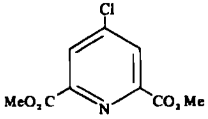
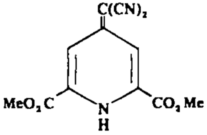
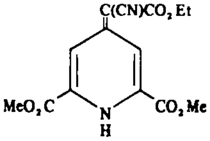
3-PyCH$_2$Cl	(α-naphthyl)CH$_2$CN	NaNH$_2$, Et$_2$O	3-PyCH$_2$CH(α-naphthyl)CN	46.5%	b.p. 189–190°/1.0 mm; m.p. 45–47°	302
4-PyBr	PhCH$_2$CN	NaNH$_2$, PhMe, 45 min; 100°, 2 hr	4-PyCHPhCN		b.p. 133–136°/0.35 mm; m.p. 76–76.5°	45
	PhCH$_2$CN + isoPr$_2$N(CH$_2$)$_2$Cl	NaNH$_2$, PhMe, 105°, 1 hr; amine added, 108–110°, 3.5 hr; R.T., 12 hr	4-PyCPh(CN)(CH$_2$)$_2$NisoPr$_2$		b.p. 164–168°/0.7 mm	45
	NCCH$_2$CO$_2$CH$_2$Ph	Me$_3$CO$^{\ominus}$K$^{\oplus}$, Me$_3$COH, reflux 5–12 hr		60%	m.p. 204° (decomp.)	84
	NCCH$_2$CO$_2$Et	same as above		52%	b.p. 177–178°	84
	CH$_2$(CN)$_2$	50% NaH, DMF, 50°; 120°, 4.5 hr.			m.p. 218–219° (decomp.); sodium salt, m.p. 291°	303
	CH$_2$(CN)CO$_2$Et	Na, EtOH, 30 min			m.p. 149°; sodium salt, m.p. 207–208° (decomp.)	190, 303

TABLE XI-22. Pyridylation of Nitriles (Continued)

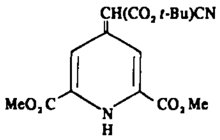
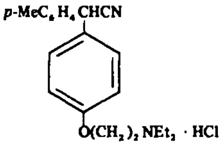
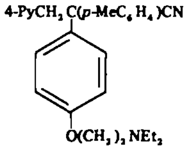
Halide	Condensed with	Conditions	Product	Yield	Properties	Ref.
	$CH_2(CN)CO_2(t\text{-}Bu)$	50% NaH, DMF, 50°; 120°, 4.5 hr; HCl, EtOH			m.p. 175° (decomp.); sodium salt, m.p. 247° (decomp.)	303
$4\text{-}PyCH_2Cl$		Na, liq. NH_3		57%	p*Ka* = 8.02	43

Table XI-23. Alkylation of Pyridylacetonitriles

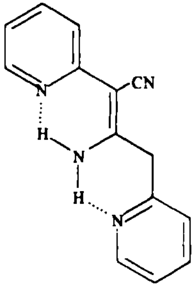
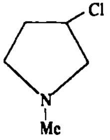
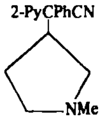
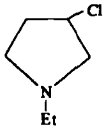
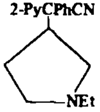
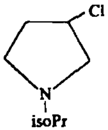
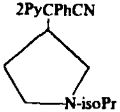
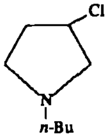
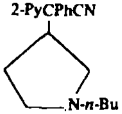
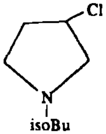
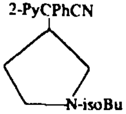
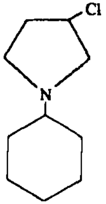
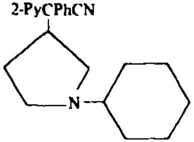
PyCHRCN	R'X	Conditions	Product	Yield	Properties	Ref.
2-PyCH$_2$CN	EtBr	NaNH$_2$, PhMe, 1 hr; halide reflux 2 hr	2-PyCHEtCN	10 g → 8.5 g	b.p. 75–77°/0.05 mm; picrate, m.p. 132–133°	178
	PhCl	NaNH$_2$	2-PyCHPhCN		m.p. 87–88°	304
	p-MeOC$_6$H$_4$Cl	NaNH$_2$	2-PyCH(*p*-MeOC$_6$H$_4$)CN			304
	PhCH$_2$Cl	NaNH$_2$, Et$_2$O	2-PyCH(CN)CH$_2$Ph +	6 g → 4.5 g	m.p. 67.5–68.5°; b.p. 153–154°/3.0 mm; picrate, m.p. 161–162°	305
			2-PyC(CN)(CH$_2$Ph)$_2$	6 g → 3.5 g	m.p. 93–97.5°	
	PhCH$_2$OAc	Na, PhCH$_2$OH, reflux 2 hr, 170–180°	2-PyCH(CH$_2$Ph)CN	84%	m.p. 66–67°	306
	2-PyCH$_2$CN	NaOEt, EtOH, reflux 2 hr		96%	m.p. 124–126°; ir; uv; nmr	163
2-PyCHPhCN		NaNH$_2$			m.p. 148–151°/0.07 mm	304

Table XI-23. Alkylation of Pyridylacetonitriles (Continued)

PyCHRCN	R¹X	Conditions	Product	Yield	Properties	Ref.
		$NaNH_2$			m.p. 110–119°	304
		$NaNH_2$			m.p. 107–109°	304
		$NaNH_2$			b.p. 170–175°/0.08 mm	304
		$NaNH_2$			b.p. 161–165°/0.07 mm	304
		$NaNH_2$			b.p. 200–208°/0.05 mm	304

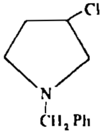
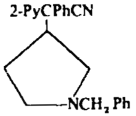
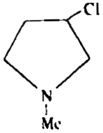
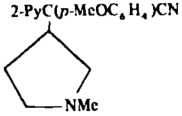
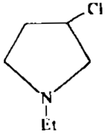
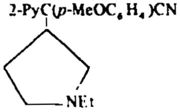
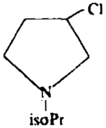
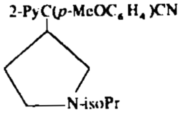
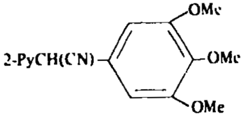
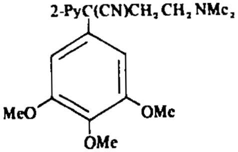
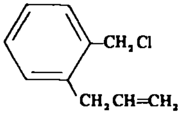
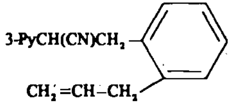
		$NaNH_2$			b.p. 200–210°/0.08 mm	304
2-PyCH(p-MeOC$_6$H$_4$)CN		$NaNH_2$			b.p. 170–173°/0.08 mm	304
		$NaNH_2$			b.p. 200–202°/0.08 mm	304
		$NaNH_2$			b.p. 190°/0.05 mm	304
	$Me_2N(CH_2)_2Cl$	Na, NH_3, Et_2O		59.5%	b.p. 191–196°/0.25 mm; picrate, m.p. 137–138°	276
2-PyCH(CH$_2$Ph)CN	$Me_2N(CH_2)_2Cl$	$NaNH_2$, PhMe heat, 2.5 hr	2-PyC(CN)(CH$_2$Ph)CH$_2$CH$_2$NMe$_2$		b.p. 155–167°/2 mm; methiodide, m.p. 167–167.5°	305

TABLE XI-23. Alkylation of Pyridylacetonitriles (Continued)

PyCHRCN	R'X	Conditions	Product	Yield	Properties	Ref.
3-$PyCH_2CN$	EtCl	$PhCH_2\overset{\oplus}{N}(CH_2CH{=}CH_2)_3\overset{\ominus}{Cl}$ 50% NaOH, < 25°	3-PyCHEtCN		b.p. 73–75°/0.1 mm	307
	o-$ClC_6H_4CH_2Cl$	NaH, PhH, DMF, R.T., 15 hr	3-$PyCH(CN)CH_2$(o-ClC_6H_4)		b.p. 125–135°/0.08 mm, m.p. 64–65°	59
		NaH, DMF; 25°, overnight				290
	$Ph(CH_2)_2Br$	NaH, DMF, R.T.; PhMe, R.T., 3 hr; R.T. overnight	3-$PyCH(CN)CH_2CH_2Ph$	60%	b.p. 143–150°/0.01 mm b.p. 147–150°/0.01 mm	308 286–289, 309, 310
	m-$ClC_6H_4(CH_2)_2Br$	same as above	3-$PyCH(CN)CH_2CH_2$(m-ClC_6H_4)	61%	b.p. 160–162°/0.05 mm	287–289, 308–310
	p-$ClC_6H_4(CH_2)_2Br$	same as above	3-$PyCH(CN)CH_2CH_2$(p-ClC_6H_4)	58%	b.p. 168–169°/0.05 mm b.p. 168–175°/0.05 mm	286–289 308–310
	p-$MeC_6H_4(CH_2)_2Br$	same as above	3-$PyCH(CN)CH_2CH_2$(p-MeC_6H_4)		b.p. 170–173°/0.04 mm	288
	isoPrCHPhCl	same as above	3-PyCH(CN)CHPhisoPr		m.p. 96–97°	286
	m-$MeOC_6H_4(CH_2)_2Br$	same as above *or*	3-$PyCH(CN)CH_2CH_2$(m-$MeOC_6H_4$)	60%	b.p. 160–163°/0.04 mm	286
		NaH, DMF; 25°, overnight		44 g → 60 g	b.p. 178–183°/0.5 mm	290

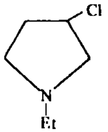
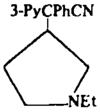
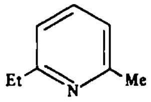
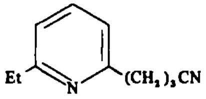
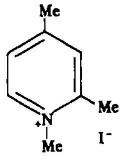
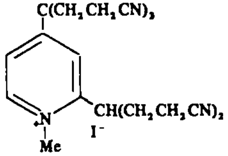
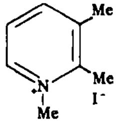
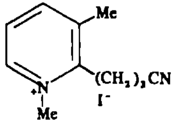
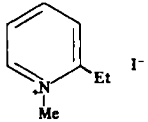
	Ph(CH$_2$)$_3$Cl	NaH, DMF, R.T.; PhMe, R.T., 3 hr; R.T., overnight	3-PyCH(CN)(CH$_2$)$_3$Ph	46%	b.p. 145–152°/0.04 mm, m.p. 96–97°	286, 288
3-PyCHPhCN		PhMe, reflux 4 hr; halide added, reflux 3 hr		57%	b.p. 168–171°/0.005 mm	57

TABLE XI-24. Synthesis of Side-Chain Nitriles by Michael Addition

Vinyl compound	Addend	Conditions	Product	Yield	Properties	Ref.
CH_2=CHCN	2-PyMe	Na, 100–110°, reflux 3–5 hr	2-Py$(CH_2)_3$CN		b.p. 95–97°/1.0 mm	311
CH_2=CHCN	2-PyMe · MeI	Et_3N, reflux 2 hr, H_2O, EtOH; 300°	2-PyCH$(CH_2CH_2CN)_2$	78%	b.p. 182°/1.2 mm; methiodide, m.p. 141–142°	312
CH_2=CHCN		Na, 100–110°; reflux 3–5 hr				311
CH_2=CHCN		Et_3N, H_2O, EtOH, reflux 48 hr		44%	methiodide, m.p. 192–193°	312
CH_2=CHCN		Et_3N, H_2O, EtOH, reflux 24 hr		44%	m.p. 192–193°	312
CH_2=CHCN		Et_3N, reflux 24 hr, EtOH, H_2O; 300°	2-PyCHMeCH$_2$CH$_2$CN	65%	b.p. 170°/45 mm; methiodide, m.p. 97°	312

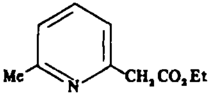
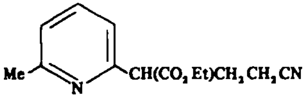
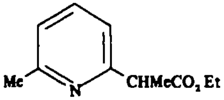
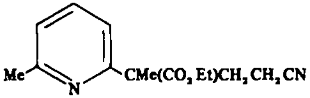
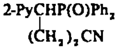
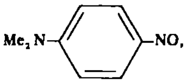
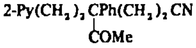
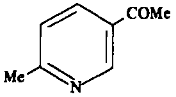
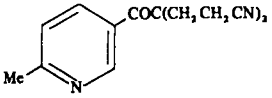
$CH_2{=}CHCN$	2-PyCH$_2$CO$_2$Et	Na, Et$_2$O, reflux 14 hr *or* Na, N$_2$	2-PyCH(CO$_2$Et)CH$_2$CH$_2$CN	75% 71%	b.p. 130–150°/0.2 mm	313 242
$CH_2{=}CHCN$		Na, 180°			n_D^{20} 1.5030	283
$CH_2{=}CHCN$		Na, 180°			b.p. 160°/1.0 mm	283
2-PyCH=CH$_2$	NCCH$_2$CO$_2$Et	Na, 100°; 100–110°, 5 hr	2-Py(CH$_2$)$_2$CH(CN)CO$_2$Et			204
$CH_2{=}CHCO_2Et$	2-PyCH$_2$CN	Na, heat, 2 hr	2-PyCH(CN)CH$_2$CH$_2$CO$_2$Et	25 g → 13 g	b.p. 143–148°/0.2 mm	178
$CH_2{=}CHCN$	2-PyCHEtCN	Na, 150°, 2 hr	2-PyCEt(CN)CH$_2$CH$_2$CN	8 g → 16 g	b.p. 108–110°/0.05 mm	178
$CH_2{=}CHP(O)(OEt)_2$	2-PyCH$_2$CN	NaOEt, EtOH, 60°	2-PyCH(CN)CH$_2$CH$_2$P(O)(OEt)$_2$	61%	n_D^{20} 1.4935; picrolonate, m.p. 102–103°	243
PhCH=CHCOMe	2-PyCH$_2$CN	30% KOH, MeOH, Et$_2$O, 20–25°, 2 hr	2-PyCH(CN)CHPhCH$_2$COMe	34 g → 27 g	m.p. 109°; phenylhydrazone, m.p. 150–151°	270
PhCH=CHCOPh (0.75 equiv.)	2-PyCH$_2$CN	30% KOH, MeOH, Et$_2$O, 20–25°, 2 hr	2-PyCH(CN)CHPhCH$_2$COPh	20 g → 35 g	m.p. 119°; phenylhydrazone, m.p. 148°	270
PhCH=CHCOPh (1 equiv.)	2-PyCH$_2$CN	30% KOH, MeOH, Et$_2$O, 20–25°, 2 hr	2-PyCH(CN)CHPhCH$_2$COPh + 2-PyC(CN)[CHPhCH$_2$COPh]$_2$	20 g → 8 g 16 g	 m.p. 212–213°	270
2-PyCH=CHCOPh	2-PyCH$_2$CN	30% KOH, MeOH, Et$_2$O, 20–25°, 2 hr	2-PyCH(CN)CH(2-Py)CH$_2$COPh	34 g → 38 g	m.p. 158°	270
$CH_2{=}CHCN$	2-PyCHMeCO$_2$Et	Na, 180°	2-PyCMe(CO$_2$Et)CH$_2$CH$_2$CN	68%	yellow oil, n_D^{20} 1.5046	283

TABLE XI-24. Synthesis of Side-Chain Nitriles by Michael Addition (Continued)

Vinyl compound	Addend	Conditions	Product	Yield	Properties	Ref.
$CH_2=CHCN$	$2\text{-PyCH}_2P(O)Ph_2$	Triton B, MeCN, overnight	 2-PyCHP(O)Ph_2 with $(CH_2)_2CN$ below CH	1 g → 0.85 g		314
$CH_2=CHCN$	2-PyCH=CH_2	 H_2O, $e^{\ominus}$, $Et_4N^{\oplus}Tos^{\ominus}$,	$2\text{-Py(CH}_2)_4CH$		b.p. 136–140°/0.5 mm	90
$CH_2=CHCN$	$2\text{-Py(CH}_2)_2CN$	heat	$2\text{-PyCH(CH}_2CN)CH_2CH_2CN$			311
$CH_2=CHCN$	$2\text{-Py(CH}_2)_2CHPhCOMe$	*t*-BuOH, 25–45°, 3 hr	 $2\text{-Py(CH}_2)_2CPh(CH_2)_2CN$ with $COMe$ below CPh	69%	b.p. 195–200°/0.1 mm	36
2-PyCH=CH_2	$PhCH_2CN$	Triton B, MeOH, reflux 3 hr	$2\text{-Py(CH}_2)_2CHPhCN$ + $(2\text{-PyCH}_2CH_2)_2CPhCN$		b.p. 72°/0.8 mm b.p. 194°/0.5 mm	167
2-PyCH=CH_2	MeCN	same as above	$2\text{-Py(CH}_2)_3CN$		b.p. 111°/1.5 mm	167
$CH_2=CHCN$		40% Triton B, dioxane, 10–20°		34 g → 10 g	m.p. 144.5–146°; picrate, m.p. 168–170°	156
	4-PyMe	Na, 100–110°; reflux 3–5 hr	$4\text{-Py(CH}_2)_3CN$		b.p. 122–125°/1.0 mm	311
$CH_2=CHCN$ (2 equiv.)	4-PyMe	same as above	$4\text{-PyCH(CH}_2CH_2CN)_2$		b.p. 140–145°	311
$CH_2=CHCN$	4-PyMe · MeI	Et_3N, H_2O, EtOH, reflux 12 hr; 300°	$4\text{-PyC(CH}_2CH_2CN)_3$	67%	m.p. 156°; methiodide, m.p. 229.5–230.5°	312

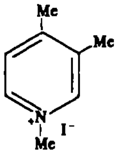
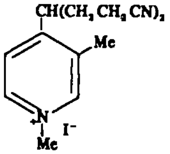
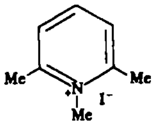
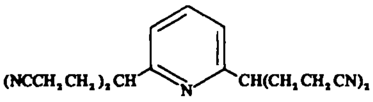
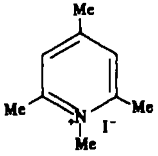
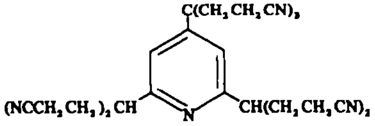
	4-PyEt · MeI	Et_3N, H_2O, EtOH, reflux 19 hr	4-PyCHMe$(CH_2CH_2CN)_2$ ·MeI	87%	m.p. 126–128°	312
	4-*n*-PrPy · MeI	Et_3N, H_2O, EtOH, reflux 24 hr; 300°	4-PyCHEt$(CH_2CH_2CN)_2$	85%	b.p. 230–235°/1.4 mm; m.p. 74.5°; methiodide, m.p. 232.5–235°	312
	4-$PyCH_2P(O)Ph_2$	Triton B, MeCN, overnight	 $\text{4-Py}\underset{\displaystyle (CH_2)_2CN}{\underset{\vert}{C}}HP(O)Ph_2$	58%	m.p. 199–200°	314
	4-$Py(CH_2)_2CN$	heat	4-PyCH$(CH_2CH_2CN)_2$		b.p. 140–145°	311
		Et_3N, H_2O, EtOH, reflux 23 hr		50%	m.p. 145–146°	312
	4-PyCOMe	Triton B, 60°, 5 hr	4-PyCO$(CH_2)_3CN$		m.p. 139–140°	117
CH_2=CHCN		Et_3N, H_2O, EtOH, reflux 24 hr; 300°		76%	m.p. 55.5–56°; methiodide, m.p. 152–153° (decomp.)	312
		Et_3N, H_2O, EtOH, reflux 22 hr; 300°		66%	m.p. 131–132.5°; methiodide, m.p. 202.5–203.5°	312

TABLE XI-24. Synthesis of Side-Chain Nitriles by Michael Addition (Continued)

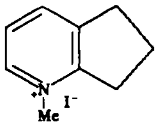
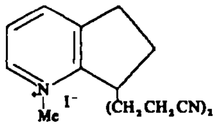
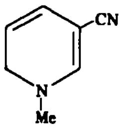
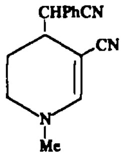
Vinyl compound	Addend	Conditions	Product	Yield	Properties.	Ref.
		Et_3N, H_2O, EtOH, reflux 17 hr		71%	methiodide, m.p. 195.5–196°	312
	$PhCH_2CN$	Triton B, 100°, N_2, 12 hr		17.5 g ↓ 11.6 g	b.p. 165–180°/0.1 mm; ir	315

TABLE XI-25. Synthesis of Side-Chain Nitriles by Knoevenagel Condensation

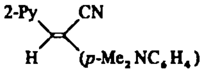
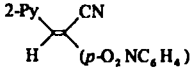
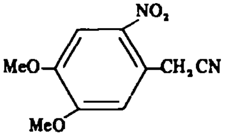
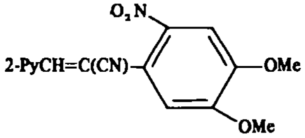
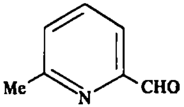
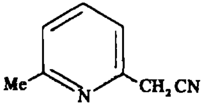
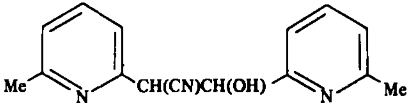
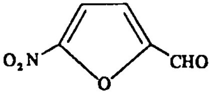
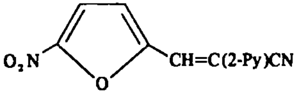
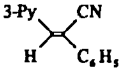
Carbonyl component	Methylene component	Conditions	Product	Yield	Properties	Ref.
2-PyCHO	$NCCH_2CO_2Et$	EtOH, piperidine; reflux 1-5 hr	2-PyCH=C(CN)CO_2Et	64%	m.p. 94.5-96°	137
	$NCCH_2CO_2Et$	EtOH	2-PyCH=C(CN)CO_2Et	88%	m.p. 94-95°	211
	$PhCH_2CN$	NaOH, EtOH, heat	2-PyCH$(CHPhCN)_2$	75%	m.p. 171-173°	211
	p-$ClC_6H_4CH_2CN$	EtOH, piperidine, reflux 1-5 hr	2-PyCH=C(CN)(p-ClC_6H_4)	67%	m.p. 165-167°	137
	p-$Me_2NC_6H_4CH_2CN$	NaOEt, EtOH, 50°; 1 hr with no heat		>70%	m.p. 136-138°; uv	98
	p-$O_2NC_6H_4CH_2CN$	EtOH, piperidine, reflux 1-5 hr	2-PyCH=C(CN)(p-$O_2NC_6H_4$)	96%	m.p. 199-201°	137
		MeOH, piperidine, heat		99%	m.p. 200-201.5°; ir; uv	164
		EtOH, piperidine reflux 1-5 hr		96%	m.p. 192.5-193.5°	137
2-PyCOMe	$PhNH_2$	$CN^{\ominus}$, HOAc	2-PyCMe(CN)NHPh		m.p. 127.5-128.5°	316
	MeCN	$NaNH_2$, Et_2O, 1.5 hr	2-PyCPh(OH)CH_2CN		m.p. 90-92°	223

TABLE XI-25. Synthesis of Side-Chain Nitriles by Knoevenagel Condensation (Continued)

Carbonyl component	Methylene component	Conditions	Product	Yield	Properties	Ref.
2-PyCOPh	EtCN	$NaNH_2$, Et_2O, 1.5 hr	2-PyCPh(OH)CHMeCN		m.p. 100–102°	223
	$PhCH_2CN$	$NaNH_2$, C_6H_6, reflux 1 hr	2-PyCPh=CPhCN		m.p. 150–151°; uv	41
	p-$ClC_6H_4CH_2CN$	$NaNH_2$, C_6H_6, reflux 1 hr	2-PyCPh=C(p-ClC_6H_4)CN		m.p. 165–167°; uv	41
	p-$MeOC_6H_4CH_2CN$	$NaNH_2$, C_6H_6, reflux 1 hr	2-PyCPh=C(p-$MeOC_6H_4$)CN		m.p. 138–140°; uv	41
MeCHO	2-$PyCH_2CN$	piperidine, HOAc C_6H_6, 45 min	2-PyC(CN)=CHMe	74%	b.p. 70–71°/0.25 mm	163
p-$O_2NC_6H_4CHO$	2-$PyCH_2CN$	piperidine, EtOH, reflux 1 hr	2-PyC(CN)=CH(p-$O_2NC_6H_4$)			68
		*N*-ethylpiperidine *or* heat only			m.p. 51–52°	130
	2-$PyCH_2CN$	Ac_2O, overnight			m.p. 197–200°	241
3-PyCHO	$NCCH_2C_6H_5$	NaOEt, EtOH, 50°; 1 hr with no heat		98%	m.p. 92–93°; uv	98

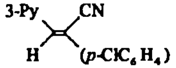
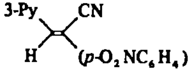
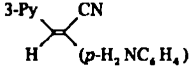
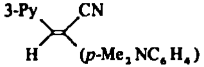
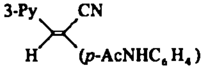
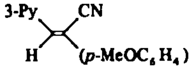
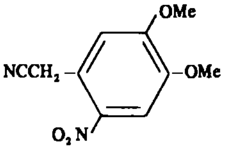
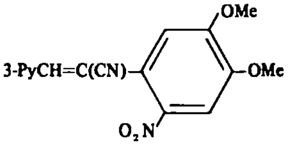
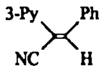
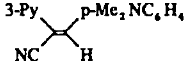
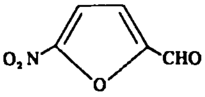
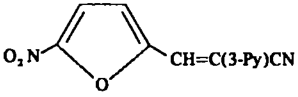
$NCCH_2(p\text{-}ClC_6H_4)$	same as above		>70%	m.p. 140–141°	98
	piperidine, MeOH, heat	3-PyCH=C(p-ClC$_6$H$_4$)CN	76%	m.p. 137–138.5°; ir, uv	164
$NCCH_2(p\text{-}O_2NC_6H_4)$	same as above	3-PyCH=C(p-O$_2$NC$_6$H$_4$)CN	88%	m.p. 156–157°	164
	NaOEt, EtOH, 50°; 1 hr with no heat		>70%	m.p. 156–157°	98
$NCCH_2(p\text{-}H_2NC_6H_4)$	same as above		>70%	m.p. 169–171°	98
$NCCH_2(p\text{-}NMe_2C_6H_4)$	same as above		>70%	m.p. 122–124°	98
$NCCH_2(p\text{-}AcNHC_6H_4)$	same as above		>70%	m.p. 223–224°	98
$NCCH_2(p\text{-}MeOC_6H_4)$	same as above		>70%	m.p. 112–114°	98
	piperidine, MeOH, reflux 4 hr		94%	m.p. 204°	10
$NCCH_2CO_2H$	MeOH, reflux 10 min	3-PyCH=C(CN)CO$_2$H	11 g → 14 g	m.p. 203°	213

TABLE XI-25. Synthesis of Side-Chain Nitriles by Knoevenagel Condensation (Continued)

Carbonyl component	Methylene component	Conditions	Product	Yield	Properties	Ref.
	$NCCH_2CO_2Et$	piperidine, EtOH reflux 1-5 hr	3-PyCH=C(CN)CO_2Et	83%	m.p. 87.5-88.5°	137
3-PyCOPh	$PhCH_2CN$	$NaNH_2$, C_6H_6, reflux 1 hr	3-PyCPh=CPhCN		m.p. 154.5-157°	41
	p-$ClC_6H_4CH_2CN$	same as above	3-PyCPh=C(p-ClC_6H_4)CN		m.p. 185-187°	41
	p-$MeOC_6H_4CH_2CN$	same as above	3-PyCPh=C(p-$MeOC_6H_4$)CN		m.p. 164-165°	41
PhCHO	3-$PyCH_2CN$	NaOEt, EtOH, 50°			m.p. 107-109°; uv	98
o-ClC_6H_4CHO	3-$PyCH_2CN$	NaOEt, 95% EtOH, R.T.	3-PyC(CN)=CH(o-ClC_6H_4)		m.p. 117-118°	59
p-$Me_2NC_6H_4CHO$	3-$PyCH_2CN$	MeOH, H_2O	3-PyC(CN)=CH(p-$Me_2NC_6H_4$)		m.p. 142-143°	317
		NaOEt, EtOH, 50°			m.p. 139-141°	98
	3-$PyCH_2CN$	Ac_2O, overnight			m.p. 167-169°	241
4-PyCHO	$NCCH_2CO_2H$	MeOH, reflux 10 min	4-PyCH=C(CN)CO_2H	68%	hemihydrate, m.p. 185°	213

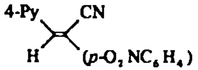
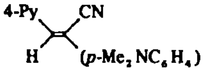
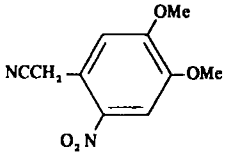
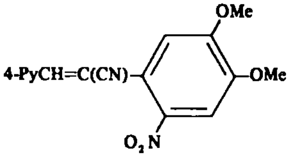
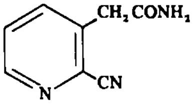
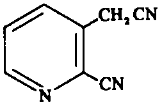
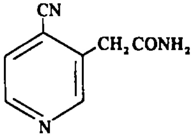
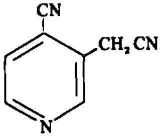
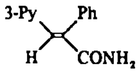
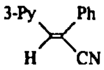
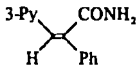
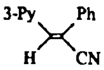
	NCCH$_2$(*p*-O$_2$NC$_6$H$_4$)	piperidine, MeOH, heat		81%	m.p. 156–157°; uv, ir	164
	NCCH$_2$(*p*-Me$_2$NC$_6$H$_4$)	NaOEt, EtOH, 50°; 1 hr with no heat		>70%	m.p. 154–157°; uv	98
		piperidine, MeOH, reflux 4 hr		99%	m.p. 200–201°; uv	10
4-PyCOPh	PhCH$_2$CN	NaNH$_2$, C$_6$H$_6$, reflux 1 hr	4-PyCPh=CPhCN		m.p. 146–148°; uv	41
	p-ClC$_6$H$_4$CH$_2$CN	same as above	4-PyCPh=C(*p*-ClC$_6$H$_4$)CN		m.p. 167–169°; uv	41
	p-MeOC$_6$H$_4$CH$_2$CN	same as above	4-PyCPh=C(*p*-MeOC$_6$H$_4$)CN		m.p. 161–166°; uv	41
o-O$_2$NC$_6$H$_4$CHO	4-PyCH$_2$CN	piperidine, MeOH, reflux 6 hr	4-PyCH(CN)CH(OH)(*o*-O$_2$NC$_6$H$_4$)	18%	m.p. 138–140°; picrate, m.p. 204.5–205.5°	99
p-O$_2$NC$_6$H$_4$CHO	4-PyCH$_2$CN	MeOH, H$_2$O	4-PyC(CN)=CH(*p*-O$_2$NC$_6$H$_4$)		m.p. 199–200°	317
p-H$_2$NC$_6$H$_4$CHO	4-PyCH$_2$CN	MeOH, H$_2$O	4-PyC(CN)=CH(*p*-H$_2$NC$_6$H$_4$)		m.p. 224–227°	317
p-Me$_2$NC$_6$H$_4$CHO	4-PyCH$_2$CN	MeOH, H$_2$O	4-PyC(CN)=CH(*p*-Me$_2$NC$_6$H$_4$)		m.p. 181–182°	317

TABLE XI-26. Side-Chain Nitrile Synthesis: Miscellaneous Methods

Starting material	Conditions	Product	Yield	Properties	Ref.
		Dehydration			
	$POCl_3$, pyridine, 65° 2.5 hr			m.p. 64–65.5°	92
	same as above		87%	m.p. 78.5–79.5°	150
	TsCl, pyridine, R.T., 1 hr		72%	m.p. 64–66°	98
	60% H_2SO_4, 100°, 3 hr; R.T., overnight				98
4-$PyCH_2CONH_2$	$POCl_3$, heat, 6 hr	4-$PyCH_2CN$	58.5%	m.p. 43–44°	168
		Metathesis			
2-$PyCH_2Br$	NaCN, Et_2SO or MeEtSO, 92–94°, 5 hr	2-$PyCH_2CN$			318
2-$PyCH_2Cl$	NaCN, DMF, 50–55°	2-$PyCH_2CN$			318

Metathesis

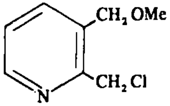
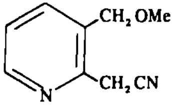
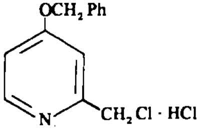
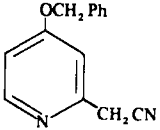
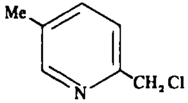
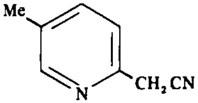
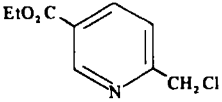
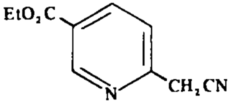
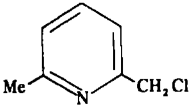
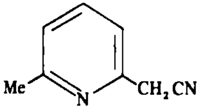
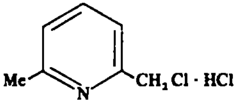
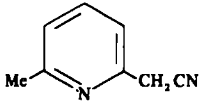
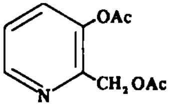
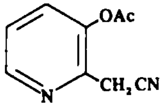
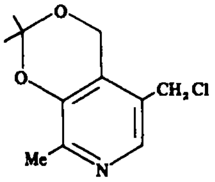
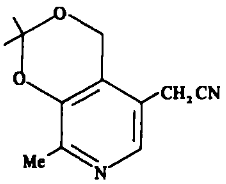
2-PyCH$_2$Cl·HCl	NaHCO$_3$, H$_2$O; NaCN, MeOH, 10 hr *or* KCN, KI, 60% EtOH, 45–50°, 9 hr *or*	2-PyCH$_2$CN	100 g → 50 g	b.p. 85–90°/1–2 mm	270 296
	NaCN, DMSO		87%	b.p. 118–120°/0.3 mm	319
	NaCN, EtOH, reflux 10 hr		83.5%	b.p. 110–115°/0.05 mm; picrate, m.p. 146–148°	9
	KCN, KI, EtOH, heat 3 hr		81%	picrate, m.p. 175°	282
	KCN, EtOH, reflux 8 hr		7 g → 5 g	b.p. 105–106°/3.0 mm	192
	NaCN, EtOH, H$_2$O, reflux 23 min		1.75 g → 1.2 g		17
	NaCN, MeOH, 13 hr *or*		65%	b.p. 105°/12 mm; picrate, m.p. 151°	200
	KCN, MeOH, steam-bath 2 hr		5 g → 2.5 g	m.p. 40–41°	130

TABLE XI-26. Side-Chain Nitrile Synthesis: Miscellaneous Methods (Continued)

Starting material	Conditions	Product	Yield	Properties	Ref.
	KCN, KI, 60% EtOH, 45–50°, 9 hr				296
2-Py$(CH_2)_2CH(OH)SO_3H$	aq. KCN	2-Py$(CH_2)_2CH(OH)CN$	63%	m.p. 81–82°	219
2-Py$(CH_2)_4CH(OH)SO_3H$	aq. KCN	2-Py$(CH_2)_4CH(OH)CN$	78.5%	m.p. 62°	219
	KCN, MeOH, 60–65°, 2 hr				18
2-PyC(Cl)=NOH or as a HCl salt	KCN, MeOH, 60°, 1 hr	2-PyC(=NOH)CN		m.p. 218–221°	320
3-Py$CH_2Cl \cdot HCl$	NaCN, 95% EtOH, H_2O, reflux 1 hr *or* NaCN, DMSO	3-PyCH_2CN	76.5–82.5%	b.p. 126°/7 mm; n_D^{20} 1.5279 b.p. 143–145°/15 mm; methiodide, m.p. 120–121°	268 319
	KCN, acetone, H_2O, reflux 16–20 hr *or* NaCN, DMSO, 140°, 15 min		86% 91%	m.p. 90–91° m.p. 89–90°; nmr	195 125

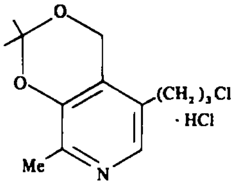
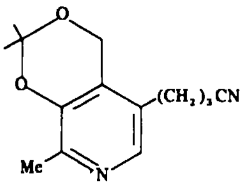
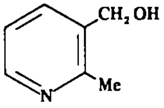
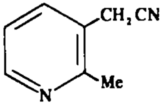
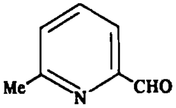
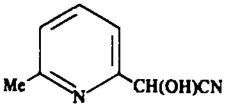
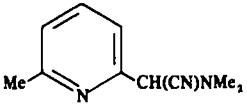
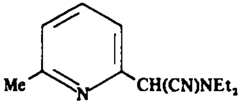
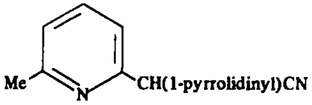
	NaCN, DMSO, 140°				125
	SOCl$_2$, reflux 2.5 hr; KI, KCN, EtOH, reflux 5 hr		119 g → 89 g	b.p. 136–137°; n_D^{25} 1.5255; picrate, m.p. 149–149.5°	174
4-PyCH$_2$Cl·HCl	KCN, MeOH, H$_2$O, reflux 2 hr	4-PyCH$_2$CN	45 g → 36 g	b.p. 92°/0.5 mm; m.p. 36°; hydrochloride, m.p. 270° (decomp.)	165
	or				
	KCN, KI, 60% EtOH, 45–50°, 9 hr			m.p. 43°	296
	or				
	NaCN, DMSO			b.p. 145°/18 mm; methiodide, m.p. 156–158°	319
4-PyC(Cl)=NOH·HCl	KCN, 60°, 1 hr, MeOH	4-PyC(=NOH)CN		m.p. 275–278° (decomp.)	320
		Strecker syntheses			
2-PyCHO	KCN, dil. HCl	2-PyCH(OH)CN			321 217
	KCN, Me$_2$NH, H$_2$O, overnight	2-PyCH(CN)NMe$_2$		b.p. 107°/0.8 mm	52
	KCN, Et$_2$NH, H$_2$O, overnight	2-PyCH(CN)NEt$_2$		b.p. 140–145°/0.4 mm	52
	KCN, pyrrolidine, H$_2$O, overnight	2-PyCH(1-pyrrolidinyl)CN		b.p. 145°/0.8 mm	52

TABLE XI-26. Side-Chain Nitrile Synthesis: Miscellaneous Methods (Continued)

Starting material	Conditions	Product	Yield	Properties	Ref.
	KCN, piperidine, H_2O, overnight	2-PyCH(piperidino)CN		b.p. 150–152°/0.5 mm; m.p. 66–67°	52
	KCN, morpholine, H_2O, overnight	2-PyCH(morpholino)CN		m.p. 90–92°	52
	KCN, $COCl_2$, H_2O, PhMe, 5°, 1 hr	$[2\text{-PyCH(CN)CO}]_2CO$	60%		322
	KCN, dil. HCl			m.p. 134°	321
	KCN, Me_2NH, H_2O, overnight			b.p. 112–113°/0.6 mm	52
	KCN, Et_2NH, H_2O, overnight			b.p. 120–125°/0.7 mm	52
	KCN, pyrrolidine, H_2O, overnight			b.p. 136–138°/0.07 mm	52

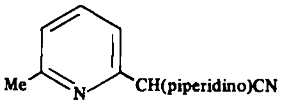
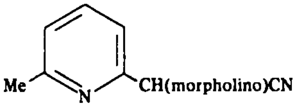
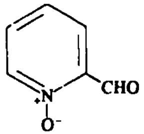
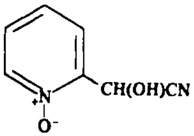
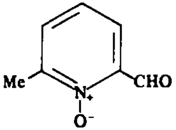
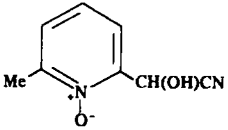
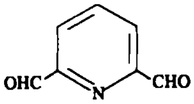
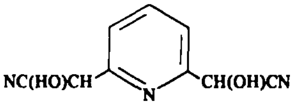
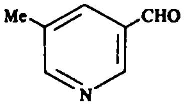
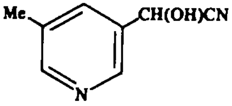
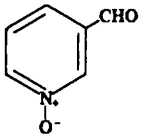
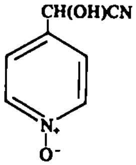
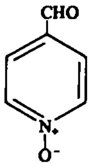
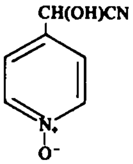
	KCN, piperidine, H_2O, overnight			b.p. 160°/1.0 mm	52
	KCN, morpholine, H_2O, overnight			b.p. 164–165°/0.25 mm	52
	KCN, R. T., 1 hr		61%	m.p. 125°	323
	KCN, R.T., 1 hr		49%	m.p. 125°	323
	KCN, dil. HCl			m.p. 105° (decomp.)	321
2-PyCOMe	KCN, dil. HCl	2-PyCMe(OH)CN		m.p. 50–51°	321
		Strecker syntheses			
3-PyCHO	same as above	3-PyCH(OH)CN			321
	KCN, NH_4Cl	3-PyCH(NH_2)CN			27

TABLE XI-26. Side-Chain Nitrile Synthesis: Miscellaneous Methods (Continued)

Starting material	Conditions	Product	Yield	Properties	Ref.
	PhCOCl, C_6H_6, -5°; aq. KCN, 4 hr	3-PyC(OH)(CN)COPh	31%	m.p. 95–96°	324
	2*N* HCl, -4 to -5° 20% aq. KCN			m.p. 99.5°	325
	KCN, R.T., 1 hr		36%	m.p. 207°	323
4-PyCHO	KCN, NH_4Cl	4-PyCH(NH_2)CN			27
	$MeNH_2$, $NaHSO_3$, EtOH; NaCN, H_2O, 15 hr	4-PyCH(NHMe)CN·2HCl		m.p. 165–166°	63
	KCN, R.T., 1 hr		98%	m.p. 118°	323

Others

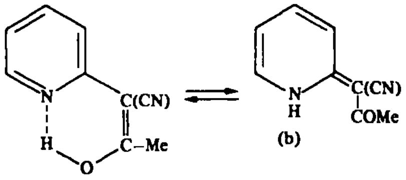
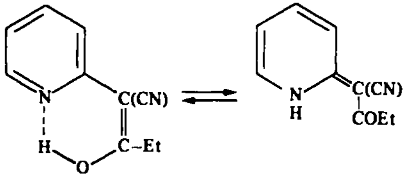
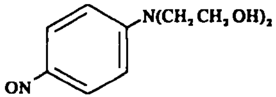
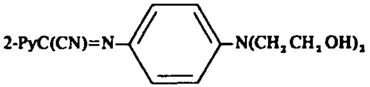
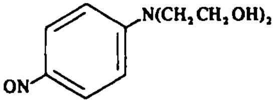
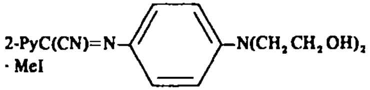
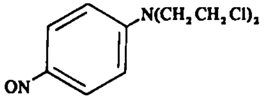
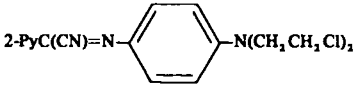
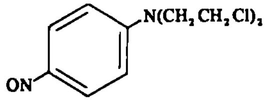
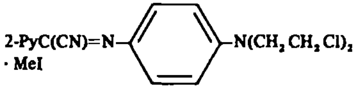
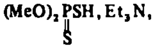
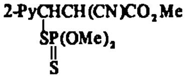
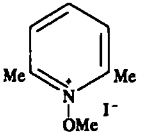
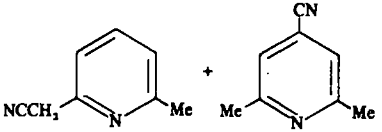
2-PyCH$_2$CN + Ac$_2$O	10 days *or* HOAc, reflux 6 hr	 (a) (b)		(a) m.p. 145°, (b) m.p. 171–172°; ir; uv; nmr	163
2-PyCH$_2$CN + (EtCO)$_2$O	same as above			m.p. 108°	163
2-PyCH$_2$CN + diketene	solvent, reflux 4 hr	2-PyCH(CN)COCH$_2$COMe		m.p. 127–172.5°	326
2-PyCH$_2$CN + 	40% KOH, EtOH		80%	m.p. 125–128°	319
2-PyCH$_2$CN MeI + 	piperidine, MeOH		57%	m.p. 170°	319

TABLE XI-26. Side-Chain Nitrile Synthesis: Miscellaneous Methods (Continued)

Starting material	Conditions	Product	Yield	Properties	Ref.
		Others			
2-PyCH$_2$CN + 	40% KOH, EtOH		72%	m.p. 96–97°	319
2-PyCH$_2$CN + · MeI 	piperidine, MeOH		67%	m.p. 154–156° (decomp.)	319
2-PyCH$_2$CH(CN)CO$_2$Me	 $(MeO)_2\underset{\underset{S}{\|}}{P}SH, Et_3N,$ steam bath, 1 hr	 $2\text{-Py}\underset{\underset{\underset{S}{\|}}{SP(OMe)_2}}{C}HCH(CN)CO_2Me$			65
2-PyC(CN)=C(OH)Me	EtI, aq. NaOH, Ag$^{\oplus}$	2-PyC(CN)=C(OEt)Me		m.p. 81–82°; ir; uv; nmr	163
2-PyCO$_2$Et	NaOH, PhMe; MeCN; reflux 4 hr; R.T. overnight	2-PyCOCH$_2$CN	18%	m.p. 93–94°	360
2-PyCO$_2$Et + PhCH$_2$CN	NaOEt, reflux	2-PyCOCHPhCN	94%	m.p. 122–123°	275
	KCN, R.T., 1 hr	 (33%) (13%)		b.p. 125–133°/22 mm; picrate, m.p. 176–179°	327

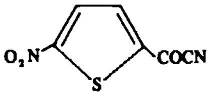
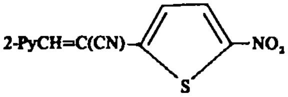
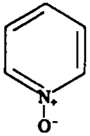
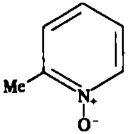
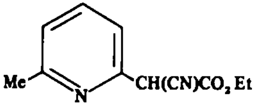
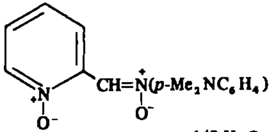
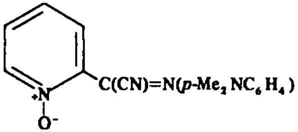
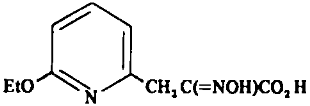
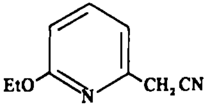
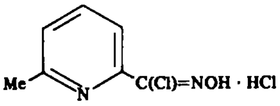
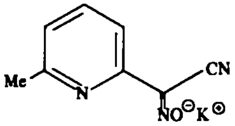
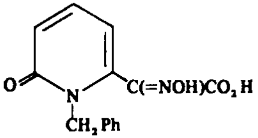
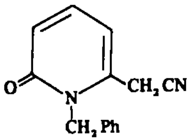
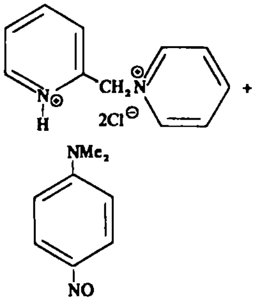
2-PyMe + 	Ac_2O, 120–130°, 1.5 hr			m.p. 240–241°	60
 + $NCCH_2CO_2Et$	Ac_2O	2-PyCH(CN)CO_2Et	28%	m.p. 107–108°	201
 + $NCCH_2CO_2Et$	Ac_2O		17%	m.p. 154–155°	201
 · 1/2 H_2O	KCN, EtOH			m.p. 183°	328
2-PyCH=CHC(=NOH)CO_2H	Cu powder, 155°, long time	2-PyCH=CHCN + 2-PyCH=CHCH=NOH	46% 17%	b.p. 160°/9.0 mm; m.p. 83.5°	213
	heat		80.6%	b.p. 95°/0.05 mm; m.p. 54°	139

TABLE XI-26. Side-Chain Nitrile Synthesis: Miscellaneous Methods (Continued)

Starting material	Conditions	Product	Yield	Properties	Ref.
		Others			
2-PyC(Cl)=NOH · HCl	KCN, 60°, 1 hr	 2-PyCCN with $\|$ $NO^{\ominus}K^{\oplus}$	11%	m.p. 218–221°	329
	KCN, 60°, 1 hr		47%	m.p. 209–210°	329
	heat		88.5%	m.p. 92°	139
	NaCN, EtOH, 0°, 3 hr	2-PyC(CN)=N(p-$Me_2NC_6H_4$)	68%	m.p. 116–118°	295

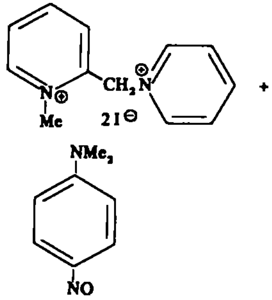
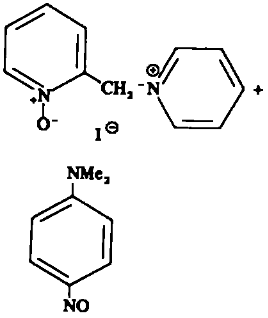
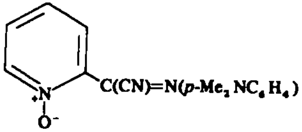
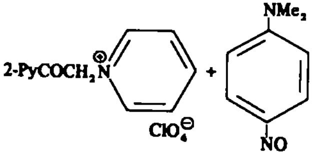
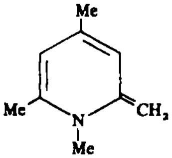
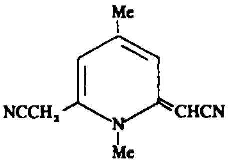
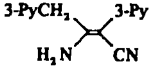
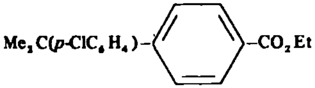
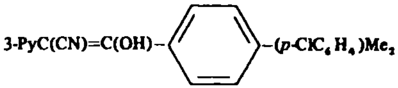
	NaCN	$2\text{-PyC(CN)=N}(p\text{-Me}_2\text{NC}_6\text{H}_4)$ · MeI	81%	m.p. 189–191°	295
	KCN, 95% EtOH, reflux 2 hr		64%	m.p. 183°	328
	NaCN	$2\text{-PyCOC(CN)=N}(p\text{-Me}_2\text{NC}_6\text{H}_4)$	97%	m.p. 160–161°	295

TABLE XI-26. Side-Chain Nitrile Synthesis: Miscellaneous Methods (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
		Others			
	ClCN, C_6H_6, 65°, 5 hr			m.p. 196–197°	330
3-PyCH$_2$CN	Et_2CO_3, NaOEt, EtOH, reflux 4 hr	3-PyCH(CO_2Et)CN	80%	m.p. 103–104°	168
3-PyCH$_2$CN + MeCO$_2$Et	NaOEt	3-PyCH(CN)COMe			331
3-PyCH$_2$CN + PhCO$_2$Et	NaOMe, EtOH, reflux 2.5 hr	3-PyC(CN)=CPhOH + 		m.p. 245–247° m.p. 117–119.5°	42
3-PyCH$_2$CN + p-ClC$_6$H$_4$CO$_2$Et	same as above	3-PyC(CN)=C(p-ClC$_6$H$_4$)OH		m.p. 248–250°	42
3-PyCH$_2$CN + p-Me$_2$NC$_6$H$_4$CO$_2$Et	same as above	3-PyC(CN)=C(p-Me$_2$NC$_6$H$_4$)OH		m.p. 165–166°	332
3-PyCH$_2$CN + 	same as above			m.p. 131–135°	332
3-PyCH$_2$CN + o-MeOC$_6$H$_4$CO$_2$Et	same as above	3-PyC(CN)=C(o-MeOC$_6$H$_4$)OH		m.p. 220–221°	332

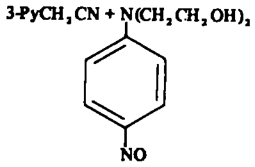
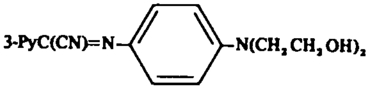
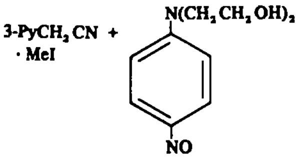
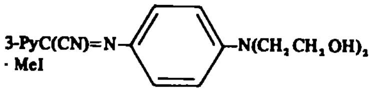
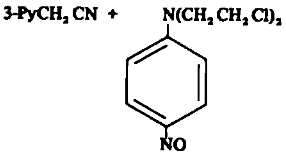
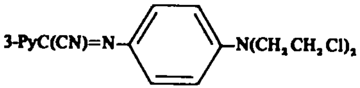
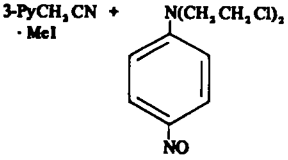
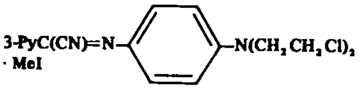
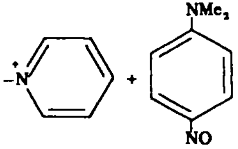
	40% KOH, EtOH		80%	m.p. 131°	319
	piperidine, MeOH		80%	m.p. 225° (decomp.)	319
	40% KOH, EtOH		72%	m.p. 120°	319
	piperidine, MeOH		98%	m.p. 203–204° (decomp.)	319

TABLE XI-26. Side-Chain Nitrile Synthesis: Miscellaneous Methods (Continued)

Starting material	Conditions	Product	Yield	Properties	Ref.
		Others			
3-PyCOCH$_2$ – 	NaCN	3-PyCOC(CN)=N(p-Me$_2$NC$_6$H$_4$)	93%	m.p. 156–157°	295
3-PyCO$_2$Et + MeCN	NaOEt *or* boiled 9 hr; alc. HCl	3-PyCOCH$_2$CN		m.p. 180–183° m.p. 182–184°	269 103
3-PyCO$_2$Et + PhCH$_2$CN	Na, EtOH, reflux	3-PyCOCHPhCN		m.p. 137–141°	225
3-PyCO$_2$Et + p-FC$_6$H$_4$CH$_2$CN	NaOMe, EtOH, reflux 2.5 hr	3-PyC(OH)=C(p-FC$_6$H$_4$)CN		m.p. 220–223°	42
3-PyCO$_2$Et + m-ClC$_6$H$_4$CH$_2$CN	same as above	3-PyC(OH)=C(m-ClC$_6$H$_4$)CN		m.p. 188–190°	42
3-PyCO$_2$Et + p-ClC$_6$H$_4$CH$_2$CN	NaOMe, EtOH, reflux 2.5 hr	3-PyC(OH)=C(p-ClC$_6$H$_4$)CN		m.p. 217–219°	42
3-PyCO$_2$Et + p-CH$_3$C$_6$H$_4$CH$_2$CN	NaOMe, EtOH, reflux 2.5 hr	3-PyC(OH)=C(p-CH$_3$C$_6$H$_4$)CN		m.p. 189–191°	42
3-PyCO$_2$Et + p-MeOC$_6$H$_4$CH$_2$CN	Na$^{\oplus}\overset{\ominus}{C}H_2$SOMe	3-PyCOCH(p-MeOC$_6$H$_4$)CN	72%	m.p. 155–156°	16
3-PyCO$_2$Et + 3-PyCH$_2$CN	NaOMe, EtOH, reflux 2.5 hr	3PyC(OH)=C(3-Py)CN		m.p. 251–252° (decomp.); uv	333
3-PyCH=CHC(=NOH)CO$_2$H	155°	3-PyCH=CHCN	79%	b.p. 161–165°/11–12 mm	213
3-PyCH=CHC(=NOH)CO$_2$H	Cu powder, 155°, long time	3-PyCH=CHCN + 3-PyCH=CHCH=NOH	32% 39%		213

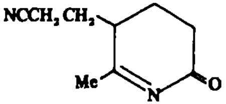
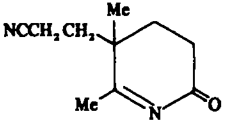
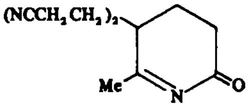
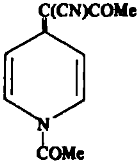
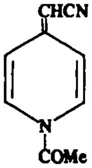
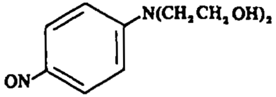
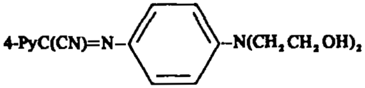
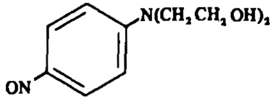
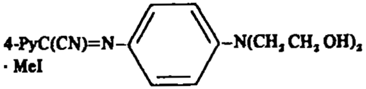
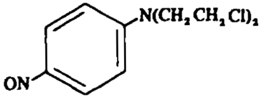
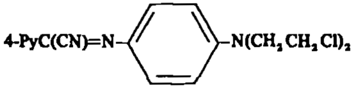
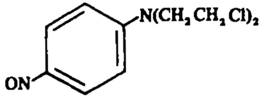
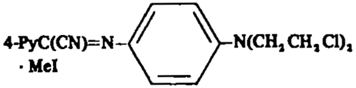
$MeCOCH(CH_2CH_2CN)_2$	Na, EtOH, reflux 6 hr		53%	m.p. 166°	334
$MeCOCMe(CH_2CH_2CN)_2$	Na, EtOH, reflux 6 hr		79.5%	m.p. 157–158°	334
$MeCOC(CH_2CH_2CN)_3$	Na, EtOH, reflux 6 hr		67%	m.p. 222–223°	334
$4\text{-}PyCN + TsCH_2CN$	NaOMe; H_2SO_4	$4\text{-}PyC(NH_2)=C(CN)Ts$	57%	m.p. 246–249°	335
$4\text{-}PyCH_2CN$	Ac_2O, heat		62%	m.p. 216–217°; ir; nmr	163
$4\text{-}PyCH_2CN$	Ac_2O, R.T., 10 min		87%	m.p. 149–150°; ir; uv; nmr	163
$4\text{-}PyCH_2CN$	Et_2CO_3, NaOEt, EtOH, reflux 4 hr	$4\text{-}PyCH(CN)CO_2Et$	64%	m.p. 210–212°	168

TABLE XI-26. Side-Chain Nitrile Synthesis: Miscellaneous Methods (Continued)

Starting materials	Conditions	Product	Yield	Properties	Ref.
		Others			
4-PyCH$_2$CN + 	40% KOH, EtOH		80%	m.p. 167–168°	319
4-PyCH$_2$CN + MeI 	piperidine, MeOH		78%	methiodide, m.p. 218–219° (decomp.)	319
4-PyCH$_2$CN + 	40% KOH, EtOH		85%	m.p. 149–150°	319
4-PyCH$_2$CN · MeI + 	piperidine, MeOH		50%	m.p. 195–196° (decomp.)	319

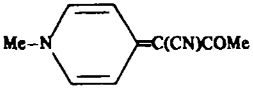
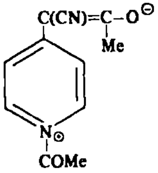
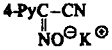
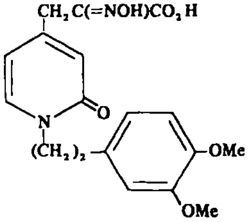
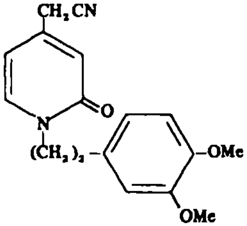
4-PyC(CN)=CMeOH	MeI, Ag$^{\oplus}$			m.p. 216–217°; ir; uv; nmr	163
	recrystallized from BuOH	4-PyC(CN)=C(OH)Me		m.p. 268–269°; pK_a = 8.40, 1.76; ir; uv; nmr	163
4-PyCO$_2$Et + MeCN	PhMe	4-PyCOCH$_2$CN		m.p. 95–96°	171
4-PyCO$_2$Et + 2-FurylCH$_2$CN	NaOMe, EtOH, reflux 2.5 hr	4-PyC(OH)=C(2-furyl)CN		m.p. 255–258°	333
4-PyC(Cl)=NOH·HCl	KCN, 60°, 1 hr	 $\mathrm{4\text{-}Py}\underset{\mathrm{NO^{\ominus}K^{\oplus}}}{\underset{\Vert}{\mathrm{C}}}\mathrm{-CN}$	54.4%	m.p. 276–278° (decomp.)	329
	heat or Ac$_2$O, steam-bath, 10 min		80%	m.p. 118–121°	3

TABLE XI-26. Side-Chain Nitrile Synthesis: Miscellaneous Methods (Continued)

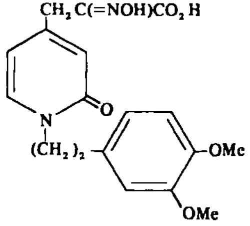
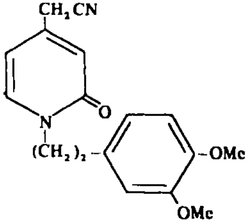
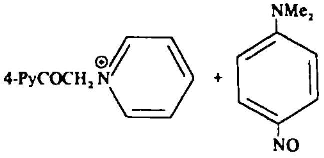
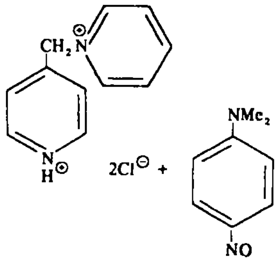
Starting materials	Conditions	Product	Yield	Properties	Ref.
		Others			
	Ac_2O			m.p. 118–120°	88
	NaCN	4-PyCOC(CN)=N(p-$Me_2NC_6H_4$)	93%	m.p. 188–189°	295
	NaCN, EtOH, 0°, 3 hr	4-PyC(CN)=N(p-$Me_2NC_6H_4$)	64%	m.p. 145–146°	295

TABLE XI-27 Solvolysis of Side-Chain Nitriles

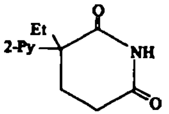
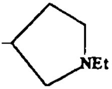
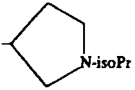
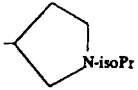
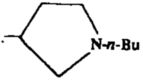
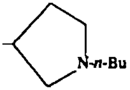
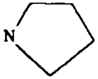
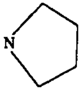
Nitrile	Conditions	Product	Yield	Properties	Ref.
2-$PyCH_2CN$	Amberlite IRA-400 (base form), reflux 2 hr	2-$PyCH_2CONH_2$		m.p. 119-120°	163
2-PyCHPhCN	96% H_2SO_4, 24 hr; MeOH, reflux 45 min	2-$PyCHPhCO_2Me$	95.2%	m.p. 74-75°	336
	96% H_2SO_4, 24 hr; EtOH, reflux 45 min	2-$PyCHPhCO_2Et$	90.6%	b.p. 158°/0.5 mm	336
	H_2S, Et_3N, pyridine, R. T., 17 hr *or* P_2S_5, xylene, heat, 4.5 hr	2-$PyCHPhCSNH_2$		m.p. 137.5-138°	166
2-$PyCH(p\text{-}ClC_6H_4)CN$	H_2S, Et_3N, pyridine, R.T., 6 hr	2-$PyCH(p\text{-}ClC_6H_4)CSNH_2$		m.p. 160-160.5°	166
2-$PyCH(CH_2Ph)CN$	98% H_2SO_4, 2 days	2-$PyCH(CH_2Ph)CONH_2$	0.5 g → 0.2 g	m.p. 123-125°	305
	MeOH, HCl, reflux	2-$PyCH(CH_2Ph)CO_2Me$	3 g → 2.7 g		305
2-$PyC(CH_2Ph)_2CN$	98% H_2SO_4, 2 days	2-$PyC(CH_2Ph)_2CONH_2$			305
2-$PyCEt(CN)CH_2CH_2CN$	HOAc, H_2SO_4, reflux			m.p. 84-86°; picrate, m.p. 152-154°	178
2-$PyCPh(CN)CH_2CH_2CN$	75% H_2SO_4, 130°, 15 hr; alc. NH_3; HOAc, 0.5 hr steam-bath	2-$PyCHPhCH_2CH_2CO_2H$	124 g ↓ 105 g	m.p. 113-114°	337
2-$PyC(p\text{-}ClC_6H_4)(CN)CH_2CH_2CN$	same as above	2-$PyCH(p\text{-}ClC_6H_4)CH_2CH_2CO_2H$		m.p. 100-101°	337

TABLE XI-27. Solvolysis of Side-Chain Nitriles (Continued)

Nitrile	Conditions	Product	Yield	Properties	Ref.
2-PyCPh(CN)- 	70 % H_2SO_4, 147°, 48 hr	2-PyCPh($CONH_2$)- 		m.p. 150-153°	304
2-PyCPh(CN)- 	same as above	2-PyCPh($CONH_2$)- 		m.p. 160-161°	304
2-PyCPh(CN)- 	same as above	2-PyCPh($CONH_2$)- 		m.p. 127.5-133°	304
2-PyCPh(CN)- 	same as above	2-PyCPh($CONH_2$)- 		m.p. 108-111°	304
2-PyCPh(CN)$CH_2CH_2NMe_2$	conc. H_2SO_4, steam-bath 4 hr	2-PyCPh($CONH_2$)$CH_2CH_2NMe_2$		Sulfuric acid salt, m.p. 206-207°	44
2-PyCPh(CN)$CH_2CH_2NEt_2$	same as above	2-PyCPh($CONH_2$)$CH_2CH_2NEt_2$		m.p. 63.5-64.5°	44
2-PyCPh(CN)$CH_2CH_2NPr_2$	same as above	2-PyCPh($CONH_2$)$CH_2CH_2NPr_2$		m.p. 63-64°	44, 45
2-PyCPh(CN)$CH_2CH_2N(isoPr)_2$	same as above	2-PyCPh($CONH_2$)$CH_2CH_2N(isoPr)_2$		m.p. 94.5-95°	44, 45
2-PyCPh(CN)CH_2CH_2N 	same as above	2-PyCPh($CONH_2$)CH_2CH_2N 		m.p. 109.5-110.5°	44

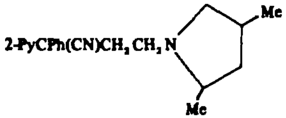
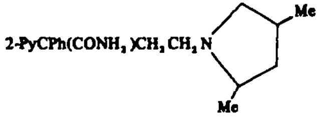
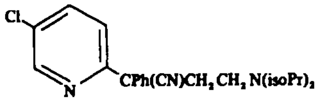
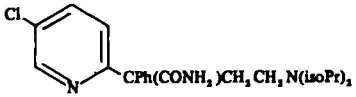
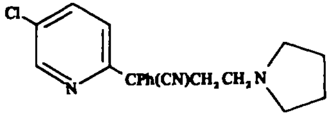
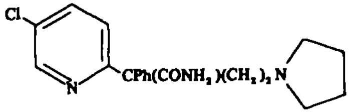
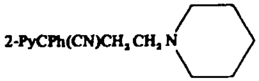
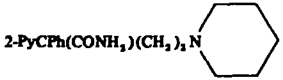
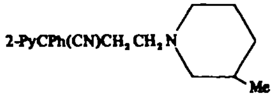
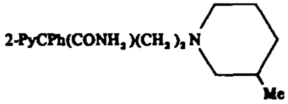
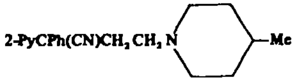
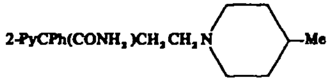
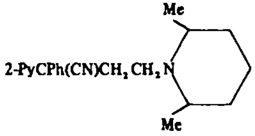
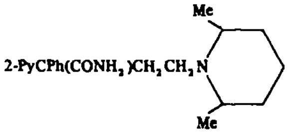
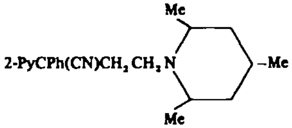
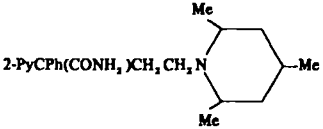
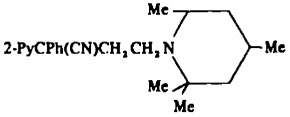
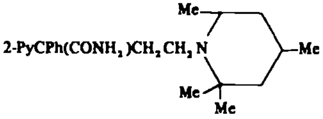
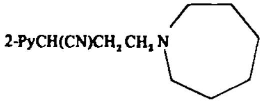
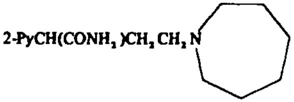
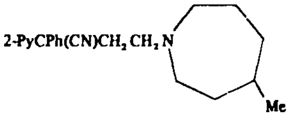
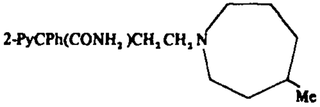
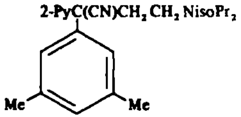
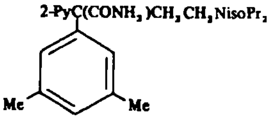
	same as above			44
	same as above			44 45
	same as above			44
	same as above		m.p. 114–115°	44
	same as above		m.p. 100–101°	44
	same as above		m.p. 144–145°	44
	same as above		m.p. 152–153°	44

TABLE XI-27. Solvolysis of Side-Chain Nitriles (Continued)

Nitrile	Conditions	Product	Yield	Properties	Ref.
	same as above			m.p. 117–119°	44
	same as above			m.p. 100–103°	44
	same as above			m.p. 123°	44
	same as above				44
2-PyC(m-MeC$_6$H$_4$)(CN)CH$_2$CH$_2$NisoPr$_2$	KOH, EtOH, H$_2$O, reflux 2 hr, *or* H$_2$SO$_4$, steam-bath 4 hr	2-PyC(m-MeC$_6$H$_4$)(CONH$_2$)CH$_2$CH$_2$NisoPr$_2$		m.p. 113–114°	44, 45
	H$_2$SO$_4$, 4 hr, steam-bath *or* KOH, EtOH, H$_2$O, reflux 2 hr				44, 45

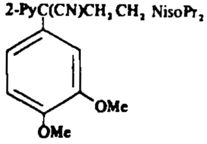
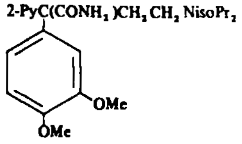
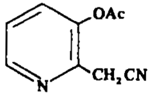
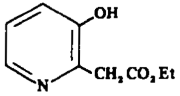
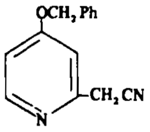
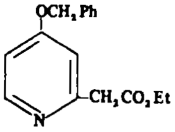
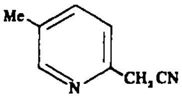
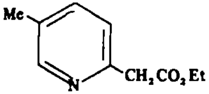
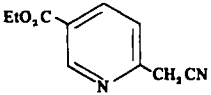
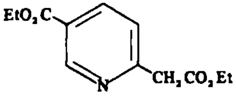
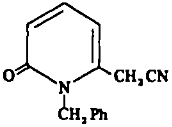
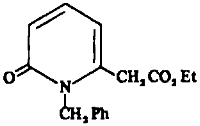
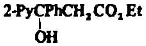
2-PyC(o-FC$_6$H$_4$)(CN)CH$_2$CH$_2$NisoPr$_2$	H$_2$SO$_4$, 4 hr, steam-bath	2-PyC(o-FC$_6$H$_4$)(CONH$_2$)CH$_2$CH$_2$NisoPr$_2$		m.p. 77–78°	45
2-PyC(p-FC$_6$H$_4$)(CN)CH$_2$CH$_2$NisoPr$_2$	same as above	2-PyC(p-FC$_6$H$_4$)(CONH$_2$)CH$_2$CH$_2$NisoPr$_2$		m.p. 77–80°, 77–78°	44, 45
2-PyC(p-ClC$_6$H$_4$)(CN)CH$_2$CH$_2$NisoPr$_2$	same as above	2-PyC(p-ClC$_6$H$_4$)(CONH$_2$)CH$_2$CH$_2$NisoPr$_2$			45
2-PyC(p-IC$_6$H$_4$)(CN)CH$_2$CH$_2$NisoPr$_2$	same as above	2-PyC(p-IC$_6$H$_4$)(CONH$_2$)CH$_2$CH$_2$NisoPr$_2$			44
2-PyC(p-MeOC$_6$H$_4$)(CN)CH$_2$CH$_2$NisoPr$_2$	H$_2$SO$_4$, steam-bath 4 hr *or* KOH, EtOH, H$_2$O, reflux 2 hr	2-PyC(p-MeOC$_6$H$_4$)(CONH$_2$)CH$_2$CH$_2$NisoPr$_2$			45
	same as above			m.p. 102–103°	44
2-PyC(CH$_2$Ph)(CN)CH$_2$CH$_2$NMe$_2$	H$_2$SO$_4$, heat, 3 hr	2-PyC(CH$_2$Ph)(CONH$_2$)CH$_2$CH$_2$NMe$_2$		m.p. 46–48°; methiodide, m.p. 170°	305
2-PyC(α-naphthyl)(CN)CH$_2$CH$_2$NisoPr$_2$	H$_2$SO$_4$, steam-bath, 4 hr	2-PyC(α-naphthyl)(CONH$_2$)CH$_2$CH$_2$NisoPr$_2$		m.p. 152–155°	45
(2-Py)$_2$C(CN)CH$_2$CH$_2$NMe$_2$	same as above	(2-Py)$_2$C(CONH$_2$)CH$_2$CH$_2$NMe$_2$		m.p. 125–126°	44
2-PyCPh(CN)(CH$_2$)$_3$NEt$_2$	same as above	2-PyCPh(CONH$_2$)(CH$_2$)$_3$NEt$_2$			44
	EtOH, HCl			b.p. 135°/0.001 mm; acetate, b.p. 110°/0.01 mm; ir	18
	EtOH, HCl, reflux 5 hr		89%	picrate, m.p. 123°; ir	282

TABLE XI-27. Solvolysis of Side-Chain Nitriles (Continued)

Nitrile	Conditions	Product	Yield	Properties	Ref.
	EtOH, HCl, 50°, 2 hr; overnight; 80°, 8 hr *or* conc. H_2SO_4, EtOH, reflux 8 hr		5 g → 1.5 g	b.p. 110–113°/4.5 mm	192
	EtOH, HCl, R.T. overnight		1.3 g → 1.4 g	b.p. 106–108°/0.1 mm; picrate, m.p. 106–107°	17
	95% EtOH, HCl, reflux 2 hr; R.T., 12 hr		98.5%	m.p. 79°	139
2-Py$(CH_2)_2CN$	EtOH, HCl, Et_2O, 10 hr; 30–40°, overnight	2-Py$(CH_2)_2CO_2Et$	89%	b.p. 76–79°/0.3 mm	148
2-PyCPh(OH)CH_2CN	EtOH, H_2SO_4, reflux 1.5 hr	 $2\text{-Py}\underset{\text{OH}}{\text{C}}\text{PhCH}_2\text{CO}_2\text{Et}$		m.p. 62°	223
2-PyCPh(OH)CHMeCN	EtOH, H_2SO_4, reflux 1.5 hr	 $2\text{-Py}\underset{\text{OH}}{\text{C}}\text{PhCHMeCO}_2\text{Et}$		m.p. 63°	223
2-PyCH_2CH(α-naphthyl)CN	KOH, $PhCH_2OH$, reflux 15 hr	2-PyCH_2CH(α-naphthyl)CO_2K	76%	m.p. 137°; free acid, m.p. 177–178° (decomp.)	338
2-PyCOCHPhCN	90% H_2SO_4, 50°, 3 hr	2-PyCOCHPh$CONH_2$	84%	m.p. 184–186°	116
2-PyCH=C(*p*-ClC_6H_4)CN	H_2SO_4, 0.5 hr, steam-bath	2-PyCH=(*p*-ClC_6H_4)CO_2H	90%-	m.p. 147–148° (decomp.)	137

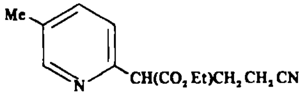
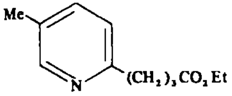
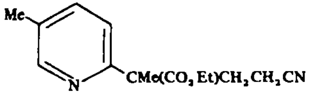
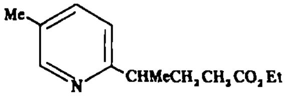
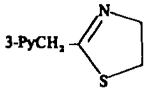
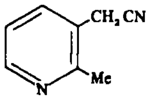
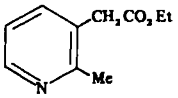
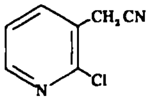
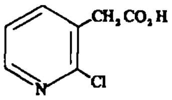
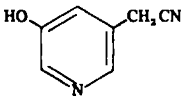
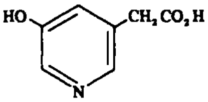
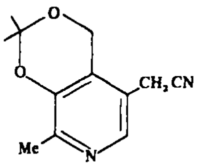
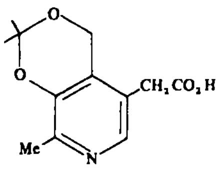
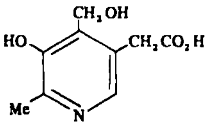
2-Py$(CH_2)_3$CN	MeOH, KOH, 3% H_2O_2, 50°, 1 hr	2-Py$(CH_2)_3$CONH$_2$	1.5 g → 1.3 g	m.p. 102°	167
	pyridine, Et_3N; H_2S, several hr	2-Py$(CH_2)_3$CSNH$_2$	3 g → 2 g	m.p. 86°	167
2-Py$(CH_2)_2$CHPhCN	KOH, MeOH, 3% H_2O_2, 50°, 1 hr	2-Py$(CH_2)_2$CHPhCONH$_2$	4.6 g → 4.3 g	m.p. 129°	167
	pyridine, Et_3N, H_2S, several hr	2-Py$(CH_2)_2$CHPhCSNH$_2$	4.6 g → 2.6 g	m.p. 159°	167
	18% HCl, reflux 3 hr; NaOH	2-Py$(CH_2)_2$CHPhCO$_2$Na	4.6 g → 5.2 g	m.p. 161-162°; sodium salt, m.p. 207°	167
	dry HCl, MeOH	2-Py$(CH_2)_2$CHPhCO$_2$Me	10 g → 7.3 g	b.p. 178°/2 mm	167
2-Py$(CH_2)_2$CH(OH)CN		2-Py$(CH_2)_2$CH(OH)CO$_2$H	41%	m.p. 93-94°; hydrochloride, m.p. 162°	219
	16% aq. HCl, reflux 10 hr; 150°, 15 min, -CO$_2$; HCl, EtOH, 3 hr			b.p. 102°/0.2 mm	283
2-PyCMe(CO$_2$Et)CH$_2$CH$_2$CN	same as above	2-PyCHMeCH$_2$CH$_2$CO$_2$Et	4.6 g → 2.2 g	b.p. 110°/1.0 mm	283
	same as above			b.p. 105°/0.3 mm	283
2-Py$(CH_2)_3$CH(OH)CN		2-Py$(CH_2)_3$CH(OH)CO$_2$H	38%	m.p. 143°	219
2-Py$(CH_2)_2$CPh(COMe)CH$_2$CH$_2$CN	46% H_2SO_4, reflux 3 hr	2-Py$(CH_2)_2$CPh(COMe)CH$_2$CH$_2$CO$_2$H	88%	m.p. 171.5-173°	36
3-PyCH$_2$CN	H_2S	3-PyCH$_2$CSNH$_2$		m.p. 135-136.5°	168

TABLE XI-27. Solvolysis of Side-Chain Nitriles (Continued)

Nitrile	Conditions	Product	Yield	Properties	Ref.
	$HSCH_2CH_2NH_2$		65%		168
	HCl, EtOH, cold for 1.5 hr *or* reflux 5 hr		45 g → 43 g	b.p. 124–125°/7 mm, n_D^{25} 1.4982; picrate, m.p. 154–155.5°	174
	conc. HCl, reflux 5.5 hr		76%	m.p. 203–204°	268
	conc. HCl, reflux 5 hr		78%	m.p. 197°	268
	10% alc. KOH, reflux 3 hr *or* NaOH, 70% EtOH, reflux 3 hr		0.7 g → 0.4 g 83%	m.p. 194° m.p. 186–187°	125 195
	conc. HCl, 40°, 45 min		43%	m.p. 217–218° (decomp.); ir; uv	195

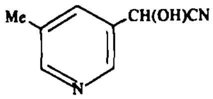
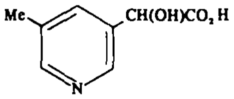
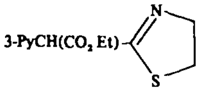
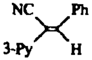
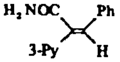
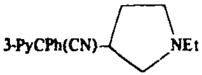
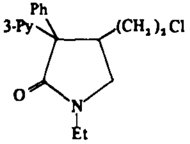
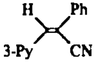
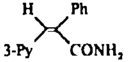
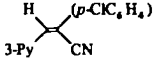
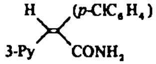
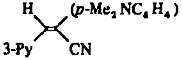
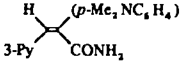
	conc. HCl, dry HCl, R.T., overnight; NaOAc buffer, Cu(OAc)$_2$, H$_2$S			m.p. 181°; hydrochloride, m.p. 221–222°	325
3-PyCH(NH$_2$)CN	conc. HCl, 80 hr	3-PyCH(NH$_2$)CO$_2$H			27
3-PyCH(CO$_2$Et)CN	HSCH$_2$CH$_2$NH$_2$, N$_2$, EtOH, reflux 3 hr		79%	hydrochloride, m.p. 166–167° (decomp.)	168
3-PyCH(CN)CH$_2$CH$_2$Ph	NaOH, 56°, 3 hr	3-PyCH(CONH$_2$)CH$_2$CH$_2$Ph		m.p. 145–146°	288
3-PyCH(CN)CH$_2$CH$_2$Ph	alc. NaOH, reflux 64 hr	3-PyCH(CO$_2$H)CH$_2$CH$_2$Ph	86%	m.p. 102–112°	286, 288
3-PyCH(CN)CH$_2$CH$_2$(*p*-MeC$_6$H$_4$)	same as above	3-PyCH(CO$_2$H)CH$_2$CH$_2$(*p*-MeC$_6$H$_4$)		m.p. 144–145°	286, 288
3-PyCH(CN)CH$_2$CH$_2$(*m*-ClC$_6$H$_4$)	same as above	3-PyCH(CO$_2$H)CH$_2$CH$_2$(*m*-ClC$_6$H$_4$)	55%	m.p. 147–148°	286, 288
3-PyCH(CN)CH$_2$CH$_2$(*p*-ClC$_6$H$_4$)	same as above	3-PyCH(CO$_2$H)CH$_2$CH$_2$(*p*-ClC$_6$H$_4$)	75%	m.p. 149–150°, 133–135°	286, 288
3-PyCH(CN)CH$_2$CH$_2$(*m*-MeOC$_6$H$_4$)	same as above	3-PyCH(CO$_2$H)CH$_2$CH$_2$(*p*-MeOC$_6$H$_4$)	64%	m.p. 93–94°	286
3-PyCH(CN)CH$_2$CH$_2$(*m*-MeOC$_6$H$_4$)	EtOH, 30% H$_2$O$_2$, 24% NaOH, 50–60°, 3 hr	3-PyCH(CONH$_2$)CH$_2$CH$_2$(*m*-MeOC$_6$H$_4$)	60 g → 40 g	m.p. 156–157°	290
3-PyCH(CN)(CH$_2$)$_3$Ph	alc. NaOH, reflux 64 hr	3-PyCH(CO$_2$H)(CH$_2$)$_3$Ph		m.p. 114–116°	288
	85% H$_2$SO$_4$, steam-bath 2 hr		18%	m.p. 151–152°; uv	98
	70% H$_2$SO$_4$, 130–140°, 48 hr; HCl, SOCl$_2$, CHCl$_3$, 3 hr		29%	m.p. 100–103°	57

TABLE XI-27. Solvolysis of Side-Chain Nitriles (Continued)

Nitrile	Conditions	Product	Yield	Properties	Ref.
3-PyCPh(CN)CH_2CH_2NisoPr$_2$	conc. H_2SO_4, steam-bath 4 hr	3-PyCPh($CONH_2$)CH_2CH_2NisoPr$_2$			44
3-PyCH_2CH(p-$NH_2C_6H_4$)CN	MeOH, dry HCl, 3–4 hr; MeOH, 10–11% NaOH, reflux 3 hr	3-PyCH_2CH(p-$NH_2C_6H_4$)CO_2H	63%	m.p. 181–183°	164
3-PyCH_2CH(α-naphthyl)CN	KOH, PhCH_2OH, reflux 15 hr	3-PyCH_2CH(α-naphthyl)CO_2K	84%	m.p. 222–224° (decomp.); free acid, m.p. 192.5–193.5°	338 302
3-PyCOCHPhCN	90% H_2SO_4, 50°, 3 hr	3-PyCOCHPh$CONH_2$	71%	m.p. 136–137°	116
3-PyCOCH(p-MeOC_6H_4)CN	HCl, EtOH, overnight	3-PyCOCH(p-MeOC_6H_4)CO_2Et	15%	m.p. 70–71°	16
3-PyCH=CHCN	aq. KOH, reflux 4 hr; pH 4 with HCl	3-PyCH=CHCO_2H		m.p. 234.5°;	213
	85% H_2SO_4, steam-bath 2 hr		65%	m.p. 134–137° (PrOH-2-PrOAc), m.p. 129–130° (Me_2CO-pentane); uv	98
	85% H_2SO_4, steam-bath 2 hr		39%	m.p. 155–159°; uv	98
	50% H_2SO_4, steam-bath 2 hr		95%	m.p. 201–203°; uv	98
3-PyC(OH)=C(p-MeC_6H_4)CN	conc. H_2SO_4, R.T., 1 hr	3-PyC(OH)=C(p-MeC_6H_4)$CONH_2$		m.p. 136–138°	42
3-PyC(OH)=C(3-Py)CN	conc. fuming H_2SO_4, 25%, 3 hr	3-PyC(OH)=C(3-Py)$CONH_2$			333
4-PyCH_2CN	Et_3N, EtOH, H_2S, 3 hr	4-PyCH_2CSNH_2		m.p. 168–169° (decomp.)	168

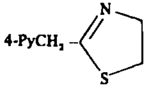
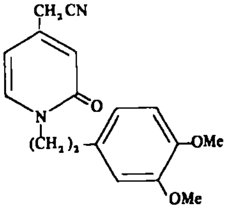
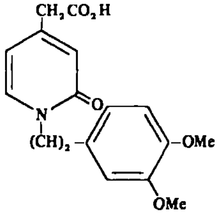
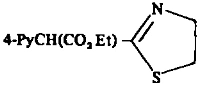
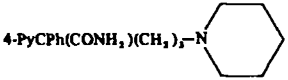
	$HSCH_2CH_2NH_2$		57%		168
	NaOH, EtOH, reflux overnight			m.p. 156.5-157° (decomp.)	3, 88
4-PyCH(NH_2)CN	conc. HCl, R.T., 5 days	4-PyCH(NH_2)CO_2H·HCl	172 g → 132 g		27
4-PyCH(CO_2Et)CN	$HSCH_2CH_2NH_2$, N_2, EtOH, reflux 3 hr		64%	m.p. 100-101°	168
4-PyCH(CN)CH(OH)(o-$O_2NC_6H_4$)	75% H_2SO_4; base	4-PyC($CONH_2$)=CH(o-$O_2NC_6H_4$)	0.7 g → 0.2 g	m.p. 208-209°	99
4-PyCPh(CN)CH_2CH_2NisoPr$_2$	H_2SO_4, steam-bath, 4 hr	4-PyCPh($CONH_2$)CH_2CH_2NisoPr$_2$		m.p. 138.5-139°	44, 45
4-PyCPh(CN)(CH_2)$_3NC_5H_{10}$	conc. H_2SO_4, steam-bath, 4 hr				44
4-PyCH_2CH(p-$H_2NC_6H_4$)CN	HCl, MeOH, 3-4 hr; MeOH, 10-11% NaOH, reflux 3 hr.	4-PyCH_2CH(p-$H_2NC_6H_4$)CO_2H	27%	m.p. 196-198°	164
4-PyCH_2CH(α-naphthyl)CN	KOH, PhCH_2OH, reflux 15 hr	4-PyCH_2CH(α-naphthyl)CO_2K	89%	m.p. 211-212.5°	338
4-PyCOCHPhCN	90% H_2SO_4, 50°, 3 hr	4-PyCOCHPh$CONH_2$	97%	m.p. 161-162°	116
4-PyCH=CHCN	aq. KOH, reflux 4 hr	4-PyCH=CHCO_2H	74%	m.p. 290-291° (decomp.)	213

TABLE XI-27. Solvolysis of Side-Chain Nitriles (Continued)

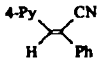
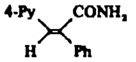
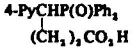
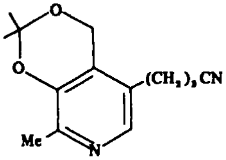
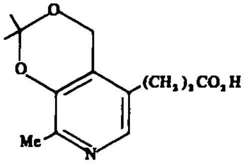
Nitrile	Conditions	Product	Yield	Properties	Ref.
	85% H_2SO_4, steam-bath 2 hr		54%	m.p. 178–180°	98
 4-PyCHP(O)Ph_2 with $(CH_2)_2CN$ on the CH	HCl	 4-PyCHP(O)Ph_2 with $(CH_2)_2CO_2H$ on the CH	57%	m.p. 200°	314
	10% alc. KOH, 3 hr			m.p. 160–161°	125

TABLE XI-28. Reduction of Side-Chain Nitriles

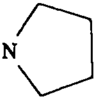
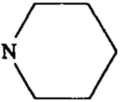
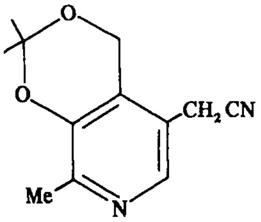
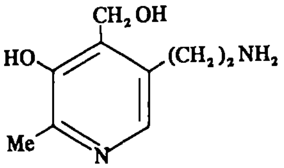
Nitrile	Conditions	Product	Yield	Properties	Ref.
2-Py(CH$_2$)$_2$CN	H$_2$, Ra-Ni, NH$_3$, EtOH, 70–75°	2-Py(CH$_2$)$_3$NH$_2$			285
2-Py(CH$_2$)$_3$CN	H$_2$, Ra-Ni, Et$_2$NH, 2000 atm, 75–100°	2-Py(CH$_2$)$_4$NEt$_2$			236
	H$_2$, Ra-Ni, pyrrolidine, 2000 atm, 75–100°	2-Py(CH$_2$)$_4$ –N 			236
	H$_2$, Ra-Ni, piperidine, 2000 atm, 75–100°	2-Py(CH$_2$)$_4$ –N 			236
2-PyCH(CN)(CH$_2$)$_2$CO$_2$Et	H$_2$, PtO$_2$, EtOH, 2 atm	2-PyCH(CH$_2$NH$_2$)CH$_2$CH$_2$CO$_2$Et		picrate, m.p. 128–129°	178
2-Py(CH$_2$)$_2$CHPhCN	LAH, Et$_2$O	2-Py(CH$_2$)$_2$CHPhCH$_2$NH$_2$	13.8 g → 8 g		167
3-PyCH$_2$CN	Δ^1-*p*-menthene, 10% Pd-C, 200 min	3-PyEt			170
	LAH, Et$_2$O, 0°, 1 hr		45%		195

TABLE XI-28. Reduction of Side-Chain Nitriles (Continued)

Nitrile	Conditions	Product	Yield	Properties	Ref.
3-PyCH=CHCN	Δ^1-*p*-menthene, 10% Pd-C, 210 min	3-*n*-PrPy			170
4-PyCHPhCN	H_2, Ra-Ni, MeOH	4-PyCHPhCH$_2$NH$_2$			339

TABLE XI-29. Reactions of 2-Pyridineacetonitriles with Organometallic Reagents

Starting material	Reagent	Conditions	Product	Yield	Ref.
2-PyC(CH$_2$Ph)(CN)CH$_2$CH$_2$NMe$_2$	EtMgBr	Et$_2$O, reflux 4 hr	2-PyC(CH$_2$Ph)(COEt)CH$_2$CH$_2$NMe$_2$	0.93 g → 0.73 g	305

TABLE XI-30. Carbonyl Reactions of Keto Acids

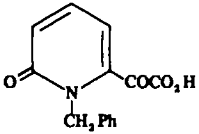
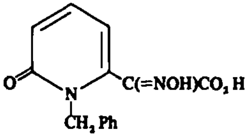
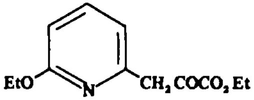
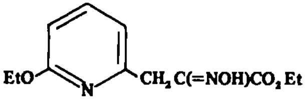
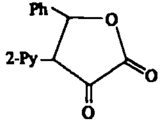
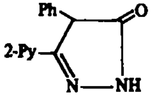
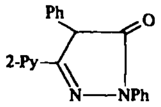
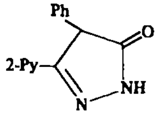
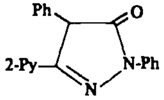
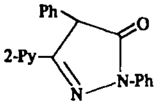
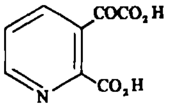
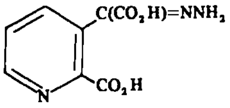
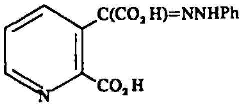
Starting material	Reagent and conditions	Product	Yield	Properties	Ref.
2-PyCOCO$_2$Et	PhOH, 87% H$_2$SO$_4$, 4-5 hr overnight	2-PyCH(p-HOC$_6$H$_4$)$_2$			340
	NH$_2$OH · HCl, NaOH, 36 hr		91.4%	m.p. 191°	139
2-PyCOCHPhCO$_2$Me	PhNHNH$_2$ · HCl, MeOH-H$_2$O, reflux, Py, 1 hr	2-PyC(=NNHPh)CHPhCO$_2$Me	89%	m.p. 142-144°	341
	NH$_2$OH · HCl, Py, EtOH, steam-bath, 3 hr		92.4%	m.p. 73°	139
2-PyCH=CHCOCO$_2$H	NH$_2$OH · HCl, aq. KOAc	2-PyCH=CHC(=NOH)CO$_2$H	90%	m.p. 129°	213
2-PyCH$_2$COCO$_2$Et	PhCHO		0.5 g → 0.3 g	m.p. 225-226°	86
2-PyCOCHPhCO$_2$Me	NH$_2$CONHNH$_2$ · HCl		78.7%	m.p. 228-230°; picrate, m.p.210°	341

TABLE XI-30. Carbonyl Reactions of Keto Acids (Continued)

Starting material	Reagent and conditions	Product	Yield	Properties	Ref.
	$PhNHNH_2$, isoBuOH, reflux 3 hr			m.p. 188–189°	341
2-PyCOCHPhCONH$_2$	$NH_2CSNHNH_2$				341
	$PhNHNH_2$, 100–110°, 2 hr				341
2-PyC(=NNHPh)CHPhCO$_2$Me	PhMe *or* isoBuOH, reflux 4 hr		82%		341
3-PyCOCO$_2$H	$CH_2(CO_2H)_2$, Py, steam-bath, 1 hr	3-PyC(OH)(CO$_2$H)CH$_2$CO$_2$H	66%	m.p. 217–218°	218
	$NH_2NH_2 \cdot H_2SO_4$, NaOAc, H_2O, R.T., overnight		74%	m.p. 302° (decomp.); ir	260
	$NH_2NHPh \cdot HCl$, NaOAc, H_2O, R.T., overnight		5 g → 6.2 g	m.p. 218–220° (decomp.); ir	260

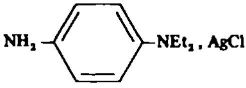
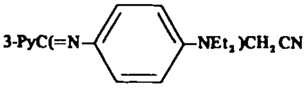
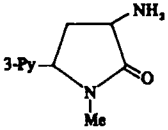
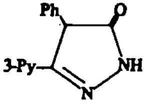
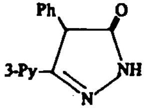
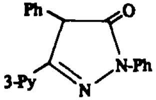
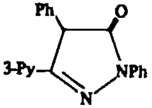
3-$PyCOCH_2CO_2Me$	$NH_2OH \cdot HCl$, MeOH, heat, 2–3 min	3-$PyC(=NOH)CH_2CO_2Me \cdot HCl$		m.p. 125°	26
3-$PyCOCH_2CO_2Et$	$H_2NNHCSNH_2$, boiling alcohol, 5–6 min	3-$PyC(CH_2CO_2Et)=NNHCSNH_2$		m.p. 153°	25
	dry HCl, PCl_5, C_6H_6, 2 hr, 0°; R.T., 2 hr; 80°, 20 min	3-$PyC(Cl)=CHCO_2Et$ + 3-$PyC(Cl)_2CH_2CO_2Et$ + 3-$PyC(Cl_2)Me$ + 3-$PyC(Cl)=CH_2$		b.p. 85°/0.01 mm; n_D^{20} 1.5578	175
	CH_2N_2, Et_2O, 3 days	3-$PyC(OMe)=CHCO_2Et$	11%	b.p. 86°/0.1 mm; n_D^{20} 1.5479; picrate, m.p. 139–140°; ir	175
3-$PyCOCHPhCO_2Me$	$PhNHNH_2$, R.T., 24 hr	3-$PyC(=NNHPh)CHPhCO_2Me$		m.p. 207–209°	341
3-$PyCOCH_2CN$	, AgCl, Na_2CO_3, 1 hr, EtOH-H_2O		0.36 → 0.06 g	m.p. 99–101°	103
3-$PyCO(CH_2)_2CO_2Me$	$NH_2OH \cdot HCl$, Py	3-$PyC(=NOH)CH_2CH_2CO_2Me$		m.p. 70°	22
3-$PyCO(CH_2)_2CO_2Et$	$NH_2OH \cdot HCl$	3-$PyC(=NOH)CH_2CH_2CO_2Et$		m.p. 132–133°	2
3-$PyCOCH_2CONHPh$	$PhNH_2$, $PhNH_2 \cdot HCl$, benzene, reflux	3-$PyC(NHPh)=CHCONHPh$			292
3-$Py^{14}COCH_2CH_2CO_2H$	$MeNH_2$, EtOH, overnight, R.T.; H_2, 5% Pt-$BaSO_4$, 6 hr	(±)$Py^{14}CH(NHMe)CH_2CH_2CO_2H$	53%	m.p. 120–123°	24
3-$PyCO(CH_2)_3CO_2H$	$NH_2OH \cdot HCl$, aq. KOH, 7 hr	3-$PyC(=NOH)CH_2CH_2CH_2CO_2H$		m.p. 161–163°	75
3-$PyCH_2COCH_2CONHMe$	$NH_2OH \cdot HCl$, 10% NaOH, overnight, R.T.	3-$PyCH_2C(=NOH)CH_2CONHMe$		m.p. 160–165°	22

TABLE XI-30. Carbonyl Reactions of Keto Acids (Continued)

Starting material	Reagent and conditions	Product	Yield	Properties	Ref.
3-PyCH=CHCOCO$_2$H	NH$_2$OH · HCl, aq. KOAc	3-PyCH=CHC(=NOH)CO$_2$H	quantitative	m.p. 176° (decomp.)	213
3-PyCOCH$_2$CH(NHAc)CO$_2$H	MeNH$_2$, Ra-Ni, H$_2$, 4 hr, 85°; 5*N* HCl, reflux 5 hr				1
3-PyCOCHPhCONH$_2$	NH$_2$CSNHNH$_2$			m.p. 255–257°; picrate, m.p. 231–235°	341
3-PyCOCHPhCO$_2$Me	NH$_2$CONHNH$_2$ · HCl		89.2%		341
3-PyCOCHPhCO$_2$Me	PhNHNH$_2$, N$_2$, isoBuOH, reflux		90.2%	m.p. 221–223°; picrate m.p. 208–211°	341
3-PyC(=NNHPh)CHPhCO$_2$Me	isoBuOH or PhMe, reflux 4 hr				341

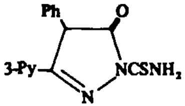
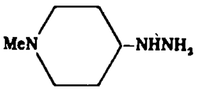
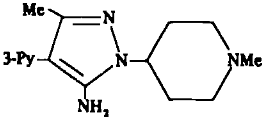
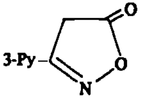
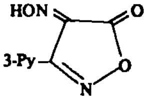
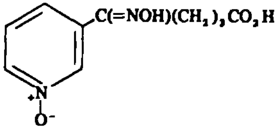
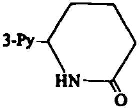
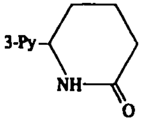
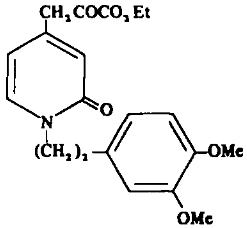
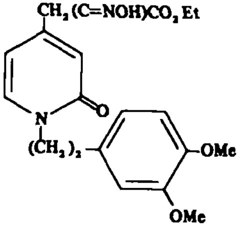
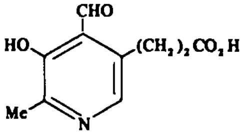
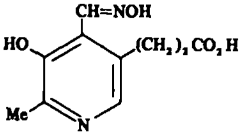
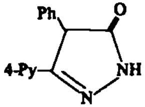
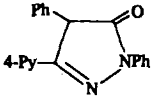
3-PyC(CH_2CO_2Et)=NNHCSNH$_2$				m.p. 236°	25
3-PyCH(CN)COMe + 	EtOH, 1 hr, R.T.; reflux 3 hr				331
3-PyC(=NOH)CH_2CO_2Me · HCl	aq. $NaHCO_3$			m.p. 164°	26
3-PyC(=NOH)CH_2CO_2Me · HCl	aq. $NaNO_2$			m.p. 180–185°	26
	Zn, HOAc			*dl*, m.p. 137–138.5° *l*, m.p. 146–147°, $[\alpha]_D^{21}$ −61°	75
3-PyCO(CH_2)$_3CO_2H$	$(NH_4)_2CO_3$, 85% HCO_2H, 140°, 90 hr		65%	m.p. 170–171°	102
4-PyCOCH$_2CO_2Et$	$NH_2NHCSNH_2$, alcohol, boiled 5–6 hr	4-PyC(CH_2CO_2Et)=NNHCSNH$_2$		m.p. 169–170°	25

TABLE XI-30. Carbonyl Reactions of Keto Acids (Continued)

Starting material	Reagent and conditions	Product	Yield	Properties	Ref.
4-PyCOCHPhCO$_2$Me	PhNHNH$_2$, R.T., 24 hr	4-PyC(=NNHPh)CHPhCO$_2$Me		m.p. 241–243°	341
4-PyCOCH$_2$CONHPh	PhNH$_2$, PhNH$_2$ · HCl C$_6$H$_6$, reflux	4-PyC(NHPh)=CHCONHPh		m.p. 192–193°	292
	NH$_2$OH · HCl, NaOAc, EtOH, reflux 30 min		82%	m.p. 186.5–189.5°	3, 88
	NH$_2$OH · HCl, NaAc, EtOH, reflux 3 hr		76%	m.p. 211–212°	279
4-PyCOCHPhCO$_2$Me	NH$_2$CONHNH$_2$ · HCl		90.6%	m.p. 269–271°; picrate, m.p. 229–230°	341
4-PyCOCHPhCO$_2$Me	PhNHNH$_2$, N$_2$, isoBuOH, reflux		87.9%	m.p. 235–237°; picrate, m.p. 246–249°	341

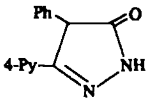
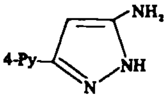
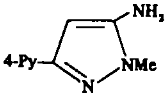
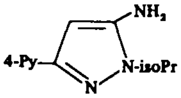
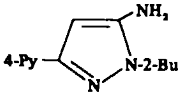
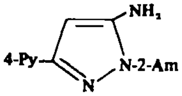
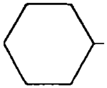
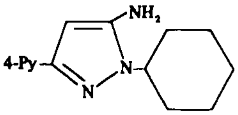
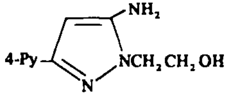
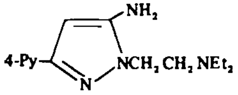
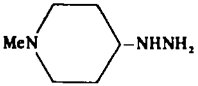
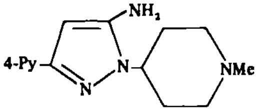
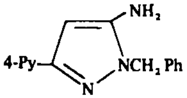
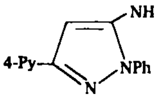
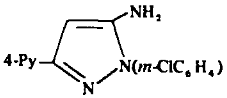
4-PyCOCHPhCONH$_2$	NH$_2$CSNHNH$_2$		341
4-PyCOCH$_2$CN + N$_2$H$_4$	abs. EtOH, reflux		171
4-PyCOCH$_2$CN + MeNHNH$_2$	abs. EtOH, reflux		171
4-PyCOCH$_2$CN + isoPrNHNH$_2$	abs. EtOH, reflux		171
4-PyCOCH$_2$CN + 2-BuNHNH$_2$	abs. EtOH, reflux		171
4-PyCOCH$_2$CN + 2-AmNHNH$_2$	same as above		171
4-PyCOCH$_2$CN +  -NHNH$_2$	Na, 98% EtOH, reflux 10 hr		171

TABLE XI-30. Carbonyl Reactions of Keto Acids (Continued)

Starting material	Reagent and conditions	Product	Yield	Properties	Ref.
4-PyCOCH$_2$CN + HOCH$_2$CH$_2$NHNH$_2$	abs. EtOH, reflux				171
4-PyCOCH$_2$CN + Et$_2$NCH$_2$CH$_2$NHNH$_2$	same as above				171
4-PyCOCH$_2$CN + 	Na, 98% EtOH, reflux 10 hr				171
4-PyCOCH$_2$CN + PhCH$_2$NHNH$_2$	abs. EtOH, reflux				171
4-PyCOCH$_2$CN + PhNHNH$_2$	same as above				171
4-PyCOCH$_2$CN + m-ClC$_6$H$_4$NHNH$_2$	same as above				171

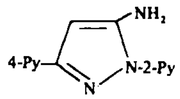
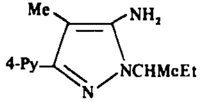
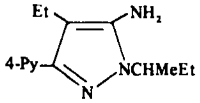
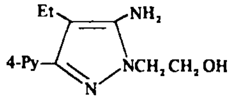
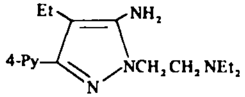
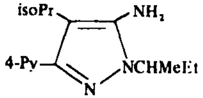
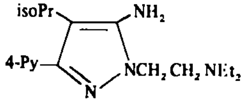
$\mathrm{4\text{-}PyCOCH_2CN + 2\text{-}PyNHNH_2}$	same as above		171
$\mathrm{4\text{-}PyCOCHMeCN}$ + $\mathrm{MeCHEtNHNH_2}$	same as above		171
$\mathrm{4\text{-}PyCOCHEtCN}$ + $\mathrm{MeCHEtNHNH_2}$	same as above		171
$\mathrm{4\text{-}PyCOCHEtCN}$ + $\mathrm{HOCH_2CH_2NHNH_2}$	same as above		171
$\mathrm{4\text{-}PyCOCHEtCN}$ + $\mathrm{Et_2NCH_2CH_2NHNH_2}$	same as above		171
$\mathrm{4\text{-}PyCOCH(isoPr)CN}$ + $\mathrm{EtCHMeNHNH_2}$	same as above		171
$\mathrm{4\text{-}PyCOCH(isoPr)CN}$ + $\mathrm{Et_2NCH_2CH_2NHNH_2}$	same as above		171

TABLE XI-30. Carbonyl Reactions of Keto Acids (Continued)

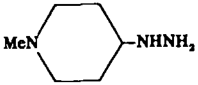
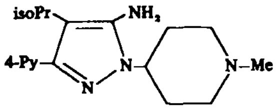
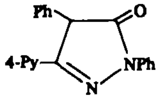
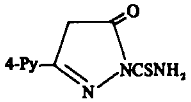
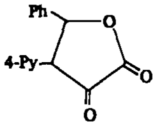
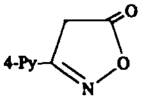
Starting material	Reagent and conditions	Product	Yield	Properties	Ref.
4-PyCOCH(isoPr)CN + 	same as above				171
4-PyC(=NNPh)CHPhCO$_2$Me	isoBuOH or PhMe, reflux 4 hr			m.p. 235–237°; picrate, m.p. 246–249°	341
4-PyC(CH$_2$CO$_2$Et)=NNHCSNH$_2$				m.p. 222–223°	25
4-PyCH$_2$COCO$_2$Et	PhCHO		0.5 g → 0.2 g	m.p. 266–267°	86
(4-PyCOCHCO$_2$Et)$_2$CHPh	NH$_2$OH · HCl			m.p. 194–195° (decomp.)	105

TABLE XI-31. Introduction of a Double Bond

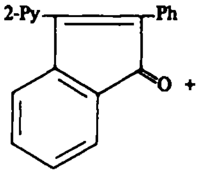
Starting material	Conditions	Product	Yield	Properties	Ref.
2-PyCPh(OH)CH$_2$CO$_2$H	SOCl$_2$, reflux 2 hr; 10% NaOH, 1 hr	2-PyCPh=CHCO$_2$H	53%	m.p. 203–204°	54
2-PyCPh(OH)CH$_2$CO$_2$Et	H$_2$SO$_4$, 90 min	2-PyCPh=CHCO$_2$Et		m.p. 47–48.5°	222
2-PyCPh(OH)CHMeCO$_2$Et	H$_2$SO$_4$, 60 min	2-PyCPh=CMeCO$_2$Et		m.p. 96–98°	222
2-PyCPh(OH)CHPhCO$_2$H	98% H$_2$SO$_4$, 1 hr	 +			172
		2-PyCPh=CPhCO$_2$H		m.p. 190–195° (decomp.)	
2-PyC(SMe)$_2$CH$_2$CO$_2$Et	DMSO, 40–50° *or* Me$_2$SO$_4$, 1–2 hr, 90–100°; boiled 10–15 min, Me$_3$S$^{\oplus}$ MeSO$_4^{\ominus}$	2-PyC(SMe)=CHCO$_2$Et		m.p. 157–158°	342
3-PyCPh(OH)CH$_2$CO$_2$H	SOCl$_2$, reflux 2 hr; 10% NaOH, 1 hr	3-PyCPh=CHCO$_2$H	56%	m.p. 201–202°	54
4-PyCPh(OH)CH$_2$CO$_2$H	same as above	4-PyCPh=CHCO$_2$H	78%	m.p. 241–242°	54
4-PyCPh(OH)CH$_2$CO$_2$Et	P$_2$O$_5$, C$_6$H$_6$, reflux 8 hr *or* 98% H$_2$SO$_4$, 20°, 45 min	4-PyCPh=CHCO$_2$Et		m.p. 104–105°	222

TABLE XI-31. Introduction of a Double Bond (Continued)

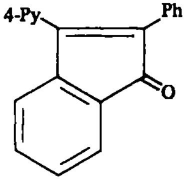
Starting material	Conditions	Product	Yield	Properties	Ref.
4-PyCPh(OH)CHMeCO$_2$Et	P$_2$O$_5$ or H$_2$SO$_4$, 15 min	4-PyCPh=CMeCO$_2$Et		m.p. 53–55°	222
4-PyCPh(OH)CHPhCO$_2$H	98% H$_2$SO$_4$, 1 hr	4-PyCPh=CPhCO$_2$H + 		m.p. 248–255°	172
4-PyC(SMe)$_2$CH$_2$CO$_2$Et	DMSO, 40–50° *or* Me$_2$SO$_4$, 1–2 hr, 90–100°; boiled 10–15 min, Me$_3$S$^{\oplus}$MeSO$_4^{\ominus}$	4-PyC(SMe)=CHCO$_2$Et		m.p. 67–68°	342

TABLE XI-32. Addition Reactions of Unsaturated Side-Chains

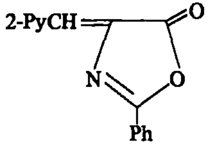
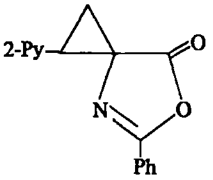
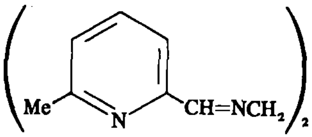
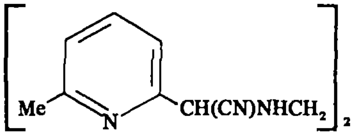
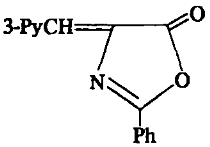
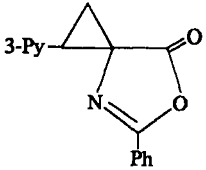
Starting material	Reagent and conditions	Product	Yield	Properties	Ref.
$(2\text{-PyCH=NCH}_2)_2$	HCN, 5-10°	$[2\text{-PyCH(CN)NHCH}_2]_2$	65.7%	m.p. 96-102° (decomp.)	343
	CH_2N_2 or DMSO		12% 19%	m.p. 141°	94
	HCN, 5-10°		72.2%		343
	CH_2N_2 or DMSO		15% 25%	m.p. 145°	94
3-PyC(Cl)=$CHCO_2Et$ + 3-PyCCl_2CHCO_2Et (mixture)	Et_2NH, 80°, 24 hr	$3\text{-PyC(NEt}_2)\text{=CHCO}_2Et$	44.7%	b.p. 101°/0.01 mm; n_D^{20} 1.5582; picrate, m.p. 110°	175

TABLE XI-32. Addition Reactions of Unsaturated Side-Chains (Continued)

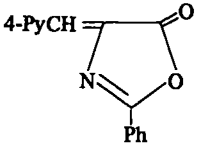
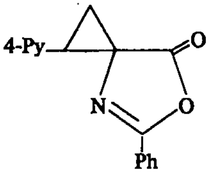
Starting Material	Reagent and Conditions	Product	Yield	Properties	Ref.
	morpholine, C_6H_6, reflux 4 hr	3-PyC(morpholino)=$CHCO_2Et$	57.5%	b.p. 129–131°/0.01 mm; n_D^{20} 1.5728; picrate, m.p. 125°	175
	piperidine, C_6H_6, reflux 4 hr	3-PyC(Piperidino)=$CHCO_2Et$	68%	b.p. 128°/0.01 mm; n_D^{20} 1.5788; picrate m.p..111°	175
	pyrrolidine, C_6H_6, reflux 4 hr; H_2; EtOH, Py, 5% Pd-C	3-PyC(1-pyrrolidinyl)=$CHCO_2Et$	71%	b.p. 130–131°/0.01 mm; n_D^{20} 1.5869; picrate, m.p. 127°	175
	CH_2N_2 or DMSO		17% 22%	m.p. 152°	94

TABLE XI-33. Pyridine Side-Chain Hydrazides, Hydroxamic Acids, Amidines, and Imides

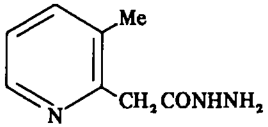
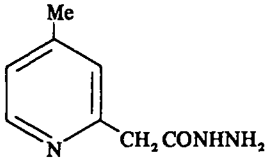
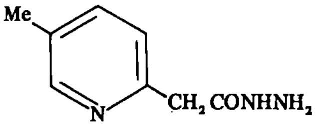
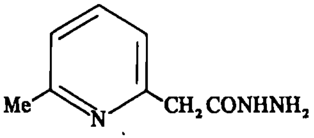
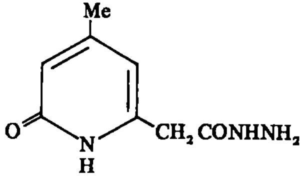
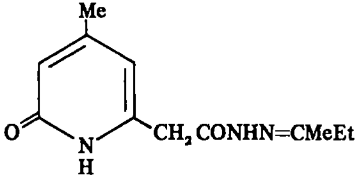
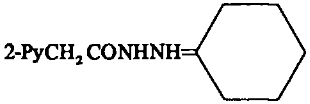
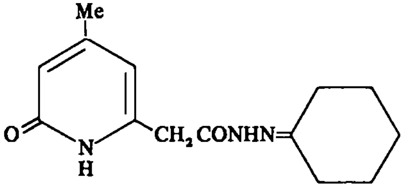
Compound	b.p./mm	m.p.	Derivative	Ref.
2-PyCH$_2$CONHNH$_2$		120° 117–119° 117–118°	hydrochloride, m.p. 175–177° hydrochloride, m.p. 195–199° picrate, m.p. 138–139°	351 362 291
		136–138°		34
		105.5° 106.5°		34
		122–123°		34
		143–144.5°		34

TABLE XI-33. Pyridine Side-Chain Hydrazides, Hydroxamic Acids, Amidines, and Imides (Continued)

Compound	b.p./mm	m.p.	Derivative	Ref.
		189–190°		363
		171–172°		363
		99–102°		362
		229–230°		363

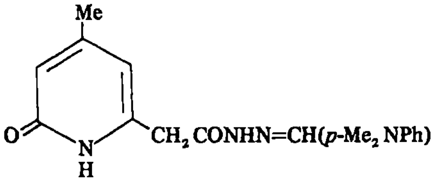
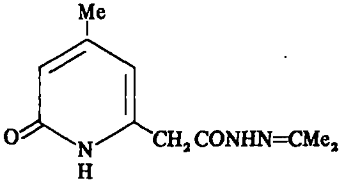
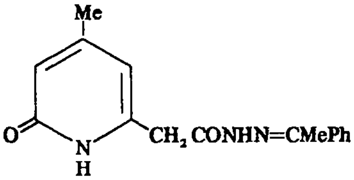
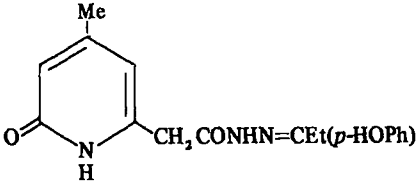
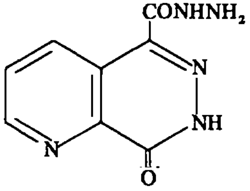
2-PyCH$_2$CONHNH=CH(p-Me$_2$NPh)	181–184°	362
	220–221°	363
	229–239° (decomp.)	363
	206–207°	363
	206–207°	363

TABLE XI-33. Pyridine Side-Chain Hydrazides, Hydroxamic Acids, Amidines, and Imides (Continued)

Compound	b.p./mm	m.p.	Derivative	Ref.
2-PyCHMeCONHNH$_2$		77-78°		34
2-PyCH(OH)CONHNH$_2$		102°		35
2-Py(CH$_2$)$_2$CONHNH$_2$	143-149°/0.002		*p*-Me$_2$NPhCHO derivative, m.p. 142-145°	34
3-PyCH$_2$CONHNH$_2$		108-109°	hydrochloride, m.p. 182-185°	351
3-PyCH$_2$CONHNHCHMe(3-Py)		122-124°		159
3-PyCH$_2$CONHN=CMe(3-Py)		156-158° (decomp.)		159
3-PyCH(OH)CONHNH$_2$		141°		35
		296° (decomp.)		260

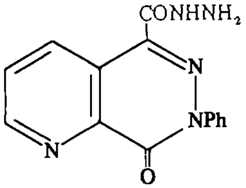
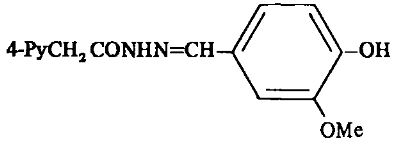
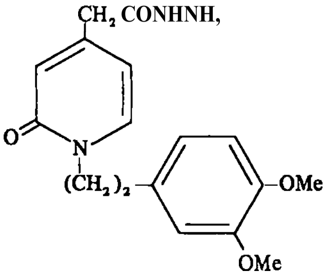
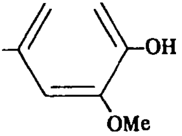
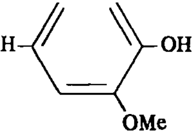
		198"		260
3-PyCOC(=NH)NHC(=NH)NH$_2$		150–151"		162
3-PyCOCH$_2$ CONHC(=NH)NH$_2$		283-288° (decomp.)		161
3-PyCOCONHC(=NH)NH$_2$		283–288" (decomp.)		161
4-PyCH$_2$ CONHNH,		90–91"		364
			hydrochloride, m.p. 185–188"	351
4-PyCH$_2$ CONHNH,		94–95"		**58**
4-PyCH$_2$ CONHNHisoPr	no data			58
4-PyCH$_2$ CONHNHCH, Ph		119–120"		159
4-PyCH$_2$ CONHN=CHPh		69–71" (hydrate) 116–1**17"**		159 364
4-PyCH$_2$ CONHN=CH(*p*-HOPh)		2**1**7–218"		364
4-PyCH$_2$ CONHN=CH(*p*-AcNHPh)			hydrate, m.p. 226–227"	364

TABLE XI-33. Pyridine Side-Chain Hydrazides, Hydroxamic Acids, Amidines, and Imides (Continued)

Compound	b.p./mm	m.p.	Derivative	Ref.
 4-PyCH$_2$CONHN=CH–		208–209"		364
4-PyCH$_2$CONHN=CMe$_2$	no data			58
		110–112"		8
4-PyCH(CH$_2$Ph)CONHNH$_2$		138"		166
4-Py(CH$_2$)$_2$CONHNH$_2$		61–62°		364
		84"	hydrate, m.p. 64°	166
4-Py(CH$_2$)$_2$CONHNHCHMe$_2$		74°		160
4-Py(CH$_2$)$_2$CONHN=CH(*p*-HOPh)		199–200°		364

4-Py(CH$_2$)$_2$CONHN=CH(*p*-AcNHPh)		198–199"	364
4-Py(CH$_2$)$_2$CONHN=CH– 		212–214"	364
4-Py(CH$_2$)$_2$CONHN=CMe$_2$	no data		160
4-PyCH=CHCONHNH$_2$		109–110°	29
4-PyCH=CHCONHN=CH(*p*-AcNHPh)		169–171°	364
4-PyCH=CHCONHN=CH– 		124–126"	364

References

1. H. McKennis, Jr., L. B. Turnbull, E. R. Bowmann, and E. Tamaki, *J. Org. Chem.,* 28, 383 (1963).
2. F. Zymalkowski and B. Trenktrog, *Arch. Pharm.* (Weinheim), **292,** 9 (1959).
3. M. Barash and J. M. Osbond, *J. Chem. Soc.,* 2157 (1959).
4. M. Barash, J. M. Osbond, and J. C. Wickens, *J. Chem. Soc.,* 3530 (1959).
5. J. M. Bobbitt and D. A. Scola, *J. Org. Chem.,* 25,560 (1960).
6. A. Cohen and J. M. Osbond, U.S. patent, 2,877,227 (1959); *Chem. Abstr.,* **55,** 7444e (1961).
7. M. Kirisawa, *Chem. Pharm. Bull.* (Tokyo), **7,** 35 (1959).
8. M. Kirisawa, *Chem. Pharm. Bull.* (Tokyo), **7,** 38 (1959).
9. Y. Sato, *Chem. Pharm.* Bull. (Tokyo), 7,241 (1959).
10. J. T. Suh and B. M. Puma, *J. Org. Chem.,* 30,2253 (1965).
11. A. Jackson and J. A. Joule, *Chem. Commun.,* 459 (1967).
12. E. Wenkert, K. G. Dave, R. C. Lewis, and P. W. Sprague, *J. Amer. Chem. Soc.,* 89, 6741 (1967).
13. J. A. Weisbach, J. L. Kirkpatrick, K. R. Williams, E. L. Anderson, N. C. Yim, and B. Douglas, *Tetrahedron Lett.,* 3457 (1965).
14. F. Bohlmann, E. Winterfeldt, H. Laurent, and W. Ude. *Tetrahedron,* 19, 195 (1963).
15. B. Frydman, M. E. Despuy, and H. Rapoport, *J. Amer Chem. Soc.,* 87,3530 (1965).
16. C. E. Cook, R. C. Corley, and M. E. Wall, *J. Org. Chem.,* 30,4114 (1965).
17. I. G. Morns and A. R. Pinder, *J. Chem. Soc.,* 1841 (1963).
18. F. Bohlmann, E. Winterfeldt, D. Schumann, and B. Catscheff, *Chem. Ber.,* 98, 653 (1965).
19. F. Bohlmann, E. Winterfeldt, D. Schumann, U. Zarnack, and P. Wandrey, *Chem. Ber.,* 95,2365 (1962).
20. M. Pailer and R. Libiseller, *Monatsh. Chem.,* 93, 511 (1962); *Chem. Abstr.* **57,** 4708f (1962).
21. M. Beroza, *J. Org. Chem.,* 28, 3562 (1963).
22. H. McKennis, Jr., E. R. Bowman, and L. B. Turnbull, *J. Amer. Chem. Soc.,* 82,3974 (1960).
23. H. McKennis, Jr., S. L. Schwartz, L. B. Turnbull, E. Tamaki, and E. R. Bowman, *J. Biol. Chem.,* 239,3981 (1964).
24. P. L. Morselli, H. H. Ong, E. R. Bowman, and H. McKennis, Jr., *J. Med. Chem.,* 10, 1033 (1967).
25. C. Belzecki and T. Urbański, *Rocz. Chem.,* 32,779 (1958); *Chem. Abstr.* **53,** 10188b (1959).
26. C. Caradonna, M. L. Stein, and M. Ikram, *Ann. Chim.* (Rome), 49, 2083 (1959); *Chem. Abstr.,* **54,** 19646c (1960).
27. L. C. Cheney and J. C. Codfrey, U.S. patent, 3,202,653 (1965); *Chem Abstr.,* 63, 18094c (1965).
28. A. Fujita, T. Yamamoto, J. Matsumoto, S. Minami, and H. Takamatsu, *Yakugaku Zasshi,* 85,565 (1965); *Chem. Abstr..* **63,** 9909f (1965).
29. S. Kakimoto, J. Nishie, and K. Yamamoto, *Japan J. Tuberc..* 7, 76 (1959); *Chem. Abstr..* **54,** 21079h (1960).
30. F. Leonard and W. Tschannen, *J. Med. Chem.,* 9,140 (1966).
31. R. B. Moffett, *J. Med. Chem.,* 9,475 (1966).
32. R. B. Moffett, U.S. patent, 3,255,186 (1966); *Chem. Abstr.,* **65,** 8928c (1966).

33. Y. G. Perron, L. C. Cheney, and J. C. Godfrey, Belg. patent, 631,631 (1963); Chem. Abstr., 61, 7021h (1964).
34. J. Izdebski, Rocz. Chem., 39, 717 (1965); Chem. Abstr., 64, 3465e (1966).
35. E. G. Brain and J. H. C. Nayler, Brit. patent, 986,544 (1965); Chem. Abstr., 62, 16255c (1965).
36. E. J. Cragoe, Jr., A. M. Pietruszkiewicz, and C. M. Robb, J. Org. Chem., 23, 971 (1959).
37. J. Heider and D. Jerchel, Ger. patent 1,166,190 (1964); Chem. Abstr., 60, 159474 (1964).
38. J. Heider and D. Jerchel, Ger. patent 1,180,367 (1964); Chem. Abstr., 62, 1725f (1965).
39. J. Heider and D. Jerchel, U.S. patent, 3,167,544 (1965); Chem. Abstr., 62, 11887c (1965).
40. J. Heider and D. Jerchel, U.S. patent, 3,314,854 (1967); Chem. Abstr., 67, 108849f (1967).
41. G. M. K. Hughes, U.S. patent, 3,094,533 (1963); Chem. Abstr., 60, 2912e (1964).
42. W. L. Bencze and G. N. Walker, U.S. patent, 3,337,568 (1967); Chem. Abstr., 68, 87179r (1968).
43. M. Perelman and S. Mizsak, J. Med. Chem., 6, 533 (1963).
44. J. W. Cusic and H. W. Sause, Belg. patent, 617,730 (1962); Chem. Abstr., 58, 12522d (1963).
45. J. W. Cusic and H. W. Sause, U.S. patent, 3,225,054 (1965); Chem. Abstr., 64, 6625f (1966).
46. J. A. Meschino, U.S. patent, 3,185,707 (1965); Chem. Abstr., 63, 2934f (1965).
47. J. A. Meschino, U.S. patent, 3,254,092 (1966); Chem. Abstr., 65, 12179d (1966).
48. R. B. Moffett, J. Med. Chem., 7, 446 (1964).
49. R. B. Moffett, U.S. patent, 3,156,697 (1964); Chem. Abstr., 62, 5257 (1965).
50. A. D. Cale, Jr., H. Jenkins, B. V. Franko, J. W. Ward, and C. D. Lunsford, J. Med. Chem., 10, 214 (1967).
51. R. W. Temple and L. F. Wiggins, Brit. patent, 930,459 (1963); Chem. Abstr., 59, 13956b (1963).
52. E. Seeger and A. Kottler, Ger. patent 1,026,318 (1958); Chem. Abstr., 54, 11058a (1960).
53. Smith, Kline, and French Laboratories, Nether. patent appl., 6,507,155 (1965); Chem. Abstr., 65, 761c (1966).
54. F. J. Villani, M. S. King, and F. J. Villani, J. Med. Chem., 6, 142 (1963).
55. Laboratori Panacea S.r.l., Belg. patent, 628,483 (1963); Chem. Abstr., 60, 14509a (1964).
56. C. D. Lunsford and A. D. Cale, Jr., Belg. patent, 613,734 (1962); Chem. Abstr., 58, 507g (1963).
57. C. D. Lunsford and A. D. Cale, Jr., U.S. patent, 3,192,207 (1965); Chem. Abstr., 63, 11503a (1965).
58. T. S. Gardner, E. Wenis, and J. Lee, J. Med. Pharm. Chem., 5, 503 (1962).
59. W. L. Bencze, Belg. patent 620,631 (1963); Chem. Abstr.. 59, 11449b (1963).
60. S. Minami, A. Fujita, J. Matsumoto, K. Fujimoto, M. Shimizu, and Y. Takase, Jap. patent, 23,662 (1965); Chem. Abstr., 64, 3504b (1966).
61. S. Minami, A. Fujita, K. Yamamoto, K. Fujimoto, M. Shimizu, and Y. Takase, Jap. patent, 6,908 (1966); Chem. Abstr., 65, 7154b (1966).
62. S. Minami, A. Fujita, K. Yamamoto, K. Fujimoto, and Y. Takase, Jap. patent, 1,178 (1967); Chem. Abstr., 66, 94912m (1967).

63. H. M. Taylor, U.S. patent, 3,313,683; ***Chem. Absrr.,*** 67,64073s (1967).
64. Farbenfabriken Bayer AG, Nether. appl., 6,605,907 (1966); ***Chem. Abstr.,*** 67,22013s (1967).
65. M. A. McCall and R. L. McConnell, U.S. patent, 3,106,566 (1963); ***Chem. Abstr.,*** 60, 4115g (1964).
66. M. Samejima, ***Yakugaku Zasshi. 80,*** 1706 (1960); ***Chem. Abstr., 55,*** 10439b (1961).
67. Kodak, Soc. anon., Belg. patent, 588,862 (1960); ***Chem. Abstr.. 55,*** 1251i (1961).
68. N. J. Doorenbos, U.S. patent, 2,953,561 (1960); ***Chem. Abstr.. 55,*** 1250d (1961).
69. Tanabe Seiyaku Co. Ltd., Belg. patent, 671,385 (1966); ***Chem. Abstr.,*** 65, 15348g (1966).
70. M. Anderson and A. W. Johnson, ***J. Chem. Soc., C,*** 1075 (1966).
71. S. J. Norton and E. Sanders, ***J. Med. Chem.,*** 10,961 (1967).
72. C. H. Kao, ***K'o Hsüch T'ung Pao No.*** 14, 434 (1957); ***Chem. Abstr., 55,*** 235221 (1961).
73. K. Horibata, H. Taniuchi, M. Tashiro, S. Kuno, O. Hayaishi, T. Sakan, T. Tokuyama, and S. Seno, ***Koso Kagaku Shinpojiumu, 15,*** 117 (1961); ***Chem. Abstr.. 56,*** 5113g (1962).
74. J. W. Hylin, ***Arch. Biochem. Biophys..*** 83, 528 (1959); ***Chem. Abstr..*** 53, 22246a (1959).
75. Y. L. Gol'dfarb, F. D. Alashev, and V. K. Zvorykina, ***Izv. Akad. Nauk SSR, Otd. Khim. Nauk,*** 2209 (1962); ***Chem. Abstr., 58,*** 14014d (1963).
76. S. Senoh, S. Imamoto, and Y. Maeno, ***Tetrahedron Lett.,*** 3431 (1964).
77. R. Hiltmann and H. Wollweber, Ger. patent, 1,073,497 (1960); ***Chem. Abstr., 55,*** 19956a (1961).
78. J. Izdebski, ***Rocz. Chem.,*** 39,1625 (1965); ***Chem. Abstr., 64,*** 17536b (1966).
79. Z. Dabrowski and J. T. Wrobel, ***Chem. Ind.*** (London), 1758 (1964).
80. J. A. Gautier, I. Marszak, M. Olomucki, and M. Miocque, Bull. ***Soc. Chim. Fr.,*** 2569 (1965).
81. J. A. Gautier, I. M. Olomycki, and M. Miocque, C. R. ***Acad. Sci., Paris, Ser. C,*** 251, 562 (1960); ***Chem. Abstr., 55,*** 9397e, 11407g (1961).
82. O. Martensson and E. Nilsson, ***Acta Chem. Scand.,*** 14,1129 (1960).
83. G. V. Boyd and A. D. Ezekiel, ***J. Chem. Soc., C,*** 1866 (1967).
84. R. E. Willette, ***J. Chem. Soc.,*** 5874 (1965).
85. E. D. Amstutz and M. M. Besso, ***J. Org. Chem.,*** 25,1687 (1960).
86. M. M. Besso, PhD thesis, Lehigh University, Bethlehem, Pa. (1959).
87. G. N. Walker and B. N. Weaver, ***J. Org.*** Chem., 26,4441 (1961).
88. J. M. Osbond, Brit. patent, 808,046 (1959); ***Chem. Abstr.,*** 53,18063 (1959).
89. Y. Noike, ***Yakugaku Zasshi,*** 79, 1514 (1959); ***Chem. Abstr.,*** 54, 11021b (1960).
90. M. M. Baizer, U.S. patent, 3,218,245 (1965); ***Chem. Abstr., 64,*** 17554f (1966).
91. S. L. Shapiro, V. Bandurco, and L. Freedman, ***J. Org. Chem.,*** 27,174 (1962).
92. R. Tan and A. Taurins, ***Tetrahedron*** Lett.. 1233 (1966).
93. H. Hellmann and H. Piechota, ***Ann. Chem.,*** 631, 175 (1960).
94. G. Slater and A. W. Somerville, ***Tetrahedron,*** 13,2823 (1967).
95. S. J. Norton, C. G. Skinner, and W. Shive, ***J. Org. Chem..*** 26,1495 (1961).
96. S. Hauptmann and K. Hirshberg, ***J. Prakt. Chem.,*** 34, 272 (1966); Chem. ***Absrr., 66,*** 55360k (1967).
97. J. Wrobel and Z. Dabrowski, Rocz. ***Chem.,*** 39, 1239 (1965); ***Chem. Abstr., 64,*** 15936g (1966).
98. F. H. Clarke, G. A. Felock, G. B. Silverman, and C. M. Watnick, ***J. Org. Chem.,*** 27, 533 (1962).

99. W. Herz and D. R. K. Murty, *J.* Org. Chem., 26,418 (1961).
100. G. Galiazzo, Gazz. Chim. *Ital.*, 95,1322 (1965).
101. J. A. T. Beard and A. R. Katritzky, Rec. Trav. Chim. Pays-Bas, 78,592 (1959).
102. G. B. D. de Graaff, W. Ch. Melger, J. Van Bragt, and S. Schukking, Rec. Trav. Chim. Pays-Bas, 83,910 (1964).
103. N. S. Vul'fson and L. I. Lukashina, *Sbornik* Statei, *Nauch.-Issledovatel. Inst.* Org. Poluprod. *i Krasitelei* No. 2, 137 (1961); Chem. Abstr., **56**, 10094e (1962).
104. W. Wunderlich, *J. Prakt.* Chem., 2,302 (1955); Chem. Abstr., **54**, 4579i (1960).
105. O. Y. Magidson, Zh. Obshch. Khim., 29, 165 (1959); Chem. Abstr., **54**, 530d (1960).
106. K. W. Merz and R. Barchet, Arch. Pharm. (Weinheim), 297,423 (1964).
107. N. S. Vul'fson, V. E. Kolchin, and L. K. Artemchick, Zh. Obshch. Khim., 32, 3382 (1962); Chem. Abstr., 59, 1784e (1963).
108. N. S. Vul'fson and V. E. Kolchin, Zh. Obshch. Khim., 34,2381 (1964); Chem. Abstr., **61**, 14818c (1964).
109. Nishimoto and T. Nakashima, Yakugaku Zasshi, 81, 88 (1961); Chem. Abstr., 55, 13420h (1961).
110. K. Winterfeld and H. Buschbeck, Arch. Pharm. (Weinheim), 294,468 (1961).
111. D. R. Bragg and D. G. Wiberley, *J.* Chem. *Soc., C,* 5074 (1961).
112. G. VanZyl, D. L. DeVries, R. H. Decker, and E. T. Niles, *J.* Org. Chem., 26, 3373 (1961).
113. H. Hellmann and D. Dieterich, *Ann.* Chem., **656**, 53 (1962).
114. R. Lukeš, J. N. Zvonkova, A. F. Mironov, and M. Ferles, Collect. Czech. Chem. *Commun.*, 25,2668 (1960); Chem. *Abstr.*, **55**, 4501d (1961).
115. M. S. Brown and H. Rapoport, *J. Org.* Chem.. 28,3261 (1963).
116. L. Kuczynski, Z. Machon, and L. Wykret, Dissertationes Pharm., 16, 479 (1964); Chem. Abstr., **63**, 11491f (1965).
117. J. Čejka, M. Fereles, S. Chládek, J. Labsky, and M. Zelinka, Collect Czech. Chem. *Commun.*, 26, 1429 (1961); Chem. Abstr., **55**, 27309b (1961).
118. A. L. Davis, C. G. Skinner, and W. Shive, Arch. *Biochem. Biophys.*, 87, 88 (1960); Chem. Abstr., 55,25133 (1961).
119. M. E. Kuehne, *J.* Amer. Chem. *Soc.*, 84,837 (1962).
120. A. Mustafa and M. M. M. Sallam, *J.* Org. Chem., 27,2406 (1962).
121. L. Neilande, A. Karklins, V. Veiss, and G. Vanags, *Latvijas* PSR *Zinatnu* Akad. *Vestis,* Kim Series 7 (1964); Chem. Abstr., **61**, 3699g (1964).
122. E. Wenkert, K. G. Dave, and F. Haglid, *J.* Amer. Chem. *Soc.*, 87,5461 (1965).
123. E. Zbiral and E. Werner, Tetrahedron Lett., 2001 (1966).
124. E. Zbiral and E. Werner, Monatsh. Chem., 97, 1797 (1966); Chem. Abstr., **66**, 85824g (1967).
125. W. Kornytnyk, B. Paul, A. Bloch, and C. A. Nichol, *J.* Med. Chem., 10,345 (1967).
126. Dr. Karl Thomae GmbH, Belg. patent, 621,453 (1963); Chem. *Abstr.*, 59, 10185f (1963).
127. A. Stempel, Belg. patent, 635,615 (1964); Chem. Abstr., **61**, 10661e (1964).
128. G. Giacomello, F. Gualtieri, F. M. Riceieri, and M. L. Stein, Tetrahedron Lett., 1117 (1965).
129. F. Korte and H. J. Schulze-Steinen, Chem. *Ber.*, 95,2444 (1963).
130. W. Baker, K. M. Buggle, J. F. W. McOmie, and D. A. M. Watkins, *J.* Chem. *Soc.*, 3594 (1958).
131. M. J. Betts and B. R. Brown, *J.* Chem. *Soc., C,* 1730 (1967).
132. G. N. Walker, J. *Org.* Chem., 27,2966 (1962).

133. E. Wenkert, K. G. Dave, F. Haglid, R. G. Lewis, T. Oishi, **R. V.** Stevens, and T. Terashima, *J. Org. Chem.,* 33,747 (1968).
134. A. Mironov, M. Fereles, and M. Pergal, *Sb. Vysoke Skoly Chem.-Technol. Praze, Org. Technol,* 5, 83 (1961); *Chem. Abstr.,* **62,** 13017b (1965).
135. **V.** Boekelheide and R. J. Windgasse, Jr., *J. Amer. Chem. Soc.,* 81,1456 (1959).
136. G. N. Walker, *J. Amer. Chem. Soc.,* 77, 3844 (1955).
137. **J. Sam,** *J. Phurm. Sci.,* 56,1360 (1967).
138. I. Murakoski, A. Kubo, J. Saito, and **J.** Haginiwa, *Chem. Phurm. Bull.* (Tokyo), 12, 747 (1964).
139. R. Adarns and W. Reifschneider, *J. Amer. Chem. Soc.,* 81, 2537 (1959).
140. T. Miyadera and I. Iwai, *Chem. Phurm.* Bull. (Tokyo), 12,1338 (1964).
141. D. **R.** Bragg and D. G. Wibberley, *J. Chem. Soc.,* 2627 (1962).
142. D. R. Bragg and D. G. Wibberley, *J. Chem. Soc.,* 3277 (1963).
143. J. Hurst, T. Melton, and D. G. Wibberley, *J. Chem. Soc.,* 2948 (1965).
144. T. Kappe, *Monatsh. Chem.,* 98, 1858 (1967); Chem. *Abstr.,* 68, 39447e (1968).
145. T. Melton and D. G. Wibberley, *J. Chem. Soc., C,* 983 (1967).
146. K. Winterfeld and W. Erning, *Arch. Phurm.* (Weinheim), 298,220 (1965).
147. D. R. Bragg and D. G. Wibberley, J. *Chem. Soc., C,* 2120 (1966).
148. K. Winterfeld and W. Erning, *Arch. Phurm.* (Weinheim), 298, 220 (1965); *Chem. Absrr.,* 63, 14809h (1965).
149. H. Pacheco and R. Gatto, *Bull. Soc. Chim. Fr.,* 95 (1960).
150. **R.** Tan and A. Taurins, *Tetruhedron Lett.,* 2737 (1965).
151. H. E. Baumgarten, H. C. F. Su, and **R.** P. Barkley, J. *Heterocycl. Chem,* 3, 357 (1966).
152. B. M. Ferrier and N. Campbell, *Proc. Roy. Soc. Edinburgh Sect. A,* 65, 231 (1959-60); *Chem. Abstr..* **55,** 24748e (1961).
153. H. **Junek,** *Monatsh. Chem.,* **96,** 2046 (1965); *Chem. Abstr.,* **64,** 11167h (1966).
154. ***R.*** Dohmori, *Chem. Phurm. Bull.* (Tokyo), 12,595 (1964).
155. T. Naito, R. Dohmori, and M. Shimoda, *Phurm. Bull.* (Japan), **3,** 34 (1955).
156. M. Maruoka, K. Isagawa, T. Kuki, and **Y.** Fushizaki, *Nippon Kaguku Zasshi,* 83,218 (1962); *Chem. Abstr.,* 59, 3879d (1963).
157. **O.** Martensson and E. Nilsson, *Actu Chem. Scund.,* 15,1026 (1961).
158. W. A. Schuler and A. Gross, **U.S.** patent, 2,953,562 (1960); *Chem. Absrr.,* 55, 4552f (1961).
159. H. Bojarska-Dahlig, Polish patent 47,469 (1963); *Chem. Abstr.,* **61,** 10661g (1964).
160. **Roussel** UCLAF, Fr. patent, M3268 (1965); *Chem. Abstr.,* **63,** 16314c (1965).
161. R. P. Mariella and J. J. Zelko, *J. Org. Chem.,* 25,647 (1960).
162. K. Odo and E. Ichikawa, Jap. patent 9565 (1967); *Chem. Abstr.,* **67,** 64250x (1967).
163. C. D. Gutsche and H. W. Voges, *J. Org. Chem.*,32,2685 (1967).
164. G. N. Walker, J. *Med. Chem..* 8,583 (1965).
165. B. E. Betts and W. Davey, *J. Chem. Soc.,* 3333 (1961).
166. H. W. Sause, Belg. patent, 669,165 (1966); *Chem Abstr.,* **65,** 13666c (1966).
167. E. Profft and W. Steinke, *Chem. Ber.,* 94,2267 (1961).
168. A. Banashek and **M.** N. Shckukina, *Zh. Obshch. Khim., 31,* 1479 (1961); *Chem. Abstr., 55,* 24739e (1961).
169. G. F. Holland and J. N. Pereira, *J. Med. Chem.,* 10, 149 (1967).
170. K. Kindler and K. **Lührs,** *Chem. Ber.,* 99,227 (1966).
171. CIBA Ltd., Belg. patent 612,971 (1962); *Chem. Abstr., 58,* 3438f (1969).
172. R. DeFazi and A. **Marsili,** *Gazz. Chim. Ital.,* 89,1709 (1959); *Chem. Abstr.,* 55, 4502g (1961).

173. G. N. Walker and B. N. Weaver, *J. Org. Chem.*. 25,484 (1960).

174. Y. Sato, T. Iwashige, and T. Miyadera, *Chem. Phurm. Bull.* (Tokyo), 8,427 (1960).

175. K. M. Naef and H. Schaltegger, *Helv. Chim. Actu,* 45,1018 (1962).

176. W. E. Hahn and T. Zieliński, *Łódź. Towarz. Nauk., Wydzial III,* No. 6, 23 (1960); *Chem. Abstr.,* 55, 5525d (1960).

177. J. A. Meschino and C. H. Bond, *J. Org. Chem.,* 28,3129 (1963).

178. V. Carelli, *Ann. Chim.* (Rome), 51,713 (1961); *Chem. Abstr.,* 56,47201 (1962).

179. V. C. Arsenijevic, H. Lapin, and A. Horeau. *C. R. Acud. Sci., Paris, Ser. C, 248,* 3309 (1959).

180. H. Lapin and A. Horeau, *Chimia,* 15,551 (1961); *Chem. Abstr.,* 59, 560d (1963).

181. B. M. Ferrier and N. Campbell, *J. Chem. Soc.,* 3513 (1960).

182. F. Johnson, J. P. Panella, A. A. Carlson, and D. H. Hunneman, *J. Org. Chem.,* 27, 2473 (1962).

183. H. Junek, *Monatsh. Chem.,* 95,1473 (1964); *Chem. Abstr.,* 62, 13124b (1965).

184. H. Junek, *Monatsh. Chem.,* 95,1201 (1964); *Chem. Abstr.,* 62, 1629g (1965).

185. F. Cuiban, S. Cilianu-Bibian, S. Popescu, and 1. Rogozea, Fr. patent 1,366,064 (1964); *Chem. Abstr.,* 61, 14643c (1964).

186. H. Kato, T. Ogawa, and M. Ohta, *Bull. Chem. Soc. Jap.,* 33, 1468 (1960); *Chem. Abstr.,* 55, 27301b (1961).

187. H. W. R. Williams, Brit. patent, 980,417 (1965); *Chem. Abstr.,* 62, 7864d (1965).

188. H. Kato, T. Ogawa, and M. Ohta, *Chem. Ind.* (London), 1300 (1960).

189. E. Profft and R. Stumpf, *J. Prakt. Chem.*. 19, 266 (1963); *Chem. Abstr.,* 59, 15252b (1963).

190. Y. L. Gol'dfarb, F. D. Alashev, and V. K. Zyorykina, *Izv. Akad. Nauk SSSR, Ser. Khim,* 2241 (1964); *Chem. Abstr.,* 62, 7819g (1965).

191. F. H. Clarke and C. M. Watnick, *J. Org. Chem.,* 24,1574 (1959).

192. Y. Arata and K. Achiwa, *YukugukuZusshi,* 79,108 (1959); *Chem. Abstr.,* 53, 10211d (1959).

193. A. L. Logothetis, *J. Org. Chem.,* 29,1834 (1964).

194. G. W. J. M. Groenendaal, Rec. *Truv. Chim. Pays-Bus,* 78,446 (1959).

195. I. Tomita, H. G. Brooks, and D. E. Metzler, *J. Heterocycl. Chem., 3,* 178 (1966).

196. Y. Arata, *Yakugaku Zusshi,* 80,709 (1960); *Chem. Abstr.,* 54, 21084d (1960).

197. B. J. Calvert and J. D. Hobson, *J. Chem. Soc.,* 5378 (1964).

198. A. Jart, A. J. Bigler, and V. Bitsch, *Anal. Chim. Actu,* 31,472 (1964); *Chem. Abstr.,* 62, 1082d (1965).

199. D. E. Ames and B. T. Warren, *J. Chem. Soc.,* 5518 (1965).

200. F. Bohlmann, E. Winterfeldt, G. Boroschewski, R. Mayer-Mader, and B. Gatscheff, *Chem. Ber.,* 96,1792 (1963).

201. M. Hamama and M. Yamazaki, *Chem. Phurm. Bull.* (Tokyo), 11,415 (1963).

202. S. Boatman, T. M. Harris, and C. R. Hauser, *J. Amer. Chem. Soc.,* 87,5198 (1965).

203. G. A. Taylor, *J. Chem. Soc.,* 3332 (1965).

204. J. Mills, U.S. patent, 2,903,459 (1959); *Chem. Abstr.,* 54, 5702a (1960).

205. S. Ohki, Y. Noike, T. Ohishi, K. Nara, and T. Kato, *Yakugaku Zusshi,* 79, 1522 (1959); *Chem. Abstr.,* 54, 11022h (1960).

206. F. Bohlmann, E. Winterfeldt, P. Studt, H. Laurent, G. Borosehewski, and K. M. Kleine, *Chem. Ber.,* 94,3151 (1961).

207. V. Boekelheide and R. Scharrer, *J. Org. Chem.,* 26,3802 (1961).

208. M. Maruoka, K. Isagawa, and Y. Fushizaki, *Nippon Kagaku Zusshi,* 82, 1279 (1961); *Chem. Abstr.,* 59, 563b (1963).

209. A. M. Parsons, Brit. patent, 847,051 (1960); *Chem. Abstr.*. 55, 7441c (1961).

210. E. E. Mikhlina and M. V. Rubtsov, ***Zh. Obshch. Khim.,*** 32, 2177 (1962); ***Chem. Abstr.,*** 58, 9024g (1963).
211. E. Profft, F. Schneider and H. Beyer, ***J. Prakt. Chem.,*** 2,147 (1955).
212. E. D. Bergmann and I. Shahak, ***J. Chem. Soc.,*** 4033 (1961).
213. M. Strell and E. Kopp, ***Chem. Ber.,*** 91,1621 (1958).
214. G. Pappalardo, B. Tornetta, and G. Seapini, ***Farmaco, Ed. Sci.,*** 21,740 (1966); ***Chem. Abstr..*** 66, 46363m (1967).
215. B. M. Ferrier and N. Campbell, ***Chem. Znd.*** (London), 1089 (1958).
216. R. Walter and H. Zimmer, ***J. Heterocycl. Chem.,*** 1,205 (1964).
217. M. Viscontini and H. Raschig, ***Helv. Chim. Acta,*** 42,570 (1959).
218. D. Jerchel, J. Heider, and H. Wagner, ***Ann. Chem.,*** 613,153 (1958).
219. E. Profft and R. Stumpf, ***Arch. Pharm.*** (Weinheim), 296, 79 (1963).
220. T. S. Cardner, E. Wenis, and J. Lee, ***J. Org. Chem.,*** 26,1514 (1961).
221. Finanz and Kompensationanstalt, Fr. patent, 1,427,135 (1966); ***Chem. Abstr.,*** 65, 7151c (1966).
222. R. DeFazi, S. Carboni, and A. Marsili, ***Gazz. Chim. Ital.,*** 89, 1701 (1959); ***Chem. Abstr.,*** 55, 4497c (1961).
223. C. Runti and L. Sindellari, ***Boll. Chim. Farm.,*** 99, 499 (1960); ***Chem. Abstr..*** 55, 10468a (1961).
224. H. K. Hall, Jr., ***J. Amer. Chem. Soc.,*** 82,1209 (1960).
225. F. J. Vini, U.S. patent, 3,301,863 (1967); Chem. ***Abstr.,*** 67, 21833x (1967).
226. L. Horner and E. O. Reuth, ***Ann. Chem.,*** 703, 37 (1967).
227. P. Truitt and S. G. Truitt, ***J. Med. Chem.,*** 9,637 (1966).
228. W. Korytnyk, ***J. Med. Chem.,*** 8, 112 (1965).
229. H. N. Wingfield, Jr., ***J. Org. Chem.,*** 24, 872 (1959).
230. J. Canceill, J. J. Basselier, and J. Jacques, ***Bull. Soc. Chim. Fr.,*** 1024 (1967).
231. C. Bonsall and J. Hill, ***J. Chem. Soc., C,*** 1836 (1967).
232. H. Hellmann, H. Piechota, H. Henecka, and H. Timmler, Ger. patent, 1,081,896 (1960); ***Chem. Abstr.,*** 55, 19813a (1961).
233. J. Jančulev and M. Jančevska, ***Bull. Sci, Conseil Acad. RPF Yougoslavie,*** 6, 1 (1961); ***Chem. Abstr.,*** 55, 27305h (1961).
234. S. Fatutta and A. Stener, ***Gazz. Chim. Ital.,*** 88, 89 (1958); ***Chem. Abstr.,*** 53, 2244f (1959).
235. C. C. Chu and P. C. Teague, ***J. Org. Chem.,*** 23,1578 (1958).
236. Finanz and Kompensationsanstalt, Fr. patent, M3143 (1965); Chem. ***Abstr.,*** 63, 2933d (1965).
237. G. Queguiner and P. Pastour, ***C. R. Acad. Sci.. Pans, Ser. C,*** 258,5903 (1964); ***Chem. Abstr.,*** 61, 6987c (1964).
238. R. P. Eustigneeva and N. A. Preobrazhenskii, ***Zh. Obshch. Khim.,*** 28, 3085 (1958); ***Chem. Abstr.,*** 53, 10215a (1959).
239. H. Sliwa and P. Maitte, ***C. R. Acad. Sci. Paris, Ser. C,*** 259,2255 (1964); ***Chem. Abstr.,*** 62, 2760d (1965).
240. L. Neilande and G. Vanags, ***Latvijas PSR Zinatnu Akad. Vestis, Kim. Ser.,*** 203 (1964); ***Chem. Abstr.,*** 61, 6999d (1964).
241. H. Takamatsu, S. Minami, A. Fujita, K. Yamamoto, K. Fujimoto, M. Shimizu, Y. Takase, and I. Nakajima, Jap. patent 6233 (1965); ***Chem. Abstr.,*** 63, 5609e (1965).
242. K. Winterfield and R. Knieps, ***Arch. Pharm.*** (Weinheim), 293,478 (1960).
243. E. Maruszewska-Wieczorkowska and J. Michalski, Rocz. ***Chem..*** 37, 1315 (1963); ***Chem. Abstr.,*** 60, 5546a (1964).

244. W. Schulze and H. Willitzer, J. *Prakt. Chem.*, **23**, 20 (1964); *Chem. Abstr.*, 60, 13219h (1964).
245. I. Matsuo, K. Sugimoto, and S. Ohki, *Chem. Pharm.* Bull. (Tokyo), 14,691 (1966).
246. K. W. Merz and R. Barchet, *Arch. Pharm.* (Weinheim), 297,412 (1964).
247. Badische Anilin und Soda-Fabrik AG, Nether. appl. 6,514,088 (1966); *Chem. Abstr.*, **65**, 13605g (1966).
248. M. Freifelder, *J. Org. Chem.*, 28,602 (1963).
249. V. Carrelli, F. Liberatore, and F. Morlacchi, Ann. *Chim.* (Rome), **51**, 467 (1961); *Chem. Abstr.*, **56**, 7273i (1962).
250. W. Shaeffer and R. Wegler, Ger. patent, 1,149,356 (1963); *Chem. Abstr.*. **59**, 11441c (1963).
251. N. Sperber, M. Sherlock, D. Papa, and D. Kender, *J. Amer. Chem. Soc.*, 81, 704 (1959).
252. H. E. Ramsden, Brit. patent, 820,083 (1959); *Chem. Abstr.*, **54**, 24818c (1960).
253. F. Dallacker, P. Kratzer, and M. Lipp, *Ann. Chem.*, **643**, 97 (1961).
254. R. A. Jones and A. R. Katritzky, *Aust. J. Chem.*, 17,455 (1964); *Chem. Abstr.*. 60, 15824e (1964).
255. T. Naito and T. Kotake, Jap. patent, 428 (1959); *Chem. Abstr.*, **54**, 6763e (1960).
256. T. Naito and T. Kotake, Jap. patent, 2929 (1960); *Chem. Abstr.*, 54,248121 (1960).
257. T. Naito, R. Dohmori, and T. Kotake, *Chem. Pharm.* Bull. (Tokyo), 12, 588 (1964).
258. O. Červinka, *Collect. Czech. Chem. Commun.*, *25*, 2675 (1960); *Chem. Abstr.*, *55*, 4507b (1961).
259. O. Červinka, *Collect. Czech. Chem. Commun.*, *25*, 1174 (1960); *Chem. Abstr.*, 54, 13126b (1960).
260. I. Matsuura, F. Yoneda, and Y. Nitta, *Chem. Pharm.* Bull. (Tokyo), 14, 1010 (1966).
261. K. Osugi, *Yakugaku Zasshi*, 78, 1353 (1958); *Chem. Abstr.*, **53**, 8112f (1959).
262. H. Ahlbrecht and F. Kroehnke, *Ann. Chem.*, 704,133 (1967).
263. F. Eiden and P. Peter, *Arch. Pharm.* (Weinheim), **297**, 1 (1964).
264. F. E. Cislak, U.S. patent, 3,069,427 (1962); *Chem. Abstr.*, **58**, 125220c (1963).
265. M. J. Martell, Jr., and T. O. Soine, J. *Phann. Sci.*, 52,331 (1963).
266. H. McKennis, Jr., L. B. Turnbull, E. R. Bowman, and S. L. Schwartz, J. *Amer. Chem. Soc.*, 84,4598 (1962).
267. Daiichi Seiyaku Co. Ltd., Nether. appl. 6,607,005 (1966); *Chem. Abstr.*, 67, 32593v (1967).
268. S. Okuda and M. M. Robison, J. *Amer. Chem. Soc.*, 81,740 (1959).
269. N. S. Vul'fson, L. I. Lukashina, and S. L. Davydova, *Khim. Tekhnol. i Primenenie Proizv. Piridina i Khinolina. Materialy Soveshch., Inst. Khim. Akad. Nauk Latv. SSR, Riga,* 243 (1957); *Chem. Abstr.*, **57**, 16604a (1962).
270. H. Beyer and K. Leverenz, *Chem. Ber.*, 94,263 (1961).
271. T. J. Kasper and D. E. Rivard, U.S. patent, 3,116,297 (1963); *Chem. Abstr.*, 61, 645h (1964).
272. A. Buzas, C. Dufour. and J. Roy, U.S. patent, 2,827,465 (1958); *Chem. Abstr.*, 53, 413d (1959).
273. A. Buzas, C. Dufour, J. Roy, and Société d'Etudes et d'Applications Chimiques, Fr. patent, 1,214,807 (1960); *Chem.* Abstr., *55*, 19955 (1961).
274. Laboratories Fher SA, Span. patent, 273,594 (1962); *Chem. Abstr.*, **60**, 508b (1964).
275. L. Kuczynski, Z. Machon, and L. Wykret, *Dissertationes* Pharm., 13, 299 (1961); *Chem. Abstr.*. **57**, 8540h (1962).
276. L. T. DiFazio and P. F. Smith, *J. Med. Chem.*, 9,631 (1966).

277. R. H. Mizzone and R. P. Mull, Belg. patent, 654,416 (1965); Chem. *Abstr.,* 64, 14171e (1966).
218. P. M. Quan and L. D. Quin, J. Org. Chem., 31,2487 (1966).
279. C. Iwata and D. E. Mekler, J. *Heterocycl.* Chem., 4,319 (1967).
280. J. Piťha and I. Ernest, Chem. *Listy,* 52, 1937 (1958); Chem. *Abstr.,* 53, 3258a (1959).
281. T. Maruyama, N. Kuraki, and K. Konishi, Kogyo *Kagaku* Zusshi, 68, 2428 (1965); Chem. *Abstr.,* 65, 13849f (1966).
282. F. Bohlmann, E. Winterfeldt, and H. Brackel, Chem. *Ber.,* 91,2194 (1958).
283. J. Wrobel and Z. Dabrowski, *Rocz.* Chem., 40, 317 (1966); Chem. *Abstr.,* 65, 684f (1966).
284. F. Mareš and M. Hudlický, Chem. *Listy,* 52, 1933 (1958); Chem. *Abstr.,* 53, 3257g (1959).
285. L. W. Walter and P. Margolis, J. *Med.* Chem., 10,498 (1967).
286. W. L. Bencze and L. I. Barsky, J. *Med.* Phurm. Chem., 5, 1298 (1962).
287. W. L. Bencze, Belg. patent, 626,022 (1963); Chem. *Abstr.,* 60, 14481h (1960).
288. W. L. Bencze, U.S. patent, 3,238,218 (1966); Chem. *Abstr.,* 65, 694c (1966).
289. W. L. Bencze, Belg. patent, 611,278 (1962); *Chem. Abstr.,* 57, 15080f (1962).
290. Upjohn Co., Brit. patent, 1,053,312 (1966); Chem. *Abstr.,* 66, 85701q (1967).
291. Y. Morimoto, *Yakugaku* Zusshi, 82,386 (1962); Chem. *Abstr.,* 58, 3421g (1963).
292. J. Moszev and B. Fisher, Zesz. *Nauk. Univ. Jagiellon,* Pr. Chem., 11, 103 (1966); Chem. *Abstr.,* 68, 114382k (1968).
293. CIBA Ltd., Brit. patent 974,137 (1964); Chem. *Abstr.,* 62, 7737f (1965).
294. C. E. Loader and C. J. Timmons, J. Chem. Soc., 1078 (1966).
295. F. Kröhnke and K. F. Gross, Chem. *Ber.,* 92, 22 (1959).
296. R. Tschesche and G. Sturm, U.S. patent, 3,290,312 (1966); *Chem. Abstr.,* 66, 37958g (1967).
297. R. Barchet and K. W. Merz. *Tetrahedron Lett.,* 2239 (1964).
298. H. Burford, A. R. Gault, S. T. Coker, and W. L. Nobles, J. *Amer. Pharm. Assoc. Sci.* Ed., 48,669 (1959); Chem. *Abstr.,* 54, 3859d (1960).
299. N. P. Buu-Hoi and P. Jacquignon, Fr. patent, M2379 (1964); Chem. *Abstr.,* 61, 1840g (1964).
300. J. B. Marco, Span. patent 275,507 (1962); Chem. *Abstr.,* 60, 1713d (1964).
301. W. J. Middleton, U.S. patent, 2,914,534 (1959); Chem. *Abstr.,* 54, 9962e (1960).
302. E. Szarvasi, Fr. patent Addn., 83,531 (1964); Chem. *Abstr.,* 62, 535a (1965).
303. Y. Ormote, K. T. Kuo, and N. Sugiyama, Bull. Chem. *Soc.* Jup., 40, 1695 (1967); Chem. *Abstr.,* 68, 21803h (1968).
304. C. D. Lunsford and A. D. Cale, Jr., U.S. patents 3,192,210, 3,192,221, and 3,192,210 (1965); Chem. *Abstr.,* 63, 11504b (1965).
305. T. Kato, T. Atsumi, and H. Sasaki, *Yakugaku* Zusshi, 85, 812 (1965); Chem. *Abstr.,* 63, 18018g (1965).
306. S. Miyano and N. Abe, Tetrahedron *Lett.,* 1509 (1966).
307. T. Urbanski, B. Serafinowa, C. Belzecki, J. Lange, H. Makurukowa, and M. Makosza, Polish patent, 47,902 (1964); Chem. *Abstr.,* 61, 4279g (1964).
308. W. L. Bencze, Belg. patent, 622,295 (1963); Chem. *Abstr.,* 59, 10001h (1963).
309. C. F. Huebner and W. L. Bencze, Belg. patent, 626,200 (1963); Chem. *Abstr.,* 60, 10620e (1964).
310. C. F. Huebner and W. L. Bencze, Belg. patent, 626,201 (1963); Chem. *Abstr.,* 60, 9221b (1964).
311. F. E. Cislak, U.S. patent, 2,868,794 (1959); Chem. *Abstr.,* 53, 10255d (1959).
312. J. A. Adamick and R. J. Flores, J. *Org.* Chem., 29,572 (1964).

313. R. K. Hill, C. E. Glassick, and L. J. Fliedner, *J. Amer.* Chem. *Soc.*, 81,737 (1959).
314. E. Maruszewska-Wieczorkowska and J. Michalski, Rocz. **Chem.**, 38, 625 (1964); Chem. Abstr., 61, 10702h (1964).
315. K. Schenker and J. Druey, *Helv. Chim. Acta*, 42,2571 (1959).
316. J. **S.** Walia, L. Heindl, H. Lader, and P. **S.** Walia, Chem. *Ind.* (London), 155 (1968).
317. W. L. Bencze, Belg. patent 626,962 (1963); Chem. Abstr., 60, 6828f (1964).
318. K. Fukui, M. Kondo, and H. **Kitano**, Jap. patents, 12,418 and 12,419 (1961); Chem. Abstr., 56, 8536d (1962).
319. **W**. Schulze, J. *Prakt.* Chem., 19, 91 (1962); Chem. Abstr., 58, 12509f (1963).
320. E. J. Poziomek and A. R. Melvin, **U.S.** patent, 3,209,008 (1965); Chem. Abstr.. 63, 18041g (1965).
321. W. Sauermilch and A. Wolf, *Arch.* Pharm. (Weinheim), 292, 38 (1959).
322. F. Gude, Ger. patent, 1,217,384 (1966); *Chem.* Abstr.. 65,53748 (1966).
323. W. Mathes and W. Sauermilch, *Ann.* Chem., 618, 152 (1958).
324. A. Banashek and M. N. Shchukina, Zh. Obshch. Khim., 32,205 (1962); Chem. Abstr.. 57, 16586b (1962).
325. W. Mathes and W. Sauermilch, Chem. *Ber.*, 93,286 (1960).
326. T. Kato and T. Atsumi, Yakugaku Zasshi, 87, 961 (1967); Chem. Abstr., 68, 49422g (196*8)*.
328. H. Hamana, B. Umezawa, Y. Goto, and K. Noda, Chem. Pharm. Bull. (Tokyo), 8,692 (1960); Chem. Absrr., 55, 18723d (1961).
329. E. J. Poziomek and **A.** R. Melvin, J. *Org.* Chem., 26,3769 (1961).
330. **O.** Weissel, Ger. patent, 1,118,784 (1961); *Chem.* Absfr., 57, 4639c (1962).
331. E. Jucker and A. J. Lindemann, U.S. patent, 3,041,343 (1962); Chem. Abstr., 57, 13764c (1962).
332. W. L. Bencze and G. N. Walker, U. **S.** patent, 3,337,565 (1967); Chem. Abstr., 68, 114446j (1968).
333. G. N. Walker, **W.** L. Bencze, and J. B. Ziegler, U.S. patent, 3,337,566 (1967); *Chem.* Abstr., 68, 29608u (1968).
334. Dynamit-Nobel, Belg. patent, 635,427 (1963); *Chem.* Abstr., 61, 11977f (1964).
335. H. J. Kabbe, Ann. Chem., 704,144 (1967).
336. J. Kreidl, **S.** Jager, and B. Benke, Hung. patent, 149,888 (1962); **Chem.** Abstr., 60, 9253e (1964).
337. G. Ehrhart, H. Ruschig, and K. Schmitt, Ger. patent, 1,116,226 (1961); *Chem.* Abstr.. 57, 2199c (1962).
338. E. Szarvasi, ***C.*** R. Acad. Sci. Paris, Ser. *C*, 259, 166 (1964); *Chem.* Abstr., **61**, 8266e (1964).
339. Smith, Kline, and French Labs., Nether. patent appl., 6,512,616 (1966); Chem. Abstr., 65, 7095c (1966).
340. R. Fusco and G. Bianchetti, Brit. patent, 879,247 (1961); Chem. Abstr., 56, 12859f (1962).
341. L. Kuczynski and L. Wykret, Dissertations Pharm., 16, 485 (1964); Chem. Abstr., 11537b (1965).
342. J. Grosselck, L. Beress, H. Schenk, and G. Schmidt, *Angew.* Chem. Intern. Ed., **4**, 1080 (1965).
343. A. E. Frost and H. H. Freedman, *J. Org.* Chem., 24, 1905 (1959).
344. R. Selleri, G. Orzalesi, and **O.** Caldini, Boll. Chim. Farm., 105, 117 (1966); Chem. Abstr., 65, 3821 (1966)..
345. S. Tatsuoka, ***Y*.** Yeno, K. Tanaka, and T. Ueyanagi, Jap. patent, 11,831 (1962); Chem. Abstr., 59, 10006c (1963).

346. K. Patzelt and J. Ctvrtnik, Czech. patent, 117,825 (1966); Chem. ***Abstr.,*** 66, 2481j (1967).
347. Lepetit S.p.A., Belg. patent, 624,836 (1963); Chem. ***Abstr.,*** **59,** 11445g (1963).
348. G. Jommi, F. Pelizzoni, and A. Fiecchi, *Ann.* Chim. (Rome), **51,** 1340 (1961); *Chem.* ***Abstr..*** 56, 15478d (1962).
349. A. R. Katritzky, J. A. T. Beard, and N. A. Coats, **J.** Chem. *Soc.,* 3680 (1959).
350. J. A. Weisbach, K. R. Williams, N. Yim, J. L. Kirkpatrick, E. L. Anderson, and B. Douglas, Chem. Ind. (London), 662 (1966).
351. F. Zymalkowski and B. Trentrog. ***Arch. Pharm.*** (Weinheim), 293, 47 (1960); Chem. ***Abstr.,*** **55,** 21108e (1961).
352. K. H. Biichel and F. Korte, Z. ***Anal. Chem..*** 190,243 (1962); Chem. ***Abstr.,*** **58,** 6333b (1962).
353. M. Saunders and E. H. Gold, *J.* ***Org.*** Chem., 27, 1439 (1962).
354. W. Ciusa and G. Barbiroli, *Ann.* Chim. (Rome), 56, 3 (1966); Chem. ***Abstr.,*** **65,** 3828d (1966).
355. I. A. Calo, **V.** Evdokimoff, and C. Cardini, Rend. ***Ist. Super. Sanita,*** 25, 529 (1962); ***Chem. Abstr.,*** **59,** 2808d (1963).
356. **V.** Quercia, *Boll.* Chim. ***Farm.,*** 100,834 (1961); *Chem. Abstr.,* 57,58831 (1962).
357. G. A. Robison and F. W. Schueler, J. *Pharm.* ***Sci.,*** 50,602 (1961).
358. **W.** Bruegel, ***Z. Elektrochem.,*** 66, 159 (1962); Chem. ***Abstr.,*** **57,** 307b (1962).
359. K. Hoffmann, J. **Heer,** E. Sury, and E. Urech, U.S. patent, 2,957,879 (1960); *Chem.* ***Abstr., 55,*** 10478f (1961).
360. F. H. Case and W. A. Butte, *J. Org.* Chem., 26,4415 (1961).
361. **1.** Kelemen and R. Wizinger, ***Helv.*** Chim. ***Acta,*** **45,** 1908 (1962).
362. J. Swiderski and J. Izdebski, *Rocz.* Chem., 36,963 (1962); Chem. ***Abstr.,*** 58, 5625a (1963).
363. A. Zaitsev, **M.** M. Shestaeva, and **V.** A. Zagorevskii, Khim ***Geterotsikl Soedin,*** 168 (1967); *Chem.* ***Abstr.,*** **67,** 73498m (1967).
364. E. **S.** Nikitsikaya, E. E. Mikhlina, L. N. Yakontov, and **V.** Ya Furshtatova, Zh. Obschch. ***Khim.,*** 28,2186 (1958); ***Chem. Abstr.,*** **53,** 9207d (1959).
365. **M.** Freyrnann, R. Freymann, and C. Geissner-Prettre, ***Arch. Sci.*** (Geneva) 13, **Spec.** No. 506 (1960); ***Chem. Abstr.,*** **58,** 3289d (1963).
366. A. Roedig and K. Grohe, ***Chem. Ber.,*** 98,923 (1965).
367. J. R. Geigy A. G., Nether. appl. 6,600,522 (1966); *Chem.* ***Abstr..*** **65,** 16948b (1966).

Chemistry of Heterocyclic Compounds, Volume 14
Edited by R. A. Abramovitch

CHAPTER XII

Pyridinols and Pyridones

HOWARD TIECKELMANN

State University of New York
Buffalo, New York

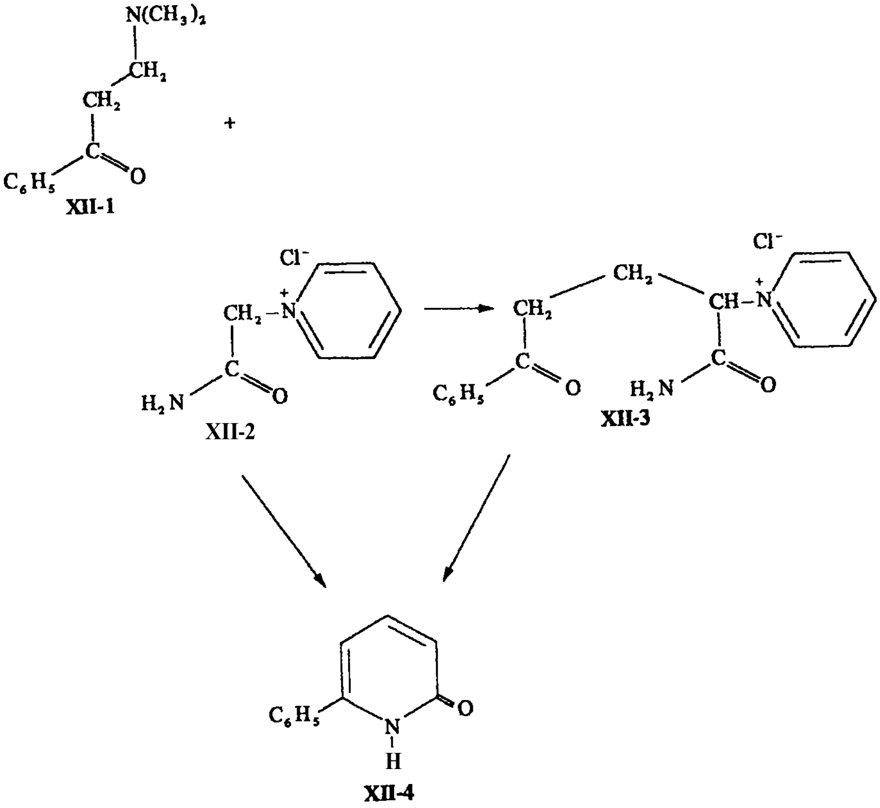
I. Preparation

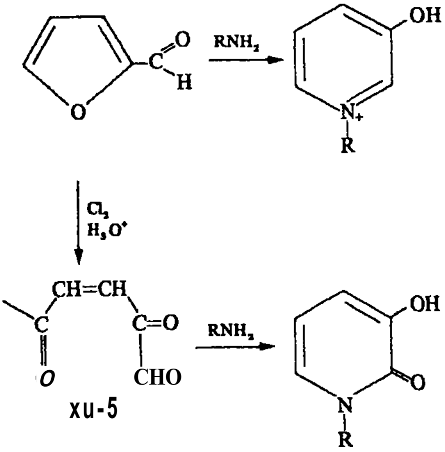
A large variety of ring closure reactions have been applied to the direct formation of pyridinols and pyridones. Judicious choices of open-chain intermediates often can provide excellent routes to a variety of substituted pyridines and fused ring systems.

The ring closures presented in this section are classified according to the number of ring carbons furnished by each reagent: (1) one reactant provides all five ring carbons; (2) one reactant provides four ring carbons; and (3) one reactant provides three ring carbons.

This classification of ring closure is arbitrary. The isolation of an acyclic intermediate often is the choice of the investigator. For example, 6-phenyl-2-pyridone (XII-4) has been directly prepared from XII-1 and XII-2 or from the isolable intermediate XII-3.[1]

The further classification used here and earlier' into (1) ring closures and (2) preparations from other rings is also arbitrary and often appears inappropriate in that a useful relationship such as that between furfural and the acyclic 2-oxoglutaconaldehyde (XII-5) may not be apparent.[3]

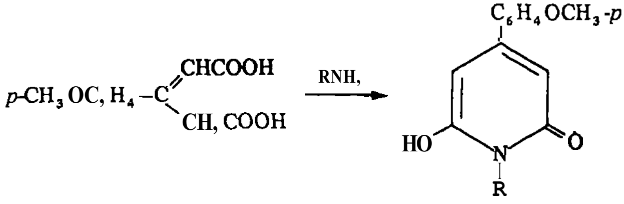

N(CH3)2
CH2
CH2
C
O
C6H5
XII-1
+
Cl−
CH2−N+
C
H2N
O
XII-2
CH2
CH2
C
O
C6H5
CH−N+
Cl−
C
H2N
O
XII-3
C6H5
N
H
O
XII-4


O
C
O
H
RNH2
OH
N+
R
Cl2
H3O+
H
CH=CH
C
O
C=O
CHO
XII-5
RNH2
OH
O
N
R

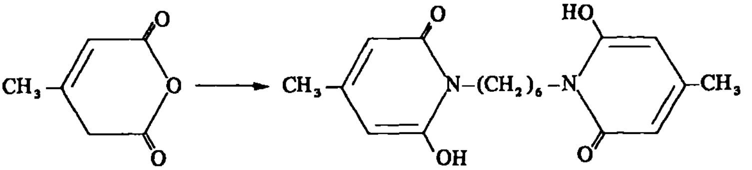
1. Ring Closures of Acyclic Compounds That Provide Five Ring Carbons

A. *Glutaconic Acid and Its Derivatives*

Glutaconic acid derivatives have been used extensively for the synthesis of **2,6-pyridinediols**;[4] however, there has been relatively little interest in these compounds during the past ten years. **β-(*p*-Methoxyphenyl)glutaconic** acid (XII-6) and methylamine or benzylamine give N-methyl- or *N*-benzyl-6-hydroxy-**4-(*p*-methoxyphenyl)-2-pyridone (XII-7)**.[5] β-Methylglutaconic anhydride and hexamethylenediamine give the dipyridone (XII-8) when boiled in **xylene**.[6]



XII-6 **xn-7**

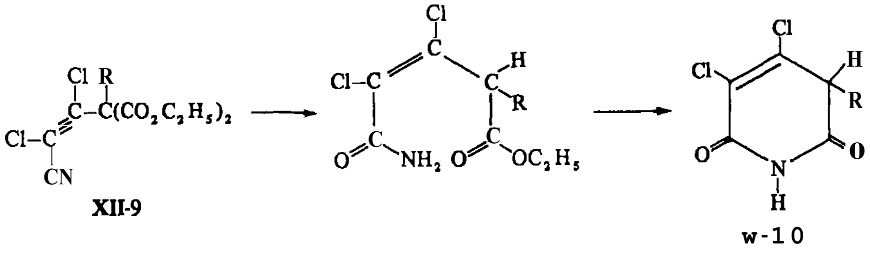


XII-8

In addition to cyclizations where glutaconic acid derivatives provide five ring carbons, cyclizations are known where a glutaconate provides four ring carbons and a 2-pyridone is formed (Section I.2.B., p. 616).

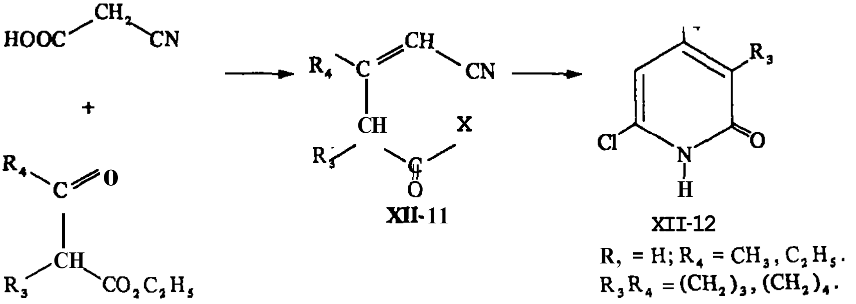
Alkylations of diethyl α-alkylmalonates with trichloroacrylonitrile give the β-cyanovinylmalonates (XII-9), which cyclize in sulfuric acid to 3-alkyl-4,5-**dichloro-2,6-pyridinediones** (XII-10) in good yield.'

β-Ketoesters and cyanoacetic acid in benzene containing ammonium acetate and acetic acid give ethyl γ-cyano-2-butenoates (XII-11, X = OC_2H_5), which are saponified to the corresponding acids (XI-11, X = OH) and then are converted to the acyl chlorides (XII-11, **X** = Cl) with phosphorus pentachloride. The acyl chlorides cyclize to 6-chloro-2-pyridones **(W-12)** in n-butyl ether containing hydrogen chloride.'



XII-9

w-10

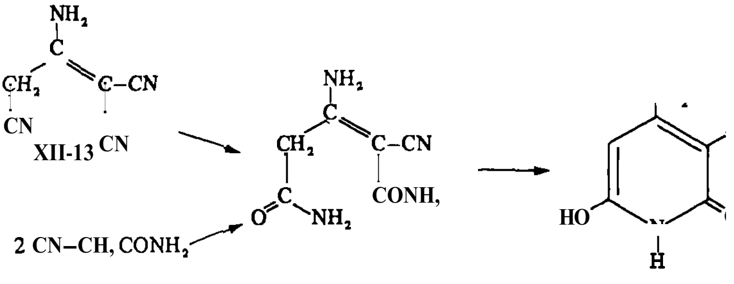


XII-11

XII-12

$R_1 = H; R_4 = CH_3, C_2H_5.$
$R_3R_4 = (CH_2)_3, (CH_2)_4.$

When the dimer of malononitrile, 2-amino-1,1,3-tricyanopropene (**XII-13**) is heated with hydrochloric acid, it gives glutazinamide (**XII-14**; R = $CONH_2$, 77% yield). Cyanoacetamide and sodium ethoxide in ethanol form glutazinonitrile (**XI-14**, R = CN).[9]

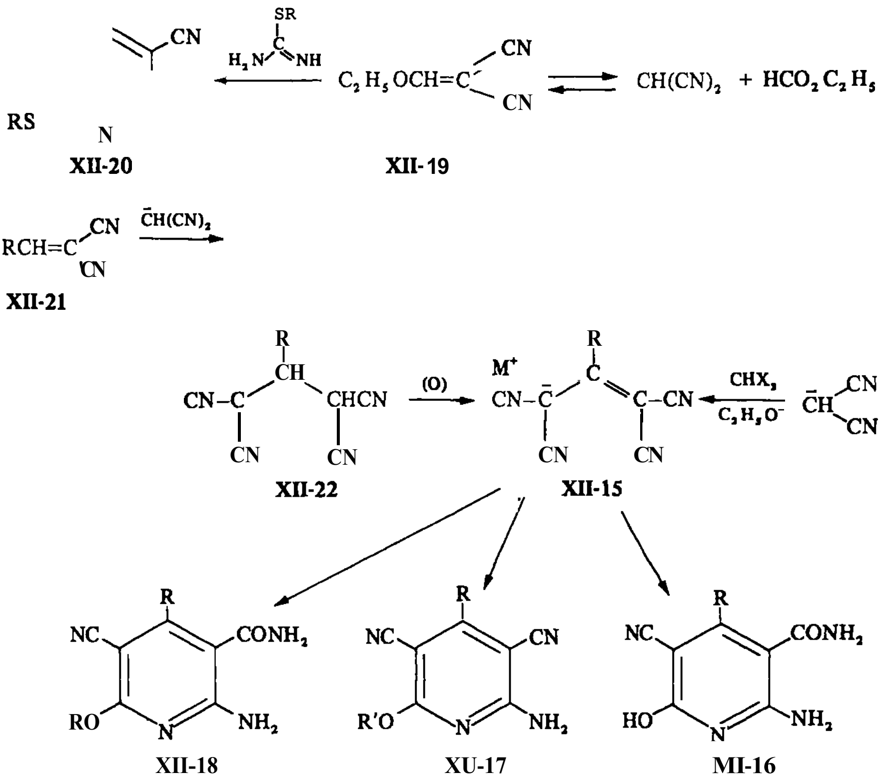


XII-13

XII-14

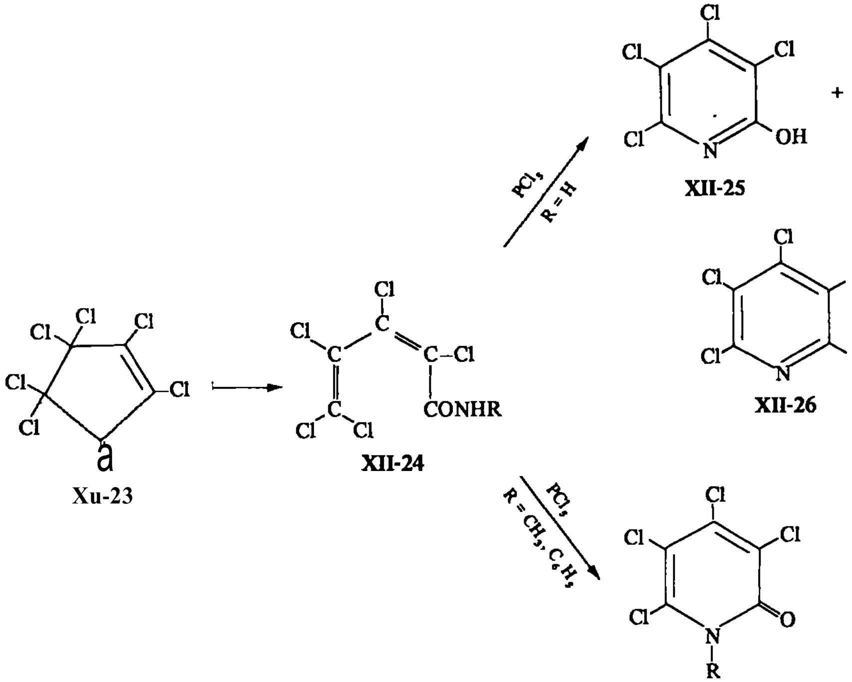
The potassium salt of tetracyanopropene (**MI-15**, M = K) gives 2-amino-5-cyano-6-hydroxy-3-pyridinecarboxamide (**XII-16**, R = H) when heated in aqueous alkali. " In aqueous alcohols, **MI-15** forms **6-alkoxy-2-amino-3,5-dicyanopyridines** (**XII-17**; R = **H**, **R'** = CH_3, C_2H_5) or **6-alkoxy-2-amino-5-cyano-3-pyridinecarboxamide** (**XII-18**, R = H) depending on conditions." Bromoform and chloroform react with malononitrile in the presence of sodium alkoxides to give **XI-17** (R = H).[11]

Ethoxymethylenemalononitrile (XII-19), a useful intermediate for the synthesis of 4-amino-5cyanopyrimidines **(XII-20)**, gives **MI-17** (**R** = **H**, R' = C_2H_5) in aqueous alcohol. A retrocondensation of **W-19** forms some malononitrile, which reacts with more **MI-19** to form **XII-15** (R = **H**) and then **XII-17** (R = H).[10] Benzylidenemalononitrile (**XII-21**, **R** = C_6H_5) reacts similarly. However, a Michael addition of the malononitxile anion to **MI-21** gives the anion of 2-phenyltetracyanopropane (**MI-22**, R = C_6H_5), which, through autooxidation or hydride transfer, forms **MI-15** (R = C_6H_5).[12] Aldehydes and malononitrile have been used to form **MI-17** (R = alkyl, aryl; R' = C_2H_5) in one step.[13]



B. *Pentadienoic Acid Derivatives*

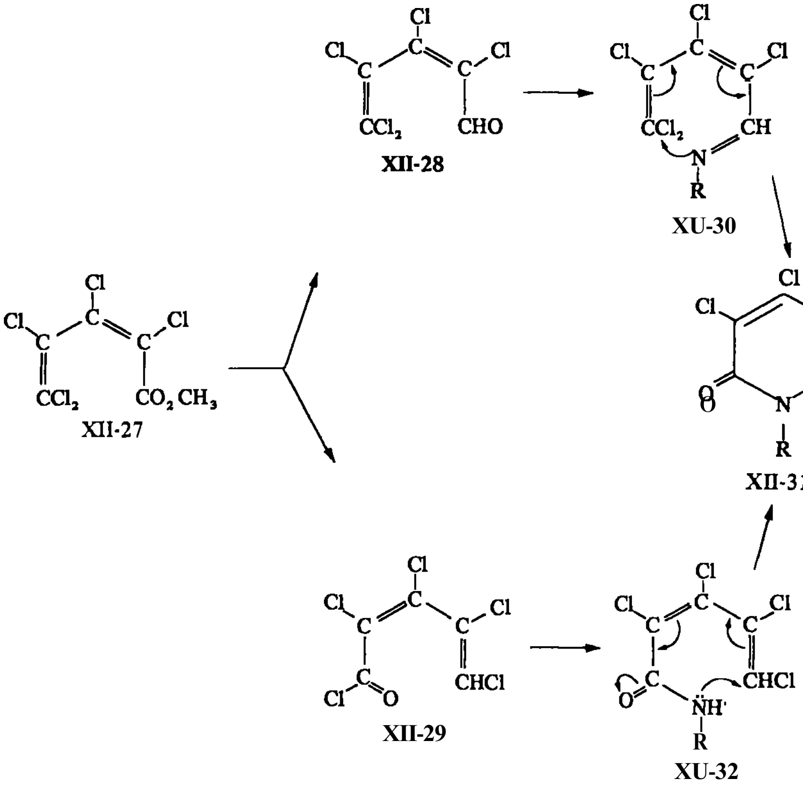
Condensation of perchloropropene with trichloroethylene gives 4H-nonachloro-1-pentene, which can be converted to **perchlorocyclopentene-3-one (XII-23)**[14] or converted to **perchloro-2,4-pentadieneamides (MI-24)** *via* perchloro-2,4-pentadienoic acid.[15] When **MI-23** is treated with ammonia, ring opening occurs to give XII-24. Cyclization of W-24 with PCl_5 gives perchloro-2-pyridinol **(XII-25)** and pentachloropyridine **(XII-26,** 67%).[16] N-Substituted amides (XII-24; R = CH_3,C_6H_5) can be cyclized to pyridone by heating them alone or with PCl_5.[15]

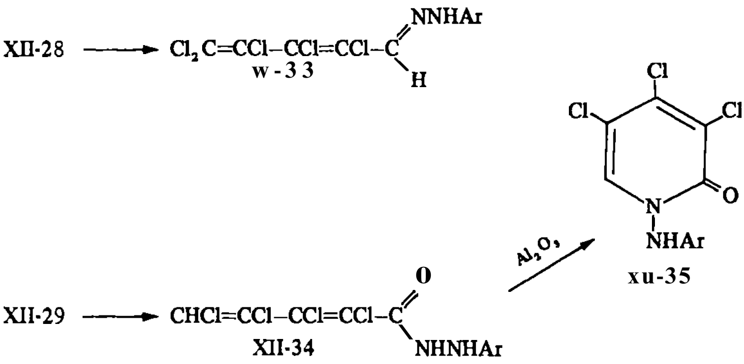


Lithium aluminum hydride and methyl **perchloro-2,4-pentadienoate (XII-27)**[17] at -78" form dienes XII-28 and **XII-29.**[15] The mixture of isomers **XII-28** and XII-29, or pure **XII-28,** is converted to W-29 by heating in CCl_4.[17] The mixture reacts with aryl hydrazines *via* hydrazones (W-30, R = arylamino) to form *N*-**arylamino-3,4,5-trichloro-2-pyridones** (XII-31), with semicarbazide to form *N*-ureido-3,4,5-trichloro-2-pyridone (XII-31, R = ureido) (Section IV.3., p. 839) and with ammonia or primary amines to form amides (XII-32), which are readily cyclized to pyridones **(XII-31).**[15]

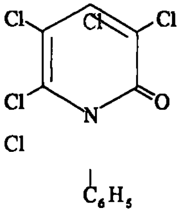
Compounds **XII-28** and W-29 react with **2,4-dinitrophenylhydrazine** to form isomeric products W-33 and **W-34,** which cyclize to 3,4,5-trichloro-**1-(2,4-dinitroanilino)-2-pyridone (XII-35).**[17]

Perchloropentadienoyl chloride'' and **2,3,4,5-tetrachloro-5-bromo-2,4-pentadienoyl chloride''** react with aniline to form *N*-phenylperchloro-2-pyridone **(MI-36)** *via* the corresponding *N*-phenylamide. The 2-pyridones **XII-37** and **XII-38** are prepared similarly from the appropriate bromo **analogs.''**

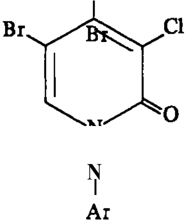




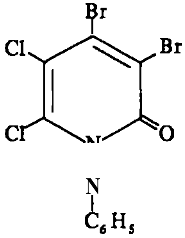
2,3,4,5-Tetrachloro-5-phenyl-2,4-pentadienamide (XII-39), prepared from perchloropentadienoyl chloride *via* a Friedel Crafts phenylation, is cyclized to 3,4,5-trichloro-6-phenyl-2-pyridone (XII-40) by pyrolysis or by heating with sodium hydroxide in methanol.[20]



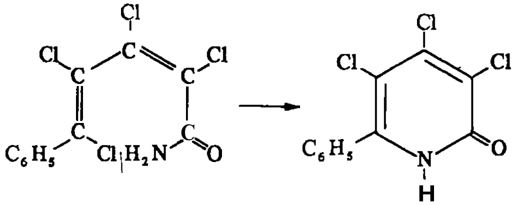
XII-36



W37



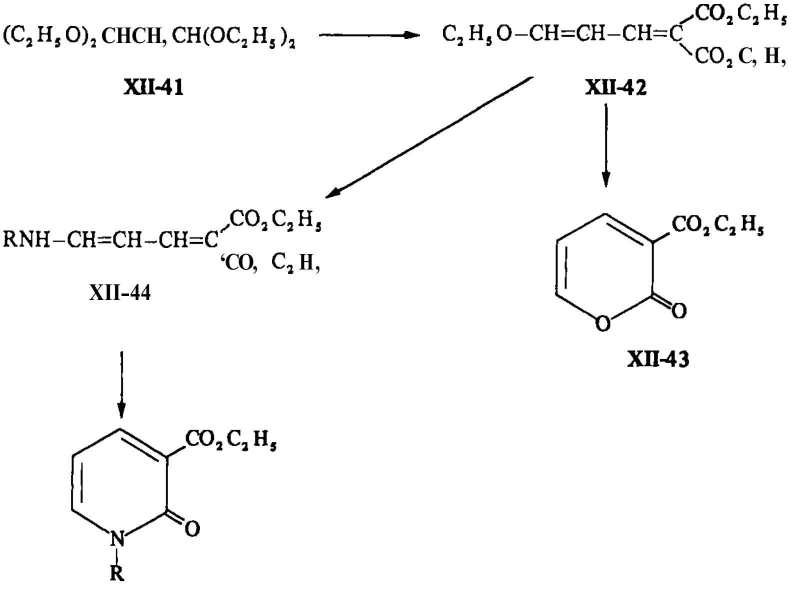
XII-38



XII-39

XII-40

1,1,3,3-Tetraethoxypropane (malonaldehyde tetraethylacetal) **(XII-41)** and diethyl malonate in acetic anhydride give diethyl 3-ethoxyallylidenemalonate **(XII-42)**, which cyclizes in polyphosphoric acid or formic acid to the pyrone **XII-43**. Reaction of **W42** with ammonia or benzylamine forms 3-aminoallylidenemalonates **(XII-44**; R = H, $CH_2C_6H_5$), which are cyclized to the ethyl a-pyridone-3carboxylates **(XII-45)** in alcoholic sodium ethoxide or piperidine.[21]



XII-41

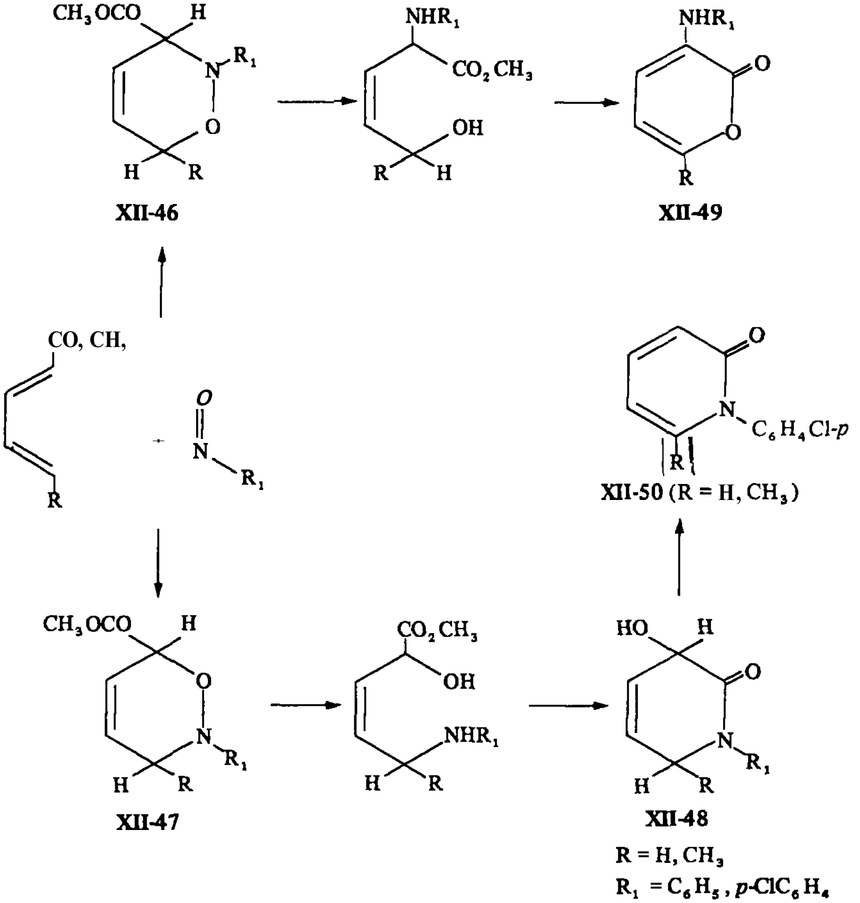
XII-42

XII-44

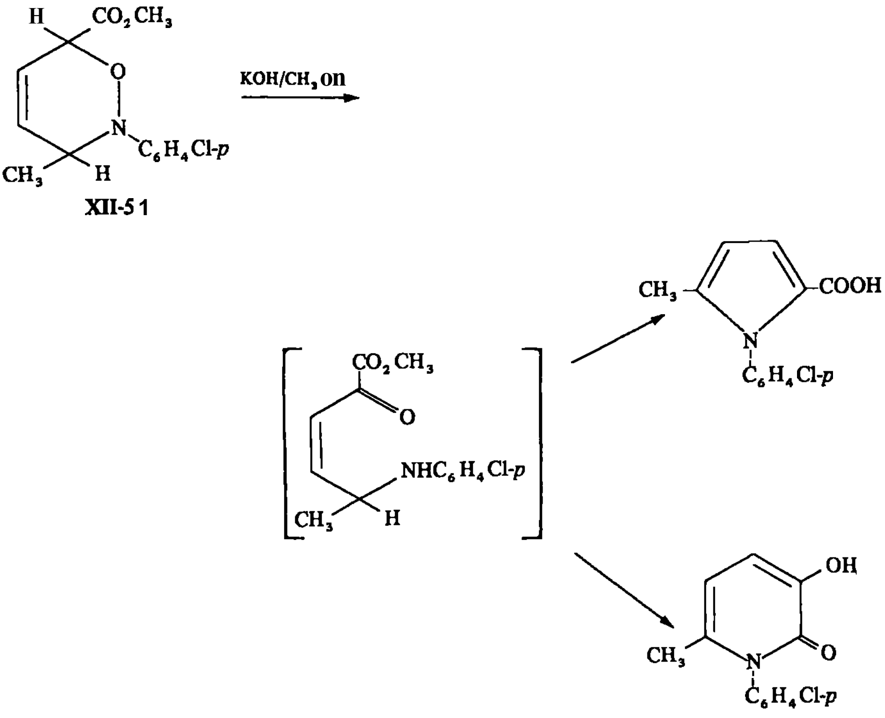
XII-43

XII-45

Nitroso compounds and carbomethoxydienes form Diels-Alder adducts, the 3,6-dihydro-1,2-oxazines XII-46 and XII-47,[22, 23] which are reduced by zinc in acetic acid to the 3,6-dihydro-2-pyridones (XII-48) and the 2-pyrones (MI-49)respectively. Because of the directive effect of the carbomethoxy group, W47, if not formed exclusively, is the major product. Dehydration of XII-48 to 1-aryl-6-substituted-2-pyridones (MI-50) occurs on heating with concentrated hydrochloric acid.[24]



The oxazines of structure W47 form pyrroles when they are treated with potassium hydroxide in methanol. However, under appropriate conditions W-51 in methanolic KOH forms 63% of 3-hydroxy-6-methyl-*N*-(*p*-chlorophenyl)-2-pyridone (W-52) and 33% of 1-(*p*-chlorophenyl)-5-methyl-2-pyrrolecarboxylic acid.[24]



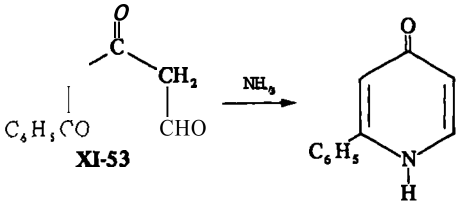
XII-51

XII-52

C. Triketones, Ketodialdehydes (Oxoglutaconaldehydes), and Ketodicarboxylic Acid Derivatives

Hauser and co-workers have prepared a number of triketones by (1) acylation of benzoylacetone with aliphatic esters employing lithium amide,” (2) by twofold aroylation of acetone with methyl esters using sodium **hydride,**[26] (3) by aroylation and acylation of aliphatic diketones with potassium amide in liquid ammonia[27] and (4) by aroylation of sodioacetoacetaldehyde[28] in the presence of potassium **amide.**[27] Disodio- and dipotassiobenzoylacetone are not acylated by ethyl acetate or by phenyl propionate.[25, 29] However, dilithiobenzoylacetone and dilithioacetylacetone with an excess of lithium amide are acylated by aliphatic esters. It is usually more convenient to synthesize 4-pyridones directly from these triketones by cyclization with ethanolic ammonia rather than by way of the intermediate Qpyrone.”

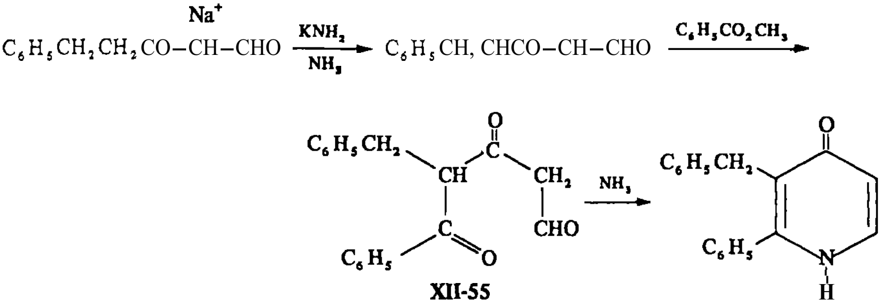
5-Phenyl-3,5-diketopentanal (W-53) is converted to 2-phenyl-4-pyridone (XII-54) in good yield with ethanolic ammonia.’ [7]



XI-53

XII-54

The γ-benzyl derivative of XII-53 (W-55) prepared from the sodium salt of **5-phenyl-1,3-pentanedione**, potassium amide, and methyl benzoate, was not isolated but was converted to 5-benzyl-6-phenyl-4-pyridone with ammonia in ethanol.[27]



$$C_6H_5CH_2CH_2CO\!-\!\overset{Na^+}{CH}\!-\!CHO \xrightarrow[NH_3]{KNH_2} C_6H_5CH_2CHCO\!-\!CH\!-\!CHO \xrightarrow{C_6H_5CO_2CH_3}$$

XII-55

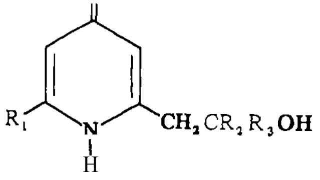
Condensation at the terminal methyl group of 1-phenyl and 1-(p-methoxyphenyl)-1,3,5-hexanetrione (W-56) with benzophenone or anisaldehyde in the presence of three equivalents of sodamide in liquid ammonia gives the hydroxytriketones (XII-57), which cyclize with ammonia to give the 4-pyridones (XII-58a–c).[30]

$$R_1COCH_2COCH_2COCH_3 \longrightarrow$$

XII-56

$$R_1COCH_2COCH_2COCH_2CR_2R_3OH \longrightarrow$$

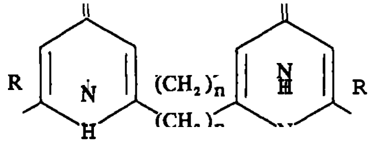
XII-57



XII-58a-c

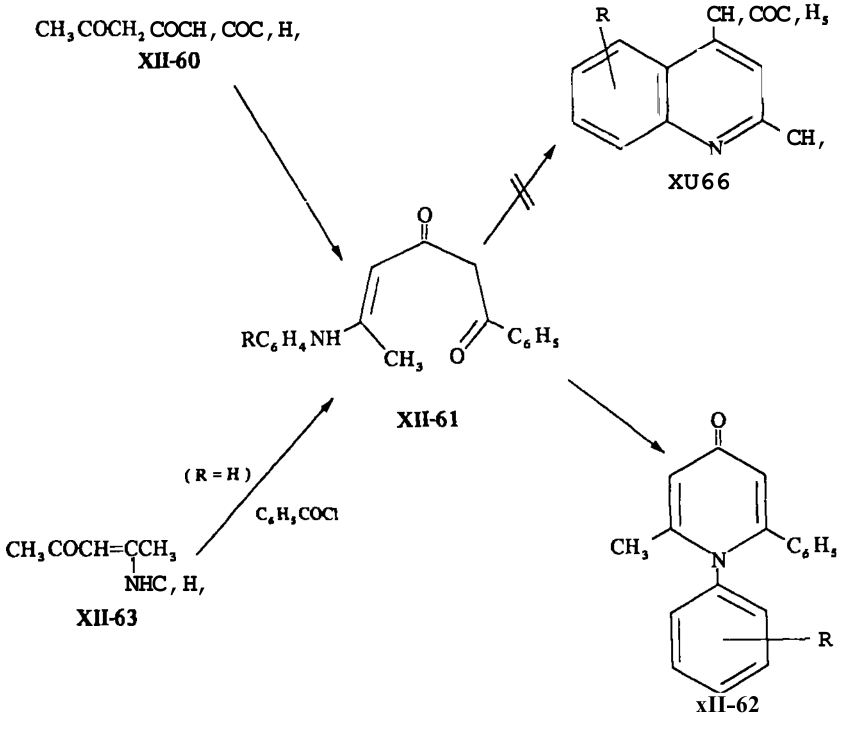
	R_1	R_2	R_3
a:	C_6H_5	C_6H_5	C_6H_5
b:	C_6H_5	p-$CH_3OC_6H_4$	H
c:	p-$CH_3OC_6H_4$	C_6H_5	C_6H_5

The trisodio salts of **W-56** are also alkylated with α,ω-dibromoalkanes to give the corresponding bis(triketones), which can be converted to the polymethylene-**bis-2-(6-aryl-4-pyridones)** (*W-59*, n = 5,6) with **ammonia.**[30a]

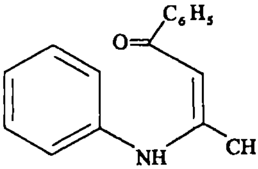


XII-59

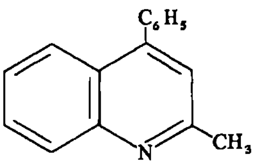
Although three different carbonyl groups are available, **6-phenyl-2,4,6-hexanetrione (XII-60)** reacts with aromatic amines to form the ketoenamines (XII-61; R = H, *o*-Cl, *p*-Cl, *p*-OCH$_3$), which cyclize to ***N*-aryl-2-methyl-6-phenyl-4-pyridones (XII-62)** in hot polyphosphoric acid. *n*-Butylamine and ***W-60*** give the corresponding ketoenamines, but these could not be cyclized to the pyridone by



this method. Instead they gave the **pyrone.**[31] The enamine (XII-63) forms a dipotassio salt with potassium amide in liquid ammonia, which reacts with benzoyl chloride to give the diketoenamine (XII-61, R = H).[32] Although the ketoenamine (XII-64) is cyclized to the quinoline (XII-65) by sulfuric **acid,**[33] quinolines (XII-66) were not detected in these **studies.**[31]

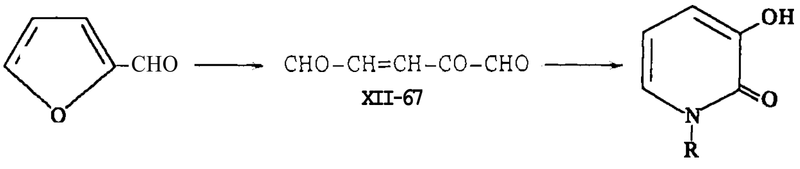


XII-64



XII-65

When furfural is oxidized with chlorine or bromine in an aqueous acidic medium, a solution of hydrates of oxoglutaconaldehyde (XII-67), to which the trivial name endialone has been given, is formed in high **yield.**[3] Endialone and ammonia or aliphatic amines give 3-hydroxy-2-pyridones (XII-68), usually in low **yield.**[3] Endialone **(XII-67)** and sulfamic acid give **XII-69** (43%) and **XII-70** (31%), which are slowly transformed to XII-71 and **XII-68 (R = H)**, respectively,

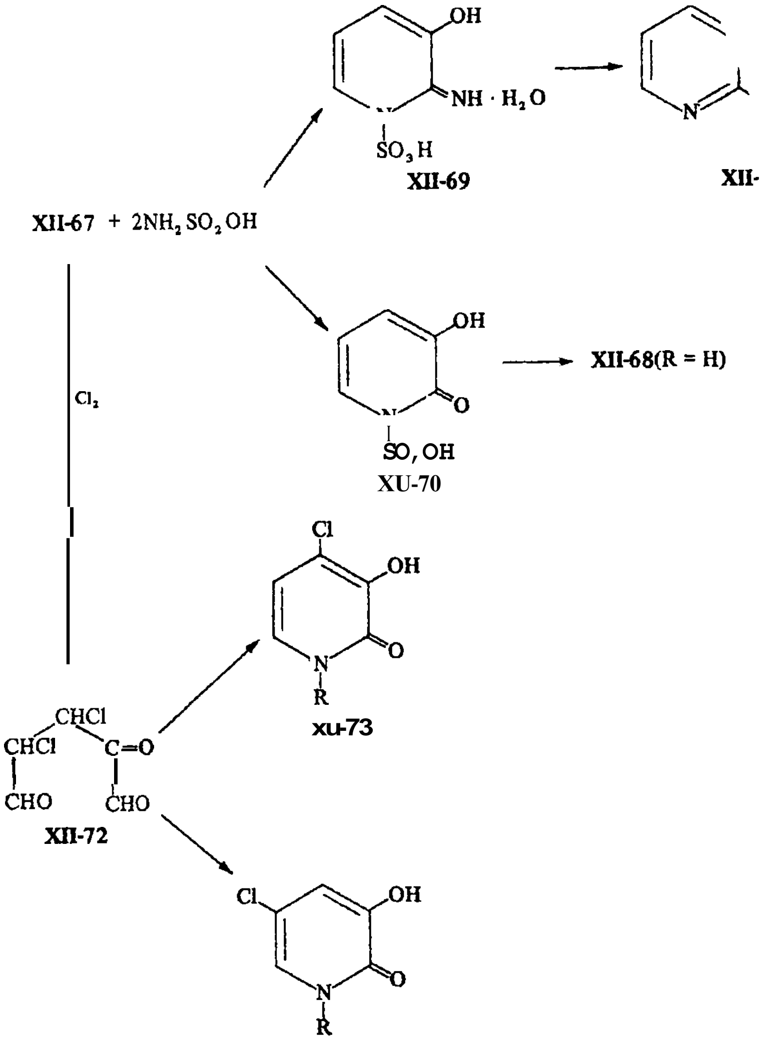


XII-68

R = H(69%), CH_3(19%), $(CH_2)_3N(CH_3)_2$(24%), CH_2COOH(8%)

on standing. Chlorine adds to XII-67 to form **2,3-dichloro-4-oxoglutaraldehyde** (XII-72), which reacts with ammonia at pH 7, with methylamine at pH 7.5, to give **4-chloro-3-hydroxy-2-pyridone** (W-73; R = H, CH_3), with anilines in strongly acidic solution to give **5-chloro-3-hydroxy-2-pyridones (XII-74, R =** aryl), and with sulfamic acid to give **W-74** (R = **H).**[3]

Diethyl **acetone-1,3-dicarboxylate** and a mixture of cold aqueous ammonia and liquid ammonia (1:1) are converted to **4,6-diamino-2-pyridone (XII-75).**[34]



XII-69

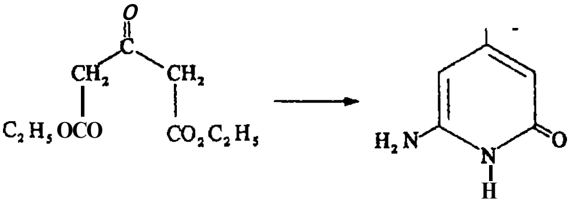
XII-71

XU-70

xu-73

XII-72

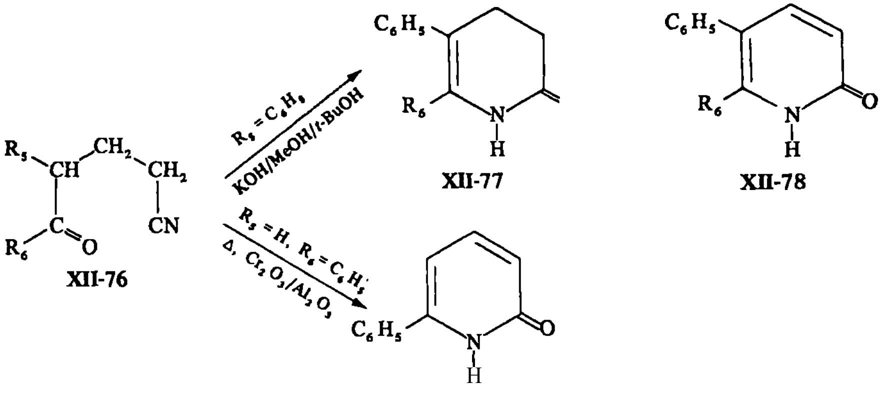
XII-74



xu-75

D. δ-Ketonitriles (3.4-Dihydro-2-pyridones)

Monocyanoethylation of deoxybenzoin and phenylacetone.in *t*-butyl alcohol gives γ-cyanoketones (XU-76;$R_5 = C_6H_5$, $R_6 = CH_3$, C_6H_5), which are cyclized by potassium hydroxide in t-butyl alcohol/methanol to **3,4-dihydro-5-phenyl-6-substituted-2-pyridones** (XII-77), which can be dehydrogenated to 5-phenyl-6-substituted-2-pyridones **(XII-78)**.[35] **When** γ-benzoylbutyronitrile is passed over Al_2O_3 at 400" or over Cr_2O_3/Al_2O_3 at 300 to 310°, 6-phenyl-2-pyridone **(W-79)**is **formed.**[36] Mixtures of products can be formed in these reactions; for example, γ-acetylvaleronitrile **(W-76, R_5** = R_6 = CH_3) is converted to 2,3-dimethylpyridine (6.6%), 5,6-dimethyl-1,6-dehydropiperidone (23%), and **5,6-dimethyl-3,4-dihydro-2-pyridone** (6%) at 340 to 360". At **400** to 410" some **5,6-dimethyl-2-pyridone** (6.6%) is formed.[36]



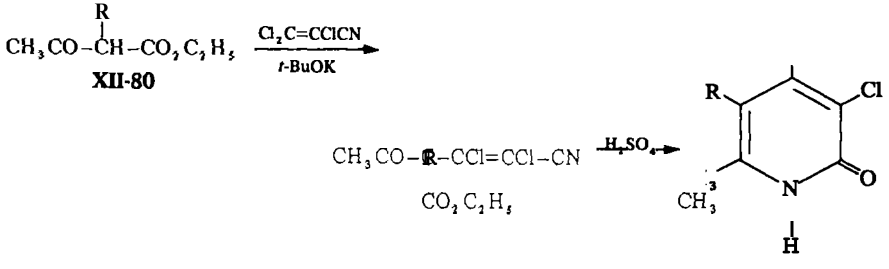
XII-76

XII-77

XII-78

XII-79

Trichloroacrylonitrile and ethyl α-alkylacetoacetates (XII-80) give **XII-81**, which cyclizes with sulfuric acid to **5-alkyl-3,4-dichloro-6-methyl-2-pyridones (XII-82).**[37]



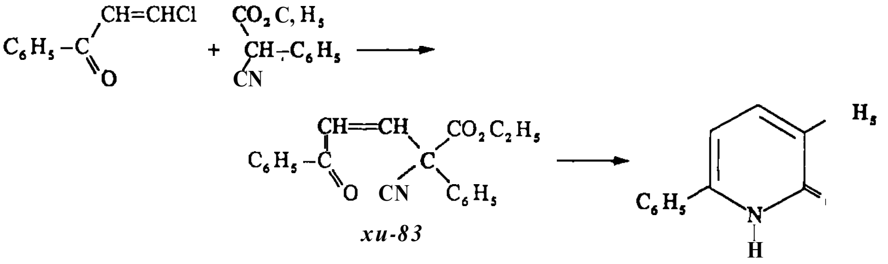
XII-80

XII-81

XII-82

R = H, CH, ,C, H_5 ,*n*-C_4H_9, $C_6H_5CH_2$

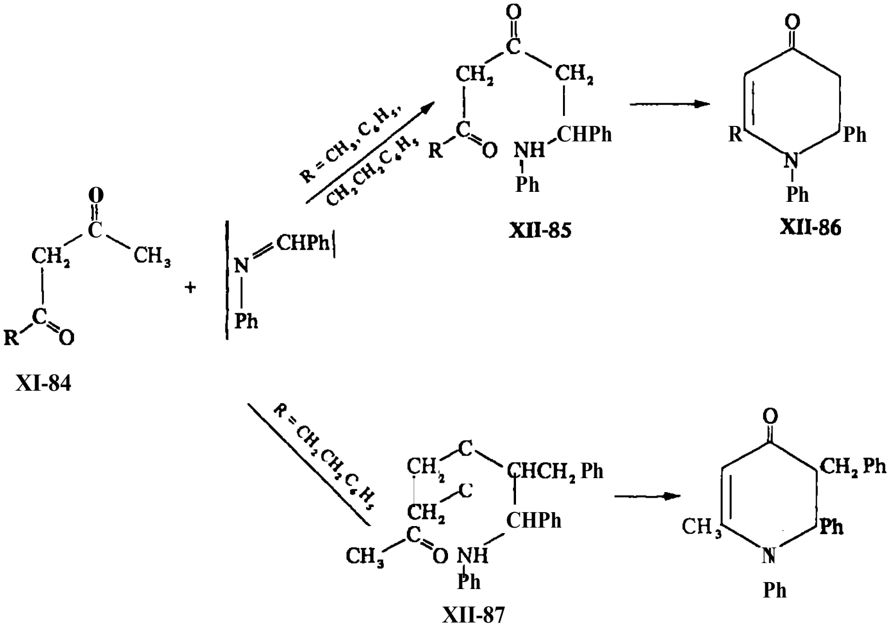
4-Carbethoxy-4-cyano-1,4-diphenyl-2-butene-1-one **(XII-83)**, from ethyl α-cyano-α-phenylacetate and phenyl β-chlorovinyl ketone, is cyclized in 86% sulfuric acid to **3,6-diphenyl-2-pyridone.**[38]



xu-83

E. *Miscellaneous*

β-Diketones **(XII-84**; R = CH_3, C_6H_5) condense **with** benzylideneaniline, but not with aliphatic Schiff bases, in the presence of potassium amide to give **2,3-dihydro-4-pyridones** *(W-86)*either directly (R = CH_3) or by treatment of **XII-85** (R = C_6H_5) with sulfuric acid. Under these conditions 6-phenyl-2,4-hexanedione **(XII-84**, R = $CH_2CH_2C_6H_5$) gives 1-anilino-1,7-diphenyl-3,5-heptanedione (MI-85, R = $CH_2CH_2C_6H_5$), which forms MI-86 (R = $CH_2CH_2C_6H_5$) on treatment with sulfuric acid. The isomeric dihydropyridone



XII-85

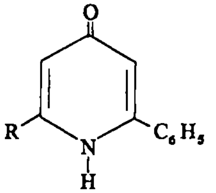
XII-86

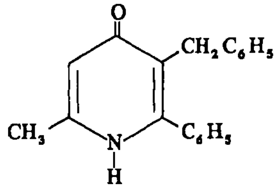
XI-84

XII-87

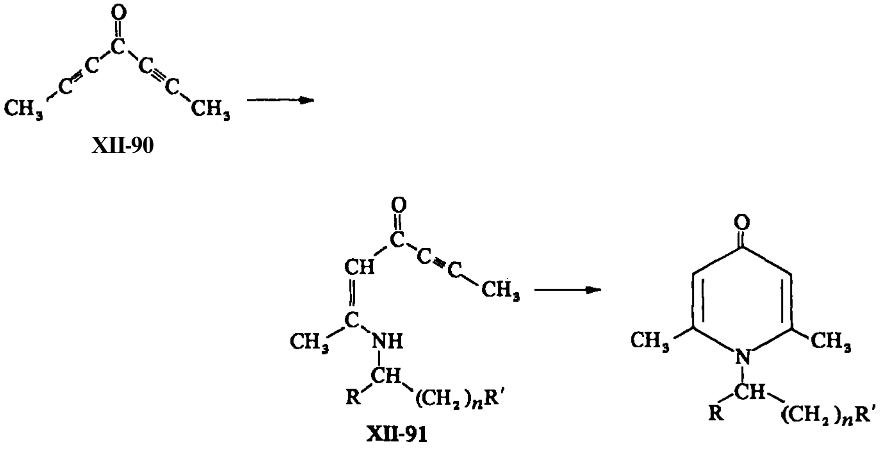
is a by-product in the formation of **W-86** (R = $C_6H_5CH_2CH_2$) presumably *via* **XII-87**.[39]

The β-diketones **(XII-84**; R = CH_3, C_6H_5, $C_6H_5CH_2CH_2$) are condensed with benzonitrile and potassium amide to give the 6-substituted-2-phenyl-4-pyridones (XII-88) directly.[40] The possible products *W-89*, isomeric with **XII-88** (R = $C_6H_5CH_2CH_2$), which could arise from the condensation of benzonitrile at C-5, were not isolated?'


XII-88


XII-89

Di-1-propynyl ketone (MI-90) and primary amines (ethylamine, isopropylamine) or amino acids that are unsubstituted in the a-position (glycine, β-alanine, ε-aminocaproic acid, glycylglycine, glycylleucine, alanylglycine) give enamines (**W-91**), which form *N*-substituted lutidones when their sodium salts are heated in water or their esters are heated in xylene. When 2-substituents are present, cyclization occurs when their calcium salts or amides are heated in aqueous alkali. When heated in the presence of Triton B and DMF, α-alanylamide and di-1-propynyl ketone give the lutidone.[41]

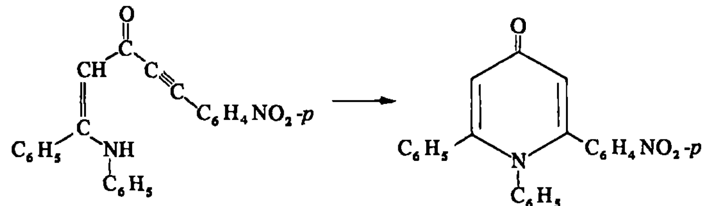

XII-90

XII-91

p-Nitrophenylpropiolyl chloride and sodium phenylacetylene give the diynone (**XII-92**), which reacts with aniline in alcohol to give XII-93, which cyclizes in boiling xylene to **1,6-diphenyl-2-(*p*-nitrophenyl)-4-pyridone**.[42]

$$p\text{-}NO_2C_6H_4\text{-}C{\equiv}C\text{-}COCl \xrightarrow{C_6H_5C{\equiv}CNa} p\text{-}NO_2C_6H_4\text{-}C{\equiv}C\text{-}CO\text{-}C{\equiv}C\text{-}C_6H_5 \longrightarrow$$

XII-92

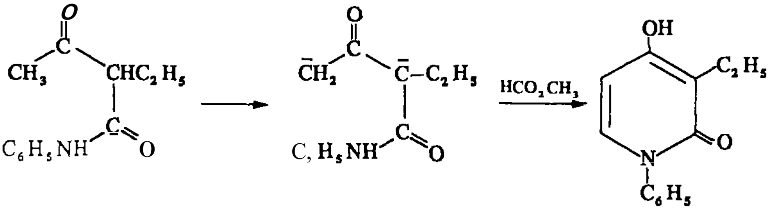


XII-93

2. Ring Closures in Which One Acyclic Compound Provides Four Ring Carbons

A. *Ketoamides*

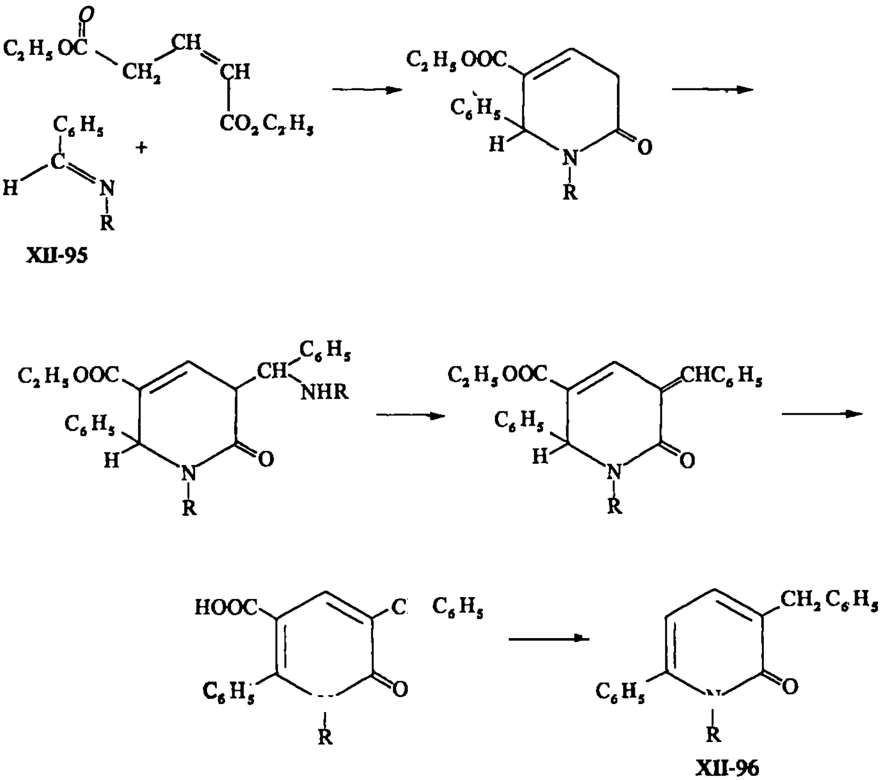
α,α-Diethylacetoacetamide reacts with methyl formate in the presence of sodium ethoxide in toluene to form **3,3-diethyl-2,4-pyridinedione.**[43] Using two equivalents of sodium, α-ethylacetoacetanilide, and methyl formate in toluene/methanol gives 3-ethyl-4-hydroxy-1-phenyl-2-pyridone **(XII-94).**[44]



XII-94

B. *Unsaturated Acid Derivatives*

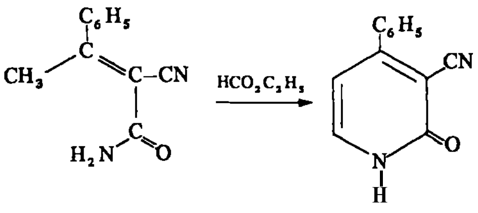
Diethyl glutaconate and two moles of *N*-benzylidenemethylamine (XII-95, R = CH_3) or benzylideneaniline (XII-95, R = C_6H_5) in xylene condense to give compounds characterized as 1-substituted-3-benzylidene-5-carbethoxy-2-oxo-6-phenyl-Δ^4-piperidenes (interpretation of NMR), which form 1-substituted-3-**benzyl-5-carboxy-6-phenyl-2-pyridones** after heating in methanolic potassium hydroxide. The carboxypyridones have been decarboxylated to XII-96.[45] α-Cyano-β-methylcinnamide and ethyl formate are cyclized in the presence of sodium hydride to 3-cyano-4-phenyl-2-pyridone **(XII-97).**[46]



XII-95

XII-96

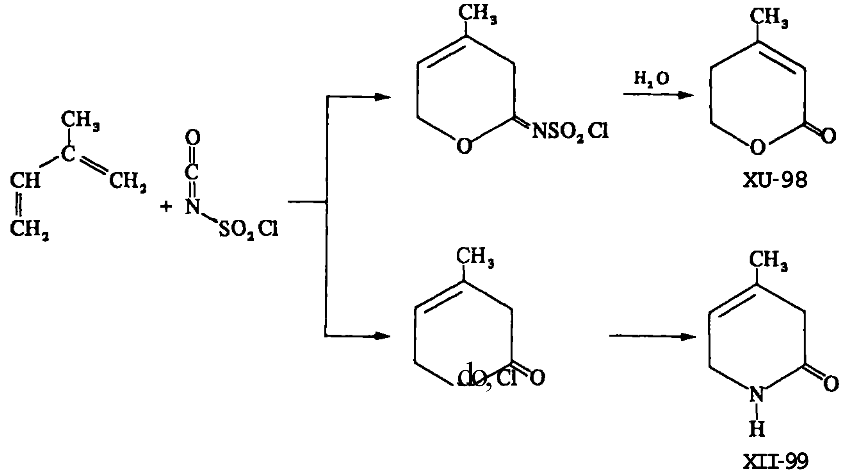
R = CH, ,C_6H_5



XII-97

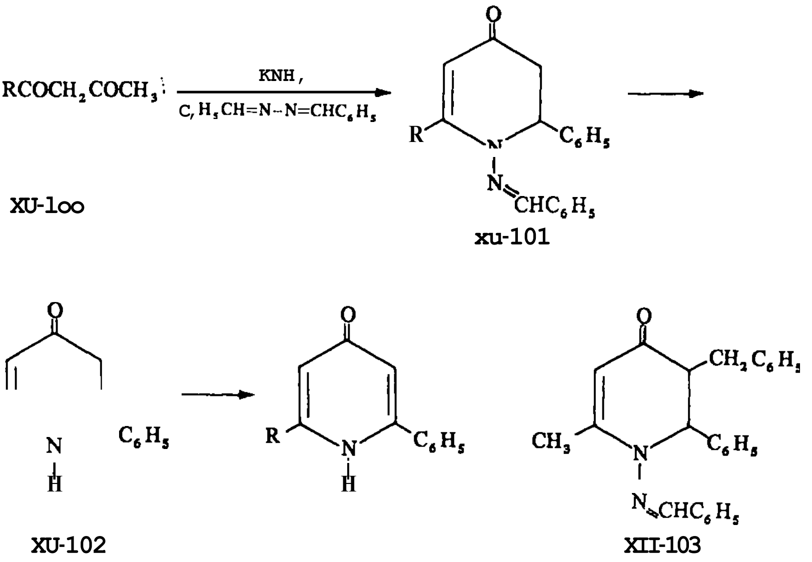
C. *Dienes*

Chlorosulfonyl isocyanate and isoprene in ether give 5-hydroxy-3-methyl-2-pentenoic acid lactone (4-methyl-5,6-dihydro-2-pyrone, XII-98) and 5-amino-3-methyl-3-pentenoic acid lactam (4-methyl-3,6-dihydro-2-pyridone, XII-99) by hydrolysis of intermediate N-sulfochlorides that were not isolated:'



D. *Diketones*

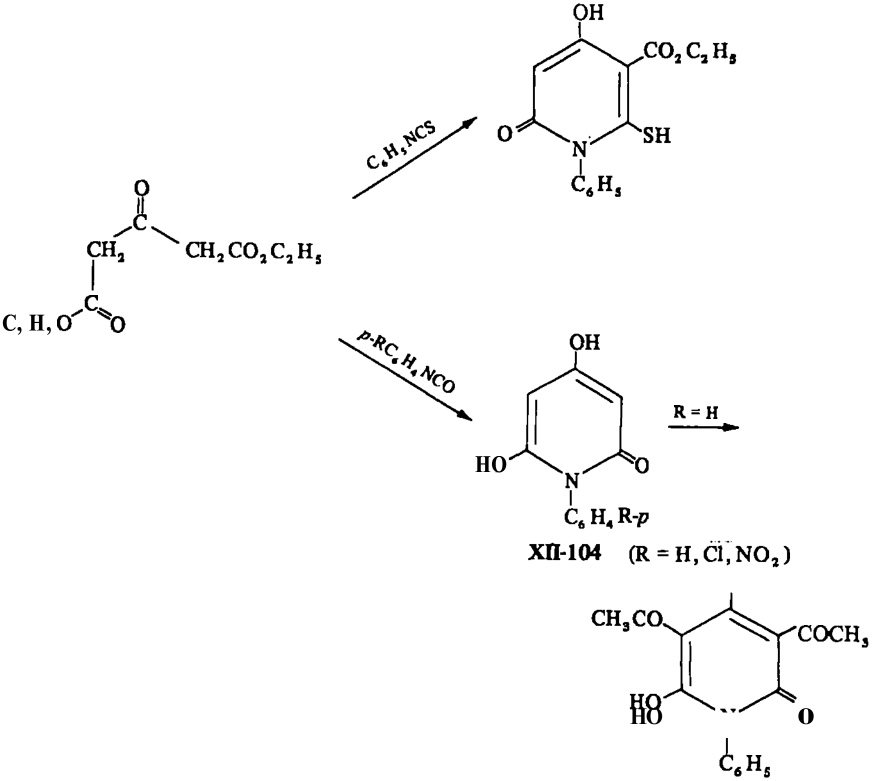
β-Diketones (XU-100) and benzaldazine give 1-benzylideneimino-2,3-dihydro-4-pyridones (XII-101), which can be converted *to* the corresponding 2,3-dihydro-4-pyridones (XI-102) by hydrogenolysis. Dehydrogenation with chloranil gives the 4-pyridone.



When **6-phenyl-2,4-hexanedione** **(MI-100**, R = $C_6H_5CH_2CH_2$) was used, **W-101** (R = $CH_2CH_2C_6H_5$, 52%) and the isomeric pyridone **(XII-103, 21%)** were **formed.**[48] The β-diketones **(MI-100)** and benzylideneaniline give *N*-phenyl derivatives of **XII-102.**[39]

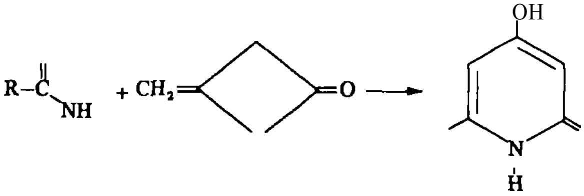
E. *β-Ketoesters*

The sodium salt of diethyl acetonedicarboxylate reacts with aryl isocyanates to give **1-aryl-4,6-dihydroxy-2-pyridones (XU-104)** and with phenyl isothiocyanate to give **3-carbethoxy-4-hydroxy-2-mercapto-1-phenyl-6-pyridone.**[49] Th'e compound formed on treatment of **XI-104** (R = H) with acetic anhydride has been proposed to be **3,5-diacetyl-4,6-dihydroxy-1-phenyl-2-pyridone.** Characterization was based on the infrared spectrum.[49]



XII-104 (R = H, Cl, NO_2)

Thioamides react with diketene in acetic acid or xylene to form **6-substituted-4-hydroxy-2-pyridones (XII-105).**[50]

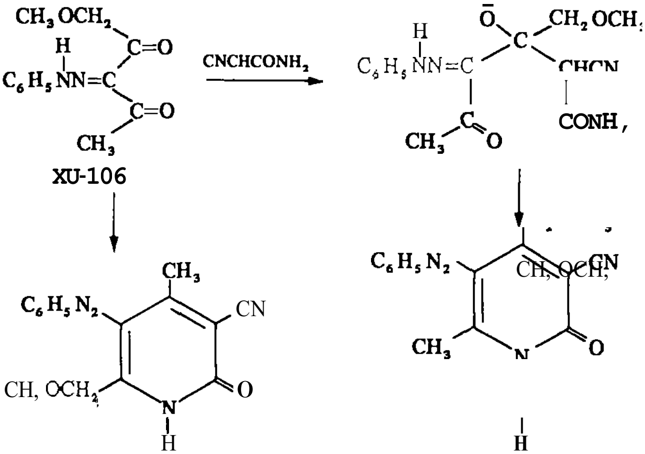


XII-105
R = alkyl, aryl

3. Ring Closures in Which One Acyclic Compound Provides Three Ring Carbons

A. *β-Diketones, β-Ketoaldehydes, and Malonaldehyde*

There are two possible orientations for ring closure between reactants furnishing two and three carbons, respectively, to the ring. When the carbonyl reagent is an unsymmetrical diketone, the electrophilicity of the two carbonyl groups often is similar and both possible products are detected. The methylene group of cyanoacetamide prefers to react with the more electrophilic or the less hindered carbonyl.[51] Reaction of 1-methoxy-3-phenylhydrazono-2,4-pentanedione (**XII-106**) and cyanoacetamide employing sodium ethoxide gives both possible products (**XII-107** and **XII-108**), with **XII-107** predominating.[52] Presumably the inductive effect of the 1-methoxy group makes the 2-carbonyl more electrophilic, and it is preferentially attacked by the conjugate base of cyanoacetamide [for leading references see (53)].

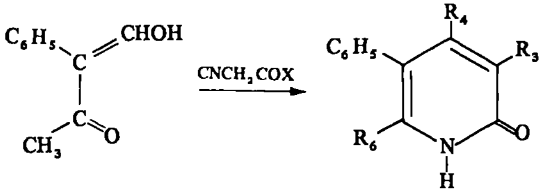


XII-106

XII-108

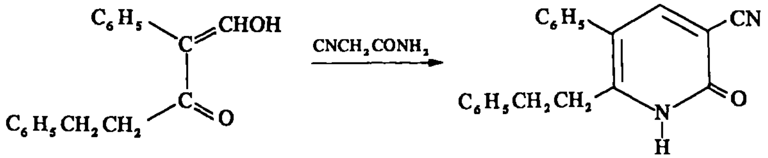
XII-107

1-Hydroxymethylene-1-phenyl-2-propanone **(XU-109)** condenses with cyanoacetamide in piperidine to give **3-cyano-6-methyl-5-phenyl-2-pyridone (XII-110a)** in low yield. Cyanoacetamide and the sodium salt of **XII-109** give **3-cyano-4-methyl-5-phenyl-2-pyridone (XII-110b)**. With ethyl cyanoacetate in methanol containing piperidine, **3-carbomethoxy-6-methyl-5-phenyl-2-pyridone (XII-110c)** is formed. It has been suggested that the formation of the sodium salt of the hydroxymethylene group of **XU-109** blocks attack by the methylene of cyanoacetamide at that **carbon.**[53] **2,5-Diphenyl-1,3-pentanedione** and cyanoacetamide in aqueous sodium carbonate give **3-cyano-5-phenyl-6-(β-phenylethyl)-**2-pyridone **(XII-111)**.[27]



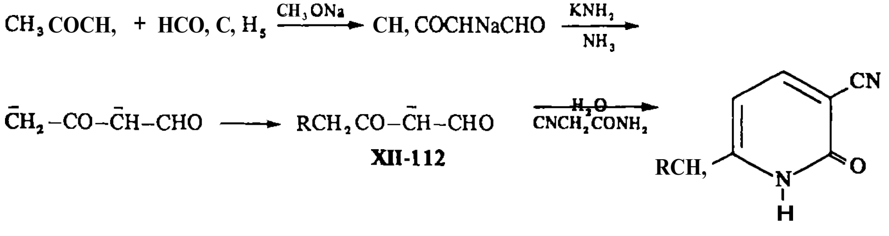
XII-109 **XII-110**

a: R_3 = CN, R_4 = H, R_6 = CH_3
b: R_3 = CN, R_4 = CH_3, R_5 = H
c: R_3 = CO_2CH_3, R_4 = H, R_6 = CH_3



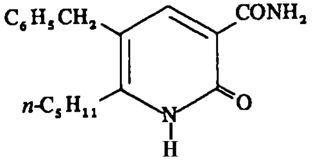
XII-111

The dicarbanion of acetoacetaldehyde is alkylated in the γ-position to give salts and copper chelates of β-ketoaldehydes **(W-112** ;R = $C_6H_5CH_2$, CH_3, n-C_4H_9 and n-C_8H_{17}), which are converted to 3-cyano-2-pyridones **(XII-113**; R = CH_3, $C_6H_5CH_2$, n-C_4H_9) by reaction with cyanoacetamide. n-Butylation of the dianion of α-benzylacetoacetaldehyde followed by cyclization with aqueous cyanoacetamide gives **5-benzyl-3-carboxamido-6-*n*-pentyl-2-pyridone (XII-114)**.[54]



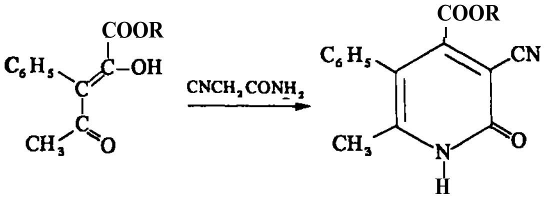
XII-112

XU-113



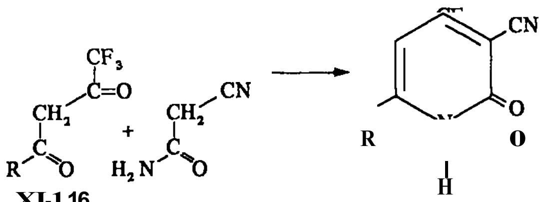
XII-114

Ethyl 2-keto-3-phenyllevulinate and cyanoacetamide in methanol containing piperidine give a mixture of methyl and ethyl 3-cyano-6-methyl-5-phenyl-2-pyridone-4-carboxylates (**XII-115**).[53]



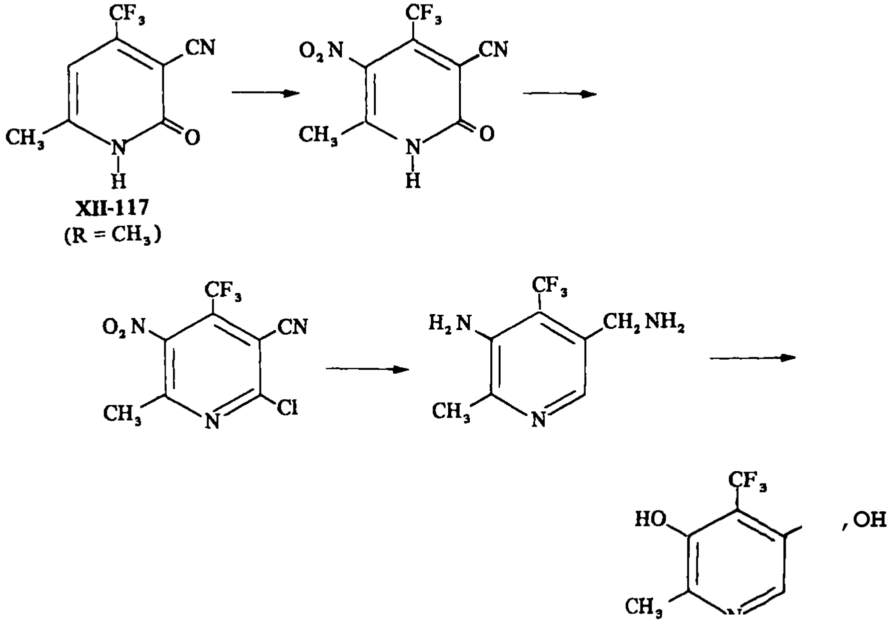
XII-115
R = CH_3, C_2H_5

A series of **3-cyano-4-trifluoromethyl-2-pyridones** (**W-117**) has been prepared employing trifluoromethyldiketones (**XU-116**) or ethyl 4,4,4-trifluoroacetoacetate (Section I.3.B., p. 625) and cyanoacetamide.[55] The strongly



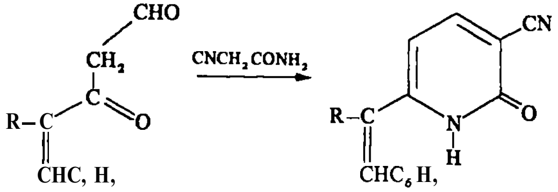
XII-117
R = CH_3, CF_3, C_6H_5, 2-thienyl

electron-withdrawing trifluoromethyl group in the diketones activates the carbonyl group to give products **W-117** rather than the isomeric **6-trifluoromethyl-4-alkylpyridones.**[55] The conversion of **XII-117** (R = CH_3) to the vitamin B_6 analog, **5-hydroxy-6-methyl-4-trifluoromethyl-3-pyridinemethanol** (**XII-118**), illustrates a utility of this **compound.**[56] Reactions of cinnamoylacetaldehydes with cyanoacetamides give 3-cyano-6-styryl-2-pyridones (**XII-119**).[57]



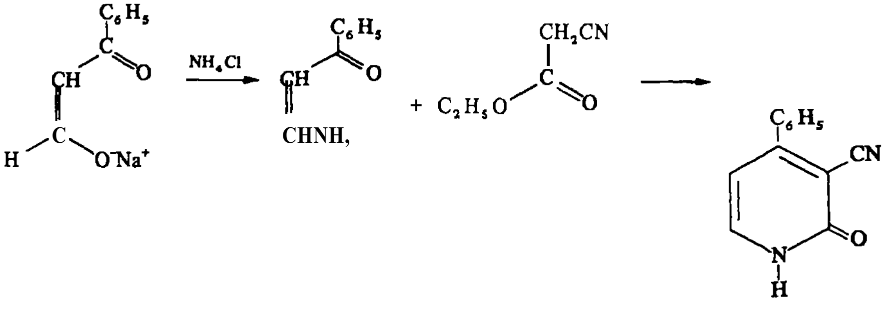
XII-117
(R = CH_3)

XII-118



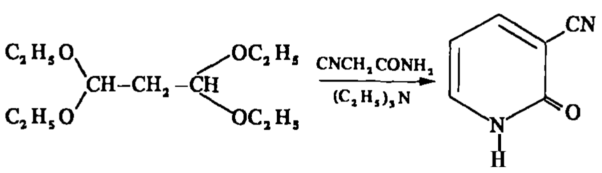
XU-119

Ethyl cyanoacetate and 1-amino-2-benzoylethylene cyclize to 3-cyano-4-phenyl-2-pyridone (XII-120) in the presence of sodium ethoxide.[46]



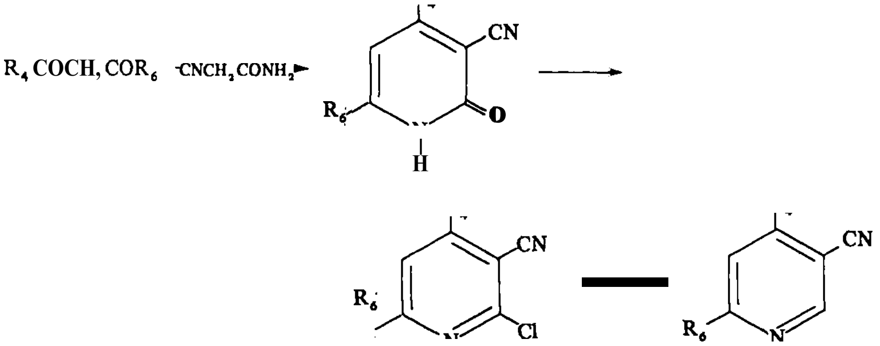
XII-120

1,1,3,3-Tetraethoxypropane (malonaldehyde diethyl acetal) and cyanoacetamide in aqueous triethylamine give 3-cyano-2-pyridone (XII-123, 57%).[58]

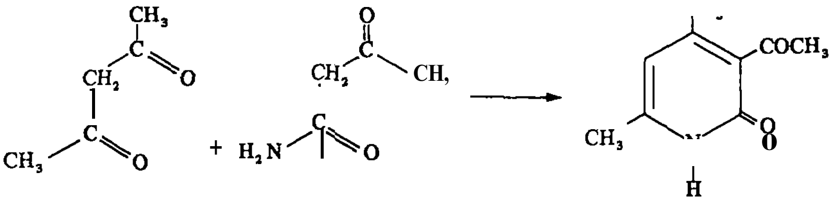


MI-123

The reaction between β-dicarbonyl compounds and cyanoacetamide to form the corresponding **3-cyano-2-pyridones,** followed by conversion to the 2-halo derivatives and reduction in the presence of 5% Pd-C, is a useful route to 3-cyano-4- and 3-cyano-6-substituted pyridines (MI-121).[59] Acetoacetamide and acetylacetone in 10%ethanolic hydrogen chloride give **3-acetyl-4,6-dimethyl-2-pyridone (XII-122).**[60]

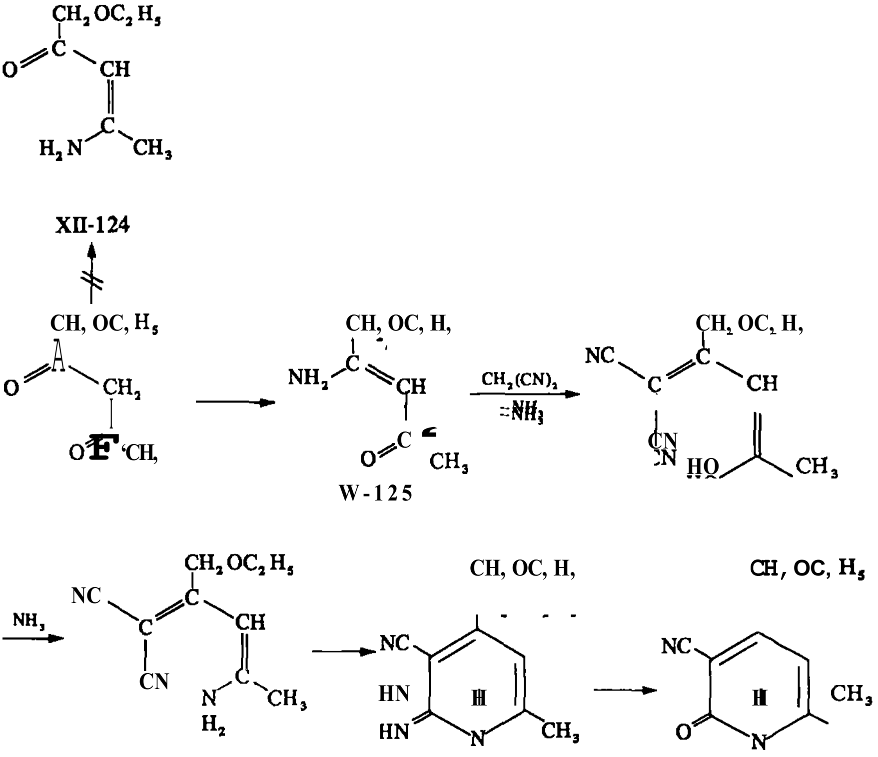


XII-121



xu-122

An enamine from **1-ethoxy-2,4-pentanedione,** previously described as **XII-124**[61, 62] has been shown to be **XII-125,** which has been prepared also from ethoxyacetonitrile and **acetone.**[63] The pyridone **W-126** is formed by treatment of **W-125** with malononitrile followed by ammonia and **cyclization.**[63]



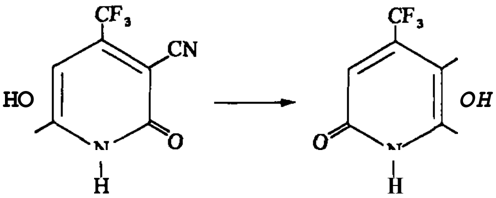
XII-124

W-125

XII-126

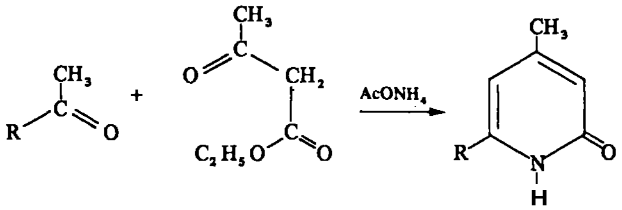
B. β-Ketoacid Derivatives

Cyclizations of β-ketoesters with cyanoacetamide or with ethyl cyanoacetate and ammonia give 5-cyano-6-hydroxy-2-pyridones.[64] Ethyl 4,4,4-trifluoroacetoacetate and cyanoacetamide in the presence of sodium methoxide form 3-cyano-6-hydroxy-4-trifluoromethyl-2-pyridone (XII-127) after crystallization from 15% hydrochloric acid. This pyridone appears to tautomerize in the solid state to 5-cyano-6-hydroxy-4-trifluoromethyl-2-pyridone.[55]



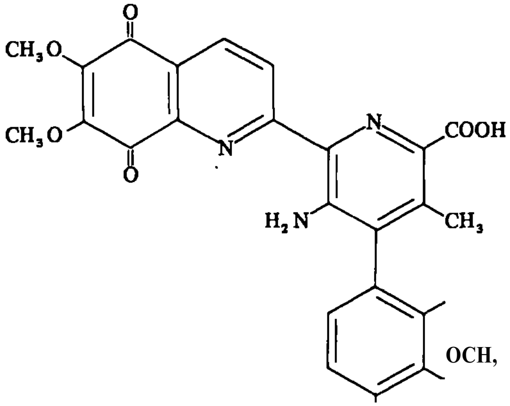
XII-127

Only small amounts of 6-aryl-4-methyl-2-pyridones (XU-128; R = C_6H_5, 6%; α-$C_{10}H_7$, 8.5%) are formed from ethyl acetoacetate, aryl methyl ketones and ammonium acetate.[65]

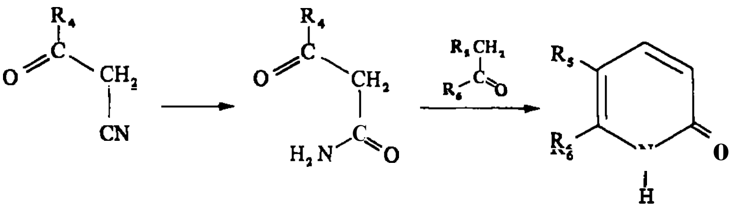


XII-128

The procedure of Hauser and Eby[66] has been used to prepare several substituted 4-phenyl-2-pyridones related to streptonigrin (XII-129). In model experiments, aroylacetonitriles and ketones in polyphosphoric acid give 4-aryl-2-pyridones (XU-130). 5,6-Dimethyl-4-phenyl-2-pyridone (XII-130a) was



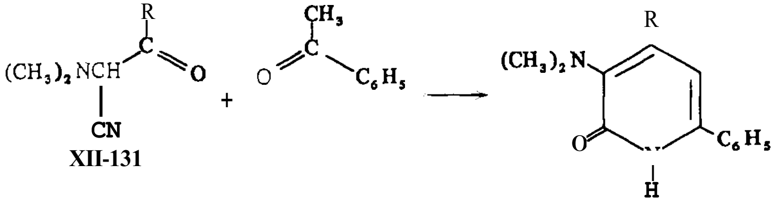
XII-129



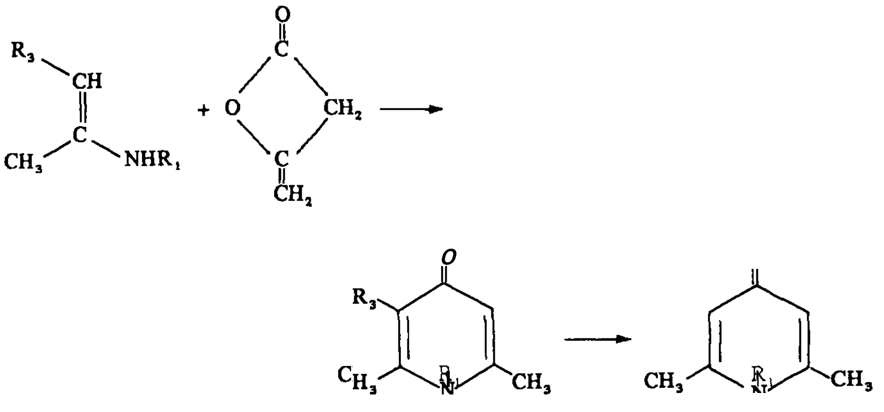
XII-130 a, b

	R_4	R_5	R_6
a:	C_6H_5	CH_3	CH_3
b:	2,3,4-$(CH_3O)_3C_6H_2$	H	CH_3

the only pyridone isolated when ethyl methyl ketone and benzoylacetonitrile were **used.**[67] Dimethylaminoacetonitrile can be aroylated to give **α-aroyl-α-*N*,*N*-**dimethylaminoacetonitriles **(W-131;** R = **C_6H_5, *p*-$CH_3OC_6H_4$, *p*-ClC_6H_4),** which are cyclized with acetophenone to **4-aryl-3-dimethylamino-6-phenyl-2-**pyridones.[68]


XII-131

Primary and secondary enamines prepared from ethyl acetoacetate or β-diketones react with diketene to form 4-pyridones **(XU-132).** The 3-carbethoxy-4-pyridones **(W-132, R_3** = **CO_2**Et) are readily saponified and

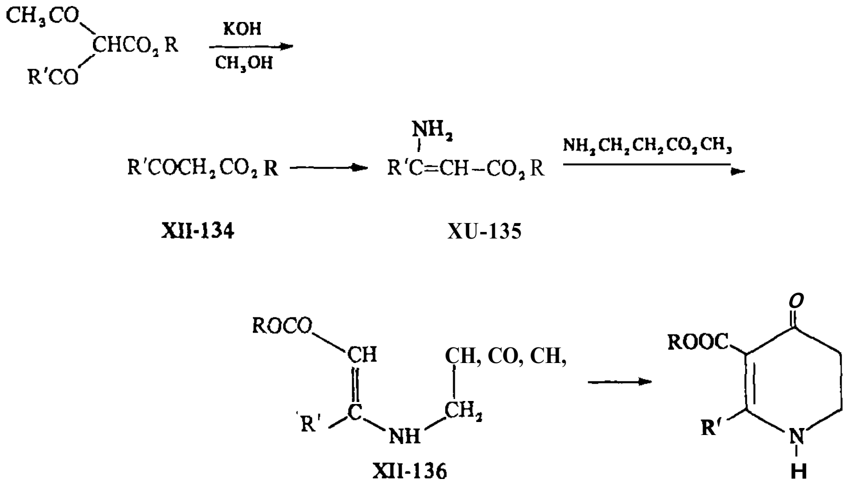

XII-132 XII-133

R_1 = H, $C_6H_5CH_2$, C_6H_5; R_3 = $CO_2C_2H_5$.

R_1 = H; R_3 = $COCH_3$, COC_6H_5.

decarboxylated to *N*-substituted-4-lutidones **(XU-133, R_1 = H, C_6H_5).**[69]

Acylated acetoacetic esters are cleaved with methanolic potassium hydroxide to give XII-134, which can be converted to enamines XII-135 with ammonia in the presence of **a** small amount of ammonium nitrate. Methyl β-alanate and XII-135 in ethanol give the enamines **XII-136,** which are cyclized to **the 5,6-dihydro-4-pyridones using** sodium methoxide in methanol.'' When the



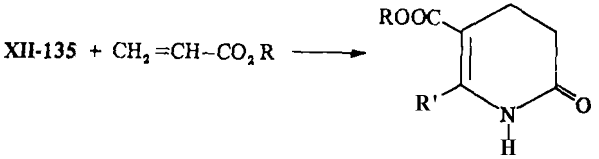
XII-134

XU-135

XII-136

R	R'
CH_3	$C_6H_5CH_2-$
t-Bu	$C_6H_5CH_2-$
CH_3	$p\text{-}CH_3OC_6H_4CH_2-$
CH_3	$3,4\text{-}(CH_3O)_2C_6H_3CH_2-$
CH_3	CH_3

enamines **XII-135** are boiled under reflux with acrylic esters, 3,4-dihydro-2-pyridones (**XII-137**) are formed.[70]

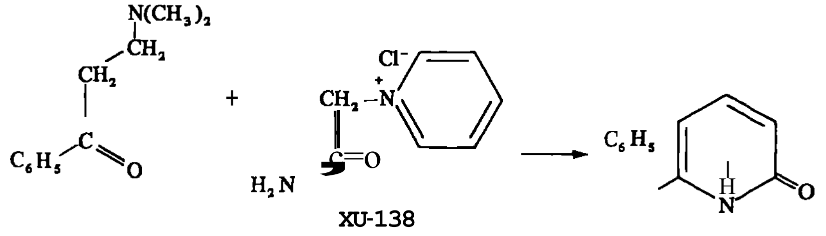


XII-137

R	R'
C_2H_5	CH_3
CH_3	$CH_2C_6H_5$

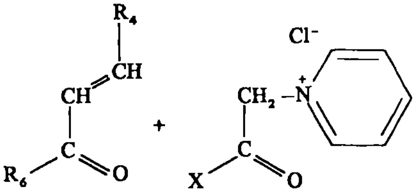
C. *β-Substituted Ketones*

Both dialkylamine and pyridine can function as leaving groups in this type of pyridone synthesis. For example, 6-phenyl-2-pyridone can be formed from ω-dimethylaminopropiophenone and *N*-(carbamylmethyl)pyridinium chloride (**XII-138**)[1] (Section I.1., p. 599).

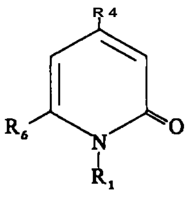


D. *Unsaturated Carbonyl Compounds*

Compound **W-138** or its N-methyl derivative in methanol containing dimethylamine or sodium hydroxide, or in acetic acid containing ammonium acetate, reacts with **benzylideneacetophenone**, benzylideneacetone, cinnamaldehydes, or ω-4-(picolinylidenyl)acetophenone probably by paths initiated by a Michael addition to give **XII-140.**[1, 71–74] *N*-Carbethoxymethylpyridinium bromide (**W-139**) and ammonium acetate in acetic acid has



X = NH, (XU-138)
X = OC_2H_5 (XII-139)

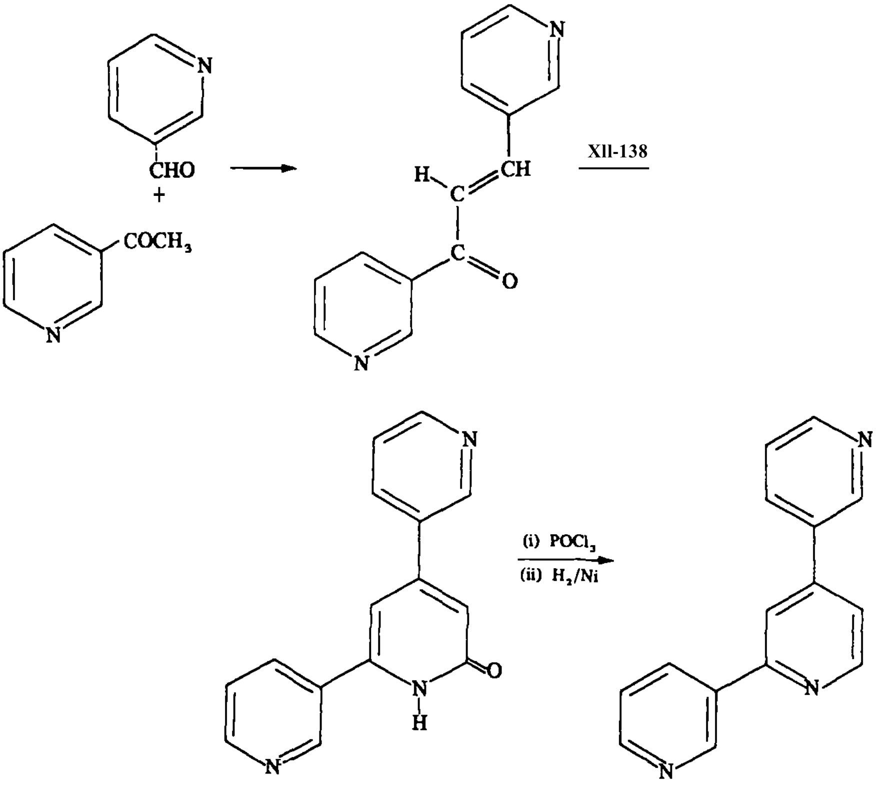


XU-140

	R_1	R_4	R_6
a–c:	H	C_6H_5	H, CH_3, C_6H_5
d:	CH_3	C_6H_5	C_6H_5
e:	H	4-pyridyl	C_6H_5
f:	H	C_6H_5	3-pyridyl
g, h:	H	*p*-$NO_2C_6R_4$	C_6H_5, 2-pyridyl
i:	H	*o*-$NO_2C_6H_4$	H

advantages over **W-138** for synthesis of **XII-140e-g.**[72] Benzylideneacetophenone and **W-138** or **W-139** with ammonium acetate in acetic acid at 140” give both XII·140a and **2,4,6-triphenylpyridine.**[74] A retrocondensation of benzylideneacetophenone occurs to form benzaldehyde and acetophenone, which react with benzylideneacetophenone and ammonium acetate to form triphenylpyridine *via* a typical Chichibabin **reaction,**[75] which includes a dehydrogenation.

Nicotellin (**XII-141**), a tobacco alkaloid, has been synthesized from XII-138 and the Claisen condensation product of nicotinaldehyde and 3-acetylpyridine.[1]

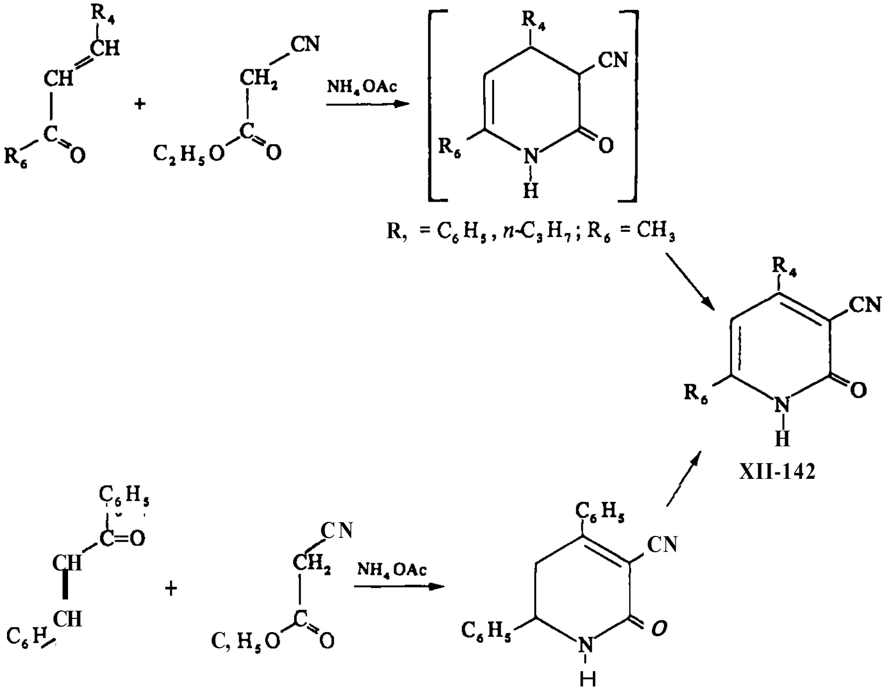


XII-141

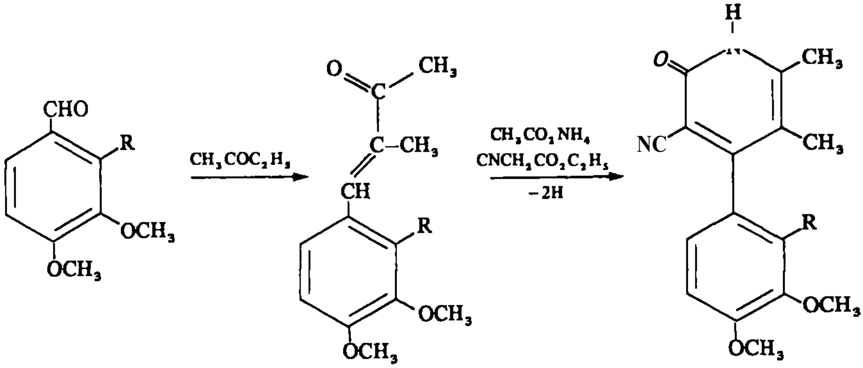
Vinyl ketones, ethyl cyanoacetate and ammonium acetate give 4,6-disubstituted 3-cyano-2-pyridones (**XU-142**) by a reaction path that includes a Michael addition and a dehydrogenation. The intermediate **3,4-dihydro-2-pyridones** were not detected. When benzylideneacetophenone was used in benzene, the reaction proceeded by a Knoevenagel condensation and it was possible to isolate the intermediate **3-cyano-5,6-dihydro-4,6-diphenyl-2-pyridone**, which was dehydrogenated to **MI-142** by boiling in acetone.[76]

Condensation of 2-substituted veratrals with ethyl methyl ketones gives substituted vinyl ketones that react with ethyl cyanoacetate in the presence of ammonium acetate to give **4-aryl-3-cyano-5,6-dimethyl-2-pyridones (XII-143)**.[77]

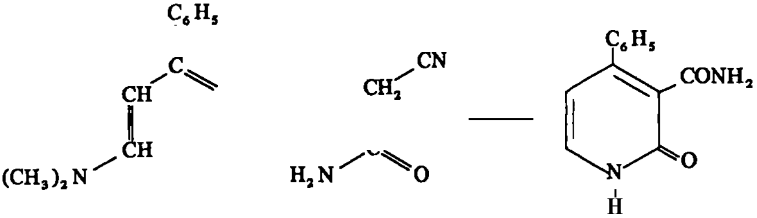
Cyanoacetamide and 1-dimethylamino-3-phenyl-1-**propene-3-one** in acetic acid give **3-carboxamido-4-phenyl-2-pyridone (XII-144)**.[78]



XII-142

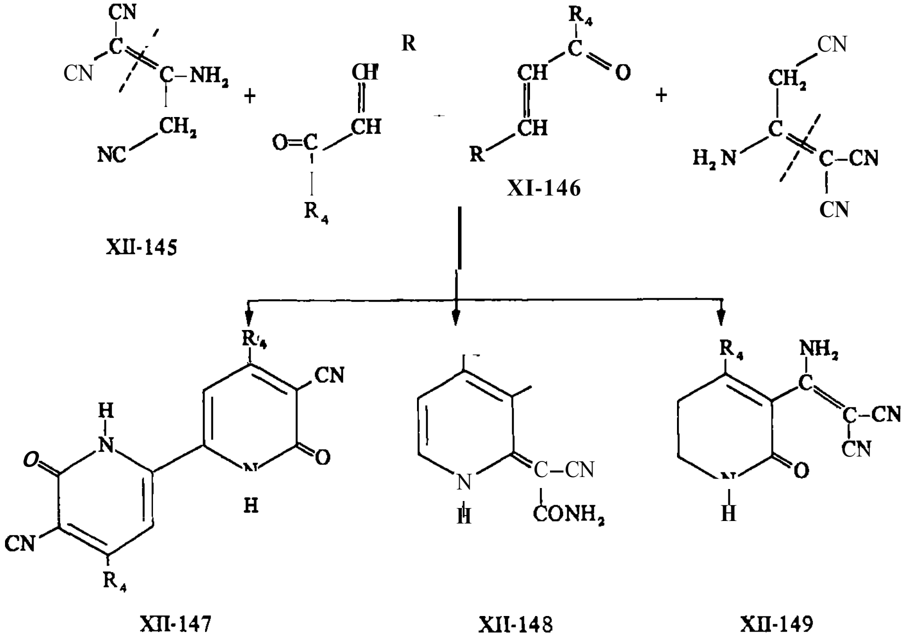


XII-143

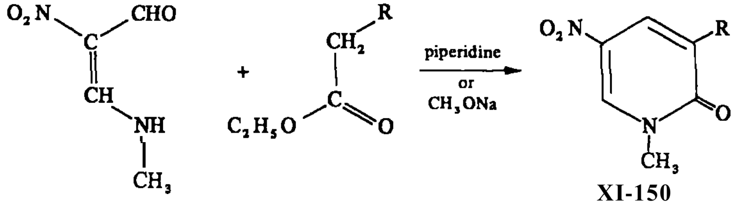


XII-144

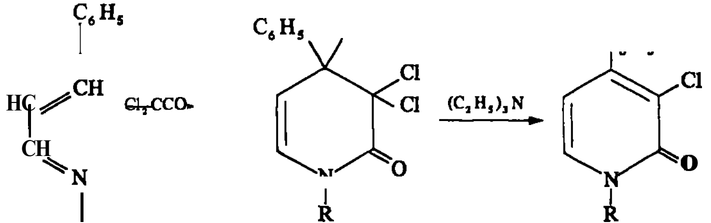
1,3,3-Tricyano-2-aminopropene(dimeric malononitrile) (XI-145) and enaminoketones (XII-146; R = $NHCH_3$, $N(CH_3)_2$, R_4 = C_6H_5, p-$CH_3C_6H_4$, 2,4-$(CH_3)_2C_6H_3$, p-$CH_3OC_6H_4$) in acetic acid give bipyridonyls (XII-147), as well as smaller amounts of W-148 and the 5,6-dihydro-2-pyridone (MI-149) in a reaction that is not influenced by radical inhibitors or initiators or by the exclusion of oxygen.[78-80]



Although imino derivatives of nitromalonaldehyde and active methylene compounds often give linear condensation products that could not be cyclized,[81] α-nitro-β-methylaminoacrolein reacts with diethyl malonate to give ethyl 1-methyl-5-nitro-2-pyridone-3-carboxylate (W-150, R = $CO_2C_2H_5$). Similarly, ethyl a-nitroacetate gives W-150 (R = NO_2).[82]



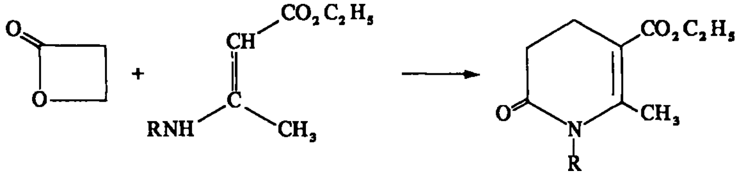
Dehydrochlorination of dichloroacetyl chloride by triethylamine in the presence of a Schiff's base with a cinnamaldehyde structure **through** cycloaddition gives dihydro-2-pyridones (W-151), which are converted to 3-chloro-2-pyridones (W-152) by an excess of triethylamine.[83]



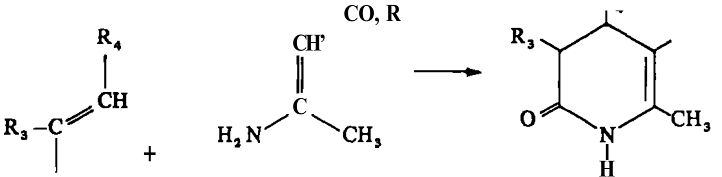
XII-151 XII-152

R = C_6H_5, $CH_3C_6H_4$, $C_6H_5CH{=}CH{-}CH{=}N{-}$

Enamines W-153, W-154, and W-155 and propiolactone or acrylic acids form dihydropyridones, W156,W-157, and XII-158, when boiled in chlorobenzene.[84]

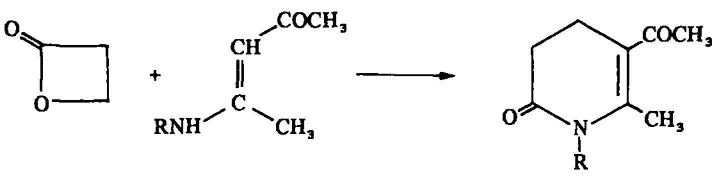


XII-153 XU-156



XII-154 XU-157 a-c

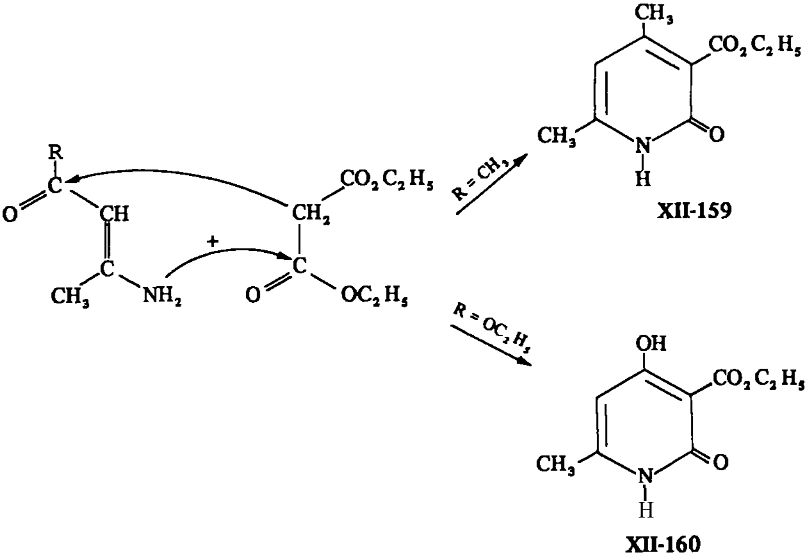
	R_3	R_4	R
a:	H	H	t-Bu
b:	CH,	H	C_2H_5
c:	H	CH,	C_2H_5



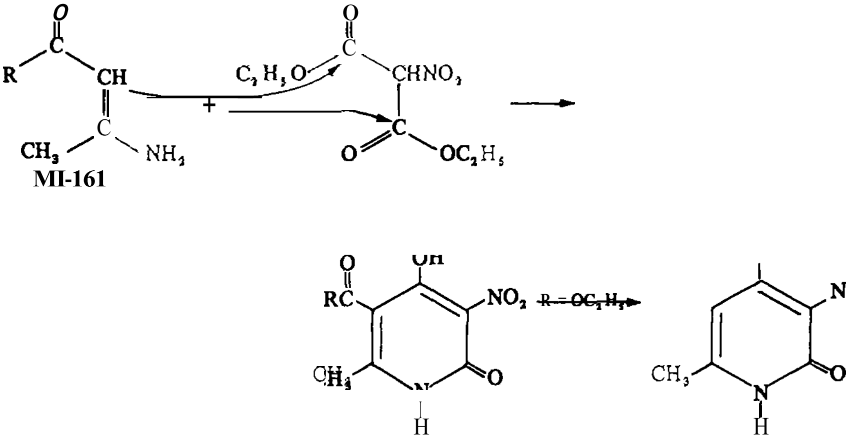
XII-155 XU-158

E. *Malonic Acid Derivatives*

In the presence of alkoxides, diethyl malonate reacts with acetylacetone imine to give the **4,6-dimethyl-2-pyridone** **(XI-159)** and with ethyl β-aminocrotonate to give the 4-hydroxy-2-pyridone **(XII-160).**[85] In these reactions, ethyl malonate, like ethyl cyanoacetate and cyanoacetamide, provides two of the ring carbons. Ethyl nitromalonate, which cannot form a 2-pyridone by this path, reacts with enamines **(MI-161;** R = C_6H_5, OC_2H_5) through its two carbethoxy groups to give the **5-substituted-4-hydroxy-3-nitro-2-pyridones** **(MI-162).** The 5-carbethoxy-2-pyridone (XII-162, R = OC_2H_5) is readily saponified and **decarboxylated.**[86] In contrast, it had been suggested earlier that when the related ethyl alkylmalonates are used, intermediates are formed which undergo aromatization through loss of a carbethoxy group from the malonate **moiety.**[85]



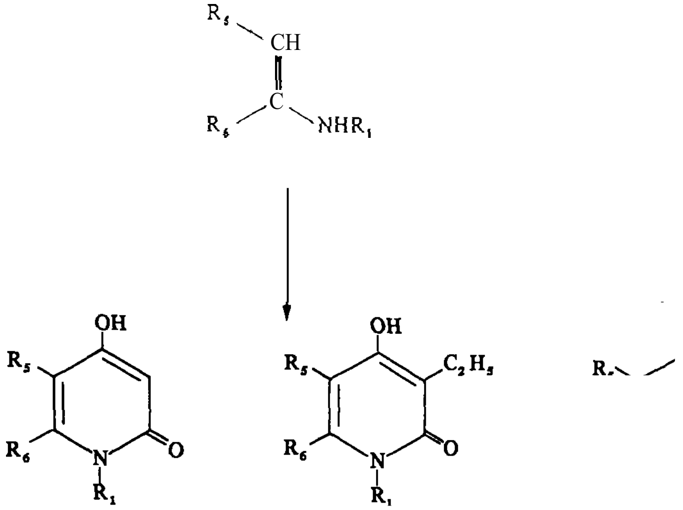
Primary and secondary enamines and anils **(XII-163)** react with carbon suboxide **(MI-164)** to form **3-unsubstituted-4-hydroxy-2-pyridones** **(XII-165),**[87,88] with carbethoxy ethyl ketene **(XI-166)** to form 3-ethyl-4-hydroxy-2-pyridones **(XII-167),**[89] and with malonyl chloride **(MI-168)** or malonic acids and acetic anhydride **(XI-169)** to give **3-substituted-4-hydroxy-2-pyridones** **(XII-170)**[90-92] (Table **XII-1). Anils** of cyclic ketones **(MI-163,** R_5R_6 = $(CH_2)_n$ where *n* = 3,4,5,6; R_1 = aryl) and substituted malonyl chlorides (R_3 = alkyl) give **5,6-polymethylene-4-hydroxy-2-pyridones.**[93] A comparison



MI-161

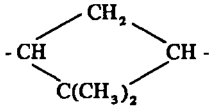
XII-162

with known isomeric pyridones[94] showed that the product formed from benzoylacetonearnine (**XII-163; R_5** = $COCH_3$, R_6 = C_6H_5, R_1 = H) and carbon suboxide **(XII-164)** is **5-acetyl-4-hydroxy-6-phenyl-2-pyridone** (**XII-165; R_1** = H, R_5 = $COCH_3$, R_6 = C_6H_5) and not the isomeric 5-benzoyl-4-hydroxy-6-methyl-2-pyridone[87, 95] (Section I.S.C., p. **658**).

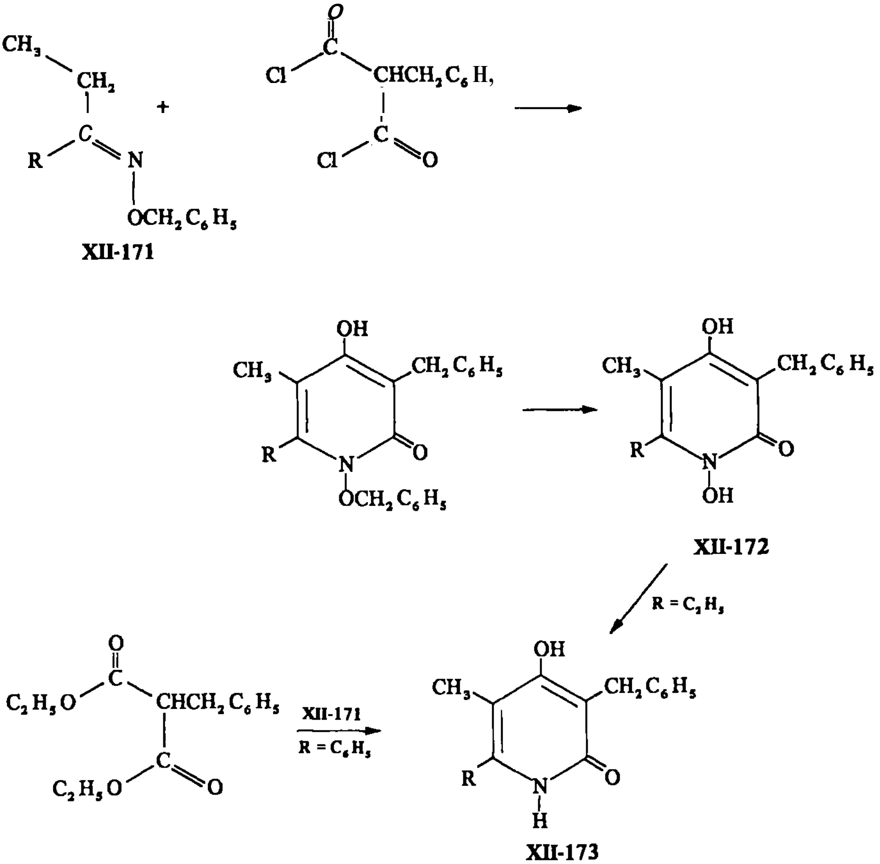


The benzyl ether of diethyl ketoxime (**W-171**, R = C_2H_5) and benzylmalonyl chloride in benzene give 3-benzyl-1-benzyloxy-6-ethyl-4-hydroxy-5-methyl-2-

TABLE XII-1. 4-Hydroxy-2-pyridones from Derivatives of Malonic Acid

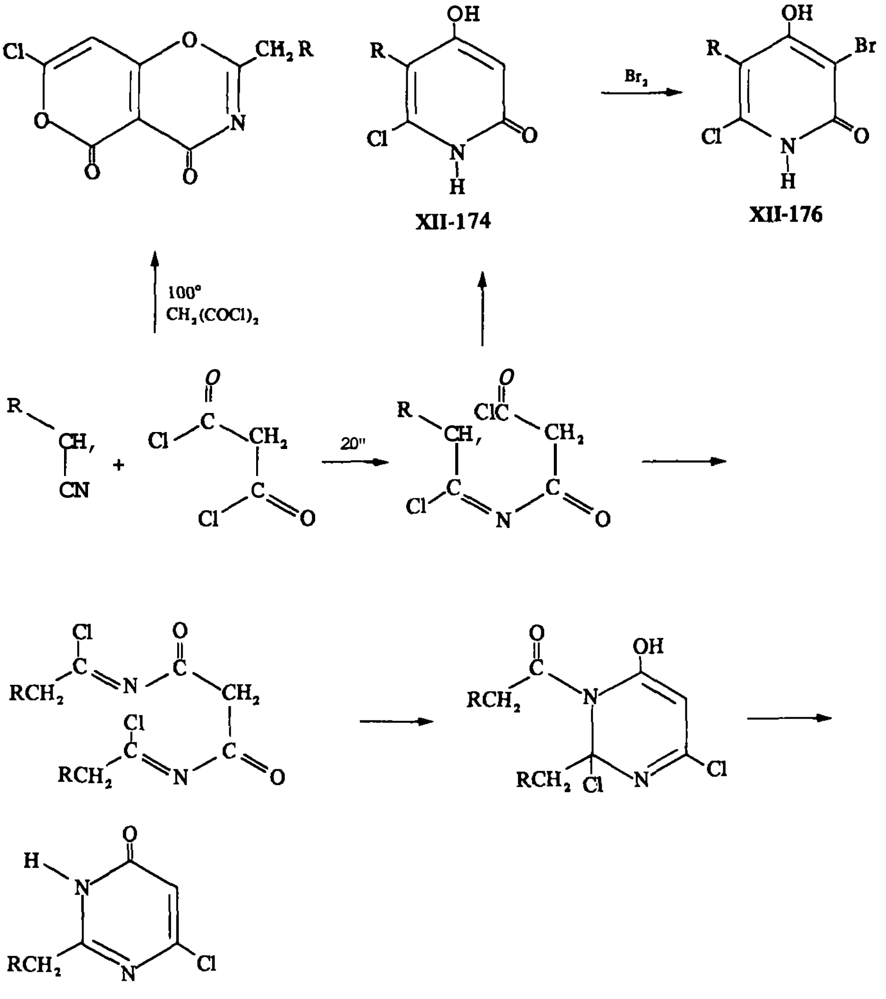
R_1	R_3	R_5	R_6	Reagent	%Yield	Ref.
H	H	$CO_2C_2H_5$	CH_3	XI-164	56	87
H	H	$CO_2C_2H_5$	C_2H_5	XI-164	31	87
H	H	$CO_2C_2H_5$	n-C_3H_7	XI-164	47	87
C_6H_5	H	$CO_2C_2H_5$	CH_3	XI-164	38	87
$(CH_3)_2C_6H_3$	H	$CO_2C_2H_5$	CH_3	XI-164	46	87
				XI-168	100	90
p-$CH_3OC_6H_4$	H	$CO_2C_2H_5$	CH_3	XI-164	41	87
				XI-168	100	90
H	H	$COCH_3$	CH_3	XI-164	80	87
				XI-169	42	90
C_6H_5	H	$COCH_3$	CH_3	XI-164	46	87
$C_6H_5CH_2$	H	$COCH_3$	CH_3	XI-164	92	87
H	H	$COCH_3$	C_6H_5	XI-164	74	87
				XII-169	33	90
C_6H_5	H	$COCH_3$	C_6H_5	XI-164	31	87
				XI-168	61	90
CH_3	H	$COCH_3$	C_6H_5	XI-164	38	87
C_6H_5	H	$(CH_2)_3$		XI-164	46	88
C_6H_5	H	$(CH_2)_4$		XI-164	48	88
C_6H_5	H	$(CH_2)_5$		XI-164	46	88
C_6H_5	H	$(CH_2)_6$		XI-164	19	88
C_6H_5	C_2H_5	$(CH_2)_4$		XI-166	26	89
H	C_2H_5	CH_3CO	CH_3	XI-166	39	89
				XI-168	33	93
C_6H_5	H	$CO_2C_2H_5$	H	XI-168	68	90
H	$C_6H_5CH_2$	$COCH_3$	C_6H_5	XI-168	92	90
H	$C_6H_5CH_2$	$COCH_3$	CH_3	XI-168	54	90
				XI-169	58	90
C_6H_5	$C_6H_5CH_2$	$COCH_3$	CH_3	XI-168	29	90
H	C_2H_5	CH_3	C_6H_5	XI-168	65	91
H	$CH_2C_6H_5$	CH_3	C_6H_5	XI-168	68	91
H	$C_6H_5CH_2$			MI-168	30	91
C_6H_5	$C_6H_5CH_2$	H	C_6H_5	XI-168	42	92
C_6H_5	$CH(CH_3)_2$	H	C_6H_5	XI-168	56	92
p-$CH_3C_6H_4$	$C_6H_5CH_2$	H	C_6H_5	XI-168	82	92
p-CH_3C_6	n-C_4H_9	H	C_6H_5	XII-168	42	92
p-$CH_3C_6H_4$	$CH(CH_3)_2$	H	C_6H_5	XI-168	66	92
C_6H_5	$C_6H_5CH_2$	CH_3	C_6H_5	XI-168	38	92
C_6H_5	$C_6H_5CH_2$	C_2H_5	C_6H_5	XI-168	39	92

pyridone, which on hydrogenolysis gives **3-benzyl-6-ethyl-1,4-dihydroxy-5-methyl-2-pyridone** (MI-172, R = C_2H_5).' The pyridone (W-173) is formed by heating XII-172 at reduced pressure. When the benzyl ether of propiophenone oxime (W-171, R = C_6H_5) is heated at 250 to 280" with diethyl benzylmalonate, the pyridone (W-173, R = C_6H_5) is obtained directly.[96]



Nitriles condense with malonyl chloride to give **2-chloro-4,6-dihydroxypyridines** (MI-174) in 23 to 63% yield[g7] and/or the pyrimidones (XII-175)[98] or chloropyranooxazines (Section I.5.C.) depending on conditions.[97, 99]

5-Bromo-3-carbethoxy-2-chloro-4,6-dihydroxypyridine (XII-176, R = $CO_2C_2H_5$) is prepared either by bromination of MI-174 (R = CO_2Et) or by cyclization of bromomalonyl chloride and ethyl cyanoacetate. Methylmalonyl chloride did not react with propionitrile.[97] The product from acetonitrile and malonyl chloride, first described as **2-chloro-4,6-dihydroxypyridine** (MI-174, R = H),[97] is 6-chloro-2-methyl-4-pyrimidone (XI-175, R = H).[98]



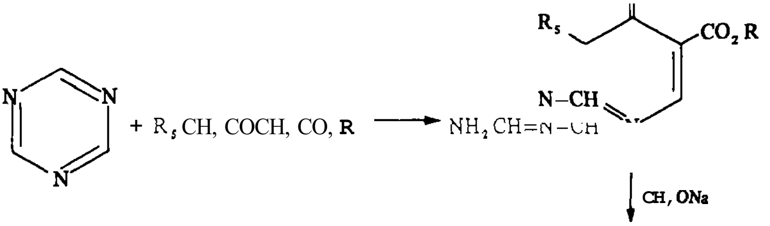
XII-174

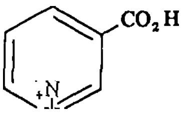
XII-176

XII-175

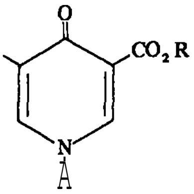
F. *Acetone Derivatives*

Dimethyl acetonedicarboxylate or ethyl acetoacetate can provide the 3-, **4-**, and 5-carbons to give **3,5-disubstituted-4-pyridones (XI-177, R_5 = CH_3CO, CO_2CH_3)**. *s*-Triazine has been used to provide the 2- and 6-carbons.[100] A compound, previously described as **4-hydroxy-3-pyridinecarboxylic** acid (XII-177, R = R_5 = H)[101] was shown to be nicotinic acid-1-oxide **(XII-178)**.[100]





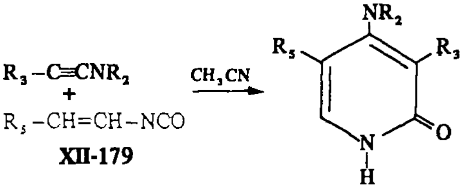
XII-178



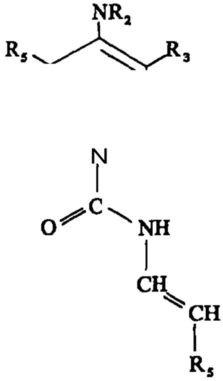
XII-177

G. Isocyanates

In isocyanates the incipient ring carbons are not in a continuous carbon chain. Styryl isocyanates **(XII-179)** react with ynamines in acetonitrile to give 4-amino-5-substituted-2-pyridones by 1,4-cycloaddition. Further reaction occurs under these conditions to give **1-(*N*-substituted-carbamoyl)-2-pyridones** (XII-180), which are readily decomposed **thermally.**[102]



XII-179

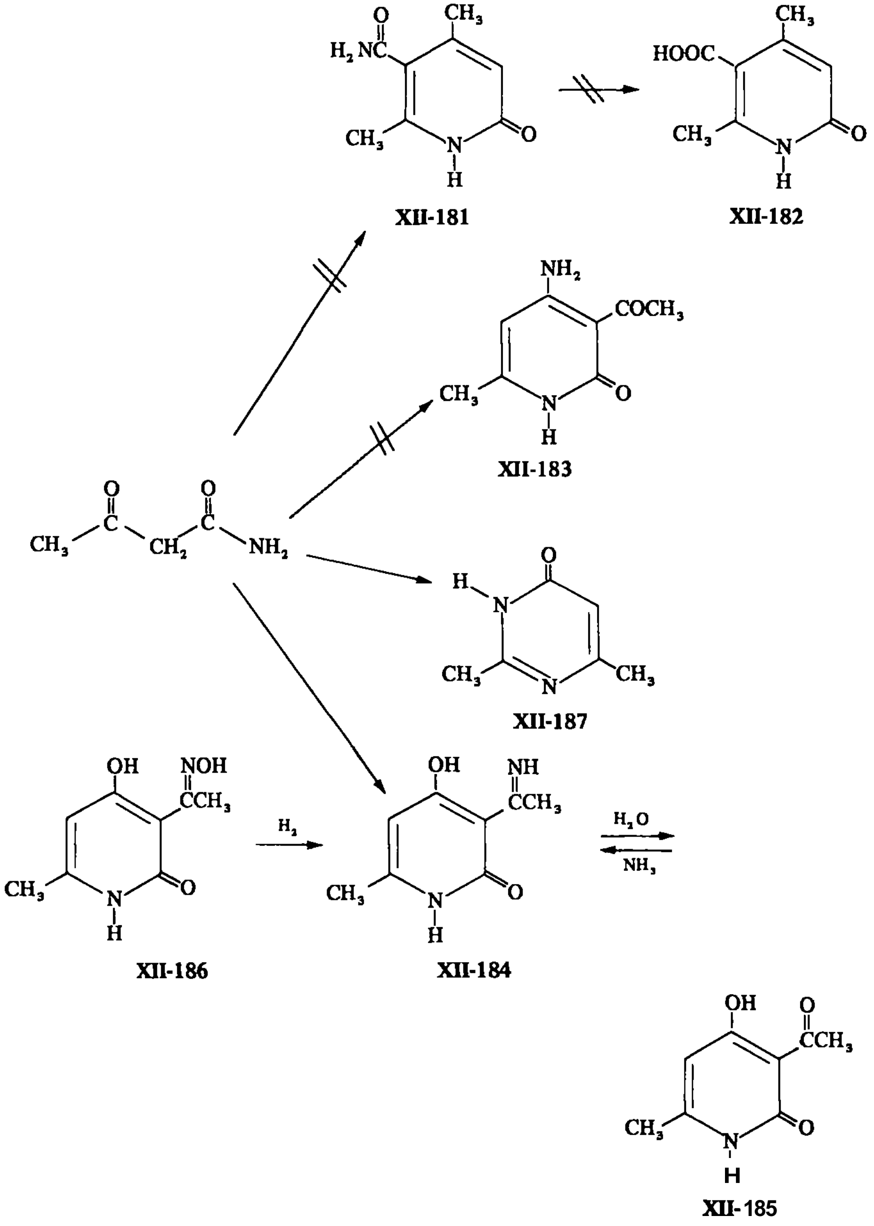


XII-180

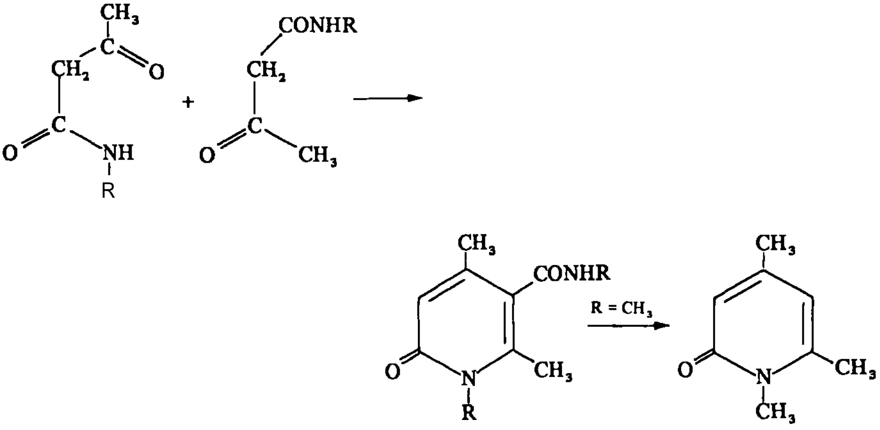
4. Miscellaneous Ring Closures

A. *Autocondensations*

There is some confusion in the literature that describes autocondensations of acetoacetamides. In 1902, Claisen and **Meyer**[103] proposed that the pyridone product formed by heating acetoacetamide was 5-carboxamido-4,6-dimethyl-2-pyridone (XU-181) and its hydrolysis product was XII-182.[103] A reinvestigation of this reaction led to assignment of XI-183 as the structure because it gives the



known **3-acetyl-4-hydroxy-6-methyl-2-pyridone (MI-185)** on hydrolysis.'[04] However, easy conversion of **MI-185** to the original cyclization product with ammonia suggested the structure **XII-184** for the latter.'"' Product **XII-184** was also prepared by reduction of the corresponding oxime **(MI-186).** The main product of cyclization of acetoacetamide is **2,6-dimethyl-4-pyrimidone (MI-187,** 52%). When acetoacetamide was heated under reduced pressure, the yield of **XU-184** could be increased from 3% to 30–45%.[105] A small amount of **XII-185** is formed during the formation of acetoacetamide from diketene and **ammonia.**[106] *N*-Alkylacetoacetamides also undergo auto-condensations when heated, but the yields of pyridones are low once more. Water formed appears to hydrolyze the reactant to acetone, carbon dioxide, and amine. The products have been characterized as **5-(*N*-alkylcarbamoyl)-2-pyridones (XII-188**; R = CH_3, C_2H_5) because the 1-methyl homolog **(MI-188,** R = CH_3) was hydrolyzed and decarboxylated to **1,4,6-trimethyl-2-pyridone.**[107]

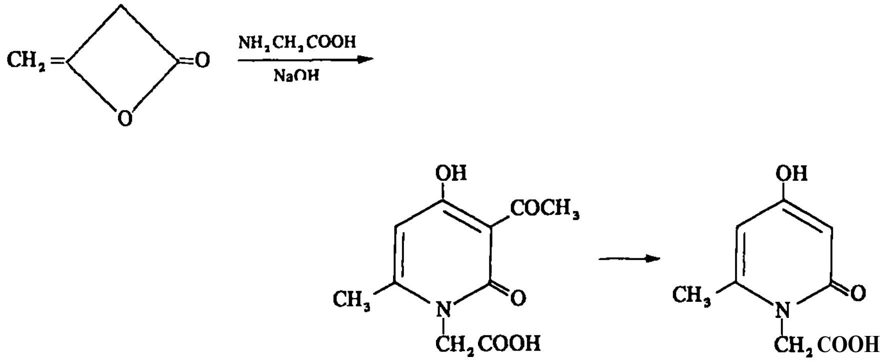


XII-188

β-Ketoamides substituted in the a-position cannot give products analogous to **MI-188** but react to give **5,6-dialkyluracils.**[107]

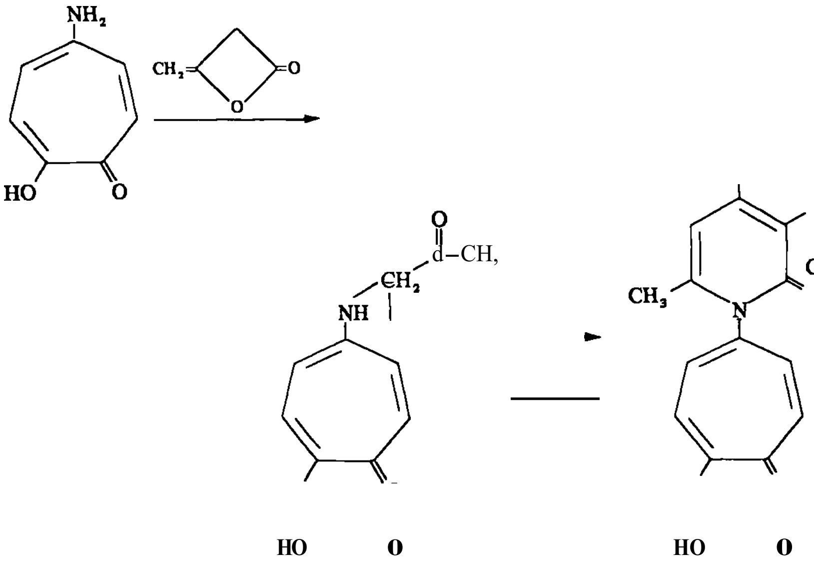
Diketene and glycine in a basic solution give 3-acetyl-1-carboxymethylene-4-**hydroxy-6-methyl-2-pyridone (XII-189)** by a reaction path in which dehydroacetic acid is not an intermediate. However, *N*-acetoacetylglycine was not detected.[154] Deacylation of **XII-189** to **XII-190** occurs in sulfuric acid.

5-Aminotropolone and diketene give **3-acetyl-4-hydroxy-6-methyl-(5-tropolonyl)-2-pyridone (XII-192)** directly, in the presence of triethylamine. In the absence of triethylamine, 5-acetoacetamidotropolone **(MI-191)** could be isolated.[109]



XII-189

XII-190

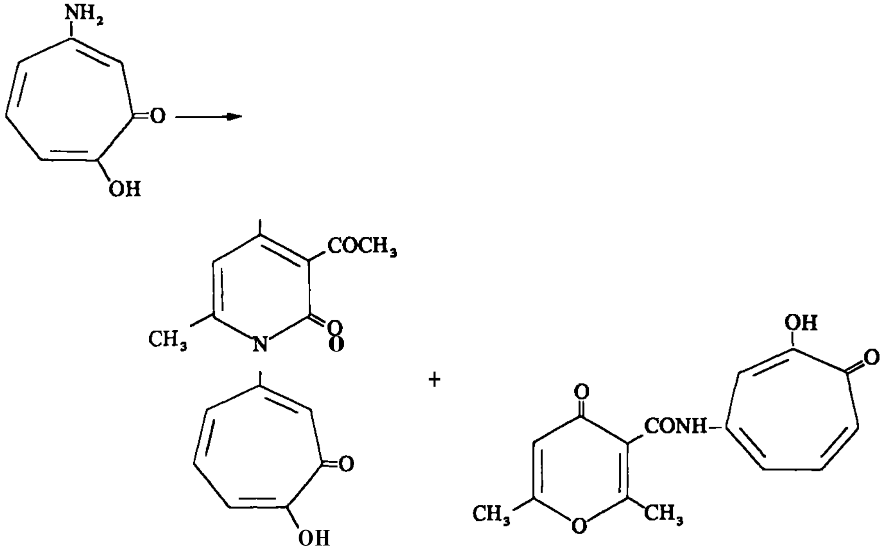


XII-191

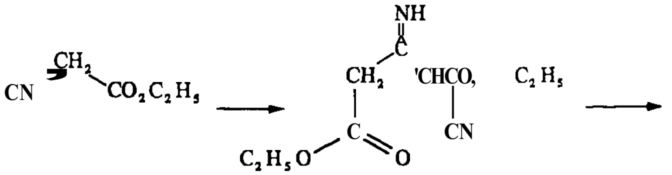
XII-192

4-Aminotropolone and diketene form 3-acetyl-4-hydroxy-6-methyl-1-(tropolon-4-yl)-2-pyridone (MI-193) and N-(tropolon-4-yl)-2,6-dimethyl-4-oxo-4*H*-pyran-3-carboxamide(XII-194).[110]

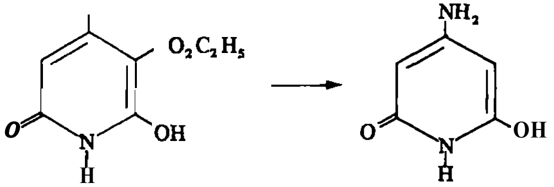
A preparation of glutazine (XU-196) from ethyl cyanoacetate has been improved.[34] 3-Carbethoxyglutazine is readily prepared from ethyl α-cyano-β-iminoglutarate (XI-195) and can be decarboxylated by heating with ammonia to glutazine (XU-196) in an overall yield of 35%.[34]



XU-193 XII-194



XII-195

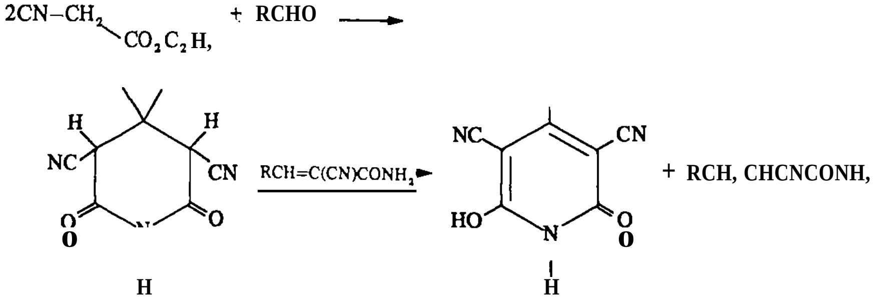


W-1%

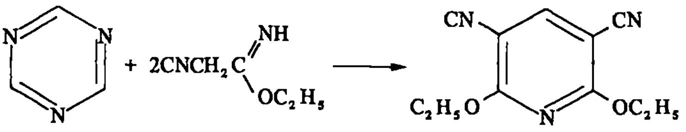
B. *Cyclizations* of *Three or More Acyclic Molecules*

The condensation of an aldehyde with ethyl cyanoacetate and ammonia to give 4-alkyl-3,5-dicyano-6-hydroxy-2-pyridone (XII-198) probably proceeds through the oxidation of an intermediate glutaric acid imide (MI-197). Only small amounts of the reduction products (XI-199) could be isolated. Additional pathways for the oxidation of W-197 to XII-198 were not excluded."'

s-Triazine and ethyl a-cyanoacetimidate give 3,5-dicyano-2,6-diethoxypyridine (XII-200).[100]

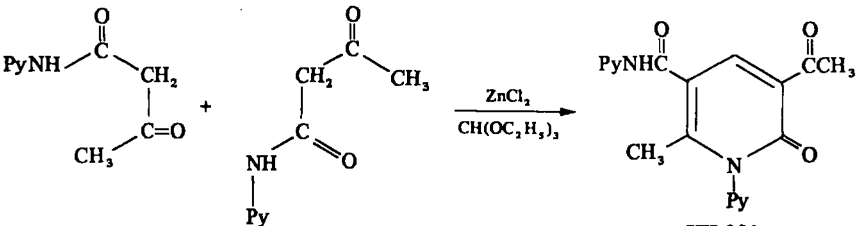


XII-197 XII-198 XII-199

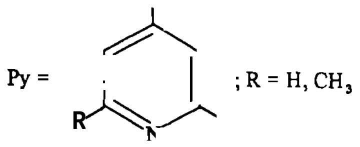


XII-200

Treatment of α-unsubstituted-*N*-(2-pyridyl)acetoacetamides with triethyl orthoformate and zinc chloride in ethanol gives 3-acetyl-6-methyl-1-(2-pyridyl)-5-(*N*-2-pyridylcarboxamido)-2-pyridone (XII-201).[112]



XII-201

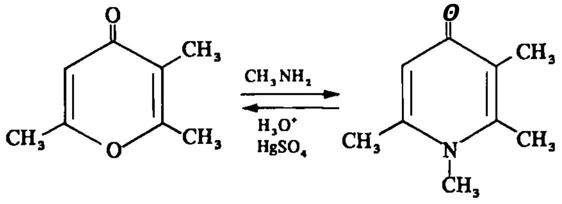


5. From Other Ring Compounds

A. *2-Pyrones*

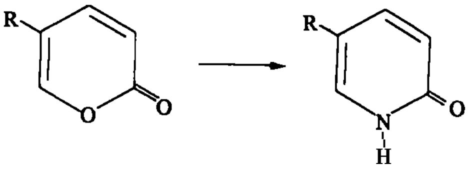
Ammonia, primary amines, and related acyclic nitrogen nucleophiles react with a large variety of pyrones to form pyridones. These reactions often have been used to characterize the pyrones or to remove them from mixtures. Under these circumstances, yields are often not reported and experimental conditions are not optimal, and, therefore, in many instances these reactions are difficult to evaluate, particularly as alternative routes to the somewhat more carefully studied direct ring closures to form pyridones.

Although pyrones and pyridones are potentially interconvertible, the conversion of pyridones to pyrones has been reported only occasionally. For example, **2,3,6-trimethyl-4-pyrone** in aqueous methylamine gives **1,2,3,6-tetramethyl-4-pyridone** (**XII-202**) (59%, isolated). The pyridone is converted to the pyrone (31%, isolated) in dilute sulfuric acid containing mercuric **sulfate.**[113]



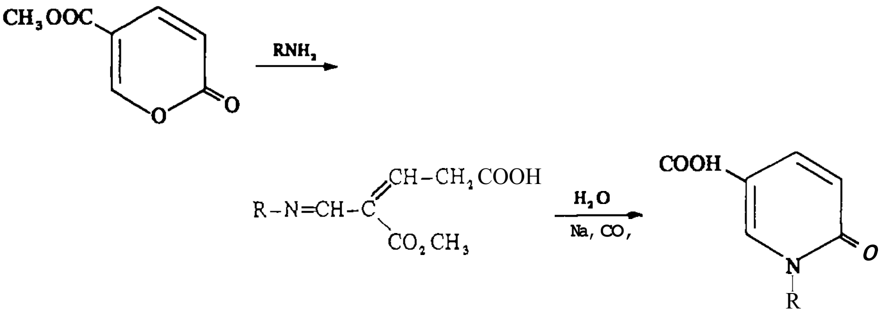
XII-202

A wide range of experimental conditions has been used to effect these transformations. For example, scillaridin A, a **17-β-(5-pyronyl)-steroid** (**XII-203**) does not react with ammonia in methanol or with ammonium acetate in boiling acetic acid and gives only a low yield of pyridone with ammonia in aqueous methanol at 120". It gives the pyridone (**XII-204**) in *58%* yield with ammonium acetate and acetic acid in dimethylformamide at 175" in a sealed **tube.**[114]



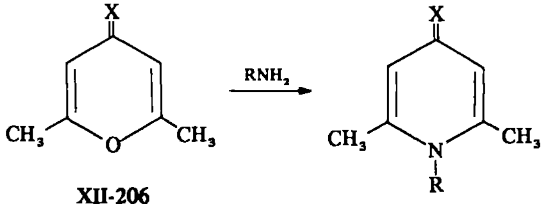
XU-203 **XII-204**

Methyl coumalate reacts with amines to give Schiff's bases that can be cyclized in aqueous sodium carbonate to *N*-substituted-2-pyridones [**XII-205**, R = 2-thiazolyl, 2-pyridyl, **4-methyl-2-pyridyl, 2-(**1,3,4-thiadiazolylmethyl)].[115] After boiling under reflux for 4 hours, 2-pyrone-6-carboxylic acid and ammonium acetate in acetic acid give a 51% yield of 2-pyridone-6-carboxylic acid.[116] 4-Methyl-6-phenyl-2-pyridone is prepared in **98%** yield by heating the corresponding a-pyrone in methanolic ammonia at 100°.[117]



XII-205

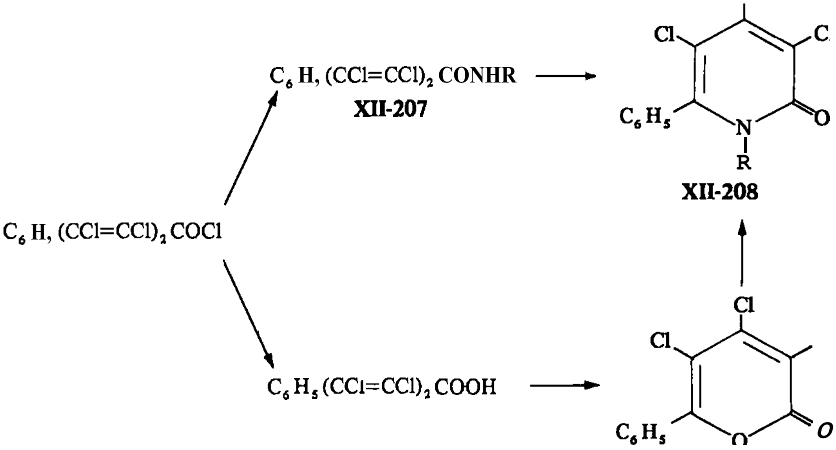
Butylamine and **2,6-dimethyl-4-pyrone** (**XII-206**, **X = O)** and 2,6-dimethyl-4-thiopyrone **(MI-206, X = S)** give the corresponding 4-pyridone and thiopyridone, respectively. Benzylamine, a weaker base and weaker nucleophile, reacts with the thiopyrone but not with the pyrone.[118]

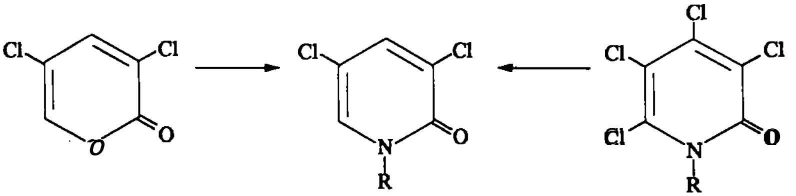


XII-206

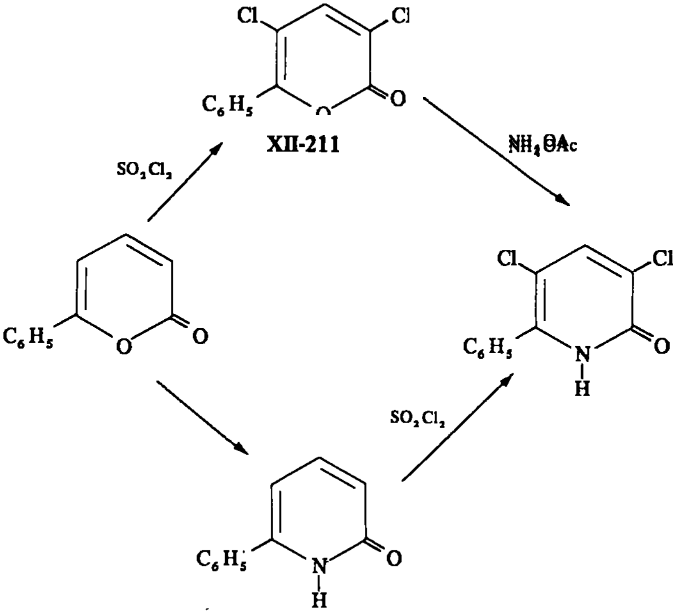
3,4,5-Trichloro-6-phenyl-2-pyridone (XU-208, R = H) can be prepared from the corresponding a-pyrone by boiling it under reflux for 36 hours with ammonium acetate in acetic anhydride and acetic acid. It is, however, more conveniently prepared by cyclization of the amide **XII-207**.[20] **3,5-Dichloro-2-**pyridone (**XII-209**, R = **H)** is formed in low yield from the pyrone. The pyridones **MI-209** (R = **H**, CH_3, C_6H_5) are, however, formed in good yield by reduction of **XII-210** (see Section 1.1.B., p. 604).[18]

3,5-Dichloro-6-phenyl-2-pyridone can be prepared from 6-phenyl-2-pyrone by chlorination with sulfuryl chloride to give **XU-211**, which is then treated with ammonium acetate, or by chlorination of 6-phenyl-2-pyridone.[119] Perchloro-2,4-pentadienoyl chloride and the corresponding methyl ester **(XII-212)** are reduced

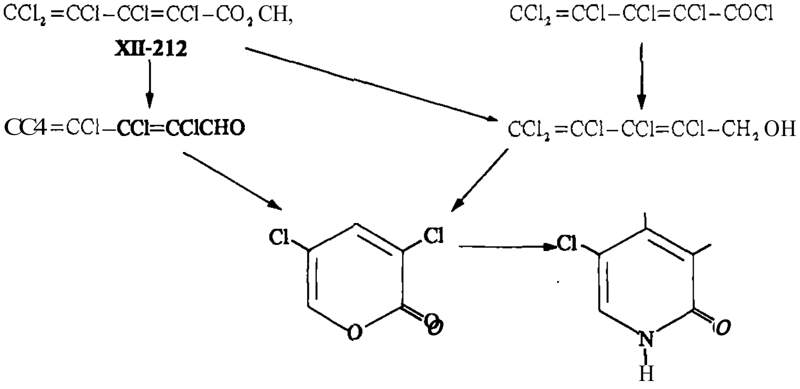




XII-209 **XII-210**

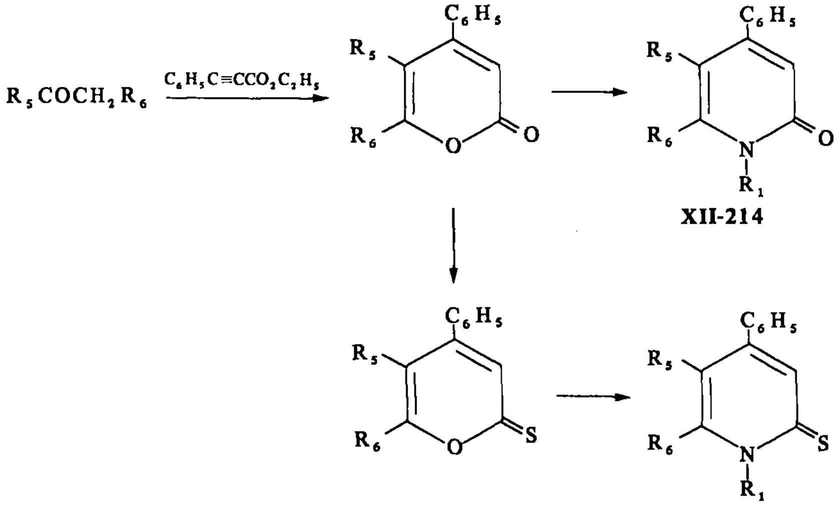


by lithium aluminum hydride at -10° to **perchloro-2,4-pentadien-1-ol.** Cyclization in the presence of manganese dioxide or chromic acid in *t*-butyl alcohol gives **3,4,5-trichloro-2-pyrone,** which is converted to the 2-pyridone **(W-213)** with ammonium acetate in acetic acid'' (see Section I.1.B., p. 604). **3,4,5-Trichloro-2-pyridone (XII-213)** can be formed also from perchloro-2,4-pentadienal by heating in acetic acid.''



XII-213

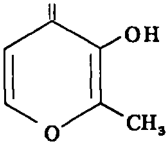
w-Methoxy- and w-aryloxyacetophenones and benzyl phenyl ketones condense with ethyl phenylpropiolate to give **5-methoxy-**[120] and 5-aryloxy-4,6-**diphenyl-2-pyrones,**[121] and **4,5,6-triaryl-2-pyrones.**[122] Ammonia and methylamine give the corresponding 2-pyridones **(XII-214).** *N*-Methyl-2-thiopyridones (MI-215) are formed from 2-thiopyrones and **methylamine.**[122]

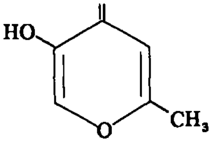


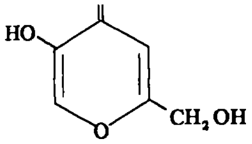
XII-215

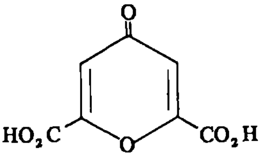
B. *4-Pyrones*

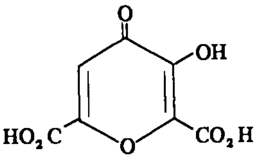
Maltol **(XII-216)**, allomaltol **(XII-217)**, kojic acid **(XII-218)**, chelidonic acid **(XII-219)**, meconic acid **(XII-220)**, and comenic acid **(MI-221, R = H)** are examples of well-known natural products and their derivatives that have been

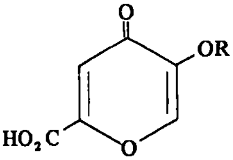

XII-216


XII-217


XII-218


XII-219


xu-220

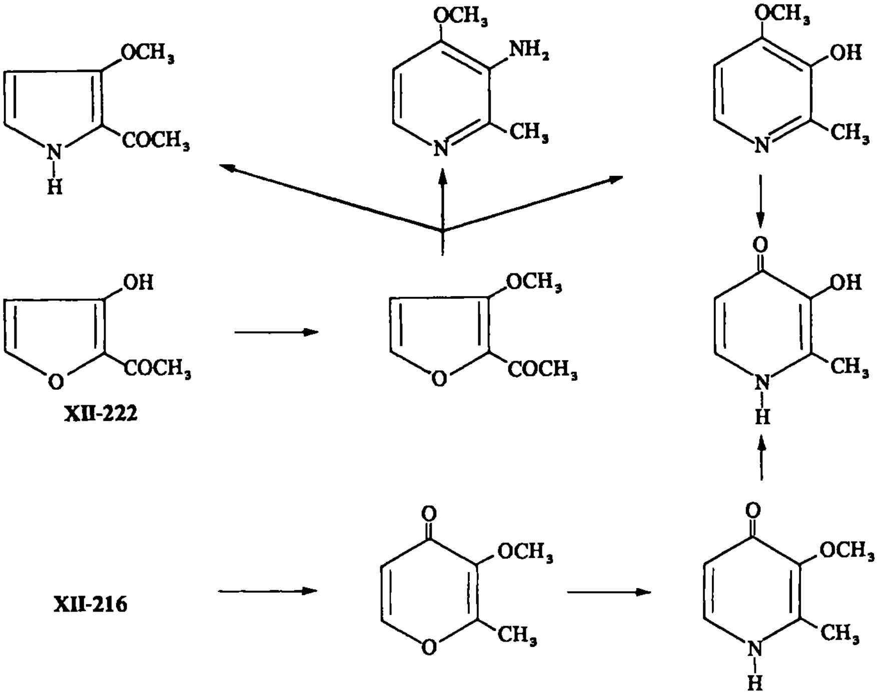

w-221

converted to 4-pyridones. Many of these conversions have been instrumental in elucidating structures of naturally occurring furanols and pyrones.[123]

Isomaltol, first described as a pyrone, has been shown to be 3-hydroxy-2-furyl methyl ketone **(XII-222)**.[124, 125] This structure has been confirmed by its conversion to **3-hydroxy-2-methyl-4-pyridone**,[125] which has been synthesized from maltol **(XII-216)**.[125, 126]

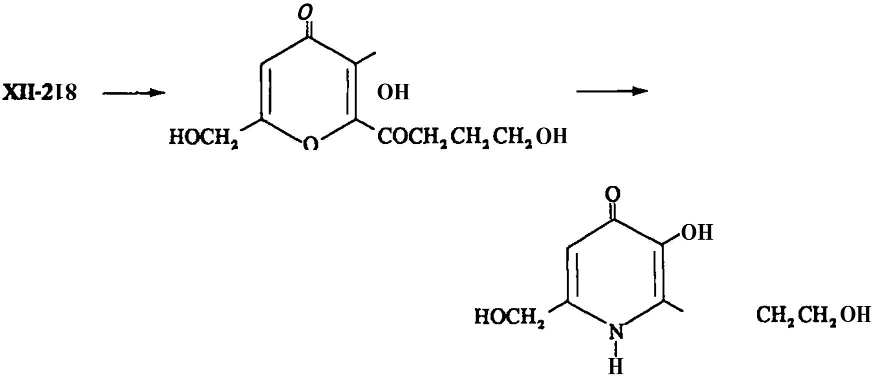
Kojic acid **(MI-218)** is acylated in the 2-position by butyrolactone in trifluoroacetic acid. The product and aqueous ammonia give **3-hydroxy-2-(γ-hydroxybutyryl)-6-hydroxymethyl-4-pyridone**.[127]

Treatment of **MI-220** or **MI-221** (**R** = H, CH_3) with aromatic amines in water gives **1-aryl-5-hydroxy(or methoxy)-4-pyridone-2-carboxylic** acids, which are readily decarboxylated to **XII-223**, (R = H, CH_3) or converted to ethyl esters.[128, 129] **2-Hydroxymethyl-5-methoxy-4-pyrone**, a monomethyl ether of kojic acid, and 2-dialkylaminoethylamines in water give 1-(2-dialkylaminoethyl)-2-hydroxymethyl-5-methoxy-4-pyridones **(MI-224**; R = CH_3, C_2H_5**)**.[130] Natural maltol glucoside and ammonia or primary amines give the corresponding pyridones **(XU-225)** when boiled in methanol.[131]

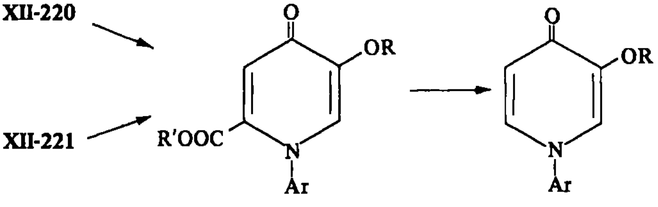


XII-222

XII-216



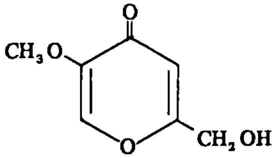
XII-218

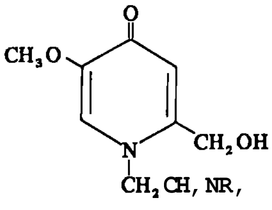


XII-220

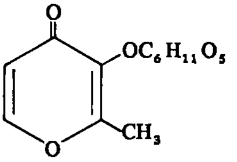
XII-221

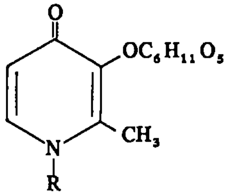
XII-223





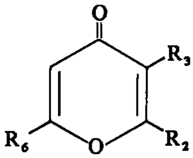
XII-224



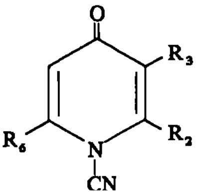


XII-225

γ-Pyrones and cyanamide in aqueous ethanol give *N*-cyano-4-pyridones (**W-226**); however, reactions of **XI-226** with acids or bases have not given characterizable products.[132]



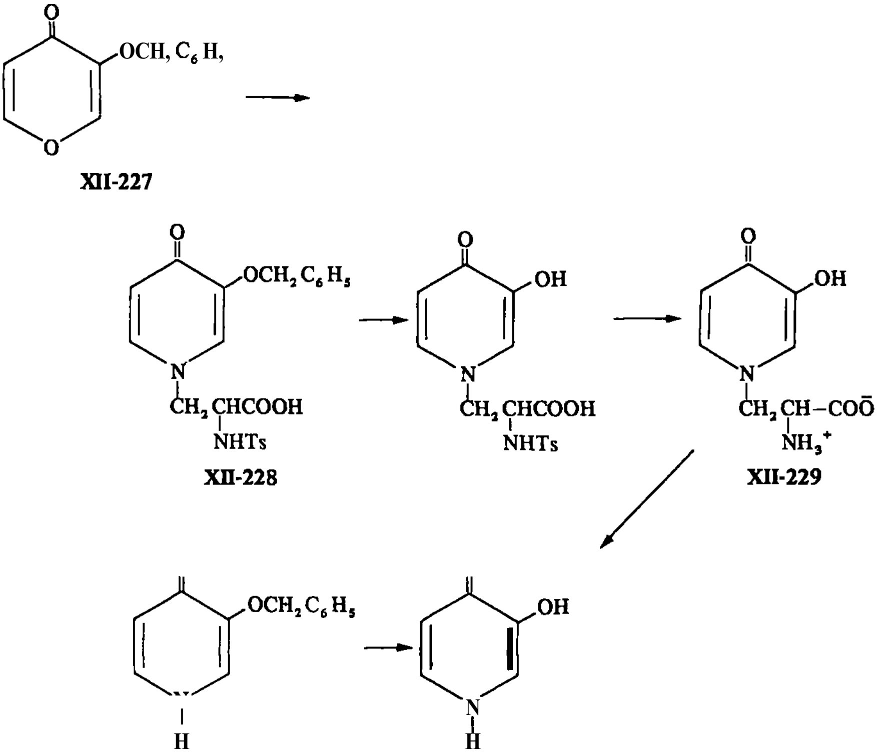
R_2 = H,CH_3; R_3 = H,OH,OCH_3; R_6 = CH_2OH,CH_2Cl,CH_3



W-226

The naturally occurring amino acid mimosine (leucaenine; **W-229**) has been synthesized from meconic acid (**XII-220**), which is decarboxylated and then converted to the benzyl ether (**W-227**). Mimosine is obtained *via* **XII-228**.[133] 3-Hydroxy-4-pyridone was formed by treatment of mimosine with zinc dust or by hydrogenolysis of 3-benzyloxy4-pyridone in a procedure designed to locate the label from aspartic acid incorporation into 4-pyridone in *Mimosa pudica*.[134]

Although the Cpyridones **W-230** can be prepared from the pyrones, it is more convenient to obtain them directly from triketones by treatment with ammonia in ethanol'' (see Section I.1.C., p. 608). **1-Phenyl-1,3,5-hexanetrione** is acetylated and cyclized by boron trifluoride and acetic anhydride to the 4-pyrone (**W-231**). Conversion to **3-acetyl-2-methyl-6-phenyl-4-pyridone** in low yield is accomplished in anhydrous ammonia.[135] **1,5-Diphenyl-1,3,5-pentanetrione** gives **3-benzoyl-2-methyl-6-phenyl-4-pyrone** (**XII-232**), which reacts with



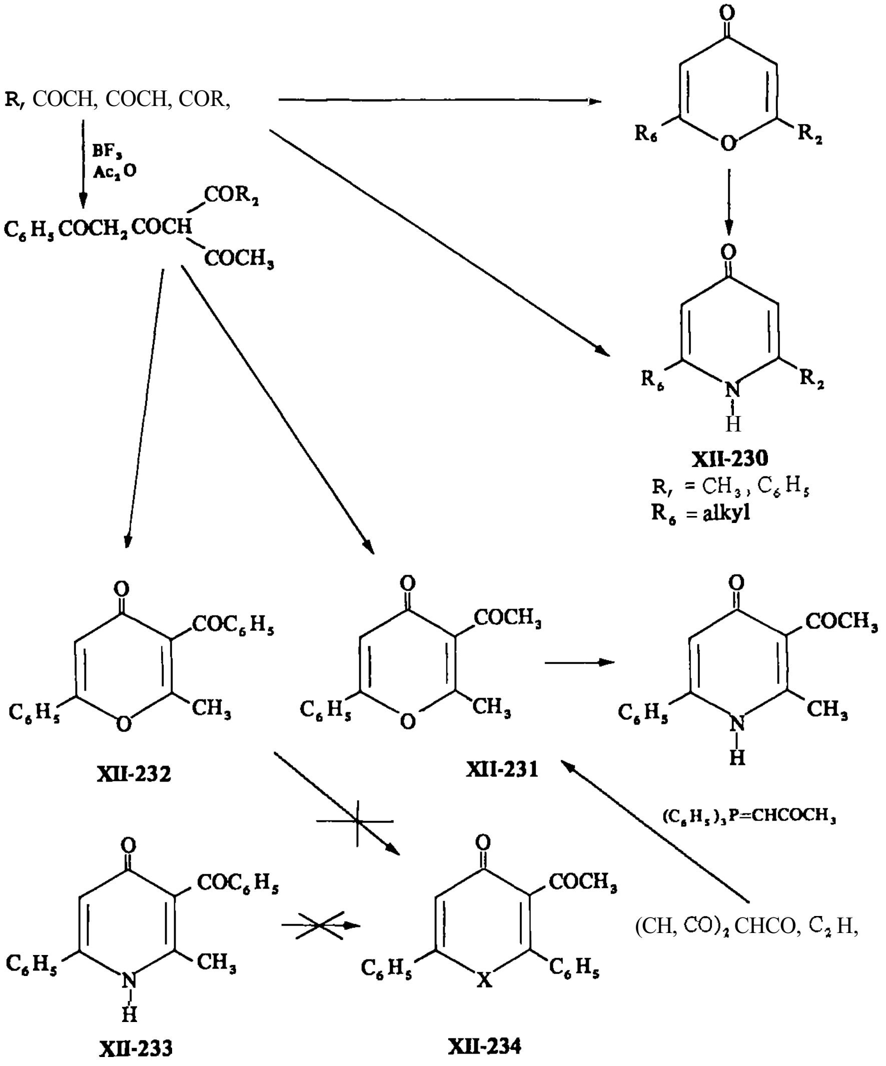
XII-227

XII-228

XII-229

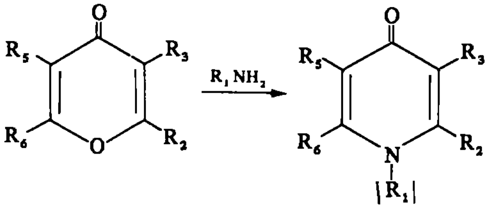
liquid ammonia to form the pyridone XI-233 in 86% yield. Products isomeric with XII-232 and XII-233, such as XII-234 (X = O, NH), were not found.[135] β-Ketoesters react with acyl and aroyl phosphorus ylids to give the same 4-pyrones. For example, ethyl a-acetylacetoacetate and benzoylmethylenetriphenylphosphorane give XII-231.[136] Additional conversions of 4-pyrones to 4-pyridones are summarized in Table XI-2.

Lutidones rather than 4-hydroxy-2-pyridones are formed from dehydroacetic acid (XII-235) and ammonia or primary amines.[142] With one equivalent of aqueous or ethanolic primary amine at ambient temperatures, dehydroacetic acid gives **3-(α-alkylaminoethylidene)-6-methylpyran-2,4-diones** (XI-236). An excess of amine (R = Me, Et, *n*-Pr, n-Bu, $CH_2C_6H_5$, $CH_2CH_2C_6H_5$) and dehydroacetic acid give **2,6-bisalkylaminohepta-2,5-dien-4-ones** (XII-237) or the lutidones (XII-238), depending on conditions.[108, 143-148] Aqueous ammonia and dehydroacetic acid give some 3-carboxylutidone XII-239, which is not decarboxylated under the reaction conditions and therefore is not an intermediate in the formation of lutidone under these conditions.[147, 148] These dienones

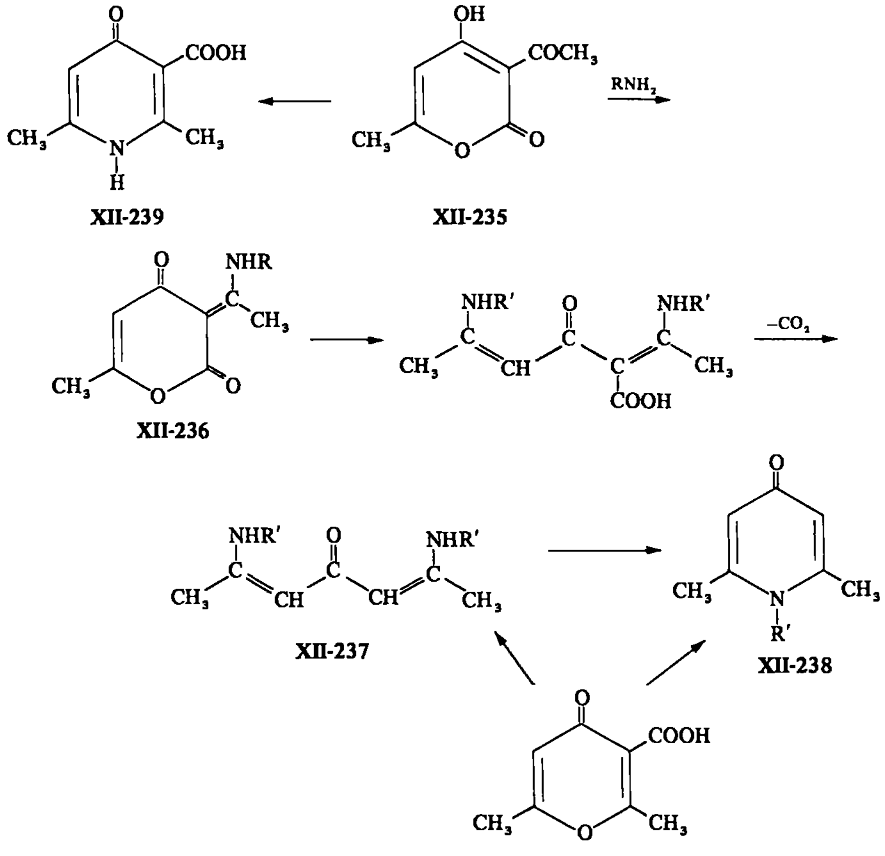


(XU-237) in which the two alkyl groups are different were not isolated on treatment of W-236 (R = Et) with **methylamine.**[108] Aqueous dimethylformamide has been used as the solvent to give **XII-236.**[145] Compounds **XII-236** could not be converted directly to the lutidones **XII-238,**[143] which indicates that the *N*-methyllutidone is not formed by rearrangement of XII-236 through an intramolecular nucleophilic attack by the nitrogen on C-6.[143] However, XII-236 (R = $CH_2CH_2C_6H_5$, $CH(CH_3)CH_2C_6H_5$) in dilute mineral acid does give **XII-238.**[145] Under appropriate conditions diacetylacetone and amines give **the**

TABLE XI-2. Conversion of 4-Pyrones to 4-Pyridones



R1	R2	R3	R5	R6	%Yield	Ref.
H	CH_3	H	H	CH_3	65	137
H	CH_3	H	H	2-quinolylmethyl	80	138
CH_3	H	CH_3	CH_3	H	74	139
CH_3	CH_3	H	H	CH_3	–100	140
H	CH_3	$COCH_3$	H	CH_3	–	141



XII-239

XII-235

XII-236

XII-237

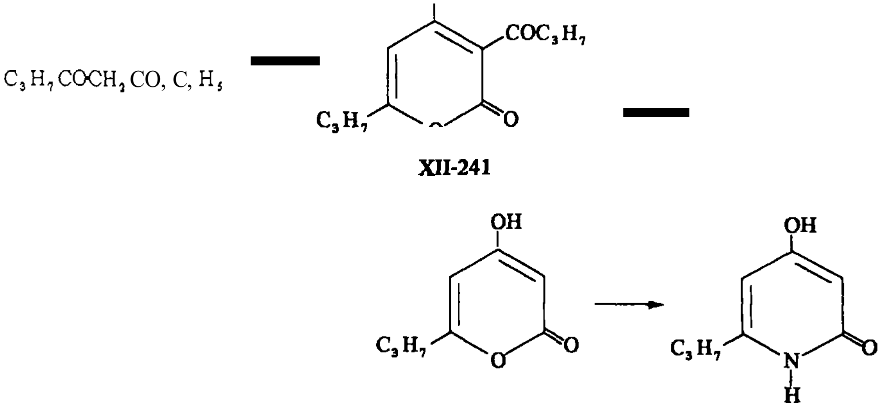
XII-238

MI-240

dienone **MI-237** or the lutidone XII-238.[143,144] **3-Carboxy-2,6-dimethyl-4-pyrone (XII-240)** and amines **also** give **XU-237** or **XII-238.**[149] Ethanolamine and dehydroacetic acid give **XII-236 and** XII-238 (R' = CH_2CH_2OH), but not **XII-237.**[147,148] *N*-Phenyllutidone **(XU-238,** R = C_6H_5) is prepared from dehydroacetic acid and aniline by boiling in concentrated hydrochloric acid for 2 **hours.**[147]

C. *4-Hydroxy-2-pyridones from Pyrones*

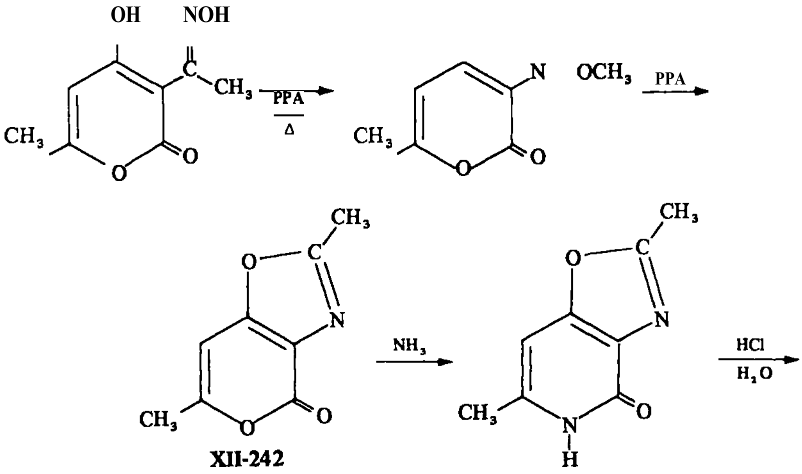
Ethyl n-butyroacetate, **on** treatment with sodium bicarbonate, gives the dehydroacetic acid homolog **W-241,** which, **on** treatment with 90% H_2SO_4, is converted to **4-hydroxy-6-propyl-2-pyrone,** which gives 4-hydroxy-6-*n*-propyl-2-pyridone in low yield when treated with ammonia.' [50]



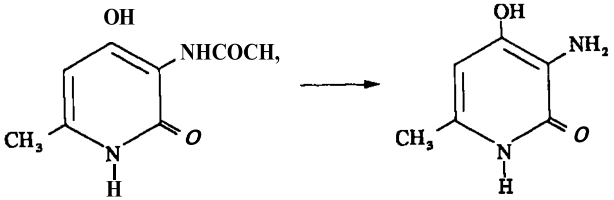
XII-241

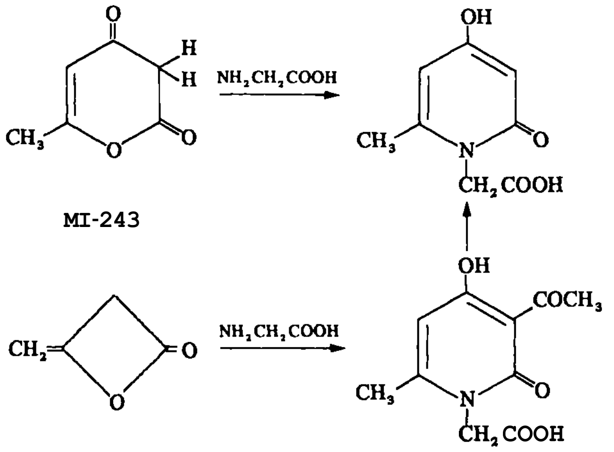
Dehydroacetic acid oxime rearranges in polyphosphoric acid to 3-acetamid04 **hydroxy-6-methyl-(2*H*)-2-pyrone** and **2,6-dimethyl-(4*H*)-pyrano**[3,4-*d*] oxazol-4-one **(W-242).** Treatment of **W-242** with ammonia gives 2,6-dimethyl-(5*H*)-oxazolo[4,5-*c*]-4-pyridone, which, in turn, gives 3-acetamido-4-hydroxy-6-methyl-2-pyridone with hydrochloric acid at room temperature and **3-amino-4-hydroxy-6-methyl-2-pyridone** on heating.' [51]

Reactions between triacetic acid lactone **(MI-243)** and ammonia or amines to give 4-hydroxy-6-methyl-2-pyridones are well **known.**[152,153] For example, glycine and **XII-243** give **1-carboxymethylene-4-hydroxy-6-methyl-2-pyridone.'** [54] This latter 4-hydroxy-2-pyridone has also been formed from diketene and glycine in aqueous base *via* **XU-244,** which can be deacetylated in concentrated sulfuric acid. Dehydroacetic acid does not appear to be an intermediate in the formation of **XII-244.** Under these conditions it reacted with glycine to form **an** isomeric product, which, however, was not characterized.[154]



XII-242



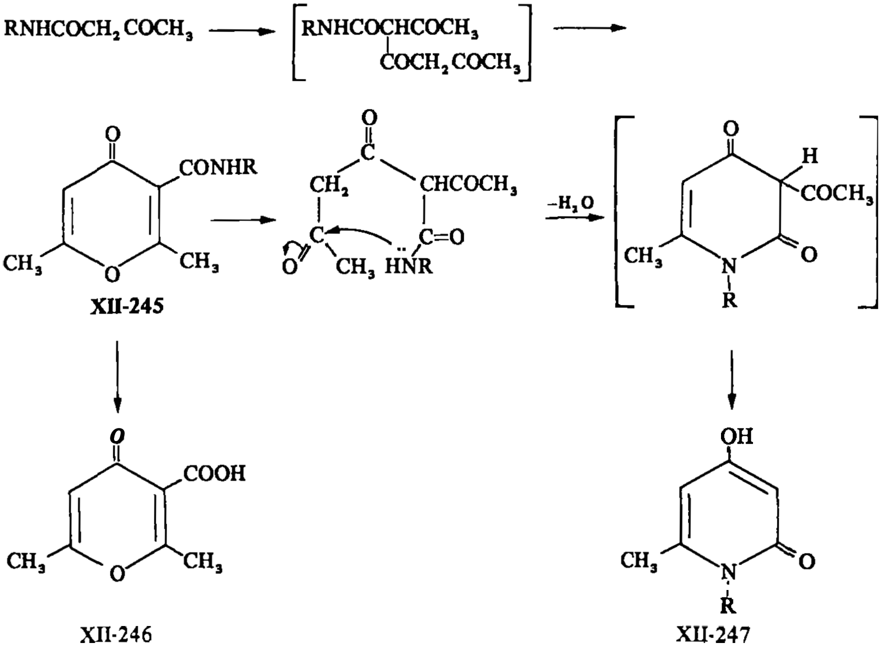


MI-243

XII-244

On heating with polyphosphoric acid *o*-haloacetoacetanilides give mixtures of 4-hydroxyquinaldines and 3-arylcarbamyl-2,6-dimethyl-4-pyrones (**XII-245**; R = 2-ClC$_6$H$_4$, 2,4-Cl$_2$C$_6$H$_3$, 2,5-Cl$_2$C$_6$H$_3$, 2-BrC$_6$H$_4$). The 4-pyrones (**XU-245**) are hydrolyzed in 70% sulfuric acid to give mixtures of the 4-pyrone-3-carboxylic acids (MI-246) and the **N-aryl-4-hydroxy-6-methyl-2-pyridones (XII-247)**.[149]

A compound previously described as **3-benzoyl-6-phenyl-2,4-(1*H*,3*H*)** pyridinedione **(XII-248)**[155] and earlier as **2,6-diphenyl-4-pyridone**,[156] which is formed

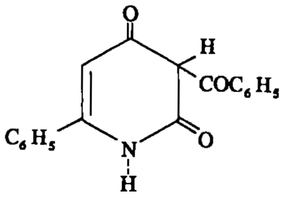


XII-245

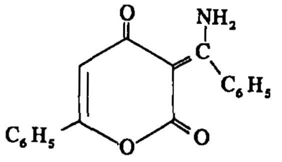
XII-246

XII-247

from **3-benzoyl-6-phenylpyran-2,4-(3*H*)-dione** and ammonia, has been shown to be **3-α-aminobenzylidene-6-phenyl-2*H*-pyran-2,4-(3*H*)dione (XII-249)**[143] (see also XII-236, p. 653).



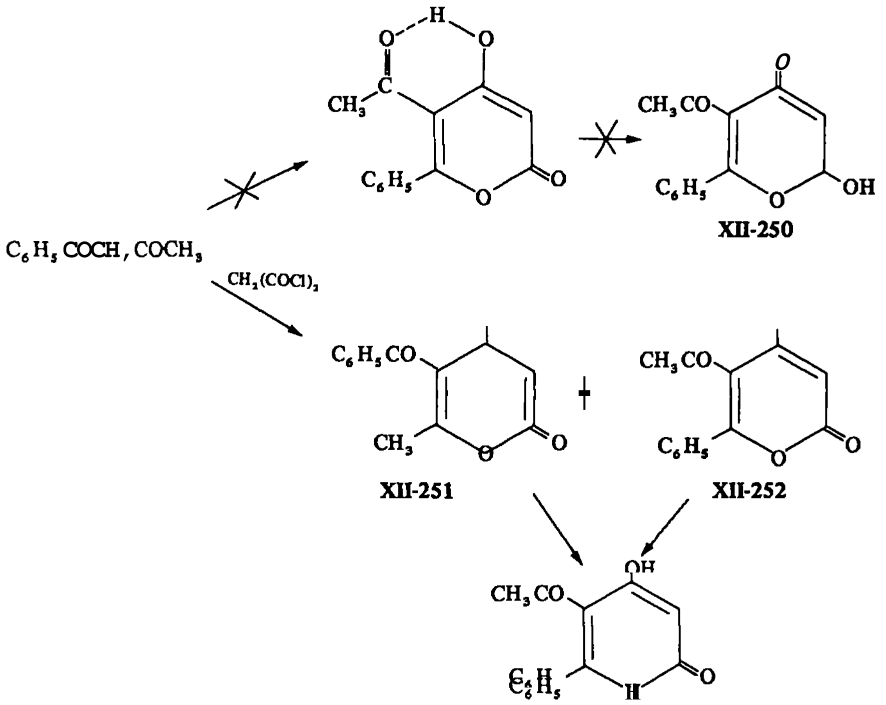
XII-248



XII-249

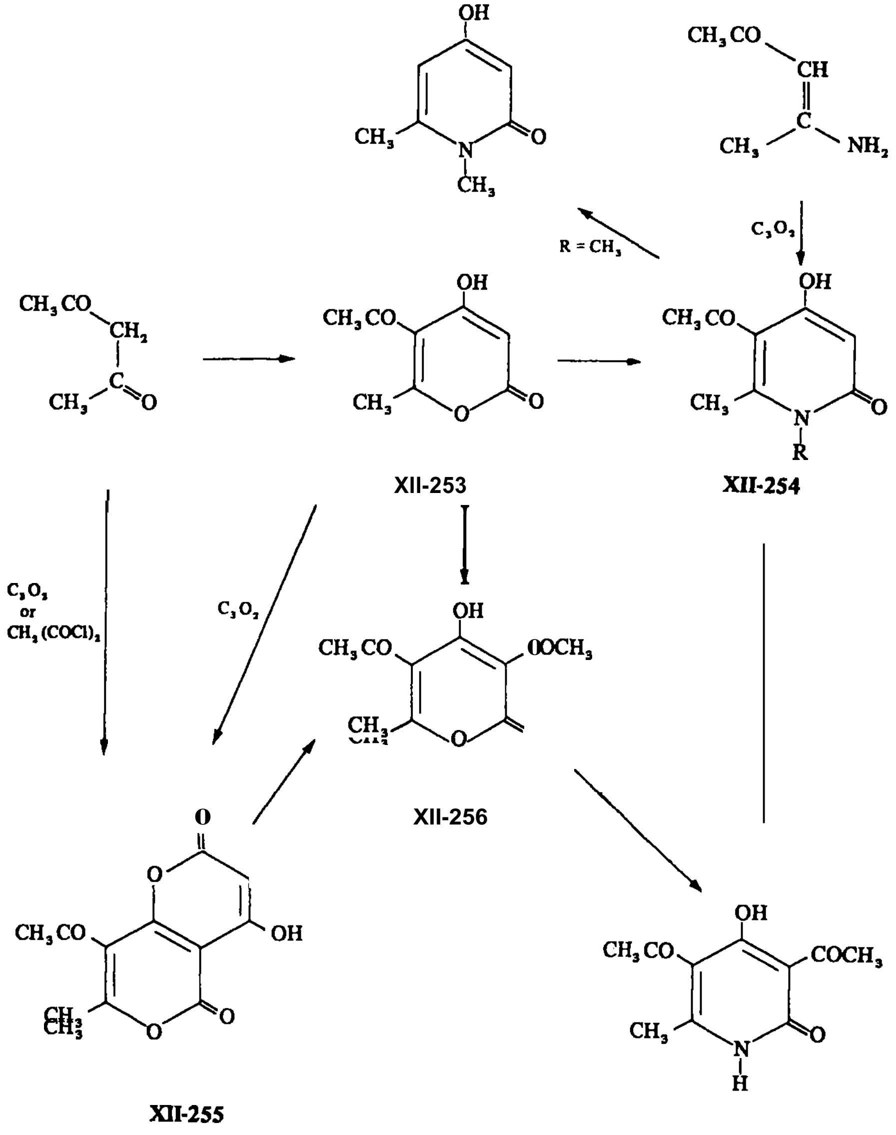
Although ketones, including ethyl acetoacetate and several related compounds, react with malonyl chloride to form chloropyranodioxins (this section, p. 661), **1,3-diketones** give pyrones. It was proposed originally that benzoylacetone forms the 4-hydroxy-2-pyrone that tautomerizes to the 2-hydroxy-4-pyrone

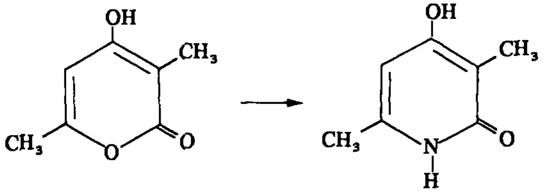
(XII-250).[94] It was shown later, however, that the reaction gives a mixture of the isomers **W-251** **(60%)** and **XI-252** **(40%)** and that both give **5-acetyl-4-hydroxy-6-phenyl-2-pyridone** on treatment with aqueous ammonia?’



Acetylacetone and malonyl chloride give 5-acetyl-4-hydroxyd-methyl-2-pyrone (XII-253), a positional isomer of dehydroacetic acid, which reacts with aqueous ammonia or aqueous methylamine to form XII-254 (R = H, CH_3),[94] which can also be prepared from the enamine of acetylacetone and carbon suboxide[87] (see Section **I.3.E.**, p. 635). The *N*-methylpyridone XII-254 (R = CH_3) is deacetylated to **4-hydroxy-1,6-dimethyl-2-pyridone** with sulfuric acid; however, W-254 (R = H) was not deacetylated under these **conditions.**[94] Acetylacetone and carbon suboxide give 8-acetyl-4-hydroxy-7-methylpyrano-**[4,3-*b*]** pyrane-2,5-dione (XI-255) with catalytic amounts of sulfuric acid. This is also formed from acetylacetone and malonyl chloride or from carbon suboxide and the intermediate **5-acetyl-4-hydroxy-6-methyl-2-pyrone (XII-253).**[157] **3,5-Diacetyl-4-hydroxy-6-methyl-2-pyrone** (XI-256) can be formed by acetylation of XII-253 with acetic acid and phosphorus oxychloride or by degradation of XII-255. **3,5-Diacetyl-4-hydroxy-6-methyl-2-pyridone** can be prepared quantitatively from W-256 and ammonia or by acetylation of XII-254.[157]

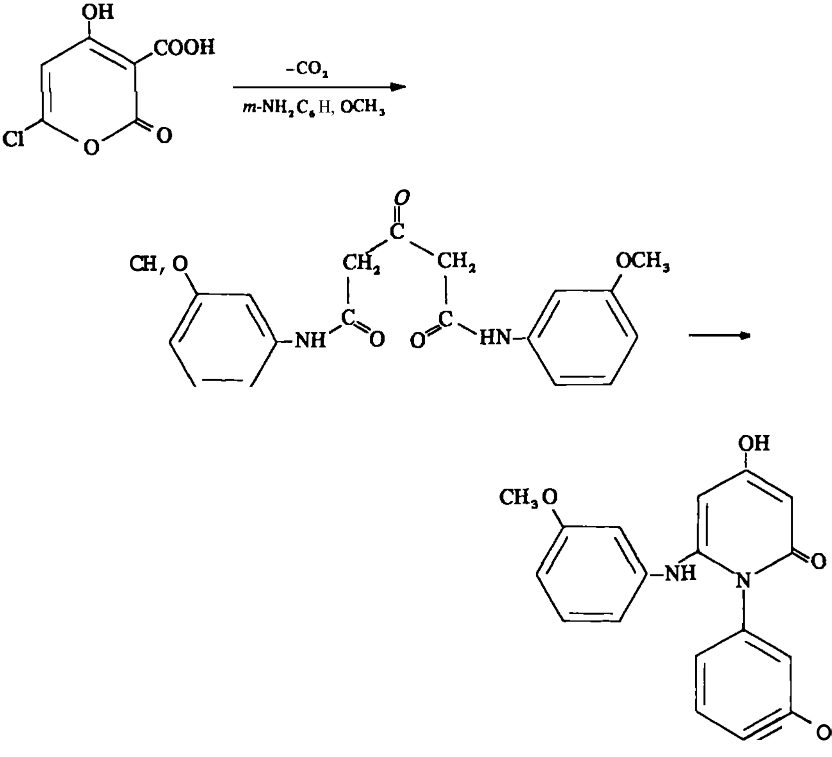
A product of the tropolone-producing mold *Penicillium stipitaturn* was identified as 3,6-dimethyl-4-hydroxy-2-pyrone by its conversion to 3,6-dimethyl-4-hydroxy-2-pyridone (W-257) with ammonia in a sealed tube at 120° and to the *N*-methyl-2-pyridone with aqueous methylamine.[158, 159]





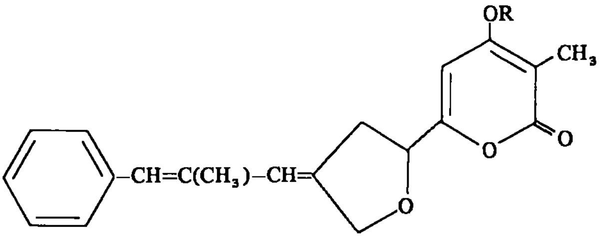
XII-257

Treatment of **2-bromo-6-hydroxymethyl-3-methoxy-4-pyrone** with aqueous ammonia or aqueous methylamine gives **4-hydroxy-2-pyridones.**[160] 6-Chloro-4 hydroxy-2-pyrone-3-carboxylic acid and *m*-anisidine give *N,N*-di-*m*-methoxy**phenylacetonedicarboxamide,** which can be converted to **4-hydroxy-*N*-(*m*-methoxyphenyl)-6-(*m*-methoxyanilino)-2-pyridone** (XII-258) by heating with phosphorus **oxychloride.**[161]



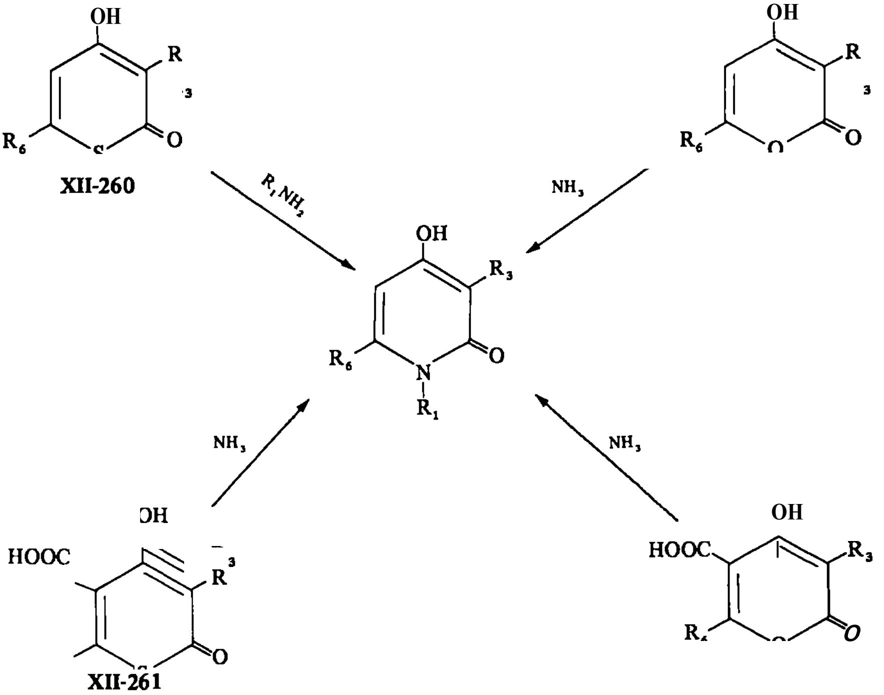
XII-258

Ammonia or ammonium acetate in acetic acid and aureothin, desmethylisoaureothin **(W-259,** R = H), and isoaureothin **(XII-259,** R = CH_3) give nitrogen-containing products. Only the product from **XII-259** (R = H) could, however, be identified as the corresponding pyridone.[162]



XII-259

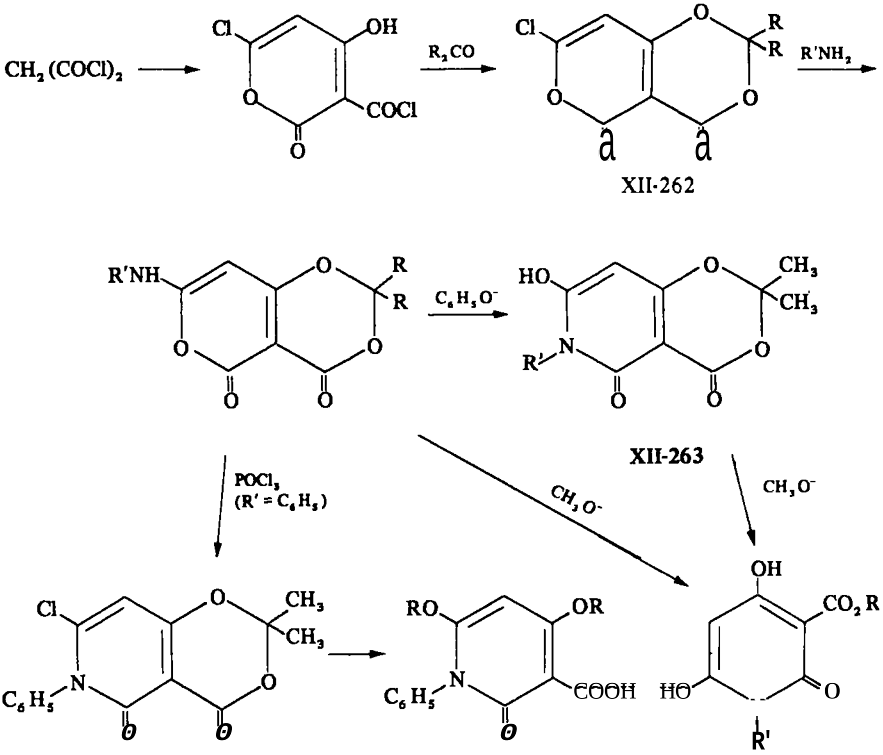
1-Thiopyran-2-ones (**XII-260, XII-261**), as well as the corresponding pyrones, give pyridones when treated with ammonia or amines. Under the conditions used (18 hr at 120°) decarboxylation at the 5-position occurs.[163]



XII-260

XII-261

7-Chlorodioxopyrano-1,2-dioxins (**XII-262**), prepared from malonyl chloride and ketones,[164-166] are converted to 7-substituted aminodioxopyrano-1,3-dioxins when treated with amines.[164, 167] The 7-amino derivatives isomerize in the presence of alkoxides to **6-aryl-2,2-dimethyl-7-hydroxy-4,5-dioxopyrido**[4,3-*d*]-**1,3-dioxins (XII-263)**, which are converted to **3-carbomethoxy-4,6-dihydroxy-2-**pyridones **(XII-264)**.[167-169] The intermediate pyridodioxins **(MI-263) are** isolated when sodium phenoxide is **used**.[170] The 7-aminopyranodioxin (R' = C_6H_5) and phosphorus oxychloride form the 7-chloropyridinodioxin, which gives **4,6-dialkoxy-3-carboxy-*N*-phenyl-2-pyridones (XII-265**; R = CH_3, C_2H_5) when treated with alkoxide **ion**.[167]



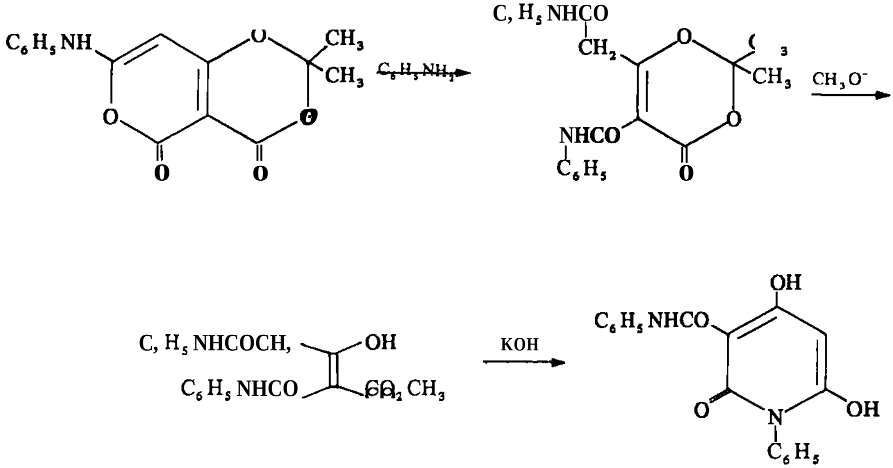
XII-262

XII-263

XII-265

XII-264

2,2-Dimethyl-7-phenylamino-4,5-dioxopyrano[4,3-*d*]-1,3-dioxin reacts with aniline to form a **1,3-dioxindiamide**, which gives an acetone-tricarboxylic acid derivative when treated with sodium **methoxide**.[164] Cyclization to 4,6-dihy-

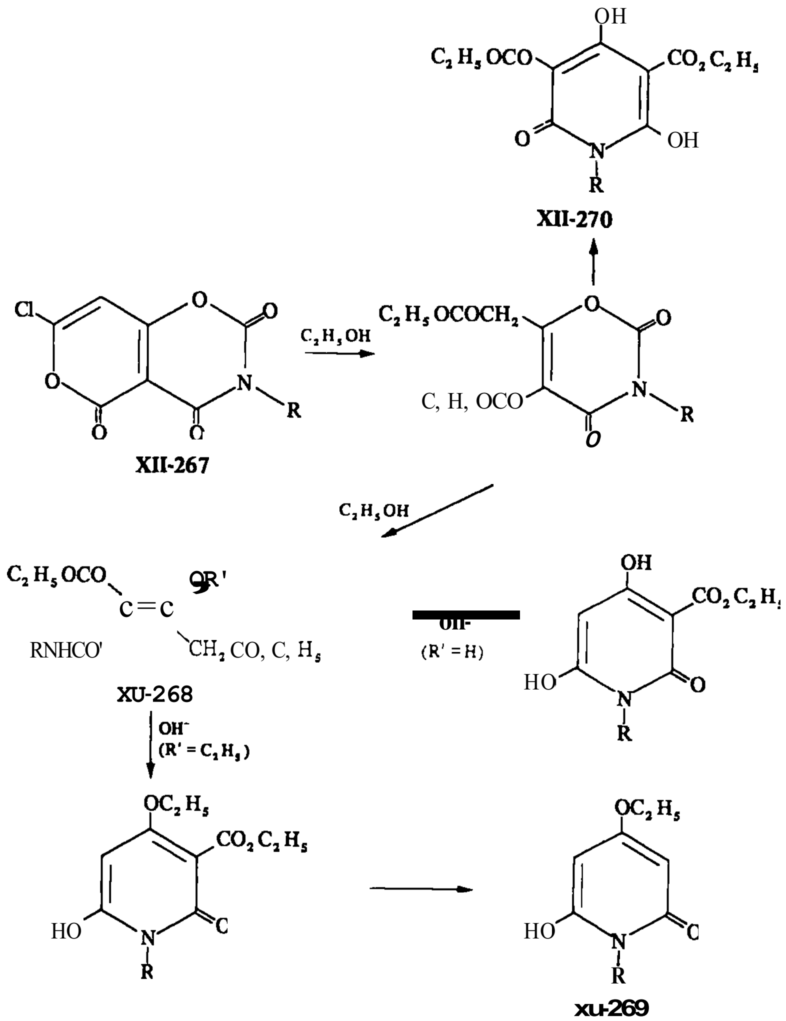


XII-266

droxy-1-phenyl-3-(*N*-phenylcarbamoyl)-2-pyridone (XII-266) occurs on boiling with methanol containing potassium **hydroxide.**[171, 172]

Isocyanates and malonyl chloride or isocyanates and 6-chloro-4-hydroxy-2-oxopyran-3-carbonyl chloride give **7-chloro-2,4,5-trioxopyrano**[3,4-*e*]-1,3-oxazines (**XII-267**), which can be converted to 2,4-dioxo-**1,3-oxazines** and diethyl 2-carbamoyl-3-ethoxy-2-pentenedioates (MI-268, R = Et) when heated with ethanol. Isothiocyanates react similarly to form thio analogs. When MI-268 (R = Et) is heated in ethanolic potassium hydroxide, **3-carbethoxy-4-ethoxy-6-**hydroxy-2-pyridones are formed that can be saponified and decarboxylated to MI-269. Hydrolysis of the enol ethers (MI-268) gives the enol (XU-268, R = H), which can be cyclized in ethanolic potassium hydroxide to the *N*-substituted-3-**carbethoxy-4,6-dihydroxy-2-pyridone.** The dioxo-oxazines in ethanolic potassium hydroxide give **3,5-dicarbethoxy-4,6-dihydroxy-2-pyridones (XII-270).**[171]

7-Amino-2,4,5-trioxo-3-phenylpyrano[3,4-*e*]-**1,3-oxazines**[172] and sodium phenoxide in phenol as solvent give **6-hydroxy-2-oxo-4-phenoxy-1**-substituted pyridine-3-carboxanilides (W-271; R_1 = aryl, R = phenyl). It has been suggested that the aryloxy ion attacks the ring with concomitant loss of CO_2 followed by isomerization to the product. Intermediates could not be **isolated.**[172, 173] Alcoholic potassium hydroxide and the oxazines give MI-271 (R = H).[174]

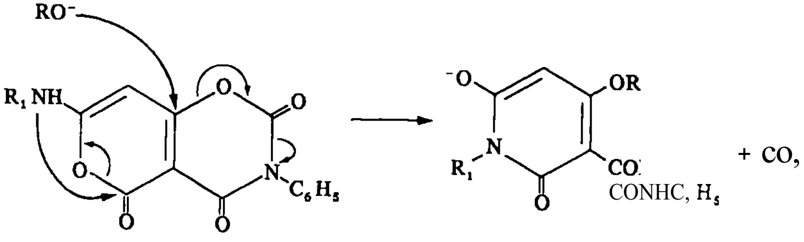


XII-270

XII-267

XU-268

xu-269

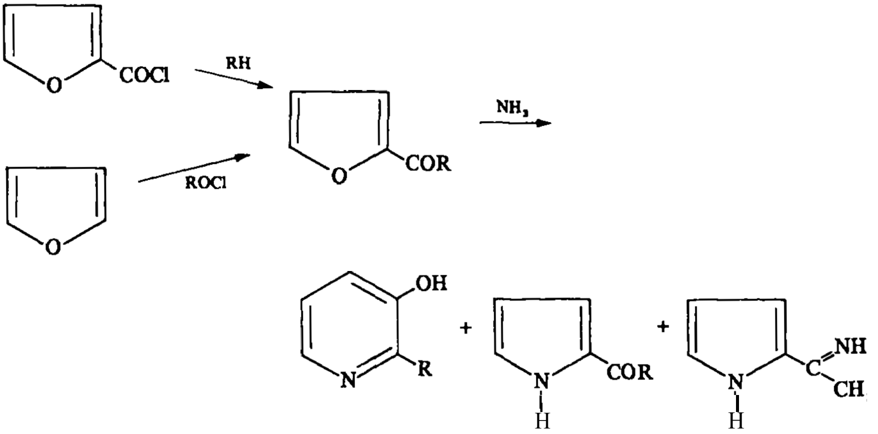


XII-271

$R_1 = C_6H_5$; *o*-, *m*-, and *p*-CH_3C_6H, ;*o*-, *m*-, and *p*-CH_3OC_6H,, m-OHC, H_4, $CH_2=CH-CH_2$, isoC_4H_9.

D. *3-Pyridinols from Furans*

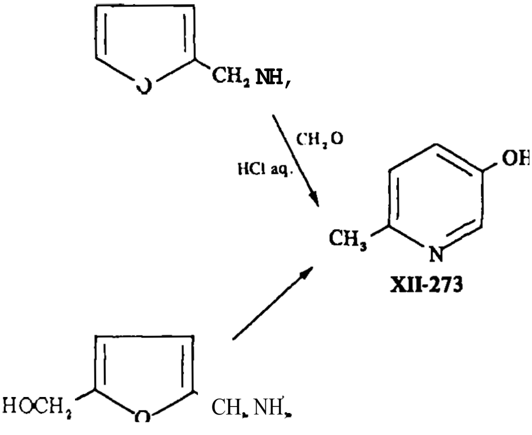
Acylfurans, convenient intermediates for the synthesis of 2-substituted-3-hydroxypyridines,[175] are synthesized by acylation of furans or by acylation of aromatic substrates with 2-furoyl halides. 3-Pyridinols **(XII-272)**, pyrrolyl ketones, and pyrroyl ketimines are formed on treatment with ammonia.[176-182]



XII-272

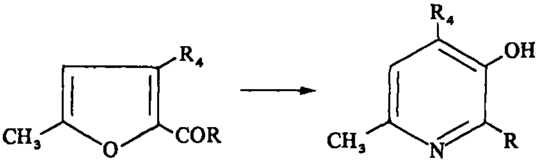
The products can be separated conveniently by **"sublimatography"**.[179-181]

6-Methyl-3-pyridinol **(MI-273)** can be prepared directly from furfurylamine and formalin in hydrochloric acid[183] or by way of **2-aminomethyl-5-hydroxy-**methylfuran.[184]



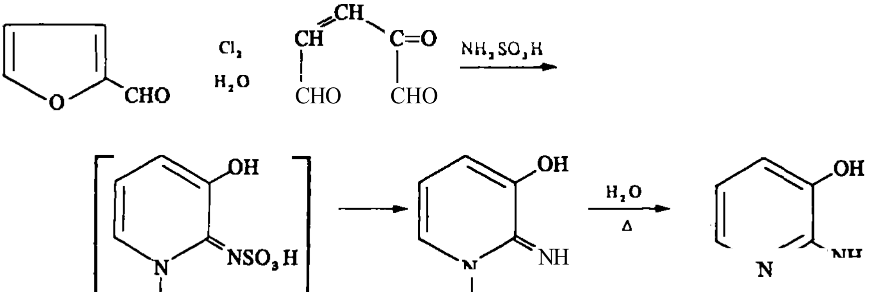
XII-273

The reaction of 2-acylfurans to form 3-pyridinols is not prevented by **small** alkyl groups at C-3. 3-Methyl- and **3-ethyl-5-methyl-2-acetylfuran (XI-274**; R = CH_3, R_4 = CH_3, CH_3CH_2)[185] and 2-aroyl-3-methylfurans (**XI-274**; R = aryl, R_4 = CH_3)[186] form 3-pyridinols without difficulty.



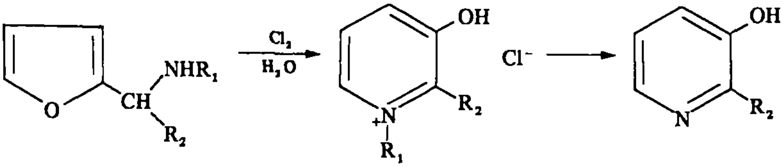
XII-274

Oxidation of furfural with chlorine water or sodium hypochlorite followed by treatment of the product (see Section I.1.C.) with sulfamic acid gives **3-hydroxy-2-imino-1(2*H*)-pyridinesulfonic** acid, which is converted to 2-amino-3-pyridinol (**XI-275**) on hydrolysis.[187, 188]



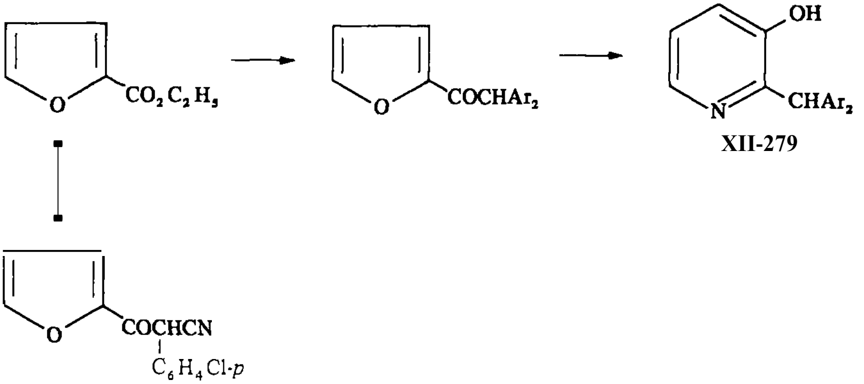
XII-275

Oxidation **of** *N*-**monosubstituted-2-(α-aminoalkyl)furans (XU-276)** with chlorine water gives *N*-**alkyl-3-hydroxypyridinium** chlorides (**XI-277**; R_1 = alkyl, R_2 = H, CN, $CONH_2$). The 2-cyanomethylfurans (XII-276; R_1 = alkyl, R_2 = CN) are prepared from furfural by a Strecker reaction and hydrolyzed to the amides (**XI-277**, R_2 = $CONH_2$). Pyridinium salts of the amides (**XI-277**, R_1 = CH_3, C_2H_5, $CH_2C_6H_5$; R_2 = $CONH_2$) give 3-hydroxypicolinamide (**XI-278**, R_2 = $CONH_2$) on **heating**.[189]

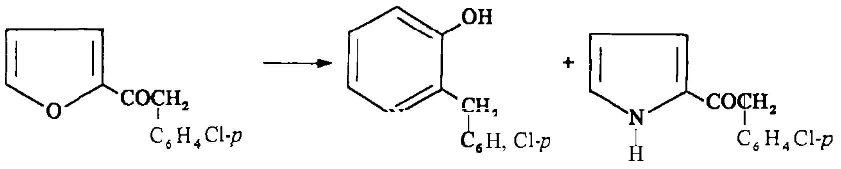


XII-276 **XII-277** **XII-278**

A variety of 2-substituted-3-pyridinols can be prepared by well-known methods.[190] For example, diarylmethyl 2-furyl ketones are prepared in good yield from ethyl furoate and diarylmethanes using KNH_2 or $NaNH_2$ in liquid ammonia and are conveniently converted to **XII-279**. *p*-Chlorobenzyl 2-furyl ketones, which can be converted to **XII-280**, can be prepared from p-chlorophenylacetonitrile and ethyl furoate by condensation in the presence of alkoxide followed by hydrolysis and decarboxylation. 2-Pyrryl ketones are also formed in the last step. Several 2-furyl ketones are cleaved under these reaction conditions and do not give 3-pyridinols.[191]

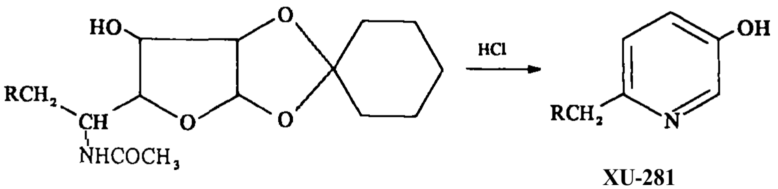


XII-279



XII-280

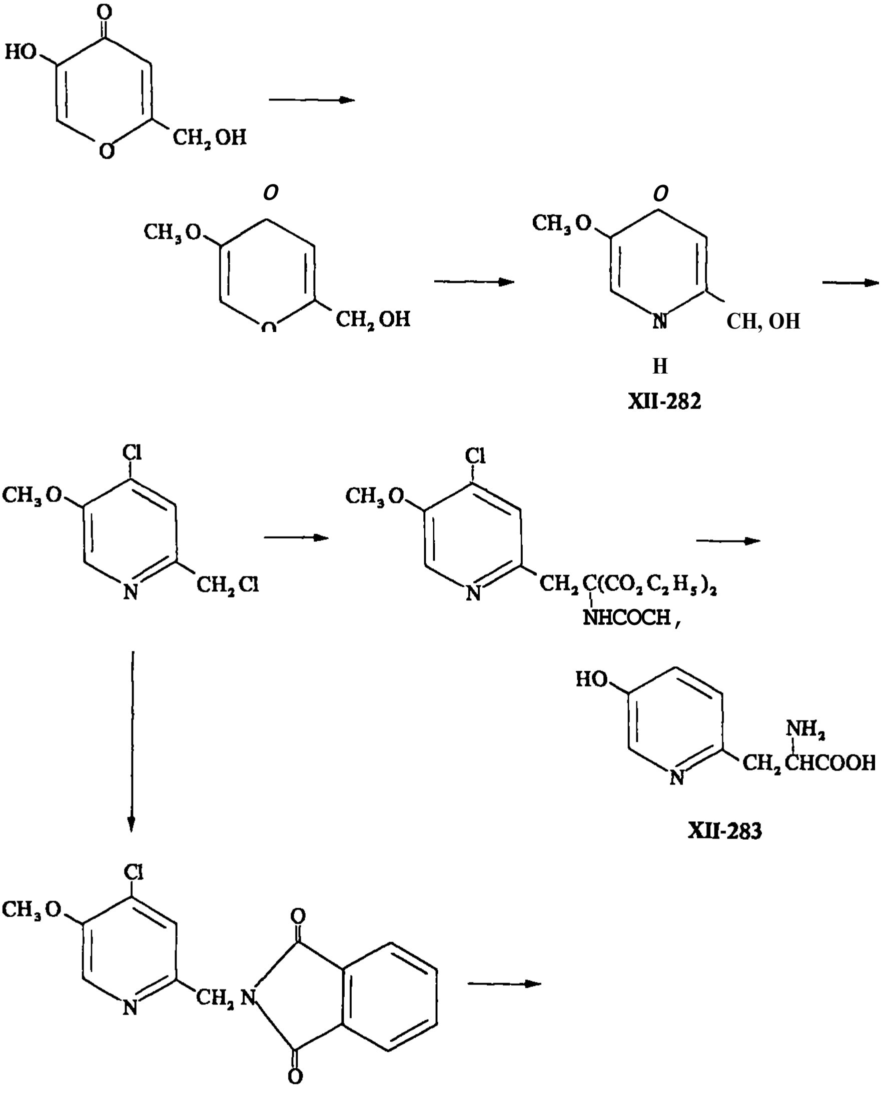
Derivatives of 5-aminoaldoses have been partially characterized by conversion to 3-pyridinols. For example, 6-amino- and 6-nitro-5-acetamido-1,2-*O*-cyclohexylidene-5,6-dideoxy-L-iodofuranose and the corresponding D-glucofuranoses when boiled under reflux with hydrochloric acid form 6-aminomethyl- and 6-nitromethyl-3-pyridinol (**XII-281**, R = NH_2, NO_2).[192, 193]



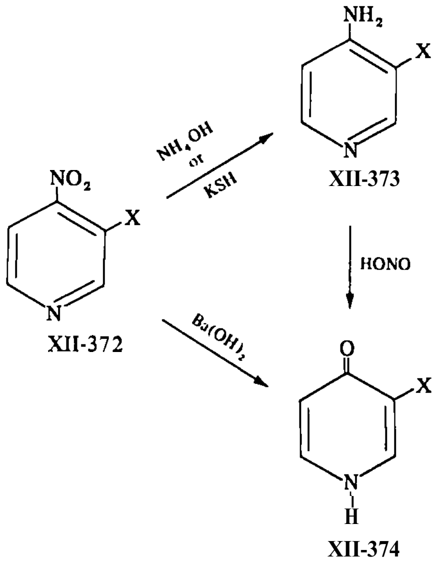
XU-281

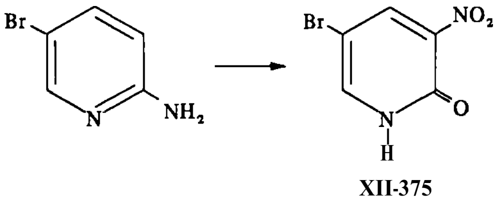
E. *3-Pyridinols from Pyrones*

3-Pyridinols have been prepared indirectly from kojic acid **(XII-218,** p. 649), which reacts with dimethyl sulfate to give 2-hydroxymethyl-5-methoxy-4*H*-pyran-4-one, which can be converted to 2-hydroxymethyl-5-methoxy-4-pyridone **(XII-282)** with aqueous ammonia. Treatment of **XII-282** with phosphorus

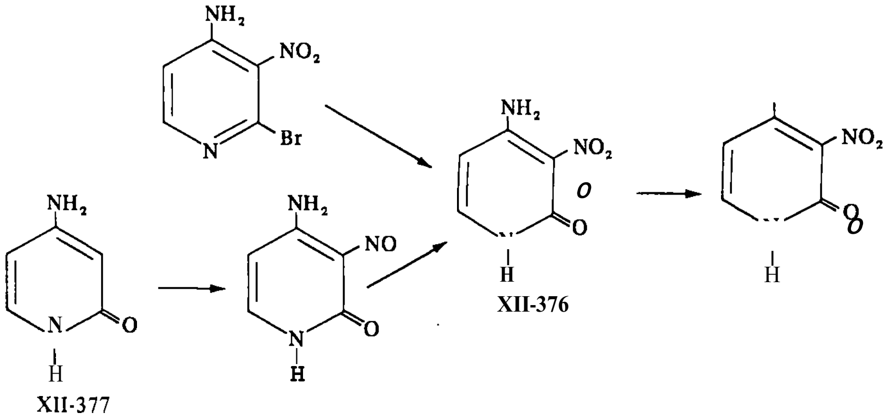

XII-282

XII-283





the nitramine can be converted to **4-amino-3-nitro-2-pyridone (XI-376)** with potassium hydroxide containing hydrogen peroxide. 3-Nitro-4-hydroxy-2-pyridone has been formed from **XII-376** by treatment with nitrous acid.[305]

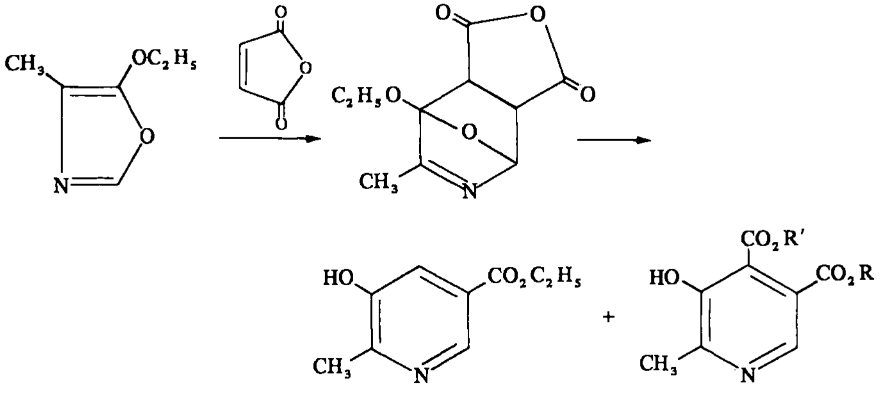


5-Ethoxy-4-methyloxaole has been used to form pyridoxine (**MI-286,** R = H). With maleic anhydride it gives an adduct that, on treatment with ethanolic hydrogen chloride, forms the products **W-287** and **XII-288** (R = R’ = Et) and a monoester (XII-288; R = Et, R’ = H or R = H, R’ = Et).[199] The diethyl ester **MI-288** is also formed from ethyl maleate or ethyl fumarate and 5-ethoxy-4-methyloxazole.[200] Fumaronitrile and 5-ethoxy-4-methyloxazole give 4,5-dicyano-2-methyl-3-pyridinol,[199, 201] also a known precursor to pyridoxine. 5-Ethoxy-4-methyloxaoles and 2-butene-1,4-diol give pyridoxine (XII-286, R = H), which is difficult to purify when prepared in this way (assay, 23%).

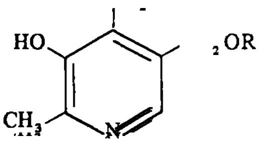
TABLE XII-3. Reactions of 5-Alkoxyoxazoles with Maleimide and Maleic Anhydride

R_2	R_6	R	% XII-284 Ref. 196	% XII-285 Ref. 197
CH_3	H	C_2H_5	43	54
C_2H_5	H	C_2H_5	80	41
n-C_3H_7	H	C_2H_5	77	31
n-C_4H_9	H	C_2H_5	83	42
n-C_5H_{11}	H	C_2H_5	81	40
C_6H_5	H	C_2H_5	43	0
CH_3	CH_3	CH_3	36	36
C_2H_5	CH_3	CH_3	73	25
n-C_5H_{11}	CH_3	CH_3	68	16
CH_3	C_2H_5	C_2H_5	85	0

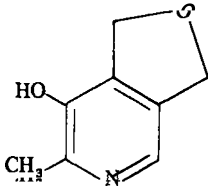
5-Ethoxy-4-methyloxazole reacts similarly with a variety of ethers and esters of 2-butene-1,4-diol.[202] 1,4-Dimethoxy-2-butene forms XII-286 (R = CH_3); 2,5-dihydrofuran forms the pyridoxine cyclic ether (**MI-289**)[199, 201] and 1,4-diacetoxy-2-butene forms pyridoxine.’”



XII-287 XII-288

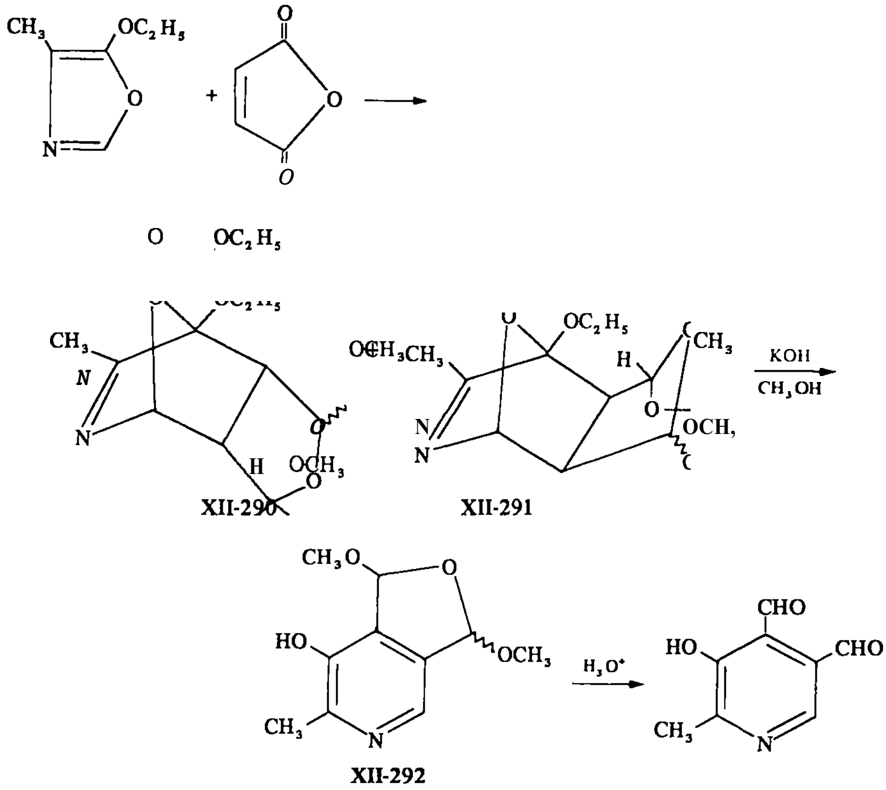


MI-286

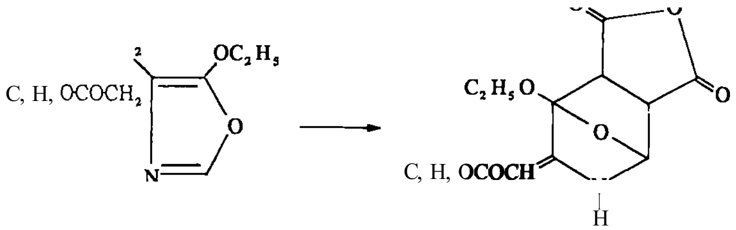


XII-289

5-Ethoxy-4-methyloxazole reacts with *cis*- and *trans*-2,5-dimethoxy-2,5-dihydrofuran to form both *endo*- (XII-290) and *exo*- (XII-291) adducts. All four adducts have been characterized. The adducts give cis- or *trans*- **XII-292** when treated with base. Both of the latter isomers give **3-hydroxy-2-methylpyridine**-4,5-dicarboxaldehyde on treatment with hydrochloric acid.[203]

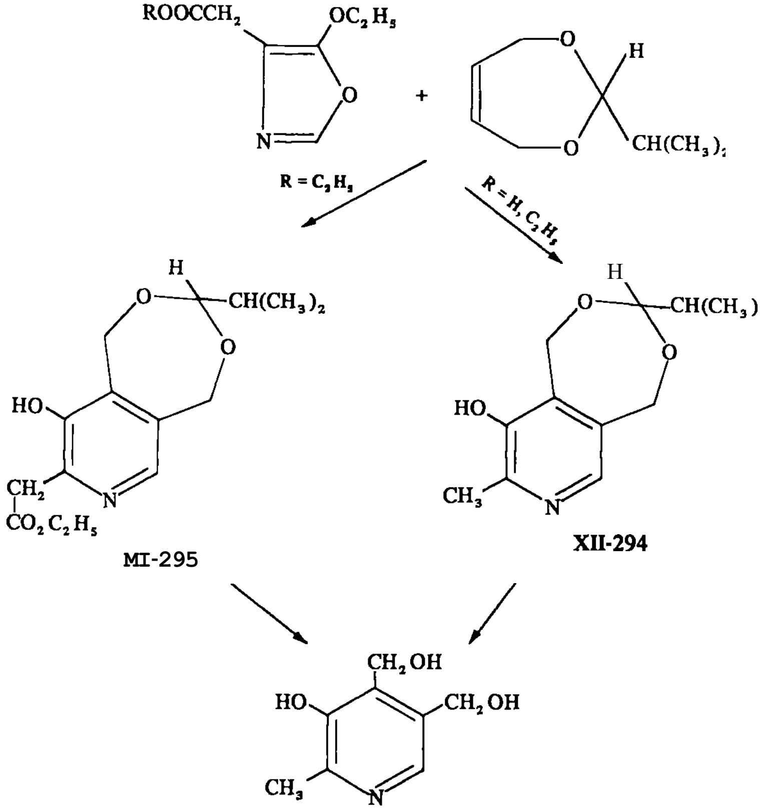


An unstable anhydride has been isolated from the reaction between maleic anhydride and ethyl 5-ethoxy-4-oxazolylacetate and has been characterized as XII-293.[204]



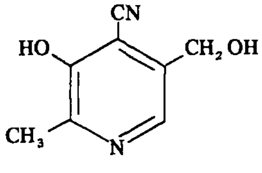
XII-293

4-Carboxymethyl-5-ethoxyoxazole reacts with fumaronitrile to give 4,5-dicyano-2-methyl-3-pyridinol.[205] It reacts with 4,7-dihydro-1,3-dioxepine to give W-294, which is hydrolyzed with dilute hydrochloric acid to pyridoxine. The ethyl ester of Ccarboxymethyl-5-ethoxyoxazole reacts with 1,3-dioxepine to form XII-294 and XII-295, which can also be hydrolyzed to pyridoxine. 5-Cyano-4-methyloxazole and 4,7-dihydro-1,3-oxepines have been used to



MI-295

XII-294

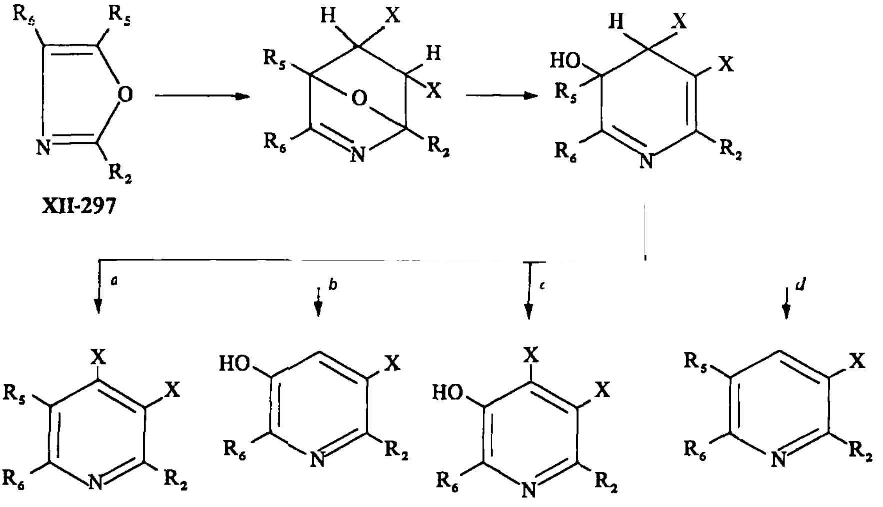


XU-296

prepare pyridoxine by a route in which cyano is the leaving group during the degradation of the adduct.[206]

Both 4-methyl-[207] and 4-carboxymethyl-5-ethoxyoxazole[208] and γ-hydroxycrotonitrile give 4-cyano-5-hydroxymethyl-2-methyl-3-pyridinol (XII-296).

Products from the four reaction paths (*a-d*) are observed in Diels-Alder additions to oxazoles (XII-297), depending on the nature of the groups on the 4- and 5-positions of the incipient pyridine ring.[209] A 5-unsubstituted oxazole can give a 3-pyridinol even though the dienophile is an alkene, if the dienophile can provide to the adduct a leaving group (X) alternate to the 3-hydroxyl that is produced by cleavage of the oxygen bridge (path b). 3-Pyridinols can also be formed by dehydrogenation (path *c*, R, = H). The yields of 3-pyridinols are usually low, however, when 5-unsubstituted oxazoles are used because of competing reactions. 4-Methyloxazole reacts with acrylonitrile in toluene to give 4-cyano-2-methylpyridine (path *a*), 2-methyl-3-pyridinol (XI-298) (path b) and 5-amino-6-methylnicotinonitrile (by dehydrogenation, path *c*, R_5 = H), all in low yields. A similar reaction in aqueous acetic acid gave only XII-298 (28%) and hydrogen cyanide. 4-Phenyloxazole and 2,4-dimethyloxazole in acetic acid

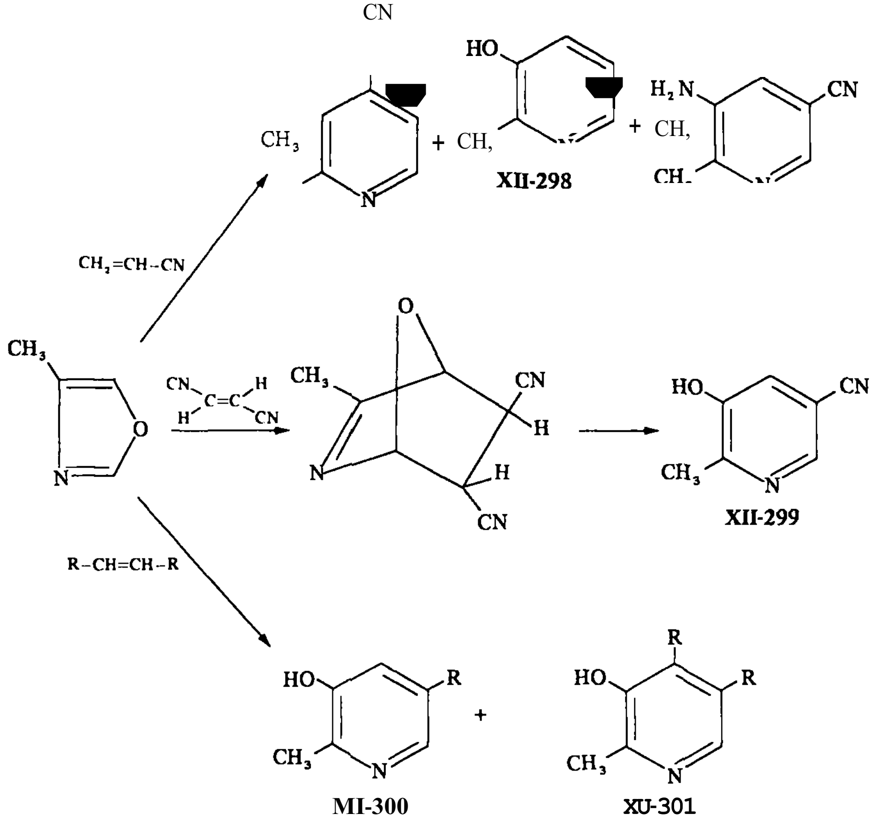


XII-297

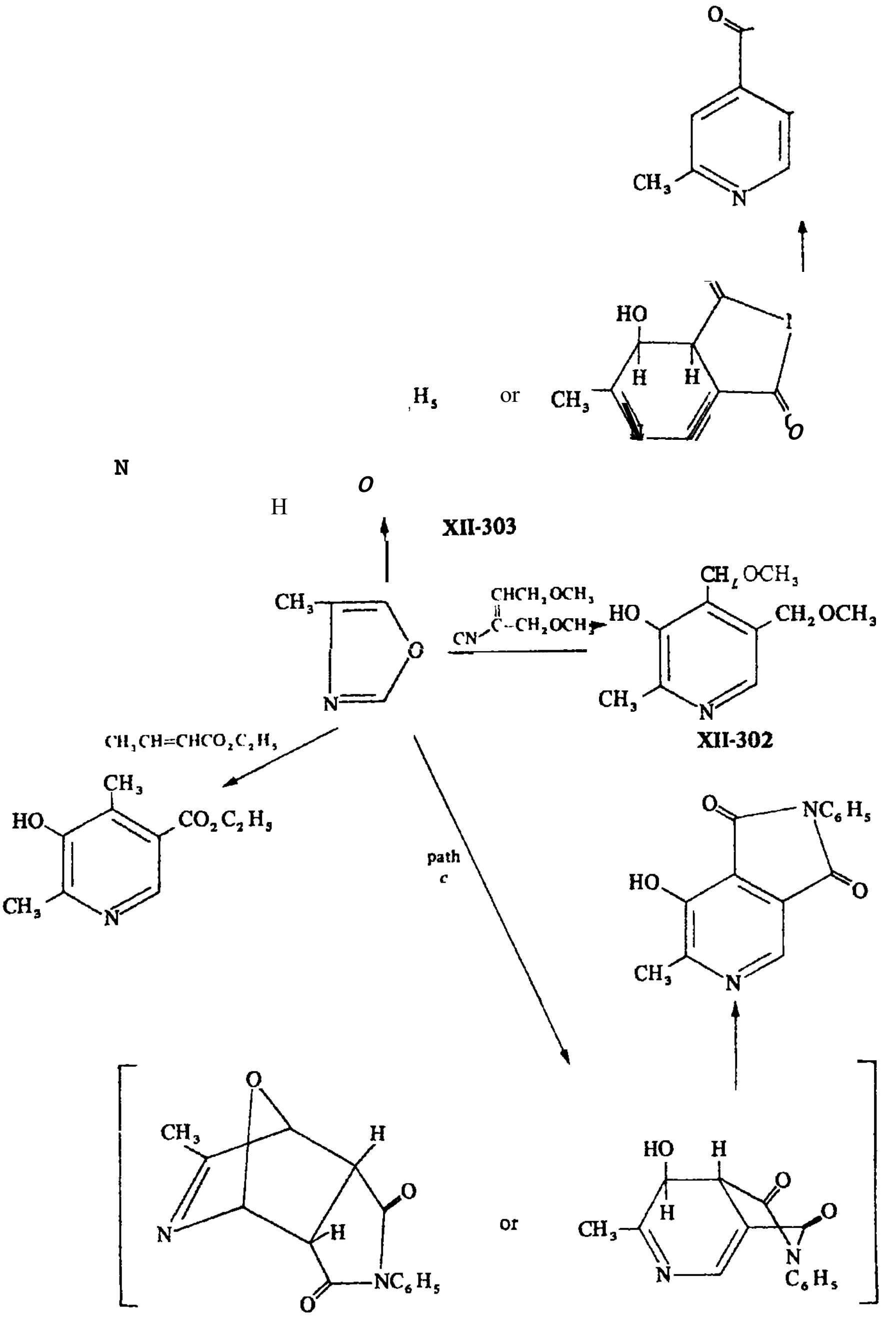
R_5 = H, OR, CN, and so on

react with acrylonitrile to give 2-phenyl-3-pyridinol and **2,6-dimethyl-3-pyridinol**, respectively.'''

Fumaronitrile and Cmethyloxazole give 5-cyano-2-methyl-3-pyridinol (**XII-299**) in unusually high yieid for this type of reaction (71%). Both diethyl fumarate **and** diethyl maleate give low yields of **W-300** and of **XII-301** (R = $CO_2C_2H_5$), which is formed by dehydrogenation (path *c*).[211] Ethyl



trans-3-cyanoacrylate gives both possible products of structure XII-300 (R = $COOC_2H_5$, CN). Ethyl acrylate gives XI-300 (R = H) and 5-carbethoxy-2-methyl-3-pyridinol (XII-300, R = $CO_2C_2H_5$).[211] **5-Carbethoxy-2,4-dimethyl-3-pyridinol**, a precursor for 4-deoxypyridoxine, and **W-302**, a pyridoxine intermediate, also can be formed from **4-methyloxazole.**[212] Depending on conditions, 4-methyloxazole and *N*-phenylmaleimide in ethyl acetate form either of two adducts (**XII-303** or **XII-304**) that were not completely characterized and that give 6-methyl-*N*'-phenyl-3,4-pyridinedicarboximide, (path *a*) and 5-hydroxy-6-methyl-*N*'-phenyl-3,4-pyridinedicarboximide (path *c*), respectively.[209] Similar



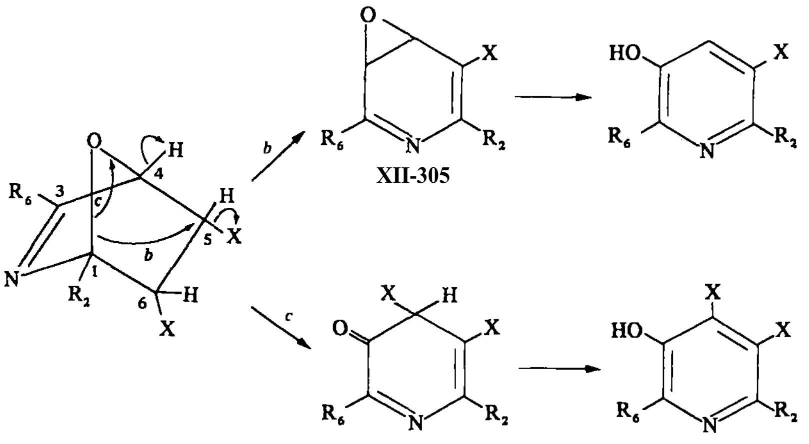
XII-303

XII-302

XII-304

Diels-Alder reactions have been reported for 2,4-dimethyloxazole, ethyl 4-methyl-5-oxazolocarboxylate, 4-methyl-5-oxazolocarbonitrile, 4-methyl-5-oxazolocarboxylic acid and 2-amino-4,5-dimethyloxazole.[209] The formation of a trace of diethyl 2-methyl-3,5-pyridinedicarboxylate from ethyl 4-methyl-5-oxazolecarboxylate and diethyl fumarate is the only example cited for path *d*.[209]

It has been suggested that in paths *b* and *c* reaction of the adduct occurs *via* C_1—O cleavage of the oxygen bridge followed by nucleophilic attack at C_5 to displace X and to give **XII-305**, or at C_4 to displace hydride and give **XII-306**.[195]



XII-305

XII-306

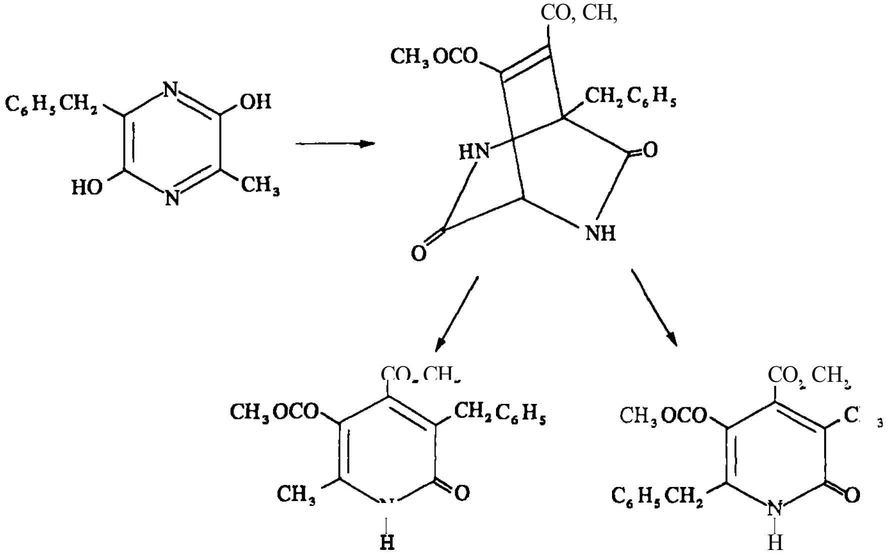
The dehydrogenation product is usually formed in small amounts; however, in the presence of hydride acceptors such as hydrogen peroxide or nitrobenzene the amount of dehydrogenation is increased.[195]

G. 3-Pyridinols and Pyridones from Other Nitrogen-Containing Heterocycles

Diels-Alder addition of dimethyl acetylenedicarboxylate to 3-benzyld-methyl-2,5-dihydroxypyrazine gives an adduct that decomposes on heating to give equal amounts of the 2-pyridones **MI-307** and **XII-308**.[213]

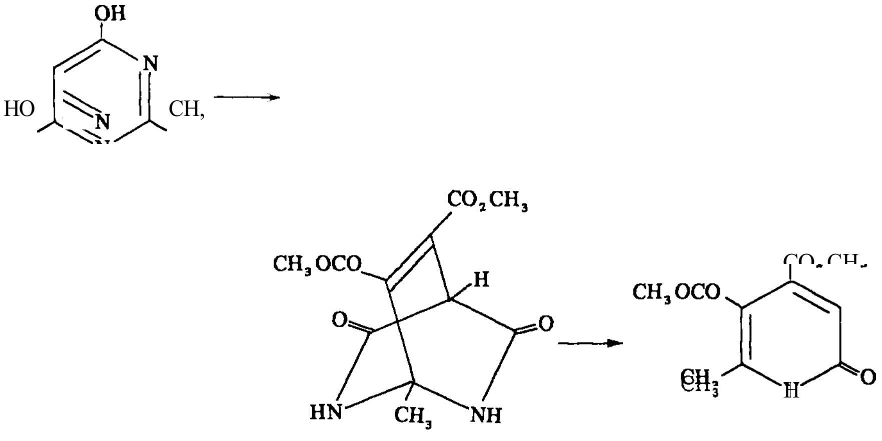
4,6-Dihydroxy-2-methylpyrimidine and dimethyl acetylenedicarboxylate form an unstable adduct that decomposes to give the pyridone **XII-309**.[213]

Acetophenone-anil and benzylmalonic acid react in acetic anhydride to form 5-benzyl-2-methyl-4,6-dioxo-2,3-diphenylhexahydro-1,3-oxazine, which rearranges to 3-benzyl-4-hydroxy-1,6-diphenyl-2-pyridone (**MI-310**) when heated with phosphorus pentoxide. A number of tetrahydrocarbostyrils have been prepared similarly from cyclohexanone-anil *via* **XII-311**.[214]



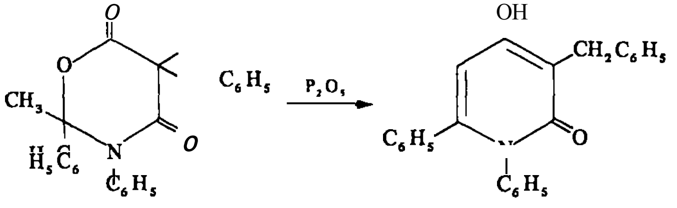
XII-307

XII-308

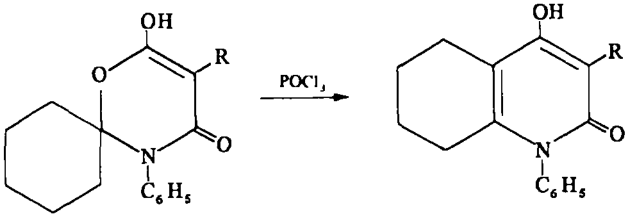


XU-309

2,3-Dihydro-1,2-diazabicyclo[3.2.0]-3-hepten-6-ones **MI-312** and **XII-313** and diazepinones **XII-314** are readily interconvertible ring systems[215-217] and all three can give 1-amino-3-pyridinol salts (see Section IV.3., p. 839) or 3-pyridinols.[218,219] When heated in methanol, the 2-acetyl- or 2-benzoyl-derivative of **MI-313** rearranges to several products including 6-acetamido- or 6-benzamido-3-hydroxy-4-methyl-5-phenylpyridine (**XII-317**) in 17% and 68% yield, respectively, presumably through intermediates such as **XII-315** and



XII-310



XII-311

XII-316. In basic aqueous solution XII-313 (R = CH_3) is converted to 4-amino-3-hydroxy-4-methyl-5-phenyl-5-piperidein-2-one (**XII-320**) and 3-hydroxy-4-methyl-5-phenyl-2-pyridone (**MI-321**) by a process beginning with **XI-318**, involving hydration, azetinone ring opening, disproportionation to **XI-319**, and recyclization.[220, 221]

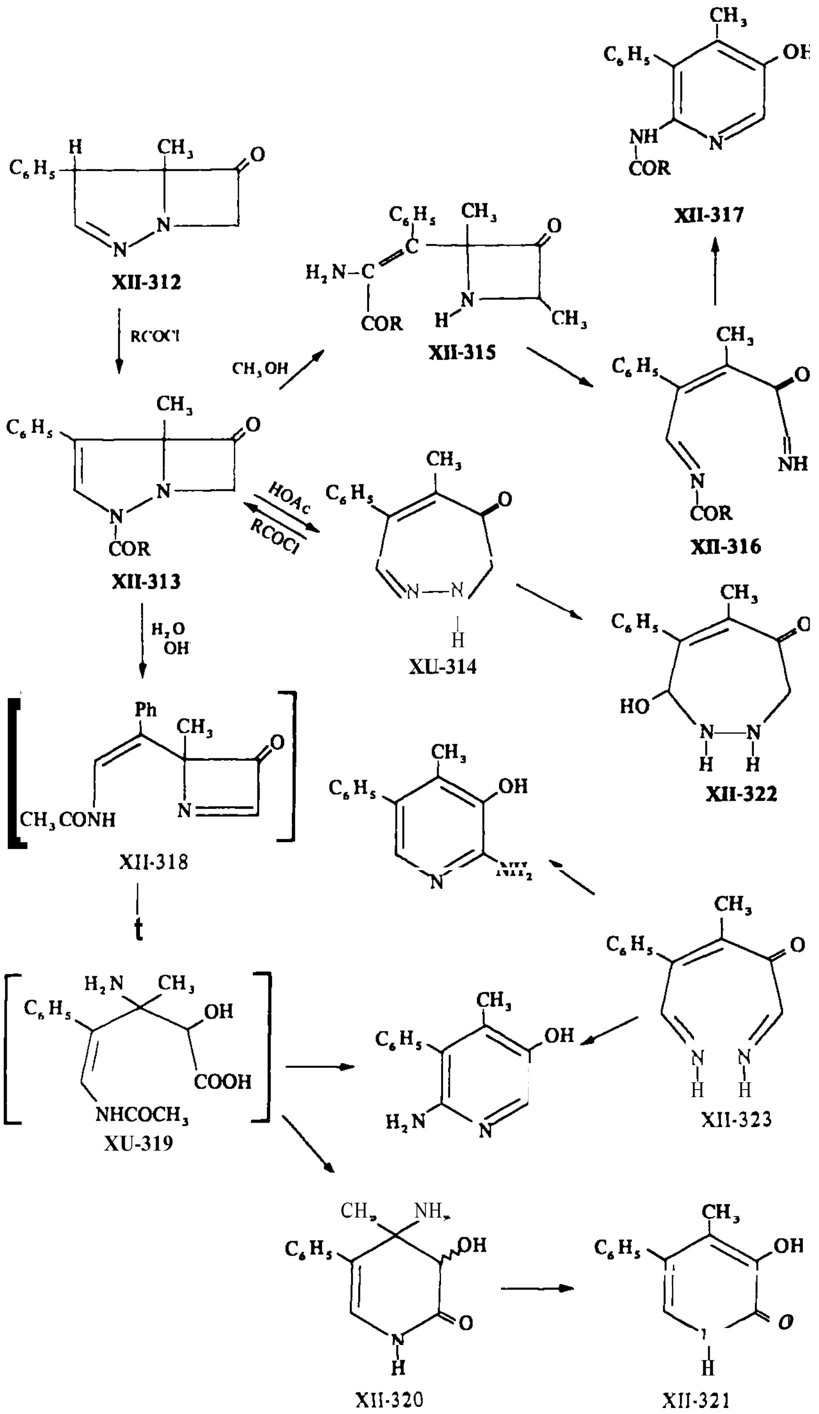
Although earlier reports indicated that XII-314 did not react with aqueous base, later work has shown that it rearranges to *6-* and 2-amino-4-methyl-5-phenyl-3-pyridinol, presumably through intermediates XI-322 and **XII-323.**[222, 223]

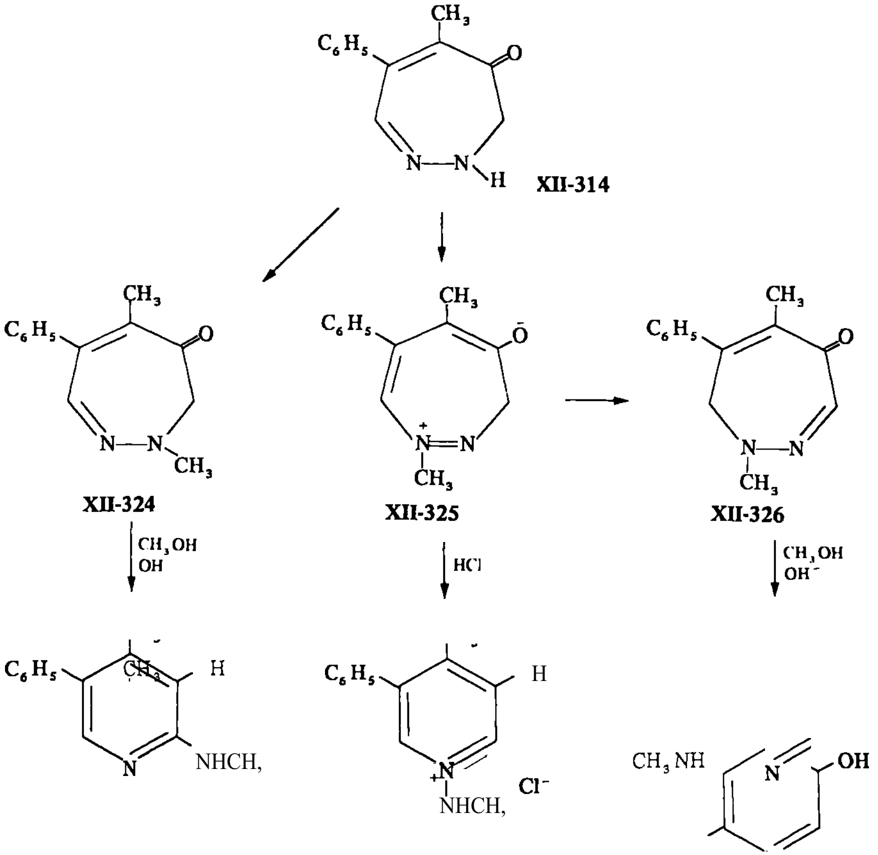
Dimethyl sulfate and **XII-314** give equal amounts of the two *N*-methyl derivatives XII-324 and **XII-325.**[216] Tautomerization of XII-325 to **MI-326** occurs on standing. The betaine **XII-325** rearranges to 3-hydroxy-4-methyl-1-methylamino-5-phenylpyridinium chloride when treated with hydrochloric acid." [6] The *N*-methyldihydroazepinones **XII-324** and **XII-326** rearrange to 3-pyridinols when warmed with methanolic alkali.[222, 224, 225]

The alkaloid dendrobine gives 4-isopropyl-2-pyridone (**MI-327**) when heated with selenium at 300°.[226]

2-Ethyl-5-methyl-3-pyridinol (XII-328) has been characterized as a degradation product of the steroid alkaloid leptinidine.[227]

The acid azide XII-329, freshly prepared from (2,3-diphenylcycloprop-2-enyl)-acetyl chloride, gives 3,4-diphenyl-2-pyridone (**MI-332**) (60–70%) and a small amount of the urethane (**MI-333**) on treatment with boiling ethanol. When heated, **XII-329** rearranges quantitatively to the isocyanate (**XII-330**).[228, 229] It has been suggested that **XII-332** is formed *via* **XII-331** through an intramolecular cycloaddition.[228] Photolysis of **XII-329**, followed by treatment with ethanol at


XII-312
RCOCl
XII-313
CH3OH
XII-315
XII-317
XII-316
HOAc
RCOCl
XU-314
XII-322
H2O
OH
XII-318
t
XU-319
XII-323
XII-320
XII-321

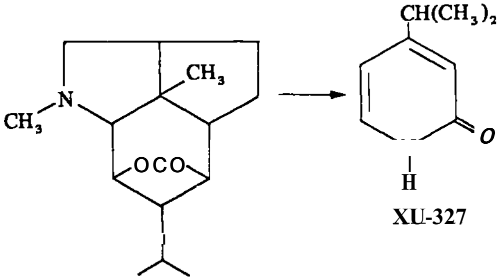


XII-314

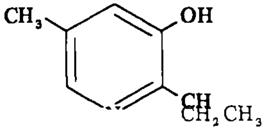
XII-324

XII-325

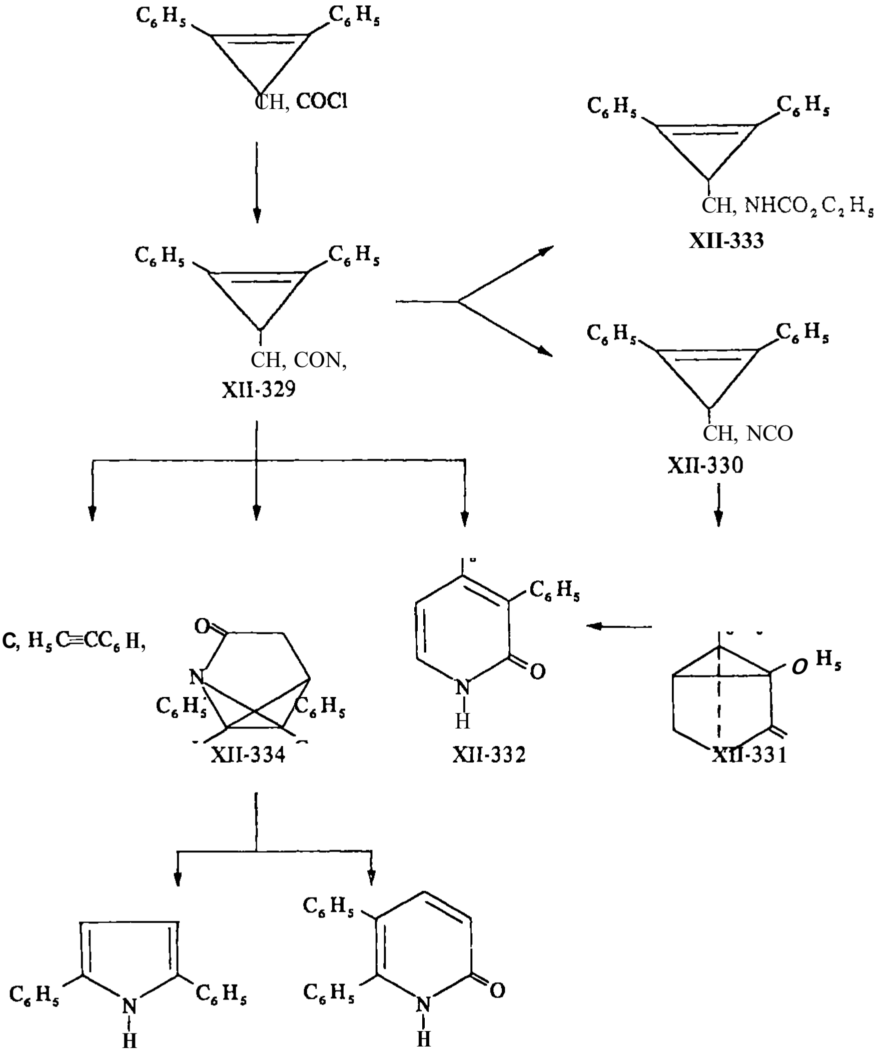
XII-326



XU-327



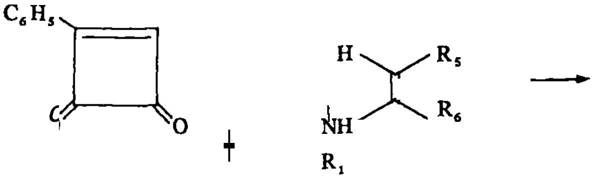
XII-328



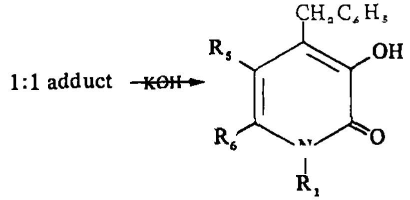
55°, gives 2,5-diphenylpyrrole (6%), **5,6-diphenyl-2-pyridone** (5%), diphenylacetylene, and XII-332. The nitrene adduct XII-334 is postulated as a common intermediate in the formation of 2,5-diphenylpyrrole and **5,6-diphenyl-2-pyridone.**''' **(1,2,3-Triphenylcycloprop-2-enyl)acetyl azide** gives, on similar treatment with ethanol, the corresponding carbamate and 3,4,5-triphenyl-2-pyridone (6–8%).[230] Photolysis gives **4,5,6-triphenyl-2-pyridone.**[230]

H. *Pyridinols and Pyridones From Carbocyclics*

Phenylcyclobutenediones and enamines give 1:1 adducts that rearrange with bases to 3-hydroxy-2-pyridones **(XII-335)**.[231]

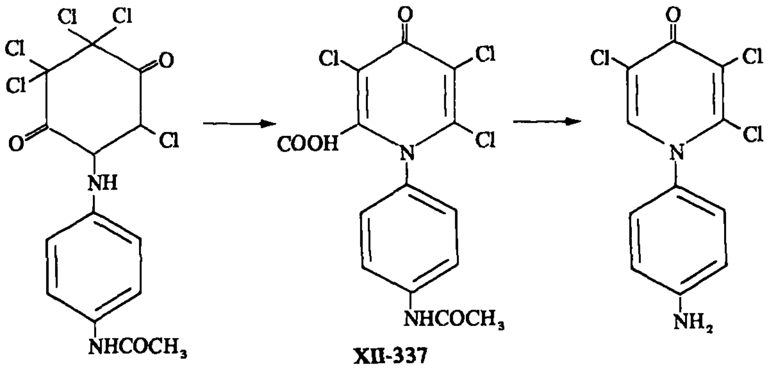


R_1 and R_6 = H, alkyl, aryl
R_5 = CO, R, COR, CN



XII-335

The secondary amine XII-336, which can be prepared conveniently from chloranil, reacts with aqueous sodium hydroxide to give the 4-pyridone **MI-337**, which is decarboxylated and deacetylated by hydrochloric acid in isopropyl alcohol to **_N_-(_p_-aminophenyl)-2,3,5-trichloro-4-pyridone**.[232]



XII-336

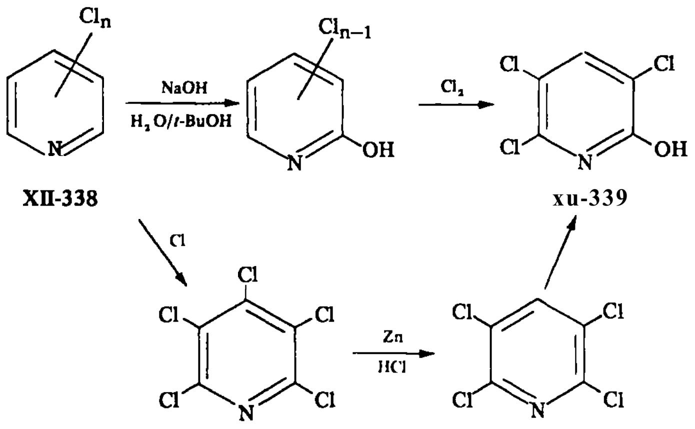
XII-337

6. From Other Pyridine Derivatives

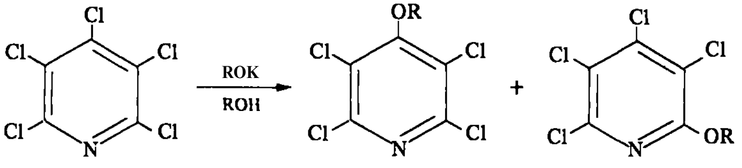
The activating influence of the ring nitrogen provides an important versatility for the synthesis of pyridones, pyridinols, and pyridine ethers, by nucleophilic substitution at the 2- and 4- and even the 3-position. Further, the potential of accomplishing these substitutions *via* pyridine *N*-oxides contributes to the scope of this method.

A. *Halopyridines*

The preparation of pyridinols from halopyridines has generally not been important. More often pyridinols have been the source for the halopyridines. However, the recent development of new routes to several halopyridines has made them available as pyridinol precursors (see also Chapter VI). For example, polyhalopyridines, formed by direct ring closure[233] or through treatment of glutarimide with phosphorus pentachloride,[234] give polychloro 2- and 4-pyridones on hydrolysis[235] and 4-alkoxypolychloropyridines when treated with alkoxides.[236] Glutarimide and phosphorus pentachloride form a mixture (**XI-338**) of 2,6-dichloro- (10%), 2,3,6-trichloro- (75%) and 2,3,5,6-tetrachloropyridine (15%)[234, 235] that is hydrolyzed to a mixture of 2-pyridinols by sodium hydroxide in aqueous t-butyl alcohol at 150 to 160°.[235] Further chlorination of the acidified hydrolysate gives 3,5,6-trichloro-2-pyridinol (**XII-339**).[235] 2,6-Dichloropyridine is converted to 6-chloro-2-pyridinol by sodium hydroxide in t-butyl alcohol-water.[237] Photochlorination of **XII-338** gives pentachloropyridine, which forms 2,3,5,6-tetrachloropyridine by reductive dehalogenation.

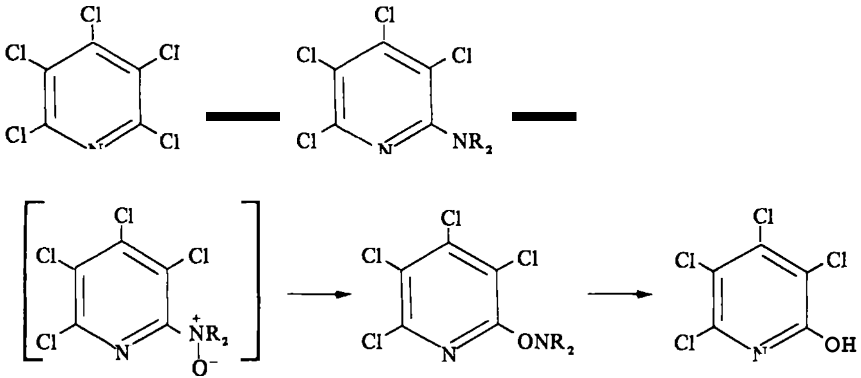


Hydrolysis gives **MI-339** in high yields, but the product by this route is more difficult to purify.[235] Pentachloropyridine can also be prepared from perchlorocyclopentenone[16] (see Section I. 1.B.) or from 2,6-diaminopyridine by chlorination in hydrochloric acid followed by treatment with phosphorus oxychloride and phosphorous trichloride.[238] Pentachloropyridine and nucleophiles give mixtures of 2- but mainly 4-substituted products, with bulkier reagents giving increased amounts of substitution at the less sterically hindered 2-position. The ratios of monosubstituted products (**XII-340:XII-341**) formed by treatment of pentachloropyridine with alkoxides are 85:15 (R = CH_3), 65:35 (R = C_2H_5), and 57:43 (R = n-C_4H_9).[238] 4-Methoxyperchloropyridine is converted to the 4-pyridinol in concentrated hydrochloric acid at 170°.[239]



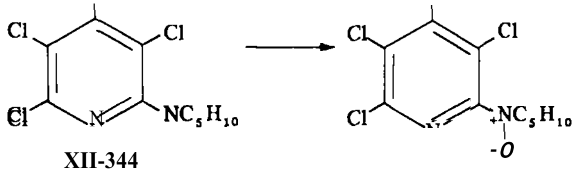
XII-340 XII-341

Perchloropyridine also reacts with secondary amines to form mainly 2- and some 4-substituted aminotetrachloropyridines. Oxidation with peroxyacids is followed by intramolecular rearrangement to give *O*-pyridylhydroxylamines. Perchloro-2-pyridinol (**XII-343**) has been formed in good yields from perchloropyridine through formation and oxidation of 2-dialkylaminotetrachloropyridines followed by pyrolysis.[240] Electron withdrawal by the chlorine atoms and the ring nitrogen favors the rearrangement of the intermediate N-oxide (**XI-342**) to the hydroxylamine. Although 4-methoxy-2-piperidinoperchloropyridine gives the hydroxylamine on oxidation, the corresponding 4-pyridinol (**XII-344**) gives the stable piperidine N-oxide, presumably because of



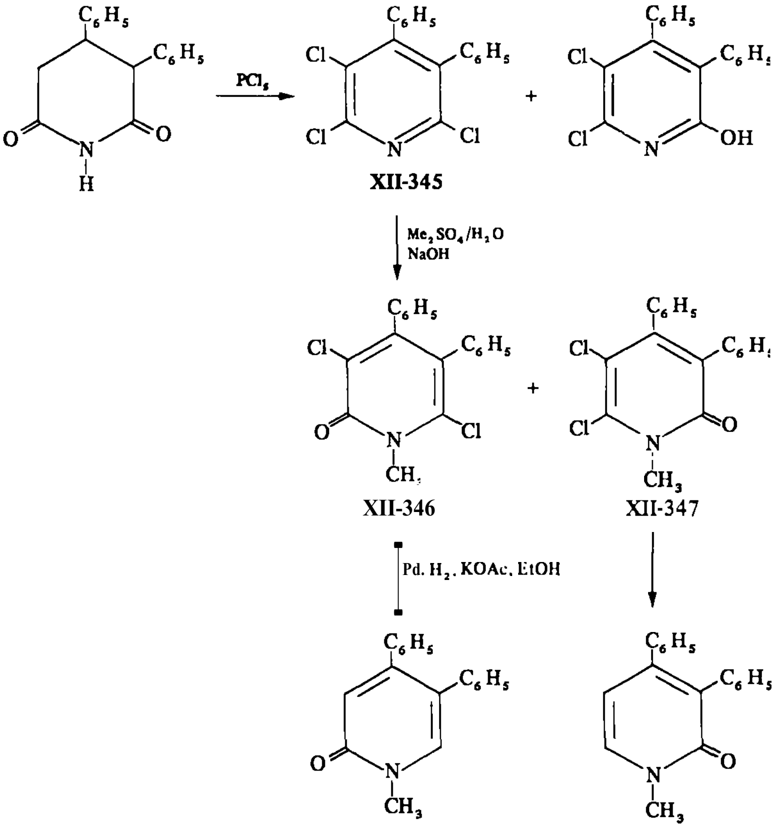
XII-342 XII-343

electron release by the 4-oxygen that exists in the hydroxyl form.[240, 241] Performic acid oxidations of the less highly substituted 2-chloro-6-piperidinopyridine also gives the *N*-oxide and no rearrangement.[240]



XII-344

2,3-Diphenylglutarimide and phosphorus pentachloride give 2,5,6-trichloro-3,4-diphenylpyridine (**XII-345**) and 5,6-dichloro-3,4-diphenyl-2-pyridinol. Treatment of **XI-345** with dimethyl sulfate in water and then with aqueous sodium hydroxide gives the pyridones **W-346** and **XII-347**, which are hydrogenated to 4,5- and 3,4-diphenyl-1-methyl-2-pyridone, respectively.[242]

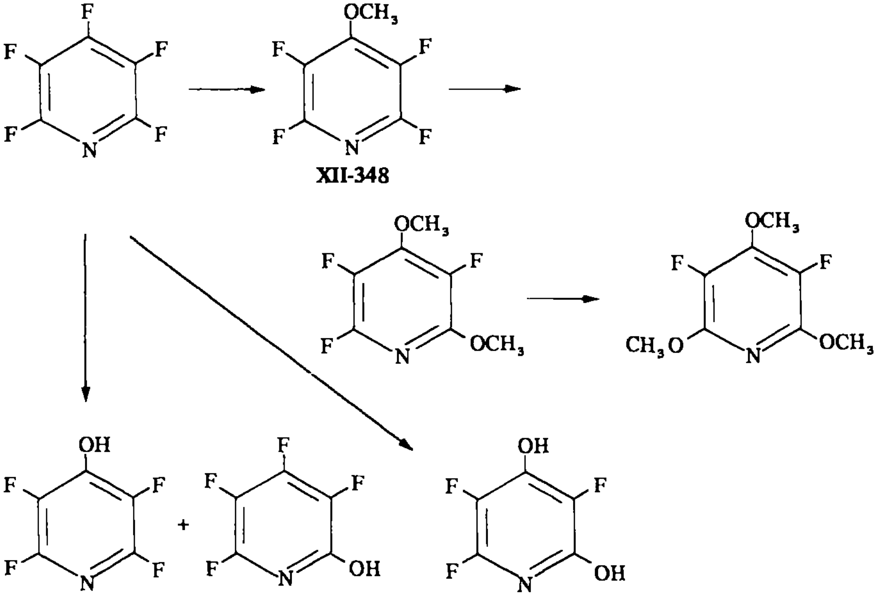


XII-345

XII-346

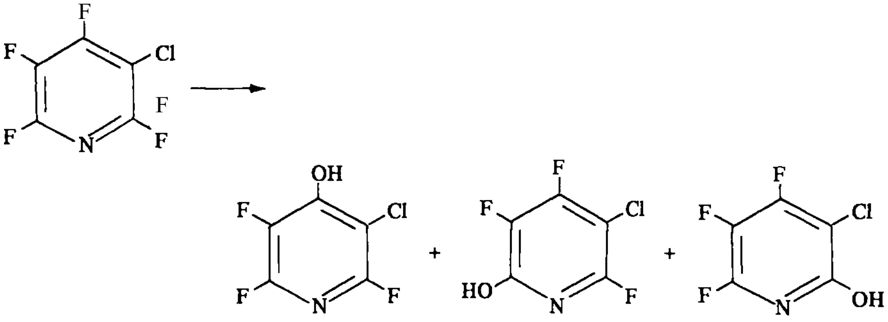
XII-347

Pentafluoropyridine, 3-chlorotetrafluoropyridine, and 3,5-dichlorotrifluoropyridine, can be obtained from pentachloropyridine[243, 244] and are convenient compounds for the preparation of chlorofluoropyridinols[244-247] *(vide infra)*. Pentafluoropyridine can also be prepared from pyridine *via* undecafluoropiperidine, although less conveniently.[244, 248] It usually reacts with nucleophiles to give the 4-substituted product initially. With sodium methoxide it gives 4-methoxytetrafluoropyridine (XII-348), 2,4-dimethoxytrifluoropyridine, and 2,4,6-trimethoxydifluoropyridine.[245, 248] Under very mild conditions it is possible to isolate MI-348 in good yield.[245] When t-butyl alcohol is used in the hydrolysis, a steric participation by solvent is indicated. Dilute aqueous sodium or potassium hydroxide and perfluoropyridine give only 4-hydroxytetrafluoropyridine[246, 248] but with potassium hydroxide in t-butyl alcohol, 4- and 2-hydroxyperfluoropyridine are formed in the ratio of 9:1.[246] 3,5,6-Trifluoro-2,4-dihydroxypyridine (XII-349) is formed from pentafluoropyridine by treatment with 40% aqueous sodium hydroxide.[248] 3-Chlorotetrafluoropyridine and aqueous potassium hydroxide form 3-chloro-2,5,6-trifluoro-4-hydroxypyridine (XU-350) and 5-chloro-3,4,6-trifluoro-2-hydroxypyridine (MI-351) in a ratio of 9:1, but in t-butyl alcohol MI-350, MI-351, and 3-chloro-4.5,6-trifluoro-2-hydroxypyridine (XII-352) are formed in the ratio of 5.5:3.5:1.[246] Aqueous potassium hydroxide and 3,5-dichlorotrifluoropyridine give an 85% yield of the two hydroxypyridines XII-353 and MI-354 also in a 9:1 ratio. In

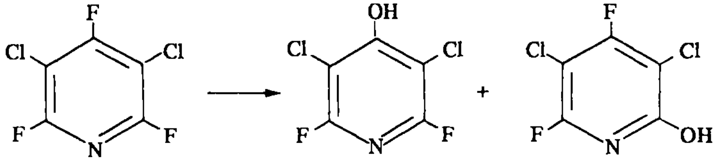


XII-348

XII-349



XII-350 XII-351 XII-352



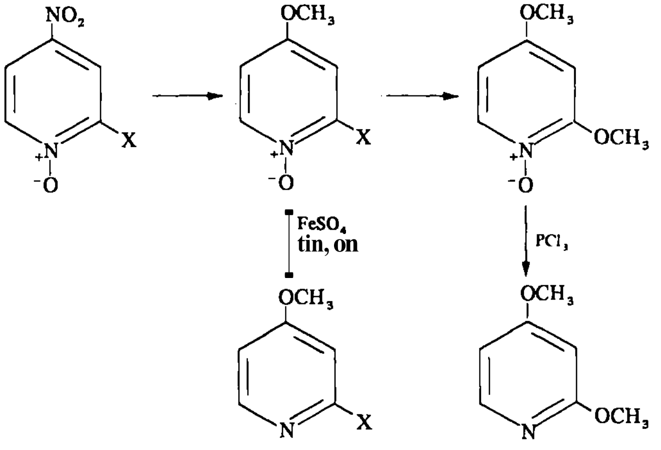
XII-353 XII-354

t-butyl alcohol, the ratio is 7:3.[246] 4-Bromotetrafluoropyridine and potassium hydroxide in *t*-butyl alcohol form 4-bromo-3,5,6-trifluoro-2-hydroxypyridine in high yield.[247]

An increase in susceptibility to nucleophilic substitution of halogen at all ring positions by an N-oxide function has been observed. Relative reactivities toward sodium methoxide have been reported for 4-chloropyridine, 4-chloro-2,6-lutidine, 4-chloro-3-nitro-2,6-lutidine, and their *N*-oxides,[249] and for 2-bromo-, 2-bromo-3-methyl- and 2-bromo-5-methylpyridine, and their *N*-oxides.[250]

In the reactions of 2-halopyridines and their *N*-oxides with methanolic potassium methoxide, the order of reactivities is 2-X > 2-X-3-CH_3 > 2-X-5-CH_3 (X = Cl, Br), which is not predictable on the basis of steric and inductive effects of the methyl group. Arrhenius parameters have been obtained for these reactions and have been used to rationalize observations. For example, it has been suggested that ion-dipole attraction between the 3-methyl and attacking methoxide is in part responsible for the greater reactivity of 2-bromo-3-methylpyridine over 2-bromo-5-methylpyridine. However, in 2-chloropyridine it is suggested that bond breaking is more important in the rate-determining step."' Toward thiophenoxide ion in methanol, the order 2-Br-3-CH_3 > 2-Br- > 2-Br-5-CH_3 is observed.[251] Further extensions of these reactions to include 2,3- and 2,5-dibromopyridine indicate that more than one *ortho* effect appears to be operative.[251]

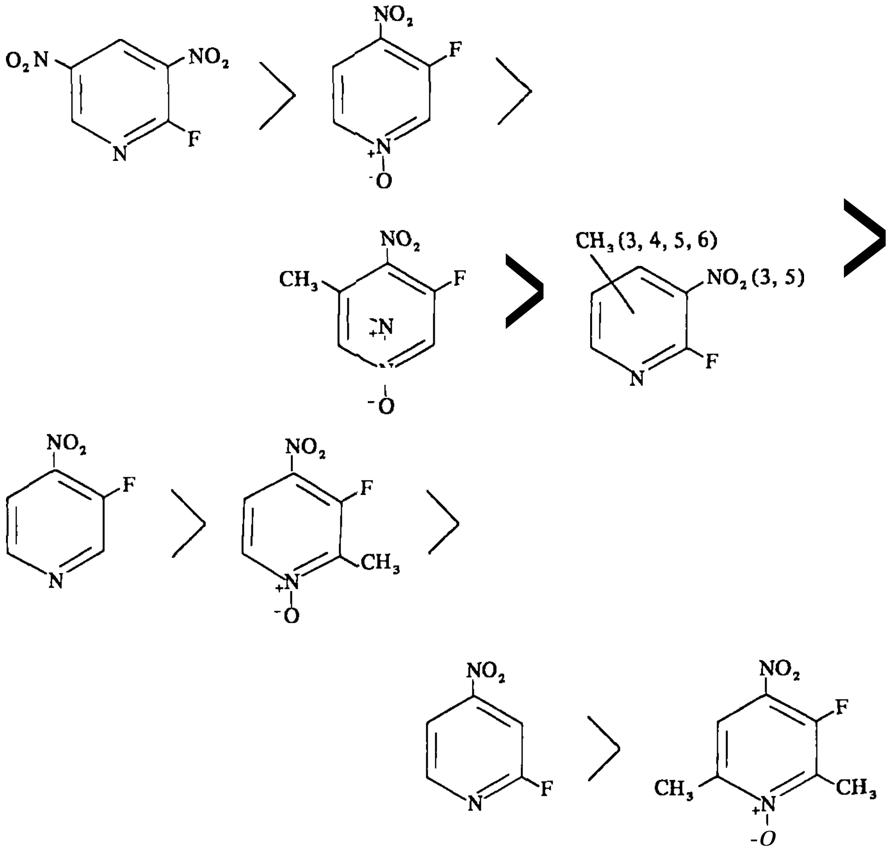
The syntheses and nucleophilic reactivities of a number of chloro and fluoronitropyridines have been studied extensively by Talik and Talik. In studies with 2-halo4-nitropyridine N-oxides, it was demonstrated that the 4-nitro group is more reactive than the 2-halo function toward aqueous alkali and alkoxides. The ethers **XI-355** and **XII-356** have been formed by reduction.[252, 253] Toward diethylamine the 2-halo is more reactive than the 4-nitro group (Br > Cl> I).[252]



XII-355 **XII-356**

3-Halo-4-nitropyridines and their *N*-oxides react at the C-nitro group when treated with bases or alkoxides to give **XII-357** or **MI-358** (X = Cl, Br, I). However, 3-fluoro-4-nitropyridine and its 1-oxide form 4-nitro-3-pyridinols and 4-nitro-3-alkoxypyridines, respectively.[254–256a] The 3-alkoxy-4-nitropyridine-1-oxides have been converted to 3,4-dialkoxypyridine-1-oxides.[256] Because of this marked reactivity of the 3-fluoro substituent, these studies have been extended to 3-fluoro-5-methyl-4-nitropyridine-1-oxide,[257] 3-fluoro-2-methyl-4-nitropyridine-1-oxide,[258] and 2,6-dimethyl-3-fluoro-4-nitropyridine-1-oxide.[258] Several of these fluoronitropyridines have been extensively studied as potential reagents for formation of amino acid derivatives.[256a–260] 2-Fluoro-3,5-dinitropyridine, a typical example, is hydrolyzed by hot water and reacts with hot alcohols to form 2-alkoxy-3,5-dinitropyridines and reacts with amino acids and their derivatives to give well-defined products.[260] The reactions of a number of fluoronitropyridines and their N-oxides have been summarized by Talik and Talik[261] and the relative reactivities toward simple nucleophiles have been observed,[258,262] as shown on p. 689.

2-Fluoro-3-nitropyridines are prepared from the corresponding 2-aminopyridines in only fair yield but are hydrolyzed in good yield to the 2-pyridinols.[259] 2-Fluoro-6-methyl-5-nitropyridine,[263] 2-fluoro-3,5-dinitro-4-methylpyridine,[264] 2-fluoro-3,5-dinitro-6-methylpyridine[264] and 2-chloro-3,5-dinitropyridine[265]

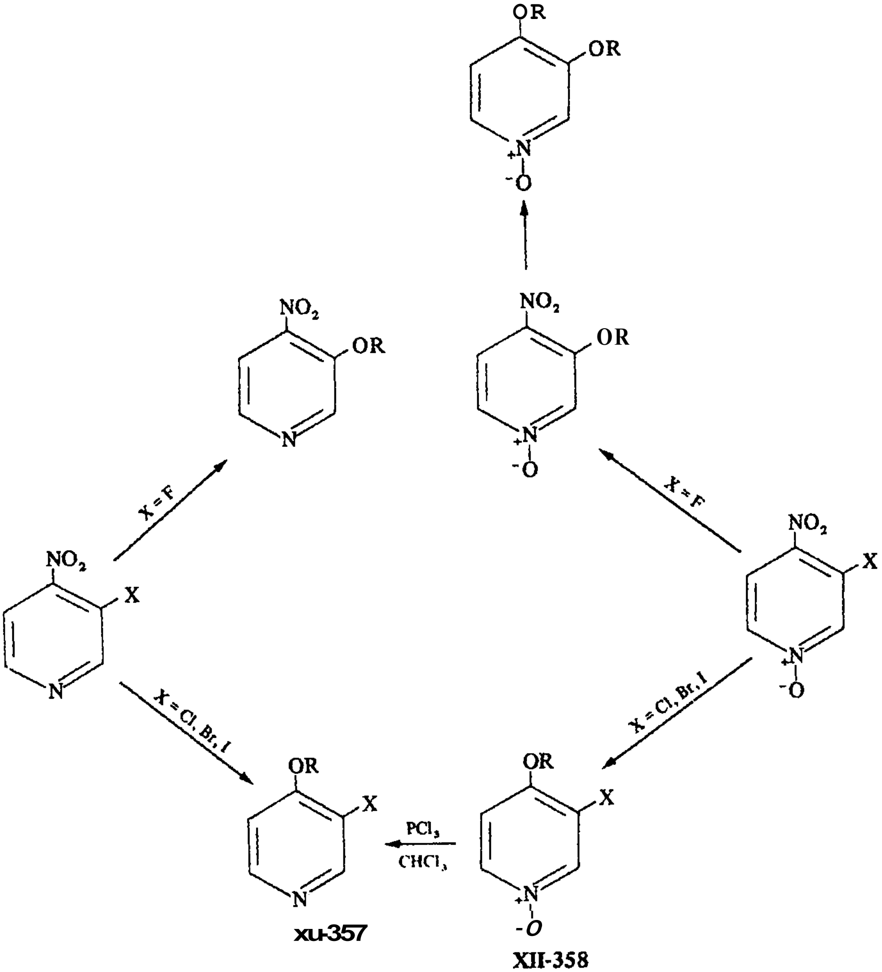


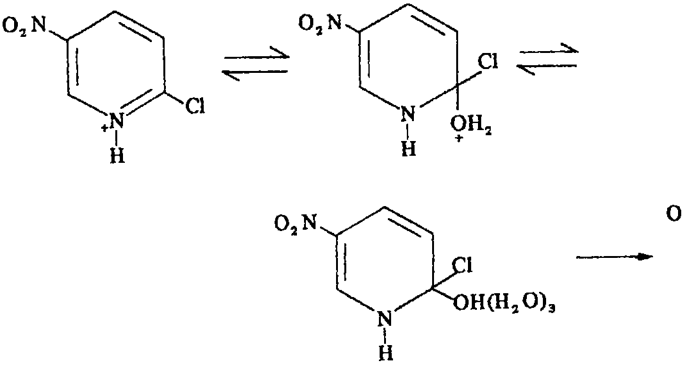
have also been converted to the corresponding ethers and 2-pyridones by solvolyses.

4-Cyano-2-fluoropyridine is hydrolyzed by aqueous acid to 2-hydroxy-4-pyridinecarboxylic acid.[266]

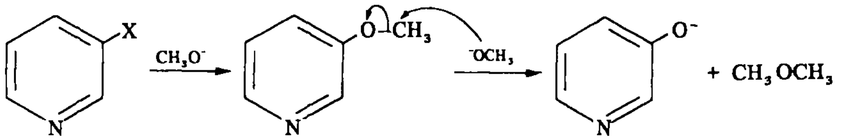
The rate of displacement of the halogen in 2-chloro- and 2-iodo-5-nitropyridine by water decreases with increasing acid concentration and is proportional to the **4th** power of a_{H_2O} and to the fraction of the halopyridine protonated in acetic acid-water and dioxane-water. Rates in D_2O with D_2SO_4 give an isotope effect of 2.36. The following mechanism has been suggested:[267]

2-, 3- and 4-Methoxypyridine are cleaved to the pyridone by sodium methoxide in methanol. 3-Chloro- and 3-bromopyridine react with methoxide ion to give 3-methoxypyridine (XII-359), which is then cleaved by methoxide in


OR
OR
+N
-O
NO₂
OR
N
NO₂
OR
+N
-O
X = F
X = F
NO₂
X
N
NO₂
X
+N
-O
X = Cl, Br, I
X = Cl, Br, I
OR
X
N
PCl₃
CHCl₃
OR
X
+N
-O
xu-357
XII-358

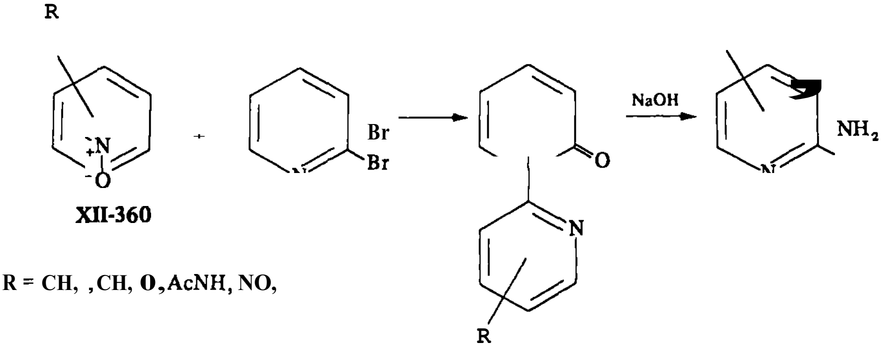

O₂N
+N
H
Cl
O₂N
Cl
N
H
OH₂
+
O₂N
Cl
OH(H₂O)₃
N
H
O

an S_N2 mechanism.[268] Treatment of 3-bromopyridine with methanolic potassium hydroxide has been reported to give an 87% yield of 3-methoxypyridine.[269] However, a reinvestigation of this reaction has shown that the yield of 3-methoxypyridine rises to 36% after 9 hours and then decreases.[268] The ratios of second-order rate constants at 218” for formation of 3-methoxypyridine[268, 270] and its subsequent cleavage are 0.53 for 3-chloropyridine and 0.75 for 3-bromopyridine.[268] 3-Chloropyridine and sodium methoxide in methanol at 230° give 3-pyridinol in 70% yield, a reaction that appears to have preparative value.[268] Reactions of 2- and 4-chloropyridines with methoxide are relatively fast and ether cleavage is not an important side reaction.[268, 270] 4-Methoxypyridine with methoxide in aqueous methanol gives both ether and alcohol by cleavage and undergoes a more rapid methoxyl exchange as shown by experiments with methanol-d_3 and deuterium oxide.[268]



XII-359

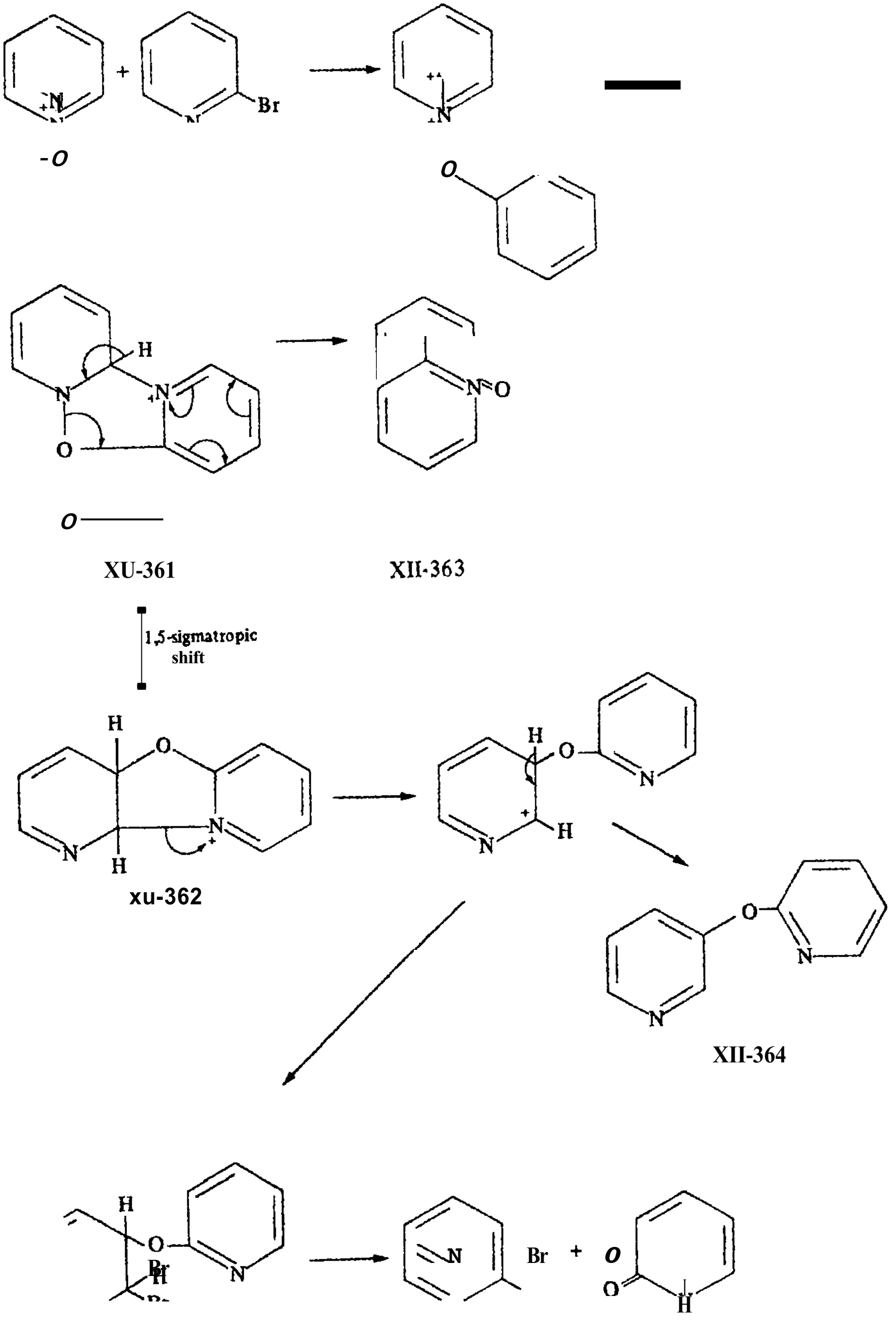
Treatment of 2-, 3-, and 4-substituted pyridine-1-oxides (XU-360) with 2-bromopyridine gives 1-(substituted-2-pyridyl)-2-pyridones, usually in low yields, 2,3′-dipyridyl ethers, and 2-pyridones (see also Chapter IV). In several instances, the N-(2-pyridyl)-2-pyridones have been hydrolyzed to aminopyridine with aqueous sodium hydroxide.’[71] Electron donating substituents, particularly at the 3-position, favor, and electron withdrawing groups on the 2- or 4-position prevent, pyridyl-2-pyridone formation.



XII-360

R = CH, ,CH, O,AcNH, NO,

Observations of the reaction between pyridine-1-oxide, quinoline-1-oxide, and isoquinoline-2-oxide with 2-bromopyridine, 2-bromoquinoline, or 1-bromoiso-



XU-361

XII-363

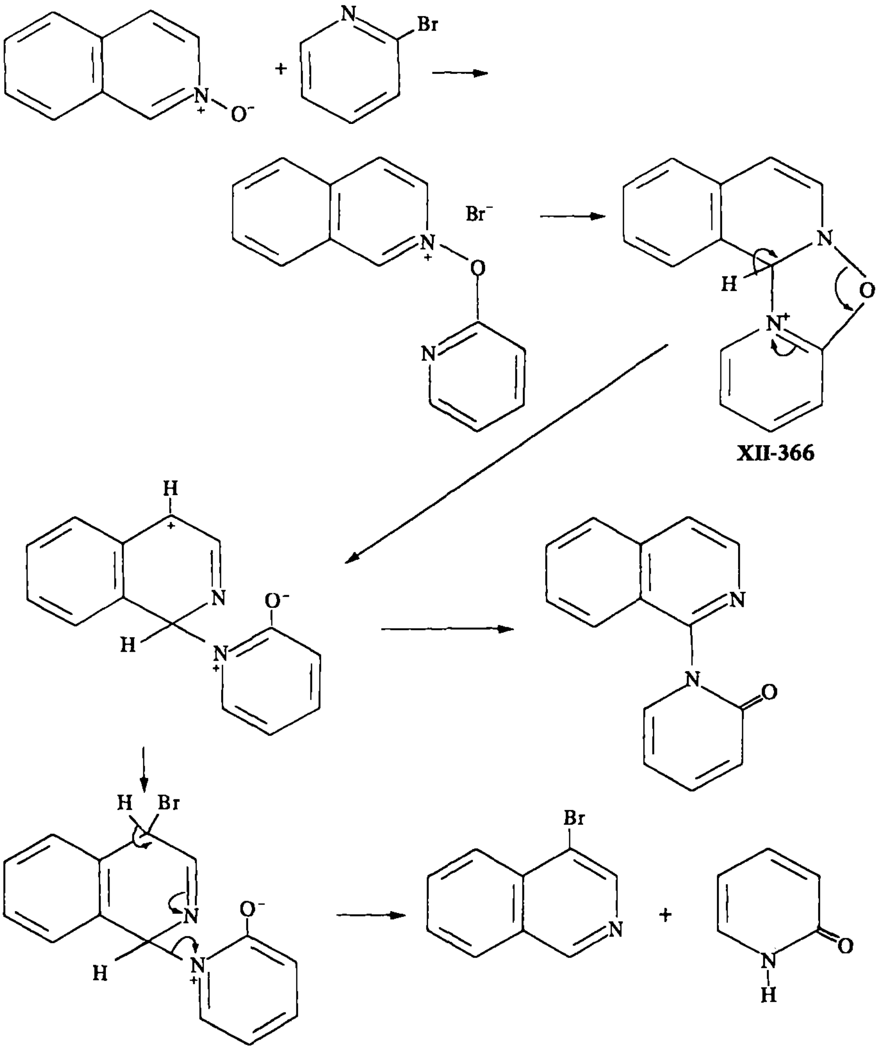
xu-362

XII-364

XII-365

quinoline are not consistent with previously proposed mechanisms[272] and have led to the suggestions that nucleophilic attack by pyridine-1-oxide on the a-carbon of 2-bromopyridine followed by ring closure gives the intermediate **XI-361** which rearranges to XII-362 through cleavage of the N—O bond. Subsequent cleavages of the C—N or C—0 bond give the observed products XII-363 to **XII-365.**[273]

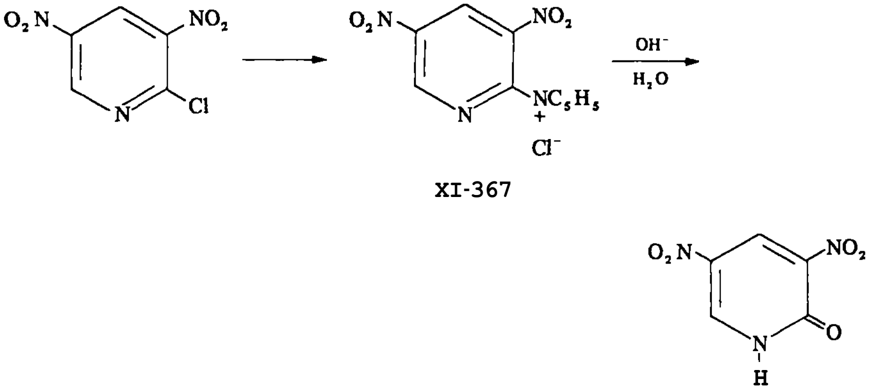
The intermediate XII-366, formed by cyclization at the 1-position of **isoquinoline-2-oxide,** cannot rearrange to a cyclic intermediate comparable to **XII-362,** and an ether product analogous to **XII-364** is not formed.[274]



XII-366

4-Alkoxypyridines rearrange at elevated temperatures to *N*-alkyl-4-pyridones. Isomerizations of this kind are catalyzed by acids and alkyl halides. Spinner and White, however, have prepared 4-methoxypyridine from 4-chloropyridine and sodium methoxide in 86% yield through temperature control and by neutralization of the reaction mixture with solid carbon dioxide.[275]

2-(3,5-Dinitro-2-pyridyl)pyridinium chloride (XII-367), formed from 3,5-dinitro-2-chloropyridine and pyridine in benzene or ether, is readily hydrolyzed in an alkaline medium to 3,5-dinitro-2-pyridone.[276]

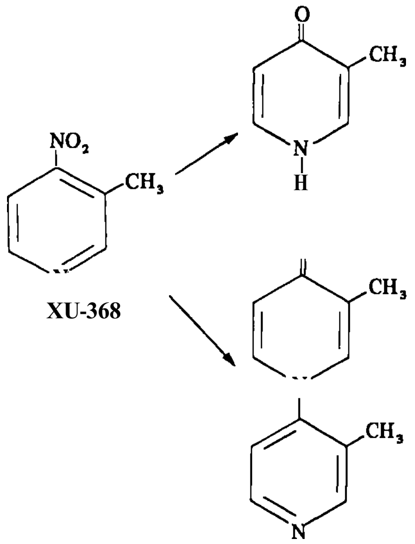


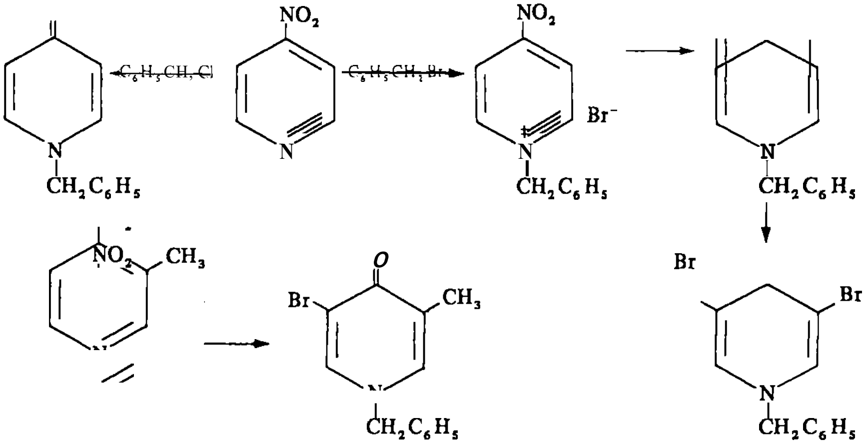
XI-367

B. *Nitropyridines*

A nitro group in the 2- or 4-position of the pyridine ring is susceptible to nucleophilic substitution under relatively mild conditions, and in these reactions it competes with a 3- or 5-halogen.[277] 3-Halo-4-nitropyridines (halo = Cl, Br, I) react with aqueous barium or potassium hydroxide to form 3-halo-4-pyridones and with alkoxides to form 4-alkoxy-3-halopyridines.[254] However, 3-fluoro-4-nitropyridine is converted to 4-nitro-3-pyridinol or 3-alkoxy-4-nitropyridines.[256a] The corresponding *N*-oxides react similarly.[256] (See Section I.6.A., p. 688).

4-Nitro-3-picoline (MI-368) is hydrolyzed on standing to 1-(3′-methyl-4′-pyridyl)-3-methyl-4-pyridone and 3-methyl-4-pyridone.[278] 4-Nitropyridine and benzyl bromide give *N*-benzyl-3,5-dibromo-4-pyridone (MI-369) in 33% yield. The quaternary salt first formed is hydrolyzed to the 4-pyridone. Oxidation of hydrogen bromide by the nitrous acid product provides the bromine and water. The yield is increased to 71%by the addition of bromine. 3,5-Dibromo-4-chloropyridine and benzyl bromide in base also give XII-369.[279] Similarly, 3-methyl-4-nitropyridine and benzyl bromide give *N*-benzyl-3-bromo-5-methyl-4-

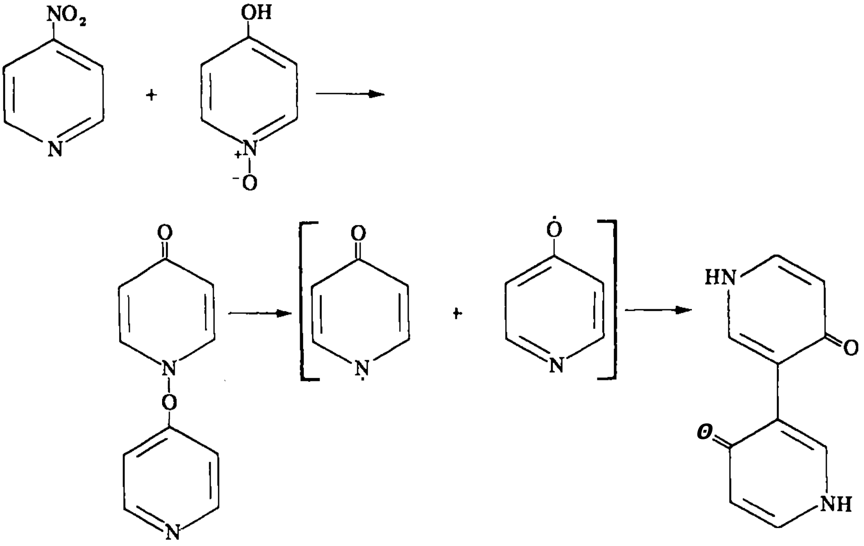




XII-370 **XII-369**

pyridone (MI-370). *N*-Benzyl-4-pyridone is prepared in 74% yield from 4-nitropyridine and benzyl chloride.

4-Nitropyridine and 4-hydroxypyridine-1-oxide in boiling methanol react to give *N*-(4′-pyridyloxy)-4(1*H*)pyridone (MI-371), which rearranges to 3,3′-(4,4′-dihydroxy)bipyridyl on heating at 100° in benzene or dioxane. Evidence supports a homolytic fission of the N–O bond in XII-371 to give a biradical intermediate.[80]



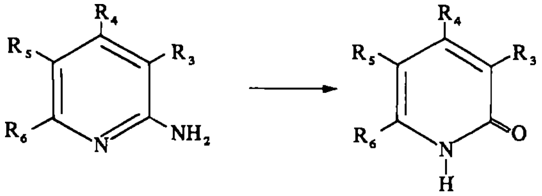
XII-371

C. *Aminopyridines*

Although many 3-aminopyridines can be diazotized and coupled, the ring nitrogen activates the diazonium ions from 2- and 4-aminopyridines, and they are rapidly converted to pyridones. A relatively large number of pyridinols and pyridones have been formed by this route. Examples are listed in Tables **XII-4** to **XII-6.**

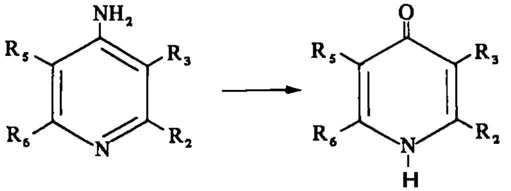
Although aminopyridines can be prepared by the reduction of nitropyridines, 2- or 4-nitro groups are readily displaced by nucleophiles. For example, 3-halo-4nitropyridines (XII-372) can be converted to the intermediate 4-amino-3-halopyridines(XII-373) by reduction with potassium hydrosulfide or by displacement with ammonia, or they can be hydrolyzed directly to 3-halo-4pyridones **(XII-374)**.[254] In those cases where both methods have been used to prepare pyridones the route XI-372 → XI-373 → XI-374 usually gives lower yields.[299] Nitration of 2-amino-5-bromopyridine with warm sulfuric acid-nitric acid gives **5-bromo-3-nitro-2-pyridone (XII-375)**.[304] However, 4-amino-2-bromo-3-nitropyridine prepared from 4-amino-2-bromopyridine *via*

TABLE XII-4. 2-Pyridones from 2-Aminopyridines



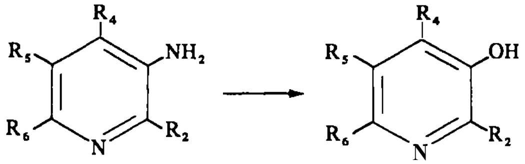
R_n					
3	4	5	6	% Yield	Ref.
CH_3				73	281
		CH_3		58	281
C_2H_5	CH_3			mixture, 75	281
	CH_3	C_2H_5		same as above	281
		CH_3		75	282
	C_2H_5			69	283
	EtO	Br		85	284
NO_2				mixture, 88	285
		NO_2		same as above	285
	NO_2			85	286
	NO_2	NO_2		80	286
NO_2		I		75	281
I		NO_2		80	281
NO_2	CH_3		CH_3	97	288
	CH_3	NO_2	CH_3	–	288
	CH_3	Br	CH_3	50	289
NO_2	CH_3	Br	CH_3	–	289
Br		NO_2		67	290
NO_2		Br		83	290
Cl		NO_2		72	291
NO_2		Cl		70	291
		OH		–	292
C_6H_5	CH_3	OH		60	292
	p-$C_6H_4NO_2$		C_6H_5	61	74
	$CH(CH_3)_2$			73	226

TABLE XII-5. 4-Pyridones from 4-Aminopyridines

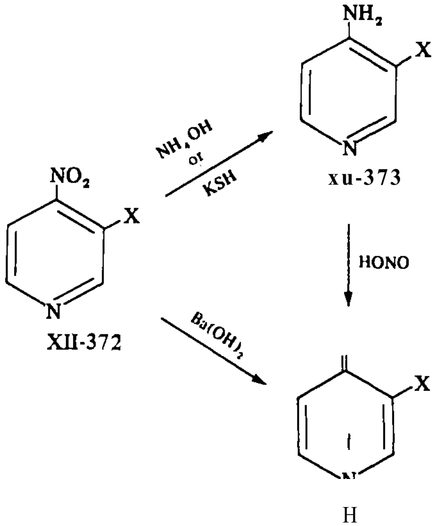


R_n					
2	3	5	6	% Yield	Ref.
CH_3				80	293
CH_3			CH_3	85	294
CH_3			CH_3	33	295
Cl			Cl	65	296
F				79	266
	F			58	266
CH_3		CH_3		60	297
	Br			45	299
	I			–	299

TABLE XII-6. 3-Pyridinols from 3-Aminopyridines



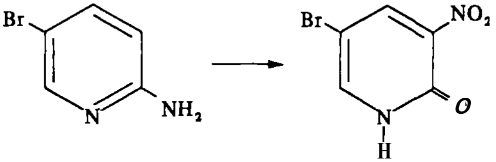
R_n					
2	4	5	6	% Yield	Ref.
CH_3			CH_3	62	300
CH_3	CH_3		CH_3	52	300
			C_6H_5CONH	54	292
		OH		20.7	301
	$COCH_3$			76	302
$COCH_3$				52	302
I			I	14	298
CH_3	COOH	COOH		80	303



XII-372

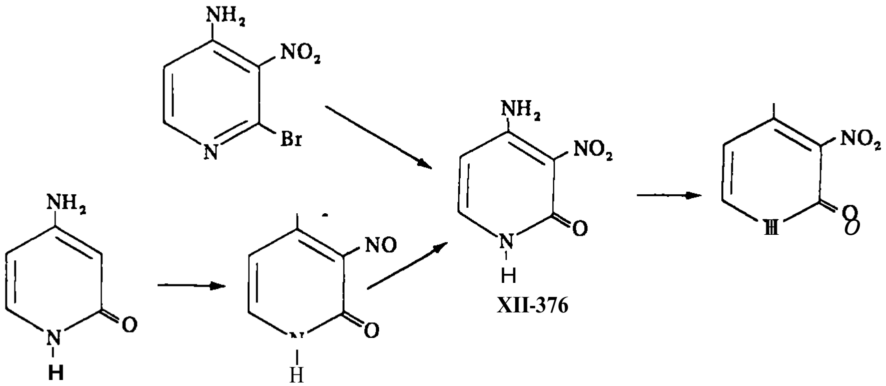
xu-373

xu-374



XII-375

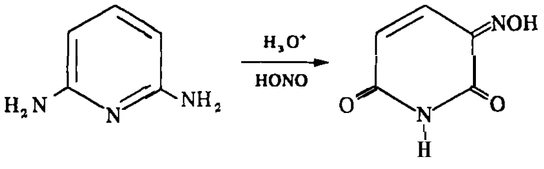
the nitramine can be converted to 4-amino-3-nitro-2-pyridone **(MI-376)** with potassium hydroxide containing hydrogen peroxide. 3-Nitro-4-hydroxy-2-pyridone has been formed from **MI-376** by treatment with nitrous acid.[305]



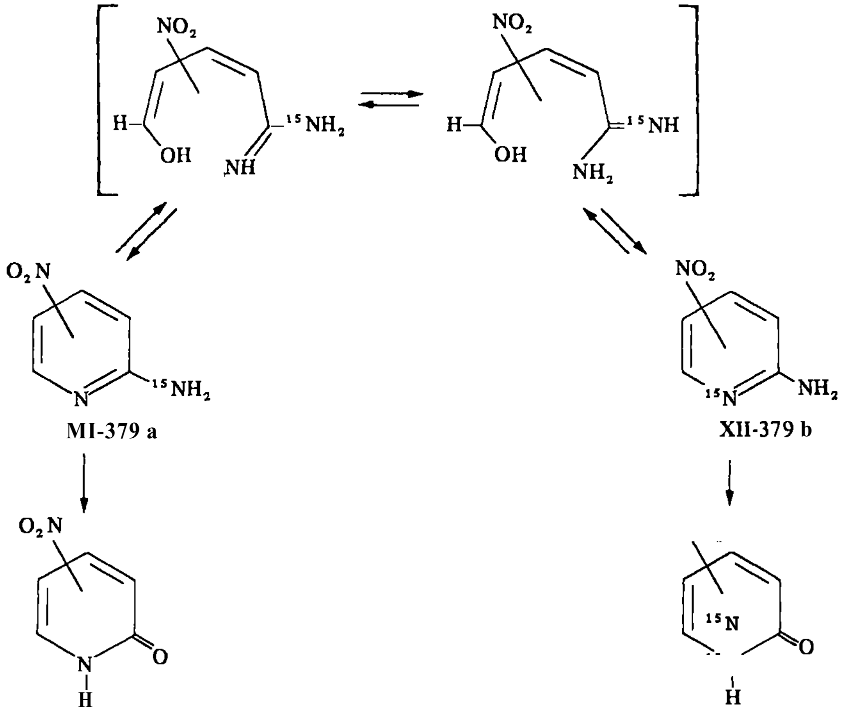
XII-376

XII-377

Both 4-amino-2-pyridone **(XII-377)**[305] and **4-amino-1,6-dimethyl-2-pyridone**[306] form 3-nitroso derivatives when treated with nitrous acid. Oxidation of **4-amino-3-nitroso-2-pyridone** also gives **XII-376.**[305] 2,6-Diaminopyridine is nitrosated and diazotized with nitrous acid in aqueous sulfuric acid. Ultraviolet, infrared and nuclear magnetic resonance spectra are consistent with the **1,2,3,6-tetrahydro-3-hydroxyimino-2,6-pyridinedione** structure **XII-378.**[307] Under mild hydrolytic conditions the nitrogens of the ring and of the amino group in 3- and 5-nitro-2-aminopyridine **MI-379** exchange positions (a Dimroth rearrangement). In reactions with nitrous acid, kinetic studies with **MI-379** indicate that the intact pyridines and not the ring-opened species react preferentially, **(MI-379a→ XII-380a, MI-379b→ XII-380b).**[308, 309]



MI-378



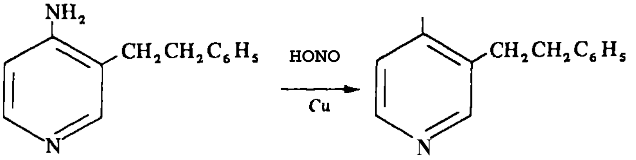
MI-379 a

XII-379 b

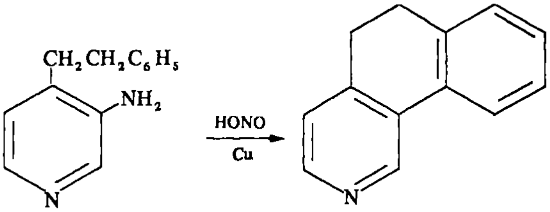
MI-380 a

XII-380 b

4-Amino-3-(β-phenylethyl)pyridine and nitrous acid give 4-hydroxy-3-(β-phenylethyl)pyridine (**XII-381**) with or without Gattermann copper powder, but **3-amino-4-(β-phenylethyl)pyridine** undergoes a Pschorr cyclization to **MI-382** in the presence of copper.[310]

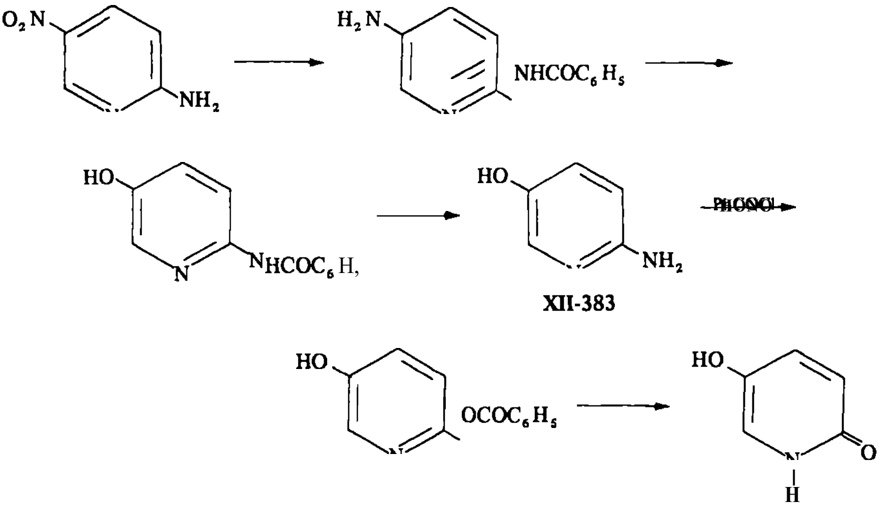


XII-381



XI-382

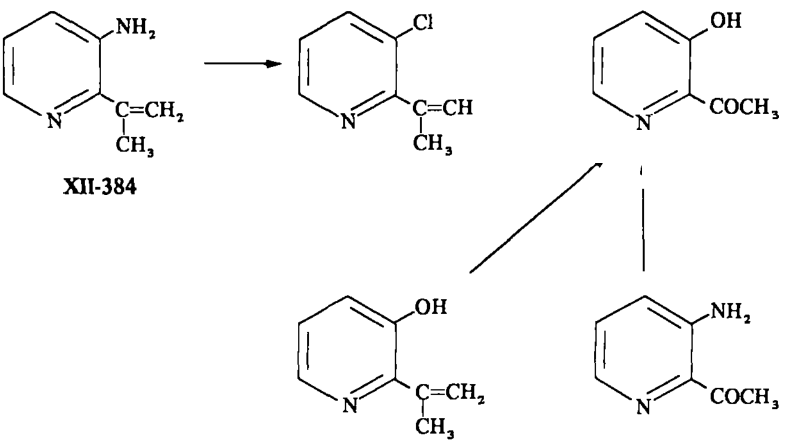
2-Amino-5-pyridinol (**W-383**) and 5-hydroxy-2-pyridone can be prepared from 2-amino-5-nitropyridine. After protecting the 2-amino group by benzoylation, hydrogenation followed by treatment with nitrous acid and acid hydrolysis gives **XII-383**. 5-Hydroxy-2-pyridone can be isolated as the monobenzoate from the reaction between **W-383** and nitrous acid after



XII-383

treatment with benzoyl chloride.[292] It has been prepared in low yield from 2-aminopyridine[311] or from 3-ethoxypyridine[312] or more conveniently and in improved yields by the Elbs peroxydisulfate oxidation of 2-pyridone.[313]

2-(3-Amino-2-pyridyl)propene (XII-384), on treatment with nitrous acid in hydrochloric acid, gives 3-chlbro-2-isopropenylpyridine and 2-acetyl-3-pyridinol. Bicyclic products were not detected. Nitrous acid oxidation of 2-isopropenyl-3-pyridinol or treatment of 2-acetyl-3-aminopyridine with nitrous acid also gives 2-acetyl-3-pyridinol.[302]



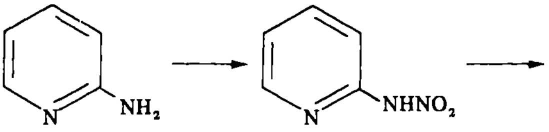
XII-384

The composition of a mixture of 3- and 5-ethyl-2-aminopyridines from the direct amination of 3-ethylpyridine has been estimated by conversion to *N*-methyl-2-pyridones.[314]

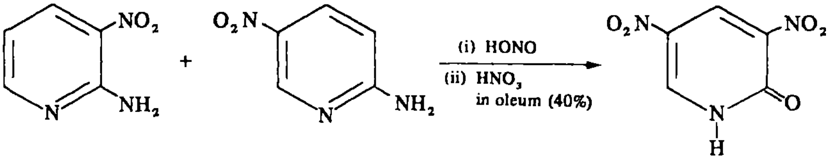
D. *Nitramines*

Nitration of aminopyridines with mixed acid gives nitramines. 2- and 4-Nitraminopyridines when heated with sulfuric acid rearrange to aminonitropyridines. For example, 2-nitraminopyridine (XII-385) gives a mixture of 3-nitro- and 5-nitro-2-aminopyridine and only a trace of 2-pyridone. The yield of 2-pyridone is increased significantly by using acetic acid-acetic anhydride in place of sulfuric acid. 3-Nitraminopyridine when treated with sulfuric acid or acetic acid-acetic anhydride gives 3-pyridinol as the major product.[315] 2-Aminopyridine has been used to prepare 3,5-dinitro-2-pyridone in an overall yield of 37% *via* the nitramine (XII-385) and the aminonitropyridines.[285]

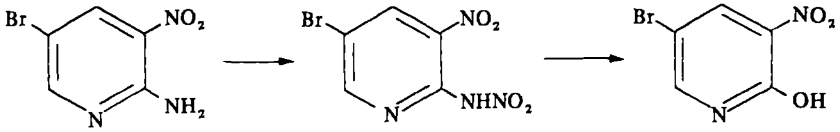
2-Amino-5-bromo-3-nitropyridine and nitric acid in sulfuric acid give the 2-nitramine, which reacts further with sulfuric acid-nitric acid to give



XII-385

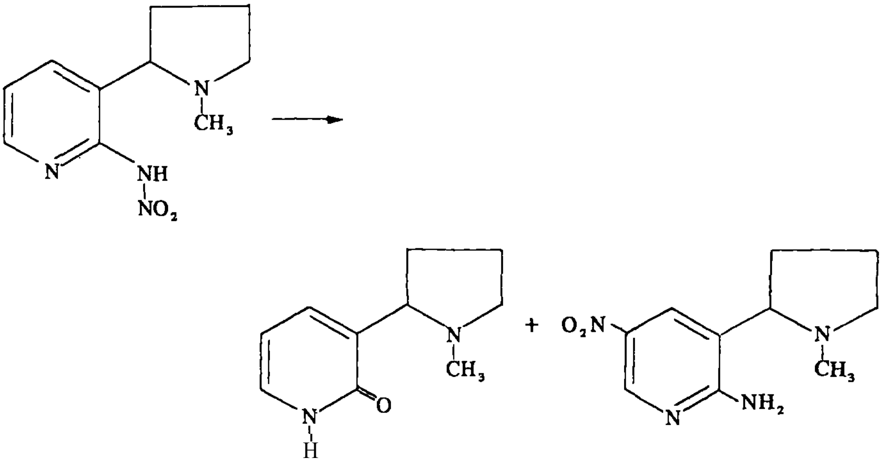


5-bromo-3-nitro-2-pyridone **(XII-386)**,[304] a behavior characteristic of 3,5-disubstituted-2-nitramines.[315]



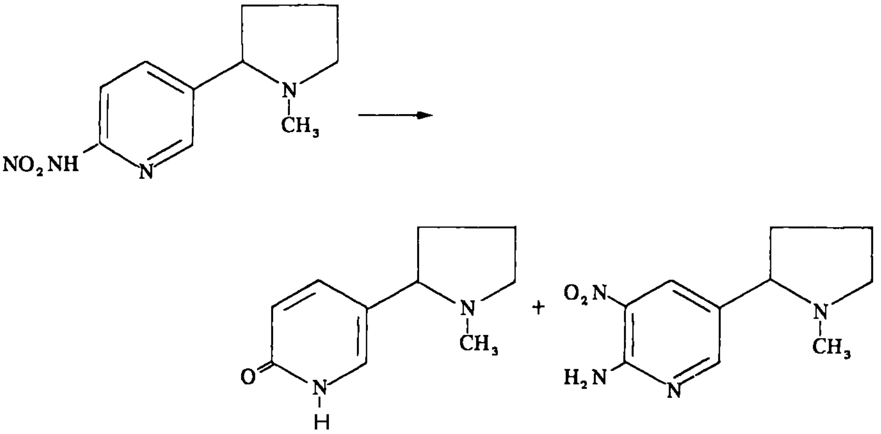
XII-386

2-Nitraminonicotine and 6-nitraminonicotine and sulfuric acid give nitrous oxide and hydroxynicotines **(XII-387, 54%;XI-388, 74%)**and amino-5-nitronicotines. The nitraminonicotines and acetic anhydride in acetic acid give some



XII-387

hydroxynicotine, tars, and nitrogen. Also with an equimolecular amount of triethylamine in acetic anhydride, 2-nitraminopyridine reacts similarly to give a good yield of nitrogen, 2-pyridone and some diethylacetamide. It has been suggested that an intermediate oxidation of the *N*-methylpyrrolidine ring or of triethylamine by the nitramine is responsible for nitrogen formation **(XI-389, XII-390)**.[316]



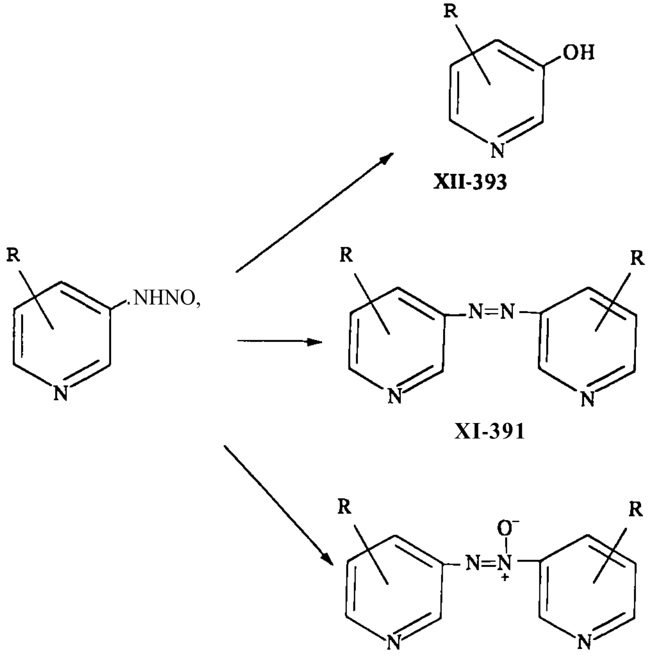
XII-388

$$RNHNO_2 + Et_3N \longrightarrow ROH + N_2 + Et_3NO \qquad \text{(XII-389)}$$

$$Et_3NO + Ac_2O \longrightarrow AcNEt_2 + CH_3CHO + AcOH \qquad \text{(XI-390)}$$

Czuba has studied 3-nitramines in some detail.[317] Nitramines of the four chloro-3-aminopyridines,[318] 3-amino-5-ethoxypyridine, 5-aminonicotinic acid, 5-aminopicolinic acid,[319] 3-amino- and 5-amino-2-pyridinesulfonic acids,[320] 3-amino-4-picoline and 5-amino-3-picoline[321] have been prepared. Attempts to prepare nitramines from the four 3-aminopyridinols were unsuccessful.'[19] However, 3-amino-5-ethoxypyridine forms the nitramine that reacts in sulfuric acid to give 5-ethoxy-3-pyridinol.[319]

3-Nitraminopyridines that normally do not rearrange when heated with sulfuric acid give azopyridines (**XII-391**; R = 6-Cl, 2-Cl, 5-Cl, 4-Cl, 5-COOH) or azoxypyridines (**XI-392**, R = 6-COOH) in addition to 3-pyridinols (**XII-393**; R = 5-Cl, 5-OC_2H_5, 4-CH_3, 5-CH_3, 2-SO_2OH).'" 5-Nitramino-2-pyridinesulfonic acid gives 3-pyridinol.[320]



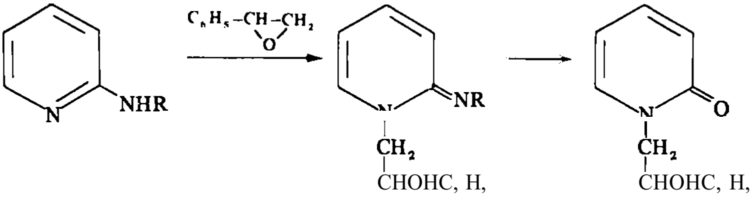
XII-393

XI-391

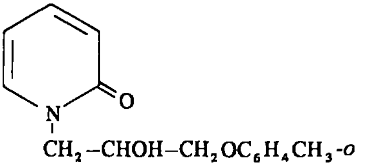
XII-392

E. *Pyridonimines*

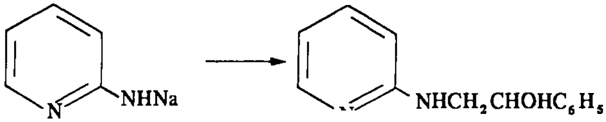
2- or 4-Pyridonimines can be prepared by treatment of aminopyridines with alkyl halides and then with silver **oxide.**[322] 2-Aminopyridines and styrene oxides in aqueous ethanol form **N-(β-hydroxy-β-phenylethyl)-2-pyridonimines (XII-394; R = H, CH_3).**[323] Treatment of **W-394** with aqueous alkali gives N-(β-hydroxy-β-phenylethyl)-2-pyridone.[323, 324] 2-Aminopyridine and **3-(0-**tolyloxy)propylene oxide give **W-395** after **hydrolysis.**[325] In the presence of sodamide in liquid ammonia N-alkylation of 2-aminopyridine occurs to give **XII-396.**[324]



XI-394



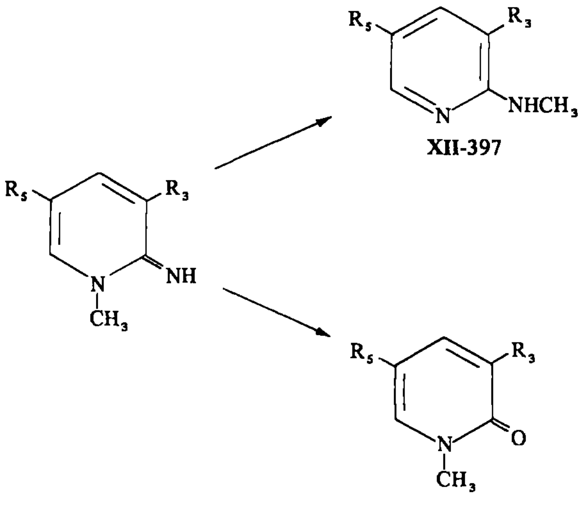
XII-395



XII-396

1-(β-Hydroxyalkyl)-2-pyridones can be synthesized by the direct alkylation of 2-pyridone with alkylene oxides.[326]

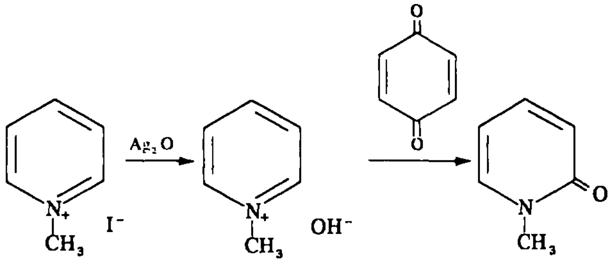
Although 3- and 5-nitro-1-methyl-2-pyridonimines undergo the Dimroth rearrangement rapidly to give XII-397 when treated with base, analogs similarly substituted with less powerful electron withdrawing groups ($R_3 = R_5 = H$; $R_3 = R_5 = Cl$; $R_5 = Cl$; $R_3 = H$) undergo hydrolysis to give the *N*-methyl-2-pyridone. The corresponding 5-cyano-2-imino-1-methylpyridine did not react under the conditions used.[327]



XII-397

F. *Quaternary Salts*

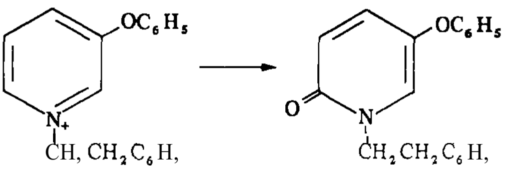
Alkaline potassium ferricyanide oxidation of *N*-substituted pyridinium salts often is a method of choice for the preparation of *N*-alkyl-2-pyridones. For example, *N*-methyl-2-pyridone is prepared conveniently from pyridine by conversion to the quaternary methosulfate followed by oxidation with potassium ferricyanide.[328] Certain quinones with high redox potentials are reduced by *N*-methylpyridonium methosulfate, but in these reactions *N*-methyl-2-pyridone could not be isolated.[329] However, *N*-methyl-2-pyridone is isolated when aqueous methylpyridinium hydroxide (**XI-398**) is treated with *p*-benzoquinone.[329, 330]



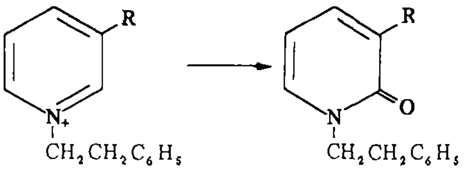
XU-398

Dipole moments have indicated that the oxidation of 1-phenethyl-3-phenoxypyridinium salts by alkaline ferricyanide gives the 6-pyridone (**XII-399**) and that the corresponding 3-bromo- and 3-cyanopyridinium salts (R = Br, CN) form the 2-pyridones (**XII-400**).[331] Subsequently these structures have been confirmed.[332] The acetal of *N*-(3,4-dimethoxyphenethyl)-3-ethyl-4-formylpyridinium bromide gives about equal amounts of the 2- and 6-pyridones.[333]

Substituents on the 3-position can contribute both electronic and steric effects.[333-335] It has been shown that a 3-methyl group is slightly activating



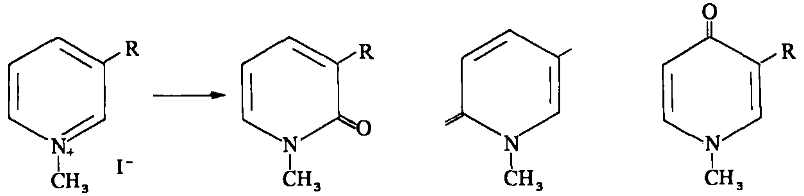
XII-399



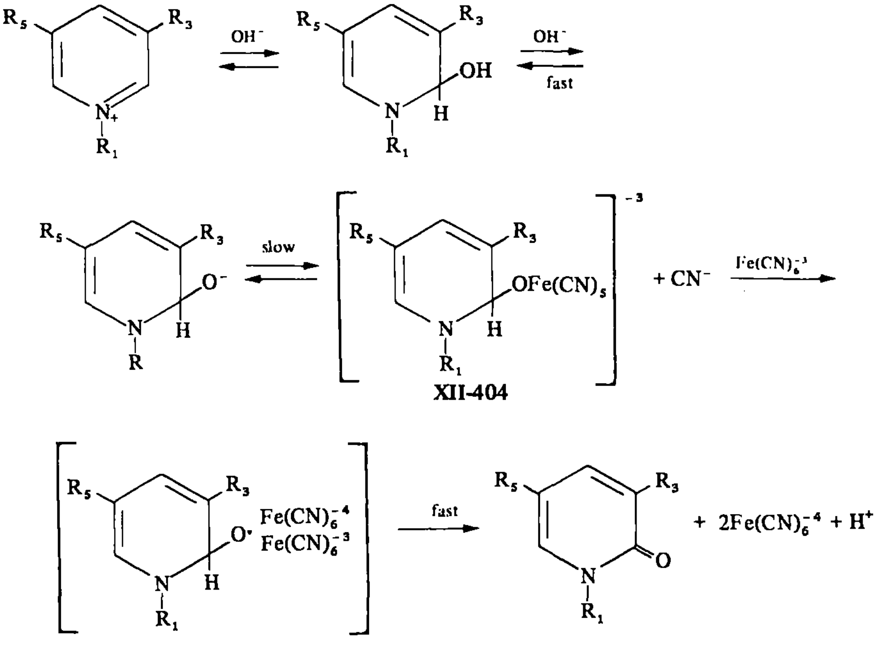
XII-400

and directs oxidation to the 2-position (XII-401:XII-402–96.6:3.4). The 3-cyano group is appreciably activating and also directs oxidation to the

2-position but 6- and 4-pyridones (XI1402 and XII-403) are also formed (83.1: 15.9:1). The carbomethoxy group is deactivating and directs only to the 6-position.[334] Neither C—H bond breaking nor the addition of hydroxide ion is ratedetermining. It has been suggested that the rate-determining step is the formation of a complex (XII-404) that then reacts with more ferricyanide to form a second complex that gives the pyridone.[334]



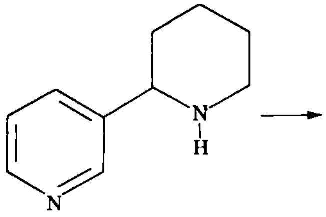
XII-401 xII-402 XII-403



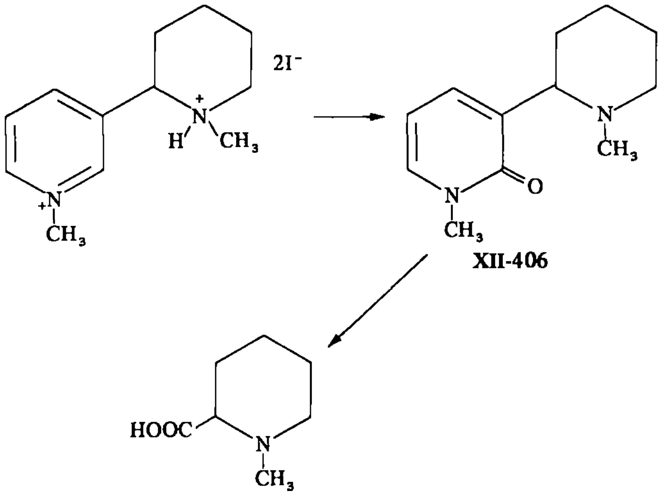
XII-404

The alkylation of the alkaloid anabasin (XII-405) with methyl iodide gives the hydroiodide of *N*-methylanabasin iodomethylate which gives *N,N'*-dimethylanabasone (XII-406) when treated with potassium ferricyanide.[336]

The oxidation of MI406 to 2(S)(−)-*N*-methylpipecolinic acid has established the absolute configuration of XII-405.[336]

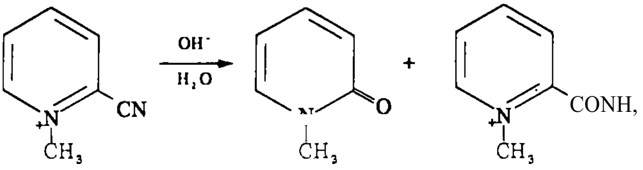


XII-405

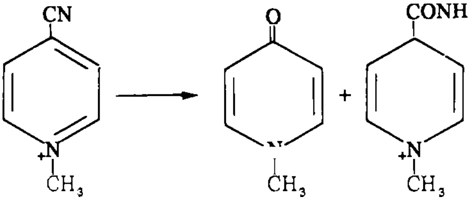


1-(1-Methyl-2-phenylethyl)-2-pyridone,[337] 1-β-(3,4-dimethoxyphenethyl)-2-pyridone,[338] 1-(3,4-dimethoxyphenethyl)-5-(1-methyl-2-pyrrolidinyl)-2-pyridone,[339] 1,1′-hexamethylene-di-2-pyridone,[6] and 1-[3-(3,4-methylenedioxyphenyl)propyl]-2-pyridone[340] have been formed by oxidation of pyridinium salts by alkaline potassium ferricyanide. However, attempts to oxidize 1-(β-6-methoxy-1-naphthylethyl)pyridinium bromide[341] or 1-methyl-3-pyridinol[342] to the pyridone with alkaline potassium ferricyanide have been unsuccessful.

Cyano-, halo-, and amino- groups on the 2- and 4-positions of pyridinium ions are susceptible to nucleophilic substitution. For example, 2- and 4-cyano-1-methylpyridinium perchlorate (XII-407 and XII-408) and aqueous sodium hydroxide give both amides and pyridones. The ratio of rates of reaction of the nitrile group are 50:5.7:1 (2-CN > 4-CN > 3-CN) and at the ring carbon are 1100:43:1 (2-CN > 4-CN > 6-position of 3-CN).[343] 1-Methyl-3-cyanopyridinium perchlorate (XII-409, X = ClO_4) in aqueous sodium hydroxide has been reported to give 3-carbamidopyridinium perchlorate (87%) and smaller amounts

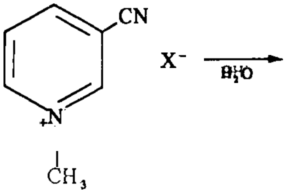


XII-407

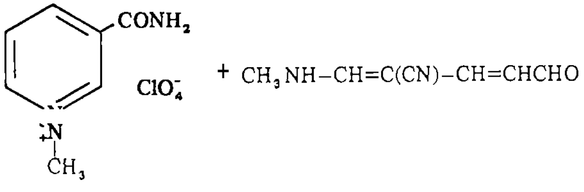


XII-408

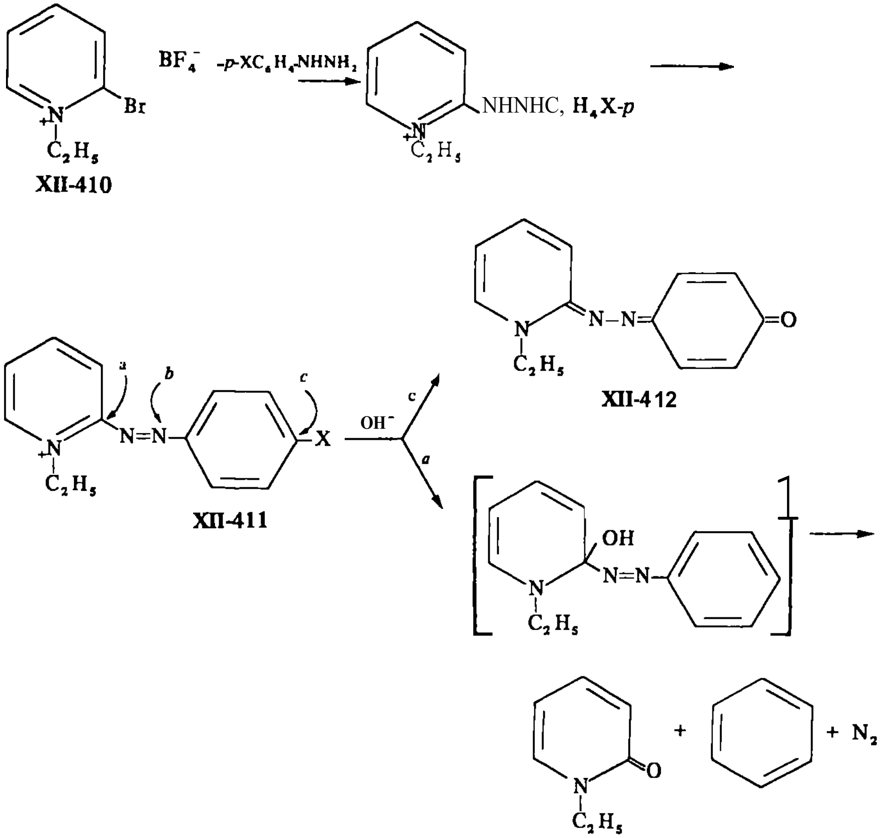
of 4-cyano-5-methylamino-2,4-pentadienal *(6%)* and 1-methyl-5-cyano-2-pyridone (~1%).[343] However, oxidation of the corresponding iodide (XII-409, X = I) with alkaline aqueous potassium ferricyanide has been shown to give only the 3-cyano-N-methylpyridones and no hydrolysis products.[334]



XII-409



4- And 2-bromo-1-alkylpyridinium fluoroborates (XII-410) and para-substituted phenylhydrazines form phenylhydrazino derivatives that are oxidized by nitrous acid to the arylazopyridinium fluoroborates (XII-411)[344] that can be attacked by nucleophiles at positions *a*, *b*, or *c*.[345, 346] Reaction between alkali and XII-411 (X = H) gives N-ethyl-2-pyridone and benzene.[344, 345] When X is H or Cl only 1% of XII-412 is formed (attack at c). Sulfinates and sodium bisulfite react at *b* to give adducts.

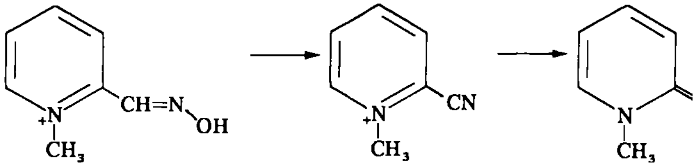


XII-410

XII-411

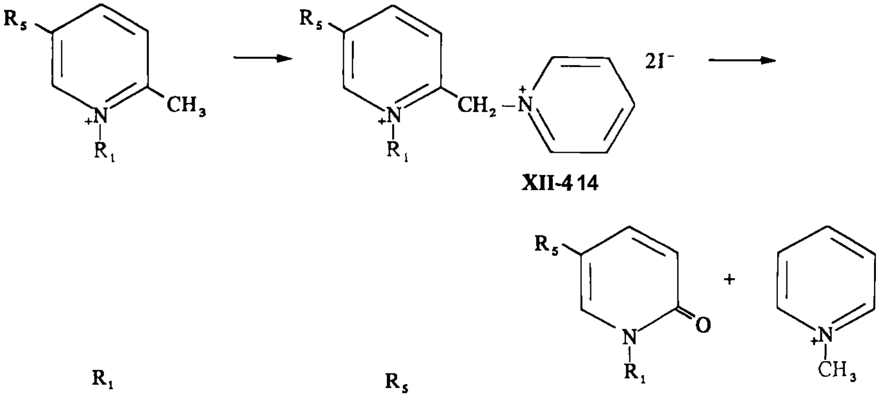
XII-412

The **2-cyano-N-methylpyridinium** ion, the 2-carboxy-1-methylpyridinium ion and N-methyl-2-pyridone have been identified as metabolites of *N*-methylpyridinium-2-aldoxime iodide (2-PAM) **(XII-413)**[347, 348] in rats.



XII-413

As part of a program to synthesize ipecac alkaloids, dipyridinium diiodides (XII-414), which are formed from **1,5-disubstituted-2-methylpyridinium** salts and iodine in pyridine, were converted to 2-pyridones (XII-415) with aqueous

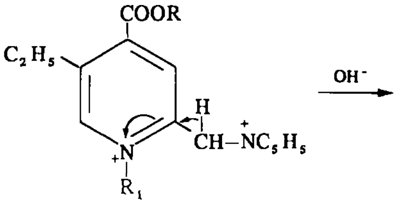


XII-414

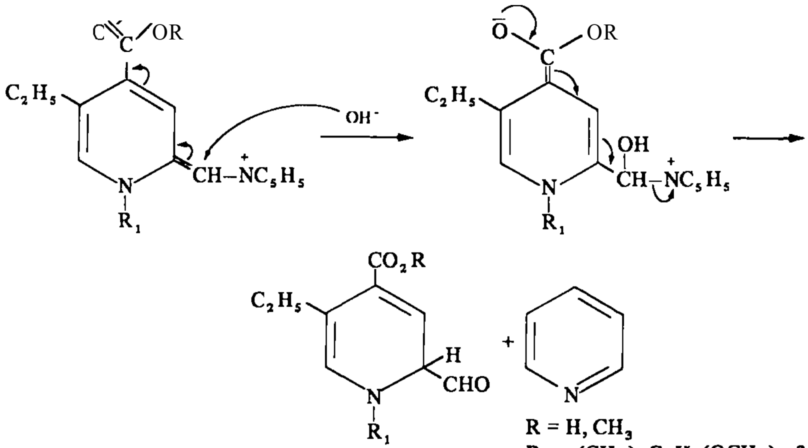
XII-415

R_1	R_5
CH_3	H
$(CH_2)_2C_6H_5$	H, C_2H_5
3, 4-$(CH_3O)_2C_6H_3(CH_2)_2$	H, C_2H_5

alkali.[349-351] An attempt to use this method with **XII-416,** which has an electron withdrawing carboxyl or carbomethoxy group in the 4-position, was unsuccessful. Cleavage gives pyridine and not the pyridone.[349, 350] The

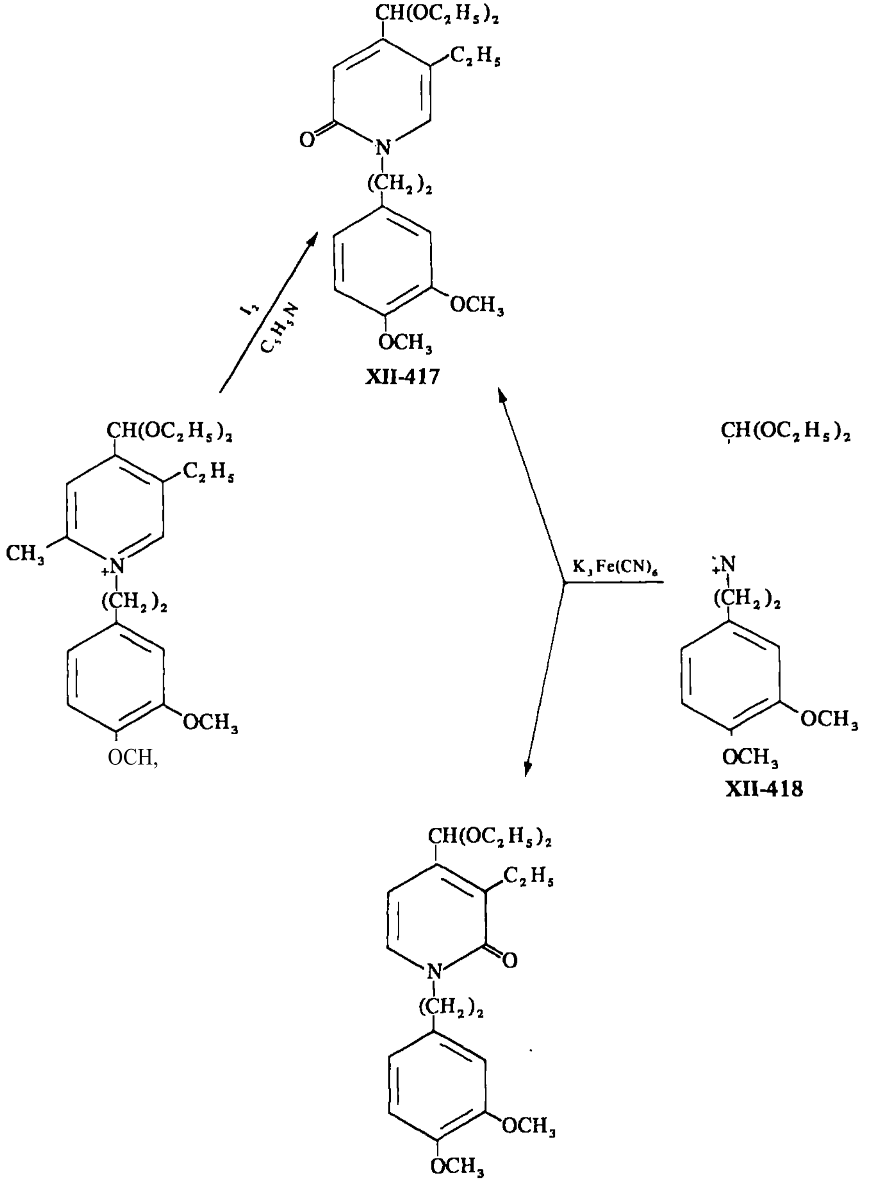


XII-416

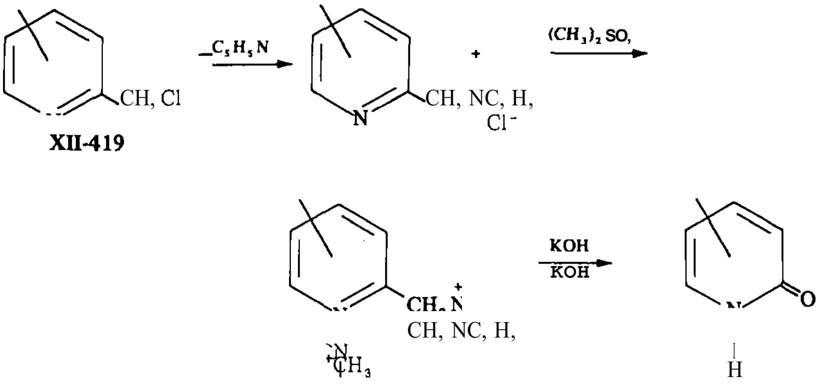


R = H, CH_3
R_1 = $(CH_2)_2C_6H_3(OCH_3)_2$-3,4

application of **this** route to the synthesis of **XI1415** [R_1 = $(CH_2)_2C_6H_5$, 3,4-$(CH_3O)_2C_6H_3(CH_2)_2$; R_5 = C_2H_5] has **also** been unsuccessful.[352] 4-(Carboxaldehydediethylacetal)-1-(3,4-dimethoxyphenethyl)-5-ethyl-2-pyridone (**XII-417**) has been prepared in low yield by this method and was used to characterize the products of alkaline ferricyanide oxidation of **XII-418**.[333]



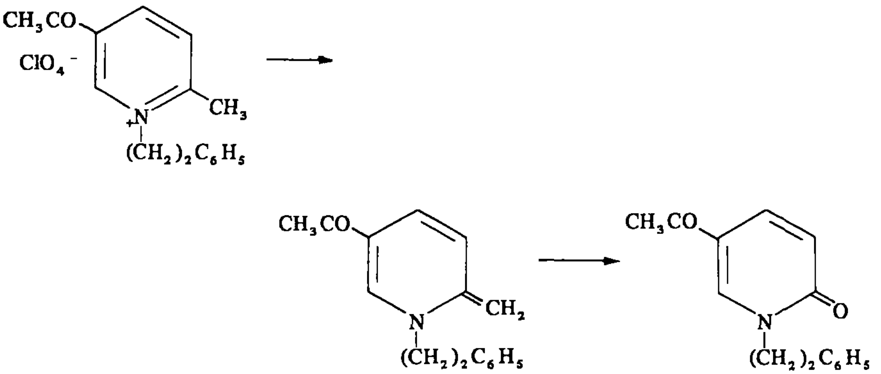
2-Methylpyridine-1-oxides react with tosyl chloride to give 2-chloromethyl derivatives **(XII-419)**, which react with pyridine to form 1-(2′-pyridylmethyl)-pyridinium chlorides. These, on methylation, give **XII-420** which form the 2-pyridone[353] by the procedure previously described.[349]



XII-419

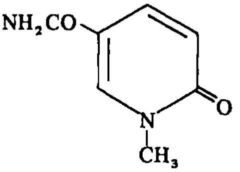
XII-420

5-Acetyl-2-methyl-1-phenylethylpyridinium perchlorate when treated with aqueous sodium hydroxide gives the anhydro base that forms 5-acetyl-1-phenethyl-2-pyridone **(XII-421)** with potassium permanganate in acetone.[354]

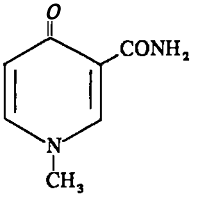


XII-421

A single *N*-methylnicotinamide oxidase apparently is responsible for the oxidation of *N*-methylnicotinamide to *N*-methyl-2-pyridone-5-carboxamide **(XII-422)** and *N*-methyl-4-pyridone-3-carboxamide **(XII-423)** and the oxidation of pyridoxal to pyridoxic acid in man. A xanthine oxidase appears to oxidize *N*-methylnicotinamide ion to **XII-422** but not to **XII-423**.[355]



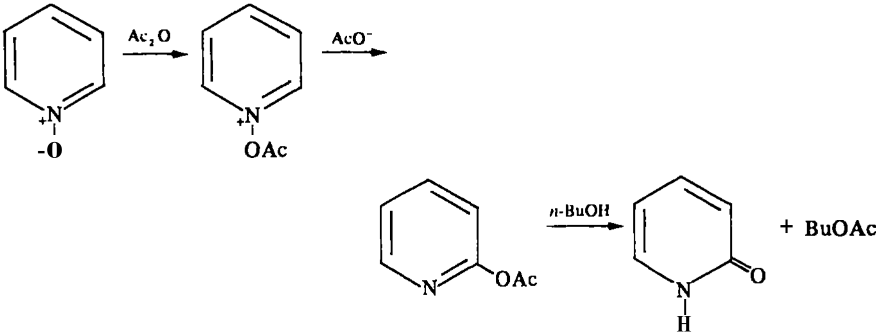
XII-422



XII-423

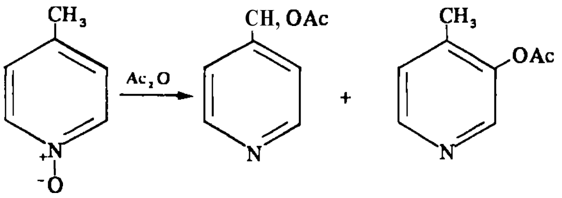
G. N-Oxides and Anhydrides

When pyridine-1-oxides and related heterocyclic *N*-oxides in which there are no alkyl groups at the 2- or 4-positions are heated with acetic anhydride, *O*-acetylation occurs. This is followed by rearrangement to the acetoxypyridine **(XII-424)**, which is hydrolyzed readily to the pyridone.[356-360] Acetoxylation usually occurs at the 2-position[361-364] (see also Chapter IV).

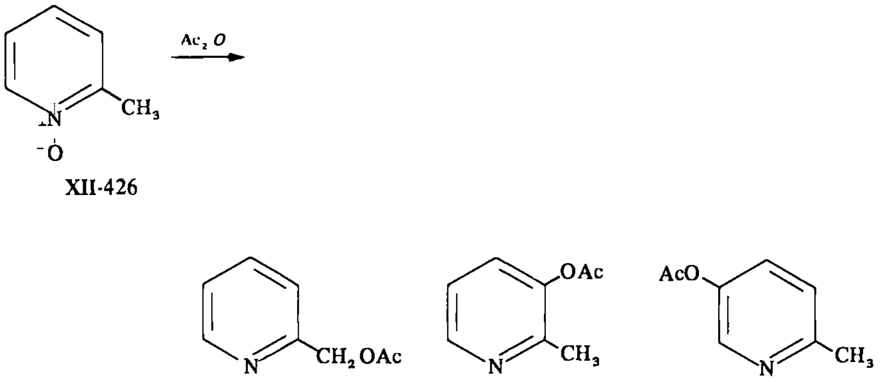


XII-424

A method of preparation of 2-pyridone from pyridine in 50% overall yield *via* the N-oxide and **XII-424** is recommended by Chumakov.[365] The 2-pyridone, free of water and acetic acid, is prepared from **XII-424** by heating with *n*-butyl alcohol.[365] When an alkyl group occupies the 2- or 4-position (e.g., **XII-425** to **XII-427**) substitution at the a-position of the side-chain predominates and is usually accompanied by some reaction at the

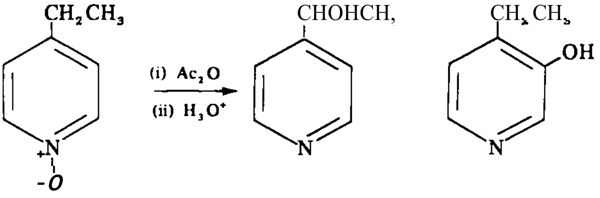


XII-425 (53%) (7%)



XII-426

(60%) (16%) (18%)



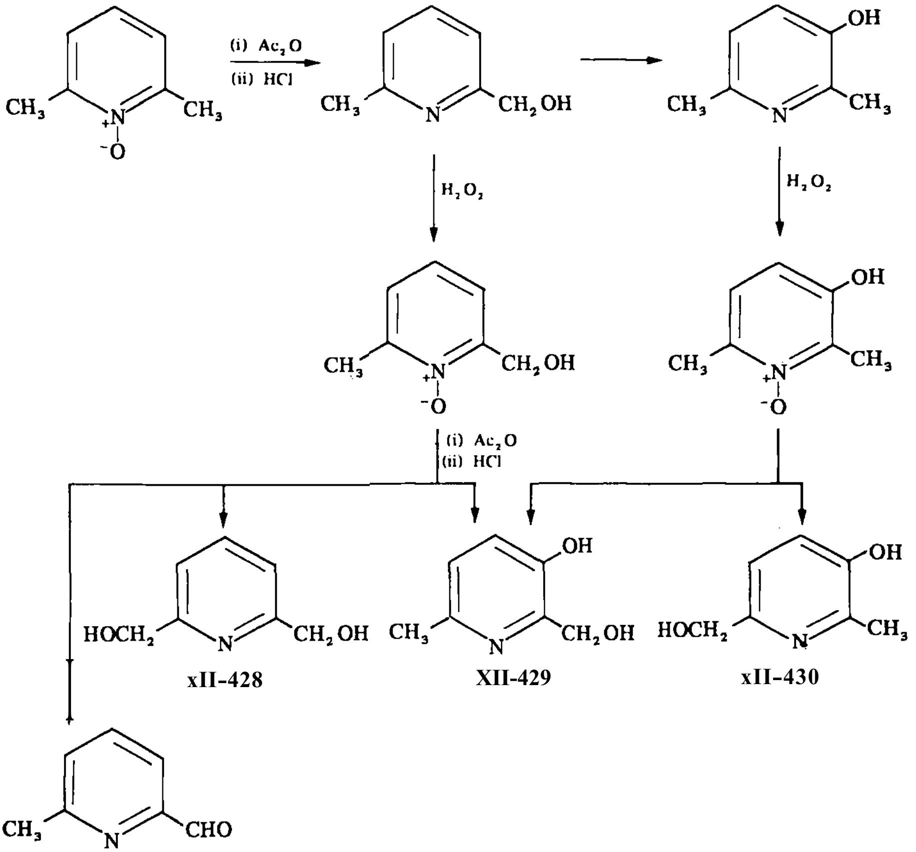
XII-427 (27%) (6%)

3-position.[366, 367] Further treatment of *N*-oxides of rearrangement products with acetic anhydride gives diols and aldehydes after hydrolysis. For example, 2,6-lutidine-1-oxide has been converted to the aldehyde and the diols (XII-428 to **XII-430**).[368, 369] All possible pyridinols and pyridinylcarbinols are formed from 2,4-lutidine-1-oxide and from 2,4,6-collidine-1-oxide when treated with acetic anhydride.[370]

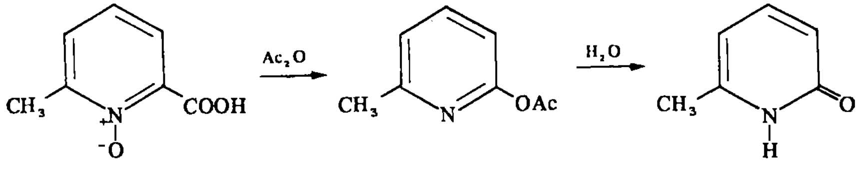
The product of rearrangement of 6-methylpicolinic acid-1-oxide (XII-431) and acetic anhydride, previously characterized as 2-acetoxymethylpyridine,[371] has been shown to be 6-acetoxy-2-picoline (**XII-432**).[372] The observation that 2-picoline-1-oxide (XII-426), the decarboxylation product of XII-431, gives mainly 2-acetoxymethylpyridine indicates that decarboxylation, N—O cleavage, and acetoxylation of **XI1431** at C-2 are concerted.[372]

The preparation of 6-methyl-2-pyridone from 2,6-lutidine *via* **XII-431** appears to be preferred[372] over diazotization and hydrolysis of 6-methyl-2-aminopyridine.[373]

2-Carboxypyridine-1-oxide is decarboxylated quantitatively with acetic anhydride.[361, 362, 374] However, conversion to the methyl ester blocks decarboxylation and methyl 2-pyridone-6-carboxylate is formed after hydrol-



xII-428 XII-429 xII-430



XII-431 XII-432

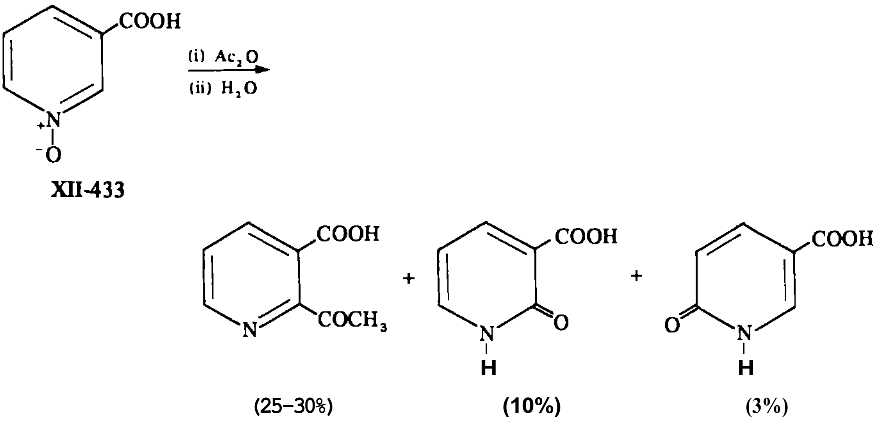
ysis.[360] Methyl isonicotinate-1-oxide gives methyl 2-pyridone-4-carboxylate in poor yield after **hydrolysis.**[283]

2-Trifluoromethylpyridine-1-oxide and acetic anhydride give a poor yield of 6-trifluoromethyl-2-pyridone. 4-Trifluoromethylpyridine-1-oxide does not react with acetic anhydride. It has been suggested that in the latter case the *N*-oxygen is not acetylated because of a strong hyperconjugative electron withdrawal by the 4-trifluoromethyl group.[375]

Studies with 3-substituted pyridines indicate that the product distribution depends on the substituent. When the group in the 3-position is methyl, the two isomeric 2-pyridones are formed in about equal amounts. However, when the group is inductively electron withdrawing, the 3-substituted-2-pyridone either predominates or is the only isolated product. 3-Picoline-1-oxide and acetic anhydride give 3-methyl-2-pyridone (35–40%), 5-methyl-2-pyridone (35–40%), and 3-methyl-1-(5-methyl-2-pyridyl)-2-pyridone (4%) after hydrolysis with water.[361] In a later study, much less 3-methyl-2-pyridone was detected.[376]

3-(Trimethylsilyl)pyridine-1-oxide and acetic anhydride give 5-(trimethylsilyl)- and 3-(trimethylsilyl)-2-pyridone in a ratio of approximately 1.5:1.[377]

3-Acetylamino-2,6-lutidine rearranges to the acetate of 3-acetylamino-6-methyl-2-pyridinemethanol.[378] However, 3-hydroxypyridine-1-oxide and acetic anhydride give 2,3-dihydroxypyridine only,[361] and 3-halopyridine-1-oxides give the 2-acetoxy-3-halopyridines.[363] 3-Nitropyridine-I-oxide gives 3-nitro-2-pyridone in 50% yield.[364] Although only 3- and 5-carbomethoxy-2-pyridone are isolated from a reaction between methyl nicotinate-1-oxide and acetic anhydride,[362] nicotinic acid-1-oxide (XII-433) forms 2-acetylnicotinic acid and smaller amounts of 2- and 6-hydroxynicotinic acid after hydrolysis.[361]

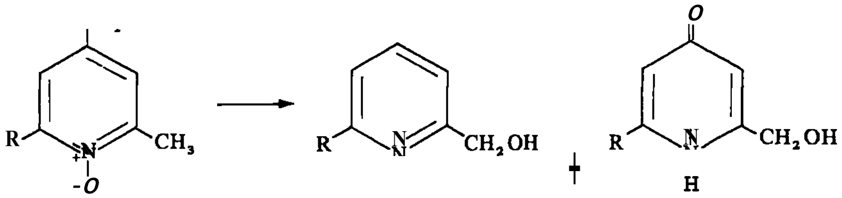


XII-433

(25–30%) (10%) (3%)

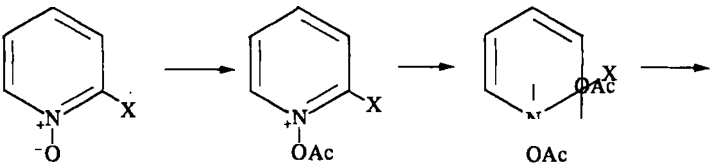
3-Trifluoromethylpyridine-1-oxide and acetic anhydride give an 83% yield of 3-trifluoromethyl-2-pyridone.[375]

A nitro group at position 3 or 5 of 2,4-[379] or 2,6-dimethylpyridine-1-oxide[295, 379] or of *sym*-collidine-1-oxide has no effect on the ease of rearrangement but has some effect on the product distribution. Decreases in the yields of 4-hydroxymethyl containing products and of pyridinols are observed.[379] The 4-nitro group of methylpyridine-I-oxides is a reactive leaving group in nucleophilic **substitutions.**[380] 4-Nitro-2-picoline-1-oxide **(XII-434,** R = **H)** and **4-nitro-2,6-lutidine-1-oxide (XII-434,** R = CH_3) and acetic anhydride give the 4-nitro-2-hydroxymethylpyridine and the 2-hydroxymethyl-4-pyridone.[381] **4-Nitro-2,5-lutidine-1-oxide** forms 2-hydroxymethyl-5-methyl-4-nitropyridine and **2,5-dimethyl-4-pyridone.**[297]

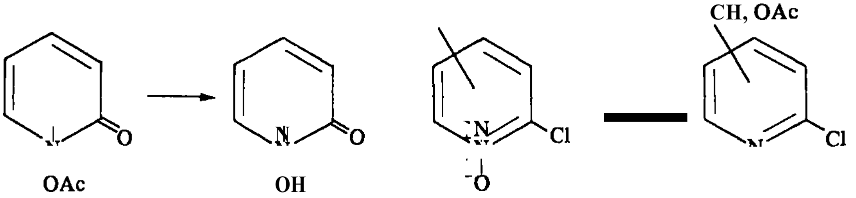


XII-434

2-Chloro-, 2-ethoxy-, and 2-phenoxypyridine-1-oxides **(XII-435)** do not rearrange but form **1-hydroxy-2-pyridones** after hydrolysis. However, 2-chloro-4-methylpyridine-1-oxide **(XII-436,** R = 4-CH_3) and 2-chloro-6-methylpyridine-1-oxide **(XII-436,** R = 6-CH3) give the corresponding **acetoxymethyl-2-chloropyridines.**[374]

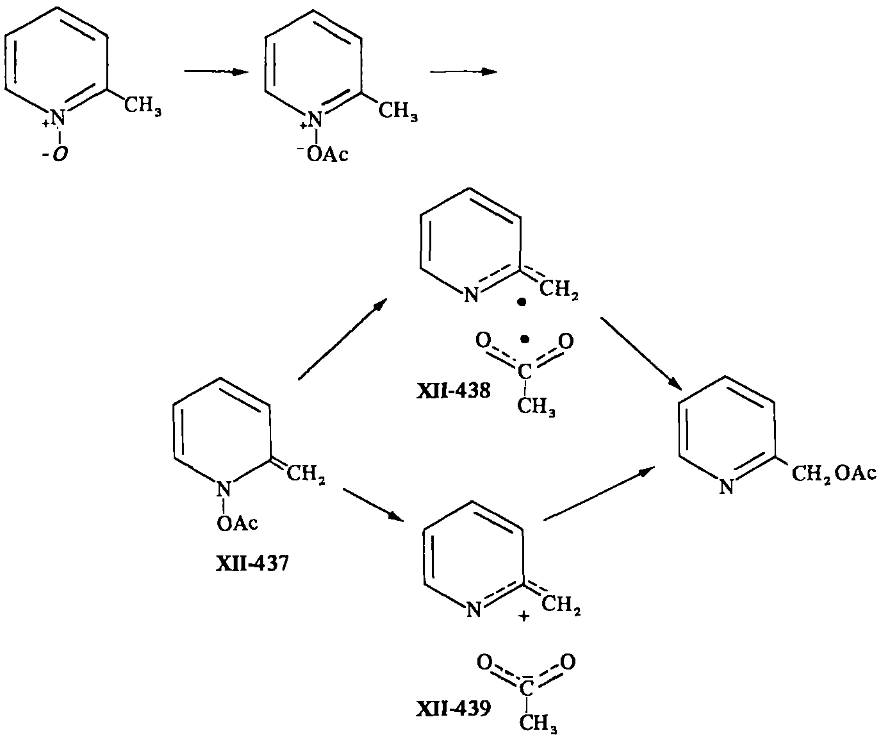


XII-435



XII-436

Considerable attention has been devoted to the mechanisms of these reactions during the past decade and with only partial success. It should be emphasized that rearrangement to the nucleus at the 2- or 3-position or to the α-carbons of the side-chain on the 2- or 4-positions are different kinds of reactions. Studies with ^{18}O labeled acetic anhydride show that rearrangement of 2-picoline-1-oxide is intramolecular and that equilibration of the two oxygens from the *N*-acetyloxy group takes **place.**[382, 383] Although this suggests a "radical pair" intermediate and many investigators earlier favored a radical mechanism (XII-438), later work has shown that 2- and 4-picoline-1-oxides react through anhydro bases (e.g., XII-437) and has suggested that 2-picoline-I-oxide reacts by an intramolecular path *via* an ion pair intermediate (XII-439).[360-362, 366, 383-398] (See also Ch. IV).



XII-437

XII-438

XII-439

Studies using 1-acetoxy-2-(α,α-dideuterobenzyl)pyridinium perchlorate, sodium acetate, and acetic acid show that proton transfer to form the anhydro base is irreversible.[389] Relatively large isotope effects (k_H/k_D) for reactions of *N*-oxides of 2-benzylpyridine, 2-picoline, and 4-picoline also show that proton removal to form the anhydro base is the rate-determining step.[396]

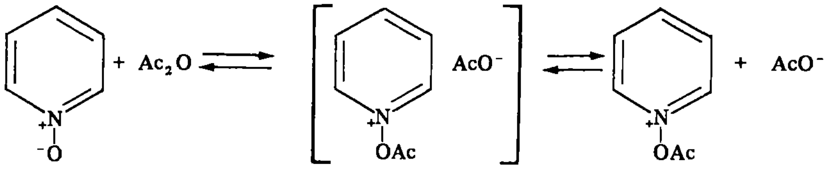
in the intramolecular rearrangement of 2-picoline-1-oxides it appears that after N—O cleavage, the rearrangement process is completed so quickly that the oxygen atoms of the acetoxy are not completely scrambled. The extent of scrambling appears to be related to the structure and conformational preference of the anhydro base.[399]

It has been suggested that in 2-picoline-1-oxide either a (1,3)-sigmatropic shift of the nitrogen atom between the two oxygen atoms of the acetoxy group before the N → C_α migration or competitive (1,3)- and (3,3)-sigmatropic rearrangements of the anhydro base could be operative.[397]

The rearrangement of the anhydro base from 4-picoline-1-oxide may be intramolecular (through ion-pairs or radical pairs) or intermolecular depending on solvent and concentration.[387, 390, 391] Experiments with ^{18}O-acetic anhydride indicate that, in the absence of solvent or in acetic acid, 4-acetoxymethylpyridine, and 3-acetoxy-4-methylpyridine are formed by intermolecular nucleophilic attack of the acetate on the anhydro base.[392] Recently, chemically induced nuclear spin polarization during the reaction of 4-picoline-1-oxide with acetic anhydride has provided direct evidence for the intermediate formation of a radical pair and strengthens the suggestion that a dual mechanism is operative involving cleavage of the anhydro base to both radical and ion pairs.[400] MO consideration of data from the action of acetic anhydride on 2- and 4-methoxypyridine-1-oxides has led to the conclusion that this rearrangement is concerted and ionic.[369]

The observation that rearrangements to the 4-methyl group do not occur with 3-nitro-2,4- and 5-nitro-2,4-lutidine-1-oxide and 3-nitro-2,4,6-collidine-1-oxide indicates a greater stabilization of the 2- rather than the 4-methylene anhydro base by the 3-nitro group. The 3-nitro group also increases the reactivity of the methylene group relative to that of the pyridine nucleus.[379]

The reaction of pyridine-1-oxide with acetic anhydride to form 2-acetoxypyridine, which cannot proceed through an analogous anhydro base, exhibits pseudo-first-order kinetics and a secondary isotope effect (2,6-d_2-; k_H/k_D = 0.92). An ionic process is consistent with the kinetic data and with the effects of 3-substituents on product distribution. The pathway involves attack of acetate ion within the ion pair (XII-440) or attack of acetate at C-2 of the cation, but does not involve intramolecular rearrangement of the free cation.[360]



XII-440

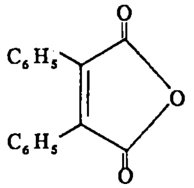
A study with ^{18}O labeled acetic anhydride suggests that the rearrangement of 3-picoline-1-oxide to give a mixture of 3- and 5-methyl-2-acetoxypyridines proceeds by an intermolecular ionic process.[394]

In addition to rearrangement, pyridine-I-oxides undergo redox reactions on treatment with acid anhydrides to give carbon dioxide, an aldehyde or ketone, the parent acid, and the pyridine as well as pyridinols and alkylated pyridines.[387, 398, 401, 402] When 2- and 4-picoline-I-oxides are treated with phenylacetic anhydride in benzene, at least 46% and 79% respectively of the N-oxides are consumed by redox reactions[401] (e.g., equations XII-441 and XII-442). Additional products from 2-picoline-1-oxide are 2-(β-phenylethyl)-

$$2C_6H_7NO + (C_6H_5CH_2CO)_2O \longrightarrow$$

$$C_6H_5COOH + C_6H_5CHO + CO_2 + 2\,C_6H_7N \qquad \text{(XII-441)}$$

$$2C_6H_7NO + 3(C_6H_5CH_2CO)_2O \longrightarrow$$



$$+\ 4C_6H_5CH_2COOH + 2\,C_6H_7N \qquad \text{(XII-442)}$$

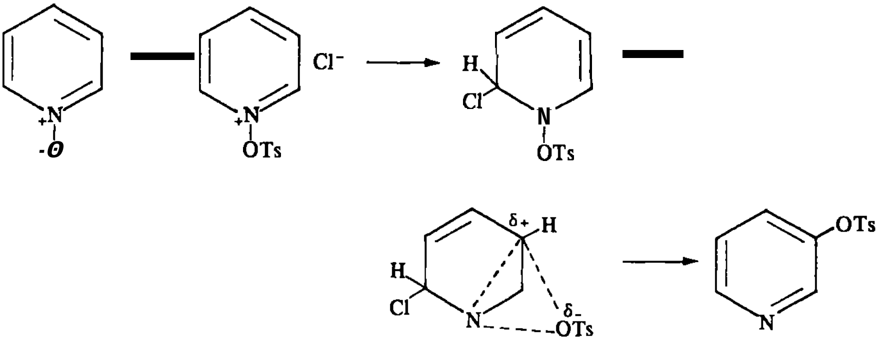
pyridine, benzylpicolines, hydroxypicolines and toluene.[401] Pyridine-1-oxide reacts with acetic anhydride at a relatively slow rate to give 2-acetoxypyridine as the principal product[403, 404] but reacts with higher normal and branched chain anhydrides and phenylacetic anhydride to give considerable amounts of redox products (Table XII-7).[405, 406] Higher carboxylic acid anhydrides can be replaced by mixtures of acetic anhydride and the corresponding carboxylic acid with similar results.[405, 406] Although radicals are present in these mixtures, ionic mechanisms are available and appear to be more reasonable to many investigators.[402, 405-407]

TABLE XII-7. Redox Reaction Products from Pyridine-1-oxide and Anhydrides

Anhydride	Solvent	Product (% yield)	% Yield CO_2	Ref.
Phenylacetic	Benzene	Benzaldehyde (69)	76	406
Diphenylacetic	Benzene	Benzophenone (68)	83	406
Isobutyric	Toluene	Acetone (39)	69	406
Butyric	Xylene	Propionaldehyde (12)	19	406
Acetic	Xylene, neat	2-Pyridone (65)	nil	403,406
p-Nitrophenylacetic	Neat	p-Nitrobenzaldehyde (20)	21	407

3-(Trimethylsilyl)pyridine-1-oxide and phosphorus oxychloride give 2- and 4-chloro-3-(trimethylsilyl)pyridine, which are difficult to separate but which have been converted to the pyridones by conversion to the benzyl ethers followed by hydrogenolysis.[377]

Acetyl or benzoyl chloride and 2-picoline-1-oxide in nonaqueous solvents give the acetate or benzoate of 2-pyridinemethanol and a small amount of 2-pyridylmethyl chloride?''' Pyridine-1-oxide and tosyl chloride in benzene give 2,3-dipyridyl ether, **N-(2'-pyridyl)-2-pyridone**, **N-(2'-pyridyl)-5-chloro-2-pyridone**, **N-(2'-pyridyl)-3-chloro-2-pyridone**, and **3-tosyloxypyridine**.[409] Tracer studies have suggested that the 3-tosyloxypyridine is formed *via* an intimate ion pair **(XII-443)**.[410] (For alternate suggestion, see Ch. I).



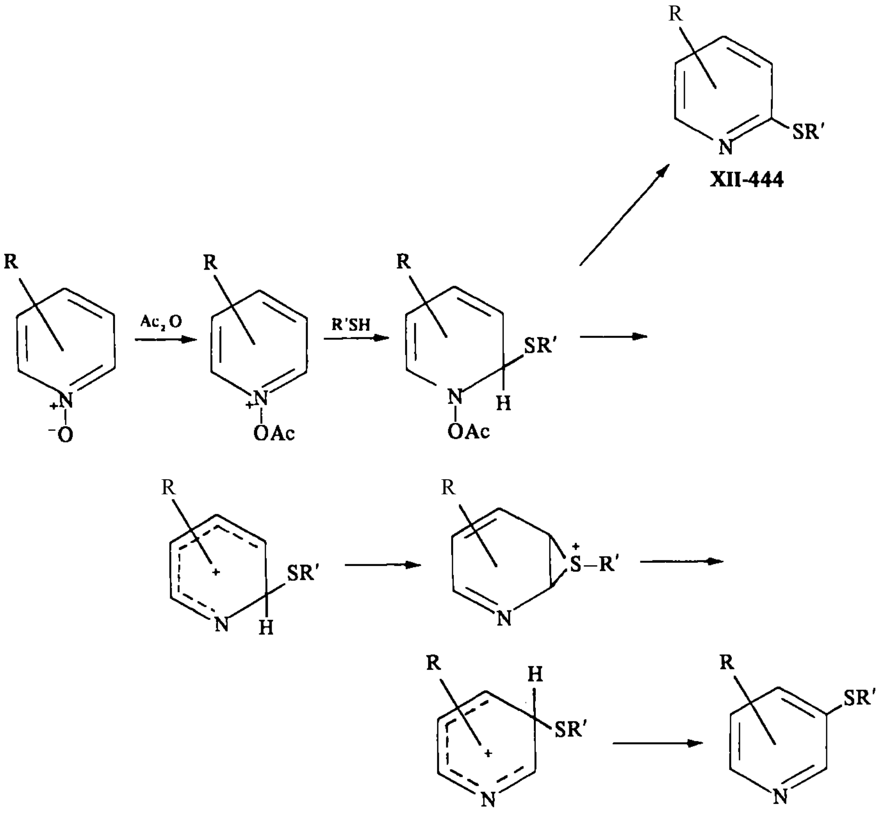
XII-443

4-Picoline-1-oxide, 2,6-lutidine-1-oxide, and **4-nitro-2,6-lutidine-1**-oxide react with ketene to form the corresponding hydroxymethylpyridine and the corresponding 3-pyridinol in relatively low yields. N-oxides of 3-picoline, 4-nitropyridine, and 4-nitro-2-picoline did not give comparable products when treated with ketene.[411]

N-Oxides undergo deoxidative substitution in the presence of acetic anhydride and mercaptans to give mainly 2- and 3-alkylthiopyridines, (XII-444 and XII-445). 4-Alkylthiopyridines were not detected but acetates are formed by rearrangement of the intermediate N-acetoxypyridinium salt. The mechanism, which is consistent with observations,[412-444] has been proposed, as shown in mechanisms XII-44 and **X11-45**.

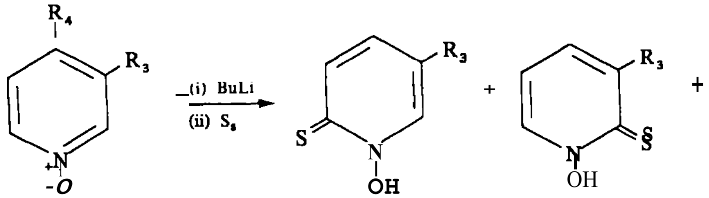
Pyridine N-oxides and butyllithium give lithiopyridine N-oxides that react with oxygen to form hydroxamic acids in poor yield. They react with sulfur to give 1-hydroxy-2-pyridinethiones (XII-446 to XII-448) in better yields; however, no attempt was made to optimize yields.[415] (See also Chs. VII and XV).

3-Hydroxy-1-methoxypyridinium methyl sulfate and the sodium salt of n-butyl mercaptan give **2-butylthio-3-hydroxypyridine** (XII-449).[416]



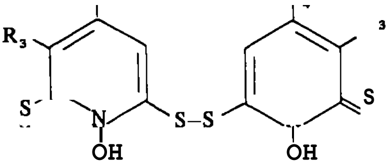
XII-444

XII-445



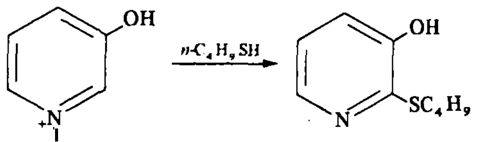
XII-446

XII-447



XII-448

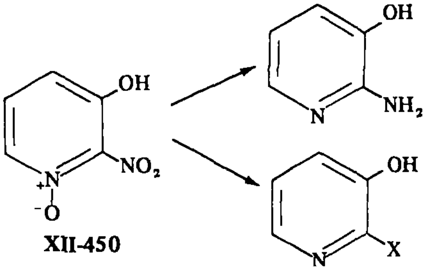
		% Yield		
R_3	R_4	**XII-446**	XII-447	XII-448
H	H	8	–	–
H	CH_3	39	–	–
CH_3	Cl	11.5	–	–
CH_3	CH_3	24	12.5	31.4



XII-449

H. *N-Oxides (by Reduction)*

Pyridine-I-oxides are comparatively resistant to reduction because of resonance stabilization by the aromatic system. Typical reagents that have been used for the formation of pyridones and pyridinols are Raney Nickel in methanol, palladium-on-charcoal, phosphorous trichloride, or phosphorus oxychloride in ethyl acetate.[380] The N-oxides of pyridoxine, pyridoxal, and pyridoxamine have been deoxygenated catalytically.[417] 4-Alkoxy-3-halopyridine-1-oxides are *N*-deoxygenated by phosphorous trichloride in chloroform.[255] 2-Amino-3-pyridinol can be prepared from 2-nitro-3-pyridinol-1-oxide (XII-450) in acetic acid by treatment with iron and mercuric chloride and then with zinc.[418] 2-Halo-3-pyridinols can be prepared from XII-450 by treatment with phosphorous trihalides in chloroform!' [8] 2,4-Diiodo- and 2,4,6-triiodo-3-



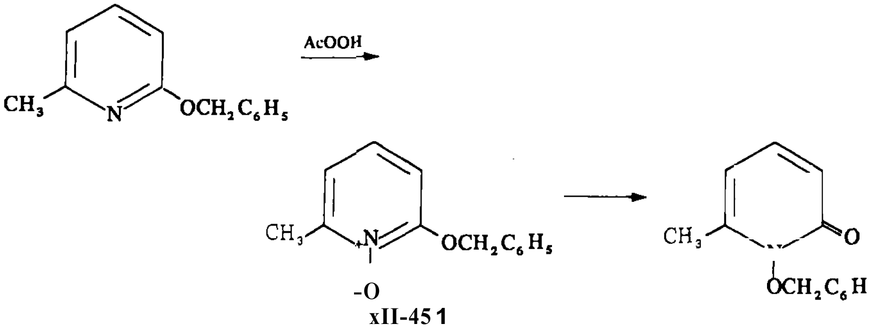
XII-450

pyridinol can be formed from their N-oxides by deoxygenation with iron and acetic acid.[298]

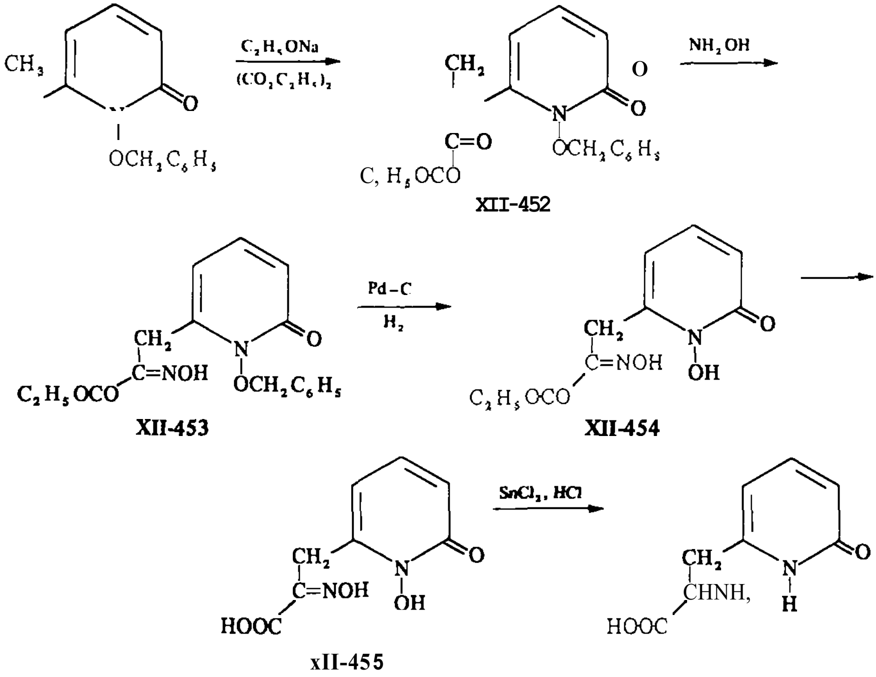
Irradiation of pyridine-1-oxides in the gas phase with ultraviolet light can lead to deoxygenation. In benzene the pyridine and some phenol are often formed. Other products include 3-pyridinols, 2-pyridones, and 2-formyl- or acylpyrroles.[419, 420] 2-Picoline-1-oxide gives small amounts of both 2- and 6-methyl-3-pyridinol, in addition to other products.[421, 422] Irradiation of 2,6-lutidine-1-oxide in benzene gives phenol, 2,6-lutidine, 2,6-dimethyl-3-pyridinol, and 2-acetyl-5-methylpyrrole.[420, 421] In ether, 2,5-dimethyl-3-formylpyrrole and 3-acetyl-2-methylpyrrole are also formed.[420, 422] Both 2,3,6- and 2,4,6-collidine-1-oxide give some of the corresponding 3-pyridinol.[420]

The 1-benzyloxy- group has been used as a protecting group in pyridone syntheses. 2-Benzyloxypyridine-1-oxides undergo facile rearrangement to

N-benzyloxy-2-pyridone even at ambient temperature.[423] For example, a compound previously described as **2-benzyloxy-6-methylpyridine-1-oxide (XII-451)**[424] was later shown to be **1-benzyloxy-6-methyl-2-pyridone.**[425] The intermediate **XII-451** can be isolated under mild **conditions.**[423]

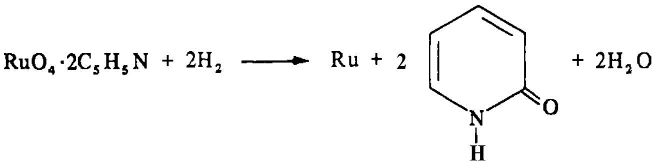


Although *m*-chloroperbenzoic acid oxidation of **2-benzyloxy-4-methylpyridine** gives the ***N*-oxide,**[426] **this** oxidizing agent and **1-benzyloxy-6-methyl-2-pyridone** give only the rearranged product.[425] **1-Benzyloxy-6-methyl-2-pyridone** condenses smoothly with ethyl oxalate to give the *β*-(6-pyridonyl)pyruvate **(XII-452)**, which can be converted to **6-(*β*-alanyl)-2-pyridone** via the oximes **(MI453** to XII-455) and the **1-hydroxy-6-(*β*-alanyl)-2-pyridone.**[425]



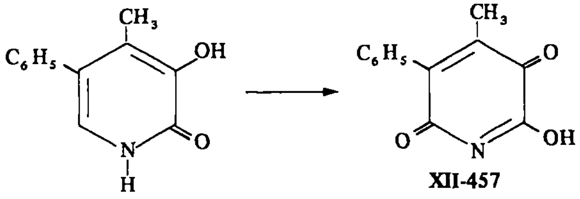
I. *Direct Hydroxylation*

2-Pyridone has been oxidized to 5-hydroxy-2-pyridone by the Elbs method with potassium **peroxidisulfate.**[342] 2-Pyridone has been formed by ^{60}**cobalt** y-radiation of an aqueous solution of pyridine.[427] The mechanism of attack and reactivity of OH radicals with pyridine have been studied.[428] Rates of reactions of pyridines with the electrophilic hydroxyl radicals are predictably somewhat slower than analogous rates of reactions of benzene derivatives, which are very fast and approach diffusion control rates. For β-substituted pyridines, good correlation **was** obtained between rate data and σ_m. Rates for pyridines containing a-, or γ-substituents that are affected by the ring nitrogen, did not correlate with σ_o and σ_p. Hydroxylations occurred at both carbon and nitrogen.[429] 2-Pyridone has been isolated as a minor product from the reaction of nitrobenzenes with pyridine at 600°.[430] Ruthenium tetroxide and pyridine in carbon tetrachloride give a 1:2 complex that yields ruthenium and 2-pyridone when heated in a stream of hydrogen (equation **XII-456).**[431]



(XII-456)

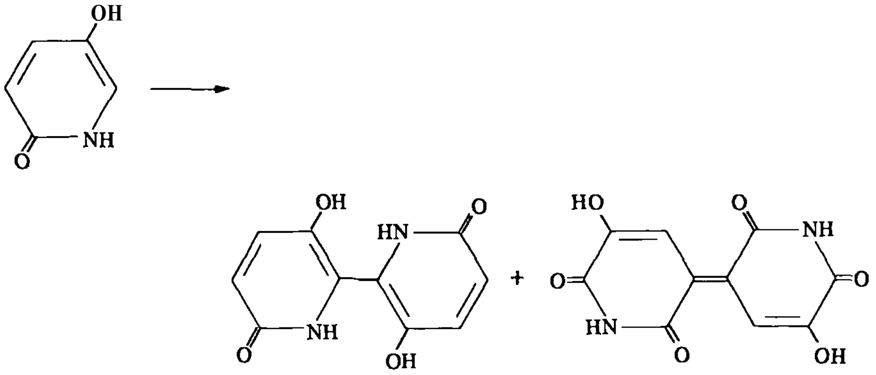
3-Hydroxy-4-methyl-5-phenyl-2-pyridone and sodium nitrite in sulfuric acid give **2-hydroxy-4methyl-5-phenyl-1-**azaquinone **(XII-457).**[221]



XII-457

The three monohydroxypyridines and 4-hydroxy-2-pyridone are not oxidized by hydrogen peroxide and peroxidase. However, 5-hydroxy-2-pyridone is oxidized to XII-458 and **XII-459.**[432]

A relatively large number of metabolic products of 3-acetylpyridine, an antimetabolite of nicotinamide, have been isolated and identified. They include **3-(α-hydroxyethyl)pyridine,**[433] its **glucuronide,**[434] and its **N-oxide,**[435] **3-(α-hydroxyethyl)-6-pyridone,**[435] **5-acetyl-2-pyridone,**[436–438] 5-acetyl-1-methyl-Zpyridone,[437] 3-carboxamido-**1-methyl-4-pyridone**[435] and 3-carbox-

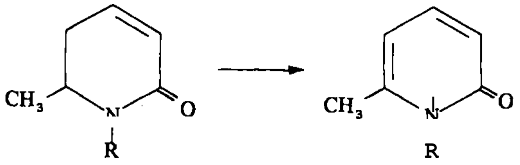


XII-458 XII-459

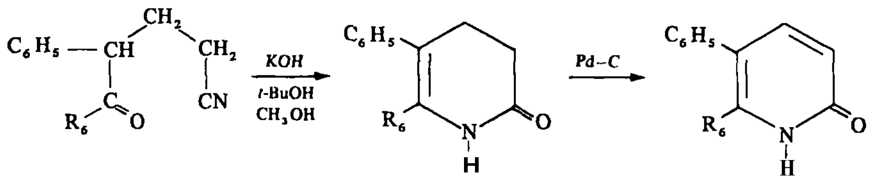
amido-1-methyl-6-pyridone.[435] 3-Hydroxy-4-pyridone is an intermediate in the metabolism of 4-pyridone by *Agrobacterium sp.*[439,440]

J. *Hydropyridinols*

Pyridinols and pyridones are sometimes prepared by dehydrogenation of hydropyridinols. For example, the available 1-phenyl- and 1-methyl-5,6-dihydro-2-pyridones (XII-460; R = CH_3, C_6H_5)[441] are readily dehydrogenated to the pyridones with palladium-on-carbon.[442] y-Acetyl- and γ-benzoyl-γ-phenylbutyronitriles cyclize to 5,6-disubstituted-3,4-dihydro-2-pyridones (XII-461),[35,443] which are also conveniently dehydrogenated to 2-pyridones with palladium-on-carbon.[35] The potassium salt of benzylcyanoacetic acid and propiophenone give



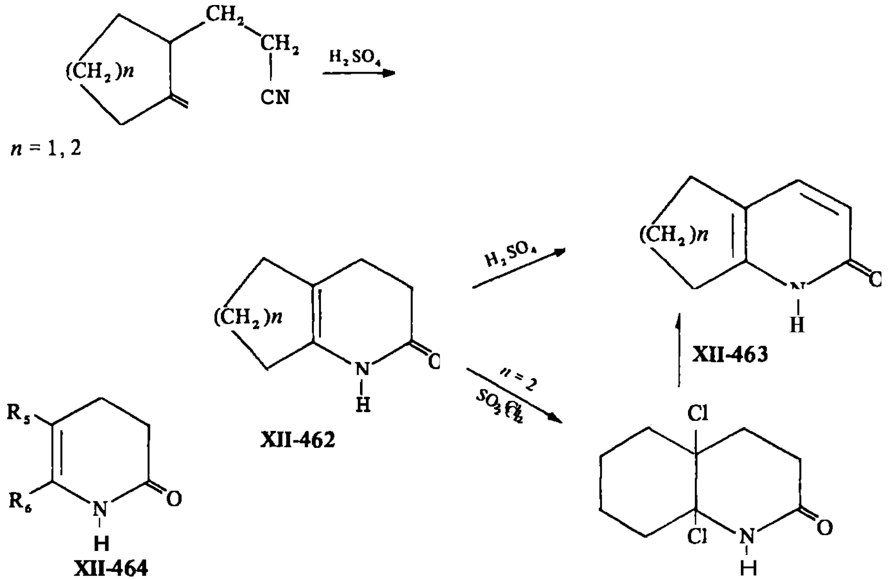
XII-460



XII-461

2-cyano-3,4-diphenyl-4-acetylbutanoic acid, which cyclizes and decarboxylates on standing to **6-methyl-4,5-diphenyl-3,4-dihydro-2-pyridone.**[444]

Cycloalkano-2-pyridones **(XII-463)** are formed from 2-(2-cyanoethyl)cycloalkanones by cyclization to **XII-462** with cold concentrated sulfuric acid, which is reduced to sulfur dioxide in a subsequent aromatization.[445]



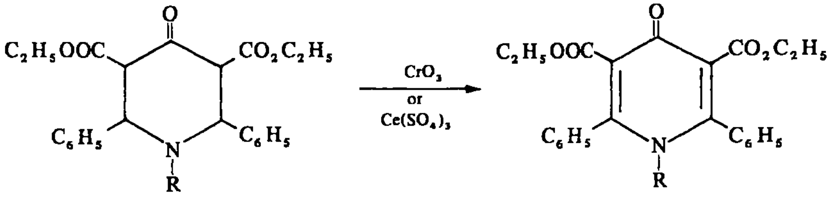
XII-462

XII-463

XII-464

Treatment of **5,6-dialkyl-3,4-dihydro-2-pyridones (XII-464;** $R_5 = R_6 = CH_3$, $R_5 = C_3H_7$, $R_6 = CH_3$) with **bromine**[446] or sulfuryl **chloride**[447] results in addition of halogen, which is followed by dehydrohalogenation to the 2-pyridone. The tetrahydroquinolone **(XII-463,** $n = 2$) was **also** prepared by this route from **XII-462.**[447]

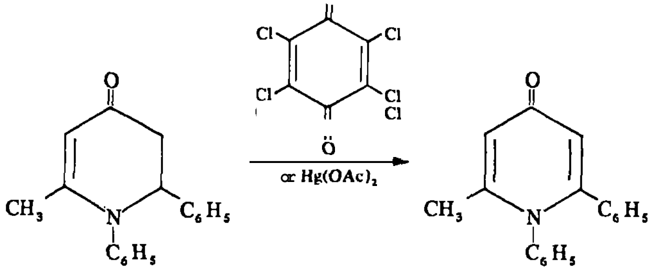
Diethyl **2,6-diphenyl-4-piperidone-3,5-dicarboxylates (XII-465)** are dehydrogenated by chromic oxide or ceric sulfate to the 4-pyridone (XII-466; R = **H**, CH_3, $C_6H_5CH_2$, $CH_2{=}CH{-}CH_2$). Some dealkylation of the *N*-substituted piperidones occurs to give the pyridone **(XII-466,** R = **H)** when chromic oxide is



XII-465

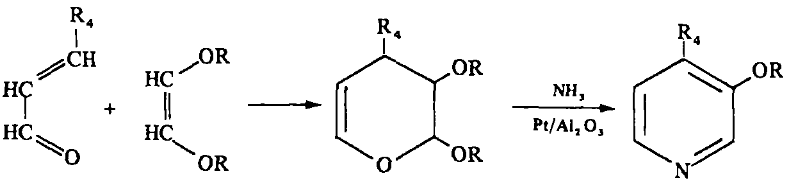
XII-466

1,2-Diphenyl-2,3-dihydro-6-methyl-4-pyridone (XII-467) and chloranil in tetrahydrofuran or mercuric acetate in water form **1,2-diphenyl-6-methyl-4-pyridone.**[449]



XII-467

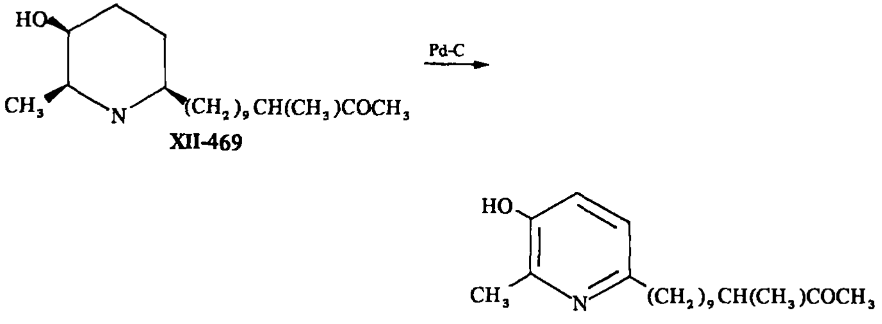
Acrolein **(XII-468, R_4 = H)** and crotonaldehyde (XII-468, R_4 = CH_3) react with **1,2-dialkoxyethylenes** to form **2,3-dialkoxy-3,4-dihydro-1,2-pyrans**, which have been converted to 3-alkoxypyridines with ammonia in the presence of Pt/Al_2O_3 at 180 to 300°.[450]



XI-468

R_4 = H; R = C_2H_5 ,C_3H_7
R_4 = CH_3 ; R = C_2H_5 .

Cassine (XII-469), a crystalline alkaloid from the legume *Cassia excelsa* Shrad., has been dehydrogenated to **2-methyl-6-(10-acetylundecyl)-3-pyridinol** with palladium-on-carbon at 220°.[451]



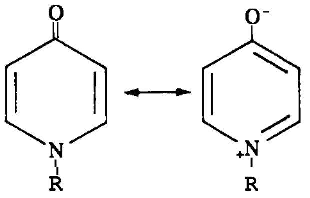
XII-469

11. Properties and Structure

1. Physical Methods

No attempt will be made here to review and correlate the large number of ultraviolet, infrared, nuclear magnetic resonance, and mass spectra that have been recorded, interpreted, and used in structure determination of pyridinols and pyridones. Articles that contain significant spectral data and/or discussions are noted in the Tables. The role of spectroscopic techniques, ionization constants, and dipole moments in the studies of structure and tautomerism of heterocyclic compounds has been reviewed recently by Albert.[452] Although ionization constants have been used to estimate pyridinol-pyridone equilibrium constants with some success,[241, 453-457] caution must be exercised about drawing conclusions from this type of data.[458]

The infrared literature was reviewed by Katritzky and Ambler in 1963.[459] Interpretation of infrared bands of pyridinols and pyridones has, however, been the subject of several investigations during recent years and merits a brief discussion. The infrared spectrum of 4-pyridone (XII-470a, R = H) in the solid state contains three significant bands in the double bond stretching region. A band near 1590 cm^{-1} (I = 0.25) that disappears on both *N*-deuteration and *N*-methylation is assigned to NH in-plane bending.[460] A high frequency band at 1635 cm^{-1} at one time was assigned to carbonyl stretching. The low frequency band at 1534 cm^{-1} was assigned to C=C bond stretching. Subsequently, because of an inability to correlate these bands with those of analogous oxygen heterocycles it was suggested that these assignments be reversed.[461] In solution, the low frequency band (solid, 1550 cm^{-1}) in *N*-methyl-4-pyridone (**XII-470**, R = CH_3) was more sensitive than the high frequency band to changes in solvent ($CHCl_3$, 1581 cm^{-1}; C_6H_6, 1598 cm^{-1}), a characteristic of carbonyl group absorptions, which also supported a reversal of the assignment.[461] The low carbonyl stretching frequency was presumably due to the polar nature of that bond attributed to contributions to XII-470a from XII-470b.



XII-470 a **XII-470 b**

A comparison of the infrared spectra of 4-pyridone and 1-methyl-4-pyridone in the solid states shows that the bands at 1635 cm^{-1} are not much different but that the 1534 cm^{-1} band of 4-pyridone is shifted to near 1550 cm^{-1} and sharpens in 1-methyl-4-pyridone, consistent with the expected shift from a hydrogen bonded to a nonhydrogen bonded carbonyl.[461] However, a comparison of the spectra of 3,5-dihalo-, 3,5-dihalo-1-methyl-, 2,3,5,6-d_4, 1-d-, and I-methyl-4-pyridones has led to the conclusion that both C=O and C=C stretchings are extensively mixed to give composite vibrations at both frequencies.[460,462] These difficulties have not negated the earlier structure assignments of 4-pyridones that have been based on infrared interpretations.

In 1-methyl-2-pyridone the higher frequency bands have been assigned to a carbonyl stretching vibration.[461] The inductive effect of the nitrogen alpha to the carbonyl operates in a direction opposite to that of the resonance effect and this less polar carbonyl gives a higher frequency band than that observed for 4-pyridones.[461] However, 2-methoxypyridinium hexachloroantimonate, which does not have a carbonyl group, shows a strong ring mode absorption at 1638 cm^{-1} [463,464] A comparison of the spectra of 2-pyridone and 2-pyridone-^{18}O also shows extensive mixing of vibrations.[463,465]

The assignments of the 1477–1443 cm^{-1} bands of 2-pyridone to skeletal stretching[466] has been questioned[463,465,467] since these bands are sensitive to phase, solvent, and isotopic substitution.[465]

2. Association of 2- and 4-Pyridones

2-Pyridone and its thio and seleno analogs all form strong dimers in chloroform[466] and in benzene.[468] Hydrogen bonding in sulfur and selenium analogs is lower than in 2-pyridone but nevertheless all three are classified as powerful hydrogen bonders.[469] 2-Pyridone forms an exceptionally strong hydrogen bonded dimer in nonpolar solvents.[469-471] This is supported by NMR studies where an unusually low field resonance for the enolizable proton is observed, indicative of strong hydrogen bonding.[465,472] NMR studies indicate that 4-pyridone is more strongly associated in solution than is 2-pyridone. In dilute solution in chloroform, it has a molecular weight that corresponds approximately to a trimer.[462]

In solid 2-pyridone, hydrogen bonding is of the NH···O type.[473] 6-Chloro-2-pyridinol exists as the pyridinol tautomer in the solid state and forms hydrogen bonded dimers of the OH–N type.[474] Molecular weight determinations in chloroform show that concentrated solutions of 4-methyl-, 4-phenyl-, 3,4-trimethylene-, and 3,4-tetramethylene-6-chloro-2-pyridone contain mainly hydrogen bonded dimers.[457]

Rate and equilibrium constants have been measured for the hydrogen bond dimerization of 2-pyridone in chloroform-dimethyl sulfoxide and in carbon tetrachloride-dimethyl sulfoxide[475] and of 2-pyridone and 2-thiopyridine in chloroform,[471] by ultrasonic attenuation, ultraviolet, infrared, and NMR methods. In the first solvent system, association appeared to be diffusion controlled. In the second solvent it was suggested that solvation-desolvation of 2-pyridone by dimethyl sulfoxide is rate limiting.[475]

3. The Pyridone Structure

2- And 4-pyridones are aromatic and do not have the properties of simple unsaturated lactams. It has been estimated that 2-pyridones have about 35% of the aromaticity of benzene as defined by their ability to sustain an induced ring current[476] and as calculated by the SCF treatment.[477]

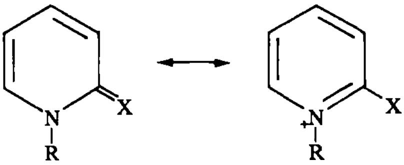
The infrared spectra of 2- and 4-pyridones are consistent with the pyridone structure.[478] A comparison of the infrared spectra of 2-pyridone and 2-pyridone-^{18}O indicates that the lactam description is better than the dipolar one.[463] A comparison of infrared and Raman spectra of 4-pyridone (**XII-470**, R = H) with those of 4-pyridinium ions and a rationalization of the dipole moment has led to the estimate that the upper limit of the contribution to 4-pyridone by the dipolar form (**XII-470b**, R = H) is 10 to 15%.[460]

The chemical shifts of the y-protons of several 2-substituted pyridines including 2-pyridone, the 2-pyridone anion, and 2-phenoxy- and 2-methoxypyridine have been correlated with the electron donating and withdrawing properties of the substituents.[479]

Charge distributions and dipole moments have been calculated by a modified Hückel method for *N*-methyl-2-pyridone (μ = '4.0 D) and *N*-methyl-4-pyridone (μ = 6.7, 6.4 D).[480, 481] Dipole moments have been measured in benzene for *N*-methyl-2-pyridone (μ = 4.15 D;[453] 4.0 D;[482] 4.04 D[469]) and for *N*-methyl-4-pyridone (μ = 6.9 D[453]).

4. Tautomerism

In water, the ultraviolet spectra of 2-pyridone, 2-thiopyridone, and 2-selenopyridone resemble the spectra of their respective *N*-methyl derivatives, and all exist as the amide tautomer (>99%).[454, 468, 483, 484] 2-Pyridinethiones (XII-471; X = S, R = CH_3, μ = 5.26 D) and 2-pyridineselenones (XII-471; X = Se, R = CH_3, μ = 5.73 D) in benzene have progressively higher dipole moments than 2-pyridones[469] because of increasing contributions of structure **XII-471a** (X = O, S, Se) to **XII-471**.[485] Acid strengths are in the expected order: **XII-471**: R = H, X = O, pK_a 11.62, S, 9.97; Se, 9.36.[468]

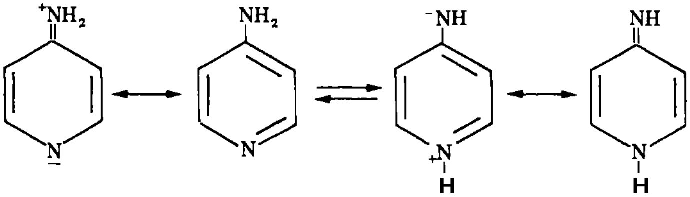


XII-471 a XII-471 b

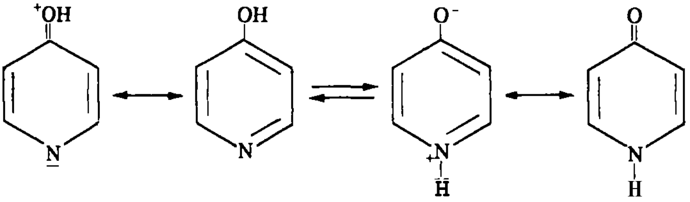
The **NMR** spectrum of 4-pyridone in aqueous solution is consistent with a pyridone **structure.**[486] In deuterochloroform, the NMR spectra of 2- and **4-pyridone-^{15}N** show a very rapid intermolecular exchange of the enolizable **proton.**[462,465] The observed ^{15}N–H coupling of 90 Hz at low temperature indicates that the relative amount of the 2-pyridinol tautomer is less than 2%.[465] A study **of** ''nitrogen-hydrogen coupling in 4-pyridone was thwarted by its poor solubility at lower **temperatures.**[462]

It **has** been demonstrated that appreciable pyridinol tautomer is present in the vapor of **2-pyridone**[487] and **6-phenyl-2-pyridone.**[488]

Unlike the corresponding pyridones, 2- and 4-aminopyridines prefer the amino forms **(XII-472).**



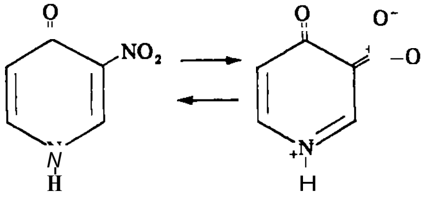
XII-472 a XII-472 b XII-473 a XII-473 b



XII-474 a XII-474 b XII-475 a XII-475 b

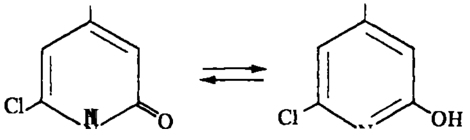
In **4-aminopyridine,** stabilization of **XII-472** and **XII-473** by charge separated forms **(XII-472a** and **XII-473a)** are similar and moderate and the aromatic nature of **XII-472b** is responsible for the predominance of **XII-472.** However, in 2- and 4-pyridone, stabilization of **XII-474** by the charge separated form **XII-474a** where oxygen bears a positive charge is much less than stabilization of XII-475 by XII-475a where oxygen is negatively charged, and **XII-475** predominate~ .[489]~ ~ '

Although 2-pyridone, 4-pyridone, and many of their derivatives appears to exist predominantly in the pyridone form under all conditions, electron withdrawing groups alpha to the nitrogen shift the equilibrium in favor of the pyridinol tautomer.[7, 241, 242, 246, 456, 457, 490-497] For example, tetrafluoro-4-pyridinol (pK_a = 3.21; 20°, H_2O), which is a stronger acid than pentafluorophenol (pK_a = 5.53, 25") exists mainly (>95%) in the pyridinol form.[248] Electron withdrawing substituents increase the acidity of NH of the pyridone tautomer and decrease the basicity of the pyridinol nitrogen. Both effects lead to a relative stabilization of the pyridinol form.[241] Groups in the 3-position usually produce smaller effects. For example, 3-nitro-4-pyridone, in which the nitro group has an inductive base-weakening effect on both forms (—4.0 pK units), exists as the pyridone by a factor of $10^{3.4}:1$, presumably by stabilization of the pyridone by canonical form XII-476.[497] Comparable contributing structures to the pyridinol, requiring the positive charge to be on oxygen, are not important.[497]

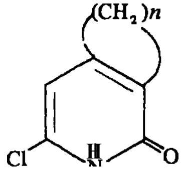


XII-476

Tautomeric equilibrium constants K_t = [pyridone]/[pyridinol] have been measured for a number of 2-pyridones (Table XII-8). The constant K_t has been estimated by a Hiickel approximation for 2- and 4-pyridone.[498] The K_t values obtained from ultraviolet spectra and those obtained from acidity constants are in poor agreement for 6-chloro-4-substituted-2-pyridones (XII-477; R = CH_3, C_6H_5) and 6-chloro-3,4-polymethylene-2-pyridones (XII-478; n = 3,4) in water.[457] For example, in XII-477 where R = CH_3, values of 6% and 44% respectively of pyridinol tautomer (XII-477b) are obtained from ultraviolet data and from acidity constants. However, values obtained from ultraviolet studies appear to be more reliable.[457, 458]

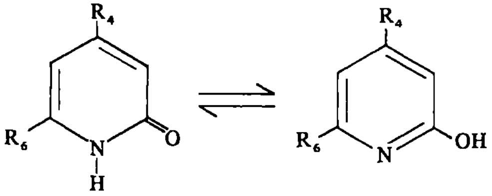


XII-477 a XII-477 b



xII-478

TABLE XI-8. Tautomeric Equilibrium Constants: K_t = [pyridone]/[pyridinol]

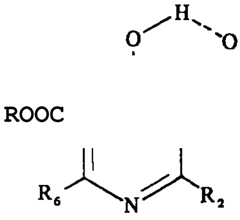


R_4	R_6	Solvent	K_t	Method	Ref.
H	Cl	98%H_2O, 2% EtOH	1.66	uv	494
		50% H_2O, 50% EtOH	1.16		
		EtOH	0.14		
		50%EtOH, 50% Dioxane	0.09		
		Dioxane	0.07		
H	NH_2	Ethanol	99	uv	494
		50% EtOH, 50% Dioxane	46.6		
		Dioxane	0.64		
CH_3	Cl	H_2O (20")	15	uv	457
CH_3	Cl	H_2O (20")	1.3	p*K*	
CH_3	Cl	Methanol	0.48	uv	
		Chloroform	0.79	uv	
		Dimethyl sulfoxide	0.04	uv	
		Cyclohexane	0.05	uv	

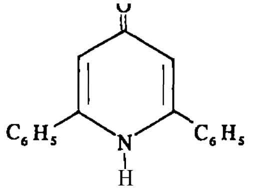
The equilibrium shifts toward the pyridinol as the medium becomes less polar[241, 458, 489, 490, 494-496] (Table XI-8) and as the solvent becomes less able to solvate the carbonyl group.[457] Protic solvents favor the pyridone tautomer (Table XII-8) by hydrogen bonding to the carbonyl.[457] For example, in both dimethyl sulfoxide (ε = 45.0) and cyclohexane (ε = 2.0) the pyridinol form predominates (85-96%) for XII-477 and XII-478. The pyridinol content is less (28-69%) in protic solvents and in chloroform. In the solid state, these compounds exist in the pyridone form.[457] The temperature dependence of the tautomeric equilibrium for 6-amino-, 6-bromo-, and 6-chloro-2-pyridone has been studied in several solvents.[496] Heteroaromatic tautomer equilibria changes with solvent for 6-chloro-2-pyridone, 2,3,5-trichloro-4-pyridone, 2-chloro-4-pyridone, 3-pyridinol and 2,6-di-(methoxycarbonyl)-4-pyridone have been correlated by equation XII-478a,[490] where K_{T1} is the equilibrium constant in one solvent and P_1 is the polarity of the solvent (ethanol-water, methanol-water, ethylene glycol, acetonitrile, chloroform, and isooctane) and Kosower *Z* values are used as a measure of solvent polarity.[499] An abnormality has been observed for 2,6-di-(methoxycarbonyl)-4-pyridone, which exists as the pyridone in chloroform and carbon tetrachloride but not in isooctane.[490]

$$\ln \frac{K_{T1}}{K_{T2}} = a(P_1 - P_2) \qquad \text{XII-478a}$$

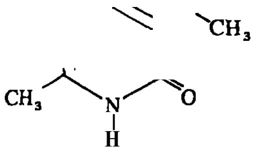
The ultraviolet and infrared spectra of the dimethyl and diethyl esters of 3,5-dicarboxy-4-pyridones (XII-479; $R_2 = R_6$ = phenyl, α-pyridinyl, aquinolinyl) indicate they exist as conjugate pyridinol chelates in chloroform, carbon tetrachloride and ethanol.[448, 500]



XII-479

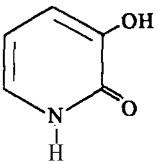


XII-480

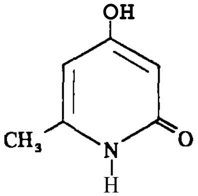


xII-481

The dimethyl and diethyl esters of 2,6-di-α-pyridinyl- and 2,6-di-α-quinolinyl-4-hydroxy-3,5-pyridinedicarboxylic acids (XII-479) also exist in the solid state as conjugate chelates.[500] 2,6-Diphenyl-4-pyridone, which does not possess the *ortho*-hydroxy ester structural feature of XII-479, exists as the pyridone (XII-480) in the solid state and in solution.[448] 3-Acetyl-4,6-dimethyl-2-pyridone (W-481) exists as the pyridone tautomer in methanol. Stabilization of the pyridinol form by hydrogen bonding does not occur.[60] The infrared (KBr) and ultraviolet spectra (ethanol) of 3-hydroxy-2-pyridone are consistent with the pyridone structure (XII-482).[501]



XII-482

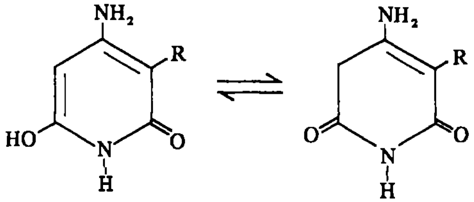


XII-483

The 4-hydroxy-6-methyl-2-pyridone structure (XII-483) is consistent with its NMR, ir, and uv spectra[502] and is similar to that of 4-hydroxy-2-pyridone.[503]

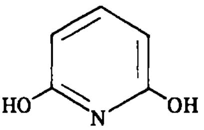
Ultraviolet spectra in water and ethanol and infrared spectra (KBr) show that glutazine and several of its derivatives (XII-484; R = H, CN, $CONH_2$, CO_2Et) exist as an equilibrium mixture of the 4-amino-6-hydroxy-2-pyridone (XII-484a) and the 4-amino-2,6-pyridinedione (XII-484b).[504]

Glutaconimide, which exists predominately in lactam forms,[467] is mainly 6-hydroxy-2-pyridone (XII-485a:b:c = 25:60:15) in water, as shown by a comparison of its ultraviolet spectra with those of model compounds.[455] The

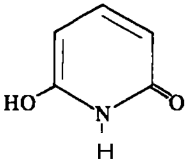


XII-484 a **XII-484 b**

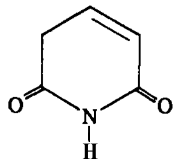
relatively large amounts of the pyridinediol **(XII-485a)** at equilibrium is considered to be related to the reduced basicity of the glutaconimide nitrogen compared to that of the nitrogen of 2-pyridones, which have only one



XII-485 a

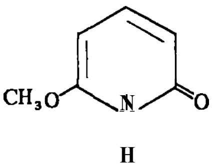


XII-485 b

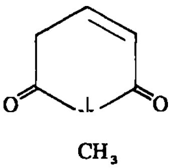


XII-485 c

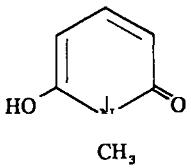
α-oxygen.[455] The *O*-methyl derivative appears to exist mainly as structure **XII-486** and the *N*-methyl derivative as approximately equal amounts of **XII-487a** and **XII-487b** in aqueous solution; only the diketo tautomer **(XII-487a)** is observed in chloroform solution, however.[505]



XII-486

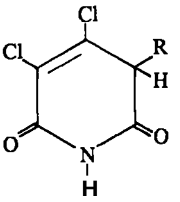


XII-487a



XII-487b

The infrared spectra of **XI-488** (R = CH_3, C_2H_5, n-C_4H_9, n-C_5H_{11}) in the solid state exclude tautomers containing **OH** groups; in carbon tetrachloride solution, however, absorptions due to **OH** containing tautomers are observed.[7]

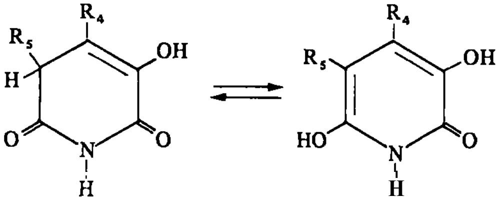


XII-488

TABLE XII-9. Tautomerism Constants (K_T = [CH form]/[OH form]) for 3-Hydroxy-2, 6-pyridinediones (XII-489)

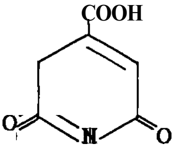
R_4	R_5	K_T(DMSO-d_6)	K_T(CF_3COOH)
H	CH_3	0.4	0
CH_3	CH_3	2.0	0
CH_3	H	4.2	0.3

3-Hydroxy-2,6-pyridinediones (XII-489) have been obtained in both the CH and OH forms. Tautomeric constants have been calculated from NMR data. In DMSO, the CH form predominates when there is a methyl group at the Cposition. In trifluoroacetic acid, the OH form either exists exclusively or predominates[506] (Table XI-9).

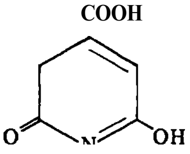


XII-489

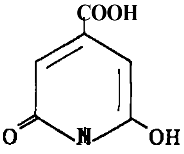
Infrared studies have ruled out XII-490a and XII-490b as structures for crystalline citrazinic acid. Esters of citrazinic acid exist in form XII-490c in



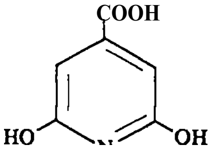
XII-490 a



XII-490 b



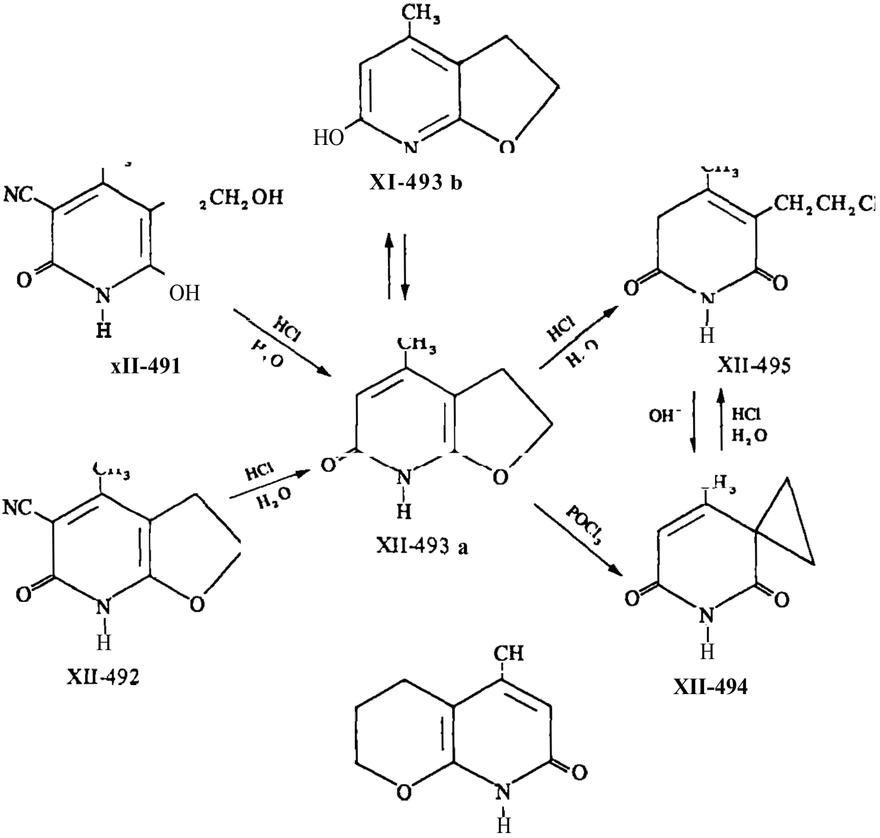
XII-490 c



XII-490 d

methanol and in the imide form (XII-490a) in chloroform, dioxane, and acetonitrile.[507]

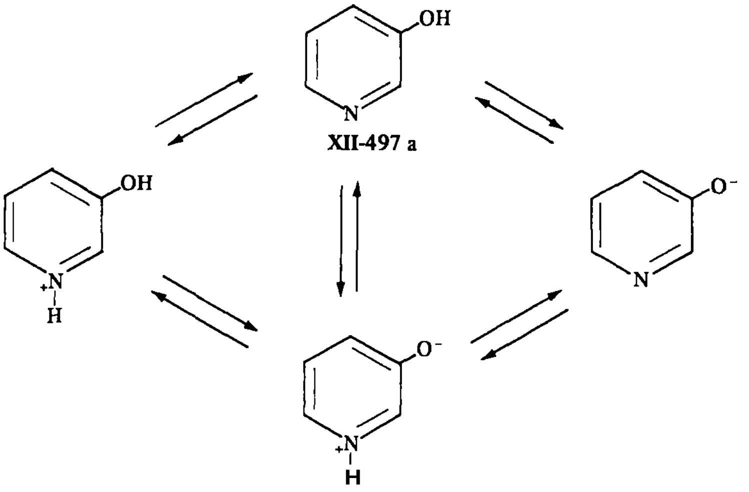
The reaction of either the cyanoglutaconimide XII-491 or the cyanofuropyridone XII-492 with hydrochloric acid gives two isomeric products that were first considered to be the furopyridone (XII-493a) and the furopyridinol (XII-493b).[508] Subsequently it has been demonstrated that only one tautomer can be isolated[458, 509] and that the compound earlier identified as XII-493a is probably 4-methyl-3-spirocyclopropane-2,6-pyridinedione (XII-494),[510] which is formed from XII-495 during alkaline workup of the reaction mixture.[510]



In ethanol. **2,3-dihydro-6-hydroxy-4-methylfuro**[2,3-*b*] pyridine exists mainly as the pyridinol **(XII-493b)**, while the corresponding 2,3-dihydropyranopyridine XII-496 exists mainly as the pyridone. Under the same conditions 6-methoxy-2-pyridone exists as equal amounts of the two tautomers. The preference, on energetic grounds, by a five membered ring for exo double bonds (a possible Kékulé localization for XII-493b) and the preference by the dihydropyrano ring for endo double bonds can account for these observations.[458]

5. 3-Pyridinols

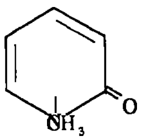
Spectroscopic data and p*K* measurements have indicated that 3-pyridinol in aqueous solution is present in a tautomeric equilibrium between approximately equal amounts of XII-497a and XII-497b[511] among other ionic forms.[511, 512] The infrared spectrum of 3-pyridinol in the solid state[513] and its NMR spectrum in nonpolar solvents[514] show the presence of intermolecular hydrogen bonding that is compatible with a dipolar structure. A comparison of the NMR spectra of 2-methyl-3-pyridinol and 1,2-dimethyl-3-hydroxypyridinium iodide has provided additional evidence for the existence of the zwitterion form in aqueous solution.[515] Calculated singlet-singlet transition energies of the zwitterionic form of 3-pyridinol by the Pariser-Parr-Pople method are in good agreement with experimental data, but the discrepancies are higher than those realized for the enolic and anionic forms.[516]



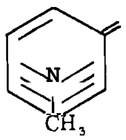
XII-497 a

XII-497 b

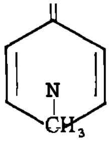
Anhydro 3-hydroxy-N-methylpyridinium hydroxide, "*N*-methyl-3-pyridone," (XII-499) has been prepared and characterized and has been classified as a mesionic compound.[517] The similarity of spectral properties of the three *N*-methylpyridones (XII-498, XII-499, *W-500)* and the observations that dipolar structures make *only* a small contribution to M1498 and XII-500 has suggested that there is also only a small contribution by the polar structure XII-499a to "1-methyl-3-pyridone." A delocalization of the negative charge into the ring that is accommodated through canonical structures XI1499b-d can account for the carbonyl properties of XII-499. It has been suggested that formulas such as XII-499e be employed for mesionics;[517] however, undesirable connotations such as an implication of *d* orbital participation could result from this notation. A PPP ASMO calculation also predicts that 2-, 3-, and 4-pyridone should all have similar properties.' [17, 518]



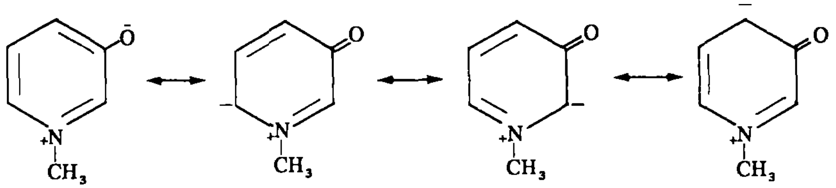
XII-498



XII-499 e

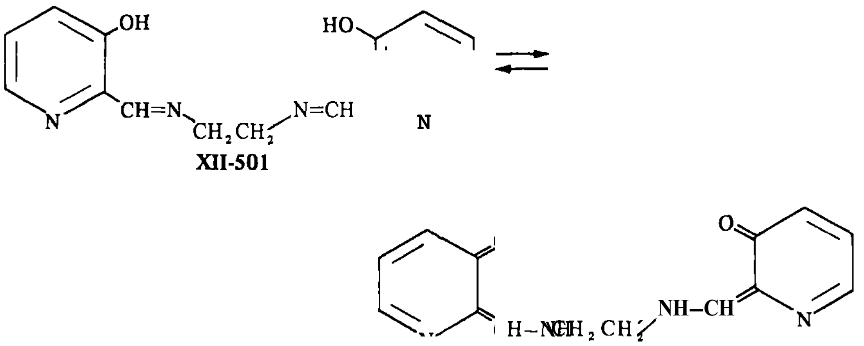


XII-500



XII-499 a **XII-499 b** **XII-499 c** **XII-499 d**

The ultraviolet spectra of bis(3-hydroxy-2-pyridylmethylene)ethylenediamine (XII-501) indicate that in ethanol the keto form predominates and that protonation occurs on the annular nitrogen atoms.[519]



XII-501

Chemical shifts have been used to evaluate pi electron densities for several 2-, 4-, and 6-alkyl- and 2-, and 6-aminomethyl-3-pyridinols. Reasonable agreement is observed in a comparison of these charge distributions and those obtained by MO LCAO calculations.[520]

Earlier data have indicated that 3-pyridinol[453, 521] is a weaker base than pyridine.[522] A reexamination of these basicities suggests that the reverse is true and that the 3-hydroxyl group is electron releasing here and its introduction increases the basicity of the nitrogen of pyridine and alkylpyridines.[523] p*K* values for the individual acid dissociation steps for pyridoxamine, pyridoxal, 3-hydroxypyridine-4-carboxaldehyde, and 3-hydroxypyridine-2-carboxaldehyde have been obtained by NMR measurements in D_2O solution.[524]

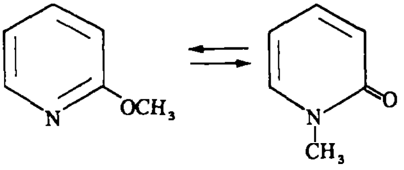
6. Fluorescence

Fluorescence studies have been reported for several 3-pyridinols including pyridinols of the vitamin B$_6$ series, and 2- and 4-pyridones.[512, 525-527] 4-Pyridone and 4-methoxypyridine are not fluorescent at any p*H* values.[525] The cations, anions, and dipolar ions of 3-pyridinol derivatives are fluorescent, but neutral forms are not.[525, 526] All forms of 2-pyridone and its derivatives are

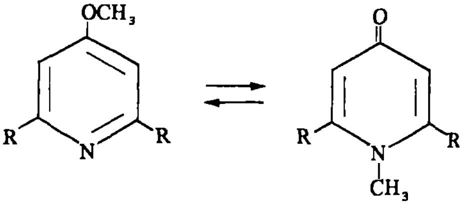
Excited state ionization (ionization of acids and bases in the excited state at p*H* ranges where unexcited molecules do not ionize)[528] has been studied for cations of 3-pyridinols,[525, 528] pyridoxine,[525, 527, 528] pyridoxamine,[525, 527, 528] pyridoxal,[525, 527, 528] 2-pyridone,[525] and *N*-methyl-2-pyridone and *N*-methyl-3-pyridinol.[525] Excited state pK_a values for the 3-pyridinol anion and cation have been studied using photopotentiometry, the measurement of the potential developed between one illuminated electrode and one dark electrode in solution.[529]

7. Relative Stabilities of *N*-Alkylpyridones and Alkoxypyridines

In equilibration studies in the liquid state by using the corresponding *N*-methyl-2-(or)4-methoxypyridinium tetrafluoroborate as the catalyst, it has been determined that the N-methyl isomer is more stable than the 0-methyl isomer for both pairs: 2-methoxypyridine $\rightleftharpoons$ *N*-methyl-2-pyridone ($\Delta G^\circ > -9.3$ kcal/mole) (XII-502 $\rightleftharpoons$ W-503) and 4-methoxypyridine $\rightleftharpoons$ *N*-methyl-4-pyridone (MI-504 $\rightleftharpoons$ XII-505) ($\Delta G^\circ > -7.4$ kcal/mole) at 130°.[530, 531] On the other hand, the sulfur analog of XII-502 is more stable than the *N*-methylpyridinethione.[532]

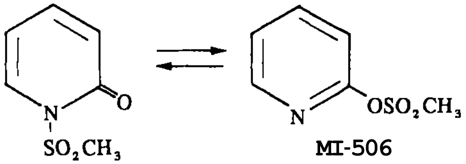


XII-502 XI-503



XII-504 XI-505

The relative stabilities of these two sulfur analogs should be compared with the tautomeric equilibrium of 2-thiopyridine where the pyridinethione tautomer predominates in aqueous solution. These observations demonstrate that tautomeric equilibria in protic systems cannot be used reliably to predict the relative stabilities of the methylated isomers.[532] It has been shown recently that *O*-mesyloxypyridines **(MI-506)**are more stable than *N*-mesyl-2-pyridones.[533]



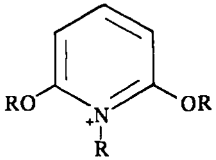
MI-506

4-Methoxy-2,6-diphenylpyridine **(XII-504,** R = C_6H_5) is more stable than *N*-methyl-2,6-diphenyl-4-pyridone due to 1,2,6-steric interactions.[530,531]

8. Protonation of 2- and 4-Pyridones

Although it had been suggested on the basis of Raman and infrared evidence that 2- and 4-pyridone are protonated on nitrogen,[534] subsequent information has established that protonation occurs on oxygen.[464,472,486,535-542]

Protonated 6-methoxy-2-pyridone, 6-methoxy-1-methyl-2-pyridone, 6-hydroxy-1-methyl-2-pyridone, and 2,6-dimethoxypyridine all exist as structure **XII-507.**[455]



MI-507

The crystal structure of 2-hydroxypyridinium chloride monohydrate and 2,6-dihydroxypyridinium chloride have been determined. The cations are essentially planar and are in the mono- and dipyridinol forms respectively.[543]

9. The Pyridone Anion

Although at one time there was some disagreement as to the location of the charge on the 2-pyridone anion in its ground state,[544,545] later work has demonstrated that the charge lies mainly on the oxygen atom.[472,546]

III. Reactions

1. Involving *O* and *N*

A. *O*- and *N*-Alkylation and Arylation

a. **GENERAL** Alkylations of 2-pyridones have been studied extensively and usually are accomplished by reactions between the pyridone anion and an alkyl halide or dialkyl sulfate or between the pyridone and a diazoalkane. Tosylates, alkenes, and epoxides have been used as alkylating agents, but less extensively. Although there are fewer reports of 3-pyridinol and 4-pyridone alkylations, interest in 3-pyridinols has increased over the past decade, but the course of their alkylations and the structures of products have been less clearly elucidated. O- and/or *N*-Alkylations usually are observed, although side-chain a-C-alkylation can be accomplished. It has been shown in alkylations of 2-pyridone salts, that the product distribution in these reactions results from kinetic control and depends on the nature of the pyridone, the cation, the alkylating agent, and the solvent.

b. **2-PYRIDONES** The course of alkylations of 2-pyridone salts is far more sensitive to changes in cation and solvent than are comparable alkylations of 2-pyrimidone salts.[547,548] The pi-electron deficiency in pyrimidones due to two ring nitrogens imposes more severe restrictions on polarizability than are observed in alkylations of pyridones. In alkylations of alkali metal and silver 2-pyridone salts with halides, important solvent effects are observed. Solvent has the greatest effect on silver salt alkylations, where alkoxypyridine formation is favored in poor ion-solvating media.[547,549] Under heterogeneous conditions many alkylations give only 2-alkoxypyridines.[549] For example, the silver salt of 2-pyridone and methyl iodide give *N*-methyl-2-pyridone as the major product in dimethylformamide but give 2-methoxypyridine (97%) when benzene is used.[547] Alkylations of alkali metal salts are less solvent sensitive but an increase in rate and more *O*-alkylation are observed in dimethylformamide[547] and dimethyl sulfoxide[550] compared with protic and nonpolar solvents. Although alkali metal salts of 2-pyridone and methyl iodide in dimethylformamide give *N*-methyl-2-pyridone as the major product (>90%), *O*-alkylation increases as the halide is varied from methyl to ethyl and predominates with isopropyl iodide due to a steric effect (Table XII-10).[547] The potassium salt of 6-acetamino-2-pyridone in ethanol-water is *N*-alkylated by isoamyl bromide.[551] The "traditional" solvents employed in 2-pyridone salt alkylations, methanol and ethanol, appear to be relatively poor for ethylations and isopropylations of 2-pyridone; considerable elimination occurs as is evidenced by 2-pyridone formation.[547]

In alkylations of silver salts in DMF, considerable amounts of 2-pyridone are also regenerated. An S_N2 alkyl-oxygen cleavage of 2-methoxypyridine may be responsible for the pyridone that is formed (see Section IV). Only elimination is observed with the silver salt of 2-pyridone and isopropyl bromide in DMF (Table XII-11).[547]

Although the product distributions listed in Tables XI-10 and XI-11 are calculated from gas chromatographic data, simple procedures have been developed for bench-scale preparations by direct alkylation to form chromatographically pure 2-isopropyloxypyridine (76%), 2-benzyloxypyridine (78%), and 2-methoxypyridine (57%). These procedures avoid the more circuitous route where a 2-halopyridine is treated with an alkoxide to form the ether.[547]

In view of the relatively large solvent effects on the alkylation site of the silver salt of 2-pyridone, generalizations concerning the site of alkylation of ring-substituted 2-pyridone salts need to be reconsidered. These generalizations sometimes have been made by comparing reactions run in different solvents and

TABLE XI-10. Alkylation of Salts of 2-Pyridone in DMF[547]

Alkylating agent	Cation	% Yield	Product Composition, %		
			N-Alkyl	*O*-Alkyl	2-Pyridone
MeI	Na	93	95	5	
EtBr	Na	94	77	23	
IsoPrBr	Na	84	29	68	3
$C_6H_5CH_2Br$	Na	95	97	3	
MeI	Ag	81	74	12	21
EtBr	Ag	80	20	38	42
IsoPrBr	Ag	No alkylation, only 2-pyridone was formed			
$C_6H_5CH_2Br$	Ag	85	54	46	

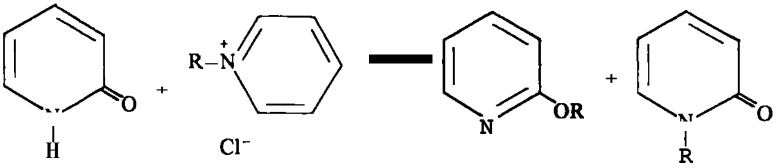
TABLE XII-11. Solvent Effects on Alkylations of Salts of 2-Pyridone[547]

Alkyl halide	Solvent	Cation	% Yield	Product Composition, %		
				N-Alkyl	*O*-Alkyl	2-Pyridone
EtBr	DMF	Na	94	77	23	
EtBr	MeOH	Na	80	66	5	29
EtBr	$(CH_3O)_2(CH_2)_2$	Na	88	87	6	7
EtBr	DMF	Ag	80	20	38	42
EtI	$(CH_3O)_2(CH_2)_2$	Ag	90	21	54	19
EtI	EtOH	Ag	91	1	80	19
EtI	C_6H_6	Ag	100		100	
$C_6H_5CH_2Br$	C_6H_6	Ag	100		100	
IsoPrI	C_6H_6	Ag	100		100	

by comparing reactions where only a part of the total reaction products were identified.[547, 552]

It has been verified by comparing alkylations of sodium salts and silver salts of 2-pyridone, 5-nitro-2-pyridone, and 5-carbethoxy-2-pyridone that electron withdrawing groups at the 5-position cause increased *N*-alkylation. This substituent effect, like the solvent effect, is more pronounced in alkylations of silver salts.[549] When electron withdrawing groups occupy both the 3- and 5-positions, *N*-alkylation is strongly favored. For example, silver salts of 3-halo-5-nitro-2-pyridones and methyl iodide in ethanol give mainly the *N*-methyl-2-pyridones and only small amounts of the ethers (3–6%).[287, 290, 291] 3-Bromo-1-methyl-5-nitro-2-pyridone has also been prepared from the sodium salt and dimethyl sulfate.[290]

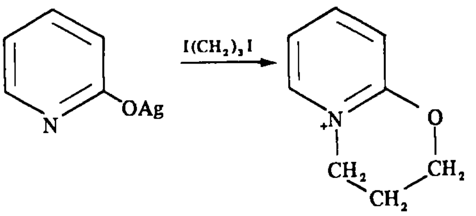
By melting a mixture of 2-pyridone and picrylpyridinium chloride, the O- and *N*-alkylated products (W-508 and W-509) are formed in 17% and 82% yield, respectively. Rearrangement of XII-508 to XII-509 occurs at its melting point.[553] The silver salt of 2-pyridone and picryl chloride in benzene gives 97% of XII-508 and 3% of XII-509.[553]



XII-508
R = Picryl

XII-509

The silver salt of 2-pyridone and trimethylene iodide in dioxane gives 2,3-dihydropyrido[2,1-*b*]oxinium iodide (XII-510).[554] Potassium salts of

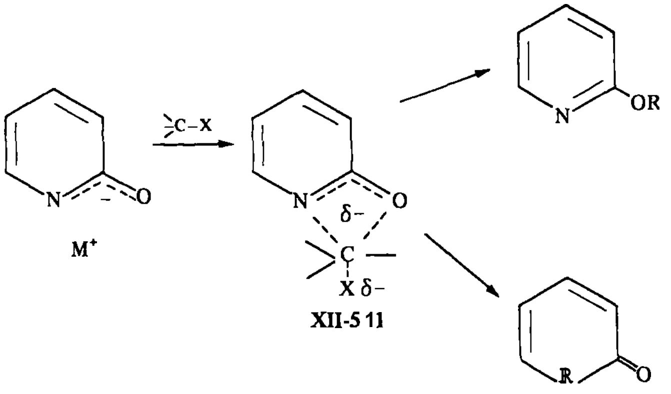


XII-510

3,4,5,6-tetrafluoro-2-pyridinol and 2,3,5,6-tetrafluoro-4-pyridinol are methylated on oxygen by methyl iodide in methanol and by dimethyl sulfate.[246]

Silver salts of 4,5,6-triphenyl-2-pyridone and 4,6-diphenyl-5-phenoxy-2-pyridone are mainly *O*-alkylated by methyl iodide in methanol or benzyl chloride in benzene. The potassium salt of 4,5,6-triphenyl-2-pyridone in an excess of methyl iodide gives more *N*-alkylation product, but the sodium salt and benzyl chloride in ethanol gives more *O*-alkylation product.'" This appears to be due to a steric effect, since sodium salts of 2-pyridones that are unsubstituted in the 3- and 6-position give similar product distributions in reactions with benzyl halides and with methyl iodide under similar conditions.[547, 549] This steric effect has been observed in the benzylation of 6-methyl-2-pyridone.[555]

Butylation of the sodium salt of 2-pyridone in dimethyl sulfoxide gives 2-n-butoxypyridine and *N*-*n*-butyl-2-pyridone, in the same product ratio at a pressure of 1 atm and at 1360 atm. Similarly, the product distribution in benzylation of the potassium salt in ethanol does not vary with pressure, and therefore the transition states leading to O- and *N*-alkylation have nearly identical molar volumes.[550] It has been concluded from these data that the branching of the reaction pathway occurs at or beyond the transition state. The model for the transition state (XII-511) implies that the products are determined by minor differences in conformation and energy distribution.[550]

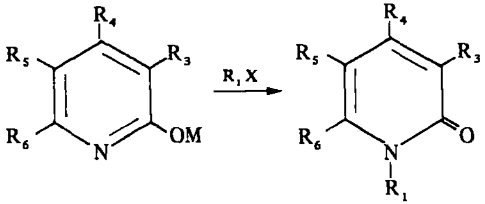


XII-511

A variety of alkali metal salts of 2-pyridones have been alkylated in polar solvents to give *N*-alkyl-2-pyridones (Table XI-12).

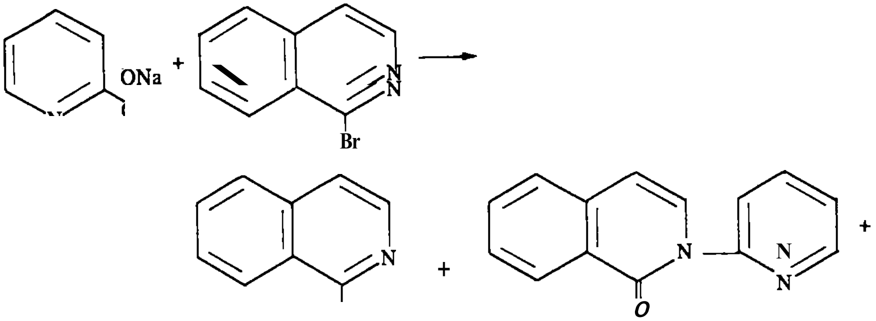
The sodium salts of 2-pyridone and 4-pyridone react with 1-bromoisoquinoline and copper-bronze to give mixtures of products. For example, under Ullmann conditions the sodium salt of 2-pyridone gave 39% of *N*-(2-isoquinolyl)-2-pyridone (XII-512) and minor amounts of 2-(2-pyridyl)isocarbostyril, 2-(1-isoquinolyl)isocarbostyril, 1-(2-pyridyl)-2-pyridone and isocarbostyril.[560] (See also Section I.6.A., p. 691.) Under these conditions, 3-acetamido-2-bromopyridine forms 1-(3-acetamido-2-pyridyl)-2-pyridone, which can be hydrolyzed to the aminopyridyl-2-pyridone and then cyclized in the presence of polyphosphoric acid to dipyrido[1,2-*a*:3,2-*d*] imidazole (XII-513).[271]

TABLE XI-12. *N*-Alkylation of Alkali Metal Salts of 2-Pyridones

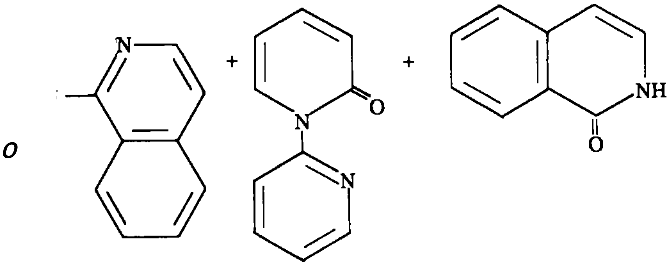


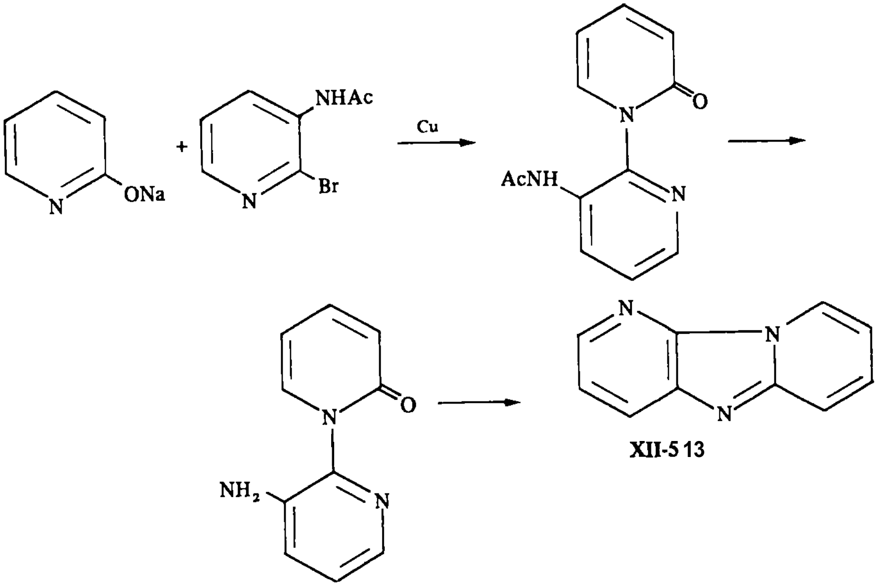
R$_1$	R$_3$	R$_4$	R$_5$	R$_6$	M	X	Solvent	% Yield	Ref.
CH$_3$	NO$_2$	H	H	H	K	I	EtOH/H$_2$O	80	5.56
CH$_3$	CH$_3$	NEt$_2$	C$_6$H$_5$	H	Na	1	MeOH/H$_2$O	95	102
CH, =CHCH$_2$	H	H	H	H	Na	Cl	EtOH	64	557
p-NCC$_6$H$_4$CH$_2$	H	H	H	H	Na	Cl	MeOH	>3 d	558
2-Cl-4-NO$_2$C$_6$H$_3$CH$_2$	H	H	H	H	K	Br	EtOH	81	558
CH$_3$	CH$_3$	H	H	H	K	I	EtOH		559
CH$_3$	H	CH$_3$	H	H	K	I	EtOH		559
CH$_3$	H	H	CH$_3$	H	K	I	EtOH		559
CH$_3$	H	H	H	CH$_3$	K	I	EtOH	56	559
3,4-(CH$_3$O)$_2$C$_6$H$_3$CH$_2$CH$_2$	H	CH$_3$	C$_2$H$_5$	H	K	I	BuOH	64	281

'Yield reported is for the product of hydrolysis, *N*-(*p*-carboxybenzyl)-2-pyridone.



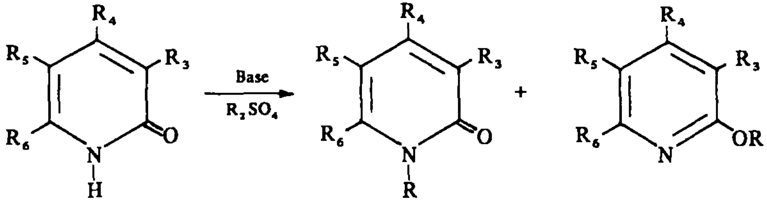
XII-5 12

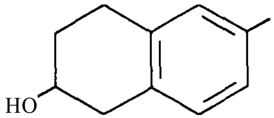




XII-5 13

TABLE XII-13. Alkylations of 2-Pyridones and 2-Pyridinols with Dialkyl Sulfates



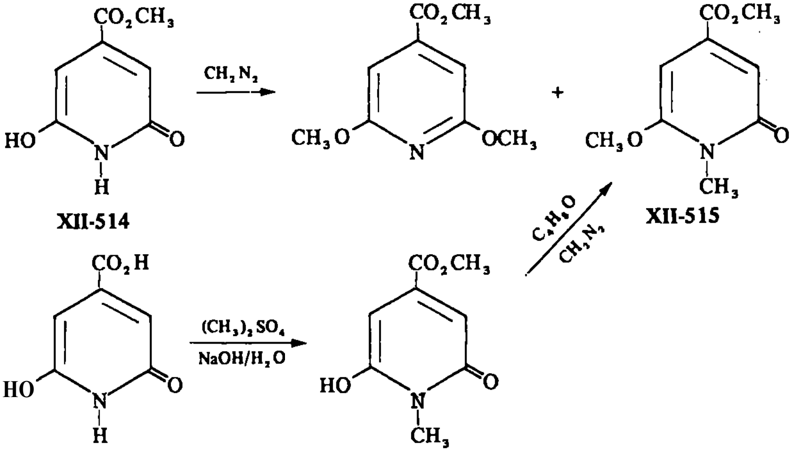
R	R_3	R_4	R_5	R_6	Base	N-Alkyl (%)	O-Alkyl (%)	Ref.
CH_3	C_2H_5			Mixture	CH, ONa	15		314
CH_3			C_2H_5	Mixture	CH_3ONa	15		314
CH_3				CH_3	NaOH	51		306
C_2H_5				CH, CONH	NaOH		52	551
CH_3					C_2H_5ONa	48	29[a]	568
CH_3		COOH		OH	NaOH	75[b]		507
CH_3		CH_3		Cl	CH, ONa	38		a
CH_3		C_6H_5		Cl	CH_3ONa	67		8
CH_3	$(CH_2)_3$			Cl	CH, ONa	88		8
CH_3	$(CH_2)_4$			Cl	CH, ONa	18		a

[a] **6-(6-Methoxy-1,2,3,4-tetrahydro-2-naphthyl)-2-pyridone** was also formed.
'Methyl N-methylcitrazinate.

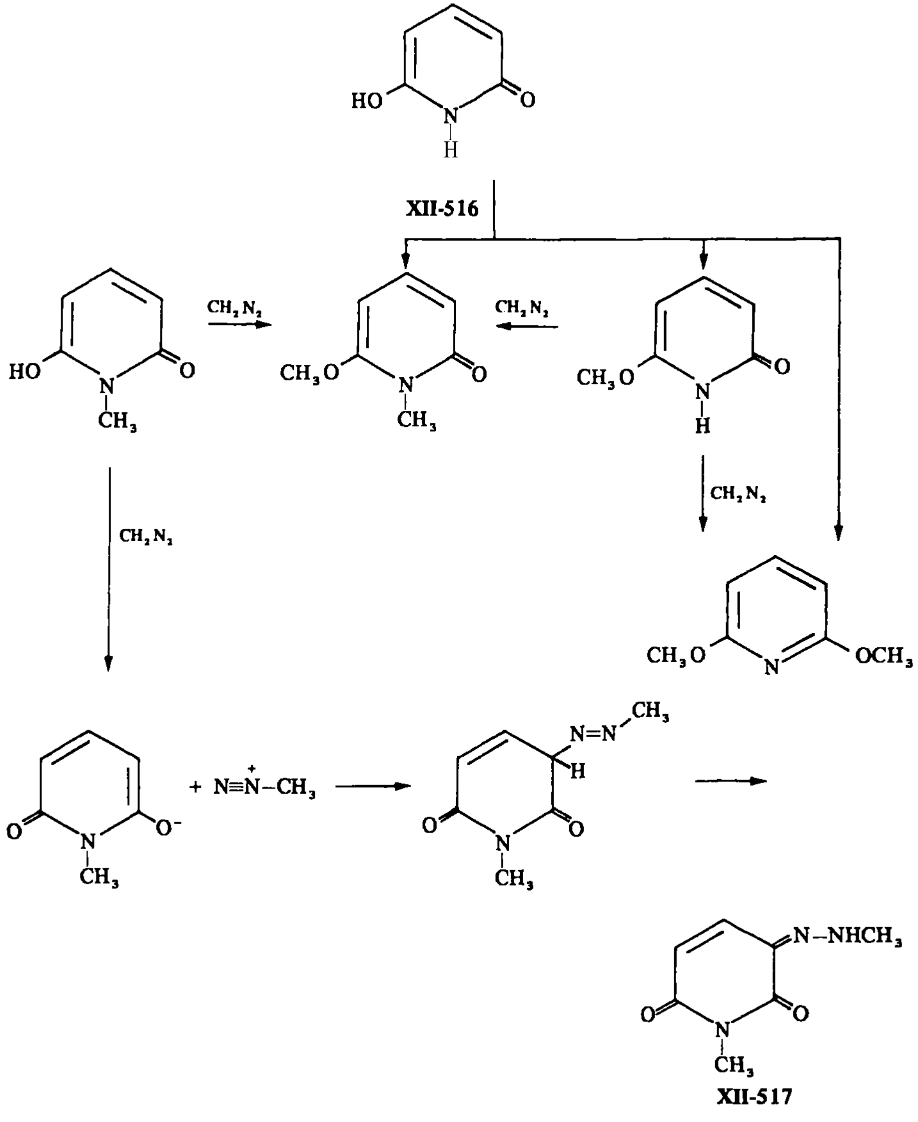
A large number of *N*-substituted-2-pyridones have been synthesized as potential pharmaceuticals, principally by Gogolimska[561–563] and Raczka[337, 564, 565] and Sacha.[566, 567] These compounds have been prepared by alkylation of alkali metal salts with halides,[337, 561–564] by modification of the *N*-substituent,[561–567] and by oxidation of pyridinium salts with ferricyanide.[337] Careful analyses of product distribution from alkylations of 2-pyridones with dialkyl sulfates are not generally reported. When dimethyl sulfate is used with salts of 2-pyridones that are unsubstituted or have small groups or chlorine at the 6-position, *N*-alkylation appears to predominate. For example, 3- and 5-ethyl-2-pyridone,[314] 6-chloro-2-pyridones' and 6-methyl-2-pyridone[306] are *N*-alkylated by dimethyl sulfate and base (Table XI-13). On the other hand, the sodium salt of 6-acetamido-2-pyridone and diethyl sulfate give 2-acetamido-6-ethoxypyridine.[551] 6-(6-Hydroxy-1,2,3,4-tetrahydro-2-naphthyl)-2-pyridone and dimethyl sulfate give the products of O- and *N*-alkylation[568] (Table XII-13).

Although it had been assumed earlier that diazomethane and 2-pyridone give exclusive *O*-alkylation,[569] it has been shown that both *N*-methyl-2-pyridone and 2-methoxypyridine (Table XII-14) are formed and that the product ratio is the same in methanol-ethyl ether as in methylene chloride-ethyl ether. An increase in 0-alkylation of 2-pyridone by diazoethane as compared with alkylation by diazomethane (Table XII-14) has been rationalized on steric grounds or as resulting from a decrease in the S_N2 character of a graded S_N1–S_N2 factor.'"

4,5,6-Triphenyl-2-pyridone and 5-phenoxy-4,6-diphenyl-2-pyridone are reported to be 0-alkylated by diazomethane.[121] Citrazinic acid and its methyl ester (XII-514) give mixtures of the products of O- and *N*-methylation. 4Carbomethoxy-6-methoxy-1-methyl-2-pyridone (XII-515) can be prepared from citrazinic acid by dimethyl sulfate to give methyl *N*-methylcitrazinate (Table XII-13, which is then treated with diazomethane.



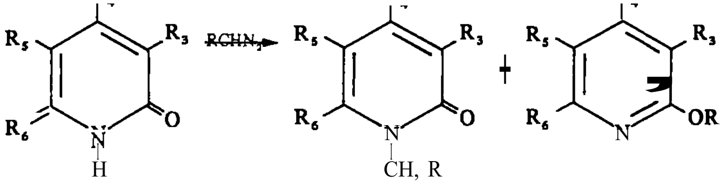
6-Hydroxy-2-pyridone **(XU-516)** and a large excess of diazomethane give 6-methoxy-2-pyridone (2%), 6-methoxy-1methyl-2-pyridone (4%), 2,6-dimethoxypyridine (8%), and the **3-(β-methylhydrazone)** of 1-methyl-2,3,6-pyridinetrione **(XU-517) (14%)**.[505] 6-Methoxy-2-pyridone and diazomethane give a mixture of *O*- and *N*-methylation products. 6-Hydroxy-1-methyl-2-pyridone gives 6-methoxy-1methyl-2-pyridone and **XII-517**.[505]



XII-516

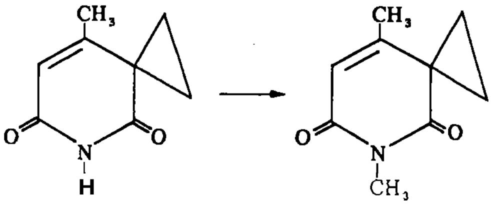
XII-517

TABLE XII-14. Alkylations of 2-Pyridones and 2-Pyridinols with Diazoalkanes

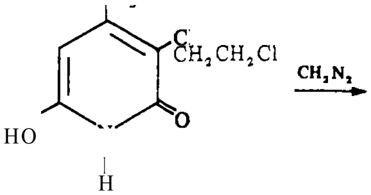


R	R$_3$	R$_4$	R$_5$	R$_6$	*N*-Alkyl (%)	*O*-Alkyl (%)	Ref.
H	H	H	H	H	55	35	570
CH$_3$	H	H	H	H	66	24	570
H				NH$_2$	37	48	494
H				Cl	57	17	494
CH$_3$		C$_2$H$_5$O	Br			62	284

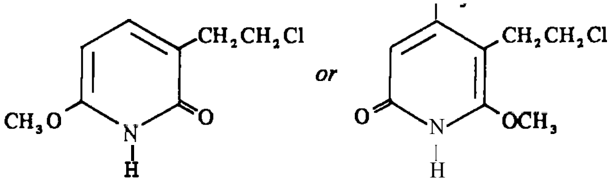
4-Methyl-3-(spirocyclopropane)-2,6-pyridinedione (XII-518) and diazomethane in methanol-ether give the *N*-methyl derivative.



XII-518

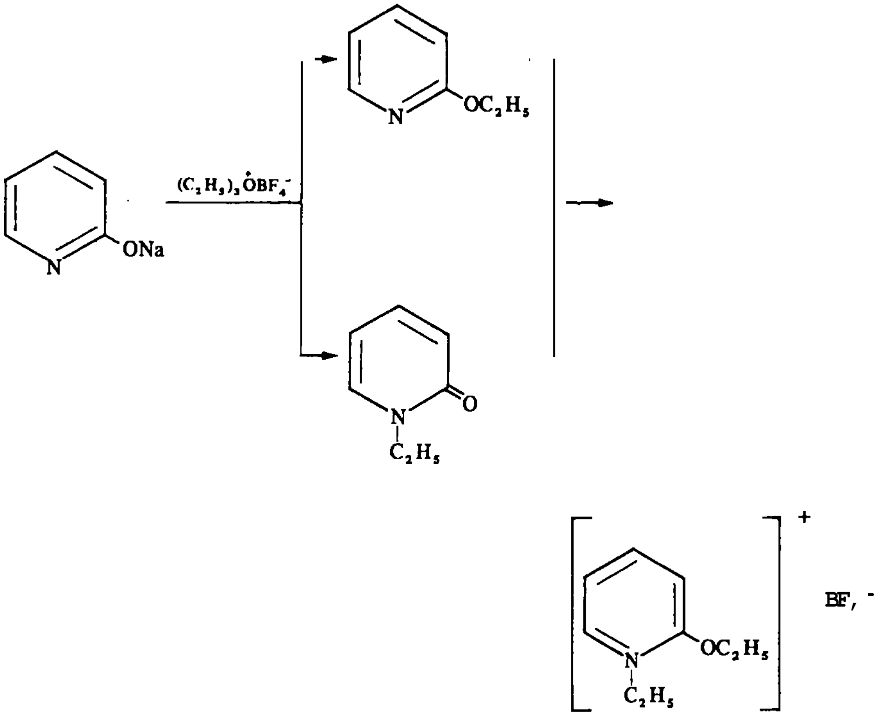


XII-519



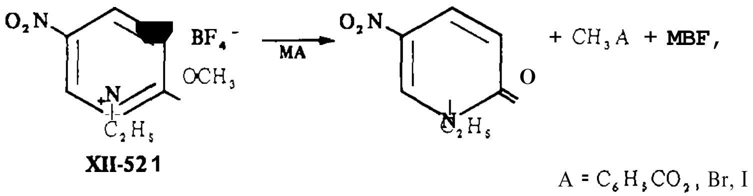
On the other hand, 3-(β-chloroethyl)-4-methyl-2,6-pyridinediol (XII-519) gives a product of *O*-alkylation that was not characterized.[510] Additional alkylations of 2-pyridones by diazomethane and diazoethane are summarized in Table XII-14.

The sodium salt of 2-pyridone and triethyloxonium tetrafluoroborate in methylene chloride gives 2-ethoxypyridine (21%), *N*-ethyl-2-pyridone (40%), and *N*-methyl-2-ethoxypyridinium tetrafluoroborate (XII-520), 29%.[571] A slower alkylation of the sodium salt by XII-520 produces 2-ethoxypyridine (9%) and *N*-ethyl-2-pyridone (79%).[571] The product distribution in this alkylation changes with time.[571] In ethanol and with an excess of triethyloxonium tetrafluoroborate, the monoethylation products are formed in 19% and 77% yield, respectively.[570] Product XII-520 can be formed in 97% yield from 2-ethoxypyridine and is hydrolyzed with aqueous sodium hydroxide to *N*-ethyl-2-pyridone (89%).[571]

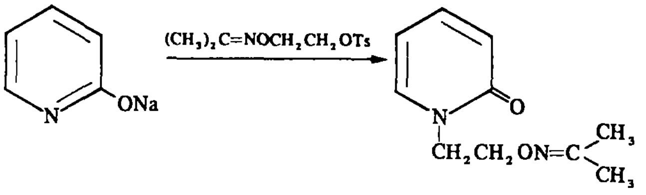


XII-520

1-Ethyl-2-methoxy-5-nitropyridinium tetrafluoroborate (XII-521) is a strong methylating agent. Sodium benzoate, sodium iodide, and lithium bromide are methylated by this reagent.[572]

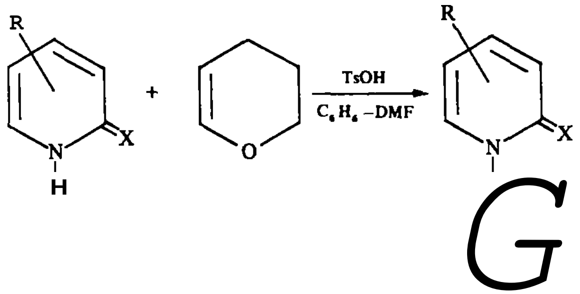


The sodium salt of 2-pyridone and *O*-(2-hydroxyethyl)acetoneoxime p-toluenesulfonate gives the *N*-alkylation product **XII-522.**[573]



XII-522

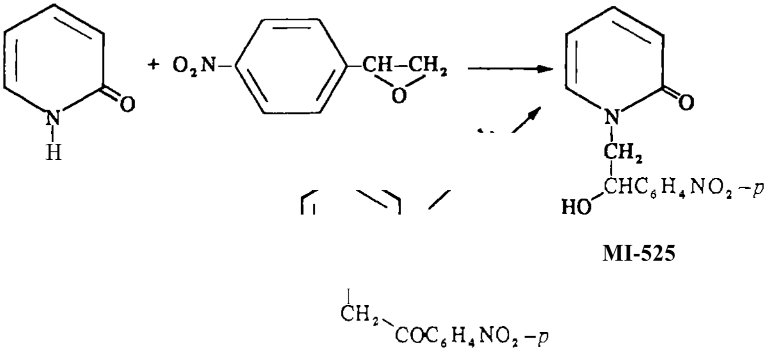
Treatment of 2-pyridones (**MI-523,** X = **O**) or 2-pyridinethiones (**XII-523,**X = **S**) with dihydropyran in the presence of p-toluenesulfonic acid gives **1-tetrahydropyranyl-2-pyridones** or **1-tetrahydropyranyl-2-pyridinethione (XII-524).**[574]



XII-523 XII-524

2-Pyridone and *p*-nitrostyrene oxide **give 1-(*β*-hydroxy-*β*-*p*-nitrophenethyl)-2-**pyridone (**XII-525**), which was also synthesized by alkylation of 2-pyridone with ω-bromo-*p*-nitroacetophenone to give the ketone **MI-526,** which was reduced with sodium **borohydride.**[326]

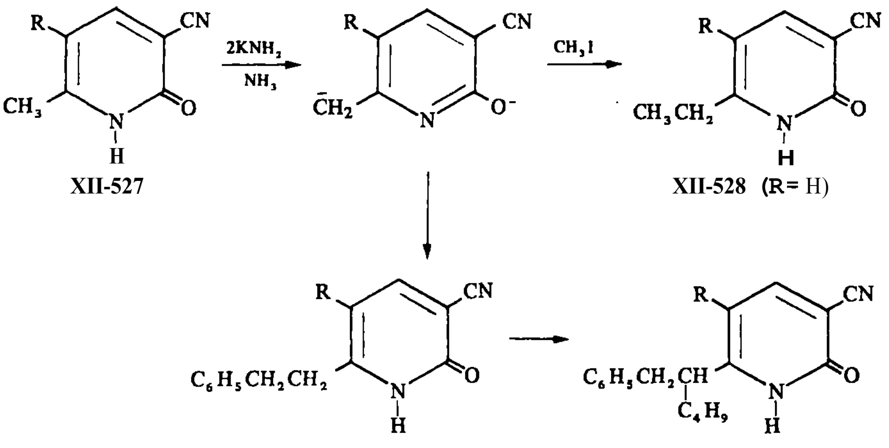
Dianions *of* 4- and 6-alkyl-3-cyano-2-pyridones can be formed from the pyridone by treatment with two equivalents of potassium amide in liquid ammonia and can be alkylated, aroylated, or acylated selectively on the



MI-525

XII-526

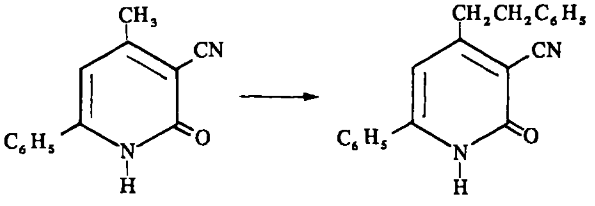
side-chain in good yields. By this method 6-methyl-2-pyridones **(MI-527)** are methylated to give the 6-ethylpyridone (XII-528) and benzylated to give the 6-phenethyl-2-pyridones (XII-529), which can be alkylated further. 3-Cyano-4-methyl-6-phenyl-2-pyridone (XII-530) gives the 4-phenethyl derivative in 90% yield.[575–577]



XII-527

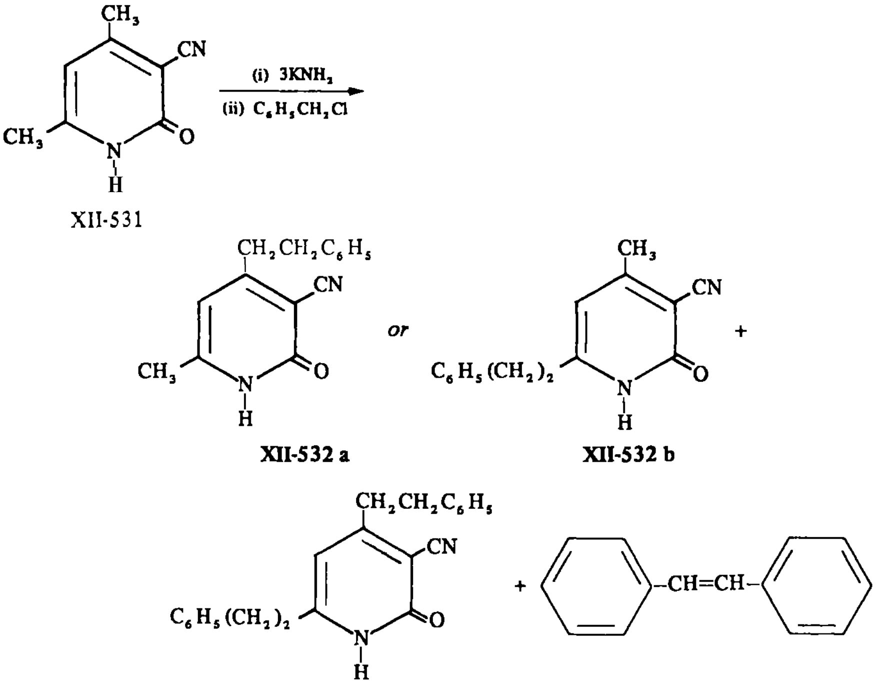
XII-528 (R= H)

XII-529



XII-530

The dianion of **3-cyano-4,6-dimethyl-2-pyridone (XII-531)** and benzyl chloride give only one product, which was not characterized. However, **XII-531** and three equivalents of potassium amide and an excess of benzyl chloride give a 30% yield of stilbene and 35% each of a monobenzyl- (**XII-532a** or **XII-532b**) and the dibenzyl- derivatives.[575] This method gives better yields of the

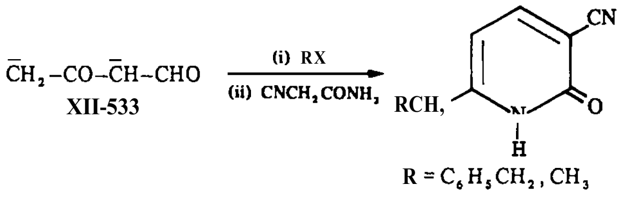


XII-531

XII-532 a

XII-532 b

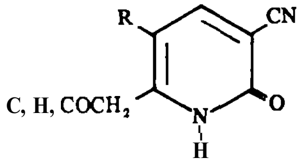
6-alkyl-3-cyano-2-pyridones than the route where dicarbanions of β-keto-aldehydes or β-diketones **XII-533** are alkylated and then cyclized with cyanoacetamide.[54] In the latter method, mixtures of products are formed,



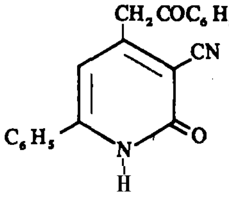
XII-533

although the use of an imine of a β-diketone has overcome this disadvantage.[578]

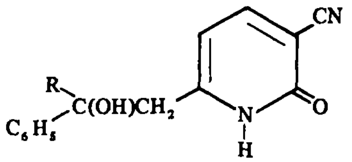
The dianions from **XII-527** (R = H, C_6H_5) and **XII-530** are aroylated with methyl benzoate to give the ketones **XII-534** and **XII-535**. They react with benzaldehyde and benzophenone to give the alcohols **XU-536.** Benzophenone and the dianion **W-530** give **XII-537.**[576]



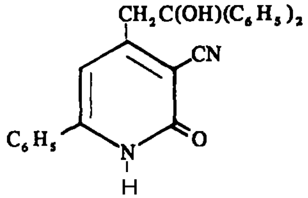
XII-534 (R = H, C_6H_5)



XII-535

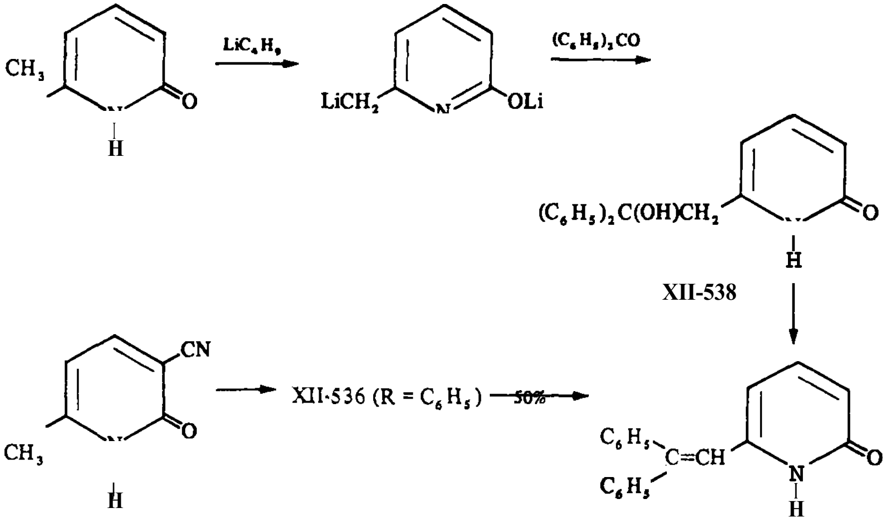


XII-536



XII-537

The monoanion of 6-methyl-2-pyridone is not sufficiently acidic to form a satisfactory dipotassium salt when treated with two equivalents of potassium amide. It does, however, react with *n*-butyllithium in tetrahydrofuran or ether to give the dilithio salt, which condenses readily with carbonyl compounds[579], *e.g.*, to give the tertiary alcohol **XII-538** in 94% yield. Less conveniently, the dehydration product of **XII-538** was prepared from the dipotassium salt of **XII-527** (R = H) *via* XII-536 (R = C_6H_5). 4-Methyl- and 3-methyl-2pyridones as

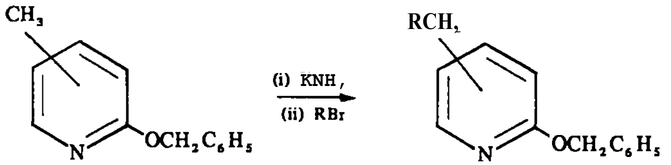


XII-538

XII-527 (R = H)

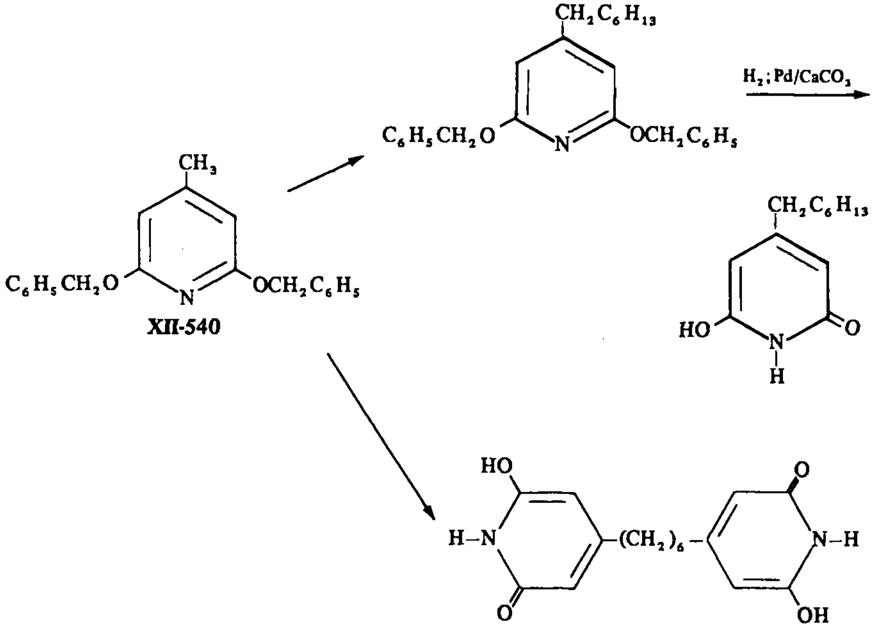
well as 3-methyl- and 6-methyl-2-pyridinethiones form dilithio salts that react similarly.[579] Alkylation of the side-chain of methylpyridines has been extended to 2-benzyloxymethylpyridines (MI-539,MI-540,XII-541). The products can be converted to alkyl-2-pyridones by hydrogenolysis.[6, 581]

Attempted alkylations of 3-benzyloxy-6- and 2-benzyloxy-5-methylpyridine with tetramethylene dibromide have been unsuccessful.[6]



XII-539

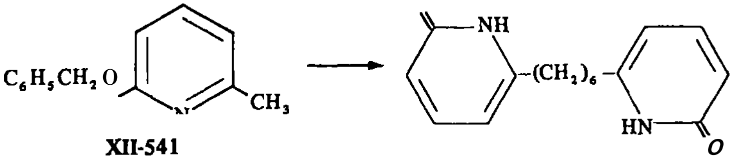
R = 3-, 4-,5- and 6-hexyl; 4-, and 5-undecyl; 4-benzyl.



XII-540

2-Pyridinethione and 1-bromo-2-chloroethane in dimethylformamide containing potassium carbonate give 2,3-dihydrothiazolo[3,2-*a*]pyridinium bromide[582]

(R.I. 1145). **3-Hydroxy-2-pyridinethione (W-542, R = H)** and 3-hydroxy-6-methyl-2-pyridinethione **(XII-542, R = CH_3)** and ethylene bromide in methanol containing sodium methoxide react to give dihydrothiazolo[3,2-*a*] pyridinium 8-oxides **(XII-543)**.[583] Methyl 2,3-dibromopropionate and **XII-542** form



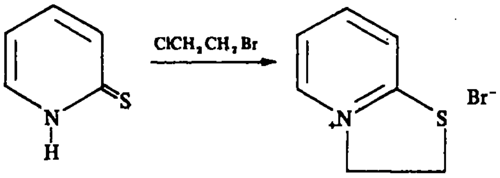
XII-541

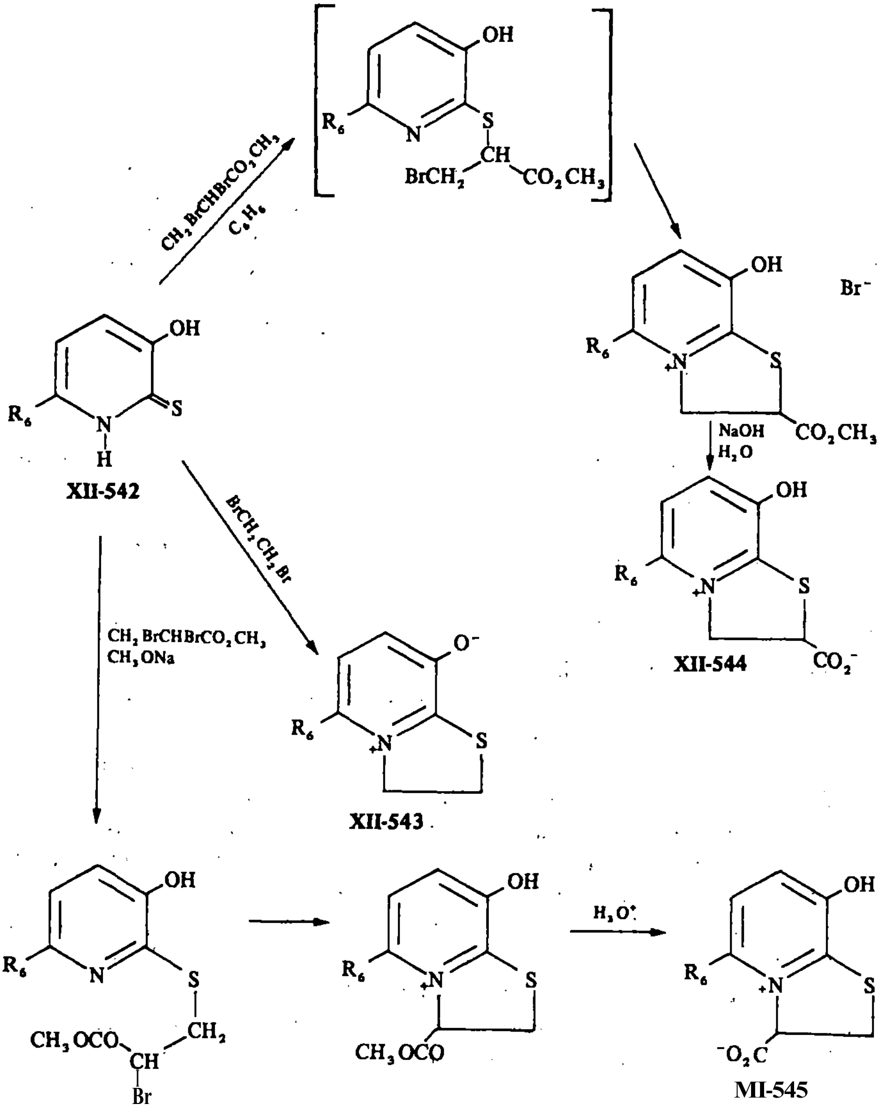
8-hydroxy-dihydrothiazolo[3,2-*a*] pyridinium 2-carboxylates **(MI-544)** after heating in benzene, followed by saponification. These reactants, in the presence of sodium methoxide in methanol, give the 3-carboxylate **(XII-545)** after hydrolysis, presumably *via* β-elimination of the ester to give ethyl a-bromoacrylate, which then reacts with **XII-542**.[583] 8-Hydroxy-5-methyldihydrothiazolo[3,2-*a*] pyridinium 3-carboxylate **(XU-545, R_6 = CH_3)** is a blue fluorescent material that has been isolated from bovine liver hydrolysates.[584]

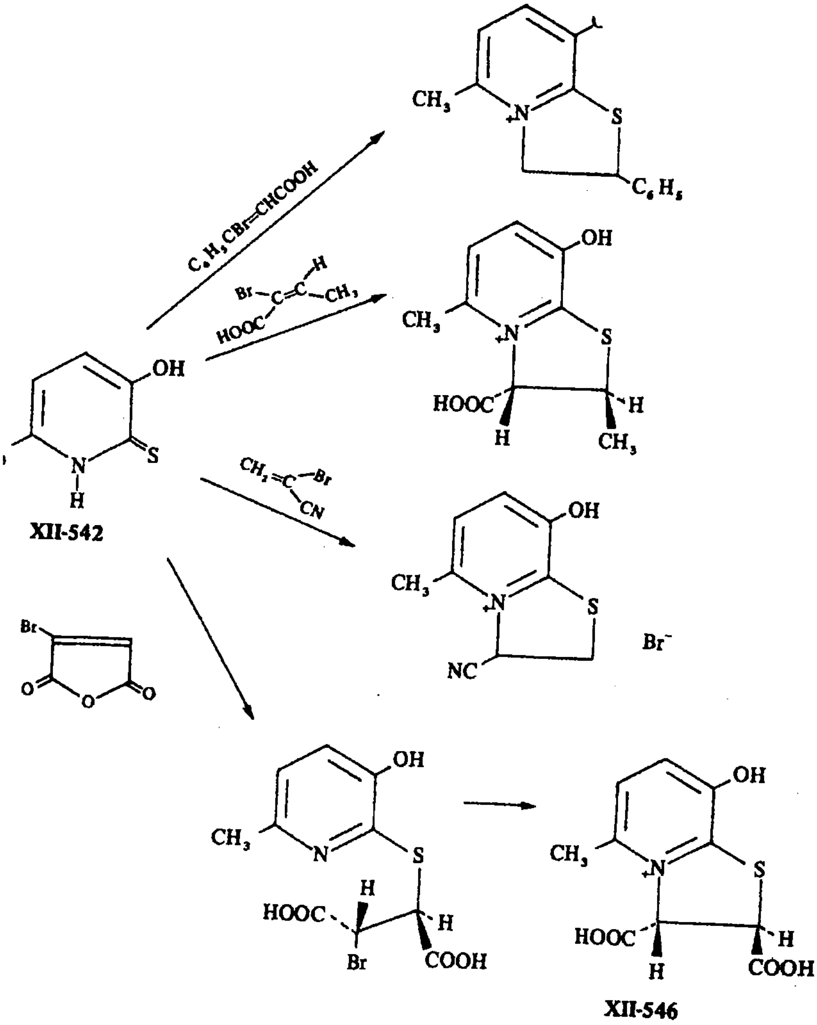
Similarly, **MI-542** reacts with α-bromoacrylonitrile to give the 3-cyano derivatives and with α-bromo-α-unsaturated acids by *trans* addition to form substituted **3-carboxyldihydrothiazolo[3,2-*a*]** pyridinium compounds that are readily decarboxylated.[585] Under these conditions **MI-542** does not react with β-bromostyrene.

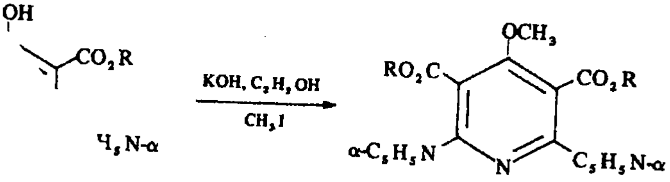
The *trans* product **XII-546** from bromomaleic anhydride and **MI-542** requires that the anhydride ring of the intermediate adduct be opened to assume the conformation necessary for *trans* displacement of Br by the annular nitrogen.[585]

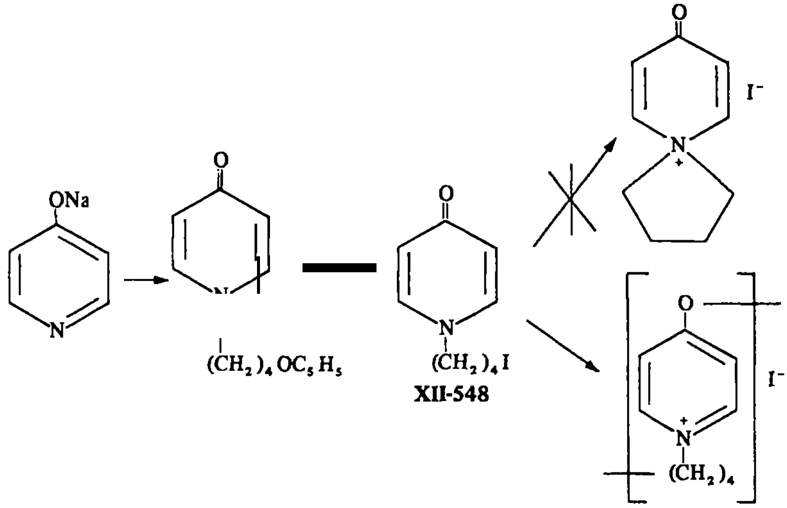
c. 4-PYRIDONES A combination of *ortho* and electronic effects appears to determine the course of alkylations of 4-pyridones. *N*-Alkylation is more sensitive to steric effects than is *O*-alkylation. For example, the potassium salt of 3-nitro-4-pyridone is *N*-alkylated by methyl iodide,[586] and the sodium salt of **3,5-diiodo-4-pyridone** is N-alkylated by ω-bromoalkanoates in ethanol.’” On the other hand, the dimethyl and diethyl esters of **2,6-di-(α-pyridyl)-4-hydroxy-3,5-pyridinedicarboxylic** acid **(XII-547; R = CH_3, C_2H_5)** undergo *O*-alkylation with methyl iodide in alcoholic potassium hydroxide,[500] and the potassium salt of tetrafluoro-4-pyridone and either methyl iodide or dimethyl sulfate in methanol give tetrafluoro-4-methoxypyridine. The product of *N*-methylation was not detected.[246] Alkylation of the sodium salt of 4-pyridone with 4-phenoxybutyl bromide followed by treatment with hydriodic acid gives ***N*-(4-iodobutyl)-4-pyridone (XII-548)**, which forms a polymer in water rather than the *N*-spiro derivative.[588] Dehydrohalogenation of **2-chloro-3-(β-chloro-**


ClCH₂CH₂Br
S
N
H
+N
S
Br⁻

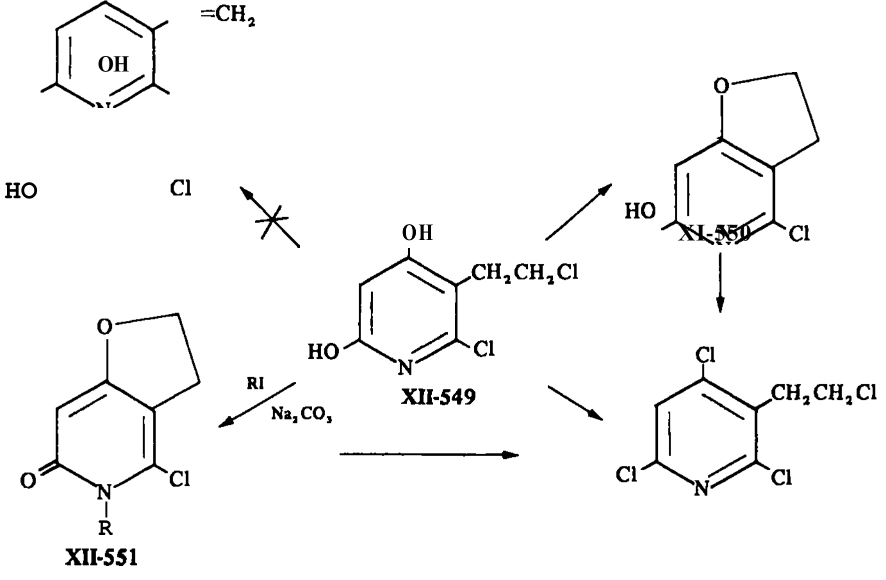

CH₂BrCHBrCO₂CH₃
C₆H₆
OH
R₆
N
S
CH
BrCH₂
CO₂CH₃
Br⁻
+N
NaOH
H₂O
XII-542
BrCH₂CH₂Br
XII-544
CO₂⁻
CH₂BrCHBrCO₂CH₃
CH₃ONa
O⁻
XII-543
CH₃OCO
CH₂
Br
H₃O⁺
⁻O₂C
MI-545


XII-542
OH
S
N
H
C₆H₅CBr=CHCOOH
Br—C=C—CH₃
HOOC
H
CH₂=C—Br
CN
Br
O
O
O
CH₃
N
S
C₆H₅
OH
HOOC
H
CH₃
NC
Br⁻
COOH
XII-546


OH
CO₂R
Ч₅N-α
KOH, C₂H₅OH
CH₃I
OCH₃
RO₂C
CO₂R
α-C₅H₅N
N
C₅H₅N-α



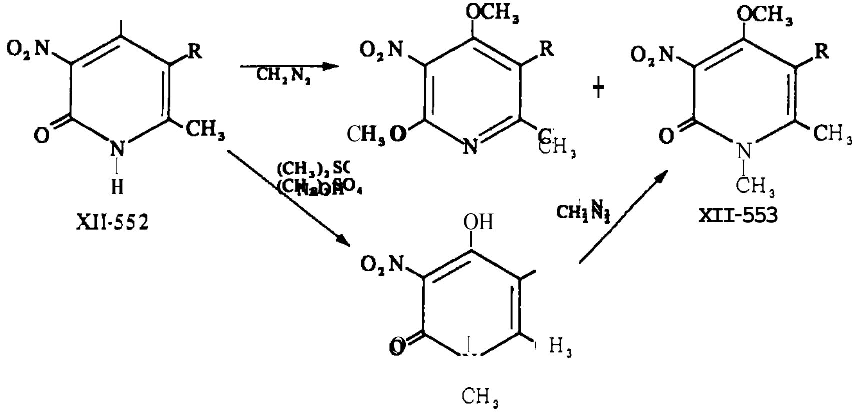
ethyl)-4,6-dihydroxypyridine (XI-549) in ethanolic ammonia gives **4-chloro-2,3-**dihydro-6-oxofuro[3,2-*c*]pyridine **(XII-550)**'[89] and not **2-chloro-3-vinyl-4,6-**pyridinediol as previously reported.'[90] Treatment of **XII-549** with sodium carbonate and methyl or ethyl iodide produces **5-alkyl-4-chloro-2,3-dihydro-6-**oxofuro[3,2-*c*]pyridine **(XII-551)** (R.I. 1306). The *N*-alkylfuro[3,2-*c*]pyridines **(XII-551**; R = CH_3,C_2H_5) and phosphorus oxychloride give 2,4,6-trichloro-3-β-chloroethylpyridine,[589] which can be prepared directly from **XII-549** or **XII-550**.[590]



5-Acetyl-4-hydroxy-6-methyl-2-pyridone and dimethyl sulfate in sodium methoxide give the *N*-methyl-2-pyridone (40%) but diazomethane causes O-methylation **(52%).**[94]

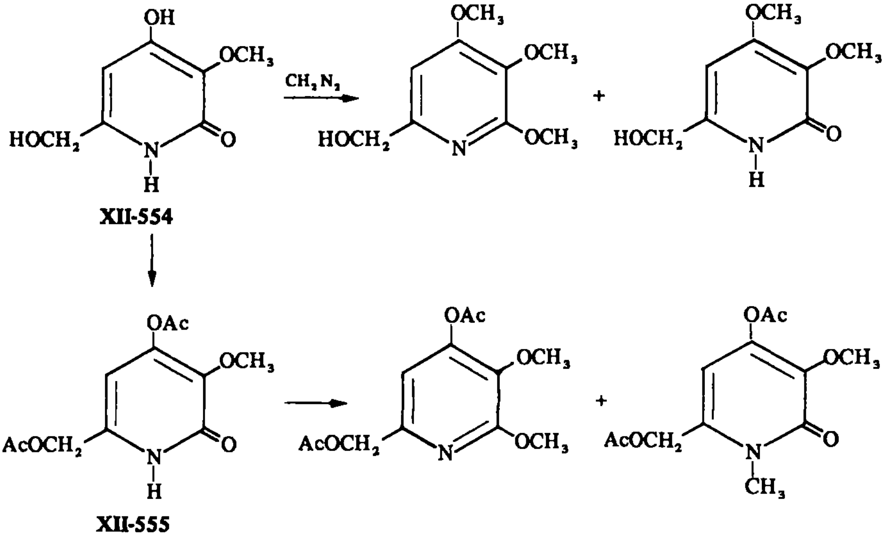
Alkylation of 4-hydroxy-6-methyl-3-nitro-2-pyridone **(MI-552 ,**R = H) and its 5-carbethoxy derivative **(MI-552 ,**R = $CO_2C_2H_5$) with diazomethane in ether or benzene gives a mixture of the 2,4-dimethoxypyridine and the 4-methoxy-*N*-methyl-2-pyridone **(XII-553).**[86] Alkylation of **MI-552** (R = H) with an excess of dimethyl sulfate gives a good yield of the 4-hydroxy-*N*-methyl-2-pyridone, which gives XII-55 3 on treatment with **diazomethane.**[86]

4-Hydroxy-6-hydroxymethyl-3-methoxy-2-pyridone (XI-554) and diazomethane in ether-ethanol give both **6-hydroxymethyl-2,3,4-trimethoxypyridine** and **6-hydroxymethyl-3,4-dimethoxy-2-pyridone.**[591] Acetylation *of* **XII-554**



XII-552

XII-553

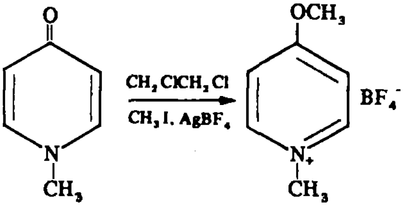


XII-554

XII-555

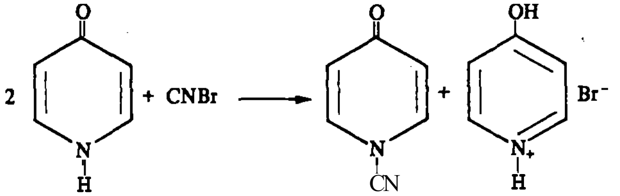
gives **MI-555**, which reacts with diazomethane to give both 4-acetoxy-6-acetoxy-**methyl-2,3-dimethoxypyridine** and **4-acetoxy-6-acetoxymethyl-3-methoxy-N-methyl-2-pyridone**.[591]

N-Methyl-4-pyridone and methyl iodide in ethylene chloride containing silver tetrafluoroborate give **4-methoxy-N-methylpyidinium** tetrafluoroborate (**XII-556**).[139]



XII-556

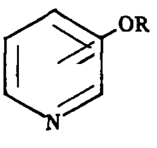
4-Pyridone and cyanogen bromide in chloroform give N-cyano-4-pyridone (**XII-557**).[460]



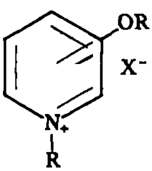
XII-557

d. 3-PYRIDINOLS Alkylations of 3-pyridinols have been reported to give four types of products: 3-alkoxypyidines (XII-558), 3-hydroxypyridinium salts (**XII-559**, R = H), betaines (XII-560), and betaine complexes (**MI-561**).

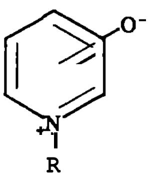
Shapiro, Weinberg, and Freedman[592] have assigned the betaine hydrohalide structure to a number of *N*-alkylation products, several of which are considered



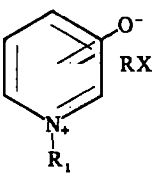
XII-558



XII-559



MI-560



MI-561

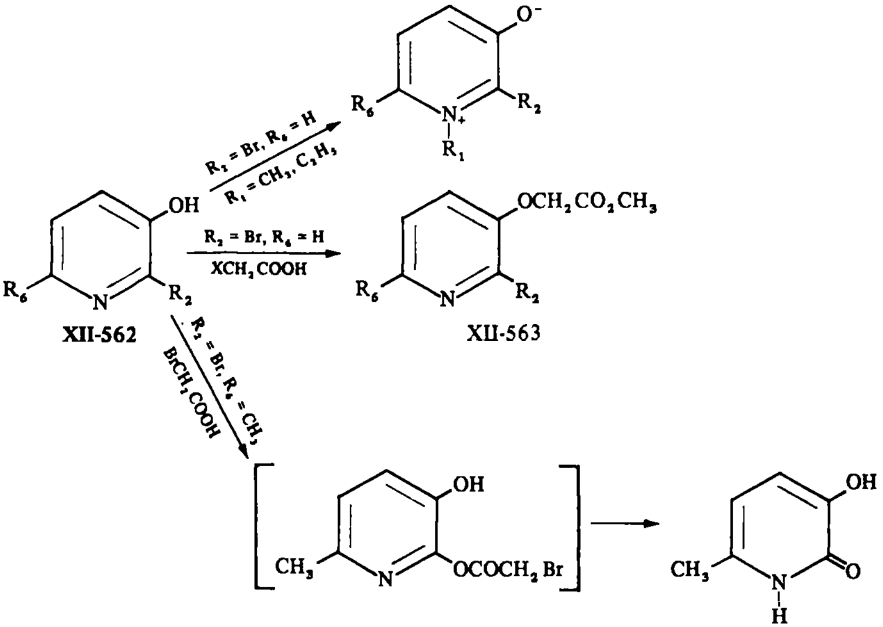
by others to be pyridinium **salts**.[189, 342, 593] For example, the *N*-methylation product from 3-pyridinol and methyl iodide has been described as *N*-methyl-3-oxypyridyl betaine hydroiodide (**MI-561**; R_1 = CH_3, R = H, X =

I)[592] and more often has been assigned the *N*-methyl-3-hydroxypyridinium iodide structure **(XII-559).**[342, 593, 594] Alkylation of 3-methoxypyridine ***(W-558,*** R = CH_3) with benzyl halides gives *N*-benzyl-3-methoxypyridinium halides (XII-559; R = $CH_2C_6H_5$, X = Br; R = $CH_2C_6H_4Cl$-*o* and *p*).[594] Salts of structure *XU-559* (R = H, R_1 = alkyl, aryl) have been prepared from furfural and amines[190] (see Section I.5.D.) Alkylations of 3-pyridinols have often given low yields of 3-alkoxypyridines. Reactions usually take place at nitrogen to give the pyridinium salt[595, 596] or the betaine. The synthesis of 3-methoxypyridine from 3-pyridinol or its sodium salt and dimethyl sulfate appears to be unsatisfactory.[594] Alkylation with diazomethane at ambient temperature gives only a low yield of 3-methoxypyridine and considerable amounts of *N*-alkylation; the yield, however, can be increased to 75% by carrying out the reactions in t-butyl alcohol at -15 to -20°.[594] Following this procedure, 2-bromo-3-methoxy-6-methylpyridine has been prepared in 90% yield.[597] Sodium salts of 3-pyridinols are preferentially 0-alkylated by alkyl halides in dimethyl sulfoxide or dimethylformamide. By this method, thirty-five new 3-alkoxypyridines have been prepared in good yield in dimethyl sulfoxide.[596] 3-Pyridinol is 0-alkylated by ethyl α-bromopropionate in 37% yield in sodium ethoxide in ethanol and in 21% yield in ethanolic potassium hydroxide. Using sodium hydride in dimethyl sulfoxide, a 67% yield is realized.[595] Ethyl 3-hydroxyisonicotinate is alkylated similarly by ethyl bromoacetate and ethyl α-bromopropionate. 3-Alloxypyridine is prepared in only 5% yield from allyl bromide and the sodium salt of 3-pyridinol in dimethylformamide.[598] The yield is increased to 45% when sodium hydride in dimethyl sulfoxide is used.[595]

The course of alkylation of 2- and 6-substituted-3-pyridinols is subject to a steric effect. Sodium salts of 3-pyridinol in ethanol are N-alkylated by methyl bromo- or iodoacetate. However, 2-bromo-3-pyridinol is N-alkylated by methyl and ethyl iodide in dimethylformamide but is O-alkylated by haloacetates to **XII-563** (R_2 = Br, R_6 = H). **2-Bromo-6-methyl-3-pyridinol (XII-562,** R_2 = Br, R_6 = CH_3) is *N*-alkylated by methyl and ethyl iodide and *O*-alkylated by diazomethane, but reacts with bromoacetic acid in chlorobenzene to give **3-hydroxy-6-methyl-2-pyridone** (XII-565), possibly *via* **2-(α-bromoacetoxy)-6-**methyl-3-pyridinol **(XII-564).**[597] With **6-methyl-2-methylthio-3-pyridinol** (XII-562; R_2 = CH_3S, R_6 = CH_3), *N*-alkylation should be favored electronically, particularly by electron release by the 2-methylthio group. However, quaternization is difficult even with the simple alkyl halides and only 0-alkylation is observed when methyl iodoacetate is used.[597]

2,4,6-Triiodo-3-pyridinol, potassium carbonate, and ethyl chloroacetate in methyl ethyl ketone give the *O*-alkylation product **(XI-566)** in 80% **yield.**[599]

2-Diphenylmethyl-3-pyridinol and dimethyl sulfate in alkaline water-dioxane give both **2diphenylmethyl-3-methoxypyridine** and 2-diphenylmethyl-3-hydroxy- 1-methylpyridinium hydroxide.[191]

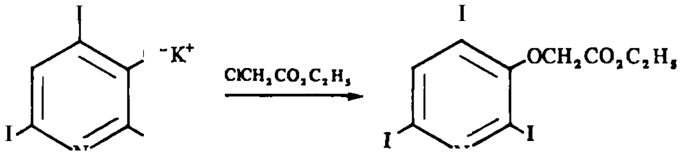


XII-562

XII-563

XII-564

XII-565

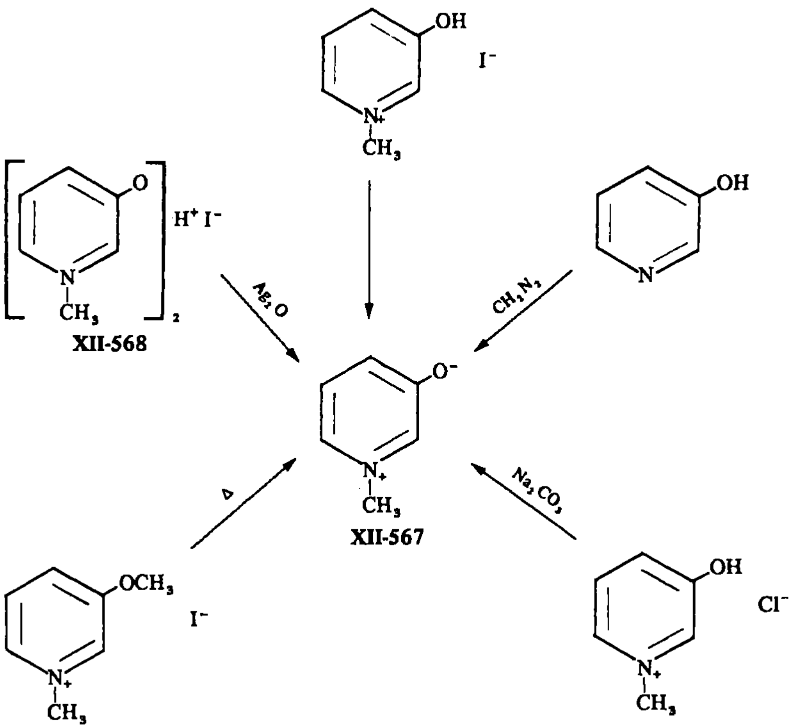


XU-566

The alkaloid Syphilobin F, a 2-substituted-3-pyridinol (see Section VI., p. 861), is *O*-methylated by diazomethane in diethyl ether-benzene in 43% yield.[600]

Anhydro-3-hydroxy-N-methylpyridiniumhydroxide (XII-567) can be formed by the reaction between 3-pyridinol and diazomethane, by the reaction of *N*-methyl-3-hydroxypyridinium chloride with anhydrous sodium carbonate and by thermal decomposition of 3-methoxypyridine iodomethylate. However, its preparation from the dimer complex of *N*-methyl-3-hydroxypyridinium iodide (XII-568)[593] by treatment with silver oxide was the most convenient method.[517] It has also been prepared from the quaternary iodide.[755]

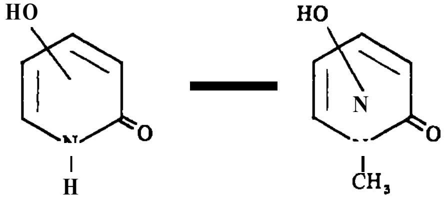
Paoloni notes that the ground state properties of XII-567 are in line with those of its isomers *N*-methyl-2-pyridone and *N*-methyl-4-pyridone and suggests that this is a mesionic compound for which the betaine structure is unsatisfactory[517, 518] (see, however Section 11.5.).



XII-568

XII-567

The two diols, 3- and 5-hydroxy-2-pyridone (XII-569, 3-OH, 5-OH) are converted to the corresponding *N*-methyl-2-pyridones by treatment with excess methyl iodide.[342]



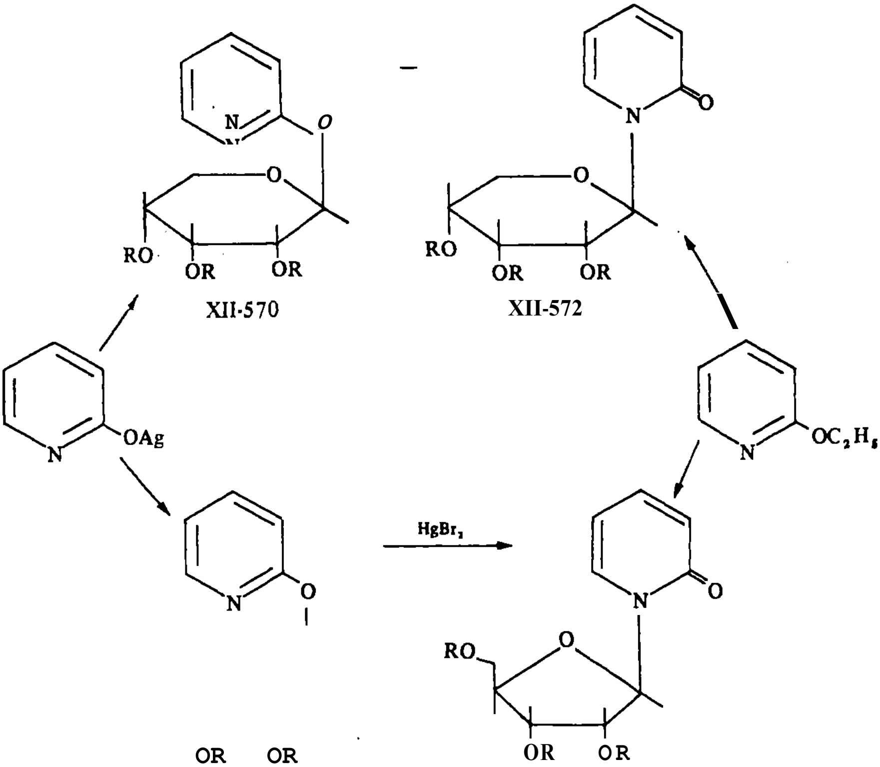
XII-569

B. *Pyridine Nucleosides*

The chemistry of pyridine nucleoside analogs is similar to that of the more widely studied pyrimidine nucleosides. The nucleosides are prepared from pyridone salts or alkoxypyridines or trimethylsilyloxypyridines and halogenoses. The products of direct alkylation of salts appear to be the O-glycosides, but rearrangements can occur *in situ* or by subsequent treatment with mercuric bromide.

The silver salt of 2-pyridone gives the O-glycoside (XI-570) when treated with 1-bromo-2,3,4-tri-*O*-benzoyl-D-ribopyranose. O-Ribofuranosides (XII-571 and XII-574) are formed from silver salts of 2- and 4-pyridone and 1-chloro-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose in boiling toluene. Rearrangements of the *O*-glycosides to N-glycosides (XII-572, XII-573, XII-575; R = C_6H_5CO) are accomplished by heating with mercuric bromide in toluene.[601, 602] Deblocking to the nucleoside analogs [XII-572 and MI-573 (R = H)] is accomplished by trans-esterification with sodium methoxide in methanol.[602]

The blocked nucleosides XII-572 and MI-573 can also be prepared from 2-ethoxypyridine and the halogenoses. 4-Ethoxypyridine and 1-chloro-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose gives both the β- (MI-575) and α-anomers (XI-576).[602] *N*-(D-Glucopyranosyl)-2-pyridone is prepared from the silver salt

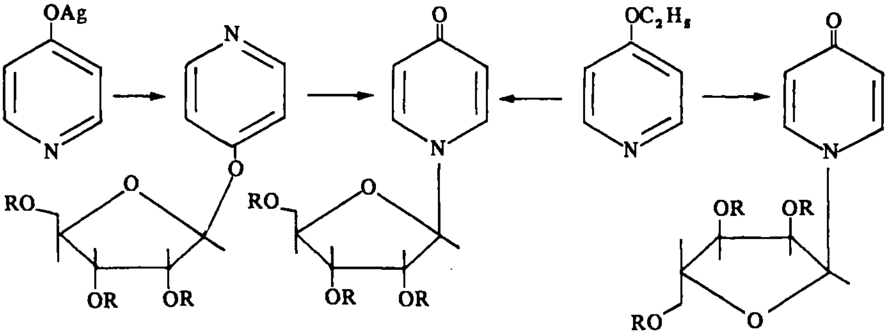


XII-570

XII-572

XII-571

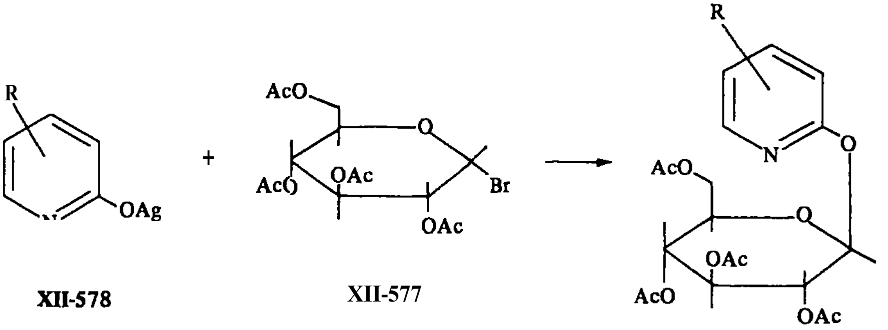
XII-573



XII-574 XII-575 XII-576

of 2-pyridone and tetra-*O*-acetyl-α-D-glucopyranosyl bromide (XII-577) by similar procedures. It can also be prepared from 2-ethoxypyridine or the mercuri-chloride salt of 2-pyridone with the halogenose.[603]

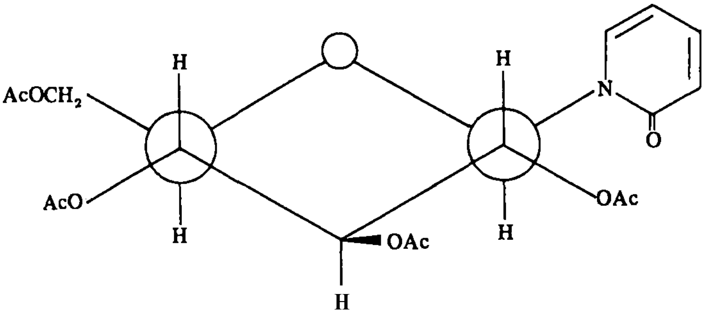
Silver salts of substituted 2-pyridones (W-578; R = 3-CO_2CH_3, 4-CO_2CH_3, 6-CO_2CH_3, 4-C_6H_5, 6-C_6H_5, 5-NO_2, 5-CN, 5-Cl, 5-Br, 5-I) and XII-577 give *O*-β-glucosides. The 6-substituted-*O*-β-glucosides (6-CO_2CH_3, 6-C_6H_5) do not, however, rearrange when heated with mercuric bromide in toluene.[604] Some β → α anomerization occurs[605,606] when the silver salts of 5-halopyridones are rearranged. When R is the electron withdrawing 5-NO_2 or 5-CN, only anomerization is observed.[605]



XII-578 XII-577

In the preferred conformation of the *N*-β-glucosides, the aglycone moiety is perpendicular to the axis of the sugar group and the C=O or C=S group is aligned with the vicinal proton (XII-579).[607]

3-Substituted and 3,5-disubstituted 2-(tetra-*O*-acetyl-β-D-glucopyranosyloxy)-pyridones also undergo O → N rearrangement when heated with mercuric bromide[608] and often are accompanied by some formation of the *O*-α-anomer.[609,610]

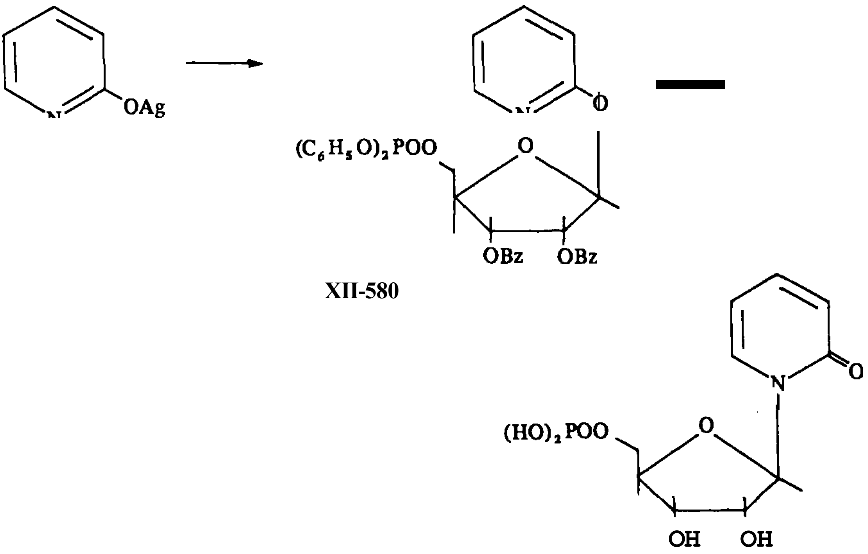


XII-579

The silver salt of 2-pyridone and **2-deoxy-3,5-di-*O*-(*p*-tolyl)-α-D-ribofuranosyl** chloride give both the a- and β-*O*-glycosides. Rearrangement of either anomer in the presence of mercuric bromide gives the N-deoxyribosides with an α:β ratio of 1:2.[611, 612]

The silver salt of 3-carbamoyl-6-pyridone and 1-chloro-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose give **3-carbamoyl-*N*-(β-D-ribofuranosyl)-6-pyridone** after rearrangement and deblocking with sodium methoxide. This nucleoside has been converted to 3-carbamoyl-6-pyridone adenine **dinucleotide.**[613]

The silver salt of 2-pyridone and **1-bromo-2,3-di-*O*-benzoyl-5-*O*-diphenylphosphoryl-D-ribofuranose** in toluene gives the *O*-riboside (**XII-580**), which in

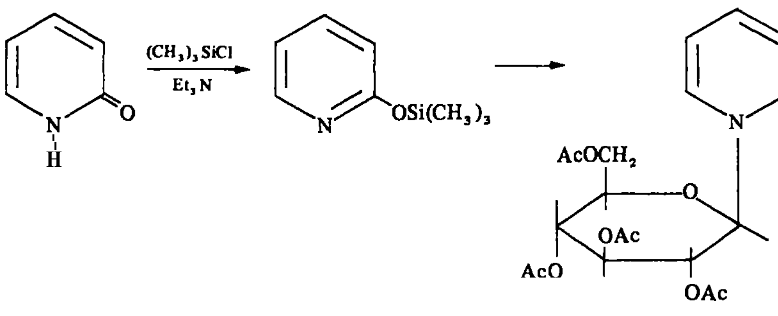


XII-580

turn gives the *N*-riboside 5’-phosphate after rearrangement and then hydrolysis first with alkali and then with phosphordiesterase.[614]

The nucleotide can also be prepared from *N*-(2′,3′-*O*-isopropylidene-β-D-ribofuranosyl)-2-pyridone through phosphorylation with β-cyanoethyl phosphate in the presence of *N*,*N*′-dicyclohexylcarbodiimide followed by deblocking.[615]

2-Pyridone and trimethylchlorosilane in toluene containing triethylamine form 2-(trimethylsilyloxy)pyridine, which reacts with tetra-*O*-acetyl-α-D-glucopyranosyl bromide to give **N-(tetra-O-acetyl-D-glucopyranosyl)-2-pyridone (XII-581).**[616] 2,4-Bis(trimethylsilyloxy)pyridine and **2,3,5-tri-O-benzoyl-D-**ribofuranosyl bromide in acetonitrile give the *N*-riboside after boiling in ethanol. **4-Hydroxy-N-(β-D-ribofuranosyl)-2-pyridone** (3-deazauridine) **(MI-582)** is formed by deblocking with alcoholic **ammonia.**[616]



XII-581

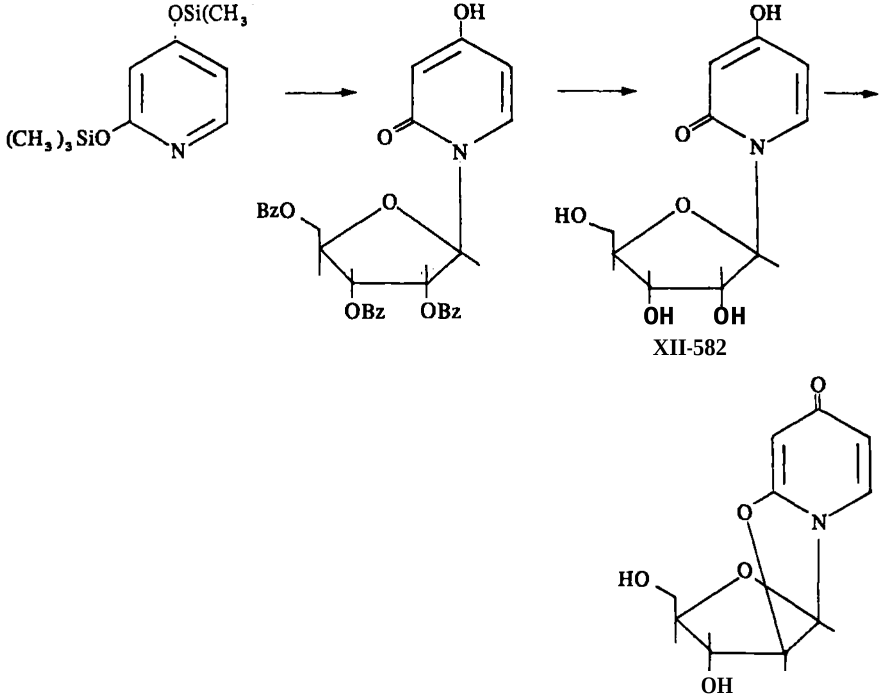
Reaction of **MI-582** with diphenyl carbonate gives **2,2′-anhydro-2-hydroxy-N-β-D-arabinosyl-4-pyridone (XII-583).**[617]

The “1-deazauridine” **(XU-587)** has been prepared from **3-bromo-2,6-di-**benzyloxypyridine by means of conversion to the 3-pyridyllithium and then to the di-3-pyridylcadmium **(XU-584)**. Treatment of **XII-584** with 1-chloro-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose gives a **2,6-dibenzyloxy-3-(D**-ribofuranosyl)-pyridine **(MI-585)** and the benzylidene derivative **(MI-586)**. Hydrogenolysis of XII-585 gives a **3-ribosyl-2,6-dihydroxypyridine (XII-587).**

The cadmium derivative **MI-584** is converted to a 2′-deoxyribofuranoside **(MI-588)** by **a** similar procedure beginning with **3,5-di-p-toluyl-2′-deoxy-D-**ribofuranosyl **chloride.**[618]

The configurations of anomers of **N-(5′-toluyl-2′-deoxy-D**-ribofuranosyl)-2-pyridone and the corresponding Odeoxyribofuranosides have been determined from their chemical shifts and coupling **constants.**[619]

The silver salt of 2-pyridone has also been used to prepare **N-(β-D-glucopyranosyl)-2-pyridone**[620] and **N-(5′-deoxy-β-D-ribofuranosyl)-2-pyridone.**[621] Pyridyl ethers have been used to prepare **N-(β-2′-deoxyribofuranosyl)-2-pyridone,**[622] **N-(β-D-glucopyranosyl)-4-pyridone,**[623] and 5-nitro-I-(β-D-gluco-



XII-582

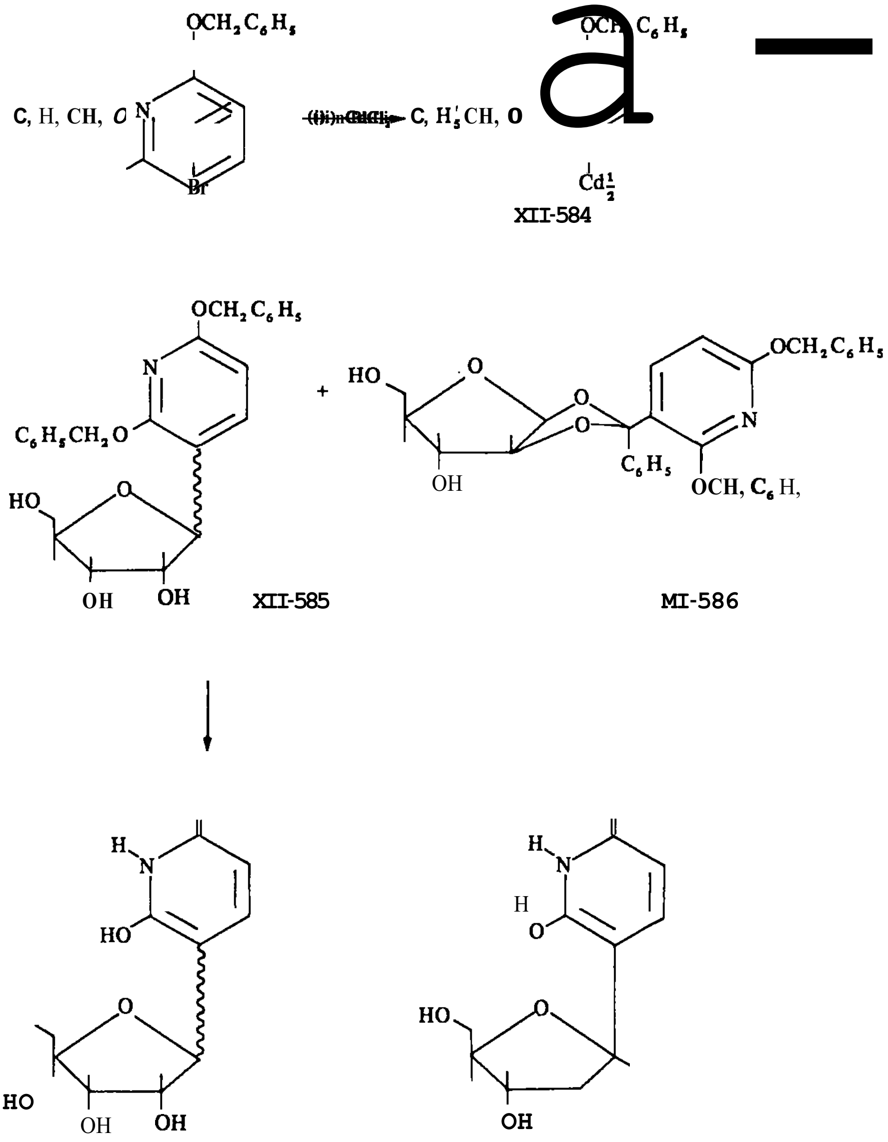
XII-583

pyranosyl)-2-pyridone.[624] The mercuric salt method has been used to prepare *N*-(β-glucopyranosyl)-2-pyridone,[620] *N*-(β-D-ribofuranosyl)-2-pyridone,[625] and *N*-(β-2-deoxyribofuranosyl)-2-pyridone.[622]

Sodium salts of 2-pyridone and of a number of 3- and 5-substituted 2-pyridones and 3,5-disubstituted-2-pyridones when treated with tetra-*O*-acetyl-α-D-glucopyranosyl bromide in acetone give both the O- and *N*-β-glucosides.[624, 626]

Blocked pyridine nucleosides have been phosphorylated with β-cyanoethyl phosphate and dicyclohexylcarbodiimide,[615, 625, 627] diphenyl phosphorochloridate,[615, 628] and with triethyl phosphate followed by oxidation.[627]

N-(β-D-Ribofuranosyl)-2-pyridone 5′-diphosphate (XI-590) has been prepared from *N*-(2′,3′-*O*-ethoxymethylene-β-D-ribofuranosyl)-2-pyridone by phosphorylation with triimidazoyl phosphate to give XII-589, which is treated with bis(tributylammonium) orthophosphate and deblocked with hydrochloric acid.[628] The synthesis of *N*-(3′-*O*-phosphoryl-β-D-ribofuranosyl)-2-pyridone (3′ → 5′) uridine has been reported.[627]



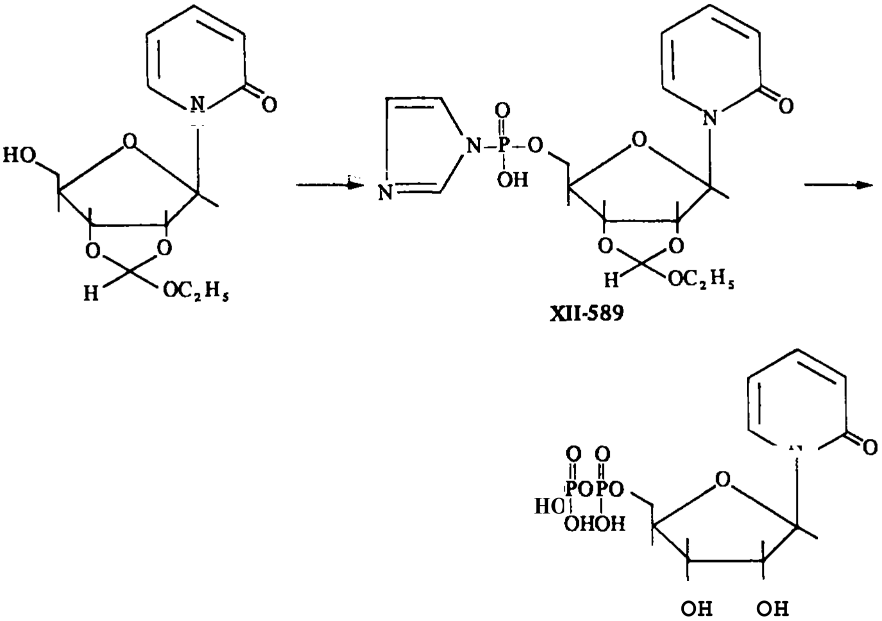
XII-584

XII-585

MI-586

MI-587

MI-588



XII-589

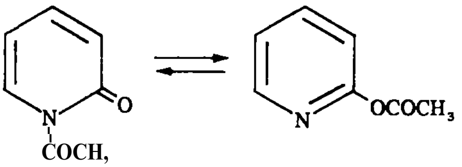
XII-590

C. *O*- and *N*-Acylation

Esters of pyridinols and pyridones are readily prepared by conventional procedures, although early investigators experienced some difficulty in the preparation of esters of 2- and 4-pyridones because of their reactivity, particularly their susceptibility to hydrolysis.[629] *N*-Acylated pyridones have been elusive until recently.

It has been suggested that *N*-acylations have often been overlooked and that *N*-acylations of 2-pyridones may be general but that rapid rearrangement of the *N*- to the *O*-acylpyridine occurs.[630]

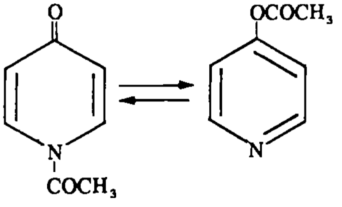
N-Acetyl-2-pyridone (XU-591) was first prepared by acetylation of the thallium(I) salt of 2-pyridone that gives both MI-591 and 2-acetoxypyridine.



MI-591

The reaction product contains approximately 40% of **XII-591** at -40"; at ambient temperatures the mixture is almost entirely 2-acetoxypyridine (approximately 90%).[631] Treatment of 2-pyridone with acetyl chloride in the presence of a tertiary amine catalyst gives a 46:54 mixture of 2-acetoxypyridine and *N*-acetyl-2-pyridone (**MI-591**). After 24 hours in dimethyl sulfoxide, the mixture contains 92% of 2-acetoxypyridine. This *N* → O migration is accelerated by 2-pyridone.[632]

Acetylation of 4-pyridone or its thallium salt with acetic anhydride gives *N*-acetyl-4-pyridone (**XII-592**).[633] Earlier this product had been described as 4-acetoxypyridine.[634,635] In methylene chloride, **MI-592** equilibrates with



XII-592

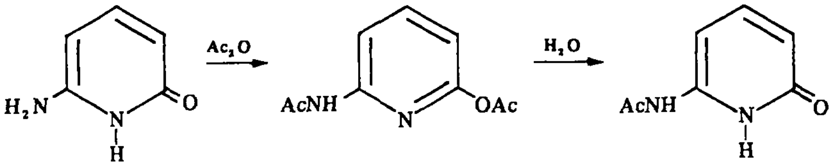
4-acetoxypyridine in the ratio 53:47.[633] 4-Pyridyl benzoate, however, exists entirely in this form in methylene chloride.[633] The isomeric pyridyl benzoates are prepared conveniently from benzoyl chloride and the pyridinol by boiling in chloroform.[636]

2- And 3-acetoxypyridine have been examined as potential acetylating agents.[637] Generally 2-acetoxypyridine gives better yields with the amines and phenols surveyed. *n*-Butyl alcohol is acetylated in 92% yield after 3 hours with 2-acetoxypyridine in tetrahydrofuran at ambient temperatures, but requires 7 hours under reflux (93%) with 3-acetoxypyridine in tetrahydrofuran.

3-Acetoxypyridine and benzoic acid in boiling xylene give 3-benzoyloxypyridine in 85% yield.[637] 2-Butyroxypyridine is prepared in 80% yield from n-butyric acid and 2-acetoxypyridine in xylene by distilling off the acetic acid as it is formed. 2-Benzoyloxypyridine is formed in 63% yield by this method. The corresponding acylthiopyridines are prepared from 2-acetylthiopyridine.[638] These reactions are subject to considerable steric effects.

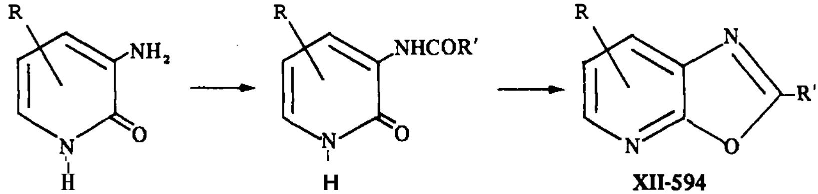
2-Pyridyl methacrylate has been prepared from the sodium salt of 2-pyridone and methacryl chloride and has been polymerized by radicals but not by anions.[639] 2-Pyridone and phosgene (1:4) in dry tetrahydrofuran or benzene with or without pyridine form di-(α-pyridyl)carbonate, which is a useful reagent for the formation of the benzoate and the monophenyl phosphate of 2-pyridone.[640]

2-Amino-6-pyridone and acetic anhydride in water give the diacetylated material (**XII-593**), which can be hydrolyzed to give 2-acetamido-6-pyridone; this can be *O*-alkylated conveniently.[641]



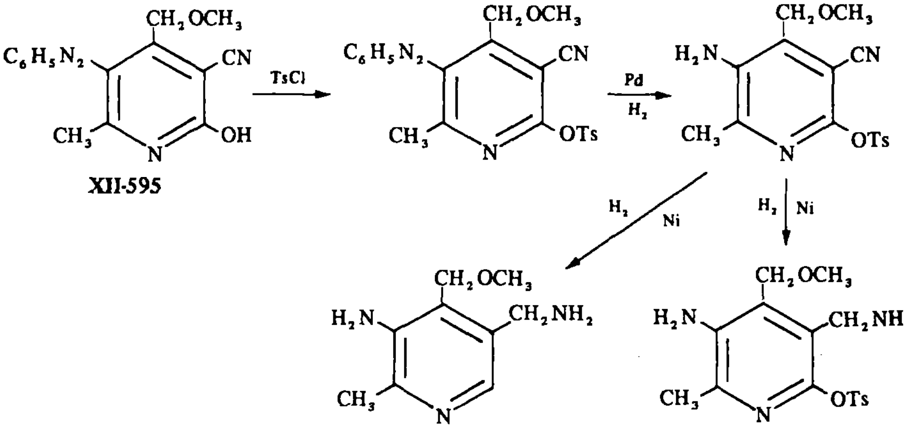
XII-593

2-Alkyl(or aryl)oxazolo[5,4-*b*-]pyridines (**MI-594**) are formed by acylation of 3-amino-2-pyridones followed by distillation from P_2O_5.[556,642,643] **6-Bromo-2-phenyloxazolo[5,4-*b*]pyridine** (**XII-594**; R = **6-Br**, R' = C_6H_5) is prepared directly from 3-amino-5-bromo-2-pyridone and benzoic **anhydride**.[643]



XII-594

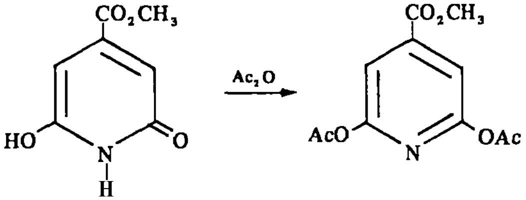
Treatment of **5-cyano-4-methoxymethyl-2-methyl-3-phenylazo-6-pyridone** (**XII-595**) with tosyl chloride in acetone-pyridine gives the tosylate; this can be hydrogenated in **two** steps to **3-amino-5-aminomethyl-4-methoxymethyl-2-methylpyridine** (XII-596) or to **3-amino-5-aminomethyl-4-methoxymethyl-2-methyl-6-tosyloxypyridine** in the presence of Raney Nickel, depending on conditions.[52]



XII-595

XII-596

4-Hydroxy-2-pyridones form 4-acetoxy-2-pyridones readily. 4-Acetoxy-1,6-dimethyl-2-pyridone[644] and 4-acetoxy-5-acetyl-6-methyl-2-pyridone[87] have been prepared employing acetic anhydride. 4-Acetoxy-6-methyl-1-phenyl-2-pyridone has been formed with phosphoryl chloride and acetic acid.[645] Methyl citrazinate (XI-597) and acetic anhydride give methyl 2,6-diacetoxyisonicotinate.[507]



XII-597

3-Nitro-4-pyridone and 3-amino-4-pyridone are N-acylated by ethyl chloroformate in aqueous sodium carbonate.[586]

Reactions of 3-pyridinols with organic and inorganic acid derivatives to give esters are well known.[646] Recently 2-nitro-3-pyridinol was converted to 3-acetoxy-2-nitropyridine with acetyl chloride in benzene-pyridine. 6-Nitro-3-pyridinol and acetyl chloride in acetone containing sodium carbonate gave the acetate quantitatively.[647]

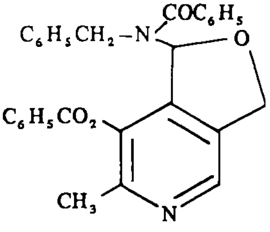
3-Pyridinol or 2-nitro-3-pyridinol and chlorosulfonic acid in chloroform containing dimethylaniline give the 3-pyridyl bisulfate. 2-Pyridone gives the unstable *N*-sulfonate and 4-pyridone gives both the *N*-sulfonate and the 4-pyridyl bisulfate, all isolated as their potassium salts.[648] 3-Methanesulfonoxypyridine is prepared from 3-pyridinol and methanesulfonyl chloride in chloroform containing 2,6-lutidine.[649]

Pyridoxylidenebenzylamine (MI-598) and benzoyl chloride in ether-pyridine form 7-benzoyloxy-1-(*N*-benzylbenzamido)-6-methylfuro[3,4-*c*] pyridine (MI-599). However, treatment of MI-598 with acetic anhydride in pyridine gives *N*-(α^4-acetoxy-3,O^5-diacetylpyridoxyl)-*N*-acetylbenzylamine.[650]

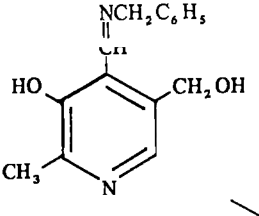
3,5-Pyridinediol and acetic acid containing sodium acetate form the diacetate. Benzoylation is accomplished with benzoyl chloride *in* pyridine.[301]

3-Pyridinol and benzyl chloroformate in tetrahydrofuran give benzyl-3-pyridyl carbonate (XII-600), which has been used to introduce the *N*-benzyloxycarbonyl group into amino acids. It reacts with L-lysine in waterdimethylformamide to give ε-(*N*-benzyloxycarbonyl)-L-lysine (33%). Somewhat higher yields are obtained from benzyl 8-quinolyl carbonate and 4-nitrobenzyl-8-quinolyl carbonate employing 3-pyridinol as a catalyst.[651]

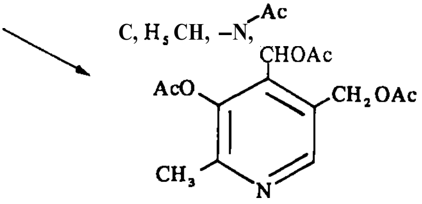
N-Benzyloxycarbonylamino acids and 3-pyridinol form 3-pyridyl esters in the presence of dicyclohexylcarbodiimide. The esters in ethyl acetate are treated with an amino acid ethyl ester hydrochloride and triethylamine to give peptides

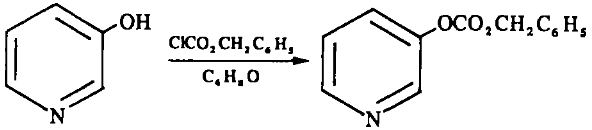


XII-599

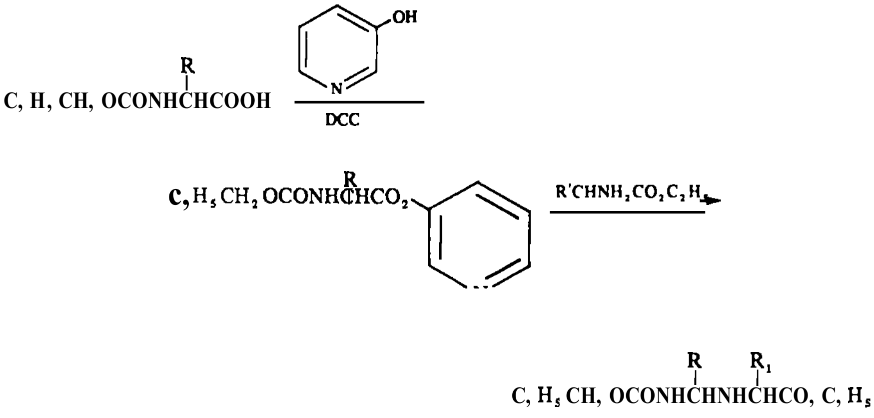


XII-598





XII-600

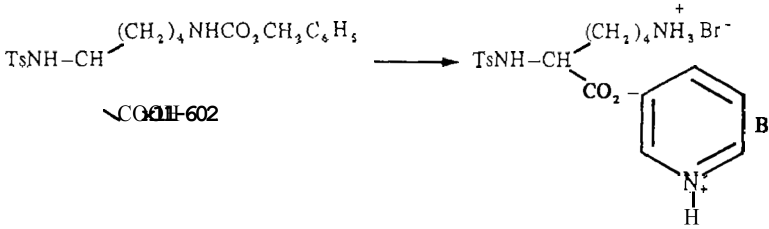


$$C_6H_5CH_2OCONH\overset{R}{C}HCOOH \xrightarrow[\text{DCC}]{\text{3-pyridinol}} C_6H_5CH_2OCONH\overset{R}{C}HCO_2\text{-}(3\text{-pyridyl}) \xrightarrow{R'CHNH_2CO_2C_2H_5} C_6H_5CH_2OCONH\overset{R}{C}HNH\overset{R_1}{C}HCO_2C_2H_5$$

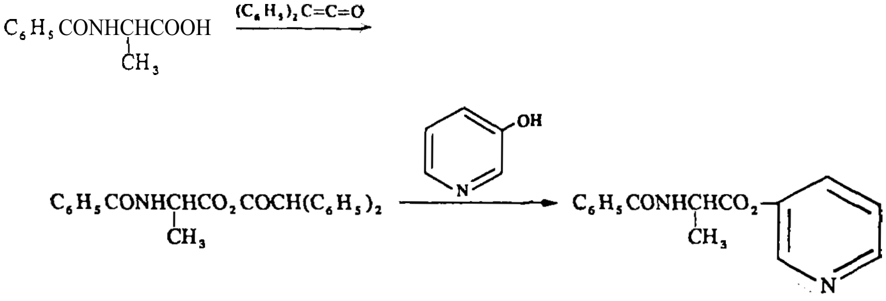
XII-601

(XII-601).[652,653] Similarly, 2-methyl-4-nitro-3-pyridinol, 2,6-dimethyl-4-nitro-3-pyridinol, 2-isobutyl-6-methyl-4-nitro-3-pyridinol, and 2-methyl-6-(*N*-methylpiperidyl)-3-pyridinol have been converted to *N*-benzyloxycarbonylamino acid esters for use in peptide synthesis.[654]

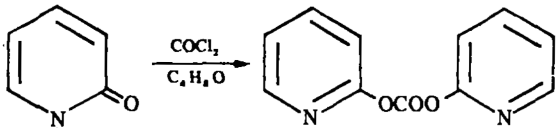
ε-(*N*-Benzyloxycarbonyl)-α-*N*-toluene-*p*-sulfonyl L-lysine (**XII-602**), 3-pyridinol, and *N*,*N*'-dicyclohexylcarbodiimide in tetrahydrofuran give the pyridyl ester, which can be converted to the hydrobromide by hydrogen bromide in nitromethane.[655] Esterification of the *N*-tosyl derivatives of phenylalanine, *N*-methylphenylalanine, and L-valine with 3-pyridinol in the presence of *N*,*N*'-dicyclohexylcarbodiimide yields 3-pyridyl esters that can be isolated as their hydrochlorides.[656]

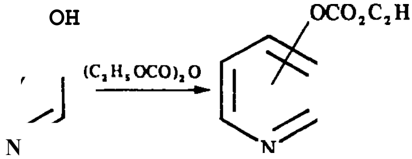

XII-602

The 3-pyridyl ester of *N*-benzoyl-DL-alanine (XII-603) has been prepared from a mixed anhydride and 3-pyridinol.[657]


XII-603

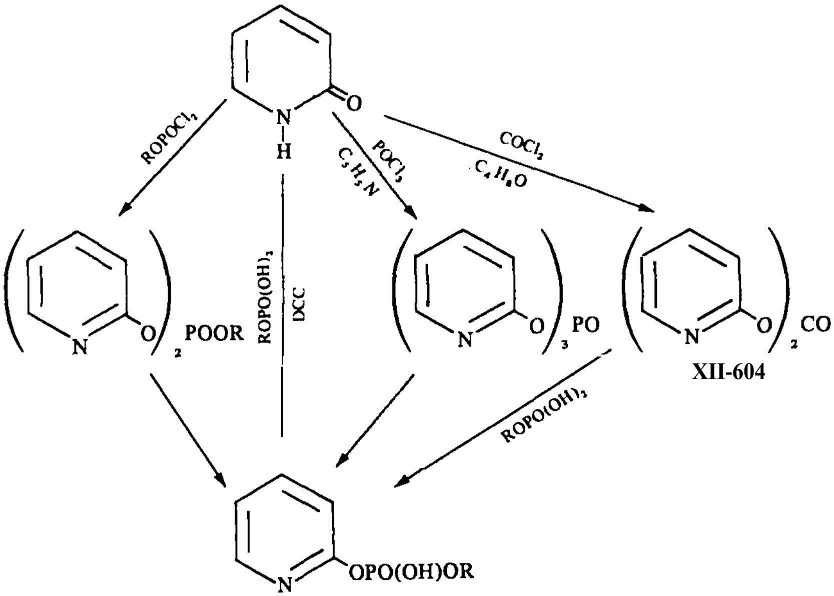
2-Pyridone and phosgene in tetrahydrofuran give di-(2-pyridyl) carbonate (**XII-604**).[658] Ethyl pyrocarbonate and pyridinols in aqueous ethanol give the corresponding pyridyl ethyl carbonates.[659]


XII-604



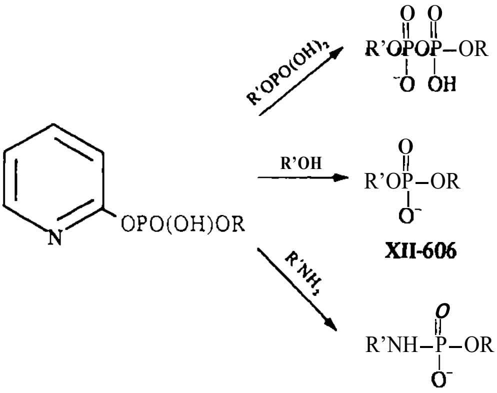
D. *Pyridyl Phosphates*

α-Pyridyl phosphates (XII-605; R = thymyl, benzyl, β-naphthyl, phenyl, p-chlorophenyl) can be prepared from di-(2-pyridyl) carbonate (XII-604) and monoesters of phosphoric acid and isolated as their cyclohexylammonium or sodium salts. Some of these mixed phosphates (XII-605; R = C_6H_5, p-ClC_6H_4, C_2H_4CN) can also be prepared from 2-pyridone and aryl phosphorodichloridates or from 2-pyridone and monoesters and N,N'-dicyclohexylcarbodiimide (DCC). 2-Pyridone and phosphorus oxychloride and pyridine give the tripyridyl phosphate, which is readily hydrolyzed to the dipyridyl phosphate (XII-605, R = $-C_5H_4N$).[658]



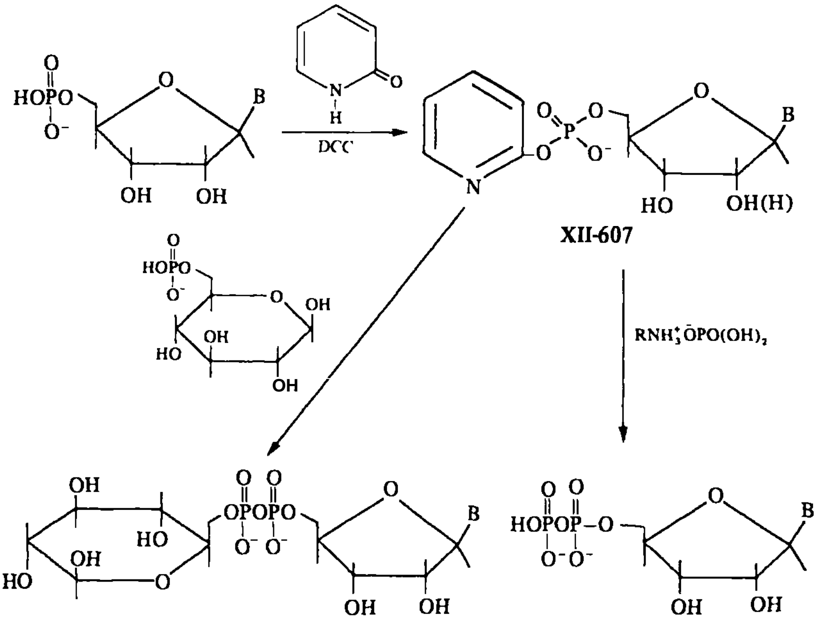
XII-605

Because of the reactivity of the α-pyridyl moiety, phosphates of structure XII-605 are convenient reagents for the formation of derivatives of phosphoric acid. They react with monoesters of phosphoric acid to give pyrophosphates, with alcohols to form dialkyl phosphates (XII-606), and with amines to form monoalkyl phosphoramides.[660]



XII-606

α-Pyridyl esters of nucleoside 5′-phosphates (XII-607) can be prepared from the 5'-phosphate and 2-pyridone using **DCC**. The α-pyridyl ester **XII-607** and monose phosphate **give** the unsymmetrical *P*,*P*′-pyrophosphate diesters **(XII-608)**. With phosphoric acid salts the pyrophosphate XII-609 is formed.[661]

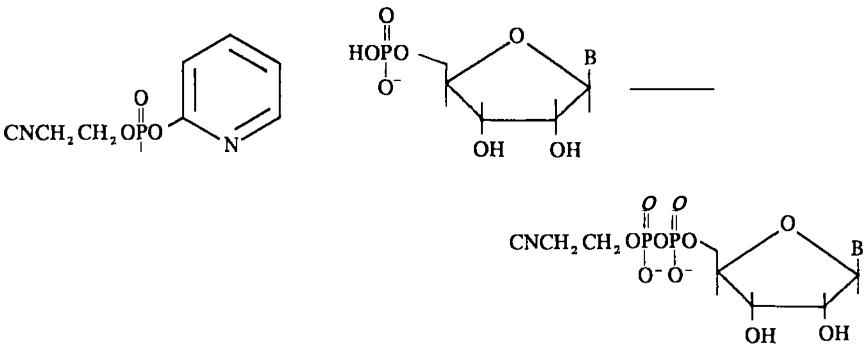


XII-607

XII-608

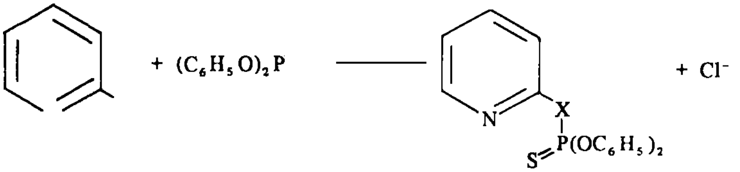
XII-609

β-Cyanoethyl 2-pyridyl phosphate and uridine-, cytidine-, and adenosine-5′-phosphates give the *P,P′*-pyrophosphate diesters **(XII-610)** which can be converted to the pyrophosphate with base.[662]



XII-610

2-Pyridone and 2-pyridinethione anions react with *O,O′*-diphenylphosphorochloridothioate to give *O,O′*-diphenyl *O*-2-pyridyl phosphorothioate **(XII-611, X = O)** and *O,O′*-diphenyl S-2-pyridyl phosphorodithioate **(XII-611, X = S)**.



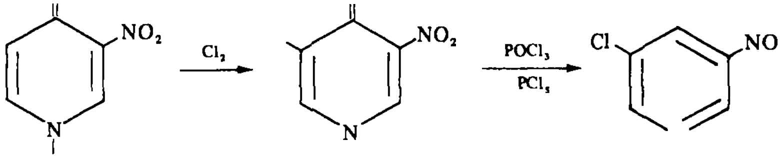
XII-611

Phosphates and phosphorothioates are insensitive to anion polarizability in this reaction. 2-Pyridone is a better nucleophile than 2-pyridinethione (relative rates = 28:1). The rates of these reactions have been correlated with acidities for several carboxylic acids, phenols, and thiophenols.[663]

E. *Displacement by Halogen*

2- And 4-halopyridines are often prepared from the corresponding pyridones (Tables **XII-15** and XII-16). 3-Pyridinols, like phenols, are unreactive toward direct displacement, but 3- and 5-halopyridines can be obtained by direct halogenation. Di- and trihalopyridines can be prepared by combinations of these procedures.[98, 287, 291, 294, 664, 665] For example, **3,4-dichloro-5-nitro-**

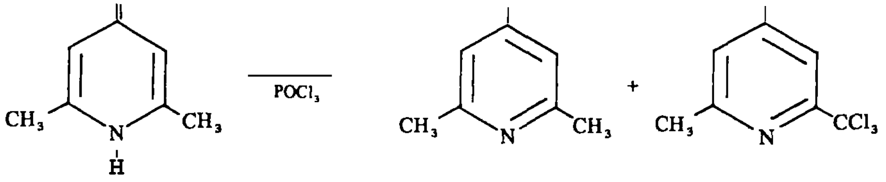
pyridine **(XII-612)**, an intermediate used in the preparation of γ-carbolines, has been prepared from 3-nitro-4-pyridone by chlorination to give 3-chloro-5-nitro-4-pyridone, which is then treated with phosphoryl chloride and phosphorus pentachloride.[664]



XII-612

Direct displacement of hydroxyl by halogen is accomplished with phosphoryl chloride,[34, 97, 98, 291, 305, 338, 502, 510, 666-668] phosphorus pentachloride,[37, 293, 669] a mixture of phosphoryl chloride and phosphorus pentachloride,[53, 282, 290, 291, 294, 306, 664, 665, 670-675] phosphorus pentachloride and phosphorous trichloride,[102] phosphoryl chloride or thionyl chloride in dimethylformamide,[676] phosphoryl chloride with dimethylaniline,[98] and phenylphosphoric dichloride.[672] 2-Pyridones are converted to 2-bromopyridines with phosphorus pentabromide.[287, 290, 291]

In the conversion of 2,6-dimethyl-4-pyridone to 4-chloro-2,6-lutidine a small amount of 4-chloro-2-methyl-6-trichloromethylpyridine **(MI-613)** is isolated.[670]

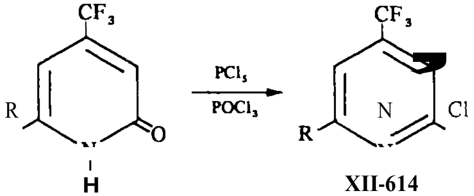


XII-613

3-Cyano-6-substituted-4-trifluoromethyl-2-pyridones are not converted to the 2-chloro derivatives under a number of conditions, but several 6-substituted-4-trifluoromethyl-2-pyridones do react to give **XII-614**.[672]

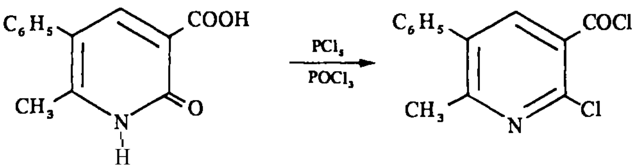
Under conditions where 3-carboxy-6-methyl-5-phenyl-2-pyridone **(XII-615)** forms a 2-chloro-3-chlorocarbonylpyridine, only the carboxy function of **XII-616** reacted with phosphorus pentachloride-phosphorus oxychloride to give **MI-617**.[53]

Heating ammonium salts of 4-alkyl-3,5-dicyano-6-hydroxy-2-pyridone and phosphorus oxychloride under pressure at 220" is required to form 4-alkyl-2,6-dichloro-3,5-dicyanopyridines **(XII-618)**. The salts are also converted to **XII-618** by heating with phenylphosphonic dichloride at 200°.[111]

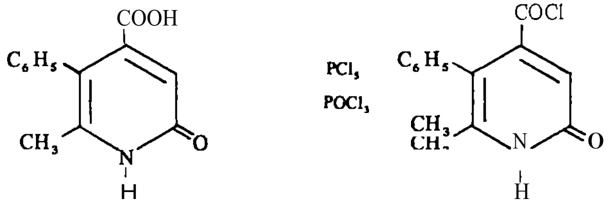


XII-614

R = C, H,, 2-C_4H_3S, CH,



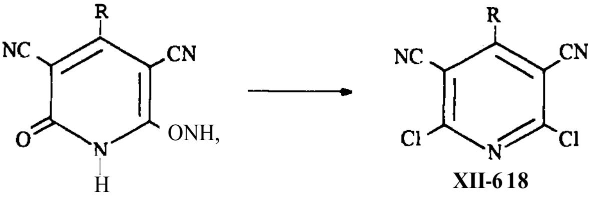
XII-615



XII-616

XII-617

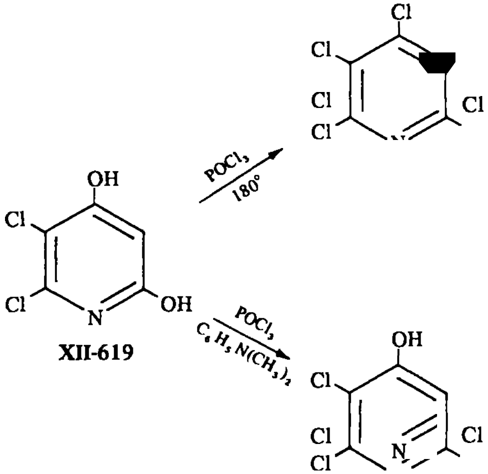
4-Hydroxy-2-pyridone is converted to 2,4-dichloropyridine[502] and 5,6-dichloro-2,4-pyridinediol (**MI-619**) is converted to 2,3,4,6-tetrachloropyridine by phosphoryl chloride. In the presence of dimethylaniline. **XII-619** is converted to 2,3,6-trichloro-4-pyridinol.[98]



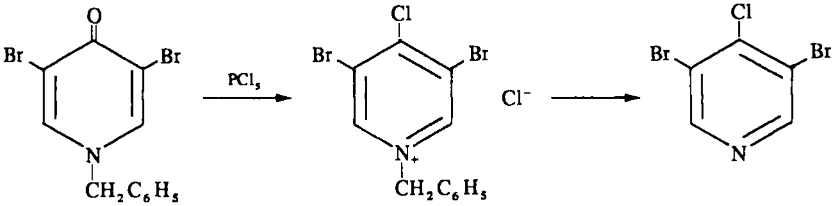
XII-618

R = CH_3, C_2H_5, $CH_2CH_2CH_3$, C_6H_{13}

N-Alkylpyridones are demethylated when undergoing substitutions of this kind or are converted to pyridinium salts.[677] For example, *N*-benzyl-3,5-dibromo-4-pyridone (**MI-620**) and phosphorus pentachloride in toluene form 3,5-dibromo-4-chloropyridine and a small amount of N-benzyl-3,5-dibromo-4-chloropyridinium chloride.' [79] *N*-Methyl-5-nitro-2-pyridone and thionyl chloride in dimethylformamide give 2-chloro-1-methyl-5-nitropyridinium chloride.[676]



XII-619



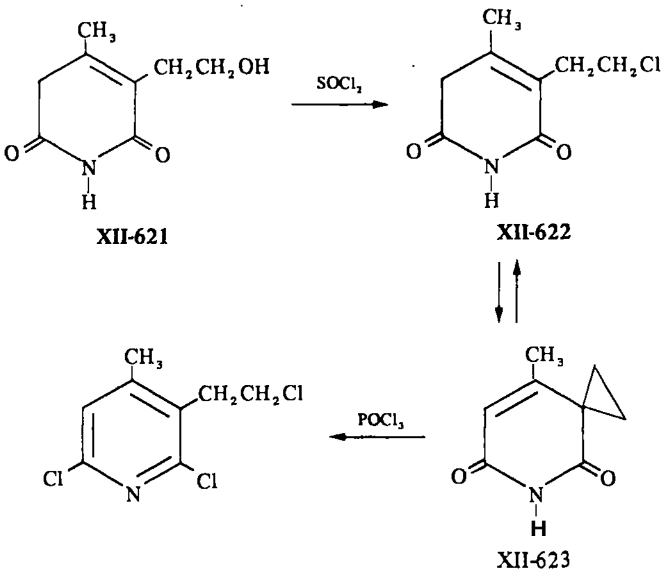
XII-620

4-Chloro-1,6-dimethyl-2-pyridone is, however, formed from 4-hydroxy-1,6-dimethyl-2-pyridone and phosphoryl chloride-phosphorus pentachloride[306] and 3-carbomethoxy-4,6-dichloro-1-methyl-2-pyridone can be formed from 3-carbomethoxy-4,6-dihydroxy-1-methyl-2-pyridone.[169]

Treatment of 3-(β-hydroxyethyl)-4-methyl-2,6-pyridinediol (**MI-621**) with thionyl chloride gives 3-(β-chloroethyl)-4-methyl-2,6-pyridinediol (**XII-622**), which cyclizes to the spirane **XII-623** with triethylamine. **XII-623** forms 2,6-dichloro-3-(β-chloroethyl)-4-methylpyridine with phosphoryl chloride or is reconverted to **XII-622** with hydrochloric acid.[510]

N-Methyl- and *N*-ethyl-4-chloro-2,3-dihydro-6-oxofuro[3,2-*c*]pyridine (**XII-624**) and phosphorus oxychloride give 3-(β-chloroethyl)-2,4,6-trichloropyridine in 68% and 71% yields, respectively.[589]

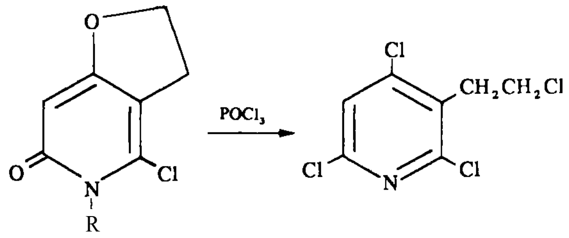
N-Substituted-2-pyridones can be used as substrates for ring closure to a number of polyheterocyclic systems, as an alternate to the Pschorr cyclization[678, 679] or to the cyclizations of the corresponding *N*-alkyl-2-halopyridinium halides. 2-Substituted pyridines (**MI-625**; X = Cl, Br, OC_2H_5) and 3-(2-bromoethyl)indole give *N*-[2-(3-indolyl)ethyl]-2-substituted pyridinium bromide



XII-621

XII-622

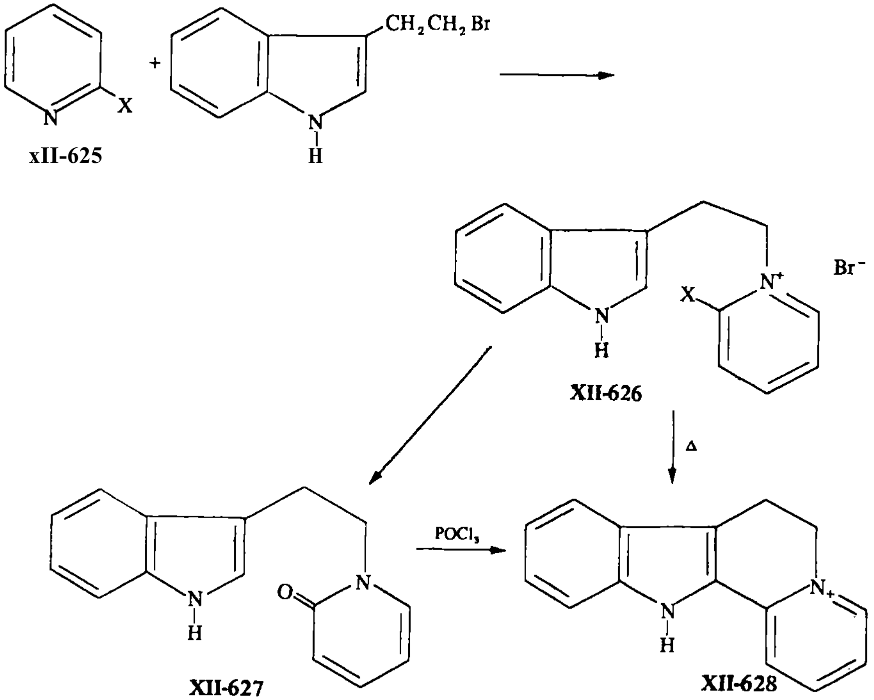
XII-623



XII-624

(XII-626), hydrolysis of which gives the pyridone **(XI-627)** in 80% yield. Ring closure of **XII-626** **(X** = Br) by fusion in an oil bath or by treatment of **XI-627** with phosphorus oxychloride gives 6,7-dihydro-12*H*-indolo[2,3-*a*] quinolizinium salts **(XI-628)**. In this series the best yields are obtained in the direct sequence **XII-626** **(X** = Br) → **XII-628**.[680]

A reaction between *N*-arylethyl-2-pyridones **(MI-629)** and phosphorus oxychloride was originally reported to give quinolizinium salts.[681] Reports that the 5-carbethoxy-[349] and 5-ethyl-[682] derivatives of **XII-629** do not cyclize led to reinvestigations of earlier work, which have shown that quinolizinium salts were not formed, but that this reaction gives N-arylethyl-2-chloropyridinium salts instead.[341,683,684] Additional conversions of pyridones to halopyridines are listed in Tables **XII-15** to **XII-18**.

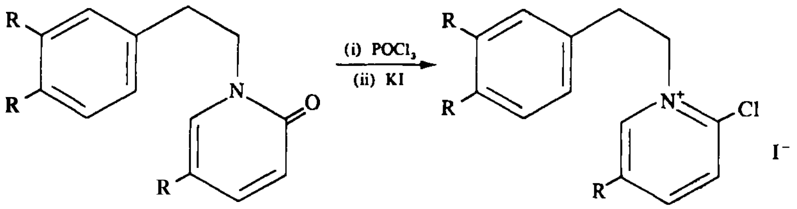


xII-625

XII-626

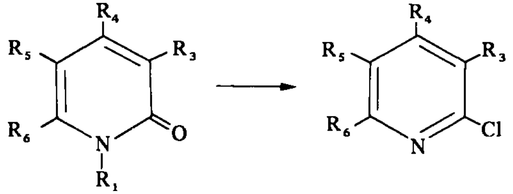
XII-627

XII-628



XII-629

TABLE XII-15. Conversion of 2-Pyridones to 2-Chloropyridines

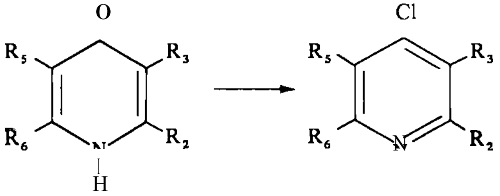


R_1	R_3	R_4	R_5	R_6	Reagent	% Yield	Ref.
	CN	CX_3	NO_2	CH_3	$PCl_5/POCl_3$	54	674
			CH_3		$PCl_5/POCl_3$		282
	NO_2	CH_3	NO_2		$PCl_5/POCl_3$	27	675
	NO_2		NO_2	CH_3	$PCl_5/POCl_3$	83	675
		CF_3		C_6H_5	$PCl_5/POCl_3$	88	672
		CF_3		CH_3	$PCl_5/POCl_3$	66	672
		CF_3		2-C_4H_3S	$C_6H_5POCl_2$	80	672
		CF_3		2-C_4H_3S	$PCl_5/POCl_3$	[a]	672
	Cl	Cl	Cl		PCl_5	92	669
	Cl	Cl	CH_3	CH_3	PCl_5	96	37
	CH_3	$N(C_2H_5)_2$	C_6H_5		PCl_5/PCl_3	75	102
	NO_2		Br		PCl_5/PCl_3	95	665
	NO_2				$POCl_3$/DMF	97	676
			NO_2		$POCl_3$/DMF	95	676

CH_3			NO_2		$SOCl_2$/DMF	40		676
	Br		NO_2		$POCl_3/PCl_5$	78		290
	Cl		NO_2		$POCl_3/PCl_5$	86		291
	NO_2		Cl		POCl ,	60		291
	NO_2	C_6H_5		CH_3	POCl,	58		666
							mixture	
		C_6H_5	NO_2	CH_3	$POCl_3$	58		666
	NO_2		NO_2		POCl, $/PCl_5$	48		673
	NO_2	CH_3		CH_3	PCl_5			288
		CH ,	NO_2	CH_3	PCl_5			288
	NO_2		NO_2		$POCl_3$/DMF	96		676
	I		NO_2		$POCl_3/PCl_5$	86		287
$C_6H_5CH_2CH_2$					POCl,			338
	NO_2	NH_2			$POCl_3$	89		305
	COOH		C_6H_5	CH_3	$POCl_3/PCl_5$			53
	NH_2			n-C_3H_7	Pocl,			150
	CN	CF_3	NO_2	CH_3	PCl_5			56
		CH_3		Cl	POCl,	68		8
		C_6H_5		Cl	POCl,	88		8
		3,4-(CH_2),-		Cl	Pocl,	78		8

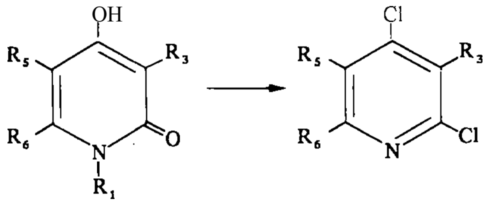
‘Treatment of 6-(2-thienyl)-4-trifluoromethyl-2-pyridone with PCl, $/POCl_3$ gave 6-(5-chloro-2-thienyl)-4-trifluoromethyl-2-pyridone (25%) and 2-chloro-6-(5-chloro-2-thienyl)-4-trifluoromethylpyridine (18%)

TABLE XI-16. Conversion of 4-Pyridones to 4-Chloropyridines



R_2	R_3	R_5	R_6	Reagent	% Yield	Ref.
CH_3	Cl	NO_2	CH_3	$PCl_5/POCl_3$	92	294
CH_3	NO_2		CH_3	$PCl_5/POCl_3$	88	294
	Cl	NO_2		$PCl_5/POCl_3$	68	664
	NO_2	NO_2		$POCl_3$/DMF	95	616
	NO_2			$POCl_3$		668
CH_3		CH_3		POCI, $/PCl_5$		297
COOH		CH_3		$SOCl_2$		297
CH_3		NO_2		PCl_5	35	293
$C(CH_3)_3$			$C(CH_3)_3$	POCI, $/PCl_5$		671
CH_3	NO_2		CH_3	$POCl_3$	61	670
CH_3			CH_3	POCI, $/PCl_5$	68	670

TABLE XI-17. Conversion of 2,4-Pyridinediols and 4-Hydroxy-2-pyridones to 2,4-Dichloropyridines

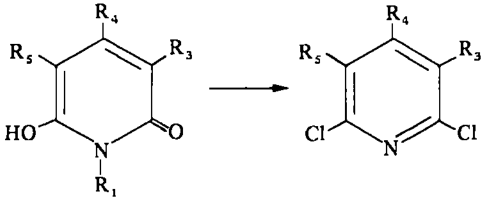


R_1	R_3	R_5	R_6	Reagent	% Yield	Ref.
	NO_2		$n\text{-}C_3H_7$	POCI,	50^a	150
		$CO_2C_2H_5$		POCI,		667
		CH_3	Cl	$POCl_3$	58	97
	.	Cl	Cl	$POCl_3$		98
		Cl	Cl	$POCl_3/C_6H_5N(CH_3)_2$		98
CH_3			CH_3	POCI, $/PCl_5$	b	306
			CH_3	POCI,	65	502
		CH, CH, Cl		POCI,	64.5	589

UForty-five percent of 4-chloro-3-nitro-6-*n*-propyl-2-pyridinol was obtained under mild conditions.

[b] Reaction occurred only at the 4-position to give 1,6-dimethyl-4-chloro-2-pyridone.

TABLE MI-IS. Conversion of 2,6-Pyridinediols and *N*-Substituted Derivatives *to* 2,6-Dichloropyridines



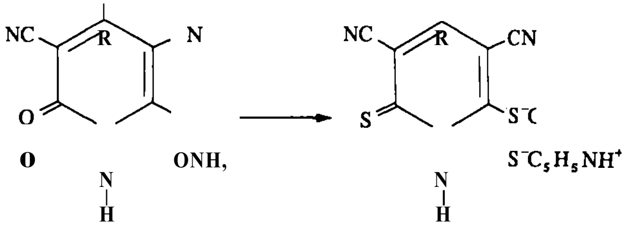
R_1	R_3	R_4	R_5	Reagent	% Yield	Ref.
		NH_2		$POCl_3$	60	34
C_6H_5	$CONHC_6H_5$	OC_6H_5		$POCl_3$	90[a]	172
C_6H_5	$CONHC_6H_5$	$OC_6H_4CH_3$-*o*		$POCl_3$	50[b]	173
H	CH_3	Cl	Cl	PCl_5	96	7

[a] Product was 6-chloro-4-phenoxy-1-phenyl-2-pyridone-3-carboxanilide.

[b] Product was 6-chloro-1-phenyl-4-(*o*-tolyloxy)-2-pyridone-3-carboxanilide.

F. *Miscellaneous Replacements*

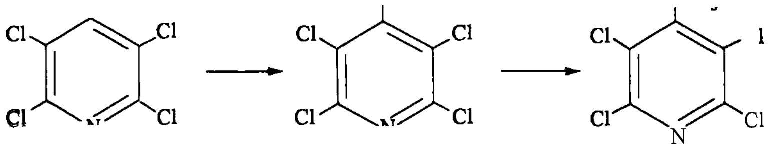
Pyridinols and pyridones and phosphorus pentasulfide give predictable products. 4-Pyridinol and phosphorus pentasulfide in pyridine give 4-pyridinethione,[685] while 2,6-di-*t*-butyl-4-pyridone gives bis[4-(2,6-di-*t*-butylpyridinyl)] sulfide.[671] *N*-Alkyl-3,5-dibromo-2,6-dimethyl- and *N*-alkyl-3,5-dibromo-2,6-diphenyl-4-pyridone are converted to the corresponding 4-pyridinethiones.[118] Ammonium salts of 4-alkyl-3,5-dicyano-6-hydroxy-2-pyridones and phosphorus pentasulfide in xylene and pyridine form pyridinium salts of the corresponding 6-mercapto-2-pyridinethiones(XII-630).[111]



XII-630

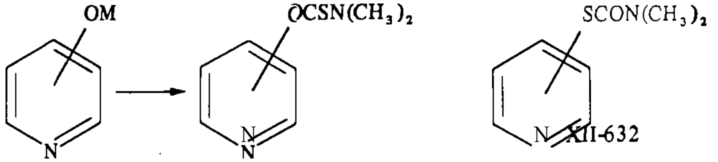
Pentachloropyridine and phosphorus pentasulfide give 4-mercaptotetrachloropyridine (XII-631), which can be methylated readily with dimethylsulfate in aqueous alkali.[686]

A method has been described for the conversion of phenols to thiophenols employing dimethylthiocarbamoyl chloride. 2- And 4-pyridone and 3-pyridinols were typical among twenty-nine compounds studied. The carbamyl chloride and



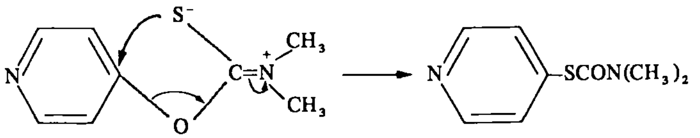
X11-631

the sodium salt of 2-pyridone or 3-pyridinol, or the silver salt of 4-pyridone in dimethylformamide gives the *O*-pyridyl dimethylthiocarbamate. Thermal rearrangement gives the *S*-pyridyl dimethylthiocarbamates **(XII-632)**.[687]



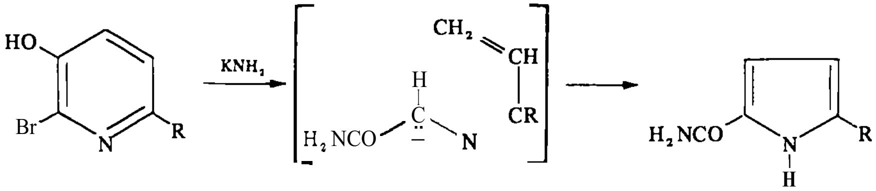
XII-632

The boron trifluoride and hydrogen chloride salts of 2- and 4-pyridyl *N*,*N*'-dimethylthiocarbamate rearrange at room temperature. The lower temperature requirement for phenols substituted with electron withdrawing groups supports a mechanism involving nucleophilic attack by sulfur **(XII-633 → XII-634)**.[687] When 4-pyridone is heated with sodium bisulfite a small amount of 4-pyridinesulfonic acid is formed.[685]



XII-633 XII-634

Ring contractions are sometimes observed when halopyridines or halopyrimidines are treated with potassium amide. 2-Bromo-3-pyridinol **(XII-635**, R = **H)** and an excess of potassium amide in liquid ammonia give pyrrole-2-carboxamide **(XI-636**, R = **H)**. 2,6-Dibromo-3-pyridinol **(XII-635**, R = Br) forms 5-bromo-pyrrole-2-carboxamide **(XII-636**, R = **Br)**.[688]

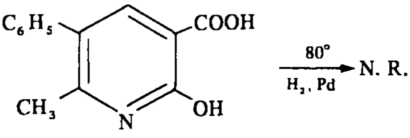


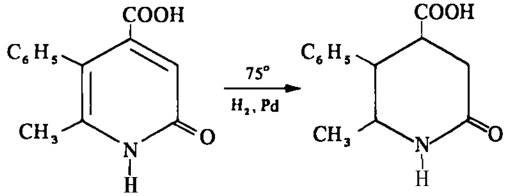
XII-635 XII-636

2. Involving the Nucleus

A. *Reduction*

2-Pyridones are usually hydrogenated employing a Raney Nickel catalyst at elevated temperatures and pressures, most often with ethanol as the solvent, although palladium and platinum catalysts have been used (Table XI-19). At temperatures that are higher than optimum for piperidone formation, piperidines are formed.[283] N-Benzyl-2-pyridone gives *N*-cyclohexylmethyl-2-piperidone (81%) when hydrogenated at 100 atm and at 150° in ethanol employing a Raney Nickel catalyst, but gives *N*-benzyl-2-piperidone at 50 atm of hydrogen and 70".[689] 6-Methyl-5-phenyl-2-pyridone-3-carboxylic acid is not hydrogenated under conditions where the 4-carboxylic acid **(MI-637)** is reduced to 6-methyl-5-phenyl-2-piperidone-4-carboxylic acid. It was suggested that these properties are a consequence of the pyridinol structure of the 3-carboxylic acid and the pyridone structure of **XII-637**.[53] More direct information is needed to verify this



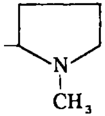


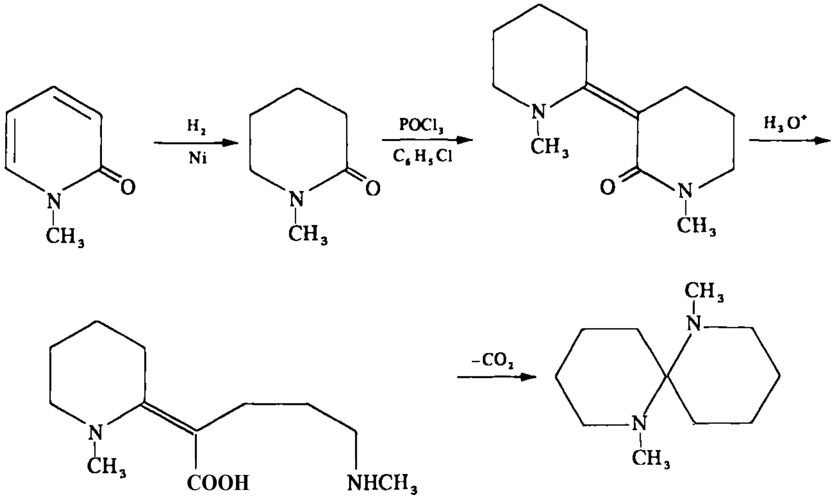
XII-637

conclusion.[489] N-Methyl-2-pyridone has been used for the synthesis of 1,7-dimethyl-1,7-diazaspiro[5,5]undecane **(XI-638)** *via* N-methyl-2-piperidone in 43% overall yield.[692]

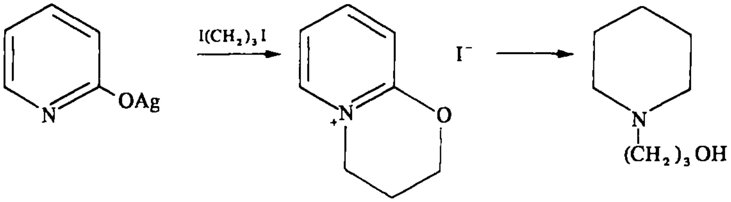
2,3-Dihydro-4*H*-pyrid[2,1-*b*]oxazinium iodide (XII-639), prepared by alkylation of the silver salt of 2-pyridone with trimethylene iodide, is hydrogenated in the presence of platinum to *N*-(γ-hydroxypropyl)piperidine.[554]

TABLE **XII**-19. Hydrogenation of 2-Pyridones to 2-Piperidones

R_1	R_3	R_4	R_5	R,	Catalyst	Temperature	P_{atm}	% Yield	Ref.
H	H	H	H	H	Raney Ni	150	100	72	689
$C_6H_5CH_2$	H	H	H	H	Raney Ni	70	50	80	689
H	CH_3	H	H	H	Raney Ni	200–240	120	80	283
H	H	C_2H_5	H	H	Raney Ni	200–240	120	80	283
H	H	CO_2CH_3	H	H	Raney Ni	260	120	50	283
H	H	COOH	C_6H_5	CH_3	Pd-C	75	45 p.s.i.	100	53
CH_3	H	H	H	H	Raney Ni	50	150	96	692
C_2H_5	CH_3	H	H	H	Raney Ni	150–160	135	64	690
$(CH_2)_2C_6H_3(OCH_3)_2$-3,4	H	H		H	Pt, O-$PdCl_2$	40			339
CH_3	H	H	$(CH_2)_4\underset{\displaystyle CH_3}{\underset{\vert}{N}}COC_6H_5$	H	Raney Ni	−78		85	691
CH_3	H	H	$-CH{=}CH(CH_2)_2\underset{\displaystyle CH_3}{\underset{\vert}{N}}COC_6H_5$	H	Raney Ni	−78		95	691
CH, C, H_4COOH-*p*					Raney Ni	70	50	60	558
$CH_2C_6H_4NH_2$-*p*					Raney Ni	70	50	63	558
CH, C, H, NH, -*m*					Raney Ni	70	50	27	558
					Raney Ni	70	50	10	558
					Raney Ni	70	50	60	558
CH, C, H, Br-*o*					Raney Ni	70	50	40	558
					Raney Ni		atm	83	340



XI1438

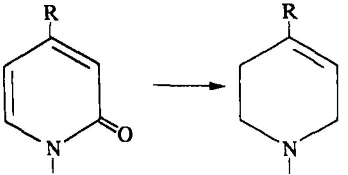


XII-639

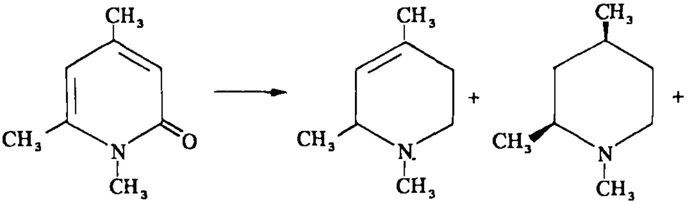
Hydrogenations of 2-aralkyl-3-pyridinols with platinum catalysts give mixtures of products where either or both the pyridyl ring and the phenyl ring are reduced. However, the major product of low pressure, controlled hydrogenation of 2-diphenylmethyl-3-pyridinol at 50" is 2-(α-cyclohexylbenzyl)-3-pyridinol. Hydrogenation of the corresponding methyl ethers, 2-aralkyl-3-methoxypyridines over a platinum catalyst gives cleaner products.[191] 2-Diphenylmethyl-3-pyridinol in dioxane containing Raney Nickel is hydrogenated at 130 to 135° and 125 kg/cm^2 to 2-diphenylmethyl-3-piperidinol (~70%) and smaller amounts of 2-(α-cyclohexylbenzyl)-3-piperidinol and 2-dicyclohexylmethyl-3-piperidinol.[191]

Although early attempts were unsuccessful, it is possible to reduce *N*-methyl-2-pyridones with lithium aluminum hydride and aluminum chloride in tetrahydrofuran or ether, or without aluminum chloride in tetrahydrofuran.[693] N-Methyl-2-pyridone (**MI-640**, R = H) gives 1-methyl-3-piperideine (**XII-641**, R = H) as the major product and 1,4-dimethyl-2-pyridone (XII-640, R = CH$_3$) gives

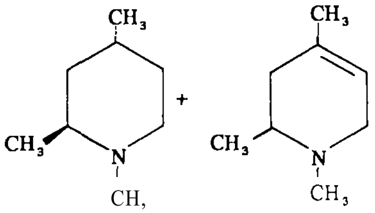
1,4-dimethyl-3-piperideine (XII-641, R = CH_3). However, 1,3-, 1,5-, and 1,6-dimethyl-2-pyridone and 1,4,6-trimethyl-2-pyridone give mixtures of the corresponding piperidines and piperideines.[693,694] For example, reduction of 1,4,6-trimethyl-2-pyridone with lithium aluminum hydride gives **XII-642** as the major product along with **XII-643**, **XII-644**, and **XII-645**. In the presence of aluminum chloride, the less stable of the piperidines, the trans isomer (**XII-644**) is not detected[694] and **Xn-645** is the major product. The product distribution



XII-640 **XII-641**

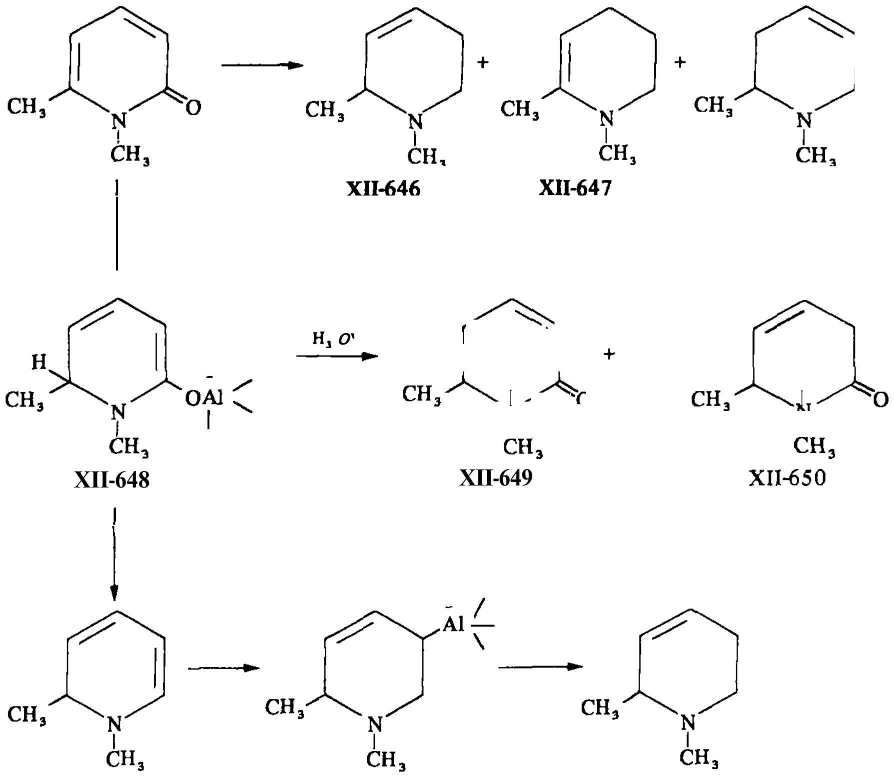


XII-642 **XII-643**



xII-644 **XII-645**

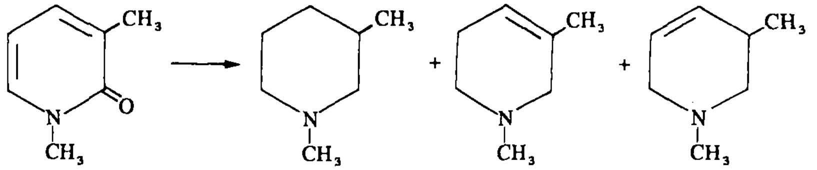
has been rationalized through steps initiated by 1,6-, 1,4-, or 1,2-addition involving the carbonyl group.[695] 1,6-Dimethyl-2-pyridone and two moles of lithium aluminum hydride per mole of pyridone gives mainly 1,2-dimethyl-3-piperideine (**XII-646**) and 1,2-dimethyl-2-piperideine (**MI-647**) and a small amount of 1,6-dimethyl-3-piperideine. As an illustration, 1,6-addition of the aluminum hydride ion to 1,6-dimethyl-2-pyridone gives **XII-648**, which is followed by reductive cleavage to the enamine **XII-651**; this reacts with more aluminum hydride ion to give **Xn-646** after hydrolysis.[695] With an excess of the



XII-646 **XII-647** **XII-648** **XII-649** **XII-650** **XII-651** **XII-646**

2-pyridone the dihydropyridones **XII-649** and XII-650 are isolated after hydrolysis. The product of 1,4-addition XII-647 was isolated in good yield from 1,6-dimethyl-2-pyridone, but products of reactions initiated by 1,4-addition are not detected when other *N*-methyl-2-pyridones were reduced.[695]

Electrolytic reductions of N-methyl- and *N*-ethyl-2-pyridone have given mainly 1-alkylpiperidine and some 1-alkyl-3-piperideine. Both 1,3-dimethyl- (**XII-652**) and 1,6-dimethyl-2-pyridone give mainly the piperidine (e.g., **XII-653**) and equal but smaller amounts of the two isomeric piperideines (e.g., **XII-654**, **XII-655**).[696]

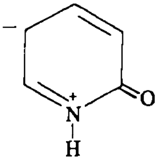


XII-652 **XII-653** **XII-654** **XII-655**

N-Benzyl-5,6-dihydro-6-methyl-2-pyridone[697] and 3,4-dihydro-5,6-diphenyl-2-pyridone[443] have been hydrogenated to the corresponding 2-piperidones in the presence of platinum. Piperidones can be converted to piperidines with lithium aluminum hydride.[697]

B. *Electrophilic Substitution—General*

Electrophilic substitutions of pyridinols and pyridinol ethers have been reviewed recently.[698] Although pyridine reacts with difficulty, aminopyridines, pyridinols, and pyridones, undergo electrophilic substitution readily under moderate conditions. The annular NH—CO group of 2-pyridone, which acts as an electron releasing group in these reactions, has an acid strengthening effect on a second substituent. This group, therefore, appears to be electron withdrawing in its ground state and electron releasing (+E effect) in electrophilic substitution transition states through contributions from structures such as **XI-656** at the demand of cationic reagents.[699] A study of electrophilic substitution of pyridones is complicated because of the variety of forms that could react. Several studies have, however, been reported for nitration in acid solutions where the reacting species have been determined.[700,701]



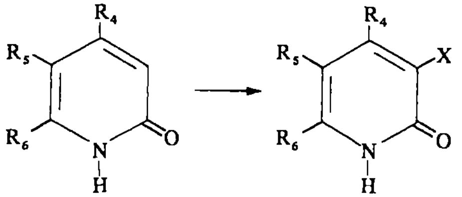
XII-656

C. *Halogenation*

Halogenation of 2- and 4-pyridones occurs at the 3- and 5-positions and, even under mild conditions, the monohalogenated product from 2-pyridones unsubstituted in the 3- and 5-positions is usually not isolated.[698,702] Recent contributions to the literature describe product distributions that are consistent with earlier chemistry[702] (Tables XII-20 to XII-22).

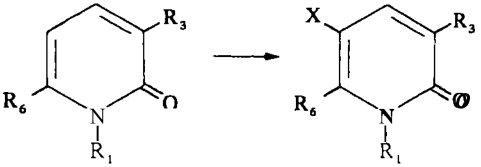
Although treatment of 4-methyl-, 1-methyl-, 1,4-dimethyl-, and 1,6-dimethyl-2-pyridone with *N*-bromosuccinimide (NBS) gives 3,5-dibromo-2-pyridones, side-chain bromination occurs with 1,3- and 1,5-dimethyl-2-pyridones to give 3- and 5-bromomethyl-*N*-methyl-2-pyridone, respectively. 3- And 5-methyl-2-pyridone give oils that decompose on distillation.[559]

TABLE XI-20. 3-Halo-2-pyridones by Halogenation



R_4	R_5	R_6	Reagent	% Yield	Ref.
	NO_2		HCI, KCIO,	60	291
	NO_2		Br_2	91	290
	NO_2		KI, KIO,, H^+	80	287
OH	CH,	Cl	Br, , C_2H_5OH	95	97

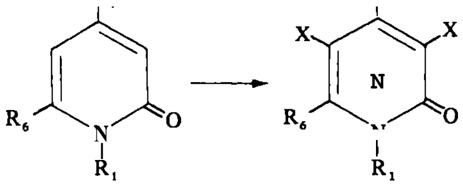
TABLE XI-21. 5-Halo-2-pyridones by Halogenation



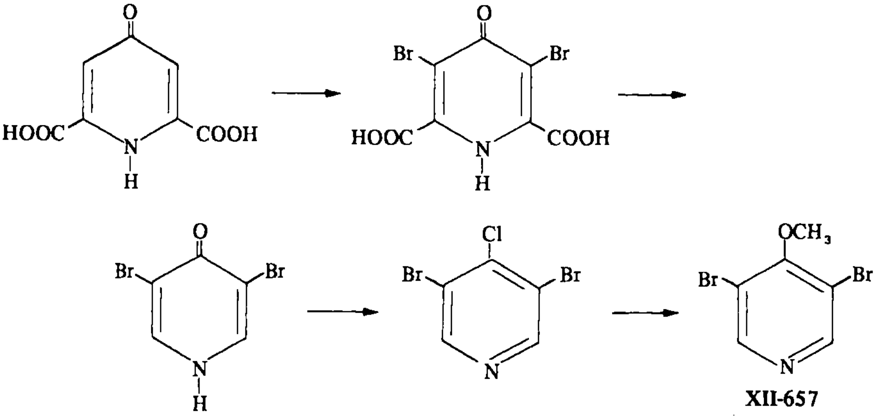
R_1	R_3	R_4	R_6	Reagent	%Yield	Ref.
	NO_2			HCl, $KClO_3$	45	291
	NO_2			KI, KIO,, H^+	60	287
	CH_3			Br, , HOAc		559
C_6H_5	$CONHC_6H_5$	OC_6H_5	OH	Br,, $CHCl_3$	67	172
C_6H_5	$CONHC_6H_5$	$OC_6H_4CH_3$-*m*	OH	Br_2, CCl_4	50	173
C_6H_5	CONHC, H,	OC, H, CH_3-*o*	OH	Br, , CCl_4	50	173
m-$CH_3OC_6H_4$	CO_2CH_3	OH	OH	Br_2, CHCl,	80	169
	NO_2	OH	CH,	Br_2, HOAc	74	502

Iodination of 2-pyridone with aqueous iodine-potassium iodide gives 5-iodo-2-pyridone and 3,5-diiodo-2-pyridone and iodination of 4-pyridone gives 3-iodo-4-pyridone (50%) and 3,5-diiodo-4-pyridone (21%).[704] 3,5-Dibromo-4-methoxypyridine (XII-657) has been prepared from chelidamic acid by bromination, followed by decarboxylation, treatment with phosphorus oxychloride, and then with potassium methoxide.[705]

TABLE XII-22. 3, 5-Dihalo-2-pyridones by Halogenation



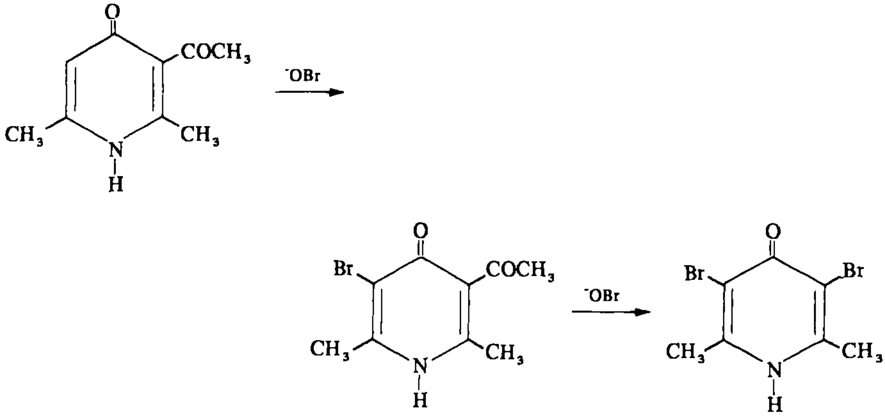
R_1	R_4	R_6	Reagent	% Yield	Ref.
H	CH,	H			
CH,	CH,	H	Br_2 , HOAc	75-90	559
CH,	H	CH_3			
CH,	H	H			
H	CH,	H	NBS, benzoyl peroxide	75	559
CH,	CH,	H	NBS, benzoyl peroxide	45	559
CH,	H	CH_3	NBS, benzoyl peroxide	57	559
CH,	H	H	NBS, $AlCl_3$	79	559
H	H	Cl	HCl, H_2O, , HOAc	80	703
H	H	Cl	Br,, 33% H_2SO,	93	703
			KI, I_2	15	704



XII-657

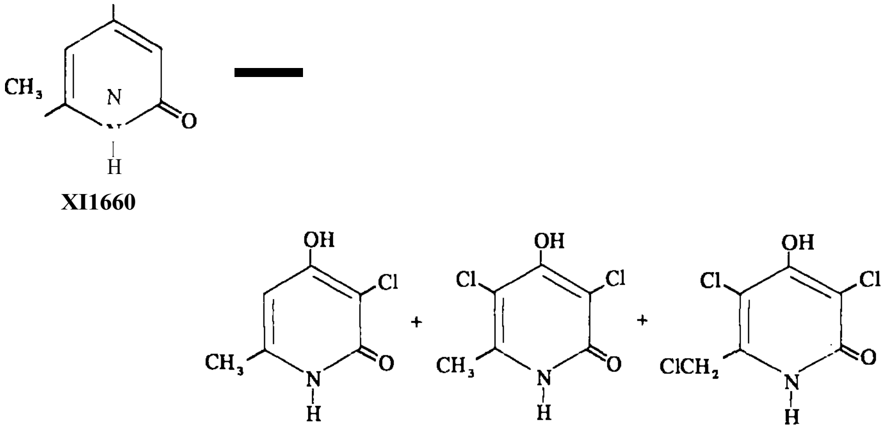
3,5-Dibromo-1-methyl-4-pyridone has been prepared from *N*-methyl-4-pyridone by modifications[139] of an earlier procedure.[706] *N*-(*n*-Butyl)-2,6-dimethyl-4-pyridone is also brominated in acetic acid to the 3,5-derivative.[118] 3-Nitro-4-pyridone[664] and 2,6-dimethyl-3-nitro-4-pyridone[294] are halogenated at the 5-position to give 5-bromo- and 5-chloro-2,6-dimethyl-3-nitro-4-pyridone, which have been converted to the corresponding 4-chloropyridines for use in γ-carboline synthesis.

3-Acetyl-2,6-dimethyl-4-pyridone and sodium hypobromite form 3-acetyl-5-**bromo-2,6-dimethyl-4-pyridone** (XII-658), which then gives 3,5-dibromo-2,6-dimethyl-4-pyridone **(XII-659)**[141]



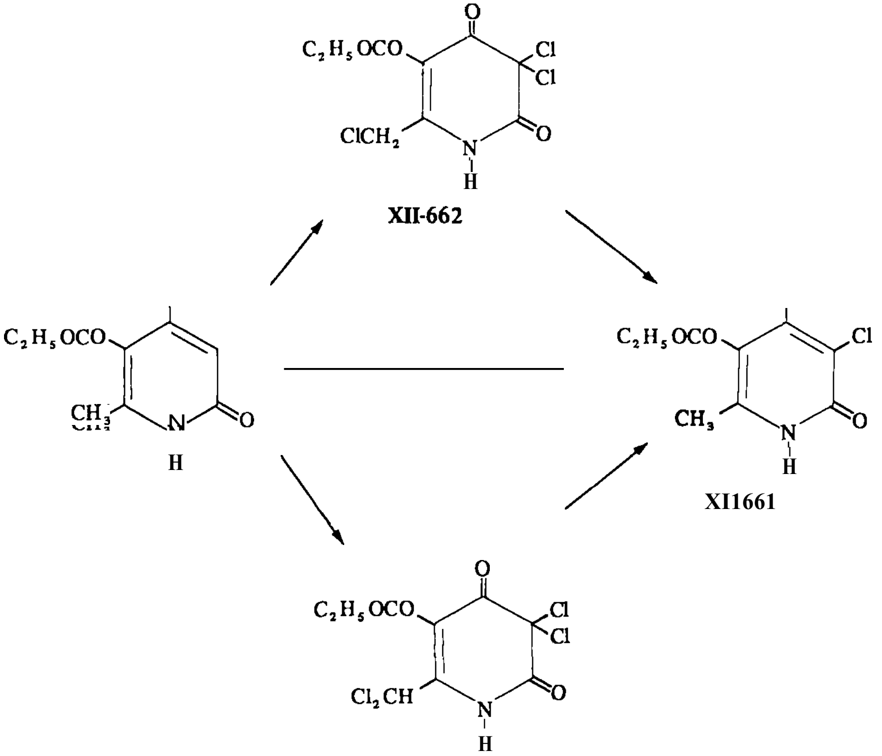
XII-658 **XII-659**

Chlorination of **4-hydroxy-6-methyl-2-pyridone (MI-660)** in water at **40"** gives 3-chloro- and **3,5-dichloro-6-methyl-2,4-pyridinediol** and 6-chloromethyl-3,5-dichloro-4-hydroxy-2-pyridone in a ratio of 4:4:1.[502]



XI1660

Chlorination of 5-carbethoxy-4-hydroxy-6-methyl-2-pyridone with SO_2Cl_2 gives **XII-661**, **MI-662**, or **XII-663**, depending on conditions. Products **XII-662** and **XII-663** are converted to **XII-661** with zinc and acetic acid.[707]



XII-662

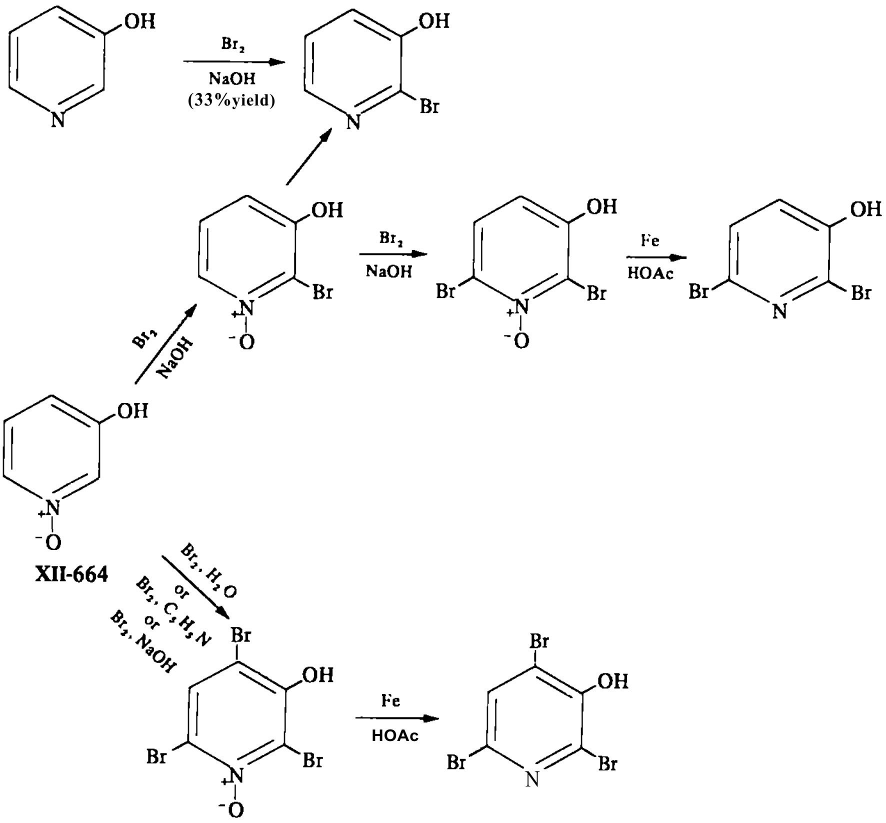
XI1661

XII-663

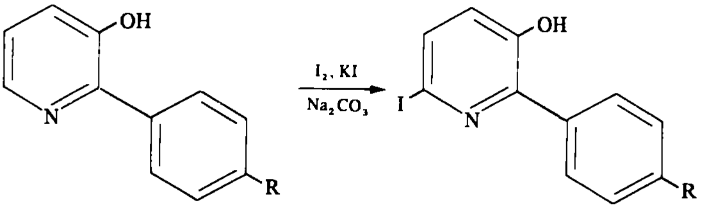
3-Pyridinol is converted to 2-bromo-3-pyridinol by an alkaline solution of bromine. Additional activation of the ring can be provided by conversion to the *N*-oxide. 3-Hydroxypyridine-1-oxide (**XII-664**) can give 2-bromo- (47%) or 2,4,6-tribromo-3-hydroxypyridine-1-oxide (78%), depending on conditions. Further bromination of 2-bromo-3-hydroxypyridine-1-oxide can give 2,6-dibromo-3-hydroxypyridine-1-oxide (36%). The *N*-oxides are reduced to the corresponding 3-pyridinols by iron and acetic acid.[708]

6-Methyl-3-pyridinol is brominated in pyridine to give 2-bromo- and then 2,4-dibromo-6-methyl-3-pyridinol. Iodination with sodium iododichloride gives 2-iodo-6-methyl-3-pyridinol.[583] Iodination of 2-(*p*-substituted phenyl)-3-pyridinols (**XII-665**; R = H, CH_3, C_2H_5, $CH(CH_3)_2$, $C(CH_3)_3$, Cl, OCH_3) gives 2-aryl-6-iodo-3-pyridinols.[709] This should be contrasted with nitration of these pyridinols, which occurs first on the phenyl group[710, 711] (Section III.2.D., p. 810).

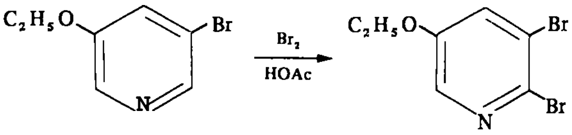
Bromination in acetic acid of 3-bromo-5-ethoxypyridine (**XII-666**) gives 2,3-dibromo-5-ethoxypyridine. Similar treatment of 2-bromo-6-ethoxypyridine (XII-667) gives 2,3-dibromo-6-ethoxypyridine.[712]



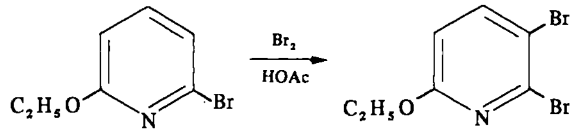
XII-664



XII-665



XII-666



XII-667

D. *Nitration*

The preparative nitration of pyridones has been reviewed recently.[698] The nitrations of several 2- and 4-pyridones have been studied kinetically.[700, 701] Pyridones with $pK_a < 1.5$ are nitrated as their free bases under all conditions. 4-Pyridone (pK_a 3.27) is nitrated as the free base in 65 to 85% sulfuric acid but as the conjugate acid in 85 to 98% H_2SO_4.[700] 6-Hydroxy-2-pyridone and its *N*- and O-methyl derivatives are rapidly converted to the 3-nitro-derivative *via* the free bases in 70 to 77% sulfuric acid. At higher acidities the reactions were too fast to be followed kinetically.[701]

Since 2-pyridones are nitrated mainly as their free bases and are probably in the pyridone form,[700] it is not likely that a transition state involving hydrogen-bond participation by OH as has been suggested for ortho-nitration of phenol[713] and for nitration of 2-substituted-3-pyridinols at the 4-position[714] (this section, p. 809) is responsible for the formation of 3-nitro-2-pyridone, the major product.[714]

3,5-Dinitro-2-pyridone is usually prepared by direct nitration of 2-pyridone.[673, 676, 715] It can be formed in 50% yield employing fuming nitric acid in oleum[676] or in 37% yield from 2-aminopyridine (MI-668) *via* its nitramine. *In situ* rearrangement to a mixture of 3- and 5-nitro-2-aminopyridines. is followed by conversion to the pyridones and nitration (Table XII-23).[285]

Nitration of 6-methyl-4-phenyl-2-pyridone (XI1–669) gives a mixture of the 3- and 5-mononitro derivatives that could not be separated because of its insolubility in organic solvents and that did not react with triethyl phosphite. Conversion to the 2-chloro derivatives gave a mixture that could be converted to the *β*-carbolines W-670 and XII-671 when treated with triethyl phosphite, presumably through nitrene intermediates.[666]

Mixtures of 3- and 5-nitro-4-methyl-2-pyridone and of 3- and 5-nitro-6-methyl-2-pyridone have been converted to the corresponding 3,5-dinitro-2-pyridones with nitric acid in oleum.[675]

A procedure has been described for the preparation of 3-nitro-4-pyridone from 4-pyridone and mixed acids that avoids the oleum used by previous investigators (Table XII-24).[667] Both 4-hydroxy-2-picoline and 4-ethoxy-2-picoline are nitrated at the 3- and 5-positions but give more 3-nitration.[293] 4-Hydroxy-2-

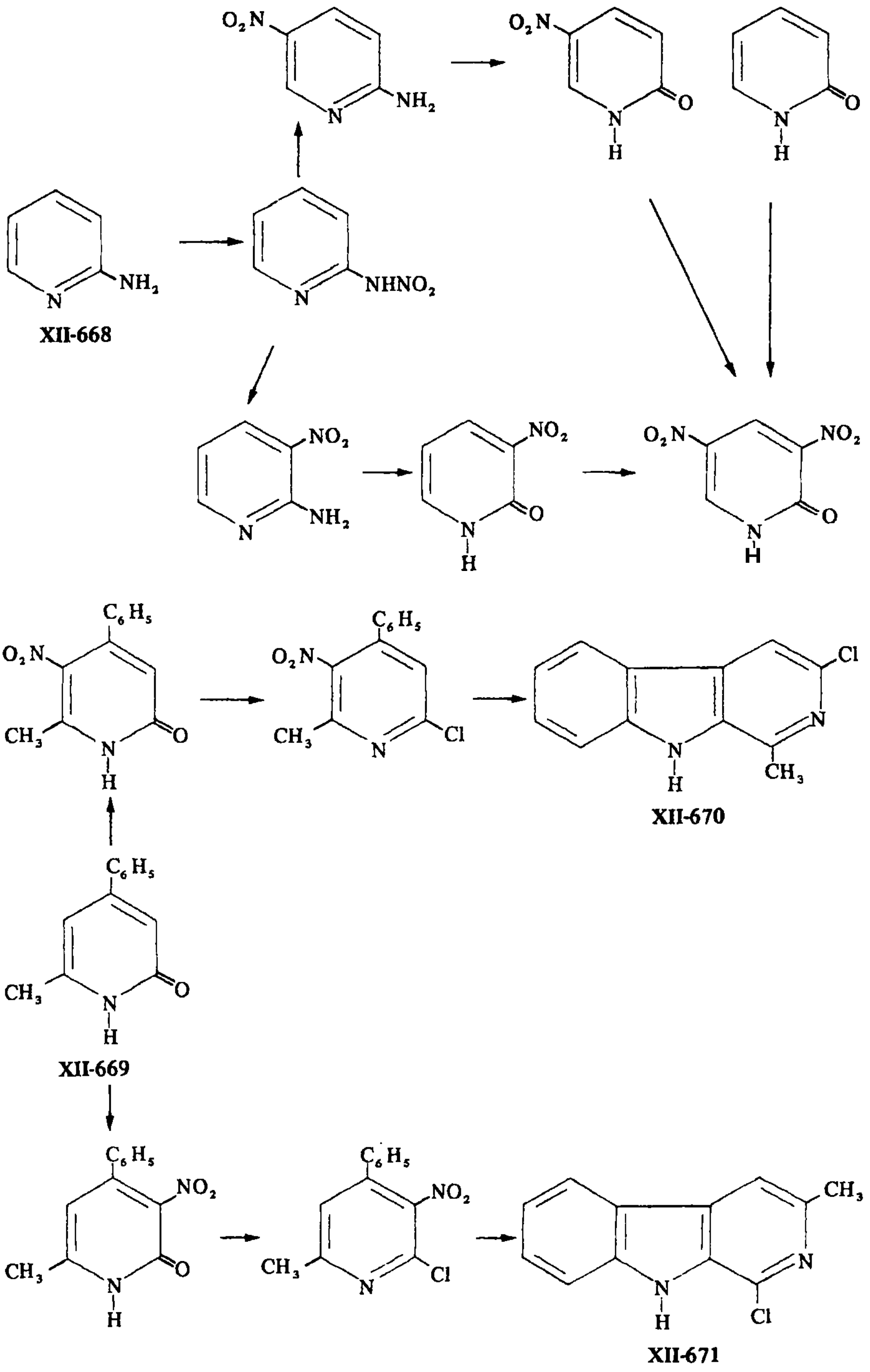
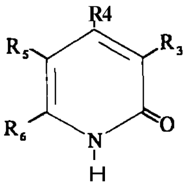

XII-668
XII-669
XII-670
XII-671

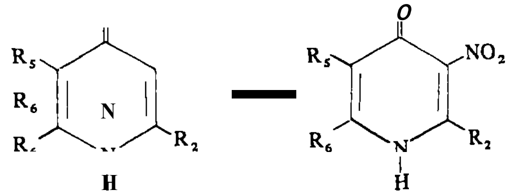
TABLE XII-23. Nitration of 2-Pyridones



R_3	R_4	R_5	R_6	Reagent	% Yield 3-NO_2	 5-NO,	Ref.
NO_2				40%oleum HNO,		50	285
		NO_2					285
CN	CF_3		CH_3	HNO_3 (fuming, d1.5) H, SO, (conc.)		72	56
	OH		CH_3	10% HNO,	only 3-NO_2 82		502
	OH		n-C_3H_7	83% HNO,	50		150
	OH	Cl	Cl	50% HNO,	77		98
	OH	CH_3	Cl	50% HNO,	94		97

pyridones are usually nitrated at the 3-position (Table XII-23). Additional nitrations of 2-pyridones and 4-pyridones are summarized in Tables XII-23 and XII-24.

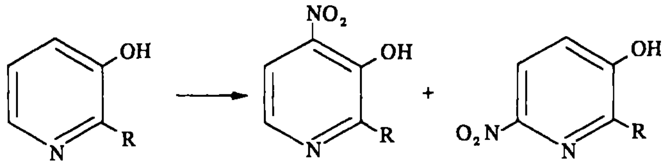
TABLE XII-24. 3-Nitro-4-pyridones



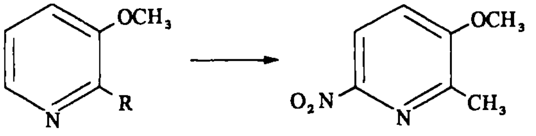
R_2	R_5	R_6	Reagent	%Yield	Ref.
H	H	H	HNO, (*d* 1.5), H_2SO_4 (*d* 1.84)	61	667
CH,	H	CH,	HNO, (*d* 1.5), H_2SO_4 (*d* 1.84)		670
CH,	H	CH,	HNO, (*d* 1.5), H_2 SO.,(*d* 1.84)	83	294
CH,	H	CH,	HNO, (*d* 1.5), H_2 SO.,	70	295
H	NO,	H	HNO, (fuming) ,30%oleum	92	716

3-Pyridinol and 3-methoxypyridine undergo nitration with nitric acid in sulfuric acid as their conjugate acids.[701] 3-Pyridinol with sulfuric and nitric acid[647] or with fuming acids[701] gives 2-nitro-3-pyridinol in good yield along with a small amount of 6-nitro-3-pyridinol.[647] Further nitration in acetic acid-acetic anhydride gives 2,6-dinitro- and then 2,4,6-trinitro-3-pyridinol.[717] Generally, in electrophilic substitutions of 3-pyridinols, the 4-position is less reactive than the 2- or the 6-position. However, in the nitrations of 2-alkyl- or 2-halo-3-pyridinol **(Xn-672)** at lower temperatures (0-5°) formation of the 4-nitro-2-substituted-3-pyridinol predominates.[647, 718] In fact, several 4-nitro-3-pyridinols were first reported to be 6-nitro-3-pyridinols[719] but were later correctly described.[718] It has been suggested that in these series, hydrogen-bonded 6-membered transition states involving the 3-hydroxy group are energetically favored and are responsible for the preferred reactivity of the 4-position over the 6-position when the 2-position is occupied.[714] The weakening or absence of this hydrogen-bonding should influence orientation. Thus, in the nitration of 2-methyl-3-pyridinol **(W-672**, R = CH_3**)** at higher temperatures (55°), the 6-nitro product predominates, and the nitration of 3-methoxy-2-methylpyridine **(XII-673)** gives only the 6-nitro derivative.[714] 2-Nitro-3-pyridinol **(XII-674)**, which is a hydrogen-bonded substrate, is also nitrated preferentially at the 6-position to give 2,6-dinitro-3-pyridinol **(XII-675)**.[714] However, the rate profiles for the nitration of 3-pyridinol and 3-methoxypyridine to give 2-nitro derivatives are similar.[701]

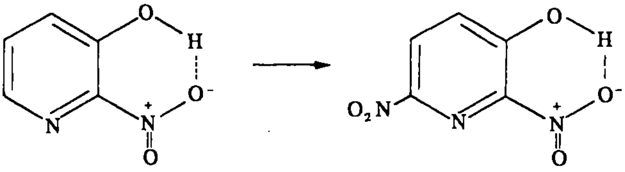
2,6-Dialkyl-3-pyridinols are nitrated in good yield at the 4-position using nitric acid and sulfuric acid.[719] Nitration of **2,6-dimethyl-3-pyridinol** with sodium nitrate in oleum gives **2,6-dimethyl-4-nitro-3-pyridinol** in only 10% yield.[295]



XII-672

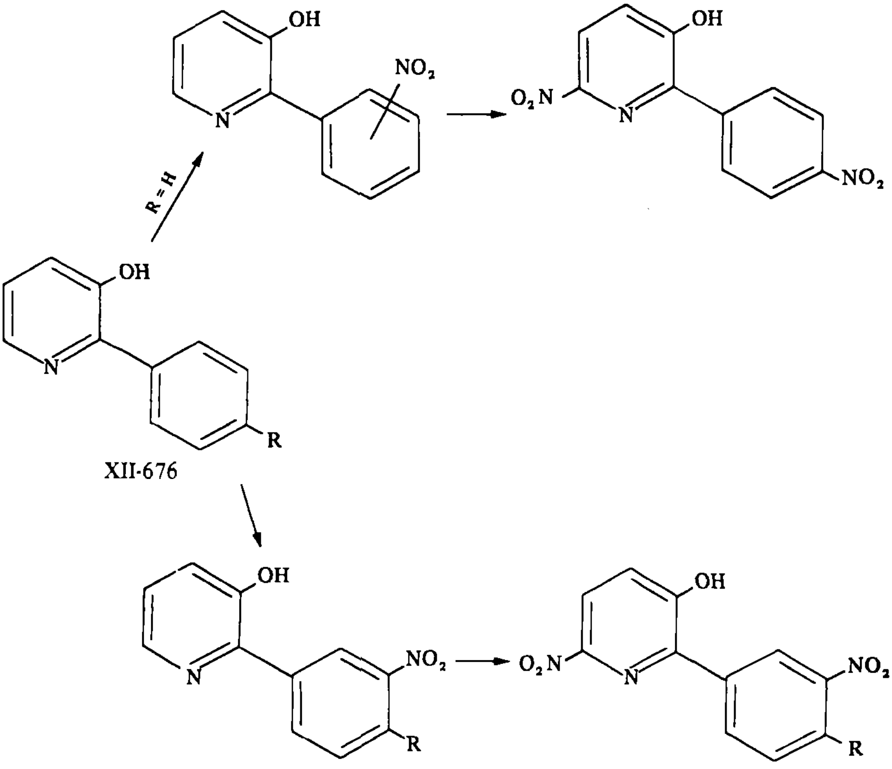


XII-673



XII-674 **XII-675**

With concentrated sulfuric acid and nitric acid (*d* 1.34) 2-phenyl-3-pyridinol (**XI-676,** R = H) is nitrated first at the phenyl group (*88%* in the *para* position) rather than at the cationic pyridinol ring, to give mainly **2-(*p*-nitrophenyl)-3-**pyridinol, which reacts further at the 6-position of the pyridine ring to give **6-nitro-2-(*p*-nitrophenyl)-3-pyridinol.**[710] When the *para* position of the phenyl ring contains *ortho-para-* directing substituents, nitration occurs at the position *ortho* to the substituent to give **2-(3-nitro-4-substituted phenyl)-3-pyridinols** (**XII-677**; R = CH_3, C_2H_5, $CH(CH_3)_2$, $C(CH_3)_3$, OCH_3, Cl). Further nitration of **MI-677** (R = CH_3) again occurs at the 6-position of the pyridinol ring.[711] Iodination of **MI-676** in the presence of sodium carbonate occurs only at the 6-position of the pyridinol ring.[709]



XII-676

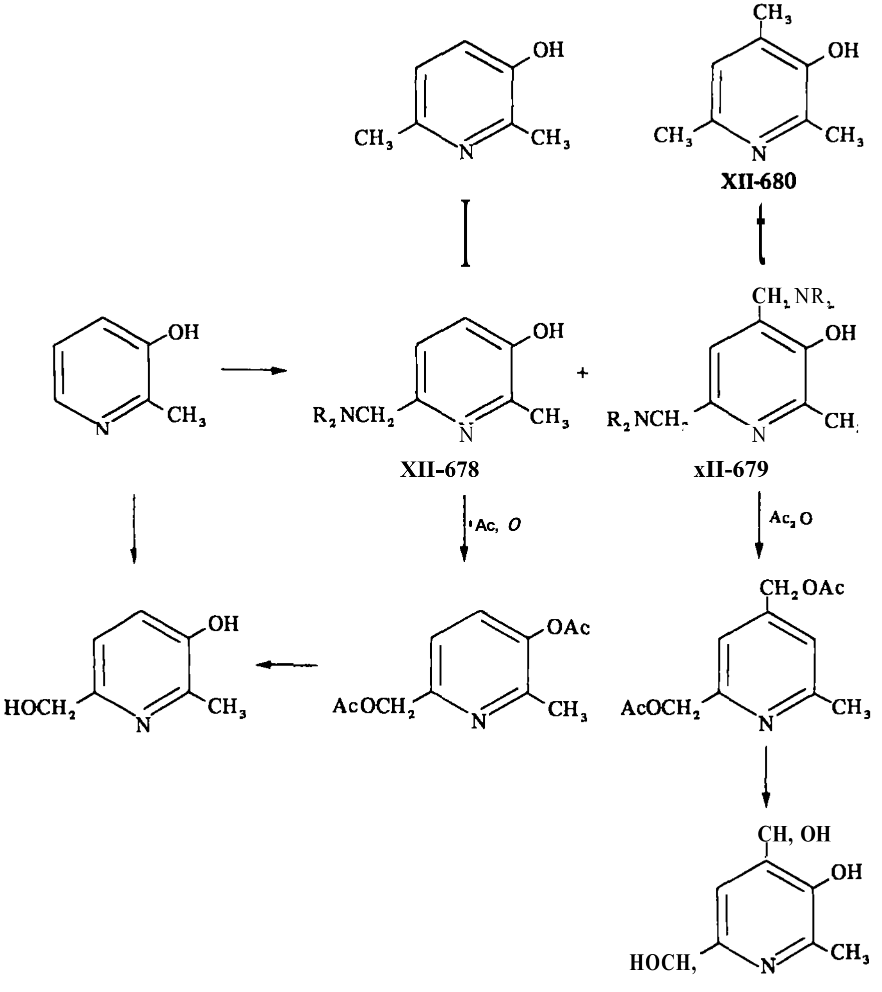
XII-677

E. The Mannich Reaction

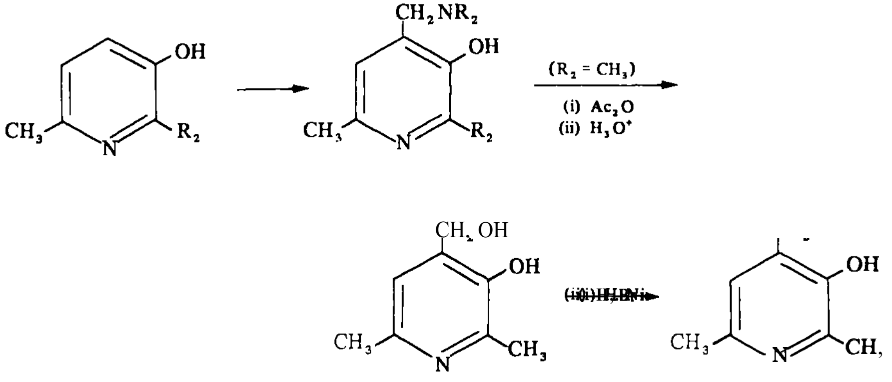
Although 3-pyridinol is not sufficiently reactive to undergo chloromethylation or Friedel Crafts alkylation or arylation it is readily aminomethylated. The ease of reaction appears to be in the order of 2- > 6- > 4-positions in the absence of steric influences. 3-Pyridinol reacts with secondary amines and formaldehyde at the 2- and then the 6-positions and 6-methyl-3-pyridinol reacts at the 2-position. However, reaction at the 4-position is not observed, even under drastic conditions[720] (unless the a-positions are blocked—see below). Although dimethylamine and piperidine react with formaldehyde and 3-pyridinol to give both the 2-mono- and 2,6-bis-products, diethylamine and 3-pyridinol give only 2-diethylaminomethyl-3-pyridinol, a behavior that is similar to that observed in hydroxymethylation.[720]

2-Methyl-3-pyridinol reacts with secondary amines and formaldehyde to form the 6-dialkylaminomethyl- (**XII-678**) and **4,6-bis(dialkylaminomethyl)-2-methyl-**

3-pyridinol **(MI-679)**. Hydroxymethyl-3-pyridinols are formed by converting the Mannich products **(XI-678** and **XII-679**, R = CH_3) to the acetate followed by hydrolysis. Hydrogenation of the Mannich products gives the expected **2,6-dimethyl-** and **2,4,6-trimethyl-3-pyridinol** (XII-680), **respectively.**[721] Higher 2-alkyl-3-pyridinols also react stepwise with formaldehyde and piperidine or dimethylamine to form 4,6-bisdialkylamino products. When the group at the 2-position is bulky (R = isobutyl, isoamyl), the formation of the bis product requires more severe conditions because of steric influence of the alkyl group on the activating effects of the 3-hydroxyl group."

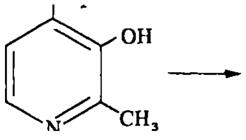


2-Ethyl-6-methyl- and **2,6-dimethyl-3-pyridinol** react with piperidine, dimethylamine, and morpholine in aqueous formaldehyde to form 4-dialkylaminomethylated products that have been used to prepare vitamin B_6 analogs **XII-681** and **XII-682**.[723] Reaction at the side-chain is not observed.[724]

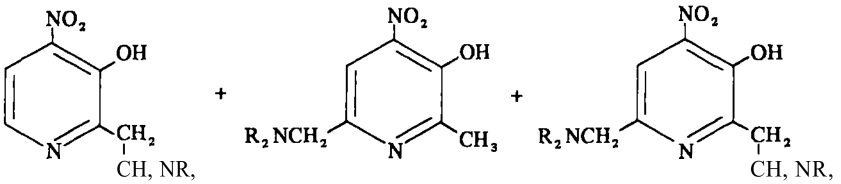


XII-681 **XII-682**

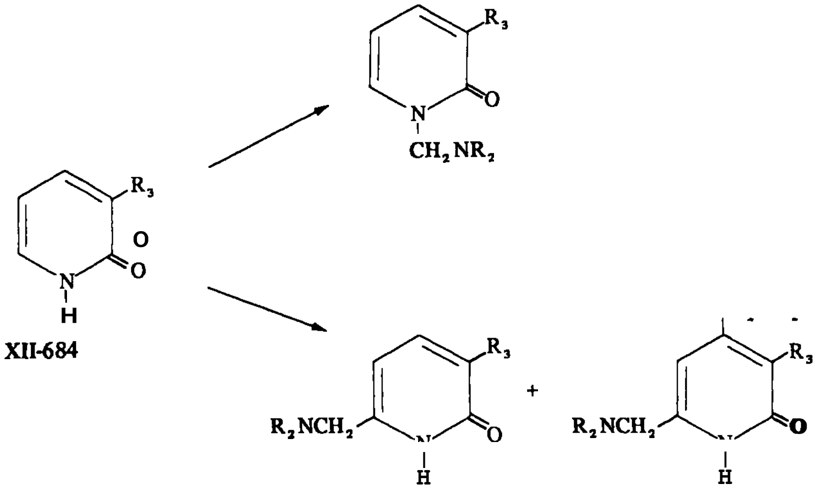
2-Nitro-3-pyridinol forms 6-dialkylaminomethyl-2-nitro-3-pyridinols that do not react further even under forcing conditions.[725] A compound previously described as 2-methyl-6-nitro-3-pyridinol[726] and later identified as 2-methyl-4-nitro-3-pyridinol **(XII-683)**[726a] reacts with formalin and dialkylamines to give both 6-dialkylaminomethyl- and 2-(β-dialkylaminoethyl)-3-pyridinols.



XII-683

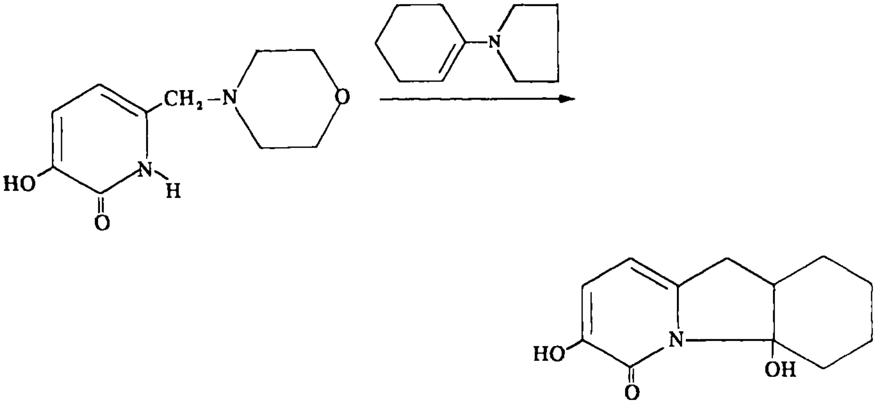


2-Pyridone and 3-methoxy-2-pyridone (XII-684; R_3 = H, CH_3O) give 1-dialkylaminomethylpyridones, but 3-hydroxy-2-pyridone (MI-684, R_3 = OH) forms the 6- and 4,6- Mannich products.[501] The 6-morpholino- Mannich product



XII-684

reacts with cyclohexanone pyrrolidine enamine to give the dihydroxyhexahydrobenzo[*b*] indolizinone **XII-685**.[501]



XII-685

Aminomethylation of **2-(*p*-anisyl)-3-pyridinol** gives 6-mono- and 4,6-bis(dimethylaminomethyl)-2-(*p*-anisyl)-3-pyridinol. Aminomethylation at the anisyl group is not observed. Aminomethylation of **2-(*p*-hydroxyphenyl)-3-pyridinol** occurs at both the 3- and 5-position of the *p*-hydroxyphenyl group, followed by aminomethylation at the 6- and then the 4-position of the pyridinol ring.[727]

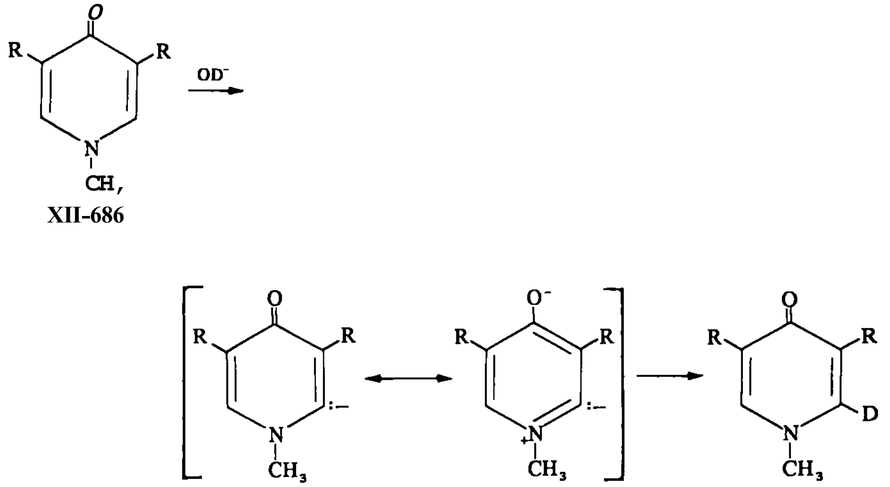
Proton chemical shifts and **LCAO** calculated charge distributions have been correlated with reactivity and substitution sequences in the Mannich reactions of 3-pyridinols.[520, 728]

F. *Hydroxymethylations*

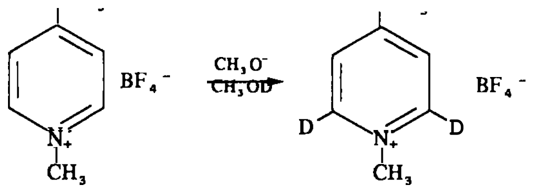
1-Methyl-2-pyridone, formaldehyde, and hydrochloric acid give 5-hydroxymethyl-1-methyl-2-pyridone. Addition of acetic anhydride and sodium acetate to the reaction mixture appears to be necessary to obtain a good yield. A similar reaction using 5-ethyl-1-methyl-2-pyridone gives 5-ethyl-3-hydroxymethyl-1-methyl-2-pyridone.[729] 2-Methyl-3-pyridinol undergoes only 6-hydroxymethylation when treated with formaldehyde in aqueous base;[721] with formaldehyde and secondary amines, however, 4,6-bis products can be isolated (see Section III.2.E.).

G. Hydrogen-Deuterium Exchange

It has been suggested that deuteration of N-methyl-2-pyridone occurs at the methyl group.[730] Base-catalyzed hydrogendeuterium exchange, however, takes place at the 2- and 6-positions of 4-pyridones (**MI-686**, R = H, CH_3, Br) and 4-methoxy-1-methylpyridinium tetrafluoroborate (**MI-687**) and at the 6-position of *N*-methyl-2-pyridone in deuterium oxide *via* an ylide mechanism.[139, 731, 732] The rates of exchange relative to *N*-methyl-4-pyridone are: *N*-methyl-2-pyridone (D_2O at 100"), $10^{-0.8}$; 4-methoxy-1-methylpyridinium tetrafluoroborate (**XII-687**) (CH_3OD at 40°), $10^{5.3}$.[732] The high rate of incorporation into **MI-687** is due to the positive charge that lowers the activation energy for hydrogen-abstraction.[732] *N*-methyl-2,6-dimethyl-4-



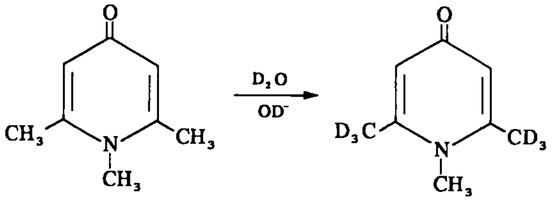
XII-686



xII-687

pyridone (XI-688)undergoes exchange at the α-side-chains.[139]

Acid-catalyzed hydrogen-deuterium-exchange occurs on the 3- and 5-positions of pyridones.[137, 537, 733-736] Over a wide range of acidities (pH 4 - H_0 -10), the



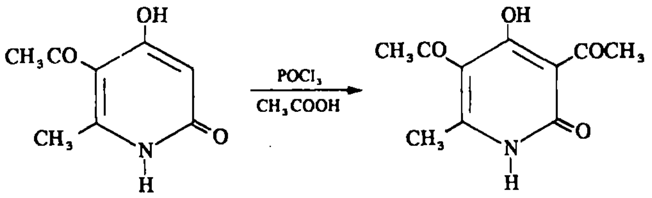
XII-688

rates of deuterium exchange vary by relatively small increments for 4-pyridone, 1-methyl-4-pyridone, and 3- and 5-methyl-2-pyridone, consistent with the suggestion that these compounds react as the free bases.[734] Methyl substitution at the 2- and 6-positions activates the much less reactive conjugate acids. 2,6-Dimethyl-4-pyridone exchanges as the free base at lower acidities but as the conjugate acid at acidities above H, -3.5. A similar changeover in mechanism occurs at H_0 -2.7 for 1,2,6-trimethyl-4-pyridone.[137, 733] A comparison of rate data from 1,2,6-trimethyl-4-pyridone, 4-methoxy-2,6-dimethylpyridine and 2,6-dimethyl-4-pyridone, indicates that exchange occurs on the pyridone form of the free base.[137] The deactivating effect of the positively charged nitrogen of the conjugate acids has been compared with effects of heterocyclic analogs containing $=\overset{+}{N}OH-$, $=\overset{+}{N}(O^-)-$, $=\overset{+}{O}-$ and $=\overset{+}{S}-$.[137] 4-Methoxypyridine does not exchange under these conditions.[734, 735] The 3- and 5-positions of 2-pyridone appear to be deuterated at approximately the same rate in 23% deuterosulfuric acid.[736]

H. *Acetylation*

5-Acetyl-4-hydroxy-6-methyl-2-pyridone and phosphoryl chloride in acetic acid give 3,5-diacetyl-4-hydroxy-6-methyl-2-pyridone (XII-689).[157] 4-Hydroxy-6-methyl-2-pyridone (XII-690, R = H), 1,6-dimethyl-4-hydroxy-2-pyridone

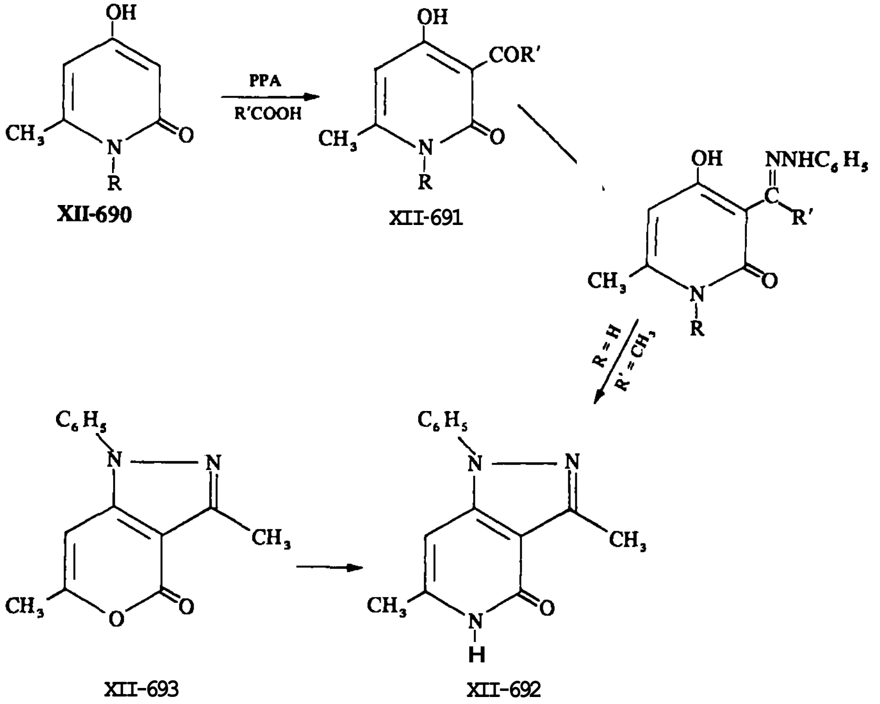
(**XII-690**, R = CH_3), and 4-hydroxy-6-methyl-1-phenyl-2-pyridone (**XII-690**, R = C_6H_5) and acetic acid in phosphoryl chloride give the 4-acetoxy product.[645] In polyphosphoric acid (PPA), 3-acylation can occur to give XII-691 (R = R' = CH_3; R = H, R' = CH_3, C_2H_5, n-C_3H_7, n-C_4H_9, isoC_4H_9, n-C_5H_{11}).[644, 645, 737] Structure assignments have been based on infrared



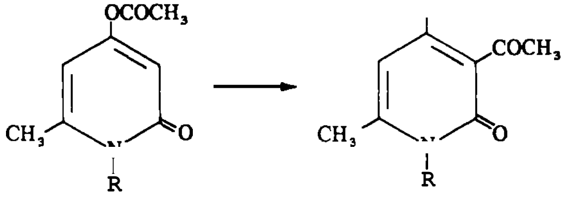
XII-689

spectroscopy and on the synthesis of 3,6-dimethyl-1-phenylpyrazolo[4,3-*c*]pyridin-4-one (**XII-692**) (R.I. 1186), which was also prepared from the known 3,6-dimethyl-1-phenylpyrano[4,3-*c*]pyrazol-4-one (**XII-693**).

Both **4-acetoxy-6-methyl-2-pyridone (XII-694,** R = H) and 4-acetoxy-6-methyl-1-phenyl-2-pyridone (**XII-694,** R = C_6H_5) undergo the Fries rearrange-



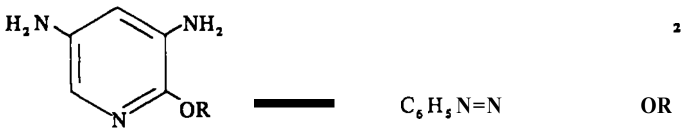
ment in the presence of aluminum chloride to give the corresponding 3-acetyl-4-hydroxy-2-pyridone.[644, 645]



XII-694

I. *Coupling with Diazonium Salts*

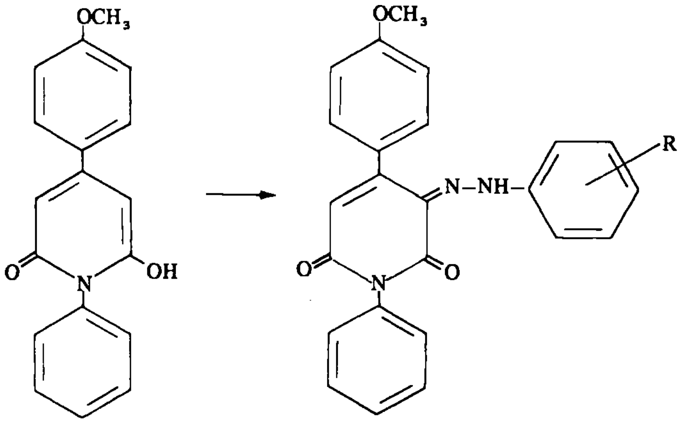
Pyridinols, pyridones, and alkoxypyridines that are sufficiently activated can be coupled with diazonium salts. 2-Alkoxy-3,5-diaminopyridine gives 2-alkoxy-3,5-diamino-6-phenylazopyridine (XII-695) with benzenediazonium



XII-695

(R = H, CH$_3$, C$_2$H$_5$, C$_3$H$_7$, ^{i}C$_4$H$_9$, C$_5$H$_{11}$)

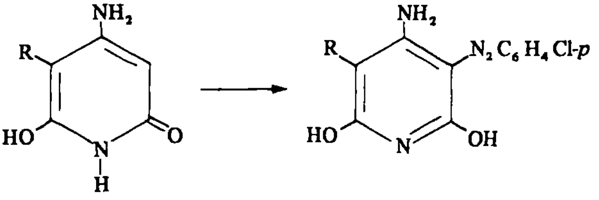
2-Hydroxy-4-(*p*-methoxyphenyl)-1-phenyl-6-pyridone couples with diazonium salts to give colored products XII-696.[739]



XII-696

(R = H, 4-CH$_3$, 2-OCH$_3$, 4-OCH$_3$, 2-, 3-, 4-NO$_2$, 2-, 3-, 4-Cl, 4-Br)

3-Pyridinol and p-nitrobenzenediazonium chloride form 6-(*p*-nitrophenylazo)-3-pyridinol as the major product. A low yield of the 2-isomer can be increased to 17% in a neutral or slightly acidic medium.[292] Glutazine (**W-697**, R = H) and 3-carbethoxyglutazine (**XII-697**, R = $CO_2C_2H_5$) react with *p*-chlorobenzenediazonium chloride to give 3-p-chlorophenylazo derivatives.[34] 6-Hydroxy-2-pyridone and benzenediazonium chloride give both 3-phenylazo- and 3,5-bis-(phenylazo)-6-hydroxy-2-pyridone.[740]

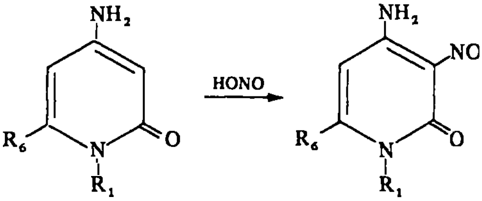


XII-697

In contrast to nitration[295, 719] and aminomethylation,[724] 2,6-dimethyl-3-pyridinol does not couple with benzenediazonium or p-nitrobenzenediazonium chloride in weakly acid or alkaline medium. Only 6-substitution occurs when 2-methyl-3-pyridinol is coupled with diazonium salts.[741]

J. *Nitrosation*

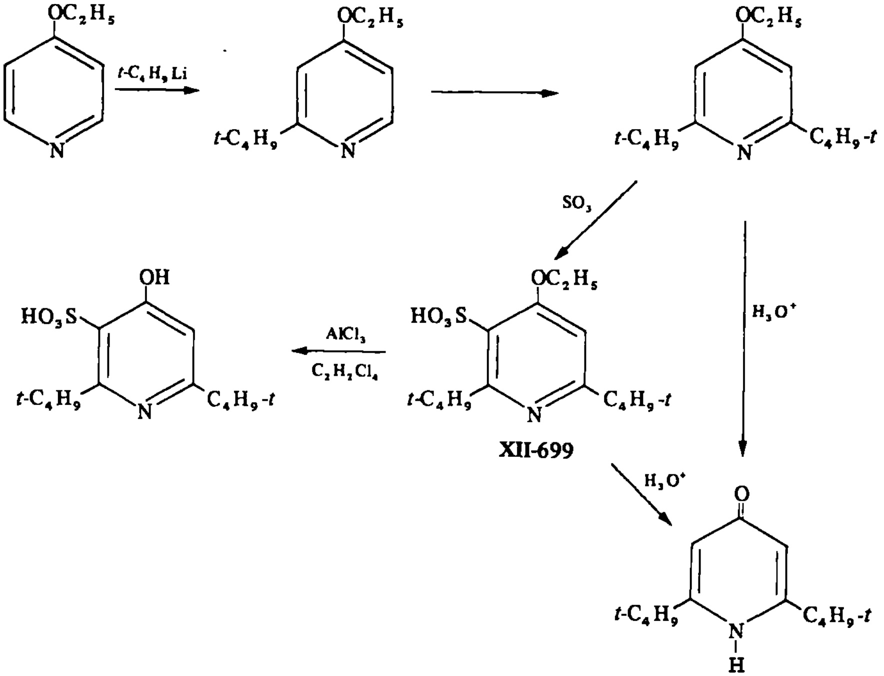
Both 4-amino-2-pyridone (**W-698**, R_1 = R_6 = H)[305] and 4-amino-1,6-dimethyl-2-pyridone (XII-698, R_1 = R_6 = CH_3)[306] react with nitrous acid to give a 4-amino-3-nitroso-2-pyridone rather than a diazonium salt.



XII-698

K. *Nucleophilic Substitution*

There are a few instances in which direct amination or arylation of pyridones has been reported.[742] 2-Methyl-4-pyridone and sodamide give 6-amino-2-methyl-Cpyridone in 79% yield.[743] 4-Ethoxypyridine and t-butyllithium give 2-t-butyl-and **2,6-di-*t*-butyl-4-ethoxypyridine.** Hydrolysis of the ether to 2,6-di-*t*-butyl-4-pyridone **(XI-700)** is accomplished with hot hydrochloric acid. Similar treatment of the 3-sulfonic acid derivatives **XII-699** with hydrochloric acid leads to displacement of the sulfonic acid group to give **MI-700**;on the other hand, **XII-699** and aluminum chloride in tetrachloroethane give the 4-hydroxypyridinesulfonic acid (75%).[671] 3-Methoxypyridine and phenyllithium react to



XII-699

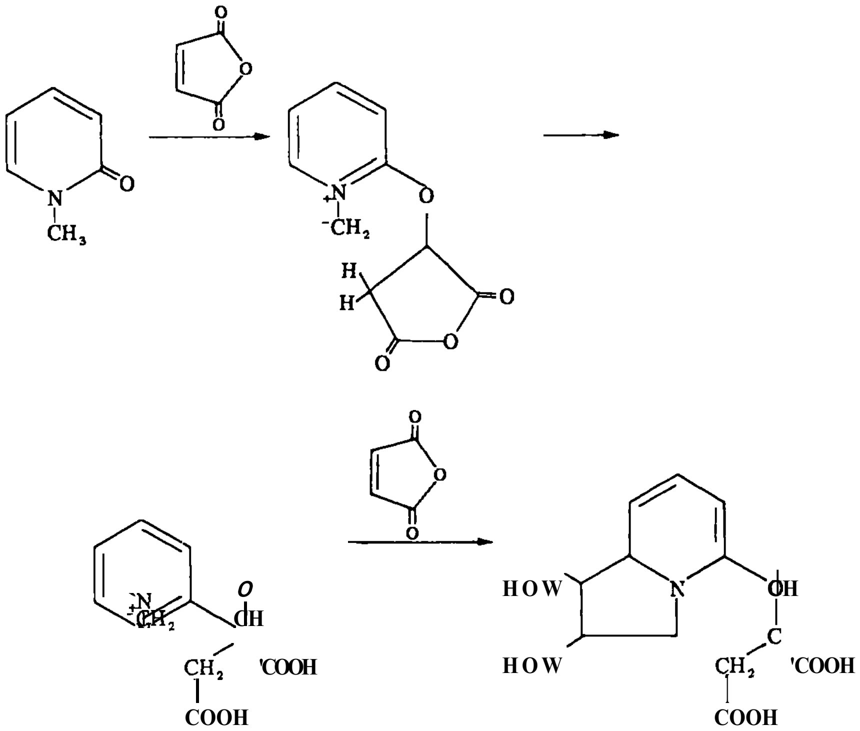
XII-700

give **3-methoxy-2-phenylpyridine** exclusively. It has been suggested that a reaction path involving coordination of the oxygen electrons to the lithium is operative.[744]

L. *Diels-Alder Dienophiles*

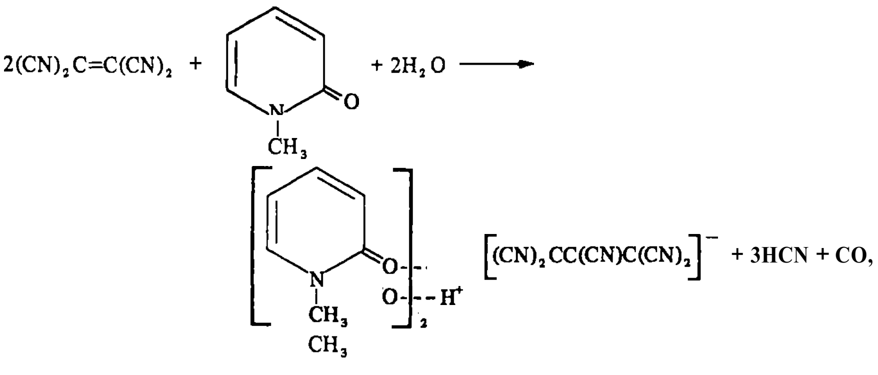
The structures of 2-pyridone and its *N*-alkyl derivatives suggest that they could perform as dienes in Diels-Alder reactions. When maleic anhydride and *N*-methyl-2-pyridone are heated alone or in toluene at 100" a 2:1 adduct is formed (24%) that dissociates into the pyridone and maleic anhydride in polar solvents or when heated to its melting point or when sublimed. The structure

W-701 has been proposed for this adduct, and its formation has been rationalized according *to* the following scheme:[730]



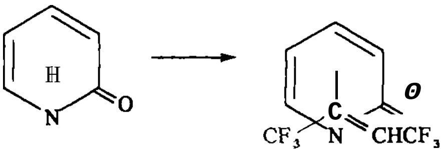
XII-701

N-Methyl-2-pyridone and tetracyancethylene in diisopropyl ether give a 2:1 pentacyanopropene salt **(XII-702)**.[745]



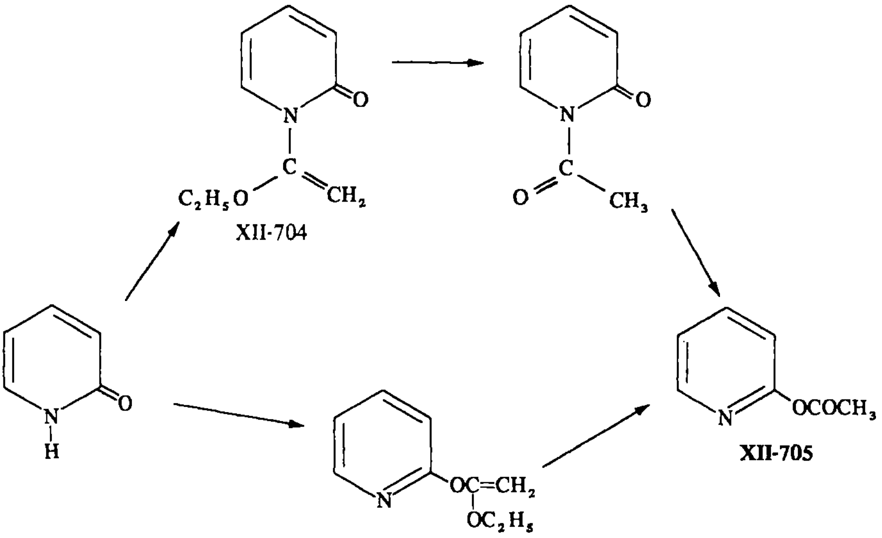
xu-I02

When heated with perfluoro-2-butyne at 175” for 12 hours, 2-pyridone gives 1-[3,3,3-trifluoro-1-(trifluoromethyl)propenyl]-2-pyridone (XII-703). *N*-Methyl-2-pyridone, a compound that cannot undergo this addition, gives no characterizable products with perfluoro-2-butyne.[746]

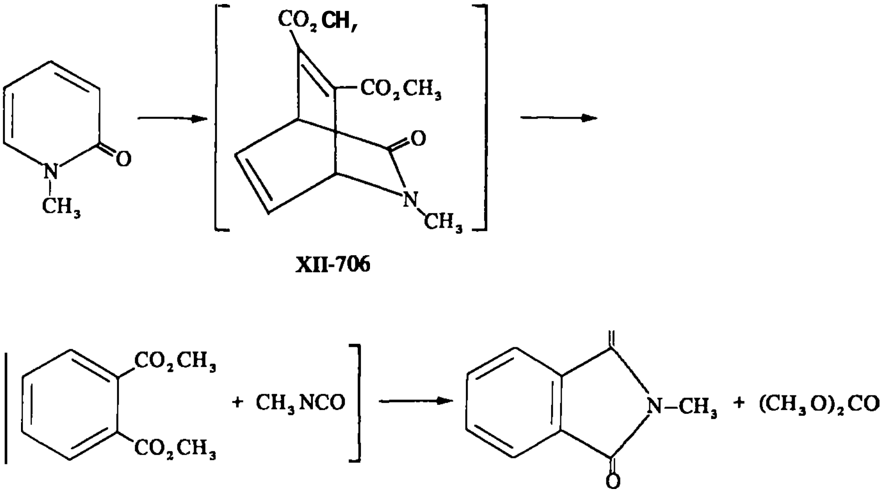


XI-703

2-Pyridone and ethoxyacetylene in chloroform-hexane were heated for 27 days to give a mixture of 2-acetoxypyridine (XII-705) (67%) and *N*-(1-ethoxyvinyl)-2-pyridone (XII-704) (33%). Similarly, 4-pyridone and ethoxyacetylene gave 4-acetoxypyridine (41%) and *N*-(1-ethoxyvinyl)-4-pyridone (17%) after 5 days. It has been suggested that XII-705 is formed by rearrangement of MI-704 *via* *N*-acetyl-2-pyridone, or through a ketene ketal intermediate by hydrolysis.[747]



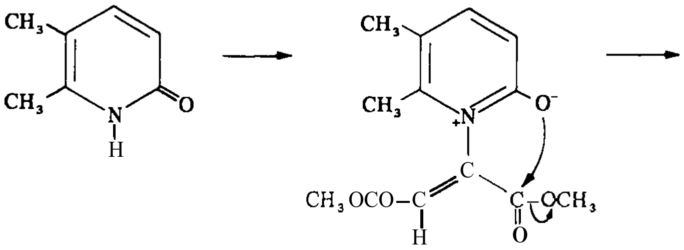
2-Pyridone, 6-methyl-2-pyridone,[748] 5,6-tetramethylene-2-pyridone, and 5,6-dimethyl-2-pyridone[749] give the products of 1,2-addition to dimethyl acetylenedicarboxylate. *N*-Methyl-2-pyridone gives *N*-methylphthalimide, which is probably formed by decomposition of the Diels-Alder adduct **XII-706**.[748]



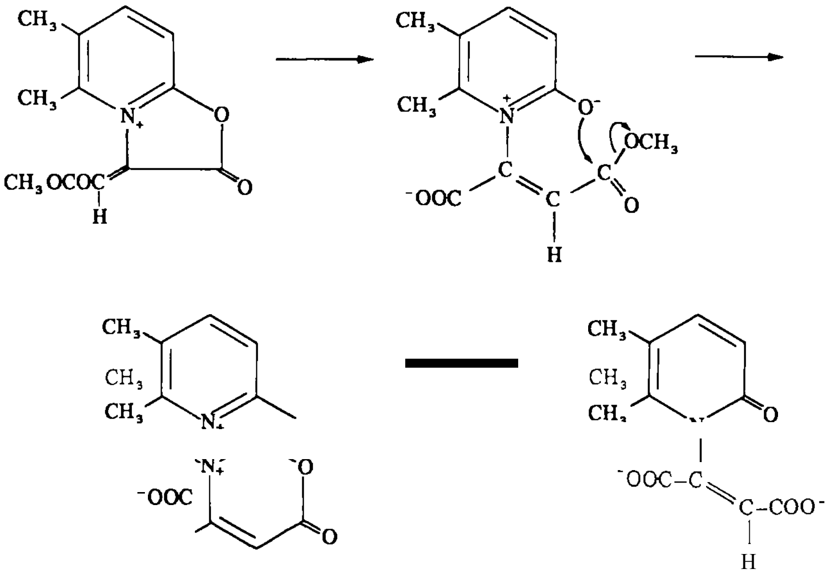
XII-706

2-Pyridon-1-yl fumarates (**XII-707**), products of addition of 5,6-dimethyl-2-pyridone to dimethylacetylene dicarboxylates are rapidly saponified in cold aqueous alkali to the acids (**XII-708**), presumably by an intramolecular catalysis involving the pyridone oxygen.[749]

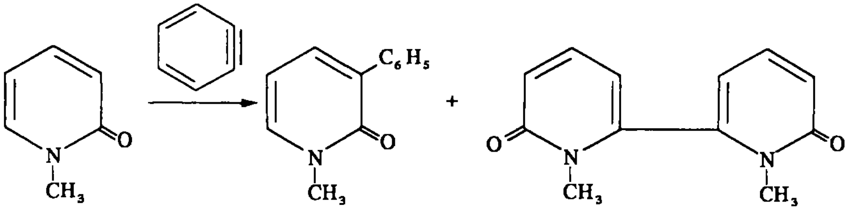
Benzyne, from chlorobenzene and sodamide, and *N*-methyl-2-pyridone give 3-phenyl-1-methyl-2-pyridone in 5.4% yield, together with a small amount of 1,1′-dimethyl-2,2′-bipyridyl-6,6′-dione (**XII-709**).[750] 2-Pyridone undergoes *N*- and O-arylation in low yield when treated with benzyne prepared from diazotized anthranilic acid.[750, 751] A small amount of acridone is formed also. However, *N*-methyl-2-pyridone and the methyl-1-methyl-2-pyridones react with benzyne from anthranilic acid to form the Diels-Alder adducts (**XII-710**).[750, 751]



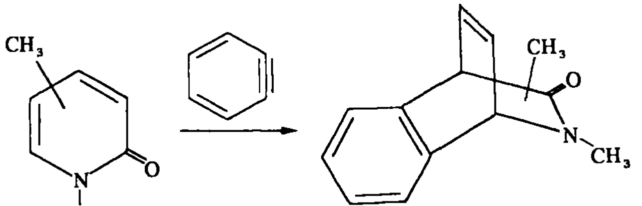
XII-707



XII-708

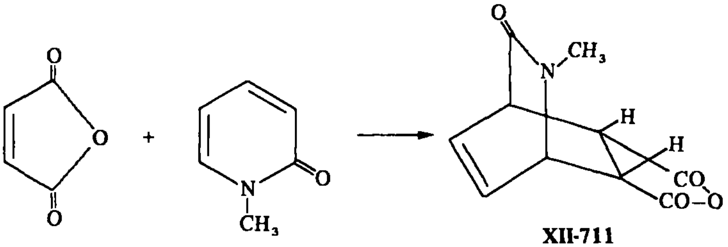


XII-709

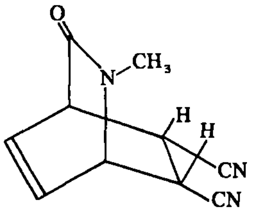


XII-710

Recently a successful Diels-Alder addition of maleic anhydride to 1-methyl-2-pyridone was accomplished by heating the reactants in toluene for 72 hours, yielding the *endo* product (**XII-711**).[752,753] 1-Methyl-2-pyridone and fumaronitrile, when boiled for 111 hours in toluene formed the adduct **XII-712**, but only in 3%yield.[754]

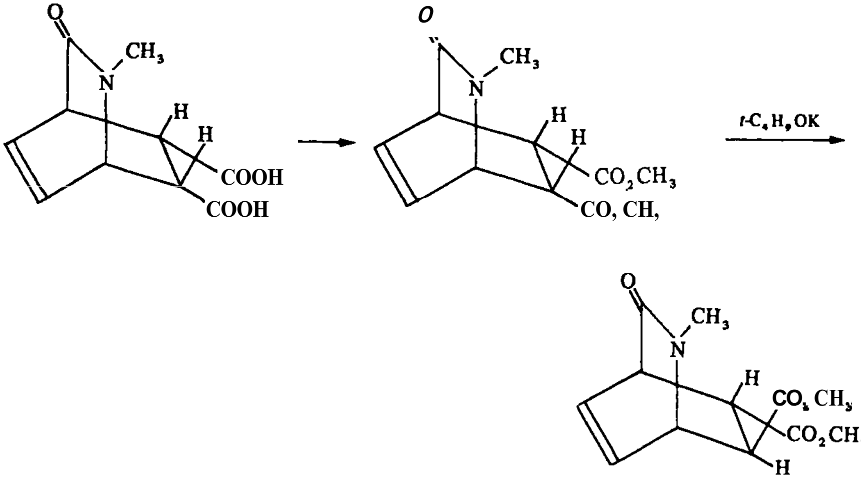


XII-711

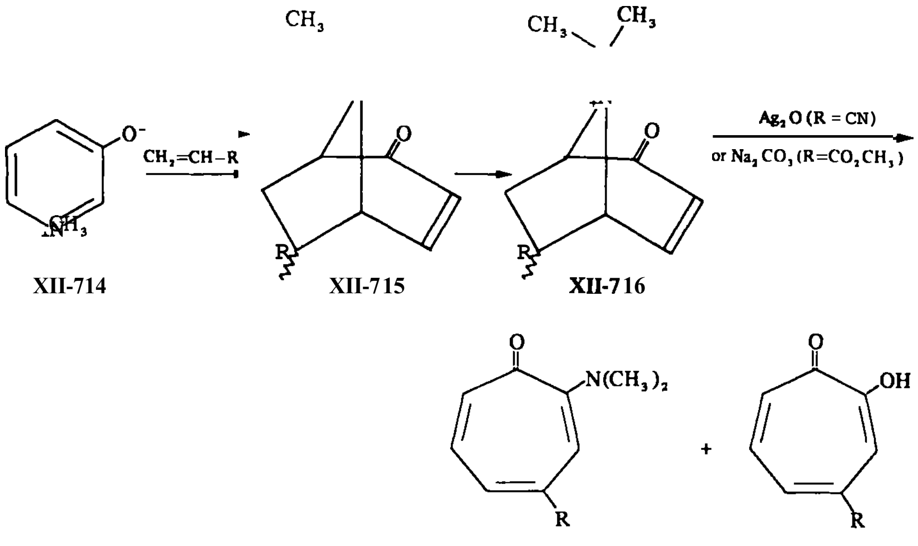


XII-712

The *endo* dicarboxylic acid can be converted to the dimethyl ester, which isomerizes to **MI-713** in good yield on treatment with potassium *t*-butoxide.[754] Anhydro-3-hydroxy-1-methylpyridinium hydroxide (**MI-714**) and *N*-phenylmaleimide, acrylonitrile, or methyl acrylate give adducts that are conveniently converted to tropones and tropolones. Acrylonitrile and methyl acrylate and **XI-714** give **MI-715** (**R** = *exo*-CN; R = CO_2CH_3, *endo*:*exo*, 1:1), which, after treatment with methyl iodide, gives **XII-716**. This forms 6-dimethylamino-5-oxo-1,3,6-cycloheptatriene-1-carbonitrile (**MI-717**, R = CN) and the 1-carbomethoxy derivative (**W-717**, R = CO_2CH_3) on reaction with silver oxide.[755] Treatment of **MI-716** with sodium bicarbonate gives **XII-717** and **MI-718** (**R** = CN, CO_2CH_3).



XII-713



XII-714

XII-715

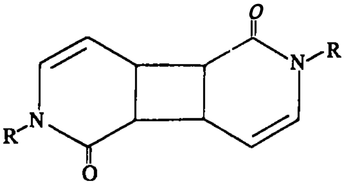
XII-716

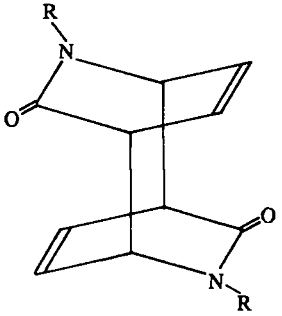
XII-717

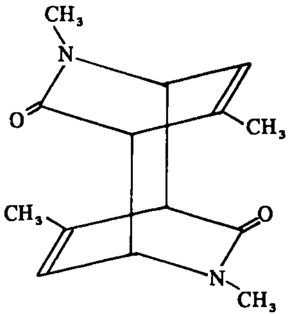
XII-718

M. *Photochemistry*

Ultraviolet irradiation of aqueous solutions of 2-pyridone and *N*-methyl-2-pyridone gives dimers to which the structure **XII-719** (R = H,CH_3, respectively) was first assigned,[756] but which subsequently have been shown to be *trans*-3,7-diazatricyclo$[4.2.2.2^{2,5}]$ dodeca-9,11-dien-4,8-diones (XII-720).[757-760] The NMR spectrum of the photodimer (XII-721) from 1,4-dimethyl-2-pyridone shows that the methyl group is at the double bond rather than at the bridgehead,[757] as would be required by the ring system in XII-719.


XII-719


XII-720

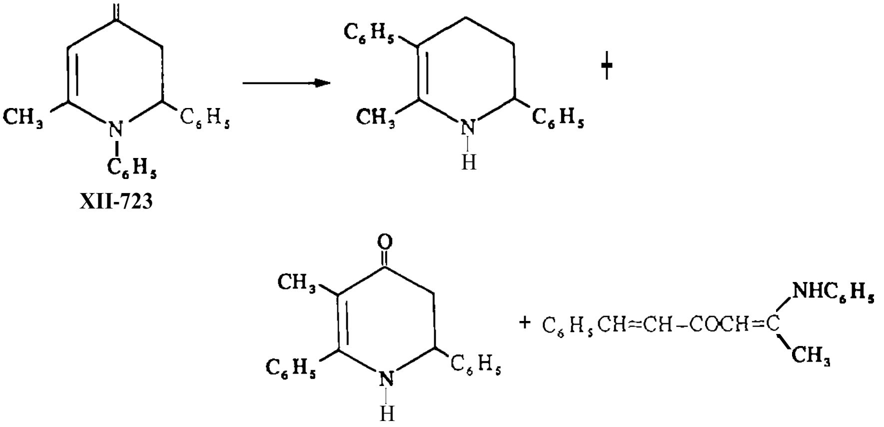

XII-721

Several substituted-2-pyridones have been dimerized to XII-720.[758, 761, 762] A photoinduced diradical intermediate was suggested as the species leading to dimerization.[762] When irradiated in water *N*-benzyl-2-fluoropyridinium bromide gives the same dimer as is formed from *N*-benzyl-2-pyridone in ethanol.[763] Photoisomerization of *N*-methyl-2-pyridone in ether, followed by careful workup of products, gives XII-722.[764]

O

XII-722

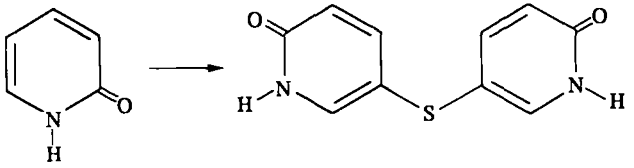
Ultraviolet irradiation of 2,3-dihydro-1,2-diphenyl-6-methyl-4-pyridone (MI-723) in methanol gives 2,5-diphenyl-6-methyl- and 2,3-dihydro-2,6-diphenyld-methyl-4-pyridone and 5-aniline 1-phenyl-1,4-hexadiene-3-one.[765]



XII-723

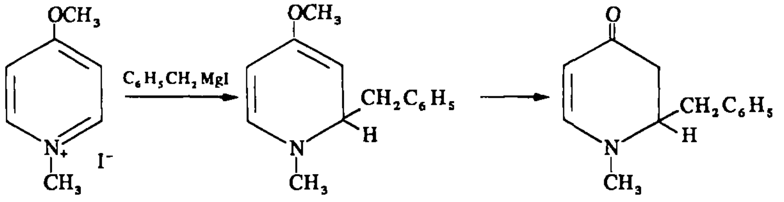
N. *Miscellaneous*

2-Pyridone and sulfur dichloride in benzene give 2,2′-dihydroxy-5,5′-dipyridyl sulfide **(XI-724)**. 3-Pyridinol and SCl_2 form a poorly defined product and 4-pyridone did not react.[766]



XII-724

4-Methoxy-1-methylpyridinium iodide **(XI-725)** and benzylmagnesium iodide in ether give 2-benzyl-1,2-dihydro-4-methoxy-1-methylpyridine, an air-sensitive red oil, which forms 2-benzyl-2,3-dihydro-1-methyl-4-pyridone when heated with sodium hydroxide in aqueous methanol.[767]

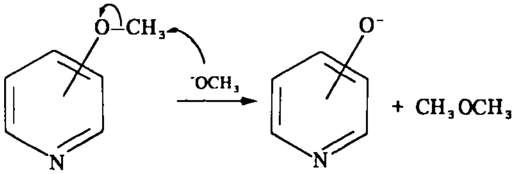


XII-725

IV. O- and N-Substitution Products

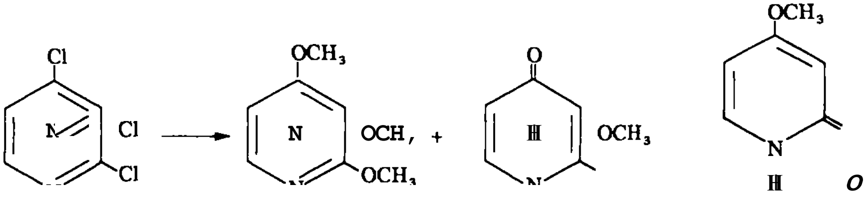
1. Reactions of Ethers (See also Section I.6.A)

The annular nitrogen of pyridine ethers, like a nitro group, performs not only as an activating group in nucleophilic substitutions but also increases the susceptibility to alkyl-oxygen cleavage of the alkoxy group by an S_N2 mechanism. The relative rates of cleavage at 164.7° of 2-, 3-, and 4-methoxypyridine (**XII-726**) by sodium methoxide in methanol to give the anion and dimethyl ether are 1.0: 1.1:2.8.[268] **2,4-Dichloropyridine** and sodium methoxide in methanol not only give 2,4-dimethoxypyridine (**XI-727**) as the major product but also 2-methoxy-4-pyridone (**XI-728**) and minor amounts of 4-methoxy-2-pyridone. **2-Chloro-4-methoxypyridine** gives **XII-727** and **XII-728**.[768] This



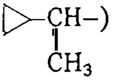
XII-726

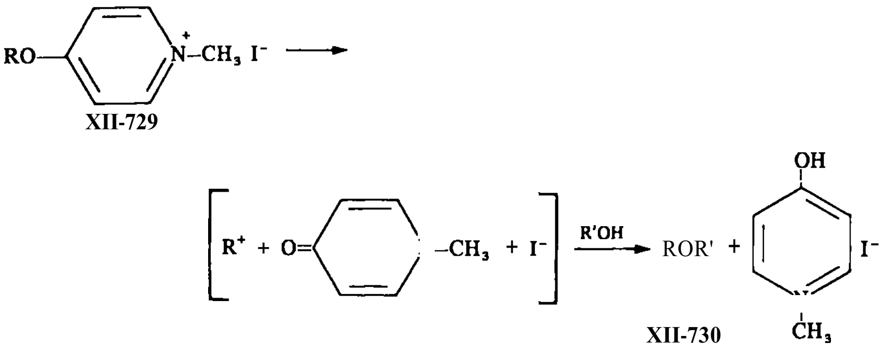
cleavage reaction is observed also as a side reaction during the formation of a Meisenheimer adduct from 2-methoxy-3,5-dinitropyridine and methanol.[769]



XII-727 XII-728

4-Alkoxy-1-methylpyridinium salts (**XII-729**) have been used to study the behavior of carbonium ions in solvolyses. They are easy to prepare and purify, and in solvolyses the leaving group does not undergo internal return. The solvolysis of **4-(cyclopropylcarbinyloxy)-1**-methylpyridinium iodide (**XII-729**, R = CH_2–◁) in 80% ethanol gives some cyclopropylcarbinol, cyclobutanol, and allylcarbinol but mainly the corresponding ethyl ethers (**XII-730**; R = cyclopropylcarbinyl, cyclobutyl, allylcarbinyl; R' = C_2H_5) in a ratio of 3.6:1.5:1.0.

Hydrolysis of optically active 4-(cyclopropylmethylcarbinyloxy)-1-methylpyridinium iodide (**XII-729**, R =  $\triangleright\!-\underset{CH_3}{CH}-$) in the presence of lithium carbonate gives cyclopropylmethylcarbinol that is 95.6% racemic.[770]

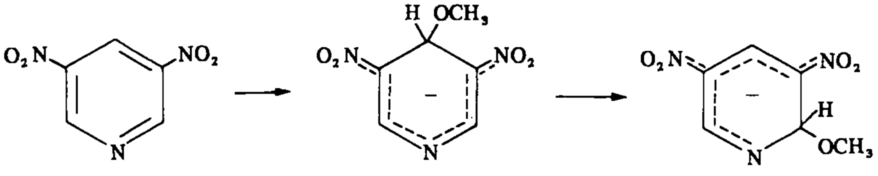


XII-729

XII-730

A methoxy group *meta* to a reaction site is normally activating in aromatic nucleophilic substitutions (σ_m is positive). However, the methoxy group of 2-chloro-4-methoxypyridine retards the reaction with sodium methoxide relative to that with 2-chloropyridine (k_{MeO}/k_H = 0.71 at 15"). It has been proposed that a conjugative interaction between the electron releasing methoxyl group and the ring nitrogen reduces the activation of the 2-halo by nitrogen.[768] Sigma complexes, formed from sodium methoxide and polynitroanisoles, have been studied extensively to shed light on the nature of nucleophilic aromatic substitution.[771] These studies have been extended recently to heterocyclic systems including 3,5-dinitropyridine,[772,773] 4-methoxy-3,5-dinitropyridine,[774-777] and 2-methoxy-3,5-dinitropyridine[769,774,777] whose properties are similar to those of the nitroanisoles.

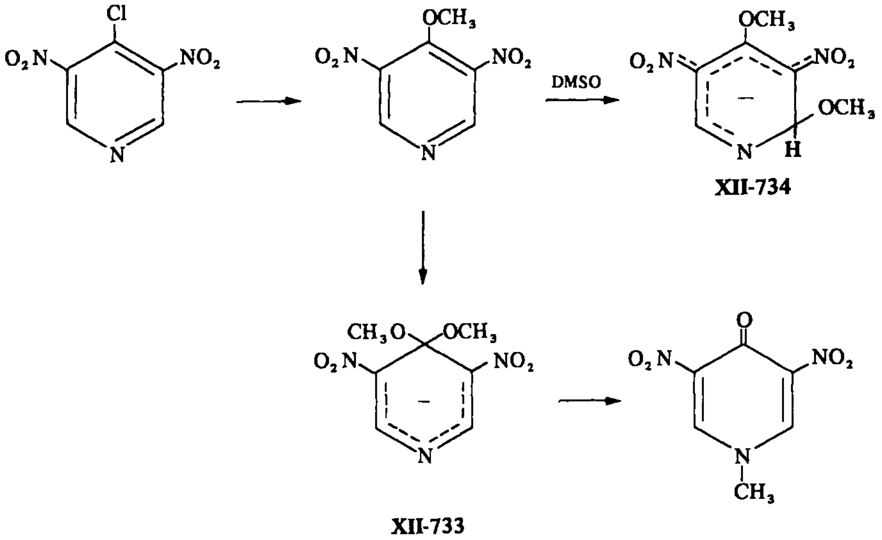
Addition of sodium methoxide to a solution of 3,5-dinitropyridine in dimethyl sulfoxide gave the anion **XII-731**, which rapidly rearranged to **XII-732** ($t_{0.5}$ 10min).[773] This was the only anion observed in methanol.



XII-731

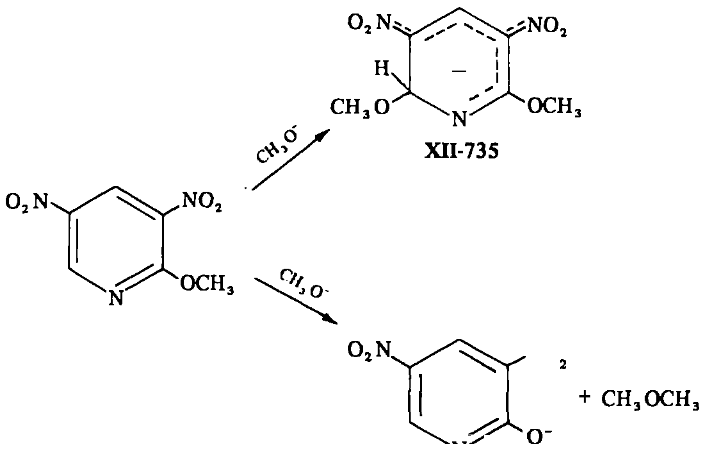
XII-732

4-Chloro-3,5-dinitropyridine[775] or **4-methoxy-3,5-dinitropyridine**[776] and sodium methoxide in methanol give sodium 4-aza-1,1-**dimethoxy-2,6-dinitro**-cyclohexadienate **(MI-733)**. In dimethyl sulfoxide the adduct **XII-734** is **formed**,[774] which may be an intermediate in the formation of **XII-733**.[776] The product of rearrangement, *N*-**methyl-3,5-dinitro-4-pyridone**, is formed by treatment of a solution containing XII-733 with acetic acid or by heating **4-methoxy-3,5-dinitropyridine**.[776, 777] The conversion of 2,6-dinitrochloro-



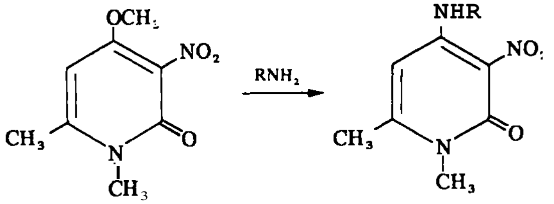
benzene to the methyl ether is faster in dimethyl sulfoxide than in methanol, which solvates the methoxide ion. When **3,5-dinitro-2-methoxypyridine** is treated with sodium methoxide in methanol, excess solvent causes irreversible formation of the sodium salt of **3,5-dinitro-2-pyridone** by a competitive rather than a consecutive **reaction**.[769] The only Meisenheimer adduct observed is the **2-aza-1,3-dimethoxy-4,6-dinitrocyclohexadienate** anion (XII-735), which is more conveniently formed in dimethyl **sulfoxide**.[769, 777] However, the behavior of **3,5-dinitro-2-methoxypyridine** in dimethyl sulfoxide could not be related directly to nucleophilic heteroaromatic substitution because of the failure of W-735 to rearrange to the 1,1-**adduct**.[769, 777]

The preferred structure of the sigma complex presumably depends on steric effects. The methine complex XII-734 experiences adverse steric interactions between the methoxyl group bound to the sp^2 carbon and the other nitro groups. This compression is enhanced in protic solvents where XII-733 predominates. In **3,5-dinitro-2-methoxypyridine**, the annular nitrogen provides **only** a small steric effect and the methine complex XII-735 is **observed**.[777]



Equilibrium constants[775, 776] and rates of formation[776] for the adduct MI-733 have been measured and compared with those of 2,4,6-trinitroanisole. An annular nitrogen in the 4-position to a reactive center results in a relative decrease in stability of the Meisenheimer compound and an increase in its rate of formation when compared to the effect of a p-nitro

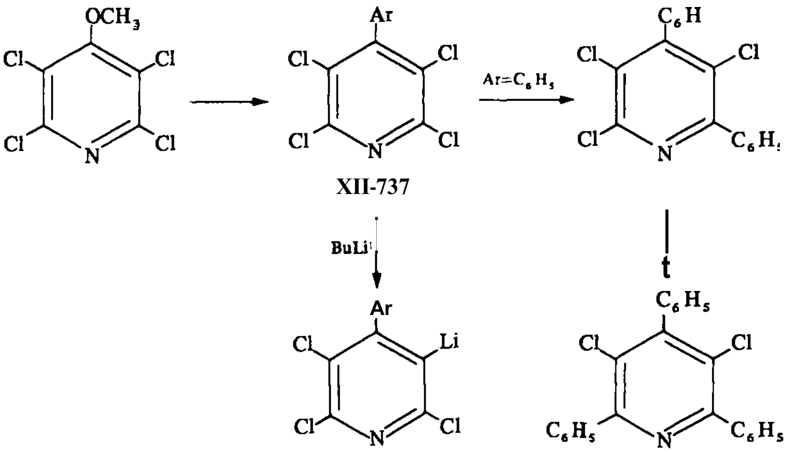
The 4-methoxypyridone (W-736) has been used to prepare a number of 4-hydrazino- and substituted-4-amino-1-methyl-2-pyridones.[86]



XII-736

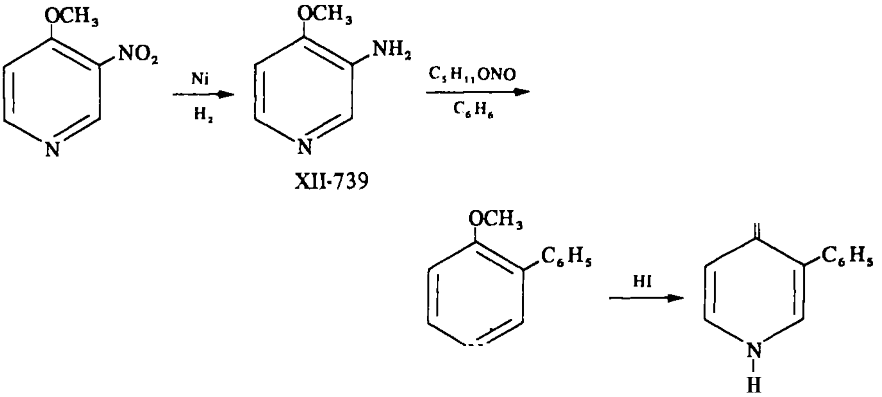
Grignard[778] and organolithium reagents[778, 779] react with tetrachloro-4-methoxypyridine to form 4-alkyl- and 4-aryltetrachloropyridines. Phenyllithium and tetrachloro-4-methoxypyridine form tetrachloro-4-phenyl- (MI-737, Ar = C_6H_5)[778, 779] trichloro-4,6-diphenyl- and dichloro-2,4,6-triphenylpyridine.[779] Under mild conditions a series of aryllithium compounds form 4-aryltetrachloropyridines (XII-737) that react with butyllithium to give 4-aryl-trichloro-3-pyridyllithium (XII-738).[778, 779]

3-Phenyl-4-pyridone has been prepared from 4-methoxy-3-nitropyridine by a diazotization of 3-amino-4-methoxypyridine (XII-739) with pentyl nitrite in the presence of benzene and in the absence of added acid.[780]



XII-737

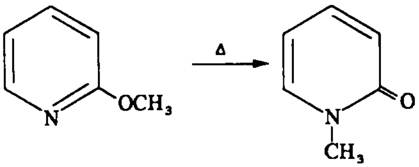
XII-738



XII-739

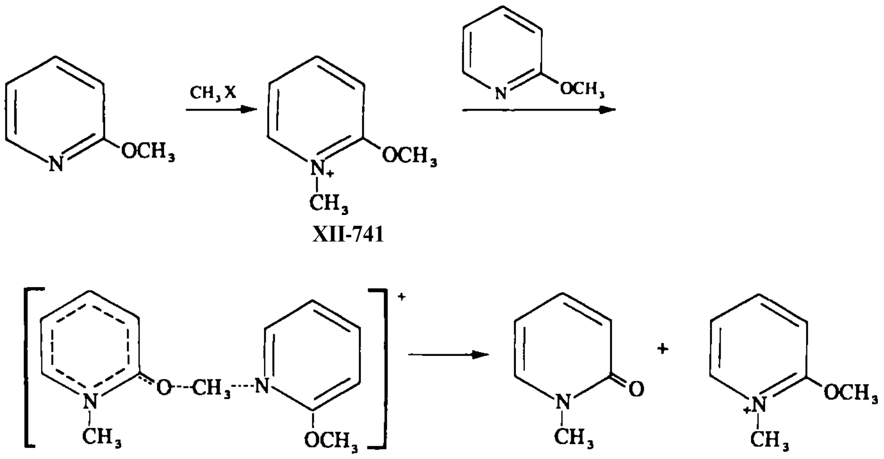
2. O → *N*-Rearrangement

Although it has been shown that the thermal rearrangement of 2-methoxypyridine to N-methyl-2-pyridone (**XII-740**) is intermolecular and is catalyzed by benzoyl peroxide,[781] these features of *O* → N rearrangements are not universal.[782, 783] Four centered mechanisms have been suggested for rearrangements of methoxypyrroline[782] or 2-alkoxypyrimidines.[783] However, intramolecularity in rearrangements of 2-alkoxypyrimidines has not been demonstrated.[784] Ion-pair intermediates have been suggested for the rearrangement of 4-methoxypyridine to *N*-methyl-4-pyridone and for the rearrangements of 2-alkoxypyrimidines to N-alkyl-2-pyrimidones.[783]



XII-740

The O → *N* rearrangement of 4- and 2-alkoxypyridines are catalyzed by alkyl halides through quaternary nitrogen derivatives (e.g., **MI-741).** Catalytic amounts of methyl iodide have been used to convert the methoxypyridines to *N*-methylpyridones under relatively mild **conditions.**[139, 530]

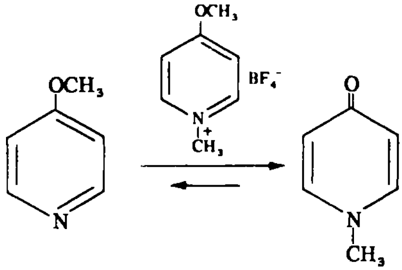


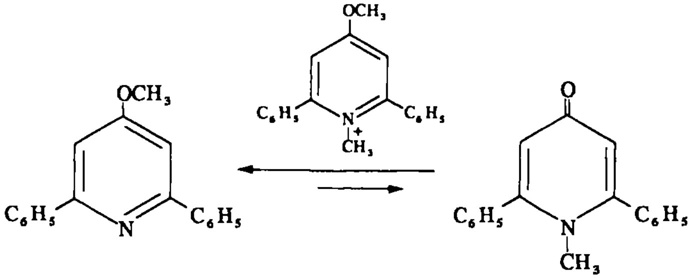
XII-741

XII-742

Acid and alkyl halide-catalyzed rearrangements have been considered to involve an intermolecular ion-pair **intermediate.**[783]

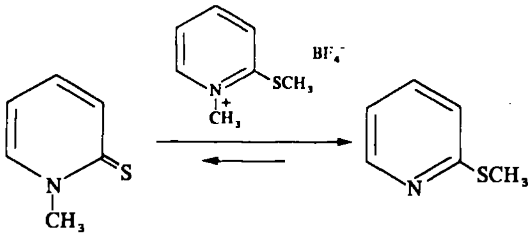
2-Methoxypyridine, 4-methoxypyridine, and **2,6-diphenyl-4-methoxypyridine** have been equilibrated in the liquid phase (130–250”) with their respective pyridone isomers in the presence of the corresponding methoxy-1-methyl-pyridinium tetrafluoroborate presumably *via* a species isomeric with **XI-742.** Although the pyridone (e.g., **XII-743)** is more stable in the above cases, **4-methoxy-2,6-diphenylpyridine** is more stable than 2,6-diphenyl-1-methyl-4-pyridone **(XII-744)** because **of 1,2,6-steric interactions.**[530] Experiments using 2-methoxy- and 4-methoxypyridine in the presence of isotopically labeled catalysts showed that oxygen to oxygen transfer occurs in addition to oxygen to nitrogen transfer, but that nitrogen to oxygen transfer does not **occur.**[530]


XII-743

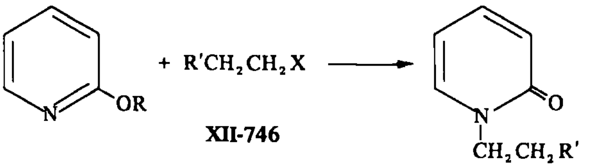

XII-744

Equilibration of ***N*-methyl-2-pyridinethione** (XII-745) with 2-methylthiopyridine in the presence of *N*-methyl-2-methylthiopyridinium tetrafluoroborate showed that the thioether is the more stable in the liquid phase [$K_{eq.}$ = **14.4 (188°), 10.7 (145°)**].[532]

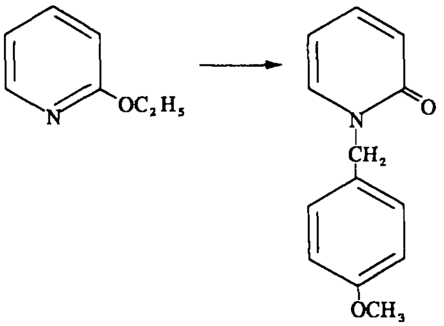
The alkyl halide-catalyzed rearrangement can be extended to reactions where R ≠ R' and provides a convenient route to *N*-alkylpyridones as an alternative to direct alkylation. For example, although alkylations of 2-pyridone salts with **β-(6-methoxy-1-naphthyl)ethyl** halides (**MI-746**, R' = 6-methoxy-1-naphthyl) appear to be unsuccessful, 2-ethoxypyridine and **XI-746** [X = Br, R' = 1-(6-$CH_3OC_{10}H_6$), C_6H_5] give the *N*-arylethyl derivative in good yield.[341]


XII-745

p-Anisyl chloride and an excess of 2-ethoxypyridine give a quantitative yield of 1-(*p*-methoxybenzyl)-2-pyridone (**MI-747**) when heated without a solvent.[762]



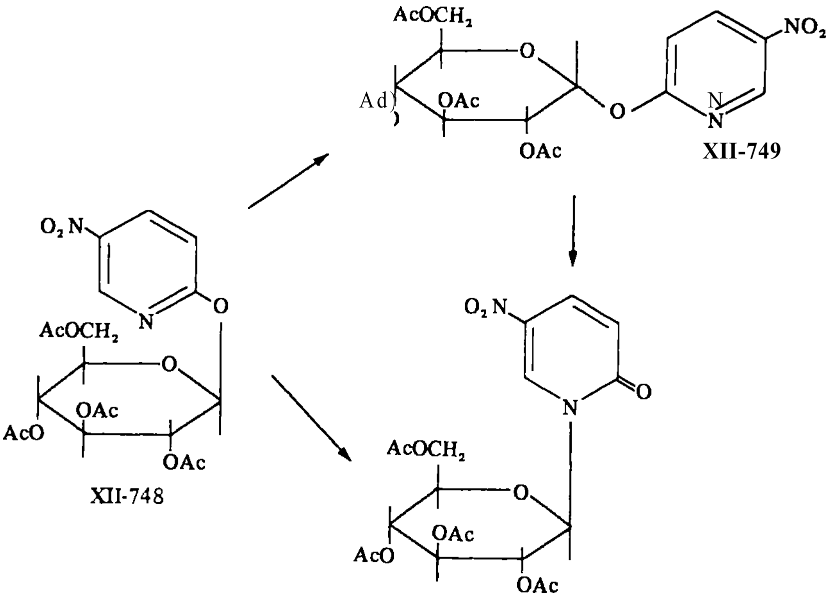
XII-746



XII-747

The product of direct alkylation of a pyridone or pyrimidone salt is the alkoxy derivative if the reagent is bulky. For example, O-glycosides are formed from halogenoses and these heterocycles, but can be rearranged to Nglycosides by heating with mercuric bromide in a solvent such as toluene. (See section on alkylation, III.1.A.). Recently, catalysis of rearrangement by other Lewis acids has been reported.[609] For example, the main product obtained from the silver salt of 5-nitro-2-pyridone and acetobromoglucose is the *β*-*O*-acetoglucoside (**XII-748**), which rearranges to the *α*-*O*-glucoside (**MI-749**) and the *β*-*N*-glucoside (**MI-750**) when treated with mercuric bromide in boiling toluene.[605, 609] Stannic chloride, titanium chloride, or antimony chloride and **XII-748** in benzene at room temperature or zinc chloride or cadmium chloride in boiling benzene also give **XII-750**. The *α*-anomer (**XU-749**) and mercuric chloride or stannic chloride in benzene also gives **XII-750**.[609]

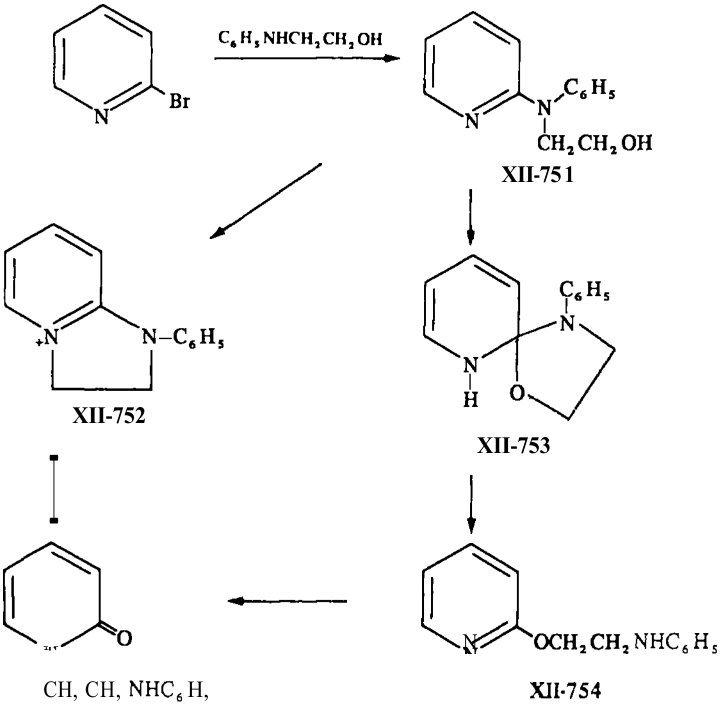
Treatment of 2-bromopyridine with *N*-phenylethanolamine gives *N*-(*β*-anilinoethyl)-2-pyridone.[785] It has been suggested that 2-(*N*-*β*-hydroxyethylanilino)-pyridine (**MI-751**) is first formed and that subsequent rearrangement occurs *via* **XII-752** or *via* **XII-753** and **XII-754**.[785]



XII-748

XII-749

XII-750



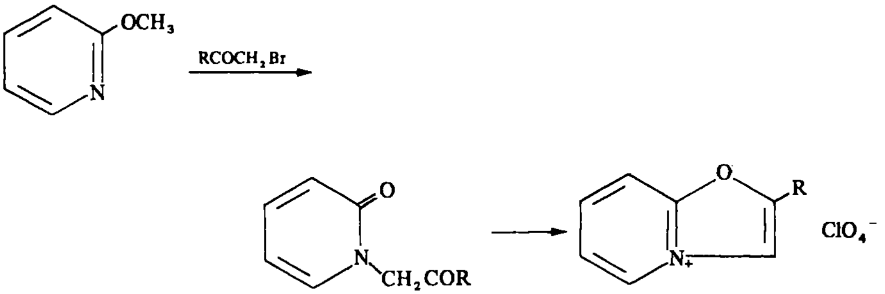
XII-751

XII-752

XII-753

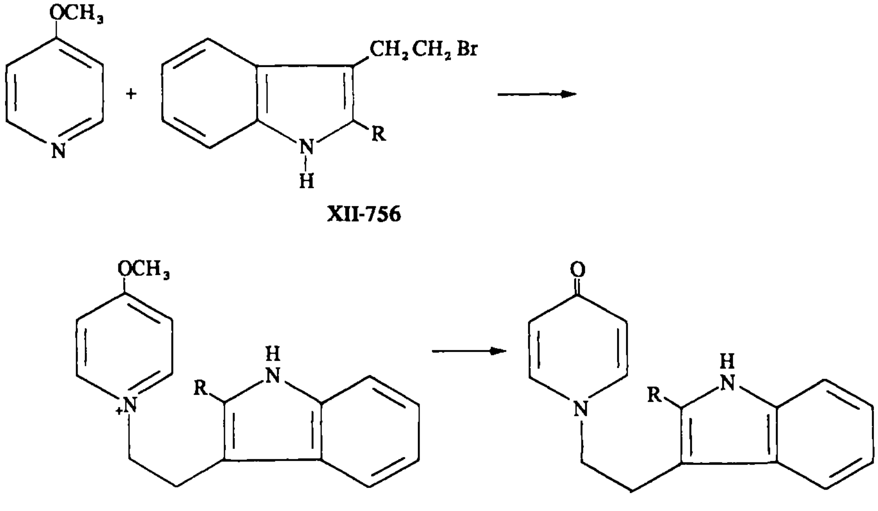
XII-754

Alkylation of 2-methoxypyridine with a phenylacyl bromide or bromoacetone gives *N*-phenacyl- or *N*-acetonyl-2-pyridone, which can be cyclized in sulfuric acid or perchloric acid to oxazolo[3,2-*a*]pyridinium salts (RJ. 1115), which have been isolated as their perchlorates **(XII-755)**.[786, 787]



XII-755

4-Methoxypyridine and β-(3-indolyl)ethyl bromides (W-756 ; R = H, CH_3) in ethanol give 1-[β-(3-indolyl)ethyl]-4-methoxypyridinium bromide, which is converted to indolylethylpyridones **(XII-757)** by treatment with sodium hydroxide in ethanol.[788] 4-Methoxy-3-pyridinecarboxamide and methyl iodide give 3-carboxamido-1-methyl-4-pyridone.[789]

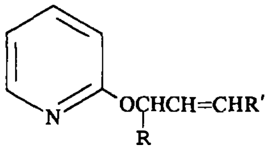


XII-756

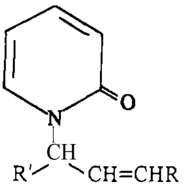
XII-757

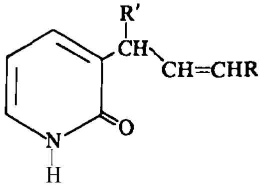
2-Allyloxy- (W-758 , R = R' = H),[598, 790] 2-methallyloxy- (XII-758; R = CH_3, R' = H)[790] and 2-crotoxypyridine (XI-758 ; R = H, R' = CH_3)[790] give *N*- and

3-substituted pyridones by a normal Claisen rearrangement when heated in dimethyl- or diethylaniline.[790] When 2-crotoxypyridine is rearranged neat, a



XU-758



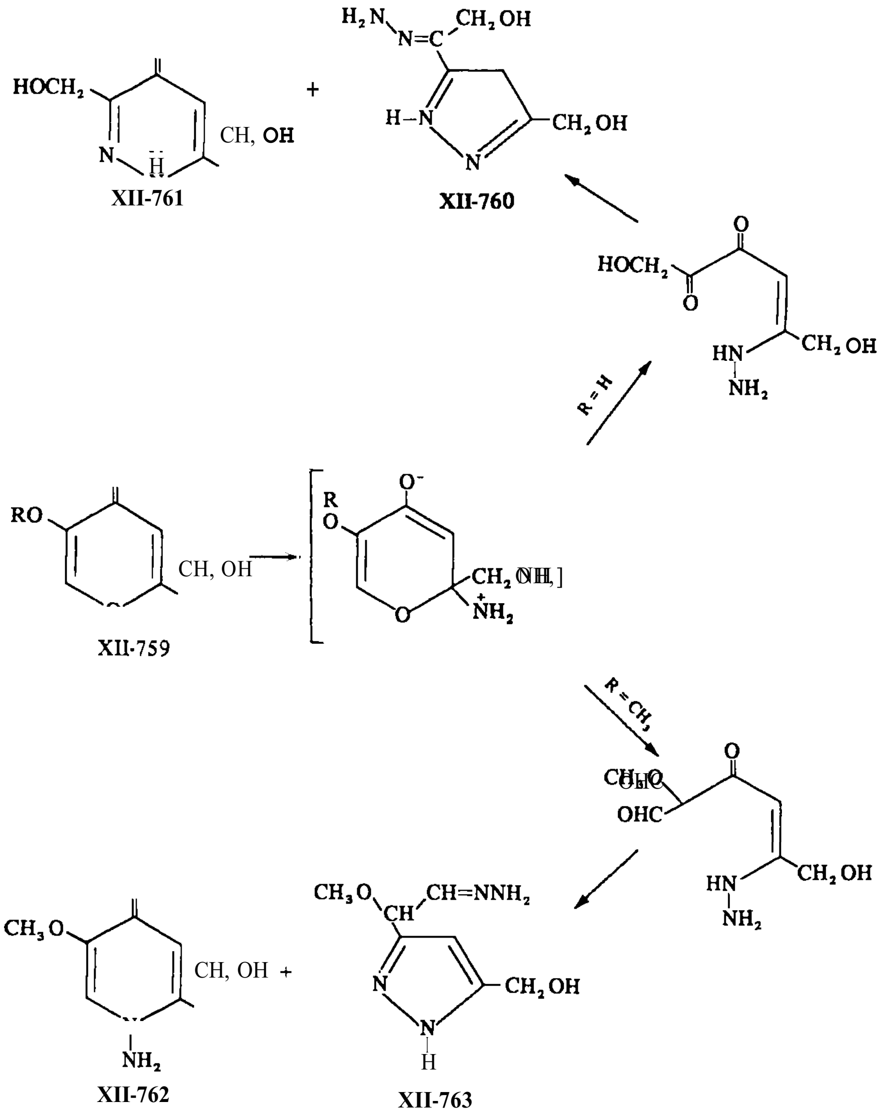


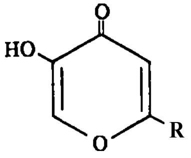
normal Claisen rearrangement gives **3-methallyl-2-pyridone**, but the rearrangement to nitrogen provides both the Claisen product, ***N*-methylallyl-2-pyridone,** and ***N*-crotyl-2-pyridone,** an abnormal **product.**[790] Possibly, the abnormal product could be formed by a [1,3]-sigmatropic process that competes with the Claisen rearrangement, a [3,3]-sigmatropic rearrangement. Attempted rearrangement of 4-allyloxypyridine was **unsuccessful.**[598]\ 2-Allyloxypyridines, like alkyloxypyridines, rearrange in good yield to ***N*-allyl-2-pyridones,** in the presence of Lewis acids. 2-Crotoxypyridine rearranges to *N*-methallyl-2-pyridone in the presence of chloroplatinic acid but gives *N*-crotoxy-2-pyridone and some 3-crotyl-2-pyridone in the presence of boron trifluoride etherate, demonstrating the different roles of the two **catalysts.**[791]

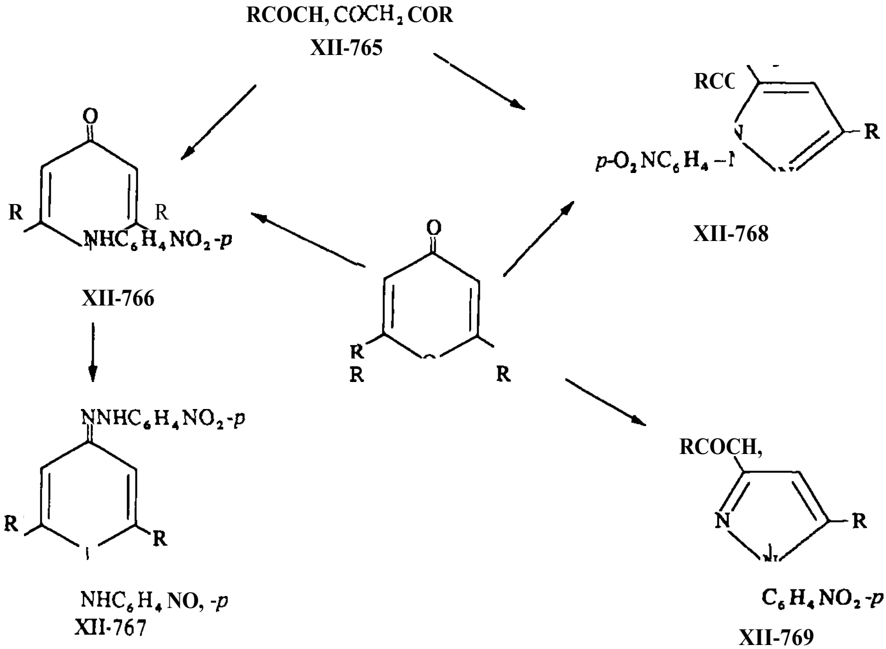
3. *N*-Amino Derivatives

Kojic acid (XII-759, R = H) and hydrazine give the corresponding pyrazole derivative (XII-760) and **3,6-bis(hydroxymethyl)-4-pyridazinone (XII-761).**[792, 793] However, **2-hydroxymethyl-5-methoxy-4-pyrone** (Kojic acid 5-monomethyl ether) **(XII-759,** R = CH_3), which contains a blocked 5-position, gives 1-**amino-2-hydroxymethyl**d**-methoxy-4-pyridone** **(XII-762)** (20%) and **α-(3-hydroxymethyl-5-pyrazolyl)-α-methoxyacetaldehyde** hydrazone **(XII-763)** (35%). These results suggest a nucleophilic attack by hydrazine at the a-position of the pyrone, followed by ring opening and nucleophilic attack by nitrogen at the 4-, 5-, or **6-carbon.**[794, 795] Allomaltol **(XII-764,** R = CH_3**)** and pyromeconic acid (XII-764, R = H) also give pyridazine and pyrazole **derivatives.**[794] α-(3-Pyrazolyl)acetaldehyde hydrazone was the only product isolated from 4-pyrone and hydrazine **hydrate.**[796, 797]

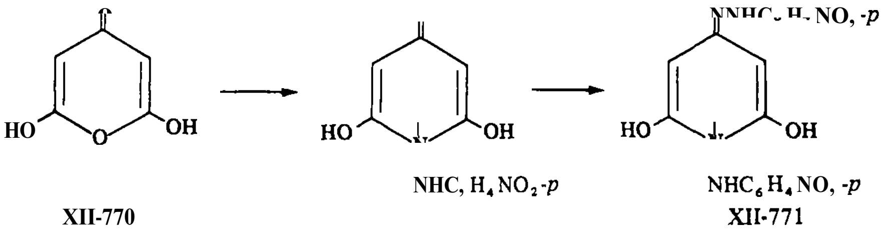
Products formed from 1,3,5-triketones **(XII-765)** or γ-pyrones and *p*-nitrophenylhydrazine had originally been assigned the structures **XII-766** and **XII-767.**[798, 799] However, it has been shown that 4-pyrone and *p*-nitrophenylhydrazine give the *p*-nitrophenylhydrazone of the pyrazole (XII-768, R = H).[797]


XII-761 XII-760 XII-759 XII-762 XII-763

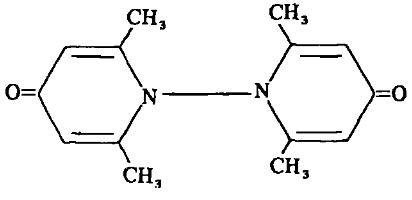

XII-764



It has been proposed subsequently that diacetylacetone (**MI-765**, R = CH_3) and *p*-nitrophenylhydrazine form **XII-768** or **XI-769** (R = CH_3) and that a second compound that is described as the 4-pyridone **MI-766** (R = CH_3) is formed from **2,6-dimethyl-4-pyrone**. Reaction of **XI-766** with additional p-nitrophenylhydrazine gives **XII-767** (R = CH_3).[140] It is proposed that acetonedicarboxylic anhydride (**XII-770**) and phenylhydrazines give the pyridone derivatives.[140, 800, 801] For example, **XI-770** and p-nitrophenylhydrazine give the **N-(*p*-nitroanilino)-4-pyridone** and its *p*-nitrophenylhydrazone (**XII-771**).[800]

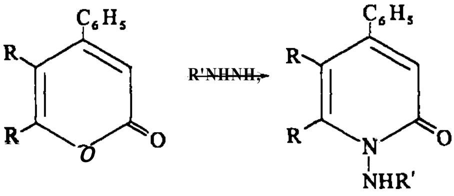


Hydrazine and **2,6-dimethyl-4-pyrone** appear to give the bipyridone **XII-772**.[140] Triaryl-2-pyrones react with hydrazine and phenylhydrazine to give



XII-772

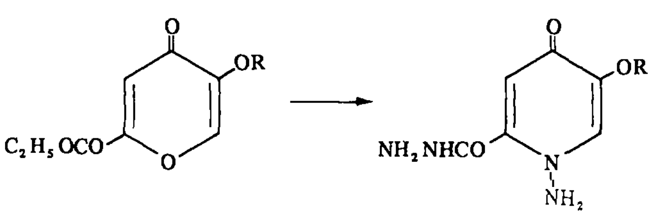
the *N*-amino- and *N*-phenylamino-2-pyridones (XII-773), respectively.[120-122, 802]



XII-773

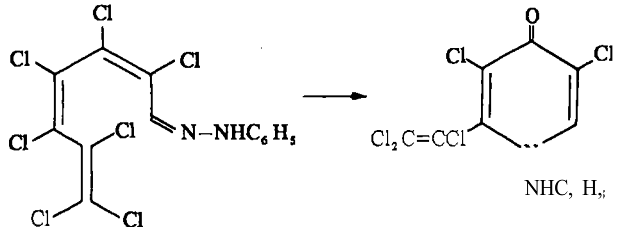
R' = C_6H_5, H; R = C_6H_5, p-BrC_6H_4-, p-$CH_3C_6H_4$-

Reactions of the 1-amino group of 1-amino-4,5,6-triaryl-2-pyridones have been studied.[802] The ethyl esters of 3-benzoyloxy-4-oxo-4*H*-pyran-6-carboxylic acid and hydrazine in ethyl alcohol are reported to give the hydrazide of 1-amino-3-benzoyloxy-4-pyridone-6-carboxylic acid (XII-774, R = C_6H_5CO) but only in 8% yield. Similarly, 6-carbethoxy-3-methoxy-4-pyrone and hydrazine give MI-774 (R = CH_3).[803]



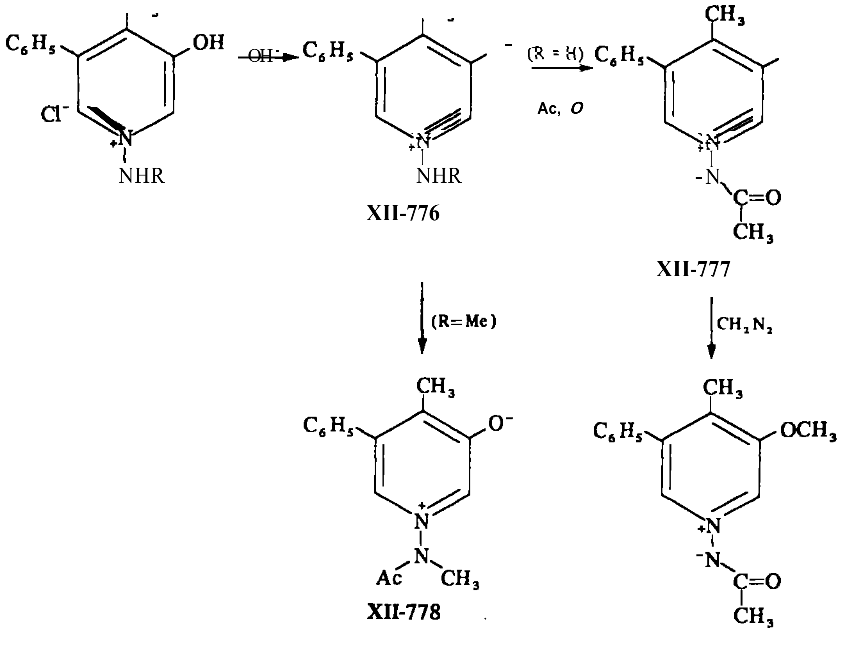
XII-774

cis,cis-2,4,6-Perchloroheptatriene-6-al phenylhydrazone (MI-775) gives 1-anilino-3,5-dichloro-2-trichlorovinyl-4-pyridone when heated in aqueous ethanol. The corresponding 2,4-dinitrophenylhydrazone required heating in acetic acid-hydrochloric acid to effect cyclization. The bromo analog was prepared similarly.[233]



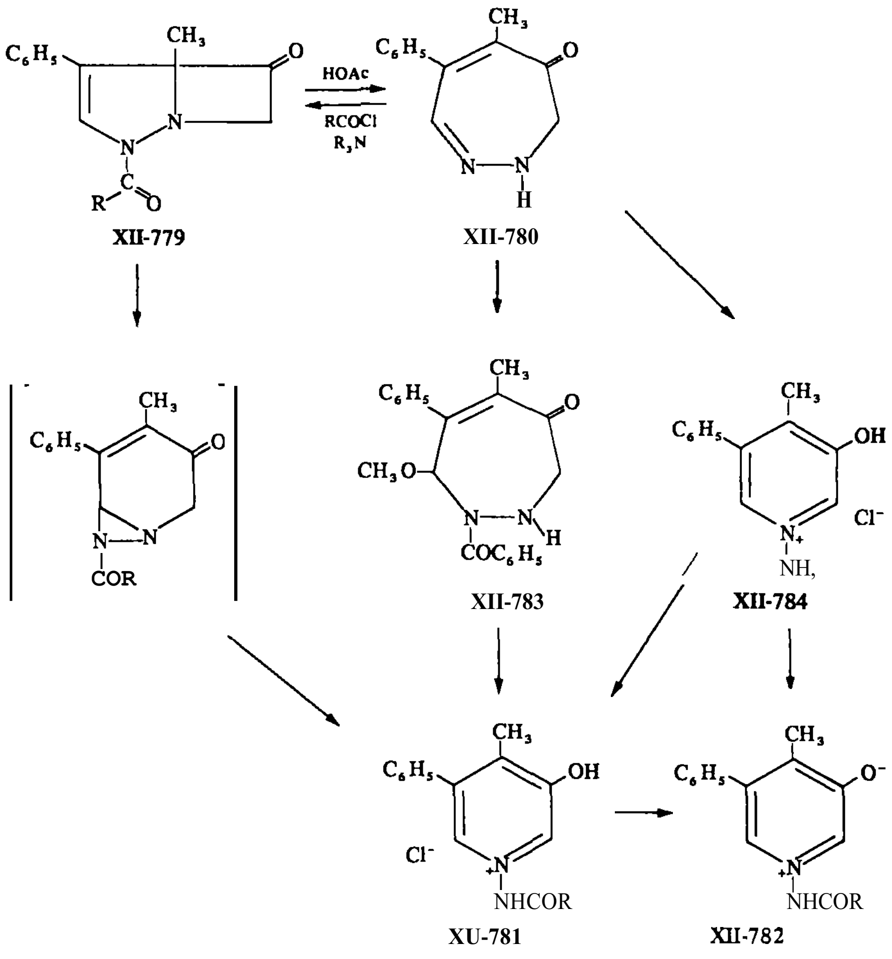
XII-775

1-Amino- and **1-methylamino-3-hydroxy-4-methyl-5-phenylpyridinium** chloride react with alkali or carbonate to form the corresponding pyridinium betaines (**XII-776**). The amino group of **XII-776** (R = H) is not basic but has the

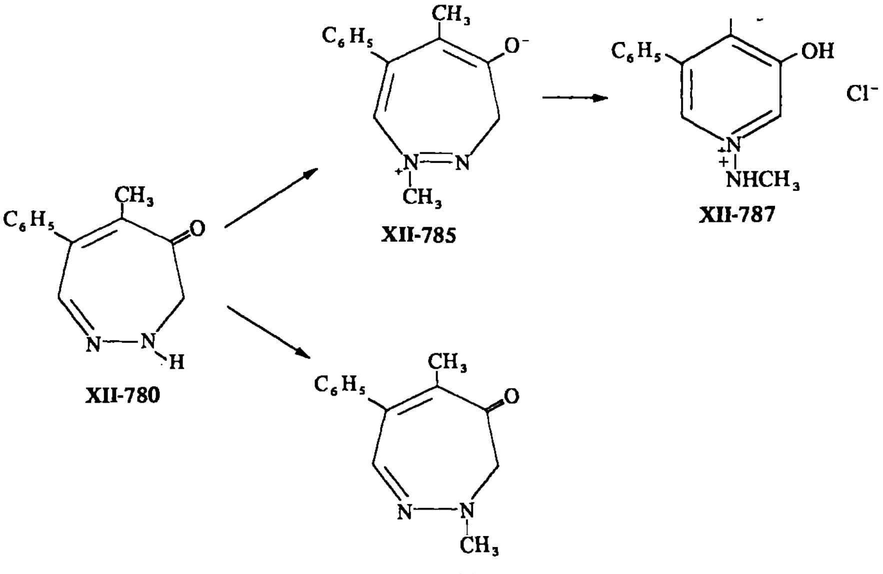


reactivity of a primary amine. For example, **W-776** (R = H) reacts with acetic anhydride to form the ylid (**XII-777**), which is *O*-alkylated with diazomethane. Trifluoroacetic anhydride and benzoyl chloride react similarly with **XII-776** (R = H). Acetylation of the *N*-methylaminopyridinium betaine (**W-776**, R = CH_3) gives the betaine **XII-778**, which, in contrast to **W-777**, is labile to hydrolysis.[219]

The interconvertible ring systems XII-779 and **W-780** can give amino-3-pyridinols when treated with aqueous acids. In hydrochloric acid-methanol, 2-acetyl- and **2-benzoyl-5-methyl-4-phenyl-1,2,-diazabicyclo**[3.2.0]-3-hepten-**6-one (MI-779)** rearrange to *N*-acetamido- and *N*-benzamido-3-hydroxy-4-methyl-5-phenylpyridinium chloride (**MI-781**; R = CH_3, C_6H_5) by an allylic shift of the bridging bond from C-5 to C-3 (see the section on 3-pyridinols for a discussion of this interconversion).[220,804] The pyridinium salts XII-781 are converted to betaines (XII-782) by treatment with pyridine or by neutralization with base.[804] When the diazapine (**W-780**) is treated with benzoyl chloride and pyridine in methanol, the 1-**benzoyl-7-methoxytetrahydrodiazepinone (W-783)** is isolated and forms XII-781 on treatment with acid. Treatment of XII-780 with **10%** hydrochloric acid gives 1-**amino-3-hydroxy-4-methyl-5-phenylpyridinium** chloride (**XII-784**),[216, 220] which gives **XI-781** on treatment with benzoyl chloride in pyridine.[804]



Dimethyl sulfate and **XII-780** give the *N*-methylated products **XII-785** and **XI-786.** The hydrochloride **of XII-785** rearranges to **XII-787.**[216]



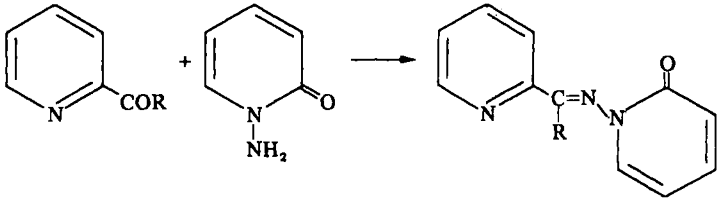
XII-780

XII-785

XII-787

XU-786

1-Amino-2-pyridone and 2-pyridinecarboxaldehyde in methanol give ***N*-(1-pyridyl-2-one)-2-pyridinealdimine** (XII-788, R = H). **Although** the Schiffs base from 1-amino-2-pyridone and 2-acetylpyridine (**W-788,** R = CH_3) is not easily isolated, it forms complexes with iron(II), nickel(II), and Co(II) **perchlorates**[805] (see Section IV.5.).

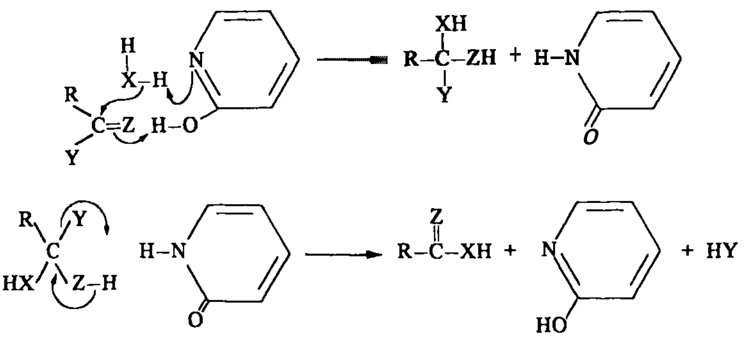


XII-788

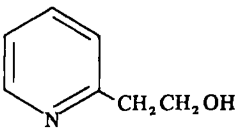
4. Bifunctional Catalysis

Although early investigators considered that general acid-general base catalysis was operative in the mutarotation **of** tetramethyl-D-glucose in benzene[806] and in the aminolysis of p-nitrophenyl acetate,[807] recent studies have demonstrated that tautomeric catalysis is consistent with observations. It has been suggested that this mechanism is prevalent particularly in reactions of carbonyl compounds where bifunctional catalytic effects have been observed and where 2-pyridone and similar tautomeric catalysts are effective.[807] The existence of a concerted general acid-base reaction mechanism has not been substantiated.[808]

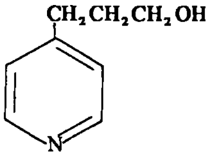
A tautomeric catalyst is defined as a "molecule that repeatedly cycles between two tautomeric states during the course of catalysis in a chemical reaction."[807] A concerted mechanism has been proposed:



It has, however, been observed that 2-(β-hydroxyethyl)pyridine (XII-789) and 4-(γ-hydroxypropyl)pyridine (XII-790), which appear to act as bifunctional catalysts, are somewhat more effective than 2-pyridone in the hydrolysis of



XII-789



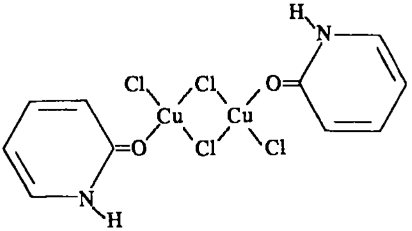
XII-790

p-nitrophenyl acetate.[809] 2-Pyridone, which acts as a bifunctional catalyst in peptide synthesis,[810-812] does not cause racemization in the synthesis of *N*-benzyloxycarbonyl-L-leucyl-L-phenylalanyl-L-valine t-butyl ester from *N*-benzyloxycarbonyl-L-leucyl-L-phenylalanine p-nitrophenyl ester and L-valine t-butyl ester in acetonitrile,[811] and in condensations in ethyl acetate solution of carbobenzoxy-β-cyano-L-alanine with methyl glycinate to give methyl carbobenzoxy-β-cyanoalanyl glycine.[812]

Bifunctional catalysis of the reaction between fluoro-2,4-dinitrobenzene and piperidine and chloro-2,4-dinitrobenzene and piperidine by 2-pyridone, but not by *N*-methyl-2-pyridone, has been reported.[813] 2-Pyridone has been evaluated as a catalyst for the polyurethane forming **process**.[814] The oxidation of 1-dodecanethiol by tetramethylene sulfoxide is catalyzed by 2-pyridone and has been considered to be general acid and general base **catalyzed**.[815]

5. Complexes and **Organometallic** Compounds

2-Pyridone forms 1:1 adducts with $MnCl_2$, $CoCl_2$, $NiCl_2$, and $CuCl_2$. In addition, $CuCl_2$ forms a 1:2 adduct, **$CuCl_2 \cdot 2(Py\text{-}2\text{-}OH)_2$** and $CoCl_2$ forms a 1:3 adduct, **$CoCl_2 \cdot 3(Py\text{-}2\text{-}OH)$**. Powder diffraction data for the $CuCl_2$ 1:1 adduct support a chlorine bridged dimeric structure **(W-7 91)**. Generally, properties of the other 1:1 adducts are consistent with the dimeric **structure**.[816]



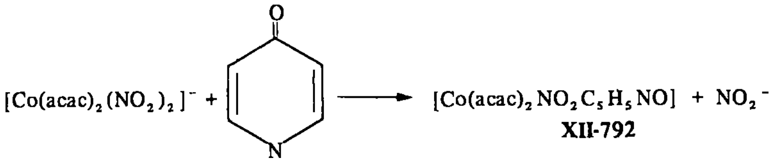
XII-791

N-Methyl-2-pyridone forms 1:1 adducts with $HgCl_2$,[817,818] $CdCl_2$,[818] and **$ZnCl_2$**[818] and forms a 1:2 adduct with $SnBr_4$.[818] **1,2,6-Trimethyl-4-pyridone** forms 1:1 complexes with $HgCl_2$, $ZnCl_2$, and $CdCl_2$. *N*-Ethyl-2,6-dimethyl-4-pyridone forms 1:1 adducts with $HgCl_2$, $CdCl_2$, and $CoCl_2$.[819] Infrared spectra indicate that the donor site of these N-methylpyridones is the carbonyl and not the **nitrogen**.[818,819]

2- And 4-pyridone coordinate at oxygen to form 1:1 adducts, **$Co(NH_3)_5PyOH(ClO_4)_3$**, with pentamminecobalt(III), which are isolated as their perchlorates. 3-Pyridinol does not react with aquopentamminecobalt(III) **perchlorate**.[820] 2-Pyridone is reduced by Cr(II) ***via*** the outer sphere mechanism, while Qpyridone is reduced ***via*** ligand transfer!''

Complexes of 2-pyridone with the structure **$M(Py\text{-}2\text{-}OH)_6(anion)_2$**, (M = **Mn**, Fe, Co, Ni, **Zn**, Cd; anion = ClO_4^-, **BF_4^-**) have the ligand in the lactam form coordinated to metal ions also *via* the carbonyl. **$Ca(Py\text{-}2\text{-}OH)_8(ClO_4)_2$** and **$Al(Py\text{-}2\text{-}OH)_6(ClO_4)_3$** have been described **also**.[822]

4-Pyridone and sodium dinitro-bisacetylacetonato carbonate(III) form a stable nonionic complex **(W-792)** that appears to be the *trans*-isomer.[823] 4-Pyridone and hydrated cobalt chloride in alcohol give a blue tetrahedral complex **$Co(Py\text{-}4\text{-}OH)_2Cl_2$**.[824]

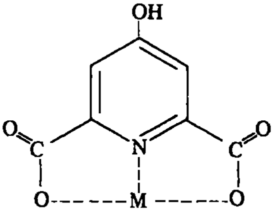


XII-792

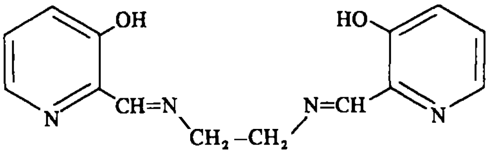
Stability constants have been determined for 1 :1 bivalent metal complexes of UO_2 , Cu, Pb, Zn, Be, Ni, Co, Cd, and rare earths with **3-hydroxy-2-pyridone.**[825]

Stability constants of 1:1 complexes **(XI-793)** formed by chelidamic acid (H_3L) and Ca^{2+}, Ba^{2+}, Sr^{2+}, Mg^{2+}, and Mn^{2+}, and of 1:1 and 1:2 complexes, $M(HL)_2$, from chelidamic acid and Co^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+} have been determined. These complexes are stabilized by loss of the phenolic proton in alkaline **solution.**[826]

Bis(3-hydroxy-2-pyridylmethylene)ethylenediamine **(HI-794)** forms 2:3 copper(II) and nickel(II) **complexes.**[827] The 1:1 complex formed from Fe(III) perchlorate and 2-pyridone has been examined spectroscopically in aqueous **solution.**[828] The Mossbauer spectrum of several substituted pyridine iron(II) derivatives has been measured, including a **bis(1,2-cyclohexadienonedioxime)-**iron(II) complex with 3-pyridinol, $Fe(II)(Niox)_2$**(Py-3-OH)**$_2$.[829]



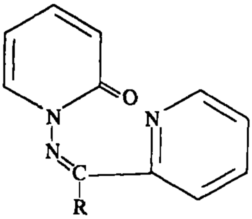
XII-793



XII-794

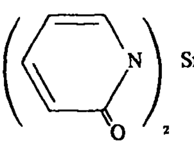
N-Amino-2-pyridone and its Schiff's bases **(XI-795)** (R = **H**, CH_3) from 2-pyridinecarboxaldehyde or 2-acetylpyridine have been studied as ligands for transition metal ions [Fe(II), Co(II), Ni(II)] .Two series of complexes have been isolated from 1-amino-2-pyridone: **ML_2Cl_2** from **the** metal chlorides and

ML$_3$(ClO$_4$)$_2$ from the perchlorates. Complexes of the general formula (ML$_2$)(ClO$_4$)$_2$ were formed from **XII-795**, a tridentate ligand that coordinates through two nitrogens and one oxygen.[805]

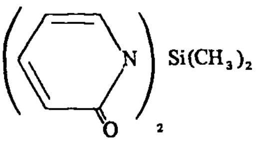


XII-795

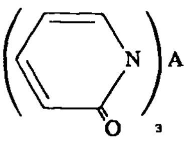
2-Pyridone reacts with dibutyl dimethyloxytin to form dibutyldi-(2-pyridonato-1)tin (**XII-796**), with dimethyl dichlorosilane to form dimethyldi-(2-pyridinato-1)silane (**XII-797**), and with aluminum ethoxide to form tri-(2-pyridinato-1)aluminum (**XII-798**). Infrared spectra are consistent with an *N*-substituted pyridone structure.[830]



XII-796

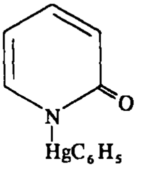


XII-797

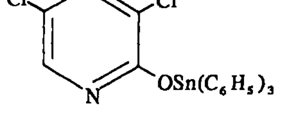


XII-798

A comparison of the ultraviolet spectra of arylmetallic derivates of pyridones with the spectra of their *N*- and 0-methyl derivatives indicates that phenylmercury derivatives of 2-pyridone, 3,5-dichloro-2-pyridone 3,5-dichloro-4-pyridone, and 4-pyridone have the lactam structure (e.g., **XII-799**), while the triphenyl tin and triphenyl lead compounds have the lactim structure (e.g., **XII-800**).[831]



XII-799



XII-800

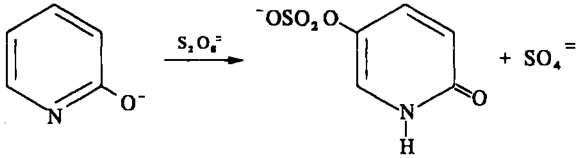
The rate of substitution of bromide in [Pt(dien)Br]$^+$ by a series of pyridine derivatives including 2-pyridone and 3-pyridinol has been considered to be governed by steric properties of the entering group rather than by its basicity.[832]

Ethyl 4,6-dihydroxy-5-nitrosonicotinate has been studied as an analytical reagent for a photometric determination of iron.[833] 3-Nitroso-2,6-pyridinediol has been studied as an analytical reagent for the photometric determinations of osmium,[834] ruthenium,[833] and palladium.[835] Ruthenium chloride appears to form a 3:1 3-nitroso-2,6-pyridinediol to ruthenium anionic complex.[836] A 2:1 complex is formed from palladium(II) chloride.[835] Methyl and ethyl esters of 1-aryl-5-hydroxy-4-pyridone-2-carboxylic acids can be used as chelating agents for the extraction and separation of niobium(V) and tantalum(V) from oxalate solutions.[837] Triethylborane and 2-pyridone form a 1:1 dimer.[838] *N*-Methyl-2-pyridone and cyclomethylenetetranitroamineform a 2:1 complex.[839]

V. Polyhydroxypyridines

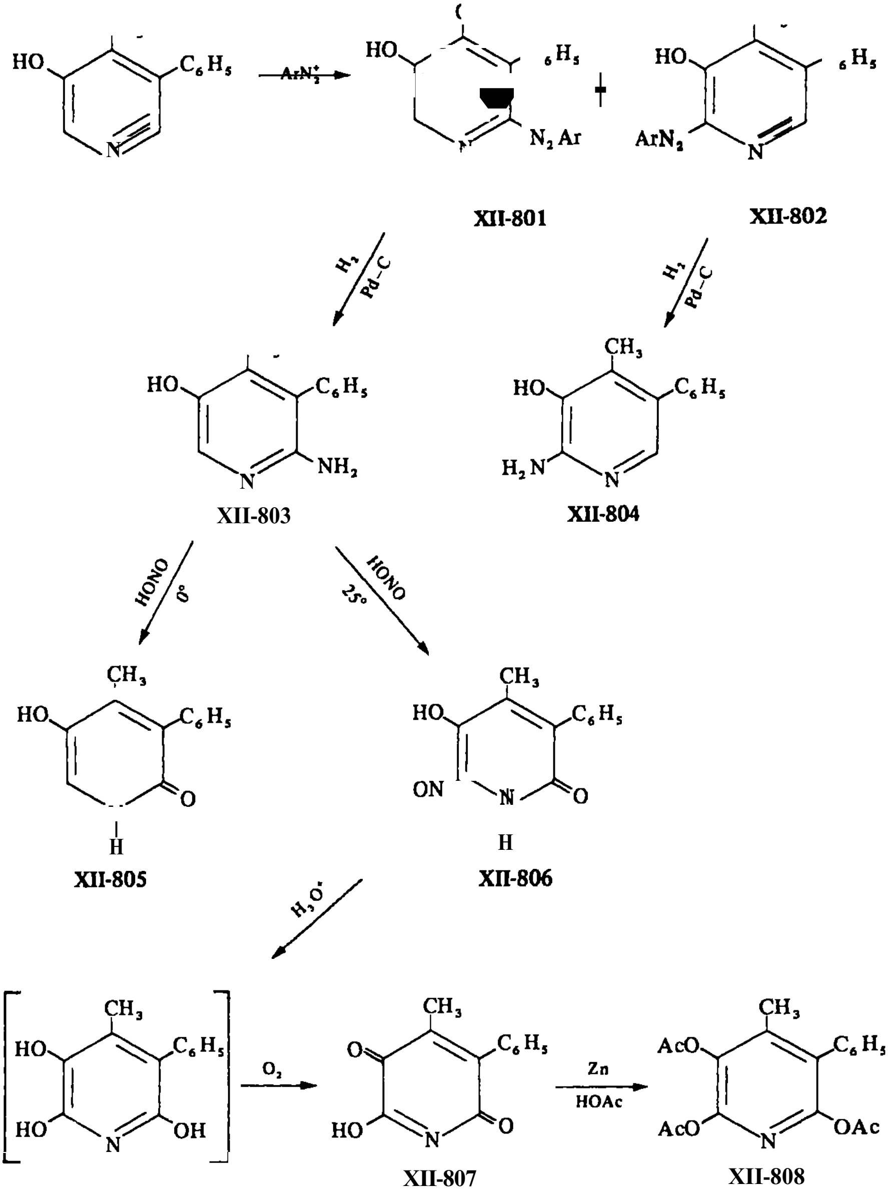
A number of 2,4- and 4,6-dihydroxy-2-pyridones can be prepared from polyhalopyridines that are available by ring closure and by direct halogenation.[15,233-235,244-248]

2-Pyridone, 4-pyridone, and 3-pyridinol undergo the Elbs peroxydisulfate oxidation, a reaction characteristic of phenols and aromatic amines. A bimolecular ionic reaction in which the 2-pyridyloxy ion attacks the peroxy-bond of the persulfate ion with displacement of sulfate ion to give 2-pyridone-5-sulfate is consistent with the observations.[840,841]

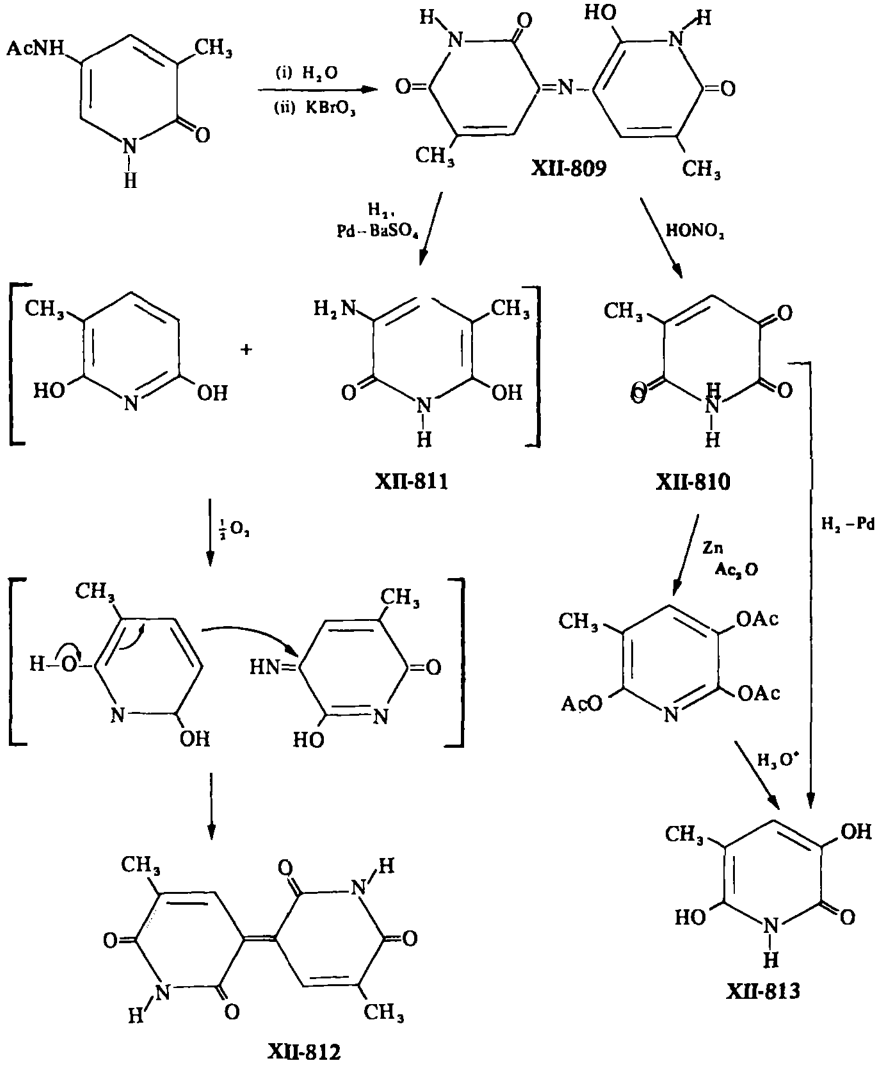


4-Methyl-5-phenyl-3-pyridinol couples with p-nitrobenzenediazonium chloride to give XII-801 and W-802 (Ar = p-$NO_2C_6H_4$), which can be hydrogenated to the corresponding aminopyridinols (XII-803 and XII-804). Treatment of XII-803 with nitrous acid gives XII-805, XII-806, or XII-807, depending on condition ~The autooxidation product W-807 can be converted to the triacetate of 4-methyl-5-phenyl-2,3,6-pyridinetriol (XII-808) by treatment with zinc dust in acetic anhydride.[292]

Compounds formed by bromate or chromium trioxide oxidation of 3- and 5-amino-2-pyridone and 3-amino-5-methyl- and 5-amino-3-methyl-2-pyridone were first described as possessing monomeric azaquinone or azaquinhydrone-type structures.[842] It has, however, been shown that after hydrolysis and oxidation with potassium bromate, 5-acetamido-3-methyl-2-pyridone forms 3-hydroxy-6-methyl-2-aza-1,4-benzoquinone-4-(2,6-dihydroxy-5-methylpyridyl)-3-imine



(XII-809).[843] Oxidation of XII-809 with nitric acid produces 5-methyl-2,3,6-pyridinetrione (XII-810). Hydrogenation of (XII-809) over Pd-BaSO$_4$ gives 4,4'-dihydroxy-5,5'-dimethyl-3,3'-diaza-2,2'-diphenoquinone (XII-812), through autooxidation of the intermediate 3-amino-5-methyl-2,dpyridinediol (XII-



XII-809

XII-811

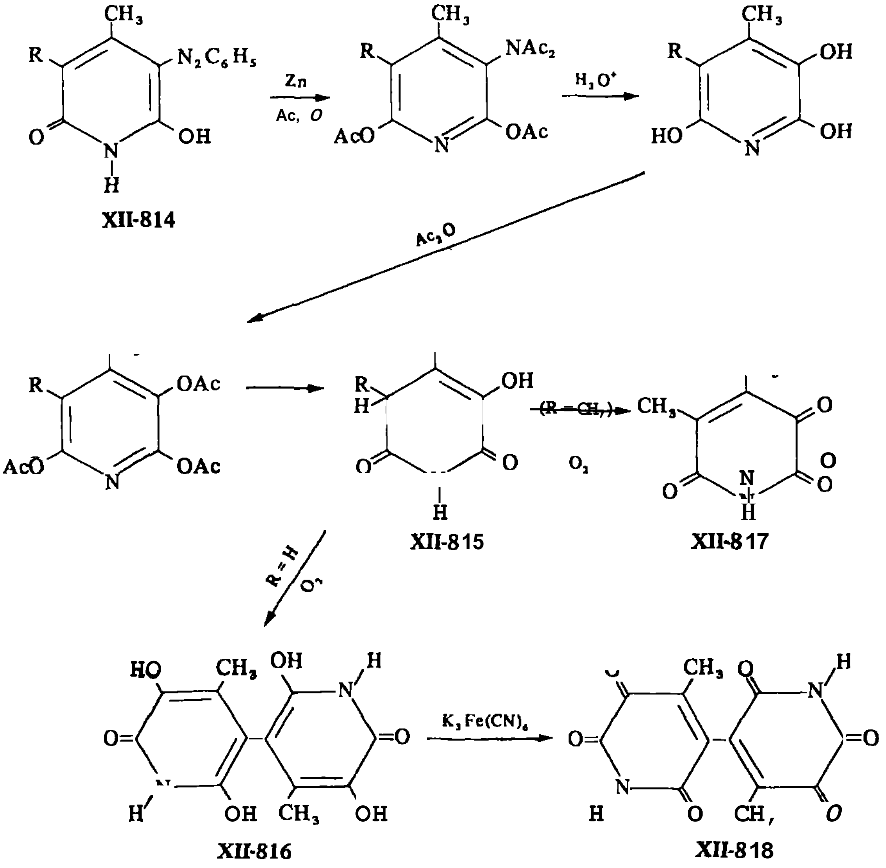
XII-810

XII-812

XII-813

811).[843] Reduction of **XII-810** with zinc in the presence of acetic anhydride gives 2,3,6-triacetoxy-5-methylpyridine, which is hydrolyzed in sulfuric acid to **XII-813,** isolated as the hydrochloride hydrate. Hydrogenation of **XII-810** over palladium also gives **XII-813.**[506]

4-Methyl-3-phenylazo-2,6-pyridinediol (XII-814, R = H**)** and 4,5-dimethyl-3-**phenylazo-2,6-pyridinediol (XII-814,** R = CH_3**)** and zinc in acetic anhydride form **2,6-diacetoxy-3-diacetylaminopyridines** that *can* be converted to the 2,3,6-triacetoxypyridine and then to **3-hydroxy-4-methyl-2,6-pyridinediones**

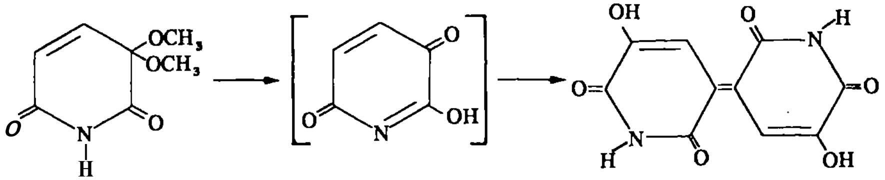


(XII-815). Autooxidation of XII-815 (R = H) gives the corresponding bipyridyl (XII-816). Autooxidation of W-815 (R = CH_3) gives the deep blue azaquinone XII-817. Oxidation of XII-816 with potassium ferricyanide gives the bisazaquinone (XII-818).[506]

Hydrolysis of the azoquinone ketal (XII-819) gives a product that had been described earlier as *3-hydroxy-2-azabenzoquinone* (XII-820),[844] but has been shown to be the diazadiphenoquinone (XII-821).[843]

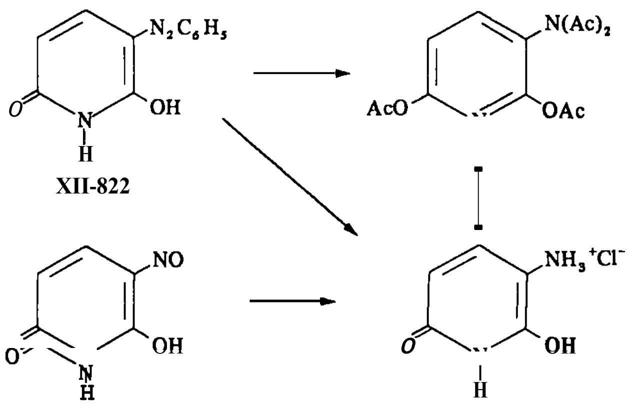
Compounds described as 4-methyl- and 4,5-dimethyltrihydroxypyridines[845] do not have the properties expected from these structures[843] and are probably products of autooxidation.

Although earlier attempts to prepare 3-amino-2,6-pyridinediol were unsuccessful[740] this compound has been prepared from 3-phenylazo-2,6-pyridinediol (XII-822).[846] Hydrogenation of W-822 employing Raney Nickel in the presence



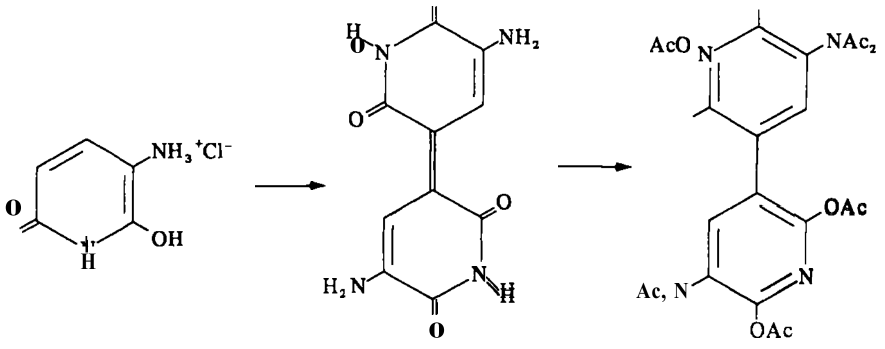
XII-819 XII-820 XII-821

of acetic anhydride gives the tetraacetate. Reduction of **XII-822** or of **3-nitroso-2,6-pyridinediol (XII-823)** with tin and hydrochloric acid gives the hydrochloride of **3-amino-2,6-pyridinediol (XII-824)**.[846] Free 3-amino-2.6-pyridinediol cannot be isolated conveniently because of its autooxidation. When its hydrochloride is dissolved in sodium bicarbonate solution indigoidin **(W-825)** is formed. (See Section VI, p. 860.) Hydrogenation of XII-825 in acetic anhydride gives 5,5′-bisdiacetylamino-2,6,2′,6′-tetraacetoxy-3,3′-bipyridyl.[846]



XII-822

XII-823 XII-824

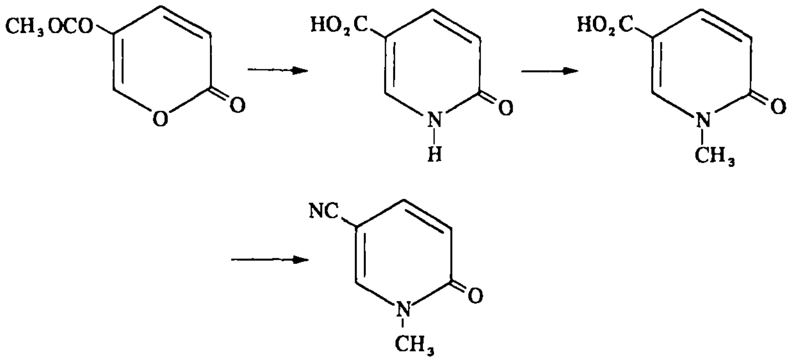


XII-825

VI. Ricinine[847] and Other Pyridine Alkaloids

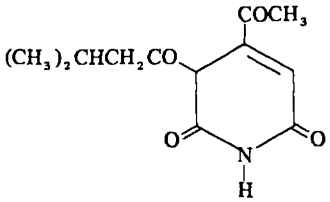
Succinic acid is incorporated into the 2-, 3- and 7-carbon atoms of ricinine (3-cyano-4-methoxy-1-methyl-2-pyridone). Carbon 1 of succinic acid becomes the nitrile carbon of ricinine.[848-850] Nicotinic acid and nicotinamide are highly incorporated into ricinine, which suggests that these two compounds are closer to ricinine than is succinic acid.[849,851] Ricinine and nicotine show labeling patterns that are consistent with a pathway where succinic acid or a related dicarboxylic acid is a precursor to nicotinic acid, which is an intermediate in the formation of nicotine and ricinine.[849,852,853] The α-carbon of lysine is incorporated into carbon 6 of ricinine and the ε-carbon of α-aminoadipic acid is incorporated into carbons 2 and 6.[854]

Nudiflorine (5-cyano-1-methyl-2-pyridone) (XII-826), an isomer of ricinidine (demethoxyricinine), has been isolated from the leaves of *Trewia nudiflora* Linn. It has been synthesized from 5-carbomethoxy-2-pyrone by treatment with ammonia to form 6-oxonicotinic acid, which is alkylated *via* its sodium salt to the *N*-methyl derivative. Esterification, followed by conversion to the amide and dehydration, gives nudiflorine. It has been suggested that both ricinidine and nudiflorine arise from nicotinic acid."'' 4-Acetyl-5-isovaleryl-2,6-pyridinedione (XII-827), an antibiotic with strong activity against gram-positive and gram-negative bacteria, has been isolated from *Aspergillus flavipes*, a thermophilic

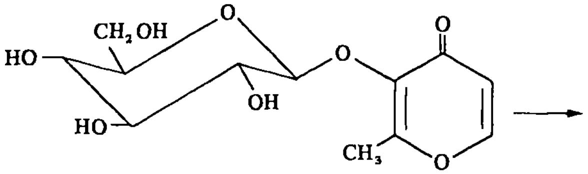


XII-826

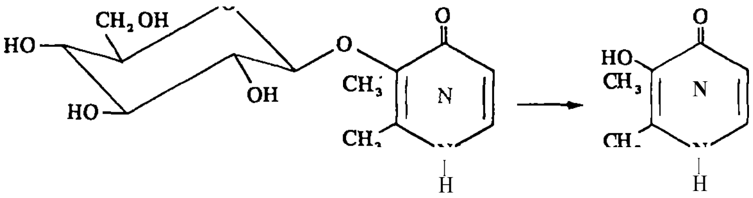
Innovanamine, 2-methyl-3-β-D-glucopyranosyl-4-pyridone (XII-829) has been isolated from fallen leaves of *Evodiopanax innovans*,[857] and has been prepared from the natural maltol glucoside (XII-828).[131] Hydrolysis by hydrochloric acid in methanol or in the presence of emulsin gives 3-hydroxy-2-methyl-4-pyridone and glucose.[858]



XII-827

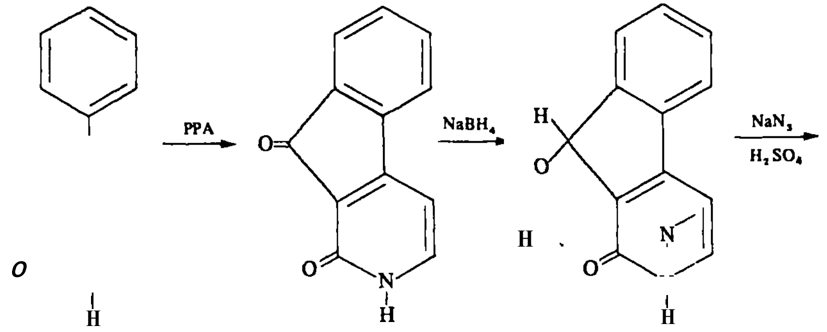


XII-828

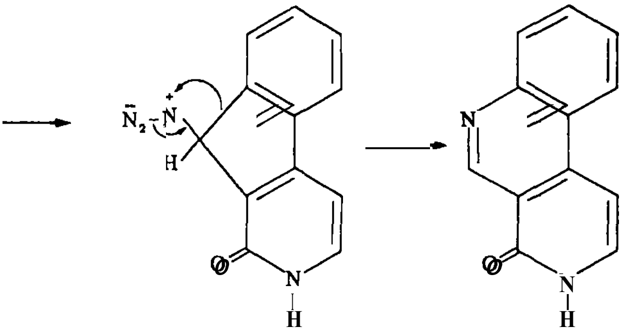


XII-829

Perlolidine (XII-833), a minor alkaloid first isolated from the New Zealand perennial rye grass *Lolium perenne* L., has been synthesized from 3-cyano-4-phenyl-2-pyridone (see Section I.2.B.) *via* **XII-830, XII-831,** and **XII-832.**[46]

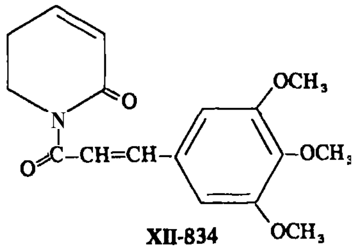


XII-830 **XII-831**

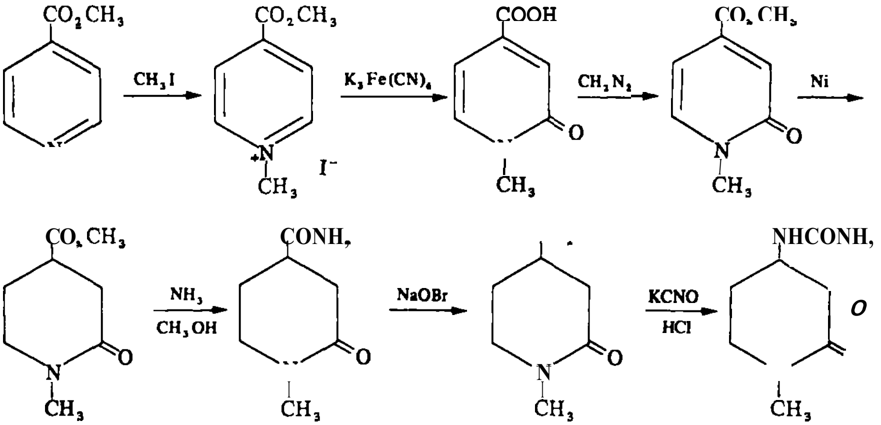


XII-832 **XII-833**

The alkaloid piplartine **XII-834**, isolated from the roots of *Piper longum* Linn., is identical with piperlongumine.[859, 860] A 3,4-dihydro-2-pyridone structure was first proposed,[859] but a detailed NMR study has shown it to be *N*-[β-(3,4,5-trimethoxyphenyl)acrylyl]-5,6-dihydro-2-pyridone (**XII-834**).[860] Blastidone (**XII-835**), a degradative component of blasticidine S by mild alkaline hydrolysis, has been prepared from methyl isonicotinate through the following sequence:[861, 862]

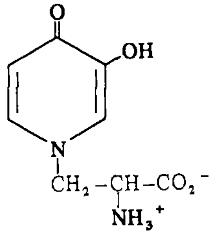


XII-834

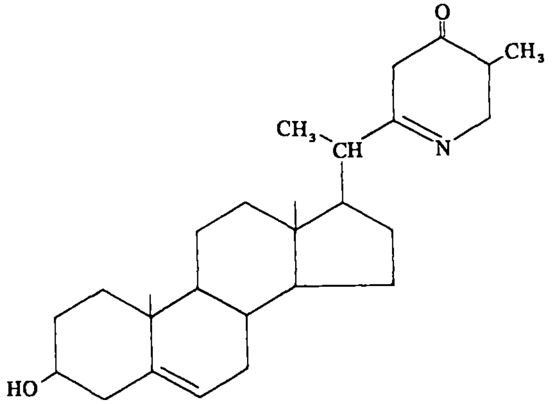


XII-835

The C-3 of aspartic acid is specifically incorporated into the pyridone nucleus of mimosine **(XII-836)**.[134] Lysine is incorporated into the pyridone nucleus of **XII-836** in *L. Glauca*.[863] The alkaloid tomatillidine has been assigned the structure **XII-837**.[864]

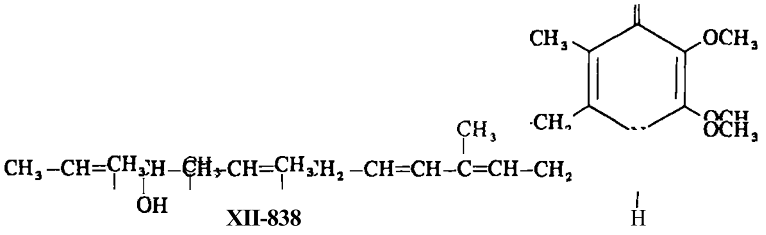


XII-836



XII-837

The structure of piericidin A, a natural insecticide[865] and inhibitor of mitochondrial electron transport,[866] has been elucidated as **XII-838**.[160, 591, 867–869] Evidence has been presented to assign the *S* configuration to C-9 and C-10 of the side chain and a *trans* arrangement at each side-chain double bond.[870] Piericidin B, isolated along with Piericidin A from mycellia of



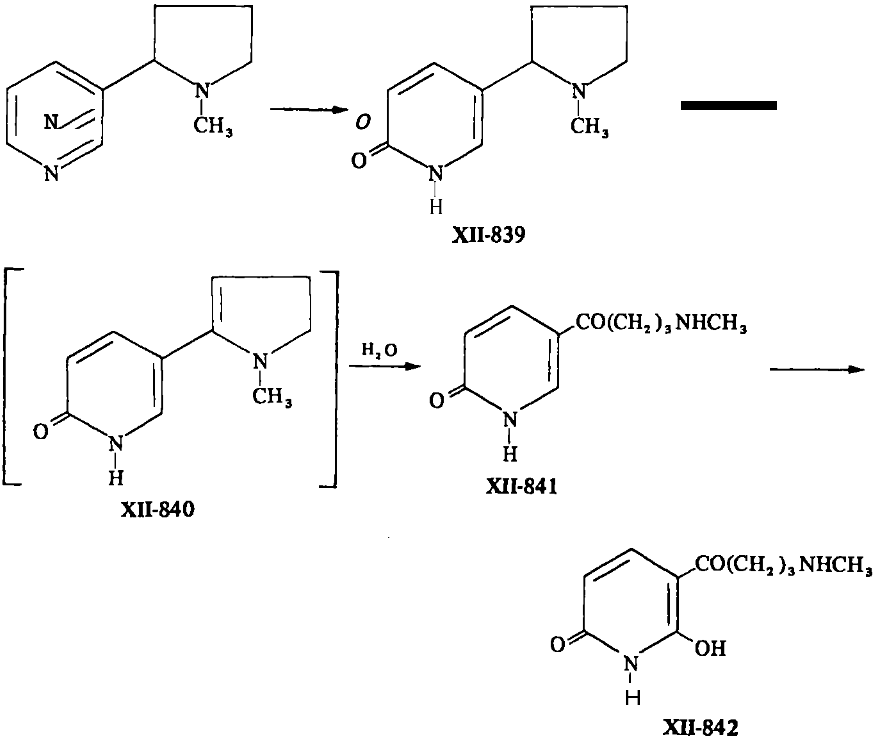
XII-838

Streptomyces mobaraensis, has been identified as the 10-methyl ether of Piericidin A.[871, 872] The biosynthesis of Piericidin A and B has been studied.[873]

The metabolism of nicotine by several microorganisms has been studied. Included as products are 6-hydroxynicotine (XII-839), 6-hydroxy- (XII-841) and 2,6-dihydroxy-3-(γ-methylaminobutyryl)pyridine (XII-842), which are obtained from nicotine in a reaction catalyzed by cell-free preparation of a soil bacterium.[874-877] and from a *Pseudomonas*.[878] 6-Hydroxynicotine (W-839) and W-842 are produced from nicotine by oxidation by a cell-free extract of *Arthrobacter oxydans*[879, 880] and by a species of *Arthrobacter* present on the roots of tobacco plants.[881]

L-Nicotine oxidation by cell-free extracts of *Arthrobacter oxydans* yields L-6-hydroxynicotine exclusively.[882] When *Arthrobacter oxydans* is grown on DL-nicotine, L- and D-6-hydroxynicotine oxidases are produced and have been separated.[883] L-6-Hydroxynicotine oxidase converts L-6-hydroxynicotine to 5-(γ-methylaminobutyryl)-2-pyridone (XII-841) in the presence of oxygen by a mechanism that consists of dehydrogenation followed by hydrolysis of the intermediate enamine (XII-840).[884]

2-Pyridone and 4-pyridone are the major persistent metabolites arising from the breakdown of pyridine nucleotides following administration of 7-C^{14}



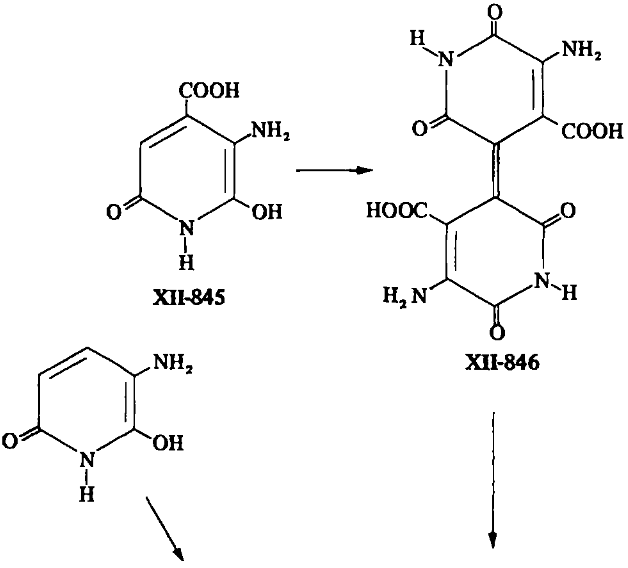
XII-839

XII-840

XII-841

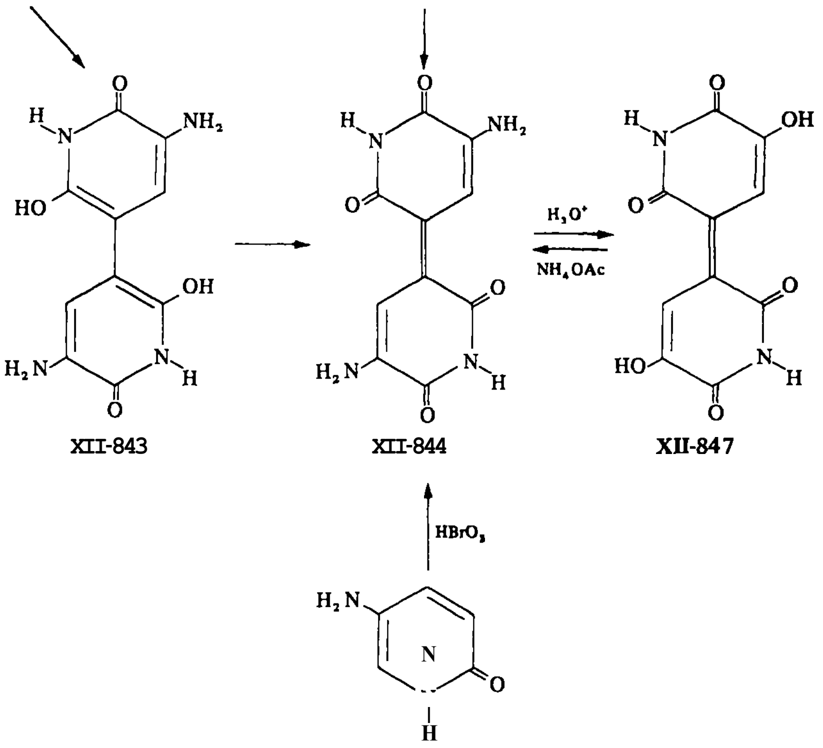
XII-842

nicotinic acid intramuscularly into a pig.[885] A bacillus isolated on nicotinic acid is shown to oxidize this compound to 6-hydroxynicotinic acid and 2,6-dihydroxynicotinic acid, which is then decarboxylated to 2,6-dihydroxypyridine.[886] Bacteria utilizing 2- and 3-hydroxypyridine convert these substrates to pyridine-2,5-diol.[439] A number of bacteria produce green or blue pigments by oxidation of 2-pyridone,[887] 5-hydroxy-2-pyridone,[888] nicotine or nicotinic acid,[889, 890] 2,6-dihydroxynicotinic acid,[891] isonicotinic acid,[892] and citrazinic acid.[892] The blue oxidation products are either indigoidin **(XII-844)** or related compounds. Indigoidin is a blue compound produced by various bacteria, ***P.*** indogofera, *C. insidiosum, A. atrocyaneus,* and *A. polychromogenes.*[893-895] The assignment of structure XII-844 was based on comparison of its uv, ir, and NMR spectra, and acidities with data on structurally related compounds. It has been prepared directly and in good yield by potassium ferricyanide oxidation of aminocitrazinic acid **(XII-845)**, by decarboxylation of the dicarboxylic acid **XII-846**,[894] by the bromic acid oxidation of 5-amino-2-pyridone,[894] bY treatment of the indigoidin hydrolysis product **(W-847)** with ammonium acetate, and by the autooxidation of 3-amino-2,6-pyridinol.[846] When the hydrochloride of 3-amino-2,6-pyridinediol is dissolved in sodium bicarbonate solution, a deep blue color is formed that rapidly disappears. On further oxidation, the solution turns blue again and deposits indigoidin **(W-844)**. Presumably a blue semiquinoid intermediate is formed that dimerizes to the leuco-indigoidin **(XII-843)**, which is oxidized to XII-844. The hydrolysis product **(XII-847)** is accessible from nitrosocitrazinic acid, from 3,3′-dipyridyl, from 3-amino-2-pyridone, or from citrazinic acid directly.[894]

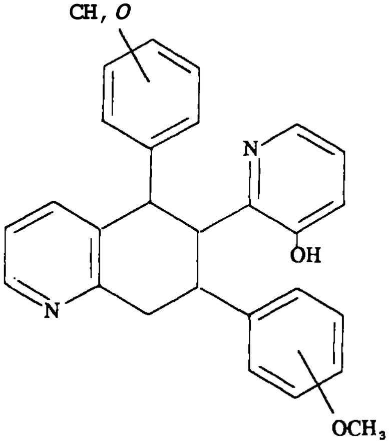


XII-845

XII-846



Two alkaloids, syphilobin F (XII-848) and syphilobin A, its 3-deoxy derivative, have been isolated from *Lobelia syphilitic* L.[600]



XII-848

VII. Acknowledgments

The author is indebted to Dolores D. Georger who typed the drafts and manuscript, and to Priscilla B. Clarke for many hours of proofreading.

VIII. Tables of Physical Data

BY PRISCILLA B. CLARKE AND HOWARD TIECKELMANN

Tables **XII-25** to XII-145 represent a list of pyridinols and pyridones that have been described in the literature from 1960 to 1970. A few compounds reported during 1958 and 1959 are also included. Melting points boiling points, and/or analytical data, and references are given for each compound. When the nitrogen atom is unsubstituted, the pyridinol structure has been used throughout the tables, which have been divided into the following major categories: 2-, 3-, and 4-pyridinols; 2-, and 4-pyridones; ethers of 2-, 3-, and 4-pyridinols; pyridinediols, ethers of pyridinediols, pyridinetriols and ethers of pyridinetriols.

Format of Tables

To facilitate the location of a specific compound the tables have been subdivided into the following categories:

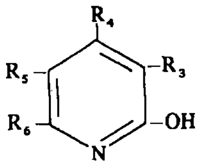
Alkyl and Aryl; Alkyloxy, Aryloxy, and Hydroxy; Amino, Substituted Amino, and Imino; Carboxylic Acids, Aldehydes, Amides and Esters; Nitriles; Halo; Nitro and Nitroso; and Sulfur Containing Pyridinols and Pyridones.

If there is more than one substituent on the pyridine ring the compound will be found in the table with the functional group listed last in the above list. For example, 4-chloro-3-nitro-6-*n*-propyl-2-pyridinol is listed in the table with the heading Nitro and Nitroso 2-Pyridinols. In all cases except sulfur containing pyridinols and carboxylic acids and their derivatives, the functional group is directly attached to the pyridine ring. In the latter cases the sulfur or carboxylic acid may appear in any location on the substituent.

Reference Code

a = Molecular orbital calculation
b = Crystal data studies
c = Column chromatography
d = Explosive properties
e = Electron spin resonance
f = R_f values
g = Gas chromatography
h = Fluorescence
i = Infrared absorption data
j = Transition energies
k = Optical rotation
l = Ligand field spectra
m = Mass spectroscopy
n = Nuclear magnetic resonance
o = Optical rotatory dispersion
p = Photochemical decomposition
q = Molar conductivity
r = Raman spectra
s = Spot test
t = Thin layer chromatography
u = Ultraviolet spectroscopy
v = Visible absorption data
w = Electronic structure
x = X-Ray data
y = Stability constants
z = Dipole moments

TABLE XII–25. Alkyl and Aryl 2-Pyridinols



R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
H	H	H	H	106–108" b.p. 130°/1 mm		342 (t); 365 (m.p.); 404 (f), (g); 463 (i); 465 (i); 472 (n); 478 (i), (r); **479** (n); 487 (i); 525 (u), (h); 546 (i), (r); 550 (b.p.) 648 (u); 659 (u); 673 (m.p.); 735 (n); 896 (i); 897 (m); 898 (i); 899 (n); 900 (f); 901 (n); 902 (i); 903 (n); 904 (u); 905 (m.p.), (u); 906 (a); 907 (m); 908 (n); 909 (u); 910 (j); **911** (t); 912 (u); 913 (i); 914 (m.p.), (u); **915** (m); 916 (n); 917 (u); 918 (s); 919 (i);
					^{15}N	465 (i), (n);
					^{18}O	463 (i) ;465 (i); 903 (m);
					2-*O*-acetyl b.p. 74°/0.95 mm	404 (f), (g); 631 (i), (n); 747 (b.p.), (i), (n), (u);
					aluminum complex m.p. 186–190"	920 (m.p.);
					aluminum perchlorate complex.m.p. 200'	822 (m.p.), (i);
					barium salt	921 (i);
					cadmium perchlorate complex.m.p. 90–95°	822 (m.p.), (i);

calcium perchlorate complex. m p. **96–99'**	**822 (m.p.), (i);**
cobalt tetrafluoroborate complex. **m.p. 158–161"**	**822 (m.p.), (i), (l);**
$CoCl_2$ 1:1 adduct and 1:3 adduct	**816 (i), (u), (v), (x);**
cobalt perchlorate complex. m.p. **174"**	**821 (i), (u);**
	822 (m.p.), (i), (l);
copper tetrafluoroborate complex, m.p. 139°	**822 (m.p.), (i), (l);**
$CuCl_2$ 1:1 adduct and 1:3 adduct	**816 (i), (u), (v), (x);**
copper perchlorate complex. m.p. **142"**	**822 (m.p.), (i), (l);**
dibutyltin complex, m.p. **- 80"**	**920 (m.p.);**
hexachloro antimonate, **m.p. 126"**	**464 (m.p.), (i); 542 (i);**
	546 (i);
hexachloro stannate. m.p. 100"	**464 (m.p.), (i);**
hydrochloride	**546 (i);**
hydrochloride hydrate	**543 (b);**
iron perchlorate complex. **m.p. 145'**	**822 (m.p.), (i), (l);**
lithium salt	**921 (i);**
manganese tetrafluoroborate complex. m.p. 105°	**822 (m.p.), (i);**
$MnCl_2$ 1:1 adduct	**816 (i), (u), (v), (x);**
manganese perchlorate complex. **m.p. 125"**	**822 (m.p.), (i);**
magnesium perchlorate complex. m.p. 133°	**822 (m.p.), (i);**
mercuri chloride salt, m.p. **205°**	**603 (m.p.);**
nickel tetrafluoroborate complex. m.p. 171°	**822 (m.p.), (i), (l);**
$NiCl_2$ 1:1 adduct	**816 (i), (u), (v), (x);**
nickel perchlorate complex. m.p. **188'**	**822 (m.p.), (i), (l);**
pentaammine cobalt III complex	**820 (i), (u);**
pentacyano propene salt, m.p. 102–104°	**745 (m.p.), (u);**

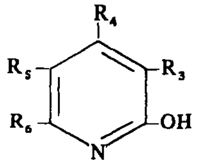
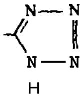


TABLE XII-25. Alkyl and Aryl 2-Pyridinols (Continued)

R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
					dimethyl silicon compkx, b.p. 113°/0.8 mm	920 (b.p.);
					phosphorus complex, m.p. 75'	920 (m.p.);
					potassium salt	921 (i);
					silver salt	921 (i);
					sodium salt	545 (i), (r); 921 (i);
					trichloroacetyl b.p. 58°/0.7 mm	922 (b.p.), (i), (n);
					zinc tetrafluoroborate complex, m.p. 118°	822 (m.p.), (i);
					zinc perchlorate complex, m.p. 139"	822 (m.p.), (i);
CH_3				139–143°		281 (m.p.), (u); 361 (m.p.); 376 (m.p.), (i), (u); 467 (u); 546 (i), (u); 735 (m.p.), (n); 899 (n); 903 (m); 923 (n); 924 (m.p.);
					picrate, m.p. 157–159'	376 (m.p.);
					$HgCl_2$ m.p. 131–132"	376 (m.p.);
					$HCl \cdot H_2O$	546 (i), (u);
	CH_3			124–125"		467 (i), (u); 546 (i), (u); 903 (m); 907 (m); 923 (n); 924 (m.p.);
					$HCl \cdot H_2O$	546 (i), (u);
		CH_3		184–188'		281 (m.p.), (u); 282 (m.p.); 361 (m.p.); 376 (m.p.), (i), (u); 467 (i), (u); 546 (i), (r), (u);

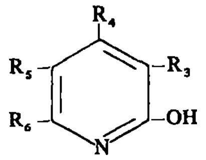
						735 (n), 903 (m);
						923 (n); 924 (m.p.); 925 (t);
					picrate, m.p. 146–148°	376 (m.p.);
					$HgCl_2$, m.p. 206–208°	376 (m.p.);
					hydrochloride	546 (i), (u);
			CH_3	158–164°		372 (m.p.), (i), (n), (u); 420 (m.p.), (i), (m), (n), (u); 422 (i), (n); 467 (i), (u); 903 (m); 907 (m); 923 (n); 924 (m.p.); 925 (t);
					hydrochloride	546 (i), (u);
		CH_2OH		148°		880 (m.p.);
		$COCH_3$				436 (t);
						437 (i), (n), (t), (u);

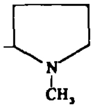
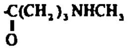
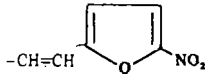
E67



			CH_3	310–312°		59 (m.p.);
		$-\underset{OH}{CHCH_3}$				435 (u);
	CH_3		CH_3	177–186°		60 (i), (n); 420 (m.p.), (i), (n), (u); 926 (m.p.);
		CH_3	CH_3	205–207°		927 (m.p.);
	C_2H_5			126°		283 (m.p.);
$-CH_2CH=CH_2$				124–128°		598 (m.p.), (i), (n), (u);
						790 (m.p.);
		$COCH_3$	CH_3			899 (n);
CH_3	CH_3	CH_3		76–78°		928 (m.p.), (i);
C_2H_5	CH_3			169–172°		281 (m.p.), (u);
	CH_3	C_2H_5		160–162°		281 (m.p.), (u);
C_2H_5			CH_3	102–103°		929 (m.p.), (i), (n), (u);
						930 (m.p.);
	isoC_3H_7			oil		226 (i);
					picrate, m.p. 146–147°	226 (m.p.);
CH_2OH		CH_2OH	CH_3	181–182°		931 (m.p.), (i), (n);
$Si(CH_3)_3$				91–92°		377 (m.p.), (i);
	$Si(CH_3)_3$			102–103°		377 (m.p.), (i);
crotyl				114–116°		790 (m.p.);
$-\underset{CH_3}{CH}CH=CH_2$				oil		790 (g);
$COCH_3$	CH_3		CH_3	218–219°		60 (m.p.), (i), (n), (u);

TABLE XII-25. Alkyl and Aryl 2-Pyridinols (Continued)



R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
$n\text{-}C_3H_7$			CH_3	79–82°		929 (m.p.), (i), (n), (u); 930 (m.p.);
		$n\text{-}C_3H_7$	CH_3	127–128°		927 (m.p.); 932 (m.p.);
						878 (m.p.), (u);
				106"		882 (i), (u);
				120–122°		881 (m.p.), (u);
					picrate, m.p. 212–215°	316 (m.p.);
					picrate. m.p. 165–166'	881 (m.p.), (u);
		 $-\underset{\underset{O}{\|}}{C}(CH_2)_3NHCH_3$		211–213°		878 (u); 880 (m.p.);
		$n\text{-}C_4H_9$	CH_3	93"		932 (m.p.);
	$C_6H_4NO_2\text{-}o$			21 1–212°		73 (m.p.), (i); 933 (m.p.);
				279'		934 (m.p.); 935 (m.p.); 936 (m.p.); 937 (m.p.);
	C_6H_5			227–235°		1 (m.p.); 46 (m.p.), (i), (m), (u); 71 (m.p.; 907 (m);
			C_6H_5	197°		71 (m.p.); 488 (i); 907 (m); 938;
$-N{=}NC_6H_4OH\text{-}p$				251'		939 (m.p.), (m), (u);
	$C_6H_4NH_2\text{-}o$			236–23T		73 (m.p.), (i), (u); 933 (m.p.);
					N-formyl. m.p. 245–247°	73 (m.p.), (i); 933 (m.p.);
					N'-acetyl, m.p. 264–266°	73 (m.p.), (i); 933 (m.p.);

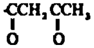
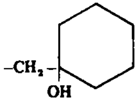
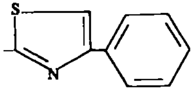
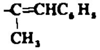
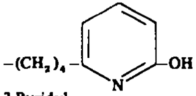
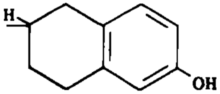
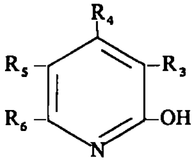
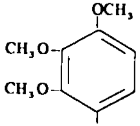
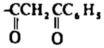
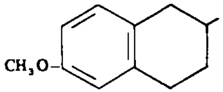
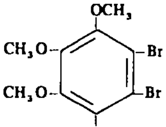
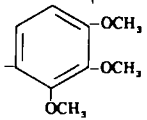
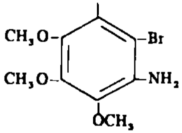
 $-C(=O)CH_2C(=O)CH_3$	CH_3		CH_3	180-182°	60 (m.p.), (i);
		C_6H	CH_3	214-215°	35 (m.p.);
	CH_3		C_6H_5	181-182°	65 (m.p.), (i), (n); 117 (m.p.);
	C_6H_5		CH_3	204-205°	1 (m.p.);
				165-167°	579 (m.p.), (i);
			$-CH=CHC_6H_5$	210-216°	57 (m.p.); 579 (m.p.), (i);
	C_6H_5	CH_3	CH_3	257-258°	67 (m.p.), (i), (n); 940 (n), (u);
$-CH_2CH_2C_6H_5$				188°	579 (m.p.), (i);
	$-CH_2CH_2C_6H_5$			168-169°	579 (m.p.), (i);
			$-CH_2CH_2C_6H_5$	155-156°	579 (m.p.), (i);
			 $-CH_2CH_2CH(OH)C_6H_5$	148-149°	579 (m.p.), (i);
				218°	116 (m.p.);
			 $-C(CH_3)=CHC_6H_5$	175°	57 (m.p.), (i), (u);
 $-C(=NH)CH_3$		C_6H_5	CH_3	230°	53 (m.p.), (i);
				283°	579 (m.p.), (i);
	3-Pyridyl		3-Pyridyl	270-282°	1 (m.p.); 71 (m.p.);
				300°	568 (m.p.), (u);

TABLE XII-25. Alkyl and Aryl 2-Pyridinols (Continued)



R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
			CH_3	227–229°		67 (m.p.), (i); 940 (n);
	$C_6H_4NO_2$-*p*		2-Pyridyl	310°		72 (m.p.);
	4-Pyridyl		C_6H_5	242°		72 (m.p.);
	C_6H_5		3-Pyridyl	237°		72 (m.p.);
	CH_3		α-Naphthyl	204–206°		65 (m.p.), (i), (n);
$-\underset{\text{O}}{\underset{\Vert}{\text{C}}}CH_2\underset{\text{O}}{\underset{\Vert}{\text{C}}}C_6H_5$	CH_3		CH_3	220°		60 (m.p.), (i ;
				239–240°		58 (m.p.) (u);
		H	CH_3			940 (n), (u);
		CH	CH_3	20		67 (m.p.), (i), (n); 940 (n), (u);
		CH_3	CH_3	23 -234		940 (m.p.), (i);

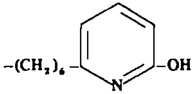
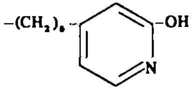
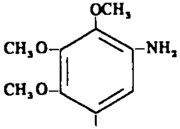
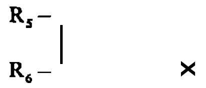
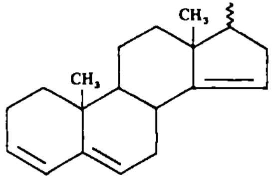
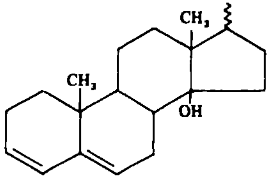
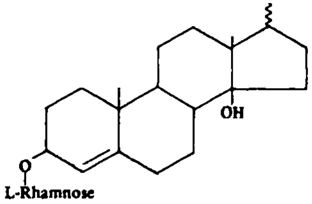
				239–244°	6 (m.p.); 579 (m.p.);
				284–285°	6 (m.p.);
		CH_3	CH_3	280'	940 (m.p.), (i);
	$C_6H_4NO_2$-*p*		C_6H_5	278–279°	74 (m.p.);
C_6H_5			C_6H_5	260–261°	38 (m.p.), (i);
C_6H_5	C_6H_5			285'	228 (m.p.), (i), (n), (u);
					242 (m.p.), (i), (u);
	C_6H_5		C_6H_5	206–210°	1 (m.p.); 71 (m.p.);
					74 (m.p.);
					941 (m.p.), (i), (u);
		C_6H_5	C_6H_5	262–263'	35 (m.p.);
				272–273'	229 (m.p.);
	$(CH_2)_{11}CH_3$			88–89°	581 (m.p.);
	$C_6H_4OCH_3$-*p*		C_6H_5	225–226°	941 (m.p.), (i), (u);
$-CH{=}C(C_6H_5)_2$				225–226"	579 (m.p.), (i);
	$-CH{=}C(C_6H_5)_2$			168–170°	579 (m.p.), (i);
			$-CH{=}C(C_6H_5)_2$	211–213"	576 (m.p.), (i), (u);
					580 (m.p.);
$-CH_2\underset{OH}{C}(C_6H_5)_2$				294–295°	579 (m.p.), (i);
	$-CH_2\underset{OH}{C}(C_6H_5)_2$			259–260°	579 (m.p.), (i);
			$-CH_2\underset{OH}{C}(C_6H_5)_2$	271–272°	580 (m.p.);
	C_6H_5	C_6H_5	C_6H_4Br-*p*	288"	122 (m.p.);
C_6H_5	C_6H_5	C_6H_5		323–325°	230 (m.p.), (i), (u),
C_6H_5	C_6H_5		C_6H_5	300–301°	938 (m.p.), (i);
	C_6H_5	C_6H_5	C_6H_5	277"	121 (m.p.), (i), (u);
					122 (m.p.), (i); 230 (m.p.);

TABLE XII-25. Alkyl and Aryl 2-Pyridinols (Continued)



R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
	C_6H_5	C_6H_5	$C_6H_4CH_3$-*p*	270°		122 (m.p.), (i);
	C_6H_5	C_6H_5	$C_6H_4OCH_3$-*p*	245°		802 (m.p.), (i);
				67-2 2		114 (m.p.), (i);
				330-345°		114 (m.p.), (i);
				2 9 92		114 (m.p.), (i);

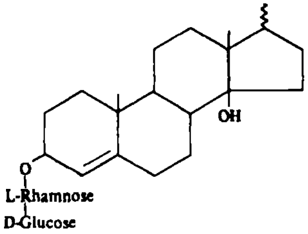
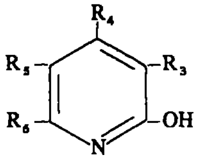
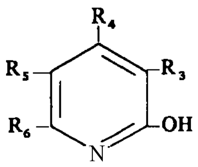
	283–284°		114 (m.p.), (i);
		hexaacetyl, m.p. 239–270°	114 (m.p.);

TABLE XII-26. Alkyloxy and Aryloxy 2-Pyridinols

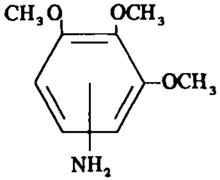


R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OCH_3				114–116°		501 (m.p.), (i);
			OCH_3	102–104°		455 (m.p.), (n), (u); 505 (m.p.), (n), (t);
OCH_3	OCH_3		CH_2OH	176–177°		160 (m.p.), (i), (u);
	OCH_3	$COCH_3$	CH_3	230°		94 (m.p.), (n), (u);
			$OCH_2C_6H_5$	128–129°		618 (m.p.), (i), (n);
	C_6H_5	OCH_3	C_6H_5	203°		120 (m.p.); 121 (i);
	C_6H_5	OCH_3	$C_6H_4CH_3$-*p*	228°		120 (m.p.);
	C_6H_5	OCH_3	$C_6H_4OCH_3$-*p*	206°		120 (m.p.);
	C_6H_5	OC_6H_4Cl-*p*	C_6H_5	241°		121 (m.p.);
	C_6H_5	OC_6H_4Br-*p*	C_6H_5	241°		121 (m.p.);
	C_6H_5	OC_6H_5	C_6H_5	233°		121 (m.p.), (i), (u);
	C_6H_5	$OC_6H_4CH_3$-*p*	C_6H_5	252°		121 (m.p.);

TABLE XII-27. Amino 2-Pyridinols



R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
NH_2						906 (a);
					hydrobromide, m.p. 225-230°	740 (m.p.), (i);
	NH_2					906 (a);
		NH_2				906 (a);
			NH_2			494 (i), (u); 918 (s); 942 **(b);**
	NH_2		NH_2	178"		34 (m.p.), **(i);**
-$NHCHO$				223–224"		642 (m.p.);
-$NHCSNH_2$				220"		642 (m.p.);
-$NHCONH_2$				>310°		642 **(m.p.), (u);**
-$NHCOCH_3$				215"		642 (m.p.), (u);
			-$NHCOCH_3$	212–213"		641 (m.p.);
CH_3		–$NHCOCH_3$		246"		843 (m.p.), (u);
-$NHCOC_2H_5$				166"		642 (m.p.);
-$NHCOOC_2H_5$				187"		642 (m.p.);
NH_2			*n*-**C_3H_7**		picrate, m.p. 167-168°	150 (m.p.);
NH_2	**NH_2**		*n*-**C_3H_7**		picrate, m.p. 198"	150 (m.p.);
-$N(COCH_3)_2$				133–134"		642 (m.p.);
-$NHCOCH_3$		-$NHCOCH_3$		267–269"		943 (m.p.);
CH_3		-$NHCOCH_3$			2-*O*-acetyl, m.p. 150–151"	843 (m.p.), (u);
-$N(COC_2H_5)_2$				102-103°		642 (m.p.);

$-NHCOC_6H_5$				189–192"	642 (m.p.); 740 (m.p.), (i), (n);
$-NHSO_2C_6H_4CH_3$–*p*				211–212"	642 (m.p.);
CH_3	$-N(C_2H_5)_2$	C_6H_5		232"	102 (m.p.), (i), (u);
NH_2		CH_3	CH_3	226–227"	67 (m.p.), (i);
CH_3	$-N(C_2H_5)_2$	$C_6H_4OCH_3$–*p*		232"	102 (m.p.), (i), (u);
		$-O\underset{\overset{\|}{O}}{C}C_6H_5$	$-NHCOC_6H_5$	243–244°	292 (m.p.);
$-N(CH_3)_2$	C_6H_4Cl-*p*		C_6H_5	272–275°	68 (m.p.), (i);
$-N(CH_3)_2$	C_6H_5		C_6H_5	231–234"	68 (m.p.), (i);
C_6H_5	$N(CH_3)_2$	C_6H_5		250"	102 (m.p.), (i), (u);
$-N(CH_3)_2$	$C_6H_4OCH_3$–*p*		C_6H_5	259–262"	68 (m.p.), (i);
C_6H_5	$-N(CH_3)_2$	$C_6H_4OCH_3$–*p*		266"	102 (m.p.), (i), (u);

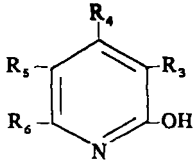
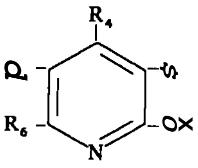


TABLE XII-28. 2-Pyridinol Carboxylic Acids and Derivatives

R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
COOH		CHO		219"		880 (m.p.);
				246-250°		362 (m.p.);
				225°		101 (m.p.);
				262°		21 (m.p.), (u);
					methyi ester, m.p. 153"	101 (m.p.);
					ethyl ester, m.p. 139"	21 (m.p.), (u);
	COOH			328"		266 (m.p.);
					methyl ester, m.p. 211–212°	283 (m.p.), 362 (m.p.);
		COOH		325"		262 (m.p.); 899 (n);
				301–302"		101 (m.p.); **855** (m.p.);
					methyl ester, m.p. 164"	101 (m.p.); **699** (m.p.);
					ethyl ester, m.p. 143–144"	362 (m.p.);
					m.p. 150"	880 (m.p.);
		CONH,		325–327"		613 (m.p.);
			COOH	273–282"		57 **(m.p.), (i),** (u);
						101 (m.p.); 362 (m.p.);
					methyl ester, m.p. 109-116"	116 (m.p.); 362 (m.p.);
					ethyl ester, m.p. 164"	116 (m.p.);
			CONH,	251"		116 (m.p.);
			CONHCH,	176°		116 (m.p.);
			$CONHC_2H_5$	176"		116 (m.p.);
COOH			COOH	304"		57 **(m.p.),** (i), (u);
	COOH		COOH	3**18–3**19"		57 (m.p.), (i);
COOH		COOH	**NH_2**	218–220"		10 (m.p.);

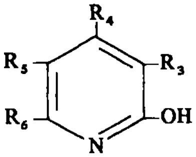
			CH_2COOH		ethyl ester, m.p. 170°	944 (m.p.);
			$-CH_2CONH_2$	254°		944 (m.p.);
$CONH_2$			CH_3	305–306°		575 (m.p.), (i), (u);
$COOH$	$COOH$		$COOH$		hydrate, m.p. 262°	57 (m.p.), (i), (u);
$COOH$			$COCH_3$	271°		57 (m.p.), (i), (u);
$COOH$		$COOH$	CH_3		diethyl ester, m.p. 196–198°	931 (m.p.), (i), (n);
	$COOH$	$COOH$	CH_3		dimethyl ester, m.p. 169–171°	213 (m.p.);
$COOH$	CH_3		CH_3	260–262°		674 (m.p.);
					hydrate m.p. 251–252°	926 (m.p.);
$COOH$	CH_3		CH_3		ethyl ester, m.p. 134–135°	60 (i), (n), (u);
						674 (m.p.);
			$-CH_2\underset{\underset{NH_2}{\vert}}{CH}COOH$	278–280°		425 (m.p.), (i);
$COOH$	$COOH$		$COCH_3$	254°		57 (m.p.), (i);
					oxime, m.p. 350°	57 (m.p.);
			$-CH_2CH{=}CHCOOH$	199–200°		944 (m.p.);
$CONH_2$	C_6H_5			285–287°		46 (m.p.), (i), (m) (u);
$-\underset{\underset{O}{\Vert}}{C}CH_2\underset{\underset{O}{\Vert}}{C}COOH$	CH_3		CH_3		ethyl ester, m.p. 175–176°	60 (m.p.), (i);
$COOH$			COC_6H_5	257°		57 (m.p.), (i), (u);
$COOH$		C_6H_5	CH_3	269–271°		53 (m.p.), (i), (u);
					methyl ester, m.p. 230–232°	53 (m.p.), (i), (u);
$CONHCH_3$		C_6H_5	CH_3	316–318°		53 (m.p.), (i), (u);
$CONHNH_2$		C_6H_5	CH_3	>350°		53 (m.p.), (i);
	$COOH$	C_6H_5	CH_3	280°		53 (m.p.), (i);
					methyl ester, m.p. 183–185°	53 (m.p.), (i);
					ethyl ester, m.p. 154–155°	53 (m.p.), (i);
C_6H_5	CH_3	$CONH_2$		350–352°		218 (m.p.);
$COOH$			$-CH{=}CHC_6H_5$	256°		57 (m.p.), (i), (u);
	$COOH$		$-CH{=}CHC_6H_5$	343°		57 (m.p.), (i);
$COOH$	$COOH$	C_6H_5	CH_3	225–230°		53 (m.p.), (i);
$CONH_2$			$-CH_2COC_6H_5$	287–289°		576 (m.p.);

TABLE XII-28. 2-Pyridinol Carboxylic Acids and Derivatives (Continued)



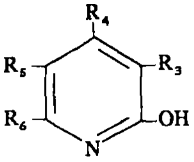
R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
			$-CH_2CHC_6H_5$ $\quad\vert$ COOH		methyl ester, m.p. 197-198°	579 (m.p.), (i);
COOH		C_6H_5	$-CH{=}CCOOH$ $\quad\vert$ OH	190°		53 (m.p.), (i);
COOH			$-C{=}CHC_6H_5$ $\vert$ CH_3	2[illegible]°		57 (m.p.) (i) ( );
	COOX		$-C{=}CHC_6H_5$ $\vert$ CH_3	314°		57 (m.p.);
$CH_2C_6H_5$	COOH	COOH	CH_3		dimethyl ester, m.p. 178–179°	213 (m.p.);
CH_3	COOH	COOH	$CH_2C_6H_5$		dimethyl ester, m.p. 191–193°	213 (m.p.);
$CONHC_2H_5$		C_6H_5	CH_3	249–251°		53 (m.p.), (i), (u);
COOH		C_6H_5	$-CH{=}CCOOH$ $\quad\vert$ OH		diethyl ester, m.p. 168–170°	53 (m.p.), (i), (u);
$-CONHCH_2CH_2N(C_2H_5)_2$		C_6H_5	CH_3	180–182°		53 (m.p.), (i);
$-CONH(CH_2)_3N(C_2H_5)_2$		C_6H_5	CH_3	181–182°		53 (m.p.), (i);
$-CONH(CH_2)_2C_6H_5$		C_6H_5	CH_3	248–250°		53 (m.p.), (i):

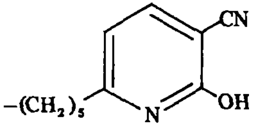
TABLE XII-29. 2-Pyridinol Nitriles



R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
			CN	214°		116 (m.p.);
CN			COOH		hydrate, m.p. 275°	57 (m.p.), (i), (u);
CN			CH_3			437 (u); 575 (n);
CN		$CONH_2$	NH_2		potassium salt hydrate, m.p. 327–332°	10 (m.p.);
CN	CF_3		CF_3	119–121°		55 (m.p.), (i), (u);
					sodium salt, m.p. 253–255°	55 (m.p.);
CN	CF_3		CH_3	232–234°		55 (m.p.), (i), (u);
CN			$COCH_3$	213°		57 (m.p.), (i), (u);
					oxime, m.p. 284°	57 (m.p.);
CN	$CONH_2$		CH_3	300°		945 (m.p.);
CN	CH_3		CH_3			575 (n);
CN			CH_2CH_3	246–248°		575 (m.p.), (u);
CN	CN	CH_3	CH_3	283°		209 (m.p.), (i);
CN	CH OO×		CH_3	228°		945 (m.p.);
CN			isoC_3H_7	208–210°		946 (m.p.);
CN	CH_2OCH_3	NH_2	CH_3	240°		52 (m.p.);
CN	CH_3	NH_2	CH_2OCH_3	206°		52 (m.p.);
CN	CH_2COOH		C_2H_5	205°		945 (m.p.);
CN	CH_2CH_2COOH		CH_3	217°		945 (m.p.);
CN	CH_2CH_2COOH		CH_2CH_3	211°		945 (m.p.);
CN	C_6H_5			233–234°		46 (m.p.);
CN			COC_6H_5	253°		57 (m.p.), (i), (u);

TABLE XII-29. 2-Pyridinol Nitriles (Continued)



R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CN	C_6H_5		CONH,	280"		79 (m.p.), (i);
CN	CH_3	C_6H_5		190-192°		53 (m.p.), (i), (u);
CN	CH_3		C_6H_5			575 (n);
CN		C_6H_5	CH_3	294-296°		53 (m.p.), (i), (u); 575 (n);
CN	CH,	C_6H_5	NH_2	346"		218 (m.p.);
CN			$-CH{=}CHC_6H,$	304"		57 (m.p.), (i), (u);
CN			$-CH_2COC_6H,$	199-205"		576 (m.p.), (i), (n), (u);
CN	COOH	C_6H_5	CH_3		methyl ester, m.p. 198-199"	53 (m.p.), (i), (u);
					ethyl ester, m.p. 165-167"	53 (m.p.), (i);
CN	C_6H_5	CH_3	CH_3	302-304°		77 (m.p.), (i), (n);
CN			CH, CH, $C_6H,$	204-205°		575 (m.p.), (n), (u);
CN	CH_3	C_6H_5	CH_3	354-356"		575 (m.p.), (i), (u);
CN			$-CH_2\underset{\substack{\mid\\ OH}}{C}HC_6H_5$	205-206"		576 (m.p.), (i), (u);
CN			$-\underset{\substack{\mid\\ CH_3}}{C}{=}CHC_6H_5$	238"		57 (m.p.), (i), (u);
CN			$-CH_2\underset{\substack{\mid\\ OCOCH_3}}{C}HC_6H,$	200-308"		576 (m.p.), (i), (u);
CN				269-270°		575 (m.p.), (i), (u);

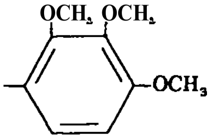
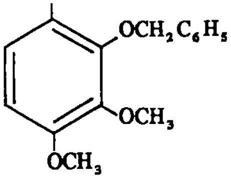
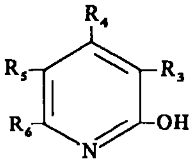
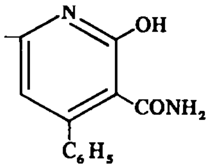
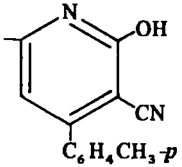
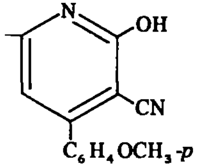
CN		CH_3	CH_3	253–254"	77 (m.p.), (i), (n);
CN			$-\underset{C_4H_9}{CH}CH_2C_6H_5$	127–128"	575 (m.p.), (i), (u);
CN			$-\underset{C_6H_5}{C}=CHC_6H_5$	257"	57 (m.p.), (i), (u);
CN			$-CH=C(C_6H_5)_2$	242–244"	576 (m.p.), (i), (u); 577 (m.p.), (i), (u);
CN	$-CH_2COC_6H_5$		C_6H_5	248–250"	576 (m.p.), (i), (n), (u);
CN		C_6H_5	$-CH_2COC_6H_5$	247–248°	576 (m.p.), (i), (n), (u);
CN	$-CH_2CH_2C_6H_5$		C_6H_5	241–242"	575 (m.p.), (i), (n), (u);
CN		C_6H_5	$-CH_2CH_2C_6H_5$	284–286"	27 (m.p.), (i); 575 (m.p.), (n), (u);
CN			$-CH_2\underset{OH}{C}(C_6H_5)_2$	215–216"	576 (m.p.), (i), (u); 577 (m.p.), (i), (u);
CN			$-CH_2\underset{C_6H_5}{CH}CH_2COC_6H_5$	227–228"	576 (m.p.), (i), (n), (u);
CN	$-CH_2CH_2C_6H_5$		$-CH_2CH_2C_6H_5$	179–180°	575 (m.p.), (i), (n), (u);
CN		CH_3	CH_3	239–240"	77 (m.p.), (i), (n);

TABLE XII-29. 2-Pyridinol Nitriles (Continued)



R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CN	C_6H_5			[illegible]0°		79 (m.p.);
CN	$-CH=C(C_6H_5)_2$		C_6H_5	275–276°		576 (m.p.), (i) (u);
CN	$C_6H_4CH_3$-*p*			> 300°		79 (m.p.);
CN	$C_6H_4OCH_3$-*p*			> 300°		79 (m.p.);
CN	$-CH_2C(OH)(C_6H_5)_2$		C_6H_5	250–252°		576 (m.p.), (i), (u);

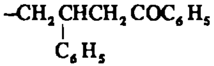
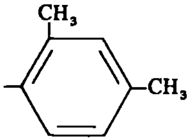
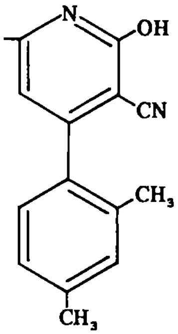
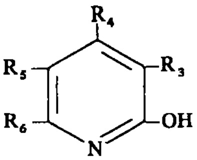
CN	 $-CH_2\underset{\mid \atop C_6H_5}{C}HCH_2COC_6H_5$	C_6H_5	2≤1-262°	576 (m.p.), (i), (n), (u);
CN			242°	79 (m.p.);

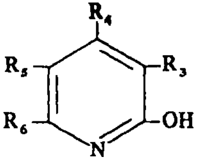
TABLE XII-30. Halo 2-Pyridinols

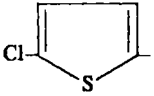
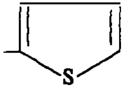


R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
F				166–167°		363 (m.p.) (u);
					2-*O*-acetyl, b.p. 82°/1 mm	363 (b.p.);
Cl				181–183°		363 (m.p.), (u); 467 (i), (u); 546 (i), (u);
					hexachloro-antimonate·H_2O	546 (i) (u);
					2-*O*-acetyl, b.p. 54°/1 mm	360 (b.p.);
		Cl				327 (u); 467 (i), (u); 546 (i), (r), (u);
					hexachloro-antimonate	546 (i), (u);
					hydrochloride	546 (i), (u);
			Cl			241 (u); 474 (b); 494 (i);
Br				181–187°		363 (m.p.), (u); 476 (i), (u); 546 (i), (u); 947 (m.p.);
					2-*O*-acetyl b.p. 77–78°	363 (b.p.);
		Br				467 (i), (u); 546 (i), (r), (u);

					hydrochloride	546 (i), (u);
		I		189–191"		467 (i), (u); 546 (i), (r), (u); 704 (m.p.), (u);
					hydrochloride	546 (i), (u);
Cl		Cl		178–179"		15 (m.p.); 467 (i), (u); 546 (i), (u); 831 (i);
					hexachloro-antimonate	546 (i), (u);
Br		Br				467 (i), (u); 546 (i), (u); 831 (i);
					hexachloro-antimonate	546 (i), (u);
I		I		264–265"		467 (i), (u); 546 (i), (u); 704 (m.p.), (u);
Cl	Cl	Cl		228–229"		15 (m.p.), (u);
Cl		Cl	Cl	172–174"		703 (m.p.); 948 (p);
Br		Br	Cl	189–192°		703 (m.p.);
F	F	Cl	F			246 (n);
Cl	F	F	F			246 (n);
F	Br	F	F	130–131°		247 (m.p.), (n); 949 (m.p.);
a	F	Cl	F	149–153"		246 (m.p.), (i), (n); 950 (m.p.); 951 (m.p.);
Cl	Cl	a	F	172–176"		951 (m.p.);
Cl	Cl	Cl	Cl	221–226"		18 (m.p.); 240 (m.p.); 241 (i), (u);
Br	Br	Br	Br	240–241"		952 (m.p.), (i);
NH_2		Br		182°		643 (m.p.);
CF_3				153–154"		375 (m.p.), (i), (n);
			CF_3	120–121"		375 (m.p.), (n);
Cl	OCH_3	Cl	F	179–180"		953 (m.p.);
Cl	OCH_3	Cl	Cl	197"		240 (m.p.);
Br	OCH_3	Br	Br	210"		952 (m.p.), (i);
Cl	Cl		CH_3	204–206°		37 (m.p.);

TABLE XX-30. Halo 2-Pyridinols (Continued)



R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
Br	CH_3	Br		196–197"		559 (m.p.);
	CH_3		Cl	156–158"		8 (*m.p.*); 457 (*i*), (*n*), (*u*);
Br	CH_3					923 (n);
CH_3		Br		166–167"		559 (m.p.);
Br		CH_3		155–156°		954 (m.p.), (i);
NHCOCH,		Br		>310°		642 (u); 643 (m.p.);
	CF_3		CH_3	133–135"		672 (m.p.);
Cl	Cl	CH_3	CH_3	278–280°		37 (m.p.);
Br		NHCOCH,		249–250°		290 (m.p.);
$NHCOCH_3$		Br		232–233"		642 (u); 643 (m.p.);
	CH_3	Br	CH_3	238"		289 (m.p.);
	OC_2H_5	Br		205–206"		284 (m.p.), (u);
$-CH_2CH_2CH_2-$			Cl	182–184"		8 (m.p.); 457 (i), (n), (u);
Cl	Cl	C_2H_5	CH_3	218–219"		37 (m.p.);
	CH_3	C_2H_5	Cl	174–176"		281 (m.p.);
$-CH_2$ CH, CH, CH, $-$			Cl	187–190"		8 (m.p.); 457 (i), (n), (u);
C_2H_5	CH_3	CH_3	Cl	198°		928 (m.p.), (i);
Cl		$n\text{-}C_3H_7$	CH_3	179–181"		447 (m.p.);
	CF_3		 Cl S	234–236"		672 (m.p.);
	CF_3		 S	201–203"		672 (m.p.);

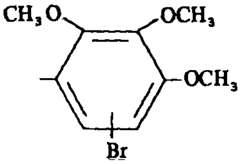
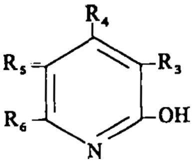
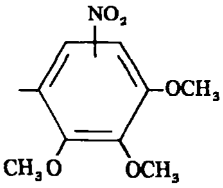
Cl	Cl	n-C_4H_9	CH_3	175–176"	37 (m.p.);
Cl	Cl	Cl	C_6H_5	282"	20 (m.p.), (u);
Cl		Cl	C_6H_5	252"	119 (m.p.), (i);
C_6H_5		Cl	Cl	205–208"	242 (m.p.), (i), (u);
	C_6H_5		Cl	166–168°	8 (m.p.); 457 (i), (n), (u);
	CF_3		C_6H_5	188–189°	672 (m.p.);
$-NHCOC_6H_5$		Br		252–253"	643 (m.p.);
CN	CF_3		C_6H_5	300–301"	55 (m.p.), (i), (u);
$CONH_2$	CF_3		C_6H_5	326–327"	672 (m.p.);
Br	C_6H_5	CH_3	CH_3	231–232"	67 (m.p.), (i), (n); 940 (n), (u);
Br		CH_3	CH_3	127–128"	67 (m.p.), (i);
C_6H_5	C_6H_5	Cl	Cl	210–212"	242 (m.p.), (i), (u);
$C_6H_4OCH_3$-p	$C_6H_4OCH_3$-p	Cl	Cl	231"	242 (m.p.), (u);

TABLE XII-31. Nitro and Nitroso 2-Pyridinols



R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
NO_2				224–226"		**364** (m.p.); **467** **(i), (u);** **899** **(n)**; **955** (u); **956** (u);
	NO_2			242"		**261** (m.p.); **262** (m.p.); **286** (m.p.);
		NO_2		184–187°		**467** **(i), (u); 943** (m.p.); **957** **(u)**; **958** (i);
NO_2		Cl		240°		**291** (m.p.);
Cl		NO_2		194–196°		**291** (m.p.);
NO_2		Br		244"		**290** (m.p.);
Br		NO_2		213"		**290** (m.p.);
NO_2		I		248°		**287** (m.p.);
I		NO_2		203"		**287** (m.p.);
NO	NH_2			330°		**305** (m.p.);
NO_2		NO_2		175–178"		**260** (m.p.); **261** (m.p.); **265** (m.p.); **673** (m.p.), (i); **676** (m.p.); **959** (i); **960** **(u)**;
					silver salt hydrate	**961** (d);
					sodium salt, m.p. **293"**	**769** (m.p.), **(n)**; **961** (d);
					copper(II) salt	**961** **(d)**;
					mercury(II) salt	**961** (d);
					lead(II) salt	**961** (d);

					bismuth salt	961 (d);
	NO_2	NO_2		207"		286 (m.p.);
NO_2	NH_2			314-315°		305 (m.p.);
NH_2		NO_2		199-201°		943 (m.p.); 959 (i);
NO_2	CH_3	NO_2		233-237"		675 (m.p.);
				254"		264 (m.p.);
NO_2		NO,	CH_3	238-240°		264 (m.p.); 675 (m.p.);
NO_2	CH_3			229"		259 (m.p.);
NO_2		CH_3		251-252"		259 (m.p.); 700 (m.p.), (u);
CH_3		NO_2		229-230°		259 (m.p.); 700 (m.p.), (u);
	CH_3	NO_2		186"		259 (m.p.);
		NO,	CH,	230"		263 (m.p.);
NO_2			OCH_3	172-173"		701 (m.p.);
NO_2	CH_3	Br	CH,	223"		289 (m.p.);
$NHCOCH_3$		NO_2		281°		943 (m.p.);
NO_2	CH_3		CH_3	248"		288 (m.p.);
	CH_3	NO,	CH,	150"		288 (m.p.);
CN	CH_3	NO,	CH,	271-272"		674 (m.p.);
COOH	CH_3	NO,	CH,	234-235"		674 (m.p.);
					ethyl ester, m.p. 194-195°	674 (m.p.);
NO_2	Cl		n-C_3H_7	182-183"		150 (m.p.);
NO_2	NH_2		n-C_3H_7	193"		150 (m.p.);
NO_2	C_6H_5	CH,	CH,	258°		67 (m.p.), (i), (n);
NO_2		CH,	CH,	263-264"		**67 (m.p.), (i);**

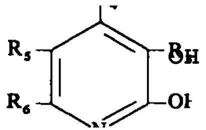
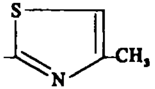
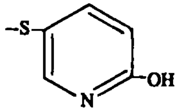
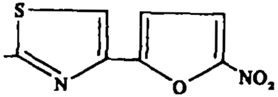
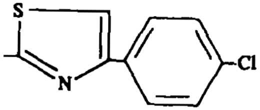
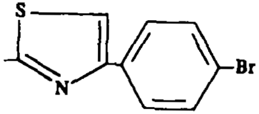
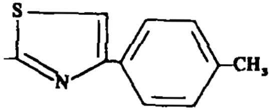
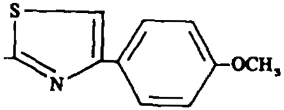


TABLE XI-32. Sulfur containing 2-Pyridinols

R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
			CSNH,	236''		116 (m.p.);
		SCH_3		75–76''		962 (m.p.);
		$-SOCH_3$		153–155'		962 (m.p.);
		SO_2CH_3		247-249°		962 (m.p.);
SC_2H_5		Cl		158–159		962 (m.p.);
$-SOC_2H_5$		Cl		216-217°		962 (m.p.);
		SC_2H_5		79-800		962 (m.p.);
			SC_2H_5	150–156'		962 (m.p.);
			$-SOC_2H_5$	107-110°		962 (m.p.);
			$-SO_2C_2H_5$	122–124''		962 (m.p.);
		$SCH(CH_3)_2$		53-54°		962 (m.p.);
		$-SO_2CH(CH_3)_2$		105-107''		962 (m.p.);
				124°		116 (m.p.);
		SC_2H_5		138-140°		962 (m.p.);
				260-263°		766 (m.p.), (n), (u);
CN	CF_3		2-Thienyl	300–303°		55 (m.p.);
		SC_6H_5		180–182°		962 (m.p.)
	$OSO_2C_6H_4Cl$-*p*		CH_3	173-175°		502 (m.p.);

	$OSO_2C_6H_5$	CH_3	193 195	6Z (m.p.) ( ), (u);
		CH_3	[illegible] 37°	93 (m.p.);
			Z21	116 (m.p.);
			225–226°	[illegible] (m.p.);
			184°	116 (m.p.);
			158°	116 (m.p.);

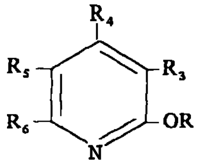
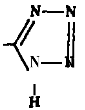
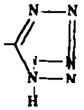


TABLE XII-33. Ethers and Esters of Alkyl and Aryl 2-Pyridinols

R	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3					b.p. 141–143°	 hydrochloride hexachloro-antimonate, m.p. 252–254°	472 (n); 479 (n); 482 (z); 525 (h), (u); 530 (b.p.), (n); 901 (n); 964 (j); 965 (i); 546 (i); 136 (m.p.), (i); 542 (i); 546 (i);
CH_3					158–160°		59 (m.p.);
CH_3					204°		59 (m.p.);
CH_3	CH_3				b.p. 63°/20 mm	picrate, m.p. 121–122°	700 (b.p.); 700 (m.p.);
CH_3			CH_3		b.p. 163°/722 mm	hydrochloride	467 (b.p.), (u); 546 (i), (u);
C_2H_5					b.p. 63°/25 mm		570 (b.p.); 965 (i);
$-CH_2CH=CH_2$					b.p. 30°/1.5 mm	picrate, m.p. 105–107°	557 (b.p.); 557 (m.p.);
$-\underset{\mathrm{OH}}{\mathrm{P}}\mathrm{OOCH_2CH_2CN}$						cyclohexyl ammonium salt, m.p. 110–111°	658 (m.p.),(u);
$-N=C(CH_3)_2$					b.p. 85°/2.3 mm		966 (b.p.);

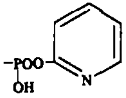
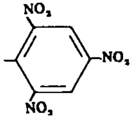
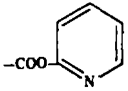
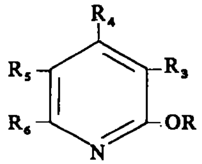
$n\text{-}C_3H_7$		b.p. 43°/7 mm	hydrochloride, m.p. 148–149°	966 (m.p.); 557 (b.p.);
isoC_3H_7		b.p. 92°/75 mm	picrate, m.p. 116–118°	557 (m.p.); 547 (b.p.), (g), (u);
$Si(CH_3)_3$		b.p. 63°/12 mm		616 (b.p.);
$-COC(CH_3)=CH_2$		m.p. -15° b.p. 90°/4 mm		639 (m.p.), (b.p.), (i), (n);
C_3H_5	CH_3CN	54°		944 (m.p.);.
Crotyl		b.p. 94°/12 mm		790 (b.p.);
$-CH(CH_3)CH\ CH_2$		b.p. 86°/20 mm		790 (b.p.);
$-CO(CH_2)_3CH_3$		b.p. 104°/5 mm		638 (b.p.), (i);
$n\text{-}C_4H_9$		b.p. 194°/65 mm		550 (b.p.); 899 (n);
			cyclohexyl ammonium salt, m.p. 154–155°	658 (m.p.);
$-P(OH)OO\text{-}$Thymyl		118–120°		967 (m.p.);
β-D-Xylose		121–123°		626 (m.p.), (f), (k);
		148–150°		553 (m.p.), (i), (n);
$-P(OH)OOC_6H_4Cl\text{-}p$		162–164°		967 (m.p.);
			cyclohexyl ammonium salt, m.p. 162–164° sodium salt	658 (m.p.), (u); 658;
		110–112°		658 (m.p.); 967 (m.p.);

TABLE XII-33. Ethers and Esters of Alkyl and Aryl 2-Pyridinols (Continued)



R	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
C_6H_5					38–42°		479 (n); 750 (m.p.); 751 (m.p.);
$-\underset{\mid}{P}OOC_6H_5$ OH						cyclohexyl ammonium salt, m.p. 166–167° sodium salt	658 (m.p.); 967 (m.p.); 658;
$-CO(CH_2)_4CH_3$					b.p. 122°/4 mm		638 (b.p.), (i);
β-D-Glucosyl					170–173°	tetraacetyl, m.p. 110–111°	603 (m.p.), (f); 620 (m.p.); 626 (m.p.);
isoC_3H_7		CH_3	C_2H_5		b.p. 132°/7.2 mm		281 (b.p.);
$-COC_6H_4NO_2-p$					116–117°		967 (m.p.);
$CH_2C_6H_5$					b.p. 110°/3 mm m.p. 39–40°		550 (b.p.); 965 (i); 967 (m.p.)
$-\underset{\mid}{P}OOCH_2C_6H_5$ OH						cyclohexyl ammonium salt, m.p. 142°	658 (m.p.), (u);
α-D-Glucosyl	CH_3				161-16P		626 (m.p.), (f), (k);
β-D-Glucosyl	CH_3				95–98°		626 (m.p.), (f), (k);
β-D-Glucosyl		CH_3			104–111°		626 (m.p.), (f), (k);
β-D-Glucosyl				CH_3	14–76		626 (m.p.), (f), (k);
$CH_2C_6H_5$	CH_3				b.p. 79°/0.1 mm		581 (b.p.);
$CH_2C_6H_5$			CH_3		b.p. 118°/0.1 mm m.p.30–31°		6 (b.p.), (m.p.);
3-Quinolyl					50–51°	picrate, m.p. 187–189°	273 (m.p.); 273 (m.p.);
CH_3				$-CH{=}CHC_6H_5$	118°		57 (m.p.);

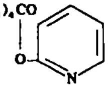
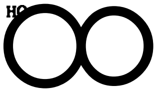
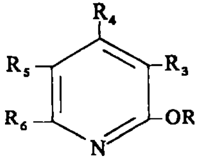
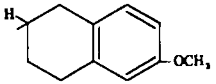
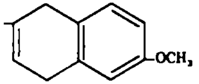
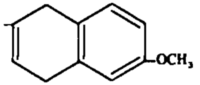
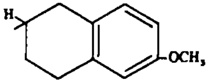
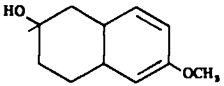
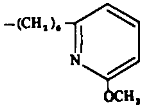
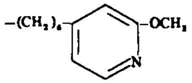
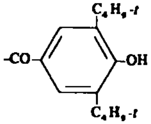
$-\underset{\mid}{\mathrm{P}}\mathrm{OO}$(5'-Uridine) OH					morpholine carbonic acid-4-(N,N'-dicyclohexyl-amidinium salt	661 (f), (u);
$-\underset{\mid}{\mathrm{P}}\mathrm{OO}$(5'-Cytidine) OH					morpholine carbonic acid-4-(N-N'-dicyclohexylamidinium salt	661 (f), (u);
$-\underset{\mid}{\mathrm{P}}\mathrm{OO}$(β-Naphthyl) OH					cyclohexylammonium salt, m.p. 172–173°	658 (m.p.), (u);
$-$PO(O-2-Pyridyl)$_2$				73–75°		658 (m.p.);
$-\underset{\mid}{\mathrm{P}}\mathrm{OO}$(5'-Adenosine) OH					morpholine carbonic acid-4-(N,N'-dicyclohexyl-amidinium salt	661 (f), (u);
$-\underset{\mid}{\mathrm{P}}\mathrm{OO}$(5'-Guanosine) OH					morpholine carbonic acid-4-(N,N'-dicyclohexyl-amidinium salt	661 (f), (u);
$-$CH$_2$C$_6$H$_5$	CH$_2$OH	CH$_2$OH	CH$_3$	f		931 (m.p.), (i), (n);
$-\underset{\mid}{\mathrm{P}}\mathrm{OO}$(Thymyl) OH					cyclohexyl ammonium salt, m.p. 118–120°	658 (m.p.), (u);
$-\underset{\mid}{\mathrm{P}}\mathrm{OO}$(5'-Thymidine) OH					ammonium salt	661 (f), (u);
$-\underset{\mid}{\mathrm{P}}\mathrm{OOC_6H_4Cl}$-p O-2-Pyridyl				96–97°		658 (m.p.);
$-\underset{\mid}{\mathrm{P}}\mathrm{OOC_6H_5}$ O-2-Pyridyl				56–57°		658 (m.p.);
$-$CO(CH$_2$)$_4$CO 				98-100°		967 (m.p.);
α-L-Arabinose					triacetyl hygroscopic	626 (k);
β-D-Xylosyl					triacetyl m.p. 114–116°	626 (m.p.), (k);
C$_2$H$_5$				b.p. 155°/0.1 mm		568 (b.p.), (u);
					perchlorate, m.p. 164–165°	568 (m.p.), (u);

TABLE XII-33. Ethers and Esters of Alkyl and Aryl 2-Pyridinols (Continued)



R	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
β-D-Glucosyl		C_6H_5			165"		604 (m.p.);
α-D-Glucosyl				C_6H_5	186–188°		604 (m.p.);
β-D-Glucosyl				C_6H_5	170–173°		604 (m.p.);
CH_3						perchlorate, m.p. 168–170°	568 (m.p.), (u);
β-D-Lactosyl					182–183°		626 (m.p.), (f), (k);
CH_3		C_6H_5		C_6H_5	82°		941 (m.p.), (i), (u);
C_2H_5					105-106°		568 (m.p.), (u);
C_2H_5					7 k		568 (m.p.), (u);
C_2H_5					b.p. 160'10.6 mm	perchlorate, mp. 162–163°	568 (b.p.), (u); 568 (m.p.);
C_2H_5					89-90°	perchlorate, m.p. 169–170'	568 (m.p.), (u); 568 (m.p.);
CH_3					b.p. 142°/0.1 mm		6 (b.p.);

CH_3					60–61°		6 (m.p.);
CH_3		$C_6H_4OCH_3$-*p*		C_6H_5	105		941 (m.p.), (i), (u);
β-D-Galactosyl						tetraacetyl, amorphous	626 (k);
α-D-Glucosyl						tetraacetyl m.p. 84–85°	606 (m.p.), (k);
β-D-Glucosyl						tetraacetyl, m.p. 110–111°	603 (m.p.); 620 (m.p.);
$CH_2C_6H_5$	*n*-C_7H_{15}				b.p. 148°/0.3 mm		581 (b.p.);
$CH_2C_6H_5$		*n*-C_7H_{15}			b.p. 140°/0.3 mm		581 (b.p.);
$CH_2C_6H_5$			*n*-C_7H_{15}		b.p. 142°/0.3 mm		581 (b.p.);
$CH_2C_6H_5$				*n*-C_7H_{15}	b.p. 120°/0.5 mm		581 (b.p.);
$-CH_2C_6H_5$		$-CH_2CH_2C_6H_5$			b.p. 184°/0.15 mm		581 (b.p.);
					181–183°		1013 (m.p.);
α-D-Glucosyl	CH_3					tetraacetyl, m.p. 119–120°	626 (m.p.), (k);
β-D-Glucosyl	CH_3					tetraacetyl, m.p. 79–81°	626 (m.p.), (k);
β-D-Glucosyl		CH_3				tetraacetyl, m.p. 129–131°	626 (m.p.), (k);
β-D-Glucosyl				CH_3		tetraacetyl, m.p. 102–104°	626 (m.p.)
CH_3		C_6H_5	C_6H_5	C_6H_4Br-*p*	181°		122 (m.p.), (i);
CH_3		C_6H_5	C_6H_5	C_6H_5	144–145°		121 (m.p.);
β-D-Ribofuranosyl-5′-desoxy-5′-iodo						2′, 3′-di-*O*-benzoyl, syrup	621 (f), (t);
α-D-Ribofuranosyl-2′-desoxy						di-*O*-toluyl, m.p. 115–118°	511 (m.p.); 619 (n);
β-D-Ribofuranosyl-2′-desoxy						di-*O*-toluyl, m.p. 85–87°	611 (m.p.); 619 (n);
$-CH_2C_6H_5$		$-(CH_2)_{11}CH_3$			b.p. 182°/0.2 mm		581 (b.p.);
$-CH_2C_6H_5$			$-(CH_2)_{11}CH_3$		b.p. 190°/0.4 mm		581 (b.p.);
CH_3		C_6H_5	C_6H_5	$C_6H_4CH_3$-*p*	152°		122 (m.p.), (i);

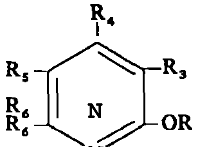


TABLE XII-33. Ethers and Esters of Alkyl and Aryl 2-Pyridinols (Continued)

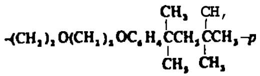
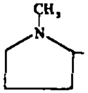
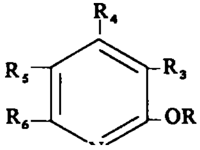
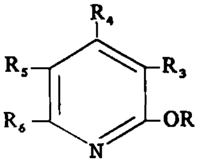
R	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
β-D-Glucosyl		C_6H_5				tetraacetyl, m.p. 129–130°	604 (m.p.);
α-D-Glucosyl				C_6H_5		tetraacetyl, m.p. 147–149°	604 (m.p.);
β-D-Glucosyl				C_6H_5		tetraacetyl, m.p. 185–186°	604 (m.p.);
 $-(CH_2)_2O(CH_2)_2OC_6H_4C(CH_3)_2CH_2C(CH_3)_2CH_3\text{-}p$					78–79°		1014 (m.p.);
$CH_2C_6H_5$		C_6H_5	C_6H_5	C_6H_5	150°		121 (m.p.);
β-D-Ribofuranosyl						2,3,5-tri-*O*-benzoyl, m.p. 112–114° 2′,3′-di-*O*-benzoyl-5′-*O*-diphenylphosphoryl, m.p. 83–85°	601 (m.p.); 602 (m.p.); 614 (m.p.), (k); 615 (m.p.), (k), (t);
β-D-Ribopyranosyl						2,3,5-tri-*O*-benzoyl, amorphous	601; 602;
β-D-Lactosyl						heptaacetyl, amorphous	626 (k);

TABLE XII-34. Ethers of Alkyloxy and Aryloxy 2-Pyridinols



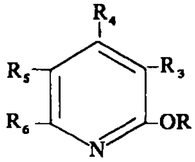
R	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
β-D-Glucosyl		OC_2H_5			130–133"		604 (m.p.);
						tetraacetyl m.p. 106-107°	604 (m.p.);

TABLE XII-35. Ethers of Amino 2-Pyridinols



R	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3				NH_2	b.p. 117°/20 mm		494 (b.p.), (i), (u);
C_2H_5	NH_2				31-32°		319 (m.p.);
						picrate, m.p. 135-137°	319 (m.p.);
C_2H_5				NH_2	b.p. 120°/16 mm		641 (b.p.), (i), (n);
						N′-acetyl, m.p. 137–139	641 (m.p.);
$-(CH_2)_2CH(CH_3)_2$				NH_2	b.p. 162°/23 mm		641 (b.p.);
						N′-acetyl, m.p. 115-116°	641 (m.p.);
C_6H_5	N_3				40°		968 (m.p.);
C_6H_5	NH_2				106°		968 (m.p.);
C_6H_5		NH_2			57-58°		969 (m.p.);
						picrate, m.p. 176-177°	969 (m.p.);
C_6H_5				NH_2	62-63°		969 (m.p.);
						picrate, m.p. 208-209°	969 (m.p.);

TABLE XII-35. Ethers of Amino 2-Pyridinols (Continued)



R	R₃	R₄	R₅	R₆	m.p.	Derivatives	Ref.
β-D-Glucosyl	NH_2				147–153°	tetraacetyl, m.p. 147–148°	608 (m.p.), (f), (k); 608 (m.p.), (k);
β-D-Glucosyl			NH_2			5-acetyl, m.p. 210° tetraacetyl, m.p. 59–63°	605 (m.p.), (f), (k); 605 (m.p.), (k);
CH_3	NH_2		NH_2	$-N{=}NC_6H_5$		dihydrochloride, m.p. 141°	738 (m.p.);
C_2H_5	NH_2		NH_2	$-N{=}NC_6H_5$		dihydrochloride, m.p. 119°	738 (m.p.);
β-D-Glucosyl	$NHCOCH_3$					tetraacetyl, m.p. 129–131°	608 (m.p.), (k);
β-D-Glucosyl			$NHCOCH_3$			tetraacetyl, m.p. 176–177°	605 (m.p.), (k);
n-C_4H_9				$-NHCH_2CH_2$ CH_3N CH_3	b.p. 127°/0.05 mm	hydrochloride, m.p. 104–105°	970 (b.p.); 970 (m.p.);
$-(CH_2)_2N(CH_3)_2$				$-NHC_4H_9$-n	b.p. 120°/0.02 mm	hydrochloride, m.p. 122–124°	970 (b.p.); 970 (m.p.);
n-C_3H_7	NH_2		NH_2	$-N{=}NC_6H_5$		dihydrochloride, m.p. 122°	738 (m.p.);
n-C_4H_9	NH_2		NH_2	$-N{=}NC_6H_5$		dihydrochloride, m.p. 126°	738 (m.p.);
n-C_4H_9				$-NHCH_2CH_2$ C_2H_5N C_2H_5	b.p. 163°/0.2 mm	hydrochloride, m.p. 76–77°	970 (b.p.); 970 (m.p.);
$-(CH_2)_2N(C_2H_5)_2$				$-NHC_4H_9$-n	b.p. 135°/0.02 mm	hydrochloride, m.p. 95–97°	970 (b.p.); 970 (m.p.);
n-C_5N_{11}	NH_2		NH_2	$-N{=}NC_6H_5$		dihydrochloride, m.p. 96°	738 (m.p.);

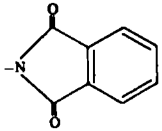
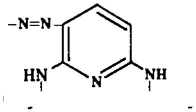
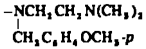
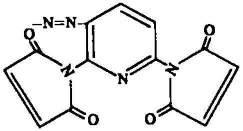
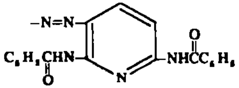
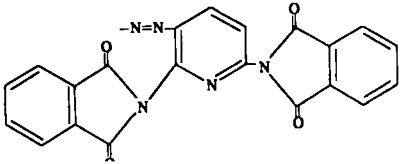
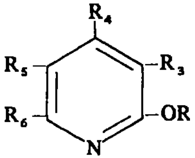
n-C_4H_9					63-165°		971 (m.p.);
CH_3	CH_3	$-N(C_2H_5)_2$	C_6H_5		p. 125°/0.01 mm		102 (b.p.), (i), (u);
β-D-Glucosyl			$NHCOC_6H_5$		175-180°	tetraacetyl m.p. 253-255°	605 (m.p.), (f), (k); 605 (m.p.), (k);
n-C_4H_9					p. 190°/1 mm		971 (b.p.);
n-C_4H_9				 $-\underset{CH_2C_6H_4OCH_3\text{-}p}{NCH_2}CH_2N(CH_3)_2$	p. 195 /0.4 mm	hydrochloride m.p. 129-130°	970 (b.p.); 970 (m.p.);
n-C_4H_9					145-147°		971 (m.p.);
n-C_4H_9					[illegible]		971 (m.p.);
n-C_4H_9					[illegible]		971 (m.p.);

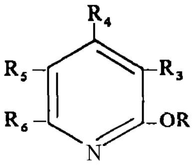
TABLE XII-36. Ethers of 2-Pyridinol Carboxylic Acids and Derivatives

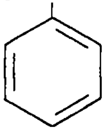


R	R$_3$	R$_4$	R$_5$	R$_6$	m.p.	Derivatives	Ref.
CH_3			COOH			ethyl ester	**549 (g);**
C_2H_5			COOH			ethyl ester, b.p. 125°/0.7 mm	**549 (b.p.);**
CH_3	COOH	COOH		COOH		trimethyl ester, m.p. 132"	**57** (m.p.);
CH_3	COOH			$COCH_3$		methyl ester, m.p. 80°	**57** (m.p.), **(i), (u);**
isoC_3H,			COOH			ethyl ester	**549;**
C_2H_5				CH_2COOH		ethyl ester, m.p. **80°**	**944** (m.p.);
CH_3	COOH	COOH		$COCH_3$		dimethyl ester, m. p. 80°	57 (m.p.), **(i);**
C_2H_5				$-CH_2COCOOH$		ethyl ester, m.p. **99"**	**944** (m.p.);
						oxime, m.p. 129"	**944** (m.p.);
C_2H_5				$CH_2\underset{\underset{NOH}{\|}}{C}COOH$		ethyl ester, m.p. **73°**	**944** (m.p.);
β-D-Glucosyl	COOH					methyl ester, m.p. 80–82°	**604** (m.p.);
$CH_2C_6H_5$			COOH			ethyl ester, m.p. **50-51°**	**549 (m.p.);**

CH_3	COOH			−CX ∈HC$_6$H$_5$		methyl ester, m.p. 63°	57 (m.p.), (i), (u);
CH_3		COOX		$-CH{=}CHC_6H_5$		methyl ester, m.p. 98°	57 (m.p.), (i);
$CH_2C_6H_5$	COOH		COOH	CH_3	186° softens 260°		931 (m.p.), (i);
CH_3	OOOX			$-\underset{\mid\atop CH_3}{C}{=}CHC_6H_5$		methyl ester, m.p. 73°	57 (m.p.), (i), (u);
CH_3		OOH		$-\underset{\mid\atop CH_3}{C}{=}CHC_6H_5$		methyl ester, m.p. 128°	57 (m.p.);
β-D-Gl c syl	$OOOCH_3$					tetraacetyl, m.p. 110–113°	604 (m.p.);
β-D-Glucosy l		$OOOCH_3$				tetraacetyl, m.p. 93–95°	604 (m.p.);
β-D-Glucosy l				$COOCH_3$		tetraacetyl, m.p. 171–173°	604 (m.p.);
β-D-Gluco-pyranosyl			$CONH_2$			tetraacetyl, m.p. 179°	613 (m.p.);
β-D-ribo-furanosyl			$CONH_2$			2,3,5-tri-*O*-benzoyl, m.p. 177°	613 (m.p.);

TABLE **XII-37.** Ethers of 2-Pyridinol Nitriles



R	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	CN			COOH		methyl ester, m.p. 124°	57 (m.p.), (i), (u);
CH_3	CN		CN	NH_2	258–259°		10 (m.p.);
C_2H_5	CN		$CONH_2$	NH_2	272–273°		10 (m.p.);
C_2H_5	CN	CH_3	CN	NH_2	235–237°		13 (m.p.);
C_2H_5	CN	C_2H_5	CN	NH_2	203–204°		13 (m.p.), (i), (n), (u);
β-D-Glucosyl			CN		180–182°		605 (m.p.), (f), (k);
C_2H_5	CN	$n\text{-}C_3H_7$	CN	NH_2	156–157°		13 (m.p.), (i), (n), (u);
C_2H_5	CN	isoC_3H_7	CN	NH_2	234–235°		13 (m.p.), (i), (n), (u);
C_2H_5	CN	2-furyl	CN	NH_2	203–204°		13 (m.p.), (i), (u);
C_2H_5	CN	$n\text{-}C_4H_9$	CN	NH_2	142–144°		13 (m.p.), (i), (n), (u);
C_2H_5	CN	$t\text{-}C_4H_9$	CN	NH_2	230–231°		13 (m.p.), (i), (u);
CH_3	CN	C_6H_5	CN	NH_2	259–261°		13 (m.p.), (i), (u);
C_2H_5	CN	3-Pyridyl	CN	NH_2	258°		13 (m.p.), (i), (u);
C_2H_5	CN	$-CH(C_2H_5)_2$	CN	NH_2	123–124°		13 (m.p.), (i), (n), (u);
C_2H_5	CN	$C_6H_4Cl\text{-}o$	CN	NH_2	263–264°		13 (m.p.), (i), (u);
C_2H_5	CN	$C_6H_4Cl\text{-}p$	CN	NH_2	180–181°		13 (m.p.), (i), (u);
CH_3	CN			–CH=CH 	122°		57 (m.p.), (i), (u);

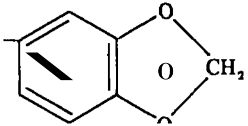
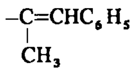
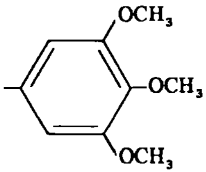
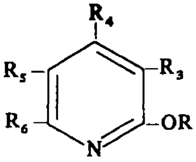
C_2H_5	CN	C_6H_5	CN	NH_2	238-239"	13 (m.p.), (i), (u);
C_2H_5	CN	C_6H_{11}	CN	NH_2	159-161°	13 (m.p.), (i), (u);
C_2H_5	CN	n-C_6H_{13}	CN	NH_2	oil	13 (i);
C_2H_5	CN		CN	NH_2	174-175°	13 (m.p.), (i), (u);
CH_3	CN			 $-\underset{CH_3}{\underset{\mid}{C}}=CHC_6H_5$	13"	57 (m.p.), (i), (u);
C_2H_5	CN	$CH_2C_6H_5$	CN	NH_2	140-141"	13 (m.p.), (i), (n), (u);
C_2H_5	CN	$C_6H_4CH_3$-m	CN	NH_2	230-231"	13 (m.p.), (i), (u);
C_2H_5	CN	$C_6H_4CH_3$-p	CN	NH_2	192-194"	13 (m.p.), (i), (u);
isoC_3H_7	CN	C_6H_5	CN	NH_2	205-207"	13 (m.p.), (i), (u);
n-C_3H_7	CN	C_6H_5	CN	NH_2	224-225°	13 (m.p.), (i), (u);
C_2H_5	CN	$C_6H_4OCH_3$-p	CN	NH_2	199-200"	13 (m.p.), (i), (n), (u);
C_2H_5	CN	$C_6H_4N(CH_3)_2$-p	CN	NH_2	270-271"	13 (m.p.), (i), (n), (u);
C_2H_5	CN		CN	NH_2	219-221"	13 (m.p.), (i), (u);
β-D-Glucosyl	CN				tetraacetyl, m.p. 197-201"	608 (m.p.), (k);
α-D-Glucosyl			CN		tetraacetyl, m.p. 125-130"	605 (m.p.), (k);
β-D-Glucosyl			CN		tetraacetyl, m.p. 153-155°	605 (m.p.), (k);

TABLE XII-38. Ethers and Esters of Halo 2-Pyridinols



R	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	Cl				b.p. 107°/52 mm	hexachloro-antimonate·HCl	467 (b.p.), (u); 546 (i), (u);
CH_3		Cl			27–28° b.p. 71°/17 Torr		768 (m.p.), (b.p.);
CH_3			Cl			hydrochloride, m.p. 121° eff.	467 (m.p.), (u); 546 (i), (u);
CH,				Cl	b.p. 73°/15 mm		241 (u); 494 (b.p.);
CH_3	Br				b.p. 98°/26 mm	hydrochloride	467 (b.p.), (u); 546 (i), (u);
CH_3			Br			hydrochloride, m.p. 125" eff.	467 (m.p.), (u); 546 (m.p.), (i), (u);
CH_3			I		b.p. 106°/30 mm	hydrochloride, m.p. 146–147"	467 (b.p.), (u); 467 (m.p.); 546 (i), (u);
CH_3	Cl		Cl		38–40"	hexachloro-antimonate·HCl	467 (m.p.), (u); 831 (i), (u); 546 (i);

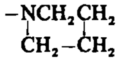
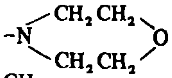
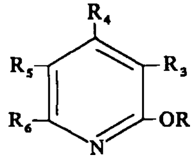
CH_3	Br		Br		48–49°		467 (m.p.), (u); 831 (i);
						hexachloro-antimonate·HCl	546 (i), (u);
CH_3	F		F	F	b.p. 146°/760 mm		247 (b.p.); 949 (b.p.);
CH_3	F	F	F	F	b.p. 135°/760 mm		246 (b.p.), (g), (i), (n);
CH_3	F	Br	F	F	b.p. 193°/760 mm		247 (b.p.), (n); 949 (b.p.);
CH_3	Br	Br	Br	Br	173°		952 (m.p.);
$CONHCH_3$	Cl	Cl	Cl	Cl	220–223"		972 (m.p.);
C_2H_5	Cl	Cl	Cl	Cl			241 (u);
CH_2CH_2OH	Cl	Cl	Cl	F	82-83"		953 (m.p.);
$CONHCH_3$	Cl		Cl	Cl	121–123°		972 (m.p.);
CH_3	Cl	CH_3	Cl	Cl	82"		778 (m.p.), (n);
$N(CH_3)_2$	Cl	Cl	Cl	Cl	83"		240 (m.p.);
$CONHCH_3$	Cl			Cl	129–132"		972 (m.p.);
C_2H_5			Br	Br	41-42"		712 (m.p.);
$PO(OCH_3)_2$	Cl		Cl	Cl	86-88"		703 (m.p.);
CH_3		CH_3		Cl	b.p. 105°/12 mm		8 (b.p.); 457 (i), (n), (u);
$PO(NHCH_3)_2$	Cl		Cl	Cl	86-89"		973 (m.p.);
					146–148"		973 (m.p.);
$CON(CH_3)_2$	Cl	Cl	Cl	Cl	118–120"		972 (m.p.);
	Cl	Cl	Cl	Cl	71°		240 (m.p.);
	Cl	Cl	Cl	Cl	130"		240 (m.p.);
CH_3	$-CH_2CH_2CH_2-$			Cl	b.p. 145°/14 mm		8 (b.p.); 457 (i), (n), (u);
$-PO(OC_2H_5)_2$	Cl		Cl	Cl	43–44°		703 (m.p.); 974 (g), (c);

TABLE **XII-38.** Ethers and Esters of Halo 2-Pyridinols (Continued)



R	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
$-\underset{\text{OCH}_3}{\underset{\mid}{\text{P}}}\text{ONHCH(CH}_3)_2$	Cl		Cl	Cl	117–119"		973 (m.p.);
$-\underset{\text{CH}_3\text{NH}}{\underset{\mid}{\text{P}}}\text{OOCH}_2\text{CH}_2\text{CH}_3$	Cl		Cl	Cl	68–71"		973 (m.p.);
$-\text{N(CH}_2)_5$	Cl	Cl	Cl	Cl	87°		240 (m.p.);
C_6H_5	Cl	Cl	Cl	Cl	94"		240 (m.p.);
$-\text{N(CH}_2)_6$	Cl	Cl	Cl	Cl	54"		240 (m.p.);
β-D-Glucosyl	Cl		Cl		160–162"		608 (m.p.), (f), (k);
						tetraacetyl, m.p. 164–166"	608 (m.p.), (k);
β-D-Glucosyl	Br		Br		159–160"		608 (m.p.), (f), (k);
						tetraacetyl, m.p. 152–154"	608 (m.p.), (k);
β-D-Glucosyl	Cl					tetraacetyl, m.p. 147–149"	608 (m.p.), (k);
β-D-Glucosyl	Br					tetraacetyl, m.p. 135–137"	608 (m.p.), (k);
α-D-Glucosyl			Cl			tetraacetyl, m.p. 124–125°	606 (m.p.), (k), (n); 610 (m.p.), (n);
β-D-Glucosyl			Cl		152-155"		605 (m.p.), (f), (k);

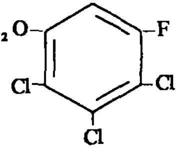
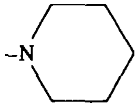
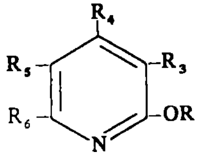
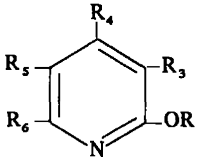
						tetraacetyl,	
						m.p. 126–129	**605 (m.p.), (k);**
							606 (m.p.), (k);
β-D-Glucosyl			Br		164-165°		**605 (m.p.), (f), (k);**
						tetraacetyl,	
						m.p. 143–144"	**605 (m.p.), (k);**
α-D-Glucosyl			I			tetraacetyl,	
						m.p. 139–142"	**605 (m.p.), (k);**
β-D-Glucosyl			I		159-162°		**605 (m.p.), (f), (k);**
						tetraacetyl,	
						m.p. 166–169"	605 (m.p.), **(k);**
CH_3		CON(Et)$_2$		Cl	b.p. 153°/3 mm		975 (b.p.);
isoC_3H_7		CH_3	C, H,	Cl	b.p. **78°/0.8** mm		281 (b.p.);
Sn(C_2H_5)$_3$	Cl		Cl		b.p. 145°/2 mm		831 (b.p.), **(i), (u);**
Sn(C_2H_5)$_3$	Br		Br		b.p. 180°/6 mm		831 (b.p.);
–CH_2CH_2O– 	**Cl**	Cl.	Cl	**F**	124-125°		953 (m.p.);
CH_3		**C_6H_5**		Cl	65"		**8** (m.p.); 457 (i), **(n), (u);**
$CH_2C_6H_5$		CH_3	C_2H_5	Cl	b.p. 150°/0.6 mm		281 (b.p.);
–N(CH_2)$_5$	Cl		**Cl**	Cl	82"		240 (m.p.);
CH_3	C_6H_5	C_6H_5	Cl	Cl	164–166"		**242 (m.p.), (u);**
CH_3	Cl	**C_6H_5**	C_6H_5	Cl	152"		**242 (m.p.), (u);**
C_2H_5	Cl	**C_6H_5**	C_6H_5	Cl	110"		**242 (m.p.), (m), (u);**
$CH_2C_6H_5$	NHCH, C_6H_5			Br	78-80"		**740 (m.p.), (i), (n);**

TABLE **XII-38.** Ethers and Esters of Halo 2-Pyridinols (Continued)



R	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
$CH(C_6H_5)_2$		CH_3	C_2H_5	Cl	104–105°		**281 (m.p.);**
$CH(C_6H_5)_2$	C_2H_5	CH_3		Cl	94–95"		281 **(m.p.);**
$Pb(C_6H_5)_3$	Cl		Cl		120"		**831 (m.p.)**, (i), **(u);**
$Sn(C_6H_5)_3$	Cl		Cl		112–113"		**831 (m.p.), (i), (u);**
$Sn(C_6H_5)_3$	Br		Br		127–130°		**831 (m.p.)**, (i);

TABLE **XII-39.** Ethers of Nitro 2-Pyridinols



R	R_3	R_4	R_5	**R_6**	**m.p.**	Derivatives	Ref.
CH_3	**NO_2**		NO_2	D	**89–91°**		**769 (m.p.)**, (n);
CH_3	**Cl**		**NO_2**		**58"**		**291 (m.p.)**, (i);
CH_3	**NO_2**		Cl		**90"**		**291 (m.p.);**
CH_3	Br		**NO_2**		**84"**		**290 (m.p.), (i);**
CH_3	I		**NO_2**		**74"**		**287 (m.p.);**

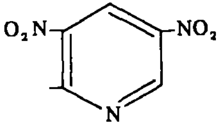
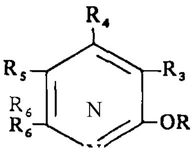
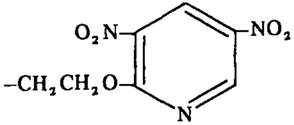
CH_3	NO_2		NO_2		89-94°	260 (m.p.); 261 (m.p.); 265 (m.p.); 769 (m.p.), (n); 773 (m.p.), (n), (u); 960 (u);
CH_3	NO_2					956 (u);
CH_3		NO_2			106°	261 (m.p.); 262 (m.p.);
CH_3			NO_2			957 (u); 958 (i);
CH_3	NO_2		NO_2	$NHNH_2$	180-182°	769 (m.p.), (n); 265 (m.p.);
C_2H_5	NO_2		NO_2		65-71°	260 (m.p.); 261 (m.p); 265 (m.p.);
CH_3	NO_2	CH_3	NO_2		129°	264 (m.p.);
CH_3	NO_2		NO_2	CH_3	54°	264 (m.p.);
CH_3	CH_3		NO_2		93-95°	700 (m.p.);
CH_3			NO_2	CH_3	68°	263 (m.p.);
C_2H_5	NO_2	CX:	NO_2		87°	264 (m.p.);
C_2H_5	NO_2		NO_2	CH_3	63°	264 (m.p.);
isoC_3H_7			NO_2		51-53°	549 (m.p.);
n-C_4H_9			NO_2			899 (n);
	NO_2		NO_2		255-257°	265 (m.p.); 276 (m.p.);
$C_6H_4NO_2$-p	NO_2		NO_2		127°	265 (m.p.);
C_6H_5	Cl		NO_2		92°	291 (m.p.);
C_6H_5	Br		NO_2		121°	290 (m.p.);
C_6H_5	NO_2		NO_2		159°	265 (m.p.);
C_6H_4OH-m	NO_2				168°	968 (m.p.);
β-D-Glucosyl			NO_2		165-167°	605 (m.p.), (f), (k);

TABLE XII-39. Ethers of Nitro 2-Pyridinols (Continued)



R	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
	NO_2				147–148°		265 **(m.p.)**;
β-D-Glucosyl	NO_2		Br			tetraacetyl, m.p. 162–165°	608 (m.p.), (k);
β-D-Glucosyl	Br		NO_2			tetraacetyl, m.p. 188–193° sublimes at 160"	608 **(m.p.)**, (k);
β-D-Glucosyl	NO_2		NO_2			tetraacetyl, m.p. 155–161°	608 (m.p.), (k);
α-D-Glucosyl			NO_2			tetraacetyl, m.p. 166–167°	605 (m.p.), **(k)**;
β-D-Glucosyl			NO_2			tetraacetyl, m.p. 149-150°	**605 (m.p.), (k); 609 (n);**
β-D-Glucosyl	NO_2					tetraacetyl, m.p. 138–140"	608 **(m.p.)**, (k);
β-D-Glucosyl	CN		NO_2			tetraacetyl, m.p. 185-188°	608 (m.p.), (k);

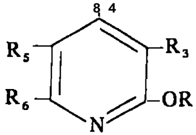
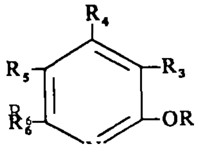


TABLE XII-40. **Ethers and Esters of Sulfur** Containing 2-Pyridinols

R	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
COSCH,	Cl	Cl	Cl	Cl	80–82°		976 (m.p.);
COSCH,		Cl		Cl	57–58°		976 (m.p.);
$PS(OCH_3)_2$	Cl		Cl	Cl	43–44°		703 (m.p.);
$-PSOCH_3$ | NHCH,	**Cl**		Cl		84-86°		973 (m.p.);
$-PSOCH_3$ | NHCH,	**Br**		**Br**		93–95"		973 (m.p.);
$-PSOCH_3$ | NHC_2H_5	Cl		Cl		89–91°		973 (m.p.);
$-PSOC_2H$, | NHCH,	**Cl**		Cl		71–73"		973 (m.p.);
$-PSOC_2H_5$ | NHCH,	**Br**		**Br**		88–89"		973 (m.p.);
$COS(CH_2)_2CH$,	Cl		Cl	Cl	45–46°		976 (m.p.);
$PS(OC_2H_5)_2$	Cl	Cl	Cl	Cl	4749"		973 (m.p.);
$PS(OC_2H_5)_2$	**Cl**		Cl	Cl	4243"		703 (m.p.); 973 (m.p.); 977 (g);
$PS(OC_2H_5)_2$	**Cl**	Cl		Cl	53–55"		973 (m.p.);
$PS(OC_2H_5)_2$	**Br**		Br	Cl	60–61°		703 (m.p.); 973 (m.p.);

TABLE XII-40. Ethers and Esters of Sulfur Containing 2-Pyridinols (Continued)



R	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
$-\underset{\underset{OCH_3}{\vert}}{P}SNHCH(CH_3)_2$	Cl	Cl	Cl	Cl	77–81"		973 (m.p.);
$-\underset{\underset{OCH_3}{\vert}}{P}SNHCH(CH_3)_2$	Cl	Cl		Cl	79–82°		973 (m.p.);
$-\underset{\underset{OCH_3}{\vert}}{P}SNHCH(CH_3)_2$	Cl		Cl	Cl	79–81"		973 (m.p.);
$-\underset{\underset{NHCH_3}{\vert}}{P}SOCH_2CH_2CH_3$	Cl				52–55"		973 (m.p.);
$-\underset{\underset{NHCH_3}{\vert}}{P}SOCH(CH_3)_2$	Cl		Cl		86–89°		973 (m.p.);
$-\underset{\underset{OCH_3}{\vert}}{P}SNHCH(CH_3)_2$	Cl		Cl		52–56"		973 (m.p.);
$-\underset{\underset{OCH_3}{\vert}}{P}SNHCH(CH_3)_2$		Cl		Cl	51–54"		973 (m.p.);
$-\underset{\underset{OC_2H_5}{\vert}}{P}SNHC_2H_5$	Cl		Cl		68–70"		973 (m.p.);
$-\underset{\underset{OCH_3}{\vert}}{P}SNHCH(CH_3)_2$	Br		Br		63–68"		973 (m.p.);

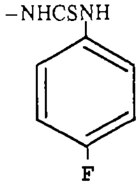
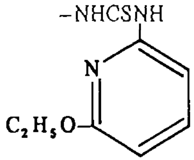
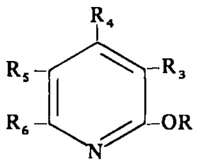
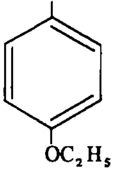
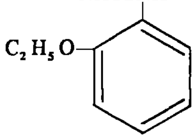
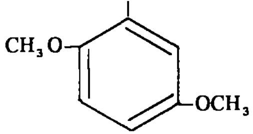
-PSOCH(CH$_3$)$_2$ NHCH,	Br		Br		85–87"	973 (m.p.);
-PSCH(CH$_3$)C$_2$H$_5$ NHCH,	Cl		Cl		82–86"	973 (m.p.);
-PSOC$_4$H$_9$ NHCH,	Cl		Cl		62–64"	973 (m.p.);
PSOCH, CH(CH$_3$)$_2$ NHCH,	Cl		Cl		76–18"	973 (m.p.);
PS(OC$_2$H$_5$)$_2$			SO, CH,		56–58"	978 (m.p.);
PS(OC$_2$H$_5$)$_2$	SOC, H$_5$		Cl		47–49"	978 (m.p.);
PSOCH, CH, CH, NHCH, CH, CH,	Cl		Cl		60–62°	973 (m.p.);
COSC, H$_5$	Cl	Cl	Cl	Cl	103–104"	976 (m.p.);
COSC$_6$H$_5$	Cl		Cl	Cl	109–110"	976 (m.p.);
COSC$_6$H$_5$		Cl		Cl	63"	976 (m.p.);
COSC, H$_5$				Cl	88–89"	976 (m.p.);
C$_2$H$_5$	CN	**2-Thienyl**	CN	NH$_2$	176–178"	13 (m.p.), (i), (u);
C$_2$H$_5$					182–183"	641 (m.p.);
C$_2$H$_5$					176–177"	641 (m.p.);

TABLE XII-40. Ethers and Esters of Sulfur Containing 2-Pyridinols (Continued)



R	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
$-SO_2$GH_4CH_3-*p*	CN	CH_2OC[illegible]	NH_2	CH_3	126°		52 (m.p.);
[illegible]				$-NHCSNH$ 	160–161°		641 (m.p.);
C_2H_5				$-NHCSNH$ 	171–172°		641 (m.p.);
C_2H_5				$-NHCSNH$ 	163–164°		641 (m.p.);
$-SO_2C_6H_4CH_3$-*p*	$-CH_2NH_2$	CH_2OCH_3	NH_2	[illegible]		picrate, m.p. 188°	52 (m.p.);

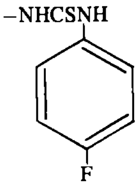
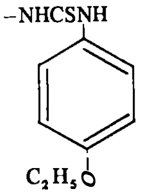
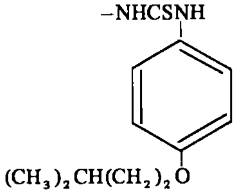
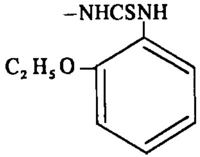
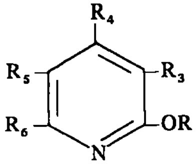
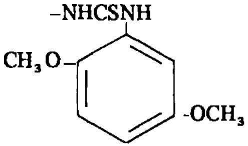
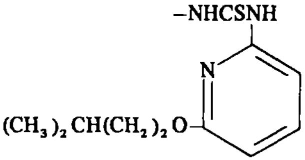
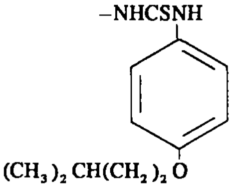
$-PS(OC_6H_5)_2$		oil	≤63 (u);
$isoC_5H_{11}$		150-151°	≤41 (m.p.)
$isoC_5H_{11}$		171-172°	≤41 (m.p.);
C_2H_5		121-122°	641 (m.p.);
$isoC_5H_{11}$		128-129	≤41 (m.p.);

TABLE XII-40. Ethers and Esters of Sulfur containing 2-Pyridinols (Continued)



R	R₃	R₄	R₅	R₆	m.p.	Derivatives	Ref.
isoC$_5$H$_{11}$					104–105°		641 (m.p.);
isoC$_5$H$_{11}$					140-141°		641 (m.p.);
isoC$_5$H$_{11}$					115-116°		641 (m.p.);

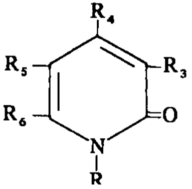
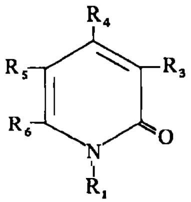


TABLE XII-41. Alkyl and Aryl 2-Pyridones

R	R	ρ	R	R	4	D t	ɑf
D							465 (i); 487 (i);
D						^{15}N	465 (i);
D						^{18}O	465 (i);
H	H	H	H	H		$B(C_2H_5)_3$ complex	838 (n);
						C_6H_5Hg complex,	
						m.p. 217–218°	831 (m.p.), (i), (u);
						$Si(CH_3)_2$ complex,	
						b.p. 116°/1 mm	830 (b.p.);
						Al complex	
						m.p. 121°	830 (m.p.);
						$Sn(C_4H_9)_3$ complex	830;
CD_3							485 (n); 907 (m);
CH_3	D(H)		D(H)	D	b.p. 80°/0.4 mm		530 (b.p.), (n);
CH_3					b.p. 63°/0.5 mm		465 (i); 472 (n);
					b.p. 115°/10 mm		476 (b.p.), (n); 481 (z);
							525 (h), (u); 530 (b.p.);
							541 (i); 616 (b.p.), (i);
							692 (b.p.), (i); 764 (m);
							923 (n); 979 (c);
							342 (t);
							348 (f), (g), (h), (u);
							353 (b.p.); 466 (i);
							480 (i); 482 (z);
							485 (n); 745 (u);
							907 (m); 919 (i);
							980 (w); 981 (b.p.), (i);
							982 (a), (u); 983 (i);
							984; 985 (n);
							1157 (n);
						^{15}N	465 (i);
						^{18}O	465 (i);
						picrate,	
						m.p. 142–143°	351 (m.p.); 353 (m.p.);
							745 (m.p.), (u);
						hydrochloride,	
						m.p. 170–172°	540 (m.p.), (i);
						hydrobromide,	
						m.p. 175–176°	540 (m.p.), (i);

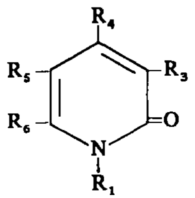
TABLE XII-41. Alkyl and Aryl 2-Pyridones (Continued)

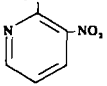
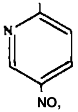


R$_1$	R$_3$	R$_4$	R$_5$	R$_6$	m.p.	Derivatives	Ref.
						hydroiodide .H_2O m p 73-15"	540 (m.p.), (i);
						hydroiodide, m.p 116-119°	540 (m.p.), (i);
						$HSbCl_4$ m p. 128-131°	540 (m.p., (i);
						H_2SnBr_6 m.p. 132-135°	540 (m.p.), (i);
						H_2SnCl_6	540 (m.p.), (i);
						m.p. 167-169°	464 (m.p.), (i);
						m.p. 250-252°	464 (m.p.), (i);
						$HSbCl_4$	540 (m.p.), (i);
						m p. 186-189°	542 (i);
						2 1 complex with cyclomethylene tetranitraamine	839 (i), (x);
						pentacyanopropene salt, m.p. 135-136'	745 (m.p.), (u);
						1 1 complex BF_3 m p. 124-126°	818 (i); 986 (m.p.);
						BCl_3 complex, m.p 115-123° hygroscopic	818 (m.p.), (i);
						BBr_3 complex, m.p. 106-109°	818 (m.p.), (i);
						$CuCl_2$ complex, m.p. >290°	818 (m.p.), (i),
						$HgCl_2$ m.p. 126-133°	817 (m.p.); 818 (m.p.), (i);
						$SbCl_3$ complex m.p. 85-87' hygroscopic	818 (m.p.), (i);
						$SnBr_4$ complex, m.p. 225-227°	818 (m.p.), (i);
						$ZnCl_2$ complex m.p. 124-12 T	818 (m.p.), (i);
CH_2CD_3							907 (m);
$-CH=CH_2$					121-123°		785 (m.p.); 907 (n), (u);

CD_2CH					b.p. 144°/0.5 mm		987 (b.p.); 907 (m);
$COCH_3$							631 (i), (n);
CH_2CH					62-65° hygroscopic		988 (m.p.);
						hydrochloride, m.p. 151-154°	988 (m.p.); 989 (m.p.);
CH	CH_2Br				98-99°		559 (m.p.);
CH			i·B		119°		559 (m.p.);
CH	CH_3				b.p. 78°/0.5 mm		476 (b.p.), (i), (n); 559 (b.p.); 907 (m); 924 (b.p.); 982 (u), (u);
CH		i			58-59° b.p. 110°/3 mm		353 (b.p.); 559 (m.p.); 907 (m); 923 (n); 924 (m.p.); 982 (a), (u);
						picrate, m.p. 163-164	353 (m.p.);
			CH_3		b.p. 88°/0.5 mm		476 (m.p.), (i), (n);
					b.p. 185°/29 mm m.p. 40-41°		559 (b.p.); 700 (b.p.); (u); 907 (m); 924 (b.p.); 982 (a), (u); 984;
				CH	55-58° b.p. 80°/<0.5 mm b.p. 116°/3 mm		353 (b.p.); 442 (b.p.), (m.p.); 476 (m.p.), (n); 485 (n); 559 (m.p.); 907 (m); 924 (m.p.); 982 (a), (u); 984;
						picrate m.p. 133-134°	353 (m.p.);
						hydrochloride, m.p. 198-203°	306 (m.p.); 442 (m.p.);
					b.p. 140°/0.5 mm b.p. 118°/7 mm		485 (n); 570 (b.p.); 907 (m); 987 (b.p.);
						$HgCl_2$ complex, m.p. 108-109°	346 (m.p.); 351 (m.p.);
						pentacyanopropene, salt, m.p. 116-117°	745 (m.p.), (u);
CH					95-97° b.p. 198°/10 mm		988 (m.p.), (b.p.);
CH			CH_2OH		106-108°		729 (m.p.), (i), (n), (u);
						5-*O*-acetyl, m.p. 45-47°	729 (m.p.), (i), (n);
CH ,CNH_2						hydrochloride, m.p. 197-198°	573 (m.p.); 990 (m.p.);
CH CH_2Cl					131-132°		554 (m.p.);
CH $=CH_2$					b.p. 88°/1.5 mm		557 (b.p.); 991 (b.p.);
						picrate, m.p. 104-106°	557 (m.p.);
CH			$COCH_3$				437 (i), (n), (u); 438 (n);
CH		d	CH_3				476 (n); 984;

TABLE XII-41. Alkyl and Aryl 2-Pyridones (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3		CH_3		CH_3	85–89° b.p. 152°/10 mm		60 (n); 107 (m.p.); 476 (m.p.), (n); 694 (b.p.), (m.p.); 907 (m); 982 (a), (u);
CH_3	C_2H_5				picrate, m.p. 59–60°		314 (m.p.);
CH_3			C_2H_5		b.p. 114°/3 mm	picrate, m.p. 122-123°	353 (b.p.), (i); 314 (m.p.); 353 (m.p.);
C_3H_7		CH_3			32°		907 (m.p.), (m);
C_2H_5			CH_3				467 (u);
n-C_3H_7					b.p. 123°/13 mm	picrate, m.p. 95–97° pentacyanopropene salt, m.p. 97'	557 (b.p.); 907 (b.p.), (m); 557 (m.p.); 745 (m.p.), (u);
isoC_3H_7							485 (n);
CH_3			$CH(OH)CH_3$				435 (i), (n);
$CF_3C=CHCF_3$					55–56°		746 (m.p.), (i), (u);
$-CH_2CH=CHCH_3$					b.p. 94°/0.1 mm		790 (b.p.), (g);
$CH_2=COC_2H_5$					b.p. 108°/1.2 mm		747 (b.p.), (i), (n), (u);
n-C_4H_9					b.p. 172°/33 mm		550 (b.p.);
CH_3	CH_2OH		C_2H_5		71–79'		729 (m.p.), (i), (n);
					172–174°		271 (m.p.); 1012 (m.p.);
					179–180°		271 (m.p.);

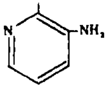
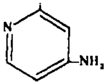
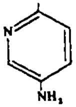
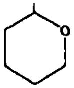
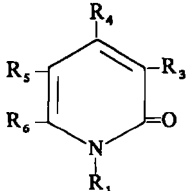
2-Pyridyl				50–52		403 (m.p.); 404 (f), (g); 409 (g);
					picrate, m.p. 116–118°	403 (m.p.); 992 (m.p.);
					$HgCl_2$ m.p. 170–172°	403 (m.p.);
					$HCl \cdot H_2O$ m.p. 263–265°	993 (m.p.);
				146–147°		271 (m.p.); 994 (m.p.);
					picrate, m.p. 181–182°	271 (m.p.);
					N'-acetyl, m.p. 243–244°	271 (m.p.);
				169–170°		271 (m.p.);
					picrate, m.p. 256–258°	271 (m.p.);
					N'-acetyl, m.p. 205–206°	271 (m.p.);
				157–158°		271 (m.p.); 994 (m.p.);
					picrate, m.p. 198–199°	271 (m.p.);
					N'-acetyl, m.p. 210–211°	271 (m.p.);
5'-Desoxy-5'-iodo-β-D-ribofuranosyl				122–124°		621 (m.p.), (k), (t);
					2', 3'-*O*-isopropylidene, m.p. 95–96°	621 (m.p.), (k), (t);
					2', 3'-di-*O*-benzoyl, amorphous	621 (f), (k), (t);
				oil		574 (f);
CH_3	$COCH_3$	CH_3	CH_3			60 (l), (n), (u);
2'-Desoxy-α-D-ribofuranosyl				132°		611 (m.p.), (k);
				96–98°		622 (m.p.), (n), (o), (u);
					3', 5'-di-*p*-toluyl, m.p. 152–159°	611 (m.p.), (k); 619 (n); 622 (m.p.);

TABLE XII-41. Alkyl and Aryl 2-Pyridones (Continued)



R_1	R	R_4	R_5	R	.p.	Derivativ	R
2'-Desoxy-β-D-ribofuranosyl					115–116°		611 (m.p.), (k); 622 (m.p.), (o), (u);
						3', 5'-di-*O*-toluyl, m.p. 112–115°	611 (m.p.), (k); 619 (n);
5'-Desoxy-β-D-ribofuranosyl					syrup		621 (f), (k);
						2', 3'-*O*-isopropylidene, m.p. 85–87°	621 (m.p.), (f), (k), (t);
						2'-3'-di-*O*-benzoyl, m.p. 108–111°	621 (m.p.), (k), (t);
α-L-Arabinosyl					227–228°		626 (m.p.), (f), (k);
						triacetyl, amorphous	626 (k);
β-D-Ribofuranosyl					151–152°		601 (m.p.); 602 (m.p.); 615 (u); 625 (m.p.), (i), (u); 628 (u);
						2'-phosphate	627 (u);
						3'-phosphate	627 (u);
						5'-phosphate barium salt	615 (u);
						5'-phosphate	628 (u);
						5'-diphosphate	628 (u);
						2', 3'-cyclophosphate	627 (c);
						2', 3'-isopropylidene, m.p. 92–93°	615 (m.p.), (t);
						2', 3'-isopropylidene 5'-phosphate bistriethyl ammonium salt	615 (u);
						2', 3'-*O*-ethoxymethylene	628 (t);
						5'-phenylphosphate barium salt	615 (u);
						5'-imidazolyl phosphate 2', 3'-*O*-ethoxymethylene	628;
						2', 3'-di-*O*-benzoyl m.p. 226–228°	615 (m.p.), (k), (t);
						5'-*O*-trityl,	

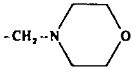
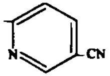
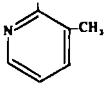
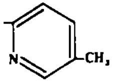
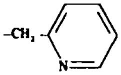
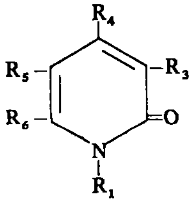
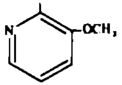
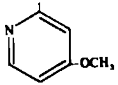
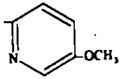
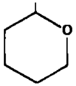
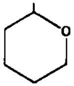
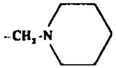
			amorphous	625 (f), (i), (u); 627 (t);
			2, 3, 5-tri-*O*-benzoyl m.p. 139–142°	601 (m.p.); 602 (m.p.);
			2, 3-di-*O*-benzoyl 5'-diphenyl phosphate, m.p. 118–119°	614 (m.p.), (i), (k); 615 (m.p.), (k), (t);
β-D-Ribopyranosyl		207–208°		601 (m.p.); 602 (m.p.);
			tri-*O*-benzoyl amorphous	601; 602;
β-D-Xylosyl		92–93°		626 (m.p.), (f), (k);
			triacetyl, m.p. 223–225°	626 (m.p.), (k);
$-CH_2CH_2ON{=}C(CH_3)_2$		b.p. 125°/0.3		573 (b.p.); 990 (b.p.);
			hydrochloride, m.p. 115–116°	573 (m.p.); 990 (m.p.);
		79°		501 (m.p.);
CH_3 **$-(CH_2)_2N(CH_3)_2$**	**t-C_4H_9**			485 (n);
			dihydrochloride, m.p. 83–85°	562 (m.p.);
$C_6H_2(NO_2)_3$-2, 4, 6		**206–208°**		**553 (m.p.), (i), (n);**
		**204–206°**		**271 (m.p.);**
C_6H_4Cl-*m*		**134–136°**		**565 (m.p.);**
C_6H_4Cl-*p*		**133°**		**24 (m.p.);**
C_6H_4Br-*m*		**145–147°**		**565 (m.p.);**
$C_6H_4NO_2$-*m*		**185–187°**		**564 (m.p.);**
C_6H_5		**124–128°**		**750 (m.p.); 907 (m);** **988 (m.p.), (m), (n);**
C_6H_4OH-*m*		**175–176°**		**565 (m.p.);**
$C_6H_4NH_2$-*m*		**183–185°**		**564 (m.p.);**
		**107–109°**		**361 (m.p.), (u);**
		**93–95°**		**361 (m.p.), (u);**
		**93°**		**562 (m.p.);**

TABLE XII-41. Alkyl and Aryl 2-Pyridones (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
					146–147°		271 (m.p.);
					106–107°		271 (m.p.);
					125–127°		271 (m.p.);
	CH				oil		574 (f);
		CH			oil		574 (f);
β-D-Galactosyl					204–205°		626 (m.p.), (f), (k);
						tetraacetyl, amorphous	626;
β-D-Glucopyranosyl					203–205°		603 (m.p.), (f); 620 (m.p.);
						tetraacetyl, m.p. 190°	603 (m.p.); 607 (n); 616 (m.p.); 620 (m.p.); 626 (m.p.), (k);
						0.5 H_2O, m.p. 66°	501 (m.p.), (i);

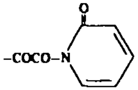
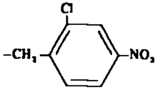
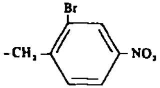
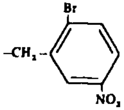
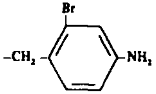
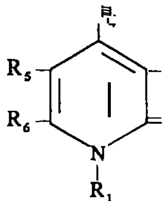
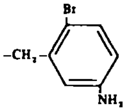
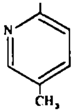
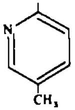
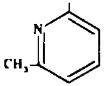
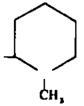
$-CH_2CH_2N(C_2H_5)_2$				mm		1015 (b.p.);
CH_3		$-(CH_2)_4NHCH_3$			dihydrochloride, m.p. 171°	691 (m.p.);
					picrate, m.p. 164-165°	691 (m.p.);
						1016 (m.p.);
						558 (m.p.);
						561 (m.p.);
						561 (m.p.);
$-CH_2C_6H_4$-F-*o*				76-78°		562 (m.p.);
$-CH_2C_6H_4$-Cl-*o*				72°		561 (m.p.), (u);
$-CH_2C_6H_4$-Br-*o*				105-106		1017 (m.p.);
$-CH_2C_6H_4$-Br-*p*				97-98°		561 (m.p.);
$-CH_2C_6H_4$-I-*o*				121-122		561 (m.p.), (u);
$-CH_2C_6H_4$-NO_2-*o*				135-136		564 (m.p.); 1018 (m.p.);
$-CH_2C_6H_4$-NO_2-*m*				114-115		564 (m.p.);
$-CH_2C_6H_4$-NO_2-*p*				147-149		564 (m.p.);
$-CH_2C_6H_5$						466 (i); 689 (i);
CH_3	C_6H_5			130-132		750 (m.p.), (m), (n);
C_6H_5			H	136-139		24 (m.p.); 442 (m.p.);
					hydrochloride, m.p. 201-204°	442 (m.p.);
$C_6H_4CH_3$-*o*						907 (m);
						561 (m.p.);

TABLE XII-41. Alkyl and Aryl 2-Pyridones (Continued)



R₁	i.	d	i.	R.	m.p.	D t	ɑt
					119-120°		561 (m.p.);
$-CH_2C_6H_4NH_2$-*o*					133-134°		564 (m.p.);
$-CH_2C_6H_4NH_2$-*m*					133-134°		564 (m.p.);
$-CH_2C_6H_4NH_2$-*p*					110-112°		564 (m.p.);
	B				110-111°		361 (m.p.), (i), (u);
			B		102 103		361 (m.p.), (i), (u);
				CH_3	202°		993 (m.p.);
CH_3					206-210°	6,6'-dimer	750 (m.p.), (m), (n);
β-D-Glucopyranosyl	B					tetraacetyl, amorphous	610 (i);
β-D-Glucosyl		H			hygroscopic powder		626 (f), (k);
						tetraacetyl, m.p. 163-165°	626 (m.p.), (k);
CH_3					95-96° b.p. 154°/0.8 mm		336 (b.p.), (m.p.), (k);

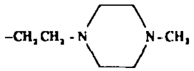
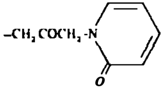
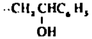
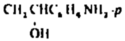
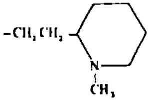
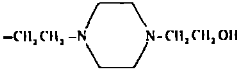
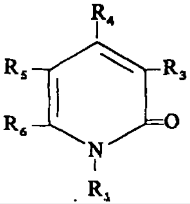
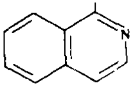
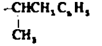
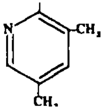
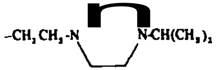
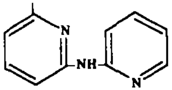
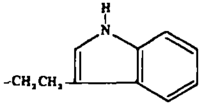
			dihydrochloride m.p. 217–219°	567 (m.p.);
CH_3	$-(CH_2)_4N(CH_3)_2$	b.p. 170°		691 (b.p.);
			dihydrochloride, m.p. 186–188°	691 (m.p.);
			dipicrate, m.p. 124–126°	691 (m.p.);
$-CH_2COC_6H_4Br$-*p*		168–170°		786 (m.p.); 787 (m.p.);
$-CH_2COC_6H_5$		156–158°		786 (m.p.); 787 (m.p.);
		223–225°		554 (m.p.);
			p-nitrophenylhydrazone, m.p. 245–248°	554 (m.p.);
 $-CH_2\underset{OH}{C}HC_6H_4NO_2$-*p*		190–191°		1019 (m.p.);
			β-acetyl, m.p. 172–174°	1019 (m.p.);
$-CH_2CH_2C_6H_5$		104–105°		338 (m.p.), (i), (n);
				341 (m.p.), (u);
 $-CH_2\underset{OH}{C}HC_6H_5$		118–128°		323 (m.p.); 324 (m.p.);
			hydrochloride, m.p. 156–158°	324 (m.p.);
$-CH_2C_6H_4OCH_3$-*p*		84–86°		762 (m.p.); 924 (m.p.);
$-CH_2CH_2NHC_6H_5$		108–109°		785 (m.p.), (i), (u);
			$0.5\ H_2O$ m.p. 109–110°	785 (m.p.);
$-CH_2CH_2NHC_6H_5$			*N'*-acetyl, m.p. 100–104°	785 (m.p.);
			N'-acetyl·HCl, m.p. 118–124°	785 (m.p.);
 $CH_2\underset{OH}{C}HC_6H_4NH_2$-*p*		185–186°		1019 (m.p.);
		46–47°		562 (m.p.);
			dihydrochloride, m.p. 208–211°	566 (m.p.); 1020 (m.p.);

TABLE XII-41. Alkyl and Aryl 2-Pyridones (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
					188–189°	 picrate, m.p. 149°	214 (m.p.); 1021 (m.p.); 214 (m.p.);
$CH_2C_6H_5$				$-CH_2CN$	92°		944 (m.p.);
$-CH_2COC_6H_4OCH_3$-*p*							787;
 $-\underset{CH_3}{CH}CH_2C_6H_5$					73°		337 (m.p.);
	CH_3		CH_3		104–105°		316 (m.p.), (i);
						dihydrochloride, m.p. 237–240°	566 (m.p.);
						dihydrochloride, m.p. 214–216°	567 (m.p.);
					159–160°	picrate m.p. 224–225°	271 (m.p.); 271 (m.p.);
					170–171°		680 (m.p.), (i), (u);
$-CH_2CH_2C_6H_5$			$-COCH_3$				354 (u);

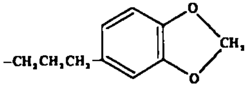
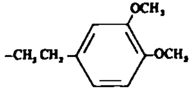
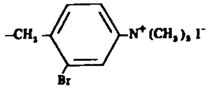
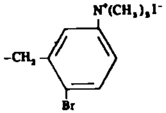
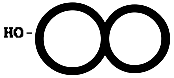
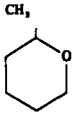
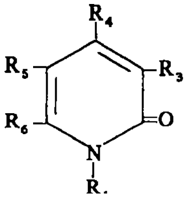
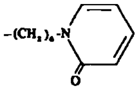
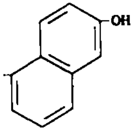
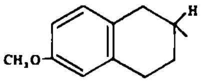
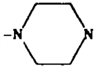
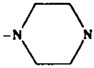
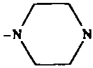
		102-103°		340 (m.p	
$-CH_2CH_2C_6H_5$	3	56-57°		349 (m.p	
			picrate m.p. 105-106°	349 (m.p	
$-(CH_2)_4OC_6H_5$		b.p. 180°/0.8 mm		588 (b.p.	
			picrate, m.p. 86-88°	588 (m.p	
		oily, m.p. 82-83° m.p. 67-68°		350 (m.p 338 (m.p	
			chloroplatinate, m.p. 100-103°	351 (m.p	
			picrate, m.p. 126-127°	350 (m.p	
$-CH_2\underset{\mid}{C}HCH_2OC_6H_4CH_3\text{-}o$ OH		81-83°		325 (m.	p.);
		175-176°		561 (m.	
		174-175°		561 (m.	
		254°		568 (m.	
	C_6H_5	128-130°		574 (m.	
$-(CH_2)_3OC_6H_4NO_2\text{-}p$		103°		1023 (n	

TABLE XII-41. Alkyl and Aryl 2-Pyridones (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
$-(CH_2)_6-$ 					94–95°		6 (m.p.);
2-Pyridyl			$-COC_6H_5$		168–169°		115 (m.p.);
$-CH_2CH_2-$ 					202–203°	 0.5 HBr, m.p. 187–188°	341 (m.p.), (u); 341 (m.p.);
CH_3				CH_3O- 	144–146°		568 (m.p.), (u);
β-D-Glucosyl		C_6H			286–289°	 tetraacetyl, m.p. 135°	604 (m.p.); 604 (m.p.);
$-CH_2CH_2-N$  $N-C_6H_4Cl$-*o*						hydrochloride, m.p. 236–239°	566 (m.p.); 1024 (m.p.);
$-CH_2CH_2-N$  $N-C_6H_4Cl$-*m*						hydrochloride, m.p. 240–243°	566 (m.p.); 1024 (m.p.);
$-CH_2CH_2-N$  $N-C_6H_4Cl$-*p*						hydrochloride, m.p. 209–218°	566 (m.p.); 1024 (m.p.);

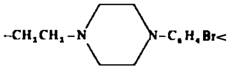
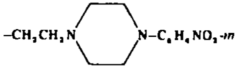
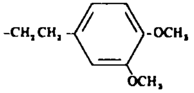
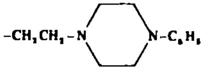
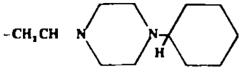
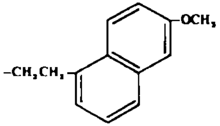
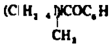
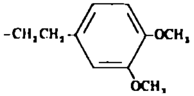
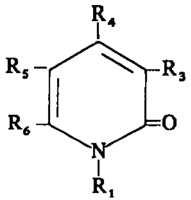
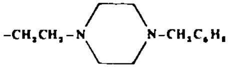
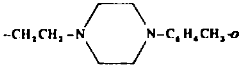
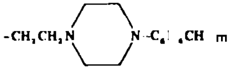
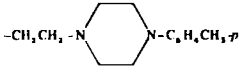
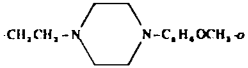
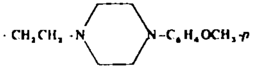
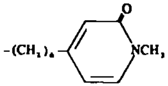
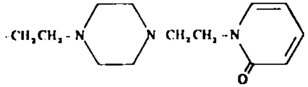
						hydrochloride, m.p. 241–244°	566 (m.p.);
						hydrochloride, m.p. 252–253°	567 (m.p.);
			C_2H		57–58° b.p. 220°/3.5 m		350 (b.p.), (m.p.), (i), (u);
						picrate, m.p. 99–100°	350 (m.p.);
						hydrochloride, m.p. 212–215°	988 (m.p.); 1024 (m.p.);
						dihydrochloride, m.p. 261–264°	566 (m.p.); 567 (m.p.); 1020 (m.p.);
CH_3	C_6H_5	C_6H_5			176°		242 (m.p.), (i), (n), (u);
CH_3		C_6H_5	C_6H		108°		242 (m.p.) (f), (i), (n), (u);
CH_3		C_6H_5		C_6H_5	91°		71 (m.p.); 941 (m.p.)
					102–103°		1025 (m.p.); 1 (m.p.);
					104–106°		341 (m.p.), (u);
$-CH_2CH_2-$ $_4Cl$ -m						hydrochloride, m.p. 227–229°	567 (m.p.);
CH_3			 $(CH_2)_4\underset{CH_3}{N}COC_6H$		112–113°		691 (m.p.);
		H	CH_3		72–76°		281 (m.p.);

TABLE XII-41. Alkyl and Aryl 2-Pyridones (Continued)



R1	R3	R4	R5	R6	m.p.	Derivative	Ref.
						dihydrochloride, m.p. 252–256°	988 (m.p.); 1024 (m.p.);
						hydrochloride, m.p. 262–266°	988 (m.p.); 1024 (m.p.);
						dihydrochloride, m.p. 193–201°	988 (m.p.); 1024 (m.p.);
						hydrochloride, m.p. 227–230°	988 (m.p.); 1024 (m.p.);
						hydrochloride, m.p. 220–222°	67 (m.p
						dihydrochloride, m.p. 210–212°	5 7 (m p
CH_3					141–142°		6 (m.p.);
						dihydrochloride, m.p. 272–275°	566 (m.p
$-CH_2COC_6H_4C_6H_5$-p					233–236°		787 (m.p.);
CH_3	$CH_2C_6H_5$			C_6H_5	71–73°		45 (m.p.), (i), (n), (u);
CH_3		$C_6H_4OCH_3$-p		C_6H_5	115°		941 (m.p.), (i), (u);

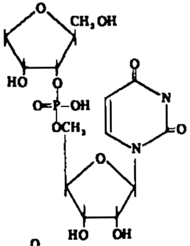
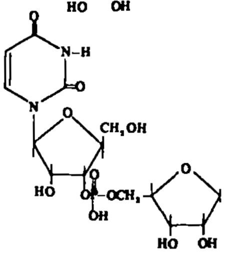
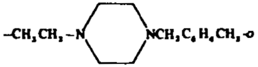
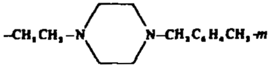
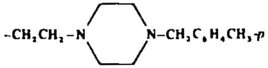
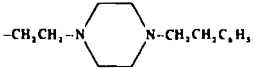
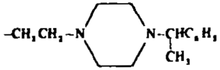
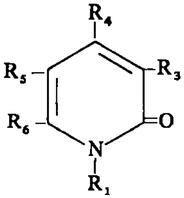
		627 (u);
		627 (u);
	dihydrochloride, m.p. 247–250°	988 (m.p.); 1024 (m.p.);
	dihydrochloride, m.p. 246–249°	*988* (m.p.); 1024 (m.p.):
	dihydrochloride, m.p. 256–259°	988 (m.p.); 1024 (m.p.);
	dihydrochloride m.p. 254–258°	*988* (m.p.); 1024 (m.p);
	dihydrochloride, m.p. 244–247°	566 (m.p.);

TABLE XII-41. Alkyl and Aryl 2-Pyridones (Continued)



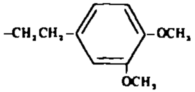
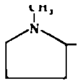
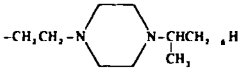
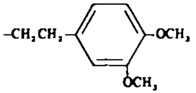
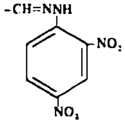
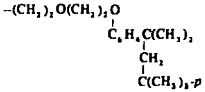
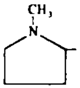
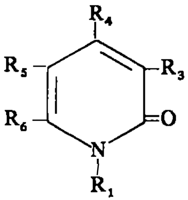
R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
					b.p. 208°/0.002 mm	 perchlorate, m.p. 199°	339 (b.p.); 339 (m.p.);
						dihydrochloride, m.p. 245–248°	566 (m.p.); 567 (m.p.);
n-C_4H_9		C_6H_5		C_6H_5	98–99°		1025 (m.p.), (u);
CH_3		C_6H_5	C_6H_5	C_6H_4Br-p	170°		122 (m.p.);
CH_3		C_6H_5	C_6H_5	C_6H_5	189°		**121 (m.p.), (i), (u);**
$-CH_2C_6H_5$		C_6H_5		C_6H_5	133–134°		1025 (m.p.), (u);
C_6H_5	$-CH_2C_6H_5$			C_6H_5			45 (i), (n), (u);
			C_2H_5		268–269°		333 (m.p.), (i);
CH_3		C_6H_5	C_6H_5	$C_6H_4CH_3$-p	158°		122 (m.p.);
 $-(CH_2)_2O(CH_2)_2O-C_6H_4C(CH_3)_2CH_2C(CH_3)_3$-$p$					68–69°		1014 (m.p.), (k);

TABLE XII-42. Alkyloxy, Aryloxy, and Hydroxy 2-Pyridones



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
					148-149°		466 (i); 995 (m.p.);
						thallium salt,	
						m.p. 191-192°	996 (m.p.);
						1-*O*-acetyl,	
						m.p. 93-95°	995 (m.p.), (u);
							996 (m.p.); 997 (m.p.), (i);
OH	OH				188-190°		3 (m.p.), (n);
OH			OH		220'		3 (m.p.), (n);
OH		CH_3			129-135°		374 (m.p.); 415 (m.p.);
OH				CH_3	143-145°		374 (m.p.); 944 (m.p.);
CH_3	OH				129-132°		3 (m.p.); 342 (m.p.), (i),
							(n), (t), (u);
							998 (m.p.), (t), (u);
						3-*O*-acetyl,	
						m p. 99-101°	998 (m.p.), (t), (u);
CH_3			OH		150-153'		342 (m.p.), (i), (n), (t), (u);
CH_3				OH	152-154°		455 (m.p.), (n), (u);
OCH_3					oil		423 (i); 466 (i);
OH			OH	CH_3	228-232°		999 (m.p.), (n);
OC_2H_5					b.p. 96°/1.1 mm		423 (u); 623 (b.p.);
OH	CH_3	CH_3			169-170'		415 (m.p.);
OH		CH_3	CH_3		195'		415 (m.p.);
CH_3		OH		CH_3	224-230°		94 (m.p.); 644 (m.p.);
						4-*O*-acetyl,	
						m.p. 144-146°	644 (m.p.), (i);
							645 (i), (u);
OCH_3				CH_3	33-34°		944 (m.p.);
CH_3		OCH_3			114-116'		849 (m.p.);
CH_3				OCH_3	52-54°		455 (m.p.), (n), (u);
						hydrate,	
						m.p. 78-80"	505 (m.p.), (n), (t);
OH	CH_3	CH_3		OH	157-158°		1000 (m.p.), (i);
OH			OH	C_2H_5	167-171"		1001 (m.p.), (i), (n), (u);
$-OCH_2CH=CH_2$					b.p. 91°/0.1 mm		423 (g), (i), (u);
							1002 (b.p.); 1003 (b.p.);
CH_3	CH_3	OH		CH_3	265°		158 (m.p.), (u);
							159 (m.p. (u);
CH_3	OCH_3	OH		CH_2OH		diacetyl,	
						m.p. 93-94'	160 (m.p.), (i), (u);
$-CH_2CH=CH_2$		OH		CH_3	160-163"		1004 (m.p.);

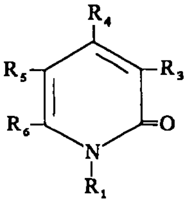
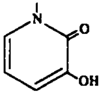
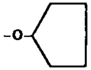
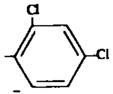
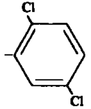


TABLE XII-42. Alkyloxy, Aryloxy, and Hydroxy 2-Pyridones (Continued)

R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	$-COCH_3$	OH		CH_3	133–135°		644 (m.p.), (i); 645 (i), (u); 1005 (m.p.);
						phenylhydrazone, m.p. 234–235°	1005 (m.p.);
CH_3		OH	$-COCH_3$	CH_3	280°		94 (m.p.), (u);
$-O(CH_2)_3CH_3$					b.p. 97°/0.1 mm		1003 (b.p.), (i), (u);
	OH				>300°		3 (m.p.);
					66–67°		1003 (m.p.); 1006 (m.p.), (c);
β-D-Ribofuranosyl		OH			228–229°		617 (m.p.), (k), (u);
CH_3	$-OP(OC_2H_5)_2$				62–63°		998 (m.p.), (t), (u);
$-(CH_2)_3N(CH_3)_2$	OH					phosphate, m.p. 213–214°	3 (m.p.);
C_6H_4Cl-*p*		OH		OH	177–179°		49 (m.p.);
$C_6H_4NO_2$-*p*		OH		OH	185°		49 (m.p.);
C_6H_5		OH		OH	198–200°		49 (m.p.);
β-D-Glucosyloxy					195–197°		623 (m.p.), (f); 1026 (m.p.), (k);
						tetraacetyl, m.p. 142–143°	623 (m.p.), (k);
CH_3		$-\overset{O}{\overset{\Vert}{P}}(OC_2H_5)_2$		CH_3	oil		1004;
		OH		CH_3		4-*O*-acetyl, m.p. 143–144°	149 (m.p.);
		OH		CH_3		4-*O*-acetyl, m.p. 135–137°	149 (m.p.);

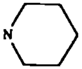
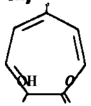
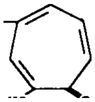
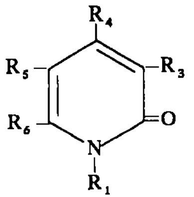
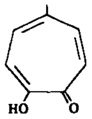
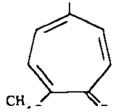
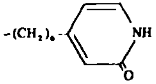
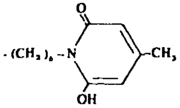
$-OCOC_6H_5$					140–144°		997 (m.p.), (i); 1010 (m.p.); 1027 (m.p.); 1028 (i);
C_6H_4Cl-*p*	OH			CH_3	147°		24 (m.p.);
C_6H_4Cl-*o*		OH		CH_3		4-*O*-acetyl, m.p. 140–141°	149 (m.p.);
C_6H_4Br-*o*		OH		CH_3		4-*O*-acetyl, m.p. 133–134°	149 (m.p.);
C_6H_5		OH		CH_3		4-*O*-acetyl, m.p. 148–149°	MJ (m.p.), (i), (u);
$-OCH_2C_6H_5$					77–79°		423 (m.p.); 466 (i); 1003 (m.p.);
$-CH_2N$ 	OCH_3					0.5 H_2O m.p. 69–71'	501 (m.p.);
CH_3	$-OCOC_6H_5$				136–138°		998 (m.p.), (t), (u);
		OH		CH_3	284–285°		109 (m.p.), (u);
4-Pyridyl	$-COCH_3$	OH		CH_3			1030 (i), (n);
$-OCH_2C_6H_5$		CH_3			78–80°		425 (m.p.), (i);
$-CH_2CH_2C_6H_5$		OH			202–204°		1008 (m.p.);
$-OCH_2CH_2C_6H_5$					b.p. 165°/0.25 mm		1003 (b.p.);
C_6H_5	C_2H_5	OH			306–309°		44 (m.p.), (u);
$-OCH_2C_6H_4OCH_3$-*p*					76–77°		1003 (m.p.);
OH		$C_6H_4OCH_3$-*p*		$-OCH_3$	194–196°		5 (m.p.), (i), (u);
β-D-Glucosyl		$-OC_2H_5$			amorphous	tetraacetyl m.p. 78–80°	604; 604 (m.p.);
C_6H_4Br-*p*	$-COCH_3$	OH		CH_3	262°		1030 (m.p.), (i), (n);
C_6H_5	$-COCH_3$	OH		CH_3	217–224°	phenyl hydrazone, m.p. 239–240°	110 (n); 645 (m.p.), (i), (u); 1005 (m.p.); 1030 (m.p.), (i), (n); 1005 (m.p.);
CH_3		OH	$-COCH_3$	C_6H_5	270		87 (m.p.);
C_6H_5		OH	$-COCH_3$	CH_3	253°		87 (m.p.);
$-CH_2CH_2C_6H_5$	$-OCH_3$				b.p. 140°/0.05 mm		1029 (b.p.);
$-OCH_3$		$C_6H_4OCH_3$-*p*		OCH_3	129–130°		5 (m.p.), (i), (u);
C_6H_4Cl-*p*	$-COCH_3$		$-COCH_3$	OH	238–240°		112 (m.p.);
C_6H_5	$-COCH_3$	OH	$-COCH_3$	OH	123–125°		49 (m.p.);
	$-COCH_3$	OH		CH_3	246'		110 (m.p.), (i), (n), (u); 1030 (i), (n);

TABLE XII-42. Alkyloxy, Aryloxy, and Hydroxy 2-Pyridones (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
	$-COCH_3$	OH		CH_3	250° 228		109 (m.p.), (i), (n), (u); 110 (m.p.), (i), (n), (u); 1030 (i), (u);
C_6H_5	CH_3	OH	$-CH_2CH_2CH_2-$		263°		93 (m.p.);
C_6H_5		OH	$-CH_2CH_2CH_2CH_2-$		325°		93 (m.p.); 214 (m.p.);
						4-*O*-acetyl m.p. 135°	214 (m.p.);
						4-*O*-benzoyl, m.p. 169°	214 (m.p.);
CH_3	OH	$-CH_2C_6H_5$	$-COCH_3$		185°		231 (m.p.);
$-CH_2C_6H_5$		OH	$-COCH_3$	CH_3	243°		87 (m.p.);
$C_6H_4CH_3$-*p*	$-COCH_3$	OH		CH_3	209-211°		1030 (m.p.), (i), (n);
$C_6H_4OCH_3$-*p*	$-COCH_3$	OH		CH_3	192-193°		1030 (m.p.), (i), (n);
C_3H_5	$-CH_2C_6H_5$	OH		CH_3	262°		163 (m.p.);
OH	$-CH_2C_6H_5$	OH	CH_3	C_2H_5	186°		96 (m.p.);
CH_3	$-COCH=CHC_6H_4Cl$-*p*	OH		CH_3	193-194°		1031 (m.p.), (u);
CH_3	$-COCH=CHC_6H_4NO_2$-*m*	OH		CH_3	235-236°		1031 (m.p.), (u);
CH_3	$-COCH=CHC_6H_4NO_2$-*p*	OH		CH_3	248-250°		1031 (m.p.), (u);
	$-COCH_3$	OH		CH_3	225°		109 (m.p.), (u);
CH_3	$-COCH=CHC_6H_5$	OH		CH_3	158-159°		1031 (m.p.), (u);
CH_3	$-COCH=CHC_6H_4OH$-*p*	OH		CH_3	262-263°		1031 (m.p.), (u);

C_6H_5		OH	$-CH_2CH_2CH_2CH_2CH_2-$		276"	214 (m.p.);
C_6H_5	CH_3	OH	$-CH_2CH_2CH_2CH_2-$		274"	93 (m.p.); 214 (m p.);
C_6H_5		OCH_3	$-CH_2CH_2CH_2CH_2-$		198"	214 (m p);
C_6H_5	C_2H_5	OH	$-CH_2CH_2CH_2-$		273'	93 (m.p.);
$-OCH_2C_6H_5$	CH_3	OH	CH_3	C_6H_5	191°	96 (m.p.);
OH					205–207"	6 (m.p.);
C_6H_5		OH		C_6H_5	308°	92 (m.p.);
OH		C_6H_5		C_6H_5	162°	941 (m p), (i), (u);
C_6H_5		OH	$-CH_2CH_2CH_2CH_2CH_2CH_2-$		287"	214 (m.p.);
C_6H_5	CH_3	OH	$-CH_2CH_2CH_2CH_2CH_2-$		277"	93 (m p.);
C_6H_5	C_2H_5	OH	$-CH_2CH_2CH_2CH_2-$		282'	89 (m p.); 93 (m.p.); 214 (m.p.);
C_6H_5	isoC_3H_7	OH	$-CH_2CH_2CH_2-$		272'	93 (m p.);
$C_6H_4CH_3$-*o*	CH_3	OH	$-CH_2CH_2CH_2CH_2-$		236"	93 (m.p.);
C_6H_5		OH	$-CO(CH_2)_3CH_3$	CH_3	210"	1032 (m.p.);
OH		C_6H_5	$-OCH_3$	C_6H_5	211°	120 (m.p.); 121 (m.p.), (i);
CH_3	$-COCH{=}CHC_6H_4N(CH_3)_2$-*p*	OH		CH_3	236–237°	1031 (m.p.), (u);
C_6H_5	CH_3	OH	$-CH_2CH_2CH_2CH_2CH_2CH_2$		281'	93 (m p.);
C_6H_5	C_2H_5	OH	$-CH_2CH_2CH_2CH_2CH_2-$		274"	93 (m.p.);
C_6H_5	isoC_3H_7	OH	$-CH_2CH_2CH_2CH_2-$		280"	93 (m.p I;
$C_6H_4CH_3$-*o*	C_2H_5	OH	$-CH_2CH_2CH_2CH_2-$		240'	93 (m.p.);
C_6H_5		OH	$-CO(CH_2)_4CH_3$	CH_3	193'	1032 (m.p.);
		CH_3		OH	180–1820	6 (m.p.);
C_6H_5		OH	$-COCH_3$	C_6H_4Cl-*p*	299'	1032 (m.p.);
C_6H_5		OH	$-COCH_3$	C_6H_5	299–300°	87 (m.p.); 90 (m.p.);
$CH_2C_6H_5$	$-OCH_2C_6H_5$				115–116°	596 (m.p.), (i);
$-CH_2CH_2C_6H_5$	3 (or 5)-Phenoxy				121–123°	1011 (m.p.), (z);
OH		C_6H_5	OCH_3	$C_6H_4CH_3$-*p*	195–196'	121 (m.p.);
C_6H_5	C_2H_5	OH	$-CH_2CH_2CH_2CH_2CH_2CH_2-$		264"	93 (m.p.);
C_6H_5	*n*-C_4H_9	OH	$-CH_2CH_2CH_2CH_2-$		245°	93 (m.p.);
$C_6H_4CH_3$-*o*	isoC_3H_7	OH	$-CH_2CH_2CH_2CH_2-$		230'	93 (m.p.);
C_6H_5		OH	$-CO(CH_2)_5CH_3$	CH_3	176"	1032 (m.p.);
CH_3	OH	$-CH_2C_6H_5$	$-COC_6H_5$		167–168"	231 (m.p.);
C_6H_5		OH	$COCH_3$	$C_6H_4CH_3$-*p*	310'	1032 (m.p.);
C_6H_5	isoC_3H_7	OH		C_6H_5	325"	92 (m.p.);
$OCH_2C_6H_5$		$C_6H_4OCH_3$-*p*		OCH_3	142–143°	5 (m.p.), (i), (u);
$C_6H_4CH_3$-*o*	*n*-C_4H_9	OH	$-CH_2CH_2CH_2CH_2-$		213"	93 (m.p.);
C_6H_5	$-COCH{=}CHC_6H_4Cl$-*p*	OH		CH_3	219–220°	1031 (m.p.), (u);
C_6H_5	$-COCH{=}CHC_6H_5$	OH		CH_3	211–213°	1031 (m.p.), (u);
C_6H_5	$-COCH{=}CHC_6H_4OH$-*p*	OH		CH_3	271–272°	1031 (m.p.), (u);
C_6H_5	$N_2C_6H_4NO_2$-*p*	OH	$-CH_2CH_2CH_2CH_2-$		206°	214 (m.p.);

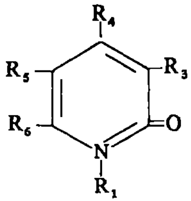


TABLE XII- 2. Alkyloxy, Aryloxy, and Hydroxy 2-Pyridones (Continu d)

R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref
C_6H_5	C_6H_5	OH	$-CH_2CH_2CH_2CH_2-$		243°		93 (m.p.);
C_6H_5	NC. _ H.	OH	$-CH_2CH_2CH_2CH_2-$		200°		214 (m.p.);
C_6H_5	$-CH_2C_6H_5$	OH	$-COCH_3$	CH_3	246–247°		90 (m.p.);
$C_6H_4CH_3$-*p*	isoC_3H_7	OH		C_6H_5	360°		92 (m.p.);
C_6H_5	$-CH_2C_6H_5$	OH	$-CH_2CH_2CH_2CH_2-$		260°		93 (m.p.); 214 (m.p.);
C_6H_5	C_6H_5	OH	$-CH_2CH_2CH_2CH_2CH_2$		264'		93 (m.p.);
C_6H_5	$-CH_2C_6H_5$	OH		*s*-C_4H_9	279–281°		92 (m.p.);
$C_6H_4CH_3$-*p*	*n*-C_4H_9	OH		C_6H_5	295–297°		92 (m.p.);
$-OCH_2C_6H_5$	$-CH_2C_6H_5$	OH	CH_3	C_2H_5	168°		96 (m.p.);
OH		C_6H_5	C_6H_5	C_6H_4Br-*p*	216°		122 (m.p.), (i);
OH		C_6H_5	C_6H_5	C_6H_5	232–233°		121 (m.p.), (i);
OH		C_6H_5	OC_6H_5	C_6H_5	224–225°		121 (m.p.), (i);
CH_3	$-COCH{=}CHC_6H_5$	OH		$-CH{=}CHC_6H_5$	199–201°		1031 (m.p.), (u);
C_6H_5	$-COCH{=}CHC_6H_4N(CH_3)_2$-*p*	OH		CH_3	272–27Y		1031 (m.p.), (u);
C_6H_5	C_6H_5	OH	$-CH_2CH_2CH_2CH_2CH_2CH_2-$		240"		93 (m.p.);
C_6H_5	$-CH_2C_6H_5$	OH	$-CH_2CH_2CH_2CH_2CH_2-$		269"		93 (m.p.);
$C_6H_4CH_3$-*o*	$-CH_2C_6H_5$	OH	$-CH_2CH_2CH_2CH_2-$		233'		93 (m p.);
CH_3		C_6H_5	$-OC_6H_4Cl$-*p*	C_6H_5	200°		121 (m.p.);
CH_3		C_6H_5	$-OC_6H_4Br$-*p*	C_6H_5	209°		121 (m.p.);
C_6H_5	$-CH_2C_6H_5$	OH		C_6H_5	275–287°		92 (m.p.); 214 (m.p.);
						4-O-acetyl, m.p. [illegible]–154°	92 (m.p);
$-OCH_3$		C_6H_5	C_6H_5	C_6H_5	163°		122 (m.p.), (i);
CH_3		C_6H_5	$-OC_6H_5$	C_6H_5	167°		121 (m.p.), (i), (u);
$-OCH_3$		C_6H_5	$-OC_6H_5$	C_6H_5	162'		122 (m.p.), (i);
C_6H_5	$-CH_2C_6H_5$	OH	$-CH_2CH_2CH_2CH_2CH_2CH_2$		282°		93 (m.p.); 214 (m.p.);
C_6H_5	$-CH_2C_6H_5$	OH	CH_3	C_6H_5	228–230°		92 (m.p.);
						acetate, m.p. 157–159'	92 (m.p.);
CH_3		C_6H_5	$-OC_6H_4CH_3$-*p*	C_6H_5	180°		121 (m.p.);
$C_6H_4CH_3$-*p*	$-CH_2C_6H_5$	OH		C_6H_5	299–300°		92 (m.p);
						acetate, m.p. 147–149°	92 (m.p.);
C_6H_5	OH	$-CH_2C_6H_5$	$-COC_6H_5$	CH_3	232–235°		231 (m.p.);
C_6H_5	$-CH_2C_6H_5$	OH	C_2H_5	C_6H_5	283–285°		92 (m.p.);
C_6H_5		OH	$-CH_2C_6H_5$	$-CH_2CH_2C_6H_5$	220'		1033 (m.p.), (i);
$-CH_2C_6H_5$	OH	$-CH_2C_6H_5$	$-COC_6H_5$	CH_3	185'		231 (m.p.);
$-OCH_2C_6H_5$		C_6H_5	C_6H_5	C_6H_5	174–175°		121 (m p.);

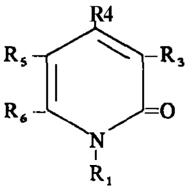
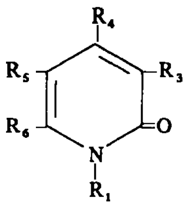
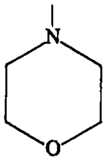
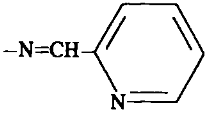
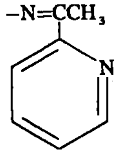


TABLE XII-43. Amino 2-Pyridones

R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
NH_2						$CoCl_2 \cdot 5H_2O$ complex $Co(ClO_4)_2 \cdot H_2O$ complex $FeCl_2$ complex $Fe(ClO_4)_2 \cdot H_2O$	805 (i), (q); 805 (i), (q); 805 (i), (q); 805 (i), (q);
OH		NH_2				1,4-diacetyl, m.p. 215-217°	1007 (m.p.);
NH_2	OH				161-163"		3 (m.p.);
$-NHCONH_2$	OH				233-235"		3 (m.p.);
CH_3	NH_2					picrate, m.p. 204" *N*'-acetyl, m.p. 165-166"	556 (m.p.); 556 (m.p.);
CH_3				NH_2	163-165"		494 (m.p.), (i), (u);
CH_3		NH_2		CH_3	257-258"		306 (m.p.);
$-N(CH_3)_2$	OH				81-83"	 acetate, m.p. 48-49° benzoate, m.p. 137-138°	3 (m.p.); 3 (m.p.); 3 (m.p.);
CH_3	NH_2	NH_2		CH_3	233"		86 (m.p.);

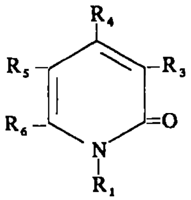
TABLE XII-43. Amino 2-Pyridones (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
	OX				177–179°		3 (m.p.);
						$Co(ClO_4)_2$ complex $Cu(ClO_4)_2$ complex $Fe(ClO_4)_2$ complex $Ni(ClO_4)_2$ complex H_2O $Zn(ClO_4)_2$ complex	305 (q); 305 (i), (q); 305 (i), (q); 305 (q); 805 (i), (q);
CH_3	NH_2	$-NHC_4H_9$		$\sqsubset X_3$		hydrochloride m.p. 256–257°	 36 m.p.);
						$Co(ClO_4)_2$ complex $Fe(ClO_4)_2$ complex $Ni(ClO_4)_2$ complex	305 (i), (q); 305 (i), (q); 305 (q);

$-CH_2CH_2C_6H_5$	NH_2					N'-acetyl·HCl, m.p. 92–93"	332 (m.p.);
$-CH_2CH$, C, H,		NH_2				hydrochloride, m.p. 166–169"	1008 (m.p.);
$-CH_2CH_2C_6H_5$			NH_2			$HCl{\cdot}H_2O$ m.p. 203–205°	1008 (m.p.);
CH_3		$-NHNHC_6H_5$		CH_3	271"		306 (m.p.);
NH_2		C_6H_5		C_6H_5	166"		941 (m.p.), (i), (u);
						diacetate, m.p. 120°	941 (m.p.);
CH_3	CH_3	$-N(C_2H_5)_2$	C_6H_5		96"		102 (m.p.), (i), (u);
NH_2		C_6H_5	$-OCH_3$	C_6H_5	186"		120 (m.p.); 121 (i);
						N'diacetyl, m.p. 128°	121 (m.p.);
NH_2		$C_6H_4OCH_3$-*p*		C_6H_5	163"		941 (m.p.) (i);
NH,		C_6H_5	$-OCH_3$	$C_6H_4CH_3$-*p*	174"		120 (m.p.);
NH,		C_6H_5	$-OCH_3$	$C_6H_4OCH_3$-*p*	148"		120 (m.p.);
$C_6H_4OCH_3$-*m*		OH		NHC, H, OCH, -*m*	258"		161 (m.p.);
$-CH_2CH$, C_6H_5			$-NH\underset{\underset{O}{\|}}{C}OCH_2C_6H_5$		134"		1008 (m.p.);
NH_2		C_6H_5	C_6H_5	C, H_4Br-*p*	197°		122 (m.p.), (i);
						N'-acetyl, m.p. 252"	122 (m.p.), (i);
						N'diacetyl, m.p. 195°	122 (m.p.), (i);
NH_2		C_6H_5	$-OC_6H_4Cl$-*p*	C_6H_5	203"		121 (m.p.);
						N'diacetyl, m.p. 159°	121 (m.p.);
NH_2		C_6H_5	$-OC_6H_4Br$-*p*	C_6H_5	222"		121 (m.p.);
						N'diacetyl, m.p. 160°	121 (m.p.);

TABLE XII-43. Amino 2-Pyridones (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
NH_2		C_6H_5	C_6H_5	C_6H_5	199"		**121 (m.p.), (i), (u);**
						N-acetyl, m.p. 246"	**121 (m.p.);**
						N'diacetyl, m.p. 167	121 (m.p.);
						$CuCl_2$ complex, m.p. 246"	**802 (m.p.), (i);**
NH_2		C_6H_5	OC_6H_5	C_6H_5	181"		**121 (m.p.), (i),(u);**
						N'-acetyl, m.p. 234"	121 (m.p.);
						N'-diacetyl, m.p. 158°	121 (m.p.);
$-N{=}CHC_6H_5$		C_6H_5		C_6H_5	179"		941 (m.p.);
NH_2		C_6H_5	C_6H_5	$C_6H_4CH_3$-*p*	189°		122 (m.p.), (i);
$-NHCH_3$		C_6H_5	OC_6H_5	C_6H_5		*N'*-acetyl, m.p. 173"	121 (m.p.);
NH_2		C_6H_5	C_6H_5	$C_6H_4OCH_3$-*p*	157–158"		802 (m.p.);
						$CuCl_2$ complex, m.p. 231–232"	802 (m.p.), (i);
NH_2		C_6H_5	$-OC_6H_4CH_3$-*p*	C_6H_5	202"		121 (m.p.);
						N'-acetyl, m.p. 258"	121 (m.p.);

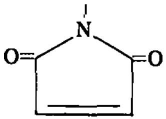
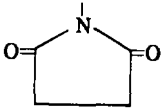
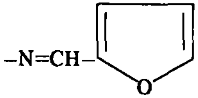
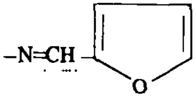
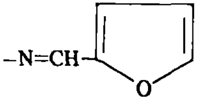
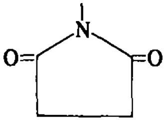
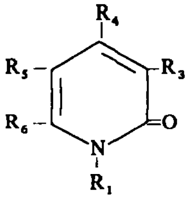
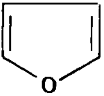
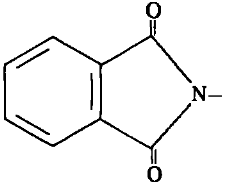
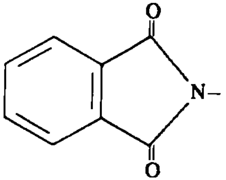
					N'diacetyl, m.p. 164"	121 (m.p.);
−N=CHC$_6$H$_5$	C$_6$H$_5$	−OCH$_3$	C$_6$H$_5$	164"		121 (m.p.);
−N=CHC$_6$H$_5$	C$_6$H$_4$OCH$_3$-*p*		C$_6$H$_5$	168"		941 (m.p.), (i);
NHCH,	C$_6$H$_5$	OC$_6$H$_4$CH$_3$-*p*	C$_6$H$_5$		*N'*-acetyl, m.p. 176"	121 (m.p.);
NHCOC$_2$H,	C$_6$H$_5$	C$_6$H$_5$	C$_6$H$_5$	217–218°		802 (m.p.), (i);
	C$_6$H$_5$	C$_6$H$_5$	C$_6$H$_5$	230"		802 (m.p.), (i);
	C$_6$H$_5$	C$_6$H$_5$	C$_6$H$_5$	247"		802 (m.p.), (i);
	C$_6$H$_5$	OC$_6$H$_4$Cl-*p*	C$_6$H$_5$	216"		121 (m.p.);
	C$_6$H$_5$	C$_6$H$_5$	C$_6$H$_5$	183"		121 (m.p.);
	C$_6$H$_5$	OC$_6$H$_5$	C$_6$H$_5$	195–196"		121 (m.p.);
	C$_6$H$_5$	C$_6$H$_5$	C$_6$H$_4$OCH$_3$-*p*	196–197°		802 (m.p.), (i);

TABLE XII-43. Amino 2-Pyridones (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
–N=CH– 		C_6H_5	$OC_6H_4CH_3$-*p*	C_6H_5	220"		121 (m.p.);
$N(COC_2H_5)_2$		C_6H_5	C_6H_5	C_6H_5	185"		802 (m.p.);
–N=CHC_6H_5		C_6H_5	C_6H_5	C_6 H, Br-p	188°		122 (m.p.);
Salicylideneiminato		C_6H_5	C_6H_5	C_6H_5	273°	biscopper (II) complex	802 (m.p.);
–N=CHC_6H_4NO, -*o*		C_6H_5	C_6H_5	C_6H_5	193"		802 (m.p.);
–N=$CHC_6H_4NO_2$-*m*		C_6H_5	C_6H_5	C_6H_5	190"		802 (m.p.), (i);
–N=$CHC_6H_4NO_2$-*p*		C_6H_5	C_6H_5	C_6H_5	210°		802 (m.p.), (i);
–N=CHC_6H_5		C_6H_5	C_6H_5	C_6H_5	158"		121 (m.p.); 802 (m.p.), (i);
–N=CHC_6H_5		C_6H_5	OC_6H_5	C_6H_5	236°		121 (m.p.);
–N=CHC_6 H, OH-*o*		C_6H_5	C_6H_5	C_6H_5	128"		802 (m.p.), (i);
–N=CHC_6H_4OH-*m*		C_6H_5	C_6H_5	C_6H_5	262"		802 (m.p.), (i);
–N=CHC_6H_4OH-*p*		C_6H_5	C_6H_5	C_6H_5	267°		802 (m.p.), (i);
–$NHOCH_2C_6H_5$		C_6H_5	C_6H_5	C_6H_5	252"		121 (m.p.);
–$NHOCH_2$ C, H_5		C_6H_5	OC_6H_5	C_6H_5	242"		121 (m.p.);

	C_6H_5	C_6H_5	C_6H_5	**255–256°**		**802** (m.p.);
Salicylideneiminato	C_6H_5	C_6H_5	$C_6H_4OCH_3$-*p*	**247°**	biscopper (II) complex	**802** (m.p.), **(i);**
$-N{=}CHC_6H_5$	C_6H_5	C_6H_5	$C_6H_4OCH_3$-*p*	**202"**		**802** (m.p.), (i);
$-N{=}CHC_6H_5$	C_6H_5	$OC_6H_4CH_3$-*p*	C_6H_5	**246"**		**121** (m.p.);
$-N{=}CHC_6H_4OCH_3$-*p*	C_6H_5	C_6H_5	C_6H_5	**209"**		**802** (m.p.), (i);
$-N{=}CHC_6H$, OH-*o*	C_6H_5	C_6H_5	$C_6H_4OCH_3$-*p*	**230"**		**802** (m.p.), (i);
$-N{=}CHC_6H$, OH-*m*	C_6H_5	C_6H_5	$C_6H_4OCH_3$-*p*	**259"**		**802** (m.p.), (i);
$-N{=}CHC_6H_4OH$-*p*	C_6H_5	C_6H_5	$C_6H_4OCH_3$-*p*	**215"**		**802** (m.p.), **(i);**
$-NHOCH_2C_6H_5$	C_6H_5	$OC_6H_4CH_3$-*p*	C_6H_5	150"		**121** (m.p.);
	C_6H_5	C_6H_5	$C_6H_4OCH_3$-*p*	**294"**		**802** (m.p.), (i);
$-N{=}CHC_6H_4N(CH_3)_2$-*p*	C_6H_5	C_6H_5	C_6H_5	**242"**		**802** (m.p.), **(i);**
$-N(OCH_2C_6H_5)_2$	C_6H_5	C_6H_5	C_6H_5	**212"**		**121** (m.p.);
$-N(OCH_2C_6H_5)_2$	C_6H_5	OC_6H_5	C_6H_5	**219"**		**121** (m.p.);
$-N(OCH_2C_6H_5)_2$	C_6H_5	$OC_6H_4CH_3$-*p*	C_6H_5	**198"**		**121** (m.p.);

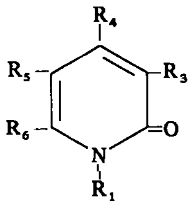


TABLE XII-44. 2-Pyridone Carboxylic Acids and Derivatives

R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	COOH					amide. m.p. **216–217"**	**1009 (m.p.);**
						cyanomethyl, **m.p. 106-107°**	**1009 (m.p.);**
CH_3		COOH				methyl ester, m.p. 177-178°	**861 (m.p.), (i);**
CH_3			COOH		238-243°		**·101 (m.p.), (u);** **699 (m.p.); 855 (m.p.);**
						oxime, m.p. **186-187°**	**998 (m.p.), (t), (u);**
						amide, m.p. 209-210°	**855 (m.p.);**
						ethyl ester, **m.p. 65-67"**	**729 (m.p.), (i), (n);**
						N'-benzamido-, m.p. 133-135°	**1009 (m.p.);**
						methyl ester, m.p. 139"	**101 (m.p.); 855 (m.p.);** 1009 (i);
						tropyl ester methiodide, m.p. 330–334	998 **(m.p.), (t),** (u);
						1-methyl-2-oxo- 3-pyridyl. m.p. 249-251°	998 **(m.p.),** (t), **(u);**
CH_2COOH	OH				217–219°		3 (m.p.);
CH_3	COOH	OH		OH		methyl ester. **m.p. 202"**	169 **(m.p.),** (i), (u);
						ethyl ester, m.p. 170'	171 **(m.p.),** (i), (u);
						morpholine salt, m.p. **144'**	171 (m.p.);

$\mathrm{OC(O)NHCH_3}$					149–151°		1010(m.p.);
$\mathrm{CH_3}$	COOH		$\mathrm{NH_2}$			ethyl ester·HCl m.p. 187° ethyl ester·picrate, m.p. 189°	82 (m.p.); 82 (m.p.);
OH				$\mathrm{CH_2}\underset{\mathrm{NOH}}{\underset{\Vert}{\mathrm{C}}}\mathrm{COOH}$	178°	 ethyl ester. m.p. 190–191°	425 (m.p.), (i); 425 (m.p.), (i);
$\mathrm{C_2H_5}$			COOH			ethyl ester. b.p. 130°/0.7 mm	549 (b.p.);
$\mathrm{CH_3}$				$\mathrm{CH_2COOH}$		ethyl ester. m.p. 100–101°	944 (m.p.);
$\mathrm{CH_3}$		COOH		$\mathrm{OCH_3}$		methyl ester. m.p. 83–84°	507 (m.p.), (t);
$\mathrm{CH_2CH_3}$	COOH	OH		OH		methyl eater. m.p. 184° morpholinium salt, m.p. 142° ethyl ester, m.p. 185°	168 (m.p.), (i), (u); 168 (m.p.); 168 (m.p.), (i), (u);
$\mathrm{CH_3}$	$\mathrm{OCONHCH_3}$				135–137°		998 (m.p.), (t), (u);
OH				$\mathrm{CH_2}\underset{\mathrm{NH_2}}{\underset{\vert}{\mathrm{C}}}\mathrm{HCOOH}$		hydrochloride, m.p. 208–210°	425 (m.p.), (i);
$\mathrm{CH_3}$	$\mathrm{NH_2}$	$\mathrm{NH_2}$	COOH	$\mathrm{CH_3}$		ethyl ester, m.p. 163°	86 (m.p.);
$-\underset{\mathrm{COOH}}{\underset{\vert}{\mathrm{C}}}{=}\mathrm{CHCOOH}$						dimethyl ester, m.p. 103–104°	78 (m.p.), (i), (m), (n), (u);
$\mathrm{OCH_3}$				$\mathrm{CH_2COCOOH}$		ethyl ester. m.p. 153°	944 (m.p.);
$\mathrm{CH_2COOH}$	$\mathrm{OCH_2COOH}$					dimethyl ester. m.p. 102–103°	596 (m.p.), (i);
iso$\mathrm{C_3H_7}$			COOH			ethyl ester, m.p. 91–92°	549 (m.p.);
$\mathrm{CH_3}$	$\mathrm{OCON(CH_3)_2}$				143–144°		998 (m.p.), (t), (u);
$\mathrm{CH_3}$	$\mathrm{OCONHC_2H_5}$				142–144°		998 (m.p.), (t), (u);
$-\underset{\mathrm{COOH}}{\underset{\vert}{\mathrm{C}}}{=}\mathrm{CHCOOH}$				$\mathrm{CH_3}$		dimethyl ester, m.p. 120–121°	748 (m.p.), (i), (m), (n), (u);
$n\text{-}\mathrm{C_4H_9}$	COOH	OH		OH		methyl ester, m.p. 182°	168 (m.p.), (i), (u);

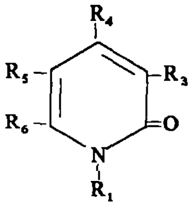
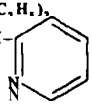
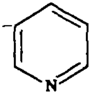


TABLE XII-44. 2-Pyridone Carboxylic Acids and Derivatives (Continued)

R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
isoC$_4$H$_9$	COOH	on		OH		ethyl ester. m.p. 160°	168 (m.p.), (i);
						methyl ester. m.p. 158'	168 (m.p.), (i), (u);
						ethyl ester. m.p. 170"	168 (m.p.), (i), (u);
CH_3		CH_3	$-CONHCH_3$	CH_3	198–199°		107 (m.p.);
2-Pyridyl			COOH		277–279°		115 (m.p.);
						methiodide, m.p. 266–267°	115 (m.p.);
						amide	115;
						methyl cater. m.p. 163–165'	1IS (m.p.);
						1-pyrrolidine amide, m.p. 183–185°	115 (m.p.);
						1-morpholine amide, m.p. 199–200°	115 (m.p.);
2-Pyridyl			$-CON(C_2H_5)_2$		149–150°		·115 (m.p.);
2-Pyridyl			–CONH– 		281–282°		115 (m.p.);
						dimethiodide, m.p. 233–235°	115 (m.p.);
2-Pyridyl			–CONH– 		266–268°		115 (m.p.);
						methiodide, m.p. 284–285°	115 (m.p.);

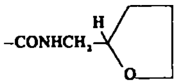
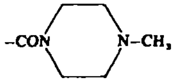
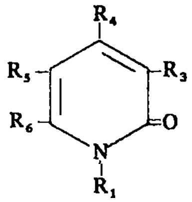
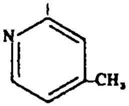
2-Pyridyl			 $-CONHCH_2-$		193–194°		115 (m.p.);
2-Pyridyl			 $-CON\ \ N-CH_3$		152–153'		115 (m.p.);
2-Pyridyl			$CONH(CH_2)_2N(C_2H_5)_2$		141–143°		**115 (m.p.);**
$-C=CHCOOH$ COOH			CH_3	CH_3	145–147'		**749 (m.p.);**
CH_3	$-COCH_3$	CH_3	COOH	CH_3		**ethyl ester, m.p. 91–92°**	**476 (m.p.), (n);**
β-D-Ribosyl			$CONH_2$		**219–220°**		**613 (m.p.), (t);**
						2',3'-*O*-isopropylidene m.p. 159–161"	**613 (m.p.);**
CH_3	$-OCON(C_2H_5)_2$				**80–81°**		**998 (m.p.), (t), (u);**
C_6H_4Cl-*o*	COOH	OH		OH		methyl ester, m.p. 184°	**169 (m.p.), (i), (u);**
C_6H_4Cl-*m*	COOH	OH		OH		methyl ester, m.p. 197'	**168 (m.p.), (i), (u);**
						morpholinium salt, m.p. 183°	**168 (m.p.);**
C_6H_4Cl-*p*	COOH	OH		OH		methyl ester. m.p. 170°	**168 (m.p.), (i), (u);**
C_6H_4Cl-*o*	COOH	OH		OH		ethyl ester. m.p. 192°	**169 (m.p.), (i), (u);**
C_6H_4Cl-*m*	COOH	OH		OH		ethyl ester. m.p. 188'	**168 (m.p.), (i), (u);**
C_6H_4Cl-*p*	COOH	OH		OH		ethyl ester, m.p. 178'	**168 (m.p.), (i), (u);**
C_6H_4Br-*m*	COOH	OH		OH		methyl ester, m.p. 188'	**168 (m.p.), (i), (u);**
C_6H_4Br-*p*	COOH	OH		OH		methyl ester, m.p. 196°	**168 (m.p.);**
C_6H_4Br-*m*	COOH	OH		OH		ethyl ester. m.p. 192"	**168 (m.p.), (i), (u);**
C_6H_4Br-p	COOH	**OH**		**OH**		ethyl ester. m.p. 203'	**168 (m.p.);**
$C_6H_4NO_2$	COOH	**OH**		OH		ethyl ester, **m.p. 190°**	**169 (m.p.), (i), (u);**

TABLE XII-44. 2-Pyridone Carboxylic Acids and Derivatives (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
C_6H_5	COOH	OH		OH		methyl ester, m.p. 210° or m.p. 176° morpholine salt, m.p. 196"	168 (m.p.); 169 (m.p.), (i), (u); 171 (m.p.); 171 (m.p.);
C_6H_5	COOH	OH		OH		ethyl ester, m.p. 204–205° or m.p. 163' morpholine salt, m.p. 182° carboxanilide, m.p. 234'	169 (m.p.), (i), (u); 171 (m.p.), (i), (u); 171 (m.p.), (u); 171 (m.p.), (u);
C_7H_4OH-*m*	COOH	OH		OH		methyl ester. m.p. 193'	169 (m.p.), (i), (u);
			COOH		259–261"		115 (m.p.);
β-D-Glucosyl	COOH					methyl ester, m.p. 212–213" methyl ester. amorphous	115 (m.p.); 604;
β-D-Glucosyl	$COOCH_3$					tetraacetyl, m.p. 75–76'	604 (m.p.);
β-D-Glucosyl		COOH				methyl ester, amorphous	604;
β-D-Glucosyl		$COOCH_3$				tetraacetyl, m.p. 186–189°	604(m.p.);
β-D-Glucosyl			$CONH_2$		220–221°		613 (m.p.), (t);

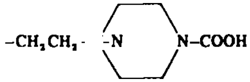
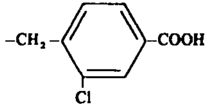
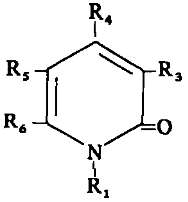
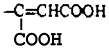
						tetraacetyl, m.p. 216–217°	613 (m.p.);
						ethyl ester·HCl m.p. 197-199°	567 (m.p.); 1020 (m.p.);
C_2H_5		CH_3	$CONHC_2H_5$	CH_3	145–147°		107 (m.p.);
C_6H_5	COOH	OH	COOH	OH		dimethyl ester, m.p. 232°	171 (m.p.), (u);
						morpholine salt, m.p. 192°	171 (m.p.);
						diethyl ester, m.p. 214°	171 (m.p.), (i), (n), (u);
					265–266°		82 (m.p.)
$C_6H_4CH_3$-*m*	COOH	Cl	Br	OH		methyl ester, m.p. 118°	169 (m.p.);
[illegible]	COOH				130°		21 (m.p.);
						ethyl ester, oil	21 (u);
$CH_2C_6H_5$			COOH			ethyl ester, m.p. 60–61°	549 (m.p.);
$CH_2C_6H_4COOH$-*p*					206–207°		558 (m.p.);
C_6H_5		OH	COOH	CH_3		ethyl ester, m.p. 175°	87 (m.p.); 90 (m.p.); 1034 (m);
$CH_2C_6H_5$	COOH	OH		OH		methyl ester, m.p. 178°	169 (m.p.), (i), (u);
						morpholine salt, m.p. 167°	169 (m.p.);
						ethyl ester, m.p. 168°	169 (m.p.), (i), (u);
$C_6H_4CH_3$-*o*	COOH	OH		OH		methyl ester, m.p. 182°	168 (m.p.), (i), (u);
						morpholine salt, m.p. 176°	168 (m.p.);
						ethyl ester, m.p. 191°	168 (m.p.), (i)

TABLE XII-44. 2-Pyridone Carboxylic Acids and Derivatives (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
$C_6H_4CH_3$-*m*	COOH	OH		OH		methyl ester. m.p. 190° ethyl ester. m.p. 196°	169 (m.p.); 169 (m.p.), (i), (u);
$C_6H_4CH_3$-*p*	COOH	OH		OH		methyl ester. m.p. 198° morpholine salt. **m.p.** 180° ethyl ester. m.p. 199°	168 (m.p.); 168 (m.p.); 168 (m.p.);
C_6H_5	COOH	OCH_3		OH		methyl ester m.p. **252°**	171 (m.p.), (u);
$C_6H_4OCH_3$-*o*	COOH	OH		OH		methyl ester. m.p. 198° ethyl ester. m.p. 190°	169 (m.p.), (i), (u); 169 (m.p.), (i), (u);
$C_6H_4OCH_3$-*m*	COOH	OH		OH		methyl ester, m.p. 190° ethyl ester. **m.p. 180°**	169 (m.p.), (i), (u); 169 (m.p.), (i), (u);
$C_6H_4OCH_3$-*p*	COOH	OH		OH		methyl ester. m.p. 193° ethyl ester, m.p. 205°	167 (m.p.), (i), (u); 168 (m.p.), (i), (u); 168 (m.p.), (i), (u);
 $-\underset{\text{COOH}}{\underset{\vert}{C}}=CHCOOH$			$-CH_2CH_2CH_2CH_2-$		190–191°	 hydrate. **m.p. 165–166°**	749 (m.p.); 749 (m.p.);

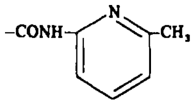
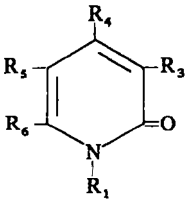
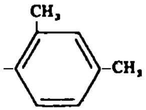
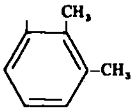
–CHCOOH CHCOOH 1-(2-Pyridone)						dimethyl ester, m.p. 189–190°	748 (m.p.), (i), (m), (n), (u);
$CH_2C_6H_5$				CH_2COOH	169°		944 (m.p.);
						amide, m.p. 250–252°	944 (m.p.);
						ethyl ester, m.p. 79°	944 (m.p.);
$-CH_2CH_2C_6H_5$	COOH				161–163°		332 (m.p.);
						ethyl ester, b.p. 191°/0.015 mm	332 (b.p.);
						$NHNH_2\cdot HCl\cdot H_2O$, m.p. 88–90°	332 (m.p.);
$-CH_2CH_2C_6H_5$		COOH			260°		1008 (m.p.);
						ethyl ester, m.p. 102–104°	1008 (m.p.);
						$NHNH_2$ m.p. 191–193°	1008 (m.p.);
$-CH_2CH_2C_6H_5$			COOH			ethyl ester, m.p. 55–56°	1008 (m.p.);
						$NHNH_2\cdot HCl\cdot H_2O$ m.p. 252°	1008 (m.p.);
C_6H_5	COOH	OCH_3		OCH_3	195–197°		167 (m.p.), (u);
C_6H_5	COOH	OC_2H_5		OH		ethyl ester. m.p. 160°	171 (m.p.), (i), (n), (u);
$C_6H_4OCH_3$-*p*		OH	COOH	CH_3		ethyl ester, m.p. 208°	87 (m.p.); 90 (m.p.); 1034 (m);
$C_6H_4OCH_3$-*o*	COOH	OH		OCH_3		methyl ester. m.p. 205°	169 (m.p.);
C_6H_4Cl-*p*	$COCH_3$		COOH	CH_3	212–274°		112 (m.p.), (n);
						methyl ester, m.p. 207°	112 (m.p.);
						ethyl ester, m.p. 185–187°	112 (m.p.), (n);
						t-butyl ester. m.p. 228°	112 (m.p.);
C_6H_4Cl-*p*	$COCH_3$			CH_3	215–218°		112 (m.p.), (n);
$CH_2C_6H_5$				$-CH_2COCOOH$	211°		944 (m.p.);
						a-oximino, m.p. 191°	944 (m.p.);

TABLE XII-44. 2-Pyridone Carboxylic Acids and Derivatives (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
C_6H_4COOH-*p*	$COCH_3$	OH		CH_3		ethyl ester. m.p. 176-177°	1030 (m.p.), (i), (n);
CH_3	OH	$CH_2C_6H_5$	COOH	CH_3		ethyl ester. m.p. 141°	231 (m.p.);
		OH	COOH	CH_3		ethyl eater	1034 (m);
		OH	COOH	CH_3		ethyl ester. m.p. 198-199°	87 (m.p.); 90 (m.p.);
α-$C_{10}H_7$	COOH	OH		OH		methyl ester, m.p. 250° m.p. 203° ethyl ester. m.p. 208-210° morpholine salt. m.p. 188°	171 (m.p.), (u); 169 (m.p.), (i), (u); 171 (m.p.), (i), (u); 169 (m.p.), (i), (u); 171 (m.p.), (u);
β-$C_{10}H_7$	COOH	OH		OH		methyl ester. m.p. 205° morpholine salt. m.p. 178° ethyl ester. m.p. 184°	168 (m.p.), (i), (u); 168 (m.p.); 168 (m.p.), (i), (u);

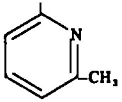
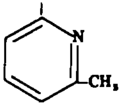
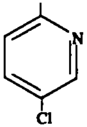
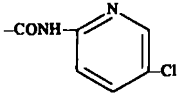
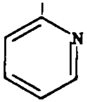
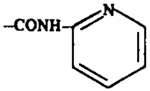
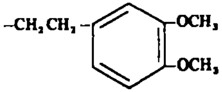
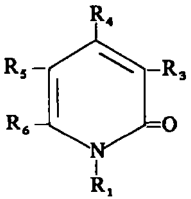
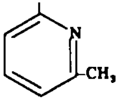
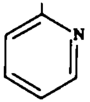
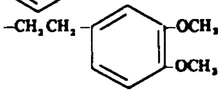
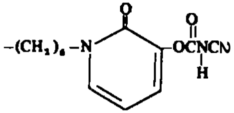
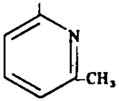
	$COCH_3$		$COOH$	$-CH_2COOH$		dimethyl ester, m.p. 172°	112 (m.p.);
C_6H_5	$COOH$	OC_2H_5		OC_2H_5	197°		167 (m.p.), (u);
α-$C_{10}H_7$	$COOH$	OH	$COOH$	OH		dimethyl ester, m.p. 214°	171 (m.p.), (u);
						morpholine salt, m.p. 208°	171 (m.p.);
						diethyl ester, m.p. 209°	171 (m.p.), (u);
	$COCH_3$		$-CONHC_3H_7$-*n*	CH_3	21[illegible]		112 (m.p.);
	$COCH_3$			CH_3	216–219°		112 (m.p.), (n);
	$COCH_3$			CH_3	228–229		112 (m.p.), (n);
		CH_2COOH	C_2H_5		154°		281 (m.p.), (u);
						hydrochloride, m.p. 160–163°	281 (m.p.);

TABLE XII-44. 2-Pyridone Carboxylic Acids and Derivatives (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
	$COCH_3$		–C NC$_4$H$_9$ *t*	CN	243 24		1 Z (m.p.)
CH_3	$-CH_2C_6H_5$		COOH	C_6H_5	293–294°		45 (m.p.), (i), (u);
						methyl ester, m.p. 119–120°	45 (m.p.), (n);
						ethyl ester, m.p. 95–96°	45 (m.p.), (i), (n), (u);
C_6H_5	OH	$CH_2C_6H_5$	COOH	CH_3		ethyl ester, m.p. 142°	231 (m.p.);
	$-COCH_3$		$-CONHC_6H_5$	CH_3	230–232°		112 (m.p.);
		$-CH_2COCOOH$	C_2H_5			ethyl ester, m.p. 141–143°	281 (m.p.);
	$-OCONHCH_3$				166–168°		998 (m.p.), (t), (u);
	$COCH_3$		$CONHC_6H_4Cl$-*p*	CH_3	231–233°		112 (m.p.), (n);

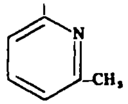
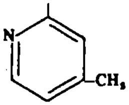
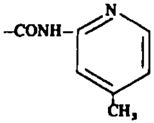
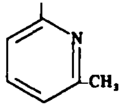
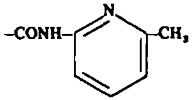
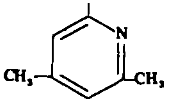
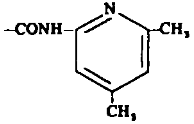
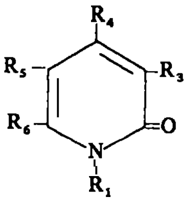
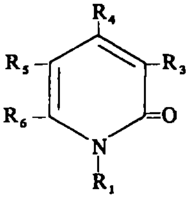
$-CH_2C_6H_5$	OH	$-CH_2C_6H_5$	COOH	CH_3		ethyl ester, m.p. 160"	231 (m.p.);
	$COCH_3$		$-CONHC_6H_5$	CH_3	210–212'		112 (m.p.);
	$COCH_3$			CH_3	235–237°		112 (m.p.);
	$COCH_3$			CH_3	252–253°		112 (m.p.), (n);
CH_3	$-\underset{C_6H_5}{\underset{\vert}{C}}HOC_2H_5$		COOH	C_6H_5		ethyl ester, m.p. 88–90°	45 (m.p.), (i), (n), (u);
	$COCH_3$			CH_3	253–255°		112 (m.p.), (n);
$-CONHC_6H_5$	CH_3	$N(C_2H_5)_2$	C_6H_5		165'		102 (m.p.), (i), (u);
C_6H_5	$CH_2C_6H_5$		COOH	C_6H_5	251–252°		45 (m.p.), (i), (u);
C_6H_5	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*o*		OH	180°		173 (m.p.), (i), (u);
						morpholine salt, m.p. 165–166°	173 (m.p.);
C_6H_5	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*m*		OH	195		173 (m.p.), (i), (u);
						morpholine salt, m.p. 163°	173 (m.p.);
$-CONHCH{=}CHC_6H_5$	CH_3	$N(C_2H_5)_2$	C_6H_5		165°		102 (m.p.), (i), (u);
$-CH_2C_6H_5$	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*o*		OH	157°		173 (m.p.), (i), (u);
$-CH_2C_6H_5$	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*m*		OH	201'		173 (m.p.);
C_6H_5	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*o*		OCH_3	238"		173 (m.p.), (u);
C_6H_5	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*m*		OCH_3	219°		173 (m.p.);

TABLE XII-44. 2-Pyridone Carboxylic Acids and Derivatives (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
$C_6H_4CH_3$-*o*	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*o*		OH	175°		173 (m.p.), (i), (u);
$C_6H_4CH_3$-*o*	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*m*		OH	211°		173 (m.p.), (i), (u);
$C_6H_4CH_3$-*o*	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*o*		OH	170°		173 (m.p.), (i), (u);
$C_6H_4CH_3$-*m*	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*m*		OH	177°		173 (m.p.), (i), (u);
$C_6H_4CH_3$-*p*	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*o*		OH	178°		173 (m.p.), (i), (u);
$C_6H_4CH_3$-*p*	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*m*		OH	204°		173 (m.p.);
$C_6H_4OCH_3$-*o*	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*o*		OH	200°		173 (m.p.), (i), (u);
$C_6H_4OCH_3$-*o*	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*m*		OH	201°		173 (m.p.);
$C_6H_4OCH_3$-*m*	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*o*		OH	182°		173 (m.p.), (i), (u);
$C_6H_4OCH_3$-*m*	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*m*		OH	210°		173 (m.p.);
$C_6H_4OCH_3$-*p*	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*o*		OH	205°		173 (m.p.), (i), (u);
$C_6H_4OCH_3$-*p*	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*m*		OH	223°		173 (m.p.);
$-NHCO(CH_2)_2COOH$		C_6H_5	C_6H_5	C_6H_5	170°		802 (m.p.), (i);
$-CONHCH{=}CHC_6H_4OCH_3$-*p*	CH_3	$N(C_2H_5)_2$	$C_6H_4OCH_3$-*p*		154°		102 (m.p.), (i), (u);
$-CONHCH{=}CHC_6H_5$	C_6H_5	$N(CH_3)_2$	C_6H_5		176°		102 (m.p.), (i), (u);
α-$C_{10}H_7$	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*o*		OH	210°		173 (m.p.), (i), (u);
α-$C_{10}H_7$	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*m*		OH	230°		173 (m.p.);
β-$C_{10}H_7$	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*o*		OH	207°		173 (m.p.); (i), (u);
β-$C_{10}H_7$	$-CONHC_6H_5$	$-OC_6H_4CH_3$-*m*		OH	232°		173 (m.p.);
$-CONHCH{=}CHC_6H_4OCH_3$-*p*	C_6H_5	$N(CH_3)_2$	$C_6H_4OCH_3$-*p*		200°		102 (m.p.), (i), (u);
$-NHCOC_6H_4COOH$-*o*		C_6H_5	C_6H_5	C_6H_5	254–256°		802 (m.p.), (i);
β-D-Ribofuranosyl			$CONH_2$			2,3,5-tri-*O*-benzoyl m.p. 232°	613 (m.p.)

TABLE XII-45. 2-Pyridone Nitriles



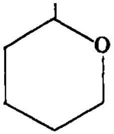
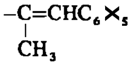
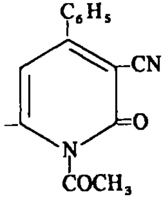
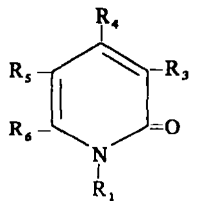
R_1	R_3	R_4	R_5	R_6	m.p.	Derivative	Ref.
CH_3			CN		157–161°		343 (m.p.); 855 (m.p.), (i), (n), (u);
CH_3	CN	OCH_3			201–202°		849 (m.p.); 854 (m.p.);
			CN		98–100°		574 (m.p.), (f);
β-D-Glucosyl			CN		214–216°		624 (m.p.), (f);
						tetraacetyl m.p. 98–100°	624 (m.p.), (f);
$CH_2CH_2C_6H_5$	CN				115–11[illegible]°		332 (m.p.); 1011 (m.p.), (z);
$CH_2CH_2C_6H_5$			CN		144–14[illegible]°		1008 (m.p.);
CH_3	CN			 $-\underset{CH_3}{\underset{\vert}{C}}=CHC_6X_5$	124°		57 (m.p.), (i), (u);
$COCX_3$	CN	C_6X_5			291°		79 (m.p.), (t);

TABLE XII-46. Halo 2-Pyridones



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OH	OH	Cl			none		3 (n);
OH	OH		Cl		> 180"		3 (m.p.), (n);
OH	Cl	Cl	Cl		202–203"		17 (m.p.);
CH_3	Cl	Cl	Cl	Cl	148–150°		18 (m.p.); 241 (u);
CH_3	Cl	Cl	Cl		193–194"		15 (m.p.), (u);
NHCONH,	Cl	Cl	Cl		235"		15 (m.p.), (u);
CH_3	Cl		Cl		140–141"		15 (m.p.); 18 (m.p.); 327 (u); 831 (i), (u);
CH_3	Br		Br		175–187"		530 (m.p.), (i), (m), (n); 559 (m.p.); 570 (m.p.), (n); 745 (m.p.); 831 (i);
CH_3			Cl				327 (u);
CH_3				Cl	61-65"		241 (m.p.), (u); 494 (m.p.), (i);
CH_3			Br				467 (u);
CH_3	OH	Cl			186–187"		3 (m.p.), (n);
CH_3	Br		NH_2		164"	 *N'*-acetyl, m.p. 244"	290 (m.p.); 290 (m.p.);
CH_3	COOH	Cl		Cl		methyl ester, m.p. 126"	169 (m.p.);

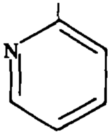
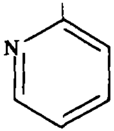
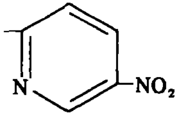
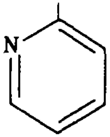
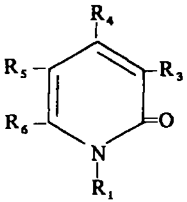
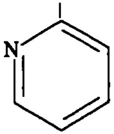
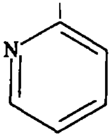
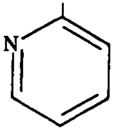
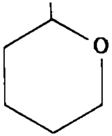
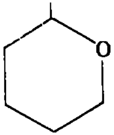
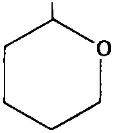
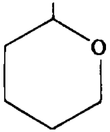
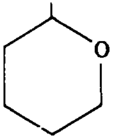
						ethyl ester, m.p. 117"	171 (m.p.), (u);
CH_3	Br	CH_3	Br		215–216"		559 (m.p.);
CH_3	Br		Br	CH_3	153–154°		559 (m.p.);
C_2H_5	Br		Br		109–110"		570 (m.p.);
CH_3		Cl		CH_3	70"		306 (m.p.);
CH_3		CH_3		Cl	62"		8 (m.p.); 457 (i), (n), (u);
$N(CH_3)_2$	OH	Cl			135–137"		3 (m.p.), (n);
CH_3	$-CH_2CH_2CH_2-$			Cl	84"		8 (m.p.); 457 (i), (n), (u);
	Cl		Cl		140–141°		409 (m.p.), (c), (g);
	Br		Br				409 (g);
	Br				231–232"		271 (m.p.);
	Cl				108–109"		409 (m.p.), (g);

TABLE XII-46. Halo 2-Pyridones (Continued)



[illegible]	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
			Cl				409 (g).,
	Br				111-112°		409 (g); 992 (m.p.);
			Br				409 (g);

	Br	Br	[illegible]0–91°	574 (m.p.), (f);
	$CH_2CH_2CH_2CH_2-$	Cl	[illegible]°	8 (m.p.); 457 (i), (n), (u);
	Cl		[illegible]0–62	574 ([illegible].) ∞;
		Cl	il	574 ∞;
	Br		oil	574 ∞;
		Br	oil	574 ∞;

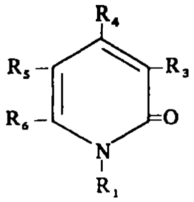
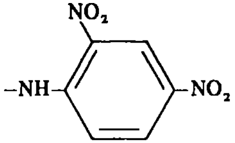
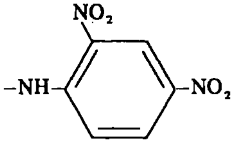
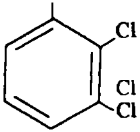


TABLE XII-46. Halo 2-Pyridones (Continued)

R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
C_6H_5	Cl	Cl	Cl	Cl	149-156°		18 (m.p.); 19 (m.p.), (u);
C_6H_5	Br	Br	Cl	Cl	156-157"		19 (m.p.), (u);
	Cl	Cl	Cl		244-252"		15 (m.p.); 17 (m.p.); 19 (m.p.);
	Cl	Br	Br		264-266"		19 (m.p.), (u);
C_6H_5	Cl	Cl	Cl		148-149"		15 (m.p.), (u);
	OH		Cl		222-223"		3 (m.p.), (n);

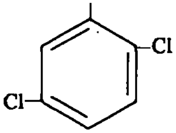
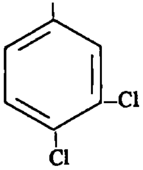
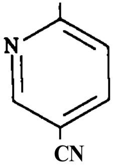
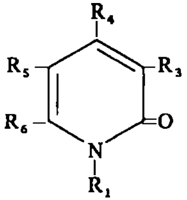
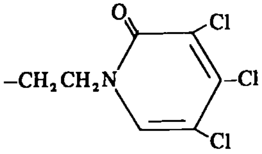
	OH		Cl	145–146"		3 (m.p.), (n);
	OH		Cl	193–194"		3 (m.p.), (n);
	Br			264–265°		271 (m.p.);
NHC_6H, NO, -*p*	Cl	Cl	Cl	223–225°		15 (m.p.);
C_6H_5	Cl		Cl	126–127"		18 (m.p.);
C_6H_5Hg–	Cl		Cl	100–102"		831 (m.p.), (i), (u);
C, H, Cl-*o*	OH		Cl	164–165°		3 (m.p.), (n);
C, H_4Cl-*m*	OH		Cl	185–186°		3 (m.p.), (n);
$-NHC_6H_5$	Cl	Cl	Cl	173–174°		15 (m.p.), (u);
C, H, NO, -*m*	OH		Cl	235–236"		3 (m.p.), (n);
C_6H_5	OH		Cl	147–149"		3 (m.p.), (n);
$-NHC_6H_5$	Cl	OH	Cl	249–250°		15 (m.p.);
β-D-Glucosyl	Cl		Cl	186–188"		624 (m.p.), (f);
					tetraacetyl, m.p. 159–161"	624 (m.p.), (f);

TABLE XII-46. Halo 2-Pyridones (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
β-D-Glucosyl	Br		Br		219–222°		624 (m.p.), (f);
						tetraacetyl, m.p. 179–180°	624 (m.p.), (f);
β-D-Glucosyl	I		I		232–234°		624 (m.p.), (f);
						tetraacetyl, m.p. 175–176°	624 (m.p.), (f);
β-D-Glucosyl	Cl					tetraacetyl, m.p. 87–90°	624 (m.p.), (f);
β-D-Glucosyl			Cl		210–212°		605 (m.p.), (f), (k);
						tetraacetyl, m.p. 229–233°	605 (m.p.);
β-D-Glucosyl			Br		217–218°		605 (m.p.), (f), (k);
						tetraacetyl, m.p. 224°	605 (m.p.), (k);
β-D-Glucosyl			I		213–215°		605 (m.p.), (f), (k);
						tetraacetyl, m.p. 199–200°	605 (m.p.);
	Cl	Cl	Cl		306–308°		15 (m.p.);

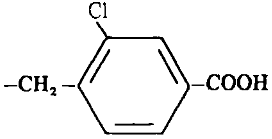
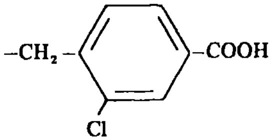
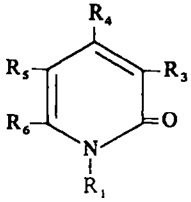
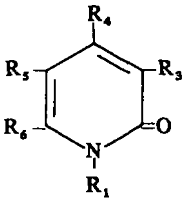
C_6H_5	COOH	Cl		Cl		methyl ester, m.p. 154" ethyl ester, m.p. 156"	171 (m.p.), (u); 171 (m.p.), (i), (n), (u);
$-CH_2C_6H_5$	Cl		Cl		86–87"		563 (m.p.);
CH_3		C_6H_5		Cl	118"		8 (m.p.); 457 (i), (n), (u);
$C_6H_4CH_3$-*o*	OH		Cl		172–173"		3 (m.p.), (n);
$C_6H_4CH_3$-*m*	OH		Cl		158–160"		3 (m.p.), (n);
$C_6H_4OCH_3$-*p*	OH		Cl		172-174°		3 (m.p.), (n);
	**Cl**		Cl		216–217"		563 (m.p.);
			Cl		235–237"		563 (m.p.);
$-CH_2C_6H_4COOH$-*p*	Cl		Cl		238–240"		563 (m.p.);
$-CH_2C_6H_4COOH$-*p*			Cl		240–242"		563 (m.p.);
$CH_2CH_2C_6H_5$	Cl				129–130"		332 (m.p.);
$CH_2CH_2C_6H_5$		Cl			101–103"		1008 (m.p.);
$CH_2CH_2C_6H_5$			Cl		122–123"		1008 (m.p.);
$CH_2CH_2C_6H_5$	**Br**				139–140"		332 (m.p.); 1011 (m.p.), (z);
$CH_2CH_2C_6H_5$			Br		114–115"		1008 (m.p.);
$CH_2CH_2C_6H_5$	I				115–116°		332 (m.p.);
$CH_2CH_2C_6H_5$			I		119–121°		1008 (m.p.);
C, H, -*n*	**OC_4H_9-*n***		Cl		46–47°		596 (m.p.), (i);

TABLE **XII-46**. Halo 2-Pyridones (Continued)



R_1	R_3	R_4	R_5	R,	m.p.	Derivatives	Ref.
$CH_2C_6H_4COO$ $(CH_2)_2$ p-$(CH_3)_2N$	Cl		Cl			hydrochloride, m.p. 182–184"	563 (m.p.);
CH_3	Cl	C_6**H_5**	C_6H_5	Cl	231–233"		242 (m.p.), (i), **(u);**
CH_3	C_6**H_5**	C_6**H_5**	Cl	Cl	135–136"		242 (m.p.), **(i), (u);**
$CH_2C_6H_4COO$ $(CH_2)_3$ p-$(CH_3)_2N$	Cl		Cl			hydrochloride, m.p. 127–128°	563 (m.p.);
C_6H_5	CONHC, H,	**OC_6**H_4CH_3-o		Cl	245"		**173 (m.p.), (u);**
C_6H_5	$CONHC_6H$,	$OC_6H_4CH_3$-o	Br	OH	165–166"		**173 (m.p.);**

TABLE XII-47. Nitro and Nitroso 2-Pyridones



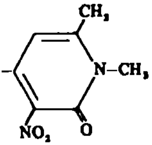
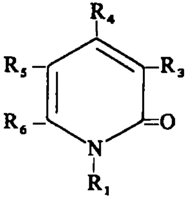
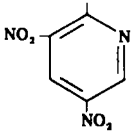
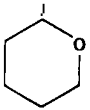
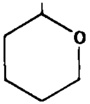
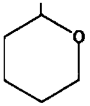
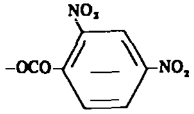
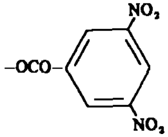
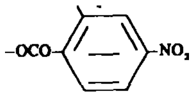
R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	Cl		NO_2		115°		291 (m.p.), (i);
CH_3	Br		NO_2		122-124°		290 (m.p.), (i);
CH_3	I		NO_2		193'		287 (m.p.), (i);
CH_3	NO_2		NO_2		174-175°		82 (m.p.);
CH_3	NO_2				179-180°		556 (m.p.);
CH_3			NO_2		172-176'		82 (m.p.); 861 (m.p.), (i);
CH_3	NO_2			on	160°		701 (m.p.);
CH_3	COOH		NO_2		204°		82 (m.p.);
						ethyl ester, m.p. 92-93'	82 (m.p.);
CH_3	NO_2		CH_3		179-180°		700 (m.p.);
C_2H_5	NO_2				122°		572 (m.p.);
CH_3	NO_2	OCH_3			172-173°		849 (m.p.), (n);
CH_3	NO_2	OH		CH_3	218-219°		86 (m.p.);
CH_3	NO	NH_2		CH_3	246		306 (m.p.);
CH_3	NO_2	NH_2		CH_3	314-315°		86 (m.p.);
CH_3	NO_2	$NHNH_2$		CH_3	191-192°		86 (m.p.);
CH_3	NO_2	NH_2	COOH	CH_3		ethyl ester, m.p. 131-13Y	86 (m.p.);
CH_3	NO_2	OCH_3		CH_3	188°		86 (m.p.);
CH_3	NO_2	$-NHCH_2CH_2NH-$ 		CH_3	324-325°		86 (m.p.);
CH_3	NO_2	$NHNH_2$	$-CONHNH_2$	CH_3	218-220°		86 (m.p.);
CH_3	NO_2	OCH_3	COOH	CH_3		ethyl ester, m.p. 131-132°	86 (m.p.);

TABLE XII-47. Nitro and Nitroso 2-Pyridones (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	NO_2	$-NHCH_2CH_2Cl$		CH_3	175°		86 (m.p.);
CH_3	NO_2	$-NHCH_2CH_2OH$		CH_3	229"		86 (m.p.);
	NO_2		NO_2		230"		276 (m.p.);
	NO_2		NO_2		137-141'		574 (m.p.), (f);
	NO_2				85-87°		574 (m.p.), (f);
			NO_2		88-90"		574 (m.p.), (f),
$-OCOC_6H_4Br$-*m*			NO_2		140-143'		1028 (m.p.), (i);
β-D-Glucosyl	Br		NO_2		amorphous		608 (f), (k);
β-D-Glucosyl	NO_2		Br		228-229°		608 (m.p.), (f), (k);
β-D-Glucosyl	NO_2				157-163"		608 (m.p.), (f), (k);

β-D-Glucosyl			NO_2		117–119"	tetraacetyl, m.p. 99–100°, or amorphous	624 (m.p.), (k); 609 (m.p.), (n), (u); 624 (f), Or);
CH_3	NO_2	NHC_6H_5		CH_3	113"		86 (m.p.);
	NO_2				191–193"		1028 (m.p.), (i);
	NO_2				214'		1028 (m.p.), (i);
			NO_2		174–175°		1028 (m.p.), (i);
$-OCOC_6H_4Cl$-*o*	NO_2				139–141°		1028 (m.p.), (i);
$-OCOC_6H_4Cl$-*p*	NO_2				135–137"		1028 (m.p.), (i);
$-OCOC_6H_4Cl$-*o*			NO_2		140–142°		1028 (m.p.), (i);
$-OCOC_6H_4Cl$-*p*			NO_2		151–153"		1028 (m.p.), (i);
$-OCOC_6H_4Br$-*m*	NO_2				135–137°		1028 (m.p.), (i);
$-OCOC_6H_4NO_2$-*m*	NO_2				170–172°		1028 (m.p.), (i);
$-OCOC_6H_4NO_2$-*p*	NO_2				197–199°		1028 (m.p.), (i);
$-OCOC_6H_4NO_2$-*m*			NO_2		186–188°		1028 (m.p.), (i);
$-OCOC_6H_4NO_2$-*p*			NO_2		198–201'		1028 (m.p.), (i);
	NO_2				118–120°		1028 (m.p.), (i);
$-OCOC_6H_5$			NO_2		149–150'		1028 (m.p.), (i);
β-D-Glucosyl	CN		NO_2		144–145°	tetraacetyl, m.p. 136–140°	608 (m.p.), (f), (k); 608 (m.p.), Or);
$-OCOC_6H_4CN$-p	NO_2				197–199°		1028 (m.p.), (i);

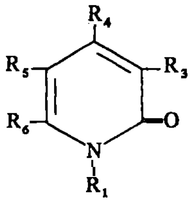
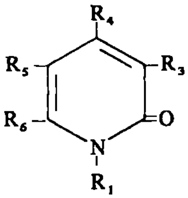


TABLE XII-47. Nitro and Nitroso 2-Pyridones (Continued)

R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
$-OCOC_6H_4CH_3$-*p*	NO_2				150–152°		1028 (m.p.), (i);
$-OCOC_6H_4CH_3$-*p*			NO_2		164–166°		1028 (m.p.), (i);
$-OCOC_6H_4OCH_3$-*p*	NO_2				156–158°		1028 (m.p.), (i);
$-OCOC_6H_4OCH_3$-*p*			NO_2		139–141°		1028 (m.p.), (i);
$-CH_2CH_2C_6H_5$	NO_2				150–151°		332 (m.p.);
$-CH_2CH_2C_6H_5$			NO_2		155–158°		1008 (m.p.);
CH_3	NO,	$-NHNHC_6H_5$		CH_3	169–171'		86 (m.p.);
CH_3	NO,	$-NHCH_2C_6H_4NO$, -*o*		CH_3	203–204°		86 (m.p.);
CH_3	NO,	$-NHCH_2C_6H_5$		CH_3	143–144°		86 (m.p.);

TABLE XII-48. Sulfur containing 2-Pyridones



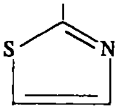
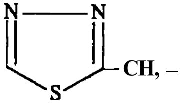
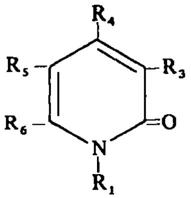
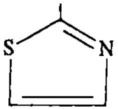
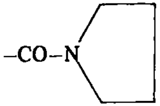
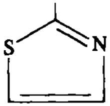
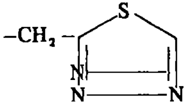
R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
SO_3H						potassium salt	648 (i), (u);
OSO_2CH_3					77–79"		995 (m.p.), (i), (u);
			COOH		264–265°		115 (m.p.);
						methiodide, m.p. 244–247"	115 (m.p.);
						amide, m.p. 268–270"	115 (m.p.);
						methyl ester, m.p. 161–163°	115 (m.p.);
			COOH		254–256"		115 (m.p.);
						methyl ester, m.p. 213–214"	115 (m.p.);
CH_3		$-OPS(OCH_3)_2$		CH_3	oil		1004;
$OSO_2C_6H_4F$-*p*					130–132"		995 (m.p.), (i), (u);
$OSO_2C_6H_5$					135–137"		995 (m.p.), (i), (u);

TABLE XII-48. Sulfur containing 2-Pyridones (Continued)



R_1	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
$CH_2CH{=}CH_2$		$-OPS(OCH_3)_2$		CH_3	54-57"		1004 (m.p.);
CH_3		$-OPS(OC_2H_5)_2$		CH_3	62-63"		1004 (m.p.);
C_6H_5		OH	COOH	SH		ethyl ester, m.p. 126-128"	49 (m.p.);
$-OSO_2C_6H_4CH_3$-*p*					101-103"		995 (m.p.), (i), (u);
$-OSO_2CH_2C_6H_5$					101-103"		1035 (m.p.), (i);
CH_3	Br		$-NHCSNHC_6H_5$		232"		290 (m.p.);
					204-207°		115 (m.p.);
			$-CON(C_2H_5)_2$		141"		115 (m.p.);
			$-CON(C_2H_5)_2$		200-201"		115 (m.p.);

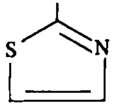
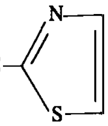
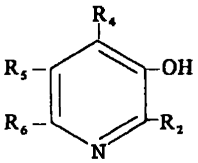
$-CH_2CH{=}CH_2$		$-OPS(OC_2H_5)_2$		CH_3	oil		10 0 ;
n-C_3H_7		$-OPS(OC_2H_5)_2$		CH_3	≦0–32°		10 0 (mp.);
	$COCH_3$		-CONX 	CH_3	259 Z≦1°		112 (m.p.), (n);
$-CH_2C_6H_5$		$-OPS(OC_2H_5)_2$		CH_3	il		10 0 ;
5′-*O*-Tosyl- β-D-ribo- furanosyl						2′,3′-*O*-iso- propylidene, m.p. 135–137°	621 (m.p.), (t);

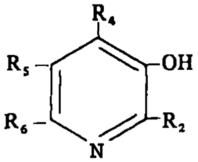
TABLE XII-49. Alkyl and Aryl 3-Pyridinols



R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
H	H	H	H	123-129'		176 (i); 227 (g), (t); 317 (m.p.); 320 (m.p.); 342 (t); 404 (f); 478 (i), (r); 512 (u); 514 (n); 520 (n); 525 (h), (u); 527; 529; 648 (u); 659 (u); 899 (n); 900 (f); 901 (n); 902 (i); 904 (u); 905 (m.p.), (u); 906 (a); 909 (u); 910 (j); 911 (t); 912 (u); 915 (m); 918 (s); 925 (t); 1036 (m.p.); 1037 (m.p.); 1038 (m.p.); 1039 (m); 1040 (f); 1041 (e); 1042 (n); 1043 (g), (u); 1044 (u);
					picrate, m.p. 205-206°	227 (m.p.);
					hydrochloride, m.p. 105-107°	1036 (m.p.);
					deuterio	1045 (i);
					sodium salt	545 (i), (r);
					O-acetyl	404 (f), (g); 414 (i), (n), (g);
			CH_3NO_2	190°		193 (m.p.);
CH_3				165-169°		176 (m.p.) (i); 178 (f); 179 (m.p.); 181 (m.p.); 210 (m.p.), (u); 369 (m.p.); 514 (n); 515 (n); 520 (n); 899 (n); 925 (t); 1036 (m.p.); 1038 (m.p.); 1039 (m); 1046 (m.p.);

					picrate, m.p. 203'	176 (m.p.);
					NH_4Cl salt, m.p. 230-231	179 (m.p.);
					hydrochloride, m.p. 225-227°	1036 (m.p.);
CH_3					*O*-acetyl, b.p. 66°/4.5 mm	367 (b.p.), (g), (i), (m); (n); 369 (b.p.), (g); 386 (g);
					O-acetyl picrate, m.p. 143°	369 (m.p.);
	CH_3			117-119°		317 (m.p.); 369 (m.p.); 925 (l);
					picrate, m.p. 200°	369 (m.p.);
					"*O* m.p. 119-121°	392 (m.p.);
					O-acetyl, b.p. 98°/4.5 mm	369 (b.p.), (g); 387 (n); 392 (g); 414 (g), (i), (n);
					O-acetyl picrate, m.p. 173"	369 (m.p.);
		CH_3		133-135°		227 (m.p.), (g), (t); 317 (m.p.);
					picrate, m.p. 189-190°	227 (m.p.);
			CH_3	164-170'		176 (i); 183 (m.p.); 369 (m.p.); 514 (n); 515 (n); 520 (n); 1047 (m.p.);
					O-acetyl, b.p. 80°/4 mm	367 (g), (i), (m), (n); 369 (b.p.), (g); 1047 (b.p.);
					picrate, m.p. 150-152°	1047 (m.p.);
					O-acetyl picrate, m.p. 144-145°	369 (m.p.);
CH_2OH						918 (s);
	CH_2NH_2				di-HCl m.p. 17P	1155 (m.p.), (u);
			CH_2NH_2	157-160'		193 (m.p.), (n);
$COCH_3$				55-56"		302 (m.p.);
CH_3	CH_3			167°		420 (m.p.), (m), (n), (u);
CH_3			CH_3	190-212°		182 (m.p.); 210 (m.p.); 300 (m.p.); 369 (m.p.);

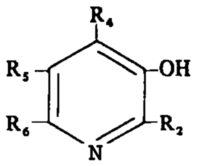
TABLE XII-49. Alkyl and Aryl 3-Pyridinols (Continued)



R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
						386 (m.p.), (i); 390 (m.p.); 420 (m.p.), (m), (n), (u); 515 (n); 520 (n); 721 (m.p.); 925 (t); 1039 (m);
					O-acetyl, b.p. 80°/0.8 mm	369 (b.p.); 386 (b.p.), (g), (i); 414 (g), (n);
	CH_3		CH_3	135°		420 (m.p.), (m), (n), (u);
C_2H_5				134°		176 (m.p.), (i); 386 (i);
					picrate, m.p. 173–174°	176 (m.p.);
					O-acetyl	386 (g);
	C_2H_5			100°		283 (m.p.), (u);
					oxalate, m.p. 231°	283 (m.p.);
			C_2H_5		O-acetyl	386 (g);
CH_3		CH_2OH			hydrochloride, m.p. 169–170°	211 (m.p.);
CH_3			CH_2OH	153°		368 (m.p.); 369 (m.p.); 721 (m.p.), (n);
					picrate, m.p. 190–191°	386 (m.p.);
					hydrochloride, m.p. 157–158°	721 (m.p.);
					3,6-diacetyl, b.p. 112°/1 mm	369 (g); 721 (b.p.), (n);
CH_2OH			CH_3	157°		368 (m.p.); 369 (m.p.);
					picrate, m.p. 174°	368 (m.p.);
					2,3-diacetyl	369 (g);
CH_2OH			CH_2OH			918 (s);
	CH_2OH	CH_2OH			hydrochloride, m.p. 125–126°	204 (m.p.), (f);
CH_3		CH_2NH_2			di-HCl, m.p. 275–277°	211 (m.p.);

	CH_2NH_2	CH_2OH				928 (u);
					di-HCl,	
					m.p. 166–168	204 (m.p.), (f);
	CH_2NH_2	$CH_2OPO_3H_2$			di-H_2O	204 (f);
CH_3	CHO	CH_2OH				1048 (n);
CH_3	CH_2OD	CH_2OD				1049 (n);
$-\underset{CH_3}{\underset{\mid}{C}}=CH_2$					hydrate, m.p. 52–53'	302 (m.p.);
CH_3	CH_2Cl	CH_2Cl			hydrochloride,	
					m.p. 175–190°	1050 (m.p.);
CH_3	CH_2Br	CH_2Br			hydrobromide.	
					m.p. 224–22F	1050 (m.p.);
CH_3	CH_2I	CH_2I			hydroiodide,	
					m.p. 120–160	1050 (m.p.);
CH_3		$COCH_3$		253–254°		204 (m.p.), (n), (t), (u);
CH_3	CH_2Br		CH_3		hydrobromide.	
					m.p. 170–171'	723 (m.p.);
CH_3	CH_2OH	CH_2Cl				1051 (e);
CH_3	CH_2Br	CH_2OH			hydrobromide,	
					m.p. 159–160°	1052 (m.p.);
CH_3	CHO	$CH_2OPO_3H_2$				1048 (n);
CH_3	CH_3	CH_3		17k		1053 (m.p.);
					hydrochloride.	
					m.p. 216'	1053 (m.p.); 1054 (m.p.);
CH_3	CH_3		CH_3	134–138°		185 (m.p.); 300 (m.p.); 370 (m.p.), (i); 386 (m.p.), (i); 390 (m.p.); 514 (n); 520 (n); 721 (m.p.), (n); 723 (m.p.); 925 (t); 1039 (m);
					picrate, m.p. 166°	370 (m.p.);
					O-acetyl, b.p. 88°/1.5 mm	386 (b.p.), (g), (i);
CH_3		C_2H_5			O-acetyl	386 (g);
C_2H_5		CH_3		134–136°		227 (m.p.), (g), (t), (u);
					picrate, m.p. 180–182°	227 (m.p.);
C_2H_5			CH_3	171–172°		182 (m.p.);
			n-C_3H_7	90–91°		386 (m.p.), (i), (n);
					O-acetyl	386 (g);
CH_3	CH_3	CH_2OH		271'		1048 (n); 1053 (m.p.);
					hydrochloride. m.p. 254°	1054 (m.p.);
CH_3	CH_2OH	CH_3			hydrochloride, m.p. 140–144'	1053 (m.p.); 1054 (m.p.);

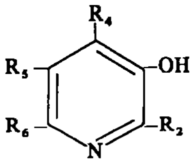
TABLE XII-49. Alkyl and Aryl 3-Pyridinols (Continued)

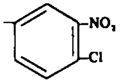
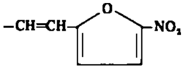


R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	CH_2OH		CH_3	160–162°		723 (m.p.);
					hydrochloride. m.p. 159–160°	723 (m.p.);
					3,4-di-*O*-acetyl, b.p. 128°/1 mm	723 (b.p.), (n);
CH_3	CH_2OH	CH_2OH		197–206°		204 (m.p.), (f), (n); 525 (h), (u); 527; 912 (u); 918 (s); 1048 (n); 1051 (e); 1055 (e); 1056 (m.p.);
					hydrochloride, m.p. 203–206°	200 (m.p.); 1057 (m.p.); 1058 (m.p.);
CH_3	CH_2OH	$^*CH_2OH$			^{14}C·HCl m.p. 208–209°	1059 (m.p.);
CH_3	CH_2OH		CH_2OH	166–167°		721 (m.p.), (n);
					hydrochloride. m.p. 130–131°	721 (m.p.);
					3,4,6-tri-*O*-acetyl, m.p. 50° b.p. 165°/0.01 mm	721 (b.p.), (m.p.), (n);
CH_3	$CH(OH)_2$	CH_2OH				525 (h), (u);
CH_3	CH_2NH_2	CH_2Br			dihydrobromide. m.p. >250°	1060 (m.p.);
CH_3	CH_2OH	$CH{=}NNH_2$		175–176°		1053 (m.p.);
CH_3	CH_3	$CH_2OPO_3H_2$				1048 (n); 1061 (u);
CH_3	CH_2OH	$CH_2OPO_3H_2$				527;
CH_3	CH_2NH_2	CH_3			di-HCl m.p. 260–263°	1054 (m.p.);
					diacetate, m.p. 176–177°	1054 (m.p.);
					ditosylate·HCl m.p. 194–195°	1054 (m.p.);
$CH_2N(CH_3)_2$				5940'		515 (n); 520 (n);
CH_3	CH_2NH_2	CH_2OH				720 (m.p.), (n); 918 (s); 524 (n); 525 (h), (u); 527; 928 (u); 1048 (n);

					di-HCl,	
					m.p. 226–227°	1062 (m.p.), (f);
					picrate,	
					m.p. 198°	1062 (m.p.);
CH_3	CH_2OH	CH_2NH_2			di-HCl	
					m.p. 17F	1063 (m.p.);
	CH_2NH_2	CH_2OH	CH_3		di-HCl,	
					m.p. 234–240.	204 (m.p.), (f);
CH_3	$CH(OH)_2$	$CH_2OPO_3H_2$				525 (h), (u);
CH_3	CH_2NH_2	$CH_2OPO_3H_2$				527; 1048 (n);
	CH_2NH_2	CH_2om$_3H_2$	CH_3		dihydrate	204 (f);
CH_3	CH_2NH_2	CH_2NH_2			hydrochloride.	
					m.p. 278–283°	1064 (m.p.);
CH_3	$-CH_2OCH_2OCH_2-$			17P		208 (m.p.);
CH_3	CH_2Cl	CH_2OCH_3			hydrochloride,	
					m.p. 139–141°	1063 (m.p.);
CH_3	C_2H_5		CH_3	120–122°		185 (m.p.);
n-C_3H_7			CH_3	161–162°		182 (m.p.);
isoC_3H_7			CH_3	189–190°		182 (m.p.); 520 (n);
CH_3	CH_2OH	$CH(OH)CH_3$			hydrochloride.	
					m.p. 159–160.	204 (m.p.), (n);
CH_3	CH_2OH	CH_2OCH_3			hydrochloride.	
					m.p. 141–142°	1063 (m.p.);
CH_3	CH_2OCH_3	CH_2OH		173°		1048 (n); 1056 (m.p.);
CH_3	$CH(OH)CH_3$	CH_2OH		177–178°		1053 (m.p.); 1065 (m.p.);
					hydrochloride,	
					m.p. 173–174°	204 (m.p.), (f), (n);
CH_3	CH_2OH	CH_2OH	CH_3	174–177.		204 (m.p.), (f);
CH_3			$CH_2N(CH_3)_2$	159–160.		520 (n); 721 (m.p.), (n);
					di-HCl,	
					m.p. 210–211°	721 (m.p.);
$CH_2N(CH_3)_2$			CH_3	68–69°		520 (n); 720 (m.p.), (n);
CH_3	CH_2NH_2	$CH(OH)CH_3$			di-HCl,	
					m.p. 188–191°	204 (m.p.);
CH_3	CH_2NH_2	CH_2OH	CH_3		di-HCl	
					m.p. 182–184°	204 (m.p.), (f);
CH_3	CH_2NH_2	$CH_2OPO_3H_2$	CH_3		dihydrate	204 (f);
CH_3	CH_2OD	$CH_2CH_2CH_2OD$				1049 (n);
CH_3	CH_2Br	$CH_2CH_2CH_2Br$			hydrobromide	1049;
n-C_4H_9			CH_3	141–143°		182 (m.p.);
isoC_4H_9			CH_3	179–180°		182 (m.p.);
isoC_5H_{11}				149–150.		722 (m.p.), (n);
			$-CH_2C(CH_3)_2$	118–119°		386 (m.p.), (i), (n);
					O-acetyl	386 (g);
CH_3	$CH_2OC_2H_5$	CH_3			picrate,	
					m.p. 13T	1054 (m.p.);

TABLE XII-49. Alkyl and Aryl 3-Pyridinols (Continued)



R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	$-\underset{\displaystyle OC_2H_5}{\underset{\mid}{CH}}-OCH_2-$					1048 (n);
CH_3	CH_2OH	$CH_2CH_2CH_2OH$			hydrochloride, m.p. 142–143°	1049 (m.p.), (i), (u);
CH_3	CH_2OCH_3	CH_2OCH_3			hydrochloride, m.p. 144–145° picrate, m.p. 168–169°	199 (m.p.), (u); 200 (m.p.); 1046 (m.p.); 1057 (m.p.); 1058 (m.p.); 1064 (m.p.); 1046 (m.p.);
CH_3	$CH_2CH_2CH_2OH$	CH_2OH			hydrochloride, m.p. 161–162°	1065 (m.p.), (i), (n);
isoC_3H_7	CH_2OH	CH_2OH			hydrochloride, m.p. 190–191°	204 (m.p.), (f);
CH_3	CH_2OH	$CH(OCH_3)_2$		167–168°		1066 (m.p.), (u);
CH_3	$CH_2N(CH_3)_2$		CH_3	b.p. 110°/2 mm	 di-HCl m.p. 255–256° *O*-acetyl, b.p. 100°/1 mm	724 (b.p.), (n); 724 (m.p.); 723 (b.p.);
$CH_2N(C_2H_5)_2$				b.p. 85°/1 mm	 di-HCl, m.p. 201–202°	520 (n); 720 (b.p.), (n); 720 (m.p.);
isoC_3H_7	CH_2NH_2	CH_2OH			di-HCl m.p. 169–170'	204 (m.p.), (f);
				325–326°		711 (m.p.), (n);
$C_6H_4NO_2$-*p*				275–276°		710 (m.p.), (n);
				238–258°		1067 (m.p.);

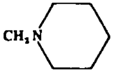
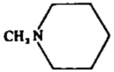
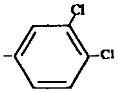
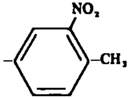
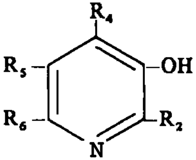
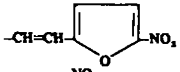
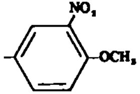
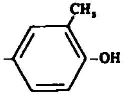
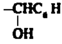
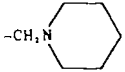
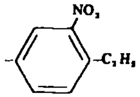
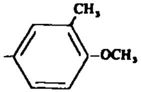
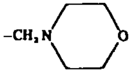
					hydrochloride. m.p. 235–241°	1067 (m.p.);
					O-acetyl, m.p. 137–140°	1067 (m.p.);
C_6H_5				202–206°		180 (m.p.), (i), (u); 210 (m.p.); 1039 (m); **1046 (m.p.);**
C_6H_4OH-*p*				218–220°		710 (m.p.);
$C_6H_4NH_2$-*p*				200–201'		710 (m.p.), (n);
				72–74'		520 (n); 720 (m.p.), (n);
			CH_3			520 (n);
n-C_4H_9	CH_2OH	CH_2OH			hydrochloride. m.p. 187–188°	204 (m.p.), (f);
CH_3			$CH_2N(C_2H_5)_2$	137–139'		515 (n); 721 (m.p.), (n);
					di-HCl m.p. 205–206'	721 (m.p.);
					O-acetyl, b.p. 110°/1 mm	721 (b.p.);
$CH_2N(C_2H_5)_2$			CH_3	b.p. 79°/1 mm		720 (b.p.), (n);
C_2H_5	$CH_2N(CH_3)_2$		CH_3	b.p. 115°/2 mm		724 (b.p.), (n);
					di-HCl m.p. 190–192°	724 (m.p.);
n-C_4H_9	CH_2NH_2	CH_2OH		b.p. 100°/1 mm	di-HCl, m.p. 163–164°	204 (m.p.), (f);
$CH_2N(CH_3)_2$			$CH_2N(CH_3)_2$			520 (n); 720 (b.p.), (n);
COC_6H_4Cl-*p*				102–103'		191 (m.p.);
	CH_3			176–177°		186 (m.p.);
COC_6H_5				63–65°		191 (m.p.);
C_6H_4Cl-*p*	CH_3			147–148°		186 (m.p.);
	C_6H_4Cl-*p*		CH_3	203–205°		1068 (m.p.), (l):
$CH_2C_6H_4Cl$-*p*				219–220.		191 (m.p.);
				223–224°		711 (m.p.), (n);

TABLE XII-49. Alkyl and Aryl 3-Pyridinols (Continued)



R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
 			CH_3	250		1047 (m.p.); 1069 (m.p.);
					O-acetyl, m.p. 167–16k	1047 (m.p.); 1069 (m.p.), (g);
 				133–134'		711 (m.p.), (n);
C_6H_5	CH_3			115–116°		186 (m.p.);
$C_6H_4CH_3$-*p*				200°		180 (m.p.), (i), (u);
	CH_3	C_6H_5		197–19k		216 (m.p.);
					O-acetyl, oil	218 (u);
					p-toluene-sulfonate, m.p. 71–72°	218 (m.p.);
 				241–242°		180 (m.p.), (i), (u);
 $-\underset{OH}{CH}C_6H_5$				117–119°		191 (m.p.);
	CH_3	C_6H_{11}		198–201°		218 (m.p.), (i), (u);
CH_3	 $-CH_2OCHOCH_2-$ $\underset{CH(CH_3)_2}{}$			163°		208 (m.p.);
CH_3			$-CH_2N$ 3	182–184°		721 (m.p.), (n);
					di-HCl m.p. 208–210°	721 (m.p.);
					O-acetyl, b.p. 115°/1 mm	721 (b.p.);

			CH_3	53–54°		720 (m.p.), (n);
CH_3	CH_2OH	$CH_2N(CH_2)_4$			hydrobromide, m.p. 200–203°	1070 (m.p.);
CH_3	$CH_2OCH_2OCH_3$	$CH_2OCH_2OCH_3$		63–65°		202 (m.p.), (u);
CH_3	$-CH(OCH_3)_2$	$-CH(OCH_3)_2$			hydrochloride, m.p. 149–150°	1066 (m.p.), (u);
n-C_4H_9			$-CH_2N(CH_3)_2$	113–114°		722 (m.p.), (n);
isoC_4H_9			$-CH_2N(CH_3)_2$	118–119°		722 (m.p.), (n);
CH_3	$-CH_2N(CH_3)_2$		$-CH_2N(CH_3)_2$	b.p. 125°/1 mm		721 (b.p.), (n);
			$-CH_2N{=}CH$ 	173–175°		193 (m.p.);
				125–126°		711 (m.p.), (n);
			$-CH_2CH_2C_6H_5$	146–147°		386 (m.p.), (i), (n);
					O-acetyl, b.p. 125°/0.4 mm	386 (b.p.), (g), (i);
				181–182°		180 (m.p.), (i), (u);
$C_6H_4OCH_3$-p	CH_3			131–132°		186 (m.p.);
CH_2NH_2	CH_3	C_6H_5			2,3-diacetyl, m.p. 135–136°	211 (m.p.), (i);
C_2H_5			CH_3	b.p. 160°/2 mm		714 (b.p.), (n);
					dihydrochloride, m.p. 227–229°	724 (m.p.);
isoC_5H_{11}			$-CH_2N(CH_3)_2$		dihydrochloride, m.p. 220–221°	112 (m.p.), (n);

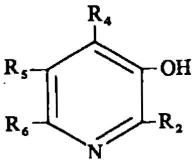
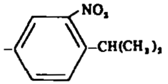
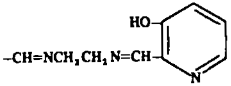
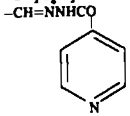
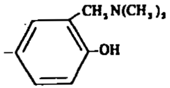
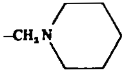
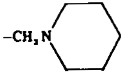
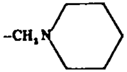
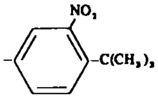
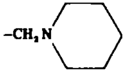
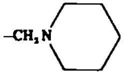
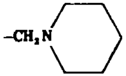


TABLE XII-49. Alkyl and Aryl 3-Pyridinols (Continued)

R₂	R₄	R₅	R₆	m.p.	Derivatives	Ref.
				190–191°		711 (m.p.), (n);
				144°		519 (m.p.), 827 (u);
CH_3	$-CH_2C_6H_5$	CH_2OH		190–191°		1065 (m.p.), (n);
CH_3		$CH_2OPO_3H_2$		260°		1061 (m.p.);
					dihydrochloride, m.p. 227–228°	727 (m.p.);
CH_3	CH_3	$-CH_2N(CH_2)_4$		117–120°		1070 (m.p.);
C_2H_5			CH_3	b.p. 155°/2 m		724 (b.p.), (n);
					dihydrochloride, m.p. 208–209°	724 (m.p.);
$n\text{-}C_3H_7$				165–166°		722 (m.p.), (n);

isoC₃H₇				155–156°		722 (m.p.), (n);
CH_3 isoC₃H₇	$-CH_2OH$ $-CH_2N(CH_3)_2$	$-CH_2N(CH_2)_4$	 $CH_2N(CH_3)_2$	128–130° b.p. 125°/1 mm	tri-HCl, m.p. 222–223°	1070 (m.p.); 722 (b.p.), (n); 722 (m.p.);
CH_3	$-CH_2Cl$	$-CH_2OCOC_6H_5$			hydrochloride. m.p. 190	1063 (m.p.);
CH_3	$-CH=NCH_2$ C_6H_4F-*p*	$-CH_2OH$				650 (n), (t);
CH_3	$-CH_2OH$	$-CH_2OCH_2C_6H_5$		117–118°		1053 (m.p.); 1065 (m.p.);
					hydrochloride. m.p. 152–153°	1065 (m.p.);
				137–138°		711 (m.p.), (n);
$C_6H_4OCH_3$-*p*			$-CH_2N(CH_3)_2$		di-HCl m.p. 225–226°	727 (m.p.);
n-C₄H₉				168–169°		722 (m.p.), (n);
isoC₄H₉				192–193°		722 (m.p.), (n);
n-C₄H₉ CH_3	$-CH_2N(CH_3)_2$ $-CH=NCH_2$ $C_6H_4OCH_3$-*p*	 CH_2OH	$-CH_2N(CH_3)_2$	180–182° 103–105°		722 (m.p.), (n); 650 (m.p.), (n);
isoC₅H₁₁				170–171°		722 (m.p.);
isoC₅H₁₁	$CH_2N(CH_3)_2$		$CH_2N(CH_3)_2$	150–151°	tri-HCl, m.p. 212–213°	722 (m.p.), (n); 722 (m.p.);
$-CHC_6H_5$ C_5H_9				263–2644'		191 (m.p.);

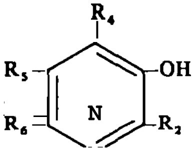
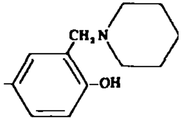
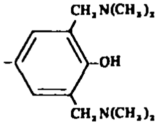
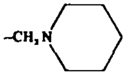
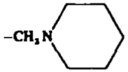


TABLE XII-49. Alkyl and Aryl 3-Pyridinols (Continued)

R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
					di-HCl, m.p. 259–260°	727 (m.p.);
CH_3	$-CH_2NH\underset{\substack{\vert\\CH_3}}{C}HCH_2C_6H_5$	CH_2OH			di-HCl, m.p. 229–230°	1052 (m.p.);
					dipicrate m.p. 168–170°	1052 (m.p.);
					tri-HCl, m.p. 230–231°	727 (m.p.);
				b.p. 125°/1 mm		520 (n); 720 (b.p.), (n);
9-Xanthyl				267–270°		919 (m.p.);
$-\underset{\substack{\vert\\C_6H_5}}{C}HC_6H_4Cl\text{-}o$				226–229°		191 (m.p.);
$-\underset{\substack{\vert\\C_6H_5}}{C}HC_6H_4Cl\text{-}p$				193–195°		191 (m.p.);
$CH(C_6H_5)_2$				221–222°		191 (m.p.); 1071 (m.p.);
					methosulfate, m.p. 152–154°	191 (m.p.);
					O-acetyl, m.p. 133–135°	1071 (m.p.);
$-\underset{\substack{\vert\\OH}}{C}(C_6H_5)_2$				168–170°		191 (m.p.); 1071 (m.p.);

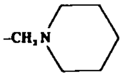
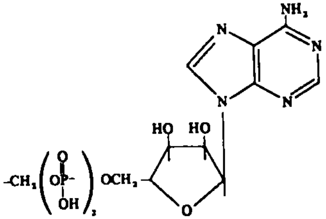
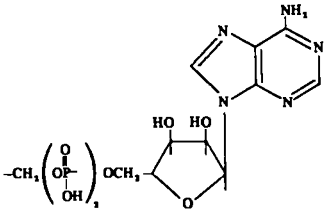
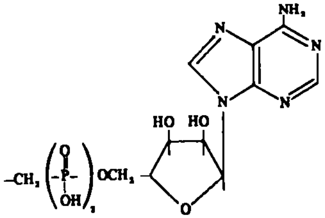
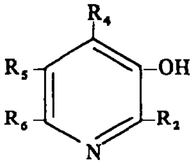
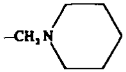
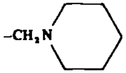
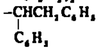
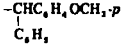
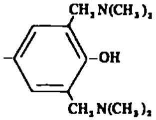
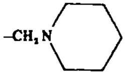
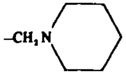
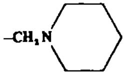
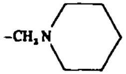
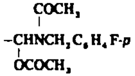
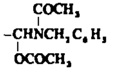
$-\underset{\displaystyle C_6H_5}{\underset{\vert}{C}}HC_5H_{11}$				22 35		191 (m.p.);
$C_6H_4OCH_3$-*p*					di-HCl, m.p. 199-200°	727 (m.p.);
CH_3	$-CHO$					1072 (i), (u);
CH_3	$-CH_2OH$					1072 (i), (u);
CH_3	$-CH_2NH_2$					1072 (i), (u);
$C_6H_4OCH_3$-*p*	$-CH_2N(CH_3)_2$		$-CH_2N(CH_3)_2$		tri-HCl, m.p. 215-216°	727 (m.p.);

TABLE XII-49. Alkyl and Aryl 3-Pyridinols (Continued)



R.	R.	R.	R.	m.p.	Derivatives	Ref
CH_3					tri-HCl m.p. 207–208°	721 (m.p.), (n);
CH_3			$(CH_2)_{11}CH_3$	101–104°		1073 (m.p.), (i), (n), (u);
$CH(C_6H_5)_2$			CH_3	195–197°		191 (m.p.); 1071 (m.p.);
$-\underset{\displaystyle C_6H_5}{CH}CH_2C_6H_5$				216–217°		191 (m.p.);
$-\underset{\displaystyle C_6H_5}{CH}C_6H_4OCH_3\text{-}p$				206–208°		191 (m.p.);
			$-CH_2N(CH_3)_2$	tetra-HCl m.p. 238–23P		121 (m.p.);
$n\text{-}C_3H_7$				b.p. 98°/1 mm		722 (b.p.), (n);
					tri-HCl, m.p. 213–214°	722 (m.p.);
isoC_3H_7				76–77°		722 (m.p.), (n);
					tri-HCl, m.p. 198–199°	722 (m.p.);
CH_3	$-\underset{\displaystyle OCOCH_3}{CH}\overset{\displaystyle COCH_3}{N}CH_2C_6H_4F\text{-}p$	CH_2OH			3,5-di-*O*-acetyl, m.p. 139–142°	650 (m.p.), (i);
CH_3	$-\underset{\displaystyle OCOCH_3}{CH}\overset{\displaystyle COCH_3}{N}CH_2C_6H_5$	CH_2OH			3,5-di-*O*-acetyl, m.p. 130°	650 (m.p.), (i), (m), (n), (u);

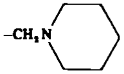
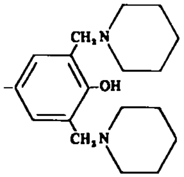
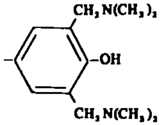
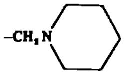
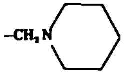
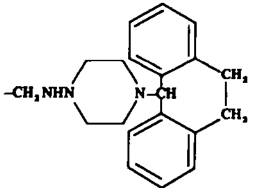
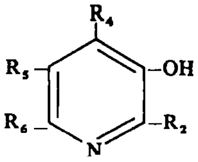
$n\text{-}C_4H_9$		$-CH_2N$ 3		tri-HCl, m.p. 224–226°	722 (m.p.), (n);
C_6H_5	C_6H_5	C_6H_5	139–141°		1074 (m.p.), (i), (n), (u);
				MHCl, m.p. 2362371	727 (m.p.);
	$CH_2N(CH_3)_2$	$CH_2N(CH_3)_2$		penta-HCl m.p. 259–261°	727 (m.p.);
$C_6H_4OCH_3\text{-}p$				tri-HCl, m.p. 246–247°	727 (m.p.);
			240–243°		1075 (m.p.);

TABLE XII-49. Alkyl and Aryl 3-Pyridinols (Continued)



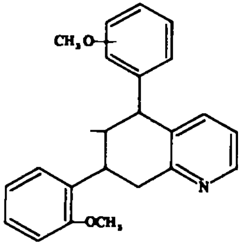
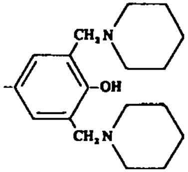
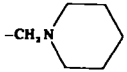
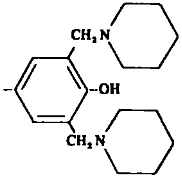
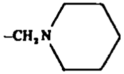
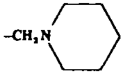
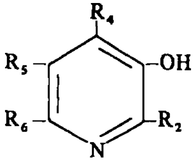
R$_2$	R$_4$	R$_5$	R$_6$	m.p.	Derivatives	Ref.
				222–223°	 CH$_3$I m.p. 244–246° *O*-acetyl, m.p. 124–125°	600 (m.p.), (f), (i), (k), (m), (u); 600 (m.p.); *600* (m.p.), (i), (m), (t);
					tetra-HCl, 243°	127 (m.p.);
					penta-HCl m.p. 246–247°	727 (m.p.);

TABLE XII-50. Alkyloxy and Aryloxy 3-Pyridinols

R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OCH_3						467 (u);
CH_3	OCH_3			162–164°		125 (m.p.), (u);
		OC_2H_5		126–128°		317 (m.p.); 319 (m.p.);

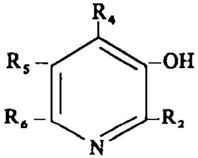
TABLE XII-51. Amino 3-Pyridinols



R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
NH_2				172–174"		187 (m.p.); 188 (m.p.); 906 (a);
					sulfate, m.p. 124–125°	187 (m.p.);
					benzamido, m.p. 95–96"	292 (m.p.);
					benzamido picrate, m.p. 237–238°	292 (m.p.);
			NH_2	116–117"		292 (m.p.);
					picrate, m.p. 225–227"	292 (m.p.);
					hydrochloride, m.p. 125–126"	292 (m.p.);
					benzamido, m.p. 181–182"	292 (m.p.), (i), (u);
					benzamido·HCl, m.p. 215–220"	292 (m.p.);
NH_2			NH_2	>300"		971 (m.p.);
NH_2			CH_3	153–155°		1076 (m.p.);
CH_3		NH_2	CH_3	259–260°		295 (m.p.);
$-N{=}NC_6H_4NO_2$-*p*				234–235°		292 (m.p.);

			$-N{=}NC_6H_4NO_2$-*p*	231–232°		292 (m.p.);
$-N{=}NC_6H_4NO_2$-*p*			CH_3	157–158°		741 (m.p.);
CH_3			$-N{=}NC_6H_4NO_2$-*p*	196–197°		741 (m.p.);
$-N{=}NC_6H_5$			CH_3	166–168°		741 (m.p.);
CH_3			$-N{=}NC_6H_5$	175–177°		741 (m.p.);
NH_2	CH_3	C_6H_5		200–210°	picrate, m.p. 260°	222 (m.p.), (u); 292 (m.p.), (u);
	CH_3	C_6H_5	NH_2	190–195°	*N*'-acetyl m.p. 110–112°	221 (m.p.); 222 (m.p.), (n); 292 (m.p.), (u); 221 (m.p.);
$NHCH_3$	CH_3	C_6H_5		200°		222 (m.p.), (n), (u);
	CH_3	C_6H_5	$NHCH_3$	155–156°		225 (m.p.), (u);
$-N{=}NC_6H_4NO_2$-*p*	CH_3	C_6H_5		230–235°		292 (m.p.);
	CH_3	C_6H_5	$-N{=}NC_6H_4NO_2$-*p*	261–269°		292 (m.p.);
$NHCOC_6H_5$	CH_3	C_6H_5			picrate, m.p. 213°	292 (m.p.);
	CH_3	C_6H_5	$NHCOC_6H_5$	216–217°		221 (m.p.), (u); 292 (m.p.);
	CH_3	C_6H_5	$-\underset{\underset{CH_3}{\vert}}{N}COC_6H_5$	150–151°		225 (m.p.), (i), (u);

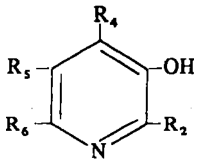
TABLE XII-52. 3-Pyridinol Carboxylic Acids and Derivatives



R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CHO				79–80°		513 (m.p.), ([illegible]; 524 (n); 1077 (i);
	CHO			133–134°		513 (m.p.), [illegible]; 524 (n); 107[illegible] ([illegible]);
			CHO			1078 (u);
	COOH				ethyl ester, m.p. 43–45°	595 (m.p.), (n);
			COOH			176 (i);
COO×			CH_3	235°		1047 (m.p.);
	CHO	CH_2OH				204 (u); 1155 (u);
					hydrochloride, m.p. 144–147°	204 (m.p [illegible] (f);
CH_3	COOH				ethyl ester, m.p. 51–54°	209 (m.p.), (i);
CH_3		COOH			ethyl ester, m.p. 201–202°	199 (m.p.), (n), (u); 211 (m.p.), (f), (i); 1079 (m.p.);
					amide, m.p. 305°	211 (m.p.);
					hydrazide, m.p. >330°	211 (m.p.);
CH_3		$COOC_2H_5$			*O*-acetyl, m.p. 201–202°	199 (m.p.), (n);

	CHO	$CH_2OPO_3H_2$			hydrate	204 (f);
CH_3	CHO	CHO		150–160"		203 (m.p.), (n), **(u);**
					$HCl\cdot H_2O$,	203 (m.p.);
					m.p. 158–161°	1066 (m.p.), **(u);**
CH_3	CH_2OH	CHO			lactone,	
					m.p. 275–277°	1059 (m.p.);
CH_3	COOH	COOH		270–272° or		199 (m.p.), **(i), (u);**
				252–254°		1064 **(m.p.);**
					dimethyl ester,	
					m.p. 140–141"	**205** (m.p.);
					diethyl ester,	
					b.p. 130°/	200 (b.p.); **205** (b.p.);
					0.5 mm	1057 (b.p.);
					diethyl	
					ester·HCl	
					m.p. 143–144"	199 (m.p.);
						200 **(m.p.);** 211 (m.p.),
						(f); 1057 (m.p.);
						1058 (m.p.);
						1064 (m.p.);
	COOH	**COOH**	**CH_3**	**239°**		197 **(m.p.), (u);**
–CH=NCH$_2$COOH					potassium salt	1077 (i);
	–CH=NCH$_2$COOH				potassium salt	1077 (i);
CH_3	**CHO**	**CH_3**				1088 (m), (n);
CH_3	CHO	CH_2OH				***204*** (u); 524 (n);
						527; 1081 (n);
					hydrochloride	1045 (i);
	CHO	CH_2OH	**CH_3**			204 (u);
					hydrochloride,	
					m.p. > 170"	***204*** (m.p.), (f);
CH_3	**CH_3**	COOH			ethyl ester,	
					m.p. 146–148"	212 (m.p.), **(i);**
CH_3	COOH	CH_2OH		256°		**1053** (m.p.);
					cation	***525*** (h), (u);
CH_3	**CHO**	$CH_2OPO_3H_2$				527; 1045 (i);
						1061 (u); 1082 (n);

TABLE XII-52. 3-Pyridinol Carboxylic Acids and Derivatives (Continued)



R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_2COOH	COOH	COOH			triethyl ester·HCl, m.p. 124–125°	1064 (m.p.);
CH_3	COOH	COOH	CH_3	269–270"		197 (m.p.), (u);
	COOH	COOH	C_2H_5	240–241"	diethyl ester, m.p. 145–147°	209 (m.p.); 197 (m.p.);
$-\mathrm{CH{=}N}\underset{\mathrm{CH_3}}{\mathrm{CH}}\mathrm{COOH}$					potassium salt	1077 (i);
	$-\mathrm{CH{=}N}\underset{\mathrm{CH_3}}{\mathrm{CH}}\mathrm{COOH}$				potassium salt	1077 (i);
CH_3	CHO	CH_2OH	CH_3	>170"		204 (m.p.), (f);
CH_3	CHO	$-\underset{\mathrm{OH}}{\mathrm{CH}}\mathrm{CH_3}$			hydrochloride, m.p. 106–107"	204 (m.p.);
CH_3	CHO	$-CH_2OPO_3H_2$	CH_3			204 (f);
CH_3	CHO	CH_2CH_2COOH		191–192"		1080 (m.p.), (i), (n), (t);
					oxime, m.p. 211–212°	1080 (m.p.);
	COOH	COOH	$CH_2CH_2CH_3$	216–217°		197 (m.p.);
CH_3	COOH	COOH	CH_2CH_3	233–235°		197 (m.p.);
isoC_3H_7	CHO	CH_2OH			hydrochloride, m.p. 119–121"	204 (m.p.), (f);
CH_3	CHO	$-CH(OCH_3)_2$		58–59"		1066 (m.p.), (u);

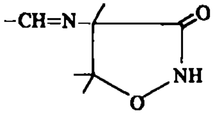
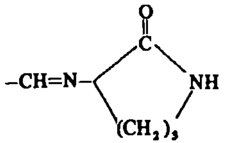
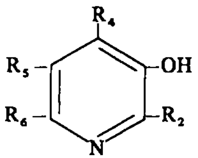
CH_3	$-CH=NOCH_3$	$-CH=NOCH_3$		106–107°		1066 (m.p.), (u);
CH_3	CH_2NH_2	CH_2CH_2COOH			di-HCl	1080 (i), (u);
CH_3	$-CH=NOH$	$-CH(OCH_3)_2$		195–197°		1066 (m.p.), (u);
$-CH=NCHCOOH$ $(CH_2)_2COOH$					dipotassium salt	1077 (i);
	$-CH=NCHCOOH$ $(CH_2)_2COOH$				dipotassium salt	1077 (i);
	$COOH$	$COOH$	$n\text{-}C_4H_9$	198–199°		197 (m.p.);
CH_3		CH_2OH				1081 (n);
$-CX=NCXCOOH$ $CX(CH_3)_2$					potassium salt	1077 (i);
	$-CH=NCHCOOH$ $CH(CH_3)_2$				potassium salt	1077 (i);
$n\text{-}C_4H_9$	CHO	CH_2OH			hydrochloride, m.p. 63–64°	204 (m.p.), (f);
CH_3	$-CH=NCHCOOH$ CH_2CH_2OH	CH_2OH				1081 (n);
	$COOH$	$COOX$	$n\text{-}C_5H_{11}$	181–183°		197 (m.p.), (u);
CH_3		CH_2OH		163–165°		1083 (m.p.);
CH_3	$COOH$	$COOH$	$n\text{-}C_5H_{11}$	213–214°		197 (m.p.), (u);
CH_2COOH	$CH(OCH_3)_2$	$CH(OCH_3)_2$			ethyl ester, b.p. 139–142°	1064 (b.p.);

TABLE XII-52. 3-Pyridinol Carboxylic Acids and Derivatives (Continued)



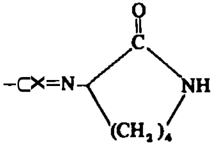
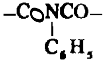
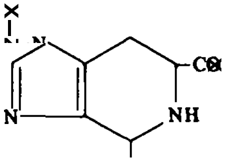
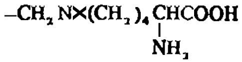
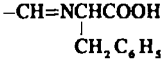
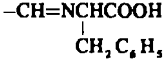
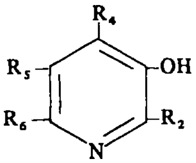
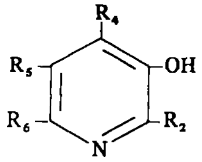
R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3		CH_2OX		Z11 213		1083 (m.p.);
CH_3	 $-CONCO-$ over C_6H_5			ZZ9 2 8°		209 (m.p.), (i);
CH_3		CH_2OH				1081 (n);
CH_3	 $-CH_2NX(CH_2)_4\underset{NH_2}{CHCOOH}$	H_2OX		214–215°		1084 (m.p.);
 $-CH=N\underset{CH_2C_6H_5}{CHCOOH}$					potassium salt $\cdot H_2O$	1077 (i);
	 $-CH=N\underset{CH_2C_6H_5}{CHCOOH}$				potassium salt $\cdot H_2O$	1077 (i);

TABLE XII-53. 3-Pyridinol Nitriles



R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3		CN		246–247"		209 (m.p.), (i); 211 (m.p.), (i), (f); 1079 (m.p.);
CH_3	CN	CN		187–191" or 120–125"	hydrate, m.p. 89°	199 (m.p.); 201 (m.p.), (u); 205 (m.p.); 1064 (m.p.), (i), (u); 205 (m.p.);
CH_3		CN	CH_3	249–251"		209 (m.p.), (i);
CH_3	CN	CH_2OH			hydrochloride, m.p. 186–190"	205 (m.p.); 207 (m.p.);
CH_2COOH	$-\underset{\underset{NH}{\Vert}}{C}OC_2H_5$	CN			ethyl ester, m.p. 164–166"	1064 (m.p.);

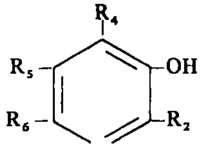
TABLE XII-54. Halo 3-Pyridinols



R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
Cl				169–170°		418 (m.p.);
		Cl		158"		317 (m.p.);
Br				185–186"		583 (n), (u); 708 (m.p.);
		Br		165–166"		319 (m.p.);
Br			Br	168–169"		708 (m.p.);
I			I	198–199"		298 (m.p.);
	I		I	230"		298 (m.p.), (n);
I	I		I	153–154"		599 (m.p.);
Br	Br		CH_3	107–109"		583 (m.p.), (n), (u);
Br			CH_3	187–189"		583 (m.p.), (i), (n), (u);
I			CH_3	174"		583 (m.p.), (i), (n), (u);
C, H_4Cl-*p*			I	162–163"		709 (m.p.), (n);
					hydrochloride, m.p. 180–181"	709 (m.p.);

[illegible]	I	15 8 159°		709 (m.p.), (n);
			hydrochloride, m.p. 165–166°	709 (m.p.);
$C_6H_4CH_3$-*p*	I	167–168°		709 (m.p.), (n);
			hydrochloride, m.p. 175–176°	709 (m.p.);
$C_6H_4OCH_3$-*p*	I	171–172°		709 (m.p.);
			hydrochloride, m.p. 187–188°	709 (m.p.);
$C_6H_4C_2H_5$-*p*	I	147–148°		709 (m.p.), (n);
			hydrochloride, m.p. 168–169°	709 (m.p.);
$C_6H_4CH(CH_3)_2$-*p*	I	144–145°		709 (m.p.), (n);
			hydrochloride, m.p. 170–171°	709 (m.p.);
$C_6H_4C(CH_3)_3$-*p*	I	140–141°		709 (m.p.);
			hydrochloride, m.p. 185–186°	709 (m.p.);

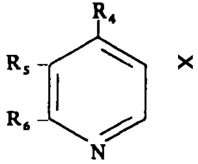
TABLE XII-55. Nitro and Nitroso 3-Pyridinols



R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
NO_2				67-69"		515 (n); 647 (m.p.), (n), (u); 648 (u);
					0-acetyl, m.p. 50–51"	647 (m.p.);
					b.p. 101°/0.03 mm	647 (b.p.);
					m.p. 76–77"	1085 (m.p.), (b.p.);
					ammonium salt, m.p. 142–145"	1086 (m.p.);
					magnesium salt, m.p. 330"	1086 (m.p.);
					sodium salt, m.p. 300°	1086 (m.p.);
	NO_2			132"		256a (m.p.); 261 (m.p.);
			NO_2	213–215"		647 (m.p.), (c), (n), (w);
					0-acetyl, m.p. 111–112"	647 (m.p.);
Cl	NO_2			70–71°		647 (m.p.), (n), (u);
Cl			NO_2	197"		647 (m.p.), (n), (u);
NO_2			NO_2			647 (n), (u);
CH_3	NO_2		NO_2	90-91"		719 (m.p.), (n);
NO_2		CH_3		133-135"		647 (m.p.), (n), (u);
NO_2			CH_3	175-176"		719 (m.p.), (n);

CH_3	NO_2			182–185°		515 (n); 647 (m.p.), (n), (u); 714 (m.p.), (n); 718 (m.p.), (n);
CH_3			NO_2	262–263°		515 (n); 647 (m.p.), (n), (u); 714 (m.p.); 718 (m.p.); 719 (m.p.), (n);
CH_3	CH_3	NO_2		155°		379 (m.p.);
CH_3	NO_2		CH_3	137–138°		295 (m.p.), (i); 719 (m.p.), (n);
CH_3		NO_2	CH_3	208°		379 (m.p.);
	CH_3	NO_2	CH_3	200°		379 (m.p.), (i);
n-C_3H_7			NO_2		ammonium salt, m.p. 116–117°	719 (m.p.);
isoC_3H_7			NO_2		ammonium salt, m.p. 164–166°	719 (m.p.);
CH_3	CH_3	NO_2	CH_3	170°		379 (m.p.), (i);
C_2H_5	NO_2		CH_3	129–130°		719 (m.p.), (n);
n-C_3H_7	NO_2			86–87°		714 (m.p.), (n); 718 (m.p.), (n); 719 (m.p.); 726 (m.p.);
					ammonium salt, m.p. 116–117°	719 (m.p.);
isoC_3H_7	NO_2			66–67°		714 (m.p.), (n); 718 (m.p.), (n); 719 (m.p.); 726 (m.p.);
					ammonium salt, m.p. 116–117°	719 (m.p.);
n-C_3H_7			NO_2	162–163°		714 (m.p.), (n); 718 (m.p.);
isoC_3H_7			NO_2	160–162°		714 (m.p.), (n); 718 (m.p.);
NO_2			$CH_2N(CH_3)_2$		ammonium *salt,* m.p. 181–182°	725 (m.p.), (n);
NO_2			$CH_2CH_2N(CH_3)_2$	88–89°		726 (m.p.);
$CH_2CH_2N(CH_3)_2$	NO_2			143–144°		726 (m.p.), (n);
n-C_4H_9	NO_2		CH_3	39–40°		719 (m.p.), (n);
isoC_4H_9	NO_2		CH_3	63–65°		719 (m.p.), (n);
isoC_5H_{11}	NO_2			72–73°		714 (m.p.), (n); 718 (m.p.) (n); 719 (m.p.);
isoC_5H_{11}			NO_2	200–202°		714 (m.p.), (n); 718 (m.p.);

TABLE XII-55. Nitro and Nitroso 3-Pyridinols (Continued)



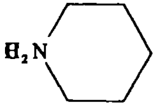
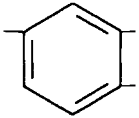
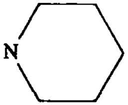
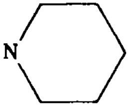
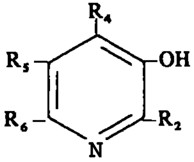
R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
NO_2			$CH_2N(C_2H_5)_2$	128–129°		725 (m.p.), (n);
C_6H_4NO-*p*			NO_2	160–161°		710 (m.p.), (n);
NO						
NO			H_2N 		ammonium salt, m.p. 172–173°	725 (m.p.), ( );
$H_2CCH_2N(C_2H_5)_2$	NO			113–114°		72[illegible] (m.p.) (n);
			NO	159–160°		711 (m.p.), (n);
NO	CH_3	C_6H_5	NH_2			
NO_2			$-CH_2CH_2N$ 			
$-CH_2CH_2N$ 	NO_2			210°	dihydrochloride m.p. 125–127°	726 (m.p.), (n); 726 (m.p.); 726 (n)
$-CH(CH_2N(CH_3)_2)_2$	NO_2					

TABLE XII-56. Sulfur containing 3-Pyridinols



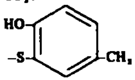
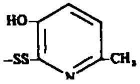
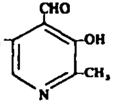
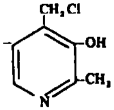
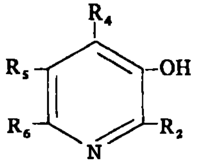
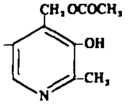
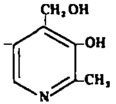
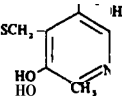
R$_2$	R$_4$	R$_5$	R$_6$	m.p.	Derivatives	Ref.
SH				144–145°		583 (m.p.), (n), (u);
SO$_3$H				300–302°		317 (m.p.); 320 (m.p.);
			CH$_3$	200–206°		416 (m.p.);
			CH$_3$	209–210°		583 (m.p.), (n), (u);
SH			CH$_3$	174–177°		583 (m.p.), (n), (u);
		CSNH$_2$		259–260°		211 (m.p.);
–CH=NNHCSNH$_2$						1078 (u);
			–CH=NNHCSNH$_2$			1078 (u);
SC$_2$H$_5$				88–90°		416 (m.p.);
	CH$_2$SH	CH$_3$			hydrochloride, m.p. 194°	1087 (m.p.);
SCH$_3$			CH$_3$	127–129°		597 (m.p.), (u);
CH$_3$	CHO	–CH$_2$SCH$_2$– 		169°		1060 (m.p.);
CH$_3$	–CH$_2$Cl	–CH$_2$SCH$_2$– 			di-HCl m.p. 205°	1088 (m.p.);
–SCH$_2$COOH			CH$_3$		hydrobromide, m.p. 168–170°	597 (m.p.), (u);

TABLE XII-56. Sulfur containing 3-Pyridinols (Continued)



R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	CH_2OCOCH_3	CH_2SCH_2– 			di-HCl, m.p. 1%'	1088(m.p.);
CH_3	CH_2OH	–CH_2SSCH_2– 		222'		**1089 (m.p.);** **1090 (m.p.), (f), (i), (u);**
CH_3	CH_2SSCH_2– 	CH_2OH		207–20k		**1091 (m.p.), (f), (u);**
CH_3	CH_2OH	CH_2SSO_3H			**sodium salt·$3H_2O$** m.p. 192'	**1090 (m.p.), (f), (i);**
CH_3	**–CH=NOH**	CH_2SO_2H		207–209'		**1092 (m.p.), (u);**
SC_2H_5			CH_3	47–49°	hydroiodide, m.p. 126–128°	597(m.p.), (u); 597 (m.p.);
CH_3	CH_2SH	CH_3			**hydrochloride,** m.p. 194'	1060(m.p.); 1051 (e);
CH_3	CH_2SH	CH_2SH				583(m.p.);
SCH_2CH_2OH			CH_3	102–104°	hydrochloride, m.p. 135–141°	**583 (m.p.);**
CH_3	CH_2SH	CH_2OH			hydrochloride, **m.p. 174–180°** **3,4,5-triacetate,** **m.p. 64'** **4,5-diacetate,** **m.p. 116°**	1051 (e); **1055 (e);** 1063(m.p.); 1087(m.p.); **1091 (m.p.);** 1063 (m.p.); 1063(m.p.);

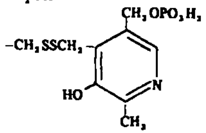
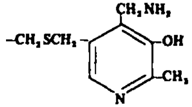
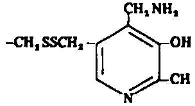
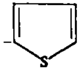
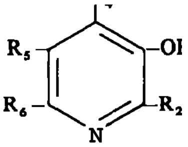
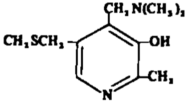
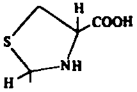
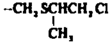
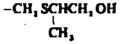
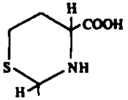
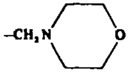
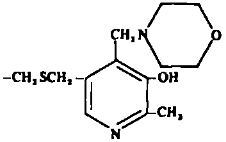
CH$_3$	CH$_2$OH	CH$_2$SH			1051 (e); 1055 (e);
CH$_3$		CH.OPO			1091 (f), (i), (u);
CH$_3$	CH$_2$OH	CH$_2$SO$_4$H	209–211°		1092 (m.p.);
CH$_3$	CH$_2$NH$_2$		tetra-HCl, m.p. 290–291°		1060 (m.p.);
CH$_3$	CH$_2$NH$_2$		210°		1091 (m.p.), (f);
				tetra-HCl m.p. 233–235°	1089 (m.p.); 1093 (m.p.);
CH$_3$	CH$_2$NH$_2$	CH$_2$SSO		sodium salt m.p. 118°	1091 (m.p.), (f), (i);
CH$_3$	CH$_2$SH	CH$_2$NH$_2$		di-HBr·2H$_2$O m.p. 198°	1063 (m.p.);
CH$_3$	CH$_2$NH$_2$	CH$_2$SH		3,4,5-triacetate, m.p. 178°	1063 (m.p.); 1087 (m.p.);
				5-acetyl, m.p. 194–195°	1093 (m.p.);
CH$_3$	CH$_2$NH$_2$	CH$_2$SO$_4$	220–221°		1092 (m.p.), (f);
CH$_3$	CH$_2$OH	CH.CNS	155–156°		1090 (m.p.), (f), (i);
S(CH$_2$)$_2$CH$_3$				dihydrate, m.p. 112°	1091 (m.p.), (f);
CH$_3$	CH$_2$SH	$_2$OCH	92–95°		416 (m.p.);
				hydrochloride, m.p. 144–146°	1063 (m.p.);
CH$_3$	CH$_2$OCH$_3$	CH$_2$SH		3,4-diacetate, m.p. 88°	1063 (m.p.);
CH$_3$	CH$_2$OH	CH$_2$SO		hydrochloride, b.p. 169–170°	1063 (m.p.);
CH$_3$	$-CH_2S\overset{}{C}NH_2$ $\|$ NH	CH.OH	219°		1094 (m.p.);
				di-HBr, m.p. 161–163°	1052 (m.p.);
	CH$_3$		206–207°		186 (m.p.);
CH$_3$	–CH=NNHCSNH$_2$		172–174°		1066 (m.p.);

TABLE XII-56. Sulfur containing 3-Pyridinols (Continued)



R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	CH_3	$CH_2SCH_2CH_2Cl$			hydrochloride, m.p. 150–152°	1070 (m.p.);
CH_3	CH_3	$CH_2SCH_2CH_2OH$		140–142°	hydrochloride, m.p. 180–182°	1070 (m.p.); 1070 (m.p.);
CH_3	CH_2OH	$CH_2SCH_2CH_2OH$			hydrochloride, m.p. 146–148°	1070 (m.p.);
CH_3	$CH_2N(CH_3)_2$			150°	tetra-HCl·4H₂O, m.p. 140°	1088 (m.p.);
CH_3		CH_2OH				1081 (n);
CH_3	CH_3	 $-CH_2S\underset{\mid \atop CH_3}{C}HCH_2Cl$			hydrochloride, m.p. 128–132°	1070 (m.p.);
CH_3	$-CH_2NH_2$	$-CH_2(C_2H_4OCS_2)$			di-HBr m.p. >230°	1093 (m.p.);
$S(CH_2)_4CH_3$			CH_3	34° b.p. 120°/1.5 mm		597 (m.p.), (b.p.), (u);
CH_3	CH_3	 $-CH_2S\underset{\mid \atop CH_3}{C}HCH_2OH$		143–146°		1070 (m.p.);
CH_3			$-N{=}NC_6H_4SO_3H$	none		741;
CH_3		CH_2OH				1081 (n);
CH_3				200°	tetra-HCl m.p. 260°	1060 (m.p.); 1088 (m.p.);

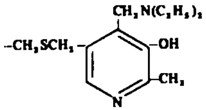
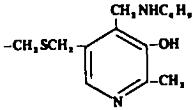
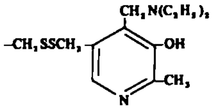
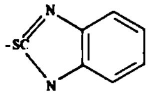
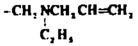
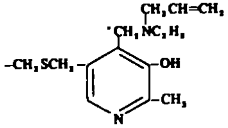
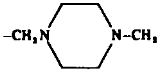
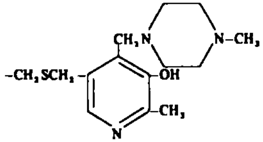
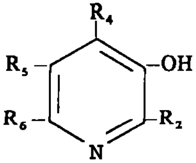
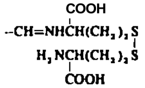
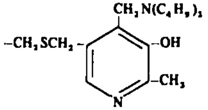
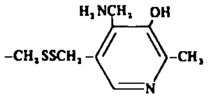
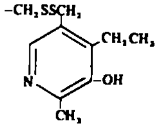
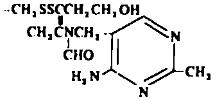
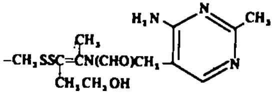
CH_3	CH_2OH	$-CH(SC_2H_5)_2$		99–100°	 3,4-diacetyl ·HCl, m.p. 132°	1066 (m.p.), (u); 1066 (m.p.), (u);
CH_3	$-CH_2N(C_2H_5)_2$			112°	 tetra-HCl, m.p. 220°	1060 (m.p.); 1088 (m.p.);
CH_3	$CH_2NHC_4H_9$				tetra-HCl, m.p. 252°	1060 (m.p.);
CH_3	$-CH_2N(C_2H_5)_2$					1093;
			CH_3	235–240°		416 (m.p.);
$-SC_6H_4CH_3$-*p*			CH_3	139–141°		597 (m.p.), (u);
CH_3	 $-CH_2\underset{C_2H_5}{N}CH_2CH=CH_2$			17°		1088 (m.p.);
CH_3				40°		1088 (m.p.);
CH_3	CH_3	$CH_2SC_6H_4Cl$-*p*		164–167°	 hydrochloride, m.p. 199–202°	1070 (m.p.); 1070 (m.p.);
CH_3	CH_2OH	$CH_2SC_6H_4Cl$-*p*			hydrochloride, m.p. 153–155°	1070 (m.p.);

TABLE XII-56. Sulfur containing 3-Pyridinols (Continued)



R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	CH_2SH	$CH_2OCOC_6H_5$		182–184°		1063 (m.p.);
					3,4-diacetyl, m.p. 142–143°	1063 (m.p.);
CH_3	 $\overset{COOH}{-CH{=}NHCH(CH_2)_2S}$ $\underset{COOH}{H_2NCH(CH_2)_2S}$	CH_2OH				1081 (n);
CH_3	$CH_2N(C_4H_9)_2$				tetra-HCl, m.p. 220"	1088 (m.p.);
CH_3	CH_2NH_2				233–255°	1095 (m.p.);
CH_3	CH_2CH_3			226221'		1095 (m.p.);
CH_3		$-CH_2OH$			di-HCl·1/2H_2O, m.p. 17k	1096 (m.p.);
CH_3	CH_2OH				di-HCl m.p. 187–188°	1096 (m.p.), (i), (u);
					di-HBr, m.p. 180–181°	1096 (m.p.);

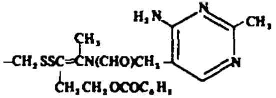
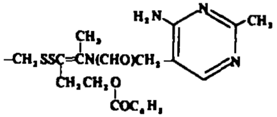
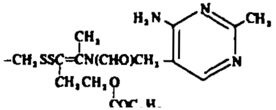
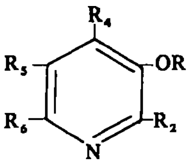
CH_3	CH_2NH_2		170–173°	1096 (m.p.), (i);
CH_3	CH_3		172°	1096 (m.p.);
CH_3		$-CH_2OH$	162°	1096 (m.p.), (i);

TABLE XII-57. Ethers and Esters of Alkyl and Aryl 3-Pyridinols



R	R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3					b.p. 68°/12 mm		525 (h), (u); 594 (b.p.), (u); 964 (j), (w); 1042 (n);
						hydrochloride, m.p. 160–161°	594 (m.p.);
						picrate, m.p. 136–139°	594 (m.p.);
CH_3	CH_3						515 (n);
$-CH_2CH_2{=}CH_2$					b.p. 90°/10 mm		595 (b.p.), (n); 598 (b.p.), (i);
						picrate, m.p. 56–58°	595 (m.p.);
CH_3	CH_3	CH_2OH	CH_2OH				1048 (n);
2-Pyridyl					30–31°		992 (m.p.);
					b.p. 97°/7 mm	picrate, m.p. 163–164°	273 (m.p.); 992 (m.p.);
$COCH(CH_3)_2$		CH_3					387 (b.p.), (n);
						picrate, m.p. 148–149°	387 (m.p.);
$-(CH_2)_4CH_3$					b.p. 116°/9 mm		596 (b.p.);
β-D-Glucosyl					187–188°		603 (m.p.), (f);
						tetraacetyl, m.p. 141–142°	603 (m.p.);
$-COC_6H_5$					49–50°		342 (m.p.);
					b.p. 168°/12 mm		637 (b.p.), (m.p.);
						picrate, m.p. 153–154°	342 (m.p.);
						$AgCl_3$ double salt, m.p. 175-176	342 (m.p.);
CH_3	$-COC_6H_4Cl$-*p*				90–93°		191 (m.p.);
CH_3	$-COC_6H_5$				bp. 140°/1 mm		191 (b.p.);
						hydrochloride,	191 (m.p.); 1071 (m.p.);
CH_3	$-CH_2C_6H_4Cl$-*p*				74–76°		191 (m.p.);
CH_3	$-CH_2C_6H_5$				b.p. 120°/3 mm m.p. 46–47°		191 (b.p.), (m.p.); 1071 (b.p.), (m.p.);

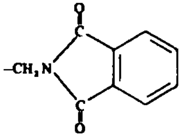
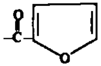
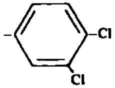
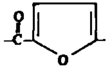
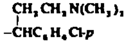
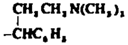
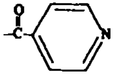
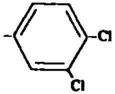
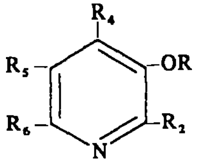
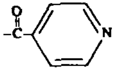
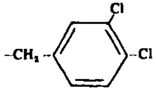
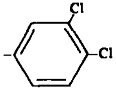
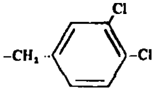
$-CH$				CH_3	27–29° b.p. 100°/0.05 m	hydrochloride, m.p. 189–190°	191 (m.p.); 6 (b.p.), (m.p.);
CH_3		CH_3	C_6H_5			hydrochloride, m.p. 152–155°	219 (m.p.), (u);
						picrate, m.p. 136–137°	219 (m.p.);
2-Quinol					98–99°		273 (m.p.);
						picrate, m.p. 176–178°	273 (m.p.);
1-Isoquin					40–42°		273 (m.p.);
						picrate, m.p. 195–196°	273 (m.p.);
					162–163°		193 (m.p.);
CH_3	CH_3	CH_2OH	$-CH_2OCH_2C_6H_5$			hydrochloride, m.p. 140–141°	1065 (m.p.);
		CH_3			151–152°		186 (m.p.);
	C_6H_4Cl-*p*	H			144°		186 (m.p.);
CH_3	 $-\overset{CH_2CH_2N(CH_3)_2}{\overset{\vert}{C}}HC_6H_4Cl\text{-}p$				b.p. 164°/1 mm		191 (b.p.);
						acid maleate, m.p. 124–127°	191 (m.p.);
	 $-\overset{CH_2CH_2N(CH_3)_2}{\overset{\vert}{C}}HC_6H_5$				b.p. 170°/2 mm		191 (m.p.);
						acid maleate, m.p. 124–126°	191 (m.p.);
		CH_3			119°		186 (m.p.);

TABLE XI-57. Ethers and Esters of Alkyl and Aryl 3-Pyridinols (Continued)



R	R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
$-\overset{O}{\overset{\|}{C}}C_6H_4N{=}NC_6H_4NO_2\text{-}p$							1097 (g);
	$C_6H_4Cl\text{-}p$	CH_3			181°		186 (m.p.);
CH_3	$-\underset{C_3H_7}{\underset{\|}{C}}HC_6H_5$				103–106°		191 (m.p.);
		CH_3			90–91°		186 (m.p.);
	$C_6H_4Cl\text{-}p$	CH_3			74°		186 (m.p.);
CH_3	$-\underset{C_6H_4Cl\text{-}p}{\underset{\|}{C}}HC_6H_5$				106–109°		191(m.p.);
CH_3	$-\underset{HO\quad C_6H_5}{C}C_6H_4Cl\text{-}p$				133–134°		191 (m.p.);
CH_3	$-CH(C_6H_5)_2$				120–122°		191 (m.p.);
CH_3	$-\underset{OH}{\underset{\|}{C}}(C_6H_5)_2$				129–131°		191 (m.p.);
CH_3	$-\underset{C_6H_{11}}{\underset{\|}{C}}HC_6H_5$				142–144°		191(m.p.);
CH_3	$-\underset{CH_2C_6H_5}{\underset{\|}{C}}HC_6H_5$				71–73°		191(m.p.);
C_2H_5	$-CH(C_6H_5)_2$				96–98.		191(m.p.);

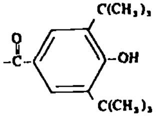
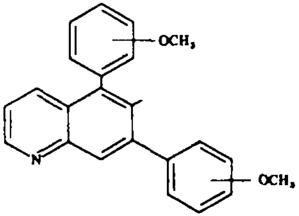
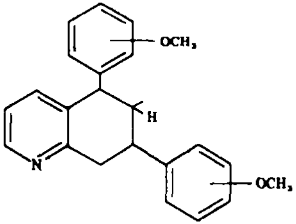
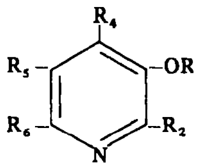
					176–177°		1013 (m.p.);
$CH_2C_6H_5$	CH_3	CH_2Cl	$-CH_2OCH_2C_6H_5$			hydrochloride, m.p. 145–148° picrate, m.p. 154–155°	1065 (m.p.); 1065 (m.p.);
$CH_2C_6H_5$	CH_3	CH_2OH	$-CH_2OCH_2C_6H_5$		68–69°		1053 (m.p.); 1065 (m.p.);
C_6H_5	C_6H_5			C_6H_5	91–95°		1098 (m.p.);
$CH_2C_6H_5$	CH_3	$-\underset{OH}{CH}CH_3$	$-CH_2OCH_2C_6H_5$		83–84°		1053 (m.p.); 1065 (m.p.), (n);
$CH_2C_6H_5$	CH_3	$-(CH_2)_3OH$	$-CH_2OCH_2C_6H_5$		64–65°		1065 (m.p.);
$CH_2C_6H_5$	CH_3	$-\underset{OH}{CH}C_6H_5$	$-CH_2OCH_2C_6H_5$		102–104°		1065 (m.p.), (n);
C_6H_4Cl-*p*	C_6H_5	C_6H_5		C_6H_4Br-*p*	171–173°		74 (m.p.);
C_6H_4Cl-*p*	C_6H_5	C_6H_5		C_6H_5	177–179°		74 (m.p.); 1098 (m.p.);
CH_3							600 (t);
CH_3					179–180.		600 (m.p.);

TABLE XII-58. Ethers and Esters of Amino 3-Pyridinols



R	R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
C_2H_5			$-NHNO_2$		160"		319 (m.p.);
C_2H_5			$-NH_2$		6"	picrate, m.p. 189–191"	319 (m.p.); 319 (m.p.);
C_2H_5				$-NH_2$	47–48°	hydrochloride, m.p. 143–145° picrate, m.p. 240–241° *N*'-acetyl, m.p. 108–109"	292 (m.p.); 292 (m.p.); 292 (m.p.); 292 (m.p.);
$-CH_2C{\equiv}CH$	$-NH_2$				b.p. 91°/0.2 mm m.p. 58–59"		596 (b.p.), (m.p.);
$-CH_2CH{=}CH_2$	$-NH_2$				b.p. 82–83" m.p. 42–44°		596 (b.p.), (m.p.);
$-CH_2CH(OCH_3)_2$	$-NH_2$				b.p. 111°/0.3 mm		596 (b.p.);
$-(CH_2)_3N(CH_3)_2$	$-NH_2$				b.p. 112°/0.2 mm m.p. 67–69°		596 (b.p.), (m.p.);
$-CH_2C_6H_5$	$-NH_2$				b.p. 150°/0.05 mm m.p. 96–97"		596 (b.p.), (m.p.);
$-COC_6H_5$				$-N(COC_6H_5)_2$	m.p. 182–183°		292 (m.p.), (i), (u);
$-COC_6H_5$		CH_3	C_6H_5	$-NHCOC_6H_5$	m.p. 198–200°		222 (m.p.), (i); 292 (m.p.), (i);
COC_6H_5	$NHCOC_6H_5$	CH_3	C_6H_5		195–196°		292 (m.p.);
COC_6H_5	$-N(COC_6H_5)_2$	CH_3	C_6H_5		182"		292 (m.p.), (i);

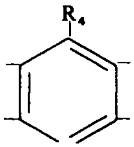
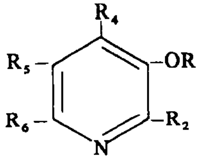


TABLE XII-59. Ethers and Esters of 3-Pyridinol Carboxylic Acids and Derivatives

R	R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
COOH						ethyl ester	659 (u);
CH_3	CHO						513 (i); 1077 (i);
CH_3		CHO			36–37"		513 (m.p.), (i); 1017 (i);
CH_3	COOH					amide, m.p. 198–200° methyl ester, b.p. 85°/0.1 mm	596 (m.p.); 596 (b.p.);
$-CH_2COOH$						ethyl ester, b.p. 118°/1 mm diethylamide, b.p. 137°/0.4 mm diethylamide·HCl m.p. 140–142°	595 (b.p.), (n); 596 (b.p.); 596 (m.p.);
$-CH_2COOH$	$COOCH_3$					amide. m.p. 185–186° methyl ester, m.p. 18–79"	596 (m.p.); 596 (m.p.);
$-CH_2COOH$	$CONH_2$					methyl ester, m.p. 141–143° diethylamide, m.p. 134–135°	596 (m.p.); 596 (m.p.);
$-CH_2COOH$	$CONHC_2H_5$					methyl ester, m.p. 109–110"	596 (m.p.);
$-CH_2COOH$		$COOC_2H_5$				ethyl ester, Oil	595 (n);

TABLE XII-59. Ethers and Esters of 3-Pyridinol Carboxylic Acids and Derivatives (Continued)



R	R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
$-\underset{CH_3}{\underset{\mid}{CHCOOH}}$						ethyl ester, b.p. 86°/0.2 mm	595 (b.p.), (n);
CH_2COOH				CH_3		methyl ester, m.p. 50–51° ethyl ester, b.p. 111°/0.1 mm, m.p. 10° amide, m.p. 154–156°	596 (m.p.); 596 (b.p.), (m.p.); 596 (m.p.);
CH_2COOH	CH_2OH					amide, m.p. 157–158°	596 (m.p.);
$-\underset{CH_3}{\underset{\mid}{CHCOOH}}$		$COOC_2H_5$				ethyl ester, oil	595 (n);
$CH_2CH{=}CH_2$	$COOH$					amide, m.p. 125–126° N'-benzylamide, m.p. 72–73° N'-*p*-methoxybenzylamide, m.p. 74–75°	596 (m.p.); 596 (m.p.); 596 (m.p.);
$-\underset{C_2H_5}{\underset{\mid}{CHCOOH}}$	$CONH_2$					ethyl ester, m.p. 101–108°	596 (m.p.);
$-COOH$	CH_3	$-CH_2NHCOOC_2H_5$	$-CH_2OX$			ethyl ester, m.p. 70–71°	659 (m.p.);
$-(CH_2)_3CH_3$	$COOH$					amide, m.p. 109–110°	596 (m.p.);

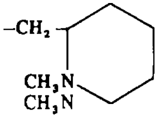
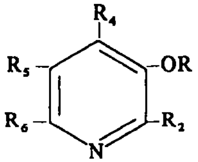
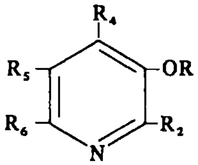
$-CH_2CH(CH_3)_2$	COOH				amide, m.p. 109-110°	596 (m.p.);
CH_3	$-CH{=}N\underset{\substack{\vert\\CH(CH_3)_2}}{C}HCOOH$				potassium salt	1077 (i);
CH_3		$-CH{=}N\underset{\substack{\vert\\CH(CH_3)_2}}{C}HCOOH$			potassium salt	1077 (i);
$-CH_2C_6H_5$	COOH				amide, m.p. 106-107"	596 (m.p.);
CH_3	$-\underset{\substack{\vert\\C_6H_5}}{C}HCOOH$				ethyl ester, b.p. 175°/2 mm m.p. 105-107"	191 (b.p.), (m.p.);
$-CH_2C_6H_5$	CH_3	CHO	$-CH_2OCH_2C_6H_5$	72"		1053 (m.p.);
					hydrate, m.p. 60-70°	1053 (m.p.);
					hemihydrate, m.p. 72°	1065 (m.p.), (n);
$-COCH_2NHCO-O-CH_2C_6H_5$				102"		654 (m.p.);
$CH_2C_6H_5$	CH_3	CH_2CH_2COOH	$CH_2OCH_2C_6H_5$		hemihydrate, m.p. 175-176°	1065 (m.p.);
$CH_2C_6H_5$	CH_3	$CH_2CH(COOH)_2$	$CH_2OCH_2C_6H_5$	173-174"	diethyl ester·HCl	1065 (m.p.);
					m.p. 109-110°	1065 (m.p.);

TABLE XII-60. Ethers of 3-Pyridinol Nitriles



R	R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	CN					111–113°	596 (m.p.);
$CH_2C_6H_5$	CN					99–101°	596 (m.p.);

TABLE XII-61. Ethers of Halo 3-Pyridinols



R	R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	Br				45° b.p. 123°/9 mm		596 (b.p.), (m.p.);
CH_3			Br		33–34°		705 (m.p.);
						hydrobromide, m.p. 178–180°	705 (m.p.);
CH_2COOH	I	I		I	202–203°		599 (m.p.);
						ethyl ester, m.p. 137–138°	599 (m.p.);
CH_2COOH	Br					methyl ester, m.p. 65–69°	596 (m.p.);

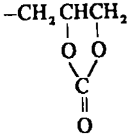
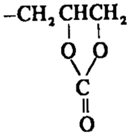
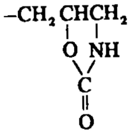
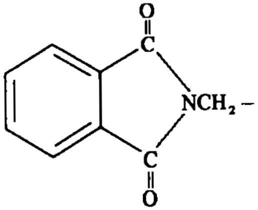
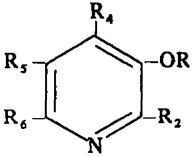
C_2H_5		Br	Br		67–69°	712 (m.p.);
$CONHCH_3$		Cl			128°	972 (m.p.);
CH_3	Br		CH_3		54°	597 (m.p.), (u);
C_2H_5		Br			8.2–8.8° b.p. 111°/5 mm	705 (b.p.), (m.p.);
	Cl				124–126°	596 (m.p.);
	Br				143–144°	596 (m.p.);
	Cl				136–138°	596 (m.p.);
$-CH_2COC_6H_5$	Br				105–107°	596 (m.p.);
CH_3		Cl			177–179°	193 (m.p.);

TABLE XII-62. Ethers and Esters of Nitro 3-Pyridinols



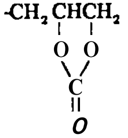
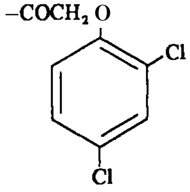
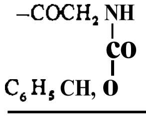
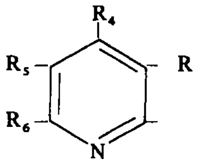
R	R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	NO_2						515;
CH_3		NO_2			46"		256a (m.p.); 261 (m.p.);
$CONHCH_3$	NO_2				132–135"		1085 (m.p.);
CH_3	NO_2			CH_3	88–89°		596 (m.p.);
CH_3	CH_3			NO_2	101–103"		714 (m.p.), (n);
C_2H_5		NO_2			40"		256a; 261 (m.p.);
	NO_2				162–164"		596 (m.p.);
	NO_2				109–1 13"		1085 (m.p.);
 $–COCH_2NH–CO–OCH_2C_6H_5$	$isoC_4H_9$	NO,		CH,	96–98"		654 (m.p.);

TABLE XII-63. Ethers and Esters of Sulfur Containing 3-Pyridinols



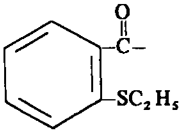
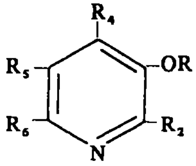
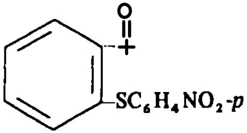
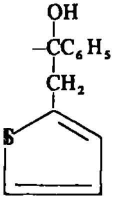
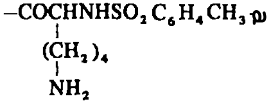
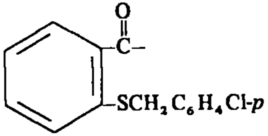
R	R₂	R₄	R₅	R₆	m.p.	Derivatives	Ref.
SO_3H	NO_2					potassium salt	648 (i), (u);
SO_3H							648 (i), (u);
SO_2CH_3					60° b.p. 103°/0.01 mm		649 (b.p.), (m.p.);
$COSCH_3$					47–48°		583 (m.p.);
$SO_2N(CH_3)_2$					b.p. 99°/0.25 mm		1099 (b.p.);
CH_2COOH	SCH_3			Cl		methyl ester, m.p. 74–75°	597 (m.p.), (i), (n), (u);
$SO_2C_6H_4Cl$-*p*	NO_2				75–77°		1085 (m.p.);
$COSC_6H_5$					60–62°		1100 (m.p.);
$S^{18}O_2C_6H_4CH$ -*p*					b.p. 170°/3 mm m.p. 78°		410 (b.p.), (m.p.);
					5 [illegible]		1101 (m.p.);
$-COCHCH(CH_3)_2$ $NHSO_2C_6H_4CH_3$-*p*					15[illegible]		656 (m.p.), (k);

TABLE XII-63. Ethers and Esters of Sulfur Containing 3-Pyridinols (Continued)



R	R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
						hydrochloride, m.p. 196°	1101 (m.p.);
H					127–129°		191 (m.p.);
 $-COCH(NHSO_2C_6H_4CH_3\text{-}p)(CH_2)_4NH_2$						hydrobromide, hygroscopic	655;
						hydrochloride, m.p. 195°	1101 (m.p.);

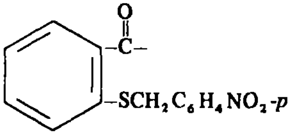
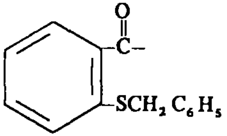
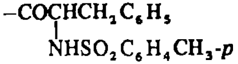
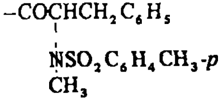
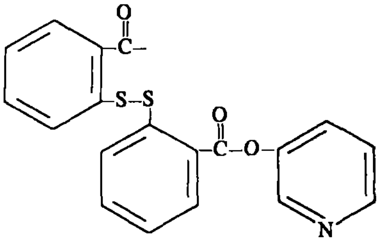
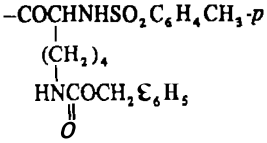
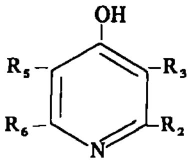
		hydrochloride, m.p. 196–197°	1101 (m.p.);
		hydrochloride, m.p. 154–155°	1101 (m.p.);
 $-\mathrm{CO}\underset{\mathrm{NHSO_2C_6H_4CH_3}\text{-}p}{\mathrm{C}}\mathrm{HCH_2C_6H_5}$		HCl·1/2H$_2$O, m.p. 173°	656 (m.p.), (k);
 $-\mathrm{CO}\underset{\underset{\mathrm{CH_3}}{\mathrm{N}}\mathrm{SO_2C_6H_4CH_3}\text{-}p}{\mathrm{C}}\mathrm{HCH_2C_6H_5}$		hydrochloride, m.p. 118° HCl·1/2H$_2$O m.p. 93°	656 (m.p.), (k); 656 (m.p.);
		dihydrochloride, m.p. >230°	1101 (m.p.);
 $-\mathrm{CO}\underset{\underset{\mathrm{HN\underset{O}{C}OCH_2Ɛ_6H_5}}{\mathrm{(CH_2)_4}}}{\mathrm{C}}\mathrm{HNHSO_2C_6H_4CH_3}\text{-}p$	96°		655 (m.p.);

TABLE XII-64. Alkyl and Aryl 4-Pyridinols



R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
H	H	H	H	148–149°		404 (f); 460 (m.p.), (i); 462 (i); 466 (i); 478 (i), (r); 486 (n); 537 (n); 648 (u); 659 (u); 735 (n); 819 (i); 899 (n); 900 (f); 901 (n); 902 (i); 904 (u); 905 (m.p.), (u); 906 (a); 909 (u); 910 (j); 911 (t); 912 (u); 915 (m); 918 (s); 1040 (f); 1102 (u); 1103 (i), (n); 1104 (u);
					picrate	1104 (u);
					^{15}N	462 (i);
					^{18}O	462 (i), (m);
					sodium salt	545 (i), (r); 921 (i);
					O-acetyl, m.p. 130–145°	404 (f); 414 (m.p.), (g), (i), (n);
					b.p. 120°/2 mm	747 (b.p.), (m.p.), (i), (u);
					O-acetyl, m.p. 80°	1105 (m.p.);
					$CoCl_2$ complex m.p. 219°	824 (m.p.), (i), (v);
					$Co(NH_3)_5$ complex	820 (i), (u);
					perchlorate	821 (i), (u);
					hydrochloride	536 (n); 1103 (i), (r);
					hydrate, m.p. 59–61°	1106 (m.p.);
					hexachloro-antimonate,	464 (m.p.), (i);
					m.p. 169–175°	542 (i);

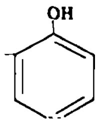
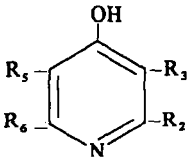
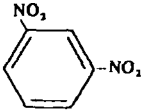
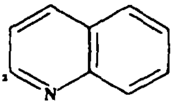
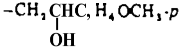
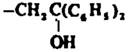
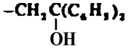
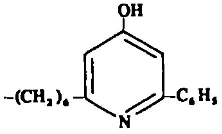
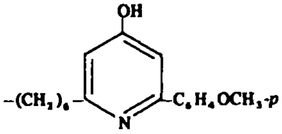
					hexachloro-stannate, m.p. 247–249°	464 (m.p.), (i);
					N-deuterio	460 (i), (r); 462 (i);
					N,O-D_2 chloride	1045 (i); 1103 (i), (r);
D	D	D	D			460 (i), (r); 1102 (u); 1103 (i);
					N,O-D_2 chloride	1103 (i), (r);
					hydrochloride	1103 (i), (r);
CH_3					nitrate, m.p. 157–161°	293 (m.p.);
	CH_3			92–98°		273 (m.p.); 278 (m.p.); 297 (m.p.); 789 (m.p.);
					picrate. m.p. 209–210°	273 (m.p.);
CH_3		CH_3		205–206°		297 (m.p.);
					picrate. m.p. 220–221°	297 (m.p.);
CH_3			CH_3	222–232°		25 (m.p.); 137 (m.p.), (n); 295 (m.p.);
					hydrochloride	536 (n);
CH_2OH			CH_3	225–227°		411 (m.p.);
C_2H_5			CH_3	118–119°		25 (m.p.);
	$Si(CH_3)_3$			174°		377 (m.p.), (i);
CH_3	$COCH_3$		CH_3	233–242°		69 (m.p.); 136 (m.p.), (u); 141 (m.p.);
					picrate, m.p. 172–174°	141 (m.p.);
						280 (i), (m), (u);
C_6H_5				156–157°		27 (m.p.);
	C_6H_5			228–230°		780 (m.p.);
C_6H_4Cl-*p*			CH_3	236–237°		29 (m.p.), (i), (u);
CH_3			C_6H_5	174–176°		25 (m.p.), (i), (u); 29 (m.p.);
					hydrochloride	40 (m.p.), (i), (u);
					m.p. 235–237°	40 (m.p.), (i), (u);

TABLE XII-64. Alkyl and Aryl 4-Pyridinols (Continued)



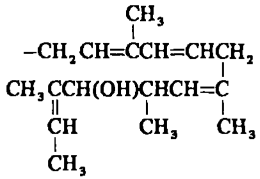
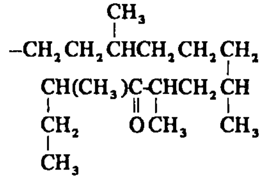
R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
	$-CH_2CH_2-$ 			191–192"		310 (m.p.);
C_3H_5			C_6H_5			**25 (m.p.), (i), (u);**
	$-CH_2CH_2C_6H_5$				hemihydrate, m.p. 162"	310 (m.p.);
$t\text{-}C_4H_9$			$t\text{-}C_4H_9$	170–172"		671 (m.p.);
					chloroaurate, m.p. 199–201"	**671 (m.p.);**
CH_3	$COCH_3$		$C_6H_4Br\text{-}p$	251°		**136 (m.p.), (u);**
CH_3	COC_6H_5		CH_3	257–258"		**69 (m.p.);**
CH_3	$COCH_3$		C_6H_5	214–215°		**135 (m.p.), (i), (m), (u);**
$isoC_3H_7$			C_6H_5	117–118"		**25 (m.p.), (i), (u);**
$-CH_2$ 			CH_3	315'		138 (m.p.), (i);
$C_6H_4Cl\text{-}p$			C_6H_5	208–212°		**29 (m.p.), (i), (u);**
C_6H_5			C_6H_5	175–179°		**29 (m.p.), (i), (u);** **40 (m.p.), (i), (n), (u);** **530 (m.p.);**
C_6H_5	$-CH_2C_6H_5$			247–248"		**27 (m.p.), (i), (u);**
$C_6H_4OCH_3\text{-}p$			C_6H_5	219–222"		**29 (m.p.), (i), (u);**
CH_3	COC_6H_5		C_6H_5	267–269°		**135 (m.p.), (i), (m), (u);**
C_6H_5			$-CH_2CH_2C_6H_5$	171–173"		**40 (m.p.), (u);**
$C_6H_4OCH_3\text{-}p$			$C_6H_4OCH_3\text{-}p$	274–275"		**26 (m.p.), (i);**

C_6H_5	 $-CH_2\underset{OH}{\underset{\vert}{C}}HC_6H_4OCH_3\text{-}p$	191–192"	30 (m.p.), (u);
n-Nonyl	C_6H_5	88–89"	25 (m.p.);
C_6H_5	 $-CH_2\underset{OH}{\underset{\vert}{C}}(C_6H_5)_2$	205–206°	30 (m.p.), (u);
$C_6H_4OCH_3\text{-}p$	 $-CH_2\underset{OH}{\underset{\vert}{C}}(C_6H_5)_2$	211–213°	30 (m.p.), (u);
	C_6H_5	247–248°	30 (m.p.), (u);
	$C_6H_4OCH_3\text{-}p$	300–301°	30 (m.p.), (u);

R_5-

R_6-

TABLE XII-65. Alkyloxy and Aryloxy 4-Pyridinols

R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	OCH_3			155–156°		125 (m.p.), (u);
CH_2OH		OCH_3		172°		794 (m.p.);
OCH_3	OCH_3		CH_2OH	94–95°		160 (m.p.), (i), (u);
					4,6-diacetyl, oil	160 (c), (i), (u);
	$OCH_2C_6H_5$			195–197°		134 (m.p.);
CH_3	β-D-Gluco-pyranosyloxy			116–118°		131 (m.p.); 858 (m.p.);
CH_2OH		$OCH_2C_6H_5$		224–226°		793 (m.p.);
OCH_3	OCH_3	CH_3	 $-CH_2CH{=}C(CH_3)CH{=}CHCH_2-$ $CH_3C(=CHCH_3)CH(OH)CH(CH_3)CH{=}C(CH_3)-$			59[illegible] ([illegible]), ( ); 87[illegible] ([illegible]);
OCH_3	OCH_3	CH_3	 $-CH_2CH_2CH(CH_3)CH_2CH_2CH_2-$ $CH(CH_2CH_3)C(=O)CH(CH_3)CH_2CH(CH_3)-$	*O*-acetyl		8≤9 (m);

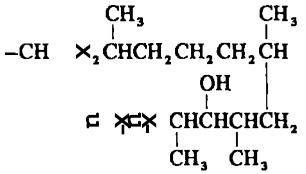
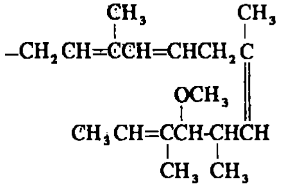
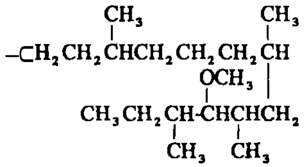
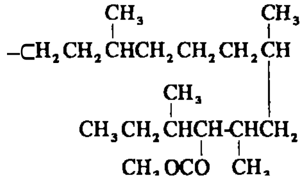
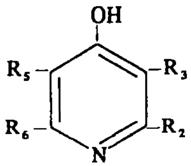
OCH_3	OCH_3	CH_3		O-acetyl	869 (m);
OCH_3	OCH_3	CH_3			871 (i), (n); 872 (i), (k), (n), (o);
				O-acetyl	872 (i), (k), (o);
OCH_3	OCH_3	CH_3		O-acetyl	872 (m);
OCH_3	OCH_3	CH_3		O-acetyl	869 (m);

TABLE XII-67. 4-Pyridinol Carboxylic Acids and Derivatives



R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
COOH					ethyl ester·HCl m.p. 126–128"	1107 (m.p.);
	COOH			250–255°		101 (m.p.), (u); 789 (m.p.), (u);
					amide, m.p. 263"	789 (m.p.), (i), (u);
					methyl ester	101 (u);
					ethyl ester, m.p. 228–230°	100 (m.p.);
					methyl ester-4-acetyl	101 (u);
COOH			COOH		diamide, m.p. 320–322"	456 (m.p.);
					dimethyl ester, m.p. 170–171"	456 (m.p.), (i), (n), (u);
					diethyl ester, m.p. 120–121°	1107 (m.p.);
	COOH	COOH			dimethyl ester, m.p. 262–264°	100 (m.p.);
CHO		**OCH_3**		176–178"		1108 (m.p.);
COOH		**CH_3**		225–226"		297 (m.p.);
					amide, m.p. 221–222°	297 (m.p.);

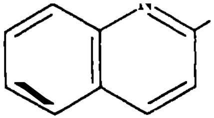
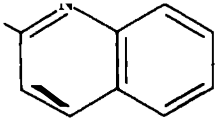
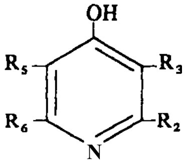
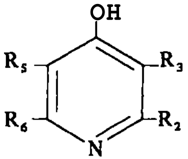
CH_3	COOH	COOH		diethyl ester, m.p. 156–158"	456 (m.p.), (i), (n), (u);
CH_3	COOH		CH_3	hydrate, m.p. 257–258"	147 (m.p.);
				ethyl ester, m.p. 162–164"	69 (m.p.), (i);
				pnitroanilide, m.p. 335-340°	1030 (m.p.);
2–Pyridyl	COOH	COOH	2-Pyridyl	dimethyl ester	500 (i);
				diethyl ester	500 (i), (u);
C_6H_5	COOH	COOH	C_6H_5	diethyl ester m.p. 199°	448 (m.p.), (i);
	COOH	COOH		dimethyl ester	500 (i);
				diethyl ester	500 (i);

TABLE XII-68. 4-Pyridinol Nitriles



R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
	CN			238–240"		789 (m.p.), (u);

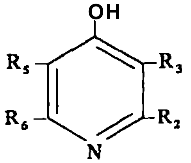
TABLE XII-69. Halo 4-pyridinols



R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
F				157"		266 (m.p.);
	F			153"		266 (m.p.);
Cl				170"		241 (u); 253 (m.p.);
	Cl			204–205"		254 (m.p.);
Br				173"		253 (m.p.);
	Br			228–230"		254 (m.p.); 299 (m.p.);
I				215°		253 (m.p.);

	I			298–301°		254 (m.p.); 299 (m.p.); 704 (u);
Cl			Cl	196"		241 (i), (u); 296 (m.p.);
	Cl	Cl				460 (i); 831 (i);
	Br	Br				460 (i), (u);
	I	I		300"		704 (u); 1109 (m.p.);
Cl	Cl	Cl		214–216"		456 (m.p.), (i), (n), (u); 1110 (m.p.);
Cl	Cl		Cl	193–195"		98 (m.p.), (i), (n), (u);
F	F	F	F	73–75" or 95–97"		246 (m.p.), (i), (n); 950 (m.p.); 951 (m.p.); 1070 (m.p.);
					anilinium salt, m.p. 132"	248 (m.p.);
F	Cl	F	F	122–124"		246 (n); 951 (m.p.);
F	Cl	Cl	F	101–102"		246 (m.p.), (i), (n); 950 (m.p.); 951 (m.p.);
					potassium salt, m.p. < 300"	951 (m.p.);
					***O*-acetyl,** m.p. 55–56"	951 (m.p.);
Cl	Cl	Cl	Cl	232–233"		239 (m.p.); 241 (i), (u);
CH_3	Br	Br		294–295°		293 (m.p.);
CH_3			Cl	156"		743 (m.p.);
CH_3	Br	Br	CH_3	282"		141 (m.p.);
Br	Br	Br	$-N(CH_3)_2$	oil		952;
					hydrochloride, m.p. 129–131°	952 (m.p.);
CH_3	$COCH_3$	Br	CH_3	295–297"		141 (m.p.);
C_4H_9-*t*	Br	Br	C_4H_9-*t*	146–147"		671 (m.p.);

TABLE XII-70. Nitro 4-Pyridinols



R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
	NO_2			270–279°		479 (u); 667 (m.p.); 700 (m.p.); 789 (m.p.); 955 (u);
	NO_2	Cl		263"		664 (m.p.);
	NO_2	NO_2		>300"		456 (i), (n), (u); 700 (m.p.); 716 (m.p.), (i);
	NH_2	NO_2		295"		556 (m.p.);
					hydrochloride, m.p. 270"	556 (m.p.);
					N'-formyl, m.p. 298"	556 (m.p.);
					N'-acetyl, m.p. 239–240"	556 (m.p.);
					N'-carbethoxy, m.p. 165,295"	556 (m.p.);
CH_3	NO_2	Br		350"		293 (m.p.);
CH_3	NO_2			213–275"		293 (m.p.);
CH_3		NO_2		247–249"		293 (m.p.);
CH_3	NO_2	Cl	CH_3	>320"		294 (m.p.);
CH_3	NO_2	Br	CH_3	340–345°		294 (m.p.);
CH_3	NO_2	I	CH_3	292–295"		294 (m.p.);
CH_3	NO_2		CH_3	294"		294 (m.p.); 670 (m.p.);
CH_3		NO_2	CH_3	296"		295 (m.p.);

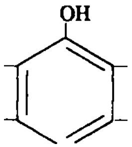
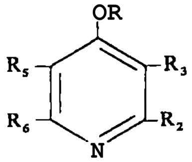


TABLE XII-71. Sulfur containing 4-Pyridinols

R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
	SC_2H_5	SC_2H_5		147–149"		962 (m.p.);
C_4H_9-*t*	SO_3H		C_4H_9-*t*	256–258"		671 (m.p.);

TABLE XII-72. Ethers and Esters of Alkyl and Aryl 4-Pyridinols



R	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	D	D	D	D			1102 (u);
CH_3					4" b.p. 107°/50 mm b.p. 185°/712 mm	picrate, m.p. 170–172" hexachloro-antimonate, m.p. 135–138"	275 (b.p.), (m.p.); 482 (z); 735 (n); 899 (n); 925 (t); 964 (j); 1102 (u); 1103 (n); 1106 (b.p.); 1106 (m.p.); 464 (m.p.), (i);
C_2H_5						hydrochloride	536 (n);
CH_3	CH_3					nitrate	293;
$CH_2CH{=}CH_2$					b.p. 104°/11 mm	picrate, m.p. 109–110°	598 (b.p.), (i), (n); 598 (m.p.);
$N{=}C(CH_3)_2$					59–60" b.p. 70°/4.5 mm	hydrochloride, m.p. 192–193"	966 (b.p.), (m.p.); 966 (m.p.);
CH_3	CH_3			CH_3	b.p. 70°/20 mm		137 (b.p.), (n);
C_2H_5	CH_3					nitrate, m.p. 84–86°	293 (m.p.);

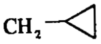
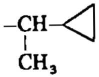
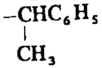
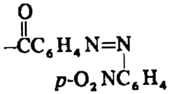
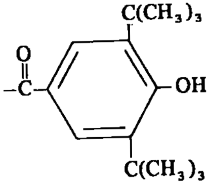
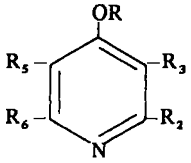
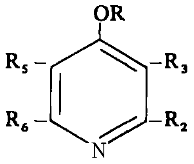
			b.p. 85°/3 mm		770 (b.p.);
C_2H_5	C_2H_5			hydrochloride, m.p. 141–142°	589 (m.p.);
			b.p. 77 /2 mm		770 (b.p.);
β-D-Glucosyl			68–171°	etraacetyl, n.p. 113–114	≤03 m.p.) (f); ≤03 (m.p.); ≤71 (b.p.);
C_2X_5	t-C_4H_9		.p. 115°/15 mm	picrate, n.p. 121–122°	671 (m.p.);
$CH_2C_6H_5$			5–56° .p. 94°/1 mm		1106 (m.p.); 770 (b.p.);
 $-CH(CH_3)C_6H_5$					
C_2H_5	$-C(CH_3)_3$	$-C(CH_3)_3$	b.p. 141°/21 mm	chloroaurate, m.p. 193–194°	671 (b.p.); 671 (m.p.);
 $-C(=O)C_6H_4N{=}NC_6H_4NO_2$-$p$					1097 (g);
CH_3	C_6H_5	C_6H_5	79–81°		530 (m.p.), (i), (n), (u);
			186°		101З (m.p.);
Tri-*O*-benzoyl- β-D-ribofuranosyl			139–140°		602 (m.p.);

TABLE XII-73. Ethers of Amino 4-Pyridinols



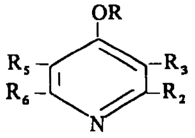
R	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
CH_3		NH_2			83°		497 (u); 789 (m.p.);
C_2H_5	CH_3	NH_2		CH_3	62–63"		294 (m.p.);

TABLE XII-74. Ethers of 4-Pyridinol Carboxylic Acids



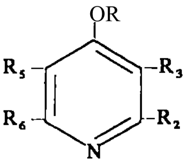
R	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
COOH						ethyl ester	**659 (u);**
CH_3		COOH				amide, m.p. 151–153°	**789** (m.p.), **(u);**
CH_3	COOH			COOH		dimethyl ester, m.p. **127–128"**	**456** (m.p.), (i), (n), (u); **107** (m.p.);
C_2H_5	COOH					ethyl ester, b.p. 127°/1.3 mm	**107** (b.p.);
						ethyl ester picrate, m.p. 104–106°	**107** (m.p.);
C_2H_5	COOH			COOH		diethyl ester, m.p. **85–87"**	**1107** (m.p.);

TABLE **XII-75.** Ethers of 4-Pyridinol Nitriles



R	R_2	R_3	R_5	**R_6**	m.p.	Derivatives	Ref.
CH_3		CN			124"		**789** (m.p.);

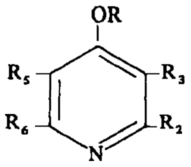
TABLE **XII-76.** Ethers and Esters of Halo 4-Pyridinols

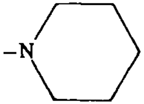


R	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	Cl				**229–230"** b.p. **106°/16** mm	 picrate, m.p. **168"**	**241 (u); 252** (m.p.); **253** (m.p.); **768** (b.p.); **252** (m.p.);
CH_3		Cl			b.p. **105°/15** mm	 picrate, m.p. **159°**	**255** (b.p.); **254** (m.p.); **255** (m.p.);
CH_3	Br				b.p. **120°/10** mm	 picrate, m.p. **115°**	**252** (b.p.); **253** (b.p.); **252** (m.p.);
CH_3		Br			b.p. **114°/12** mm	 picrate, m.p. **160"**	**255** (b.p.); **254** (m.p.); **255** (m.p.);
CH_3	I				**35"**	 picrate, m.p. **154"**	**252** (m.p.); **253** (m.p.); **252** (m.p.);
CH_3		I			**78"**	 picrate, m.p. **162"**	**254** (m.p.); **255** (m.p.); **255** (m.p.);
CH_3		Cl	**Cl**		**225–227"**		**241 (m.p.), (u);**
CH_3	Cl			Cl	**100–102"**		**241 (m.p.), (u);**

CH_3		**Br**	**Br**		85–86"		460 (i), (u); 705 (m.p.); 952 (m.p.), (n);
CH_3	Cl	Cl	Cl		60–65"		236 (m.p.); 456 (m.p.), (n), (u);
CH_3	Cl	Cl		Cl	136–138°		778 **(m.p.),** (n);
CH_3	NH_2	Cl	Cl	F	125"		953 (m.p.);
CH_3	F	Cl	**Cl**	**F**	b.p. 214"		246 (b.p.), (g), (i), **(n);** 950 (b.p.);
CH_3	F	F	F	F	b.p. 161"		245 (b.p.), **(i),** (u); 248 (b.p.), **(i),** (u); 1111 (b.p.);
CH_3	**Cl**	Cl	Cl	Cl	107–114"		236 (m.p.); 239 (m.p.); 778 (m.p.), (n);
$CONHCH_3$	a	Cl	Cl	Cl	155"		972 (m.p.);
C_2H_5	Cl	Cl	Cl	Cl			241 (u);
CH_2CH_2OH	F	Cl	Cl	F	47–48°		953 (m.p.1;
$CONHCH_3$	Cl	Cl	Cl		140"		972 (m.p.);
C_2H_5	Cl				55–57"		252 (m.p.); 253 (m.p.);
C_2H_5		Cl			b.p. 118°/20 mm	picrate, m.p. 133"	252 (m.p.); 255 (b.p.);
C_2H_5	**Br**				**38°**	picrate, m.p. 160"	254 (m.p.); 255 (m.p.); 252 (m.p.); 253 (m.p.);
C_2H_5		**Br**			b.p. 116°/12 mm	picrate, m.p. 115"	252 (m.p.); 255 (b.p.);
C_2H_5	I				b.p. 145°/11 mm	picrate, m.p. 161–162"	254 (m.p.); **255** (m.p.); 252 (b.p.);
C_2H_5		I			b.p. 143°/15 mm	picrate, m.p. 132–133"	252 (m.p.); 253 (m.p.); 255 (b.p.);

TABLE XII-76. Ethers and Esters of Halo 4-Pyridinols (Continued)



R	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
						picrate, m.p. 173"	254 (m.p.); 255 (m.p.);
C_2H_5	Br	Br			80-81"		712 (m.p.);
C_2H_5	NH_2	Br	Br		100-101°		284 (m.p.);
C_2H_5	NH_2	Br			147-148°		284 (m.p.);
C_2H_5	NH_2		Br		149-150°		284 (m.p.), (g);
$CON(CH_3)_2$	Cl	Cl	Cl	Cl	156-159"		972 (m.p.);
$CONHC_2H_5$	Cl	Cl	Cl	Cl	150°		972 (m.p.);
$CH_2CH_2OCH,$	F	Cl	Cl	F	b.p. 75°/1 mm		953 (b.p.);
$CH_2CH_2OCH,$	Cl	Cl	Cl	Cl	51-52"		236 (m.p.);
CH, CH, OCH_3	Cl	Cl	Cl		fluid		236;
$-CONHC_3H_7$-*n*	Cl	Cl	Cl	Cl	130°		972 (m.p.);
$-CONHC_3H_7$-*n*	Cl	Cl	Cl		80-85°		972 (m.p.);
C_2H_5		$-CH{=}CH_2$		Cl	70-72°		589 (m.p.);
$-COC(CH_3)_3$	F	Cl	Cl	F	63-64°		951 (m.p.);
	Cl	Cl	Cl	Cl	135"		240 (m.p.);
$-CONHC_4H_9$-*n*	Cl	Cl	Cl	Cl	113"		972 (m.p.);
$C_6H_4NO_2$-*p*	F	Cl	Cl	F	85-87"		953 (m.p.);
C_6H_5	F	Cl	Cl	F	69-71"		953 (m.p.);

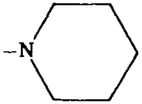
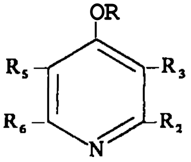
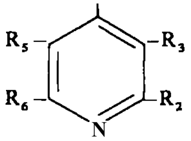
C_6H_5	Cl	Cl	Cl	Cl	111"	240 (m.p.);
CH_3	Br	Br	Br		81°	952 (m.p.);
CH, CH, OC_4H_9	Cl	Cl	Cl		oil	236;
$-Sn(C_2H_5)_3$		Cl	Cl		179–181"	831 (m.p.), (i);
$-COC_6H_5$	F	Cl	Cl	F	96–97"	951 (m.p.);
$-COC_6H_4OCH_3$-*p*	F	Cl	Cl	F	69–70"	951 (m.p.);
mesityl	F	Cl	Cl	F	b.p. 96°/0.08 mm	953 (b.p.);
$-COC_{11}H_{23}$-*n*	F	Cl	Cl	F	44–45°	951 (m.p.);
$Pb(C_6H_5)_3$		Cl	Cl		241–242"	831 (m.p.);
$Sn(C_6H_5)_3$		Cl	Cl		254–255"	831 (m.p.), (i);
$CONHC_{,8}H_{38}$	Cl	Cl	Cl	Cl	82–86"	972 (m.p.);

TABLE XII-77. Ethers of Nitro 4-Pyridinols.



R	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
CH_3		NO_2			72–74"		497 (u); 700 (m.p.); 705 (m.p.); 789 (m.p.);
CH_3		NO,	NO,		54–55°	1:1 adduct with methoxide ion	775 (n); 776 (m.p.); 776 (i), (n), (u), (v);
C_2H_5		NO_2			48–49°		705 (m.p.); 789 (m.p.); 955 (u);
C_2H_5	CH,	NO,			69–72°		293 (m.p.);
C_2H_5	CH_3		NO_2		61–63"		293 (m.p.);

TABLE XII-78. Sulfur Containing Esters of 4-Pyridinols



R	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
SO, H						potassium salt	648 (i), (u);
$-COSCH_3$	Cl			Cl	31–39"		976 (m.p.);
$-COSCH_3$	Cl	Cl	Cl		70–72"		976 (m.p.);
$-COSCH_3$	Cl	Cl	Cl	Cl	99–101"		976 (m.p.);
$-COSC_6H_5$	Cl	Cl	Cl	Cl	90–91°		976 (m.p.);
$-SO_2C_6H_4CH_3$-*p*	F	Cl	Cl	F	101–102"		951 (m.p.);

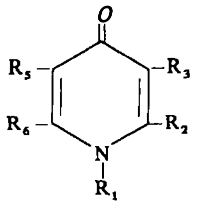


TABLE XII-79. Alkyl and Aryl 4-Pyridones

R_1	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
CD_3							1112 (m);
CH_3	D			D	91–93"		139 (m.p.), **(i), (n),** (u); 530 **(m)** ;731 (n); 1112 (m);
CH_3		D	D		92–94"		139 (m.p.), **(i),** (m), (n); **(u)**; 1112 (m);
CH_3					91–99" b.p. 178°/4 mm		139 (m.p.); 460 (i); 464 (b.p.), (m.p.); 466 (i); 478 (i); 480 (z); 481 (z); 486 **(n)**; 731 (m.p.); 735 (n); 819 (i); 980 (w); 1103 (n); 1112 (m); 1113 (i);
						^{15}N	1112 (m);
						hydrochloride	536 (n); 1103 (i), (i);
						hexachloro-antimonate, m.p. 155–159"	464 (m.p.), (i); 542 (i);
						hexachloro-stannate, m.p. 130–135"	464 (m.p.), (i);

$COCH_3$					125–135"		633 **(m.p.), (i), (n);**
CH_3	**CD_3**			CD_3	247–249"		139 **(m.p.), (i), (m), (n), (u);**
CH_3	**D**	CH_3	CH,	D	132–133"		139 **(m.p.), (i), (m), (n), (u);**
CH_3	**CH_3**			CH_3	240–250°		108 **(m.p.),** 137 **(m.p.), (n);** 139 **(m.p.), (n), (u);** 143 **(m.p.);** 147 **(m.p.);** 148 (i); 539 (i); 541 (i); 706 **(m.p.);** 819 **(m.p.),** (i);
						trihydrate, **m.p.** 110°	148 **(m.p.);** 706 **(m.p.);** 731 (n); 819 (m.p.), (i);
						picrate, **m.p.** 197–199"	148 **(m.p.);** 706 **(m.p.);**
						hydrochloride, **m.p.** 260–270°	706 **(m.p.);** 819 **(m.p.), (i),**
						$CdCl_2$ complex, **m.p.** > 300°	819 **(m.p.);**
						$HgCl_2$ complex. **m.p.** 191–193"	819 **(m.p.);**
						$ZnCl_2$ complex, **m.p.** > 300°	819 **(m.p.);**
						$CaCl_2$ complex, **m.p.** > 300"	819 (m.p.);
						$SnBr_4$ complex, **m.p.** 284–286"	819 **(m.p.);**
						hydrobromide, **m.p.** 272–273"	539 **(m.p.);**
						hydroiodide, **m.p.** 252–253"	539 (m.p.);

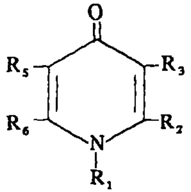
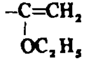


TABLE XII-79. Alkyl and Aryl 4-Pyridones (Continued)

R_1	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
						$HAsF_6 \cdot H_2O$, m.p. 124–126°	539 (m.p.);
						$HAsF_6$, m.p. 151°	539 (m.p.);
						$HSbCl_6$, m.p. 239–240°	539 (m.p.);
						$HPF_6 \cdot H_2O$, m.p. 118–119°	539 (m.p.);
						HPF_6, m.p. 150–155°	539 (m.p.);
CH_3		CH_3	CH_3		131–133°		139 (m.p.), (i), (n), (u); 731 (m.p.), (n);
 $-\underset{OC_2H_5}{\underset{\vert}{C}}{=}CH_2$					b.p. 140°/0.75 mm		746 (b.p.), (i), (n), (u);
$-(CH_2)_4Br$						hydrobromide, m.p. 132–135°	588 (m.p.);
						picrate, m.p. 112–115°	588 (m.p.);
$-(CH_2)_4I$						hydroiodide, m.p. 177–179°	588 (m.p.);
						picrate, m.p. 102–104°	588 (m.p.);

C_2H_5	CH_3	CH,	158–164°	**polymer·HI,** m.p. 210–212"	588 (m.p.), (u); 108 (m.p.); 143 (m.p.); 148 (i); 539 (i); 819 (m.p.), (i);
				hydrate, m.p. 59–74'	41 (m.p.), (u); 143 (m.p.); 144 (m.p.); 148 (m.p), (i); 541 (i); 706 (m.p.); 819 (m.p.);
				picrate, m.p. 191"	148 (i); 706 (m.p.);
				hydrochloride, m.p. 242–244"	819 (m.p.);
				$CoCl_2$ complex, m.p. 267–269"	819 (m.p.);
				$CdCl_2$ complex, m.p. 258–261"	819 (m.p.);
				$HgCl_2$ complex, m.p. 165–167°	819 (m.p.);
				$ZnCl_2$ complex, m.p. 257–262"	819 (m.p.);
				$SnBr_4$ complex, m.p. 110–114"	819 (m.p.);
				$SbCl_5$ complex, m.p. 160–165°	819 (m.p.);
				hydrobromide, m.p. 234–235°	539 (m.p.);
				hydroiodide, m.p. 208–210°	539 (m.p.);
				H_2SiF_6 complex, m.p. 150–151°	539 (m.p.);
				HClO, complex, m.p. 208–210"	539 (m.p.);

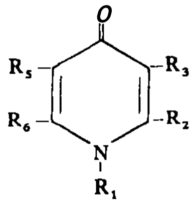


TABLE XII-79. Alkyl and Aryl 4-Pyridones (Continued)

R_1	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
						H_2SnBr_6 complex. m.p. 202–204°	539 (m.p.);
						H, $PtCl_6$ complex, m.p. 221–222°	539 (m.p.);
						H, $SnCl_6$ complex, m.p. 256–259"	539 (m.p.);
						$HBF_4 \cdot H_2O$, m.p. 68–70"	539 (m.p.);
						HBF, complex, m.p. 164–168"	539 (m.p.);
						$HAsF_6$ complex, m.p. 183–184°	539 (m.p.);
						HPF_6 complex, m.p. 165–1680	539 (m.p.);
CH_3	CH_3	CH_3		CH,	b.p. 100°/10 mm		113 (b.p.);
						hydrochloride, m.p. 252–254"	113 (m.p.);
						2,4-dinitrophenylhydrazone. m.p. 112–113"	113 (m.p.);
CH_2CH_2OH	CH_3			CH,	224–225°		147 (m.p.);
4-Pyridyl					177–178"		1104 (u); 1113 (m.p.); 1114 (m.p.);

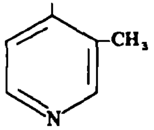
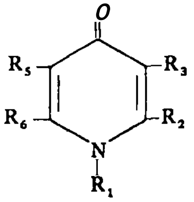
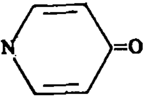
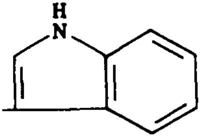
					picrate, m.p. 203–205°	1114 (m.p.);
n-C_3H_7	CH_3		CH_3		picrate, m.p. 175–176°	143 (m.p.);
isoC_3H_7	CH_3		CH_3	49–53°		41 (m.p.), (u);
$-(CH_2)_3OH$	CH_3		CH_3	188–189°		145 (m.p.);
C_6H_5Hg-				297–298°		831 (m.p.), (i);
β-D-Glucosyl				amorphous		623 (f), (k); 1026 (k);
					tetraacetyl, amorphous	623 (k); 1026 (k);
n-C_4H_9	CH_3		CH_3	65°		118 (m.p.);
					hydrate, m.p. 88–89°	143 (m.p.);
					picrate, m.p. 151–152°	143 (m.p.);
$CH_2C_6H_4Br$-*o*				121–122°		1017 (m.p.);
$CH_2C_6H_4NO_2$-*o*				136–138°		564 (m.p.);
$CH_2C_6H_4NO_2$-*m*				220–222°		564 (m.p.);
$CH_2C_6H_4NO_2$-*p*				184–185°		564 (m.p.);
				98–99°		279 (m.p.);
				109–111°		466 (m.p.), (i);
$CH_2C_6H_4NH_2$-*o*				168–169°		564 (m.p.);
$CH_2C_6H_4NH_2$-*m*				204–205°		564 (m.p.);
$CH_2C_6H_4NH_2$-*p*				206–207°		564 (m.p.);
		CH_3		197–198°		273 (m.p.); 278 (m.p.);
					picrate, m.p. 209–210°	273 (m.p.);

TABLE XII-79. Alkyl and Aryl 4-Pyridones (Continued)



R_1	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
CH_2OCH_2– 						diperchlorate, m.p. 201–202°	1115 (m.p.), (f), (t), (u);
–$(CH_2)_2N(CH_3)_2$	CH_3			CH_3	123–125°		145 (m.p.);
C_6H_5	CH_3			CH_3	196–202"		69 (m.p.), (i); 147 (m.p.);
2-Quinolyl					193–194"	picrate, m.p. 216–218°	1113 (m.p.); 1114 (m.p.); 1114 (m.p.);
1-Isoquinolyl					162–163"	picrate, m.p. 205–206°	1113 (m.p.); 1114 (m.p.); 1113 (m.p.); 1114 (m.p.);
$CH_2C_6H_5$	CH_3			CH_3		hydrate, m.p. 125–127° picrate, m.p. 183–185°	148 (m.p.), (i); 148 (m.p.);
$C_6H_4CH_3$-*o*	CH_3			CH_3	276"		1116 (m.p.);
2-Quinolyl		CH_3			162–163"	picrate, m.p. 216–218"	273 (m.p.); 273 (m.p.);
–CH_2CH_2– 					216"		788 (m.p.), (i), (u);

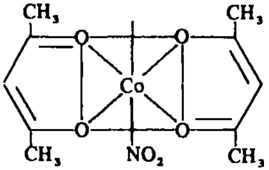
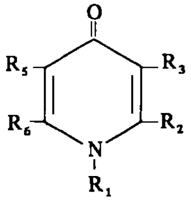
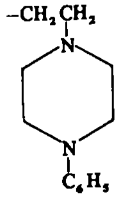
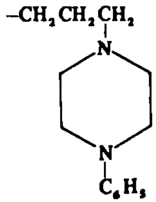
$CH_2CH_2C_6H_5$	CH_3	CH_3	164–165		145 (m.p.), (i), (u); 1117 (m.p.), (t);
				hydrate, m.p. 167–168°	148 (m.p.), (i);
				picrate, m.p. 218–220°	148 (m.p.), (i);
$-(CH_2)_4OC_6H_5$			52–55°		588 (m.p.);
				picrate, m.p. 139–141°	588 (m.p.);
				iodide. m.p. 149–151°	588 (m.p.);
				hydrate, m.p. 169°	823 (m.p.), (i), (u);
$-CH(CH_3)CH_2C_6H_5$	CH_3	CH_3		hydrochloride, m.p. 235–236°	145 (m.p.);
$-(CH_2)_2$-β- 3-indolyl	CH_3	CH_3	281–282°		145 (m.p.);
C_6H_4Cl-*o*	C_6H_5	CH_3	250–251°		31 (m.p.), (i);
C_6H_4Cl-*p*	C_6H_5	CH_3	220–221°		31 (m.p.), (i);
CH_3	C_6H_5	C_6H_5	185–190°		486 (m.p.); 530 (m.p.), (n); 706 (m.p.); 899 (m.p.);
				hydrochloride, m.p. 245°	706 (m.p.);
				picrate, m.p. 220°	706 (m.p.);
C_6H_5	C_6H_5	CH_3	241–243°		31 (m.p.), (i); 32 (m.p.), (i), (u); 706;
C_2H_5	C_6H_5	C_6H_5	oil		
				picrate, m.p. 200°	706 (m.p.);

TABLE XII-79. Alkyl and Aryl 4-Pyridones (Continued)



R_1	R_2	R_3	R_5	R_4	m.p.	Derivatives	Ref.
$C_6H_4OCH_3$-*p*	C_6H_5			CH_3	199–201°		31 (m.p.), (i);
CH_3	$C_6H_4OCH_3$-*p*			C_6H_5	oil	picrate, m.p. 164°	706; 706 (m.p.);
	CH_3			CH_3	157–158°		145 (m.p.);

C_2H_5	$C_6H_4OCH_3$-*p*	C_6H_5	oil	picrate, m.p. 199°	706; 706 (m.p.);
	CH_3	CH_3	→ 4 145		145 (m.p.);
$C_6H_4N(CH_3)_2$-*p*	*n*-C_4H_9	*n*-C_4H_9	116-118°		1118 (m.p.), (i);
$CH_2CH_2C_6H_5$	C_6H_5	C_6H_5	247-252°		145 (m.p.);
$C_6H_4N(CH_3)_2$-*p*	C_6H_5	C_6H_5	289-290°		1118 (m.p.), (i);

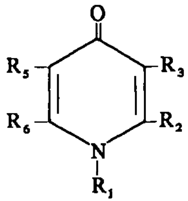
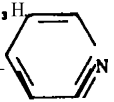
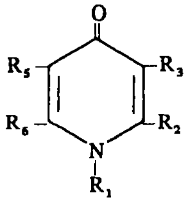


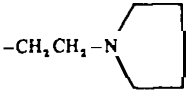
TABLE XII-80. Alkyloxy, Aryloxy, and Hydroxy 4-Pyridones

R_1	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
OCH_3							466 (i); 486 (n);
CH_3	CH_3	OH			266–268°		131 (m.p.);
C_2H_5	CH_3	OH			216–217"		131 (m.p.);
CH_2CH_2OH	CH_3	OH			204–205°		131 (m.p.);
CH_2CH_2Cl	CH_2Cl		OCH_3		151–152°		1119 (m.p.);
						hydrochloride, m.p. 195–196°	1119 (m.p.);
n-C_3H_7	CH_3	OH			164–165"		131 (m.p.);
.isoC_3H	CH_3	OH			254–256"		131 (m.p.);
–O– 					130"		**280 (m.p.), (e), (i), (m), (n), (u);**
β-D-Arabinopentofuranosyl-2-hydroxy						2,2'-anhydro, m.p. **201°/218°**	617 (m.p.), (k), (u);
C_3H_6Cl	CH_2Cl	OCH_3			117–120"		1119 (m.p.);
						hydrochloride, m.p. 169–177"	1119 (m.p.);
n-C_4H_9	CH_3	OH			126–127"		131 (m.p);
isoC_4H_9	CH_3	OH			173–174"		131 (m.p.);
C_6H_4Cl-p		OH			236–237"		129 (m.p.), (u); 1120 (u);
C_6H_4Br-p		OH			247–248"		129 (m.p.), (u); 1120 (u);
C_6H_5		OH			164°	hydrochloride, m.p. 197"	128 (m.p.);
						picrate, m.p. 172–174°	128 (m.p.);

C_6H_5	OH			OH	84°		801 (m.p.);
						hydrochloride, m.p. 205"	801 (m.p.);
						anil, m.p. 239"	801 (m.p.);
						phenyl hydrazone. m.p. >250°	801 (m.p.);
β-D-Glucosyloxy					125–127°		623 (m.p.), (f); 1026 (m.p.), (k);
						tetraacetyl, m.p. 134–136"	623 (m.p.); 1026 (m.p.), (k);
n-C_5H_{11}	CH_3	OH			127–128"		131 (m.p.);
$CH_2CH_2N(CH_3)_2$	CH_2OH		OCH_3		134–137°		130 (m.p.);
$OCH_2C_6H_5$							466 (i);
C_6H_5		OCH_3				hydrochloride. m.p. 180–181°	128 (m.p.);
						picrate, m.p. 150°	128 (m.p.);
$C_6H_4CH_3$-*o*		OH			206"		128 (m.p.);
						hydrochloride, m.p. 250–252°	128 (m.p.);
						picrate, m.p. 146"	128 (m.p.);
$C_6H_4CH_3$-*m*		OH			158–160°		128 (m.p.);
						$HCl \cdot H_2O$ m.p. 190–192"	128 (m.p.);
						picrate, m.p. 167–168°	128 (m.p.);
$C_6H_4CH_3$-*p*		OH			196°		128 (m.p.);
						hydrochloride, m.p. 215–216°	128 (m.p.);
						picrate, m.p. 174"	128 (m.p.);

TABLE XII-80. Alkyloxy, Aryloxy, and Hydroxy 4-Pyridones (Continued)



R_1	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
C_6H_{11}	CH_3	OH			206-207°		131 (m.p.);
n-C_6H_{13}	CH_3	OH			125-126°		131 (m.p.);
$CH_2CH_2N(C_2H_5)_2$	CH_3	OH			147-148°		131 (m.p.);
$CH_2C_6H_5$	CH_3	OH			204-205°		131 (m.p.);
$C_6H_4CH_3$-o		OCH_3				hydrochloride, m.p. 196-197" picrate, m.p. 187-188"	128 (m.p.); 128 (m.p.);
$C_6H_4CH_3$-m		OCH_3				$HCl\cdot.5H_2O$, m.p. 186" picrate, m.p. 163"	128 (m.p.); 128 (m.p.);
$C_6H_4CH_3$-p						HCl, m.p. 204° picrate, m.p. 164-165°	128 (m.p.); 128 (m.p.);
CH_3	CH_3	β-D-Glucosyloxy			228"		131 (m.p.);
 $-CH_2CH_2-N$	CH_2OH		OCH_3		153-155°		130 (m.p.);
n-C_7H_{15}	CH_3	OH			128-129°		131 (m.p.);
$-CH_2CH_2N(C_2H_5)_2$	CH, OH		OCH_3		90-93"	hydrochloride, m.p. 182-185"	130 (m.p.); 1119 (m.p.); 130 (m.p.);
C_2H_5	CH_3	β-D-Glucosyloxy			241-243°		131 (m.p.);
$-CH_2CH_2OH$	CH_3	β-D-Glucosyloxy			250-251°		131 (m.p.);

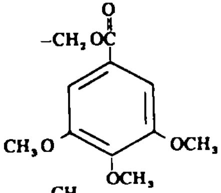
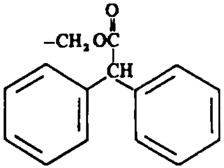
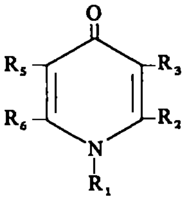
$-CH_2CH_2-N$ 	CH_2OH		OCH_3	138–140°		130 (m.p.);
$-CH_2CH(CH_2)_3CH_3$ $\quad\;|$ $\quad C_2H_5$	CH_3	OH		167–168°		131 (m.p.);
α-Naphthyl		OH		216–217°		129 (m.p.), (u); 1120 (u);
CH_2CH_2- $|$ $N(CH_2CH{=}CH_2)_2$	CH_2OH		OCH_3	86–90°		130 (m.p.);
n-C_3H_7	CH_3	β-D-Glucosyloxy		212–213"		131 (m.p.);
n-C_4H_9	CH_3	β-D-Glucosyloxy		125–127"		131 (m.p.);
isoC_4H_9	CH_3	β-D-Glucosyloxy		125–127°		131 (m.p.);
n-C_5H_{11}	CH_3	β-D-Glucosyloxy		180–182"		131 (m.p.);
C_6H_5	CH_3	β-D-Glucosyloxy		230–231"		131 (m.p.);
C_6H_{11}	CH_3	β-D-Glucosyloxy		264–266°		131 (m.p.);
n-C_6H_{13}	CH_3	β-D-Glucosyloxy		195–196'		131 (m.p.);
$C_6H_4OCH_3$-p	CH_3	β-D-Glucosyloxy		246–247°		131 (m.p.1;
n-C_7H_{15}	CH_3	β-D-Glucosyloxy		179–180°		131 (m.p.);
$-CH_2CH_2N(C_2H_5)_2$			OCH_3	116–119"		130 (m.p.);
n-$C_{12}H_{25}$	CH_3	β-D-Glucosyloxy		156–158°		131 (m.p.);
$-CH_2CH_2N(C_2H_5)_2$			OCH_3		1.5 H_2O, m.p. 63–69° di-HCl, m.p. 120–125°	130 (m.p.); 130 (m.p.);

TABLE XII-81. Amino 4-Pyridones



R_1	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
CH_3		NH_2					497 (u);
						picrate, m.p. 213°	586 (m.p.);
NH_2	CH_3		OH		248–250°		793 (m.p.);
CH_3		NH_2	NH_2			*N*^{3}-acetyl, m.p. 240–241°	556 (m.p.);
NH_2	$-CH_2OH$		OCH_3		242°		794 (m.p.), (i), (n), (u);
						1,1,2-triacetyl, m.p. 150°	794 (m.p.), (i), (n), (u);
NH_2	$-CH_2OCH_3$		OCH_3		183–185°		793 (m.p.);
						picrate, m.p. 164–166°	793 (m.p.);
						N′-acetyl, m.p. 207°	793 (m.p.);

$-NHC_6H_4NO_2$-*p*	Cl			Cl	152°		140 (m.p.);
						hydrochloride, m.p. 185°	140 (m.p.);
$-CH_2C_6H_5$		NH_2			161–162°		564 (m.p.);
$-N{=}CHC_6H_4NO_2$-*p*	CH_3		OH		259°		793 (m.p.);
NH_2	CH Cl		$-OCH_2C_6H_5$		157°		793 (m.p.);
						hydrochloride, m.p. 209°	793 (m.p.);
$-NHC_6H_4NO_2$-*p*	CH_3			CH_3	178°		140 (m.p.);
						hydrochloride, m.p. 203°	140 (m.p.);
$-NHC_6H_4NO_2$-*p*	$-OCH_3$			OCH_3	153°		140 (m.p.);
NH_2	CH_3		$-OCH_2C_6H_5$		195°		793 (m.p.);
						acetate, m.p. 206°	793 (m.p.);
NH_2	$-CH_2OH$		$-OCH_2C_6H_5$		174°		
$-\underset{\overset{\vert}{CH_3}}{N}C_6H_5$	CH_3			CH_3	155–156°		
$-N(C_6H_5)_2$	CH_3			CH_3	193–194°		1121 (m.p.);
$-NHCOC_2H_5$	$-CH_2O\underset{\overset{\vert}{C_2H_5}}{CO}$		$-OCH_2C_6H_5$		154–155°		793 (m.p.);
$-N{=}CHC_6H_4NO_2$-*p*	CH_2OH		$-OCH_2C_6H_5$		184–185°		793 (m.p.);
$-N{=}CHC_6H_5$	CH_2Cl		$-OCH_2C_6H_5$		110°, 171°		793 (m.p.);

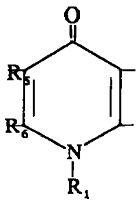
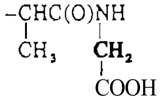
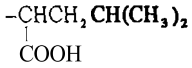


TABLE XII-82. 4-Pyridone Carboxylic Acids

R_1	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
[illegible]		NH_2				ethyl ester picrate·½H_2O, m.p. 217–218°	586 (m.p.);
CCO[illegible]		NHCOOH				diethyl ester, m.p. 85°	586 (m.p.);
CH_3		COOH				amide, 179–181°	789 (m.p.), (i), (u);
CH_3	COOH			[illegible]		dimethyl ester, m.p. 97–98°	456 (m.p.), (i), (n), (u);
$-CH_2\underset{\substack{\vert \\ NH_2}}{C}HCOOH$		[illegible]			224–226°		134 (m.p.);
$-CH_2COOH$	CH_3			CH_3	[illegible]7°		41 (m.p.), (u);
						amide, m.p. > [illegible]°	41 (m.p.), (u);
$-C$[illegible]$_2CH_2C$[illegible]	C[illegible]			CH_3			41 (u);
$-\underset{\substack{\vert \\ CH_3}}{C}$[illegible]COOH	CH_3			CH_3	[illegible]		41 (m.p.), (u);
						amide, m.p. > 320°	41 (m.p.), (u);
–[illegible]H_2C[illegible]NH–CH_2–C[illegible]	CH_3			CH_3	[illegible]00–310°		41 (m.p.), (u);

C_6H_4Cl-*p*	COOH		OH			hydrate. **m.p.** 236"	129 **(m.p.);**
						ethyl ester, **m.p.** 203–204"	129 **(m.p.), (u);** 1120 (u);
C, **H₄** Br-p	COOH		OH			hydrate, **m.p.** 192–193"	129 **(m.p.);**
						ethyl ester, **m.p.** 204–205"	129 **(m.p.), (u);** 1120 **(u);**
C, H, NO, -*m*	COOH		OH		256–257"		129 **(m.p.);**
						ethyl ester, **m.p.** 182–183"	129 **(m.p.), (u);** 1120 **(u);**
C_6H_5	COOH		**OH**		200"		128 **(m.p.);**
						methyl ester, **m.p.** 197–198"	129 **(m.p.), (u);** 1120 **(u);**
						ethyl ester, **m.p.** 177–178"	**129 (m.p.), (u); 1120 (u);**
 $-\underset{\substack{\vert\\ CH_3}}{C}HC(O)N\underset{\substack{\vert\\ CH_2\\ \vert\\ COOH}}{H}$	**CH_3**			**CH_3**		ethyl ester, **m.p.** 139"	**41 (m.p.), (u);**
C, H, CH, -*o*	COOH		OH		206"		128 **(m.p.);**
C_6 H, CH, -*m*	COOH		OH		190"		128 **(m.p.);**
$C_6H_4CH_3$-*p*	COOH		OH		197–199°		128 **(m.p.);**
						ethyl ester, m.p. 179–181°	**129** (m.p.), (u); 1120 (u);
C_6H_5	COOH		**OCH_3**		176–177"		128 **(m.p.);**
$(CH_2)_5COOH$	CH_3			CH_3		hydrochloride, **m.p.** 180–184°	**41 (m.p.), (u);**
 $-\underset{\substack{\vert\\ COOH}}{C}HCH_2\mathbf{CH(CH_3)_2}$	**CH_3**			CH_3	250–253"		**41 (m.p.), (u);**
						amide, **m.p.** 286–290°	**41 (m.p.), (u);**
C_6H_5	CH,	COOH		CH,	267–270"		69 (m.p.);

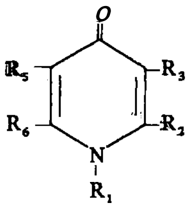
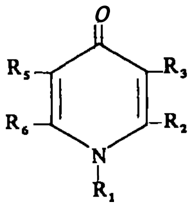


TABLE XII-82. 4-Pyridone Carboxylic Acids (Continued)

R_1	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
						ethyl ester, m.p. 150–152"	69 (m.p.);
$C_6H_4CH_3$-*o*	COOH		OCH_3		193"		128 (m.p.);
C_6H, CH,-*m*	COOH		OCH_3		177–178"		128 (m.p.);
$C_6H_4CH_3$-*p*	COOH		OCH_3		176–177°		128 (m.p.);
$-CH_2COOH$	CH_3	β-D-Glucosyloxy			236–237"		131 (m.p.);
$-CH_2C_6H_5$	CH,	COOH		CH_3		ethyl ester, m.p. 178–180"	69 (m.p.), (i);

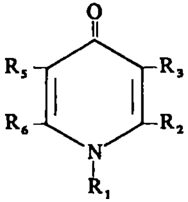
$-CH_2CONHCHCOOH$ $\quad\quad\quad\quad\ |$ $\quad\quad\quad\quad CH_2$ $\quad\quad\quad\quad\ |$ $\quad\quad\quad\quad CH(CH_3)_2$	CH_3			CH_3	305–310°		41 (m.p.), (u);
α-Naphthyl	COO×		OH		203°		129 (m.p.);
						ethyl ester, m.p. 182–183°	129 (m.p.), (u); 1120 (u);
$-CHCH_2C_6H_5$ $\ \ |$ $\ \ COO×$	CH_3			CH_3	229 231°		41 (m.p.), (u);
						amide, m.p. > 320°	41 (m.p.), (u);
CH_3	C_6H_5	COOH	COOH	C_6H_5		diethyl ester, m.p. 244°	448 (m.p.), (i);
$CH_2CH=CH_2$	C_6H_5	COOH	COOH	C_6H_5		diethyl ester, m.p. 166°	448 (m.p.), (i);
$CH_2C_6H_5$	C_6H_5	COOH	COOH	C_6H_5		diethyl ester, m.p. 204°	448 (m.p.), (i);

TABLE XII-83. 4-Pyridone Nitriles



R_1	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
CN					164–167"		460 (m.p.), (n), (u);
CN	CH, Cl		OH		164–165°		132 (m.p.), (i);
CN	CH, OH		OH		155–156°		132 (m.p.), (i);
CN	CH_3			CH_3	122–123°		132 (m.p.);
CN	CH, OH		OCH_3		169"		132 (m.p.), (i);

TABLE XII-84. Halo 4-Pyridones



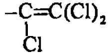
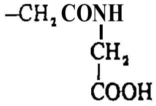
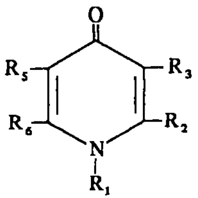
R_1	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
CH_3	D	Br	Br	D	193–194"		139 (m.p.), (i), (m), (n), (u);
CH_3	Cl				52–54"		241 (m.p.), (u);
CH_3		Cl	Cl		146–148"		241 (m.p.), (u); 460 (i);
CH_3		Br	Br		193–194"		139 (m.p.), (i), (n), (u); 460 (i), (u); 706 (m.p.);
CH_3	Cl	Cl	Cl		225–226"		456 (m.p.), (i), (n), (u);
CH_3		NH_2	Br			picrate, m.p. 195" *N'*-acetyl, m.p. 258–259"	556 (m.p.); 556 (m.p.), (i);
C_2H_5		Br	Br		157–159"		1107 (m.p.);
$-NHCONH_2$	 $-\underset{\mid}{\overset{}{C}}{=}C(Cl)_2$ with $\underset{}{Cl}$: $-C(Cl){=}C(Cl)_2$	Cl	Cl		246–247"		233 (m.p.);
CH_3	CH_3	Br	Br	CH_3	308"		706 (m.p.);
 $-CH_2\underset{OH}{\underset{\mid}{C}H}CH_2OH$		I	I		181–184"		1109 (m.p.);
 $-CH_2CO\underset{\underset{COOH}{\underset{\mid}{CH_2}}}{\underset{\mid}{N}H}$		I	I		222"		1122 (m.p.);

TABLE XII-84. Halo 4-Pyridones (Continued)



R_1	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
$CH_2CONHCH_2$ $\vert$ $COOH$		I	I			ethyl ester, m.p. **151–153"**	**1122** (m.p.);
C_2H_5	CH_3	Br	Br	CH_3	**248"**		**706** (m.p.);
$(CH,)_4COOH$		I	I		**198–199"**		**587** (m.p.);
						amide, m.p. **210–211°**	**587** (m.p.);
						methyl ester, m.p. **172"**	**587** (m.p.);
						ethyl ester, m.p. **96"**	**587** (m.p.);
						n-butyl ester, m.p. **174"**	**587** (m.p.);
						n-amyl ester, m.p. 73°	**587** (m.p.);
C_6H_5Hg-		Cl	Cl		338–340"		**831** (m.p.), (i);
$C_6H_4NH_2$-*p*	Cl	Cl	Cl			hydrochloride, m.p. **260"**	**232** (m.p.), (i);
$(CH_2)_5COOH$		I	I		**190–191"**		**587** (m.p.);
						methyl ester, m.p. **81"**	**587** (m.p.);
n-C, H_9	CH_3	Br	**Br**	CH_3	180°		**118** (m.p.);

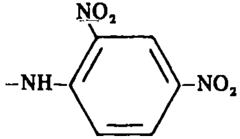
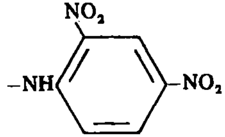
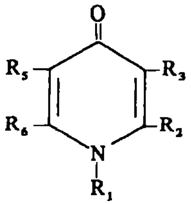
$-CH_2C_6H_5$		Br	Br			1/2 C_2H_5OH, m.p. 184–186"	279 (m.p.);
$-CH_2C_6H_5$		NH_2	I		232–233"		564 (m.p.);
$-(CH_2)_4COOCH_2$ $\quad\quad\quad\vert$ $\quad\quad CH_2OH$		I	I		86"		587 (m.p.);
	$-\underset{\vert\atop Cl}{C}=C(Cl)_2$	Cl	Cl		157–158"		233 (m.p.);
	$-\underset{\vert\atop Cl}{C}=C(Cl)_2$	Cl	Br		135–137"		233 (m.p.);
$-NHC_6H_5$	$-\underset{\vert\atop Cl}{C}=C(Cl)_2$	Cl	Cl		225"		233 (m.p.);
$-CH_2C_6H_5$		CH_3	Br		141–143"		279 (m.p.);
$-(CH_2)_7COOH$		I	I		114"		587 (m.p.);
						methyl ester, m.p. 75°	587 (m.p.);
$C_6H_4NHCOCH_3$-*p*	COOH	Cl	Cl	Cl	260–261°		232 (m.p.), (i);
$-(CH_2)_4COOCH_2$ $\quad\quad\quad\vert$ $(CH_3)_2NCH_2$		I	I		182"		587 (m.p.);
$-(CH_2)_{10}COOH$		I	I		121"		587 (m.p.);
						methyl ester, m.p. 126"	587 (m.p.);

TABLE XII-84. Halo 4-Pyridones (Continued)



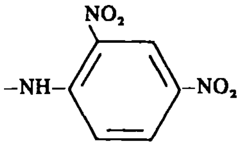
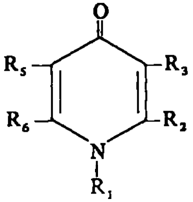
R_1	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
	C_6H_5	Cl	Cl		271–273°		233 (m.p.);
$-(CH_2)_{11}COOH$		I	I		102°		587 (m.p.);
						methyl ester, m.p. 92°	587 (m.p.);
CH_3	C_6H_5	Br	Br	C_6H_5	313°		706 (m.p.);
$-CH_2CONHCH, CH_2$ $CH_3(OCH_2CH_2)_4O$		I	I		90–91°		1123 (m.p.);
C_2H_5	C_6H_5	Br	Br	C_6H_5	285°		706 (m.p.);

TABLE XII-85. Nitro 4-Pyridones



R_1	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
COOH		NO_2				ethyl ester, m.p. 114–115°	586 (m.p.), (u);
CH_3		NO_2	NO_2		218°		456 (m.p.), (i), (n), (u); 775 (m.p.), (i), (n);
CH_3		NO_2			233°		497 (u); 586 (m.p.), (u);
CH_3		NH_2	NO_2		270°		556 (m.p.);
						N′-acetyl, m.p. 323°	556 (m.p.);
						N′-benzoyl, m.p. 244°	556 (m.p.);
$CH_2C_6H_5$		NO_2	I		175–176°		564 (m.p.);
$CH_2C_6H_5$		NO_2			113–114°		564 (m.p.);

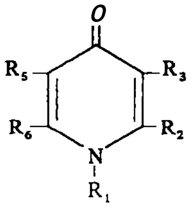


TABLE XII-86. Sulfur containing 4-Pyridones

R_1	R_2	R_3	R_5	R_6	m.p.	Derivatives	Ref.
SO, H						potassium salt	648 **(i)**, **(u)**;

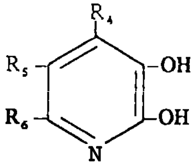


TABLE XII-87. 2,3-Pyridinediols

R_4	R_5	R_6	m.p.	Derivatives	Ref.
H	H	H	246–255°		3 (m.p.); 176 (i); 187 (m.p.); 342 (m.p.), **(t)**, (u); 361 (m.p.), (i); 467 (i), (u);
				1:1 complex with UO,	825 (y);
				1:1 complex with Cu	825 (y);
				1:1 complex with Pb	825 (y);
				1:1 complex with Zn	825 (y);

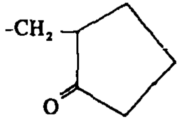
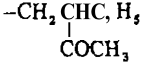
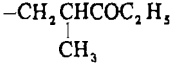
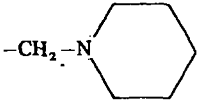
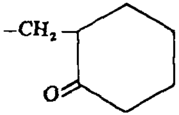
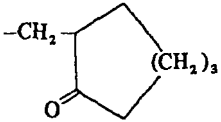
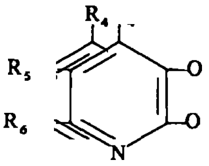
				1:1 complex with Ni	825 (y);
				1:1 complex with Co	825 (y);
				1:1 complex with Cd	825 (y);
				1:1 complex with Mn	825 (y);
		CH_3	192–194"		597 (m.p.), (u);
			219–221"		1124 (m.p.);
		 $-CH_2CH(COCH_3)C_6H_5$	192–196°		1124 (m.p.), (n);
		 $-CH_2CH(CH_3)COC_2H_5$	190–191°		1124 (m.p.), (i), (n);
			~215°		501 (m.p.), (u);
CH_3	C_6H_5		310–315"		221 (m.p.), (u);
				3-*O*-acetyl, m.p. 193–195°	221 (m.p.), (i), (n);
			236–237"		1124 (m.p.);
			239–241"		1124 (m.p.);

TABLE XII-87. 2,3-Pyridinediols (Continued)



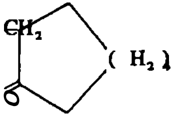
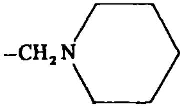
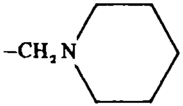
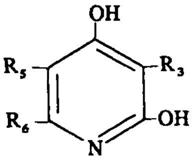
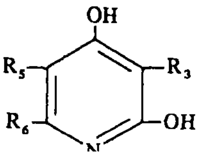
R_4	R_5	R_6	m.p.	Derivatives	Ref.
		– 	251–252°		1124 (m.p.), (i), (n);
$CH_2C_6H_5$	$-COCH_3$	$-CH_3$	210°		231 (m.p.);
$CH_2C_6H_5$	$-CO_2C_2H_5$	C_2H_5	163–164°		231 (m.p.);
			184–185°		501 (m.p.), (u);
$CH_2C_6H_5$	$-COC_6H_5$	CH_3	227°		231 (m.p.);

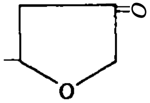
TABLE XII-88. 2,4-Pyridinediols



R_3	R_5	R_6	m.p.	Derivatives	Ref.
H	H	H			906 (a);
		CH_3	312–330"		50 (m.p.); **87** (m.p.); 109 (m.p.), **(i)**, (u); 502 (m.p.), (n), (u); 644 (m.p.); 1034(m);
				4-*O*-acetyl, m.p. 197"	644 (m.p.), (i); 645 **(i)**, (u);
	CH, CH, Cl		154–155"		589 (m.p.);
CH_3		CH_3	268–270°		158 (m.p.), (u); 159 (i); **(u);**
		C_2H_5	275"		50 (m.p.);
$COCH_3$		**CH_3**	256–261"		104 (m.p.); 106 (m.p.), **(i)**, (u); 109 (m.p.), (u); 110 (n); 644 (m.p.), (i), (u); 645 (i), (u); 1005 (m.p.);
				phenylhydrazone, m.p. 224–225°	**1005** (m.p.);
				2,4-dinitrophenylhydrazone, m.p. **305"**	106 (m.p.);
	$COCH_3$	**CH_3**	282–296"		**87** (m.p.); 90 (m.p.); 94 (m.p.), (u);

TABLE XII-88. 2,4-Pyridinediols (Continued)



R3	R5	R6	m.p.	Derivatives	Ref.
				2,4-dinitrophenylhydrazone, m.p. 240°	87 (m.p.);
				4-*O*-acetyl, m.p. 173°	87 (m.p.);
$-\overset{\text{NH}}{\overset{\Vert}{\text{C}}}\text{-CH}_3$		CH_3	314–317°		104 (m.p.); 105 (m.p.);
$-\overset{\text{NOH}}{\overset{\Vert}{\text{C}}}\text{-CH}_3$		CH_3	199°		151 (m.p.), (i), (n);
		$CH_2CH_2CH_3$	279°		150 (m.p.);
COC_2H_5		CH_3	225–226°		644 (m.p.), (i), (u); 1005 (m.p.);
				phenylhydrazone, m.p. 196–197°	1005 (m.p.);
$-COCH_3$	$COCH_3$	CH_3	264°		157 (m.p.);
C_2H_5	$COCH_3$	CH_3	197°		89 (m.p.);
$-COC_3H_7$-*n*		CH_3	183–184°		644 (m.p.), (i), (u); 1005 (m.p.);
				phenylhydrazone, m.p. 218–220°	1005 (m.p.);
		C_6H_4Cl-*p*	324°		50 (m.p.);
		C_6H_5	315–322°		50 (m.p.);
CH_3	CH_3			4-*O*-acetyl, m.p. 209–210°	162 (m.p.) (u);

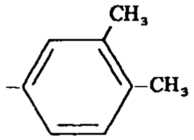
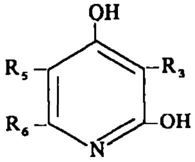
–CO[illegible] -n		CH_3	188–189°		644 (m.p.), (i), (u); 1005 (m.p.);
		CH_3		phenylhydrazone, m.p. 224–225°	1005 (m.p.);
$-COC_4H_9$ iso		CH_3	157–159°		644 (m.p.), (i), (u); 1005 (m.p.);
				phenylhydrazone, m.p. 227–228°	1005 (m.p.);
C_6H_5		CH_3	293°		163 (m.p.);
		$CH_2C_6H_5$	261°		50 (m.p.);
$-COC_5H_{11}\text{-}n$		CH_3	175–176°		644 (m.p.), (i), (u); 1005 (m.p.);
				phenylhydrazone, m.p. 194–195°	1005 (m.p.);
$-\overset{\overset{N-C_4H_9\text{-}n}{\Vert}}{C}-CH_3$		CH_3	170–171°		106 (m.p.), (i);
	OCH_3	C_6H_5	300–320°		87 (m.p.); 90 (m.p.); 94 (m.p.), (u);
$CH_2C_6H_5$		CH_3	247°		163 (m.p.);
			316°		50 (m.p.);
C_2H_5	CH_3	C_6H_5	232°		91 (m.p.);
		$C_6H_4CH(CH_3)_2\text{-}p$	276°		50 (m.p.);

TABLE XII-88. 2,4-Pyridinediols (Continued)



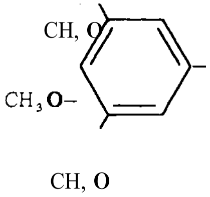
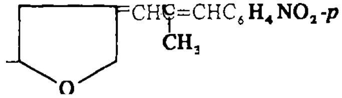
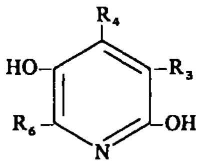
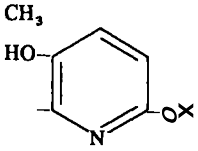
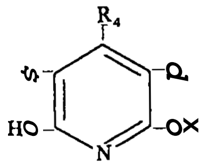
R_3	R_5	R_6	m.p.	Derivatives	Ref.
			262"		50 (m.p.);
–COCH=CHC$_6$H$_4$Cl-*p*		CH$_3$	313–314"		1031 (m.p.), (u);
–COCH=CHC$_6$H, NO, ·*m*		CH$_3$	277–278°		1031 (m.p.), (u);
–COCH=CHC$_6$H$_5$		CH$_3$	262–263°		1031 (m.p.), (u);
–COCH=CHC$_6$H$_4$OH-/I		CH$_3$	288–289"		
–CH$_2$C$_6$H$_5$	COCH,	CH$_3$	224–226"		90 (m.p.);
–CH$_2$C$_6$H$_5$	CH$_3$	C$_2$H$_5$	210"		96 (m.p.);
C$_6$H$_5$		C$_6$H$_5$	300"		163 (m.p.);
–COCH=CHC$_6$H$_4$N(CH$_3$)$_2$-*p*		CH$_3$	284–285°		1031 (m.p.), (u);
–CH$_2$C$_6$H$_5$	CH$_3$	**C$_6$H$_5$**	222–223"		91 (m.p.); 96 (m.p.);
–CH$_2$C$_6$H$_5$	COCH,	**C$_6$H$_5$**	261"		90 (m.p.);
CH$_3$	CH$_3$		238–239"		162 (m.p.), (u);
				acetate, m.p. 211–213"	162 (m.p.);

TABLE XII-89. 2,5-Pyridinediols



R$_3$	R$_4$	R$_6$	m.p.	Derivatives	Ref.
X		H	245–250°		342 (m.p.), (t), (u); 699 (u);
				2,5-di-*O*-acetyl	432 (n);
					176 (i);
				2,2′,5,5′-tetra-acetyl, m.p. 171°	432 (m.p.), (n), (u);
C_6H_5	CH_3		250–260°		296 (m.p.);



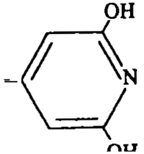
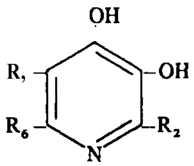
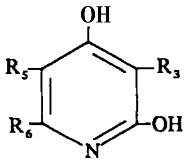
R_3	R_4	R_5	m.p.	Derivatives	Ref.
X	H	H	198 Z00°		455 (m.p.), (n), (u); 467 (i), (u); 504 (i), (u); 899 (n); 906 (a); 918 (s);
				deuterio	504 (i);
				hydrochloride	543 (b); 546 (i), (u);
	CH_3		192–194°		1000 (m.p.);
CH_3	CH_3	CH_3	179°	$HCl \cdot H_2O$ m.p. 170° (unstabl)	928 (m.p.), (i), (u); 928 (m.p.);
C_2H_5	CH_3		172–173°		510 (m.p.), (i), (n), (u);
C_2H_5	CH_3	CH_3	106°		928 (m.p.), (i), (u);
2-Deoxy-D-ribosyl			185°		618 (m.p.), (n), (u);
D-Ribosyl			190°		618 (m.p.), (u);
C H	CH_3	C_2H_5	105°	2,6-di-*O*-acetyl, m.p. 99–100°	928 (m.p.), (i), (u); 928 (m.p.);
	$-(CH_2)_6CH_6$		190–191°		6 (m.p.);
	$-(CH_2)_6-$ 		262–265°		[illegible] (m.p.);

TABLE XII-91. 3,4-Pyridinediols



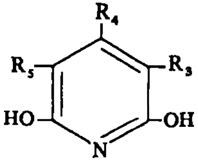
R_2	R_5	R_6	m.p.	Derivatives	Ref.
H	H	H	235-237°		134 (m.p.);
CH_3			> 250"		125 (m.p.), (u);
			293-295"		131 (m.p.); 858 (m.p.);
				hydrochloride, m.p. 184-186°	858 (m.p.);
				acetate, m.p. 205-207"	858 (m.p.);
		CH_2OH	246"		793 (m.p.);

TABLE XII-92. Alkoxy 2,4-Pyridinediols



R_3	R_5	R_6	m.p.	Derivatives	Ref.
OCH_3		CH, OH		·CH_3OH m.p. 169-171°	160 (m.p.), (i), (u);
OCH_3		CH_2OCOCH_3		4-*O*-acetyl, m.p. 143-146°	160 (m.p.), (i), (u);

TABLE XII-93. Alkoxy 2,6-Pyridinediols



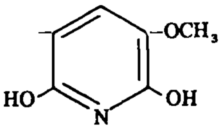
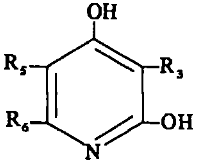
R₃	R₄	R₅	m.p.	Derivatives	Ref.
		OCH_3		2,6,2′,6′-tetraacetyl, m.p. 147"	894 (m.p.), (u);

TABLE XII-94. Amino 2,4-Pyridinediols



R₃	R₅	R₆	m.p.	Derivatives	Ref.
NH_2		CH_3		$HCl \cdot H_2O$ m.p. 283"	151 (m.p.), (i), (n);
				N′-acetyl, m.p. 245–246°	151 (m.p.), (i), (n);
				N′-acetyl-HCl, m.p. 283"	151 (m.p.);

TABLE XII-95. Amino 2,6-Pyridinediols

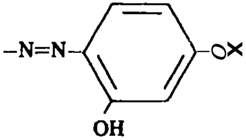
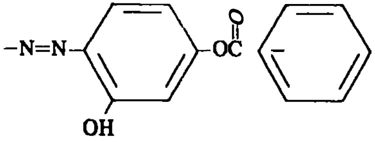
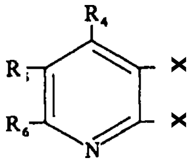
R_3	R_4	R_5	m.p.	Derivatives	Ref.
NH_2	NH_2		300°	hydrochloride *N*′-acetyl, m.p. 296–297°	846 (n), (u); 34 (m.p.); 740 (m.p.);
$N(COCH_3)_2$				2,6-di-*O*-acetyl, m.p. 89°	846 (m.p.), (n), (u);
$-N{=}NC_6H_5$			218 220°		740 (m.p.), (i), (n); 846 (m.p.), (i), (u);
			300°		939 (m.p.), (m), (u);
$-N{=}NC_6H_4Cl$-*p*	NH_2		315°		34 (m.p.);
$-N{=}NC_6H_5$		$-N{=}NC_6H_5$	200–202		740 (m.p.), (i), (n);
	$=NNHC_6H_4NO_2$-*p*			1-*p*-nitroanilino, m.p. >210°	800 (m.p.);
	$=NNHC_6H_5$			1-anilino, m.p. 188°	801 (m.p.);
			271°		939 (m.p.) (m) ( ):

TABLE XII-96. 2,3-Pyridinediol Carboxylic Acids and Derivatives



R_4	R_5	R_6	m.p.	Derivatives	Ref.
		$-CH_2\underset{\underset{CXO}{\vert}}{C}XC_5X_{11}$	172–173°		1124 (m.p.), (i), (n);
$CH_2C_6H_5$	<OOH	CH_3		ethyl ester, m.p. 148° amide, m.p. 271–272°	231 (m.p.);
		$-CH_2\underset{\underset{CXO}{\vert}}{C}XC_6H_{13}$	1≤8–ΩT0°		1124 (m.p.), (i);
$CH_2C_6H_5$	COOX	C_6H_5		ethyl ester, m.p. 174–175°	2Ξ1 (m.p.);
$CH_2C_6H_5$	COOH	$CH_2C_6H_5$		methyl ester, m.p. 192°	2Ξ1 (m.p.);

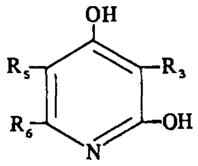


TABLE XII-97. **2,4-Pyridinediol** Carboxylic Acids and Derivatives

R_3	R_5	R_6	m.p.	Derivatives	Ref.
COOH		CH_3		ethyl ester	1034 (m);
	COOH	CH_3	280"	 ethyl ester, m.p. 228–229°	87 (m.p.); 87 (m.p.); 1034 (m);
	COOH	C_2H_5		ethyl ester, m.p. 182–183"	**87** (m.p.1; 1034 (m);
	COOH	$CH_2CH_2CH_3$		ethyl ester, m.p. 160"	87 (m.p.1; 1034 (m);

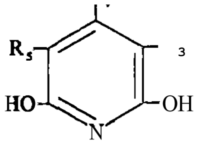
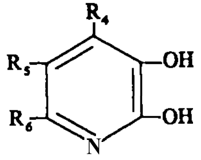


TABLE XII-98. 2,6-Pyridinediol Carboxylic Acids and Derivatives

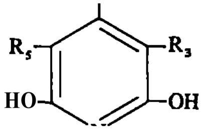
R_3	R_4	R_5	m.p.	Derivatives	Ref.
	$COOCH_3$			2,6-di-*O*-acetyl, m.p. 78–80"	507 (m.p.);
CONH,	NH_2		240°		9 (m.p.);
COOH	NH_2	$-N{=}NC_6H_4Cl$-*p*		ethyl ester, m.p. 259"	34 (m.p.);

TABLE XII-99. 2,3-Pyridinediol Nitriles



R_4	R_5	R_6	m.p.	Derivatives	Ref.
$CH_2C_6H_5$	CN	CH_3	238°		231 (m.p.);

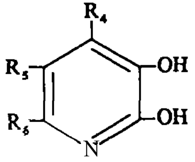
TABLE XII-100. 2,6-Pyridinediol Nitriles



R_3	R_4	R_5	m.p.	Derivatives	Ref.
CN					504 (i), (u);
				2,6-dideuterio	504 (i);
CN	NH_2		270°		9 (m.p.);
CN	CF_3			1.5 hydrate, m.p. 243–246"	55 (m.p.), (u);
				ammonium salt, m.p. 305–306"	55 (m.p.);
CN	CH_3	CN		ammonium salt, m.p. 340°	111 (m.p.), (i), (u);
				piperidinium salt, m.p. 299"	111 (m.p.), (u);

CN	C_2H_5	CN		hydrate, m.p. 216"	111 (m.p.), (i), (u);
				sodium salt·H_2O m.p. 350"	111 (m.p.), (i), (u);
				potassium salt, m.p. 330"	111 (m.p.), (i), (u);
				ammonium salt, m.p. 312°	111 (m.p.), (i), (u);
				piperidinium salt, m.p. 298"	111 (m.p.), (u);
CN	n-C_3H_7	CN		ammonium salt, m.p. 265"	111 (m.p.), (i), (u);
CN	n-C_6H_{13}	CN		ammonium salt, m.p. 304°	111 (m.p.), (i), (u);
				piperidinium salt, m.p. 288°	111 (m.p.), (u);

TABLE XII-101. Halo **2,3-Pyridinediols**



R_4	R_5	R_6	m.p.	Derivatives	Ref.
Cl			290–295"		3 (m.p.), (n);
	Cl		290–295°		3 (m.p.), (n);

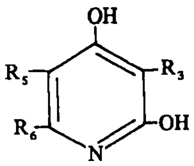


TABLE XII-102. Halo 2,4-Pyridinediols

R_3	R_5	R_6	m.p.	Derivatives	Ref.
	Cl	Cl	273–274"		**98 (m.p.), (i), (m), (n), (u);**
F	F	F	188"		**248 (m.p.), (i); 1111 (m.p.);**
Cl	Cl	F	219–221"		**953 (m.p.);**
Br	Cl	Cl	230°		**98 (m.p.), (u);**
Br	COOH	Cl		ethyl ester, m.p. 238"	**97 (m.p.);**
CN		Cl	190"		**98 (m.p.), (i);**
	CN	Cl	218–219°		**98 (m.p.), (i), (m), (n), (u);**
Cl	Cl	CH, Cl	166–170"		**502 (m.p.), (n);**
	COOH	Cl		ethyl ester, m.p. 219"	**97 (m.p.), (u);** **98 (n);**
Cl	Cl	CH_3	250–252"		**502 (m.p.), (n);**
	CH_2Cl	Cl	198°		**98 (m.p.), (i), (n);**
Br	CH_3	Cl	198°		**97 (m.p.);**
	CH, Br	Cl	220"		**98 (m.p.), (i), (n);**
Cl		CH_3	> 300°		**502 (m.p.), (n);**
	CH_3	Cl	302"		**97 (m.p.), (i), (u); 98 (n);**
Cl	COOH	CH_3		ethyl ester, m.p. 278–280"	**707 (m.p.), (i), (n);**
	CH, CH, Cl	Cl	257"		**97 (m.p.), (u);**
				2,4-di-*O*-acetyl, b.p. 178°/4 mm	**589 (b.p.);**
	C_2H_5	Cl	285"		**98 (m.p.), (n);**

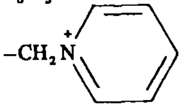
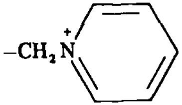
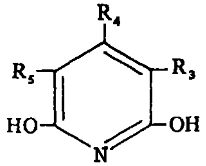
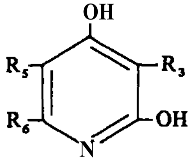
Br	$-COCH_2Br$		CH_3	180°	94 (m.p.), (n);
	$-CH_2CH_2CH_3$		Cl	305°	97 (m.p.), (u);
	$-CH_2OC_2H_5$		Cl	210°	98 (m.p.), (n);
	$-CH_2CH_2CH_2CN$		Cl	190°	98 (m.p.), (i), (m), (n), (u);
Cl	Cl		C_6H_5	270–272°	707 (m.p.);
	C_6H_4Cl-*p*		Cl	>300°	98 (m.p.), (i), (n), (u);
	$C_6H_4NO_2$-*p*		Cl	>300°	98 (m.p.), (i), (m), (n), (u);
	C_6H_5		Cl	310°	97 (m.p.), (u);
		Cl^-	Cl	>300°	98 (m.p.);
		Br^-	Cl	>300°	98 (m.p.) (n);
	$-(CH_2)_{13}CN$		Cl	250°	98 (m.p.) (i) ( ) (u);

TABLE XII-103. Halo 2,6-Pyridinediols



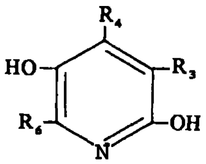
R_3	R_4	R_5	m.p.	Derivatives	Ref.
Cl	Cl	Cl	193–195"		18 (m.p.);
C_4H_9-*n*	Cl	Cl	265–270"		7 (m.p.);

TABLE XII-104. Nitro 2,4-Pyridinediols



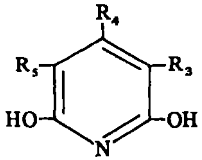
R_3	R_5	R_6	m.p.	Derivatives	Ref.
NO_2	Cl	Cl	215"		98 (m.p.), (u);
NO_2			264°		305 (m.p.);
NO_2	CH_3	Cl	233"		97 (m.p.);
NO_2	Br	CH_3	263–265°		502 (m.p.);
NO_2		CH_3	281–286"		86 (m.p.);
NO_2	COOH	CH_3		ethyl ester, m.p. 250–251"	86 (m.p.);
				n-butyl ester, m.p. 183–184"	86 (m.p.);
NO_2		CH, CH, CH,	145"		150 (m.p.);
NO_2	COC_6H_5	CH_3	219"		86 (m.p.);

TABLE XII-105. Nitroso 2,5-Pyridinediols



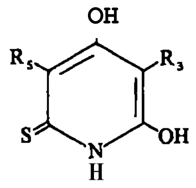
R_3	R_4	R_6	m.p.	Derivatives	Ref.
		NO	210"		292 (m.p.), (u);
C_6H_5	CH,	NO	250–253"		292 (m.p.), (u);

TABLE XII-106. Nitro 2, Pyridinediols



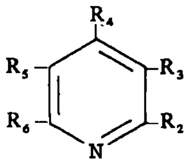
R_3	R_4	R_5	m.p.	Derivatives	Ref.
NO_2			150°		701 (m.p.);

TABLE XII-107. Sulfur Containing 2,4-Pyridinediols



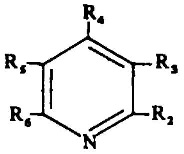
R_3	R_5	m.p.	Derivatives	Ref.
COOH	COOH		*N*-phenyl-3,5-diethyl ester, m.p. 156"	171 (m.p.), (u);

TABLE XII-108. Alkyl and Aryl 2,4-Pyridinediol Ethers



R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OCH_3		OCH_3			b.p. 89°/12 Torr		252 (b.p.);
					b.p. 200–201"		768 (b.p.);
						picrate, m.p. 158–159°	252 (m.p.); 768 (m.p.);

TABLE XII-109. Alkyl and Aryl 2,6-Pyridinediol Ethers



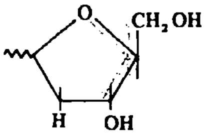
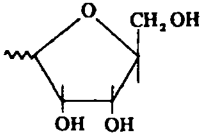
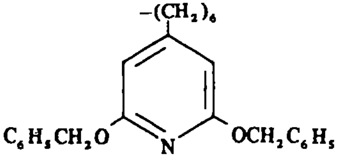
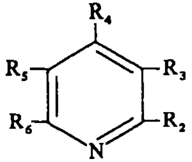
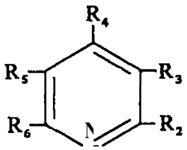
R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OCH_3				OCH_3			455 (n), (u); 505 (t);
OCH_3				CO_2H			467 (u);
$OCH_2C_6H_5$				$OCH_2C_6H_5$	74–75°		618 (m.p.), (u);
$OCH_2C_6H_5$		CH_3		$OCH_2C_6H_5$	55–56°		1000 (m.p.);
$OCH_2C_6H_5$				$OCH_2C_6H_5$	89–91°		618 (m.p.), (k), (n), (u);
$OCH_2C_6H_5$				$OCH_2C_6H_5$	184–185°		618 (m.p.), (k), (u);
$OCH_2C_6H_5$	COC_6H_5			$OCH_2C_6H_5$	117–118°		618 (m.p.), (n), (u);
$OCH_2C_6H_5$				$OCH_2C_6H_5$	90–92°		6 (m.p.);

TABLE XII-110. Alkyl and Aryl 3,5-Pyridinediol Ethers



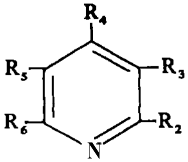
R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
	OCH_3		OCH_3			chloroplatinate, m.p. 212–213°	705 (m.p.);
C_6H_5	OC_6H_5		OC_6H_5	C_6H_5	162–164"		1098 (m.p.);

TABLE XII-111. Amino 2,4-Pyridinediol Ethers



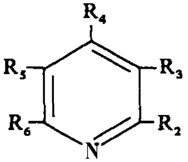
R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OC_2H_5		OC_2H_5		NH_2	35–36"		284 (m.p.);
						picrate, m.p. 176–177"	284 (m.p.);

TABLE XII-112. Amino 2,6-Pyridinediol Ethers



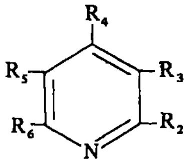
R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OCH_3		NH_2		OCH_3			504 (i), (u);
$OCH_2C_6H_5$		NH_2		$OCH_2C_6H_5$	74–75°		740 (m.p.), (i), (n);
						N′-acetyl, m.p. 88–89°	740 (m.p.), (i);

TABLE XII-113. Ethers of 2,6-Pyridinediol Carboxylic Acids



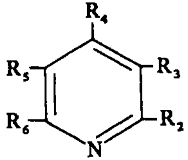
R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OCH_3	COOH			OCH_3	136–137°		618 (m.p.), (u);
OCH_3		COOH		OCH_3		methyl ester, m.p. 68–69"	507 (m.p.);
						diethylamide, m.p. 87–88"	975 (m.p.);
$OCH_2C_6H_5$	COOH			$OCH_2C_6H_5$	131–133"		618 (m.p.), (u);

TABLE XII-114. Ethers of 2,6-Pyridinediol Nitriles



R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OCH_3	CN	CH_3	CN	OCH_3	129°		111 (m.p.), (i), (u);
OCH_3	CN	C_2H_5	CN	OC_2H_5	103°		111 (m.p.), (i), (u);
OC_2H_5	CN		CN	OC_2H_5	144–145°		100 (m.p.);
OC_2H_5	CN	C_2H_5	CN	OC_2H_5	103°		111 (m.p.);

TABLE XII-115. Halo 2,4-Pyridinediol Ethers



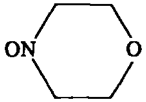
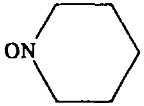
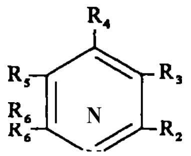
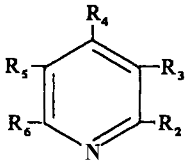
R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OCH_3	F	OCH_3	F	F	b.p. 87°/15 mm		245 (b.p.), (g), (i), (n), (u); 248 (b.p.), (i), (u); 1111 (b.p.);
OCH_3	Cl	OCH_3	Cl	F	65–68°		246 (m.p.), (g), (i); 950 (m.p.); 953 (m.p.);
OCH_3	Cl	OCH_3	Cl	Cl	116–125"		239 (m.p.), (u); 778 (m.p.), (n);
OCH_3	Br	OCH_3	Br	Br	143"		952 (m.p.);
OC_2H_5	Cl	OCH_3	Cl	F	50–51°		953 (m.p.1;
$OCH(CH_3)_2$	Cl	OCH_3	Cl	Cl	b.p. 130°/3 mm		240 (b.p.);
OC_2H_5		OC_2H_5	Br		71–72"		284 (m.p.);
	Cl	OCH_3	Cl	Cl	96"		240 (m.p.);
	Cl	OCH_3	Cl	Cl	56"		240 (m.p.);
$OC_2H_4OCH_3$	Cl	$OC_2H_4OCH_3$	Cl	F	b.p. 135°/15 mm		953 (b.p.);
$OC_6H_4NO_2$-*p*	Cl	$OC_6H_4NO_2$-*p*	Cl	F	235–236"		953 (m.p.);
O-Mesityl	Cl	*O*-Mesityl	Cl	F	154–155"		953 (m.p.);

TABLE XII-116. Halo 2,6-Pyridinediol Ethers



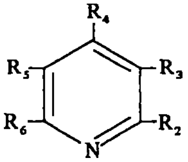
R$_2$	R$_3$	R$_4$	R$_5$	R$_6$	m.p.	Derivatives	Ref.
OCH_3	Br			OCH_3	b.p. 115°/29 mm		618 (b.p.), (u);
OCH_3	F		F	OCH_3	87"		949 (m.p.);
OCH_3	Br		Br	OCH_3	89–91°		618 (m.p.), (u);
OCH_3	F	Br	F	OCH_3	120–122"		247 (m.p.), (n); 949 (n);
OCH_3	Cl	Cl	Cl	OCH_3	140–141"		239 (m.p.), (u);
OCH_3	Br	Br	Br	OCH_3	131–132°		952 (m.p.);
OCH_3	Cl	$-NHNH_2$	Cl	OCH_3	129–132"		239 (m.p.);
OC_2H_5	Cl	Cl	Cl	OC_2H_5	105–106"		239 (m.p.);
OCH_3	Cl	$-NHNHCOCH_3$	Cl	OCH_3	201–203"		239 (m.p.);
OC_6H_{11}	Cl	Cl	Cl	OC_6H_{11}	122–123"		239 (m.p.);
$OCH_2C_6H_5$	Br			$OCH_2C_6H_5$	57–59"		618 (m.p.), (u);
$OCH_2C_6H_5$	Br		Br	$OCH_2C_6H_5$	74"		740 (m.p.), (i), (n);
$OCH_2C_6H_5$	Cl	Cl	Cl	$OCH_2C_6H_5$	98–99"		239 (m.p.);
$OCH_2C_6H_5$	Br	Br	Br	$OCH_2C_6H_5$	108–109"		740 (m.p.), (i), (n);

TABLE XII-117. Nitro 2,4-Pyridinediol Ethers



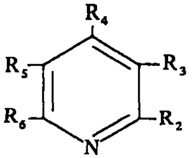
R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OCH_3	NO_2	OCH_3		CH_3	108°		86 (m.p.);
OCH_3	NO_2	OCH_3	$COOC_2H_5$	CH_3	53–54°		86 (m.p.);

TABLE XII-118. Nitro 2,6-Pyridinediol Ethers



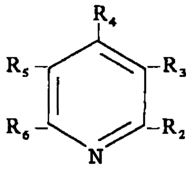
R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OCH_3	NO_2		NO_2	OCH_3			1125 (n);

TABLE XII-119. Sulfur Containing Esters of **2,4-Pyridinediols**



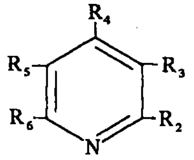
R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
$OSO_2C_6H_5$	Cl	$OSO_2C_6H_5$	Cl	CH,	97–98"		502 **(m.p.)**;
OSO, C, H,		OSO, C, H_5		CH,	54–55"		502 **(m.p.), (u)**;

TABLE XII-120. Alkyl and Aryl 2,3,6-Pyridinetriols



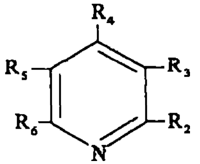
R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OH	OH	CH,		OH	209–210°		506 **(m.p.)**, (i);
						2,3,6-triacetyl, **m.p.** 69"	506 **(m.p.), (i), (u)**;
OH	OH		CH,	OH	240°		506 **(m.p.)**;
						2,3,6-triacetyl, **m.p.** 86°	506 **(m.p.)**;
OH	OH	CH,	CH,	OH		2,3,6-triacetyl, **m.p.** 102°	506 **(m.p.)**;
OH	OH	CH,	C_6H_5	OH		2,3,6-triacetyl, **m.p.** 106–107"	292 **(m.p.)**;

TABLE XII-121. Alkyl and Aryl 2,4,6-Pyridinetriols



R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OH		OH		OH			504 (i), (u);

TABLE XII-122. Ethers of 2,3,4-Pyridinetriols



R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OCH_3	OCH,	OCH,		CH_2OH	48-49"		160 (m.p.), (c), (i), (u);

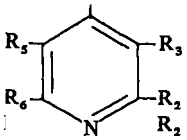


TABLE XII-123. Ethers of 2,4,6-Pyridinetriols

R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
OCH,	F	OCH,	F	OCH,	50–54"		248 (m.p.), (i), (u); 1111 (m.p.);
OCH_3	Cl	OCH,	Cl	OCH,	93–94"		16 (m.p.), 239 (m.p.);

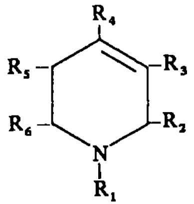


TABLE XII-124. Dihydro-2-pyridinols and Dihydro-2-pyridones

R_1	R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
	Kclo					120° or		1126 (m.p.);
						65–67°		1127 (m.p.), (i), (n), (u);
CH_3	Kclo					b.p. 129°/0.25 mm		861 (b.p.), (i);
	Keto				CH_3 ,H	103–109°		UL (m.p.), (i), (u);
								1128 (m.p.), (i), (u);
	Kclo				a,H	b.p. 109°/13 mm		UL (b.p.), (u);
								695 (b.p.); 1128 (i);
	Keto	CH,	CH_3		CH_3, H	767T		1129 (m.p.), (i), (n), (u);
	Kclo		CH_3		CH_3, CH_3	115–118°		1130 (m.p.), (u);
								1131 (m.p.), (i);
C_3H_5	Keto				CH_3, H	b.p. 111°/13 mm		1128 (b.p.), (i), (u);
	Keto	CN	CH_3		CH_3, CH_3	156–157°		1131 (m.p.), (i);
	Kclo	COOH	CH_3		CH_3, CH,	106–110°		1131 (m.p.), (i);
CH_3	Keto		CH_3		CH_3, CH_3	43–44°		1130 (m.p.), (i), (n), (m);
n-C_3H_7	Kclo				CH_3,H	b.p. 121°/15 mm		1128 (b.p.), (i);
CH_3	Kclo	CN	CH_3		CH_3, CH_3	139–140°		1130 (m.p.), (i), (n), (m);

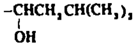
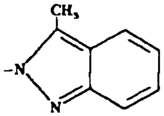
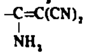
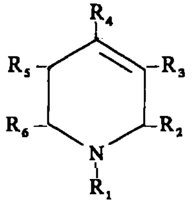
	Keto	$COCH_3$	CH_3		CH_3, CH_3	145–146°		1131 (m.p.), (i); 1132 (m.p.); 1149 (m.p.);
							semicarbazone, m.p. 245°	1131 (m.p.);
NH_2	Keto		C_6H_5			60–62°		1133 (m.p.), (n), (u);
							hydrochloride, m.p. 197–198°	1133 (m.p.);
							N'-acetyl, m.p. 205–206°	1133 (m.p.), (i), (n), (u);
							N'-diacetyl, m.p. 131–132°	1133 (m.p.), (i), (n), (u);
	Keto				CH_3, C_2H_5	121°		1132 (m.p.); 1149 (m.p.);
	Keto				CH_3, CH_3	120–122°		1149 (m.p.);
$-(CH_2)_3N(CH_3)_2$	Keto				CH_3, H	b.p. 92°/0.25 mm		1128 (b.p.), (i);
CH_3	Keto				C_6H_5, H	b.p. 186°/13 mm		441 (b.p.);
C_6H_5	Keto				CH_3, H	b.p. 180°/10 mm		441 (b.p.);
	Keto	$COCH_3$	CH_3		$-(CH_2)_4-$	134°		1132 (m.p.); 1149 (m.p.);
	Keto	COC_3H_7-n	CH_3		CH_3, CH_3	70–71°		1149 (m.p.);
	Keto	$COCH_3$	CH_3		C_2H_5, C_2H_5	87°		1132 (m.p.); 1149 (m.p.);
	Keto	$COCH_3$	CH_3		isoC_3H_7, CH_3	110–111°		1132 (m.p.); 1149 (m.p.);
	Keto	$COCH_3$	n-C_3H_7		CH_3, CH_3	109–110°		1149 (m.p.);
	Keto	$COCH_3$	isoC_3H_7		CH_3, CH_3	125–127°		1149 (m.p.);
	Keto		$COCH_3$	 $-\underset{OH}{\underset{\mid}{C}}HCH_2CH(CH_3)_2$		189–190°		856 (m.p.), (m), (n);
	Keto					188–191°		1134 (m.p.);
$-CH_2C_6H_5$	Keto				CH_3, H	b.p. 120°/0.5 mm		441 (b.p.); 697 (b.p.);
$C_6H_4OCH_3$-p	Keto				CH_3, H	b.p. 155°/0.2 mm m.p. 65–66°		1128 (b.p.), (m.p.), (i);
	Keto	$COCH_3$	CH_3		$-(CH_2)_5-$	131°		1132 (m.p.); 1149 (m.p.);
	Keto	$COCH_3$	CH_3		isoC_4H_9, CH_3	87°		1132 (m.p.); 1149 (m.p.);
	Keto	$COCH_3$	CH_3		t-C_4H_9, CH_3	123–125°		1132 (m.p.); 1149 (m.p.);
	Keto	$COCH_3$	CH_3		C_6H_5, H	40–41°		1132 (m.p.);
CH_3	Keto	C_6H_5	OC_2H_5			12–73'		1135 (m.p.), (i), (u);
	Keto	$COCH_3$	CH_3		$-(CH_2)_4-$	141°		1149 (m.p.);
	Keto	 $\underset{NH_2}{\underset{\mid}{-C}}=C(CN)_2$	C_6H_5			2400		79 (m.p.), (i);
	Keto	$COCH_3$	C_6H_5		CH_3, CH_3	160–162°		1149 (m.p.);
	Keto	$COCH_3$	CH_3		C_6H_5, CH_3	167–1690		1149 (m.p.);
	Keto	COC_6H_5	CH_3		CH_3, CH_3	158–159°		1131 (m.p.), (i), (u); 1149 (m.p.);
$CH_2C_6H_5$	Keto			isoC_3H_7, H		b.p. 162°/0.01 mm		1136 (b.p.);
	Keto	$COCH_3$	CH_3		$-(CH_2)_7-$	153–154°		1149 (m.p.);

TABLE XI-124. Dihydro-2-pyridinols and Dihydro-2-pyridones (Continued)



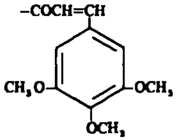
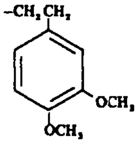
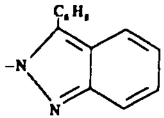
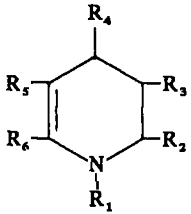
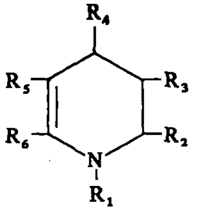
R_1	R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
	Keto	$COCH_3$	CH_3		C_6H_5, C_6H_5	169–171°		1149 (m.p.);
	Keto	$COCH_3$	CH_3		$CH_2C_6H_5$, CH_3	148–150°		1149 (m.p.);
$COCH_3$	Keto		$COCH_3$	$-\underset{\displaystyle OCOCH_3}{\underset{\vert}{C}}HCH_2CH(CH_3)_2$		175°		856 (m.p.), (k), (n);
	Keto	$COCH_3$	CH_3		$-(CH_2)_5-$	141°		1132 (m.p.);
	Keto	$COCH_3$	CH_3		$(isoC_4H_9)_2$	130–131°		1132 (m.p.); 1149 (m.p.);
C_6H_5	Keto				C_6H_5, H	187–188°		441 (m.p.);
	Keto					124°		860 (m.p.), (m), (n);
	Keto	COC_6H_5	CH_3		C_2H_5, C_2H_5	137–138°		1149 (m.p.);
	Keto			C_2H_5, H				352;
$CH_2C_6H_5$	Keto		$NHCH_2CH_2OH$	$isoC_3H_7$, H		159°		1136 (m.p.);
	Keto	$COCH_3$	CH_3		$-(CH_2)_9-$	153–154°		1132 (m.p.);
	Keto					231–236°		1134 (m.p.);
$CH_2C_6H_5$	Keto				C_6H_5, H	112–115°		441 (m.p.);
$CH_2C_6H_5$	Keto	C_6H_5	OC_2H_5			112–114°		1135 (m.p.);
$CH_2C_6H_5$	Keto	NHC_6H_5	$isoC_3H_7$, H			188°		1136 (m.p.);

TABLE XII-124a. Dihydro-2-pyridinols and Dihydro-2-pyridones



R_1	R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
	keto		CH_3			95–96°		47 (m.p.), (n);
	keto	OH, H			CH_3, H		3-*O*-acetyl m.p. 74°	24 (m.p.);
CH_3	keto				CH_3, H	b.p. 104°/13 mm		695 (b.p.); 1128 (b.p.); (i);
	keto			C_2H_5		79–80°		1127 (m.p.), (i), (n), (u);
C_2H_5	keto				CH_3, H	b.p. 106°/13 mm		1128 (b.p.), (i), (u);
$COCH_3$	OH, H	SCH_3, H			SCH_3, H		2-*O*-acetyl m.p. 115–117°	1158 (m.p.), (c), (i), (m), (u);
C_6H_4Cl-*p*	keto	OH, H				157–158°		24 (m.p.);
	keto	C_2H_5, C_2H_5	OCH_3	CH_3		b.p. 74°/6 mm		1146 (b.p.);
C_6H_4Cl-*p*	keto	OH, H			CH_3, H	103°	3-*O*-acetyl m.p. 120–124°	24 (m.p.); 24 (m.p.); 1159 (m.p.);
C_6H_5	keto	OH, H			CH_3, H	102°	3-*O*-acetyl m.p. 117°	24 (m.p.); 24 (m.p.);
$COCH_3$	OH, H	–SC_4H_9-*t*, CH_3		CH_3	OH, H		2,6-di-*O*-acetyl m.p. 125–127°	1158 (m.p.), (c), (i), (m), (u);
$COCH_3$	OH, D	SC_4H_9-*t*			SC_4H_9-*t*, D		2-*O*-acetyl m.p. 116–117°	1158 (m.p.), (i), (m);
$COCH_3$	OH, H	SC_4H_9-*t*			SC_4H_9-*t*, H		2-*O*-acetyl m.p. 116–117°	1158 (m.p.), (i), (m), (u);
$COCH_3$	OH, H	SC_4H_9-*t*	CH_3		SC_4H_9-*t*, H		2-*O*-acetyl m.p. 105–107°	1158 (m.p.), (c), (i), (m), (u);
$COCH_3$	OH, H	SC_4H_9-*t*	C_4H_9-*t*		SC_4H_9-*t*, H		2-*O*-acetyl m.p. 98–100°	1158 (m.p.), (i), (m), (u);

TABLE XII-124a. Dihydro-2-pyridinols and Dihydro-2-pyridones (Continued)



R$_1$	R$_2$	R$_3$	R$_4$	R$_5$	R$_6$	m.p.	Derivatives	Reference
$COCH_3$	OH, H	SC_4H_9-*t*	C_6H_5		SC_4H_9-*t*, H		2-*O*-acetyl m.p. 140–142°	1158 (m.p.), (i), (m), (u);
	keto				CH_3	119–120°		1160 (m.p.); 1161 (m.p.), (i), (n);
	keto			COOH	CH_3		ethyl ester m.p. 156°	70 (m.p.), (u); 84 (m.p.), (n); 1034 (m);
							r-butyl ester m.p. 127–128°	84 (m.p.);
	keto			CH_3	CH_3	130–131°		1160 (m.p.); 1162 (m.p.);
	keto			$COCH_3$	CH_3	141°		84 (m.p.); 1034 (m.p.);
CH_3	keto			COOH	CH_3		ethyl ester b.p. 105°/0.3 mm	84 (b.p.); 1034 (m);
	keto	CH_3, H		COOH	CH_3		ethyl ester m.p. 157–158°	84 (m.p.);
	keto		CH_3, H	COOH	CH_3		ethyl ester m.p. 143–147°	84 (m.p.); 1034 (m);
	keto			C_2H_5	CH_3	87–88°		1163 (m.p.);
CH_3	keto			$COCH_3$	CH_3	b.p. 97°/0.1 mm		84 (b.p.);
	keto			*n*-C_3H_7	CH_3	68–70°		1162 (m.p.); 1163 (m.p.);
	keto			*n*-C_4H_9	CH_3	57–58°		1163 (m.p.1;

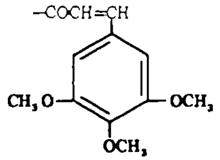
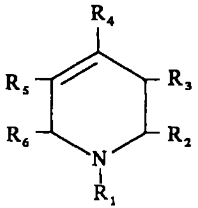
	keto				C_6H_5	148–1599		938 (n);
								1160 (m.p.);
								1162 (m.p.);
	keto			CH_3	C_6H_4Cl-*p*	159–160°		1142 (m.p.);
	keto			CH_3	C_6H_5	136–137°		1142 (m.p.);
	keto			C_6H_5	CH_3	169–170°		787 (m.p.);
	keto	OH, H	NH_2, CH_3	C_6H_5		280°		221 (m.p.), (i), (n), (u);
							3-*O*-acetyl, 4-*N*-acetyl m.p. 232–233°	221 (m.p.), (i), (n);
	keto			COOH	$CH_2C_6H_5$		methyl ester m.p. 108–110°	70 (m.p.), (u);
	keto	C_6H_5, H		CH_3	CH_3	132°		1164 (m.p.);
	keto			CH_3	$C_6H_4CH_3$-*p*	146–147°		1142 (m.p.);
	keto	CN, H	OH, H		$CH{=}CHC_6H_5$	315'		57 (m.p.), (i), (u);
							4-*O*-acetyl m.p. 289"	57 (m.p.), (i), (u);
	keto	C_6H_5, H	CH_3, CH_3		CH_3	125°		1164 (m.p.);
	keto	C_6H_5, H		C_6H_5	Br	190–192°		1165 (m.p.), (i);
	keto			C_6H_5	C_6H_5	214–215°		35 (m.p.), (i);
								443 (m.p.), (i), (u);
	keto					124"		859 (m.p.), (i), (m), (n), (u);
								1143 (m.p.), (i), (n), (u);
	keto	C_6H_5, H		C_6H_5	CH_3	194°		1164 (m.p.);
	keto		C_6H_5, H	C_6H_5	CH_3	178°		444 (m.p.), (i);
	keto	C_6H_5, H		CH_3	C_6H_5	135°		1164 (m.p.);
	keto		C_6H_5, H	CH_3	C_6H_5	187°		444 (m.p.), (i);
	keto	COOH, H	C_6H_5, H	CH_3	C_6H_5			444 (i);
	keto	C_6H_5, H		C_6H_5	C_6H_5	180–181°		1164 (m.p.);

TABLE XII-125. Dihydro-3-pyridinols and Dihydro-3-pyridones



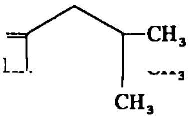
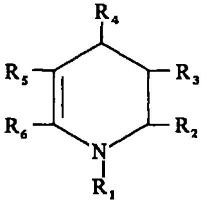
R_1	R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
$CH_2C_6H_5$		keto		OH		87–89"	hydrate	1166 (m.p.);
CH_3		OH, H	C_6H_5			104–106"		1151 (m.p.), (u); 1167 (m.p.);
							hydrochloride m.p. 211–214°	1151 (m.p.);
							3-*O*-acetyl ·HBr m.p. 230–232"	1167 (m.p.), (u);
C_6H_5	NHC, H,	keto				140–142°		1153 (m.p.), (i), (u);
$C_6H_4CH_3$-*p*	NHC, H_4CH_3-*p*	keto				164–165°		1153 (m.p.), (i), (u);
		keto		CH_3, CH_3		147°		1168 (m.p.), (i), (u);
							hydrochloride m.p. 227–229°	1168 (m.p.);
							picrate m.p. 197"	1168 (m.p.);

TABLE XII-126. Dihydro-4-pyridinolsand Dihydro-4-pyridones



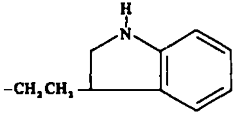
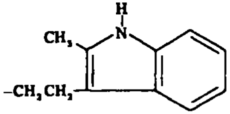
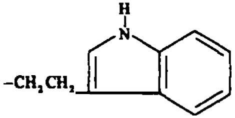
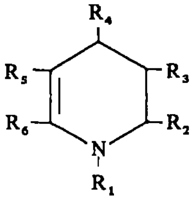
R_1	R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
	H, C_6H_5		keto		CH_3	160-161°		48 (m.p.), (i), (n), (u);
CH_3	H, $CH_2C_6H_5$		keto			68-70°		767 (m.p.), (m), (n);
	H, $CH_2CH_2C_6H_5$		keto		CH_3	143-145°		1138 (m.p.), (i), (n), (u);
			keto			164°		788 (m.p.), (i), (u);
			keto			206°		788 (m.p.), (i), (u);
	H, C_6H_5		keto		C_6H_5	149-151°		48 (m.p.), (i), (n), (u);
			keto	$COCH_3$		198°		1169 (m.p.), (i), (n), (u);
C_6H_5	H, C_6H_5		keto	I	CH_3	151°		449 (m.p.), (i), (n), (u);
C_6H_5	H, C_6H_5		keto		CH_3	84-85'		39 (m.p.), (i), (n), (u); 449 (m.p.), (i), (u); 765 (m.p.), (i), (n), (u); 1137 (n);

TABLE XII-126. Dihydro-4-pyridinols and Dihydro-4-pyridones (Continued)



R$_1$	R$_2$	R$_3$	R$_4$	R$_5$	R$_6$	m.p.	Derivatives	Ref.
							hydrobromide, m.p. 153°	449 (m.p.);
							hydrochloride. m.p. 173"	449 (m.p.);
	H, C_6H_5		keto	CH_3	C_6H_5			765 (i), (n), (t), (u);
	H, C_6H_5		keto	C_6H_5	CH_3	257°		765 (m.p.), (i), (n), (u);
$-N{=}CHC_6H_5$	H, C_6H_5	H, $CH_2C_6H_5$	keto		CH_3	176-17 P		48 (m.p.), (i), (u);
	H, C_6H_5		keto		CH_3	159-160°		48 (m.p.), (f), (n), (u);
	H, C_6H_5		keto		$CH_2CH_2C_6H_5$	124-126°		48 (m.p.), (i), (n), (u);
$-NHCH_2C_6H_5$	H, C_6H_5		keto		CH_3			48 (f), (n), (u);
C_6H_5	H, $CH{=}CHC_6H_5$		keto		CH_3	62–63'		1138 (m.p.), (i), (n), (u);
C_6H_5	H, $CH_2CH_2C_6H_5$		keto		CH_3			1138 (t);
	H, $CH_2CH_2C_6H_5$	H, $CH_2C_6H_5$	keto		CH_3			1138 (u);
	H, $CH_2CH_2C_6H_5$		keto		$CH_2CH_2C_6H_5$	144-146°		1138 (m.p.), (i), (u);
C_6H_5	H, C_6H_5		keto		C_6H_5	149–151'		39 (m.p.), (i), (n), (u);
$-N{=}CHCH{=}CHC_6H_5$	H, $CH{=}CHC_6H_5$		keto		CH_3	185–186°		1138 (m.p.), (i), (n), (u);
$-N{=}CHCH{=}CHC_6H_5$	H, $CH_2CH_2C_6H_5$		keto		CH_3	Oil		1138 (n), (u);
$-NH(CH_2)_2C_6H_5$	H, $CH_2CH_2C_6H_5$		keto		CH_3	Oil		1138 (n);
$-N{=}CHC_6H_5$	H, C_6H_5		keto		C_6H_5	178-17P		48 (m.p.), (i), (n), (u);
C_6H_5	H, C_6H_5		keto		$CH{=}CHC_6H_5$	164-165°		1137 (m.p.), (c), (f), (i), (n), (t), (u);
C_6H_5	H, C_6H_5	H, $CH_2C_6H_5$	keto		CH_3	179-180°		39 (m.p.), (i), (n), (u);

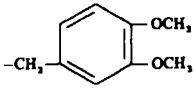
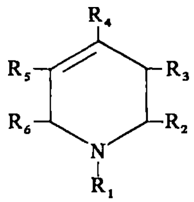
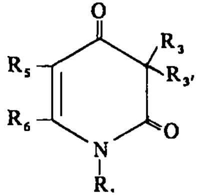
C_6H_5	H, C_6H_5		keto	$CH_2CH_2C_6H_5$	99-100°		39 (m.p.), (i), (n), (u);
C_6H_5	H, C_6H_5	H, $\underset{\mathrm{OH}}{\mathrm{C}}\mathrm{HC_6H_5}$	keto	CH_3	122-123°		1137 (m.p.), (c), (i), (n), (u);
$-N{=}CHC_6H_5$	H, C_6H_5	H, $CH_2C_6H_5$	keto	CH_3	129-131°		48 (m.p.), (i), (n), (u);
$-N{=}CHC_6H_5$	H, C_6H_5		keto	$CH_2CH_2C_6H_5$	118-121'		48 (m.p.), (i), (n), (u);
C_6H_5	H, $CH{=}CHC_6H_5$	H, $CH_2C_6H_5$	keto	CH_3	155-156'		1138 (m.p.), (i), (n), (t), (u);
C_6H_5	H, $CH{=}CHC_6H_5$		keto	$CH_2CH_2C_6H_5$	174-176°		1138 (m.p.), (i), (n), (t), (u);
$-N{=}CHCH{=}CHC_6H_5$	H, $CH{=}CHC_6H_5$		keto	C_6H_5			1138 (u);
$-N{=}CHCH{=}CHC_6H_5$	H, $CH{=}CHC_6H_5$	H, $CH_2C_6H_5$	keto	CH_3			1138 (i), (t);
$-N{=}CHCH{=}CHC_6H_5$	H, $CH{=}CHC_6H_5$		keto	$CH_2CH_2C_6H_5$			1138 (i), (n), (u);
$-NH(CH_2)_3C_6H_5$	H, $CH_2CH_2C_6H_5$		keto	$CH_2CH_2C_6H_5$			1138 (i), (n), (u);
$-NH(CH_2)_3C_6H_5$	H, $CH_2CH_2C_6H_5$	H, $CH_2C_6H_5$	keto	CH_3			1138 (i);
	CH_3	COOH	keto			methyl ester m.p. 142-145°	70 (m.p.), (u);
	$CH_2C_6H_5$	COOH	keto			methyl ester m.p. 116-1 180	70 (m.p.), (u);
						t-butyl ester m.p. 155-1580	70 (m.p.), (u);
	$-CH_2C_6H_4OCH_3$-*p*	COOH	keto			methyl ester m.p. 124-125'	70 (m.p.), (u);
		COOH	keto			methyl ester m.p. 129-131°	70 (m.p.), (u);

TABLE XII-127. Ethers of Dihydropyridinols



R_1	R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CX_3			OCH_3			b.p. [illegible]3°/760 mm	picrate m.p. 109-1[illegible]°	1170 (b.p.), (i), (n); 1170 (m.p.);
CH_3	$CH_2C_6H_5$		OCH_3				picrate m.p. 116–118°	767 (m.p.), (m), (n);
CH_3	$CH_2C_6H_4OCH_3$-*p*		OCH_3				picrate m.p. 126–127°	767 (m.p.), (i), (n);
CH_3	$CH_2C_6H_4OCH_3$-*p*		OCH_3				picrate m.p. 162–163°	1170 (m.p.), (i), (n);

TABLE XII-128. 2,4-Diketotetrahydropyridines



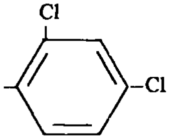
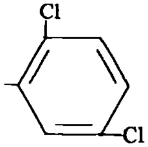
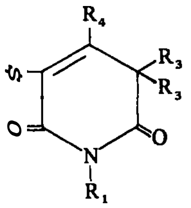
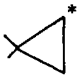
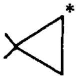
R_1	R_3	$R_{3'}$	R_5	R_6	m.p.	Derivatives	Ref.
	Cl	Cl	COOH	$CHCl_2$		ethyl ester, m.p. 161–163°	707 (m.p.), (i), (n);
	Cl	Cl	COOH	CH_2Cl		ethyl ester, m.p. 148°	707 (m.p.), (i), (n);
	CH_3	CH_3					1139 (n);
	C_2H_5	C_2H_5					1139 (n);
	Cl	Cl	Cl	C_6H_5	160–161°		707 (m.p.);
				CH_3	280–23[illegible]		149 (m.p.);
				CH_3	237 239°		149 (m.p.);
C_6H_4Cl-*o*				CH_3	263–265°		149 (m.p.);
C_6H_4Br-*o*				CH_3	278–281°		149 (m.p.);
C_6H_5	$C(=NH)CH_3$	H		CH_3	258–260°		1030 (m.p.), (i);
C_6H_5	$CH_2C_6H_5$	Cl		C_6H_5	174°		92 (m.p.);

TABLE XII-129. 2,6-Diketotetrahydropyridines



R$_1$	R$_3$	R$_{3'}$	R$_4$	R$_5$	m.p.	Derivatives	Ref.
	CH$_3$	×	Cl	Cl	196–197°		7 (m.p.);
			COOH			cyclohexyl ester, m.p. 214°	507 (m.p.);
CH$_3$							505 (n);
	CH$_3$	H		O×	oil		506;
						triacetate, m.p. 86°	506 (m.p.) (i), (u);
	C$_2$H$_5$	×	Cl	Cl	179–182°		7 (m.p.), (i), (u);
CH$_3$			COOH				507 (i);
						methyl ester, m.p. 198°	507 (m.p.);

	CH_3	CX_3				455 (n), (u);
			CH_3		175–176°	510 (m.p.), (i), (n), (u);
			CH_3	CH_3CH_2Cl	148–150°	510 (m.p.), (i), (n), (u);
CH_3			CH_3	CH_3	91–93°	1000 (m.p.), (i), (u);
CH_3			CH_3		89–90°	510 (m.p.), (n), (u);
CH_3			CH_3	CH_2CH_2Cl	82–83°	510 (m.p.), (i), (n), (m);
	n-C_5H_{11}	×	Cl	Cl	270–272°	7 (m.p.);
OH			$C_6H_4OCH_3$-*p*		216–217°	5 (m.p.), (i), (u);
	$-COCH_2\underset{\underset{\displaystyle CH_3}{\vert}}{C}HCH_3$	×	$COCH_3$		130–131°	856 (m.p.), (i), (k), (m), (n), (u);
CH_3			$C_6H_4OCH_3$-*p*		197–199°	5 (m.p.), (i), (u);
C_6H_5			OC_2H_5		200°	171 (m.p.), (i);
$-OCH_3$			$C_6H_4OCH_3$-*p*		163–166°	5 (m.p.), (i), (u);
$-OCH_2C_6H_5$			CH_3	CH_3	126–127°	1000 (m.p.), (i), (u);
C_6H_5			$C_6H_4OCH_3$-*p*			5 (i), (u);
$-CH_2C_6H_5$			$C_6H_4OCH_3$-*p*		150–152°	5 (m.p.);
$-OCH_2C_6H_5$			$C_6H_4OCH_3$-*p*		214°	5 (m.p.), (i), (u);

* = Spirocyclopropane

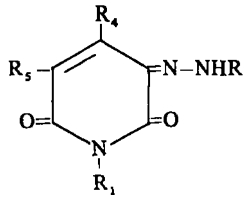
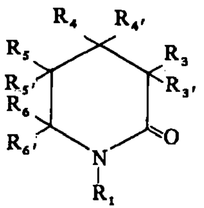


TABLE XII-130. 1,2,3,6-Tetrahydro-2,6-diketo-3-substituted hydrazonopyridines

R	R_1	R_4	R_5	m.p.	Derivatives	Ref.
CH_3	CH_3			163"		505 (m.p.), (i), (m), (n), (t), (u);
C_6H_4Cl-*o*	C_6H_5	$C_6H_4OCH_3$-*p*		287–289"		739 (m.p.);
C_6H_4Cl-*m*	C_6H_5	$C_6H_4OCH_3$-*p*		230–232"		739 (m.p.);
C_6H, Cl-*p*	C_6H_5	$C_6H_4OCH_3$-*p*		224–226°		739 (m.p.);
C_6H, Br-*p*	C_6H_5	$C_6H_4OCH_3$-*p*		233–234'		739 (m.p.);
C_6H_4NO, -*o*	C_6H_5	$C_6H_4OCH_3$-*p*		213–215"		739 (m.p.);
C_6H_4NO, -*m*	C_6H_5	$C_6H_4OCH_3$-*p*		210–212"		739 (m.p.);
$C_6H_4NO_2$-*p*	C_6H_5	$C_6H_4OCH_3$-*p*		218–220"		739 (m.p.);
C_6H_5	C_6H_5	$C_6H_4OCH_3$-*p*		245–247°		739 (m.p.);
$C_6H_4CH_3$-*p*	C_6H_5	$C_6H_4OCH_3$-*p*		230–231"		739 (m.p.);
$C_6H_4OCH_3$-*o*	C_6H_5	$C_6H_4OCH_3$-*p*		286–288'		739 (m.p.);
$C_6H_4OCH_3$-*p*	C_6H_5	$C_6H_4OCH_3$-*p*		222–224"		739 (m.p.);

TABLE XII-131. 2-Piperidones



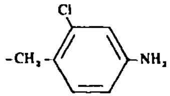
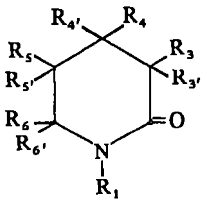
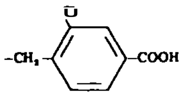
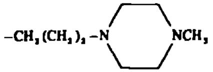
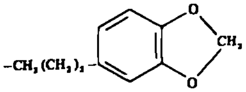
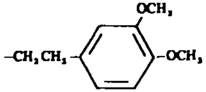
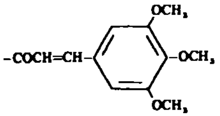
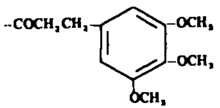
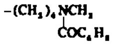
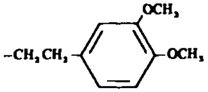
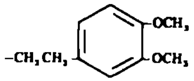
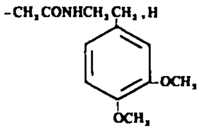
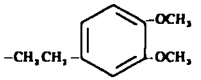
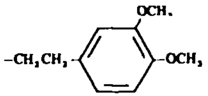
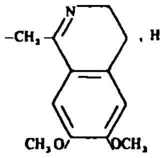
R_1	$R_3R_{3'}$	$R_4R_{4'}$	$R_5R_{5'}$	$R_6R_{6'}$	m.p.	Derivatives	Ref.
		COOH			174-176		1140 (m.p.), (l), (n);
						methyl ester, m.p. 126–127°	1140 (m.p.), (l), (n);
						ethyl ester, m.p. 108°	1140 (m.p.);
CH_3							861 (m.p.);
CH_3		NH_2			b.p. 95°/0.01 mm		861 (b.p.), (l);
CH_3		COOH				methyl ester, b.p. 120°/0.007 mm	861 (b.p.), (l);
CH_3		$-CONH_2$			194–196°		861 (m.p.), (l);
CH_3		$-NHCONH_2$			203–204°		861 (m.p.), (l);
CH_3			$-NHCONH_2$		>230°		861 (m.p.), (l);
C_2H_5	CH_3				b.p. 103°/15 mm		690 (b.p.);
	CN	CH_3		CH_3, CH_3	156–157°		1131 (m.p.);
NH_2		C_6H_5			100–102°		1133 (m.p.);
						hydrochloride, m.p. 179–180°	1133 (m.p.);
						N'-diacetyl, m.p. 122–124°	1133 (m.p.);
CH_3			$-(CH_2)_4NHCH_3$		b.p. 145°/1.5 mm		691 (b.p.);
						dihydrochloride, m.p. 166–168°	691 (m.p.);
						dipicrate, m.p. 166–167°	691 (m.p.);
$-CH_2C_6H_4F$-*o*					b.p. 159°/3 mm		689 (b.p.);
$-CH_2C_6H_4Br$-*o*					76–77°		558 (m.p.);
CH_3	C_6H_5	=NOH			151–155°		1141 (m.p.);
$-CH_2C_6H_5$					b.p. 162°/4 mm		689 (b.p.), (l);
					139–140°		558 (m.p.);
$-CH_2C_6H_4NH_2$-*m*					b.p. 218°/2 mm		558 (b.p.);
$-CH_2C_6H_4NH_2$-*p*					b.p. 220°/3 mm		558 (b.p.);
$-CH_2C_6H_{11}$					b.p. 153°/7 mm		689 (b.p.);
						hydrochloride, m.p. 132–133°	689 (m.p.);

TABLE XII-131. 2-Pipendones (Continued)



R_1	R_3,R_3'	R_4,R_4'	R_5,R_5'	R_6,R_6'	m.p.	Derivatives	Ref.
CH_3			$-(CH_2)_4N(CH_3)_2$		b.p. 134°/2 mm		691 (b.p.);
						dihydrochloride, m.p. 125–127°	691 (m.p.);
						dipicrate, m.p. 107–109°	691 (m.p.);
					225°		558 (m.p.);
$-CH_2C_6H_4COOH$-*p*					167'		558 (m.p.);
			CH_3,CH_3	OH,C_6H_4Cl-*p*	175–176°		1142 (m.p.);
			CH_3,CH_3	$OH.C_6H_4$	175–176"		1142 (m.p.);
					45°		558 (m.p.);
			CH_3,CH_3	$OH.C_6H_4CH_3$-*p*	172–174"		1142 (m.p.);
			CH_3,C_2H_5	$OH.C_6H_5$	160–161"		1142'(m.p.);
			CH_3,CH_3	$OH.C_6H_4OCH_3$-*p*	188–190°		1142 (m.p.);
$-CH_2(CH_2)_2COC_6H_5$					b.p. 108°/3 mm		558 (b.p.);
					b.p. 195°/1 mm		*340* (b.p.), (i);
$-CH_2CH_2C_6H_5$			C_2H_5,H		b.p. 130°/1 mm		352 (b.p.);
			C_2H_5,H		ail		350 (l);
					116–117"		860 (m.p.), (n), (u);

					83–84°		860 (m.p.), (n); 1143 (m.p.), (l);
$-CH_2C_6H_5$	C_2H_5, C_6H_5 C_6H_5, H	=NOH	C_2H_5, C_2H_5		176–180° 170–171°		1135 (m.p.); 1141 (m.p.);
CH_3			 $-(CH_2)_4N(CH_3)COC_6H_5$		50–52°		691 (m.p.);
		$-CH_2COOH, H$	C_2H_5, H		*cis/trans* m.p. 130°		281 (m.p.);
					trans m.p. 153–154°		352 (m.p.);
			C_2H_5, H		none		281;
CH_3	$-CH_2C_6H_5, H$		$-COOC_2H_5, H$	C_6H_5, H	105–106°		45 (m.p.), (l);
		$-CH(COOH)_2, H$	C_2H_5, H		151–153°		352 (m.p.); 1144 (m.p.);
C_6H_5	$-CH_2C_6H_5$		$-COOC_2H_5, H$	C_6H_5, H	50–51°		45 (m.p.), (l);
			C_2H_5, H			hydroiodide, m.p. 190–198°	281 (m.p.), (u);

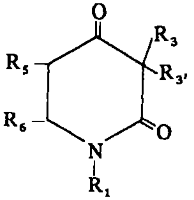
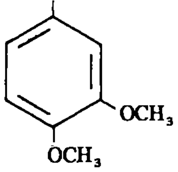


TABLE XII-132. 2,4-Diketopiperidines

R_1	R_3	$R_{3'}$	R_5	R_6	m.p.	Derivatives	Ref.
	C_2H_5	C_2H_5					1139 (n);
	C_2H_5	C_2H_5	CH_3				1139 (n);
CH_3	C_6H_5	H			136–137°		1135 (m.p.);
CH_3	C_6H_5	C_2H_5			82–84°		1135 (m.p.), (i) (u)· =
–CH_2CH_2 			C H_5 H		38–40°		281 (m.p.);
$CH_2C_6H_5$	C_6H_5	✕			139–141°		1135 (m.p.);
–$CH_2CH_2C_6H_5$	C_6H_5	H			133–135°		1135 (m.p.);
–$CH_2C_6H_5$	C_6H_5	C_2H_5			oil		1135 (i);
–$CH_2C_6H_5$	C_6H_5	C_2H_5	C ✕ C H_5				1135 (i), (u);

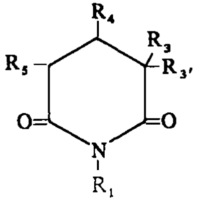


TABLE XI-133. 2,6-Diketopiperidines

R_1	R_3	R_3'	R_4	R_5	m.p.	Derivatives	Ref.
	CN		CF_3, H		158–160"		1145 (m.p.), (i);
						sodium salt, m.p. 313"	1145 (m.p.);
	CN		CF_3, CH_3		195–198°		1145 (m.p.), (i);
						sodium salt, m.p. 317"	1145 (m.p.);
	Cl	C_6H_5	C_6H_5, H		190–191°		242 (m.p.), (i), (n), (u);
	C_6H_5	H	C_6H_5, H		225–227"		242 (m.p.), (n);

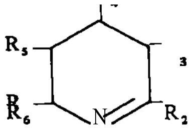
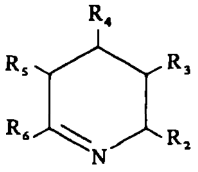


TABLE XI-134. Dehydro-4-piperidones

R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
$-OC_2H_5$	C_2H_5, C_2H_5	Keto	H, CH_3		b.p. 105°/12 mm		1146 (b.p.);

TABLE XII-135. Dehydro-2-piperidones



R_2	R_3	R_4	R_5	R_6	m.p.	Derivatives	Ref.
Keto			CH_3, $-N(C_2H_5)_2$	CH_3	b.p. 134°/5 mm	picrate. m.p. **131–132"**	**932** (b.p.); **932** (m.p.);
Keto			$(-CH_2CH_2CN)_2$	CH_3	**222–223"**		**1147** (m.p.);
Keto			n-C_3H_7, $-N(C_2H_5)_2$	CH_3	b.p. 138°/4 mm	picrate, m.p. **128–129"**	**932** (b.p.); **932** (m.p.);
Keto			n-C_4H_9, $-N(C_2H_5)_2$	CH_3	b.p. 138°/4 mm	picrate. m.p. **138–139°**	**932** (b.p.); **932** (m.p.);
Keto			n-C_3H_7, –	CH_3		triamine, m.p. 219–220°	**932** (m.p.);
Keto			isoC_3H_7, –	CH_3		triarnine, m.p. **229–230"**	**932** (m.p.);
Keto			n-C_4H_9, –	CH_3		triamine, m.p. 198–200°	**932** (m.p.);
Keto	F, F	F, F	F, F	Cl	b.p. 111°		**1148** (b.p.);
Keto	F, F,	F, F	F, F	$-OPCl_4$	b.p. 101°/4 mm		**1148** (b.p.);
Keto				CH_3	117–118"		**1147** (m.p.);
Keto			CH_3, Br	CH_3	**9193"**		**932** (m.p.);
Keto			CH_3, H	CH_3	**130–131"**		**1147** (m.p.);

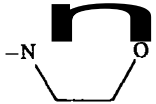
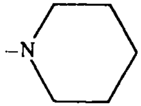
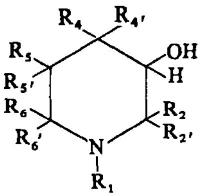
Keto	F, F	F, F	F, F		127–129"		1148 (m.p.);
Keto	F, F	F, F	F, F	$N(C_2H_5)_2$	b.p. 135°/11 mm		1148 (b.p.);
Keto			$-CH_2CH_2CN$, H	CH_3	166"		1147 (m.p.);
Keto			n-C_3H_7, Br	CH_3	113–114"		932 (m.p.);
Keto			isoC_3H_7, Br	CH_3	107–108"		932 (m.p.);
Keto			n-C_3H_7, H	CH_3	b.p. 124°/11 mm		932 (b.p.);
						picrate, m.p. 198"	932 (m.p.);
Keto	F, F	F, F	F, F		68-69"		1148 (m.p.);
Keto			$-CH_2CH_2CN, CH_3$	CH_3	157–158°		1147 (m.p.);
Keto			n-C_4H_9, Br	CH_3	108–109"		932 (m.p.);
Keto			Cl, H	C_6H_5	170–171°		447 (m.p.);
Keto				C_6H_5	152–154"		1147 (m.p.);

TABLE XII-136. 3-Piperidinols



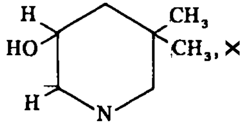
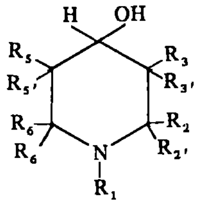
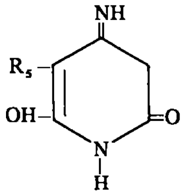
R_1	$R_2, R_{2'}$	$R_4, R_{4'}$	$R_5, R_{5'}$	$R_6, R_{6'}$	m.p.	Derivatives	Ref.
CH_3							1150 (g);
C_3H_7-*n*							1150 (g);
CH_3		H, C_6H_5			95 97°		1151 (m.p.) (n);
$CH_2C_6H_5$							1150 (g);
$CH_2CH_2C_6X_5$							1150 (g)
			CH_3, CH_3			·2HCl, m.p. 258°	1152 (m.p.) ([illegible];
CH_3		C_6H_5, C_6H_5			162–165°		1151 (m.p.), (i);

TABLE XII-137. 4-Piperidinols



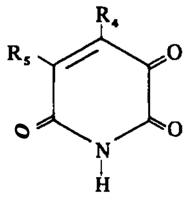
R_1	$R_2, R_{2'}$	$R_3, R_{3'}$	$R_5, R_{5'}$	$R_6, R_{6'}$	m.p.	Derivatives	Ref.
CH_3							1150 (g);
C_3H_7-*n*							1150 (g);
$CH_2C_6H_5$							1150 (g);
$CH_2CH_2C_6H_5$							1150 (g);

TABLE XII-138. Glutazines



R_5	m.p.	Derivatives	Ref.
H			504 (i), (u);
CN			504 (i), (u);
COOH		ethyl ester	504 (i), (u);
		amide	504 (i), (u);

TABLE XII-139. 1-Azaquinones



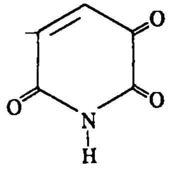
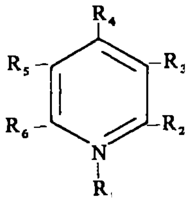
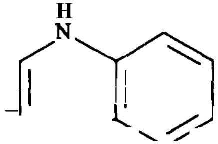
R_4	R_5	m.p.	Derivatives	Ref.
	CH_3	158–160°		843 (m.p.), (i), (n), (u);
CH_3	CH_3	126–127°		506 (m.p.), (u);
				894 (u);
CX_3	C_6H_5	160–161°		292 (m.p.), (u);

TABLE XII-140. 2-Alkoxypyridinium salts



R_1	R_2	R_3	R_4	R_5	R_6	m.p.	Anion	Ref.
CH_3	OCH_3				D	81–83"	tetrafluoroborate	530 (m.p.);
CH_3	OCH_3					81–83"	tetrafluoroborate	530 (m.p.), (i), (n), (u);
						249–250"	hexachloro-antimonate	464 (m.p.), (i); 542 (i);
C_2H_5	OCH_3			NO_2		140–145"	tetrafluoroborate	572 (m.p.);
C_2H_5	OC_2H_5					47–49"	tetrafluoroborate	571 (m.p.);
						153–154"	tetraphenylboron	571 (m.p.);
CH_2CH_2— 	OC_2H_5					134–135"	bromide	680 (m.p.), (u);

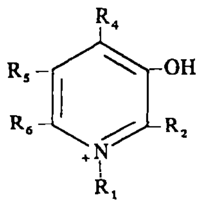


TABLE **XII-141.** 3-Hydroxypyridinium salts

R_1	R_2	R_4	R_5	R_6	m.p.	Anion	Ref.
CH_3					**179–181°**	iodide picrate	**593** (m.p.), **(u);** **594 (u);**
CH_3	CN				**209–213°**	chloride	**189** (m.p.);
CH_3	CONH,				**269"**	chloride	**189** (m.p.);
CH_3	Br			CH_3	**234–235"**	iodide	**597** (m.p.), **(u);**
C_2H_5					**108–111"**	chloride	**189** (m.p.);
C_2H_5	CN				**220–223"**	chloride	**189** (m.p.);
C_2H_5	CONH,				**249"**	chloride	**189** (m.p.);
C_2H_5	I			CH_3	**187–192°**	iodide	**597** (m.p.), **(u);**
CH_3	SCH,			CH,	**190–193"**	iodide	**597** (m.p.), **(u);**
OC_2H_5	CH_3		CN		**129–130"**	ethosulfate	**212** (m.p.);
CH_3	SC_2H_5			CH_3	**184–186°**	iodide	**597** (m.p.), **(u);**
C_6H_5					**171–176"**	bromide	**1153** (m.p.), (i);
					211–215°	chloride	**189** (m.p.); **1153** (m.p.), (i);
					65–68°	nitrate	**1153** (m.p.), (i);
					150°	perchlorate	**1153** (m.p.), (i);
					330°	sulfate	**1153** (m.p.), (i);
$CH_2C_6H_5$					**160–161"**	chloride	**189** (m.p.);
$CH_2C_6H_5$	CN				**162–164"**	chloride	**189** (m.p.);
CH, C_6H_5	CONH,				**225"**	chloride	**189** (m.p.);

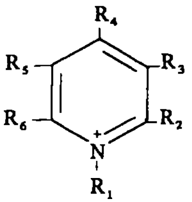


TABLE XII-142. 3-Alkoxypyridinium salts

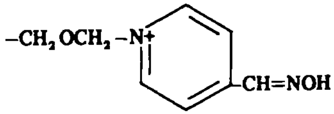
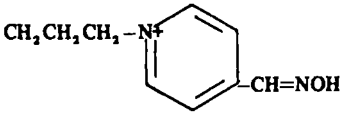
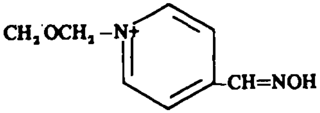
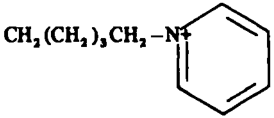
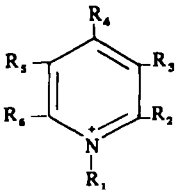
R_1	R_2	R_3	R,	R_5	R_6	m.p.	Anion	Ref.
CH_3		OSO_2CH_3				173°	iodide	649 (m.p.);
CH_3		$OCOC_6H_5$				171–173°	iodide	342 (m.p.);
NH_2		OCH_3	CH_3	C_6H_5		193–195°	chloride	219 (m.p.), (u);
						175–176°	picrate	219 (m.p.);
		OCH_3				146–147°	chloride	1154 (m.p.), (f);
		OCH_3				159–161°	bromide	1154 (m.p.), (f);
		$OCON(CH_3)_2$					chloride	1154 (f);
		OSO_2CH_3				151°	iodide	649 (m.p.);

TABLE XII-142. 3-Alkoxypyridinium salts (Continued)



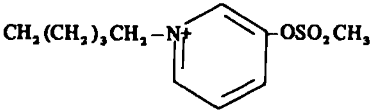
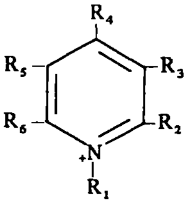
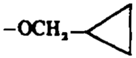
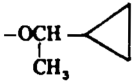
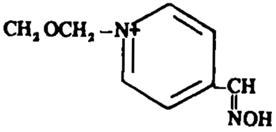
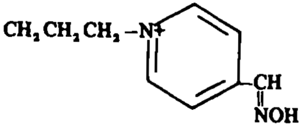
R_1	R_2	R_3	R_4	R_5	R_6	m.p.	Anion	Ref.
		OSO_2CH_3				174°	iodide	649 (m.p.);
$CH_2CH_2C_6H_5$		OC_6H_5				155-156°	bromide	211 (m.p.);

TABLE XII-143. 4-Alkoxypyridinium salts



R_1	R_2	R_3	R_4	R_5	R_6	m.p.	Anion	Ref.
CH_3			OCD_3			52-55°	tetrafluoroborate	530 (m.p.), (i), (n);
CH_3	D		OCH_3		D	55-57°	tetrafluoroborate	530 (m.p.), (i), (n);
CH_3			OCH_3			56-58°	tetrafluoroborate	139 (m.p.), (i), (n), (u);
						171-174°	hexachloroantimonate	464 (m.p.), (i);

CH_3		OC_2H_5		125°	iodide	533 (m.p.) ( ) ( );
CH_3				110–111°	iodide	7[illegible]0 (m.p.);
				87–88°	perchlorate	7[illegible]0 (m.p.);
CH_3				oil	iodide	770;
CH_3		$OCH_2C_6H_5$		149–151°	iodide	77[illegible] (m.p.);
				141–142°	perchlorate	77[illegible] (m.p.);
		OCH_3		132–133°	chloride	1154 (m.p.), (f);
		OCH_3		167–168°	bromide	1154 (m.p.);
CH_3	C_6H_5	OCD_3	C_6H_5		tetrafluoroborate	530 (i), (n);
CH_3	C_6H_5	OCH_3	C_6H_5	115–117°	tetrafluoroborate	530 (m.p.), (i), (n), (u);

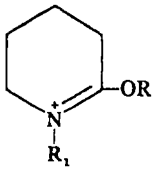


TABLE XII-144. 2-Alkoxy 3,4,5,6-tetrahydropyridinium salts

R	R_1	m.p.	Anion	Ref.
CH_3	CH_3		tetrafluoroborate, m.p. 141–143°	530 (m.p.), (i), (n);

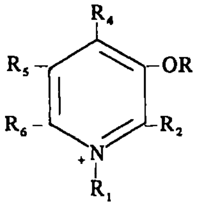


TABLE XII-145. 3-Alkoxypyridinium *N*-ylides

R	R_1	R_4	R_5	R_6	m.p.	Derivatives	Ref.
H	$:\bar{N}COCF_3$	CH_3	C_6H_5		179–180°		219 (m.p.), (u);
H	$:\bar{N}COCH_3$	CH_3	C_6H_5		216–217"		219 (m.p.), (u);
CH,	$:\bar{N}COCF_3$	CH_3	C_6H_5		134–135°		219 (m.p.), (u);
						picrate, m.p. 171–172"	219 (m.p.);
H	$:\bar{N}COCH_2CH_3$	CH,	C_6H_5		151°/175°		219 (m.p.);
CH,	$:\bar{N}COCH_3$	CH_3	C_6H_5		oil		219;
						picrate, m.p. 152–153"	219 (m.p.);

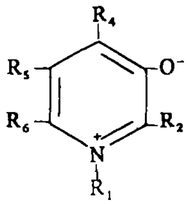
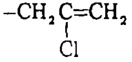


TABLE XII-146. 3-Oxypyridyl betaines

R_1	R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
CH_3						hydroiodide, m.p. 109–111° picrate, m.p. 201–202°	592 (m.p.); 592 (m.p.);
C_2H_5						hydrobromide, m.p. 99–102" picrate, m.p. 153–155°	592 (m.p.); 592 (m.p.);
$-CH_2CH_2OH$						hydrochloride, m.p. 139–144" hydrobromide, m.p. 122–123"	592 (m.p.); 592 (m.p.);
$-CH_2CH_2NH_2$						dihydrobromide, m.p. 218–222"	592 (m.p.);
 $-CH_2\underset{\mid}{C}(Cl)=CH_2$						hydrochloride, m.p. 153–155"	592 (m.p.);
$-CH_2CH=CH_2$						hydrobromide, m.p. 97–99"	592 (m.p.);
$-CH_2COCH_3$						hydrochloride, m.p. 134–136"	592 (m.p.);

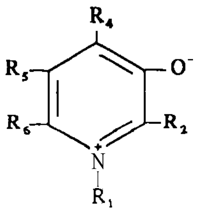
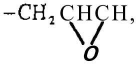
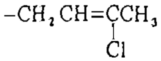
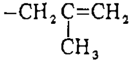


TABLE XI-146. 3-Oxypyridyl betaines (Continued)

R_1	R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
						hydrochloride, m.p. 133–135	592 (m.p.);
n-C, H,						p-toluenesulfonate, m.p. 129–130" picrate, m.p. 156–157"	592 (m.p.); 592 (m.p.l;
 $-CH_2CH{=}\underset{\mid}{C}(Cl)CH_3$						hydrochloride, m.p. 181-182°	592 (m.p.);
 $-CH_2\underset{\mid}{C}(CH_3){=}CH_2$						hydrochloride m.p. 139–144"	592 (m.p.);
n-C_4H_9						picrate, m.p. 128–130°	**592** (m.p.);
CH_3	CH,	CH_2OH	CH_2OH				1048 (n);
$-CH_2CH_2N(CH_3)_2$						dihydrochloride, m.p. 238–239" di-CH_3I, m.p. 167–171"	592 (m.p.1; 592 (m.p.);
$-(CH_2)_4CCl_3$						hydrochloride, m.p. 175–176"	592 (m.p.);
$-(CH_2)_4CN$						hydrobromide, m.p. 191–194"	592 (m.p.);

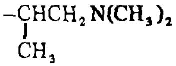
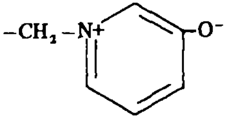
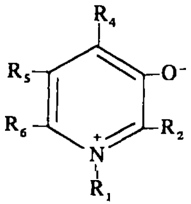
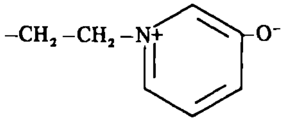
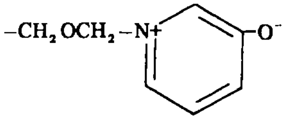
$-CH_2COOC_3H_7\text{-}n$	hydrochloride, m.p. **157–159"**	**592** (m.p.);
	1/2 H_2O, m.p. **74–78"**	**592** (m.p.);
$-(CH_2)_3N(CH_3)_2$	di-HCl, m.p. **227–233"**	**592** (m.p.);
 $-\underset{CH_3}{\underset{\vert}{C}}HCH_2N(CH_3)_2$	di-HCl, m.p. **205–209°**	**592** (m.p.);
	di-HI, m.p. **205–208"**	**592** (m.p.);
	picrate, m.p. **239"**	**592** (m.p.);
$-(CH_2)_5CN$	hydrochloride, m.p. **119–121"**	**592** (m.p.);
$-(CH_2)_3CH, OCOCH_3$	hydrobromide. m.p. **94–96"**	**592** (m.p.);
$-CH_2C_6H_4Cl\text{-}p$	hydrochloride, m.p. 184–185"	**592** (m.p.);
	picrate, m.p. **191–194"**	**592** (m.p.);
	$\cdot CH_3I$, m.p. **125–127"**	**592** (m.p.);
$-CH_2C_6H_5$	hydrochloride, m.p. **154–157"**	**592** (m.p.);
	hydrobromide, m.p. **125–128°**	**592** (m.p.);
	hydrate, m.p. **107–111"**	**592** (m.p.);

TABLE XII-146. 3-Oxypyridyl betaines (Continued)



R_1	R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
NH_2		CH_3	C_6H_5			hydrochloride, m.p. 191–195° hemihydrate, m.p. 170°/200° cyclopentanone hydrazone, m.p. 205–206°	216 (m.p.), (u); 219 (m.p); 219 (m.p.); 216 (m.p.);
						dihydrobromide, m.p. 295–296° *p*-toluenesulfate, m.p. 290–292"	592 (m.p.); 592 (m.p.);
						dihydrochloride, m.p. 211–213° picrate, m.p. 236"	592 (m.p.); 592 (m.p.);
$-CH_2COC_6H_4Cl$-*p*						m.p. 231–233"	592 (m.p.);
$-CH_2COC_6H_4Br$-*p*						hydrobromide, m.p. 255–257"	592 (m.p.);

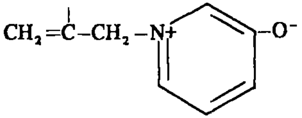
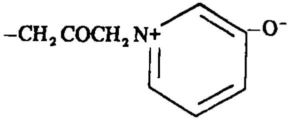
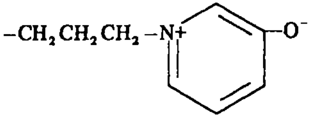
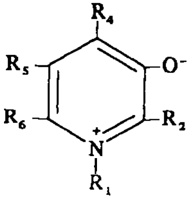
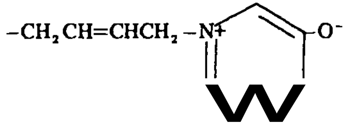
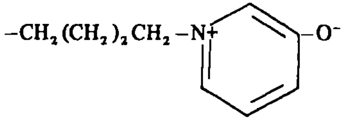
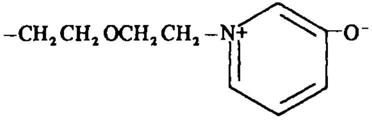
$-CH_2COC_6H_4NO_2$-*p*				hydrobromide, m.p. **235–237"**	**592** (m.p.);
$-CH_2COC_6H_5$				hydrochloride, m.p. **205–207°**	**592** (m.p.);
				di-HCl, m.p. **279"**	**592** (m.p.);
				di-HCl, m.p. **>300°**	**592** (m.p.);
NHCH,	**CH_3**	**C_6H_5**	**146–148"**		**219** (m.p.), **(u);**
				hydrochloride, m.p. **203–205°**	**216** (m.p.);
				picrate, m.p. **142–144"**	**219** (m.p.); **219** (m.p.);
				di-HCl, m.p. **226–227"**	**592** (m.p.);
				hydrobromide, m.p. **253–258"**	**592** (m.p.);
				di-HBr, m.p. **211–213"**	**592** (m.p.);
				di-CH_3I, m.p. **212–215°**	**592** (m.p.);
				di-C_2H_5I, m.p. **160–163"**	**592** (m.p.);
$-CH_2CH{=}CHC_6H_5$				hydrochloride, m.p. **137–140"**	**592** (m.p.);

TABLE XII-146. 3-Oxypyridyl betaines (Continued)



R_1	R_2	R_4	R_5	R_6	m.p.	Derivatives	Ref.
						di-HBr, m.p. 220–222°	592 (m.p.);
						di-HCl, m.p. 267–269" di-H_2O, m.p. 195–198° dipicrate, m.p. 224–226" di-CH_3I, m.p. 194–198" di-C_2H_5I, m.p. 166–167"	592 (m.p.); 592 (m.p.); 592 (m.p.); 592 (m.p.); 592 (m.p.);
						di-HCl, m.p. 169–172"	592 (m.p.);

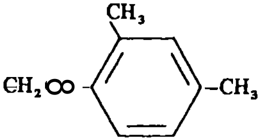
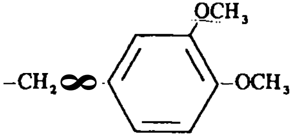
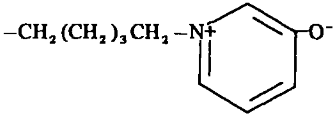
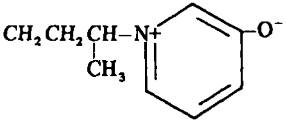
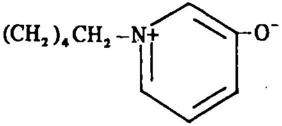
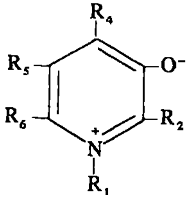
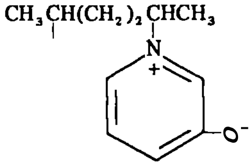
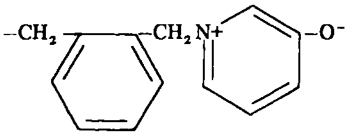
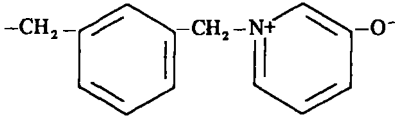
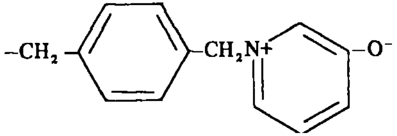
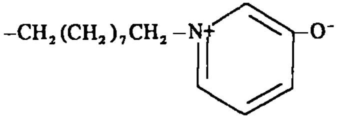
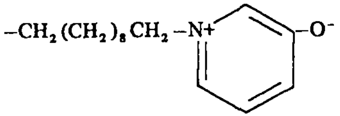
					hydrochloride, m.p. 250–252°	592 (m.p.);
					hydrochloride, m.p. 226–227°	592 (m.p.);
$CH_3CHCOOH$	C_6H_5		CH_3	144–146°		1068 (m.p.), (i), (m), (n);
$CH_3N\ OCH_3$	CH_3	[illegible]		198–200°		219 (m.p.);
					picrate, m.p. 179–180°	219 (m.p.);
					di-HCl, m.p. 217–218° di-HBr, m.p. 231–233° di-CH$_3$I, m.p. 156–159°	592 (m.p.); 592 (m.p.); 592 (m.p.);
					di-HBr, m.p. 203–206°	592 (m.p.);
					di-HBr, m.p. 274–275°	592 (m.p.);

TABLE XII-146. 3-Oxypyridyl betaines (Continued)



R$_1$	R$_2$	R$_4$	R$_5$	R$_6$	m.p.	Derivatives	Ref.
						di-HBr, m.p. 247–249°	592 (m.p.);
						di-HBr, m.p. 252-255°	592 (m.p.);

	di-HBr, m.p. 274–286"	592 (m.p.);
	di-HBr, m.p. 277–280° di-CH_3I, m.p. 203–204"	592 (m.p.); 592 (m.p.);
$-CH_2COC_6H_4C_6H_5$-*p*	hydrobromide, m.p. 235–237°	592 (m.p.);
	hydrobromide, m.p. 227–231"	592 (m.p.);
	di-HBr, m.p. 176–178°	592 (m.p.);

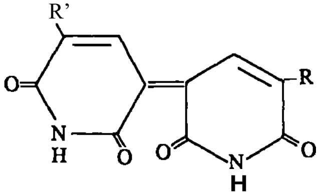


TABLE XII-147. Diazadibenzoquinones

R	R'	m.p.	Derivatives	Ref.
OH	**OH**			**894 (i), (u);**
CH_3	**CH_3**	**240°**		**843 (m.p.), (i), (n), (u);**
OCH_3	**OCH_3**			**894 (u);**

References

1. J. Thesing and A. Müller, *Chem. Ber.*, 90,711 (1957).
2. H. Meislich, in "Pyridine and Its Derivatives," E. Klingsberg, Ed., Part 3, Interscience, New York, 1962, Chapter 12.
3. J. B. Petersen, J. Lei, N. Clauson-Kaas, and K. Norris, ***Kgl. Danske Videnskab. Selskab. Mat.-Fys Medd.***, 36, 23 (1967); ***Chem. Absrr.*** 69,59063 (1968).
4. Ref. 2, pp. 511-516.
5. D. E. Ames and T. F. Grey, ***J. Chem. Soc.***, 2310 (1959).
6. D. E. Ames and J. L. Archibald, J. ***Chem. Soc.***, 1475 (1962).
7. A. Roedig, K. Grohe, and W. Mayer, ***Tetrahedron***, 24, 1851 (1968).
8. G. Simchen, ***Chem. Ber.***, 103, 389 (1970).
9. H. Junek and A. Schmidt, ***Monatsh. Chem.***, 98, 1097 (1967).
10. **S.** G. Cottis and H. Tieckelmann, J. ***Org. Chem.***, **26**, 79 (1961).
11. A. P. Krapcho and P. S. Huyffer, *J.* Org. ***Chem.***, 28, 2461 (1963).
12. M. R. **S.** Weir, K. E. Helmer, and J. B. Hyne, ***Can.*** J. ***Chem.***, 41, 1042 (1963).
13. A. S. Alvarez-Insua, M. Lora-Tamayo, and J. L. **Soto,** J. *Heterocycl. Chem.*, *7,* 1305 (1970).
14. H. J. Prins, ***Rec. Trav. Chim. Pays-Bas,*** 65,455 (1946).
15. A. Roedig and G. Märkl, ***Ann. Chem.***, 659, 1 (1962).
16. A. Roedig and K. Grohe, ***Chem. Ber.***, 98,923 (1965).
17. A. Roedig, R. Kohlhaupt, and G. Märkl, ***Chem. Ber.***, 99,698 (1966).
18. **A.** Roedig and G. Märkl, *Ann.* Chem., 636, 1 (1960).
19. A. Roedig, G. Märkl, W. Ruch, H.-G. Kleppe, R. Kohlhaupt, and H. Schaller, *Ann. Chem.*, 692, 83 (1966).
20. A. Roedig, G. Märkl, and **V.** Schaal, ***Chem. Ber.***, 95,2844 (1962).
21. T. B. Windholz, L. H. Peterson, and G. J. Kent, ***J. Org. Chem.***, 28, 1443 (1963).
22. G. Kresze and **O.** Korpiun, ***Tetrahedron***, 22, 2493 (1966).
23. G. Kresze and J. Firl, ***Terruhedron***, 24, 1043 (1968).
24. J. Firl and G. Kresze, Chem. ***Ber.***, 99, 3695 (1966).
25. S. D. Work and C. R. Hauser, J. ***Org. Chem.***, 28, 725 (1963).
26. **M.** L. Mites, T. M. Harris, and C. R. Hauser, J. Org. ***Chem.***, 30, 1007 (1965).
27. T. M. Harris, **S.** Boatman, and C. R. Hauser, ***J. Amer. Chem. Soc.***, 87, 3186 (1965).
28. R. P. Mariella, Org. ***Synth. Coll. Vol.*** IV, 210 (1963).

29. R. J. Light and C. R. Hauser, J. *Org. Chem.*, 25,538 (1960).

30. K. G. Hampton, T. M. Harris, C. M. Harris, and C. R. Hauser, *J. Org. Chem.*, 30, 4263 (1965).

30a. K. G. Hampton and C. R. Hauser, *J. Org. Chem.*, 30,2934 (1965).

31. S. Boatman, R. E. Smith, G. F. Morris, W. G. Kofron, and C. R. Hauser, *J. Org. Chem.*, 32,3817 (1967).

32. S. Boatman and C. R. Hauser, *J. Org.Chem.*, 31,1785 (1966).

33. D. Fischer, G. Scheibe, P. Merkel, and R. Muller, J. *Prakt. Chem.*, **100,** 91 (1919).

34. H. N. Rydon and K. Undheim, *J. Chem. Soc.*, 4676 (1962).

35. A. D. Campbell and I. D. R. Stevens, *J. Chem. Soc.*, 959 (1956).

36. N. P. Shusherina, K. Khua-min', and R. Ya. Levina, *Zh. Obshch. Khim.*, 33, 3613 (1963).

37. K. Grohe and A. Roedig, *Chem. Ber.*, **100,** 2953 (1967).

38. D. Münzner, H. Lettau, and H. Schubert, *Z. Chem.*, 7,278 (1967).

39. N. Sugiyama, M. Yamamoto, and C. Kashima, *Bull. Chem. Soc. Jap.*, 42, 1357 (1969).

40. C. Kashima, M. Yamamoto, S. Kobayashi, and N. Sugiyama, *Bull. Chem. Soc. Jap.*, 42,2389 (1969).

41. M. Broust-Bournazel, *Ann Chim.* (Paris), 5, 1409 (1960).

42. J. Chauvelier, M. Chauvin, and J. Aubouet, *Bull. Soc. Chim. Fr.*, 1721 (1966).

43. F. Hoffmann-LaRoche and Co. A. G., Brit. patent, 872,190 (1961); *Chem. Abstr.*, 56,462 (1962).

44. E. Gegner, *Tetrahedron Lett.* 287 (1969).

45. M. Shamma, R. W. Lagally, P. Miller, and E. F. Walker, Jr., *Tetrahedron*, 21, 3255 (1965).

46. J. C. Powers and I. Ponticello, J. *Amer.* Chem. *Soc.*, 90,7102 (1968).

47. Th. Haug, F. Lohse, K. Metzger, and H. Batzer., *Helv. Chim. Acta*, 51, 2069 (1968).

48. N. Sugiyama, M. Yamamoto, and C. Kashima, *Bull. Chem. Soc. Jap.*, 43, 901 (1970).

49. H. Junek, A. Metallidis, and E. Ziegler, *Monatsh. Chem.*, 100, 1937 (1969).

50. Th. Kappe, 1. Maninger, and E. Ziegler, *Monatsh. Chem.*, 99, 85 (1968).

51. Ref. 2, pp. 528–529.

52. U. Schmidt, *Ann. Chem.*, 657,156 (1962).

53. G. N. Walker and B. N. Weaver, J. *Org. Chem.*, 26,4441 (1961).

54. T. M. Hams, S. Boatman, and C. R. Hauser, *J. Amer. Chem. Soc.*, *85*, 3273 (1963).

55. S. Portnoy, J. *Org. Chem.*, 30, 3377 (1965).

56. J. L. Greene, Jr., and J. A. Montgomery, *J. Med. Chem.*, 6,294(1963).

57. L. Rateb, G. A. Mina, and G. Soliman, *J. Chem. Soc.*, *C*, 2140 (1968).

58. T. V. Protopopova and A. P. Skoldinov, J. *Gen. Chem. USSR*, 27, 1360 (1957).

59. G. F. Holland and J. N. Pereira, *J. Med. Chem.*, 10, 149 (1967).

60. C. Bonsall and J. Hill, *J. Chem. Soc.*, *C*, 1836 (1967).

61. Hoffman, LaRoche and Co., Swiss patent, 217,480(1941); *Chem. Abstr.*, 42,6377 (1948).

62. Otto Schnider, U.S. patent, 2,384,136 (1945) ;Chem. *Abstr.*, 40,611 (1946).

63. F. Zymalkowski and P. Messinger, *Arch. Pharm.* (Weinheim), 300, 168 (1967).

64. Ref. 2, pp. 526–527.

65. A. Sakurai and H. Midorikawa, *Bull. Chem. Soc. Jap.*, 41, 165 (1968).

66. Ref. 2, p. 540.

67. T. Kametani, K. Ogasawara, and M. Shio, *Yakugaku Zasshi*, 86,809 (1966) ;*Chem. Abstr.*, 65,20092 (1966).

68. R. E. Smith, G. F. Morris, and C. R. Hauser, J. *Org. Chem.*, 33,2562 (1968).

69. E. Ziegler, I. Herbst, and Th. Kappe, Monatsh. Chem., 100,132 (1969).
70. H. G. O. Becker, *J. Prakt.* Chem., 12,294 (1961).
71. J. Thesing, Ger. patent, 1,092,016 (1960); *Chem.* Abstr., 55,19957 (1961).
72. F. Krohnke, K.-E. Schnalke, and W. Zecher, Chem. Ber., 103,322 (1970).
73. M. A. Akhtar, W. G. Brouwer, J. A. D. Jeffreys, C. W. Gemenden, W. I. Taylor, R. N. Seelye, and D. W. Stanton, *J.* Chem. *Soc., C,* 859 (1967).
74. W. Zecher and F. Krohnke, Chem. *Ber.,* 94,698(1961).
75. W. Zecher and F. Krohnke, Chem. Ber., 94,690 (1961).
76. A. Sakurai and H. Midorikawa, Bull. Chem. *Soc.* Jap., 40,1680 (1967).
77. T. Kametani, A. Kozuka, and S. Tanaka, Yakugaku Zasshi, 90,1574 (1970); Chem. Abstr., 74,53461 (1971).
78. H. Junek, H. Sterk, and A. Schmidt, *Z. Naturforsch.,* 21B, 1145 (1966).
79. H. Junek and A. Schmidt, Monatsh. Chem., 99,635 (1968).
80. H. Junek, *Monatsh. Chem.,* 96,2046 (1965).
81. S. M. Kvitko and V. V. Perekalin, Zh. *Obshch.* Khim., 32,144 (1962).
82. S. M. Kvitko, V. V. Perekalin, and N. V. Buival, Zh. Organ. Khim., 2,2253 (1966).
83. F. Duran and L. Ghosez, Tetrahedron Lett., 245 (1970).
84. G. Schroll, P. Klemmensen, and S.-O. Lawesson, Ark. *Kemi,* 26,317 (1967).
85. Ref. 2, pp. 536–538.
86. A. Dornow and H. von Plessen, Chem. Ber., 99,244 (1966).
87. E. Ziegler and F. Hradetzky, *Monatsh.* Chem., 95,1247 (1964).
88. E. Ziegler, F. Hradetzky, and M. Eder, Monatsh. Chem., 97,1394 (1966).
89. E. Ziegler, H. Wittmann, and V. Illi, Monatsh. Chem., 100, 1741 (1969).
90. E. Ziegler, F. Hradetzky, and K. Belegratis, Monatsh. Chem., 96, 1347 (1965).
91. E. Ziegler and K. Belegratis, *Monatsh.* Chem., 98,219 (1967).
92. E. Ziegler and G. Kleineberg, Monatsh. Chem., %, 1360 (1965).
93. E. Ziegler, G. Kleineberg, and K. Belegratis, Monatsh. Chem., 98,77 (1967).
94. M. A. Butt and J. A. Elvidge, J. Chem. *Soc.,* 4483 (1963).
95. E. Ziegler and F. Hradetzky, Monatsh. Chem., 97,710 (1966).
96. E. Ziegler and K. Belegratis, Monatsh. Chem., 99,995 (1968).
97. S. J. Davis, J. A. Elvidge, and A. B. Foster, *J.* Chem. *Soc.,* 3638 (1962).
98. J. A. Elvidge and N. A. Zaidi, *J.* Chem. *Soc., C,* 2188 (1968).
99. S. J. Davis, and J. A. Elvidge, *J.* Chem. *Soc.,* 3553 (1962).
100. K. R. Huffman, F. C. Schaefer, and G. A. Peters, *J.* Org. Chem., 27,551 (1962).
101. M. L. Peterson, J. Org. Chem., 25,565 (1960).
102. R. Fuks, Tetrahedron, 26, 2161 (1970).
103. L. Claisen and K. Meyer, Chem. Ber., 35,583 (1902).
104. T. Kato, H. Yamanaka, and T. Shibata, Chem. Pharm. Bull. (Tokyo), 15, 921 (1967).
105. T. Kato, H. Yamanaka, J. Kawamata, and T. Shibata, Chem. Pharm. Bull. (Tokyo), 16,1835 (1968).
106. V. I. Gunar, L. F. Ovechkina, and S. I. Zav'yalov, *Izv.* Akad. Nauk. *SSSR,* Ser. Khim., 1885 (1965).
107. Z. Bukac and J. Sebenda, Collect. Czech. Chem. *Commun.,* 32,3537 (1967).
108. S. Garratt, *J.* Org. *Chem.,* 28, 1886 (1963).
109. S. Seto, H. Sasaki, and K. Ogura, Bull. Chem. *Soc.* Jap.. 39,281 (1966).
110. H. Toda, Yakugaku Zasshi, 87, 1351 (1967); Chem. Abstr., 69,2687 (1968).
111. J. S. A. Brunskill, *J. Chem. Soc., C,* 960 (1968).
112. M. C. Seidel, G. C. Van Tuyle, and W. D. Weir, *J.* Org. Chem., 35,1475 (1970).
113. S. A. Vartanyan, A. S. Noravyan, and V. N. Zhamagortsyan, Khim. *Geterotsikl. Soedin.,* 2,670 (1966); Chem. Abstr., 66,55339(1967).

114. F. C. Uhle and H. Schröter, *J. Org. Chem.,* 26,4169 (1961).
115. A. R. Casola and F. E. Anderson, *J. Phurm. Sci.,* **54,** 1686 (1965).
116. I. Steffan and B. Prijs, *Helv. Chim.Actu,* 44, 1429 (1961).
117. K. E. Schulte, J. Reisch, and O. Heine, *Arch. Pharm.* (Weinheim), 294,234 (1961).
118. M. A.-F. Elkaschef, **M.** H. Nosseir, and A. Abdel-Kader, J. *Chem. Soc.,* 4647 (1963).
119. N. P. Shusherina, E. A. Luk'yanets, and R. Ya. Levina, Zh. *Organ. Khim.,* 1, 679 (1965); *Chem. Abstr.,* 64, 3459 **(1966).**
120. I. E. El-Kholy, F. **K.** Rafla, and G. Soliman, *J. Chem. Soc.,* 2588 **(1959).**
121. I. E. El-Kholy, F. K. Rafla, and **G.** Soliman, J. *Chem. Soc.,* 4490 (1961).
122. I. E. El-Kholy, F. K. Rafla, and M. M. Mishrikey, J. Chem. *Soc., C,* 1950 (1969).
123. Ref. 2, pp. **552–560.**
124. J. E. Hodge and E. C. Nelson, *Cereal Chem.,* 38,207 (1961).
125. B. E. Fisher and J. E. Hodge, J. *Org.* Chem., 29, 776 (1964).
126. A. Peratoner and A. Tamburello, *Gazz. Chim. Ital., 36,* **33, 50 (1906).**
127. L. L. Woods and H. C. Smitherman, J. Org. *Chem.,* 26,2987 (1961).
128. **V.** Hahn and **S.** Kukolja, Croat. Chem. *Actu,* 33, 137 (1961).
129. K. Blazevic and **V.** Hahn, *Croat. Chem. Acta,* 38, 113 (1966).
130. C. P. Krimmel, **U.S.** patent, 2,965,641 **(1960);** *Chem. Abstr.,* 55, 13457 (1961).
131. M. Yasue, N. Kawamura, and J. Sakakibara, *Yakugaku Zusshi,* 90, 1222 (1970); *Chem. Abstr.,* 74,23102 (1971).
132. L. L. Woods, *Chem. Ind.* (London), 1567 (1960).
133. I. D. Spenser and A. D. **Notation,** *Can. J. Chem.,* 40,1374 (1962).
134. A. D. Notation and 1. D. Spenser, *Can. J. Biochem.,* 42, 1803 (1964).
135. E. **M.** Kaiser, **S.** D. Work, J. F. Wolfe, and C. R. Hauser, *J. Org. Chem.,* 32, 1483 (1967).
136. **M.** Simalty, H. Stryzelecka, and **M.** Dupre, C. *R. Acud. Sci. Ser. Puns, Ser. C., 265,* 1284 (1967).
137. P. Bellingham, C. D. Johnson, and A. R. Katritzky, *J. Chem Soc., B,* 866 (1968).
138. T. Kato and H. Yamanaka, *Chem. Pharm.* Bull. (Tokyo), **12, 18 (1964).**
139. P. Beak and J. Bonham, J. *Amer. Chem. Soc.,* 87,3365 (1965).
140. S. W. Nakhre and **S. S.** Deshapande, *Vikram* J., *Vikram Univ.,* 4, 153 (1960); *Chem. Abstr.,* 57,2185 (1962).
141. K. Hamamoto, T. Isoshima, and **M.** Yoshioka, *Nippon Kagaku Zusshi,* 79, 840 (1958).
142. Ref. 2, p. **557.**
143. J. D. Edwards, J. E. Page, and **M.** Pianka, *J. Chem. Soc.,* 5200 **(1964).**
144. D. Cook, *Can. J. Chem.,* 41,1435 (1963).
145. R. **N.** Schut, W. G. Strycker, and T. **M.** H. Liu, J. *Org. Chem.,* 28,3046 (1963).
146. *S.* Iguchi, A. Inoue, and C. Kurahashi, *Chem. Pharm. Bull.* (Tokyo), 9, 1016 **(1961).**
147. S. Iguchi, A. Inoue, and C. Kurahashi, Chem. *Pharm.* Bull. (Tokyo), 11, 385 (1963).
148. **S.** Iguchi and A. Inoue, *Chem. Pharm.* Bull. (Tokyo), 11,390 (1963).
149. A. K. Mallams, J. *Org. Chem.,* 29,3555 (1964).
150. *C.* A. Salemink, Rec. *Trav. Chim Pays-Bas,* 80,545 **(1961).**
151. T. Kato, J. Kawamata, and T. Shibata, *Yukuguku Zusshi, 88,* **106** (1968); *Chem. Abstr.,* 69,27302 **(1968).**
152. Ref. 2, p. 558.
153. C. **S.** Wang, Abst. Papers, 160th Meeting, American Chemical Society, 1970, ORGN 80.
154. **S.** Garratt and D. Shemin, J. Org. *Chem., 28,* 1372 (1963).
155. P. Petrenko-Kritschenko and J. Schottle, *Chem. Ber.,* 44, 2826 (1911).
156. F. Feist, *Chem. Ber.,* 23, 3726 (1890).

157. F. Hradetzky and E. Ziegler, *Monatsh. Chem.,* 97,398 (1966).
158. P. E. Brenneisen, T. E. Acker, and S. W. Tanenbaum, *J. Amer. Chem. Soc., 86,* 1234 (1964).
159. T. E. Acker, P. E. Brenneisen, and S. W. Tanenbaum, J. *Amer. Chem. Soc.,* 88, 834 (1966).
160. A. Suzuki, N. Takahashi, and *S.* Tamura, *Agr. Biol. Chem.* (Tokyo), **30,** 13 (1966).
161. H. Junek, H. Budschedl, and E. Ziegler, *Monatsh. Chem.,* 98,2252 (1967).
162. Y. Hirata, H. Nakata, K. Yamada, K. Okuhara, and T. Naito, *Tetruhedron,* 14,252 (1961).
163. F. K. Splinter and H. Arold, J. *Prakt. Chem.,* 311, 869 (1969).
164. S. J. Davis and J. A. Elvidge, J. *Chem. Soc.,* 2251 (1953).
165. J. A. Elvidge, *J. Chem. Soc.,* 2606 (1962).
166. S. J. Davis and J. A. Elvidge, J. *Chem. Soc.,* 3550 (1962).
167. A. Butt, I. A. Akhtar, and M. Khurshid, *Pukistun* J. *Sci. Znd. Res.,* 9, 335 (1966).
168. A. Butt, S. M. A. Hai, and I. A. Akhtar, *Tetrahedron,* 22,455 (1966).
169. A. Butt, I. A. Akhtar, S. A. Qureshi, and M. Akhtar, *Pakistan J. Sci. Ind. Res.,* 10, 240 (1967).
170. A. Butt and I. A. Akhtar, *Tetruhedron,* 21,1917 (1965).
171. M. A. Butt, J. A. Elvidge, and A. B. Foster, J. *Chem. Soc.,* 3069 (1963).
172. M. A. Butt, I. A. Akhtar, and M. Akhtar, *Tetrahedron,* 23,1551 (1967).
173. A. Butt, M. Akhtar, and R. Parveen, *Pukistun J. Sci. Ind. Res.,* 10,243 (1967).
174. A. Butt, I. A. Akhtar, and M. Akhtar, *Tetruhedron,* 23, 199 (1967).
175. Ref., pp. 560–567.
176. H. Sugisawa, and K. Aso, *Tohoku* J. *Agr. Res.,* 10, 137 (1959); *Chem. Abstr.,* 54, 11015 (1960).
177. H. Sugisawa and K. Am, *Nippon Nogei Kagaku Kaishi,* 33, 259 (1959); *Chem. Abstr.,* 59,8695 (1963).
178. H. Sugisawa, *Tohoku J. Agr. Res.,* 11,389 (1960); *Chem. Abstr.,* 55,19917 (1961).
179. H. Sugisawa, *Tohoku* J. *Agr. Res.,* 11,397 (1960); *Chem. Abstr.,* **55,** 19917–19918 (1961).
180. H. Sugisawa, H. Sugiyama, and K. Aso, *Tohoku J. Agr. Res.,* 12,245 (1961); *Chem. Abstr.,* 57, 16535 (1962).
181. H. Sugisawa and K. Aso, *Chem. Ind.* (London), 781 (1961).
182. L. D. Smirnov, S. I. Sholina, K. E. Kmglyakova, and K. M. Dyumaev, *Zzv. Akud. Nuuk SSSR. Otd. Khim.,* 890 (1963).
183. N. Clauson-Kaas and M. Meister, *Acta Chem. Scund.,* 21, 1104 (1967).
184. N. Elming and N. Clauson-Kaas, *Acta Chem.* Scund., 10, 1603 (1956).
185. L. D. Smirnov, K. M. Dyumaev, N. I. Shuikin, and I. F. Bel'skii, *Izv. Akud. Nuuk. SSSR,* 2246 (1962).
186. H. Leditschke, *Arch. Pharm.* (Weinheim), 295, 323 (1962).
187. J. R. Geigy A.G., Fr. patent, 1,477,998 (1967); *Chem. Abstr.,* 68, 29606 (1968).
188. J. R. Geigy A.G., Br. patent, 1,108,975 (1968); *Chem. Abstr.,* 69, 67226 (1968).
189. J. B. Petersen, K. Norris, N. Clauson-Kaas, and K. Svanholt, *Acta Chern. Scund.,* 23, 1785 (1969).
190. Ref. 2, pp. 560–563.
191. L. A. Walter, C. K. Springer, J. Kenney, S. K. Galen, and N. Sperber, J. *Med. Chem.,* 11, 792 (1968).
192. H. Paulsen, *Angew. Chem. Intern. Ed..* 1,454 (1962).
193. H. Paulsen, *Ann. Chem.,* 665, 166 (1963).
194. S. J. Norton, C. G. Skinner, and W. Shive, J. *Org. Chem., 26,* 1495 (1961).
195. M. Ya. Karpeiskii and *V.* L. Florent'ev, *Russ. Chem. Rev.,* 38,540 (1969).

196. G. Ya. Kondrat'eva and C.-H. Huang, ***Dokl. Akad. Nauk SSSR,*** 141, 628 (1961); ***Chem. Abstr.,*** 56, 14229 (1962).
197. G. Ya. Kondrat'eva and C.-H. Huang, ***Dokl. Akad. Nauk SSSR,*** 141, 861 (1961); ***Chem. Abstr.,*** 56,14229 (1962).
198. ***G.*** Ya. Kondrat'eva, ***Izv. Akad. Nauk SSSR, Otd. Khim. Nauk.*** 484 (1959); ***Chem. Abstr.,*** 53, 21940 (1959).
199. R. A. Firestone, E. E. Harris, and W. Reuter, ***Tetrahedron,*** 23,943 (1967).
200. K. Pfister, 111, E. E. Harris, and R. A. Firestone, **U.S.** patent, 3,227,724 (1966); ***Chem Abstr.,*** 64,8149–8150 (1966).
201. E. E. Harris, R. A. Firestone, K. Pfister, III, R. R. Boettcher, F. J. Cross, R. **B.** Currie, M. Monaco, E. R. Peterson, and W. Reuter, J. ***Org. Chem.,*** 27, 2705 (1962).
202. Merck and Co., Nether. patent, 6,614,801 (1967); ***Chem. Abstr.,*** 68,87190 (1968).
203. T. Naito, K. Ueno, M. Sano, Y. Omura, I. Itoh, and F. Ishikawa, ***Tetrahedron*** Lett., 5767 (1968).
204. N. D. Doktorova, L. **V.** Ionova, M. Ya. Karpeisky, N. Sh. Padyukova, K. F. Turchin, and ***V.*** L. Florentiev, ***Tetrahedron,*** 25, 3527 (1969).
205. T. Miki and Y. Matsuo, Jap. patent, 25,664 (1967); ***Chem. Abstr.,*** 69, 43807 (1968).
206. W. Kimel and L. Leimgruber, Fr. patent, 1,384,099 (1965); ***Chem. Abstr.,*** 63,4263 (1965).
207. T. Maruyama, E. Araki, and N. Tokai, Jap. patent, 11,745 (1967); ***Chem. Abstr.,*** 68,87177 (1968).
208. T. Miki and T. Matsuo, ***Yakugaku Zasshi,*** 87, 323 (1967); *Chem. Abstr.,* 67,32549 (1967).
209. T. Naito and T. Yoshikawa, ***Chem. Pharm.*** Bull. (Tokyo), 14,918 (1966).
210. T. Naito, T. Yoshikawa, F. Ishikawa, **S.** Isoda, Y. Omura, and I. Takamura, ***Chem. Pharm.*** Bull. (Tokyo), 13,869 (1965).
211. T. Yoshikawa, F. Ishikawa, Y. Omura, and T. Naito, ***Chem. Pharm.*** Bull. (Tokyo), 13, 873 (1965).
212. T. Yoshikawa, F. Ishikawa, and T. Naito, ***Chem. Pharm.*** Bull. (Toyko), 13, 878 (1965).
213. A. E. A. Porter and P. G. Sammes, ***Chem. Commun.,*** 1103 (1970).
214. E. Ziegler, K. Belegratis, and G. Brus, ***Monatsh. Chem.,*** 98,555 (1967).
215. J. A. Moore and R. W. Medeiros, ***J. Amer. Chem. Soc.,*** 81,6026 (1959).
216. J. A. Moore and J. Binkert, **J.** ***Amer. Chem. Soc.,*** 81,6029 (1959).
217. A. Nabeya, F. B. **Culp,** and J. A. Moore, ***J. Org. Chem.,*** 35,2015 (1970).
218. J. A. Moore and H. H. Püschner, ***J. Amer. Chem. Soc.,*** 81,6041 (1959).
219. J. A. Moore and J. Binkert, ***J. Amer. Chem. Soc.,*** 81,6045 (1959).
220. J. A. Moore, F. J. Marascia, R. W. Medeiros, and E. Wyss, J. ***Amer. Chem. Soc.,*** 84, 3022 (1962).
221. J. A. Moore, R. L. Wineholt, F. J. Marascia, R. **W.** Medeiros, and F. J. Creegan, ***J. Org. Chem.,*** 32, 1353 (1967).
222. J. A. Moore and E. C. Zoll, ***J. Org. Chem.,29,*** 2124 (1964).
223. J. A. Moore, H Kwart, G. Wheeler, and H. Bruner, ***J. Org. Chem.,*** 32, 1342 (1967).
224. R. K. Bly, E. C. Zoll, and J. A. Moore, ***J. Org. Chem.,*** 29,2128 (1964).
225. J. A. Moore and **W.** J. Theuer, **J.** ***Org. Chem.,*** 30,1887 (1965).
226. Y. Inubushi, Y. Sasaki, Y. Tsuda, B. Yasui, T. Konita, J. Matsumoto, E. Katarao, and J. Nakano, ***Tetrahedron,*** 20,2007 (1964).
227. R. Kuhn and I. Low, ***Chem. Ber.,*** 95, 1748 (1962).
228. S. Masamune and K. Fukumoto, ***Tetrahedron*** Lett., 4647 (1965).

229. N. C. Castellucci, M. Kato, H. Zenda, and S. Masamune, *Chem. Commun.*, 473 (1967).
230. A. S. Monahan and S. Tang, *J. Org. Chem.*. 33, 1445 (1968).
231. W. Ried and F. Bätz, *Ann. Chem.*. 725, 230 (1969).
232. H. Iida, I. Doi, H. Iida, *Kogyo Kagaku Zasshi,* 69, 2164 (1966); *Chem. Abstr.,* 66, 86580 (1967).
233. A. Roedig, G. Märkl, and H. Schaller, *Chem. Ber.,* 103,1022 (1970).
234. R. W. Meikle and E. A. Williams, *Nature*, 210,523 (1966).
235. W. W. Muelder and M. N. Wass, *J. Agr.* Food *Chem.,* 15,508 (1967).
236. Dow Chemical Co., Neth. patent, 6,402,443 (1965); *Chem. Abstr.,* **64,** 8152 (1966).
237. A. R. Sexton, U.S. patent, 3,355,456, (1967); *Chem. Abstr.,* 68,29602 (1968).
238. W. T. Flowers, R. N. Haszeldine, and S. A. Majid, *Tetrahedron Lett.,* 2503 (1967).
239. A. Roedig, K. Grohe, and D. Klatt, *Chem. Ber.,* 99,2818 (1966).
240. S. M. Roberts and H. Suschitzky, *J. Chem. Soc., C,* 1537 (1968).
241. A. R. Katritzky, J. D. Rowe, and S. K. Roy, *J. Chem. Soc.*, *B,* 758 (1967).
242. P. I. Mortimer, *Aust. J. Chem.*. 21,467 (1968).
243. R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc.,* 3573 (1964).
244. R. E. Banks, R. N. Haszeldine, J. V. Latham, and I. M. Young, *J. Chem. Soc.*, 594 (1965).
245. R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc.,* 3736 (1964).
246. R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc.,* 5634 (1964).
247. R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc., 5040* (1965).
248. R E. Banks, J. E. Burgess, W. M. Cheng, and R. N. Haszeldine, *J. Chem. Soc.*, 575 (1965).
249. T. Kato, H. Hayashi, and T. Anzai, *Chem. Pharm. Bull.* (Tokyo), 15, 1343 (1967).
250. R. A. Abramovitch, F. Helmer, and M. Liveris, *J. Chem. Soc.*, *B,* 492 (1968).
251. R. A. Abramovitch, F. Helmer, and M. Liveris, *J.* Org. *Chem.,* 34, 1730 (1969).
252. Z. Talik, *Rocz. Chem.,* 35,475,487 (1961).
253. Z. Talik, Rocz. *Chem.,* 36,1313 (1962).
254. T. Talik, Rocz. *Chem.,* **37, 69** (1963).
255. T. Talik, *Rocz. Chem.,* 36, 1465 (1962).
256. T. Talik and Z. Talik, Ron. *Chem.,* 38,777 (1964).
256a. T. Talik and Z. Talik, Rocz. *Chem.,* 40,1187 (1966).
257. T. Talik and Z. Talik, *Ron. Chem.,* 40,1457 (1966).
258. Z. Talik and B. Brekiesz, Rocz. *Chem.,* 41, 279 (1967).
259. T. Talik and Z. Talik, Ron. *Chem.,* 42, 1647 (1968).
260. T. Talik and Z. Talik, Rocz. *Chem.,* 41,1507 (1967).
261. T. Talik and Z. Talik, *Bull. Acad.* Pol. *Sci., 16,* 7 (1968); *Chem. Abstr.,* 69,59052 (1968).
262. T. Talik and Z. Talik, Ron. *Chem.,* 41, 1721 (1967).
263. Z. Talik and B. Brekiesz-Lewandowska, Rocz. *Chem.,* 44,1325 (1970).
264. T. Talik and Z. Talik, *Ron. Chem.,* 43,1961 (1969).
265. Z Talik and E. Plazek, *Bull. Acad.* Pol. *Sci.,* 8,219 (1960); *Chem. Abstr.,* 60,9241 (1964).
266. T. Talik and Z. Talik, Rocz. *Chem.,* 42,1861 (1968).

267. J. D. Reinheimer, J. T. Gerig, R. Garst, and B. Schrier, *J. Amer. Chem. Soc.*, 84, 2770 (1962).
268. J. A. Zoltewicz and A. A. Sale, *J. Org. Chem.*, 35,3462 (1970).
269. E. Koenigs, H. C. Gerdes, and A. Sirot, *Chem. Ber.*, 61, 1022 (1928).
270. M. Livens and J. Miller, *J. Chem. Soc.*, 3486 (1963).
271. S. Kajihara, *Nippon Kagaku Zasshi, 86,* 839 (1965); *Chem. Abstr.*, 65, 16935 (1966).
272. Ref. 2, pp. 610-611.
273. S. Kajihara, *Nippon Kagaku Zasshi, 86,* 1060 (1965); *Chem. Abstr.*, 65, 16936 (1966).
274. S. Kajihara, *Nippon Kagaku Zasshi, 86,* 93 (1965); *Chem. Abstr.*, 63, 578 (1965).
275. E. Spinner and J. C. B. White, *Chem. Ind.* (London), 1784 (1967).
276. P. Tomasik and E. Plazek, *Rocz. Chem.*, 39, 1911 (1965).
277. Ref. 2, p. 583.
278. E. C. Taylor and J. S. Driscoll, *J. Org. Chem.*. 26,3001 (1961).
279. F. Kröhnke and H. Schäfer, *Chem. Ber.*, 95, 1104 (1962).
280. T. Kosuge, H. Zenda, and Y. Suzuki, *Chem. Pharm. Bull.* (Tokyo), 18, 1068 (1970).
281. M. Barash, J. M. Osbond, and J. C. Wickens, J. *Chem. Soc.*, 3530 (1959).
282. W. Herz and D. R. K. Murty, *J. Org. Chem.*, 26, 122 (1961).
283. T. Takahashi and K. Kariyone, *Chem. Pharm. Bull.* (Tokyo), 8, 1106 (1960).
284. M. J. Pieterse and H. J. den Hertog, *Rec. Trav. Chim. Pays-Bas,* 81,855 (1962).
285. J. Kozlowska and E. Plazek, *Rocz. Chem.*, 33, 831 (1959).
286. T. Talik and Z. Talik, *Proc. Intern. Symp. Warsaw.* 81 (1963); *Chem. Abstr.*, 64, 2046 (1966).
287. T. Batkowski, *Rocz. Chem.*, 43, 1623 (1969).
288. T. Batkowski, *Rocz. Chem,* 37,385 (1963).
289. T. Batkowski and M. Tuszynska, *Rocz. Chem.*, 38,585 (1964).
290. T. Batkowski, *Rocz. Chem.*, 41,729 (1967).
291. T. Batkowski, *Ron. Chem.*, 42,2079 (1968).
292. J. A. Moore and F. J. Marascia, J. *Amer. Chem. Soc.*, 81,6049 (1959).
293. P. Nantka-Namirski, C. Kanmarczyk, and L. Toba, *Acta Pol. Pharm., 24,* 228 (1967); *Chem. Abstr.*, 69,2827 (1968).
294. P. Nantka-Namirski, *Acta Pol. Pharm.*, 18, 449 (1961); *Chem. Abstr.*, 58, 3424 (1963).
295. H. Ban-Oganowska, Z. Skrowaczewska, and L. Syper, *Rocz. Chem.*, 40, 1215 (1966).
296. T. Talik and E. Plazek, *Rocz. Chem.*, 33,387 (1959).
297. J. Koncewicz and Z. Skrowaczewska, *Rocz. Chem.*, 42,1873 (1968).
298. K. Lewicka and E. Plazek, *Ron. Chem.*, 40,1875 (1966).
299. T. Talik, *Rocz. Chem.*, 36, 1049 (1962).
300. T. Batkowski and E. Plazek, *Ron. Chem.*, 36, 51 (1962).
301. P. Tomasik and E. Plazek, *Rocz. Chem.*, 39,365 (1965).
302. C. M. Atkinson and B. N. Biddle, J. *Chem. Soc., C,* 2053 (1966).
303. C.-H. Huang and G. Ya. Kondrat'eva, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk,* 525 (1962).
304. A. Koshiro, *Yakugaku Zasshi,* 79, 1129 (1959); *Chem. Abstr.*, 54,3418 (1960).
305. *T.* Talik and Z. Talik, *Rocz. Chem.*, 37, 75 (1963).
306. A. Dornow, H. v. Plessen, and R. Huischen, *Chem. Ber.*, 99,254 (1966).
307. J. M. Cox, J. A. Elvidge, and D. E. H. Jones, *J. Chem. Soc.*, 1423 (1964).
308. M. Wahren, *Tetrahedron,* 24,441 (1968).
309. M. Wahren, *Tetrahedron,* 24,451 (1968).

310. W. Herz and D. R. K. Murty, *J. Org. Chem.*, 26,418 (1961).
311. R. Adams and T. R. Govindachari, *J. Amer. Chem. Soc.*, 69, 1806 (1947).
312. H. J. den Hertog, J. P. Wibaut, F. R. Schepman, and A. A. van der Wal, *Rec. Trav. Chim. Pays-Bus*, 69,700 (1950).
313. E. J. Behrman and B. M. Pitt, *J. Amer. Chem. Soc.*, 80,3717 (1958).
314. *Y.* Ban and T. Wakamatsu, *Chem. Ind.* (London), 710 (1964).
315. Ref. 2, pp. 591–592.
316. Y. L. Gol'dfarb, L. V. Antik, and V. A. Petukhov, *Izv. Akud. Nuuk, SSSR, Otd. Khim. Nauk*, 887 (1961); *Chem. Abstr.*, 55,22307 (1961).
317. W. Czuba, *Bull. Acud. Pol. Sci.*, 8, 281 (1960); *Chem. Abstr.*, 60, 2883 (1964).
318. W. Czuba, *Rocz.* Chem., 34, 905 (1960).
319. W. Czuba, *Rocz. Chem.*, 34,1639 (1960).
320. W. Czuba, *Rocz. Chem.*, 35,1347 (1961).
321. W. Czuba, *Rocz. Chem.*, 34,1647 (1960).
322. Ref. 2, p. 596.
323. J. Klosa, *J. Prukt. Chem.*, 8, 168 (1959).
324. A. P. Gray, D. E. Heitmeier, and E. E. Spinner, *J. Amer. Chem. Soc.*, 81, 4351 (1959).
325. K. Okamoto and *M.* Tetsuo, *Yukuguku Zusshi*, 82, 769 (1962); *Chem. Abstr.*, 58, 2433 (1963).
326. U. M. Teotino, L. PoloFriz, A. Gandini, and D. Della Bella, *Farmaco, Ed. Sci.*, 17, 988 (1962).
327. D. J. Brown and J. S. Harper, *J. Chem. Soc.*, 5542 (1965).
328. E. A. Prill and S. M. McElvain, *Org. Synth., Coll. Vol.* **II,** 419 (1943).
329. J. Gripenberg, *Tetruhedron*, 10, 135 (1960).
330. J. Gripenberg and T. Hase, *Actu Chem. Scand.*, 17, 2250 (1963).
331. Ref. 2, p. 600.
332. H. Tomisawa, T. Agatsuma, and *Y.* Kamura, *Yukuguku Zusshi*, 81, 947 (1961); *Chem. Abstr.*, 55,27301 (1961).
333. E. G. Podrebarac and W. E. McEwen, *J. Org. Chem.*, 26, 1386 (1961).
334. R. A. Abramovitchand A. R. Vinutha, *J. Chem. Soc., B*, 131 (1971).
335. Ref. 2, pp. 596–603.
336. R. Lukes, A. A. Arojan, J. Kovar, and K. Blaha, *Collect. Czech. Chem. Commun.*, 27,751 (1962).
337. A. Raczka and H. **Bojarska-Dahlig,** *Actu Pol. Pharm.*, 22, 307 (1965); *Chem. Abstr.*, 63, 13201 (1965).
338. D. W. Brown, S. F. Dyke, W. G. D. Lugton, and A. Davis, *Tetruhedron*, 24, 2517 (1968).
339. *Y.* Suzuta, *YukugukuZusshi*, 79, 1314 (1959); *Chem. Abstr.*, 54,4580 (1960).
340. *S.* Akaboshi and *S.* Ikegami, *Chem. Pharm. Bull.* (Tokyo), 14,622 (1966).
341. L. A. Paquette and N. A. Nelson, *J. Org. Chem.*, 27, 1085 (1962).
342. H. Möhrle and H. Weber, *Tetrahedron*, 26,3779 (1970).
343. E. **M.** Kosower and J. W. Patton, *Tetrahedron, 22,* 2081 (1966).
344. S. Hunig and W. Kniese, *Ann. Chem.*, 708, 198 (1967).
345. S. Hunig and W. Kniese, *Ann. Chem.*, 708,178 (1967).
346. *S.* Hünig and W. Kniese, Ann. *Chem.*, 708, 170 (1967).
347. I. Enander, A. Sundwall, and B. Sorbo, *Biochem. Phurmucol.*. 11,377 (1962).
348. P. **M.** S. Miranda and J. L. Way, *Mol. Phurmucol.*, 2, 117 (1966).
349. J. A. Berson and T. Cohen, *J. Amer. Chem. Soc.*, 78,416 (1956).
350. J. A. Berson and J. *S.* Walia, *J. Org. Chem.*, 24, 756 (1959).
351. T. Kametani and *Y.* Nomura, *Chem. Pharm. Bull.* (Tokyo), *8,* 741 (1960).

352. A, R. Battersby and J. C. Turner, *J. Chem. Soc.,* 717 (1960).

353. E. Matsumura, T. Nashima, and F. Ishibashi, Bull. *Chem. Soc. Jap.,* 43, 3540 (1970).

354. H.-J. Teuber, G. Wenzel, and U. Hochmuth, *Chem. Ber.,* %, 1119 (1963).

355. M. Stanulović and S. Chaykin, Fed. *Proc.,* 29, A343 (1970).

356. H. J. Shine, "Aromatic Rearrangements," Elsevier, Amsterdam, 1967, p. 284.

357. E. Ochiai, "Aromatic Amine *N*-Oxides," Elsevier, Amsterdam, 1967, p. 290.

358. A. R. Katritzky, *Quart. Rev.,* 10, 395 (1956).

359. V. J. Traynelis, in "Mechanisms of Molecular Migrations," B. S. Thyagarajan, Ed., Vol. 2, Interscience, New York, 1969, pp. 31–37.

360. J. H. Markgraf, H. B. Brown, Jr., S. C. Mohr, and R. G. Peterson, *J. Amer. Chem. Soc.,* 85, 958 (1963).

361. B. M. Bain and J. E. Saxton, *J. Chem. Soc.,* 5216 (1961).

362. V. Boekelheide and W. L. Lehn, *J. Org. Chem.,* 26, 428 (1961).

363. M. P. Cava and B. Weinstein, *J. Org. Chem.,* 23, 1616 (1958).

364. E. C. Taylor and J. S. Driscoll, *J. Org. Chem.,* 25, 1716 (1960).

365. Y. I. Chumakov and Z. M. Korsakova, *Mefody Polucheniya Khim. Reak. Prep,* No. 4–5, 62 (1962). (*Gos. Kom. Sov., Min. SSSR po Khim*); *Chem. Absfr., 60,* 14468 (1964).

366. T. Cohen and G. L. Deets, *J.* Amer. *Chem. Soc.,* 89, 3939 (1967).

367. P. W. Ford and J. M. Swan, *Ausf. J. Chem.,* 18, 867 (1965).

368. T. Kato, T. Kitagawa, T. Shibata, and K. Nakai, *Yakugaku Zasshi,* 82, 1647 (1962); *Chem. Abstr.,* 59, 559 (1963).

369. C. Kaneko, S. Yamada, and I. Yokoe, *Shika Zairyo Kenkyusho Hokoku,* 2, 475 (1963).

370. L. Syper, Z. Skrowaczewska, and A. Bytnar, Rocz. *Chem.,* 41, 1027 (1967).

371. W. Baker, K. M. Buggle, J. F. W. McOmie, and D. A. M. Watkins, *J. Chem. Soc.,* 3594 (1958).

372. Y. Murakami and J. Sunamoto, *Bull. Chem. Soc. Jap.,* 42, 3350 (1969).

373. R. Adams and A. W. Schrecker, *J. Amer. Chem. Soc.,* 71, 1186 (1949).

374. M. Hamana and M. Yamazaki, *Yakugaku Zasshi,* 81, 574 (1961); *Chem. Absfr.,* 55, 24743 (1961).

375. Y. Kobayashiand I. Kumadaki, *Chem. Pharm.* Bull. (Tokyo), 17, 510 (1969).

376. G. F. van Rooyen, C. v. d. M. Brink, and P. A. deVilliers, *Tydskr. Natuurwetenskappe,* 4, 182 (1964); *Chem. Absfr.,* 63, 13202 (1965).

377. Y. Sakata, K. Adachi, Y. Akahori, and E. Hayashi, *Yakugaku Zasshi,* 87, 1374 (1967); *Chem. Absfr.,* 68, 59649 *(1968).*

378. W. Sliwa and Z. Skrowaczewska, *Rocz. Chem.,* 44, 1941 (1970).

379. L. Achremowicz, T. Moroz-Banas, Z. Skrowaczewska, and L. Syper, *Rocz. Chem.,* 42, 1499 (1968).

380. Ref. 2, p. 609.

381. S. Furukawa, *Yakugaku Zasshi,* 77, 11 (1957); *Chem. Absfr.,* 51, 8745 (1957).

382. S. Oae, T. Kitao, and Y. Kitaoka, *Chem. Ind.* (London), 515 (1961).

383. S. Oae, T. Kitao, and Y. Kitaoka, *J. Amer. Chem. Soc.,* 84, 3359 (1962).

384. V. J. Traynelis and Sr. A. I. Gallagher, *J. Org. Chem.,* 35, 2792 (1970).

385. R. Bodalski and A. R. Katritzky, *Tetrahedron Lett.,* 257 (1968).

386. R. Bodalski and A. R. Katritzky, *J. Chem. Soc., B, 831* (1968).

387. V. J. Traynelis and Sr. A. I. Gallagher, *J. Amer. Chem. Soc.,* 87, 5710 (1965).

388. C. W. Muth and R. S. Darlak, *J. Org. Chem.,* 30, 1909 (1965).

389. V. J. Traynelis and P. L. Pacini, *J. Amer. Chem. Soc.,* 86, 4917 (1964).

390. S. Oae, Y. Kitaoka, and T. Kitao, *Tetrahedron,* 20, 2677 (1964).

391. **S.** Oae, **Y.** Kitaoka, and T. Kitao, ***Tetrahedron,*** 20,2685 (1964).
392. *S.* Oae, T. Kitao, and **Y.** Kitaoka, J. ***Amer. Chem. Soc.,*** 84,3362 (1962).
393. *S.* Oae, T. Kitao, and *Y.* Kitaoka, J. ***Amer. Chem. Soc.,*** 84,3366 (1962).
394. *S.* Oae and *S.* Kozuka, ***Tetrahedron,*** 20, 2691 (1964).
395. V. J. Traynelis, Sr. A. I. Gallagher, and R. F. Martello, ***J. Org. Chem.,*** 26,4365 (1961).
396. **S.** Oae, **S.** Tamagaki, T. Negoro, K. Ogino, and *S.* Kozuka, ***Tetrahedron Lett.,*** 917 (1968).
397. H. Iwamura, M. Iwamura, T. Nishida, and I. Miura, ***Tetrahedron Lett.,*** 3117 (1970).
398. T. Koenig, ***J. Amer. Chem. Soc.,*** 88,4045 (1966).
399. *S.* Oae, S. Tamagaki, T. Negoro, and *S.* Kozuka, ***Tetrahedron,*** 26,4051 (1970).
400. H. Iwamura, M. Iwamura, T. Nishida, and *S.* Sato, J. ***Amer. Chem. Soc.,*** 92, 7474 (1970).
401. T. Cohen and J. H. Fager, ***J. Amer. Chem. Soc.,*** 87,5701 (1965).
402. T. Koenig, ***Tetrahedron Lett.,*** 2751 (1967).
403. D. **M.** Pretorius and P. A. deVilliers, J. ***S. Afr. Chem. Inst.,*** **18,** 48 (1965).
404. A. Klaebe and A. Lattes, ***J. Chromatogr.,*** 27,502 (1967).
405. T. Cohen, I. H. Song, and J. H. Fager, ***Tetrahedron Lett.,*** 237 (1965).
406. T. Cohen, I. H. Song, J. H. Fager, and G. L. Deets, ***J. Amer. Chem. Soc.,*** 89,4968 (1967).
407. C. Rüchardt, O. Krätz, and *S.* Eichler, ***Chem. Ber.,*** 102,3922 (1969).
408. J. F. Vozza, ***J. Org. Chem,*** 27, 3856 (1962).
409. H. J. den Hertog, D. J. Buurman, and P. **A.** deVilliers, ***Rec. Truv. Chim. Pays-Bas,*** 80,325 (1961).
410. *S.* Oae, T. Kitao, and *Y.* Kitaoka, ***Tetrahedron.*** 19,827 (1963).
411. T. Kato, Y. Goto, and **Y.** Yamamoto, ***Yakugaku Zasshi,*** 82, 1649 (1962); ***Chem. Abstr.,*** 59, 2765 (1963).
412. L. Bauer and T. E. Dickerhofe, J. ***Org. Chem.,*** 29,2183 (1964).
413. L. Bauer and **A.** L. Hirsch, J. ***Org. Chem.,*** 31, 1210 (1966).
414. F. M. Hershenson and L. Bauer, J. ***Org. Chem.,*** 34,655 (1969).
415. R. A. Abramovitch and E. E. Knaus, J. ***Heterocycl. Chem.,*** 6,989 (1969).
416. K. Undheim, V. Nordal, and L. Borka, ***Acta Chem. Scand.,*** 23,2075 (1969).
417. *Y.* Nakai, N. Ohishi, **S.** Shimizu, and *S.* Fukui, ***Bitamin,*** 35, 213 (1967).
418. K. Lewicka and E. Plazek, ***Rec. Trav. Chim Pays-Bas,*** 78,644 (1959).
419. ***G.*** G. Spence, E. C. Taylor, and ***O.*** Buchardt, ***Chem. Rev.,*** 70,231 (1970).
420. J. Streith and C. Sigwalt, ***Bull. Soc. Chim. Fr.,*** 1157 (1970).
421. J. Streith, B. Danner, and C. Sigwalt, ***Chem. Commun.,*** 979 (1967).
422. *J.* Streith and C. Sigwalt, ***Tetrahedron Lett.,*** 1347 (1966).
423. F. J. Dinan and H. Tieckelmann, ***J.*** Org. ***Chem.,*** 29,1650 (1964).
424. R. Adams and *S.* Miyano, ***J. Amer. Chem. Soc.,*** 76,3168 (1954).
425. R. B. Greewald and C. L. Zirkle, ***J. Org. Chem.,*** 33,2118 (1968).
426. *W.* A. Lott and E. Shaw, ***J. Amer. Chem. Soc.,*** 71, 70 (1949).
427. S. A. Safarov, ***Kinet. Katal.,*** 3, 449 (1962); ***Chem. Abstr.,*** 58, 2052 (1963).
428. B. Cercek and **M.** Ebert, ***Trans. Faraday Soc.,*** 63, 1687 (1967).
429. L. G. Shevchuk, V. **S.** Zhikharev, and N. A. Vysotskaya, ***Zh. Org. Khim.,*** 5, 1655 (1969); ***Chem. Abstr.,*** 72,2784 (1970).
430. E. K. Fields and **S.** Meyerson, J. ***Org. Chem.,*** **34,** 62 (1970).
431. **Y.** Koda, ***Nagoya Kogyo Gijutsu Shikensho, Hokoku,*** 15, 155 (1966); ***Chem. Abstr.,*** 69,48876 (1968).
432. H. Loth and K. Eichner, ***Arch. Pharm.*** (Weinheim), 302, 264 (1969).

433. K. Kanig, W. Koransky, G. Munch, and P. E. Schulze, *Arch. Exp. Pathol. Pharmakol.,* **249,** 43 (1964); *Chem. Abstr.,* 62,5752 (1965).

434. V. Neuhoff and F. Kohler, *Naturwissenschaften,* 52,475 (1965).

435. V. Neuhoff and F. Kohler, *Arch. Exp. Pathol. Pharmakol.,* 254,301 (1966); *Chem. Abstr.,* 65, 11168 (1966).

436. T. Harris and V. Neuhoff, *Arch. Exp. Pathol. Pharmakol.,* 253,221 (1966); *Chem. Abstr..* 64,18424 (1966).

437. V. Neuhoff and T. Harris, *Arch. Exp. Pathol. Pharmakol.,* 249, 11 (1964); *Chem. Abstr.,* 62,8262 (1965).

438. V. Neuhoff and T. Harris, *Naturwissenschaften,* 51,290 (1964).

439. C. Houghton, K. A. Wright, and R. B. Cain, *Biochem.* J., **106, 51P** (1968).

440. C. Houghton, G. K. Watson, and *R.* B. Cain, *Bwchem.* J., 114, 75P (1969).

441. M. Shamma and P. D. Rosenstock, *J. Org.* Chem., 26,718 (1961).

442. **M.** Shamma and P. D. Rosenstock, J. *Org. Chem.,* 26,2586 (1961).

443. *O.* Y. Magidson, *Zh. Obshch. Khim.,* 33,2173 (1963).

444. P. Cordier and E. Brändli, C.R. *Acad. Sci., Pans, Ser. C,* 258,4091 (1964).

445. A. I. Meyers and G. Garcia-Muiioz, J. *Org. Chem.,* 29, 1435 (1964).

446. N. P. Shusherina, A. V. Golovin, and R. Ya. Levina, *Zh. Obshch. Khim.,* 30, 1762 (1960); *Chem. Abstr.,* 55,7410 (1961).

447. N. P. Shusherina, K. Khua-min', and R. Ya. Levina, *Zh. Obshch. Khim.,* 33, 2829 (1963); *Chem. Abstr.,* 60,4101 (1964).

448. E. Müller, R. Haller, and K. W. Merz, *Chem. Ber.,* 99,445 (1966).

449. N. Sugiyama, M. Yamamoto, and C. Kashima, *Bull. Chem. Soc. Jap.,* 42, 2690 (1969).

450. Y. I. Chumakov and V. P. Sherstyuk, *Tetrahedron Lett.,* 771 (1967).

451. R. J. Highet, *J. Org. Chem.,* 29,471 (1964).

452. A. Albert, "Heterocyclic Chemistry," 2nd Ed., Athlone Press, London, 1968.

453. A. Albert and J. N. Phillips, *J. Chem. Soc.,* 1294 (1956).

454. A. Albert and G. B. Barlin, *J. Chem. Soc.,* 2384 (1959).

455. A. R. Katritzky, F. D. Popp, and J. D. Rowe, J. *Chem. Soc., B,* 562 (1966).

456. A. A. Gordon, A. R. Katritzky, and S. K. Roy, *J. Chem. Soc., B,* 556 (1968).

457. G. Simchen, *Chem. Ber.,* 103,398 (1970).

458. E. Spinner and G. B. Yeoh, *Tetrahedron Lett.,* 5691 (1968).

459. A. R. Katritzky and A. P. Ambler, "Physical Methods in Heterocyclic Chemistry," A. R. Katritzky, Ed., Vol. **11,** Academic Press, New York, 1963, p. 259.

460. B. D. Batts and E. Spinner, *Aust. J. Chem.,* 22,2581 (1969).

461. L. J. Bellamy and P. E. Rogasch, *Spectrochim. Acta,* **16, 30** (1960).

462. R A. Coburn and G. O. Dudek, *J. Phys. Chem.,* 72,3681 (1968).

463. *G.* H. Keller, L. Bauer, and C. L. Bell, *Can.* J. *Chem.,* 46,2475 (1968).

464. J. P. Shoffner, **L.** Bauer, and C. L. Bell, J. *Heterocycl. Chem.,* 7,479 (1970).

465. R. A. Coburn and G. **O.** Dudek, J. *Phys. Chem.,* 72,1177 (1968).

466. A. R. Katritzky and *R.* A. Jones, *J. Chem. Soc.,* 2947 (1960).

467. E. Spinner and J. C. B. White, *J. Chem. Soc., B,* 991 (1966).

468. H. G. Mautner, **S.** Chu, and **C.** M. Lee, J. *Org. Chem.,* 27, 3671 (1962).

469. **M.** H. Krackov, C. M. Lee, and H. G. Mautner, J. *Amer. Chem. Soc.,* 87, 892 (1965).

470. G G. Hammes and H. *O.* Spivey, *J. Amer. Chem. Soc.,* 88,1621 (1966).

471. *G.* G. Hammes and A. C. Park, J. *Amer. Chem. Soc.,* 91.956 (1969).

472. R. **H.** Cox and A. A. Bothner-By, *J. Phys. Chem.,* 73,2465 (1969).

473. B. R. Penfold, *Acta Cryst.,* 6,591 (1953).

474. A. Kvick and I. Olovsson, *Ark. Kemi,* **30,** 71 (1969).

475. G. G. Hammes and P. I. Lillford, J. Amer. Chem. *Soc.*, 92, 7578 (1970).
476. J. A. Elvidge and L. M. Jackman, *J.* Chem. ***Soc.,*** 859 (1961).
477. G. G. Hall, A. Hardisson, and L. M. Jackman, ***Tetrahedron,*** 19, **Suppl.** 2, 101 (1963).
478. A. Albert and E. Spinner,/. Chem. ***Soc.,*** 1221 (1960).
479. H. H. Perkampus and **U.** Krüger, Chem. ***Ber.,*** 100, 1165 (1967).
480. E. **M.** Evleth, Jr., J. A. Berson, and *S.* L. Manatt, ***Tetrahedron Lett.,*** 3087 (1964).
481. J. A. Berson, E. M. Evleth, Jr., and **S.** L. Manatt, J. Amer. Chem. *Soc.*, 87, 2901 (1965).
482. H. Lumbroso and D. M. Bertin, ***Bull. Soc.*** Chim. ***Fr.,*** 1728 (1970).
483. R. A. Jones and A. R. Katritzky, J. ***Chem. Soc.,*** 3610 (1958).
484. **S.** F. **Mason**, *J.* Chem. *Soc.*, 5010 (1957).
485. **W.** E. Stewart and T. H. Siddall, **III**, ***J. Phys.*** Chem., 74,2027 (1970).
486. R. A. Y. Jones, A. R. Katritzky, and L. **M.** Lagowski, ***Chem. Ind.*** (London), 870 (1960).
487. E. **S.** Levin and G. N. Rodionova, ***Dokl. Akad. Nauk, SSSR,*** 164, 584 (1965); Chem. ***Abstr.,*** 64,4905 (1966).
488. E. **S.** Levin and G. N. Rodionova, ***Dokl. Akad. Nauk, SSSR,*** 172, 607 (1967); Chem. ***Abstr.,*** 66,115110 (1967).
489. **A.** R. Katritzky, ***Chimia,*** 24,134 (1970).
490. A. Gordon and A. R. Katritzky, ***Tetrahedron*** Left., 2767 (1968).
491. L.N. Yakhontov, D. M. Krasnokutskaya, E. M. Peresleni, Yu. N. Sheinker, and M. V. Rubtsov, ***Tetrahedron,*** 22, 3233 (1966).
492. L.N. Yakhontov, D. M. Krasnokutskaya, E. M. Peresleni, Yu. N. Sheinker, and M. V. Rubtsov, ***Dokl. Akad. Nauk, SSSR,*** 172, 118 (1967); ***Chem. Abstr., 66,*** 104506 (1967).
493. L.N. Yakhontov, D. M. Krasnokutskaya, E. M. Peresleni, Yu. N. Sheinker, and **M.**V. Rubtsov, ***Dokl. Akad. Nauk, SSSR,*** 176, 613 (1967); Chem. ***Abstr.,*** 68, 78170 (1968).
494. E.M. Peresleni, L. N. Yakhontov, D. M. Krasnokutskaya, and Yu. N. Sheinker, ***Dokl. Akad. Nauk, SSSR,*** 177,592 (1967); Chem. ***Abstr.,*** 68,95634 (1968).
495. E. M. Peresleni, M. Ya. Utritskaya, V. A. Loginova, Yu. **N.** Sheinker, and L. N. Yakhontov, ***Dokl. Akad. Nauk, SSSR,*** 183, **1102** (1968); *Chem.* ***Abstr.,*** 70,77831 (1969).
496. Yu. N. Sheinker, E. M. Peresleni, I. **S.** Rezchikova, and N. P. Zosimova, ***Dokl. Akad. Nauk, SSSR,*** 192,1295 (1970).
497. R. **A.** Jones and B. D. Roney, **J.** ***Chem. Soc., B,*** 84 (1967).
498. *V.* P. Zvolinskii, M. E. Perel'son, and **Yu. N.** Sheinker, ***Dokl. Akad. Nauk, SSSR,*** 179,1137 (1968); *Chem.* ***Abstr.,*** 69,51446 (1968).
499. E. **M.** Kosower, *J.* ***Amer.*** Chem. ***Soc.,*** 80, 3253 (1958).
500. R. Haller, ***Tetrahedron Lett.,*** 3175 (1965).
501. A. Nakamura and *S.* Kamiya, Chem. ***Pharm. Bull.*** (Tokyo), 16, 1466 (1968).
502. C. Wang, ***J. Heterocycl. Chem.,*** 7, 389 (1970).
503. H. J. den Hertog and D. J. Buurman, Rec. ***Trav.*** *Chim.* ***Pays-Bas,*** 75,257 (1956).
504. H. Sterk and H. Junek, ***Monatsh. Chem.,*** 98, 1763 (1967).
505. S. Nesnow and R. Shapiro, ***J. Org.*** Chem., 34,2011 (1969).
506. H.-J. Knackmuss, ***Chem. Ber.,*** 101,2679 (1968).
507. J. Pitha, ***Collect. Czech.*** Chem ***Commun.,*** 28, 1408 (1963).
508. J. R. Stevens, R. H. Beutel, and E. Chamberlin, J. ***Amer.*** Chem. ***Soc.,*** 64, 1093 (1942).
509. E. Ritchie, ***Aust. J.*** Chem, 9,244 (1956).

510. D. W. Jones, *J. Chem. Soc., C,* 1678 (1969).

511. Ref. 2, p. 617.

512. Y. V. Morozov, N. P. Bazhulina, V. I. Ivanov, M. Y. Karpeisky, and A. I. Kuklin, *Biofizika,* 10, 595 (1965); *Chem. Abstr.,* 63, 12527 (1965).

513. D. Heinert and A. E. Martell, *J. Amer. Chem. Soc.,* 81, 3933 (1959).

514. V. P. Lezina, V. F. Bystrov, L. D. Smirnov, and K. M. Dyumaev, *Theor. Eksp. Khim.,* 4, 379 (1968); *Chem. Abstr.,* 69, 76370 (1968).

515. V. P. Lezina, L. D. Smirnov, K. M. Dyumaev, and V. F. Bystrov, *Izv. Akad. Nauk, SSSR, Ser. Khim.,* 25, (1970); *Chem. Abstr.,* 72, 116523 (1970).

516. J. S. Kwiatkowski, *Theor. Chim. Acta,* 16, 243 (1970).

517. L. Paoloni, M. L. Tosato, and M. Cignitti, *Theor. Chim. Acta,* 14, 221 (1969).

518. G. Berthier, B. Levy, and L. Paoloni, Theor. *Chim. Acta,* 16, 316 (1970).

519. E. Suenaga, *Nippon Kagaku Zasshi,* 81, 1710 (1960); *Chem. Abstr.,* 56, 1059 (1962).

520. V. P. Lezina, V. F. Bystrov, L. D. Smirnov, and K. M. Dyumaev, *Theor. Eksp. Khim.,* 1, 281 (1965); *Chem. Abstr.,* 63, 13049 (1965).

521. D. Metzler and E. Snell, *J. Amer. Chem. Soc.,* 77, 2431 (1955).

522. H. C. Brown and *X.* Mihm, *J. Amer. Chem. Soc.,* 77, 1723 (1955).

523. I. I. Grandberg, G. K. Faizova, and A. N. Kost, *Khim. Geterotsikl. Soedin.,* 2, 561 (1966); *Chem. Abstr.,* 66, 10453 (1967).

524. O. A. Gansow and R. H. Holm, *Tetrahedron,* 24, 4477 (1968).

525. J. W. Bridges, D. S. Davies, and R. T. Williams, *Biochem. J.,* 98, 451 (1966).

526. Y. V. Morozov, N. P. Bazhulina, M. Y. Karpeisky, V. I. Ivanov, A. I. Kuklin, and *Y.* N. Breusov, *Bioenerg. Biol. Spectrofotom. Dokl. IV. Skets. Vses, Soveshch Upr. Biosin Biofiz. Pop. Krasnoyarsk. SSSR,* 179 (1965); *Chem. Abstr..* 68, 36204 (1968).

527. Y. V. Morozov, N. P. Bazhulina, and M. *Y.* Karpeisky. *Pyridoxal Catal: Enzymes, Model. Syst. Proc. Int. Symp.* 2nd Ed. 1966, p. 53; *Chem. Abstr.,* 70, 101 (1969).

528. J. W. Bridges, P. J. Creaven, D. S. Davies, and R. T. Williams, *Biochem.* J., 88, 65P (1963).

529. D. D. Rosebrook and W. W. Brandt, *J. Phys. Chem.,* 70, 3857 (1966).

530. P. Beak, J. Bonham, and J. T. Lee, Jr., *J. Amer. Chem. Soc.,* 90, 1569 (1968).

531. P. Beak and J. Bonham, *Chem. Commun.,* 631 (1966).

532. *P.* Beak and J. T. Lee, Jr., *J. Org. Chem.,* 34, 2125 (1969).

533. R. A. Abramovitch and G. N. Knaus, *J.C.S. Chern. Comm.,* 238 (1974).

534. E. Spinner, *J. Chem. Soc.,* 1226 (1960).

535. A. R. Katritzky and R. A. *Y.* Jones, *Chem. Ind.* (London), 722 (1961).

536. A. R. Katritzky and R. A. *Y.* Jones, *Proc. Chem. Soc.* (London), 313 (1960).

537. P. J. Van der Haak, and Th. J. deBoer, Rec. *Trav. Chim. Pays-Bas,* 83, 186 (1964).

538. A. R. Katritzky and R. E. Reavill, J. *Chem Soc.,* 753 (1963).

539. D. Cook, *Can. J. Chem.,* 41, 2575 (1963).

540. D. Cook, *Can. J.* Chern, 43, 749 (1965).

541. D. Cook, *Can.* J. *Chem,* 42, 2292 (1964).

542. C. L. Bell, J. Shoffner, and L. Bauer, *Chem. Ind.* (London), 1435 (1963).

543. S. A. Mason, J. C. B. White, and A. Woodlock, *Tetrahedron Lett.,* 5219 (1969).

544. Yu. N. Sheinker and Y. I. Pomerantsev, *Russ.* J. *Phys. Chem,* 33, 174 (1959).

545. E. Spinner, *J. Chem. Soc.,* 1232 (1960).

546. E. Spinner and J. C. B. White, *J. Chem. Soc., B,* 996 (1966).

547. G. C. Hopkins, J. P. Jonak, H. J. Minnemeyer, and H. Tieckelmann, *J.* Org. *Chem.,* 32, 4040 (1967).

548. G. C. Hopkins, J. P. Jonak, H. Tieckelmann, and H. J. Minnemeyer, J. *Org. Chem.,* 31,3969 (1966).
549. N. M. Chung and H. Tieckelmann, *J. Org. Chem.,* 35,2517 (1970).
550. K. R. Brower, R. L. Ernst, and J. *S.* Chen, *J. Phys. Chem.,* 68,3814 (1964).
551. N. P. Buu-Hoi, **M.** Gauthier, and N. D. Xuong, Bull. *Soc. Chim. Fr.,* 52 (1965).
552. Ref. 2, pp. 636-640.
553. K. Okon, G. Adamska, and W. Waclawek, *Rocz. Chem.,* 43,1653 (1969).
554. K. Winterfeld and M. Michael, *Chem. Ber.,* **93,** 61 (1960).
555. Ref. 2, p. 633.
556. T. Takahashi and A. Koshiro, *Chem. Pharm.* Bull. (Tokyo), 9,426 (196 1).
557. B. I. Mikhant'ev, E. I. Fedorov, A. I. Kucherova, and *V.* P. Potapova, *Zh. Obshch. Khim.,* 29,1874 (1959); *Chem. Abstr.,* 54, 8808 (1960).
558. J. Piechaczek and B. Gogolimska, *Actu Pol. Phunn.,* 25,254 (1968); *Chem. Abstr.,* 70,47245 (1969).
559. D. J. Cook, R E. Bowen, P. Sorter, and E. Daniels, J. *Org. Chem..* 26,4949 (1961).
560. S. Kajihara, *Nippon Kagaku Zasshi, 86,* 933 (1965); *Chem. Abstr.,* 65, 16936 (1966).
561. B. Gogolimska, *Acta Pol. Phurm,* 21, 363 (1964); *Chem. Abstr.,* 62,10404 (1965).
562. B. Gogolimska, *Acta Pol. Phunn. ,25,* 391 (1968).
563. B. Gogolimska, *Actu Pol. Phurm. ,*25, 397 (1968).
564. A. Raczka, A. Swirska, and H. Bojarska-Dahling, *Actu Pol. Phunn.,* 20, 137 (1963); *Chem Abstr.,* 62,1630 (1965).
565. A. Raczka and F. Zahn, *Actu Pol. Phurm.,* 22,310 (1965); *Chem. Abstr..* 63, 13201 (1965).
566. A. Sacha, *Actu Pol. Phunn.,* 23,460 (1966); *Chem. Abstr.,* 66, 104984 (1967).
567. A. Sacha, *Acta Pol. Pharm.,* 25, 123 (1968).
568. N. A Nelson and L. A. Paquette, J. *Org. Chem.,* 27,964 (1962).
569. Ref. 2, p. 641.
570. N. Kornblum and G. P. Coffey, *J. Org. Chem.,* 31,3447 (1966).
571. N. Kornblum and G. P. Coffey, J. *Org. Chem.,* 3 1, 3449 (1966).
572. T. Severin, D. Bätz, and H. Lerche, *Chem. Ber.,* 103, 1 (1970).
573. L. A. Paquette, J. *Org. Chem,* 29, 3545 (1964).
574. H. Kuhmstedt and G. Wagner, *Arch. Phunn.* (Weinheim), 301,660 (1968).
575. S Boatman, T. M. Harris, and C. R. Hauser, J. *Org. Chem.,* 30,3593 (1965).
576. S. Boatman, T. **M.** Harris, and C. R. Hauser, J. *Amer. Chem. Soc.,* 87,5198 (1965).
577. T. M. Harris and C. R. Hauser, J. *Org. Chem.,* 27,2967 (1962).
578. U. Basu, *J. Indian. Chem. Soc.,* 12,299 (1935).
579. R E. Smith, **S.** Boatman, and C. R. Hauser, *J. Org. Chem.,* 33,2083 (1968).
580. R. L. Gay, **S.** Boatman, and C. R Hauser, *Chem. Ind.* (London), 1789 (1965).
581. D. E. Ames and B. T. Warren, *J. Chem. Soc.,* Suppl. 1,5518 (1964).
582. R. W. Balsiger, J. A. Montgomery, and T. P. Johnston, *J. Heterocycl. Chem.,* 2, 97 (1965).
583. K. Undheim, **V.** Nordal, and K. Tjonneland, *Actu Chem. Scund.,* 23, 1704 (1969).
584. P. Laland, J. O. Alvsaker, F. Haugli, J. Dedichen, **S.** Laland, and N. Thorsdalen, *Nature,* 210,917 (1966).
585. K. Undheim and L. Borka, Actu *Chem. Scand.,* 23, 1715 (1969).
586. T. Takahashi and A. Koshiro, *Yakugaku Zasshi,* 79,1123 (1959); *Chem. Abstr.,* 54, 3418 (1960).
587. J. Kejha, **O.** Radek, **V.** Jelinek, and **O.** Nemecek, *Cesk. Farm.,* **16, 92** (1967); *Chem Abstr..* 67,108535 (1967).

588. J. P. Baker, A. R. Katritzky, and T. M. Moynehan, J. Chem. Soc., Suppl., 6138 (1964).

589. L. N. Yakhontov, M. Y. Uritskaya, E. I. Lapan, and M. V. Rubtsov, Khim. Geterotsikl. Soedin., 18 (1968); Chem. Abstr., 69, 106589 (1968).

590. L. N. Yakhontov, M. Y. Uritskaya, and M. V. Rubtsov, Khim. Geterotsikl. Soedin., 918 (1965); Chem. Abstr., 64, 17563 (1966).

591. N. Takahashi, A. Suzuki, and S. Tamura, Agr. Biol. Chem. (Tokyo), 30, 1 (1966); Chem. Abstr., 64, 12630 (1966).

592. S. L. Shapiro, K. Weinberg, and L. Freedman, J. Amer. Chem. Soc., 81, 5140 (1959).

593. K. Mecklenborg and M. Orchin, J. Org. Chem., 23, 1591 (1958).

594. D. A. Prins, Rec. Trav. Chim. Pays-Bas, 76, 58 (1957).

595. M. P. Mertes, R. F. Borne, and L. E. Hare, J. Heterocycl. Chem., 5, 281 (1968).

596. P. Nedenskov, N. Clauson-Kaas, J. Lei, H. Heide, G. Olsen, and G. Jansen, Acta Chem. Scand., 23, 1791 (1969).

597. K. Undheim, P. O. Tveita, L. Borka, and V. Nordal, Acta Chem. Scand., 23, 2065 (1969).

598. R B. Moffett, J. Org. Chem., 28, 2885 (1963).

599. D. Pitre and L. Fumagalli, Farmaco, Ed. Sci., 18, 495 (1963); Chem. Abstr., 59, 9971 (1963).

600. R. Tschesche, D. Klöden, and H. W. Fehlhaber, Tetrahedron, 20, 2885 (1964).

601. H. Pischel and G. Wagner, Z. Chem., 5, 227 (1965).

602. H. Pischel and G. Wagner, Arch. Pharm. (Weinheim), 300, 602 (1967).

603. G. Wagner and H. Pischel, Arch. Pharm. (Weinheim), 295, 373 (1962).

604. G. Wagner and H. Frenzel, Arch. Pharm. (Weinheim), 299, 536 (1966).

605. G. Wagner and E. Fickweiler, Arch. Pharm. (Weinheim), 298, 62 (1965).

606. G. Wagner and H. Gentzsch, Z. Chem., 7, 310 (1967).

607. P. Nuhn, A. Zschunke, and G. Wagner, Z. Chem., 9, 335 (1969).

608. G. Wagner and E. Fickweiler, Arch. Pharm. (Weinheim), 298, 297 (1965).

609. D. Thacker and T. L. V. Ulbricht, Chem. Commun., 122 (1967).

610. G. Wagner and H. Gentzsch, Arch. Pharm. (Weinheim), 301, 346 (1968).

611. D. Heller and G. Wagner, Z. Chem., 8, 415 (1968).

612. D. Heller, Pharmazie, 24, 580 (1969).

613. D. Orth and T. Wieland, Chem. Ber., 102, 196 (1969).

614. H. Pischel and G. Wagner, Z. Chem., 7, 15 (1967).

615. H. Pischel and G. Wagner, Arch. Pharm. (Weinheim), 300, 856 (1967).

616. L. Birkhofer, A. Ritter, and H.-P. Kühlthau, Chem. Ber., 97, 934 (1964).

617. M. J. Robins and B. L. Currie, Chem. Commun., 1547 (1968).

618. M. P. Mertes, J. Zielinski, and C. Pillar, J. Med. Chem., 10, 320 (1967).

619. P. Nuhn, A. Zschunke, D. Heller, and G. Wagner, Tetrahedron, 25, 2139 (1969).

620. G. Wagner and H. Pischel, Naturwissenschaften, 48, 454 (1961).

621. H. Pischel and G. Wagner, Pharmazie, 25, 45 (1970).

622. M. P. Mertes, J. Med. Chem., 13, 149 (1970).

623. G. Wagner and H. Pischel, Arch. Pharm. (Weinheim), 295, 897 (1962).

624. G. Wagner and H. Gentzsch, Arch. Pharm. (Weinheim), 301, 201 (1968).

625. T. Ukita, R. Funakoshi, and Y. Hirose, Chem. Pharm. Bull. (Tokyo), 12, 828 (1964).

626. G. Wagner and H. Pischel, Arch. Pharm. (Weinheim), 2%, 699 (1963).

627. H. Pischel and A. Holy, Collect. Czech. Chem. Commun., 34, 89 (1969).

628. H. Pischel and A. Holy, Collect. Czech. Chem. Commun., 33, 2066 (1968).

629. Ref. 2, pp. 643–645.
630. D. Y. Curtin and L. L. Miller, *J. Amer. Chem. Soc.*, 89,637 (1967).
631. A. McKillop, M. J. Zelesko, and E. C. Taylor, *Tetrahedron Lett.*, 4945 (1968).
632. A. W. K. Chan, W. D. Crow, and I. Gosney, *Tetrahedron*,,26,2497 (1970).
633. I. Fleming and D. Philippides, *J. Chem. Soc., C*, 2426 (1970).
634. F. Arndt and A. Kalischek, *Chem. Ber.*, 63,587 (1930).
635. Ref. 2, pp. 645,677.
636. J. I. G. Cadogan, *J. Chem. Soc.*, 2844 (1959).
637. Y. Ueno, T. Takaya, and E. Imoto, *Bull. Chem. Soc. Jap.*, 37, 864 (1964).
638. Y. Ueno, S. Asakawa, and E. Imoto, *Nippon Kagaku Zasshi*, 89, 101 (1968).
639. *K.* Yokota, M. Sasaki, and Y. Ishii, *J. Polym. Sci.*, 6,2935 (1968).
640. W. Kampe, *Angew. Chem. Intern. Edit.*, 2,479 (1963).
641. N. P. Buu-Hoï, M. Gauthier, and N. D. Xuong, *Bull. Soc. Chim. Fr.*, 52 (1965).
642. A. Koshiro, *Chem. Pharm. Bull.* (Tokyo), 7,725 (1959).
643. T. Takahashi and A. Koshiro, *Chem. Pharm. Bull.* (Tokyo), 7,720 (1959).
644. N. S. Vul'fson, G. M. Sukhotina, and V. N. Zheltova, *Zzv. Akad. Nauk SSSR, Ser. Khim*, 887 (1966); *Chem. Abstr.*, 65, 10556 (1966).
645. N. S. Vul'fson, G. M. Sukhotina, and L. B. Senyavina, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1605 (1966).
646. Ref. 2, pp. 643644.
647. R. C. DeSelms, *J. Org. Chem.*, 33,478 (1968).
648. A. Jerfy and A. B. Roy, Aust. *J. Chem.*, 23, 847 (1970).
649. S. Ginsburg, *J. Med. Pharm. Chem.*, 5, 1364 (1962).
650. W. Korytnyk, H. Ahrens, and N. Angelino, *Tetrahedron.* 26, 5415 (1970).
651. B. Rzeszotarska and G. Palka, *Bull. Acad. Pol. Sci.*, 16, 23 (1968); *Chem. Abstr.*, 69,59542 (1968).
652. E. Taschner, B. Rzeszotarska, and L. Lubiewska, *Angew. Chem.*, 77,619 (1965).
653. E. Taschner, B. Rzeszotarska, and L. Lubiewska, Ann. *Chem.*, 690, 177 (1965).
654. V. A. Shibnev, *K.* M. Dyumaev, T. P. Chuvaeva, L. D. Smirnov, and K. T. Poroshin, *Izv. Akad. Nauk SSSR. Ser. Khim.*, 1634 (1967); *Chem. Abstr.*, 68,22235 (1968).
655. D. T. Elmore, D. V. Roberts, and J. J. Smyth, *Biochem. J.*, 102, 728 (1967).
656. D. T. Elmore and J. J. Smyth, *Biochem.* J., 107, 103 (1968).
657. D. T. Elmore and J. J. Smyth, Proc. *Chem. Soc.* (London), 18 (1963).
658. W. Kampe, *Chem. Ber.*, 98, 1031 (1965).
659. J. Larrouquere, *Bull. Soc. Chim. Fr.*, 329 (1968).
660. *W.* Kampe, *Chem. Ber.*, 98,1038 (1965).
661. W. Kampe, *Chem. Ber.*, 99,593 (1966).
662. K.-H. Scheit and W. Kampe, *Chem. Ber.*, 98, 1045 (1965).
663. B. Miller, *J. Amer. Chem. Soc.*, 84,403 (1962).
664. P. Nantka-Namirski, *Acta Pol. Pharm.*, 18, 391 (1961); *Chem. Abstr.*, 57, 16553 (1962).
665. G. C. Finger and L. D. Starr, *J. Amer. Chem. Soc.*, 81, 2674 (1959).
666. T. Kametani, K. Ogasawara, and T. Yamanaka, *J. Chem. Soc., C*, 1006 (1968).
667. A. Albert and G. B. Barlin, *J. Chem. Soc.*, 5156 (1963).
668. J. W. Clark-Lewis and R. P. Singh, J. *Chem. Soc.*, 2379 (1962).
669. A. Roedig, K. Grohe, D. Klatt, and H.G. Kleppe, *Chem. Ber.*, 99,2813 (1966).
670. T. Kato, H. Hayashi, and T. Anzai, *Yakugaku Zasshi*, 87, 387 (1967); *Chem. Abstr.*, 67,64211 (1967).
671. H. C. van der Plas and H. J. den Hertog, *Rec. Trav. Chim. Pays-Bas*, 81,841 (1962).
672. S. Portnoy, J. *Heterocycl. Chem.*, 6, 223 (1969).

673. M. Satomi, M. Hasegawa, Y. Osawa, and K. Yamamoto, Nippon Daigaku Yakuguku Kenkyu Hokoku, 5–6, 55 (1963); *Chem.* Abstr., 61, 13275 (1964).
674. J. L. Greene, Jr., and J. A. Montgomery, J. *Med.* Chem., 7, 17 (1964).
675. W. Czuba, *Rocz.* Chem., 41, 479 (1967).
676. A. Signor, E. Scoffone, L. Biondi, and S. Bezzi, *Gazz.* Chim. Ztab, 93, 65 (1963); Chem. Abstr., 59, 2811 (1963).
677. Ref. 2, p. 649.
678. D. F. DeTar, Org. React., 9, 407 (1957).
679. R. A. Abramovitch, Adv. Free Radical Chem., 2, 87 (1967).
680. Y. Ban, R. Sakaguchi, and M. Nagai, Chem. Pharm. Bull. (Tokyo), 13, 931 (1965).
681. Ref. 2, pp. 650, 674–675.
682. R. H. Wiley, N. R. Smith, and L. H. Knabeschuh, *J. Amer.* Chem. *Soc.*, 75, 4482 (1953).
683. S. Sugasawa, S. Akaboshi, and Y. Ban, Chem. Pharm. Bull. (Tokyo), 7, 263 (1959).
684. Y. Ban, O. Yonemitsu, T. Oishi, S. Yokoyama, and M. Nakagawa, Chem. *Pharm.* Bull. (Tokyo), 7, 609 (1959).
685. R. F. Evans and H. C. Brown, J. *Org.* Chem., 27, 1329 (1962).
686. E. Ager, B. Iddon, and H. Suschitzky, *J.* Chem. *Soc.*, *C*, 193 (1970).
687. M. S. Newman and H. A. Karnes, *J.* Org. Chem., 31, 3980 (1966).
688. W. A. Roelfsema and H. J. den Hertog, Tetrahedron Lett., 5089 (1967).
689. B. Gogolimska, *Acta* Pol Pharm., 25, 248 (1968); *Chem.* Abstr., 70, 37621 (1969).
690. M. Ferles and J. Caplovic, Collect. Czech. Chem. Commun., 28, 1434 (1963).
691. Y. L. Gol'dfarb and V. V. Kiseleva, *Izv.* Akad. Nauk SSSR, Otd. Khim. Nauk. 2208 (1960); Chem. Abstr., 55, 15481 (1961).
692. K. H. Buchel, A. K. Bocz, and F. Korte, Chem. *Ber.*, 99, 724 (1966).
693. M. Ferles and M. Holik, Collect. Czech. Chem. Commun., 31, 2416 (1966).
694. M. Holik, A. Tesarova, and M. Ferles, Collect. Czech. Chem. Commun., 32, 1730 (1967).
695. M. Holik and M. Ferles, Collect. Czech. Chem. Commun., 32, 2288 (1967).
696. M. Ferles and H. Hruba, Z. Chem., 9, 450 (1969).
697. R. Lukes, Z. Koblicova, and K. Blaha, Collect. Czech. Chem. Commun., 28, 2182 (1963).
698. R. A. Abramovitch and J. G. Saha, *Adv.* Heterocycl. Chem., 6, 253 (1966).
699. A. Albert, *J.* Chem. *Soc.*, 1020 (1960).
700. P. J. Brignell, A. R. Katritzky, and H. O. Tarhan, *J.* Chem. *Soc.*, B, 1477 (1968).
701. A. R. Katritzky, H. O. Tarhan, and S. Tarhan, J. Chem. *Soc.*, B, 114 (1970).
702. Ref. 2, p. 659.
703. R. H. Rigterink and E. E. Kenaga, J. Agr. and Food Chem., 14, 304 (1966); Chem. Abstr., 65, 681 (1966).
704. F. W. Broekman and H. J. C. Tendeloo, Rec. *Trav.* Chim. Puys-Bas, 81, 107 (1962).
705. K. Clarke and K. Rothwell, J. Chem. *Soc.*, 1885 (1960).
706. M. A.-F. Elkaschef and M. H. Nosseir, J. Amer. Chem. *Soc.*, 82, 4344 (1960).
707. Th. Kappe, G. Baxevanidis, and E. Ziegler, *Monatsh.* Chem., 100, 1715 (1969).
708. K. Lewicka and E. Plazek, Rocz. Chem., 40, 405 (1966).
709. L. D. Smirnov, V. I. Kuz'min, V. P. Lezina, and K. M. Dyumaev, Izv. Akad. Nauk SSSR, Ser. Khim, 2400 (1970); Chem. Abstr., 74, 141464 (1971).
710. L. D. Smirnov, V. I. Kuz'min, V. P. Lezina, and K. M. Dyumaev, Izv. Akad. Nauk *SSSR*, Ser. Khim., 1897 (1970); Chem. Abstr., 74, 64184 (1971).
711. L. D. Smirnov, V. I. Kuz'min, V. P. Lezina, and K. M. Dyumaev, Izv. Akad. Nauk SSSR, *Ser.* Khim., 2385 (1970); Chem. Abstr., 74, 141466 (1971).

712. H. N. M. van der Lans and H. J. den Hertog, Rec. Trav. Chim. Pays-Bas, 87, 549 (1968).
713. W. A. Waters, J. Chem. Soc., 727 (1948).
714. L. D. Smirnov, R. E. Lokhov, V. P. Lezina, B. E. Zaitsev, and K. M. Dyumaev, Izv. Akad. Nauk SSSR, Ser. Khim., 1561 (1969); Chem. Abstr., 71, 112765 (1969).
715. E. Plazek, Rec. Trav. Chim. Pays-Bas, 72, 569 (1953).
716. C. O. Okafor, J. Org. Chem., 32, 2006 (1967).
717. W. Czuba and E. Plazek, Rec. Trav. Chim. Pays-Bas, 77, 92 (1958).
718. L. D. Smirnov, V. P. Lezina, B. E. Zaitsev, and K. M. Dyumaev, Izv. Akad. Nauk SSSR, Ser. Khim., 1652 (1968); Chem. Abstr., 70, 11516 (1969).
719. L. D. Smirnov, S. L. Orlova, V. P. Lezina, T. P. Kartasheva, and K. M. Dyumaev, Izv. Akad. Nauk SSSR, Ser. Khim., 2752 (1967); Chem. Abstr., 69, 86782 (1968).
120. L. D. Smirnov, V. P. Lezina, V. F. Bystrov, and K. M. Dyumaev, Izv. Akad. Nauk SSSR, Ser. Khim., 198 (1965); Chem. Abstr., 62, 11774 (1965).
721. L. D. Smirnov, V. P. Lezina, V. F. Bystrov, and K. M. Dyumaev, Izv. Akad. Nauk SSSR, Ser. Khim., 1836 (1965); Chem. Abstr., 64, 5038 (1966).
722. L. D. Smirnov, S. L. Orlova, V. P. Lezina, and K. M. Dyumaev, Izv. Akad. Nauk SSSR, Ser. Khim., 1816 (1967); Chem. Abstr., 68, 87111 (1968).
723. L. D. Smirnov, V. P. Lezina, V. F. Bystrov, and K. M. Dyumaev, Izv. Akad. Nauk SSSR, Ser. Khim., 752 (1963); Chem. Abstr., 59, 7474 (1963).
724. K. M. Dyumaev, L. D. Smirnov, and V. F. Bystrov, Izv. Akad. Nauk SSSR, Ser. Khim., 883 (1962); Chem. Abstr., 57, 12424 (1962).
725. L. D. Smirnov, T. P. Kartasheva, V. P. Lezina, and K. M. Dyumaev, Izv. Akad. Nauk SSSR, Ser. Khim., 2742 (1967); Chem. Abstr., 69, 67191 (1968).
726. L. D. Smirnov, V. P. Lezina, T. P. Kartasheva, and K. M. Dyumaev, Izv. Akad. Nauk SSSR, Ser. Khim., 198 (1968); Chem. Abstr., 69, 77086 (1968).
726a. L. D. Smirnov, Personal Communication (see ref. 726).
727. L. D. Smirnov, V. 1. Kuz'min, V. P. Lezina, and K. M. Dyumaev, Izv. Akad. Nauk SSSR, Ser. Khim., 2784 (1970); Chem. Abstr., 74, 111873 (1971).
728. K. M. Dyumaev, L. D. Smirnov, V. P. Lezina, and V. F. Bystrov, Teor. Eksp. Khim., 1, 290 (1965); Chem. Abstr., 63, 13049 (1965).
729. H. Tomisawa, Y. Kobayashi, H. Hongo, and R. Fujita, Chem. Pharm. Bull. (Tokyo), 18, 932 (1970).
730. B. S. Thyagarajan and K. Rajagopalan, Tetrahedron, 19, 1483 (1963).
731. P. Beak and J. Bonham, Tetrahedron Lett., 3083 (1964).
732. P. Beak and E. M. Monroe, J. Org. Chem., 34, 589 (1969).
733. P. Bellingham, C. D. Johnson, and A. R. Katritzky, Chem. Commun., 1047 (1967).
134. P. Bellingham, C. D. Johnson, and A. R. Katritzky, Chem. Ind. (London), 1384 (1964).
735. P. Bellingham, C. D. Johnson, and A. R. Katritzky, J. Chem. Soc., B, 1226 (1967).
736. Y. Kawazoe and Y. Yoshioka, Chem. Pharm. Bull. (Tokyo), 16, 715 (1968).
737. N. S. Vul'fson and G. M. Sukhotina, Izv. Akad. Nauk SSSR, Ser. Khim., 1785 (1966); Chem. Abstr., 66, 94944 (1967).
738. J. Barycki and E. Plazek, Ron. Chim., 38, 553 (1964).
739. A. D. Palekar and R. A. Kulkarni, Curr. Sci., 37, 229 (1968).
740. B. C. Pathak, S. P. Dutta, and T. J. Bardos, J. Heterocycl. Chem., 6, 447 (1969).
741. K. M. Dyumaev, R. E. Lokhov, B. E. Zaitsev, and L. D. Smirnov, Izv. Akad. Nauk SSSR, Ser. Khim., 2601 (1970); Chem. Abstr., 74, 113181 (1971).
742. Ref. 2, pp. 673–674.
743. H. Bojarska-Dahlig and I. Gruda, Rocz. Chem., 33, 505 (1959).
744. R. A. Abramovitch and A. D. Notation, Can. J. Chem., 38, 1445 (1960).

745. B. S. Thyagarajan, K. Rajagopalan, and P. V. Gopalakrishnan, J. *Chem. Soc.*, *B*, 300 (1968).
746. L. A. Paquette, *J. Org. Chem.*, 30,2107 (1965).
747. B. Weinstein and D. N. Brattesani, *J. Org. Chem.*, 32,4107 (1967).
748. R. M. Acheson and P. A. Taskor, J. *Chem. Soc.*, *C*, 1542 (1967).
749. N. P. Shusherina, O. V. Slavyanova and R. Ya. Levina, *Zh. Obshch. Khim.*, 39, 1182 (1969); *Chem. Abstr.*, 71, 70466 (1969).
750. L. Bauer, C. L. Bell, and G. E. Wright, *J. Heterocycl. Chem.*, 3,393 (1966).
751. E. B. Sheinin, G. E. Wright, C. L. Bell, and L. Bauer, *J. Heterocycl. Chem.*, 5, 859 (1968).
752. H. Tomisawa and H. Hongo, *Tetrahedron Lett.*, 2465 (1969).
753. H. Tomisawa and H. Hongo, *Chem. Pharm.* Bull. (Tokyo), 18,925 (1970).
754. H. Tomisawa, R. Fujita, K. Noguchi, and H. Hongo, *Chem. Pharm.* Bull. (Tokyo), **18**, 941 (1970).
755. A. R. Katritzky and Y. Tacheuchi, J. *Amer. Chem. Soc.*, 92,4134 (1970).
756. E. C. Taylor and W. W. Paudler, *Tetrahedron Lett.*, 1 (1960).
757. W. A. Ayer, R. Hayatsu, P. de Mayo, S. T. Reid, and J. B. Stothers, *Tetrahedron Lett.*, 648 (1961).
758. *G.* Slomp, F. A. MacKeller, and L. A. Paquette, J. *Amer. Chem. Soc.*, 83, 4472 (1961).
759. M. Laing, *Proc. Chem. Soc.* (London), 343 (1964).
760. E. C. Taylor, R. O. Kan, and W. W. Paudler, J. *Amer. Chem. Soc.*, 83,4484 (1961).
761. E. C. Taylor and R. O. Kan, J. *Amer.* Chem. *Soc.*, 85,776 (1963).
762. L. A. Paquette and G. Slomp, J. *Amer. Chem. Soc.*, 85,765 (1963).
763. A. Fozard and C. K. Bradsher, *J. Org.* Chem., 32,2966 (1967).
764. E. J. Corey and J. Streith, J. *Amer. Chem. Soc.*, *86*, 950 (1964).
765. C. Kashima, M. Yamamoto, Y. Sato, and N. Sugiyama, Bull. *Chem. Soc. Jap.*, 42, 3596 (1969).
766. A. Senning, *Acta* Chem. *Scand.*, 18,269 (1964).
767. **M.** Takeda, A. E. Jacobson, K. Kanematsu, and E. L. May, *J. Org. Chem.*, 34,4154 (1969).
768. M. Forchiassin, G. Illuminati, and G. Sleiter, J. *Heterocycl. Chem.*, *6*, 879 (1969).
769. C. Abbolito, C. Iavarone, G. Illuminati, F. Stegel, and A. Vazzoler, *J. Amer.* Chem. *Soc.*, 91,6746 (1969).
770. M. Vogel and J. D. Roberts, *J. Amer.* Chem. *Soc.*, 88,2262 (1966).
771. R. Foster and C. A. Fyfe, *Rev. Pure Appl. Chem.*, **16**, **61** (1966).
772. C. A. Fyfe, *Tetrahedron Lett.*, 659 (1968).
773. M. E. C. Biffin, J. Miller, A. G. Moritz, and D. B. Paul, *Ausf.* J. *Chem.*, 23, 963 (1970).
774. G. Illuminati and F. Stegel, *Tetrahedron Lett.*, 4169 (1968).
775. J. E. Dickeson, L. K. Dyall, and V. A. Pickles, *Ausf.* J. *Chem*, 21, 1267 (1968).
776. P. Bemporad, G. Illuminati, and F. Stegel, *J. Amer. Chem. Soc.*, 91, 6742 (1969).
777. **M.** E. C. Biffin, J. Miller, A. G. Moritz, and D. B. Paul, *Aust. J. Chem.*, 23, 957 (1970).
778. R. A. Fernandez, H. Heaney, J. M. Jablonski, K. G. Mason, and T. J. Ward, *J.* Chem. *Soc.*, *C*, 1908 (1969).
779. J. D. Cook and B. J. Wakefield, *J. Chem. Soc.*, *C*, 2376 (1969).
780. **W.** G. Duncan and D. W. Henry, J. *Med. Chem.*, 11,909 (1968).
781. K. B. Wiberg, T. M. Shryne, and R. R. Kintner, *J. Amer. Chem. Soc.*, 79, 3160 (1957).

782. L. A. Cohen and B. Witkop, in "Molecular Rearrangements", P. de Mayo, Ed., Vol. 2, Interscience, New York, 1964, p. 981.

783. D. J. Brown and R. V. Foster, ***J. Chem. Soc.***, 4911 (1965).

784. D. J. Brown, "The Pyrimidines," Suppl. I, Interscience, New York, 1970, pp. 280–282.

785. R. G. Hiskey and J. Hollander, ***J. Org. Chem.***, 29, 3687 (1964).

786. C. K. Bradsher and M. F. Zinn, ***J. Heterocycl. Chem.***, 1, 219 (1964).

787. C. K. Bradsher and M. F. Zinn, ***J. Heterocycl. Chem.***, 4, 66 (1967).

788. E. Winterfeldt, ***Chem. Ber.***, 97, 2463 (1964).

789. T. Wieland, C. Fest, and G. Pfleiderer, ***Ann. Chem.***, 642, 163 (1961).

790. F. J. Dinan and H. Tieckelmann, ***J. Org. Chem.***, 29, 892 (1964).

791. H. F. Stewart and R. P. Seibert, ***J. Org. Chem.***, 33, 4560 (1968).

792. A. F. Thomas and A. Marxer, ***Helv. Chim. Acta***, 41, 1898 (1958).

793. A. F. Thomas and A. Marxer, ***Helv. Chim. Acta***, 43, 469 (1960).

794. I. Ichimoto, K. Fujii, and C. Tatsumi, ***Agr. Biol. Chem.*** (Tokyo), 31, 979 (1967).

795. R. Kotani and C. Tatsumi, Bull. ***Univ. Osaka Prefect., Ser. B***, 10, 33 (1960); ***Chem. Abstr.***, 58, 11318 (1963).

796. R. G. Jones and M. J. Mann, ***J. Amer. Chem. Soc.***, 75, 4048 (1953).

797. C. Ainsworth and R. G. Jones, ***J. Amer. Chem. Soc.***, 76, 3172 (1954).

798. S. S. Deshapande, Y. V. Dingankar, and D. N. Kopil, ***J. Indian Chem. Soc.***, 11, 595 (1934).

799. D. N. Bedekar, R. P. Kaushal, and S. S. Deshapande, ***J. Indian Chem. Soc.***, 12, 465 (1935).

800. S. W. Nakhre and S. S. Deshapande, ***Vikram J., Vikram Univ.***, 4, 12 (1961).

801. S. W. Nakhre and S. S. Deshapande, ***Vikram J., Vikram Univ.***, 5, 16 (1961).

802. I. E. El-Kholy and F. K. Rafla, ***J. Chem. Soc., C***, 974 (1969).

803. V. A. Volkova and M. I. Goryaev, ***Vestn. Akad. Nauk Kaz. SSR***, 17, 38 (1961); ***Chem. Abstr.***, 55, 24743 (1961).

804. J. A. Moore, F. J. Marascia, R. W. Medeiros, and R. L. Wineholt, ***J. Org. Chem.***, 31, 34 (1966).

805. M. A. Robinson and T. J. Hurley, ***J. Inorg.*** Nucl. ***Chem.***, 28, 1747 (1966).

806. P. R. Rony, ***J. Amer. Chem. Soc.***, 90, 2824 (1968).

807. P. R. Rony, ***J. Amer. Chem. Soc.***, 91, 6090 (1969).

808. P. R. Rony, W. E. McCormack, and S. W. Wunderly, ***J. Amer. Chem. Soc.***, 91, 4244 (1969).

809. E. Sacher and K. J. Laidler, ***Can. J. Chem.***', 42, 2404 (1964).

810. H. C. Beyerman and W. M. van den Brink, ***Proc. Chem. Soc.*** (London), 266 (1963).

811. H. C. Beyerman, W. M. van den Brink, F. Weygand, A. Prox, W. Konig, L. Schmidhammer, and E. Nintz, ***Rec. Trav. Chim. Pays-Bas***, 84, 213 (1965).

812. B. Liberek and A. Michalik, Rocz. ***Chem.***, 40, 781 (1966).

813. F. Pietra and D. Vitali, ***Tetrahedron Lett.***, 5701 (1966).

814. W. C. Kuryla, ***J. Appl. Polym. Sci.***, 9, 1019 (1965).

815. T. J. Wallace and J. J. Mahon, ***J. Org. Chem.***, 30, 1502 (1965).

816. C. C. Houk and K. Emerson, ***J. Inorg.*** Nucl. ***Chem.***, 30, 1493 (1968).

817. I. Baxter and G. A. Swan, ***J. Chem. Soc.***, 3011 (1965).

818. D. Cook, ***Can. J. Chem.***, 43, 741 (1965).

819. D. Cook, ***Can. J. Chem.***, 41, 515 (1963).

820. E. S. Gould, ***J. Amer. Chem. Soc.***, 89, 5792 (1967).

821. E. S. Gould, ***J. Amer. Chem. Soc.***, 90, 1740 (1968).

822. J. Reedijk, ***Rec. Trav. Chim. Pays-Bas***, 88, 1139 (1969).

823. L. J. Boucher and J. C. Bailar, Jr., ***J.*** Inorg. Nucl. ***Chem.***, 27, 1093 (1965).

824. J. R. Wasson, K. K. Ganguli, and L. Theriot, J. *Inorg. Nucl. Chem.*, *29,* 2807 (1967).
825. D. P. Goel, Y. A. G. Dutt, and R. P. Singh, *J. Inorg. Nucl. Chem.*, 34,3119 (1970).
826. G. Anderegg, *Helv. Chim. Acfu.* 46, 1011 (1963).
827. E. Suenaga, *Nippon Kagaku Zusshi,* 79, 1551 (1958); *Chem. Abstr.,* 54, 1515 (1960).
828. S. D. Paul, M. S. Krishnan, and C. Dass, *Indian* J. *Chem.*, 7,299 (1969).
829. B. W. Dale, R. J. P. Williams, P. R. Edwards, and C. E. Johnson, *Trans. Faraday Soc.*, 64,620 (1968).
830. R. M. Ismail, *J. Organometal. Chem.*, 6,663 (1966).
831. D. N. Kravtsov, E. M. Rokhlina, and A. N. Nesmeyanov, *Izv. Akud. Nauk SSSR, Ser. Khim,* 1035 (1968); *Chem. Abstr.,* 70,4254 (1969).
832. W. R. Rimm, D. O. Johnston, C. H. Oestreich, D. G. Lambert, and M. M. Jones, *J. Znorg. Nucl. Chem.*, 29, 2401 (1967).
833. C. W. McDonald and J. H. Bedenbaugh, *Anal. Chem.*, 39, 1476 (1967).
834. C. W. McDonald and R. Carter, *Anal. Chem.*, 41, 1478 (1969).
835. C. W. McDonald and J. H. Bedenbaugh, *Mikrochim. Acfa.* 474 (1970).
836. C. W. McDonald and J. H. Bedenbaugh, *Mikrochim. Acfu,* 612 (1970).
837. M. J. Herak, M. Janko, and K. Blazevic, *Croat. Chem. Acfu,* 41, 85 (1969); *Chem. Abstr.*, 72, 6659 (1970).
838. L. H. Toporcer, R. E. Dessy, and S. I. E. Green, *Inorg. Chem.*, 4, 1649 (1965).
839. W. Selig, *Explosivsfoffe,* 15, 76 (1967); *Chem. Absfr.,* 67, 108015 (1967).
840. E. J. Behrman and P. P. Walker, *J. Amer. Chem. Soc.*, 84, 3454 (1962).
841. E. J. Behrman, *J. Amer. Chem. Soc.*, 85, 3478 (1963).
842. J. H. Boyer and *S.* Kruger, *J. Amer. Chem. Soc.,* 79, 3552 (1957).
843. H.-J. Knackmuss, *Chem. Ber.*, 101, 1148 (1968).
844. N. L. Weinberg and E. A. Brown, J. *Org. Chem.*, 31,4054 (1966).
845. D. E. Ames, R. E. Bowman, and T. F. Grey, J. *Chem. Soc.*, 3008 (1953).
846. H.-J. Knackmuss, J. *Heferocycl. Chem.*, 7, 733 (1970).
847. Ref. 2, pp. 715-719.
848. P. F. Juby and L. Marion, *Biochem. Biophys. Res. Commun.*, 5,461 (1961).
849. P. F. Juby and L. Marion, *Can.* J. *Chem.*, 41, 117 (1963).
850. G. R. Waller and L. M. Henderson, *Biochem. Biophys. Res. Commun.,* **6,** 398 (1961).
851. G. R. Waller and L. M. Henderson, *J. Biol. Chem.,* 236, 1186 (1961).
852. R. F. Dawson, D. R. Christman, A. F. D'Adamo, M. L. Solt, and A. P. **Wolf,** J. *Amer. Chem. Soc.,* 82, 2628 (1960).
853. T. Griffith, K. P. Hellman, and R. U. Byerrun, *Biochemistry,* 1, 336 (1962).
854. H. Tamir and D. Ginsburg, J. *Chem. Soc.*, 2921 (1959).
855. R. Mukherjee and A. Chatterjee, *Tetrahedron, 22,* 1461 (1966).
856. C. G. Casinovi, G. Grandolini, R. Mercantini, N. Oddo, R. Olivieri, and A. Tonolo, *TefrahedronLett.,* 3175 (1968).
857. M. Yasue and N. Kawamura, *Chem. Pharm. Bull.* (Tokyo), 14, 1443 (1966).
858. M. Yasue, N. Kawamura, and T. Kato, *Yakugaku Zasshi,* 87, 732 (1967); *Chem. Absfr.,* 67, 100382 (1967).
859. A. Chatterjee and C. P. Dutta, *Tetrahedron,* 23, 1769 (1967).
860. B. S. Joshi, V. N. Kamat, and A. K. Saksena, *Tetrahedron Lett.*, 2395 (1968).
861. T. Endo, N. Otake, S. Takeuchi, and H. Yonehara, *J. Anfibiof.* (Tokyo), *Ser.* A, 17, 172 (1964).
862. H. Yonehara, S. Takeuchi, N. Otake, T. Endo, Y. Sakagami, and *Y.* Sumiki, *J. Antibiot.* (Tokyo), *Ser. A,* 16, 195 (1963).

863. J. W. Hylin, ***Phytochernistry,*** 3, 161 (1964).
864. E. Bianchi, C. Djerassi, H. Budzikiewicz, and **Y.** Sato, J. ***Org.*** *Chem.*, 30, 754 (1965).
865. N. Takahashi, A. Suzuki, and *S.* Tamura, *J. Amer. Chem. Soc.*, 87,2066 (1965).
866. M. Jeng, C. Hall, F. L. Crane, N. Takahashi, S. Tamura, and K. Folkers, ***Biochemistry,*** 7, 1311 (1968).
867. N. Takahashi, A. Suzuki, S. Miyamoto, R. Mori, and S. Tamura, ***Agr. Biol.*** *Chem.* (Tokyo), 27, 583 (1963).
868. N. Takahashi, A. Suzuki, and S. Tamura, *Agr.* ***Biol.*** *Chem.* (Tokyo), 27, 798 (1963).
869. A. Suzuki, N. Takahashi, and S. Tamura, *Agr.* ***Biol.*** *Chem.* (Tokyo), ***30,*** 18 (1966).
870. N. Takahashi, S. Yoshida, A. Suzuki, and S. Tamura, ***Agr. Biol.*** *Chem.* (Tokyo), 32, 1108 (1968).
871. N. Takahashi, A. Suzuki, Y. Kimura, S. Miyamoto, and S. Tamura, *Tetrahedron* ***Letr.,*** 1961 (1967).
872. N. Takahashi, A. Suzuki, Y. Kimura, S. Miyamoto, S. Tamura, T. Mitsui, and J. Fukami, ***Agr. Biol.*** *Chem.* (Tokyo), 32, 1115 (1968).
873. N. Takahashi, **Y.** Kimura, and S. Tamura, ***Tetrahedron Lett.,*** 4659 (1968).
874. L. I. Hochstein and S. C. Rittenberg, ***J. Biol.*** *Chem.*, 234,151 (1959).
874a. ***L.*** I. Hochstein and S. C. Rittenberg, J. ***Biol.*** *Chem.*, 234, 156 (1959).
875. L. I. Hochstein and S. C. Rittenberg, J. **Biol** *Chem.*, 235, 795 (1960).
876. S. H. Richardson and S. C. Rittenberg, ***J. Biol.*** *Chem.*, 236,959 (1961).
877. *S.* H. Richardson and S. C. Rittenberg, ***J. Biol.*** *Chem.*, 236,964 (1961).
878. K. Deppe, ***Zentr. Bakteriol. Parasitenk. Abr.,*** **II,** 119, 589 **(1965);** *Chem.* ***Abstr.,*** 64, 14621 **(1966).**
879. K. Decker, H. Eberwein, F. A. Gries, and M. Bruhmuller, ***Z. Physiol.*** *Chem.*, 319, 279 (1960).
880. F. A. Gries, K. Decker, and M. Bruhmuller, ***Z. Physiol.*** *Chem.*, 325,229 (1961).
881. ***G.*** D. Griffith, R. U. Byerrum, and W. A. Wood, ***Proc. Soc. Exptl. Biol. Med..*** 108, 162 (1961).
882. K. Decker, H. Eberwein, F. A. Gries, and M. Bruhmuller, ***Biochem. Z.,*** 334, 227 **(1961).**
883. K. Decker and H. **Bleeg,** ***Biochim. Biophys.*** *Acta*, 105, 313 (1965).
884. K. Decker and ***V.*** D. Dai, ***Eur. J. Biochem.,*** 3,132 (1967); *Chem.* ***Abstr.,*** 68,46648 (1968).
885. M. L. **Wu** Chang and B. C. Johnson, ***J.*** *Nutr.*, 76,512 (1962).
886. J. C. Ensign, *Dissertation* ***Abstr.,*** 24, 31 (1963); *Chem.* ***Abstr.,*** 59, 15627 (1963).
887. J. C. Ensign and S. C. Rittenberg, ***Arch. Mikrobiol.,*** 47, 137 (1963).
888. J. C. Ensign and S. C. Rittenberg, ***Bact. Proc.,*** 107 (1962).
889. R. L. Gherna and S. C. Rittenberg, ***Bact. Proc.,*** 107 (1962).
890. J. C. Ensign and S. C. Rittenberg, ***Bact. Proc.,*** 54 (1963).
891. R. L. Gherna, S. H. Richardson, and S. C. Rittenberg, J. ***Biol.*** *Chem.*, 240, 3669 **(1965).**
892. J. C. Ensign and *S.* C. Rittenberg, ***Arch. Mikrobiol.,*** 51, 384 (1965).
893. R. Kuhn, H. Bauer, H.-J. Knackmuss, D. A. Kuhn, and M. P. Starr, *Naturwissen.*, 51,409 (1964).
894. R. Kuhn, **H.** Bauer, and H.-J. Knackmuss, ***Chem. Ber.,*** 98,2139 (1965).
895. R. Kuhn, M. P. Starr, D. A. Kuhn, H. Bauer, and H.-I. Knackmuss, ***Arch.*** *Mikrobiol.*, 51, 71 (1965).
896. L. J. Bellamy and P. E. Rogasch, ***Proc. Roy.*** *Soc.*, ***Ser. A,*** **257, 98 (1960).**
897. D. A. Brent, J. D. Hribar, and D. C. DeJongh, ***J. Org.*** Chern., 35, 135 (1970).

898. N. A. Broisevich and N. N. Khovratovich, ***Zh. Prikl. Spektrosk.,*** 7, 538 (1967); *Chem. Abstr.,* 68, 86651 (1968).

899. W. Brugel, ***Z. Electrochem.,*** 66, 159 (1962); *Chem. Abstr.,* 57, 307 (1962).

900. **D.** L. Gumprecht, *J. Chromatogr.,* 37, 268 (1968).

901. D. Herbison-Evans and R. E. Richards, *Mol. Phys., 8,* 19 (1964).

902. R. Isaac, F. F. Bentley, H. Sternglanz, W. C. Coburn, Jr., C. V. Stephenson, and W. S. Wilcox, ***Appl. Spectrosc.,* 17,** 90 (1963); *Chem. Abstr.,* 59, 7077 (1963).

903. G. H. Keller, L. Bauer, and C. L. Bell, ***J. Heterocycf.Chem.,*** 5,647 (1968).

904. J. Kracmar, J. Kracmarova, and J. Zyka, *Cesk. Farm.,* 17,68 **(1968); *Chem. Abstr.,*** 69,5266 (1968).

905. J. Kracmar, J. Kracmarova, and J. Zyka, ***Pharmazie.*** 23,567 (1968); ***Chem. Abstr.,*** 70,31719 (1969).

906. J. S. Kwiatkowski and J. Olzacka, Bull *Acad. Pol. Sci., Ser. Sci. Chim.,* 18, 215 (1970).

907. R. Lawrence and E. S. Waight, *J. Chem. Soc., B,* 1 (1968).

908. A. Neszmelyi and J. Bayer, *Kem. Kozlern,* 32, 221 (1969); *Chem. Abstr.,* 72, 116593 (1970).

909. K. Nishimoto, Bull. *Chem. Soc. Jap.,* 39, 645 (1966); *Chem. Abstr.,* 65, 4833 (1366).

910. K. Nishimoto and L. S. Forster, ***J. Phys. Chem.,*** 71,409 (1967).

911. H.-J. Petrowitz, G. Pastuska, and S. Wagner, *Chem.-Ztg., Chem. App.,* 89, 7 (1965); *Chem. Abstr.,* 62,11125 (1965).

912. R. **M.** Pinyazhko, ***Farm. Zh.*** (Kiev), 20, 17 **(1965); *Chem. Abstr.,*** 64,9514 (1966).

913. ***G.*** N. Rodionova and E. S. Levin, ***Dokl. Akad. Nauk SSSR,*** 174, 1132 (1967); *Chem. Abstr.,* 68,95190 (1968).

914. R. Soda, Bull. ***Natl. Inst. Ind. Health,*** 5, 32 (1961); *Chem. Abstr.* 57, 8864 (1962).

915. G. Spiteller and *M.* Spiteller-Friedmann, *Monatsh. Chem.,* 93, 1395 (1962).

916. A. Veillard, *J. Chim. Phys.,* 59, 1056 (1962).

917. V. R. Williams and J. G. Traynham, *J. Org. Chem.,* 28,2883 (1963).

918. H. W. Yurow, L. B. Morton, and S. Sass, *Microchem.* **J.,** 11, 237 (1966); ***Chern. Abstr.,*** 65, 7984 (1966).

919. B. E. Zaitsev and **Y.** N. Sheinker, ***Izv. Akad. Nauk SSSR Otd., Khim. Nauk,*** 2070 (1962); ***Chem. Abstr.,*** 58,6339 (1963).

920. R. M. **Ismail,** Fr. patent, 1,475,896 (1967); ***Chem. Abstr.,*** 68, 13178 (1968).

921. **Y.** N. Sheinker and ***Y.*** I. Pomerantzev, ***Zh. FU. Khim.,*** 33, 1819 (1959); ***Chem. Abstr.,*** 54, 12156 (1960).

922. T. Koenig and **J.** Wieczorek, **J.** ***Org. Chem.,*** 35,508 (1970).

923. C. L. Bell, R. S. Egan, and L. Bauer, **J. *Heterocycl. Chem.,*** 2,420 (1965).

924. L. A. Paquette, U.S. patent, 3,318,899 (1967); *Chem. Abstr., 68,* 49579 (1968).

925. I. I. Grandberg, G. K. Faizova, and A. N. Kost, ***Zh. Anal. Khim.,*** 20, 268 (1965); *Chem. Abstr.,* 62,15402 (1965).

926. W. Ried and **E.-U.**Kocher, *Ann. Chem.,* 647,116 (1961).

927. M. V. Lomonosov, K. Khua-min', and R. *Y.* Levina, Zh. ***Obshch. Khim.,*** 33,2829 (1963).

928. A. S. Bailey and J. *S.* A. Brunskill, *J. Chem. Soc.,* 2554 (1959).

929. E. Bullock, B. Gregory, and A. W. Johnson, ***J. Chem. Soc.,*** 1632 (1964).

930. R. F. Childs and A. W. Johnson, ***Chem. Ind.*** (London), 542 (1964).

931. B. Jaques and J. W. Hubbard, ***J. Med. Chem.,*** 11, 178 (1968).

932. N. P. Shusherina, R. **Y.** Levina, and T. G. Rymareva, ***Zh. Obshch. Khim.,*** 32, 89 (1962); ***Chem. Abstr.,*** 57, 13716 (1962).

933. R N. Seelye and D. W. Stanton, ***Tetrahedron Lett.,*** 2633 (1966).

934. Fr. Addn., 90,356 (1967); *Chem. Abstr.*, 70,87584 (1969).
935. Fr. patent, 1,458,066 (1967); *Chem. Abstr.*, 70,68183 (1969).
936. E. Haack, H. Berger and W. Vomel, Br. patent, 1,014,050 (1965); *Chem. Abstr.*, 64, 6624 (1966).
937. Nether. Appl. 6,613,362 (1967); *Chem. Abstr.*, 67, 100,007 (1967).
938. C. F. H. Allen, *Can. J. Chem.*, 43, 2486 (1965).
939. J. H. Snyders and M. J. Pieterse, *J. S. Afr. Chem. Inst.*, 22, 37 (1969); *Chem. Abstr.*, 70, 114,969 (1969).
940. T. Kametani, K. Ogasawara, M. Shio, and A. Kosuka, *Yakugaku Zasshi*, 87, 260 (1967); *Chem. Abstr.*, 67, 54317 (1967).
941. I. E. El-Kholy, F. K. Rafla, and M. M. Mishrikey, *J. Chem. Soc., C*, 1578 (1970).
942. B. D. Sharma, *Acta Crystallogr.*, 20, 921 (1966).
943. P. Tomasik and E. Plazek, *Rocz. Chem.*, 39, 1671 (1965); *Chem. Abstr.*, 64, 19549 (1966).
944. R. Adams and W. Reifschneider, *J. Amer. Chem. Soc.*, 81, 2537 (1959).
945. F. Cuiban, S. Cilianu-Bibian, S. Popescu, and I. Rogozea, Fr. patent, 1,366,064 (1964); *Chem. Abstr.*, 61, 14643 (1964).
946. J. C. Martin, U.S. patent, 3,141,880 (1964); *Chem. Abstr.*, 61, 11977 (1964).
947. J. W. Streef and H. J. den Hertog, *Rec. Trav. Chim. Pays-Bas*, 85, 803 (1966).
948. G. N. Smith, *J. Econ. Entomol.*, 61, 793 (1968); *Chem. Abstr.*, 69, 34964 (1968).
949. R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, Belg. patent, 660,873 (1965); *Chem. Abstr.*, 65, 7152 (1966).
950. R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, Brit. patent, 1,107,882 (1968); Chem. *Abstr.*, 69, 86821 (1968).
951 Imperial Chemical Industries, Ltd., Nether. Appl., 6,611,714 (1967); *Chem. Abstr.*, 68, 21842 (1968).
952. I. Collins and H. Suschitzky, *J. Chem. Soc., C*, 1523 (1970).
953. Imperial Chemical Industries, Ltd., Nether. Appl., 6,611,766 (1967); *Chem. Abstr.*, 68, 59438 (1968).
954. W. J. Link, R. F. Borne, and F. L. Setliff, *J. Heterocycl. Chem.*, 4, 641 (1967).
955. G. B. Barlin, *J. Chem. Soc.*, 2150 (1964).
956. P. Tomasik and Z. Skrowaczewska, *Rocz. Chem.*, 42, 1427 (1968).
957. P. Tomasik and Z. Skrowaczewska, *Rocz. Chem.*, 42, 795 (1968).
958. P. Tomasik, *Rocz. Chem.*, 44, 341 (1970).
959. B. Glowiak, *Bull. Acad., Pol. Sci.. Ser. Sci. Chim.*, 10, 9 (1962); *Chem. Abstr.*. 58, 501 (1963).
960. P. Tomasik and Z. Skrowaczewska, *Rocz. Chem.*, 42, 1583 (1968).
961. B. Glowiak, *Zes. Nauk Politech. Wroclaw Chem.*, 7, 49 (1961); *Chem. Abstr.*, 58, 498 (1963).
962. W. Reifschneider and J. S. Kelyman, U.S. patent, 3,335,146 (1967); *Chem. Abstr.*, 68, 87178 (1968).
963. J. K. Landquist, U.S. patent, 3,074,954 (1963); *Chem. Abstr.*, 59, 635 (1963).
964. M. Berndt and J. S. Kwiatkowski, *Theor. Chim. Acta*, 17, 35 (1970).
965. A. R. Katritzky and A. R. Hands, *J. Chem. Soc.*, 2202 (1958).
966. L. A. Paquette, U.S. patent, 3,218,329 (1965); *Chem. Abstr.*, 64, 3495 (1966).
967. F. Cramer, Ger. patent, 1,203,777 (1965); Chem. *Abstr.*, 64, 6625 (1966).
968. J. J. Eatough, L. S. Fuller, R. H. Good, and R. K. Smalley, *J. Chem. Soc., C*, 1874 (1970).
969. J. W. Streef and H. J. den Hertog, *Tetrahedron* Lett., 5945 (1968).
970. J. Buchi, S. Allisson, and W. Vetsch, *Helv. Chim. Acta*, 48, 1216 (1965).
971. M. Melandri, V. Gerosa, and A. Buttini, *Ann. Chim.* (Rome), 50, 125 (1960).

972. H. Johnston, U.S. patent, 3,249,619 (1966); ***Chem. Abstr.,*** 65,693 (1966).

973. R. H. Rigterink, Fr. patent, 1,360,901 (1964); ***Chem. Abstr.,*** 61, 16052 (1964).

974. M. C. Ivey and H. *V.* Claborn, J. ***Assoc. Offic. Anal. Chem.,*** 51, 1245 (1968).

975. T. A. Mikhailova, N. I. Kudryashova, and N. *V.* Khromov-Borisov, ***Zh. Obshch. Khim.,*** 39, 26 (1960); ***Chem. Abstr.,*** 70, 114460 (1969).

976. H. Johnston and M. S. Tomita, U.S. patent, 3,234,228 (1966); ***Chem. Abstr.,*** 64, 14173 (1966).

977. H. V. Claborn, H. D. Mann, and D. D. Oehler, J. ***Assoc. Offic. Anal. Chem..*** 51, 1243 (1968).

978. R. H. Rigterink, U.S. patent, 3,385,859 (1968); ***Chem. Abstr.,*** 69, 59105 (1968).

979. A. J. W. Brook and R. K. Robertson, ***Chem. Ind.*** (London), 2110 (1967).

980. E. M. Evleth, ***Theor. Chim. Acta,*** 11, 145 (1968).

981. T. Gramstad and W. J. Fuglevik, ***Acta Chem. Scand.,*** 16, 1369 (1962).

982. M. Holik, V. Skala, and J. Kuthan, ***Collect. Czech. Chern. Commun.,*** 33, 394 (1968).

983. A. R. Katritzky, F. W. Maine, and S. Golding, ***Tetrahedron,*** 21, 1693 (1965).

984. M. Ohtsuru, K. Tori, and H. Wantanabe, ***Chem. Pharm.*** Bull. (Toyko), 15, 1015 (1967); ***Chem. Abstr..*** 67, 112621 (1967).

985. D. W. Turner, J. ***Chem. Soc.,*** 847 (1962).

986. D. Cook, ***Chem. Ind.*** (London), 1259 (1964).

987. B. I. Mikhant'ev and E. 1. Fedorov, ***Izv. Vyssh. Ucheb. Zaved., Khim. Khim. Tekhnol., 2,*** 390 (1959); ***Chem. Abstr.,*** 54,4565 (1960).

988. A. Sacha, ***Acta Pol. Phurm.,*** 22,516 (1965); ***Chem. Abstr.,*** 64, 9723 (1966).

989. A. Sacha, Polish patent, 51,367 (1966); ***Chem. Abstr.,*** 67, 73526 (1967).

990. Upjohn Co., Nether. Appl., 6,505,770 (1965); ***Chem. Abstr., 64,*** 11185 (1966).

991. L. A. Paquette, U.S. patent, 3,432,507 (1969); ***Chem. Abstr.,*** 70,96834 (1969).

992. K. Hamamoto and T. Kajiwara, Jap. patent, 13,985 (1964); ***Chem. Abstr.,*** 65, 20108 (1966).

993. W. Sauermilch, ***Arch. Pharm.*** (Weinheim), 293,452 (1960).

994. T. Kajiwara, Jap. patent, 20,295 (1967); ***Chem. Abstr.,*** 69,27265 (1968).

995. L. A. Paquette, J. ***Amer. Chem. Soc.,*** 87, 5186 (1965).

996. E. C. Taylor, F. Kienzle, and A. McKillop, J. ***Org. Chem.,*** 35, 1672 (1970).

997. L. A. Paquette, J. ***Amer. Chem. Soc.,*** 87, 1407 (1965).

998. H. W. Chambers and J. E. Casida, ***Toxicol. Appl. Pharmacol.,*** 14, 249 (1969).

999. B. B. Greene and K. G. Lewis, ***Tetrahedron Lett.,*** 4759 (1966).

1000. D. E. Ames and T. F. Grey, J. ***Chem. Soc.,*** 631 (1955).

1001. B. B. Greene and K. G. Lewis, ***Aust. J. Chem.,*** 21, 1845 (1968).

1002. L. A. Paquette, U.S. patent, 3,213,101 (1965); ***Chem. Abstr.,*** 64, 2063 (1966).

1003. L. A. Paquette, ***Tetrahedron,*** 22, 25 (1966).

1004. P. H. Schroeder, S. Afr. patent, 07,133 (1967); ***Chem. Abstr.,*** 70, 47,309 (1969).

1005. N. S. Vul'fson and G. M. Sukhotina, ***Metody Poluch Khim., Reactiovov, Prep.,*** 83 (1966); ***Chem. Abstr.,*** 67, 32552 (1967).

1006. L. A. Paquette, U.S. patent, 3,213,100 (1965); ***Chern. Abstr.,*** 64, 2069 (1966).

1007. S. Mizukami, E. Hirai, and M. Morimoto, ***Shionogi Kenkyiesho Nempo (Shionogi Research Lab) Annual Report,*** 16, 29 (1966); ***Chem. Abstr.,*** 66, 10827 (1967).

1008. H. Tomisawa, ***Yakugaku Zasshi,*** 79, 1167 (1959); ***Chem. Abstr.,*** 54, 3416 (1960).

1009. S. Grudzinski, ***Rocz. Chem.,*** 40, 335 (1966); ***Chem. Abstr.,*** 65,681 (1966).

1010. J. Bernstein and K. A. Losee, U.S. patent, 3,356,683 (1967); ***Chem. Abstr.,*** 68, 105013 (1968).

1011. H. Tomisawa, ***Yakugaku Zasshi,*** 79, 1173 (1959); ***Chem. Abstr.,*** 54, 3417 (1960).

1012. T. Kajiwara, lap. patent, 20,294 (1967); Chem. ***Abstr.,*** 69,27264 (1968).

1013. G. M. Coppinger and E. R. Bell, *J. Phys. Chem.*, 70, 3479 (1966).

1014. E. Bernasek, U.S. patent, 3,230,226 (1966); *Chem.* Abstr., 64, 8256 (1966).

1015. L. A. Paquette, U.S. patent, 3,321,482 (1967); *Chem.* Abstr., 68, 49577 (1968).

1016. American Cyanamid Co., Nether. Appl., 6,612,653 (1967); Chem. Abstr., 68, 21847 (1968).

1017. B. Gogolimska and I. Gruda, *Acta* Pol. *Pharm.*, **20**, 130 (1963); *Chem.* Abstr., 62, 1584 (1965).

1018. B. Gogolimska, H. Bojarska-Dahlig, I. Gruda, A. Raczka, and A. Swirska, Pol. patent, 48,708 (1964); *Chem.* Abstr., 63, 18,041 (1965).

1019. J. F. Willems, A. L. VandenBerghe, and G. F. VanVeelen, Belg. patent, 706,086 (1968); Chem. Abstr., 70, 47,303 (1969).

1020. A. Sacha, Pol. patent, 55,633 (1968); *Chem.* Abstr., 70, 106,557 (1969).

1021. K. Hamamoto and T. Kajiwara, Jap. patent, 20,556 (1965); *Chem.* Abstr.. 64, 3505 (1966).

1022. H. Fugimura, K. Okamoto, and M. Tetsuo, Jap. patent, 19,649 (1964); *Chem.* Abstr., 62, 13,129 (1965).

1023. J. N. Ashley, R. F. Collins, M. Davis, and N. E. Sirett, *J. Chem. Soc.*, 3880 (1959).

1024. A. Sacha, Pol. patent, 52,123 (1966); *Chem.* Absfr., 68, 114,650 (1968).

1025. J. Faust, G. Speier, and R. Mayer, *J.* Prakt. Chem., 311, 61 (1969).

1026. G. Wagner and H. Pischel, *Z. Chem.*, 2, 308 (1962).

1027. J. K. Sutherland and D. A. Widdowson, *J. Chem. Soc.*, 4651 (1964).

1028. V. Tortorella, F. Macioci, and G. Poma, Farrnaco, Ed. Sci., 23, 236 (1968); *Chem.* Absfr., ***69,*** 59,058 (1968).

1029. H. Tomisawa and H. Hongo, ***Tohoku*** Yakka Daigaku Kenkyo *Nempo,* 39 (1963); *Chem.* Abstr., 61, 4308 (1964).

1030. T. Kato and **Y.** Kubota, Yakugaku Zasshi, 87, 1212 (1967); Chem. Absfr., 68, 95,644 (1968).

1031. N. *S.* Vul'fson and G. M. Sukhotina, Khim. *Geterotsikl. Soedin.*, 3, 682 (1967); Chem. Abstr., 68, 39,432 (1968).

1032. M. Eder, E. Ziegler, and E. Prewedourakis, *Monatsh.* Chem., 99, 1395 (1968).

1033. H. Wittmann, V. Illi, and E. Ziegler, *Monatsh. Chem.*, 98, 1108 (1967).

1034. A. M. Duffield, C. Djerassi, G. Schroll, and **S.-O.** Lawesson, Acta *Chem. Scand.*, 20, 361 (1966).

1035. M. Hamana and K. Funakoshi, Yakugaku Zasshi, 84, 23 (1964); *Chem.* Abstr., 61, 3068 (1964).

1036. N. Clauson-Kaas and N. Elming, Ger. patent, 1,134,378 (1962); *Chem.* Absfr., 58, 1438 (1963).

1037. B. F. Duesel, and **S.** Emanuele, **U.S.** patent, 3,218,330 (1965); *Chem.* Abstr., 64, 3503 (1966).

1038. N. Elming, **S.** V. Carlsten, B. Lennart, and 1. Ohlsson, Brit. patent, 862,581 (1961); *Chem. Abstr.*, 56, 11574 (1962).

1039. A. D. Filyugina, K. M. Dyumaev, A. A. Dubrovin, and I. A. Rotermel, Zh. Organ. Khim, 6, 2131 (1970); Chem. Abstr., 74, 12306 (1971).

1040. L. Fishbein and M. A. Cavanaugh, *J. Chromatogr.*, 20, 283 (1965).

1041. E. J. Poziomek, Chemist-Analyst, 55, 78 (1966).

1042. **Y.** Sasaki, M. Hatanaka, I. Shiraishi, M. Suzuki, and K. Nishimoto, Yakugaku Zasshi, 89, 21 (1969); Chem. Abstr., 70, 92,138 (1969).

1043. I. Schmeltz and R. L. **Stedman**, *Chem.* Znd. (London), 1244 (1962).

1044. P. W. Wigler and L. E. Wilson, Anal. *Biochem.*, 15, 421 (1966).

1045. F. J. Anderson and A. E. Martell, *J. Amer. Chem. Soc.*, 86, 715 (1964).

1046. T. Naito, T. Yoshikawa, F. Ishikawa, and H. Omura, Jap. patent, 22,740 (1965); *Chem. Abstr.,* 64,3496 (1966).

1047. A. Fujita, M. Nakata, S. Minami, and H. Takamatsu, *Yakugaku Zasshi,* 86, 1014 (1966); *Chem. Abstr.,* 66,75885 (1967).

1048. W. Korytnyk and R. P. Singh, *J. Amer. Chem. Soc.,* 85,2813 (1963).

1049. W. Korytnyk, *J. Med. Chem.,* 8, 112 (1965).

1050. G. E. McCasland, L. K. Gottwald, and A. Furst, *J. Org. Chem.,* 26,3541 (1961).

1051. H. Monig and R. Koch, *Biophysik..* **3,** 11 (1966).

1052. L. A. Petrova and N. N. Bel'tsova, *Zh. Obshch. Khim.,* 34, 2765 (1964); *Chem. Abstr.,* 61, 14634 (1964).

1053. W. Korytnyk and M. Ikawa, *Methods in Enzymology,* **18A,** 524 (1970).

1054. T. Naito and K. Ueno, *Yakugaku Zasshi,* 79, 1277 (1959); *Chem. Abstr.,* 54,4566 (1960).

1055. R. Koch, H. Lagendorff, and H. Monig, *Atomkernenergie,* 11, 209 (1966); *Chem. Abstr.,* 65,9302 (1966).

1056. O. Kondo, Y. Miyazaki, T. Maruyama, and M. Ikariwa, Jap. patent, 2,356 (1968); *Chem. Abstr.,* 69,67232 (1968).

1057. K. Pfister, III, E. E. Harris, and R. A. Firestone, U.S. patent, 3,227,721 (1966); *Chem. Abstr.,* 64,9689 (1966).

1058. K. Pfister, III, E. E. Harris, and R. A. Firestone, U.S. patent, 3,227,722 (1966); *Chem. Abstr., 65,* 16949 (1966).

1059. C. J. Argoudelis and F. A. Kummerow, *J. Org. Chem.,* 29,2663 (1964).

1060. G. Schorre, Ger. patent, 1,238,473 (1967); *Chem. Abstr.,* 68, 39479 (1968).

1061. T. Kuroda, *Bitamin,* 28, 211 (1963); *Chem. Abstr.,* 62,515 (1965).

1062. K. Okumura, *Bitamin,* 23,236 (1961); *Chem. Abstr..* 62, 1630 (1965).

1063. U. Schmidt and G. Geisselmann, *Ann. Chem.,* 657, 162 (1962).

1064. Tanabe Seiyaku Co., Ltd., Belg. patent, 671,385 (1966); *Chem. Abstr.,* 65, 15348 (1966).

1065. W. Korytnyk and B. Paul., *J. Med. Chem.,* 13,187 (1970).

1066. P. D. Sattsangi and C. J. Argoudelis, *J. Org. Chem.,* 33, 1337 (1968).

1067. C. F. Boehringer and Soehne, G. m.b.H., Nether. Appl., 6,402,960 (1964); *Chem. Abstr.,* 62,7732 (1965).

1068. K. Undheim and V. Nordal, *Acta Chem. Scand.,* 23, 1975 (1969).

1069. K. Nakamura, Y. Utsui, and Y. Ninomija, *Yakugaku Zasshi,* 86,404 (1966); *Chem. Abstr.,* 65, 18429 (1966).

1070. J. L. Greene, A. M. Williams, and J. A. Montgomery, *J. Med. Chem.,* **7, 20 (1964).**

1071. L. A. Walter and N. Sperber, U.S. patent, 2,997,478 (1958); *Chem. Abstr..* 56, 1434 (1962).

1072. T. Kuroda, *Bitamin,* 28, 354 (1963); *Chem. Abstr.,* 62,515 (1965).

1073. R. J. Highet and P. F. Highet, *J. Org. Chem.,* 31, 1275 (1966).

1074. P. L. Kumler and O. Buchardt, *Chem. Commun.,* 1321 (1968).

1075. J. W. Cusic, **P. Yonan, U.S.** patent, 3,377,344 (1968); *Chem. Abstr.,* 69, 52172 (1968).

1076. N. Clauson-Kaas, F. Ostermayer, E. Renk, and R. Denss, Swiss patent, 452,528 (1968); *Chem. Abstr.,* 69,96746 (1968).

1077. D. Heinert and A. E. Martell, *J. Amer. Chem. Soc.,* 84,3257 (1962).

1078. R. Tomchick and J. A. R. Mead, *Biochemical Medicine,* 4, 13 (1970).

1079. T. Naito, T. Yoshikawa, F. Ishikawa, and H. Omura, Jap. patent, 23908 (1965); *Chem. Abstr.,* 64,3495 (1966).

1080. C. Iwata and D. E. Metzler, *J. Heterocycl. Chem.,* 4, 319 (1967).

1081. E. H. Abbott and A. E. Martell, *J. Amer. Chem. Soc.,* 92, 1754 (1970).

1082. Y. Kobayashi and K. Makino, *Biochim. Biophys. Acta,* 208,137 (1970).

1083. K. Okumura, Jap. patent, 02,716 (1968) ;*Chem. Abstr.,* 69,59107 (1968).

1084. W. B. Dempsey and E. E. Snell, *Biochemistry,* 2,1414 (1963).

1085. R. C. DeSelms, U.S. patent, 3,409,624 (1968) ;*Chem. Abstr.,* 70,57665 (1969).

1086. R. C. DeSelms, U.S. patent, 3,409,630 (1968) ; *Chem. Abstr.,* 70,57663 (1969).

1087. U. Schmidt, U.S. patent, 3,075,987 (1963) ;*Chem. Abstr.,* 59,9999 (1963).

1088. G. Schorre, Ger. patent, 1,238,474 (1967) ;*Chem. Abstr.,* 68,39480 (1968).

1089. M. Iwanami, I. Osawa, and M. Nurakami, *Bitamin,* 36, 122 (1967) ;*Chem. Abstr.,* 68,12817 (1968).

1090. T. Kuroda, *Bitamin,* 30,431 (1964) ;*Chem. Abstr.,* 62,10402 (1965).

1091. T. Kuroda and M. Masaki, *Bitamin,* 30, 436 (1964) ; *Chem. Abstr.,* 62, 10402 (1965).

1092. T. Kuroda, *Bitamin,* 28,21 (1963) ;*Chem. Abstr.,* 62,515 (1965).

1093. E. Merck AG., Fr. patent, M2071 (1963) ;*Chem. Abstr.,* 60, 10656 (1964).

1094. H. Hirano, K. Masuda, and T. Fushimi, Jap. patent, 02,712 (1968) ;*Chem. Abstr.,* 69,86827 (1968).

1095. M. Murakami and M. Iwanami, Jap. patent, 19,067 (1966) ; *Chem. Abstr.,* 66, 37776 (1967).

1096. I. Utsumi, T. Watanabe, and G. Tsukamoto, *Bitamin,* 37,276 (1968) ;*Chem. Abstr.,* 69,36065 (1968).

1097. G. Neurath and W. Lüttich, *J. Chromatogr.,* 34,253 (1968).

1098. W. Zecher and F. Krohnke, *Chem. Ber.,* 94,707 (1961).

1099. C. Corral and A. M. Municio, *Anales Real. Soc. Espan. Fis. Quim., Ser. B.,* 60,341 (1964) ;*Chem. Abstr.,* 62,7670 (1965).

1100. G. Wilbert and H. Wetstein, U.S. patent, 3,284,459 (1966) ; *Chem. Abstr.,* 68, 49463 (1968).

1101. R. Ponci, A. Baruffini, and F. Gialdi, *Farmaco,* Ed. *Sci.,* 18,288 (1963) ;*Chem. Abstr..* 59,7478 (1963).

1102. B. D. Batts and E. Spinner, *J. Chem. Soc., B,* 789 (1968).

1103. B. D. Batts and E. Spinner, *Aust.* J. *Chem.,* 22,2595 (1969).

1104. J. P. Wibaut and F. W. Broekman, *Rec. Trav. Chim. Pays-Bas,* 78,593 (1959).

1105. Y. Takahasi, T. Kato, and M. Kurihara, Jap. patent, 00,055 (1969) ;*Chem. Abstr.,* 70,114853 (1969).

1106. E. Hayashi and H. Yamanaka, Jap. patent, 15,616 (1961); *Chem. Abstr.,* 56, 12863 (1962).

1107. D. G. Markees, *J. Org. Chem.,* 29,3120 (1964).

1108. H. D. Becker, *Acta Chem. Scand.,* 16, 78 (1962).

1109. A. Sugii, Y. Kabasawa, Y. Niki, and Y. Yamazaki, *Yakugaku Zasshi,* 89, 1066 (1969) ;*Chem. Abstr.,* 71,105251 (1969).

1110. M. J. Huraux and H. M. Lawson, *Symp. New Herbicides, 2nd, Pans,* 269 (1965) ; *Chem. Abstr.,* 65,12799 (1966).

1111. R. N. Haszeldine and R. E. Banks, U.S. patent, 3,317,542 (1967) ;*Chem. Abstr.,* 68, 59442 (1968).

1112. J. Bonham, E. McLeister, and P. Beak, J. *Org. Chem.,* 32,639 (1967).

1113. K. Hamamoto and T. Kajiwara, Jap. patent, 23,180 (1965) ;*Chem. Abstr.,* 64,3504 (1966).

1114. S. Kajihawa, *Nippon Kagaku Zasshi, 85,* 672 (1964) ; *Chem. Abstr.,* 62, 14624 (1965).

1115. I Christenson, *Acta Pharm. Suecica,* 5, 23 (1968) ;*Chem. Abstr.,* 68,89904 (1968).

1116. K. H. Boltze, H. D. Dell, H. Lehwald, D. Lorenz, and M. Rueberg-Schweer, *Arzeimittel-Forsch.,* 13,688 (1963) ;*Chem. Abstr.,* 63,4289 (1965).

1117. **S.** Goto, A. Kono, and *S.* Iguchi, ***J. Pharm. Sci.,*** 57,791 (1966).
1118. T. Metler, A. Uchida, and S. I. Miller, ***Tetrahedron,*** 24,4285 (1968).
1119. C. **P.** Krimmel, **U.S.** patent, 2,999,860 (1961); ***Chem. Abstr.,*** 56,4780 (1962).
1120. K. Blazevic and N. Trinajstic, ***Croatica Chem. Acta,*** 39, 25 (1967); ***Chem. Abstr.,*** 67,69116 (1967).
1121. K. H. Schuendehuette and K. Trautner, Fr. patent, 1,412,980 (1965); ***Chem. Abstr., 64,*** 8360 (1966).
1122. E. Habicht, **U.S.** patent, 2,995,561 (1959).
1123. E. Habicht and R. Zubiani, Belg. patent, 654,331 (1965); ***Chem. Abstr.,*** 64, 17553 (1966).
1124. A. Nakamura and S. Kamiya, ***Chem. Pharm.*** Bull. (Tokyo), 17,425 (1969).
1125. A. P. Chatrousse, **F.** Terrier, and **R.** Schaal, ***C.*** R. ***Acad. Sci., Paris, Ser. C.,*** 271, 1477 (1970).
1126. G. Stork and R. Matthews, ***Chem. Commun.,*** 445 (1970).
1127. R. J. Sundberg, **P.** A. Bukowick, and F. **O.** Holcombe, **J.** ***Org. Chem.,*** 32, 2938 (1967).
1128. A. J. Verbiscar and K. N. Campbell, ***J. Org. Chem.,*** 29,2472 (1964).
1129. G. DiMaio and P. A. Tardella, ***Gazz. Chim. Ital.,*** 96,387 (1966).
1130. E. Cavalieri and D. Gravel, ***Can.*** **J.** ***Chem.,*** 48, 2727 (1970).
1131. C. H. Eugster, L. Leichner, and E. Jenny, ***Helv. Chim. Acta,*** 46,543 (1963).
1132. H. Kuehnis, **R.** Denu, and C. H. Eugster, Swiss uatent, 417,591 (1967); ***Chem. Abstr.,*** 68, 39482 (1968).
1133. D. G. Cheesman, **P.** Garside, A. C. Ritchie, and J. M. Waring, **J.** ***Chem. Soc., C,*** 1134 (1967).
1134. J. C. Sheehan and M. M. Nagissu, **J.** ***Org. Chem.,*** 35,4246 (1970).
1135.' K. Hohenlohe-Oehringen and G. Zimmer, ***Monatsh. Chem.,*** 94,1225 (1963).
1136. K. Kariyone, ***Yakugaku Zasshi,*** 83, 398 (1963); *Chem.* ***Abstr.,*** 59, 7481 (1963).
1137. N. Sugiyama, M. Yamamoto, and C. Kashima, Bull. ***Chem. Soc. Jap.,*** 43, 3937 (1970).
1138. N. Sugiyama, M. Yamamoto, and C. Kashima, Bull. ***Chem. Soc. Jap.,*** 43, 3556 (1970).
1139. P. Nuhn and **W.-R.** Bley, ***Tetrahedron Lett.,*** 611 (1970).
1140. H. K. Reimschuessel, K. P. Klein, and G. J. Schmitt, *Makrolmol.* ***Chem.,*** 2, 567 (1969).
1141. K. Hohenlohe-Oehringen, Monatsh. ***Chem.,*** 96,262 (1965).
1142. P. A. Ratto and A. A. Liebman, ***J. Pharm. Sci.,*** 53,480 (1964).
1143. A. Cliatterjee and C. **P.** Dutta, ***Sci. Cult.*** (Calcutta), 29,568 (1963).
1144. A. R. Battersby, Brit. patent, 895,910 (1962); ***Chern. Abstr,,*** 58,6878 (1963).
1145. *S.* Portnoy, ***J. Heterocycl. Chem.,*** 3, 363 (1966).
1146. R. G. Glushkov and **O.** Y. Magidson, *Khim.* ***Geterotsikl. Soedin. Akad. Nauk Latv. SSR,*** 240 (1965); *Chem.* ***Abstr.,*** 63, 13259 (1965).
1147. Dynamit-Nobel, AG., Belg. patent, 635,427 (1963); ***Chem. Abstr.,*** 61, 11977 (1964).
1148. H. Ulrich, E. Kober, H. Schroeder, R. Rätz, and G. Grundmann, ***J. Org. Chem.,*** 27, 2585 (1962).
1149. H. H. Kuehnis, R. Denss, and C. H. Eugster, **U.S.** patent, 3,073,838 (1963); ***Chem. Abstr.,*** 58, 12519 (1963).
1150. R. E. Lyle, K. R. Carle, C. **R.** Ellefson, and C. K. Spicer, ***J. Org.*** *Chem.,* 35, 802 (1970).
1151. R. E. Lyle and **W.** E. Krueger, **J.** ***Org. Chem.,*** 32,2873 (1967).

1152. R. F. C. Brown, L. Subrahmanyan, and C. P. Whittle, *Aust. J. Chem.,* 20, 339 (1967).

1153. C.-T. Chen, S.-J. Yan, and J.C. Ho, *Bull. Inst. Chem. Acad. Sinica,* 13, 49 (1967); *Chem. Abstr.,* 67,118073 (1967).

1154. E. Dirks, A. Scherer, M. Schmidt, and G. Zimmer, *Arzneimittel-Forsch.,* 20, 55 (1970); *Chem. Abstr.,* 73,2338 (1970).

1155. J. E. Ayling, E. E. Snell, *Biochemistry,* 7, 1626 (1968).

1156. C. Holstead, Belg. patent, 619,423 (1962); *Chem. Abstr.,* 59, 12826 (1963).

1157. W. Seiffert and H. H. Mantsch, *Tetrahedron,* 25,4569 (1969).

1158. F. M. Hershenson and L. Bauer, *J. Org. Chem.,* 34,660 (1969).

1159. G. Kresze, G. Schulz, and F. Firl, *Angew. Chem.,* 75, 375 (1963).

1160. H. Krimm, Ger. patent 1,092, 919 (1956).

1161. J. J. Vill, T. R. Steadman, and J. J. Godfrey, *J. Org. Chem.,* 29, 2780 (1964).

1162. N. P. Shusherina, R. Ya. Levina, and K. Khua-min', *Zh. Obshch. Khim.,* 32, 3599 (1962); *Chem. Abstr.,* 58,12507 (1963).

1163. N. P. Shusherina, R. Ya. Levina, and Z. S. Sidenko, *Zh. Obshch. Khim.,* 29, 398 (1959); *Chem. Abstr.,* 54,519 (1960).

1164. A. Vigier and J. Dreux, *Bull. Soc. Chim. Fr.,* 2292 (1963); *Chem. Abstr.,* 60,5448 (1964).

1165. L. G. Duquette and F. Johnson, *Tetrahedron,* 23,4517 (1967).

1166. F. Zymalkowski and P. Messinger, *Arch. Pharm.* (Weinheim), 300, 91 (1967).

1167. R. E. Lyle and W. E. Krueger, *J. Org. Chem.,* 32,3613 (1967).

1168. R. F. C. Brown, V. M. Clark, and L. Todd, *Tetrahedron, Supplement* 8 *Part I,* 15 (1966).

1169. E. Winterfeldt, H. Radung, and P. Strehlke, *Chem. Ber.,* 99, 3750 (1966).

1170. M. Takeda, A. E. Jacobson, and E. L. May, *J. Org. Chem.,* 34,4158 (1969).

Chemistry of Heterocyclic Compounds, Volume 14
Edited by R. A. Abramovitch

Index