BROWSE | SEARCH

- Gomberg Free Radical Reaction
- Gomberg-Bachmann Reaction
- Gould-Jacobs Reaction
- Graebe-Ullmann Synthesis
- Griess Diazo Reaction
- Grignard Degradation
- Grignard Reaction
- Grob Fragmentation
- Grosheintz-Fischer-Reissert Aldehyde Synthesis
- Grundmann Aldehyde Synthesis
- Guareschi-Thorpe Condensation
- Guerbet Reaction
- Gustavson Reaction
- Gutknecht Pyrazine Synthesis
- Haack (see Vilsmeier-Haack Reaction)
- Haaf (see Koch-Haaf Carboxylations)
- Haller-Bauer Reaction
- Haloform Reaction
- Hammick Reaction
- Hantzsch Dihydropyridine Synthesis
- Hantzsch Pyrrole Synthesis
- Harries Ozonide Reaction
- Hartwig (see Buchwald-Hartwig Cross Coupling Reaction)
- Hass Cyclopropane Process
- Hauser (see Sommelet-Hauser Rearrangement)
- Haworth Methylation
- Haworth Phenanthrene Synthesis
- Hayashi Rearrangement
- Heck Reaction
- Helferich Method
- Hell-Volhard-Zelinsky Reaction
- Henkel Process
- Henkel Reaction
- Henry Reaction
- Hepp (see Fischer-Hepp Rearrangement)
- HERON Rearrangement
- Herz Reaction
- Heteroatom Rearrangements on Nitrogen
- Hilbert-Johnson Reaction
- Hillman (see Baylis-Hillman Reaction)
- Hinsberg Oxindole and Oxiquinoline Synthesis
- Hinsberg Sulfone Synthesis

- Sarett Oxidation
- Scheller Modification
- Schiemann (see Balz-Schiemann Reaction)
- Schiemann Reaction
- Schlittler-Müller Modification
- Schlotterbeck (see Buchner-Curtius-Schlotterbeck Reaction)
- Schmidt (see Bohn-Schmidt Reaction)
- Schmidt (see Claisen-Schmidt Condensation)
- Schmidt Reaction
- Schmitt (see Kolbe-Schmitt Reaction)
- Scholl Reaction
- Schöllkopf Bis-Lactim Amino Acid Synthesis
- Schöpf (see Robinson-Schöpf Reaction)
- Schotten-Baumann Reaction
- Schuster (see Meyer-Schuster Rearrangement)
- Selenium Dioxide Oxidation
- Semidine Rearrangement
- Semmler (see Wolff-Semmler Aromatization)
- Semmler-Wolff Reaction
- Senderens (see Sabatier-Senderens Reduction)
- Serini Reaction
- Shapiro Reaction
- Sharpless Dihydroxylation
- Sharpless Epoxidation
- Sharpless Oxyamination
- Shibata (see Corey-Bakshi-Shibata Reduction)
- Simmons-Smith Reaction
- Simonini Reaction
- Simonis Chromone Cyclization
- Sims (see Boyland-Sims Oxidation)
- Skraup Reaction
- Smiles (see Truce-Smiles Rearrangement)
- Smiles Rearrangement
- Smith (see Simmons-Smith Reaction)
- Sommelet Reaction
- Sommelet-Hauser Rearrangement
- Sonn-Müller Method
- Speier (see Fischer-Speier Esterification Method)
- Spengler (see Pictet-Spengler Isoquinoline Synthesis)
- SPPS
- Staudinger Reaction
- Stephen Aldehyde Synthesis

Organic Name Reactions

The Organic Name Reactions (ONR) section is intended to serve the professional chemist and student by describing organic chemical reactions which have come to be recognized and referred to by name within the chemistry community. A select group has been chosen for addition to this section. Each reaction description is designed to be informative and representative of the pertinent literature; however, it is not meant to be comprehensive. The descriptions are composed of the following: (1) name(s) associated with the reaction, (2) the original and/or primary contributor(s) connected with the discovery and/or development of the reaction, (3) a concise description of the transformation, (4) a reaction scheme, (5) key references, and (6) cross references to other ONR based on commonalities. The index included in this section also lists supplementary terms.

Abbreviations

Ac	acetyl
Ar	aryl
aq	aqueous
B	base
BBN	borabicyclo[3.3.1]nonane
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
BOC	*t*-butyloxycarbonyl
Bu	butyl
cat	catalytic
Cp	cyclopentyldienide
Δ	heat
dba	dibenzylideneacetone
DCC	dicyclohexylcarbodiimide
DEAD	diethylazadicarboxylate
DME	dimethylether
E	electrophile
ee	enantiomeric excess
Et	ethyl
EtOH	ethanol
EWG	electron withdrawing group
HA	protic acid
HMPT	hexamethylphosphoric triamide
LDA	lithium diisopropylamide
LHMDS	lithium hexamethyldisilazide
Me	methyl
NuH	nucleophile
Ph	phenyl
Pr	propyl
salen	*N*,*N'*-ethylenebis(salicylideneimine)
Tf	trifluoromethanesulfonyl
Ts	*p*-toluenesulfonyl

dppf	dichloro[1,1'-bis(diphenylphosphino) ferrocene]
dppp	1,3-bis(diphenylphosphino)propane

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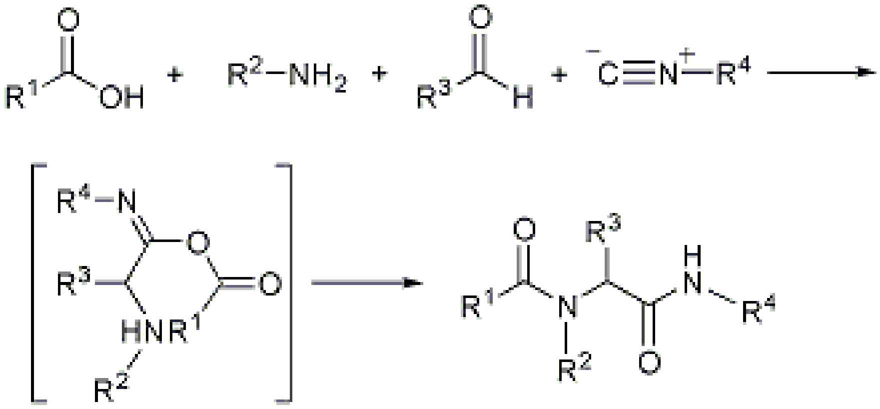
403. Ugi Reaction (Four-Component Condensation, 4CC)

I. Ugi, *Angew. Chem. Int. Ed.* **1,** 8 (1962).

The α-addition of an iminium ion and the conjugate base of a carboxylic acid to an isocyanide, followed by spontaneous rearrangement of the α-adduct to yield an α-aminocarboxamide derivative. Carbonyl compounds and amines, or their condensation products, serve as precursors to the iminium ion. The nature of the product depends primarily on the acid component:



When four discrete reactants are used, the reaction is often referred to as the four-component condensation (4CC). Diastereoselective methods development: H. Kunz *et al., Synthesis* **1991,** 1039; M. Goebel, I. Ugi, *ibid.* 1095. Synthetic applications: T. Ziegler *et al., Tetrahedron Letters* **39,** 5957 (1998); *eidem, Tetrahedron* **55,** 8397 (1999). *Reviews:* I. Ugi, *Proc. Estonian Acad. Sci. Chem.* **40,** 1-13 (1991); I. Ugi *et al., Comp. Org. Syn.* **2,** 1083-1109 (1991).

76. Claisen Condensation (Acetoacetic Ester Condensation)

L. Claisen, O. Lowman, *Ber.* **20,** 651 (1887).

Base-catalyzed condensation of an ester containing an α-hydrogen atom with a molecule of the same ester or a different one to give β-keto esters:

$$CH_3COOC_2H_5 + CH_3COOC_2H_5 \xrightarrow{C_2H_5O^-} CH_3COCH_2COOC_2H_5 + C_2H_5OH$$

C. R. Hauser, B. E. Hudson, *Org. React.* **1,** 266-322 (1942); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 734-746; J. F. Garst, *J. Chem. Ed.* **56,** 721 (1979); J. E. Bartmess *et al., J. Am. Chem. Soc.* **103,** 1338 (1981); B. R. Davis, P. J. Garratt, *Comp. Org. Syn.* **2,** 795-805 (1991). *Cf.* Dieckmann Reaction.

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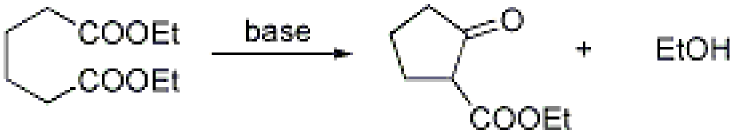
101. Dieckmann Reaction

W. Dieckmann, *Ber.* **27,** 102, 965 (1894); **33,** 595, 2670, (1900); *Ann.* **317,** 51, 93, (1901).

Base-catalyzed cyclization of dicarboxylic acid esters to give β-ketoesters, the intramolecular equivalent of the Claisen condensation, *q.v.*:



J. P. Schaefer, J. J. Bloomfield, *Org. React.* **15,** 1-203 (1967); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 740-743; H. Kwart, K. Sing in *The Chemistry of Carboxylic Acids and Esters*, S. Patai, Ed. (Interscience, New York, 1969) p 341; B. R. Davis, P. J. Garrett, *Comp. Org. Syn.* **2,** 806-829 (1991). *Cf.* Gabriel-Colman Rearrangement.

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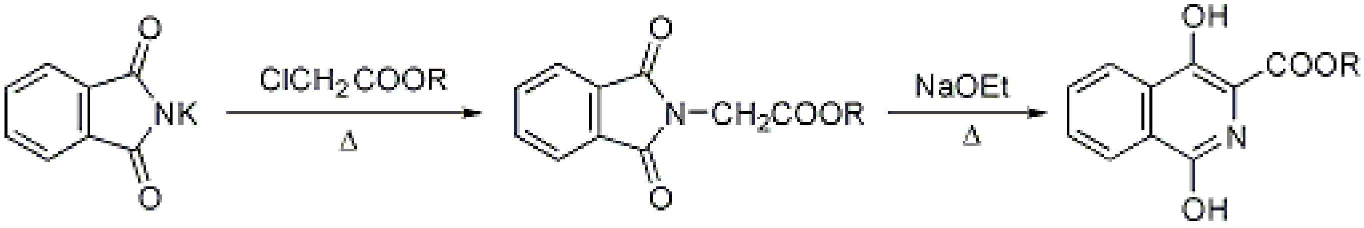
152. **Gabriel-Colman Rearrangement** (Phthalimidoacetic Ester→Isoquinoline Rearrangement, Gabriel Isoquinoline Synthesis)

S. Gabriel, J. Colman, *Ber.* **33,** 980, 996, 2630 (1900); **35,** 2421 (1902).

Formation of isoquinoline derivatives or substituted benzothiazines by the action of alkoxides on phthalimidoacetic or saccharin esters or ketones:



C. F. H. Allen, *Chem. Rev.* **47,** 284 (1950); H. Henecka, *Houben-Weyl* **8,** 578 (1952); J. H. M. Hill, *J. Org. Chem.* **30,** 620 (1965); W. C. Groutas *et al., Biochem. Biophys. Res. Commun.* **194,** 1491 (1993); *idem et al., Bioorg. Med. Chem.* **3,** 187 (1995); S.-K. Kwon, *J. Korean Chem. Soc.* **40,** 678 (1996). Mechanism: M. T. Ivery, J. E. Gready, *J. Chem. Res. (S)* **9,** 349 (1993). *Cf.* Dieckmann Reaction.

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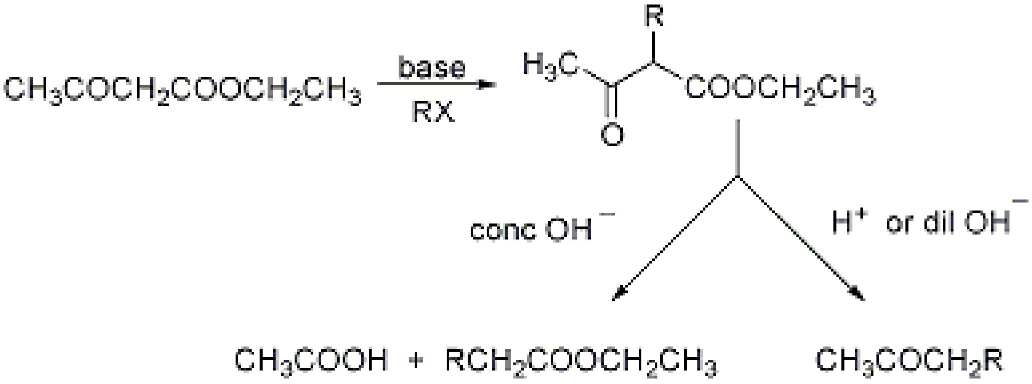
1. Acetoacetic Ester Synthesis

Base-catalyzed alkylation or arylation of β-ketoesters. Subsequent mild hydrolysis and decarboxylation yield substituted acetones. Alternately, treatment with concentrated base produces substituted esters:



Synthetic applications: R. Kluger, M. Brandl, *J. Org. Chem.* **51,** 3964 (1986); T. Yamamitsu *et al., J. Chem. Soc. Perkin Trans. I* **1989,** 1811.

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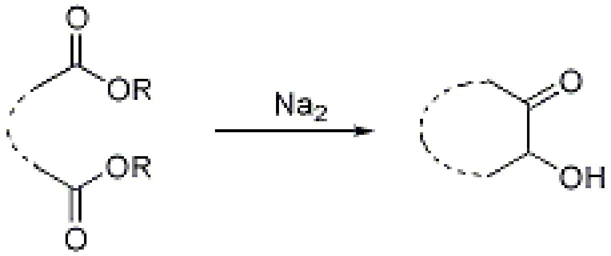
2. Acyloin Condensation

L. Bouveault, R. Loquin, *Compt. Rend.* **140,** 1593 (1905).

Reductive coupling of esters by sodium to yield acyloins (α-hydroxyketones). Yields are greatly improved in the presence of trimethylchlorosilane:



K. T. Finley, *Chem. Rev.* **64,** 573 (1964); K. Ziegler, *Houben-Weyl* **4/2,** 729-822 (1955); S. M. McElvain, *Org. React.* **4,** 256 (1948); J. J. Bloomfield *et al., ibid.* **23,** 259 (1976); R. Brettle, *Comp. Org. Syn.* **3,** 613-632 (1991). *Cf.* Benzoin Condensation.

33. Benzoin Condensation

A. J. Lapworth, *J. Chem. Soc.* **83,** 995 (1903); **85,** 1206 (1904).

Cyanide-catalyzed condensation of aromatic aldehydes to give benzoins (acyloins):

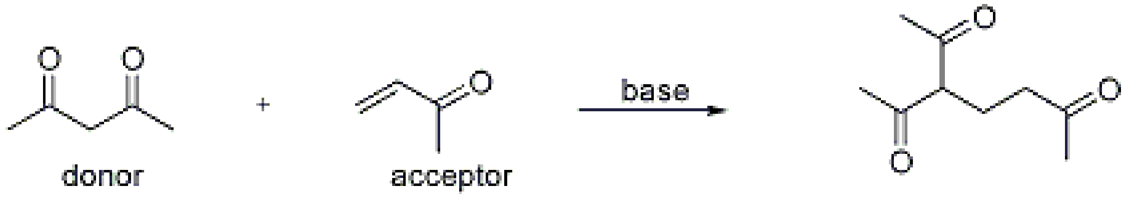
$$\mathrm{ArCHO} + \mathrm{Ar^1CHO} \xrightarrow{\mathrm{KCN}} \mathrm{ArCHOHCOAr^1}$$

H. Staudinger, *Ber.* **46,** 3530, 3535 (1913); W. S. Ide, J. S. Buck, *Org. React.* **4,** 269 (1948); H. Herlinger, *Houben-Weyl* **7/2a,** 653 (1973); A. Hassner, K. M. L. Rai, *Comp. Org. Syn.* **1,** 541-577 (1991). *Cf.* Acyloin Condensation.

258. Michael Reaction (Addition, Condensation)

A. Michael, *J. Prakt. Chem.* [2] **35,** 349 (1887).

Base-promoted conjugate addition of carbon nucleophiles (donors) to activated unsaturated systems (acceptors):



donor = malonates, cyanoacetates, acetoacetates, carboxylic esters, ketones, aldehydes, nitriles, nitro compounds, sulfones
acceptor = α,β-unsaturated ketones, esters, aldehydes, amides, carboxylic acids, nitriles sulfoxides, sulfones, nitro compounds, phosphonates, phosphoranes
base = $NaOCH_2CH_3$, $NH(CH_2CH_3)_2$, KOH, $KOC(CH_3)_3$, $N(CH_2CH_3)_3$, NaH, BuLi, LDA

Reviews: E. D. Bergmann *et al., Org. React.* **10,** 179-555 (1959); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 595-623; M. E. Jung, *Comp. Org. Syn.* **4,** 1-67 (1991). Review of organometallic nucleophiles: D. A. Hunt *et al., Org. Prep. Proced. Int.* **21,** 705-749 (1989); V. J. Lee, *Comp. Org. Syn.* **4,** 69-137, 139-168 (1991); J. A. Kozlowski, *ibid.* 169-198. Reviews of stereoselective synthesis: H.-G. Schmalz, *ibid.* 199-236; D. A. Oare, C. H. Heathcock, *Top. Stereochem.* **20,** 87-170 (1991); J. d'Angelo *et al., Tetrahedron Asymmetry* **3,** 459-505 (1992); J. Leonard *et al., Eur. J. Org. Chem.* **1998,** 2051-2061. *Cf.* Nagata Hydrocyanation; Robinson Annulation.

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268. Nagata Hydrocyanation

W. Nagata *et al.*, *Tetrahedron Letters* **1962,** 461.

Alkylaluminum-mediated 1,4-addition of hydrogen cyanide to α,β-unsaturated carbonyl compounds:

Early review: W. Nagata, M. Yoshioka, *Org. React.* **25,** 255-476 (1977). Synthetic application: T. F. Gallagher, J. L. Adams, *J. Org. Chem.* **57,** 3347 (1992). *Cf.* Michael Reaction.

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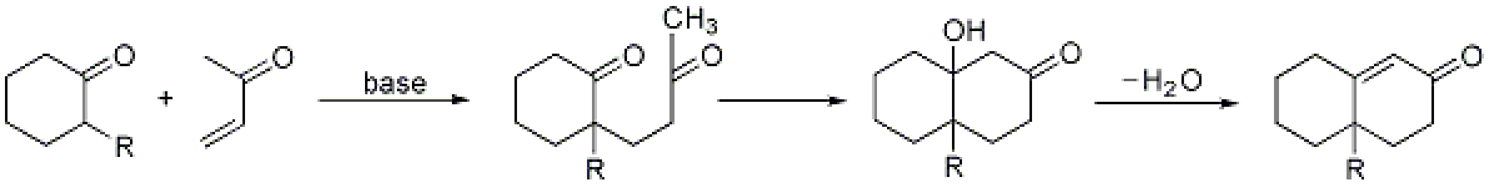
342. Robinson Annulation

W. S. Rapson, R. Robinson, *J. Chem. Soc.* **1935,** 1285.

Formation of six-membered ring α,β-unsaturated ketones by the addition of cyclohexanones to methyl vinyl ketone (or simple derivatives of methyl vinyl ketone) or its equivalents, followed by an intramolecular aldol condensation, *q.v.*:



Early review: R. E. Gawley, *Synthesis* **1976,** 777-794. Improved methodology: T. Sato *et al.*, *Tetrahedron Letters* **31,** 1581 (1990). Stereochemical study: C. Nussbaumer, *Helv. Chim. Acta* **73,** 1621 (1990). Synthetic applications: R. V. Bonnert *et al.*, *J. Chem. Soc. Perkin Trans. I* **1991,** 1225; S. Kim, P. L. Fuchs, *J. Am. Chem. Soc.* **115,** 5934 (1993). *Cf.* Michael Reaction; Wichterle Reaction.

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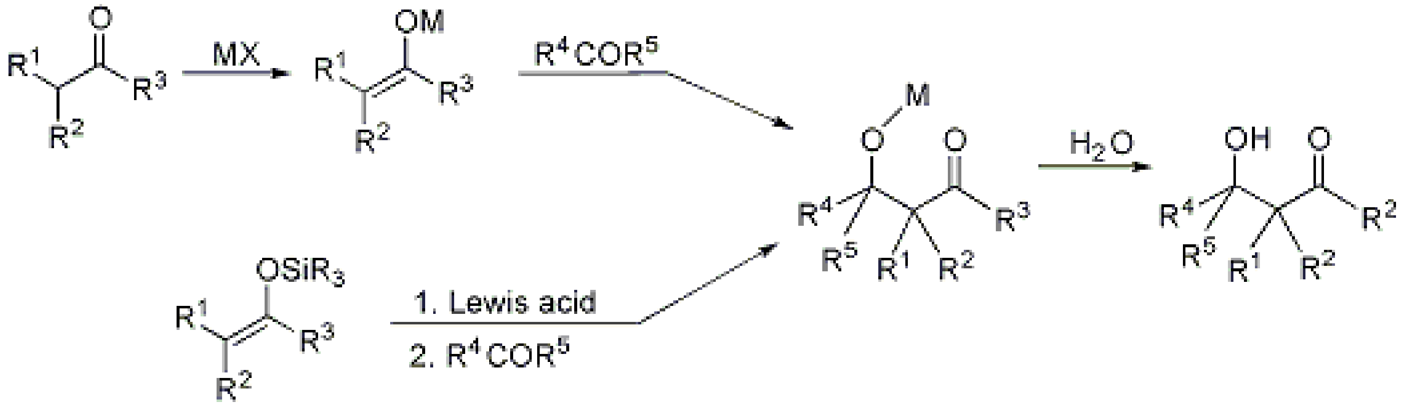
4. Aldol Reaction (Condensation)

R. Kane, *Ann. Phys. Chem., Ser. 2,* **44,** 475 (1838); *idem, J. Prakt. Chem.* **15,** 129 (1838).

Traditionally, it is the acid- or base-catalyzed condensation of one carbonyl compound with the enolate/enol of another, which may or may not be the same, to generate a β-hydroxy carbonyl compound—an aldol. The method is compromised by self-condensation, polycondensation, generation of regioisomeric enols/enolates, and dehydration of the aldol followed by Michael addition, *q.v.* The development of methods for the preparation and use of preformed enolates or enol derivatives, that dictate specific carbon-carbon bond formation, have revolutionized the coupling of carbonyl compounds:



MX = LDA, LHMDS, CH_3MgBr, Bu_2BOTf/NR_3, 9-BBNCl/NR_3, LDA + $ZnCl_2$, LDA + $(C_5H_5)_2ZrCl_2$, LDA + $Ti(O^iPr)_3Cl$

Lewis acid = $TiCl_4$, $SnCl_4$, $AlCl_3$, $BF_3 \cdot O(CH_2CH_3)_2$, $ZnCl_2$

Historical perspective: C. H. Heathcock, *Comp. Org. Syn.* **2,** 133-179 (1991). General review: T. Mukaiyama, *Org. React.* **28,** 203-331 (1982). Application of lithium and magnesium enolates: C. H. Heathcock, *Comp. Org. Syn.* **2,** 181-238 (1991); of boron enolates: B. M. Kim *et al., ibid.* 239-275; of transition metal enolates: I. Paterson, *ibid.* 301-319. Stereoselective reactions of ester and thioester enolates: M. Braun, H. Sacha, *J. Prakt. Chem.* **335,** 653-668 (1993). Review of asymmetric methodology: A. S. Franklin, I. Paterson, *Contemp. Org. Syn.* **1,** 317-338 (1994). *Cf.* Claisen-Schmidt Condensation; Henry Reaction; Ivanov Reaction; Knoevenagel Condensation; Reformatsky Reaction; Robinson Annulation.

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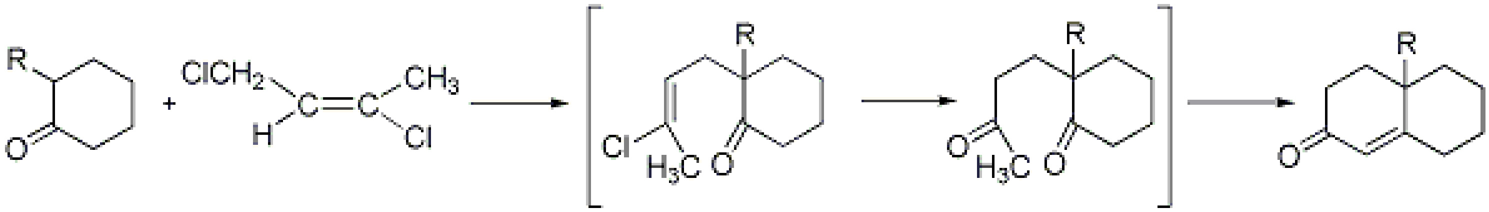
426. Wichterle Reaction

O. Wichterle *et al., Coll. Czech. Chem. Commun.* **13,** 300 (1948).

Modification of the Robinson annulation, *q.v.*, in which 1,3-dichloro-*cis*-2-butene is used instead of methyl vinyl ketone:



M. Kobayashi, T. Matsumoto, *Chem. Lett.* **1973,** 957; H. Yoshioka *et al., Tetrahedron Letters* **1979,** 3489. *Review:* M. Hudlicky, *Coll. Czech. Chem. Commun.* **58,** 2229-2244 (1993).

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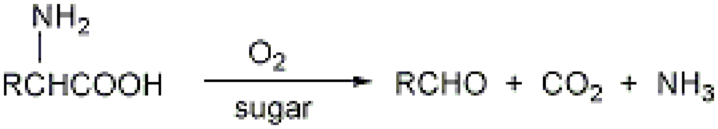
3. Akabori Amino Acid Reactions

S. Akabori, *J. Chem. Soc. Japan* **52,** 606 (1931); *Ber.* **66,** 143, 151 (1933); *J. Chem. Soc.* **64,** 608 (1943).

1. Formation of aldehydes by oxidative decomposition of α-amino acids when heated with sugars according to the equation:



$$\mathrm{RCH(NH_2)COOH} \xrightarrow[\text{sugar}]{O_2} \mathrm{RCHO} + \mathrm{CO_2} + \mathrm{NH_3}$$

2. Reduction of α-amino acids and esters by sodium amalgam and ethanolic hydrogen chloride to the corresponding α-amino aldehydes:

3. Formation of alkamines by heating mixtures of aromatic aldehydes and amino acids. No reaction was observed with tertiary amino groups.

E. Takagi *et al., J. Pharm. Soc. Japan* **71,** 648 (1951); **72,** 812 (1952); A. Lawson, H. V. Morley, *J. Chem. Soc.* **1955,** 1695; A. Lawson, *ibid.* **1956,** 307; K. Dose, *Ber.* **90,** 1251 (1957); V. N. Belikov *et al., Izv. Akad. Nauk SSSR, Ser. Khim.* **1969,** 2536.

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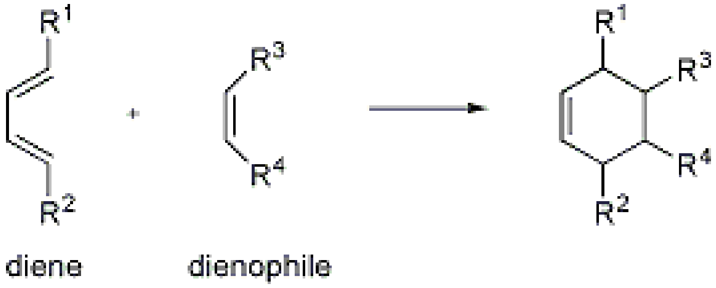
102. Diels-Alder Reaction

O. Diels, K. Alder, *Ann.* **460,** 98 (1928); **470,** 62 (1929); *Ber.* **62,** 2081, 2087 (1929).

The 1,4-addition of the double bond of a dienophile to a conjugated diene to generate a six-membered ring, such that up to four new stereocenters may be created simultaneously. The [4+2]-cycloaddition usually occurs with high regio- and stereoselectivity:



Heteroatomic analogs of the diene (e.g., CHR=CR-CR=O, O=CR-CR=O, and RN=CR-CR=NR) and dienophile (e.g., RN=NR, $R_2C=NR$, and RN=O) may also serve as reactants.

Early reviews: M. C. Kloetzel, *Org. React.* **4,** 1-59 (1948); H. L. Holmes *ibid.* 60-173; L. W. Butz, A. W. Rytina, *ibid.* **5,** 136-192 (1949). Intermolecular reactions: W. Oppolzer, *Comp. Org. Syn.* **5,** 315-399 (1991). Intramolecular reactions: E. Ciganek, *Org. React.* **32,** 1-374 (1984); W. R. Rousch, *Comp. Org. Syn.* **5,** 513-550 (1991). Use of heterodienophiles: S. M. Weinreb, *ibid.* 401-449. Use of nitroso dienophiles: J. Streith, A. DeFoin, *Synthesis* **1994,** 1107-1117. Use of heterodienes: D. L. Boger, *ibid,* 451-512. Review of diastereoselectivity: J. M. Coxon *et al.*, “Diastereofacial Selectivity in the Diels-Alder Reaction” in *Advances in Detailed Reaction Mechanisms* **3,** 131-166 (1994); T. Oh, M. Reilly, *Org. Prep. Proceed. Int.* **26,** 131-158 (1994); H. Waldmann, *Synthesis* **1994,** 535-551. *Cf.* Wagner-Jauregg Reaction.

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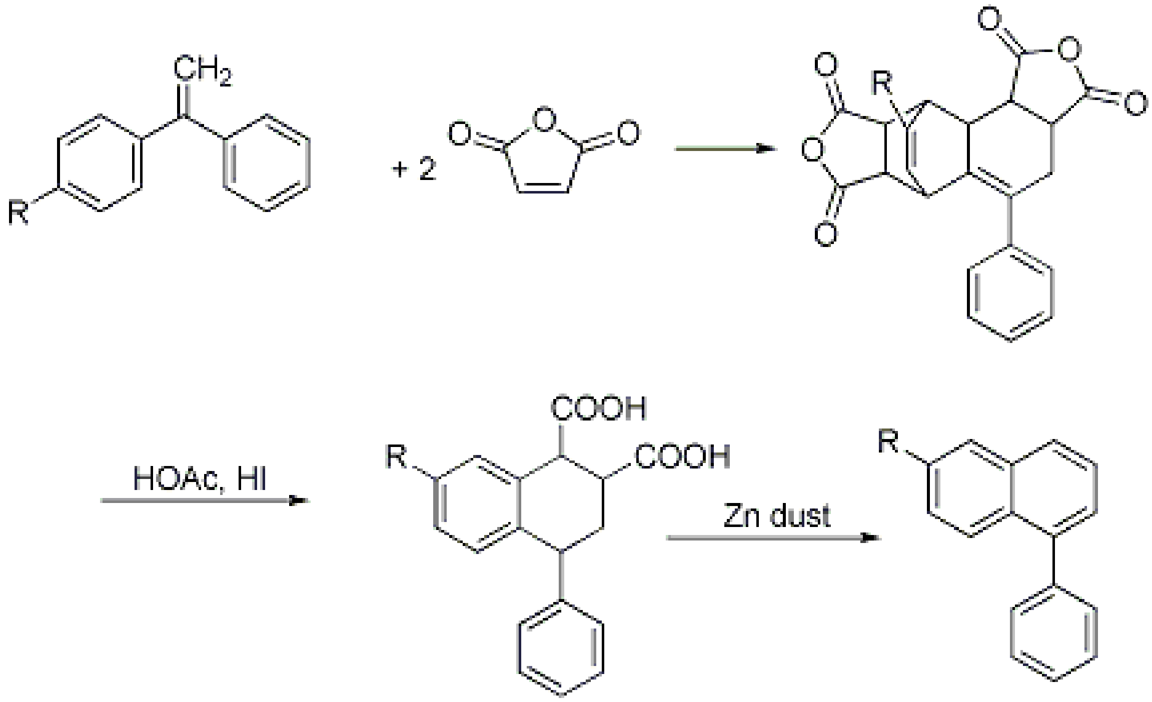
416. Wagner-Jauregg Reaction

T. Wagner-Jauregg, *Ber.* **63,** 3213 (1930); *Ann.* **491,** 1 (1931).

Addition of maleic anhydride to diarylethylenes with formation of *bis* adducts which can be converted to aromatic ring systems:



F. Bergmann *et al., J. Am. Chem. Soc.* **69,** 1773, 1777, 1779 (1947); K. Alder in *Newer Methods of Preparative Organic Chemistry*, English Ed. (Interscience, New York, 1948) p 425; M. C. Kloetzel, *Org. React.* **4,** 32 (1948). *Cf.* Diels-Alder Reaction.

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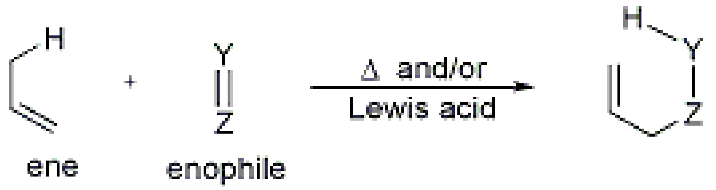
120. Ene Reaction (Alder-Ene Reaction)**;** Conia Reaction

K. Alder *et al.*, *Ber.* **76,** 27 (1943).

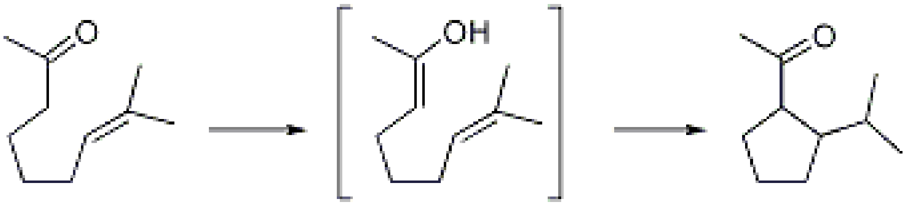
The addition of an alkene having an allylic hydrogen (ene) to a compound containing a multiple bond (enophile) to form a new bond between two unsaturated termini, with an allylic shift of the ene double bond, and transfer of the allylic hydrogen to the enophile. The mechanism is related to that of the Diels-Alder reaction, *q.v.*:



enophile = carbonyl and thiocarbonyl compounds, imines, alkenes, alkynes
Lewis acid = $BF_3 \cdot O(CH_2CH_3)_2$, $SnCl_4$, $Al(CH_2CH_3)Cl_2$, $Al(CH_3)_2Cl$

Lewis acid-promoted cyclization of 5-hexenals: J. A. Marshall, *Chemtracts-Org. Chem.* **5,** 1-7 (1992). Review of alkenes as enophiles: B. B. Snider, *Comp. Org. Syn.* **5,** 1-27 (1991). Review of carbonyl compounds as enophiles: *idem, ibid.* **2,** 527-561; in conjunction with asymmetric synthesis: K. Mikami, M. Shimizu, *Chem. Rev.* **92,** 1021-1050 (1992); K. Mikami *et al.*, *Synlett* **1992,** 255-265.

The intramolecular Ene reaction of unsaturated ketones, in which the carbonyl functionality serves as the ene component, *via* its tautomer, and the olefinic moiety serves as the enophile, is known as the **Conia reaction:**



F. Rouessac *et al., Tetrahedron Letters* **1965,** 3319. *Review:* J. M. Conia, P. Le Perchec, *Synthesis* **1975,** 1-19.

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78. Claisen-Schmidt Condensation

L. Claisen, A. Claparède, *Ber*. **14,** 2460 (1881); J. G. Schmidt, *ibid.* 1459.

Condensation of an aromatic aldehyde with an aliphatic aldehyde or ketone in the presence of a relatively strong base (hydroxide or alkoxide ion) to form an α,β-unsaturated aldehyde or ketone:

$$C_6H_5CHO + H_3C-\overset{O}{\overset{\|}{C}}-R \xrightarrow{NaOH} C_6H_5HC{=}CH-COR$$

A. T. Nielsen, W. J. Houlihan, *Org. React.* **16,** 1 (1968); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 632-639; J. A. Fine, P. Pulaski, *J. Org. Chem.* **38,** 1747 (1973). *Cf.* Aldol Reaction.

182. Henry Reaction (Nitroaldol Reaction)

L. Henry, *Compt. Rend.* **120,** 1265 (1895); J. Kamlet, **US 2151517** (1939).

Base-catalyzed aldol-type condensation, *q.v.*, of nitroalkanes with aldehydes or ketones:

Application to sugars: R. Fernández *et al., Carbohyd. Res.* **247,** 239 (1993). Reagent controlled asymmetric induction: H. Sasai *et al., Tetrahedron Letters* **34,** 855 (1993); R. Chinchilla *et al., Tetrahedron Asymmetry* **5,** 1393 (1994); R. S. Varma *et al., Tetrahedron Letters* **38,** 5131 (1997); R. Ballini, G. Bosica, *J. Org. Chem.* **62,** 425 (1997); V. J. Bulbule *et al., Tetrahedron* **55,** 9325 (1999). Catalyst effects: I. Morao, F. P. Cossio, *Tetrahedron Letters* **38,** 6461 (1997); P. B. Kisanga, J. G. Verkade, *J. Org. Chem.* **64,** 4298 (1999); D. Simoni *et al., Tetrahedron Letters* **41,** 1607 (2000). *Review:* G. Rosini, *Comp. Org. Syn.* **2,** 321-340 (1991). *Cf.* Knoevenagel Condensation.

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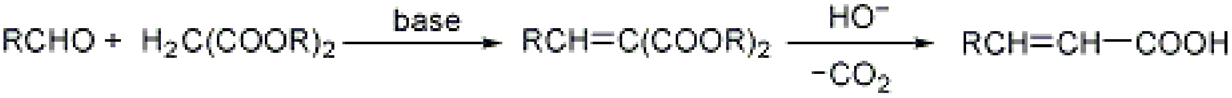
213. Knoevenagel Condensation; Doebner Modification

E. Knoevenagel *Ber*. **31,** 2596 (1898); O. Doebner, *Ber*. **33,** 2140 (1900).

Condensation of aldehydes or ketones with active methylene compounds in the presence of ammonia or amines; the use of malonic acid and pyridine is known as the **Doebner modification:**



$$RCHO + H_2C(COOR)_2 \xrightarrow{\text{base}} RCH{=}C(COOR)_2 \xrightarrow[-CO_2]{HO^-} RCH{=}CH{-}COOH$$

Early reviews: J. R. Johnson, *Org. React.* **1,** 210 (1942); G. Jones, *ibid.* **15,** 204 (1967); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 646-653. Development of enantioselective methods: L. F. Tietze, P. Saling, *Chirality* **5,** 329 (1993). Application to the synthesis of indole alkaloids: L. F. Tietze *et al., Synthesis* **1994,** 1185. Modified conditions: J. McNulty *et al., Tetrahedron Letters* **39,** 8013 (1998); B. M. Choudary *et al., J. Mol. Catal. A* **142,** 361 (1991). Synthetic applications: B. T. Watson, G. E. Christiansen, *Tetrahedron Letters* **39,** 6087 (1998); R. W. Draper *et al., Tetrahedron* **56,** 1811 (2000). *Review:* L. F. Tietze, U. Beifuss, *Comp. Org. Syn.* **2,** 341-394 (1991). *Cf.* Aldol Reaction; Henry Reaction; Ivanov Reaction.

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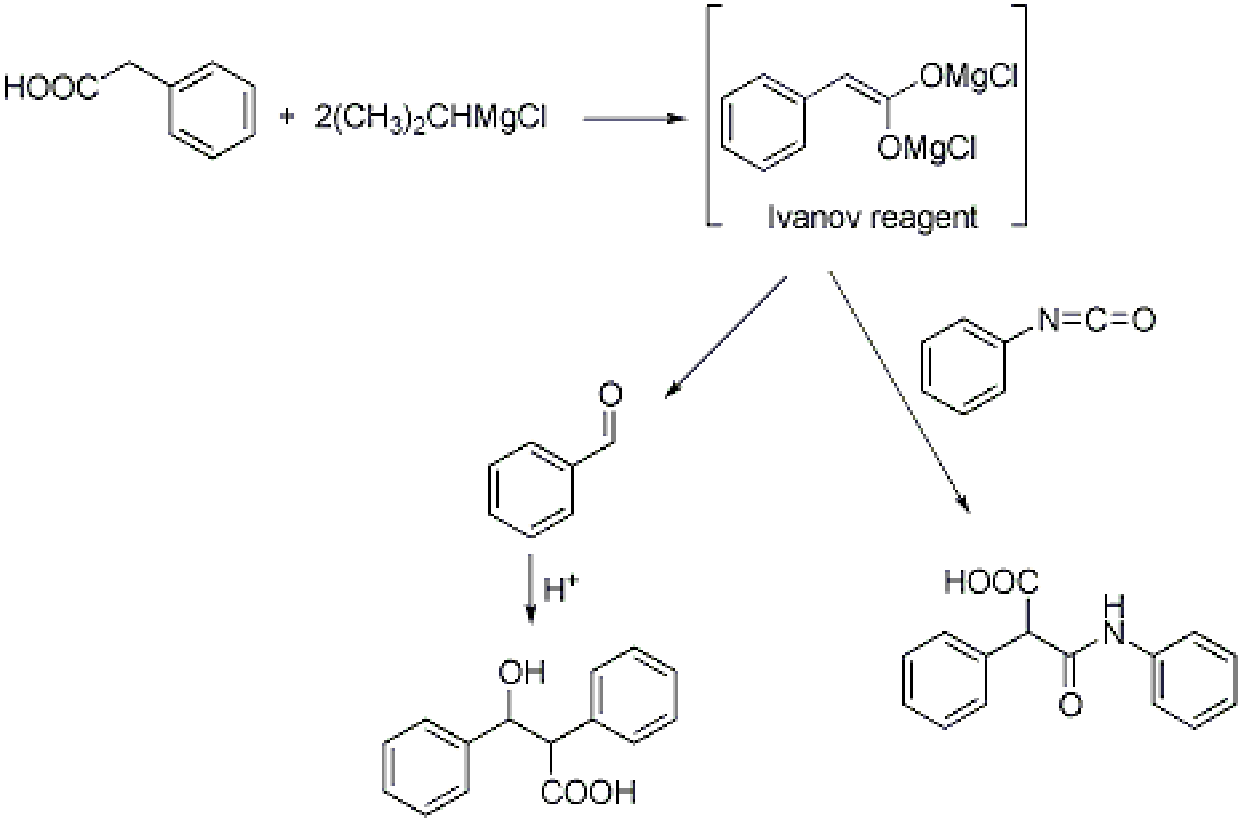
202. Ivanov Reaction

D. Ivanov, A. Spassoff, *Bull. Soc. Chim. France* **49,** 19, 375 (1931); D. Ivanov *et al., ibid.* **51,** 1321, 1325, 1331 (1932).

The addition of enediolates of aryl acetic acids (Ivanov reagents) to electrophiles, particularly carbonyl compounds:



Early reviews: B. Blagoev, D. Ivanov, *Synthesis* **1970,** 615; D. Ivanov *et al., ibid.* **1975,** 83. Synthetic application: Y. A. Zhdanov *et al., Carbohyd. Res.* **29,** 274 (1973). Kinetic and mechanistic study: J. Toullec *et al., J. Org. Chem.* **50,** 2563 (1985). Stereoselectivity: M. Mladenova *et al., Tetrahedron* **37,** 2157 (1981); M. Momtchev *et al., Bull. Soc. Chim. France* **5,** 844 (1985). *Cf.* Aldol Reaction; Knoevenagel Condensation.

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330. Reformatsky (Reformatskii) Reaction

S. Reformatskii, *Ber*. **20,** 1210 (1887); *J. Russ. Phys. Chem. Soc.* **22,** 44 (1890).

Condensation of aldehydes or ketones with organozinc derivatives of α-halo esters to yield β-hydroxy esters:

Early reviews: R. L. Shriner, *Org. React.* **1,** 1 (1942); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 671-682; M. W. Rathke, *Org. React.* **22,** 423 (1975). Use of thiocarbonyl electrophiles: M. Chandrasekharam *et al., Tetrahedron Letters* **34,** 6439 (1993). Application to the synthesis of β-keto esters: C. Kashima *et al., J. Org. Chem.* **58,** 793 (1993). Asymmetric synthesis: D. Pini *et al., Tetrahedron Asymmetry* **5,** 1875 (1994). Methods development for the synthesis of β-lactones: H. Schick *et al., Tetrahedron* **51,** 2939 (1995). *Reviews:* A. Fürstner, *Synthesis* **1989,** 571-590; M. W. Rathke, P. Weipert, *Comp. Org. Syn.* **2,** 277-299 (1991). *Cf.* Aldol Reaction; Blaise Reaction.

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46. Blaise Reaction

E. E. Blaise, *Compt. Rend.* **132,** 478 (1901).

Formation of β-oxoesters by treatment of α-bromocarboxylic esters with zinc in the presence of nitriles. The intermediate organozinc compound reacts with the nitrile and the complex is hydrolyzed with 30% potassium hydroxide:

$$R^1R^2CBrCOOC_2H_5 + Zn \longrightarrow R^1R^2C(ZnBr)COOC_2H_5 \xrightarrow{RCN}$$

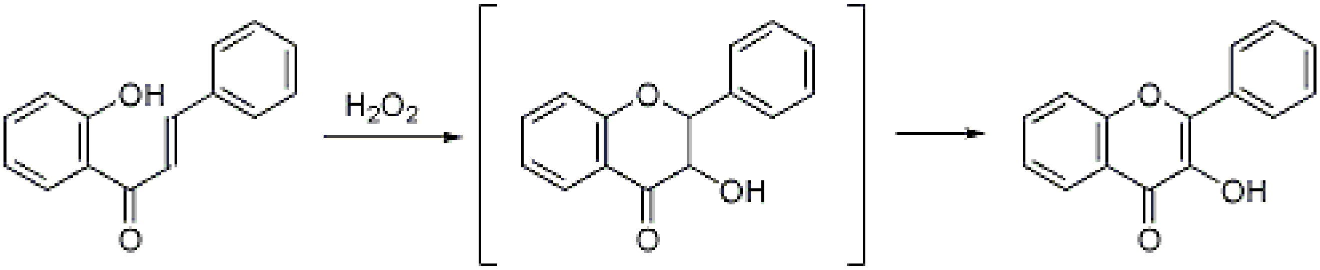
$$R^1R^2C(CR{=}NZnBr)COOC_2H_5 \xrightarrow{aq\ KOH} RCOCR^1R^2COOC_2H_5 + NH_3 + Zn(OH)Br$$

A. Horeau, J. Jacques, *Bull. Soc. Chim.* **1947,** Mem. 58; J. Cason *et al., J. Org. Chem.* **18,** 1594 (1953); H. Henecka, *Houben-Weyl* **7/2a,** 518 (1973); K. Nützel, *ibid.* **13/2a,** 829. Modified conditions: S. M. Hannick, Y. Kishi, *J. Org. Chem.* **48,** 3833 (1983); N. Zylber *et al., J. Organometal. Chem.* **444,** 1 (1993); K. Narkunan, B.-J. Uang, *Synthesis* **1998,** 1713. Stereoselectivity: J. J. Duffield, A. C. Regan, *Tetrahedron Asymmetry* **7,** 663 (1996); A. S.-Y. Lee *et al., Tetrahedron Letters* **38,** 443 (1997); J. Syed *et al., Tetrahedron Asymmetry* **9,** 805 (1998). *Cf.* Reformatsky Reaction.

5. Algar-Flynn-Oyamada Reaction

J. Algar, J. P. Flynn, *Proc. Roy. Irish Acad.* **42B,** 1 (1934); B. Oyamada, *J. Chem. Soc. Japan* **55,** 1256 (1934).

Alkaline hydrogen peroxide oxidation of *o*-hydroxyphenyl styryl ketones (chalcones) to flavonols *via* the intermediate dihydroflavonols:



T. S. Wheeler, *Record Chem. Progr.* **18,** 133 (1957); W. P. Cullen *et al., J. Chem. Soc. C* **1971,** 2848. Mechanism: T. R. Gormley, *et al., Tetrahedron* **29,** 369 (1973); M. Bennett *et al., ibid.* **54,** 9911 (1998). Synthetic applications: H. Wagner *et al., ibid.* **33,** 1405 (1977); A. C. Jain *et al., Bull. Chem. Soc. Japan* **56,** 1267 (1983). *Cf.* Auwers Synthesis.

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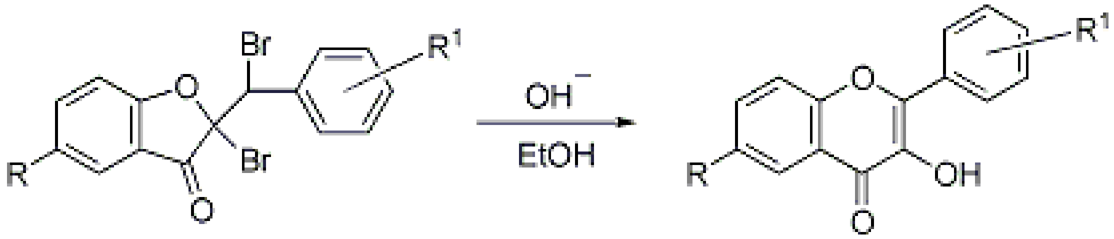
11. Auwers Synthesis

K. v. Auwers *et al.*, *Ber.* **41,** 4233 (1908); **48,** 85 (1915); **49,** 809 (1916); K. v. Auwers, P. Pohl, *Ann.* **405,** 243 (1914).

Expansion of coumarones to flavonols by treatment of 2-bromo-2-(α-bromobenzyl) coumarones with alcoholic alkali:



T. H. Minton, H. Stephen, *J. Chem. Soc.* **121,** 1598 (1922); J. Kalff, R. Robinson, *ibid.* **127,** 1968 (1925); B. H. Ingham *et al.*, *ibid.* **1931,** 895; B. G. Acharya *et al.*, *ibid.* **1940,** 817; S. Wawzonek, *Heterocyclic Compounds* **2,** 245 (1951). *Cf.* Algar-Flynn-Oyamada Reaction.

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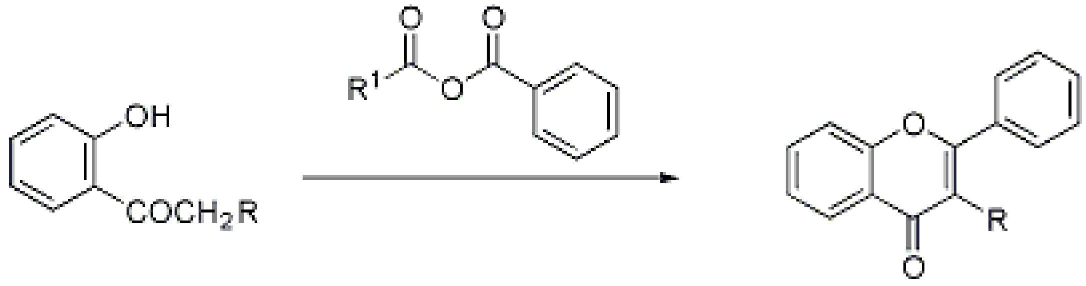
6. Allan-Robinson Reaction

J. Allan, R. Robinson, *J. Chem. Soc.* **125,** 2192 (1924).

Preparation of flavones or isoflavones by condensing *o*-hydroxyaryl ketones with anhydrides of aromatic acids and their sodium salts:



S. F. Dyke *et al., J. Org. Chem.* **26,** 2453 (1961); Seshandri in *The Chemistry of Flavonoid Compounds*, T. A. Geissman, Ed. (New York, 1962) p 182; Gripenberg, *ibid.* p 411; W. Rahman, K. T. Nasim, *J. Org. Chem.* **27,** 4215 (1962); D. L. Dreyer *et al., Tetrahedron* **20,** 2977 (1964). Synthesis applications: P. K. Dutta *et al., Indian J. Chem.* **21B,** 1037 (1982); T. Horie *et al., Chem. Pharm. Bull.* **37,** 1216 (1989); J. K. Makrandi *et al., Synth. Commn.* **19,** 1919 (1989); E. J. Corey *et al., Tetrahedron Letters* **37,** 7162 (1996); B. P. Reddy *et al., J. Heterocyclic Chem.* **33,** 1561 (1996). *Cf.* Baker-Venkataraman Rearrangement; Kostanecki Acylation.

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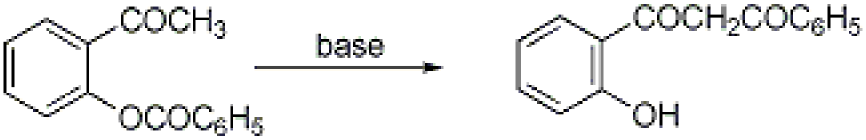
14. Baker-Venkataraman Rearrangement

W. Baker, *J. Chem. Soc.* **1933,** 1381; H. S. Mahal, K. Venkataraman, *ibid.* **1934,** 1767.

Base-catalyzed rearrangement of *o*-acyloxyketones to β-diketones, important intermediates in the synthesis of chromones and flavones:



Gripenberg in *The Chemistry of Flavonoid Compounds,* Geissman, Ed. (New York, 1962) p 410. Mechanistic studies: K. Bowden, M. Chehel-Amiran, *J. Chem. Soc. Perkin Trans. II* **1986,** 2039. Synthetic applications: P. K. Jain *et al., Synthesis* **1982,** 221; J. Zhu *et al., Chem. Commun.* **1988,** 1549; A. V. Kalinin *et al., Tetrahedron Letters* **39,** 4995 (1998); D. C. G. Pinto *et al., New J. Chem.* **24,** 85 (2000). *Cf.* Allan-Robinson Reaction; Kostanecki Acylation.

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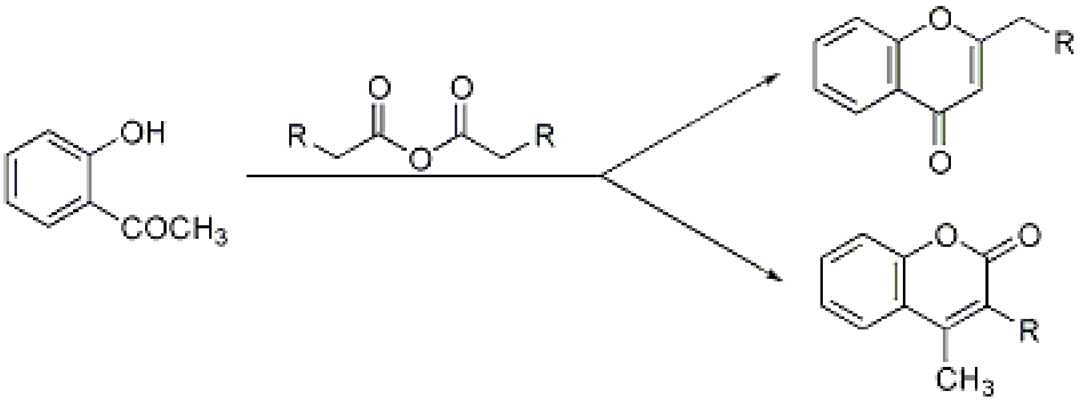
223. Kostanecki Acylation

S. von Kostanecki, A. Rozycki, *Ber*. **34,** 102 (1901).

Formation of chromones or coumarins by acylation of *o*-hydroxyaryl ketones with aliphatic acid anhydrides, followed by cyclization:



W. Baker, *J. Chem. Soc.* **1933,** 1381; C. R. Hauser, *Org. React.* **8,** 91 (1954); T. Szell *et al., Tetrahedron* **25,** 715 (1969); *idem et al., Helv. Chim. Acta* **52,** 2636 (1969); S. R. Save *et al., J. Indian Chem. Soc.* **48,** 675 (1971); Y. A. Shaikh, K. N. Trivedi, *ibid.* **49,** 599, 713 (1972); S. R. Save *et al., ibid.* **49,** 25 (1972). *Cf.* Allan-Robinson Reaction; Baker-Venkataraman Rearrangement.

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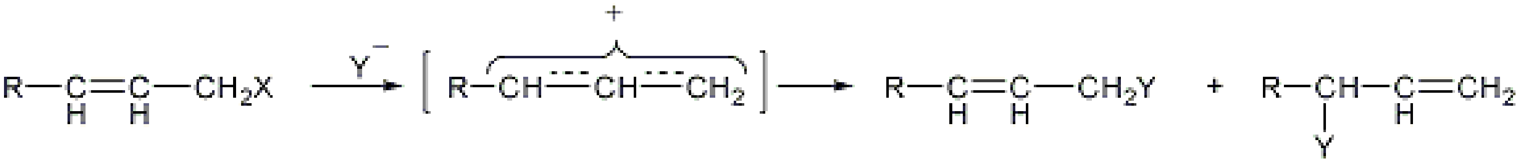
7. Allylic Rearrangements

L. Claisen, *Ber.* **45,** 3157 (1912).

Migration of a carbon-carbon double bond in a three carbon (allylic) system on treatment with nucleophiles under SN1 conditions (or under SN2 conditions when the nucleophilic attack takes place at the γ-carbon):



Reviews: J. R. DeWolfe, W. G. Young, *Chem. Rev.* **56,** 753 (1956); W. G. Young, *J. Chem. Ed.* **39,** 455 (1962); P. de la Mare in *Molecular Rearrangements* Part 1, P. de Mayo, Ed. (Wiley-Interscience, New York, 1963) pp 27-110; K. Mackenzie in *The Chemistry of Alkenes*, S. Patai, Ed. (Interscience, New York, 1964) pp 436-453; R. H. DeWolfe, W. G. Young in *ibid.* pp 681-738; J. March, *Advanced Organic Chemistry* (Wiley-Interscience, New York, 4th ed., 1992) pp 327-330.

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250. Meerwein-Ponndorf-Verley Reduction (Aluminum Alkoxide Reduction)

H. Meerwein, R. Schmidt, *Ann.* **444,** 221 (1925); W. Ponndorf, *Angew. Chem.* **39,** 138 (1926); A. Verley, *Bull. Soc. Chim. France* **37,** 537, 871 (1925).

Reduction of aldehydes or ketones to the corresponding alcohols with aluminum alkoxides (the reverse of the Oppenauer oxidation, *q.v.*):

Reviews: A. L. Wilds, *Org. React.* **2,** 178-202 (1944); R. M. Kellogg, *Comp. Org. Syn.* **8,** 88-91 (1991); C. F. de Graauw *et al., Synthesis* **10,** 1007-1017 (1994). Enantioselectivity: D. A. Evans *et al., J. Am. Chem. Soc.* **115,** 9800 (1993); M. Node *et al., ibid.* **122,** 1927 (2000). Modified conditions: P. S. Kumbhar *et al., Chem. Commun.,* **1998,** 535; T. Ooi *et al., J. Am. Chem. Soc.* **120,** 10790 (1998); Y. Nakano *et al., Tetrahedron Letters* **41,** 1565 (2000). *Cf.* Cannizzaro Reaction; Tischenko Reaction.

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286. Oppenauer Oxidation

R. V. Oppenauer, *Rec. Trav. Chim.* **56,** 137 (1937).

The aluminum or potassium alkoxide-catalyzed oxidation of a secondary alcohol to the corresponding ketone (the reverse of the Meerwein-Ponndorf-Verley reduction, *q.v.*):

$$RCHOHR^1 + CH_3COCH_3 \xrightleftharpoons{M(OC_3H_7)_3} RCOR^1 + CH_3CHOHCH_3$$

$$M = Al \text{ or } K$$

T. Beresin in *Newer Methods of Preparative Organic Chemistry,* English Ed. (Interscience, New York, 1948) p 125; C. Djerassi, *Org. React.* **6,** 207 (1951); L. Horner, U. B. Kaps, *Ann.* **1980,** 192. Intramolecular reactions: B. B. Snider, B. E. Goldman, *Tetrahedron* **42,** 2951 (1986); G. A. Molander, J. A. McKie, *J. Am. Chem. Soc.* **115,** 5821 (1993). Alternate metals: B. Byrne, M. Karras, *Tetrahedron Letters* **28,** 769 (1987); M. L. S. Almeida *et al., J. Org. Chem.* **61,** 6587 (1996); K. Krohn *et al., Synthesis* **1996,** 1341; K. Ishihara *et al., J. Org. Chem.* **62,** 5664 (1997). *Review:* C. F. de Graauw *et al., Synthesis* **1994,** 1007-1017. *Cf.* Cannizzaro Reaction.

68. Cannizzaro Reaction

S. Cannizzaro, *Ann.* **88,** 129 (1853); K. List, H. Limpricht, *Ann.* **90,** 180 (1854).

Base-catalyzed disproportionation reaction of aromatic or aliphatic aldehydes with no α-hydrogen to corresponding acid and alcohol. If the aldehydes are different, the reaction is called the “crossed Cannizarro reaction”:

$$2RCHO \xrightarrow{\text{base}} RCOO^- + RCH_2OH$$

T. A. Geissman, *Org. React.* **2,** 94 (1944); F. P. B. Van der Maeden *et al., Rec. Trav. Chim. Pays-Bas* **91**(2), 221 (1972); C. G. Swain *et al., J. Am. Chem. Soc.* **101,** 3576 (1979); R. S. McDonald, C. E. Sibley, *Can. J. Chem.* **59,** 1061 (1981). *Review:* T. Lane, A. Plagens, *Named Organic Reactions* (John Wiley & Sons, Chichester, 1998) p 40-42. *Cf.* Meerwein-Ponndorf-Verley Reduction; Oppenauer Oxidation; Tishchenko Reaction.

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397. Tishchenko Reaction

L. Claisen *Ber.* **20,** 646 (1887); V. Tishchenko, *J. Russ. Phys. Chem. Soc.* **38,** 355, 482, 540, 547 (1906); *Chem. Zentr.* **1906 II,** 1309, 1552, 1555, 1556.

Formation of esters from aldehydes by an oxidation-reduction process in the presence of aluminum or sodium alkoxides:

$$2RCHO \xrightarrow{Al(OC_2H_5)_3} RCOOCH_2R$$

O. Kamm, W. F. Kamm, *Org. Syn.* **coll. vol. I,** 104 (1941); Y. Ogata, A. Kawasaki, *Tetrahedron* **25,** 929, 2845 (1969); P. R. Stapp, *J. Org. Chem.* **38,** 1433 (1973); G. Fouquet *et al.*, *Ann.* **1979,** 1591. *Reviews:* L. Cichon, *Wiad. Chem.* **20,** 641, 783 (1966), *C. A.* **66,** 54672b, 94408b (1967). *Cf.* Cannizzaro Reaction; Meerwein-Pondorf-Verley Reduction.

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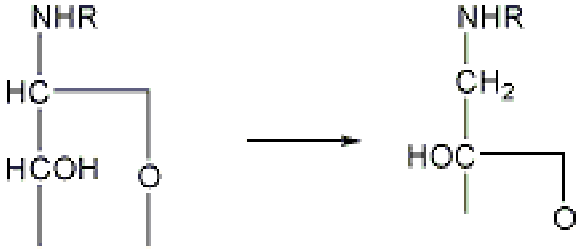
8. Amadori Rearrangement

M. Amadori, *Atti Accad. Nazl. Lincei* **2**(6), 337 (1925), *C.A.* **20,** 902 (1926); *ibid.* **9**(6), 68, 226 (1929), *C.A.* **23,** 3211, 3443 (1929).

Conversion of *N*-glycosides of aldoses to *N*-glycosides of the corresponding ketoses by acid or base catalysis:



J. E. Hodge, *Advan. Carbohyd. Chem.* **10,** 169 (1955); R. U. Lemieux in *Molecular Rearrangements* Part 2, P. de Mayo, Ed. (Wiley-Interscience, New York, 1964) p 753. ^{13}C-NMR studies: W. Funcke, *Ann.* **1978,** 2099. *Review:* K. Maruoka, H. Yamamoto, *Comp. Org. Syn.* **6,** 789-791 (1991).

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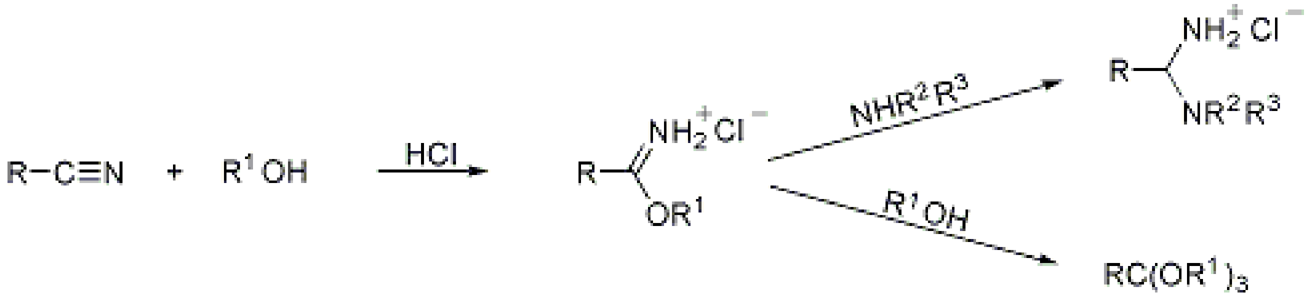
314. **Pinner Reaction** (Amidine and Ortho Ester Synthesis)

A. Pinner, F. Klein, *Ber.* **10,** 1889 (1877); **11,** 4, 1475 (1878); **16,** 352, 1643 (1883).

Formation of imino esters (alkyl imidates) by addition of dry hydrogen chloride to a mixture of a nitrile and an alcohol. Treatment of alkyl imidates with ammonia or primary or secondary amines affords amidines, while treatment with alcohols yields ortho-esters:



Reviews: R. Roger, D. Neilson, *Chem. Rev.* **61,** 179 (1961); E. N. Zil'berman, *Russ. Chem. Rev.* **31,** 615 (1962); P. L. Compagnon, M. Moeque, *Ann. Chim. (Paris)* **5,** 23 (1970); B. Decroix *et al.*, *J. Chem. Res.* **1978,** 134.

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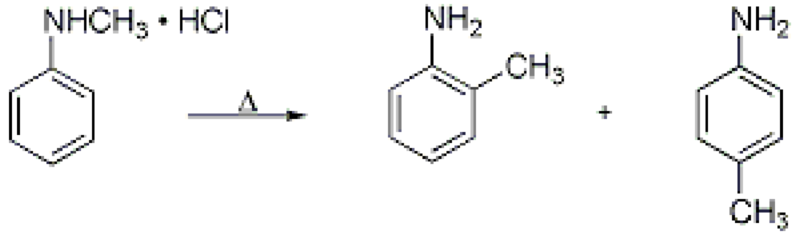
193. **Hofmann-Martius Rearrangement** (Aniline Rearrangement)

A. W. Hofmann, C. A. Martius, *Ber.* **4,** 742 (1871); A. W. Hofmann, *ibid.* **5,** 720 (1872).

Thermal conversion of *N*-alkylaniline hydrohalides to *o*- and *p*-alkylanilines:



H. Hart, J. R. Kosak, *J. Org. Chem.* **27,** 116 (1962); Y. Ogata *et al., Tetrahedron* **20,** 2717 (1964); *J. Org. Chem.* **35,** 1642 (1970); G. F. Grillot in *Mechanisms of Molecular Migration* **vol. 3,** B. S. Thyagarajan, Ed. (Wiley, New York, 1971) p 237; A. G. Giumanini *et al., J. Org. Chem.* **40,** 1677 (1975); W. F. Burgoyne, D. D. Dixon, *J. Mol. Catal.* **62,** 61 (1990); M. G. Siskos *et al., Bull. Soc. Chim. Belg.* **105,** 759 (1996).

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259. Michaelis-Arbuzov Reaction

A. Michaelis, R. Kaehne, *Ber.* **31,** 1048 (1898); A. E. Arbuzov, *J. Russ. Phys. Chem. Soc.* **38,** 687 (1906); *Chem. Zentr.* **1906,** II, 1639.

Formation of monoalkylphosphonic esters from alkyl halides and trialkyl phosphites, *via* the intermediate phosphonium salt:

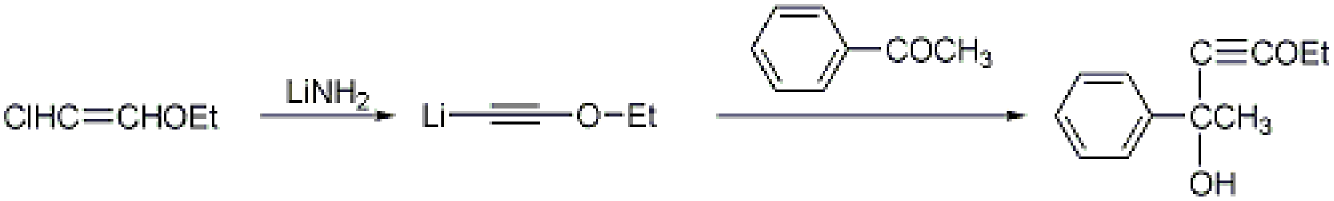
$$P(OR)_3 + R^1X \longrightarrow [(RO)_3PR^1]X \xrightarrow{\Delta} (RO)_2P(O)R^1$$

K. Sasse, *Houben-Weyl* **12/1,** 433 (1963); B. A. Arbuzov, *Pure Appl. Chem.* **9,** 307 (1964); G. M. Kosolapoff, *Org. React.* **6,** 276 (1951); D. Redmore, *Chem. Rev.* **71,** 317 (1971); G. Bauer, G. Haegele, *Angew. Chem. Int. Ed.* **16,** 477 (1977); A. K. Bhattacharya, G. Thyagarajan, *Chem. Rev.* **81,** 415 (1981); B. Faure *et al.*, *Chem. Commun.* **1989,** 805; V. K. Yadav, *Synth. Commun.* **20,** 239 (1990).

9. Arens-van Dorp Synthesis; Isler Modification

D. A. van Dorp, J. F. Arens, *Nature* **160,** 189 (1947); J. F. Arens *et al., Rec. Trav. Chim.* **68,** 604, 609 (1949); O. Isler *et al., Helv. Chim. Acta* **39,** 259 (1956).

The preparation of alkoxyethynyl alcohols from ketones and ethoxyacetylene. In the **Isler modification** the tedious preparation of ethoxyacetylene is obviated by treating β-chlorovinyl ether with lithium amide to yield lithium ethoxyacetylene, which is then condensed with the ketone:



H. Heusser *et al., Helv. Chim. Acta* **33,** 370 (1950); J. F. Arens, *Advan. Org. Chem.* **2,** 117-212 (1960); H. Meerwein, *Houben-Weyl* **6/3,** 189 (1965). *Cf.* Favorskii-Babayan Synthesis; Nef Synthesis.

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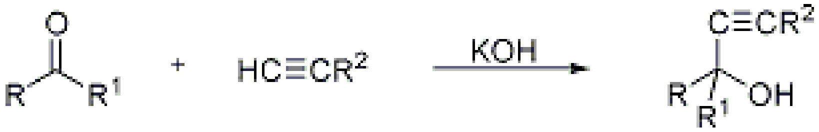
126. Favorskii-Babayan Synthesis

A. E. Favorskii, *J. Russ. Phys. Chem. Soc.* **37,** 643 (1905); *Chem. Zentr.* **1905, II,** 1018; A. Babayan *et al., J. Gen. Chem. (USSR)* **9,** 1631 (1939).

Synthesis of acetylenic alcohols from ketones and terminal acetylenes in the presence of anhydrous alkali:



A. W. Johnson, *The Chemistry of Acetylenic Compounds* **vol. 1** (London, 1946) p 14; R. A. Raphael, *Acetylenic Compounds in Organic Synthesis* (New York, 1955) p 10; M. F. Shostakovskii *et al., Zh. Org. Khim.* **4,** 1747 (1968), A. V. Shchelkunov *et al., ibid.* **6,** 930 (1970); E. M. Glazunova *et al., Zh. Org. Khim.* **12,** 516 (1976); Y. M. Vilenchik *et al., ibid.* **14,** 447 (1978). *Cf.* Arens-van Dorp Synthesis; Nef Synthesis.

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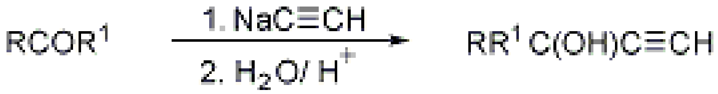
273. Nef Synthesis

J. U. Nef, *Ann.* **308,** 281 (1899).

Addition of sodium acetylides to aldehydes and ketones to yield acetylenic carbinols; occasionally and erroneously referred to as the Nef reaction, *q.v.*:



$$RCOR^1 \xrightarrow[2.\ H_2O/\ H^+]{1.\ NaC\equiv CH} RR^1C(OH)C\equiv CH$$

Farbenfabriken Bayer, **DE 280226; DE 285770** (1913); J. H. Saunders, *Org. Syn.* **20,** 40 (1940); A. W. Johnson, *The Chemistry of the Acetylenic Compounds* (London, 1946) p 11; C. D. Hurd, W. D. McPhee, *J. Am. Chem. Soc.* **69,** 239 (1947); W. Oroschnik, A. O. Mebane, *ibid.* **71,** 2062 (1949); R. A. Raphael, *Acetylenic Compounds in Organic Synthesis* (London, 1955) p 10. *Cf.* Arens-van Dorp Synthesis; Favorskii-Babayan Synthesis.

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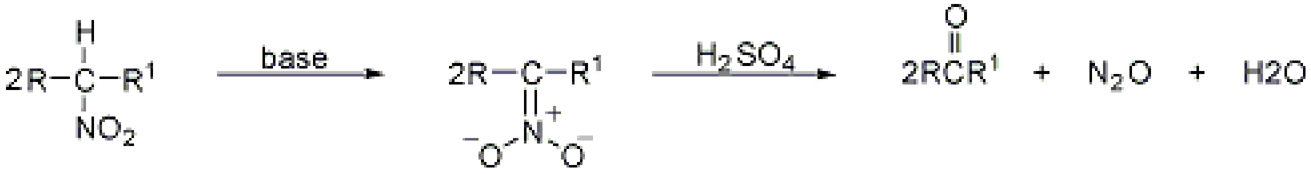
272. Nef Reaction

J. U. Nef, *Ann.* **280,** 263 (1894).

Formation of aldehydes and ketones from primary and secondary nitroalkanes, respectively, by treatment of their salts with sulfuric acid:



Modified conditions: W. Adam *et al., Synlett* **1998,** 1335; P. Ceccherelli *et al., Synth. Commun.* **28,** 3057 (1998). Application to spiroketals: T. Capecchi *et al., Tetrahedron Letters* **39,** 5429 (1998). *Reviews:* P. Salomaa in *The Chemistry of the Carbonyl Group*, S. Patai, Ed. (Interscience, N.Y., 1966) pp 177-210; H. W. Pinnick, *Org. React.* **38,** 655-792 (1990); D. S. Grierson, H.-P. Husson, *Comp. Org. Syn.* **6,** 937-944 (1991).

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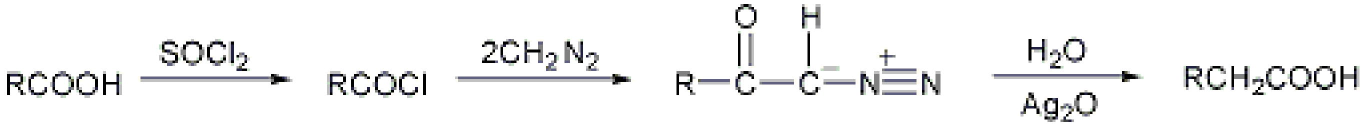
010. Arndt-Eistert Synthesis

F. Arndt, B. Eistert, *Ber*. **68,** 200 (1935).

Homologation of carboxylic acids:



Alternative reagent for diazomethane: T. Aoyama, *Tetrahedron Letters* **21,** 4461 (1980). Application to synthesis of unsaturated diazoketones: T. Hudlicky *et al., ibid.* **1979,** 2667; K. Gademann *et al., Angew. Chem. Int. Ed.* **38,** 1223 (1999); via ultrasonic activation: J-Y. Winum *et al., Tetrahedron Letters* **37,** 1781 (1996); of amino acids: R. E. Marti *et al., ibid.* **38,** 6145 (1997); R. J. DeVita *et al., Bioorg. Med. Chem. Letters* **9,** 2621 (1999). *Reviews:* W. E. Bachmann, W. S. Struve, *Org. React.* **1,** 38-62 (1942); B. Eistert in *Newer Methods in Preparative Organic Chemistry* **vol. 1** (Interscience, New York, 1948) pp 513-570; G. B. Gill, *Comp. Org. Syn.* **3,** 888-889 (1991). *Cf.* Wolff Rearrangement.

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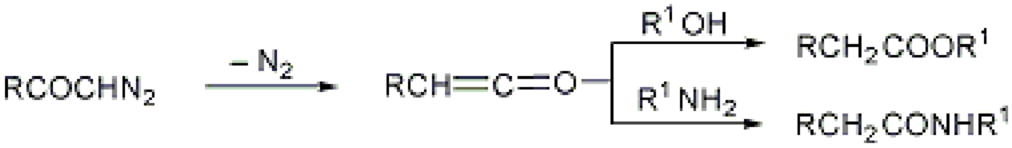
436. Wolff Rearrangement

L. Wolff *Ann.* **394,** 25 (1912).

Rearrangement of diazoketones to ketenes thermally, photochemically or catalytically. The rearrangement is the key step in the Arndt-Eistert synthesis, *q.v.*:



Reviews: P. A. S. Smith in *Molecular Rearrangements* Part 1, Ed. (Wiley-Interscience, New York, 1963) pp 528-550, 558-568; W. Kirmse, *Carbene Chemistry* (Academic Press, New York, 2nd ed., 1971) pp 475-492; H. Meier, K. P. Zeller, *Angew. Chem. Int. Ed.* **14,** 32 (1975); M. Torres, *Pure Appl. Chem.* **52,** 1623 (1980); C. B. Gill, *Comp. Org. Syn.* **3,** 887-912 (1991). Photo-induced mechanistic studies: T. Lippert *et al., J. Am. Chem. Soc.* **118,** 1551 (1996); Y. Chiang *et al., ibid.* **121,** 5930 (1999). Synthetic application: Y. R. Lee *et al., Tetrahedron Letters* **40,** 8219 (1999).

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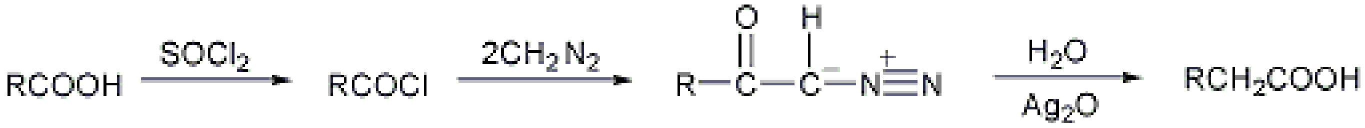
10. Arndt-Eistert Synthesis

F. Arndt, B. Eistert, *Ber.* **68,** 200 (1935).

Homologation of carboxylic acids:



Alternative reagent for diazomethane: T. Aoyama, *Tetrahedron Letters* **21,** 4461 (1980). Application to synthesis of unsaturated diazoketones: T. Hudlicky *et al., ibid.* **1979,** 2667; K. Gademann *et al., Angew. Chem. Int. Ed.* **38,** 1223 (1999); via ultrasonic activation: J-Y. Winum *et al., Tetrahedron Letters* **37,** 1781 (1996); of amino acids: R. E. Marti *et al., ibid.* **38,** 6145 (1997); R. J. DeVita *et al., Bioorg. Med. Chem. Letters* **9,** 2621 (1999). *Reviews:* W. E. Bachmann, W. S. Struve, *Org. React.* **1,** 38-62 (1942); B. Eistert in *Newer Methods in Preparative Organic Chemistry* **vol. 1** (Interscience, New York, 1948) pp 513-570; G. B. Gill, *Comp. Org. Syn.* **3,** 888-889 (1991). *Cf.* Wolff Rearrangement.

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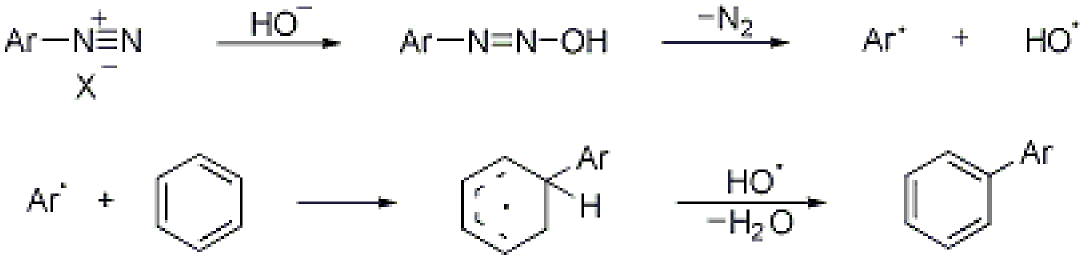
158. Gomberg-Bachmann Reaction

M. Gomberg, W. E. Bachmann, *J. Am. Chem. Soc.* **46,** 2339 (1924).

Alkali dependent formation of diaryl compounds from aryl diazonium salts and aromatic compounds.



W. E. Bachmann, R. A. Hoffman, *Org. React.* **2,** 224 (1944); O. C. Dermer, M. T. Edmison, *Chem. Rev.* **57,** 77 (1957); D. H. Hey, *Advan. Free-Radical Chem.* **2,** 47 (1966); D. E. Rosenberg, *et al.*, *Tetrahedron Letters* **21,** 4141 (1980); J. R. Beadle *et al.*, *J. Org. Chem.* **49,** 1594 (1984); T. C. McKenzie, S. M. Rolfes, *J. Heterocyclic Chem.* **24,** 859 (1987); M. Gurczynski, P. Tomasik, *Org. Prep. Proced. Int.* **23,** 438 (1991). For intramolecular version, *see* Pschorr Reaction.

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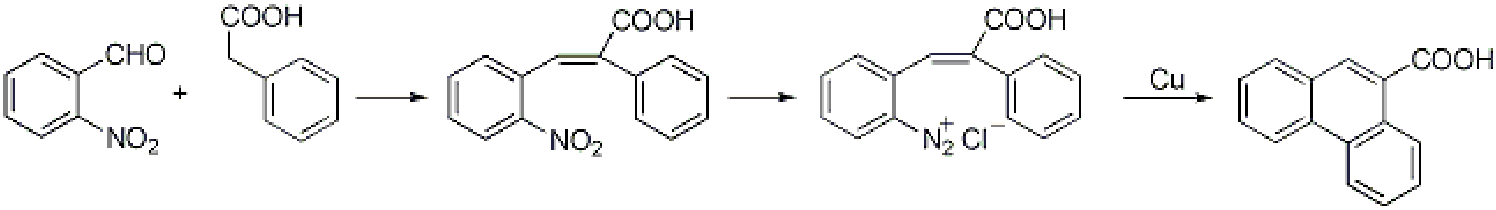
323. Pschorr Reaction

R. Pschorr, *Ber.* **29,** 496 (1896).

Synthesis of phenanthrene derivatives from diazotized α-aryl-*o*-aminocinnamic acids by intramolecular arylation:



Reviews: P. H. Leake, *Chem. Rev.* **56,** 27 (1956); D. F. De Tar, *Org. React.* **9,** 409 (1957); R. A. Abramovitch, *Advan. Free Rad. Chem.* **2,** 88 (1967); T. Kametani, K. Fukumoto, *J. Heterocyclic Chem.* **8,** 341 (1971); S. Foldeak, *Tetrahedron* **27,** 3465 (1971); T. S. Kametani *et al., ibid.* **27,** 5367 (1971); F. F. Gadallah *et al., J. Org. Chem.* **38,** 2386 (1973); S. M. Kupchan *et al., ibid.* 405; G. Daidone *et al., J. Heterocyclic Chem.* **17,** 1409 (1980). Mechanistic study: P. Hanson *et al., J. Chem. Soc. Perkin Trans II* **1999,** 49. *Cf.* Gomberg-Bachman Reaction; Meerwein Arylation.

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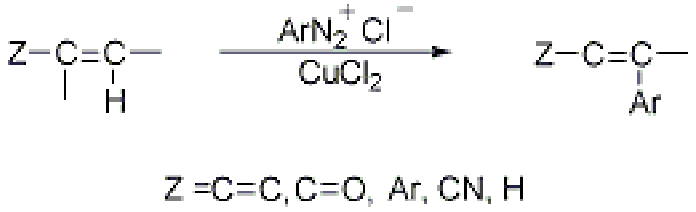
249. Meerwein Arylation

H. Meerwein *et al., J. Prakt. Chem.* **152,** 237 (1939).

Formation of arylated olefins on treatment of olefins with diazonium salts in the presence of cupric salts:



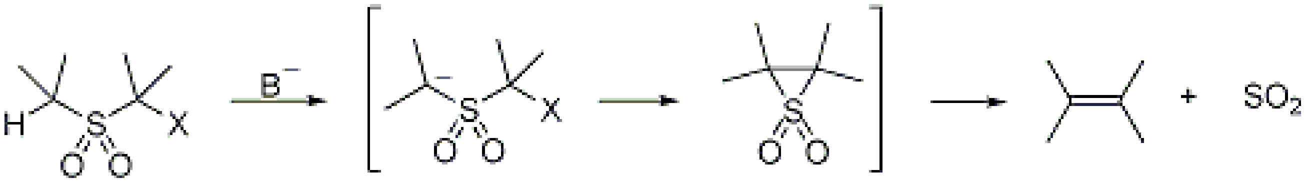
Z =C=C, C=O, Ar, CN, H

Synthetic applications: P. Sutter, C. D. Weis, *J. Heterocyclic Chem.* **24,** 69 (1987); G. Wurm, H. J. Gurka, *Pharmazie* **52,** 739 (1997); enhanced stereoselectivity: H. Brunner *et al., J. Organometal. Chem.* **541,** 89 (1997). Modified conditions: M. D. Obushak *et al., Tetrahedron Letters* **39,** 9567 (1998). *Reviews:* C. S. Rondestvedt, Jr., *Org. React.* **11,** 189 (1960); *ibid.* **24,** 225-259 (1976); C. D. Weis, *Dyes Pigment* **9,** 1-20 (1988). *Cf.* Pschorr Reaction.

327. Ramberg-Bäcklund Reaction

L. Ramberg, B. Bäcklund, *Arkiv Kemi Mineral Geol.* **13A**(27), 50 (1940), *C.A.* **34,** 4725^{5} (1940).

Reaction of α-halo sulfones with strong bases to yield alkenes:

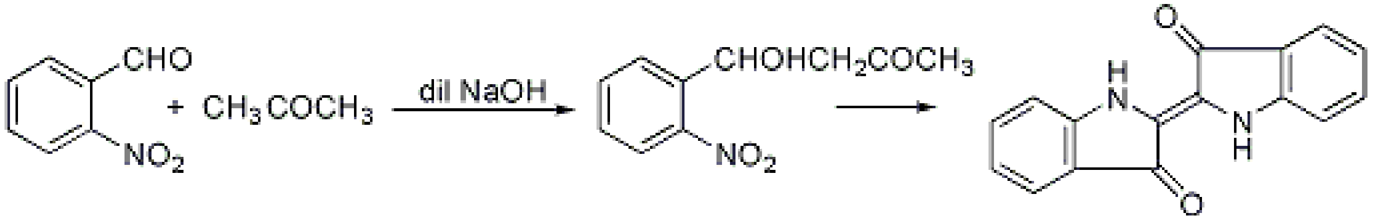


Reviews: L. A. Paquette, *Accts. Chem. Res.* **1,** 209-216 (1968); F. G. Bordwell, *ibid.* **3,** 28 (1970); L. Paquette, *Org. React.* **25,** 1 (1977); G. D. Hartman, R. D. Hartman, *Synthesis* **1982,** 504; J. M. Clough, *Comp. Org. Syn.* **3,** 861-886 (1991).

12. Baeyer-Drewson Indigo Synthesis

A. Baeyer, V. Drewson, *Ber.* **15,** 2856 (1882).

Formation of indigos by an aldol reaction, *q.v.*, of *o*-nitrobenzaldehydes to acetone, pyruvic acid or acetaldehyde; of interest mainly as a method of protecting *o*-nitrobenzaldehydes:



K. Venkataraman, *Chemistry of Synthetic Dyes* **2,** 1008 (New York, 1952); M. Sainsbury, *Rodd's Chemistry of Carbon Compounds* **IVB,** 346, 353 (1977). Synthetic applications: J. R. Mckee *et al., J. Chem. Ed.* **68,** A242 (1991); L. Fitjer *et al., Tetrahedron* **55,** 14421 (1999).

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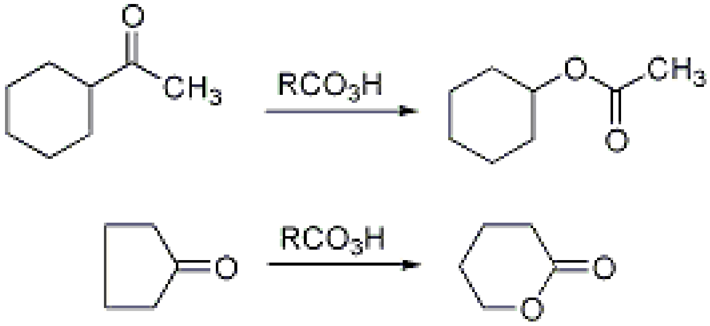
13. Baeyer-Villiger Reaction

A. Baeyer, V. Villiger, *Ber*. **32,** 3625 (1899); **33,** 858 (1900).

The oxidation of ketones to esters or lactones by peracids:



Reviews: P. A. S. Smith in *Molecular Rearrangements* Part 1, P. de Mayo, Ed. (Wiley-Interscience, New York, 1963) pp 577-591; J. B. Lee, B. C. Uff, *Quart. Rev. Chem. Soc.* **21,** 429-457 (1967); C. H. Hassall, *Org. React.* **9,** 73 (1957); G. R. Krow, *ibid.* **43,** 251-798 (1993); *idem, Comp. Org. Syn.* **7,** 671-688 (1991).

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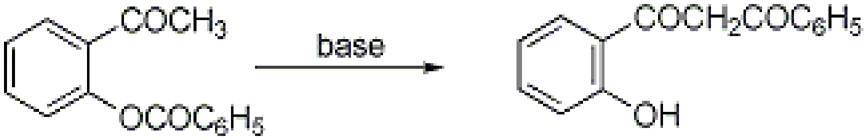
014. Baker-Venkataraman Rearrangement

W. Baker, *J. Chem. Soc.* **1933,** 1381; H. S. Mahal, K. Venkataraman, *ibid.* **1934,** 1767.

Base-catalyzed rearrangement of *o*-acyloxyketones to β-diketones, important intermediates in the synthesis of chromones and flavones:



Gripenberg in *The Chemistry of Flavonoid Compounds*, Geissman, Ed. (New York, 1962) p 410. Mechanistic studies: K. Bowden, M. Chehel-Amiran, *J. Chem. Soc. Perkin Trans. II* **1986,** 2039. Synthetic applications: P. K. Jain *et al., Synthesis* **1982,** 221; J. Zhu *et al., Chem. Commun.* **1988,** 1549; A. V. Kalinin *et al., Tetrahedron Letters* **39,** 4995 (1998); D. C. G. Pinto *et al., New J. Chem.* **24,** 85 (2000). *Cf.* Allan-Robinson Reaction; Kostanecki Acylation.

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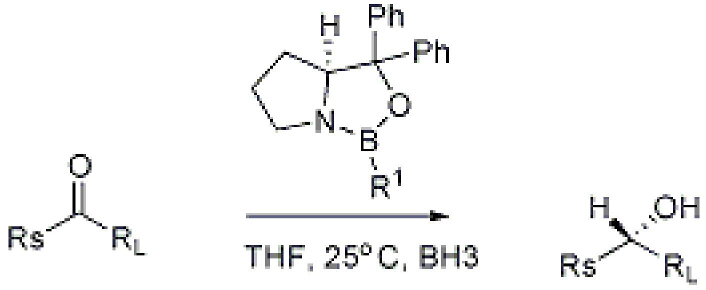
84. Corey-Bakshi-Shibata Reduction (CBS)

E. J. Corey *et al., J. Am. Chem. Soc.* **109,** 5551 (1987).

Enantioselective borane reduction of ketones catalyzed by chiral oxazaborolidines:



R_L = larger group
Rs = smaller group
R^1 = H, CH_3, C_2H_5, C_4H_9, etc.

Practical catalyst synthesis: D. J. Mathre *et al., J. Org. Chem.* **58,** 2880 (1993). Synthetic application: E. J. Corey *et al., J. Am. Chem. Soc.* **119,** 11769 (1997). *Reviews:* V. K. Singh, *Synthesis* **1992,** 605-617; L. Deloux, M. Srebnik, *Chem. Rev.* **93,** 763-784 (1993); E. J. Corey, C. J. Helal, *Angew Chem. Int. Ed.* **37,** 1986-2012 (1998).

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357. **Schiemann Reaction** (Balz-Schiemann Reaction)

G. Balz, G. Schiemann, *Ber.* **60,** 1186 (1927).

Formation of diazonium fluoroborates by diazotization of aromatic amines in the presence of fluoroborates, followed by their thermal decomposition to aryl fluorides:

$$ArNH_2 + HNO_2 + HBF_4 \longrightarrow ArN_2^+ BF_4^- \xrightarrow{\Delta} ArF + N_2 + BF_3$$

Reviews: A. Roe, *Org. React.* **5,** 193 (1949); H. Suschitzky, *Advan. Fluorine Chem.* **4,** 1 (1965); T. K. Al'sing, E. G. Sochilin, *Zh. Org. Khim.* **7,** 530 (1971); R. Bartsch *et al., J. Am. Chem. Soc.* **98,** 6753 (1976); H. G. O. Becker, G. Israel, *J. Prakt. Chem.* **321,** 579 (1979).

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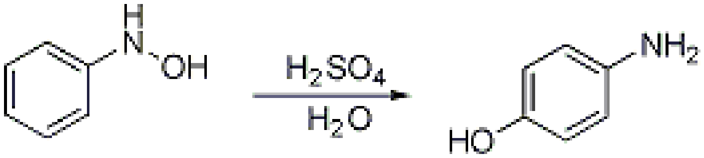
15. Bamberger Rearrangement

E. Bamberger, *Ber*. **27,** 1347, 1548 (1894).

Intermolecular rearrangement of *N*-phenylhydroxylamines in aqueous acid to give the corresponding 4-aminophenols:



Early review: H. J. Shine, *Aromatic Rearrangements* (Elsevier, New York, 1967) pp 182-190. Kinetic and mechanistic study: G. Kohnstam *et al., J. Chem. Soc. Perkin Trans. II* **1984,** 423. Synthetic application: D. Johnston, D. Elder, *J. Labelled Compd. Radiopharm.* **25,** 1315 (1988). Modified conditions: A. Zoran *et al., Chem. Commun.* **1994,** 2239; M. Tordeux, C. Wakselman, *J. Fluorine Chem.* **74,** 251 (1995).

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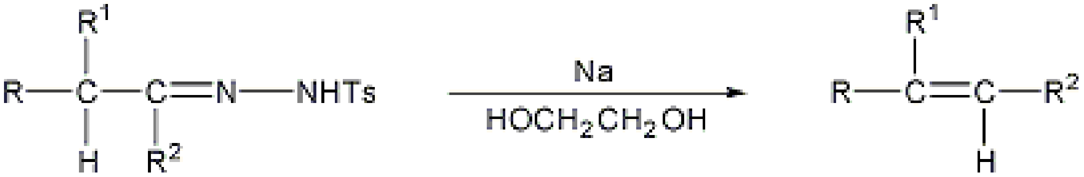
16. Bamford-Stevens Reaction; Shapiro Reaction

W. R. Bamford, T. S. Stevens, *J. Chem. Soc.* **1952,** 4735.

Formation of olefins by base-promoted decomposition of *p*-toluenesulfonylhydrazones of aldehydes and ketones:



The formation of unrearranged alkenes, generally the less substituted isomers, by treatment of ketone derived *p*-toluenesulfonylhydrazones with alkyl lithium reagents is known as the **Shapiro reaction:** R. H. Shapiro, M. J. Heath, *J. Am. Chem. Soc.* **89,** 5734 (1967). Use of *N*, *N*-diethylaminosulfonylhydrazones: J. Kang *et al., Bull. Korean Chem.* **13,** 192 (1992).

Silicon directing effect: T. K. Sarkar, B. K. Ghorai, *Chem. Commun.* **1992,** 1184. *Reviews:* R. H. Shapiro, *Org. React.* **23,** 405-507 (1976); R. M. Adlington, A. G. M. Barrett, *Accts. Chem. Res.* **16,** 55-59 (1983); K. Maruka, H. Yamamoto, *Comp. Org. Syn.* **6,** 776-779 (1991); A. R. Chamberlin, D. J. Sall, *ibid.* **8,** 944-949.

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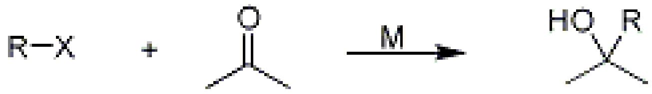
17. Barbier(-type) Reaction

P. Barbier, *C. R. Acad. Sci.* **128,** 110 (1899).

One-step procedure for the preparation of alcohols from organic halides and aldehydes or ketones:



M = Mg, Li, Sm(II), Zn   R = alkyl, aryl, vinyl, allyl   X = Cl, Br, I

Review of mechanistic studies of Sm-mediated coupling: D. P. Curran *et al.*, *Synlett* **1992,** 943-961. Book: C. Blomberg, *The Barbier Reaction and Related One-Step Processes*, K. Hafner *et al.*, Eds. (Springer-Verlag, New York, 1993) 183 pp. Zn-promoted coupling: F. Hong *et al.*, *Chem. Commun.* **1994,** 289. Sm-mediated coupling: M. Kunishima *et al.*, *Chem. Pharm. Bull.* **42,** 2190 (1994). Comparison with Ni(0) insertion chemistry for intramolecular cyclization: M. Kihara *et al.*, *Tetrahedron* **48,** 67 (1992). *Cf.* Grignard Reaction.

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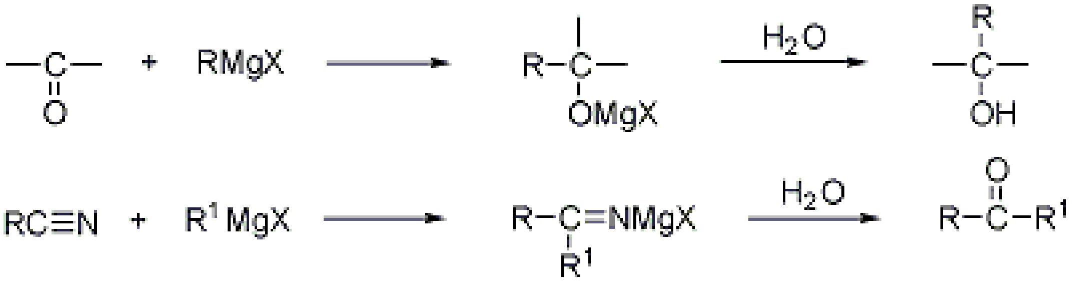
164. Grignard Reaction

V. Grignard, *Compt. Rend.* **130,** 1322 (1900).

Traditionally, it is the addition of organomagnesium compounds (Grignard reagents) to carbonyl compounds to generate alcohols. A more modern interpretation extends the scope of the reaction to include the addition of Grignard reagents to a wide variety of electrophilic substrates:



Early review: D. A. Shirley, *Org. React.* **8,** 28-58 (1954). Preparation of Grignard reagents: Y. H. Lai, *Synthesis* **1981,** 585-604. Mechanistic study: K. Maruyama, T. Katagiri, *J. Phys. Org. Chem.* **2,** 205 (1989). Review of stereoselective addition of carbonyl compounds: D. M. Huryn, *Comp. Org. Syn.* **1,** 49-75 (1991). General review: G. S. Silverman, P. E. Rakita in *Kirk-Othmer Encyclopedia of Chemical Technology* **vol. 12** (Wiley-Interscience, New York, 4th ed., 1994) pp 768-786. *Cf.* Barbier(-type) Reaction.

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18. Barbier-Wieland Degradation

H. Wieland, *Ber.* **45,** 484 (1912); P. Barbier, R. Locquin, *Compt. Rend.* **156,** 1443 (1913).

Stepwise carboxylic acid degradation of aliphatic acids (particularly in sterol side chains) to the next lower homolog. The ester is converted to a tertiary alcohol that is dehydrated with acetic anhydride, and the olefin oxidized with chromic acid to a lower homologous carboxylic acid:

$$RCH_2COOCH_3 \xrightarrow[\text{2. HX}]{\text{1. 2PhMgX}} RCH_2COHPh_2 \xrightarrow{Ac_2O} RCH{=}CHPh_2 \xrightarrow{CrO_3} RCOOH + Ph_2CO$$

H. Wieland *et al., Z. Physiol. Chem.* **161,** 80 (1926); C. W. Shoppee, *Ann. Repts.* (Chem. Soc., London) **44,** 184 (1947); W. Baker *et al., J. Chem. Soc.* **1958,** 1007; J. R. Dias, R. Ramachandra, *Tetrahedron Letters* **1976,** 3685. Synthetic applications: S. C. Wilcox, J. J. Guadino, *J. Am. Chem. Soc.* **108,** 3102 (1986); C. D. Schteingart, A. E. Hofmann, *J. Lipid Res.* **29,** 1387 (1988). *Cf.* Krafft Degradation; Miescher Degradation.

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224. Krafft Degradation

F. Krafft, *Ber.* **12,** 1664 (1879).

Conversion of carboxylic acids, especially of high molecular weight, into the next lower homolog by dry distillation of the alkaline earth salt with the corresponding acetate, followed by chromic acid oxidation of the methyl ketone:

$$(RCH_2COO)_2M + (AcO)_2M \longrightarrow RCH_2COCH_3 \xrightarrow{CrO_3} RCOOH$$

F. C. Whitmore, *Organic Chemistry* (New York, 1951) p 255; F. Klages, *Lehrbuch der organischen Chemie* **I** (Berlin, 1952) pp 262, 266, 368. *Cf.* Barbier-Wieland Degradation.

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260. Miescher Degradation

C. Meystre *et al., Helv. Chim. Acta* **27,** 1815 (1944).

Adaptation of the Barbier-Wieland degradation, *q.v.*, to permit simultaneous elimination of three carbon atoms, as in degradation of the bile acid side chain to the methyl ketone stage. Conversion of the methyl ester of the bile acid to the tertiary alcohol, followed by dehydration, bromination, dehydrohalogenation and oxidation of the diene yields the chain-shortened ketone:

$$RR^1CHCH_2CH_2COOCH_3 \xrightarrow{PhMgBr} RR^1CHCH_2CH_2C(OH)Ph_2 \xrightarrow{-H_2O}$$

$$RR^1CHCH_2CH{=}CPh_2 \xrightarrow{(CH_2CO)_2NBr} RR^1CHCHBrCH{=}CPh_2 \xrightarrow{-HBr}$$

$$RR^1C{=}CH{-}CH{=}CPh_2 \xrightarrow{CrO_3} RCOR^1 + OHCCH{=}CPh_2$$

C. W. Shoppee, *Ann. Repts.* (Chem. Soc. London) **44,** 184 (1947); F. S. Spring, *J. Chem. Soc.* **1950,** 3355; A. Wettstein, G. Anner, *Experientia* **1954,** 407; C. J. W. Brooks, *Rodd's Chemistry of Carbon Compounds* **IID,** 26 (1970); P. G. Marshall, *ibid.* 233, 253, 323.

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19. **Bart Reaction;** Scheller Modification

H. Bart, **DE 250264** (1910); **DE 254092** (1910); **DE 264924** (1910); **DE 268172** (1912); *Ann.* **429,** 55 (1922); E. Scheller, **GB 261026**; A. W. Ruddy *et al., J. Am. Chem. Soc.* **64,** 828 (1942).

Formation of aromatic arsonic acids by treating aromatic diazonium compounds with alkali arsenites in the presence of cupric salts or powdered silver or copper; in the **Scheller modification** primary aromatic amines are diazotized in the presence of arsenious chloride and a trace of cuprous chloride:

$$PhN_2^+Cl^- + Na_3AsO_3 \longrightarrow PhAsO_3Na_2 + NaCl + N_2$$

$$PhNH_2 + HNO_2 + AsCl_3 + (H_2O) \longrightarrow PhAsO_3H_2 + N_2 + 3HCl$$

The modified Bart reaction can be applied to the formation of arylstibonic acids:

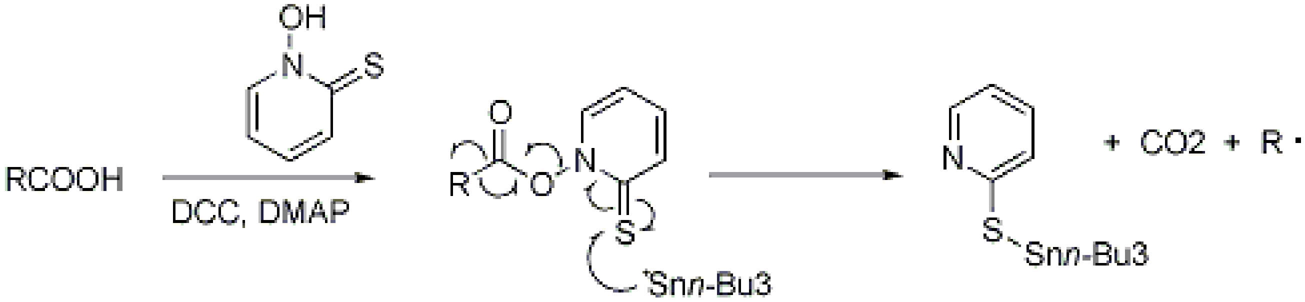
$$ArNH_2 + HNO_2 + SbCl_3 + (H_2O) \longrightarrow ArSbO_3H_2 + N_2 + 3HCl$$

C. F. Hamilton, J. F. Morgan, *Org. React.* **2,** 415 (1944); G. O. Doak, H. G. Steinman, *J. Am. Chem. Soc.* **68,** 1987 (1946); K. H. Saunders, *Aromatic Diazo-Compounds and Their Technical Applications* (London, 1949) p 330; W. A. Cowdry, D. S. Davies, *Quart. Rev.* **6,** 363 (1952).

20. Barton Decarboxylation

D. H. R. Barton *et al., Chem. Commun.* **1983,** 939; *eidem, Tetrahedron* **41,** 3901 (1985).

Radical decarboxylation of organic acids to the corresponding noralkane with tri-*n*-butyltin hydride or *t*-butylmercaptan:



Synthetic application: F. E. Ziegler, M. Belema, *J. Org. Chem.* **62,** 1083 (1997).

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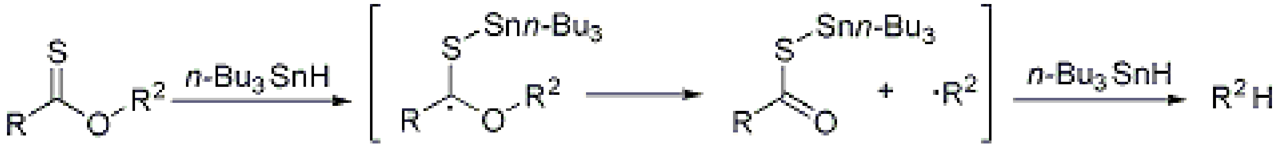
21. **Barton Deoxygenation** (Barton-McCombie Reaction)

D. H. R. Barton, S. W. McCombie, *Perkin Trans. I* **1975,** 1574.

Deoxygenation of alcohols *via* their thiocarbonyl derivatives which undergo free radical scission upon treatment with tri-*n*-butyltin hydride:



R = H, CH_3, SCH_3, Ph, OPh, imidazolyl; R^2 = alkyl

Mechanistic study: J. E. Forbes, S. Z. Zard, *Tetrahedron Letters* **30,** 4367 (1989). *Review:* M. Pereyre *et al., Tin in Organic Synthesis* (Butterworths, Boston, 1987) pp 84-96. Review of methodological improvements, particularly the replacement of tri-*n*-butyltin hydride with silicon hydrides: C. Chatgilialoglu, C. Ferreri, *Res. Chem. Intermed.* **19,** 755-775 (1993).

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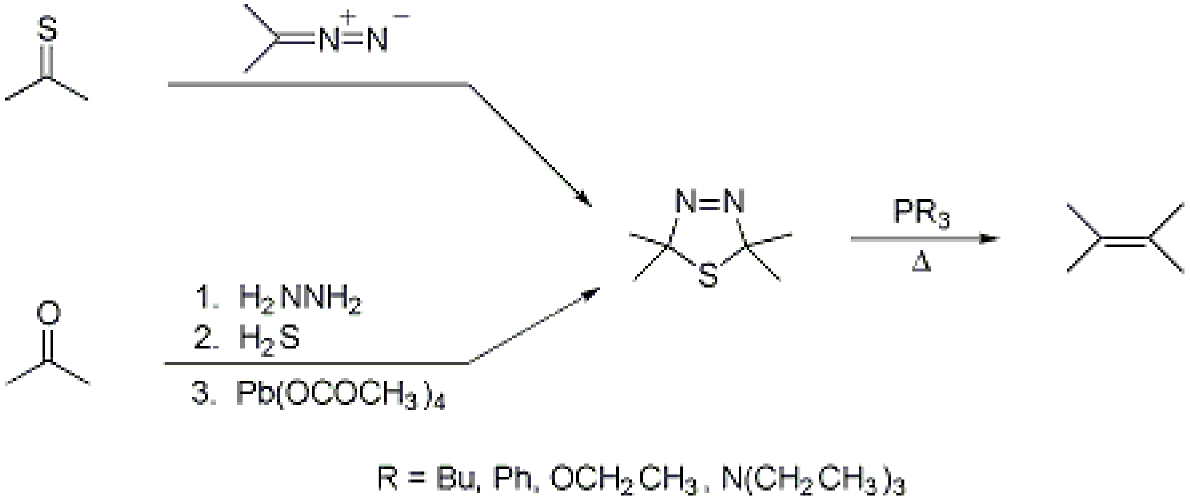
22. **Barton Olefin Synthesis** (Barton-Kellogg Reaction)

D. H. R. Barton *et al., Chem. Commun.* **1970,** 1226; R. M. Kellogg, S. Wassenaar, *Tetrahedron Letters* **1970,** 1987; R. M. Kellogg *et al., ibid.* 4689.

Olefin synthesis by two-fold extrusion of nitrogen and sulfur from a Δ^3-1,3,4-thiadiazoline intermediate. Particularly applicable to the synthesis of moderately hindered *tetra*-substituted ethylenes:



Scope and limitations: D. H. R. Barton *et al., J. Chem. Soc. Perkin Trans. I* **1974,** 1794. Synthetic applications: A. P. Schaap, G. R. Faler, *J. Org. Chem.* **38,** 3061 (1973); L. K. Bee *et al., ibid.* **40,** 2212 (1975); M. D. Bachi *et al., Tetrahedron Letters* **1978,** 4167; J. E. McMurry *et al., J. Am. Chem. Soc.* **106,** 5018 (1984); F. J. Hoogesteger *et al., J. Org. Chem.* **60,** 4375 (1995). *Cf.* McMurry Reaction.

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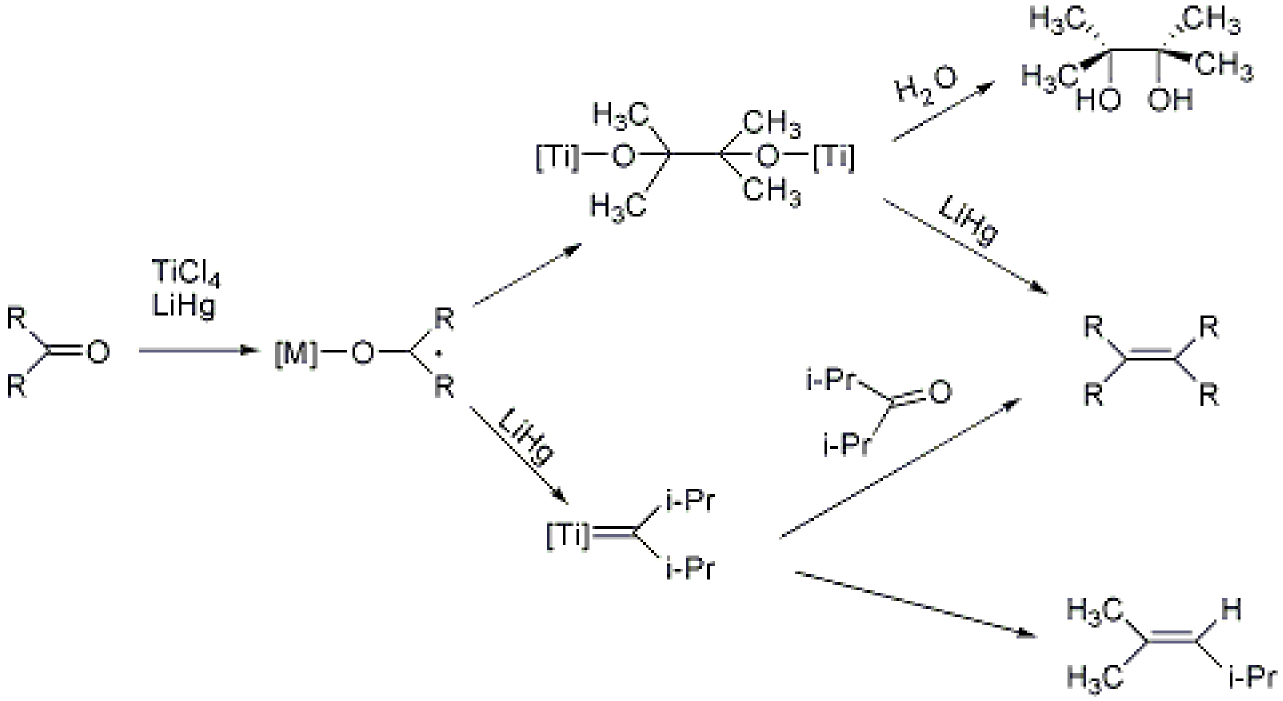
241. McMurry Coupling Reaction

J. E. McMurry, M. P. Fleming, *J. Am. Chem. Soc.* **96,** 4708 (1974); S. Tyrlik, I. Wolochowicz, *Bull. Soc. Chim. France* **1973,** 2147; T. Mukaiyama *et al., Chem. Letters* **1973,** 1041.

Deoxygenative coupling of carbonyl compounds to alkenes induced by low-valent titanium:



Synthetic application: A. Fürstner, D. N. Jumbam, *Tetrahedron* **48,** 5991 (1992); M. Rucker, R. Brückner, *Tetrahedron Letters* **38,** 7353 (1997); P. Harter *et al., Polyhedron* **17,** 1141 (1998). Modified conditions: T. A. Lipski *et al., J. Org. Chem.* **62,** 4566 (1997); S. Talukdar *et al., ibid.* **63,** 4925 (1998). *Reviews:* J. E. McMurry, *Chem. Rev.* **89,** 1513-1524 (1989); G. M. Robertson, *Comp. Org. Syn.* **3,** 583-595 (1991); T. Lectka, *Act. Met.* **1996,** 85-131; M. Ephritikhine, *Chem. Commun.* **23,** 2549-2554 (1998). *Cf.* Barton Olefin Synthesis.

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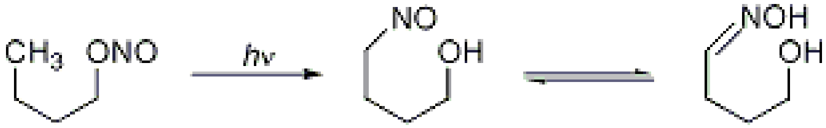
23. Barton Reaction

D. H. R. Barton *et al., J. Am. Chem. Soc.* **82,** 2640 (1960); **83,** 4076 (1961).

Conversion of a nitrite ester to a γ-oximino alcohol by photolysis involving the homolytic cleavage of a nitrogen-oxygen bond followed by hydrogen abstraction:

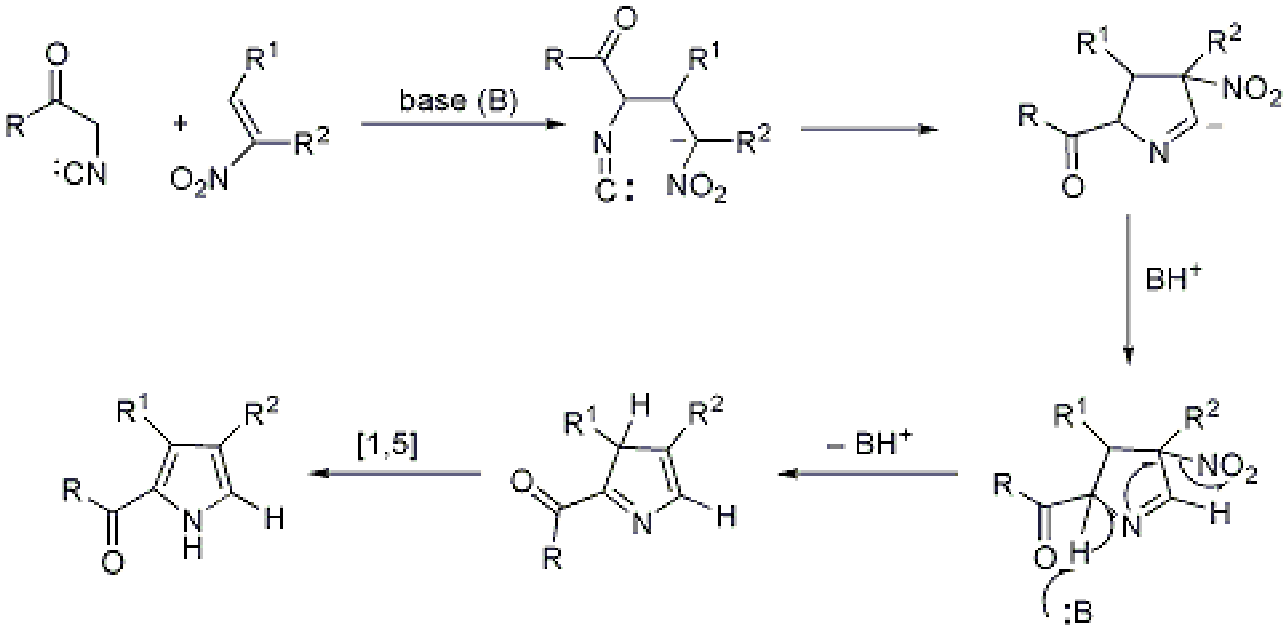


M. Akhtar, *Advan. Photochem.* **2,** 263 (1964); R. H. Hesse, *Advan. Free Radical Chem.* **3,** 83 (1969); J. Kalvoda, *Angew. Chem. Int. Ed.* **8,** 525 (1964). Mechanism: D. H. R. Barton *et al., J. Chem. Soc. Perkin Trans. I* **1979,** 1159. Synthetic application: A. Herzog *et al., Angew. Chem. Int. Ed.* **37,** 1552 (1998).

24. Barton-Zard Reaction

D. H. R. Barton *et al., Tetrahedron* **46,** 7587 (1990).

Formation of a pyrrole by condensation of a substituted nitroso-alkene with an isocyanoester:



Synthetic applications: T. D. Lash *et al., Tetrahedron Letters* **35,** 2493 (1994); *idem. et al., ibid.* **38,** 2031 (1997); E. T. Pelkey *et al., Chem. Commun.* **1996,** 1909.

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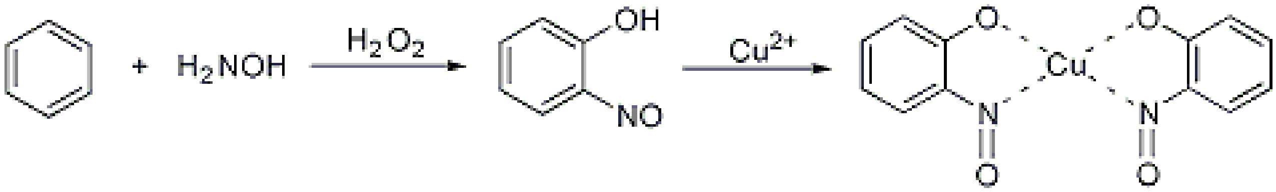
25. Baudisch Reaction

O. Baudisch *et al., Naturwiss.* **27,** 768, 769 (1939); *Science* **92,** 336 (1940); *J. Am. Chem. Soc.* **63,** 622 (1941).

Synthesis of *o*-nitrosophenols from benzene or substituted benzenes, hydroxylamine and hydrogen peroxide in the presence of copper salts:



K. Maruyama *et al., Tetrahedron Letters* **1966,** 5889; *J. Org. Chem.* **32,** 2516 (1967); *Bull. Chem. Soc. Japan* **44,** 3120 (1971); W. Seidenfaden, *Houben-Weyl* **10/1,** 1025, 1027 (1971).

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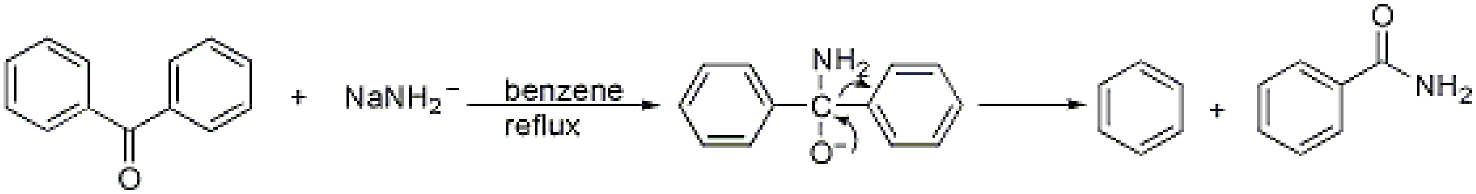
170. Haller-Bauer Reaction

A. Haller, E. Bauer, *Compt. Rend.* **148,** 70, 127 (1909); **149,** 5 (1909).

Cleavage of non-enolizable ketones with sodium amide; frequently applied to formation of trisubstituted acetic acid:



K. E. Hamlin, A. W. Weston, *Org. React.* **9,** 1 (1957); H. M. Walborsky *et al., J. Org. Chem.* **36,** 2937 (1971); E. M. Kaiser, C. O. Warner, *Synthesis* **1975,** 395. Applications: G. Mehta, M. Praveen, *J. Org. Chem.* **60,** 279 (1995); *idem et al., Tetrahedron Letters* **37,** 2289 (1996); A. Mittra *et al., J. Org. Chem.* **63,** 9555 (1998). Reviews and extension to amide formation: J. P. Gilday, L. A. Paquette, *Org. Prep. Proced. Int.* **22,** 167-201 (1990); G. Mahta, R. V. Venkateswaran, *Tetrahedron* **56,** 1399 (2000).

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361. Schotten-Baumann Reaction

C. Schotten, *Ber.* **17,** 2544 (1884); E. Baumann, *ibid.* **19,** 3218 (1886).

Acylation of alcohols or amines with acid chlorides in aqueous alkaline solution:

Review: N. O. V. Sonntag, *Chem. Rev.* **52,** 272-273 (1953). Synthetic applications: M. Tsuchiya *et al., Bull. Chem. Soc. Japan* **42,** 1756 (1969); G. I. Georg, *Bioorg. Med. Chem. Letters* **4,** 335 (1994).

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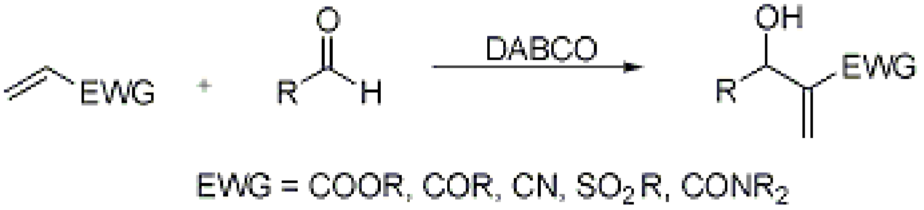
26. Baylis-Hillman Reaction

A. B. Baylis, M. E. D. Hillman, **DE 2155113;** *eidem*, **US 3743669** (1972, 1973 both to Celanese).

Coupling of activated vinyl systems with aldehydes, catalyzed by 1,4-diazabicyclo[2.2.2] octane (DABCO), to yield α-hydroxyalkylated or -arylated products:



Scope and limitations/mechanistic studies: Y. Fort *et al., Tetrahedron* **48,** 6371 (1992); E. L. M. van Rozendaal *et al., ibid.* **49,** 6931 (1993). Rate enhancement study: J. Augé *et al., Tetrahedron Letters* **35,** 7947 (1994). Use of chiral auxillary: S. E. Drewes *et al., Synth. Commun.* **23,** 1215 (1993). Synthetic applications: *idem et al., ibid.* 2807; P. Perlmutter, T. D. McCarthy, *Aust. J. Chem.* **46,** 253 (1993). *Review:* S. E. Drewes, G. H. P. Roos, *Tetrahedron* **44,** 4653-4670 (1988).

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27. Béchamp Reduction

A. J. Béchamp, *Ann. Chim. Phys.* **42**(3), 186, (1854).

Reduction of aromatic nitro compounds to the corresponding amines by iron, ferrous salts or iron catalysts in aqueous acid:

$$ArNO_2 + 2Fe + 6HCl \longrightarrow ArNH_2 + 2H_2O + 2FeCl_3$$

J. Werner, *Ind. Eng. Chem.* **40,** 1575 (1948); **41,** 1841 (1949); S. Yagi *et al., Bull. Chem. Soc. Japan* **29,** 194 (1956); A. Courtin, *Helv. Chim. Acta* **62,** 2280 (1980). *Reviews:* C. S. Hamilton, J. F. Morgan, *Org. React.* **2,** 428 (1944); R. Schröter, *Houben-Weyl* **11/1,** 394-409 (1957).

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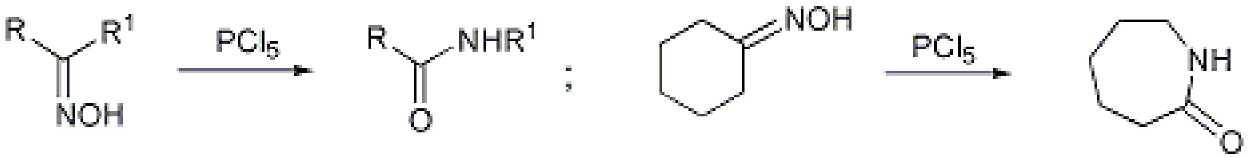
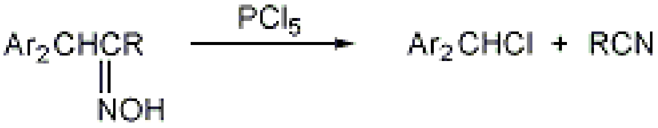
28. **Beckmann Rearrangement;** Beckmann Fragmentation

E. Beckmann, *Ber.* **19,** 988 (1886).

Acid-mediated isomerization of oximes to amides. Oximes of cyclic ketones give ring enlargements:



Certain oximes, particularly those having a quarternary carbon *anti* to the hydroxyl, are likely to undergo the **Beckmann fragmentation** to form nitriles instead of amides:



$$Ar_2CH\underset{\underset{NOH}{\|}}{C}R \xrightarrow{PCl_5} Ar_2CHCl + RCN$$

Application to steroidal oximes: P. Catsoulacos, D. Catsoulacos, *J. Heterocyclic Chem.* **30,** 1 (1993). *Reviews:* L. G. Donaruma, W. Z. Heldt, *Org. React.* **11,** 1-156 (1960); R. E. Gawley, *ibid.* **35,** 1-420 (1988); C. G. McCarty in *The Chemistry of the Carbon-Nitrogen Double Bond,* S. Patai, Ed. (Interscience, New York, 1970) pp 408-439; J. R. Hauske, *Comp. Org. Syn.* **1,** 98-100 (1991); K. Maruoka, H. Yamamoto, *ibid.* **6,** 763-775; D. Craig, *ibid.* **7,** 689-702. *Cf.* Schmidt Reaction; Tiemann Rearrangement.

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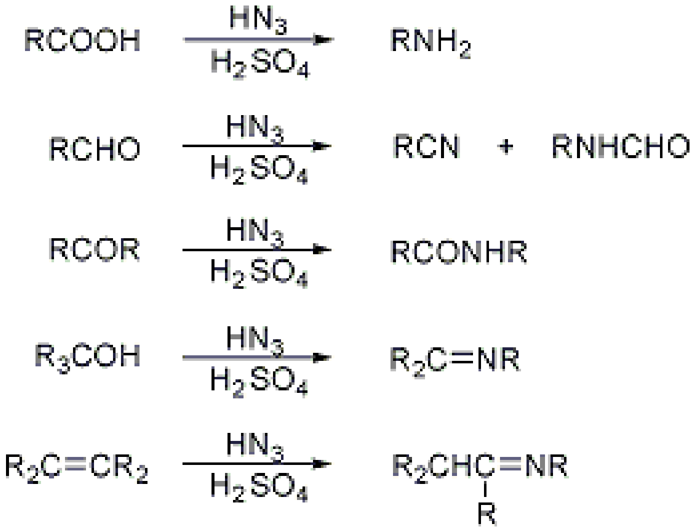
358. Schmidt Reaction

R. F. Schmidt, *Ber.* **57,** 704 (1924).

Acid-catalyzed addition of hydrazoic acid to carboxylic acids, aldehydes and ketones to give amines, nitriles and amides, respectively. Tertiary alcohols and substituted alkenes yield imines upon treatment with hydrazoic acid:



$$RCOOH \xrightarrow[H_2SO_4]{HN_3} RNH_2$$

$$RCHO \xrightarrow[H_2SO_4]{HN_3} RCN + RNHCHO$$

$$RCOR \xrightarrow[H_2SO_4]{HN_3} RCONHR$$

$$R_3COH \xrightarrow[H_2SO_4]{HN_3} R_2C{=}NR$$

$$R_2C{=}CR_2 \xrightarrow[H_2SO_4]{HN_3} R_2CH\underset{R}{C}{=}NR$$

Early reviews: H. Wolff, *Org. React.* **3,** 307-336 (1946); P. A. S. Smith in *Molecular Rearrangements* Part 1, P. de Mayo, Ed. (Wiley-Interscience, New York, 1963) pp 507-558; D. V. Banthorpe, *The Chemistry of the Azido Group,* S. Patai, Ed. (Interscience, New York, 1971) pp 405-421; G. I. Koldobskii, *Russ. Chem. Rev.* **47,** 1084 (1978). Application to cyclic ketones: A. Lévai *et al., Heterocycles* **34,** 1523 (1992); J.-Y. Mérour *et al., J. Hetereocyclic Chem.* **31,** 87 (1994); to alcohols and alkenes: W. H. Pearson *et al., J. Am. Chem. Soc.* **115,** 10183 (1993). Extension to dialkyl acylphosphonates: M. Sprecher, D. Kost, *ibid.* **116,** 1016 (1994). *Review:* T. Shioiri, *Comp. Org. Syn.* **6,** 817-821 (1991). *Cf.* Beckmann Rearrangement; Curtius Rearrangement; Hofmann Reaction; Lossen Rearrangement.

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90. **Curtius Rearrangement;** Curtius Reaction

T. Curtius, *Ber.* **23,** 3023 (1890); *idem, J. Prakt. Chem.* [2] **50,** 275 (1894).

Formation of isocyanates by thermal decomposition of acyl azides:

$$\mathrm{RCON_3} \xrightarrow{\Delta} \mathrm{R{-}N{=}C{=}O}$$

The stepwise conversion of a carboxylic acid to an amine having one fewer carbon unit, *via* the azide and isocyanate, is referred to as the **Curtius reaction:**

$$\mathrm{RCOOH} \longrightarrow \mathrm{RCON_3} \longrightarrow \mathrm{RNCO} \longrightarrow \mathrm{RNH_2}$$

Synthetic applications: R. Lo Scalzo *et al., Gazz. Chim. Ital.* **118,** 819 (1988); N. De Kimpe *et al., J. Org. Chem.* **59,** 8215 (1994). *Reviews:* P. A. S. Smith, *Org. React.* **3,** 337-449 (1946); J. H. Saunders, R. J. Slocombe, *Chem. Rev.* **43,** 205 (1948); D. V. Banthorpe in *The Chemistry of the Azido Group,* S. Patai, Ed. (Interscience, New York, 1971) pp 397-405; T. Shioiri, *Comp. Org. Syn.* **6,** 795-828 (1991). *Cf.* Bergmann Degradation; Hofmann Reaction; Lossen Rearrangement; Schmidt Reaction.

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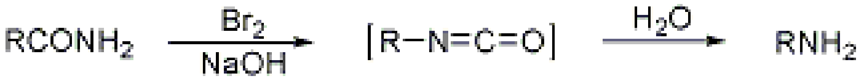
194. Hofmann Reaction

A. W. Hofmann, *Ber.* **14,** 2725 (1881).

Conversion of primary carboxylic amides to primary amines with one fewer carbon atom upon treatment with hypohalites or hydroxide *via* the intermediate isocyanate:



Early review: E. S. Wallis, J. F. Lane, *Org. React.* **3,** 267-306 (1949). Alternative reagents/strategies: S. Kajigaeshi *et al., Chem. Letters* **1989,** 463; S. Jew *et al., Arch. Pharm. Res.* **15,** 333 (1992); D. S. Rane, M. M. Sharma, *J. Chem. Tech. Biotechnol.* **59,** 271 (1994); H. Moustafa *et al., Tetrahedron* **53,** 625 (1997); Y. Matsumura *et al., J. Chem. Soc. Perkin Trans. I* **1999,** 2057. *Review:* T. Shioiri, *Comp. Org. Syn.* **6,** 800-806 (1991). *Cf.* Curtius Rearrangement; Lossen Rearrangement; Schmidt Reaction; Weerman Degradation.

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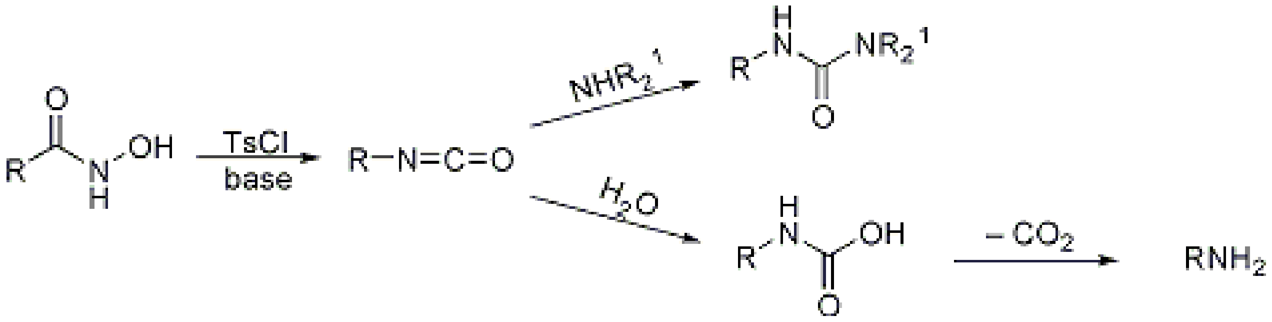
238. Lossen Rearrangement

W. Lossen, *Ann.* **161,** 347 (1872); **175,** 271, 313 (1874).

Conversion of a hydroxamic acid to an isocyanate *via* the intermediacy of its *O*-acyl, sulfonyl, or phosphoryl derivative. In the presence of amines, ureas are formed; in the presence of water, amines containing one less carbon than the starting material, are generated:



Reviews: H. L. Yale, *Chem. Rev.* **33,** 209 (1943); L. Bauer, O. Exner, *Angew. Chem. Int. Ed.* **13,** 376 (1974); T. Shiori, *Comp. Org. Syn.* **6,** 821-825 (1991). Reaction conditions leading to the formation of ureas: J. Pihuleac, L. Bauer, *Synthesis* **1989,** 61; extention to *N*-phosphinoylhydroxylamines: J. Fawcett *et al., Chem. Commun.* **1992,** 227; C. J. Salomon, E. Breuer, *J. Org. Chem.* **62,** 3858 (1997); to sulfonyloxy imides: D. A. Casteel *et al., Heterocycles* **36,** 485 (1993). Modifications: J. A. Stafford *et al., J. Org. Chem.* **63,** 10040 (1998); R. Anilkumar *et al., Tetrahedron Letters* **41,** 5291 (2000). *Cf.* Curtius Rearrangement; Hofmann Reaction; Schmidt Reaction.

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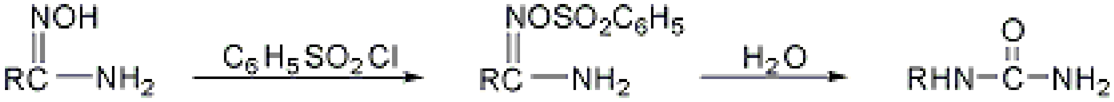
395. Tiemann Rearrangement

F. Tiemann, *Ber.* **24,** 4162 (1891).

Rearrangement of amide oximes (available from nitriles and hydroxylamine) to monosubstituted ureas by treatment with benzenesulfonyl chloride and water:

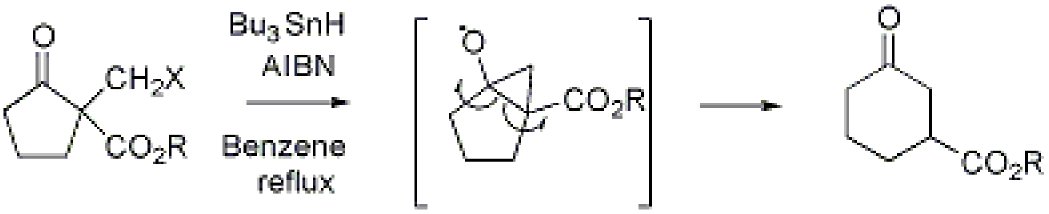


P. A. S. Smith, *Org. React.* **3,** 366 (1946); M. W. Partridge, H. A. Turner, *J. Pharm. Pharmacol.* **5,** 103 (1953); R. F. Plapinger. O. O. Owens, *J. Org. Chem.* **21,** 1186 (1956); J. Garapon *et al.*, *Tetrahedron Letters* **1970,** 4905. *Cf.* Beckmann Rearrangement.

109. Dowd-Beckwith Ring Expansion Reaction

A. L. J. Beckwith *et al., J. Am. Chem. Soc.* **110,** 2565 (1988); P. Dowd, S. C. Choi, *Tetrahedron* **45,** 77 (1989).

Free radical mediated ring expansions of haloalkyl β-ketoesters:



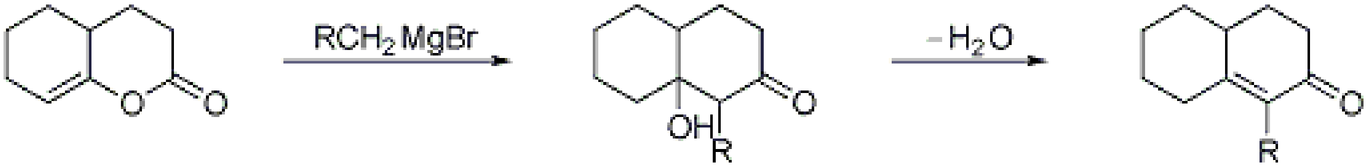
X = Br, I, SePh

Synthetic application: M. G. Banwell, J. M. Cameron, *Tetrahedron Letters* **37,** 525 (1996); C. Wang *et al.*, *Tetrahedron* **54,** 8355 (1998).

151. Fujimoto-Belleau Reaction

C. I. Fujimoto, *J. Am. Chem. Soc.* **73,** 1856 (1951); B. Belleau, *ibid.* 5441.

Synthesis of cyclic α-substituted α,β-unsaturated ketones from enol lactones and Grignard reagents prepared from primary halides:

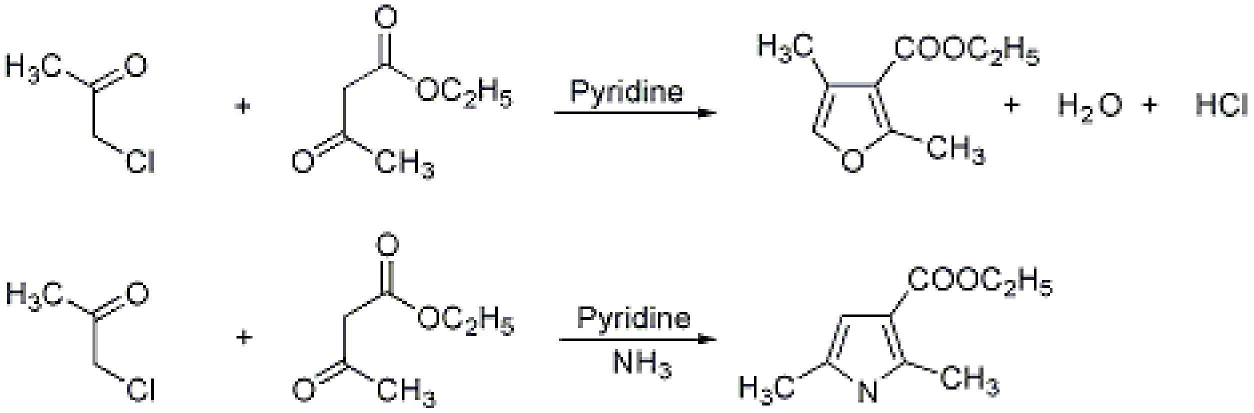


Review: J. Weill-Raynal, *Synthesis* **1969,** 49. Modified conditions: M. Aloui *et al.*, *Synlett.* **1994,** 115.

128. Feist-Bénary Synthesis

F. Feist, *Ber.* **35,** 1537, 1545 (1902); E. Bénary, *Ber.* **44,** 489, 493 (1911).

Formation of furans from α-halogenated ketones or ethers and 1,3-dicarbonyl compounds in the presence of pyridine. When ammonia is used as the condensing agent, pyrrole derivatives are always formed as secondary products:



T. Reichstein, H. Zschokke, *Helv. Chim. Acta* **14,** 1270 (1931); **15,** 268, 1105, 1112 (1932); R. C. Elderfield, T. N. Dodd, *Heterocyclic Compounds* **1,** 132 (1950); J. Kagan, K. C. Mattes, *J. Org. Chem.* **45,** 1524 (1980). Alternative substrate: R. C. Cambie *et al.*, *Synth. Commun.* **20,** 1923 (1990). *Cf.* Hantzsch Pyrrole Synthesis.

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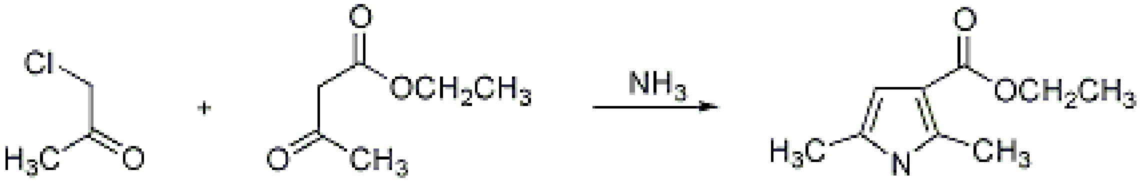
173. Hantzsch Pyrrole Synthesis

A. Hantzsch, *Ber.* **23,** 1474 (1890).

Formation of pyrrole derivatives from α-chloromethyl ketones, β-keto esters and ammonia or amines:



R. Elderfield, T. N. Dodd, Jr., *Heterocyclic Compounds* **1,** 132 (1950); A. H. Corwin, *ibid.* 290; M. W. Roomi, S. F. MacDonald, *Can. J. Chem.* **48,** 1689 (1970); K. Kirschke *et al.*, *J. Prakt. Chem.* **332,** 143 (1990); A. W. Trautwein *et al.*, *Bioorg. Med. Chem. Lett.* **8,** 2381 (1998). *Cf.* Feist-Bénary Synthesis; Knorr Pyrrole Synthesis; Paal-Knorr Pyrrole Synthesis.

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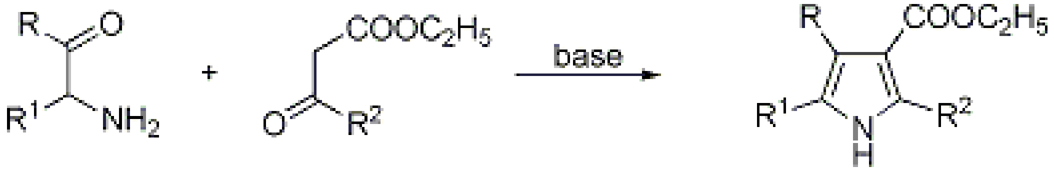
216. Knorr Pyrrole Synthesis

L. Knorr, *Ber.* **17,** 1635 (1884); *Ann.* **236,** 290 (1886); L. Knorr, H. Lange, *Ber.* **35,** 2998 (1902).

Formation of pyrrole derivatives by condensation of α-amino ketones as such or generated *in situ* from isonitrosoketones with carbonyl compounds containing active α-methylene groups:



A. H. Corwin, *Heterocyclic Compounds* **1,** 287 (1950); H. Fischer, *Org. Syn.* **coll. vol. III,** 573 (1955); S. Hauptmann, M. Martin, *Z. Chem.* **8,** 333 (1968); A. J. Castro *et al., J. Org. Chem.* **35,** 2815 (1970); Y. Tamura *et al., Chem. & Ind. (London)* **1971,** 767; H. Rapoport, J. Harbuck, *J. Org. Chem.* **36,** 853 (1971); E. Fabiano, B. T. Golding, *J. Chem. Soc. Perkin Trans. I* **1991,** 3371; A. Alberola *et al., Tetrahedron* **55,** 6555 (1999). Synthetic applications: J. A. Bastian, T. D. Lash, *ibid.* **54,** 6299 (1998); P. E. Harrington, M. A. Tius, *Org. Lett.* **1,** 649 (1999); L. Cheng, D. A. Lightner, *Synthesis* **1999,** 46. *Cf.* Hantzsch Pyrrole Synthesis; Paal-Knorr Pyrrole Synthesis.

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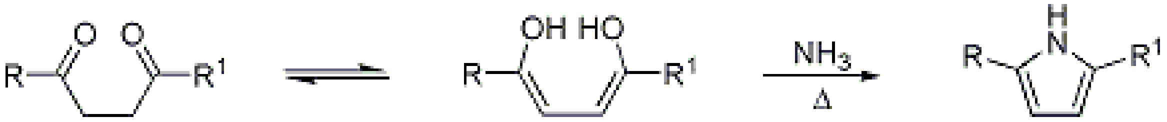
289. Paal-Knorr Pyrrole Synthesis

C. Paal, *Ber.* **18,** 367 (1885); L. Knorr, *ibid.* 299.

Formation of pyrroles via cyclization of 1,4-dicarbonyl compounds with ammonia or primary amines:



H. Fischer, H. Orth, *Die Chemie des Pyrrols* **1** (Leipzig, 1934) p 34; D. M. Young, C. F. H. Allen, *Org. Syn.* **16,** 25 (1936); A. H. Corwin, *Heterocyclic Compounds* **1,** 290 (1950); N. P. Buu-Hoi *et al., J. Org. Chem.* **20,** 639, 850 (1955); H. H. Wassermann *et al., Tetrahedron* **32,** 1863 (1976). Mechanistic studies: V. Amarnath *et al., J. Org. Chem.* **56,** 6924 (1991); *idem,* K. Amarnath, *ibid.* **60,** 301 (1995). Applications: S.-X. Yu, P. W. Le Quesne, *Tetrahedron Letters* **36,** 6205 (1995); R. Ballini *et al., Synlett* **3,** 391 (2000). *Review:* S. E. Korostova *et al., Russ. J. Org. Chem.* **34,** 1691 (1998). *Cf.* Hantzsch Pyrrole Synthesis; Knorr Pyrrole Synthesis.

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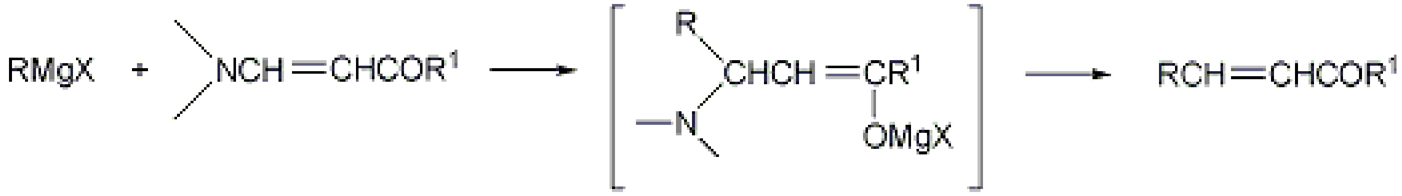
29. Bénary Reaction

E. Bénary, *Ber.* **63,** 1573 (1930); **64,** 2543 (1931).

Action of Grignard reagents on enamino ketones or aldehydes yields β-substituted α,β-unsaturated ketones or aldehydes:



T. Cuvigny, H. Normant, *Bull. Soc. Chim. France* **1960,** 515. Use of lithio derivatives instead of Grignard reagents: C. Jutz, *Ber.* **91,** 1867 (1958). Mechanism: A. Pasteur *et al.*, *Bull. Soc. Chim. France* **1965,** 2328.

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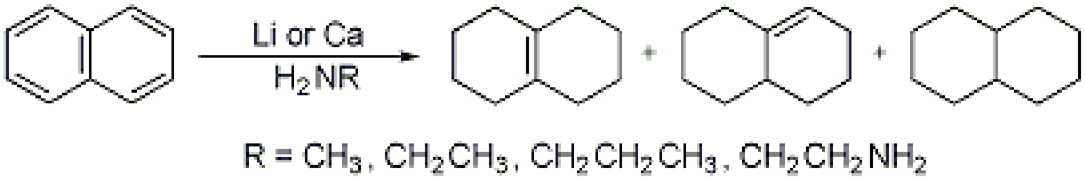
30. Benkeser Reduction

R. A. Benkeser *et al., J. Am. Chem. Soc.* **74,** 5699 (1952); **77,** 3230 (1955).

Reduction of aromatic and olefinic compounds with lithium or calcium and low molecular weight amines to monounsaturated olefins, as well as the fully reduced products. The extent of reduction and selectivity can be controlled by varying the reaction conditions:



Selectivity study: R. A. Benkeser *et al., Tetrahedron Letters* no. 16, 1 (1960). Comparative review: E. M. Kaiser, *Synthesis* **1972,** 391-415 *passim.* Scope and limitations: R. A. Benkeser *et al., J. Org. Chem.* **48,** 2796 (1983). Synthetic applications: C. Eaborn *et al., J. Chem. Soc. Perkin Trans. I* **1975,** 475; R. Eckrich, D. Kuck, *Synlett* **1993,** 344. *Cf.* Birch Reduction.

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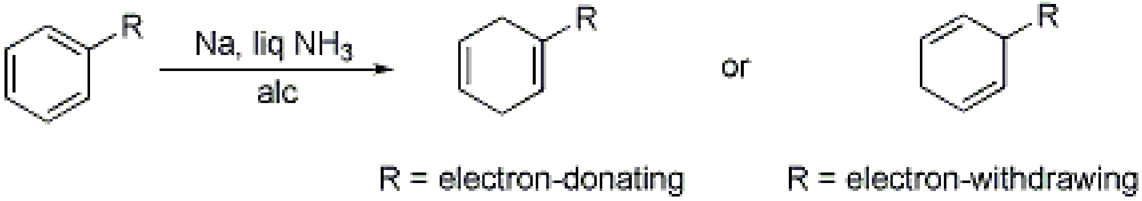
42. Birch Reduction

A. J. Birch, *J. Chem. Soc.* **1944,** 430; **1945,** 809; **1946,** 593; **1947,** 102, 1642, **1949,** 2531.

Reduction of aromatic rings by means of alkali metals in liquid ammonia to give mainly unconjugated dihydro derivatives:



Reviews: A. J. Birch, H. Smith, *Quart. Rev. (London)* **12,** 17 (1958); D. Caine, *Org. React.* **23,** 1-258 (1976); P. W. Rabideau, Z. Marcinow, *ibid.* **42,** 1-334 (1992); J. M. Hook, L. N. Mander, *Nat. Prod. Rep.* **3,** 35-85 (1986); L. N. Mander, *Comp. Org. Syn.* **8,** 489-521 (1991). *Cf.* Benkeser Reduction.

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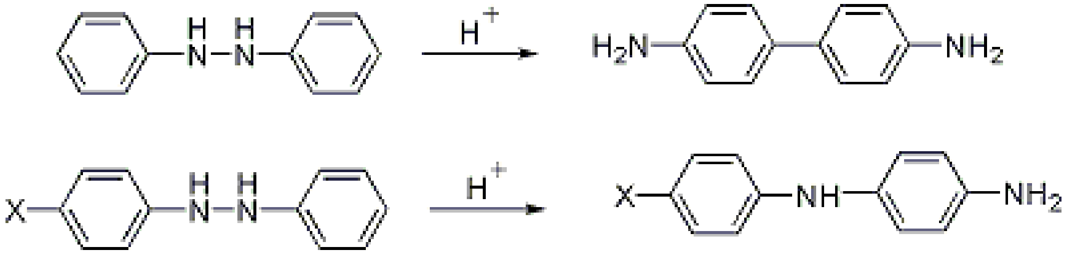
31. **Benzidine Rearrangement;** Semidine Rearrangement

A. W. Hofmann, *Proc. Roy. Soc. London* **12,** 576 (1863); P. Jacobson *et al., Ber.* **26,** 688 (1893).

Acid-catalyzed rearrangement of hydrazobenzenes to 4,4′-diaminobiphenyls. If the hydrazobenzene contains a *para* substituent, then the favored product is *p*-aminodiphenylamine **(Semidine rearrangement)**:



D. L. H. Williams, *Comprehensive Chemical Kinetics* **vol. 13,** C. H. Bamford, C. F. H. Tipper, Eds. (Elsevier, New York, 1972) pp 437-448; R. A. Cox, E. Buncel, *The Chemistry of Hydrazo, Azo and Azoxy Groups*, pt. 2, S. Patai, Ed. (Wiley, New York, 1975) pp 775-807. Mechanistic studies: H. J. Shine *et al., J. Am. Chem. Soc.* **103,** 955 (1981); **104,** 5184 (1982); **106,** 7077 (1984). Synthetic applications: T. Nozoe *et al., Chem. Letters* **1986,** 1577; K. H. Park, J. S. Kang, *J. Org. Chem.* **62,** 3794 (1997).

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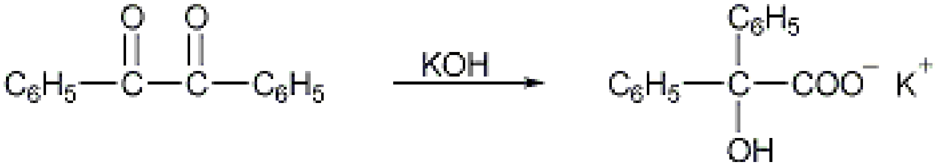
32. **Benzilic Acid Rearrangement** (Benzil-Benzilic Acid Rearrangement)

J. Liebig, *Ann.* **25,** 27 (1838); N. Zinin, *ibid.* **31,** 329 (1939).

Base-induced rearrangement of benzil to benzylic acid *via* phenyl group migration. More commonly perceived to include the migrations of other groups in α-dicarbonyl compounds:



$$C_6H_5-C(=O)-C(=O)-C_6H_5 \xrightarrow{KOH} (C_6H_5)_2C(OH)-COO^- K^+$$

Reviews: S. Selman, J. F. Eastham, *Quart. Rev.* **14,** 221 (1960); D. J. Cram, *Fundamentals of Carbanion Chemistry* (Academic Press, 1965) pp 238-243; G. B. Gill, *Comp. Org. Syn.* **3,** 821-838 (1991).

34. Bergius Process

F. Bergius, *Gas World* **58,** 490 (1913); **GB 18232** (1914).

Formation of petroleum-like hydrocarbons by hydrogenation of coal at high temperatures and pressures (*e.g.*, 450°C and 300 atm) with or without catalysts; production of toluene by subjecting aromatic naphthas to cracking temperatures at 100 atm with a low partial pressure of hydrogen in the presence of a catalyst.

B. T. Brooks, *The Chemistry of the Nonbenzenoid Hydrocarbons* (New York, 1950) p 115; *McGraw-Hill Encyclopedia of Science and Technology* **vol. 2** (New York, 1960) p 166; R. M. Baldwin in *Kirk-Othmer Encyclopedia of Chemical Technology* **vol. 6** (Wiley, New York, 4th ed., 1993) p 569. *Cf.* Fischer-Tropsch Syntheses.

139. **Fischer-Tropsch Syntheses;** Synthol Process**;** Oxo Synthesis

F. Fischer, H. Tropsch, *Ber.* **56,** 2428 (1923).

Synthesis of hydrocarbons, aliphatic alcohols, aldehydes, and ketones by the catalytic hydrogenation of carbon monoxide using enriched synthesis gas from passage of steam over heated coke. The ratio of products varies with conditions. The high pressure **Synthol process** gives mainly oxygenated products and addition of olefins in the presence of cobalt catalyst, **Oxo synthesis,** produces aldehydes. Normal pressure synthesis leads mainly to petroleum-like hydrocarbons.

C. Masters, *Adv. Organomet. Chem.* **17,** 61 (1979); C. K. Rofer-DePoorter, *Chem. Rev.* **31,** 447 (1981); W. A. Herrmann, *Angew. Chem. Int. Ed.* **21,** 117 (1982). *Reviews:* P. M. Maitlis *et al.*, *Chem. Commun.* **1996,** 1-8; H. Schulz, *Appl. Catal.* **186,** 3-12 (1999). *Cf.* Bergius Process; Oxo Process.

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288. Oxo Process (Hydroformylation Reaction)

O. Roelen, **US 2327066** (1943); R. H. Hasek (Eastman), *Org. Chem. Bull.* **27,** No. 1 (1955).

Formation of alcohols from olefins, carbon monoxide and hydrogen in the liquid phase in the presence of catalysts (metallic cobalt compounds such as Raney cobalt or cobalt carbonyls) at 115-190° and high pressures (100-200 atmospheres) in a Fischer-Tropsch-type reaction, *q.v.* The process is sometimes carried out in two stages, the initial stage giving largely aldehydes which are then reduced to the alcohols.

B. Cornils, “Hydroformylation. Oxo Synthesis, Roelen Reaction” in *New Syntheses with Carbon Monoxide*, J. Falbe, Ed. (Springer-Verlag, Berlin, 1980) pp 1-225. Reppe modification (olefin + CO + H_2O + $Fe(CO)_5$): R. Massoudi *et al., J. Am. Chem. Soc.* **109,** 7428 (1987).

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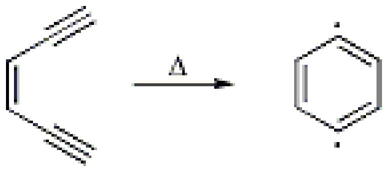
35. Bergman Reaction

R. R. Jones, R. G. Bergman, *J. Am. Chem. Soc.* **94,** 660 (1972); R. G. Bergman, *Accts. Chem. Res.* **6,** 25 (1973).

The cyclization of enediynes to generate 1,4-benzenoid diradicals:

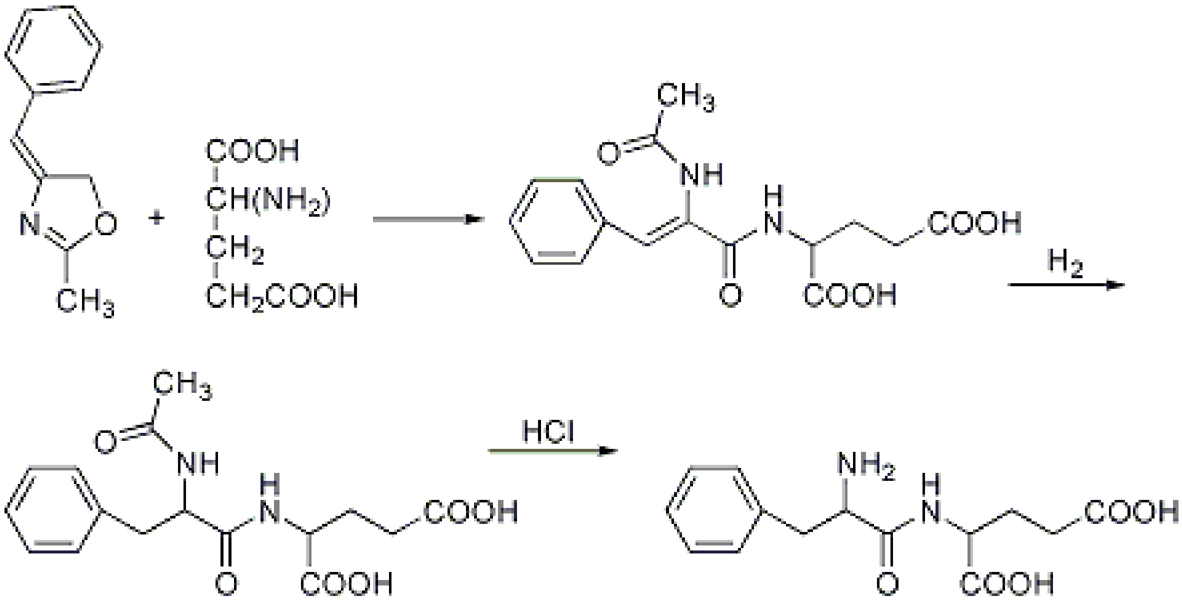


Application to ring annulation: J. W. Grissom *et al., Tetrahedron* **50,** 4635 (1994). Kinetic study: *idem et al., J. Org. Chem.* **59,** 5833 (1994). Reaction energetics: E. Kraka, D. Cremer, *J. Am. Chem. Soc.* **116,** 4929 (1994). Reviews of enediyne chemistry and its application to the development of antitumor agents: K. C. Nicolaou *et al., Proc. Nat. Acad. Sci. USA* **90,** 5881-5888 (1993); K. Nicolaou, *Chem. Brit.* **41,** 33-36, (1994).

36. Bergmann Azlactone Peptide Synthesis

M. Bergmann *et al.*, *Ann.* **449,** 277 (1926).

Conversion of an acetylated amino acid and an aldehyde into an azlactone with an alkylene side chain, reaction with a second amino acid with ring opening and formation of an acylated unsaturated dipeptide, followed by catalytic hydrogenation and hydrolysis to the dipeptide:

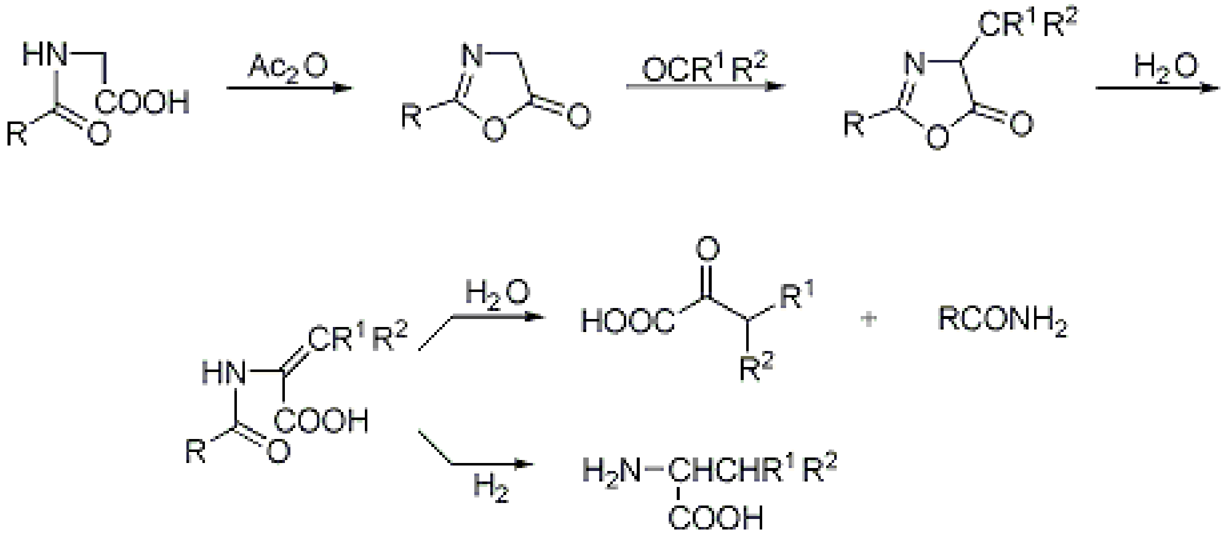


J. S. Fruton, *Advan. Protein Chem.* **V,** 15 (1949); S. Archer in *Amino Acids and Proteins*, D. M. Greenberg, Ed. (Thomas, Springfield, IL, 1951) p 181; H. D. Springall, *The Structural Chemistry of Proteins* (New York, 1954) p 29; E. Baltazzi, *Quart. Rev. (London)* **10,** 235 (1956). *Cf.* Erlenmeyer-Plöchl Azlactone and Amino Acid Synthesis.

121. Erlenmeyer-Plöchl Azlactone and Amino Acid Synthesis

E. Erlenmeyer, *Ann.* **275,** 1 (1893); J. Plöchl, *Ber.* **17,** 1616 (1884).

Formation of azlactones by intramolecular condensation of acylglycines in the presence of acetic anhydride. The reaction of azlactones with carbonyl compounds followed by hydrolysis to the unsaturated α-acylamino acid and by reduction yields the amino acid; drastic hydrolysis gives the α-oxo acid:



C. L. A. Schmidt, *The Chemistry of the Amino Acids and Proteins* (Springfield, IL, 1944) p 54; H. E. Carter, *Org. React.* **3,** 198 (1946); M. Crawford, W. T. Little, *J. Chem. Soc.* **1959,** 729; W. Steglich, *Fortschr. Chem. Forsch.* **12,** 84 (1969); J. Cornforth, D. Ming-hui, *J. Chem. Soc. Perkin Trans. I* **1991,** 2183; A. P. Combs, R. W. Armstrong, *Tetrahedron Letters* **33,** 6419 (1992). *Cf.* Bergmann Azlactone Peptide Synthesis; Perkin Reaction.

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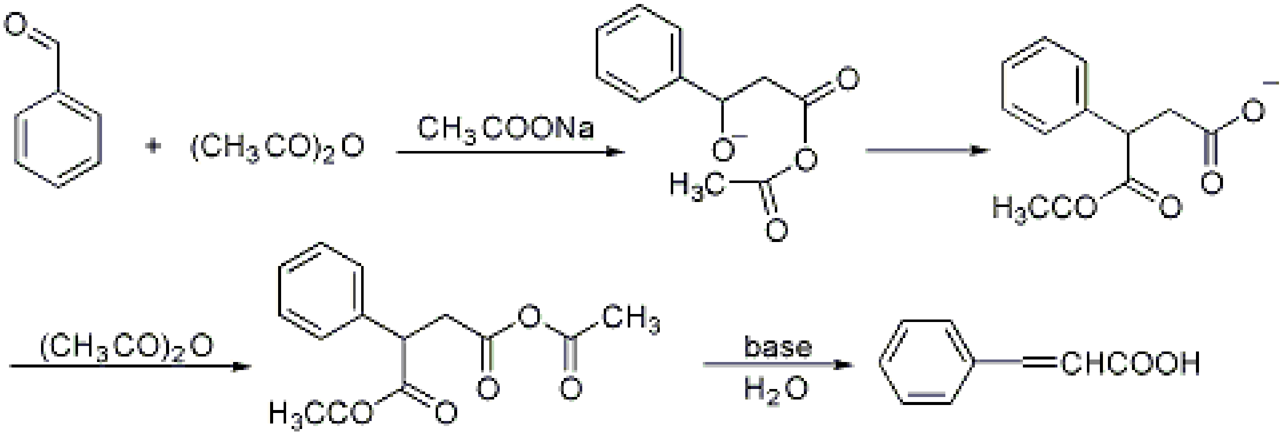
300. Perkin Reaction

W. H. Perkin, *J. Chem. Soc.* **21,** 53, 181 (1868); **31,** 388 (1877).

Formation of α,β-unsaturated carboxylic acids by aldol condensation, *q.v.*, of aromatic aldehydes and acid anhydrides in the presence of an alkali salt of the acid:



Reviews: J. R. Johnson, *Org. React.* **1,** 210 (1942); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed, 1972) pp 660-663; N. Poonia *et al., Bull. Chem. Soc. Japan* **53,** 3338 (1980); T. Rosen, *Comp. Org. Syn.* **2,** 395-408 (1991). Applications: S. Kinastowski, A. Nowacki, *Tetrahedron Letters* **23,** 3723 (1982); W. T. Brady *et al., J. Heterocyclic Chem.* **25,** 969 (1988). *Cf.* Erlenmeyer-Plöchl Azlactone and Amino Acid Synthesis; Stobbe Condensation.

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37. Bergmann Degradation

M. Bergmann, *Science* **79,** 439 (1934).

Stepwise degradation of polypeptides involving benzoylation, conversion to azides and treatment of the azides with benzyl alcohol; this treatment yields, *via* rearrangement to isocyanates, carbobenzoxy compounds which undergo catalytic hydrogenation and hydrolysis to the amide of the degraded peptide:

$$R^1CONHCHRCON_3 \xrightarrow{C_6H_5CH_2OH} R^1CONHCHRNHCOOCH_2C_6H_5 \xrightarrow[H_2O]{H_2}$$

$$R^1CONH_2 + RCHO + CO_2 + C_6H_5CH_3 + NH_3$$

M. Bergmann, L. Zervas, *J. Biol. Chem.* **113,** 341 (1936); H. D. Springall, *The Structural Chemistry of Proteins* (New York, 1954) p 321. *Cf.* Curtius Rearrangement.

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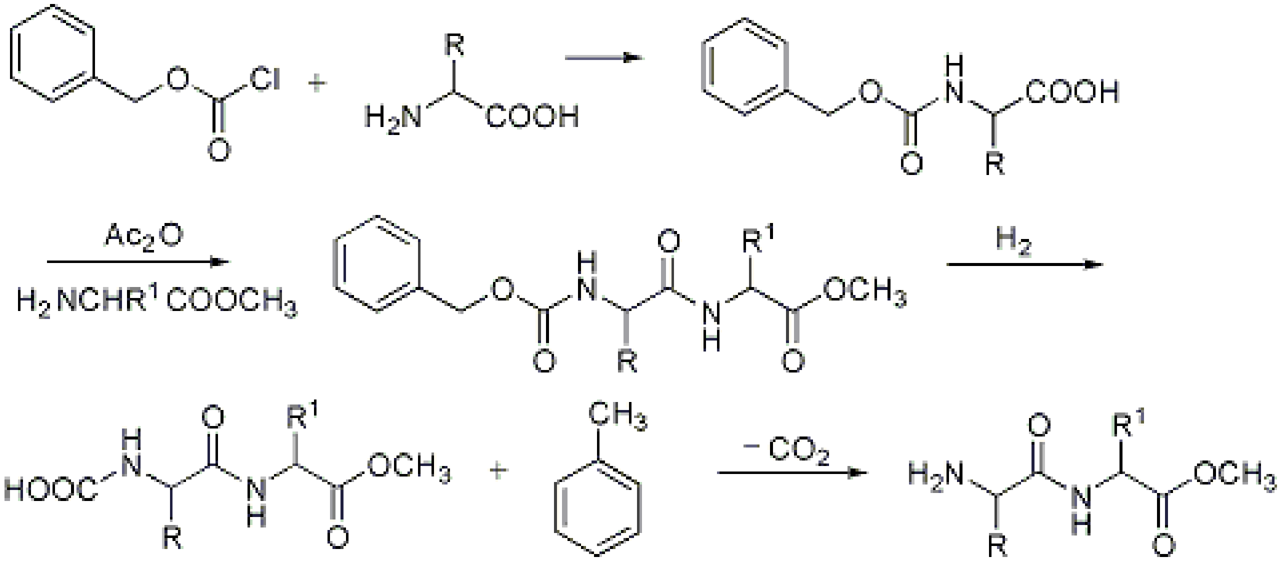
38. Bergmann-Zervas Carbobenzoxy Method

M. Bergmann, L. Zervas, *Ber*. **65,** 1192 (1932).

Formation of the *N*-carbobenzoxy derivative of an amino acid for use in peptide synthesis and liberation of the amino group at an appropriate stage of synthesis by hydrogenolysis of the labile carbon-oxygen bond:



C. L. A. Schmidt, *The Chemistry of the Amino Acids and Proteins* (Thomas, Springfield, IL, 1944) p 262; S. Archer in *Amino Acids and Proteins*, D. M. Greenberg, Ed. (Charles C. Thomas, Springfield, IL, 1951) p 177; G. W. Kenner, *J. Chem. Soc.* **1956,** 3689; T. W. Greene, *Protective Groups in Organic Synthesis* (Wiley, New York, 1981) p 239, *Cf.* Fischer Peptide Synthesis.

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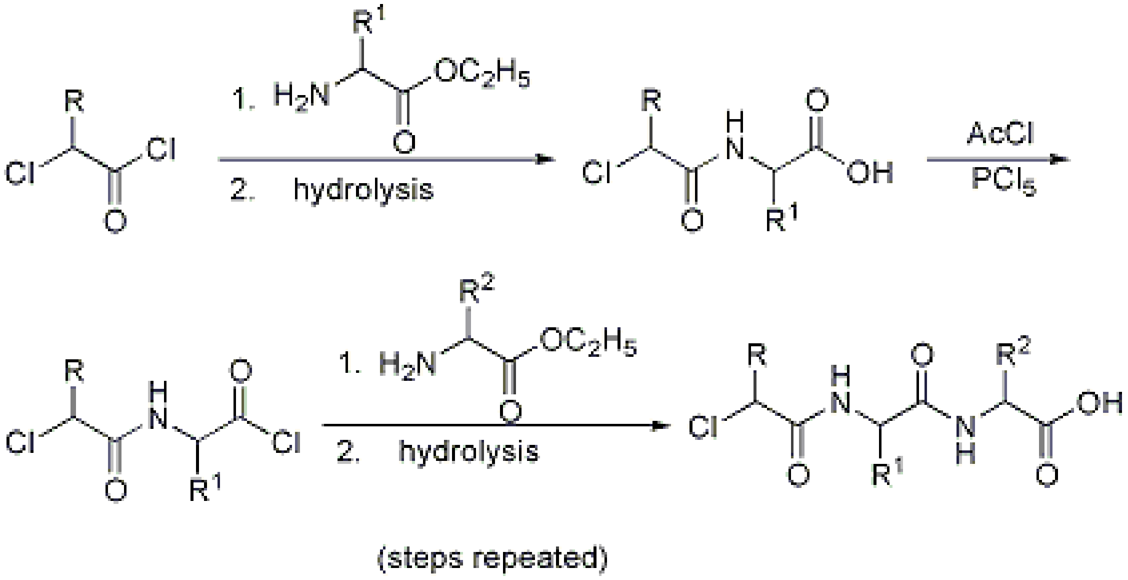
135. Fischer Peptide Synthesis

E. Fischer, *Ber.* **36,** 2982 (1903).

Formation of polypeptides by treatment of an α-chloro or α-bromo acyl chloride with an amino acid ester, hydrolysis to the acid and conversion to a new acid chloride which is again condensed with a second amino acid ester, and so on. The terminal chloride is finally converted to an amino group with ammonia:



C. L. A. Schmidt, *The Chemistry of the Amino Acids and Proteins* (Thomas, Springfield, IL, 1944) p 257; B. Rockland in *Amino Acids and Proteins,* D. M. Greenberg, Ed. (Charles C. Thomas, Springfield, IL, 1951) p 232; H. D. Springall, *The Structural Chemistry of Proteins* (New York, 1954) p 24. *Cf.* Bergmann-Zervas Carbobenzoxy Method.

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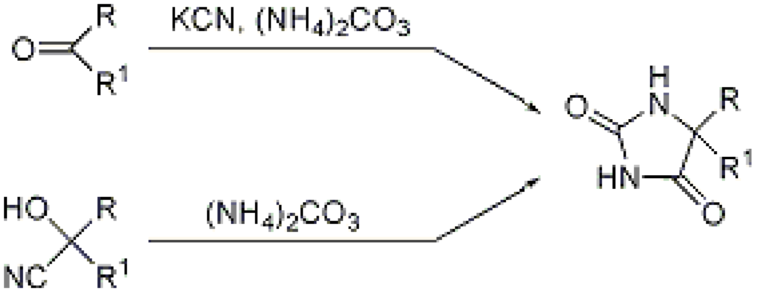
61. Bucherer-Bergs Reaction

H. T. Bucherer, H. T. Fischbeck, *J. Prakt. Chem.* **140,** 69 (1934); H. T. Bucherer, W. Steiner, *ibid.* 291; H. Bergs, **DE 566094** (1929).

Preparation of hydantoin from carbonyl compounds by reaction with potassium cyanide and ammonium carbonate, or from the corresponding cyanohydrin and ammonium carbonate:



E. Ware, *Chem. Rev.* **46,** 422 (1950); A. Rousset *et al.*, *Tetrahedron* **36,** 2649 (1980). Modified conditions: R. Sarges *et al., J. Med. Chem.* **33,** 1859 (1990). Synthetic applications to excitatory amino acids: K.-I. Tanaka *et al.*, *Tetrahedron Asymmetry* **6,** 1641, 2271 (1995); C. Domínguez *et al.*, *ibid.* **8,** 511 (1997); J. Knabe, *Pharmazie* **52,** 912 (1997). *Cf.* Strecker Amino Acid Synthesis; Urech Cyanohydrin Method.

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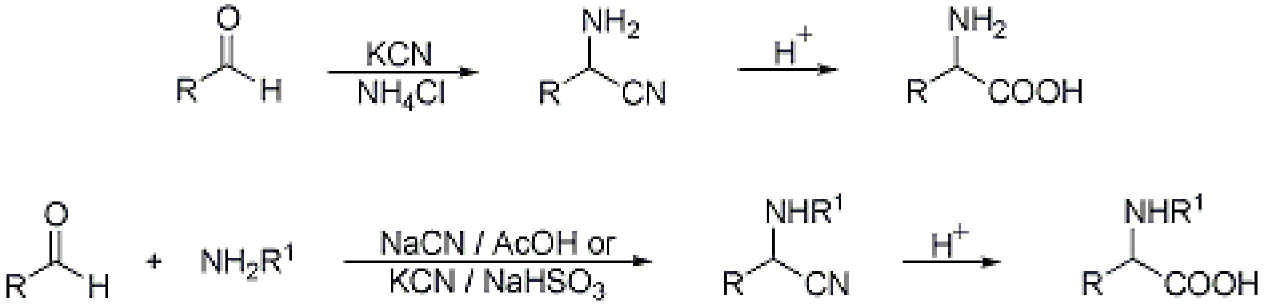
383. Strecker Amino Acid Synthesis

A. Strecker, *Ann.* **75,** 27 (1850); **91,** 349 (1854).

Synthesis of α-amino acids by reaction of aldehydes with ammonia and hydrogen cyanide followed by hydrolysis of the resulting α-aminonitriles. Safer, milder, and more selective reaction conditions have been developed, especially in regard to asymmetric synthesis. The scope of the reaction has been extended to include primary and secondary amines:



Reviews: J. P. Greenstein, M. Winitz, *Chemistry of the Amino Acids* **vol. 3** (New York, 1961) pp 698-700; G. C. Barrett, *Chemistry and Biochemistry of the Amino Acids* (Chapman and Hall, New York, 1985) pp 251, 261. Asymmetric synthesis using enantiopure sulfinimines: F. A. Davis *et al., Tetrahedron Letters* **35,** 9351 (1994); *idem et al., J. Org. Chem.* **61,** 440 (1996). Asymmetric syntheses: M. S. Sigman, E. N. Jacobsen, *J. Am. Chem. Soc.* **120,** 4901 (1998); E. J. Corey, M. J. Grogan, *Organic Letters* **1,** 157 (1999). Review of stereoselective synthesis: R. O. Duthaler, *Tetrahedron* **50,** 1539-1650 (1994); T. K. Chakraborty *et al., ibid.* **51,** 9179-9190 (1995). *Cf.* Bucherer-Bergs Reaction.

405. Urech Cyanohydrin Method; Ultee Cyanohydrin Method

F. Urech, *Ann.* **164,** 225 (1872); A. J. Ultee, *Rec. Trav. Chim.* **28,** 1 (1909).

Cyanohydrin formation by addition of alkali cyanide to the carbonyl group in the presence of acetic acid (Urech method) or by reaction of the carbonyl compound with anhydrous hydrogen cyanide in the presence of a basic catalyst (Ultee cyanohydrin method):

$$RR^1CO + KCN + CH_3COOH \longrightarrow RR^1C(OH)CN + CH_3COO^- K^+$$

$$RR^1CO + HCN \xrightarrow{HO^-} RR^1C(OH)CN$$

A. J. Ultee, *Ber.* **39,** 1856 (1906); *Rec. Trav. Chim.* **28,** 248, 257 (1909); K. N. Welch, G. R. Clemo, *J. Chem. Soc.* **1928,** 2629; H. R. Dittmar, **US 2101823** (1937); V. Migrdichian, *The Chemistry of Organic Cyanogen Compounds* (New York, 1947) p 173; D. T. Mowry, *Chem. Rev.* **42,** 231 (1948); P. Kurz, *Houben-Weyl* **8,** 274 (1952); R. F. B. Cox, R. T. Stormont, *Org. Syn.* **coll. vol. 2,** 7 (1955). *Cf.* Bucherer-Bergs Reaction; Kiliani-Fischer Synthesis.

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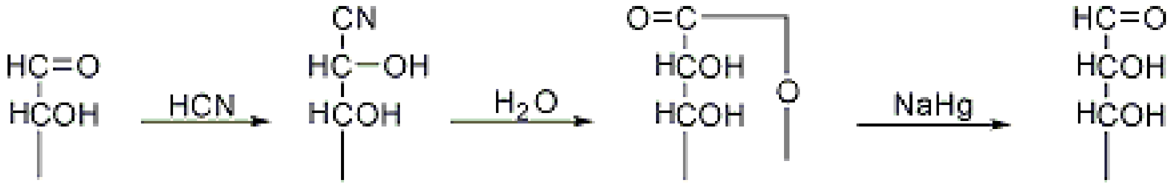
211. Kiliani-Fischer Synthesis

H. Kiliani, *Ber.* **18,** 3066 (1885); E. Fischer, *ibid.* **22,** 2204 (1889).

Extension of the carbon atom chain of aldoses by treatment with cyanide. Hydrolysis of the cyanohydrins followed by reduction of the lactone yields the homologous aldose:



Reviews: C. S. Hudson, *Advan. Carbohyd. Chem.* **1,** 2 (1945); T. Moury, *Chem. Rev.* **42,** 239 (1948); L. Hough, A. C. Richardson, *The Carbohydrates* **1A,** 118 (1972); R. Kuhn, P. Klesse, *Ber.* **91,** 1989 (1958); R. Varma, D. French, *Carbohyd. Res.* **25,** 71 (1972); R. Blazer, T. W. Whalen, *J. Am. Chem. Soc.* **102,** 5082 (1980). Mechanistic study: A. S. Serianni *et al., J. Org. Chem.* **45,** 3329 (1980). Modified conditions: N. Adjé *et al., Tetrahedron Letters* **37,** 5893 (1996). Stereoselective synthesis: J. Roos, F. Effenberger, *Tetrahedron Asymmetry* **10,** 2817 (1999). *Cf.* Urech Cyanohydrin Method.

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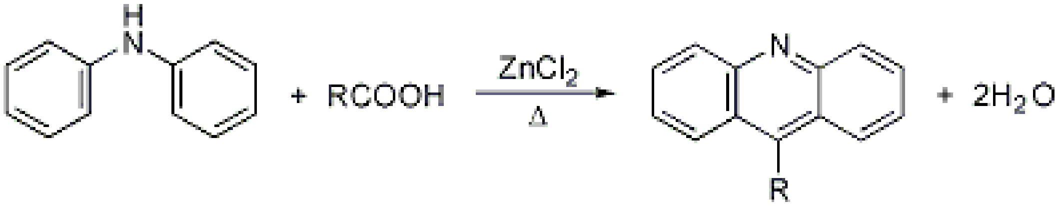
39. Bernthsen Acridine Synthesis

A. Bernthsen, *Ann.* **192,** 1 (1878); **224,** 1 (1884).

Formation of 5-substituted acridines by heating diarylamines in organic acids or anhydrides, usually in the presence of zinc chloride:



A. Albert, *The Acridines* (London, 1951) p 67; A. Albert, *Heterocyclic Compounds* **4,** 502 (1952); N. P. Buu-Hoi *et al., J. Chem. Soc.* **1955,** 1082; R. M. Acheson in *The Chemistry of Heterocyclic Compounds*, A. Weissberger, Ed., *Acridines* (Interscience, New York, 1956) pp 19-25; F. D. Popp, *J. Org. Chem.* **27,** 2658 (1962). Alkyl migration: L. H. Klemm *et al., Heterocyclic Chem.* **29,** 571 (1992).

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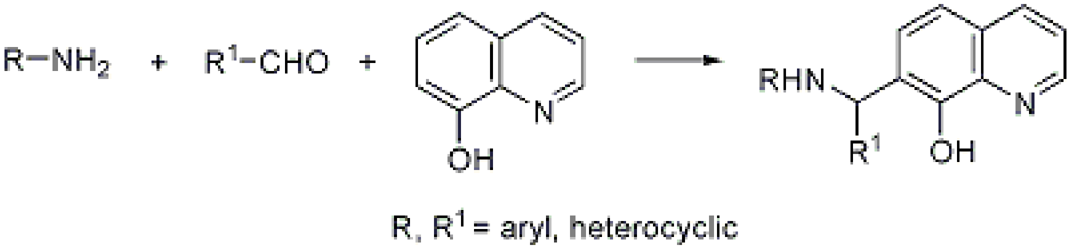
40. Betti Reaction

M. Betti, *Gazz. Chim. Ital.* **30 II,** 301 (1900); **33 II,** 2 (1903); F. Pirrone, *ibid.* **66,** 518 (1936); **67,** 529 (1937).

The reaction of aromatic aldehydes, primary aromatic or heterocyclic amines and phenols leading to α-aminobenzylphenols:



J. P. Phillips, *Chem. Rev.* **56,** 286 (1956); J. P. Phillips, E. M. Barrall, *J. Org. Chem.* **21,** 692 (1956). *Early review:* J. P. Phillips, Leach, *Trans. Kentucky Acad. Sci.* **24**(3-4), 95 (1964). Mechanistic study: H. Möhrle *et al.*, *Chem. Ber.* **107,** 2675 (1974). Stereoselectivity: C. Cardellicchio *et al.*, *Tetrahedron Asymmetry* **9,** 3667 (1998). *Cf.* Mannich Reaction.

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246. Mannich Reaction

C. Mannich, W. Krosche, *Arch. Pharm.* **250,** 647 (1912).

Reaction of compounds having an active hydrogen with non-enolizable aldehydes and ammonia or primary or secondary amines to give aminomethylated products (Mannich bases):

$$(CH_3)_2NH + HCHO + CH_3COCH_3 \longrightarrow (CH_3)_2NCH_2CH_2COCH_3 + H_2O$$

Early reviews: F. F. Blicke, *Org. React.* **1,** 303 (1942); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 654-660. *p*-Substituted phenols as substrates: D. A. Leigh, P. Linnane, *Tetrahedron Letters* **34,** 5639 (1993). In synthesis of vinylphosphonates: H. Krawezyk, *Synth. Commun.* **24,** 2263 (1994). Diastereoselectivity: P. C. B. Page *et al., J. Org. Chem.* **58,** 6902 (1993); enantioselectivity: H. Ishitani *et al., J. Am. Chem. Soc.* **119,** 7153 (1997); *eidem, Tetrahedron Letters* **40,** 2161 (1999); K. Yamada, *Angew. Chem. Int. Ed.* **38,** 3504 (1999). *Reviews:* M. Tramontini, *et al., Tetrahedron* **46,** 1791-1837 (1990); E. F. Kleinman, *Comp. Org. Syn.* **2,** 893-951 (1991); H. Heane, *ibid.* 953-973; L. E. Overman, D. J. Ricca, *ibid.* 1007-1046; M. Arend *et al., Angew. Chem. Int. Ed.* **37,** 1044-1070 (1998). *Cf.* Betti Reaction; Robinson-Schöpf Reaction.

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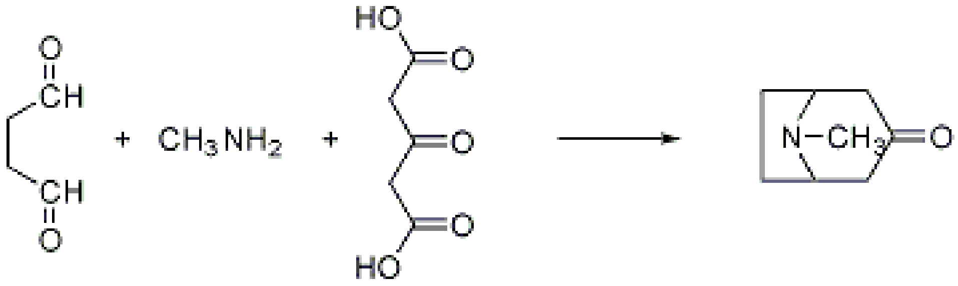
343. Robinson-Schöpf Reaction

R. Robinson, *J. Chem. Soc.* **111,** 762, 876 (1917); C. Schöpf, *Angew. Chem.* **50,** 779, 797 (1937).

Synthesis of tropinones from a dialdehyde, methylamine and acetonedicarboxylic acid:

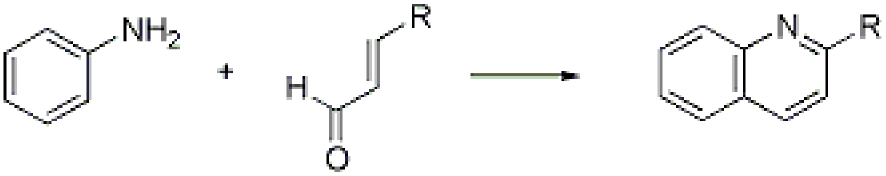


K. Alder *et al., Ann.* **601,** 147 (1956); R. D. Guthrie, J. F. McCarthy, *J. Chem. Soc. C* **1967,** 62; R. V. Stevens, A. W. M. Lee, *J. Am. Chem. Soc.* **101,** 7032 (1979); M. Langlois *et al., Synth. Commun.* **22,** 3115 (1992); T. Jarevang *et al., Acta Chem. Scand.* **52,** 1350 (1998). *Cf.* Mannich Reaction; Petrenko-Kritschenko Piperidone Synthesis.

105. **Doebner-Miller Reaction;** Beyer Method for Quinolines

O. Doebner, W. v. Miller, *Ber.* **16,** 2464 (1883).

Acid-catalyzed synthesis of quinolines from primary aromatic amines and α,β-unsaturated carbonyl compounds. When the latter are prepared *in situ* from two molecules of aldehyde or an aldehyde and methyl ketone, the reaction is known as the **Beyer method for quinolines:**



F. W. Bergström, *Chem. Rev.* **35,** 153 (1944); Y. Ogata *et al., J. Chem. Soc. B* **1969,** 805; G. A. Dauphinee, T. P. Forrest, *J. Chem. Soc. D* **1969,** 327; *Can. J. Chem.* **56,** 632 (1978); C. M. Leir, *J. Org. Chem.* **42,** 911 (1977). Applications: G. K. Lund *et al., J. Chem. Eng. Data* **26,** 227 (1981); W. Buchowiecki *et al., J. Prakt. Chem.* **327,** 1015 (1985); T. Blitzke *et al., ibid.* **335,** 683 (1993). *Cf.* Gould-Jacobs Reaction; Knorr Quinoline Synthesis.

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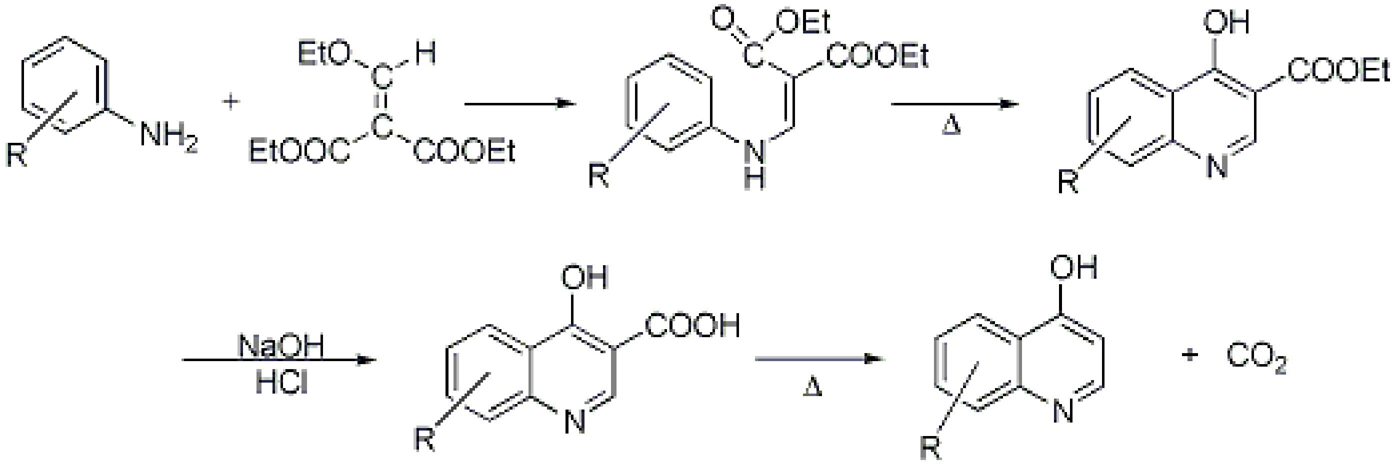
160. Gould-Jacobs Reaction

R. G. Gould, W. A. Jacobs, *J. Am. Chem. Soc.* **61,** 2890 (1939).

Synthesis of 4-hydroxyquinolines from anilines and diethyl ethoxymalonate *via* cyclization of the intermediate anilinomethylenemalonate followed by hydrolysis and decarboxylation:



R. H. Reitsema, *Chem. Rev.* **43,** 53 (1948); R. C. Elderfield, *Heterocyclic Compounds* **4,** 38 (1952); C. C. Price, R. N. Roberts, *Org. Syn.* **coll. vol. III,** 272 (New York, 1955); D. G. Markees, L. S. Schwab, *Helv. Chim. Acta* **55,** 1319 (1972); R. Albrecht, G. A. Hoyer, *Ber.* **105,** 3118 (1972); J. M. Barker *et al.*, *J. Chem. Res. (S)* **1980,** 4; A. Pipaud *et al.*, *Synth. Commun.* **27,** 1727 (1997); C. G. Dave, R. D. Shah, *Heterocycles* **51,** 1819 (1999). *Cf.* Doebner-Miller Reaction; Knorr Quinoline Synthesis.

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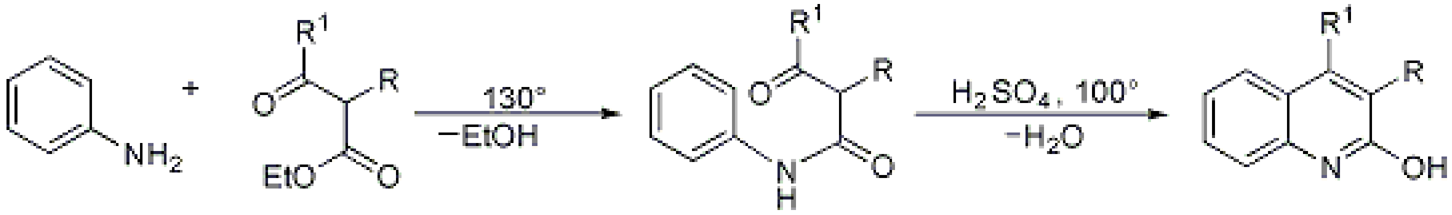
217. Knorr Quinoline Synthesis

L. Knorr, *Ann.* **236,** 69 (1886); **245,** 357, 378 (1888).

Formation of α-hydroxyquinolines from β-ketoesters and arylamines above 100°. The intermediate anilide undergoes cyclization by dehydration with concentrated sulfuric acid:



F. W. Bergstrom, *Chem. Rev.* **35,** 157 (1944); C. R. Hauser, G. A. Reynolds, *J. Am. Chem. Soc.* **70,** 2402 (1948); *Org. Syn.* **coll. vol. III,** 593 (1955); R. C. Elderfield, *Heterocyclic Compounds* **4,** 30 (1952); A. J. Hodgkinson, B. Staskum, *J. Org. Chem.* **34,** 1709 (1969). Synthetic application: P. López-Alvarado *et al., Synthesis* **1998,** 186. *Cf.* Doebner-Miller Reaction; Gould-Jacobs Reaction.

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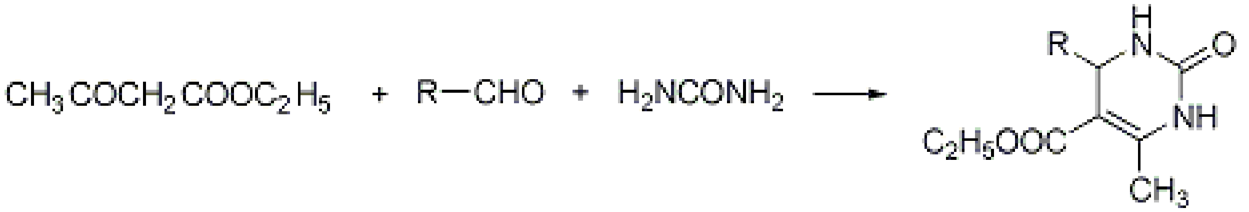
41. Biginelli Reaction

P. Biginelli, *Ber.* **24,** 1317, 2962 (1891); **26,** 447 (1893).

Synthesis of tetrahydropyrimidinones by the acid-catalyzed condensation of an aldehyde, a β-keto ester and urea:



H. E. Zaugg, W. B. Martin, *Org. React.* **14,** 88 (1965); D. J. Brown, *The Pyrimidines* (Wiley, New York, 1962) p 440; *ibid.*, Suppl. I, **1970,** p 326, F. Sweet, Y. Fissekis, *J. Am. Chem. Soc.* **95,** 8741 (1973). Synthetic applications: M. V. Fernandez *et al., Heterocycles* **27,** 2133 (1988); K. Singh *et al., Tetrahedron* **55,** 12873 (1999); A. S. Franklin *et al., J. Org. Chem.* **64,** 1512 (1999). Modified conditions: C. O. Kappe *et al., Synthesis* **1999,** 1799; J. Lu, H. Ma. *Synlett* **2000,** 63.

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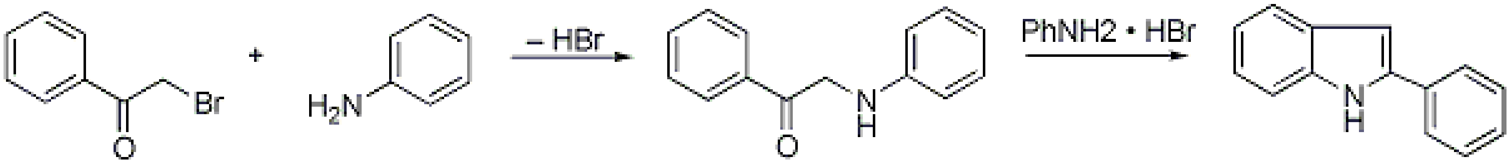
43. Bischler-Möhlau Indole Synthesis

A. Bischler *et al., Ber.* **25,** 2860 (1892); **26,** 1336 (1893); R. Möhlau, *ibid.* **14,** 171 (1881); **15,** 2480 (1882); E. Fischer, T. Schmitt, *ibid.* **21,** 1071 (1888).

Formation of 2-substituted indoles by heating ω-halogeno- or ω-hydroxy- ketones with excess aniline *via* cyclization of the intermediate 2-arylaminoketone:



P. L. Julian *et al., Heterocyclic Compounds* **3,** 22 (1952); R. J. Sundberg, *The Chemistry of Indoles* (Academic Press, New York, 1970) p 164; R. K. Brown in *The Chemistry of Heterocyclic Compounds,* A. Weissberger, E. C. Taylor, Eds., *Indoles, Part I*, W. J. Houlihan, Ed. (Wiley, New York, 1972) p 317; J. R. Henry, J. H. Dodd, *Tetrahedron Letters* **38,** 8763 (1998).

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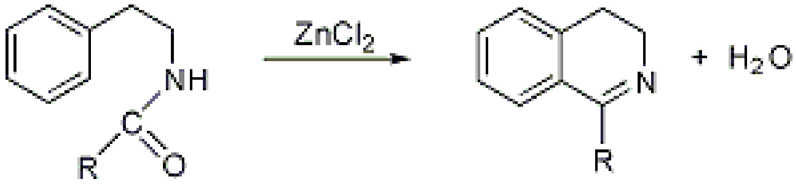
44. Bischler-Napieralski Reaction

A. Bischler, B. Napieralski, *Ber.* **26,** 1903 (1893).

Cyclodehydration of β-phenethylamides to 3,4-dihydroisoquinoline derivatives by means of condensing agents such as phosphorous pentoxide or zinc chloride:



W. M. Whaley, T. R. Govindachari, *Org. React.* **6,** 74 (1951); T. Kametani *et al., Tetrahedron* **27,** 5367 (1971); G. Fodor *et al., Angew. Chem. Int. Ed.* **11,** 919 (1972); G. Fodor, S. Nagubandi, *Tetrahedron* **36,** 1279 (1980); *eidem, Heterocycles* **15,** 165 (1981). Review of enantioselective modifications: M. O. Rozwadowska, *ibid.* **39,** 903-931 (1994). *Cf.* Bradsher Reaction; Pechmann Condensation; Pictet-Gams Isoquinoline Synthesis; Pictet-Hubert Reaction; Skraup Reaction.

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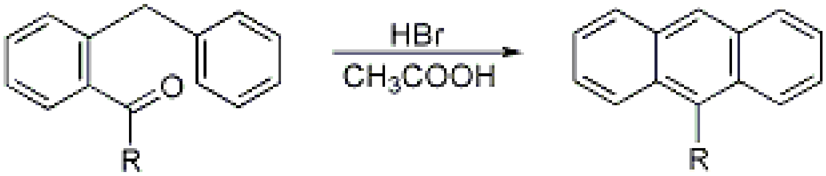
59. Bradsher Reaction

C. K. Bradsher, *J. Am. Chem. Soc.* **62,** 486 (1940).

Acid-catalyzed cyclodehydration of *o*-acyldiarylmethanes to anthracene derivatives:



Extension to an *o*-acyldiaryl ether: H. Ishibashi *et al., Tetrahedron* **50,** 10215 (1994). Application: T. Yamato *et al., J. Chem. Soc. Perkins Trans. 1* **1997,** 1193. *Review:* C. K. Bradsher, *Chem. Rev.* **87,** 1277-1297 (1987). *Cf.* Bischler-Napieralski Reaction.

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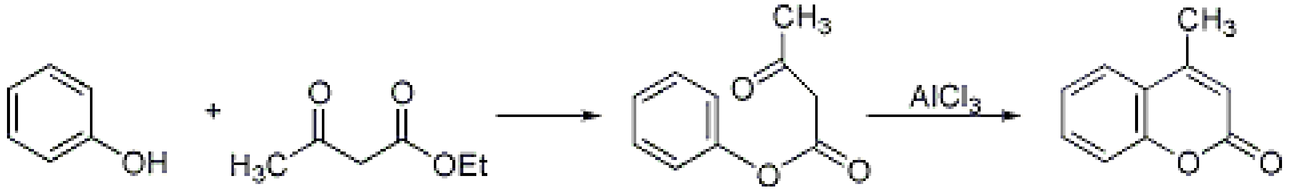
295. Pechmann Condensation

H. v. Pechmann, C. Duisberg, *Ber.* **16,** 2119 (1883).

Synthesis of coumarins by condensation of phenols with β-keto esters in the presence of Lewis acid catalysts:



Early reviews: S. Sethna, *Chem. Rev.* **36,** 10 (1945); S. Sethna, R. Phadke, *Org. React.* **7,** 1 (1953). T. Kappe, E. Ziegler, *Org. Prep. Proced.* **1,** 61 (1969); T. Kappe, C. Mayer, *Synthesis* **1981,** 524; A. G. Osborne, *Tetrahedron* **37,** 2021 (1981); D. H. Hau *et al.*, *Synlett.* **1990,** 233; T-S. Li *et al.*, *J. Chem. Res.* **1998,** 39. Modified conditions: J. E. T. Corrie, *J. Chem. Soc. Perkin Trans. I* **1990,** 2151; D. H. Hua *et al.*, *J. Org. Chem.* **57,** 399 (1992). *Cf.* Bischler-Napieralski Reaction; Simonis Chromone Cyclization.

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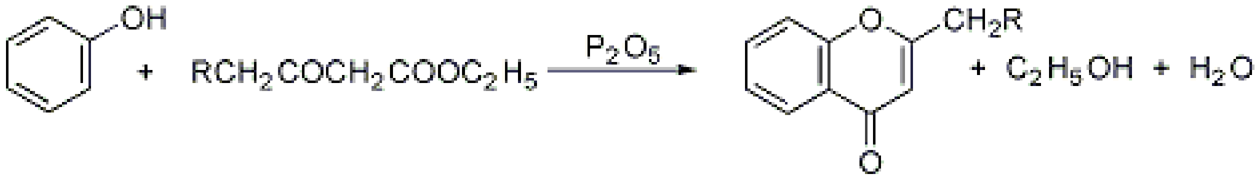
369. Simonis Chromone Cyclization

E. Petschek, H. Simonis, *Ber*. **46,** 2014 (1913).

Formation of chromones from phenol and β-keto esters in the presence of phosphorus pentoxide, phosphorus oxychloride or sulfuric acid. Coumarins may also form (Pechmann condensation, *q.v.*):



Reviews: S. M. Sethna, N. M. Shah, *Chem. Rev.* **36,** 14 (1945); S. M. Sethna, R. Phadke, *Org. React.* **7,** 15 (1953); R. N. Lacey, *J. Chem. Soc.* **1954,** 854; O. Dann, G. Illing, *Ann.* **605,** 158 (1957); S. F. Tan, *Aust. J. Chem.* **25,** 1367 (1972).

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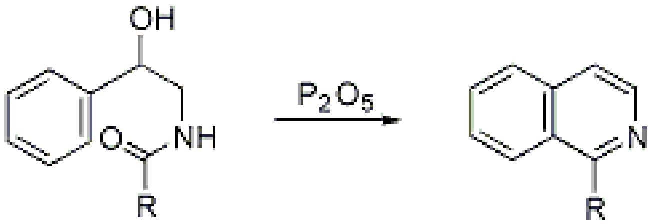
308. Pictet-Gams Isoquinoline Synthesis

A. Pictet, A. Gams, *Ber.* **43,** 2384 (1910).

Formation of isoquinolines by cyclization of acylated aminomethyl phenyl carbinols or their ethers with phosphorus pentoxide in toluene or xylene:



Reviews: W. M. Whaley, T. R. Govindachari, *Org. React.* **6,** 151 (1951); W. Y. Gensler, *Heterocyclic Compounds* **4,** 361 (1952); W. Herz, L. Tsai, *J. Am. Chem. Soc.* **77,** 3529 (1955); A. A. Bindra *et al., Tetrahedron Letters* **1968,** 2677; N. Ardabilchi *et al., J. Chem. Soc. Perkin Trans. I* **1979,** 539. *Cf.* Bischler-Napieralski Reaction.

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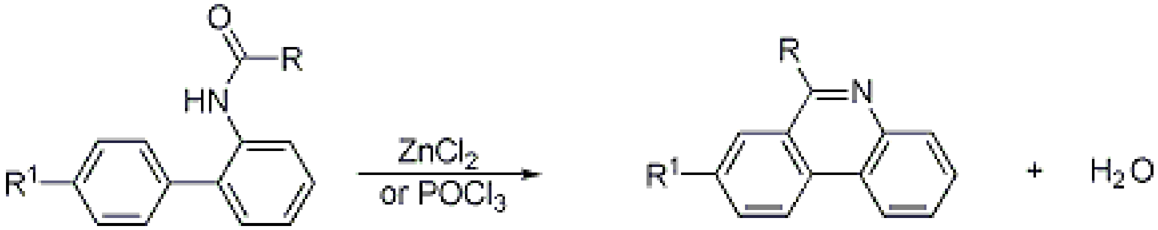
309. Pictet-Hubert Reaction; Morgan-Walls Reaction

A. Pictet, A. Hubert, *Ber*. **29,** 1182 (1896); C. T. Morgan, L. P. Walls, *J. Chem. Soc*. **1931,** 2447; **1932,** 2225.

Phenanthridine cyclization by dehydrative ring closure of acyl-*o*-aminobiphenyls on heating with zinc chloride at 250-300° (Pictet-Hubert), or with phosphorus oxychloride in boiling nitrobenzene (Morgan-Walls):



L. P. Walls, *J. Chem. Soc*. **1945,** 294; J. Cymerman, W. F. Short, *ibid*. **1949,** 703; R. S. Theobald, K. Schofield, *Chem. Rev*. **46,** 175 (1950); L. P. Walls, *Heterocyclic Compounds* **4,** 574 (1952); J. Eisch, H. Gilman, *Chem. Rev*. **57,** 525 (1957); N. Campbell, *Chemistry of Carbon Compounds* **IVA,** 691 (1957). *Cf*. Bischler-Napieralski Reaction.

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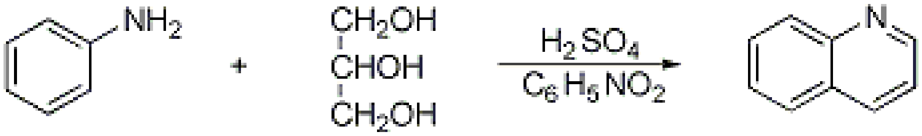
370. Skraup Reaction

Z. H. Skraup, *Ber.* **13,** 2086 (1880).

Synthesis of quinolines from aromatic amines, glycerol, an oxidizing agent and sulfuric acid:



Early review: R. H. F. Manske, M. Kulka, *Org. React.* **7,** 80-99 (1953). G. M. Badger *et al., Aust. J. Chem.* **16,** 814, 828 (1963); M. Wahren, *Tetrahedron* **20,** 2773 (1964); E. B. Mullock *et al., J. Chem. Soc. C* **1970,** 829; N. P. Buu-Hoi *et al., J. Chem. Soc. Perkin Trans. I* **1972,** 260, 263. *Cf.* Bischler-Napieralski Reaction.

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45. **Blaise Ketone Synthesis;** Blaise-Maire Reaction

E. E. Blaise, A. Koehler, *Bull. Soc. Chim.* [4] **7,** 215 (1910); E. E. Blaise, M. Maire, *Compt. Rend.* **145,** 73 (1907); E. E. Blaise, *Bull. Soc. Chim.* [4] **9,** 1 (1911).

Formation of ketones by treatment of acid halides with organozinc compounds; the use of β-hydroxy carbonyl chlorides to give β-hydroxy ketones, convertible into α,β-unsaturated ketones in boiling dilute sulfuric acid, is known as the **Blaise-Maire reaction:**

$$\mathrm{RZnCl} + \mathrm{R^1COCl} \longrightarrow \mathrm{RCOR^1} + \mathrm{ZnCl_2}$$

$$\mathrm{AcOCH_2CHRCOCl} + \mathrm{R^1ZnCl} \longrightarrow \mathrm{AcOCH_2CHRCOR^1} \longrightarrow \mathrm{HOCH_2CHRCOR^1} \longrightarrow \mathrm{H_2C{=}CRCOR^1}$$

J. Cason, *Chem. Rev.* **40,** 17 (1947); D. A. Shirley, *Org. React.* **8,** 29 (1954).

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56. Bouveault-Blanc Reduction

L. Bouveault, G. Blanc, *Compt. Rend.* **136,** 1676 (1903); *Bull. Soc. Chim. France* [3] **31,** 666 (1904).

Formation of alcohols by reduction of esters with sodium and an alcohol:

$$RCOOCH_3 \xrightarrow[R^1OH]{Na} RCH_2OH + CH_3OH$$

H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) p 150.

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47. **Blanc Reaction** (Chloromethylation)

G. Blanc, *Bull. Soc. Chim. France* [4], **33,** 313 (1923).

Introduction of the chloromethyl group into aromatic rings on treatment with formaldehyde and hydrogen chloride in the presence of zinc chloride:

$$\mathrm{ArH} + \mathrm{CH_2O} + \mathrm{HCl} \xrightarrow{\mathrm{ZnCl_2}} \mathrm{ArCH_2Cl}$$

Reviews: R. C. Fuson, C. H. McKeever, *Org. React.* **1,** 63 (1942); G. Olah, W. S. Tolgyesi, in *Friedel-Crafts and Related Reactions* **vol. II,** Part 2, G. Olah, Ed. (Interscience, New York, 1963) pp 659-784. *Cf.* Quelet Reaction.

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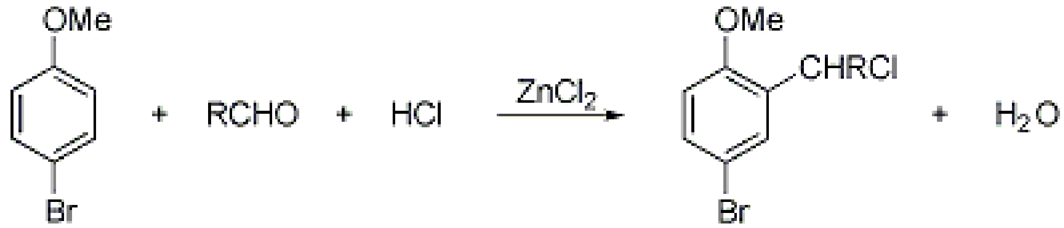
326. Quelet Reaction

R. Quelet, *Compt. Rend.* **195,** 155 (1932).

Passage of dry hydrochloric acid through a solution in ligroin of a phenolic ether and an aliphatic aldehyde in the presence or absence of a dehydration catalyst to yield α-chloroalkyl derivatives by substitution in the *para* position to the ether group or in the *ortho* position in *para*-substituted phenolic ethers:

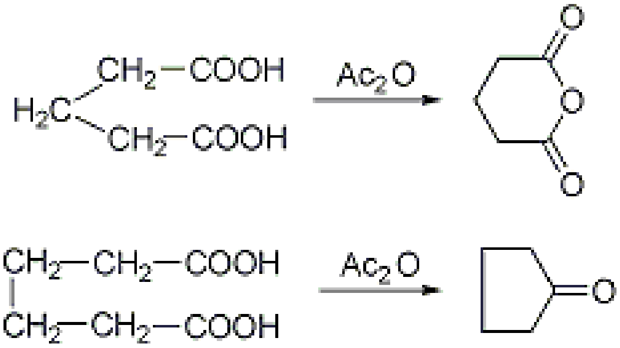


R. Quelet, *ibid.* **196,** 1411 (1933); **198,** 102 (1934); **199,** 150 (1934); **202,** 956 (1936); *Bull. Soc. Chim. France* **7,** 196 (1940); U. Neda, R. Oda, *J. Soc. Chem. Ind. Japan* **47,** 565 (1944). *Cf.* Blanc (Chloromethylation) Reaction.

48. Blanc Reaction-Blanc Rule

H. G. Blanc, *Compt. Rend.* **144,** 1356 (1907).

Cyclization of dicarboxylic acids on heating with acetic anhydride to give either cyclic anhydrides or ketones depending on the respective positions of the carboxyl groups; 1,4- and 1,5-diacids yield anhydrides, while diacids in which the carboxy groups are in 1,6 or further removed positions yield ketones:



H. Kwart, K. King in *The Chemistry of Carboxylic Acids and Esters*, J. Patai, Ed. (Interscience, London, 1969) p 362; K. D. Bode, *Houben-Weyl* **7/2,** 640 (1973). *Cf.* Ruzicka Large Ring Synthesis.

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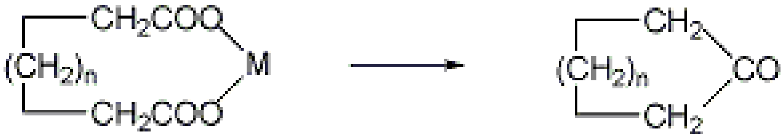
349. Ruzicka Large Ring Synthesis

L. Ruzicka *et al.*, *Helv. Chim. Acta* **9,** 249, 339, 389, 499 (1926).

Formation of large ring alicyclic ketones from dicarboxylic acids by thermal decomposition of salts with metals of the second and fourth groups of the periodic table (Ca, Th, Ce):



L. Ruzicka, *Chem. & Ind. (London)* **54,** 2 (1935); H. Gilman, *Organic Chemistry* **vol. 1** (New York, 1943) p 78; K. Ziegler, *Houben-Weyl* **4/2,** 754 (1955). *Cf.* Blanc Reaction.

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50. Bodroux Reaction

F. Bodroux, *Bull. Soc. Chim. France* **33,** 831 (1905), **35,** 519 (1906); **1,** 912 (1907); *Compt. Rend.* **138,** 1427 (1904); **140,** 1108 (1905); **142,** 401 (1906).

Formation of substituted amides by reaction of a simple aliphatic or aromatic ester with an aminomagnesium halide obtained by treatment of a primary or secondary amine with a Grignard reagent at room temperature:

$$\mathrm{RCOOR^1} + \mathrm{IMgNHR^2} \longrightarrow \mathrm{IMgOCR(OR^1)NHR^2} \xrightarrow{\mathrm{IMgNHR^2}} \mathrm{RCONHR^2}$$

H. L. Bassett, C. R. Thomas, *J. Chem. Soc.* **1954,** 1188; K. Nützel, *Houben-Weyl* **13/2a,** 278 (1973).

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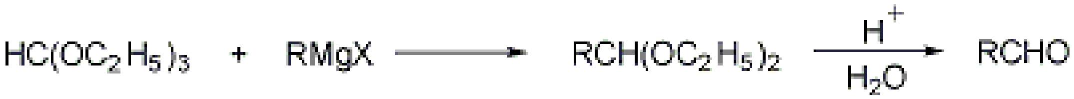
49. Bodroux-Chichibabin Aldehyde Synthesis

F. Bodroux, *Compt. Rend.* **138,** 92 (1904); A. E. Chichibabin, *Ber*. **37,** 186, 850 (1904).

Formation of aldehydes by treatment of orthoformates with Grignard reagents:



$HC(OC_2H_5)_3 + RMgX \longrightarrow RCH(OC_2H_5)_2 \xrightarrow[H_2O]{H^+} RCHO$

L. I. Smith *et al., J. Org. Chem.* **6,** 437, 489 (1941); H. W. Post, *The Chemistry of the Aliphatic Orthoesters* (New York, 1943) p 96; H. Meerwein, *Houben-Weyl* **6/3,** 243 (1965); R. H. DeWolfe, *Carboxylic Orthoacid Derivatives* (Academic Press, New York, 1970) p 224. *Cf.* Bouveault Aldehyde Synthesis.

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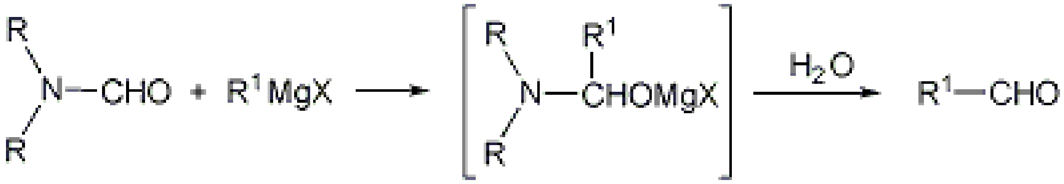
55. Bouveault Aldehyde Synthesis

L. Bouveault, *Bull. Soc. Chim. France* **31,** 1306, 1322 (1904).

Action of Grignard or organic lithium reagents on *N*,*N*-disubstituted formamides yields the homologous aldehydes:



L. I. Smith, J. Nichols, *J. Org. Chem.* **6,** 489 (1941); J. Sicé *J. Am. Chem. Soc.* **75,** 3697 (1953); E. R. H. Jones *et al., J. Chem. Soc.* **1958,** 1054. Use of lithio derivatives instead of Grignard reagents: E. A. Evans, *Chem. & Ind. (London)* **1957,** 1596. Synthetic applications using modified conditions: C. Pétrier *et al., Tetrahedron Letters* **23,** 3361 (1982); J. Einhorn, J. L. Luche, *ibid.* **27,** 1791 (1986); H. Meier, H. Aust, *J. Prakt. Chem.* **341,** 466 (1999). *Cf.* Bodroux-Chichibabin Aldehyde Synthesis.

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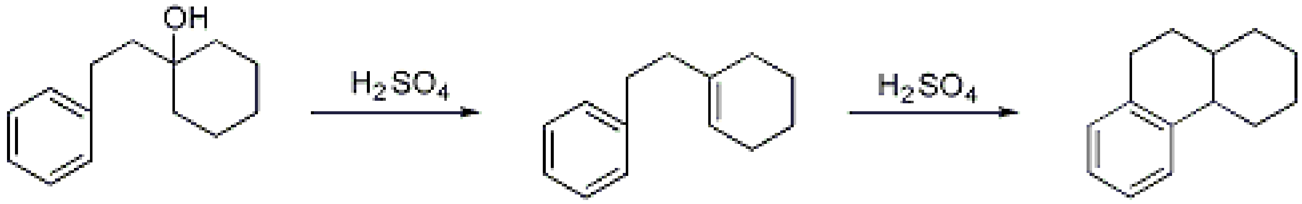
51. Bogert-Cook Synthesis

M. T. Bogert, *Science* **77,** 289 (1933); J. W. Cook, C. L. Hewett, *J. Chem. Soc.* **1933,** 1098.

Condensation of β-phenylethylmagnesium bromide with cyclohexanones followed by cyclodehydration of the tertiary alcohol with concentrated sulfuric acid with formation of octahydrophenanthrene derivatives and a small amount of spiran:



L. F. Fieser, M. Fieser, *Natural Products Related to Phenanthrene* (New York, 1949) p 90; C. Schmidt *et al., Can. J. Chem.* **51,** 3620 (1973). For a general approach to the synthesis of phenanthrenoid compounds, *see* D. A. Evans *et al., J. Am. Chem. Soc.* **99,** 7083 (1977).

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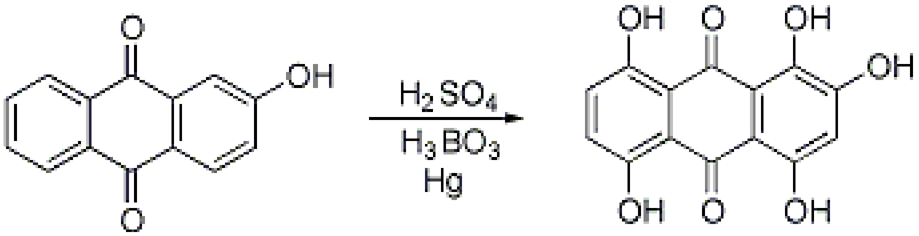
52. Bohn-Schmidt Reaction

R. Bohn, **DE 46654** (1889); R. E. Schmidt, **DE 60855** (1891).

Hydroxylation of anthraquinones containing at least one hydroxyl group by treatment with fuming sulfuric acid or sulfuric acid and boric acid in the presence of a catalyst such as mercury:

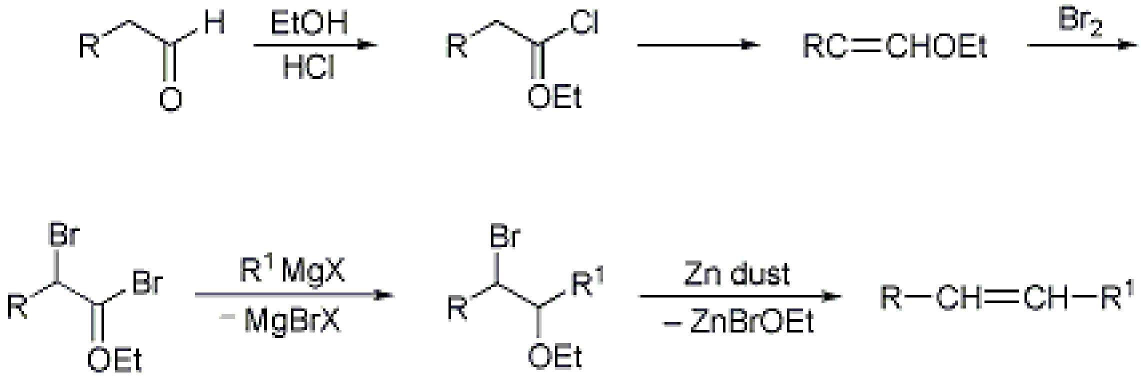


Reviews: M. Phillips, *Chem. Rev.* **6,** 168 (1929); Fieser, Fieser, *Organic Chemistry* (New York, 1956) p 903. Studies and proposed mechanism: J. Winkler, W. Jenny, *Helv. Chim. Acta* **48,** 119 (1965); B. R. Dhruva *et al., Indian J. Chem.* **14 (B),** 622 (1976).

53. Boord Olefin Synthesis

L. C. Swallen, C. E. Boord, *J. Am. Chem. Soc.* **52,** 651 (1930); **53,** 1505 (1931); **55,** 3293 (1933); H. B. Dykstra *et al., ibid.* **52,** 3396 (1930).

Regiospecific synthesis of olefins from aldehydes and Grignard reagents by zinc induced reductive elimination of halogen and alkoxy groups:



C. Niemann, C. D. Wagner, *J. Org. Chem.* **7,** 227 (1942); P. Bandart, *Bull. Soc. Chim.* **11,** 336 (1944); L. Crombie, *Quart. Rev. (London)* **6,** 131 (1952); M. Schlosser, *Houben-Weyl* **5/1b,** 213 (1972). Application to taxanes: J. S. Yadav *et al. Tetrahedron Letters* **35,** 3617 (1994); P. H. Beusker *et al., Eur. J. Org. Chem.* **1998,** 2483.

200. Hunsdiecker Reaction (Borodine Reaction)

C. Hunsdiecker *et al.*, **US 2176181** (1939); H. Hunsdiecker, C. Hunsdiecker, *Ber.* **75,** 291 (1942); A. Borodine, *Ann.* **119,** 121 (1861).

Synthesis of organic halides by thermal decarboxylation of silver salts of the corresponding carboxylic acids in the presence of halogens:

$$RCOOAg \; + \; X_2 \xrightarrow{\Delta} RX \; + \; CO_2 \; + \; AgX$$

R. G. Johnson, R. K. Ingham, *Chem. Rev.* **56,** 219 (1956); C. V. Wilson, *Org. React.* **9,** 341 (1957); S. J. Cristol, W. C. Firth, Jr., *J. Org. Chem.* **26,** 280 (1961); F. F. Knapp, Jr., *Steroids* **33,** 245 (1979); A. I. Meyers, M. P. Fleming, *J. Org. Chem.* **44,** 3405 (1979). Modified catalysis by metal salt pool: S. Chowdhury, S. Roy, *Tetrahedron Letters* **37,** 2623 (1996); D. Naskar, S. Roy, *J. Chem. Soc. Perkin Trans. I* **1999,** 2436; *eidem, Tetrahedron* **56,** 1369 (2000). *Cf.* Kochi Reaction; Simonini Reaction.

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219. Kochi Reaction

J. K. Kochi, *J. Am. Chem. Soc.* **87,** 2500 (1965).

Synthesis of organic chlorides by decarboxylation of carboxylic acids in the presence of lead tetraacetate and lithium chloride:

$$RCOOH + Pb(OAc)_4 \longrightarrow RCOOPb(OAc)_3 + AcOH \xrightarrow[\Delta]{LiCl} RCl + CO_2$$

R. A. Sheldon, J. K. Kochi, *Org. React.* **19,** 279 (1972); M. Mannier, J. P. Aycard, *Can. J. Chem.* **57,** 1257 (1979). *Cf.* Hunsdiecker Reaction.

368. Simonini Reaction

A. Simonini, *Monatsh.* **13,** 320 (1892); **14,** 81 (1893).

The preparation of aliphatic esters by the reaction of the silver salt of a carboxylic acid with iodine:

$$2RCOOAg + I_2 \xrightarrow{\Delta} RCOOR + 2AgI + CO_2$$

H. Wieland, F. G. Fischer, *Ann.* **446,** 49 (1926); J. Kleinberg, *Chem. Rev.* **40,** 381 (1947); R. G. Johnson, R. K. Ingham, *ibid.* **56,** 259 (1956); C. V. Wilson, *Org. React.* **9,** 332 (1957); N. J. Bunce, M. Hadley, *Can. J. Chem.* **54,** 2612 (1976). *Cf.* Hunsdiecker Reaction.

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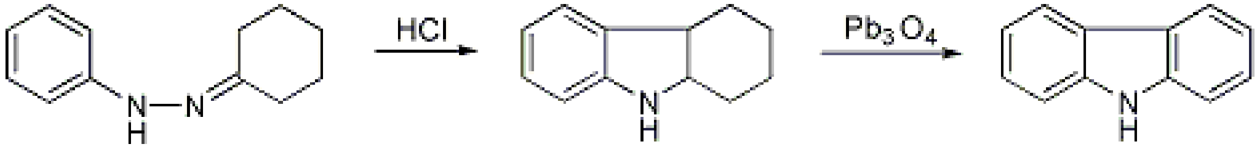
54. Borsche-Drechsel Cyclization

E. Drechsel, *J. Prakt. Chem.* **38**(2), 69 (1858); W. Borsche, M. Feise, *Ber.* **20,** 378 (1904).

Formation of carbazole by acid-catalyzed rearrangement of cyclohexanone phenylhydrazone to tetrahydrocarbazole followed by oxidation:

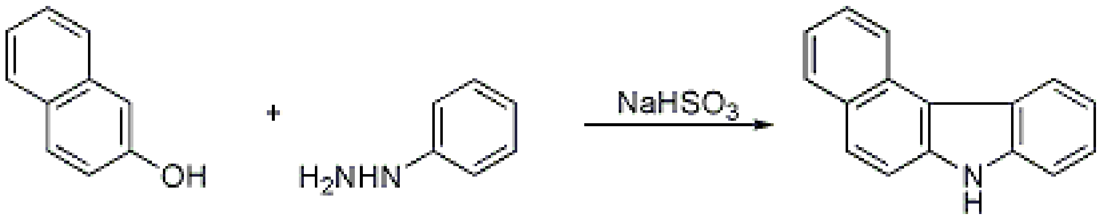


N. Campbell, B. M. Barclay, *Chem. Rev.* **40,** 361 (1947); W. Freudenberg, *Heterocyclic Compounds* **3,** 298 (1952); P. Bruck, *J. Org. Chem.* **35,** 2222 (1970). *Cf.* Bucherer Carbazole Synthesis; Fischer Indole Synthesis; Piloty-Robinson Synthesis.

62. Bucherer Carbazole Synthesis

H. T. Bucherer, F. Seyde, *J. Prakt. Chem.* **77**(2), 403 (1908).

Formation of carbazoles from naphthols or naphthylamines, aryl hydrazines and sodium bisulfite:



Reviews: N. L. Drake, *Org. React.* **1,** 114 (1942); E. Enders, *Houben-Weyl* **10/2,** 250 (1967).
Cf. Borsche-Drechsel Cyclization.

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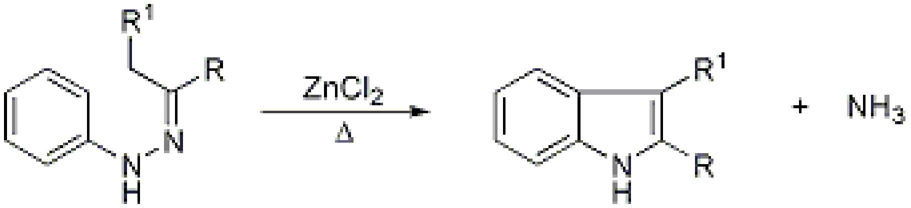
133. Fischer Indole Synthesis

E. Fischer, F. Jourdan, *Ber.* **16,** 2241 (1883); E. Fischer, O. Hess, *ibid.* **17,** 559 (1884).

Formation of indoles on heating aryl hydrazones of aldehydes or ketones in the presence of catalysts such as Lewis or proton acids:



Reviews: B. Robinson, *Chem. Rev.* **63,** 373 (1963); **69,** 227 (1969); H. Ishii, *Accts. Chem. Res.* **14,** 233-247 (1981); B. Robinson, *The Fischer Indole Synthesis* (Wiley, New York, 1982) 923 pp.; D. L. Hughes, *Org. Prep. Proced. Int.* **25,** 607-632 (1993). Modified conditions: S. M. Hutchins, K. T. Chapman, *Tetrahedron Letters* **37,** 4869 (1996); O. Miyata *et al., ibid.* **40,** 3601 (1999); S. Wagaw *et al., J. Am. Chem. Soc.* **121,** 10251 (1999). *Cf.* Borsche-Drechsel Cyclization; Piloty-Robinson Synthesis.

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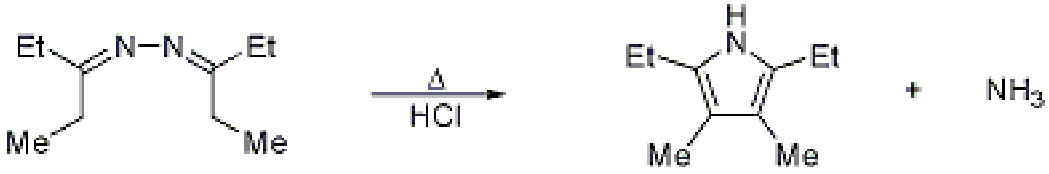
311. Piloty-Robinson Synthesis

O. Piloty, *Ber.* **43,** 489 (1910); G. M. Robinson, R. Robinson, *J. Chem. Soc.* **43,** 639 (1918).

Formation of pyrroles by heating azines of enolizable ketones with acid catalysts, usually zinc chloride or hydrogen chloride:



Review: N. V. Sidgwick, *Organic Chemistry of Nitrogen Compounds* (Oxford, 3rd ed., 1966) pp 619-641; H. Posvic *et al., J. Org. Chem.* **39,** 2575 (1974). *Cf.* Borsche-Drechsel Cyclization; Fischer Indole Synthesis.

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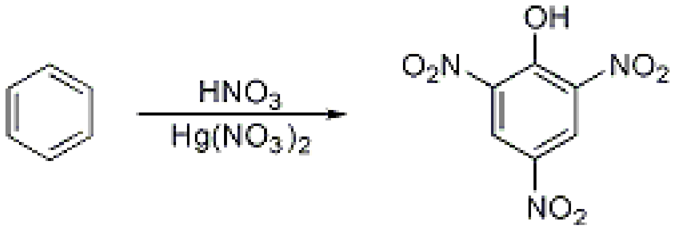
437. Wolffenstein-Böters Reaction

O. Böters, R. Wolffenstein, **DE 194883** (1906); **FR 380121** (1907); **GB 17521** (1907); **US 923761** (1909).

Simultaneous oxidation and nitration of aromatic compounds to nitrophenols with nitric acid or the higher oxides of nitrogen in the presence of a mercury salt as catalyst:



R. Wolffenstein, O. Böters, *Ber.* **46,** 586 (1913); F. H. Westheimer *et al., J. Am. Chem. Soc.* **69,** 773 (1947); M. Carmack, *et al., ibid.* 785; E. E. Aristoff *et al., Ind. Eng. Chem.* **40,** 1281 (1948); W. Seidenfaden, W. Pawellek, *Houben-Weyl* **10/1,** 815 (1971).

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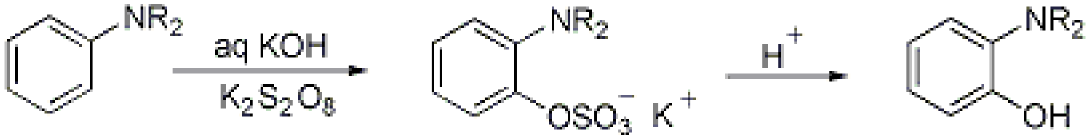
57. Boyland-Sims Oxidation

E. Boyland *et al.*, *J. Chem. Soc.* **1953,** 3623; E. Boyland, P. Sims, *ibid.* **1954,** 980.

Alkaline persulfate oxidation of aromatic amines to yield predominantly the *o*-amino aryl sulfates. Acid-catalyzed hydrolysis generates the *o*-hydroxy aryl amines:



Regioselectivity/mechanistic study: E. J. Behrman, *J. Org. Chem.* **57,** 2266 (1992). *Review: idem*, *Org. React.* **35,** 421-511 (1988). *Cf.* Elbs Persulfate Oxidation.

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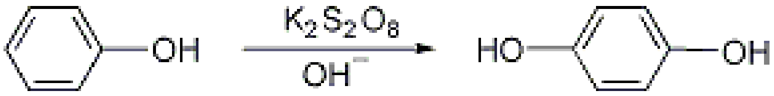
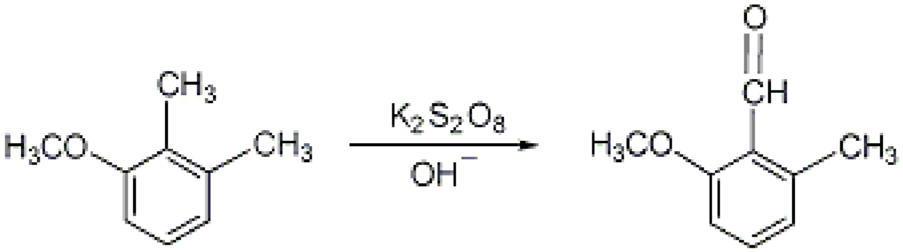
116. Elbs Persulfate Oxidation

K. Elbs, *J. Prakt. Chem.* **48,** 179 (1893).

Hydroxylation of monophenols to predominantely *p*-diphenols or oxidation of methyl-substituted aromatics by persulfates:





S. M. Sethna, *Chem. Rev.* **49,** 91 (1951); J. B. Lee, B. C. Uff, *Quart. Rev.* **21,** 453 (1967); E. J. Behrman, *Org. React.* **35,** 421-511 (1988); K. A. Parker, *et al.*, *J. Org. Chem.* **52,** 183 (1987); K. G. Watson, A. Serban, *Aust. J. Chem.* **48,** 1503 (1995). *Cf.* Boyland-Sims Oxidation.

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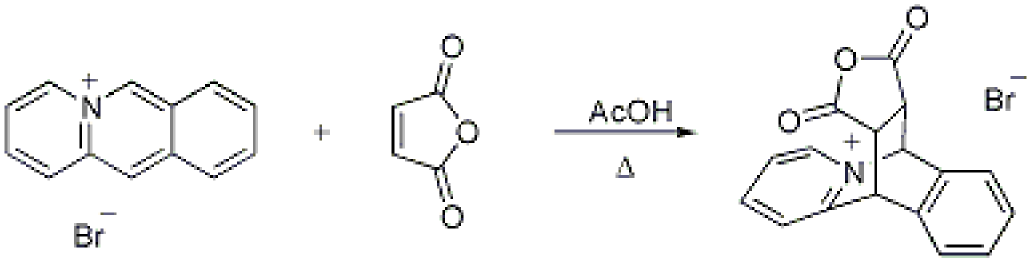
58. **Bradsher Cyclization** (Bradsher Cycloaddition)

C. K. Bradsher, T. W. G. Solomons, *J. Am. Chem. Soc.* **80,** 933 (1958).

[4 + 2] addition of a common dienophile with cationic aromatic azadienes such as acridizinium or isoquinolinium:

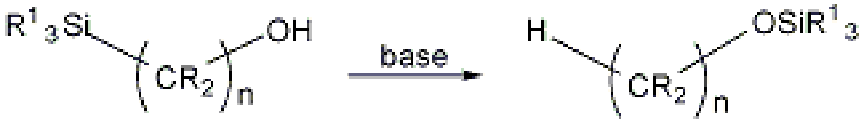


Mechanistic study: C. K. Bradsher, J. A. Stone, *J. Org. Chem.* **33,** 519 (1968). Synthetic applications: V. Bolitt *et al., J. Am. Chem. Soc.* **113,** 6320 (1991); H. Yin *et al., J. Org. Chem.* **57,** 644 (1992); T. E. Nicolas, R. W. Franck, *ibid.* **69,** 6904 (1995). *Review:* D. L. Boger, S. M. Weinreb, *Hetero Diels-Alder Methodology* in *Organic Synthesis* (Academic Press, NY, 1987) pp 239-299.

60. Brook Rearrangement

A. G. Brook, *J. Am. Chem. Soc.* **80,** 1886 (1958); *idem et al., ibid.* **81,** 981 (1959).

Base-catalyzed silicon migration from carbon to oxygen in α-, β- and γ-silyl alcohols, yielding silyl ethers:



base = NR_3, NaOH, Na/K, NaH
n = 1,2,3

Early review: A. G. Brook, *Accts. Chem. Res.* **7,** 77-84 (1974). Synthetic applications: H. J. Reich *et al., J. Am. Chem. Soc.* **112,** 5609 (1990); K. Takeda *et al., Synlett* **1993,** 841; I. Fleming, U. Ghosh *et al., J. Chem. Soc. Perkin Trans. I* **1994,** 257.

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243. Maillard Reaction ("Browning"Reaction)

L. C. Maillard, *Compt. Rend.* **154,** 66 (1912); *Ann. Chim.* **9,** 5, 258 (1916).

The reactions of amino groups of amino acids, peptides or proteins with the "glycosidic" hydroxyl group of sugars ultimately resulting in the formation of brown pigments.

G. P. Ellis, *Advan. Carbohyd. Chem.* **14,** 63 (1959); E. F. L. Anet, *ibid.* **19,** 181 (1964). Mechanism: M. Amrani-Hemaimi *et al., J. Agr. Food Chem.* **43,** 2818 (1995); high pressure effects: M. Bristow, N. S. Isaacs, *J. Chem. Soc. Perkin Trans. II* **1999,** 221. Crosslinking in proteins: K. J. Wells-Knecht *et al., J. Org. Chem.* **60,** 6246 (1995); M. O. Lederer, R. G. Klaiber, *Bioorg. Med. Chem.* **7,** 2499 (1999). *Reviews:* C. Eriksson, *Prog. Food Nutr. Sci.* **5,** 159-176 (1981); *The Maillard Reaction in Foods and Medicine,* J. O. O'Brien *et al.,* Eds. (Royal Soc. Chem., Cambridge, U.K., 1998) 464 pp.

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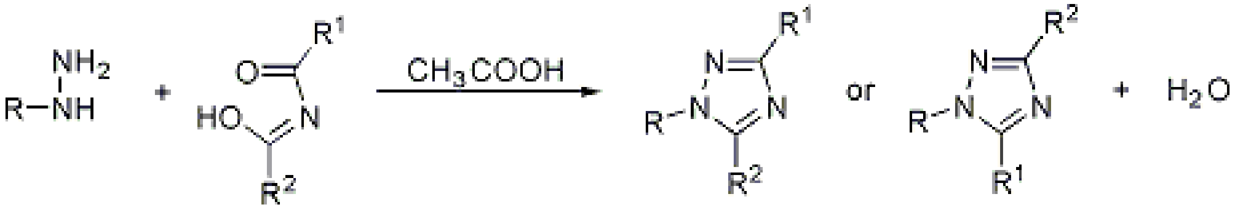
115. Einhorn-Brunner Reaction

A. Einhorn *et al., Ann.* **343,** 229 (1905); K. Brunner, *Ber*. **47,** 2671 (1914); *Monatsh.* **36,** 509 (1915).

Formation of substituted 1,2,4-triazoles by acid-catalyzed condensation of hydrazines or semicarbazides with diacylamines:

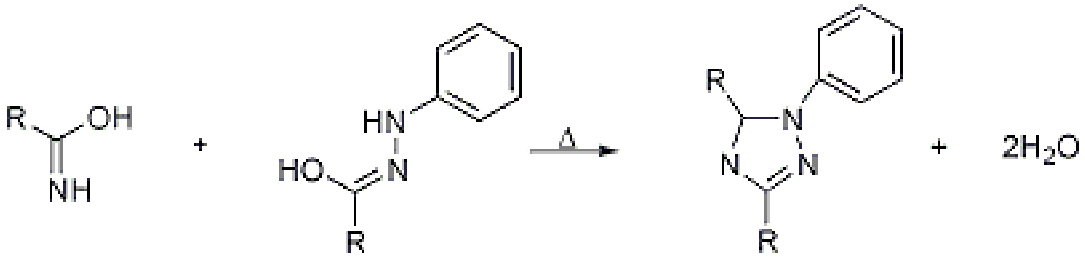


M. R. Atkinson, J. B. Polya, *J. Chem. Soc.* **1952,** 3418; **1954,** 141, 3319; Theilheimer, *Synthetic Methods* **9,** No. 449 (1955); K. T. Potts, *Chem. Rev*. **61,** 103 (1961); K. Hu *et al., J. Org. Chem.* **63,** 4786 (1998). *Cf.* Pellizzari Reaction.

297. Pellizzari Reaction

G. Pellizzari, *Gazz. Chim. Ital.* **41,** II, 20 (1911).

Formation of substituted 1,2,4-triazoles by the condensation of amides and acyl hydrazines. When the acyl groups of the amide and the acylhydrazine are different, interchange of acyl groups may occur with formation of a mixture of triazoles:



M. R. Atkinson, J. B. Polya, *J. Chem. Soc.* **1952,** 3418; P. Karrer, *Organic Chemistry* (New York, 4th ed., 1950) p 802; C. W. Bird, C. K. Wong, *Tetrahedron Letters* **1974,** 1251. *Cf.* Einhorn-Brunner Reaction.

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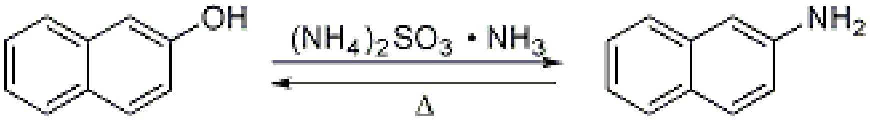
63. Bucherer Reaction

H. T. Bucherer, *J. Prakt. Chem.* [2] **69,** 49 (1904); R. Lepetit, *Bull. Soc. Ind. Mulhouse* **1903,** 326.

Reversible formation of β-naphthylamine from β-naphthol and aqueous ammonium sulfite or bisulfite *via* intermediate formation of tetralonesulfonic and tetraloneiminosulfonic acids:

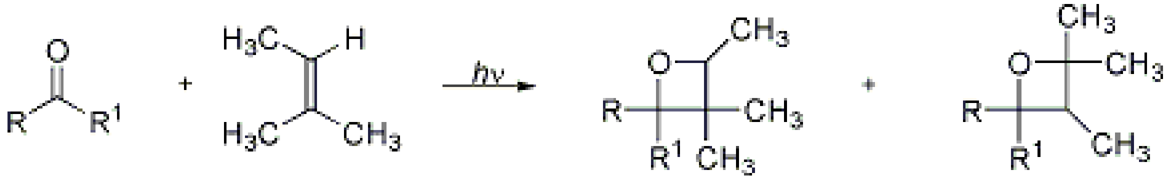


N. L. Drake, *Org. React.* **1,** 105 (1942); H. Seeboth, *Angew. Chem. Int. Ed.* **6,** 307 (1967); M. S. Gibson in *The Chemistry of the Amino Group,* S. Patai, Ed. (Interscience, London, 1968) p 37; Z. Allan *et al., Tetrahedron Letters* **1969,** 4855; W. H. Pirkle, T. C. Pochapsky, *J. Org. Chem.* **51,** 102 (1986); J. Bendig *et al., Tetrahedron* **48,** 9207 (1992).

292. Paterno-Büchi Reaction

E. Paterno, G. Chieffi, *Gazz. Chim. Ital.* **39,** 341 (1909); G. Büchi *et al., J. Am. Chem. Soc.* **76,** 4327 (1954).

Formation of oxetanes by photochemical cycloaddition of carbonyl compounds to olefins:



D. R. Arnold, *Advan. Photochem.* **6,** 301 (1968); G. Jones, II, *Org. Photochem.* **5,** 1 (1981); S. C. Freilich, K. S. Peters, *J. Am. Chem. Soc.* **103,** 6255 (1981); J. A. Porco, Jr., S. L. Schreiber, *Comp. Org. Syn.* **5,** 151-192 (1991). Mechanistic studies: D. Sun *et al., J. Org. Chem.* **64,** 2250 (1999); *eidem, J. Chem. Soc. Perkin Trans. II* **4,** 781 (1999). Stereocontrolled cycloadditions: S. A. Fleming, J. J. Gao, *Tetrahedron Letters* **38,** 5407 (1997); G. Kollenz *et al., Tetrahedron* **55,** 2973 (1999); followed by oxetane ring opening: T. Bach *et al., Ann.* **1997,** 1529; S. R. Thopate *et al., Angew. Chem. Int. Ed.* **37,** 110 (1998).

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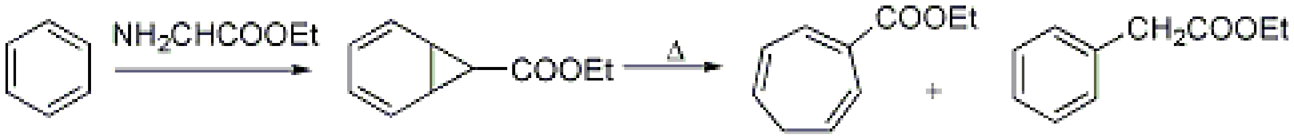
65. Buchner Method of Ring Enlargement

E. Buchner, *Ber.* **29,** 106 (1896); E. Buchner, K. Schottenhammer, *Ber.* **53,** 865 (1920).

Diazoacetic acid ester reacts with benzene and homologs to give the corresponding esters of noncaradienic acid, transformed at high temperatures to derivatives of cycloheptatriene and phenylacetic acid:



W. von F. Doering, L. H. Knox, *J. Am. Chem. Soc.* **79,** 352 (1957); W. Kirmse, *Carbene Chemistry* (Academic Press, New York, 2nd ed., 1971); A. F. Noels *et al.*, *J. Org. Chem.* **46,** 873 (1981). *Cf.* Pfau-Plattner Azulene Synthesis.

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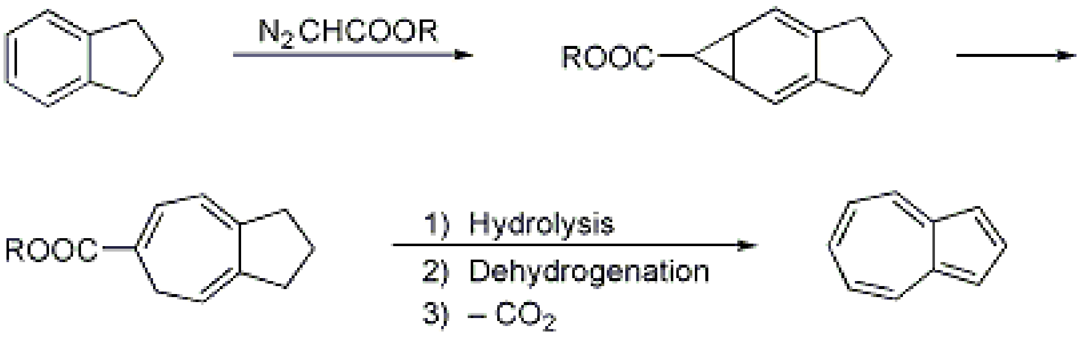
305. Pfau-Plattner Azulene Synthesis

A. St. Pfau, P. A. Plattner, *Helv. Chim. Acta* **22,** 202 (1939).

Formation of azulenes by ring enlargement of indanes on addition of diazoacetic ester, hydrolysis, dehydrogenation and decarboxylation of the resulting acid:



P. A. Plattner *et al., ibid.* **23,** 907 (1940); **24,** 483 (1941); **25,** 590 (1942); B. Eistert, *Newer Methods of Preparative Organic Chemistry* (Interscience, New York, 1948) p 555; D. H. Reid, *Chem. Soc. Spec. Publ.* **12,** 69 (1958); K. Hafner, *Angew. Chem.* **70,** 419 (1958). *Cf.* Buchner Method of Ring Enlargement.

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64. Buchner-Curtius-Schlotterbeck Reaction

E. Buchner, T. Curtius, *Ber.* **18,** 2371 (1885); F. Schlotterbeck, *Ber.* **40,** 479 (1907); **42,** 2559 (1909).

Formation of ketones from aldehydes and aliphatic diazo compounds; ethylene oxides may also be formed:

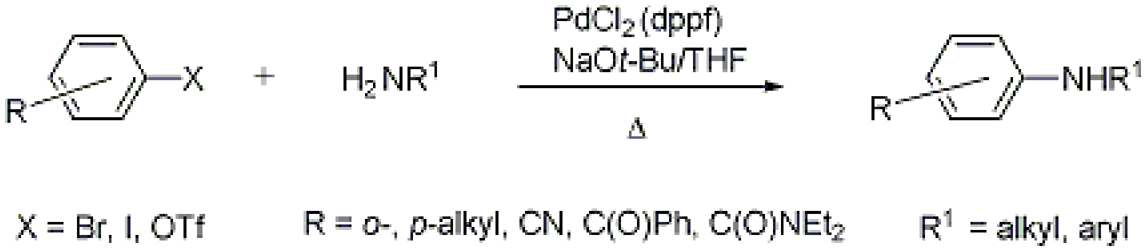
$$\mathrm{RCHN_2} + \mathrm{R^1CHO} \longrightarrow \mathrm{RCH_2COR^1} + \mathrm{N_2}$$

B. Eistert in *Newer Methods of Preparative Organic Chemistry,* English Ed. (New York, 1948) p 521; C. D. Gutsche, *Org. React.* **8,** 364 (1954); J. B. Bastus, *Tetrahedron Letters* **1963,** 955.

66. Buchwald-Hartwig Cross Coupling Reaction

J. Louie, J. F. Hartwig, *Tetrahedron Letters* **36,** 3609 (1995); A. S. Guram *et al., Angew. Chem. Int. Ed.* **34,** 1348 (1995).

Metal catalyzed formation of an arylamine by a reaction of aryl halide of triflate with primary or secondary amine:



Application: S. L. MacNeil *et al., Synlett* **1998,** 419. *Review:* J. F. Hartwig, *Angew. Chem. Int. Ed.* **37,** 2046-2067 (1998).

150. Fritsch-Buttenberg-Wiechell Rearrangement

P. Fritsch, *Ann.* **279,** 319 (1894); W. P. Buttenberg, *ibid.* 327; H. Wiechell, *ibid.* 332.

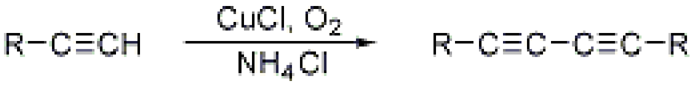
Carbene-mediated rearrangement of 1,1-diaryl-2-haloethylenes to diaryl acetylenes:

G. Köbrich, *Angew. Chem. Int. Ed.* **4,** 49 (1965); G. Köbrich, P. Buck in *Acetylenes,* H. G. Viehe, Ed. (Marcel Dekker, New York, 1969) pp 117, 131; G. Köbrich, *Angew. Chem. Int. Ed.* **11,** 473 (1972); P. J. Stang, D. P. Fox, *J. Org. Chem.* **43,** 364 (1978). Synthetic applications: V. Mouriès *et al., Synthesis* **1998,** 271; I. Creton *et al., Tetrahedron Letters* **40,** 1899 (1999). Substituent effects: T. Kawase *et al., Chem. Letters* **1995,** 499; H. Rezaei *et al., Org. Letters* **2,** 419 (2000).

157. **Glaser Coupling;** Eglinton Reaction**;** Cadiot-Chodkiewicz Coupling

C. Glaser, *Ber.* **2,** 422 (1869).

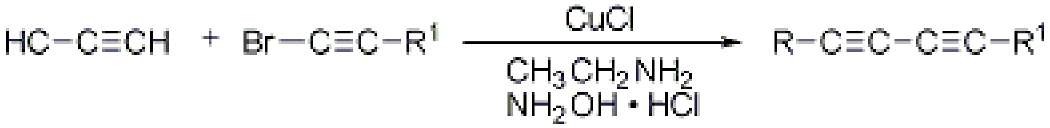
Homocoupling of terminal alkynes catalyzed by cuprous salts in the presence of an oxidant and ammonium chloride:



Synthetic applications: F. M. Menger *et al., J. Am. Chem. Soc.* **115,** 6600 (1993); L. Guo *et al., Chem. Commun.* **1994,** 243.

This coupling may also be effected by cupric salts in pyridine and is often referred to as the **Eglinton reaction.** It is particularly applicable to cyclizations: G. Eglinton, A. R. Galbraith, *Chem. & Ind. (London)* **1956,** 737; N. Hébert *et al., J. Org. Chem.* **57,** 1777 (1992).

Heterocoupling may be accomplished *via* the **Cadiot-Chodkiewicz coupling** of terminal alkynes with haloalkynes, catalyzed by cuprous salts in the presence of aliphatic amines:



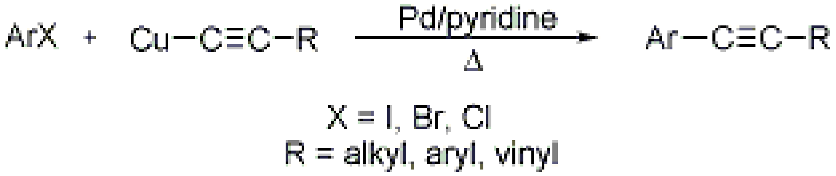
W. Chodkiewicz *et al., Compt. Rend.* **245,** 322 (1957); B. N. Ghose, *Syn. React. Inorg. Met.-Org. Chem.* **24,** 29 (1994); with supercritical CO_2 as solvent: J. Li, H. Jiang, *Chem. Commun.* **1999,** 2369.

Inclusive reviews: P. Cadiot, W. Chodkiewicz, “Couplings of Acetylenes” in *Chemistry of Acetylenes*, H. G. Viehe, Ed. (Marcel Dekker, New York, 1969) pp 597-647; K. Sonogashira, *Comp. Org. Syn.* **3,** 551-561 (1991). *Cf.* Castro-Stephens Coupling; Ullmann Reaction.

70. Castro-Stephens Coupling (Stephens-Castro Coupling, Castro Reaction)

C. E. Castro, R. D. Stephens, *J. Org. Chem.* **28,** 2163 (1963); R. D. Stephens, C. E. Castro, *ibid.* 3313; A. M. Sladkov *et al., Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1963,** 2043.

The coupling of cuprous acetylides with aryl halides to yield arylacetylenes:



Synthetic applications: J. D. Kinder *et al., Synlett* **1993,** 149; J. Kabbara *et al., Synthesis* **1995,** 299; M. S. Yu *et al., Tetrahedron Letters* **39,** 9347 (1998). Early reviews: G. H. Posner, *Org. React.* **22,** 253-400 *passim* (1975); A. M. Sladkov, I. R. Gol'ding, *Russ. Chem. Rev.* **48,** 868-896 (1979). *Cf.* Glaser Coupling.

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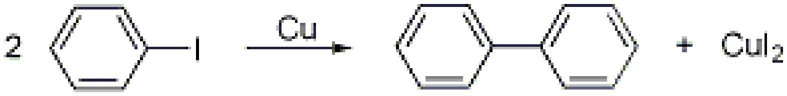
404. Ullmann Reaction

F. Ullmann, *Ann.* **332,** 38 (1904); F. Ullmann, P. Sponagel, *Ber.* **38,** 2211 (1905).

Copper-mediated coupling of aryl halides. Biaryl ether synthesis is similarly accomplished with aryl halides and phenols:

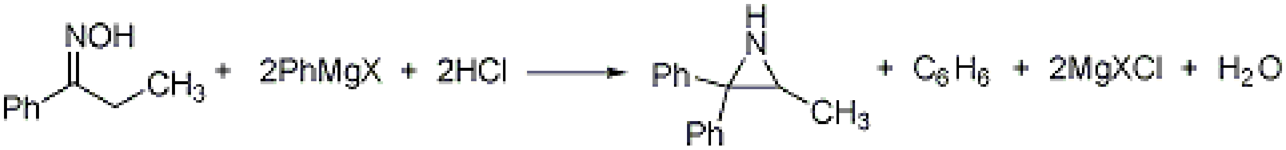


P. E. Fanta, *Chem. Rev.* **38,** 139 (1946); **64,** 613 (1964); A. A. Moroz, M. S. Shvartsberg, *Russ. Chem. Rev.* **43,** 679 (1974); P. E. Fanta, *Synthesis* **1974,** 9; M. F. Semmelhack *et al.*, *J. Am. Chem. Soc.* **103,** 6460 (1981); D. W. Knight, *Comp. Org. Syn.* **3,** 499-507 (1991). *Cf.* Glaser Coupling.

189. Hoch-Campbell Aziridine Synthesis

J. Hoch, *Compt. Rend.* **198,** 1865 (1934); K. N. Campbell, J. F. McKenna, *J. Org. Chem.* **4,** 198 (1939).

Formation of aziridines by treatment of ketoximes with Grignard reagents and subsequent hydrolysis of the organometallic complex:



K. N. Campbell *et al., J. Org. Chem.* **8,** 99, 103 (1943); **9,** 184 (1944); J. P. Freeman, *Chem. Rev.* **73,** 283 (1973); O. C. Dermer, G. E. Ham, *Ethylenimine and Other Aziridines* (Academic Press, New York, 1969) pp 65-68; E. Y. Takehisa *et al., Chem. Pharm. Bull.* **24,** 1691 (1976); T. Sasaki *et al., Heterocycles* **11,** 235 (1978); G. Alvernhe, A. Laurent, *J. Chem. Res. (S)* **1978,** 28.

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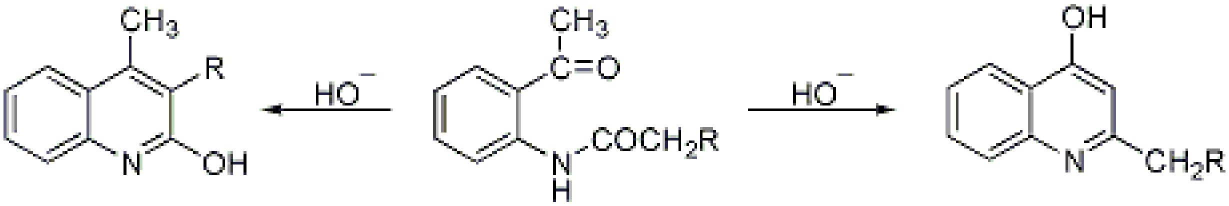
67. Camps Quinoline Synthesis

R. Camps, *Ber.* **22,** 3228 (1899); *Arch. Pharm.* **237,** 659 (1899); **239,** 591 (1901).

Formation of hydroxyquinolines from *o*-acylaminoacetophenones in alcoholic sodium hydroxide. Two isomers are produced; the relative proportions are mainly determined by the residue on the amino nitrogen:



R. H. F. Manske, *Chem. Rev.* **30,** 127 (1942); B. Witkop *et al., J. Am. Chem. Soc.* **73,** 2641 (1951); J. Bornstein *et al., ibid.* **76,** 2760 (1954); R. C. Elderfield, *Heterocyclic Compounds* **4,** 60 (1952); H. Yanagisawa *et al., Chem. Pharm. Bull.,* **21,** 1080 (1973).

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191. **Hofmann Isonitrile Synthesis** (Carbylamine Reaction)

A. W. Hofmann, *Ann.* **146,** 107 (1868); *Ber.* **3,** 767 (1870).

Formation of isonitriles by the reaction of primary amines with chloroform in the presence of alkali; the odor of the isocyanide is a test for a primary amine:

$$C_2H_5NH_2 + CHCl_3 + 3NaOH \longrightarrow C_2H_5NC + 3NaCl + 3H_2O$$

P. A. S. Smith, N. W. Kalenda, *J. Org. Chem.* **23,** 1599 (1958); M. B. Frankel *et al.*, *Tetrahedron Letters* **1959,** 5; H. L. Jackson, B. C. McKusick, *Org. Syn.* **coll. vol. IV,** 438 (1963); W. P. Weber, G. W. Gokel, *Tetrahedron Letters* **1972,** 1637.

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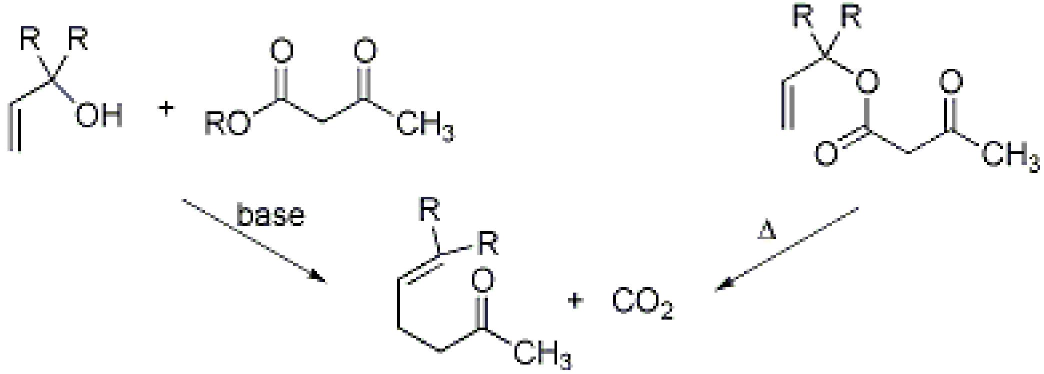
69. Carroll Rearrangement

M. F. Carroll, *J. Chem. Soc.* **1940,** 704; **1941,** 507; W. Kimel, A. C. Cope, *J. Am. Chem. Soc.* **65,** 1992 (1943).

Preparation of γ,δ-unsaturated ketones by base-catalyzed reaction of allylic alcohols with β-ketoesters or thermal rearrangement of allyl acetoacetates:

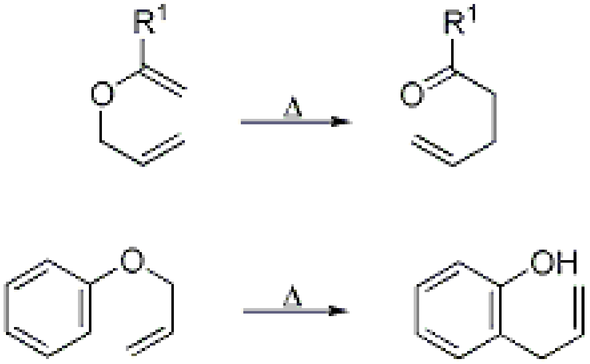


Detailed experimental: S. R. Wilson, C. E. Augelli, *Org. Syn.* **68,** 210 (1990). Synthetic applications: A. V. Echavarren *et al.*, *Tetrahedron Letters* **32,** 6421 (1991); N. Ouvrard *et al.*, *ibid.* **34,** 1149 (1993). *Cf.* Claisen Rearrangement.

77. **Claisen Rearrangement;** Eschenmoser-Claisen Rearrangement**;** Johnson-Claisen Rearrangement**;** Ireland-Claisen Rearrangement

L. Claisen, *Ber.* **45,** 3157 (1912); L. Claisen, E. Tietze, *ibid.* **58,** 275 (1925); **59,** 2344 (1926).

Highly stereoselective [3,3]-sigmatropic rearrangement of allyl vinyl or allyl aryl ethers to yield γ,δ-unsaturated carbonyl compounds or *o*-allyl substituted phenols, respectively:



When R′ = NR$_2$, the reaction is referred to as the **Eschenmoser-Claisen rearrangement:** A. E. Wick *et al., Helv. Chim. Acta* **47,** 2425 (1964); M. Lautens *et al., Tetrahedron Letters* **31,** 5829 (1990); B. Coates *et al., ibid.* **32,** 4199 (1991).

When R′ = OR, the reaction is referred to as the **Johnson-Claisen rearrangement:** W. S. Johnson *et al., J. Am. Chem. Soc.* **92,** 741 (1970); R. Bao *et al., Synlett* **1992,** 217; D. Basavaiah, S. Pandiaraju, *Tetrahedron Letters* **36,** 757 (1995).

When R′ = OSiR$_3$ or OLi, the reaction is referred to as the **Ireland-Claisen rearrangement:** R. E. Ireland, R. H. Mueller, *J. Am. Chem. Soc.* **94,** 5897 (1972); R. E. Ireland *et al., J. Org. Chem.* **56,** 650 (1991); *idem et al., ibid.* 3572; K. Hattori, H. Yamamoto, *Tetrahedron* **50,** 3099 (1994).

Inclusive reviews: S. J. Rhoads, N. R. Raulins, *Org. React.* **22,** 1-252 (1975); F. E. Ziegler, *Chem. Rev.* **88,** 1423-1452 (1988); P. Wipf, *Comp. Org. Syn.* **5,** 827-873 (1991). *Cf.* Carroll Rearrangement; Cope Rearrangement; Overman Rearrangement.

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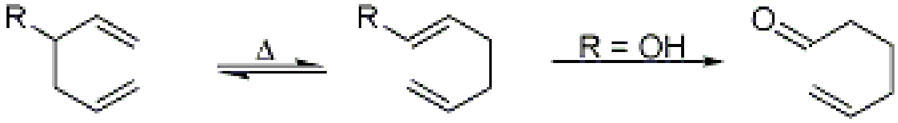
83. Cope Rearrangement; Oxy-Cope Rearrangement

A. C. Cope *et al., J. Am. Chem. Soc.* **62,** 441 (1940).

Highly stereoselective [3,3]-sigmatropic rearrangement of 1,5-dienes; “all-carbon” equivalent of the Claisen rearrangement, *q.v.*:



When R = OH, the transformation is referred to as the **oxy-Cope rearrangement:** J. Berson, M. Jones, *ibid.* **86,** 5019 (1964).

Reviews: S. J. Rhodds, N. R. Raulins, *Org. React.* **22,** 1-252 (1975); S. R. Wilson, *ibid.* **43,** 93-250 *passim* (1993); R. K. Hill, *Comp. Org. Syn.* **5,** 785-826 (1991). Review of hetero-Cope rearrangements: S. Blechert, *Synthesis* **1989,** 71-82. Brief review of synthetic applications: K. Durairaj, *Curr. Sci.* **66,** 917-922 (1994).

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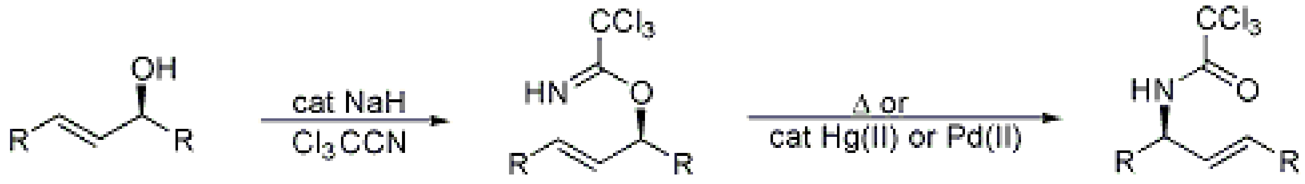
287. Overman Rearrangement

L. E. Overman, *J. Am. Chem. Soc.* **96,** 597 (1974); **98,** 2901 (1976).

Formal [3,3]-sigmatropic rearrangement of the trichloroacetimidate of allylic alcohols to allylic trichloroacetamides, thereby transposing the hydroxyl and amino functions with good chirality transfer:



Early review: L. E. Overman, *Accts. Chem. Res.* **13,** 218-224 (1980). Synthetic applications: M. Isobe *et al., Tetrahedron Letters* **31,** 3327 (1990); T. Allmendinger *et al., ibid.* 7301; J. Gonda *et al., Synthesis* **1993,** 729; C. G. Cho *et al., Synth. Commun.* **30,** 1643 (2000). Use of a chiral template and mechanistic studies: T. Eguchi *et al., Tetrahedron* **49,** 4527 (1993). Modification of reaction conditions: T. Nishikawa *et al., J. Org. Chem.* **63,** 188 (1998). *Cf.* Claisen Rearrangement.

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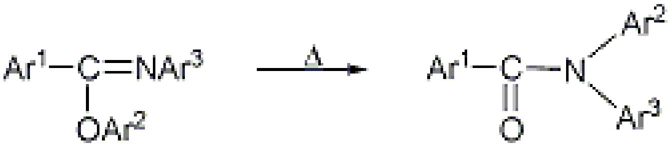
71. Chapman Rearrangement

O. Mumm *et al.*, *Ber.* **48,** 379 (1915); A. W. Chapman, *J. Chem. Soc.* **127,** 1992 (1925); **1927,** 174; **1929,** 569.

Thermal rearrangement of aryl imidates to *N*,*N*-diaryl amides:



J. W. Schulenberg *et al., Org. React.* **14,** 1 (1965); C. G. McCarty, L. Garner in *The Chemistry of Amidines and Imidates* S. Patai, Ed. (Interscience, New York, 1975) p 189. Mechanistic study: N. A. Suttle, A. Williams, *J. Chem. Soc. Perkin Trans. II* **1983,** 1369. Synthetic applications: L. H. Peterson *et al., J. Heterocyclic Chem.* **18,** 659 (1981); N. Dubau-Assibat *et al., Bull. Soc. Chim. Fr.* **132,** 1139 (1995). Chapman-like rearrangements: F. Esser *et al., J. Chem. Soc. Perkin Trans. I* **1988,** 3311; M. Dessolin *et al., Chem. Commun.* **1992,** 132.

72. Chichibabin Pyridine Synthesis

A. E. Chichibabin, *J. Russ. Phys. Chem. Soc.* **37,** 1229 (1906); *J. Prakt. Chem.* **107,** 122 (1924).

Condensation of carbonyl compounds with ammonia or amines under pressure to form pyridine derivatives; the reaction is reversible and produces different pyridine derivatives along with byproducts:

M. M. Sprung, *Chem. Rev.* **26,** 301 (1940); R. L. Frank, R. P. Seven, *J. Am. Chem. Soc.* **71,** 2629 (1949); H. S. Mosher, *Heterocyclic Compounds* **1,** 456 (1950); J. A. Gautier, J. Renault, *Bull. Soc. Chim. France* **1955,** 588; C. P. Farley, E. L. Eliel, *J. Am. Chem. Soc.* **78,** 3477 (1956); A. T. Soldatenkov, *Zh. Org. Khim.* **16,** 188 (1980). *Cf.* Hantzsch (Dihydro) Pyridine Synthesis; Kröhnke Pyridine Synthesis.

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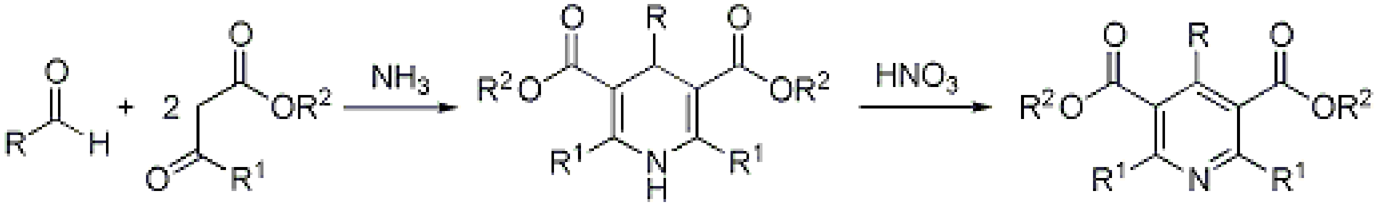
172. Hantzsch Dihydropyridine Synthesis (Pyridine Synthesis)

A. Hantzsch, *Ann.* **215,** 1, 72 (1882); *Ber.* **18,** 1744 (1885); **19,** 289 (1886).

Synthesis of dihydropyridines by condensation of two moles of a β-dicarbonyl compound with one mole of an aldehyde in the presence of ammonia. Dehydrogenation to the corresponding pyridine is accomplished with an oxidizing agent:



Note: if R at C-4 is benzyl then during oxidation cleavage will occur

H. S. Mosher, *Heterocyclic Compounds* **1,** 462 (1950); R. M. Kellog *et al., J. Org. Chem.* **45,** 2854 (1980); Y. Watanabe *et al., Synthesis* **1983,** 761. Mechanistic study: A. R. Katritzky *et al., Tetrahedron* **42,** 5729 (1986); **43,** 5171 (1987). Extension to the synthesis of unsymmetrical dihydropyridines: J. B. Sainani *et al., Indian J. Chem.* **34B,** 17 (1995); S. Visentin *et al., J. Med. Chem.* **42,** 1422 (1999). *Cf.* Chichibabin Pyridine Synthesis; Guareschi-Thorpe Condensation; Kröhnke Pyridine Synthesis.

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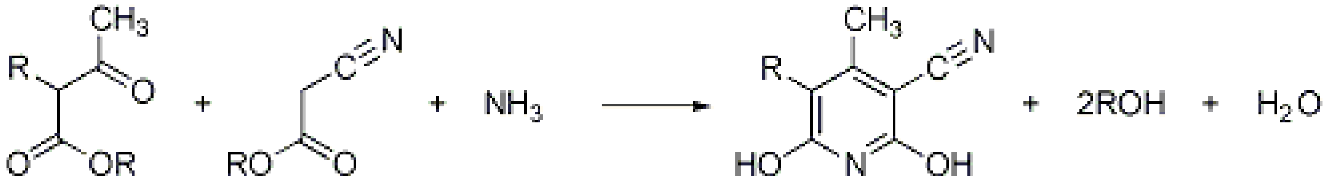
167. Guareschi-Thorpe Condensation

I. Guareschi, *Mem. Reale Accad. Sci. Torino* **II,** 46, 7, 11, 25 (1896); H. Baron, *et al., J. Chem. Soc.* **85,** 1726 (1904).

Synthesis of pyridine derivatives by condensation of cyanoacetic ester with acetoacetic ester in the presence of ammonia. In a second type of synthesis a mixture of cyanoacetic ester and a ketone is treated with alcoholic ammonia:



C. Hollins, *The Synthesis of Nitrogen Ring Compounds* (New York, 1924) p 197; V. Migrdichian, *The Chemistry of Organic Cyanogen Compounds* (New York, 1947) p 322; H. S. Mosher, *Heterocyclic Compounds* **1,** 466 (1950); R. W. Holder *et al., J. Org. Chem.* **47,** 1445 (1982); D. J. Collins, A. M. James, *Aust. J. Chem.* **42,** 215 (1989). *Cf.* Hantzsch (Dihydro)Pyridine Synthesis; Kröhnke Pyridine Synthesis.

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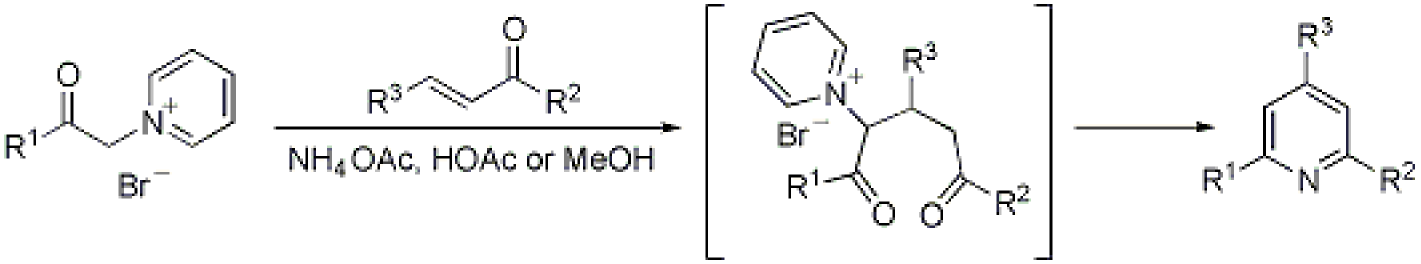
227. Kröhnke Pyridine Synthesis

W. Zecher, F. Kröhnke, *Ber.* **94,** 690, 698 (1961); *eidem, Angew. Chem. Int. Ed.* **1,** 626 (1962).

1,4-Michael addition, *q.v.*, of α-pyridinium methyl ketone salts to α,β-unsaturated ketones, generating the 1,5-dicarbonyl compounds which undergo ammonium acetate-promoted ring closure, to yield substituted pyridines:



Early review: F. Kröhnke, *Synthesis* **1976,** 1-24. Synthetic applications: J. N. Chatterjea *et al., Indian J. Chem.* **15B,** 430 (1977); G. R. Newkome *et al., J. Org. Chem.* **51,** 850 (1986); P. Lhoták, A. Kurfürst, *Coll. Czech. Chem. Commun.* **57,** 1937 (1992); T. R. Kelly *et al., J. Org. Chem.* **62,** 2774 (1997). *Cf.* Chichibabin Pyridine Synthesis; Guareschi-Thorpe Condensation; Hantzsh (Dihydro)Pyridine Synthesis.

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73. Chichibabin Reaction

A. E. Chichibabin, O. A. Zeide, *J. Russ. Phys. Chem. Soc.* **46,** 1216 (1914), *C.A.* **9,** 1901 (1915).

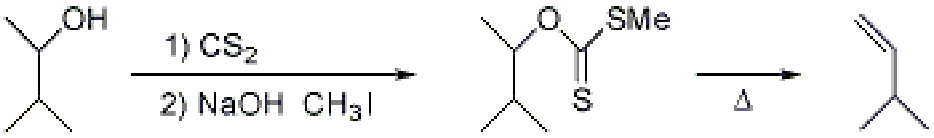
Amination of pyridines and other heterocyclic nitrogen compounds with alkali-metal amides:

H. S. Mosher, *Heterocyclic Compounds* **1,** 405 (1950); A. F. Pozharskii *et al., Russ. Chem. Rev.* **47,** 1042 (1978); H. J. W. van den Haak *et al., J. Org. Chem.* **46,** 2134 (1981). Applications: N. J. Kos *et al., ibid.* **44,** 3140 (1979); H. Tondys *et al., J. Heterocyclic Chem.* **22,** 353 (1985); E. Ciganek *et al., J. Org. Chem.* **57,** 4521 (1992). *Review:* H. C. van der Plas, M. Wozniak, *Croat. Chem. Acta* **59,** 33-49 (1986). *Cf.* Kröhnke Pyridine Synthesis.

74. **Chugaev Reaction** (Tschugaeff Olefin Synthesis)

L. Chugaev (Tschugaeff), *Ber.* **32,** 3332 (1899).

Formation of olefins from alcohols without rearrangement through pyrolysis of the corresponding xanthates *via cis*-elimination:



C. H. DePuy, R. W. King, *Chem. Rev.* **60,** 444 (1960); H. R. Nace, *Org. React.* **12,** 57 (1962); K. Harano, T. Taguchi, *Chem. Pharm. Bull. Japan* **20,** 2357 (1972); J. March, *Advanced Organic Chemistry* (John Wiley & Sons, NY, 1992) 1014-1015. Synthetic applications: X Fu, J. M. Cook, *Tetrahedron Letters* **31,** 3409 (1990); P. S. Ray, M. J. Manning, *Heterocycles* **33,** 1361 (1994). *Cf.* Cope Elimination Reaction.

82. Cope Elimination Reaction

A. C. Cope *et al., J. Am. Chem. Soc.* **71,** 3929 (1949); *idem et al., ibid.* **75,** 3212 (1953).

Formation of an olefin and a hydroxylamine by pyrolysis of an amine oxide:

Early reviews: C. H. DePuy, R. W. King, *Chem. Rev.* **60,** 448 (1960); A. C. Cope, E. R. Trumbull, *Org. React.* **11,** 317-493 *passim* (1960). Synthetic application: E. Tojo *et al., Heterocycles* **27,** 2367 (1988). Mechanistic study: R. D. Bach, M. L. Braden, *J. Org. Chem.* **56,** 7194 (1991). Methods development: A. D. Woolhouse, *J. Heterocyclic Chem.* **30,** 873 (1993). Synthetic applications of the reverse reaction (retro-Cope elimination): E. Ciganek, *J. Org. Chem.* **55,** 3007 (1990); M. B. Gravestock *et al., Chem. Commun.* **1993,** 169. *Cf.* Chugaev Reaction; Hofmann Degradation.

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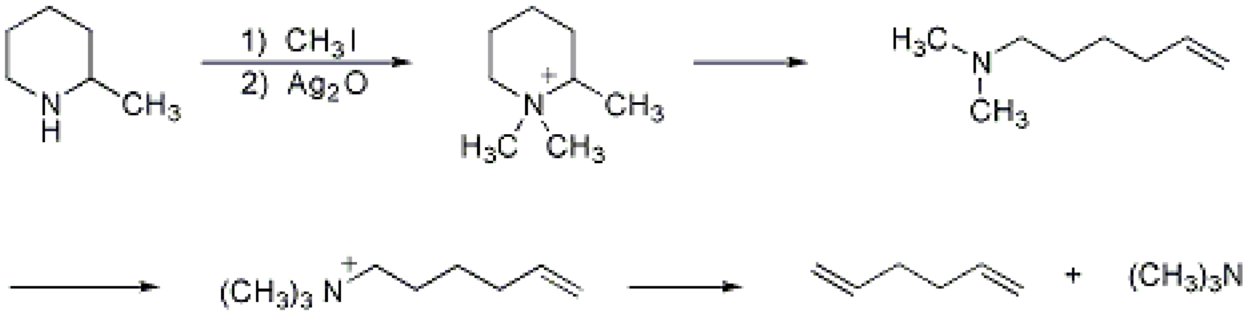
190. Hofmann Degradation (Exhaustive Methylation)

A. W. Hofmann, *Ber.* **14,** 659 (1881).

Formation of an olefin and a tertiary amine by pyrolysis of a quaternary ammonium hydroxide:



A. C. Cope, E. R. Trumbull, *Org. React.* **11,** 317-493 *passim* (1960); K. W. Bentley, G. W. Kirby in *Techniques of Organic Chemistry* **vol. IV,** Pt. 2, A. Weissberger, Ed., *Elucidation of Organic Structures by Physical and Chemical Methods* (Wiley, New York, 2nd ed., 1973) pp 255-289. Isotope effects: R. D. Bach, M. L. Braden, *J. Org. Chem.* **56,** 7194 (1991). Synthetic applications: A. D. Woolhouse *et al.*, *J. Heterocyclic Chem.* **30,** 873 (1993); D. Berkes *et al.*, *Synth. Commun.* **28,** 949 (1998). *Cf.* Cope Elimination Reaction; Emde Degradation.

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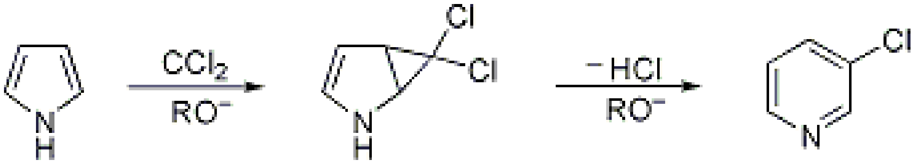
75. Ciamician-Dennstedt Rearrangement

G. L. Ciamician, M. Dennstedt, *Ber.* **14,** 1153 (1881).

Expansion of the pyrrole ring by heating with chloroform or other halogeno compounds in alkaline solution. The intermediate dichlorocarbene, by addition to the pyrrole, forms an unstable dihalogenocyclopropane which rearranges to a 3-halogenopyridine:



A. H. Corwin, *Heterocyclic Compounds* **1,** 309 (1950); H. S. Mosher, *ibid.* 475; P. S. Skell, R. S. Sandler, *J. Am. Chem. Soc.* **80,** 2024 (1958); E. Vogel, *Angew. Chem.* **72,** 8 (1960).

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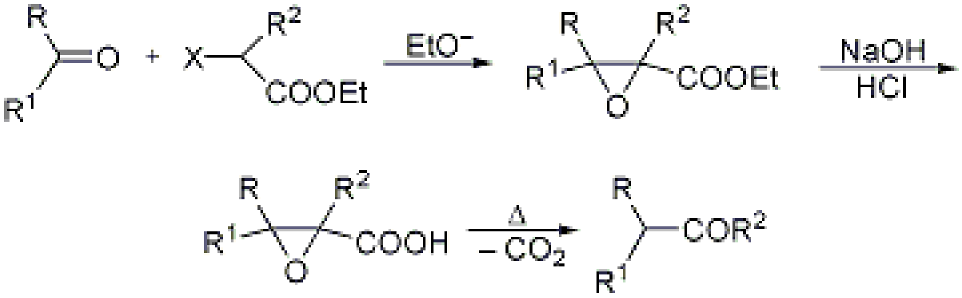
93. **Darzens Condensation** (Darzens-Claisen Reaction, Glycidic Ester Condensation)

G. Darzens, *Compt. Rend.* **139,** 1214 (1904); **141,** 766 (1905); **142,** 214 (1906).

Formation of α,β-epoxy esters (glycidic esters) by the condensation of aldehydes or ketones with esters of α-haloacids; the corresponding thermally unstable glycidic acids yield aldehydes or ketones on decarboxylation:



M. S. Newman, B. J. Magerlein, *Org. React.* **5,** 413 (1949); M. Ballester, *Chem. Rev.* **55,** 283 (1955); H. O. House, *Modern Synthetic Reactions* (W. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 666-671. Intramolecular reaction: G. Fráter *et al., Tetrahedron Letters* **34,** 2753 (1993). Enantioselectivity: D. Enders, R. Hett, *Synlett* **1998,** 961; S. Arai *et al., Tetrahedron* **55,** 6375 (1999). Modified conditions: R. F. Borch, *Tetrahedron Letters* **1972,** 3761; I. Shibata *et al., J. Org. Chem.* **57,** 6909 (1992). Review: T. Rosen, *Comp. Org. Syn.* **2,** 409-439 (1991).

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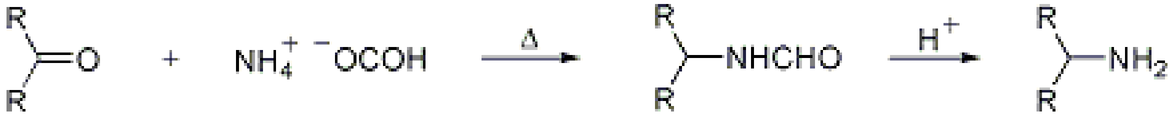
234. **Leuckart (Leukart) Reaction;** Leuckart-Wallach Reaction**;** Eschweiler-Clarke Reaction

R. Leuckart, *Ber.* **18,** 2341 (1885).

Reductive alkylation of ammonium (or amine) salts of formic acid or formamides by aldehydes or ketones:



When the reaction is performed in the presence of excess formic acid it is referred to as the **Leuckart-Wallach reaction:** O. Wallach, *Ann.* **272,** 99 (1892). Application to steroids: W. E. Solomons, N. J. Doorenbos, *J. Pharm. Sci.* **63,** 19 (1974); A. M. Bellini *et al., Steroids* **56,** 395 (1991).

The reductive methylation of primary or secondary amines employing formaldehyde and formic acid is known as the **Eschweiler-Clarke reaction:** W. Eschweiler, *Ber.* **38,** 880 (1905); H. T. Clarke, *et al., J. Am. Chem. Soc.* **55,** 4571 (1933). Synthetic applications: E. Farkas, C. J. Sunman, *J. Org. Chem.* **50,** 1110 (1985); J. Casanova, P. Devi, *Synth. Commun.* **23,** 245 (1993).

Early reviews: M. L. Moore, *Org. React.* **5,** 301-330 (1949); F. Möller, R. Schröter, *Houben-Weyl* **11/1,** 648-664 (1957). Application to deoxybenzoins: M. J. Villa *et al., Heterocycles* **24,** 1943 (1986). Mechanistic study: P. I. Awachie, V. C. Agwada, *Tetrahedron* **46,** 1899 (1990); A. G. Martinez *et al., Tetrahedron Asymmetry* **10,** 1499 (1999). Optimized procedure: R. Carlson *et al., Acta Chem. Scand.* **47,** 1046 (1993). Modified conditions: A. Loupy *et al., Tetrahedron Letters* **37,** 8177 (1996); I. Helland, T. Lejon, *Heterocycles* **51,** 611 (1999).

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79. Clemmensen Reduction

E. Clemmensen, *Ber.* **46,** 1837 (1913); **47,** 51, 681 (1914).

Reduction of carbonyl groups of aldehydes and ketones to methylene groups with zinc amalgam and hydrochloric acid:

$$RCOR^1 \xrightarrow[HCl]{Zn(Hg)} RCH_2R^1$$

E. L. Martin, *Org. React.* **1,** 155 (1942); M. Smith in *Reduction*, R. L. Augustine, Ed. (M. Dekker, New York, 1968) pp 95-170; W. Reusch, *ibid.* pp 186-194; J. G. St. C. Buchanan, P. D. Woodgate, *Quart. Rev.* **23,** 522 (1969); D. Straschewski, *Angew. Chem.* **71,** 726 (1959); E. Vedejs, *Org. React.* **22,** 401 (1975); S. Yamamura, S. Nishiyama, *Comp. Org. Syn.* **8,** 309-313 (1991). *Cf.* Haworth Phenanthrene Synthesis; Wolff-Kishner Reduction.

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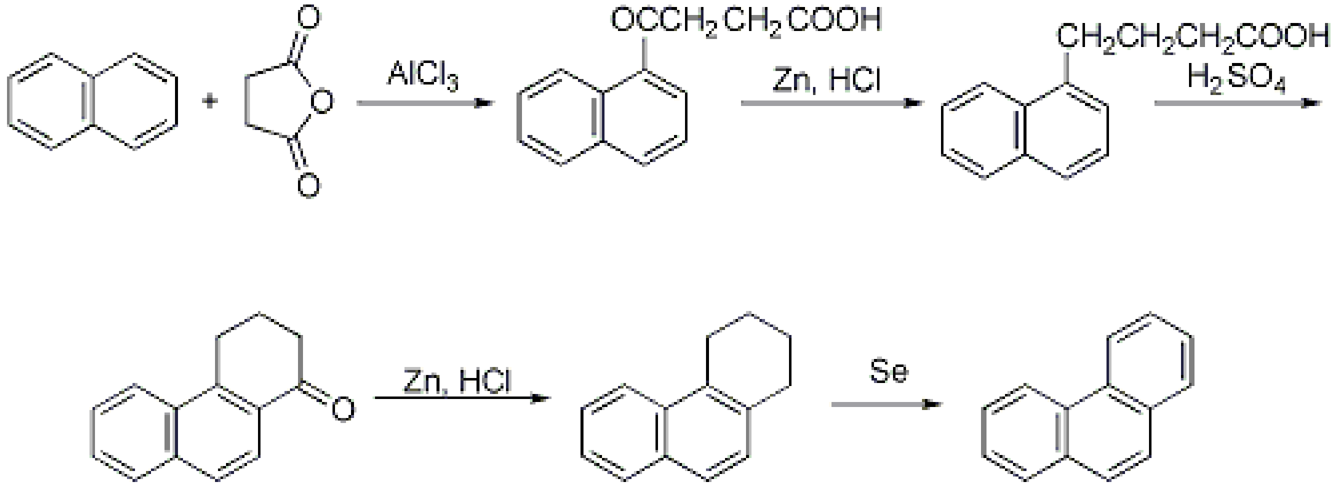
176. Haworth Phenanthrene Synthesis

R. D. Haworth, *J. Chem. Soc.* **1932,** 1125, 2717, *idem et al.*, *ibid.* 1784, 2248, 2720; **1934,** 454.

Preparation of phenanthrenes from naphthalenes *via* a series of steps including a Friedel-Crafts acylation and two Clemmensen or Wolff-Kishner reductions, *q.q.v.*:



E. Berliner, *Org. React.* **5,** 229 (1949); I. Agranat, Y. S. Shih, *Synthesis* **1974,** 865; R. Menicagli, O. Piccolo, *J. Org. Chem.* **45,** 2581 (1980). *Cf.* Friedel-Crafts Reaction.

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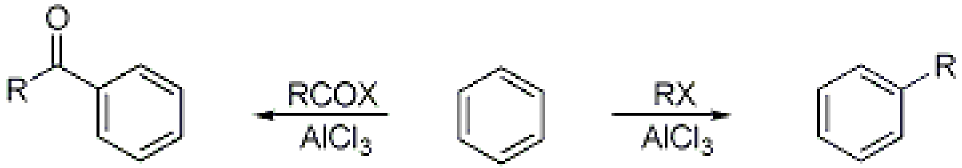
147. Friedel-Crafts Reaction

C. Friedel, J. M. Crafts, *Compt. Rend.* **84,** 1392, 1450 (1877).

The alkylation or acylation of aromatic compounds catalyzed by aluminum chloride or other Lewis acids:



RCOX = acyl halides, anhydrides
RX = alkyl halides, alkenes, alkynes, alcohols

Reviews: C. C. Price, *Org. React.* **3,** 1 (1946); G. A. Olah, *Friedel-Crafts and Related Reactions*, **vol. 1-4** (Interscience, New York, 1963-1965); J. K. Groves, *Chem. Soc. Rev.* **1,** 73 (1972); H. Heaney, *Comp. Org. Syn.* **2,** 733-752, 753-768 (1991); **3,** 293-339. Aliphatic version: S. C. Eyley, *ibid.* **2,** 707-731. Intramolecular reactions: H.-J. Knölker, *Angew. Chem. Int. Ed.* **38,** 2583 (1999); M.-C. P. Yeh *et al., J. Organometal. Chem.* **599,** 128 (2000); C.-L. Kao *et al., Tetrahedron Letters* **41,** 2207 (2000). Modified conditions: U. Bierman, J. O. Metzger, *Angew. Chem. Int. Ed.* **38,** 3675 (1999). *Cf.* Darzens-Nenitzescu Synthesis of Ketones; Haworth Phenanthrene Synthesis; Nencki Reaction.

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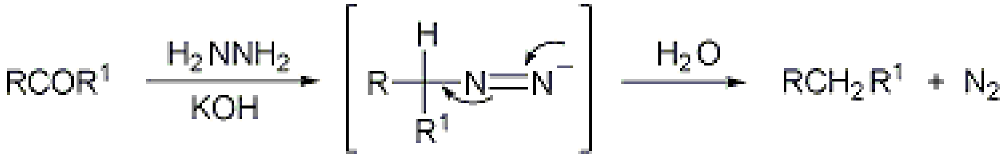
435. Wolff-Kishner Reduction; Huang-Minlon Modification

N. Kishner, *J. Russ. Phys. Chem. Soc.* **43,** 582 (1911), *C.A.* **6,** 347 (1912); L. Wolff, *Ann.* **394,** 86 (1912); Huang-Minlon, *J. Am. Chem. Soc.* **68,** 2487 (1946).

Complete reduction of carbonyl compounds to methyl or methylene groups on heating with hydrazine hydrate and a base. In the **Huang-Minlon modification** diethylene glycol is used as a solvent:



Reviews: D. Todd, *Org. React.* **4,** 378 (1948); H. H. Szmant, *Angew. Chem. Int. Ed.* **7,** 120 (1968); F. Asinger, H. H. Vogel, *Houben-Weyl* **5/1a,** 251, 456 (1970); H. Balli, *ibid.* **5/1b,** 629 (1972); R. O. Hutchins, M. K. Hutchins, *Comp. Org. Syn.* **8,** 327-343 (1991). Bond cleavage: R. P. Lemieux, P. Beak, *Tetrahedron Letters* **30,** 1353 (1989). Synthetic application: A. Srikrishna, D. Vijaykumuv, *J. Chem. Soc. Perkin Trans. I* **1999,** 1265. *Cf.* Clemmensen Reduction; Haworth Phenanthrene Synthesis.

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356. **Sarett Oxidation;** Collins Oxidation

G. I. Poos, G. E. Arth, R. E. Beyler, L. H. Sarett, *J. Am. Chem. Soc.* **75,** 422 (1953).

Oxidation of primary and secondary alcohols to aldehydes (and/or carboxylic acids) and ketones by means of CrO_3-pyridine complex:

J. R. Holum, *J. Org. Chem.* **26,** 4814 (1961); E. J. Kris, *Chem. & Ind. (London)* **1961,** 1834; V. I. Stenberg, R. J. Perkins, *J. Org. Chem.* **28,** 323 (1963); P. G. Gassman, P. G. Pape, *J. Org. Chem.* **29,** 160 (1964); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 264-273. Mechanistic studies: F. Hasan, J. Rocek, *J. Am. Chem. Soc.* **97,** 1444, 3762 (1975).

The **Collins oxidation** is characterized by a modified procedure (dichloromethane as solvent) that reliably oxidizes primary alcohols to aldehydes: J. C. Collins, *Tetrahedron Letters* **1968,** 3363; J. C. Collins, W. W. Hess, *Org. Syn.* **52,** 5 (1972); R. W. Ratcliffe, *ibid.* **55,** 84 (1976). *Cf.* Jones Oxidation.

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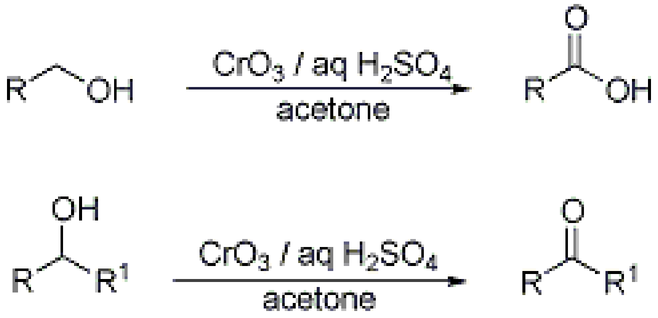
207. Jones Oxidation

K. Bowden *et al.*, *J. Chem. Soc.* **1946,** 39.

The oxidation of primary and secondary alcohols to acids and ketones, respectively, in the presence of chromic acid, aqueous sulfuric acid, and acetone. Isolated multiple bonds are not disturbed under these conditions:



P. Bladon *et al.*, *J. Chem. Soc.* **1951,** 2402; E. R. H. Jones *et al.*, *ibid.* **1953,** 457, 2548, 3019; C. Djerassi *et al.*, *J. Org. Chem.* **21,** 1547 (1956); R. N. Warriner *et al.*, *Aust. J. Chem.* **31,** 1113 (1978); S. V. Ley, A. Madin, *Comp. Org. Syn.* **7,** 253-256 (1991). Extensive synthetic applications: R. A. Epifanio *et al.*, *Tetrahedron Letters* **29,** 6403 (1988); P. A. Evans *et al.*, *Synth. Comm.* **26,** 4685 (1996); N. M. Allanson *et al.*, *Tetrahedron Letters* **39,** 1889 (1998); Y. Watanabe *et al.*, *ibid.* **40,** 3411 (1999). *Cf.* Sarett Oxidation.

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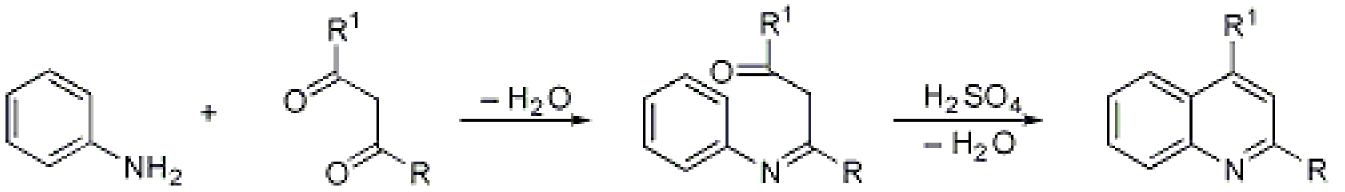
80. Combes Quinoline Synthesis

A. Combes, *Bull. Soc. Chim. France* **49,** 89 (1888).

Formation of quinolines by condensation of β-diketones with primary arylamines followed by acid-catalyzed ring closure of the intermediate Schiff base:



W. S. Johnson, F. J. Matthews, *J. Am. Chem. Soc.* **66,** 210 (1944); F. W. Bergstrom, *Chem. Rev.* **35,** 156 (1944); J. C. Perche *et al., J. Chem. Soc. Perkin Trans. I* **1972,** 260; J. Born, *J. Org. Chem.* **37,** 3952 (1972). *Cf.* Conrad-Limpach Reaction; Doebner Reaction.

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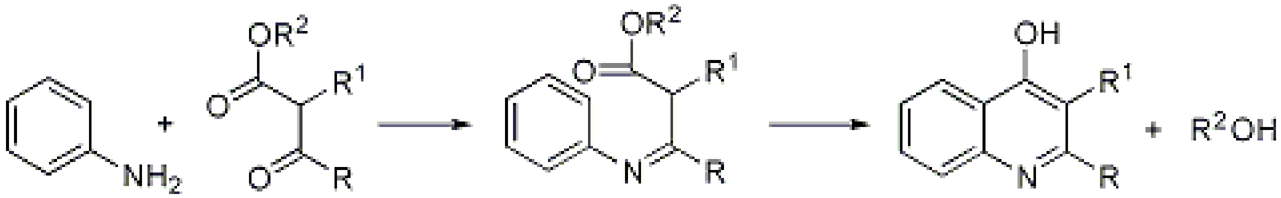
81. Conrad-Limpach Cyclization

M. Conrad, L. Limpach, *Ber.* **20,** 944 (1887); **24,** 2990 (1891).

Thermal condensation of arylamines with β-ketoesters followed by cyclization of the intermediate Schiff bases to 4-hydroxyquinolines:



R. H. Manske, *Chem. Rev.* **30,** 121 (1942); R. H. Reitsema, *ibid.* **43,** 47 (1948); H. Henecka, *Chemie der Beta Dicarbonylverbindungen* (Berlin, 1950) p 307; R. C. Elderfield, *Heterocyclic Compounds* **4,** 30 (1952); J.-C. Perche, G. Saint-Ruf, *J. Heterocyclic Chem.* **11,** 93 (1974); J. M. Barker *et al., J. Chem. Res. (S)* **1980,** 4; J. A. Moore, T. D. Mitchell, *J. Polym. Chem.* **18,** 3029 (1980). *Cf.* Combes Quinoline Synthesis; Doebner Reaction.

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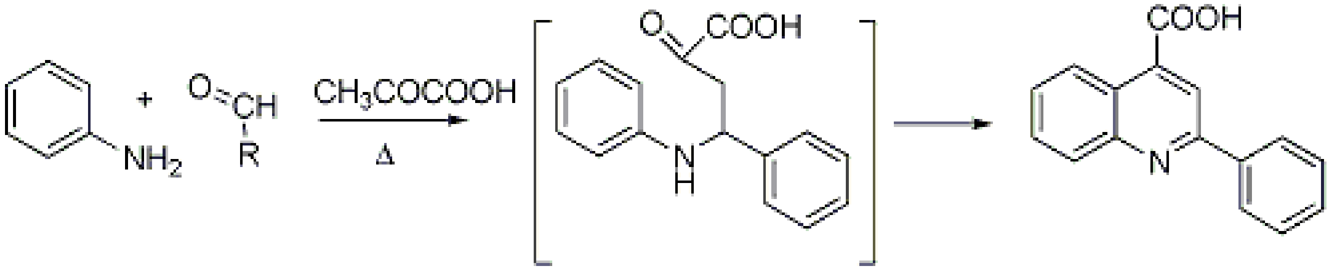
106. Doebner Reaction

O. Doebner, *Ann.* **242,** 265 (1887); *Ber*. **20,** 277 (1887); **27,** 352, 2020 (1894).

Formation of substituted cinchoninic acids from aromatic amines on heating with aldehydes and pyruvic acid:



F. W. Bergström, *Chem. Rev.* **35,** 156 (1944); R. C. Elderfield, *Heterocyclic Compounds* **4,** 25 (1952); C. Centini, *Rev. Soe. Venez. Quim.* **7**(5), 265 (1970), *C.A.* **74,** 76301x (1971); G. E. Gream, A. K. Serelis, *Aust. J. Chem.* **31,** 863 (1978). *Cf.* Combes Quinoline Synthesis; Conrad-Limpach Reaction.

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355. Sandmeyer Reaction; Gattermann Reaction; Körner-Contardi Reaction

T. Sandmeyer, *Ber.* **17,** 1633, 2650 (1884); L. Gattermann, *Ber.* **23,** 1218 (1890); G. Körner, A. Contardi, *Atti Accad. nazl. Lincei* **23 II,** 464 (1914), *C.A.* **9,** 1478 (1915).

Substitution of diazonium groups in aromatic compounds by halo or cyano groups in the presence of cuprous salts (Sandmeyer reaction), copper powder and hydrochloric or hydrobromic acid (Gattermann reaction) or cupric salts (Körner-Contardi reaction):

$$C_6H_5N_2^+ X^- \xrightarrow{CuCl} C_6H_5Cl$$

Early reviews: H. H. Hodgson, *Chem. Rev.* **40,** 251-277 (1947); W. A. Coudrey, D. S. Davies, *Quart. Rev.* **6,** 358-379 (1952); A. Roedig, *Houben-Weyl* **5/4,** 438 (1960); R. Stroh, *ibid.* **5/3,** 846 (1962). Direct conversion of aryl amines to aryl halides: M. P. Doyle, *J. Org. Chem.* **42,** 2426 (1977). Mechanistic studies: J. K. Kochi, *J. Am. Chem. Soc.* **79,** 2942 (1957); C. Galli, *J. Chem. Soc. Perkin Trans. II* **1984,** 897. Synthetic application: C. Corral *et al., Heterocycles* **23,** 1431 (1985). Improved methodology: N. Suzuki *et al., J. Chem. Soc. Perkin Trans. I* **1987,** 645; A. P. Krapcho, S. N. Haydar, *Heterocyclic Commun.* **4,** 291 (1998).

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118. Emde Degradation

H. Emde, *Ber*. **42,** 2590 (1909); *Ann.* **391,** 88 (1912).

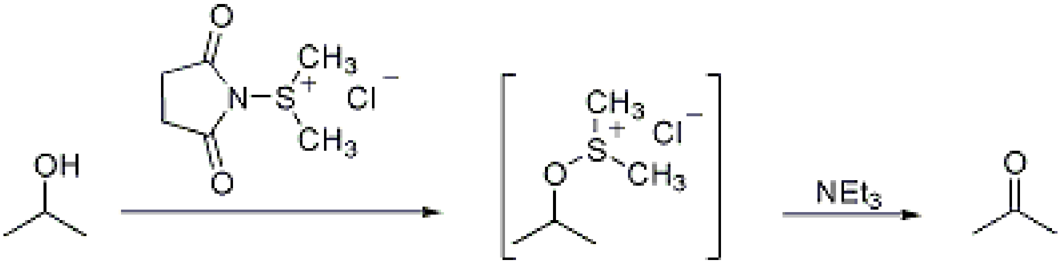
Modification of the Hofmann degradation, *q.v.*, method for reductive cleavage of the carbon-nitrogen bond by treatment of an alcoholic or aqueous solution of a quaternary ammonium halide with sodium amalgam. Also used as a catalytic method with palladium and platinum catalysts. The method succeeds with ring compounds not degraded by the Hofmann procedure:

Reviews: A. Birch, *Org. React.* **7,** 143 278 (1953); F. Möller, *Houben-Weyl* **11/1,** 973 (1955); Z. Spialter, J. A. Pappalardo, *Acyclic Aliphatic Tertiary Amines* (Macmillan, New York, 1965) pp 79-81. Photodegradation: V. Partail, *Helv. Chim. Acta* **68,** 1952 (1985). Synthetic applications: J. G. Cannon *et al., J. Med. Chem.* **18,** 110 (1975); J. Lévy *et al., Tetrahedron Asymmetry* **8,** 4127 (1997).

85. Corey-Kim Oxidation

E. J. Corey, C. U. Kim, *J. Am. Chem. Soc.* **94,** 7586 (1972).

Oxidation of primary and secondary alcohols *via* their alkoxysulfonium salts. Upon the addition of base, the salt rearranges intramolecularly to aldehydes and ketones, respectively:



Application to the synthesis of α-hydroxy ketones: E. J. Corey, C. U. Kim, *Tetrahedron Letters* **1974,** 287; of 1,3-dicarbonyl compounds: S. Katayama *et al.*, *Synthesis* **1988,** 178; J. T. Pulkkinen *et al.*, *J. Org. Chem.* **61,** 8604 (1996). *Cf.* Pfitzner-Moffatt Oxidation; Swern Oxidation.

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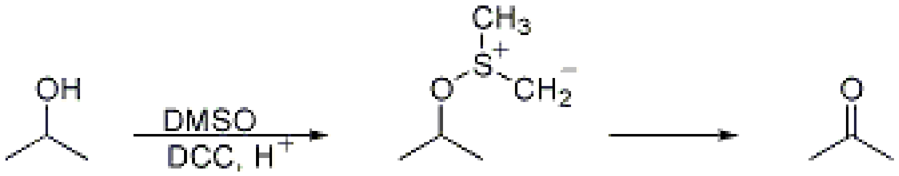
307. Pfitzner-Moffatt Oxidation (Moffatt Oxidation)

K. E. Pfitzner, J. G. Moffatt, *J. Am. Chem. Soc.* **85,** 3027 (1963).

Mild oxidation of primary and secondary alcohols, promoted by dicyclohexylcarbodiimide activation of dimethyl sulfoxide, evidently involving the alkoxysulfonium ylides, which rearrange intramolecularly to generate aldehydes and ketones, respectively:



Reviews: J. G. Moffatt, “Sulfoxide-Carbodiimide and Related Oxidations” in *Oxidation* **vol. 2,** R. L. Augustine, D. J. Trecker, Eds. (Dekker, New York, 1971) pp 1-64; T. T. Tidwell, *Org. React.* **39,** 297-572 *passim* (1990); T. V. Lee, *Comp. Org. Syn.* **7,** 291-303 *passim* (1991). *Cf.* Corey-Kim Oxidation; Swern Oxidation.

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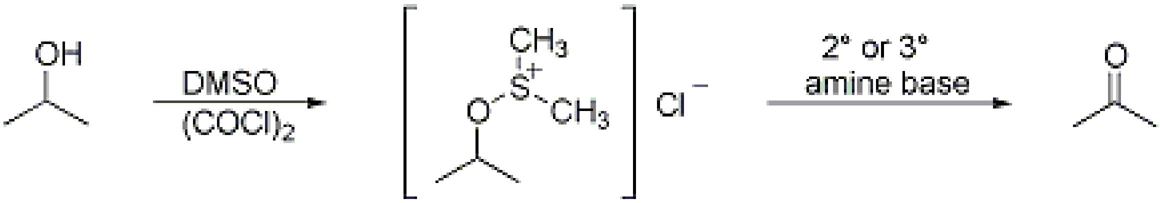
390. Swern Oxidation (Moffatt-Swern Oxidation)

K. Omura, D. Swern, *Tetrahedron* **34,** 1651 (1978).

Mild oxidation of primary and secondary alcohols, promoted by oxalyl chloride activation of dimethyl sulfoxide, evidently involving the dimethyl alkoxysulfonium salts. Upon the addition of base, the intermediates rearrange intramolecularly to generate aldehydes or ketones, respectively:

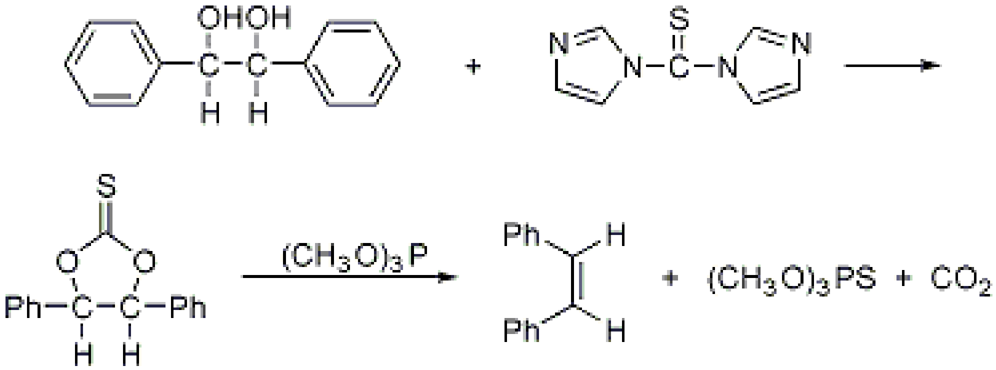


Reactivity/selectivity studies: M. Marx, T. T. Tidwell, *J. Org. Chem.* **49,** 788 (1984). *Reviews:* A. J. Mancuso, D. Swern, *Synthesis* **1981,** 165-185 *passim;* T. T. Tidwell, *Org. React.* **39,** 297-572 *passim* (1990). *Cf.* Corey-Kim Oxidation; Pfitzner-Moffatt Oxidation.

86. Corey-Winter Olefin Synthesis

E. J. Corey, R. A. E. Winter, *J. Am. Chem. Soc.* **85,** 2677 (1963).

Synthesis of olefins from 1,2-diols and thiocarbonyldiimidazole. Treatment of the intermediate cyclic thionocarbonate with trimethylphosphite yields the olefin by *cis*-elimination:



M. Tichy, J. Sicher, *Tetrahedron Letters* **1969,** 4609; E. J. Corey, P. B. Hopkiss, *ibid.* **23,** 1797 (1982); S. Kaneko *et al., Chem. Pharm. Bull.* **45,** 43 (1997). Applications in nucleotide synthesis: L. W. Dudycz, *Nucleosides Nucleotides* **8,** 35 (1989); R. L. K. Carr *et al., Org. Prep. Proced. Int.* **22,** 245 (1990); in enediynes syntheses: M. F. Semmelhack, J. Gallagher, *Tetrahedron Letters* **34,** 4121 (1993); D. Crich *et al., Synth. Commun.* **29,** 359 (1999).

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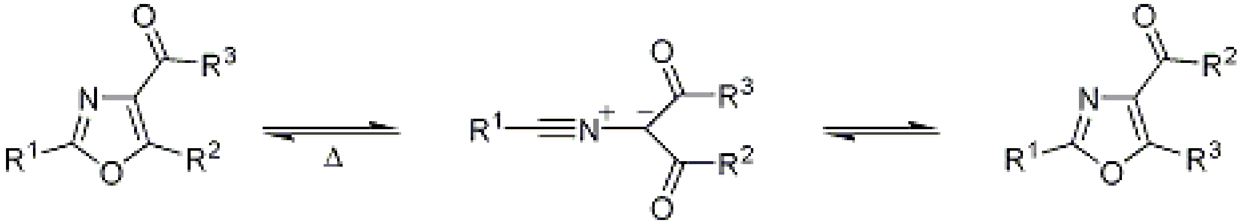
87. Cornforth Rearrangement

J. W. Cornforth, *The Chemistry of Penicillin* (Princeton University Press, New Jersey, 1949) p 700.

Thermal rearrangement of 4-carbonyl substituted oxazoles to their isomeric oxazoles *via* the postulated dicarbonyl nitrile ylides:



Mechanistic study: M. J. S. Dewar, I. J. Turchi, *J. Am. Chem. Soc.* **96,** 6148 (1974). Scope and limitations: *eidem, J. Org. Chem.* **40,** 1521 (1975). Extension to the synthesis of 5-aminothiazoles: S. L. Corrao *et al., ibid.* **55,** 4484 (1990). Synthetic application: G. L'abbé *et al., J. Chem. Soc. Perkin Trans. I* **1993,** 2259.

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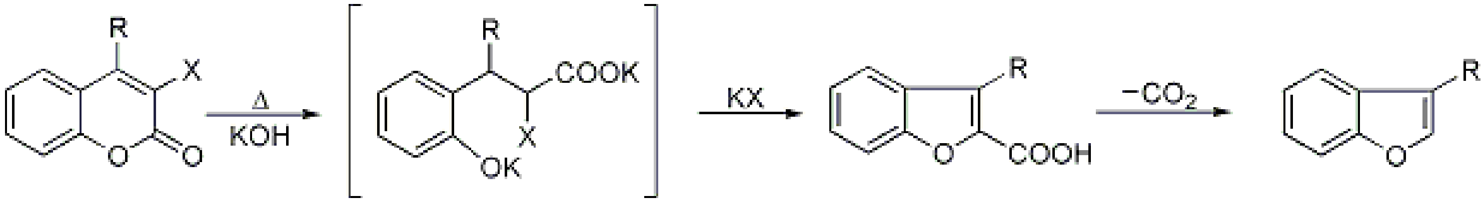
301. **Perkin Rearrangement** (Coumarin-Benzofuran Ring Contraction)

W. H. Perkin, *J. Chem. Soc.* **23,** 368 (1870).

Formation of benzofuran-2-carboxylic acids and benzofurans by heating 3-halocoumarins with alkali:



R. C. Elderfield, V. B. Meyer, *Heterocyclic Compounds* **2,** 2, 5 (1951); K. Bowden, S. Battah, *J. Chem. Soc. Perkin Trans. II* **1998,** 1604.

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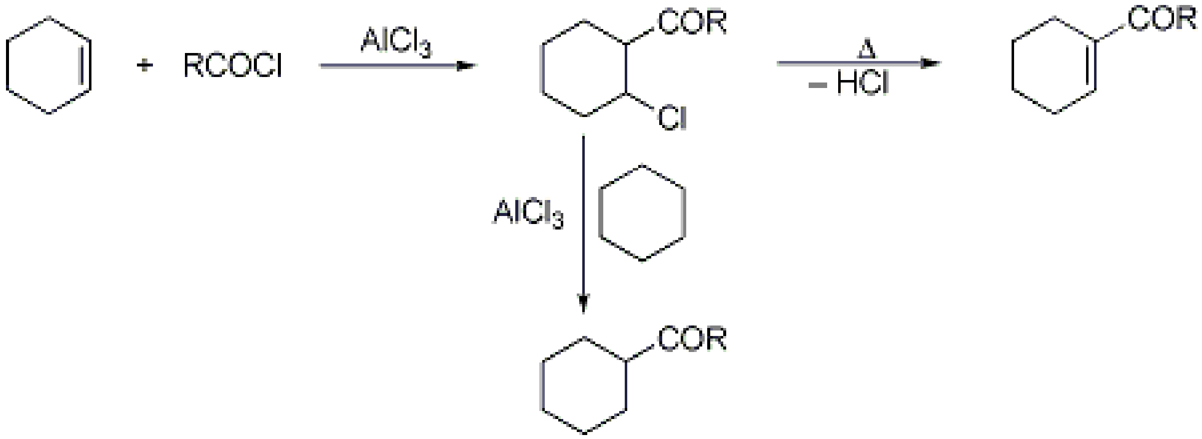
94. Darzens-Nenitzescu Synthesis of Ketones

G. Darzens, *Compt. Rend.* **150,** 707 (1910); C. D. Nenitzescu, I. P. Cantuniari, *Ann.* **510,** 269 (1934); C. D. Nenitzescu, C. Cioranescu, *Ber.* **69,** 1820 (1936).

Acylation of olefins with acid chlorides or anhydrides catalyzed by Lewis acids. When performed in the presence of a saturated hydrocarbon the product is the saturated ketone:



G. A. Olah, *Friedel-Crafts and Related Reactions* **vol. 1** (Interscience, New York, 1963) p 129; C. D. Nenitzescu, A. T. Balaban, *ibid.* **vol. 3,** Part 2, 1069 (1964); L. Ötvös *et al., Acta Chimica Acad. Sci. Hung.* **71**(2), 193 (1972); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) p 786; J. K. Groves, *Chem. Soc. Rev.* **1,** 73 (1972). Synthetic applications: D. Villemin, B. Labiad, *Synth. Commun.* **22,** 3181 (1992); S. Nakanishi *et al., ibid.* **28,** 1967 (1998). *Cf.* Friedel-Crafts Reaction; Nencki Reaction; Nenitzescu Reductive Acylation.

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275. Nencki Reaction

M. Nencki, N. Sieber, *J. Prakt. Chem.* (2) **23,** 147 (1881).

The ring acylation of phenols with acids in the presence of zinc chloride, or the modification of the Friedel-Crafts reaction, *q.v.*, by substitution of ferric chloride for aluminum chloride.

M. Nencki, W. Schmid, *ibid.* 546; M. Nencki, *ibid.* **25,** 273 (1882); U. S. Chiema, K. Venkataraman, *J. Chem. Soc.* **1932,** 918; C. W. Schellhammer, *Houben-Weyl* **7/2a,** 284 (1973); A. S. Anjaneyulu *et al., Indian J. Chem.* **33B,** 847 (1994). *Cf.* Darzens-Nenitzescu Synthesis of Ketones.

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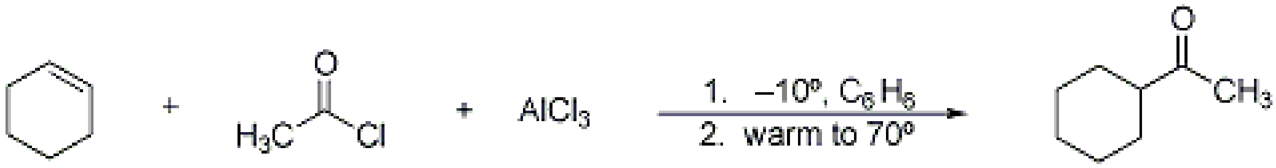
277. Nenitzescu Reductive Acylation

C. D. Nenitzescu, E. Cioranescu, *Ber.* **69,** 1820 (1936).

Hydrogenative acylation of cycloolefins with acid chlorides in the presence of aluminum chloride; with five- and six-membered rings no change in ring size occurs but with seven-membered rings rearrangement takes place with formation of a cyclohexane derivative:

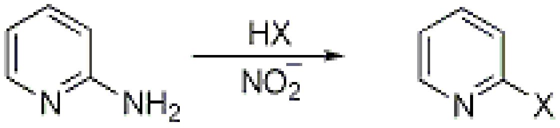


C. Nenitzescu, C. N. Ionescu, *Ann.* **491,** 189 (1931); C. D. Nenitzescu, J. P. Cantuniari, *ibid.* **510,** 269 (1934); C. D. Nenitzescu, I. Chicos, *Ber.* **68,** 1584 (1935); C. A. Thomas, *Anhydrous Aluminum Chloride in Organic Chemistry* (New York, 1941) p 759; S. L. Friess, R. Pinson, *J. Am. Chem. Soc.* **73,** 3512 (1951); Olah, *Friedel-Crafts and Related Reactions* **vol. III,** Part 2 (New York, 1964) p 1069. *Cf.* Darzens-Nenitzescu Synthesis of Ketones.

88. Craig Method

L. C. Craig, *J. Am. Chem. Soc.* **56,** 231 (1934).

Introduction of a halogen into the α-position of aminopyridines by treatment with sodium nitrite in hydrohalic acid followed by warming:

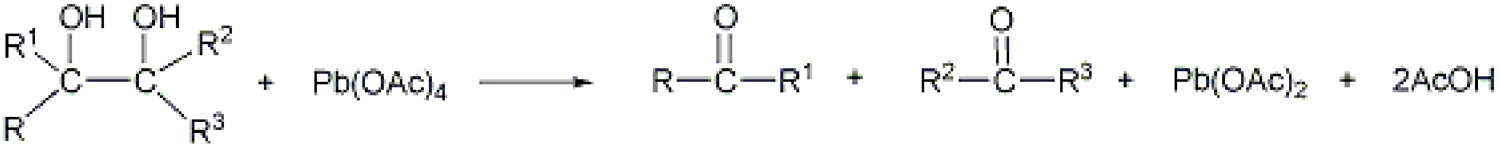


H. S. Mosher, *Heterocyclic Compounds* **1,** 515, 555 (1950); H. E. Mertel in *The Chemistry of Heterocyclic Compounds*, A. Weissberger, Ed., *Pyridine and its Derivatives Part Two*, E. Klingsberg, Ed. (Interscience, New York, 1961) p 334.

89. Criegee Reaction

R. Criegee, *Ber.* **64,** 260 (1931).

Oxidative cleavage of vicinal glycols by lead tetraacetate:



Reviews: R. Criegee in *Newer Methods of Preparative Organic Chemistry* **vol. 1** (Interscience, New York, 1948) pp 12-20; H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 359-387; K. W. Bentley in *Elucidation of Organic Structures by Physical and Chemical Methods* pt. 2, K. W. Bentley, G. W. Kirby, Eds. (Wiley, New York, 2nd ed., 1973) pp 169-177; S. Hatakeyama, H. Akimoto, *Res. Chem. Intermed.* **20,** 503-524 (1994). Mechanism: S. Chandrasekhar, C. D. Roy, *J. Chem. Soc. Perkin Trans. II* **1994,** 2141; R. Ponec *et al., J. Org. Chem.* **62,** 2757 (1997); R. M. Goodman, Y. Kishi, *J. Am. Chem. Soc.* **120,** 9392 (1998). *Cf.* Malaprade Reaction.

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244. Malaprade Reaction (Periodic Acid Oxidation)

L. Malaprade, *Bull. Soc. Chim. France* [4] **43,** 683 (1928); *Compt. Rend.* **186,** 382 (1928).

Compounds containing two hydroxyl groups, or a hydroxyl and an amino group, attached to adjacent carbon atoms, undergo cleavage of the carbon-carbon bond when treated with periodic acid to yield aldehydes:

$$\mathrm{RCHOHCHOHR^1 + HIO_4 \longrightarrow RCHO + R^1CHO + H_2O + HIO_3}$$
$$\mathrm{RCHOHCHNH_2R^1 + HIO_4 \longrightarrow RCHO + R^1CHO + NH_3 + HIO_3}$$

H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 353-359; K. W. Bentley in *Elucidation of Organic Structures by Physical and Chemical Methods*, Pt. 2, K. W. Bentley, G. W. Kirby, Eds. (Wiley, New York, 2nd ed., 1973) pp 177-185. *Cf.* Criegee Reaction.

221. Kolbe Electrolytic Synthesis; Crum Brown-Walker Reaction

H. Kolbe, *Ann.* **69,** 257 (1849).

Formation of symmetrical dimers by the electrolysis of carboxylates (decarboxylative dimerization). The coupling of two distinct carboxylates yields unsymmetrical products:

$$2RCOO^- \xrightarrow{\text{electrolysis}} R{-}R \quad + \quad 2CO_2$$

The dimerization of half-esters is known as the **Crum Brown-Walker reaction:** A. Crum Brown, J. Walker, *ibid.* **261,** 107 (1891).

$$2ROOCCH_2COO^- \xrightarrow{\text{electrolysis}} ROOCCH_2CH_2COOR \quad + \quad 2CO_2$$

Reviews: B. C. L. Weedon, *Quart. Rev.* **6,** 380 (1952); A. K. Vijh, B. E. Conway, *Chem. Rev.* **67,** 623 (1967); L. Eberson in *Organic Electrochemistry*, M. M. Baizer, Ed. (M. Dekker, New York, 1973) pp 469-507; H. J. Schäfer, *Comp. Org. Syn.* **3,** 633-658 (1991); J. Weiguny, H. J. Schäfer, *Ann.* **1994,** 225; G. Nuding *et al.*, *Synthesis* **1996,** 71; J. Hiebl *et al.*, *Tetrahedron* **54,** 2059 (1998); M. Sugiya, H. Noshira, *Chem. Letters* **1998,** 479; *eidem, Bull. Chem. Soc. Japan.* **73,** 705 (2000).

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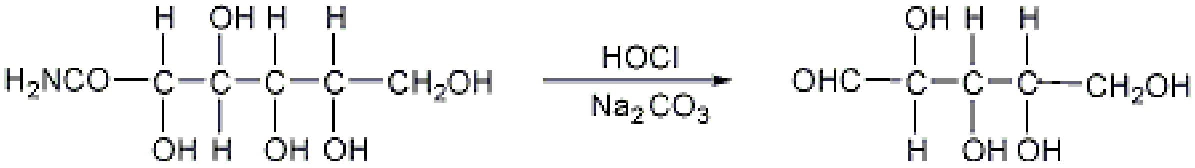
420. Weerman Degradation

R. A. Weerman, *Rec. Trav. Chim.* **37,** 1, 16 (1918).

Formation of an aldose with one less carbon from an aldonic acid by a Hofmann-type reaction, *q.v.*, of the corresponding amide. This is a general reaction of α-hydroxy carboxylic acids:



W. N. Haworth, *et al., J. Chem. Soc.* **1934,** 1722; **1938,** 1975; E. S. Wallis, J. F. Lane, *Org. React.* **3,** 275 (1946); J. C. Sowden in *The Carbohydrates*, W. Pigman, Ed. (New York, 1957) p 120; L. F. Fieser, M. Fieser, *Advanced Organic Chemistry* (New York, 1961) p 945. *Cf.* Hofmann Reaction.

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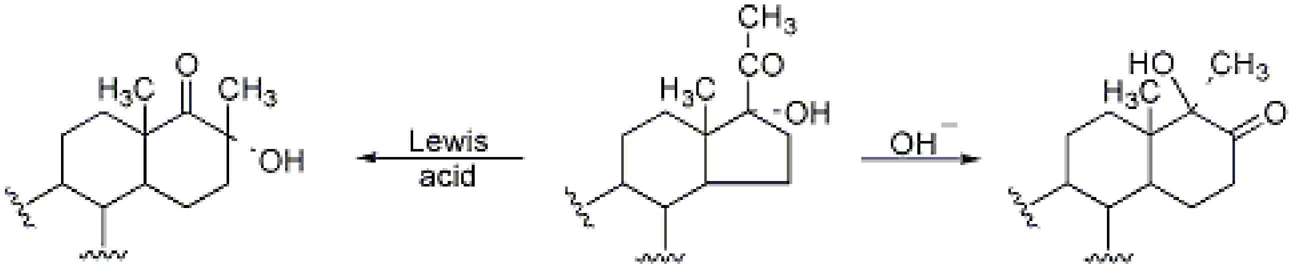
100. D-Homo Rearrangement of Steroids

L. Ruzicka, H. Meldahl, *Helv. Chim. Acta* **21,** 1760 (1938); **22,** 421 (1939).

Originally discovered in 17β-hydroxy-20-ketosteroids, but thoroughly studied in the 17α-hydroxy-20-keto series, this reaction involves an acid- or base-catalyzed acyloin rearrangement which yields a 6-membered D-ring:



R. B. Turner, *J. Am. Chem. Soc.* **75,** 3484 (1953); D. K. Fukushima *et al., ibid.* **77,** 6585 (1955); N. L. Wendler *et al., Tetrahedron* **11,** 163 (1960). *Review:* N. L. Wendler in *Molecular Rearrangements* Part 2, P. de Mayo, Ed. (Wiley-Interscience, New York, 1964) p 1114-1138. Extensive studies: D. Rabinovich *et al., Chem. Commun.* **1976,** 461; N. G. Steinberg *et al., J. Org. Chem.* **49,** 4731 (1984); L. Schor *et al., J. Chem. Soc. Perkin Trans. 1* **1990,** 163; *eidem, ibid.* **1992,** 453.

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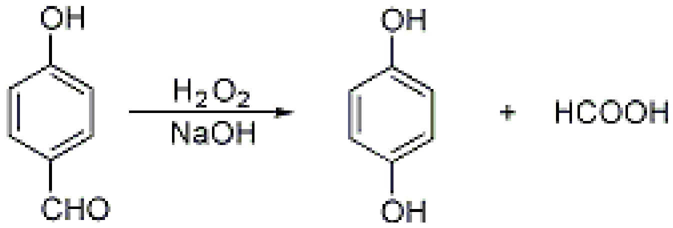
91. Dakin Reaction

H. D. Dakin, *Am. Chem. J.* **42,** 477 (1909).

Replacement of the formyl or acetyl groups in phenolic aldehydes or ketones by a hydroxyl group by means of hydrogen peroxide:

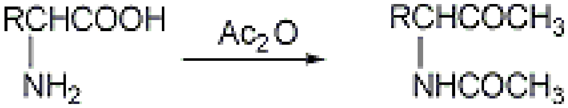


J. E. Leffler, *Chem. Rev.* **45,** 385 (1949). Mechanistic studies: M. B. Hocking, *et al., Can. J. Chem.* **55,** 102 (1977); *eidem, ibid.* **56,** 2646 (1978); M. B. Hocking *et al., J. Org. Chem.* **47,** 4208 (1982). Sodium percarbonate as oxidizing reagent: G. W. Kabalka *et al., Tetrahedron Letters* **33,** 865 (1992).

92. Dakin-West Reaction

H. D. Dakin, R. West, *J. Biol. Chem.* **78,** 91, 745, 757 (1928).

Reaction of α-amino acids with acetic anhydride in the presence of base to give α-acetamido ketones. The reaction occurs *via* the intermediate azlactone:

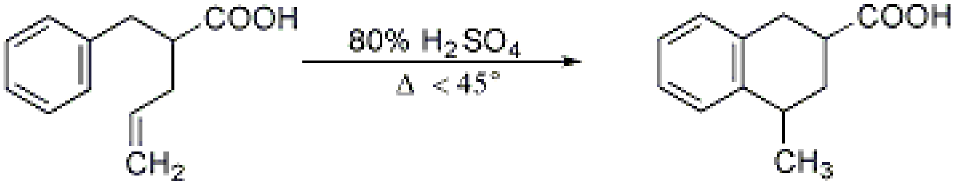


Mechanism: R. Knorr, R. Huisgen, *Ber.* **103,** 2598 (1970); W. Steglich, *et al., Chem. Ber.* **104,** 3644 (1971); G. Holfe *et al., Chem. Ber.* **105,** 1718 (1972); N. Allinger *et al., J. Org. Chem.* **39,** 1730 (1974); M. Kawase *et al., Chem. Pharm. Bull.* **48,** 114 (2000). Synthetic applications: J. R. Casimir *et al., Tetrahedron Letters* **36,** 4797 (1995); T. T. Curran, *J. Fluorine Chem.* **74,** 107 (1995). *Review:* G. L. Buchanan, *Chem. Soc. Rev.* **17,** 91 (1988).

95. Darzens Synthesis of Tetralin Derivatives

G. Darzens, *Compt. Rend.* **183,** 748 (1926).

Cyclization of α-benzyl-α-allylacetic acid type compounds by moderate heating in concentrated sulfuric acid to yield tetralin derivatives:



E. Bergmann, *Chem. Rev.* **29,** 536 (1941); J. N. Chatterjea *et al., Indian J. Chem.* **20B,** 264 (1981).

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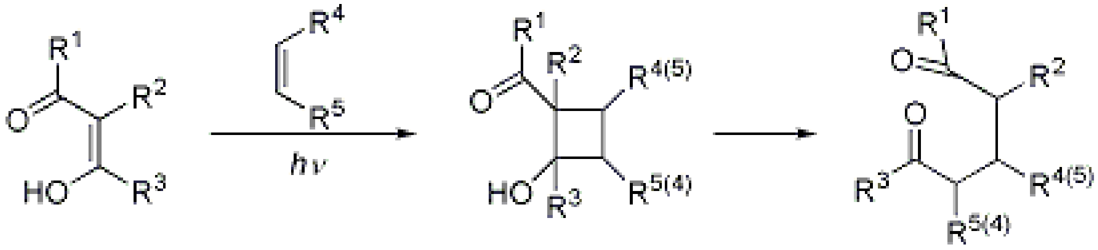
97. de Mayo Reaction

P. de Mayo *et al., Proc. Chem. Soc. London* **1962,** 119; P. de Mayo, H. Takeshita, *Can. J. Chem.* **41,** 440 (1963).

Synthesis of 1,5-diketones by photoaddition of enol derivatives of 1,3-diketones to olefins, followed by a retro-aldol reaction, *q.v.*:



P. de Mayo, *Accts. Chem. Res.* **4,** 49 (1971); H. Meier, *Houben-Weyl* **4/5b,** 924 (1975); W. Oppolzer, *Pure Appl. Chem.* **53,** 1189 (1981). Intramolecular reactions: A. J. Barker, G. Pattenden, *Tetrahedron Letters* **21,** 3513 (1980); *eidem, J. Chem. Soc. Perkin Trans. I* **1983,** 1901. Intermolecular reactions: M. Sato *et al., Chem. Letters* **1994,** 2191; P. Galatsis, J. J. Manwell, *Tetrahedron* **51,** 665 (1995); T. M. Quevillon, A. C. Weedon, *Tetrahedron Letters* **37,** 3939 (1996).

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96. **Delépine Reaction** (Delépine Amine Synthesis)

M. Delépine, *Compt. Rend.* **120,** 501 (1895); **124,** 292 (1897).

Preparation of primary amines by reaction of alkyl halides with hexamethylenetetramine followed by acid hydrolysis of the formed quaternary salts:

$$RCH_2X + C_6H_{12}N_4 \longrightarrow [RCH_2C_6H_{12}N_4]^+ X^- \xrightarrow{HX} RCH_2NH_3^+ X^-$$

S. J. Angyal, *Org. React.* **8,** 197 (1954); Y. Basace *et al., Bull. Soc. Chim. France* **1971,** 1468. Synthetic applications: S. N. Quessy *et al., J. Chem. Soc. Perkin Trans. I* **1979,** 512; S. Brandänge, B. Rodriguez, *Synth. Commun.* **1988,** 347; R. A. Henry *et al., J. Org. Chem.* **55,** 1796 (1990).

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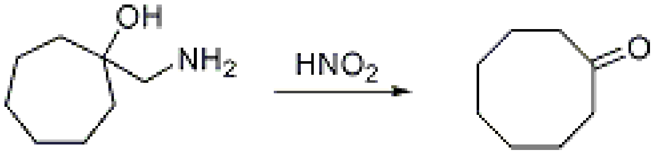
396. Tiffeneau-Demjanov Rearrangement

M. Tiffeneau *et al.*, *Compt. Rend.* **205,** 54 (1937).

Rearrangement of β-amino alcohols upon diazotization with nitrous acid to give carbonyl compounds. Cyclic alcohols yield ring expanded or contracted products:



Reviews: P. A. S. Smith, D. R. Baer, *Org. React.* **11,** 157-188 (1960); H. Metzger, *Houben-Weyl* **10/4,** 233 (1968); D. J. Coveney, *Comp. Org. Syn.* **3,** 781-782 (1991). W. E. Parham, C. S. Roosevelt, *J. Org. Chem.* **37,** 1975 (1972); D. Fattori *et al.*, *Tetrahedron* **49,** 1649 (1993). *Cf.* Demjanov Rearrangement; Pinacol Rearrangement.

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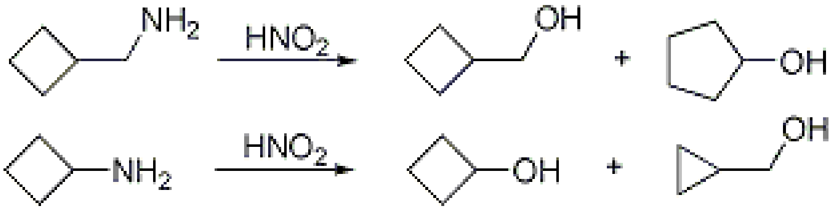
98. Demjanov Rearrangement

N. J. Demjanov, M. Lushnikov, *J. Russ. Phys. Chem. Soc.* **35,** 26 (1903); *Chem. Zentr.* **1903,** 1, 828.

Deamination of primary amines by diazotization to give rearranged alcohols. In the case of alicyclic amines, ring enlargement or contraction occurs:



P. A. S. Smith, D. R. Baer, *Org. React.* **11,** 157 (1960); H. Stetter, P. Goebel, *Ber.* **96,** 550 (1963); R. Kotani, *J. Org. Chem.* **30,** 350 (1965); V. Dave *et al.*, *Can. J. Chem.* **57,** 1557 (1979); R. K. Murray, Jr., T. M. Ford, *J. Org. Chem.* **44,** 3504 (1979); D. Fattori, *et al.*, *Tetrahedron* **49,** 1649 (1993). *Cf.* Tiffeneau-Demjanov Rearrangement; Wagner-Meerwein Rearrangement.

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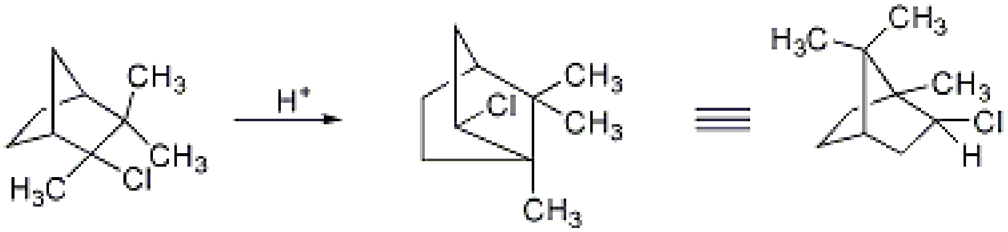
417. Wagner-Meerwein Rearrangement

G. Wagner, *J. Russ. Phys. Chem. Soc.* **31,** 690 (1899); H. Meerwein, *Ann.* **405,** 129 (1914).

Carbon-to-carbon migration of alkyl, aryl or hydride ions. The original example is the acid-catalyzed rearrangement of camphene hydrochloride to isobornyl chloride:



C. Le Drian, P. Vogel, *Helv. Chim. Acta* **70,** 1703 (1987); M. Asaoka, H. Takei, *Tetrahedron Letters* **28,** 6343 (1987); L. U. Román *et al.*, *J. Org. Chem.* **56,** 1938 (1991). Review of applications to alcohols: Y. Pocker in *Molecular Rearrangements* Part 1, P. de Mayo, Ed. (Wiley-Interscience, New York, 1963) pp 6-15; to bicyclic systems: J. Berson, *ibid.* 111-231; to terpenes: J. F. King, P. de Mayo, *ibid.* 813-840; to alkaloids: E. W. Warnhof, *ibid.* 842-879; to steroids: N. L. Wendler, *ibid.* 1020-1028. *Reviews:* R. L. Cargill *et al.*, *Accts. Chem. Res.* **7,** 106-113 (1974); H. Hogeveen, E. M. G. A. Van Kruchten, *Top. Curr. Chem.* **80,** 89-124 (1979); J. R. Hanson, *Comp. Org. Syn.* **3,** 705-719 (1991). *Cf.* Demjanov Rearrangement; Nametkin Rearrangement; Retropinacol Rearrangement.

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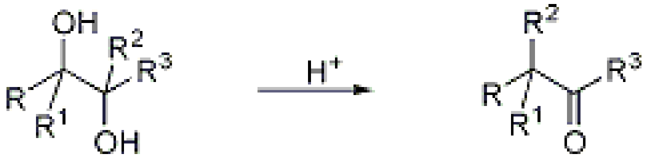
313. Pinacol Rearrangement

R. Fittig, *Ann.* **114,** 54 (1860).

Acid-catalyzed rearrangement of vicinal diols to aldehydes or ketones:



Reviews: C. J. Collins, *Quart. Rev.* **14,** 357 (1960); C. J. Collins, J. F. Eastham in *Chemistry of the Carbonyl Group*, S. Patai, Ed. (Interscience, New York, 1966) pp 762-767; B. Rickborn, *Comp. Org. Syn.* **3,** 721-732 (1991). *Cf.* Tiffeneau-Demjanov Rearrangement.

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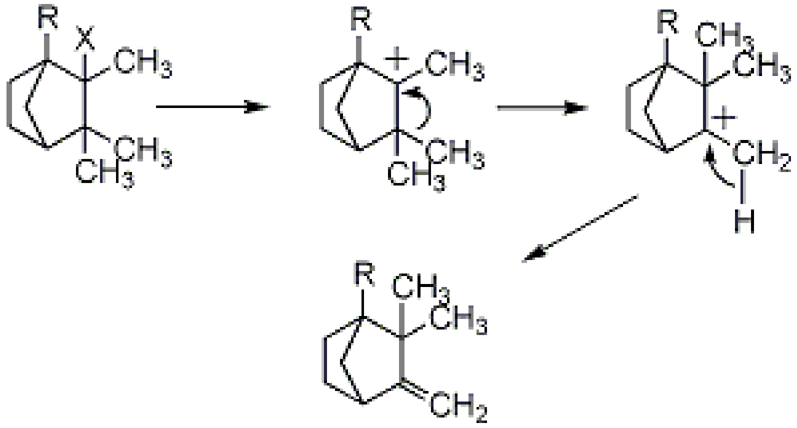
269. Nametkin Rearrangement

S. S. Nametkin, *Ann.* **432,** 207 (1923).

A special case of carbonium ion rearrangement in camphene hydrochloride derivatives involving the migration of a methyl group:



H. Henecka, *Houben-Weyl* **4/2,** 16 (1955); P. S. Moervs *et al.*, *J. Am. Chem. Soc.* **100,** 260 (1978). *Cf.* Retropinacol Rearrangement; Wagner-Meerwein Rearrangement.

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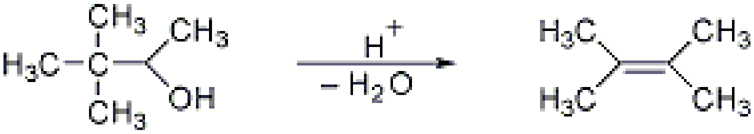
336. Retropinacol Rearrangement

N. Zelinsky, J. Zelikow, *Ber.* **34,** 3249 (1901).

Conversion of an alcohol to the rearranged olefin on treatment with acid:



Application to sterols: W. F. Johns, *J. Org. Chem.* **26,** 4583 (1961); L. M. Harrison, P. V. Fennessey, *J. Steroid. Biochem.* **36,** 407 (1990); to cyclohexanols: W. Hueckel, S. K. Gupte, *Ann.* **685,** 105 (1965). In conjunction with ring expansion: T. Kimura *et al.*, *J. Org. Chem.* **43,** 1247 (1978). *Cf.* Nametkin Rearrangement; Wagner-Meerwein Rearrangement.

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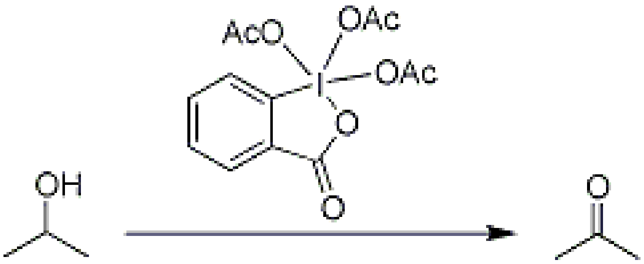
99. Dess-Martin Oxidation

D. B. Dess, J. C. Martin, *J. Org. Chem.* **48,** 4155 (1983).

Mild oxidation of primary and secondary alcohols to aldehydes and ketones, respectively, employing the triacetoxyperiodinane (the “Dess-Martin Periodinane” reagent):



Scope and limitations of fluoroalkyl-substituted carbinols as substrates: R. J. Linderman, D. M. Graves, *J. Org. Chem.* **54,** 661 (1989). Methods development: D. B. Dess, J. C. Martin, *J. Am. Chem. Soc.* **113,** 7277 (1991). Application to the synthesis of 2′- and 3′-ketonucleosides: V. Samano, M. J. Robins, *J. Org. Chem.* **55,** 5186 (1990); of substituted oxazoles: P. Wipf, C. P. Miller, *ibid.* **58,** 3604 (1993). *See* monograph: Dess-Martin Periodinane.

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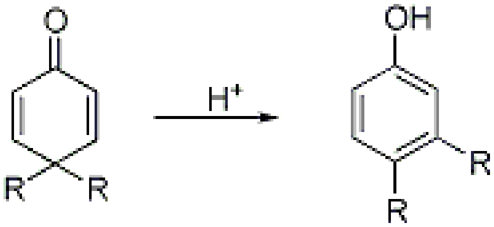
103. Dienone-Phenol Rearrangement

K. von Auwers, K. Ziegler, *Ann.* **425,** 217 (1921).

Transformation of a 4,4-disubstituted cyclohexadienone into a 3,4-disubstituted phenol upon acid treatment:

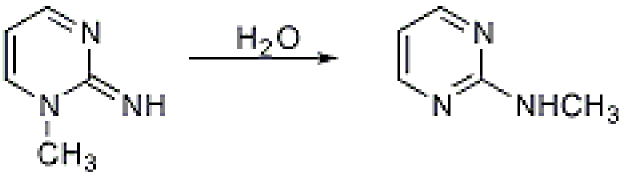


Reviews: C. J. Collins, *et al.*, in *The Chemistry of the Carbonyl Group*, S. Patai, Ed. (Interscience, New York, 1966) pp 775-778; A. J. Waring, *Adv. Alicyclic Chem.* **1,** 207 (1967); B. Miller in *Mechanisms of Molecular Migrations* **vol. 1,** B. S. Thyagarajan, Ed. (Interscience, New York, 1968) pp 275-285; B. Miller, *Accts. Chem. Res.* **8,** 277 (1975). Mechanism: G. Goodyear, A. J. Waring, *J. Chem. Soc. Perkin Trans. II* **1990,** 103. Steric effects: A. G. Schultz, N. J. Green, *Am. Chem. Soc.* **114,** 1824 (1992); A. A. Frimer *et al., J. Org. Chem.* **59,** 1831 (1994). Synthetic applications: D. J. Hart *et al., Tetrahedron* **48,** 8179 (1992); R. W. Draper *et al., Steroids* **63,** 135 (1998).

104. Dimroth Rearrangement

O. Dimroth, *Ann.* **364,** 183 (1909); **459,** 39 (1927).

Rearrangement whereby exo- and endocyclic heteroatoms on a heterocyclic ring are translocated:

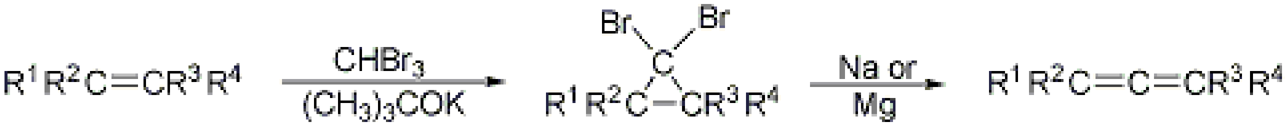


D. J. Brown, J. S. Harper in *Pteridine Chemistry*, W. Pfleiderer, E. C. Taylor, Ed. (Macmillan, New York, 1964) pp 219-230; D. J. Brown in *Mechanisms of Molecular Migrations* **vol. 1,** B. S. Thyagarajan, Ed. (Wiley-Interscience, New York, 1968) p 209; D. J. Brown in *The Pyrimidines* Suppl. I (Interscience, New York, 1970) p 287; D. J. Brown, K. Lenega, *J. Chem. Soc. Perkin Trans. I* **1974,** 372. Mechanism: K. Vaughan *et al., Heterocyclic Chem.* **28,** 1709 (1991); T. Itaya *et al., Chem. Pharm. Bull.* **45,** 832 (1997). Modified reaction: A. R. Katritzky *et al., J. Org. Chem.* **57,** 190 (1992); A. R. Pagano *et al., J. Org. Chem.* **63,** 3213 (1998). *Review:* E. S. H. El Ashry *et al., Adv. Heterocyclic Chem.* **75,** 79-167 (2000).

107. Doering-LaFlamme Allene Synthesis

W. von E. Doering, P. M. LaFlamme, *Tetrahedron* **2,** 75 (1958); **US 2933544** (1960).

Treatment of an olefin with bromoform and an alkoxide to yield the 1,1-dibromocyclopropane which reacts with an active metal to produce an allene:

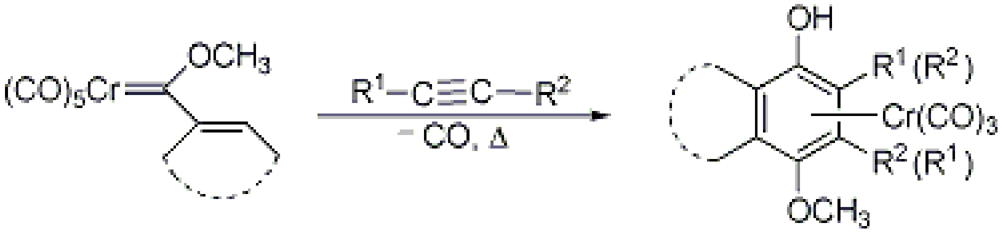


Reviews: M. Murray, *Houben-Weyl* **5/2a,** 985 (1977); V. Nair, *Comp. Org. Syn.* **4,** 1009-1012 (1991).

108. Dötz Reaction

K. H. Dötz, *Angew. Chem. Int. Ed.* **14,** 644 (1975).

Three component cyclization of an aromatic or vinylic alkoxy pentacarbonyl chromium carbene complex, an alkyne, and carbon monoxide, generating a $Cr(CO)_3$ coordinated phenol:



Solvent effects: K. S. Chan *et al., J. Organometal. Chem.* **334,** 9 (1987). Methods development: S. Chamberlin *et al., Tetrahedron* **49,** 5531 (1993); S. Chamberlin, W. D. Wulff, *J. Org. Chem.* **59,** 3047 (1994). Synthetic applications: W. D. Wulff *et al., J. Am. Chem. Soc.* **110,** 7419 (1988); D. L. Boger, I. C. Jacobson, *J. Org. Chem.* **56,** 2115 (1991). *Review:* K. H. Dötz, *New J. Chem.* **14,** 433-445 (1990).

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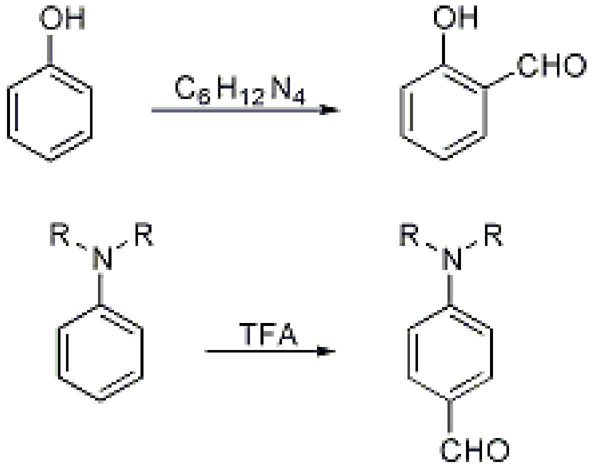
110. Duff Reaction

J. C. Duff, E. J. Bills, *J. Chem. Soc.* **1932,** 1987; **1934,** 1305; **1941,** 547; **1945,** 276.

Formylation of phenols or aromatic amines with hexamethylenetetramine in the presence of an acidic catalyst. *Ortho*-substitution is usual; however in the presence of anhydrous trifluoroacetic acid (TFA) regioselective *ortho* and *para* substitutions are observed.



L. N. Ferguson, *Chem. Rev.* **38,** 230 (1946); Y. Ogata, F. Sugiura, *Tetrahedron* **24,** 5001 (1968); F. Wada *et al.*, *Bull. Chem. Soc. Japan* **53,** 1473 (1980). Use of TFA: W. E. Smith, *J. Org. Chem.* **37,** 3972 (1972); J. F. Larrow *et al.*, *ibid.* **59,** 1939 (1994); L. F. Lindoy *et al.*, *Synthesis* **1998,** 1029. *Cf.* Reimer-Tiemann Reaction.

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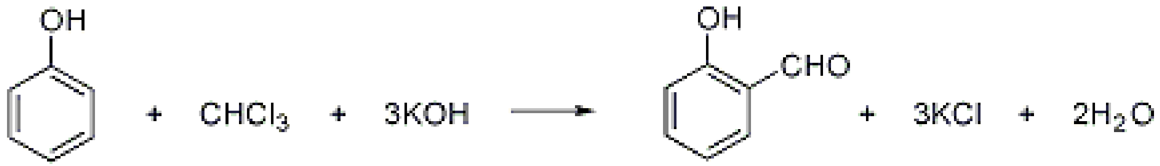
331. Reimer-Tiemann Reaction

K. Reimer, F. Tiemann, *Ber*. **9,** 824, 1268, 1285 (1876).

Formation of phenolic aldehydes from phenols, chloroform and alkali:



Review: H. Wynberg, *Chem. Rev.* **60,** 169 (1960); H. Wynberg, E. W. Meijer, *Org. React.* **28,** 2 (1982); H. Wynberg, *Comp. Org. Syn.* **2,** 769-775 (1991). *Cf.* Duff Reaction; Gattermann Aldehyde Synthesis.

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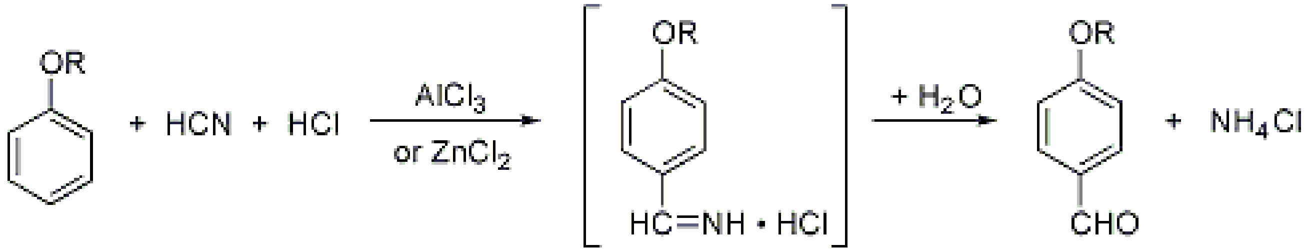
155. Gattermann Aldehyde Synthesis

L. Gattermann, *Ber.* **31,** 1149 (1898); *Ann.* **313,** (1907).

Preparation of phenolic aldehydes, phenol ethers or heterocyclic compounds by treatment of the aromatic substrate with hydrogen cyanide and hydrogen chloride in the presence of Lewis acid catalysts:



W. E. Truce, *Org. React.* **9,** 37 (1957); E. Baltazzi, L. I. Krimen, *Chem. Rev.* **63,** 526 (1963); F. M. Aslam *et al., J. Chem. Soc. Perkin Trans. I* **1972,** 892; Y. Sato *et al., J. Am. Chem. Soc.* **117,** 3037 (1995). *Cf.* Houben-Hoesch Reaction; Reimer-Tiemann Reaction.

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144. Frankland-Duppa Reaction

E. Frankland, *Ann.* **126,** 109 (1863); E. Frankland, B. F. Duppa, *Ann.* **135,** 25 (1865).

Formation of α-hydroxycarboxylic esters by reaction of dialkyl oxalates with alkyl halides in the presence of zinc, or amalgamated zinc, and acid:

$$\mathrm{ROOC{-}COOR} + 2\mathrm{R^1I} + 2\mathrm{Zn} + 2\mathrm{HCl} \longrightarrow \mathrm{R^1R^1C(OH)COOR} + \mathrm{ROH} + \mathrm{ZnI_2} + \mathrm{ZnCl_2}$$

E. Krause, A. von Grosse, *Die Chemie der metallorganischen Verbindungen* (Berlin, 1937) p 225; K. Nützel, *Houben-Weyl* **13/2a,** 741 (1973).

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111. Dutt-Wormall Reaction

P. K. Dutt, H. R. Whitehead, A. Wormall, *J. Chem. Soc.* **119,** 2088 (1921); P. K. Dutt, *ibid.* **125,** 1463 (1924).

Preparation of diazoaminosulfinates by reaction of diazonium salts with aryl- or alkylsulfonamides followed by alkaline hydrolysis to yield the corresponding sulfinic acid of the sulfonamide, and the azide:

$$ArN_2Cl \xrightarrow{H_2NSO_2R} ArN{=}NNHSO_2R \xrightarrow{HO^-} ArN_3 + HO_2SR$$

H. Bretschneider, H. Rager, *Monatsh.* **81.** 970 (1950); I. G. Laing, *Rodd's Chemistry of Carbon Compounds* **IIIC,** 107 (1973); C. Grundmann, *Houben-Weyl* **10/3,** 808 (1965).

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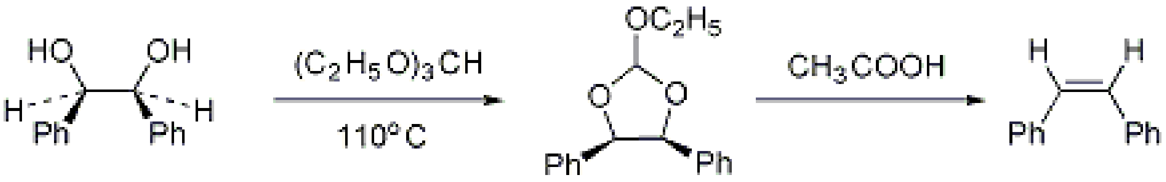
112. **Eastwood Reaction** (Eastwood Deoxygenation)

G. Grank, F. W. Eastwood, *Aust. J. Chem.* **17,** 1392 (1964).

Stereospecific conversion of vicinal diols into olefins:



Review: E. Block, *Organic Reactions* **30,** 478-491 (1984). *Cf.* Corey-Winter Olefin Synthesis.

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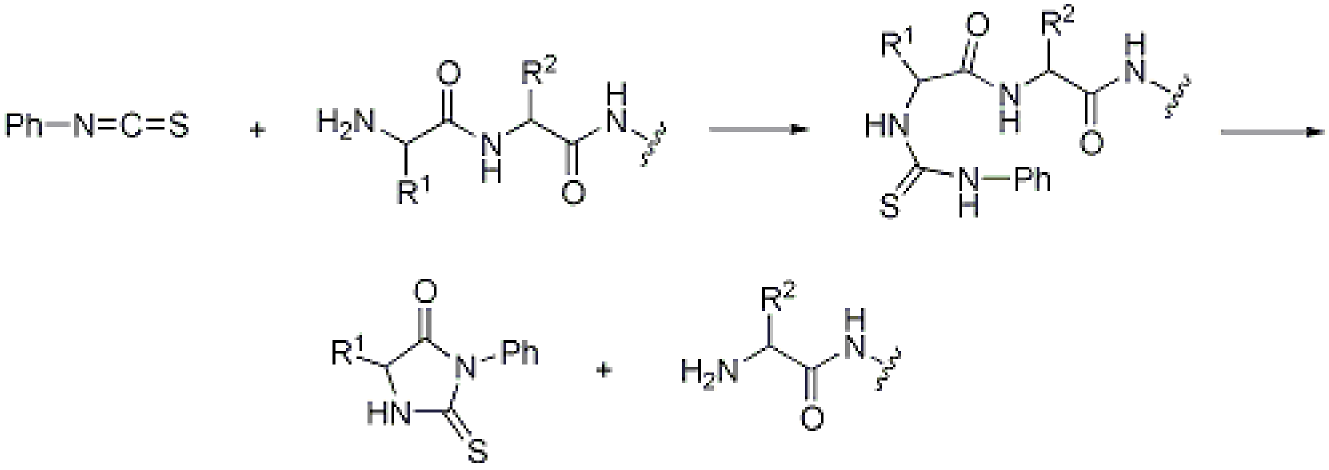
113. Edman Degradation

P. Edman, *Acta Chem. Scand.* **4,** 283 (1950).

Cyclic degradation of peptides based on the reaction of phenylisothiocyanate with the free amino group of the *N*-terminal residue such that amino acids are removed one at a time and identified as their phenylthiohydantoin derivatives:

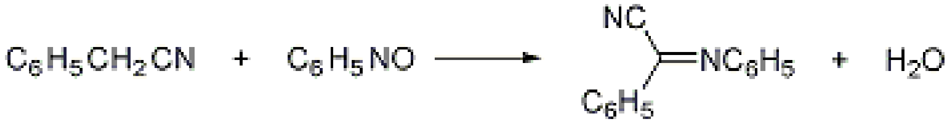


S. Bösze *et al., J. Chromatog. A* **668,** 345 (1994). *Reviews:* R. A. Laursen *et al., Methods Biochem. Anal.* **26,** 201-284 (1980); R. L. Heinrikson, “The Edman Degradation in Protein Sequence Analysis” in *Biochemical and Biophysical Studies of Proteins and Nucleic Acids,* T.-B. Lo *et al.,* Eds. (Elsevier, New York, 1984) pp 285-302; K.-K. Han *et al., Int. J. Biochem.* **17,** 429-445 (1985); C. G. Fields *et al., Peptide Res.* **6,** 39-47 (1993).

114. Ehrlich-Sachs Reaction

P. Ehrlich, F. Sachs, *Ber.* **32,** 2341 (1899).

Formation of *N*-phenylimines by the base-catalyzed condensation of compounds containing active methylene groups with aromatic nitroso compounds; nitrones also may be formed:



$$C_6H_5CH_2CN + C_6H_5NO \longrightarrow \overset{NC}{\underset{C_6H_5}{>}}C{=}NC_6H_5 + H_2O$$

F. Barrow, F. J. Thorneycroft, *J. Chem. Soc.* **1939,** 769; A. McGookin, *J. Appl. Chem.* **5,** 65 (1955); F. Bell, *J. Chem. Soc.* **1957,** 516; D. M. W. Anderson, F. Bell, *ibid.* **1959,** 3708; D. M. W. Anderson, J. L. Duncan, *ibid.* **1961,** 1631; W. Seidenfaden, *Houben-Weyl* **10/1,** 1079 (1971). Applications: F. Millich, M. T. El-Shoubary, *Org. Prep. Proced. Int.* **28,** 366 (1996); S. K. De *et al., Can. J. Chem.* **76,** 199 (1998).

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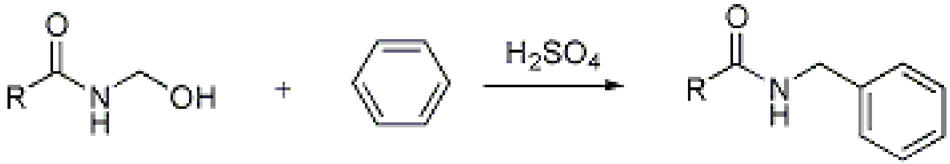
401. Tscherniac-Einhorn Reaction

J. Tscherniac, **DE 134979;** A. Einhorn *et al.*, *Ann.* **343,** 207 (1905); **361,** 113 (1908).

Introduction of the amidomethyl group into aromatic rings or activated methylene groups in the presence of sulfuric acid:



Reviews: R. Schröter, *Houben-Weyl* **11/1,** 795 (1957); Hellman *Angew. Chem.* **69,** 463 (1957); H. E. Zaugg, W. B. Martin, *Org. React.* **14,** 52 (1965); H. E. Zaugg *et al., J. Org. Chem.* **34,** 11, 14 (1969); K. Bott, *Ber.* **106,** 2513 (1973); A. R. Mitchell *et al., Tetrahedron Letters* **1976,** 3795.

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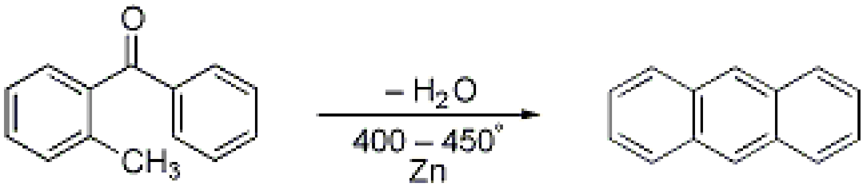
117. Elbs Reaction

K. Elbs, E. Larsen, *Ber*. **17,** 2847 (1884).

Formation of polyaromatics (*eg*. anthracene) by intramolecular condensation of diaryl ketones containing a methyl or methylene substituent adjacent to the carbonyl group:



L. F. Fieser, *Org. React.* **1,** 129 (1942); G. N. Badger, B. J. Christie, *J. Chem. Soc.* **1956,** 3435; N. P. Buu-Hoi, D. Lavit, *Rec. Trav. Chim.* **76,** 419 (1957); Cl. Marie *et al., J. Chem. Soc.* **1971,** 431; M. S. Newman, V. K. Khanna, *J. Org. Chem.* **45,** 4507 (1980).

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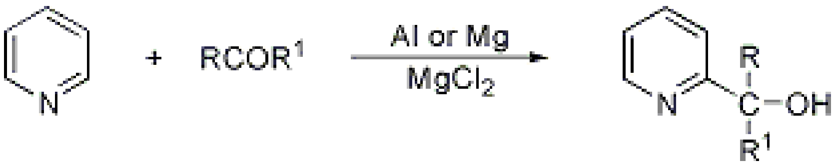
119. Emmert Reaction

B. Emmert, E. Asendorf, *Ber.* **72,** 1188 (1939); B. Emmert, E. Pirot, *ibid.* **74,** 714 (1941).

Formation of pyridyldialkylcarbinols by condensation of ketones with pyridine or its homologs in the presence of aluminum or magnesium amalgam:



C. H. Tilford *et al., J. Am. Chem. Soc.* **70,** 4001 (1948); H. L. Lochti *et al., ibid.* **75,** 4477 (1953); R. Abramovitch, R. Vinutha, *J. Chem. Soc. C* **1969,** 2104; C. A. Russell *et al., J. Chem. Soc. D* **1970,** 1406; R. Tschesche, W. Führer, *Ber.* **111,** 3502 (1978).

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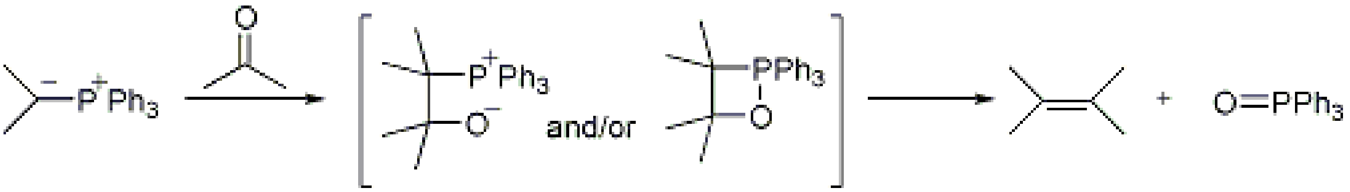
430. Wittig Reaction; Horner Reaction; Horner-Wadsworth-Emmons Reaction

G. Wittig, U. Schöllkopf, *Ber.* **87,** 1318 (1954); G. Wittig, W. Haag, *ibid.* **88,** 1654 (1955).

Alkene formation from carbonyl compounds and phosphonium ylides, proceeding primarily through the proposed betaine and/or oxaphosphetane intermediates. The stereoselectivity can be controlled by the choice of ylide, carbonyl compound, and reaction conditions:



When the ylide is replaced with a phosphine oxide carbanion, the reaction is referred to as the **Horner reaction:** L. Horner *et al., Ber.* **91,** 61 (1958); *idem et al., ibid.* **92,** 2499 (1959).

When the ylide is replaced with a phosphonate carbanion, the reaction is referred to as the **Horner-Emmons-Wadsworth reaction:** W. S. Wadsworth, Jr., W. D. Emmons, *J. Am. Chem. Soc.* **83,** 1733 (1961).

Application to the synthesis of β,γ-unsaturated amides: T. Janecki *et al., Tetrahedron* **51,** 1721 (1995). *Reviews:* A. Maercker, *Org. React.* **14,** 270-490 (1965); K. P. C. Vollhardt, *Synthesis* **1975,** 765-780; W. S. Wadsworth, Jr., *Org. React.* **25,** 73-253 (1977); I. Gosney, A. G. Rowley in *Organophosphorus Reagents in Organic Synthesis,* J. I. G. Cadogan, Ed. (Academic Press, New York, 1979) pp 17-153; B. E. Maryanoff, A. B. Reitz, *Chem. Rev.* **89,** 863-927 (1989); S. E. Kelly, *Comp. Org. Syn.* **1,** 755-782 (1991). Reviews of mechanistic studies: W. E. McEwen *et al., ACS Symposium Series* **486,** 149-161 (1992); E. Vedejs, M. J. Peterson, *Top. Stereochem.* **21,** 1-157 (1994). *Cf.* Peterson Reaction; Tebbe Reaction.

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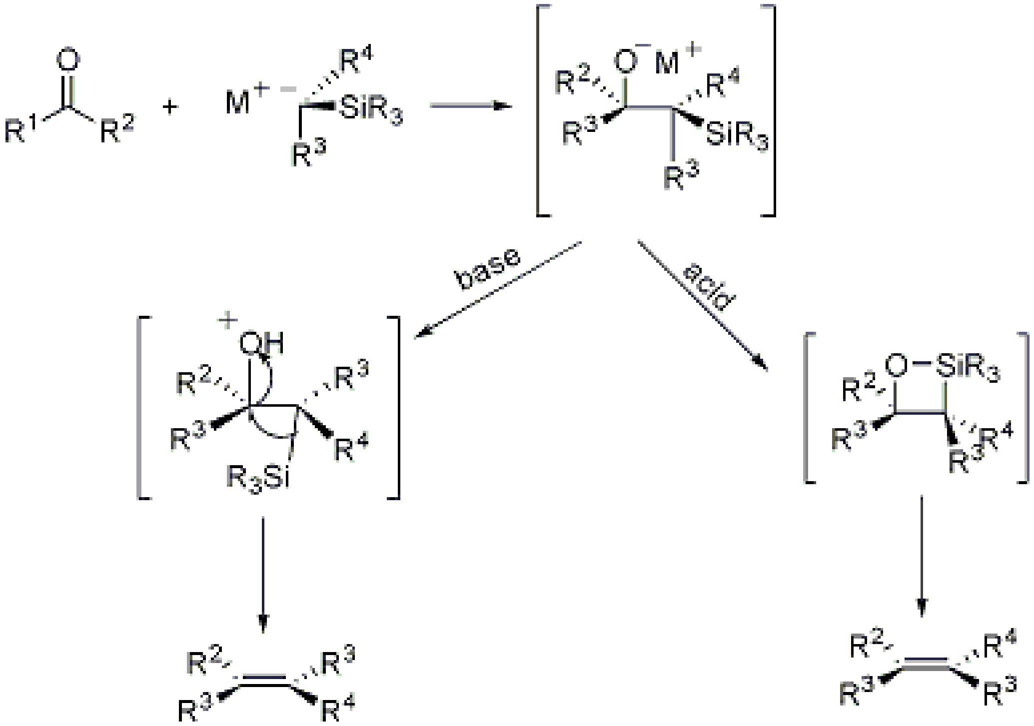
303. **Peterson Reaction** (Olefination)

D. J. Peterson, *J. Org. Chem.* **33,** 780 (1968).

Reaction of α-silyl carbanions with carbonyl compounds yielding β-silylalkoxides which undergo instantaneous elimination to afford olefins:



L. Birkofer, O. Stiehl, *Top. Curr. Chem.* **88,** 58 (1980); E. Colvin, *Silicon in Organic Synthesis* (Butterworth, London, 1981) p 143; D. J. Ager, *Synthesis* **1984,** 384-398; *idem, Org. React.* **38,** 1-223 (1990); S. E. Kelly, *Comp. Org. Syn.* **1,** 731-737, 782-783 (1991). *Cf.* Tebbe Olefination; Wittig Reaction.

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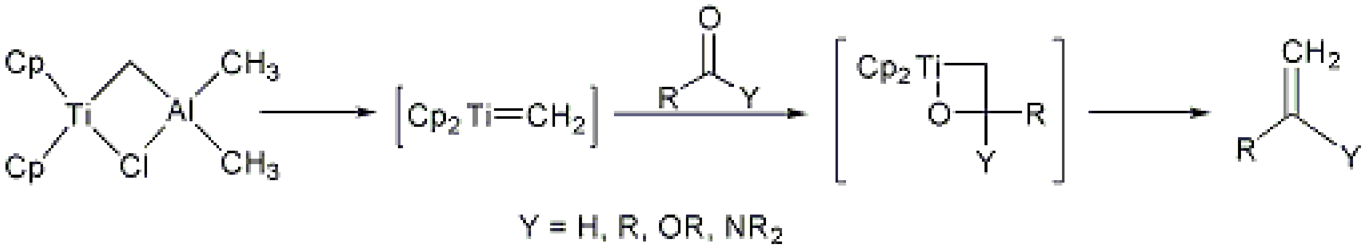
392. Tebbe Olefination (Methylenation)

F. N. Tebbe *et al., J. Am. Chem. Soc.* **100,** 3611 (1978); S. H. Pine *et al., ibid.* **102,** 3270 (1980).

Exchange of the oxygen atom of a carbonyl function for the methylene group of the proposed titanium carbene complex (the Tebbe reagent) to yield terminal alkenes:



Comparative study with Wittig reaction, *q.v.*: S. H. Pines *et al., Synthesis* **1991,** 165. *Reviews:* K. A. Brown-Wensley *et al., Pure Appl. Chem.* **55,** 1733-1744 (1983); S. E. Kelly, *Comp. Org. Syn.* **1,** 743-746 (1991); S. H. Pines, *Org. React.* **43,** 1-91 (1993). *Cf.* Peterson Reaction.

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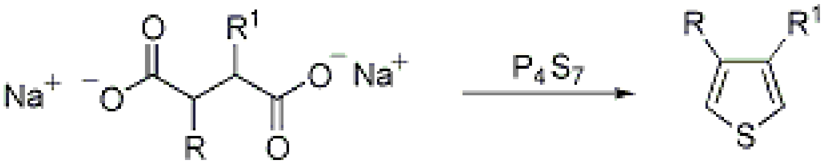
409. Volhard-Erdmann Cyclization

J. Volhard, H. Erdmann, *Ber.* **18,** 454 (1885).

Synthesis of alkyl and aryl thiophenes by cyclization of disodium succinate or other 1,4-difunctional compounds (γ-oxo acids, 1,4-diketones, chloroacetyl-substituted esters) with phosphorus heptasulfide:

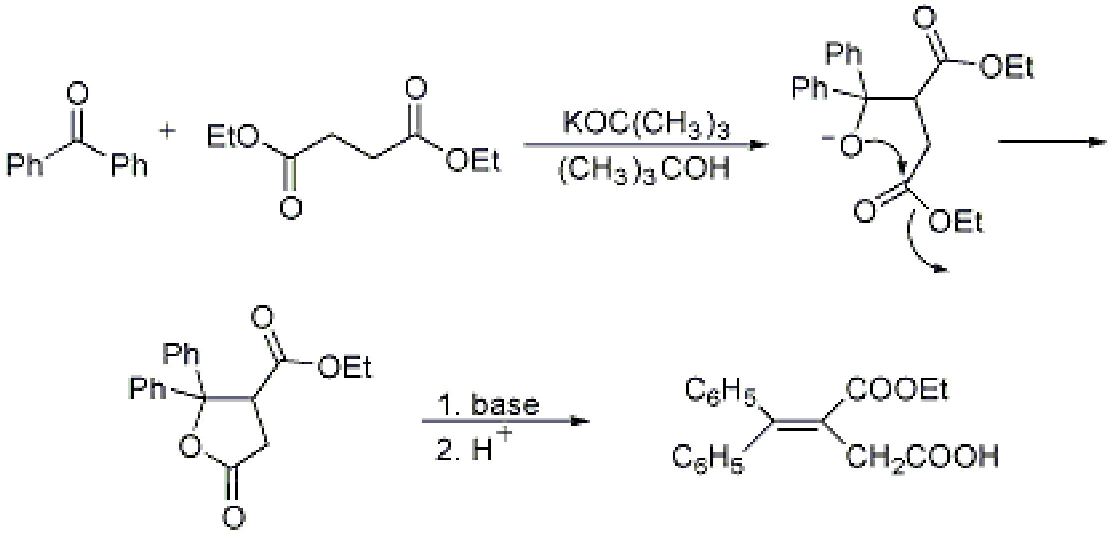


L. H. Friedburg, *J. Am. Chem. Soc.* **12,** 83 (1890); *J. Chem. Soc.* **58,** 1400 (1890); R. Phillips, *Org. Syn.* **coll. vol. II,** 578 (1943); F. F. Blicke, *Heterocyclic Compounds* **1,** 212 (1950); D. E. Wolf, K. Folkers, *Org. React.* **4,** 412 (1951); R. F. Feldkamp, B. F. Tullar, *Org. Syn.* **coll. vol. IV,** 671 (1963).

380. Stobbe Condensation

H. Stobbe, *Ber.* **26,** 2312 (1893); *Ann.* **282,** 280 (1894).

Condensation of aldehydes or ketones with diethyl succinate in the presence of a strong base to form monoesters of α-alkylidene (or arylidene) succinic acids:



Reviews: W. S. Johnson, G. H. Daub, *Org. React.* **6,** 1 (1951); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 663-666; R. J. Hart, H. G. Heller, *J. Chem. Soc. Perkin Trans. I* **1972,** 1321; N. R. El-Rayyes, *J. Prakt. Chem.* **315,** 295 (1973); V. B. Bagos *et al., Helv. Chim. Acta* **62,** 90 (1979). *Cf.* Perkin Reaction.

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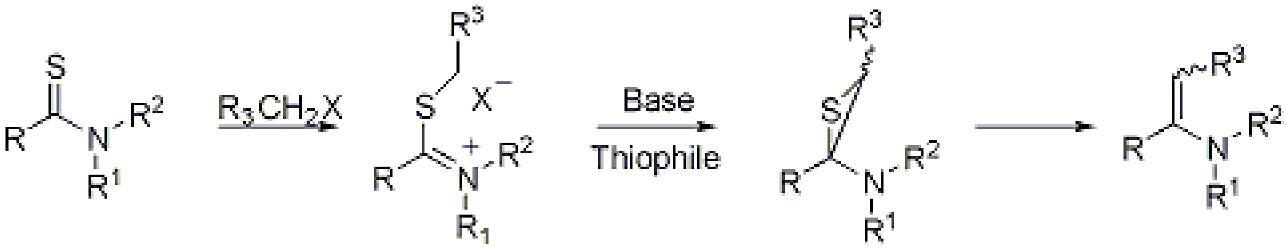
122. Eschenmoser Coupling Reaction (Sulfide Contraction)

A. Fischli, A. Eschenmoser, *Angew. Chem. Int. Ed.* **6,** 866 (1967); M. Roth *et al., Helv. Chim. Acta* **54,** 710 (1971).

Formation of vinylogous amides and urethanes by alkylation of secondary or tertiary thioamides with an electophilic agent followed by elimination of sulfur:



Synthetic applications: E. Götschi *et al., Angew. Chem. Int. Ed.* **12,** 910 (1973); O. Sakurai *et al., J. Org. Chem.* **61,** 7889 (1996), T. G. Minehan, Y. Kishi, *Tetrahedron Letters* **38,** 6811 (1997). *Review:* K. Shiosaki, *Comp. Org. Syn.* **2,** 865-894 (1991).

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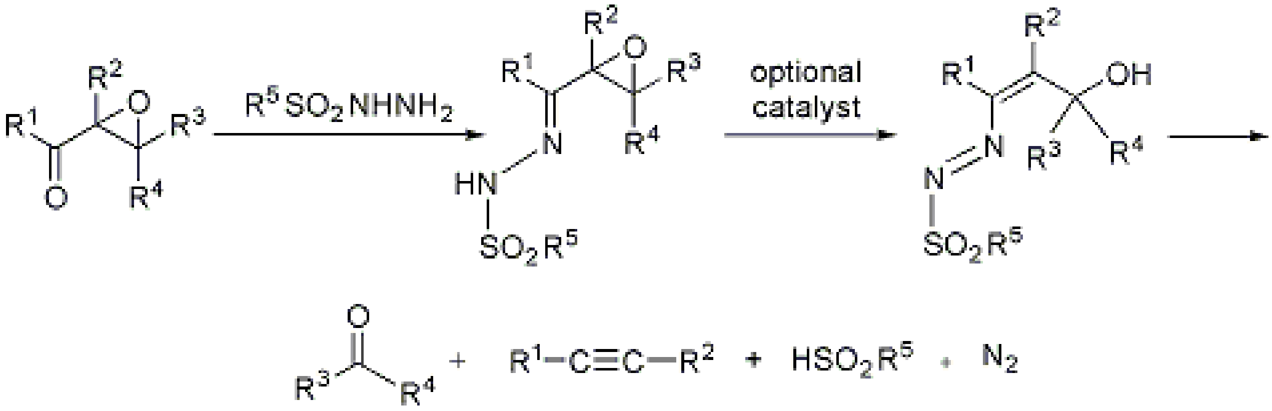
123. Eschenmoser Fragmentation (Eschenmoser-Tanabe Fragmentation)

A. Eschenmoser *et al., Helv. Chim. Acta* **50,** 708 (1967); J. Schreiber *et al., ibid.* 2101; M. Tanabe *et al., Tetrahedron Letters* **1967,** 3943.

Cleavage of α,β-epoxyketones under mild conditions, *via* sulfonylhydrazone intermediates, to yield acetylenic and carbonyl compounds:



R^5 = *p*-toluene, 2,4,6-trimethylbenzene, 2,4-dinitrobenzene
optional catalyst = C_6H_5N, $NaHCO_3$, Na_2CO_3, silica gel

Early review: D. Felix *et al., Helv. Chim. Acta* **54,** 2896-2912 (1971). Synthetic applications: C. B. Reese, H. P. Sanders, *Synthesis* **1981,** 276; W. Dai, J. A. Katzenellenbogen, *J. Org. Chem.* **58,** 1900 (1993); A. Abad *et al., Synlett* **1991,** 787. *Cf.* Grob Fragmentation; Wharton Reaction.

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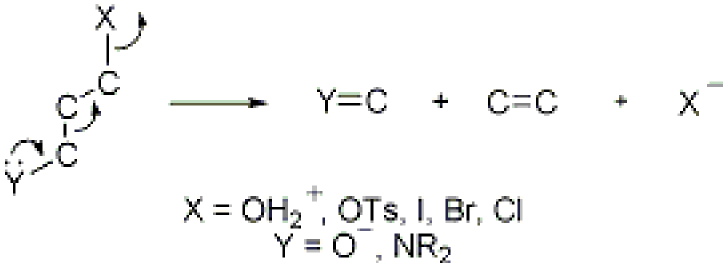
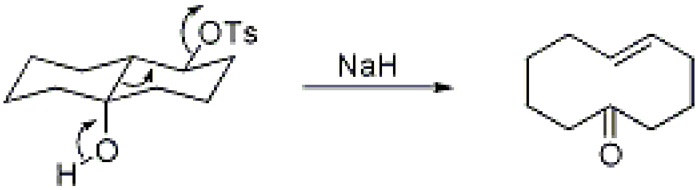
165. Grob Fragmentation

C. A. Grob, W. Baumann, *Helv. Chim. Acta* **38,** 594 (1955).

Carbon-carbon bond cleavage primarily *via* a concerted process involving a five atom system:



The intramolecular version is useful for the preparation of medium-size rings:



M. Ochiai *et al., J. Org. Chem.* **54,** 4832 (1989); S. Nagumo *et al., Tetrahedron* **49,** 10501 (1993); J.-J. Wang *et al. ibid.* **54,** 13149 (1998). Synthetic applications: S. Schreiber, *J. Am. Chem. Soc.* **102,** 6163 (1980); J. Boivin *et al., Tetrahedron Letters* **40,** 9239 (1999); A. Krief *et al., ibid.* **41,** 3871 (2000). *Reviews:* C. A. Grob, *Angew. Chem. Int. Ed.* **8,** 535-546 (1969); P. Weyerstahl, H. Marschall, *Comp. Org. Syn.* **6,** 1044-1065 (1991). *Cf.* Eschenmoser Fragmentation; Wharton Reaction.

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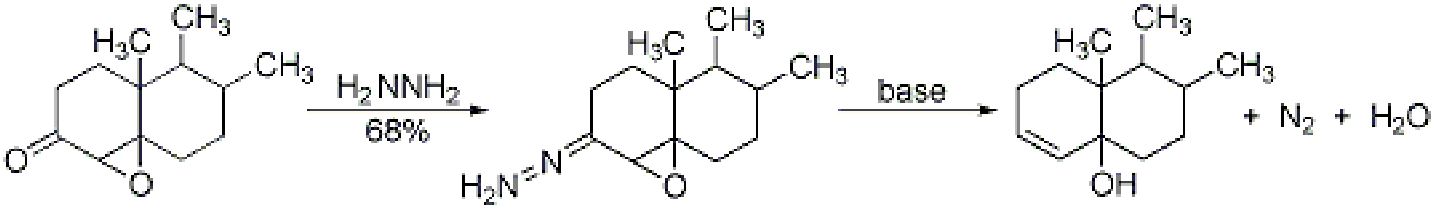
424. Wharton Reaction

P. S. Wharton, D. H. Bohlen, *J. Org. Chem.* **26,** 3615 (1961); P. S. Wharton, *ibid.* 4781.

Reduction of α,β-epoxy ketones by hydrazine to allylic alcohols:



Improved procedure: C. Dupuy, J. L. Luche, *Tetrahedron* **45,** 3437 (1989). Synthetic applications: S. Takano *et al., Synlett* **1991,** 636; T. Yoshimitsu *et al., Synthesis* **1994,** 1029; K. Yamada *et al., J. Org. Chem.* **63,** 3666 (1998). *Review:* D. Caine, *Org. Prep. Proced. Int.* **20,** 3-8 (1988); A. R. Chamberlin, D. J. Sall, *Comp. Org. Syn.* **8,** 927-929 (1991). *Cf.* Eschenmoser Fragmentation; Grob Fragmentation.

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124. Étard Reaction

A. L. Étard, *Compt. Rend.* **90,** 534 (1880); *Ann. Chim. Phys.* **22,** 218 (1881).

Oxidation of an arylmethyl group to an aldehyde by treatment with chromyl chloride:

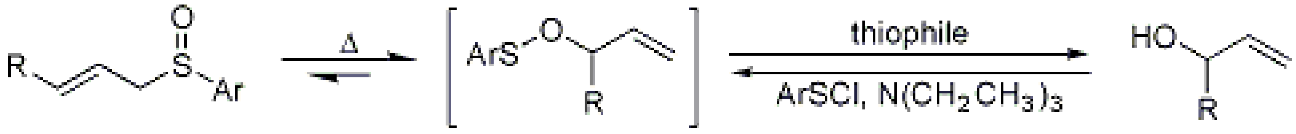
$$C_6H_5CH_3 \xrightarrow{CrO_2Cl_2} C_6H_5CHO$$

W. H. Hartford, M. Darrin, *Chem. Rev.* **58,** 1 (1958); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) p 289; C. D. Nenitzescu *et al., Rev. Roum. Chim.* **14,** 1543, 1553 (1969); I. I. Schiketanz *et al., ibid.* **22,** 1097 (1977); J. C. W. Chien, J. K. Y. Kiang, *Macromolecules* **13,** 280 (1980); F. A. Luzzio, W. J. Moore, *J. Org. Chem.* **58,** 512 (1993).

263. Mislow-Evans Rearrangement

P. Bickart *et al., J. Am. Chem. Soc.* **90,** 4869 (1968); D. A. Evans *et al., ibid.* **93,** 4956 (1971).

[2,3]-Sigmatropic rearrangement of allylic sulfoxides to allylic sulfenates which are captured by thiophiles to generate the allylic alcohols, thereby effecting the 1,3-transposition of sulfoxide and alcohol functions. The reverse process is accomplished by treating the alcohol with arylsulfenyl chloride, followed by thermal rearrangement of the sulfenate to generate the allylic sulfoxide:



thiophile = $P(OCH_3)_3$, $(CH_3CH_2)_2NH$, piperidine, PhS^-

Early review: D. A. Evans, G. C. Andrews, *Accts. Chem. Res.* **7,** 147 (1974). Acid-catalyzed modification: Y. Masaki *et al., Chem. Pharm. Bull.* **33,** 2531 (1985). Synthetic applications: H. J. Reich, S. Wollowitz, *J. Am. Chem. Soc.* **104,** 7051 (1982); G. H. Posner *et al., J. Org. Chem.* **52,** 4836 (1987); A. Padwa *et al., ibid.* **56,** 4252 (1991). Mechanistic studies: D. K. Jones-Hertzog, W. L. Jorgensen, *ibid.* **60,** 6682 (1995); *eidem, J. Am. Chem. Soc.* **117,** 9077 (1995). *Cf.* Meisenheimer Rearrangements; [2,3]-Wittig Rearrangement.

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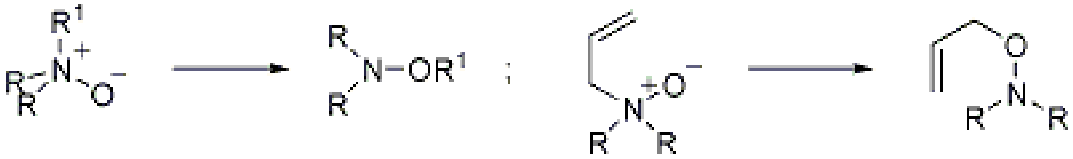
251. Meisenheimer Rearrangements

J. Meisenheimer, *Ber*. **52,** 1667 (1919).

Formation of *O*, *N*, *N*-trisubstituted hydroxylamines from tertiary amine oxides *via* [1,2]-R group migration, or [2,3]-sigmatropic rearrangement when R′ = allyl:



[1,2]-Rearrangements: N. Castagnoli, Jr. *et al., Tetrahedron* **26,** 4319 (1970); J. B. Bremner *et al., Aust. J. Chem.* **41,** 293 (1988); R. Yoneda *et al., Tetrahedron Letters* **35,** 3749 (1994); *eidem, Tetrahedron* **52,** 14563 (1996). *Cf.* Stevens Rearrangement; [1,2]-Wittig Rearrangement.

[2,3]-Rearrangements: V. Rautenstrauch, *Helv. Chim. Acta* **56,** 2492 (1973); Y. Yamamato *et al., J. Org. Chem.* **41,** 303 (1976); or [1,2]: T. Kurihara *et al., Chem. Pharm. Bull.* **42,** 475 (1994). Asymmetric syntheses: D. Enders, H. Kempen, *Synlett.* **1994,** 969; S. G. Davies, G. D. Smyth, *Tetrahedron Asymmetry* **7,** 1001 (1996); J. E. H. Buston *et al., ibid.* **9,** 1995 (1998). *Cf.* Mislow-Evans Rearrangement; Sommelet-Hauser Rearrangement; [2,3]-Wittig Rearrangement.

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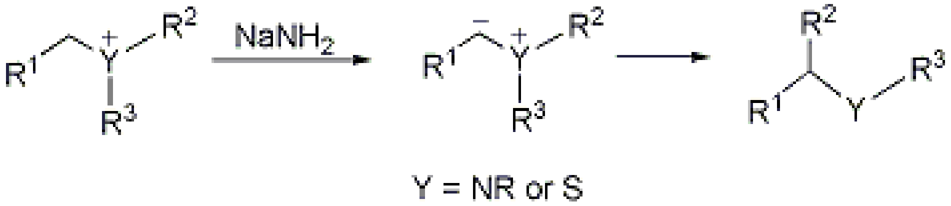
377. Stevens Rearrangement

T. S. Stevens *et al., J. Chem. Soc.* **1928,** 3193; **1930,** 2107, 2119; **1932,** 55, 1926, 1932.

Migration of an alkyl group from a sulfonium or quaternary ammonium salt to an adjacent carbanionic center on treatment with strong base. The product is a rearranged tertiary amine or sulfide:



Early reviews: H. E. Zimmerman in *Molecular Rearrangements* Part 1, P. de Mayo, Ed. (Wiley-Interscience, New York, 1963) pp 345-406; D. J. Cram, *Fundamentals of Carbanion Chemistry* (Academic Press, New York, 1965) pp 223-229; S. M. Pine, *Org. React.* **18,** 403-464 (1970). Selectivity studies vs Sommelet-Hauser rearrangement, *q.v.*: T. Kitano *et al., J. Chem. Soc. Perkin Trans. I* **1992,** 2851; T. Tanaka *et al., J. Org. Chem.* **57,** 5034 (1992). *Review:* I. E. Markó, *Comp. Org. Syn.* **3,** 913-932 (1991). *Cf.* Meisenheimer Rearrangements; [1,2]-Wittig Rearrangement.

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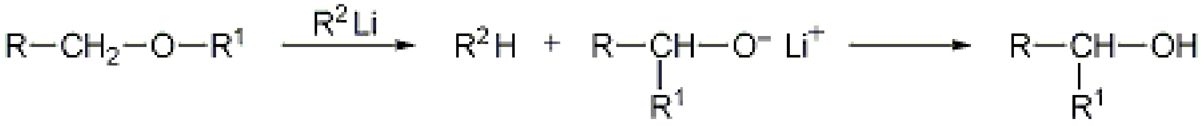
431. [1,2]-Wittig Rearrangement

G. Wittig, L. Löhmann, *Ann.* **550,** 260 (1942); G. Wittig, *Experientia* **14,** 389 (1958).

Rearrangement of ethers with alkyl lithiums to yield alcohols *via* a [1,2]-shift:



$$R-CH_2-O-R^1 \xrightarrow{R^2Li} R^2H + R-\underset{\displaystyle R^1}{\underset{|}{CH}}-O^- \, Li^+ \longrightarrow R-\underset{\displaystyle R^1}{\underset{|}{CH}}-OH$$

Reviews: H. E. Zimmerman in *Molecular Rearrangements* Part 1, P. de Mayo, Ed. (Wiley-Interscience, New York, 1963) p 372-377; L. Brandsma, J. F. Arens in *Chemistry of the Ether Linkage,* S. Patai, Ed. (Interscience, New York, 1967) pp 570-580; U. Schöllkopf, *Angew. Chem.* **82,** 795 (1970); A. R. Lepley, A. G. Giumanini in *Mechanisms of Molecular Migrations* **vol. 3,** B. S. Thyagarajan, Ed. (Interscience, New York, 1971); U. Schöllkopf, *Ind. Chim. Belg.* **36,** 1057 (1971); G. Tennant, *Ann. Rep. Progr. Chem. Sec. B* **68,** 241 (1972); R. W. Hoffmann, *Angew. Chem.* **91,** 625 (1979); *idem, Nachr. Chem. Tech. Lab.* **30,** 483 (1982). *Cf.* Meisenheimer Rearrangements; Stevens Rearrangement.

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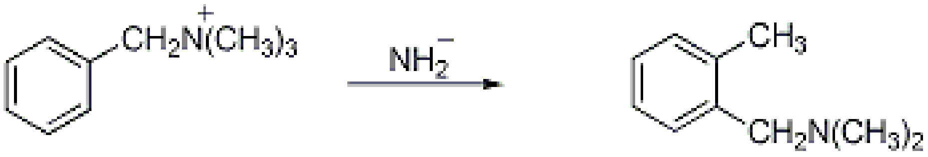
372. Sommelet-Hauser Rearrangement

M. Sommelet, *Compt. Rend.* **205,** 56 (1937).

Rearrangement of benzyl quaternary ammonium salts to *ortho* substituted benzyldialkylamines on treatment with alkali metal amides:



Early reviews: H. E. Zimmerman in *Molecular Rearrangements* Part 1, P. de Mayo, Ed. (Wiley-Interscience, New York, 1963) pp 382-391; S. H. Pine, *Org. React.* **18,** 403-464 (1970). Extension to sulfur ylides: M. Yamamoto *et al., Bull. Chem. Soc. Japan* **62,** 958 (1989); H. Ishibashi *et al., Chem. Pharm. Bull.* **39,** 2878 (1991). Effects of aromatic substitution: T. Tanaka *et al., ibid.* **40,** 518 (1992). Selectivity studies (Sommelet-Hauser rearrangement vs Stevens rearrangement, *q.v.*): T. Kitano *et al., J. Chem. Soc. Perkin Trans. I* **1992,** 2851; T. Tanaka *et al., J. Org. Chem.* **57,** 5034 (1992). *Cf.* Meisenheimer Rearrangements; [2,3]-Wittig Rearrangement.

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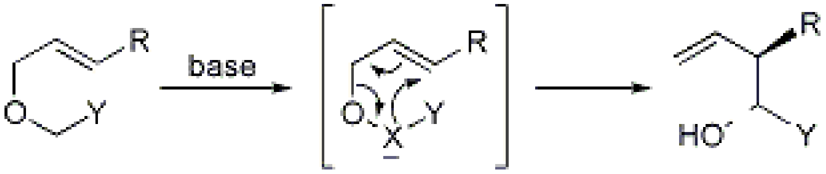
432. [2,3]-Wittig Rearrangement

J. Cast *et al., J. Chem. Soc.* **1960,** 3521; U. Schöllkopf, K. Fellenberger, *Ber.* **698,** 80 (1966); Y. Makisumi, S. Notzumoto, *Tetrahedron Letters* **1966,** 6393.

[2,3]-Sigmatropic rearrangement of the conjugate bases of allylic ethers with high regioselectivity. The stereoselectivity is highly dependent on the nature of the substrate:



Y = alkynyl, alkenyl, Ph, COR, CN
base = LDA, *n*-BuLi, $NaNH_2$

Methods development for ring contractions generating enediynes: H. Audrain *et al., Tetrahedron* **50,** 1469 (1994). Review of stereoselectivity: K. Mikami, T. Nakai, *Synthesis* **1994,** 594. *Reviews:* J. A. Marshall, *Comp. Org. Syn.* **3,** 975-1014 (1991); T. Nakai, K. Mikami, *Org. React.* **46,** 105-209 (1994). *Cf.* Meisenheimer Rearrangements; Mislow-Evans Rearrangement; Sommelet-Hauser Rearrangement.

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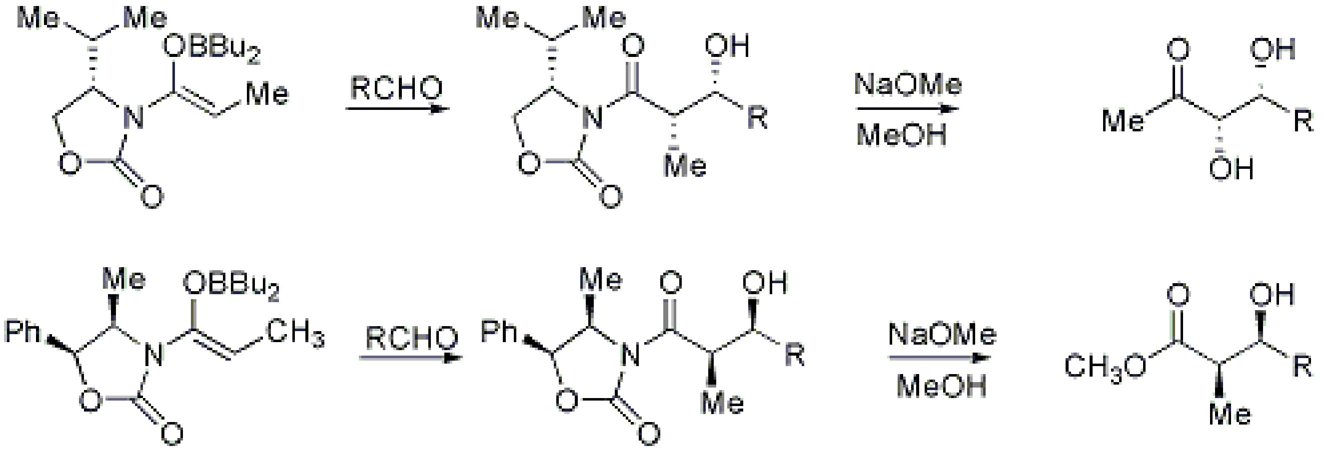
125. Evans Aldol Reaction

D. A. Evans *et al., J. Am. Chem. Soc.* **101,** 6120 (1979); **103,** 2127 (1981).

Highly enantioselective aldol condensation of the chiral *N*-acyl-oxazolidone via its dibutylboryl enolate with the appropriate aldehyde:



Mechanistic studies: D. A. Evans *et al., J. Am. Chem. Soc.* **103,** 3099 (1981). Synthetic applications: C. W. Phoon, C. Abell, *Tetrahedron Letters* **39,** 2655 (1998); C. Pearson *et al., ibid.* **40,** 411 (1999). Inversion of product stereochemistry: K. Iseki *et al., ibid.* **34,** 8147 (1993); T. Gabriel, L. Wessjohann, *ibid.* **38,** 4387 (1997). *Review:* D. A. Evans, *Aldrichchim. Acta* **15,** 23-32 (1982); B. M. Kim *et al., Comp. Org. Syn.* **2,** 239-275 (1991). *Cf.* Aldol Condensation, Mukaiyama Aldol Reaction.

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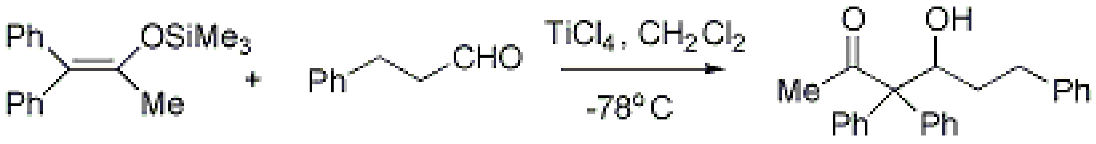
266. Mukaiyama Aldol Reaction

T. Mukaiyama *et al., Chem Lett.* **1973,** 1011; *idem et al., ibid.* **1974,** 323; *eidem, J. Am. Chem. Soc.* **96,** 7503 (1974).

Formation of β-hydroxy ketones via reaction of silyl enol ethers or ketene silyl acetals with aldehydes in presence of a Lewis acid, such as titanium tetrachloride, tin tetrachloride or boron trifluoride etherate:



Enantioselectivity: E. M. Carreira *et al., J. Am. Chem. Soc.* **116,** 8837 (1994). Diastereoselectivity: S. E. Denmark *et al., Tetrahedron* **54,** 10389 (1998). *Reviews:* H. Gröger *et al., Chem. Eur. J.* **4,** 1137-1141 (1998); E. M. Carreira in *Comprehensive Asymmetric Catalysis I-III* **vol. 3,** E. N. Jacobsen *et al.,* Eds. (Springer-Verlag, Berlin, Germany, 1999) 997-1065; K. Iseki, *ACS Symp. Ser.* **746,** 38-51 (2000). *Cf.* Aldol Reaction; Evans Aldol Reaction.

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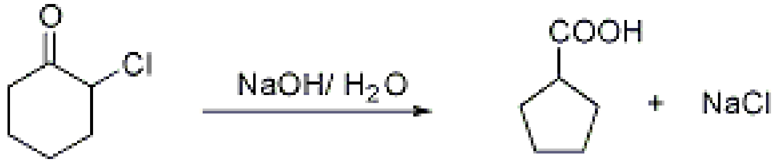
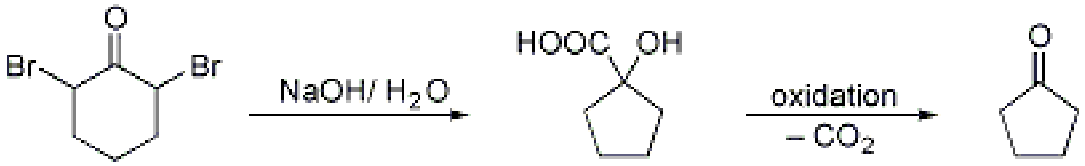
127. **Favorskii Rearrangement;** Wallach Degradation

A. E. Favorskii, *J. Prakt. Chem.* **88**(2), 658 (1913); O. Wallach, *Ann.* **414,** 296 (1918).

Base-catalyzed rearrangement of α-haloketones to acids or esters. The rearrangement of α, α′-dibromocyclohexanones to 1-hydroxycyclopentanecarboxylic acids, followed by oxidation to the ketones is known as the **Wallach degradation:**





Detailed experimental procedure: D. W. Goheen, W. R. Vaughan, *Org. Syn.* **coll. vol. 4,** 594 (1963). Application to the synthesis of carboxylic acids: T. Satoh *et al., Bull. Chem. Soc. Japan* **66,** 2339 (1993). Applications to asymmetric synthesis: *idem et al., Tetrahedron Letters* **34,** 4823 (1993); E. Lee, C. H. Yoon, *Chem. Commun.* **1994,** 479. *Reviews:* A. S. Kende, *Org. React.* **11,** 261-316 (1960); P. J. Chenier, *J. Chem. Ed.* **55,** 286 (1978); A. Baretta, B. Waegill, “A Survey of Favorskii Rearrangement Mechanisms” in *Reactive Intermediates*, R. A. Abramovitch, Ed. (Plenum Press, New York, 1982) pp 527-585; J. Mann, *Comp. Org. Syn.* **3,** 839-859 (1991).

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348. Ruff-Fenton Degradation

O. Ruff, *Ber.* **31,** 1573 (1898); **32,** 550 (1899); H. J. H. Fenton, *Proc. Chem. Soc.* **9,** 113 (1893).

Shortening of the carbon chain of sugars by the oxidation of aldonic acids (as calcium salts) with hydrogen peroxide and ferric salts:

$$RCH(OH)COOH + H_2O_2 \xrightarrow{Fe^{3+}} RCHO + CO_2 + 2H_2O$$

W. Pigman, *The Carbohydrates* (Academic Press, New York, 1957) p 118; H. S. Isbell, M. A. Salam, *Carbohyd. Res.* **90,** 123 (1981).

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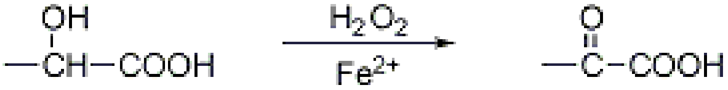
129. Fenton Reaction

H. J. H. Fenton, *Proc. Chem. Soc.* **9,** 113 (1893); *J. Chem. Soc.* **65,** 899 (1894).

Oxidation of α-hydroxy acids with hydrogen peroxide and ferrous salts (Fenton's reagent) to α-keto acids or of 1,2-glycols to hydroxy aldehydes:

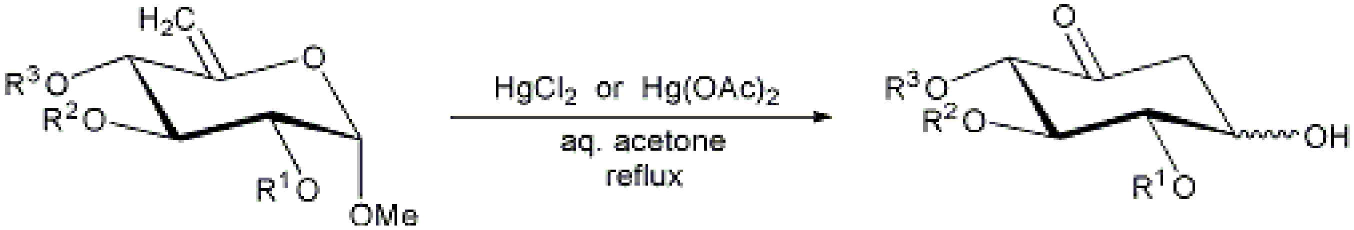


W. A. Waters in *Organic Chemistry* **vol. 4,** H. Gilman, Ed. (Wiley, New York, 1953) p 1157; G. Sosnovsky, D. Rawlinson in *Organic Peroxides* **vol. 2,** D. Swern, Ed. (Interscience, New York, 1970) pp 269-336; C. Walling, *Accts. Chem. Res.* **8,** 125 (1975); T. Tezuka *et al., J. Am. Chem. Soc.* **103,** 3045 (1981); C. Walling, K. Amarnath, *ibid.* **104,** 1185 (1982). Extension to additional substrates: aromatic alcohols: F. J. Benitez *et al., Ind. Eng. Chem. Res.* **38,** 1341 (1999); L. Lunar *et al., Water Res.* **34,** 1791 (2000); *N*-heterocyclics: M. A. Oturan *et al., New J. Chem.* **23,** 793 (1999); E. L. Bier *et al., Environ. Toxicol. Chem.* **18,** 1078 (1999); organometals: K. Banerjee *et al., Environ. Prog.* **18,** 280 (1999).

130. Ferrier Rearrangement

R. J. Ferrier, *J. Chem. Soc. Perkin Trans. I* **1979,** 1455.

The stereochemically controlled conversion of hex-5-enopyranosides into cyclohexanones (inosose derivatives), catalyzed by mercury(II) salts, such that the 5-hydroxyl and the 3-substituent of the product are predominantly in a *trans* relationship:



Stereochemical/mechanistic study: A. S. Machado *et al., Carbohyd. Res.* **233,** C5 (1992); N. Yamauchi *et al., Tetrahedron* **50,** 4125 (1994). Scope and limitations: N. Chida *et al., Bull. Chem. Soc. Japan* **64,** 2118 (1991). Synthetic applications: D. H. R. Barton *et al., Tetrahedron* **46,** 215 (1990); R. Chretien *et al., Nat. Prod. Letters* **2,** 69 (1993); A. B. Smith III *et al., Org. Lett.* **1,** 909 (1999); *eidem, ibid.* 913. Modification of catalysis: J. C. López *et al., J. Org. Chem.* **60,** 3851 (1995); T. Linker *et al., Tetrahedron Letters* **39,** 9637 (1998); B. S. Babu *et al., Synth. Commun.* **29,** 4299 (1999).

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131. Finkelstein Reaction

H. Finkelstein, *Ber*. **43,** 1528 (1910).

Reaction of alkyl halides with sodium iodide in acetone:

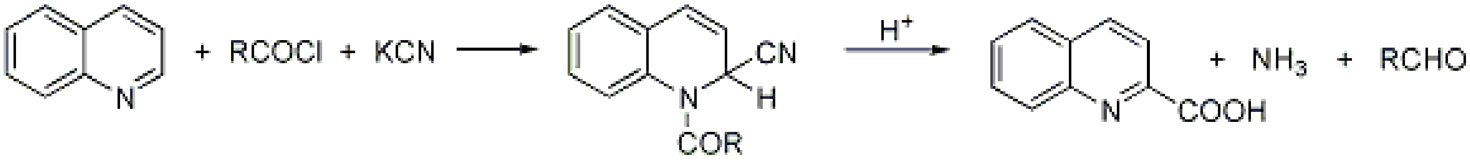
$$\mathrm{RBr} + \mathrm{NaI} \longrightarrow \mathrm{RI} + \mathrm{NaBr}$$

C. K. Ingold, *Structure and Mechanism in Organic Chemistry* (Cornell Univ. Press, London, 2nd ed., 1969) p 435; J. Hayami *et al., Tetrahedron Letters* **1973,** 385; S. Samaan, F. Rolla, *Phosphorus and Sulfur* **4,** 145 (1978); W. B. Smith, G. D. Branum, *Tetrahedron Letters* **22,** 2055 (1981). Modified conditions: D. Landini *et al., J. Chem. Soc. Perkin Trans. I* **1992,** 2309. Applications: A. J. Pearson, K. Lee, *J. Org. Chem.* **59,** 2304 (1994); A. Schmidt, M. K. Kindermann, *ibid.* **62,** 3910 (1997); T. Zoller *et al., Tetrahedron Letters* **39,** 8089 (1998).

333. Reissert Reaction (Grosheintz-Fischer-Reissert Aldehyde Synthesis)

A. Reissert, *Ber.* **38,** 1603, 3415 (1905); J. M. Grosheintz, H. O. L. Fischer, *J. Am. Chem. Soc.* **63,** 2021 (1941).

Formation of 1-acyl-2-cyano-1,2-dihydroquinoline derivatives (Reissert compounds) by reaction of acid chlorides with quinoline and potassium cyanide; hydrolysis of these compounds yields aldehydes and quinaldic acid:



Reviews: E. Mosettig, *Org. React.* **8,** 220 (1954); W. E. McEwen, R. L. Cobb, *Chem. Rev.* **55,** 511 (1955); F. D. Popp, *Advan. Heterocycl. Chem.* **9,** 1 (1968); *idem, ibid.* **24,** 187 (1979); *idem. Bull. Soc. Chim. Belg.* **90,** 609 (1981); *idem* in *The Chemistry of Heterocyclic Compounds* **vol. 32,** Part 2, G. Jones, Ed. (Wiley, New York, 1982) p 353.

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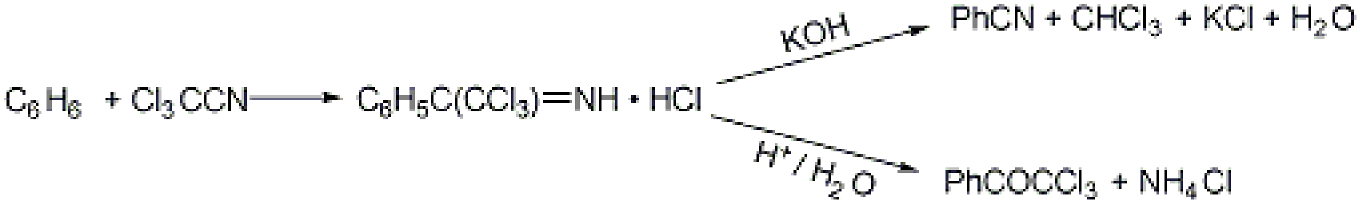
197. Houben-Fischer Synthesis

J. Houben, W. Fischer, *J. Prakt. Chem.* [2] **123,** 89, 262, 313 (1929).

Formation of aromatic nitriles by basic hydrolysis of trichloromethyl aryl ketimines. Acidic hydrolysis yields ketones:



J. Houben, W. Fischer, *Ber.* **63,** 2464 (1930); **64,** 240, 2636, 2645 (1931); **66,** 339 (1933); D. T. Mowry, *Chem. Rev.* **42,** 221 (1948); P. E. Spoerri, A. S. DuBois, *Org. React.* **5,** 390 (1949); G. Hesse, *Houben-Weyl* **4/2** 103 (1955); W. Ruske in *Friedel-Crafts and Related Reactions* **vol. III,** Part 1, G. A. Olah, Ed. (Interscience, New York, 1964) p 407. *Cf.* Houben-Hoesch Reaction.

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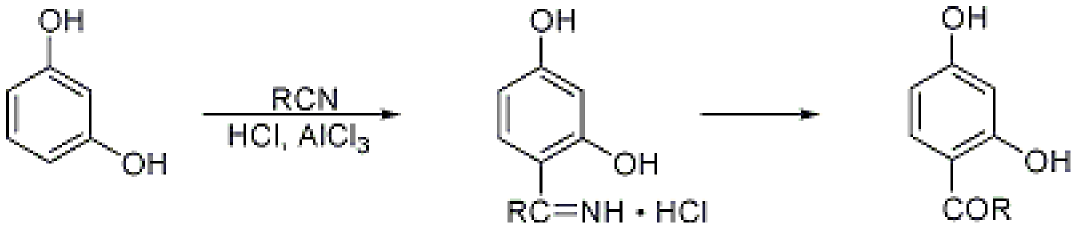
198. Houben-Hoesch Reaction

K. Hoesch, *Ber*. **48,** 1122 (1915); J. Houben, *ibid*. **59,** 2878 (1926).

Synthesis of acylphenols from phenols or phenolic ethers by the action of organic nitriles in the presence of hydrochloric acid and aluminum chloride as catalyst:



Reviews: P. E. Spoerri, A. S. DuBois, *Org. React.* **5,** 387 (1949); Thomas, *Anhydrous Aluminum Chloride in Organic Chemistry* (New York, 1941) p 504; W. Ruske in *Friedel-Crafts and Related Reactions* **vol. III,** Part 1, G. A. Olah, Ed. (Interscience, New York, 1964) p 383; M. I. Amer *et al., J. Chem. Soc. Perkin Trans. I* **1983,** 1075; V. V. Arkhipov *et al., Chem. Heterocycl. Compd.* **33,** 515 (1997); R. Kawecki *et al., Synthesis* **1999,** 751. *Cf.* Gatterman Aldehyde Synthesis; Houben-Fischer Synthesis.

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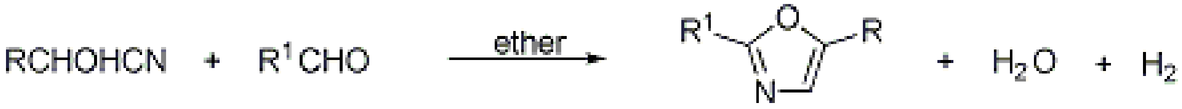
134. Fischer Oxazole Synthesis

E. Fischer, *Ber.* **29,** 205 (1896).

Condensation of equimolar amounts of aldehyde cyanohydrins and aromatic aldehydes in dry ether in the presence of dry hydrochloric acid:

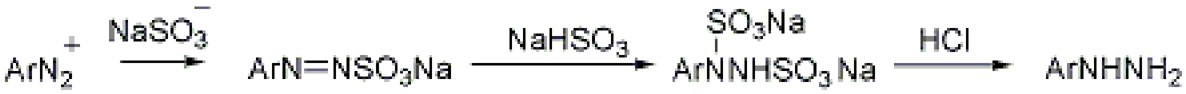


R. H. Wiley, *Chem. Rev.* **37,** 410 (1945); J. W. Cornforth, R. H. Cornforth, *J. Chem. Soc.* **1949,** 1028; J. W. Cornforth, *Heterocyclic Compounds* **5,** 309 (1957); T. Onaka, *Tetrahedron Letters* **1971,** 4391.

136. Fischer Phenylhydrazine Synthesis

E. Fischer, *Ber.* **8,** 589 (1875).

Formation of arylhydrazines by reduction of diazo compounds with excess sodium sulfite and hydrolysis of the substituted hydrazine sulfonic acid salt with hydrochloric acid. The process is a standard industrial method for production of arylhydrazines:

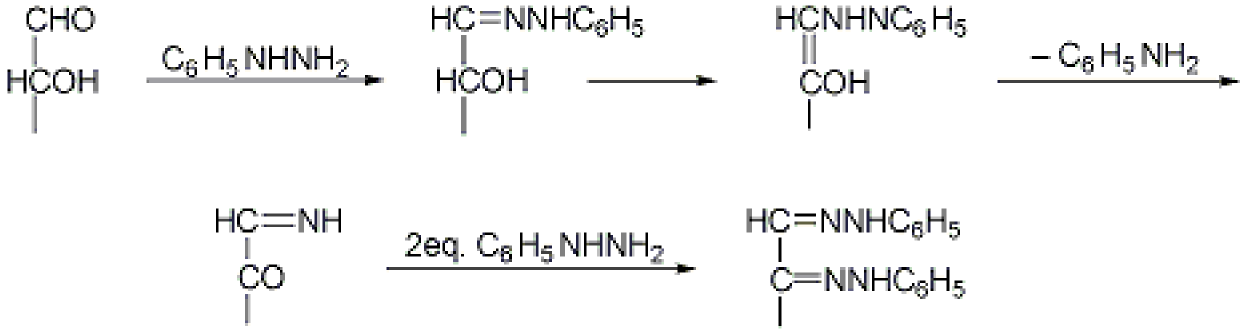


G. H. Colemann, *Org. Syn.* **coll. vol. I,** 432 (1932); K. H. Saunders, *The Aromatic Diazo-Compounds and Their Technical Applications* (London, 1949) p 183; R. Huisgen, R. Lux, *Ber.* **93,** 540 (1960).

137. Fischer Phenylhydrazone and Osazone Reaction

E. Fischer, *Ber.* **17,** 579 (1884).

Formation of phenylhydrazones and osazones by heating sugars with phenylhydrazine in dilute acetic acid:

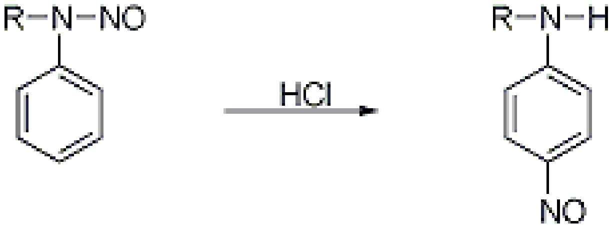


E. G. V. Percival, *Advan. Carbohyd. Chem.* **3,** 23 (1948); F. Micheel, *Chemie der Zucker und Polysaccharide* (Leipzig, 1956) p 54; W. Pigman, *The Carbohydrates* **1957,** 452, 455; H. Simon *et al., Fortschr. Chem. Forsch.* **14,** 451 (1970).

132. Fischer-Hepp Rearrangement (Nitrosamine Rearrangement)

O. Fischer, E. Hepp, *Ber.* **19,** 2991 (1886).

Rearrangement of secondary aromatic nitrosamines to *p*-nitrosoarylamines:



H. J. Shine, *Aromatic Rearrangements* (Elsevier, New York, 1967) p 231; D. L. H. Williams in *Comprehensive Chemical Kinetics* **vol. 13** (1972) p 454; S. Johan *et al., J. Chem. Soc. Perkin Trans. II* **1980,** 165. Mechanism: D. L. H. Williams, *ibid.* **1982,** 801. Applications: J. B. Kyziol, *J. Heterocyclic Chem.* **22,** 1301 (1985); P. Kannan *et al., J. Mol. Catal.* **118,** 189 (1997).

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138. Fischer-Speier Esterification Method

E. Fischer, A. Speier, *Ber*. **28,** 3252 (1895).

Esterification of acids by refluxing with excess alcohol in the presence of hydrogen chloride or other acid catalysts:

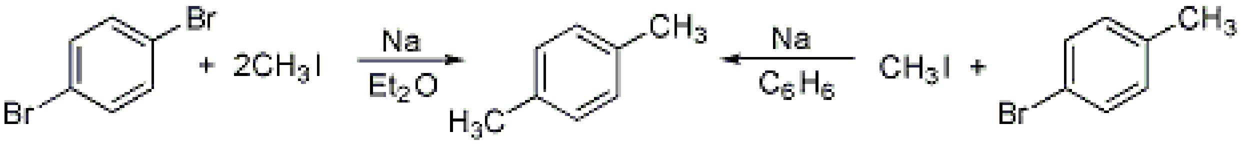
$$CH_3COOH + CH_3CH_2OH \xrightarrow{3\%\ HCl} CH_3COOCH_2CH_3 + H_2O$$

E. D. Hughes, *Quart. Rev*. **2,** 110 (1948); A. J. Kirby in *Comprehensive Chemical Kinetics* **vol. 10,** C. H. Bamford, C. F. H. Tipper, Eds. (Elsevier, New York, 1972) p 57; E. K. Euranto in *The Chemistry of Carboxylic Acids and Esters,* S. Patai, Ed. (Interscience, New York, 1969) p 505.

439. Wurtz-Fittig Reaction

B. Tollens, R. Fittig, *Ann.* **131,** 303 (1864); R. Fittig, J. König, *ibid.* **144,** 277 (1867).

Formation of alkylated aromatic hydrocarbons on coupling of an alkyl and an aryl halide with sodium:



T. L. Kwa, C. Boelhouwer, *Tetrahedron* **25,** 5771 (1969); B. J. Wakefield, *Comp. Organometal. Chem.* **7,** 45 (1982); K. Miyoshi *et al.*, *Chemosphere* **41,** 819 (2000).

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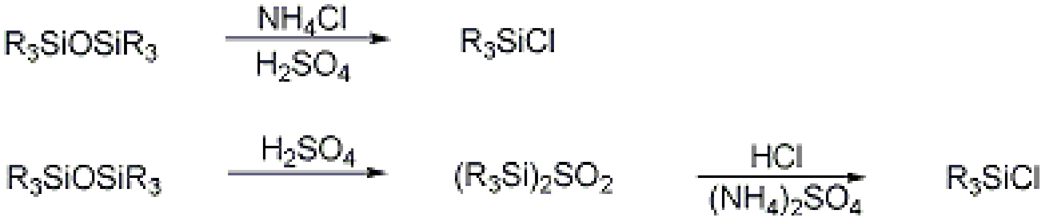
140. Flood Reaction

E. A. Flood, *J. Am. Chem. Soc.* **55,** 1735 (1933).

Formation of trialkylsilyl halides from hexaalkyldisiloxanes using concentrated sulfuric acid in the presence of ammonium chloride or fluoride, or by treatment of the intermediate silane sulfates with hydrogen chloride in the presence of ammonium sulfate:



$$R_3SiOSiR_3 \xrightarrow[H_2SO_4]{NH_4Cl} R_3SiCl$$

$$R_3SiOSiR_3 \xrightarrow{H_2SO_4} (R_3Si)_2SO_2 \xrightarrow[(NH_4)_2SO_4]{HCl} R_3SiCl$$

H. W. Post, *Silicones and Other Organic Compounds* (New York, 1949) p 64; E. G. Rochow *et al.*, *The Chemistry of Organometallic Compounds* (New York, 1957) p 158, 159. Synthetic applications: L. Birkofer, O. Stuhl, *Top. Curr. Chem.* **88,** 33 (1980).

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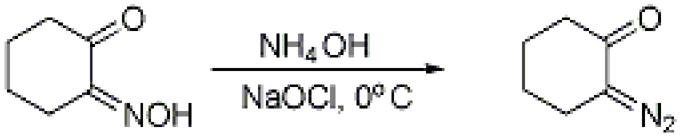
141. Forster Diazoketone Synthesis

M. O. J. Forster, *J. Chem. Soc.* **107,** 260 (1915).

Formation of diazoketones from α-oximinoketones by reaction with chloramine:



M. P. Cava, R. L. Litle, *Chem. & Ind. (London)* **1957,** 367; W. Kirmse *et al.*, *Angew. Chem.* **69,** 106 (1957). Mechanism: J. Meinwald *et al.*, *J. Am. Chem. Soc.* **81,** 4751 (1959). Application to steroids: M. P. Cava, B. R. Vogt, *J. Org. Chem.* **30,** 3776 (1965). Review and applications: F. Weygand, H. J. Bestmann, *Angew. Chem.* **72,** 535 (1960); W. Rundel, *ibid.* **74,** 469 (1962).

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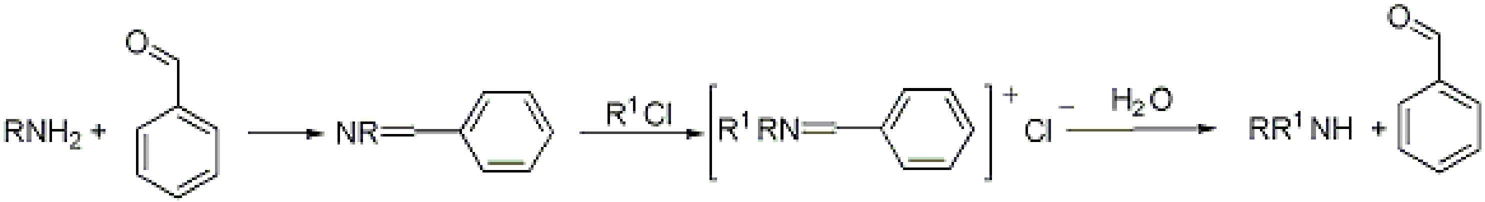
142. Forster Reaction

M. O. J. Forster, *J. Chem. Soc.* **75,** 934 (1899); H. Decker, P. Becker, *Ann.* **395,** 362 (1913).

Formation of secondary amines by condensation of a primary amine with an aldehyde, addition of alkyl halide to the Schiff base, and subsequent hydrolysis:



H. Glaser, *Houben-Weyl* **11/1,** 108 (1957); F. Möller, *ibid.* p 956.

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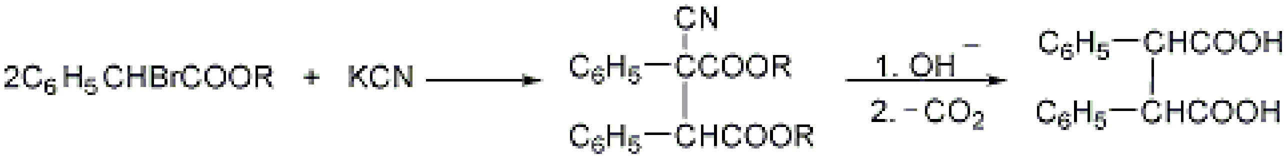
143. Franchimont Reaction

A. P. N. Franchimont, *Ber.* **5,** 1048 (1872).

Carboxylic acid dimerization to 1,2-dicarboxylic acids by treating α-bromocarboxylic acids with potassium cyanide followed by hydrolysis and decarboxylation:



N. Zelinsky, *Ber.* **21,** 3160 (1888); O. Poppe, *ibid.* **23,** 113 (1890); R. C. Fuson *et al., J. Am. Chem. Soc.* **51,** 1536 (1929); **52,** 4074 (1930); **60,** 1237 (1938); H. N. Rydon, *J. Chem. Soc.* **1936,** 593; H. Henecka, *Chemie der Beta-Dicarbonylverbindungen* (Berlin, 1950) p 176.

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145. Frankland Synthesis

E. Frankland, *Ann.* **71,** 213 (1849); **85,** 3641 (1853).

Synthesis of zinc dialkyls from alkyl halides and zinc:

$$2C_2H_5I \quad + \quad 2Zn \longrightarrow (C_2H_5)_2Zn \quad + \quad ZnI_2$$

Reviews: K. Nützel, *Houben-Weyl* **13/2a,** 570 (1973); C. R. Noller, *Org. Syn.* **coll. vol. II,** 184 (1943).

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146. Freund Reaction; Gustavson Reaction; Hass Cyclopropane Process

A. Freund, *Monatsh.* **3,** 625 (1882); G. Gustavson, *J. Prakt. Chem.* [2] **36,** 300 (1887); H. B. Hass *et al., Ind. Eng. Chem.* **28,** 1178 (1936).

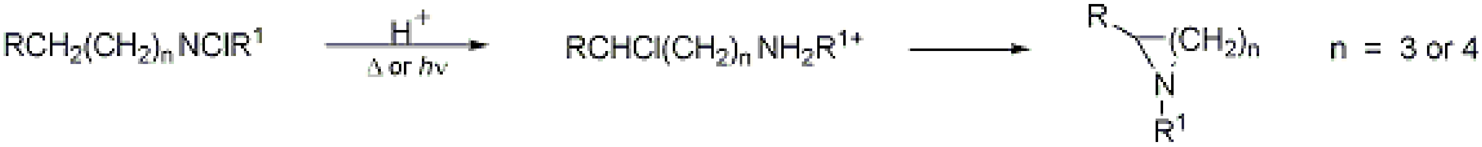
Formation of alicyclic hydrocarbons by the action of sodium (Freund reaction) or zinc (Gustavson reaction) on open chain dihalo compounds; 1,3-dichloropropane derived from the chlorination of propane obtained from natural gas is cyclized in the Hass cyclopropane process by treating with zinc dust in aqueous alcohol in the presence of catalytic sodium iodide:

H. Gilman, *Organic Chemistry* **I** (New York, 1943) p 74; J. D. Bartleson *et al., J. Am. Chem. Soc.* **68,** 2513 (1946); R. N. Shortsidge *et al., ibid.* **70,** 946 (1948); B. T. Brooks, *The Chemistry of the Nonbenzenoid Hydrocarbons* (New York, 1950) p 88; H. F. Ebel, A. Lüttringhaus, *Houben-Weyl* **13/1,** 492 (1970).

192. Hofmann-Löffler-Freytag Reaction

A. W. Hofmann, *Ber.* **16,** 558 (1883); **18,** 5, 109 (1885); K. Löffler, C. Freytag, *ibid.* **42,** 3427 (1909).

Formation of pyrrolidines or piperidines by thermal or photochemical decomposition of protonated *N*-haloamines:



M. E. Wolff, *Chem. Rev.* **63,** 55 (1963); E. J. Corey, W. R. Hertler, *J. Am. Chem. Soc.* **82,** 1657 (1960); R. Furstoss *et al., Tetrahedron Letters* **1970,** 1263; S. Titouani *et al., Tetrahedron* **36,** 2961 (1980).

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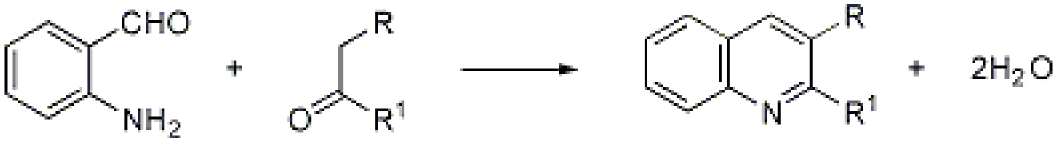
148. Friedlaender Synthesis

P. Friedlaender, *Ber.* **15,** 2572 (1882); P. Friedlaender, C. F. Gohring, *ibid.* **16,** 1833 (1883).

Base-catalyzed condensation of 2-aminobenzaldehydes with ketones to form quinoline derivatives:



Reviews: R. H. Manske, *Chem. Rev.* **30,** 124 (1942); C. C. Cheng, S. J. Yan, *Org. React.* **28,** 37 (1982). Cyclic ketones containing S, or N: G. Kempter, S. Hirschberg, *ibid.* **98,** 419 (1965); K. Rao *et al., J. Heterocyclic Chem.* **16,** 1241 (1979). Modified conditions: I.-S. Cho *et al., J. Org. Chem.* **56,** 7288 (1991); G. Sabitha *et al., Synth. Commun.* **29,** 4403 (1999). Review: R. P. Thummel, *Synlett.* **1992,** 1-12. *Cf.* Niementowski Quinoline Synthesis; Pfitzinger Reaction.

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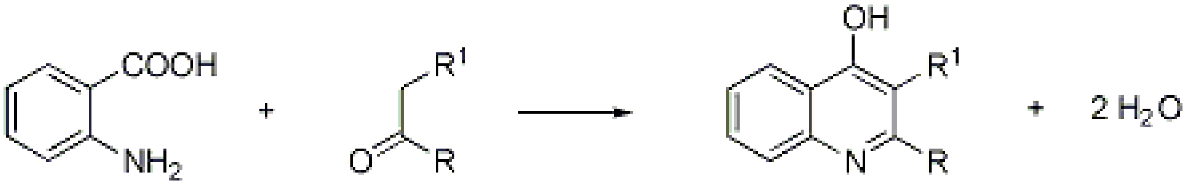
280. Niementowski Quinoline Synthesis

S. v. Niementowski, *Ber.* **27,** 1394 (1894); **28,** 2809 (1895); **38,** 2044 (1905); **40,** 4285 (1907).

Formation of γ-hydroxyquinoline derivatives from anthranilic acids and carbonyl compounds:



R. H. Manske, *Chem. Rev.* **30,** 127 (1942); T. A. Williamson, *Heterocyclic Compounds* **6,** 331 (1957); W. L. F. Armarego, *Quinazolines* (Interscience, New York, 1967) p 74; E. Cuny *et al., Tetrahedron Letters* **21,** 3029 (1980). Synthetic applications: B. P. Suthar, *Indian J. Chem.* **21B,** 588 (1982); R. J. Chong *et al., Tetrahedron Letters* **27,** 5323 (1986); M. S. Khajavi *et al., Iran. J. Chem. Chem. Eng.* **17,** 29 (1988). *Review:* T. Hisano, *Org. Prep. Proced. Int.* **5,** 145-193 (1973). *Cf.* Friedlaender Synthesis; Pfitzinger Reaction.

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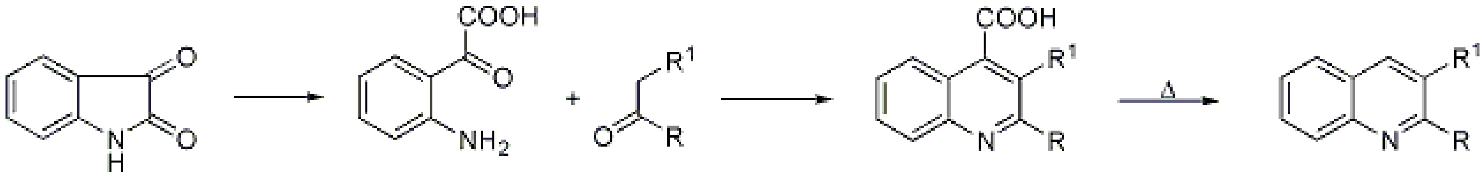
306. Pfitzinger Reaction

W. Pfitzinger, *J. Prakt. Chem.* [2] **33,** 100 (1886); **38,** 582 (1888).

Formation of quinoline-4-carboxylic acids by condensation of isatic acids from isatin with α-methylene carbonyl compounds; subsequent decarboxylation yields quinolines:



C. Hollins, *The Synthesis of Nitrogen Ring Compounds* (London, 1924) p 286; R. H. Manske, *Chem. Rev.* **30,** 126 (1942); F. W. Bergstrom, *ibid.* **35,** 152 (1944); R. C. Elderfield, *Heterocyclic Compounds* **4,** 47 (1952); N. P. Buu-Hoi *et al.*, *Bull. Soc. Chim. France* **1968,** 2476; M. H. Palmer, P. S. McIntyre, *J. Chem. Soc. B* **1969,** 539. *Cf.* Friedlaender Synthesis; Niementowski Quinoline Synthesis.

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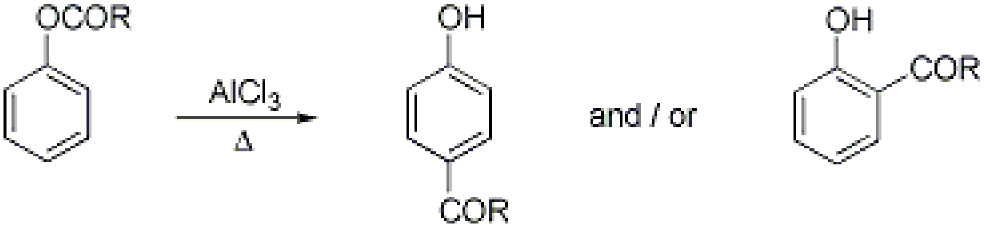
149. Fries Rearrangement

K. Fries, G. Fink, *Ber.* **41,** 4271 (1908); K. Fries, W. Pfaffendorf, *ibid.* **43,** 212 (1910).

Rearrangement of phenolic esters to *o*- and/or *p*-phenolic ketones with Lewis acid catalysts:

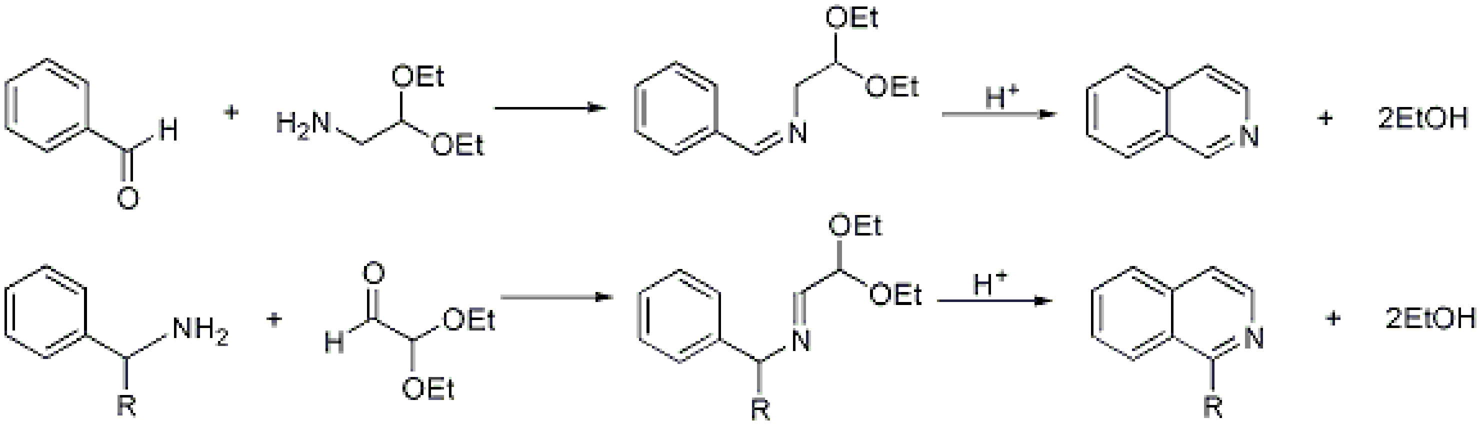


A. H. Blatt, *Org. React.* **1,** 342 (1942); A. Gerecs in *Friedel-Crafts and Related Reactions,* in **vol. 3,** Part 1; G. Olah, Ed. (Interscience, New York, 1964) pp 499-533; F. R. Jensen, G. Goldman in *ibid.* Part 2, p 1349; R. Martin *et al., Monatsh.* **81,** 111 (1980); R. Martin, *Org. Prep. Proced. Int.* **24,** 369 (1992). Photo-rearrangement: J. C. Anderson, C. B. Reese, *Proc. Chem. Soc.* **1960,** 217; D. Bellus, *Advan. Photochem.* **8,** 109 (1971); D. J. Crouse *et al., J. Org. Chem.* **46,** 374 (1981); W. Gu *et al., J. Am. Chem. Soc.* **121,** 9467 (1999). Modified conditions: K. J. Balkus, Jr. *et al., J. Mol. Catal. A* **134,** 137 (1998); B. Kaboudin, *Tetrahedron* **55,** 12865 (1999); B. M. Khadilkar, V. R. Madyar, *Synth. Commun.* **29,** 1195 (1999).

318. Pomeranz-Fritsch Reaction (Schlittler-Müller Modification)

C. Pomeranz, *Monatsh.* **14,** 116 (1893); P. Fritsch, *Ber.* **26,** 419 (1893); E. Schlittler, J. Müller, *Helv. Chim. Acta* **31,** 914, 1119 (1948).

Formation of isoquinolines by the acid-catalyzed cyclization of benzalaminoacetals prepared from aromatic aldehydes and aminoacetal; in the **Schlittler-Müller modification** the starting materials are benzyl amines and glyoxal semiacetal:



M. J. Bevis *et al.*, *Tetrahedron* **27,** 1253 (1971); E. V. Brown, *J. Org. Chem.* **42,** 3208 (1977); R. Hirsenkorn, *Tetrahedron Letters* **32,** 1775 (1991). *Reviews:* W. J. Gensler, *Org. React.* **6,** 191 (1951); *idem*, *Heterocyclic Compounds* **4,** 368 (1952); J. M. Bobbit, A. J. Bourque, *Heterocycles* **25,** 601-614 (1987).

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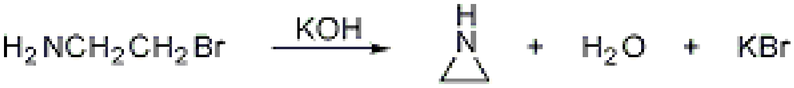
153. Gabriel Ethylenimine Method (Gabriel-Marckwald Ethylenimine Synthesis)

S. Gabriel *et al., Ber.* **21,** 1049 (1888); W. Marckwald *et al., ibid.* **32,** 2036 (1899); **33,** 764 (1900); **34,** 3544 (1901).

Formation of ethylenimines (aziridines) by elimination of hydrogen halides from aliphatic vicinal haloamines with alkali. The method can be extended to the preparation of five- and six-membered cyclic amines:



O. C. Dermer, G. E. Ham, *Ethylenimine and Other Aziridines* (Academic Press, New York, 1969) pp 1-59; R. Bartnik *et al., Pol. J. Chem.* **53,** 537 (1979); K. H. Sunwoo *et al., Dyes Pigments* **41,** 19 (1999).

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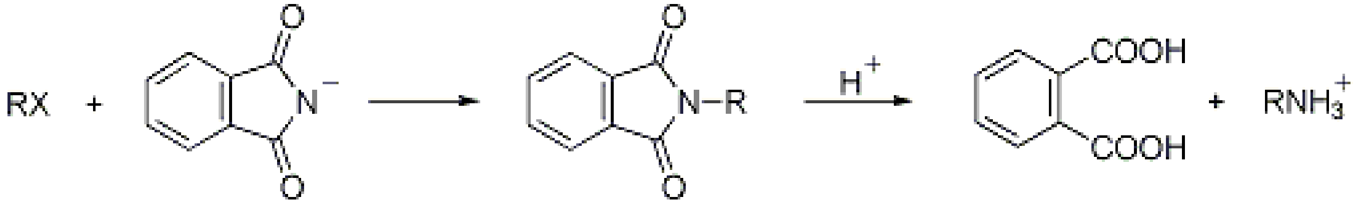
154. Gabriel Synthesis

S. Gabriel, *Ber.* **20,** 2224 (1887).

Conversion of alkyl halides to primary amines by treatment with potassium phthalimide and subsequent hydrolysis:



M. S. Gibson, R. W. Bradshaw, *Angew. Chem. Int. Ed.* **7,** 919 (1968); B. Dietrich *et al., J. Am. Chem. Soc.* **103,** 1282 (1981); O. Mitsunobu, *Comp. Org. Syn.* **6,** 79-85 (1991). Modified conditions: S. E. Sen, S. L. Roach, *Synthesis* **1994,** 756; M. N. Khan, *J. Org. Chem.* **61,** 8063 (1996). Stereoselectivity: A. Kubo *et al., Tetrahedron Letters* **37,** 4957 (1996).

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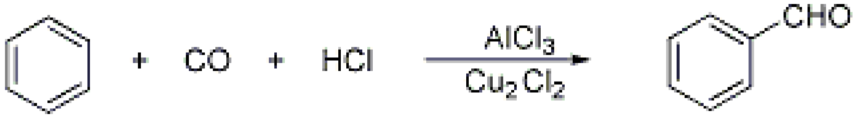
156. Gattermann-Koch Reaction

L. Gattermann, J. A. Koch, *Ber.* **30,** 1622 (1897); L. Gattermann, *Ann.* **347,** 347 (1906).

Formylation of benzene, alkylbenzenes or polycyclic aromatic hydrocarbons with carbon monoxide and hydrogen chloride in the presence of aluminum chloride at high pressure. Addition of cuprous chloride allows the reaction to proceed at atmospheric pressure:



N. N. Crounse, *Org. React.* **5,** 290 (1949); G. A. Olah, S. J. Kuhn in *Friedel-Crafts and Related Reactions* **vol. 3,** Part 2, G. Olah, Ed. (Interscience, New York, 1964) pp 1153-1156. Use of $CuCl(PPh_3)_n$: L. Toniolo, M. Graziani, *J. Organometal. Chem.* **194,** 221 (1980).

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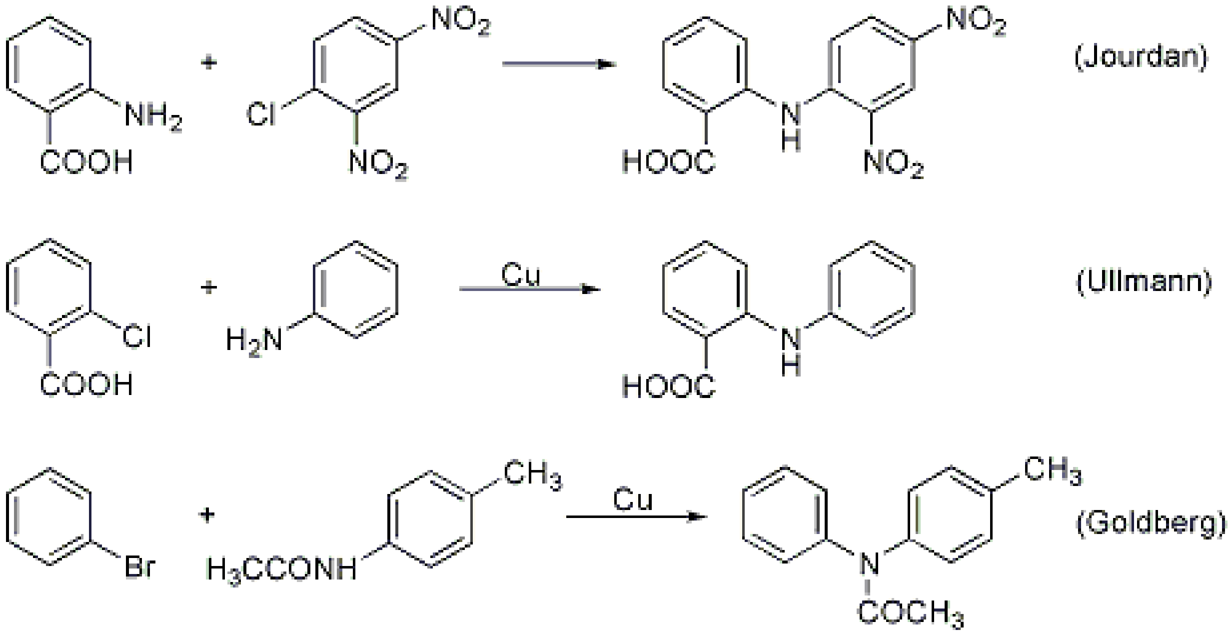
208. Jourdan-Ullmann-Goldberg Synthesis

F. Jourdan, *Ber.* **18,** 1444 (1885); F. Ullmann, *ibid.* **36,** 2382 (1903); I. Goldberg, *ibid.* **39,** 1691 (1906); **40,** 4541 (1907).

Synthesis of substituted diphenylamines, useful as intermediates in the synthesis of acridones:



Reviews: R. M. Acheson, *Acridines* (Interscience, New York, 1956) p 148; Schulenberg, Archer, *Org. React.* **14,** 19 (1965).

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159. Gomberg Free Radical Reaction

M. Gomberg, *J. Am. Chem. Soc.* **22,** 757 (1900).

Formation of free radicals by abstraction of the halogen from triarylmethyl halides with metals:

$$2(C_6H_5)_3CCl + Zn \longrightarrow 2(C_6H_5)_3C{-}Cl^{\bullet -} \longrightarrow 2(C_6H_5)_3C^{\bullet} + ZnCl_2$$

A. R. Forrester *et al.*, in *Organic Chemistry of Stable Free Radicals* (Academic Press, New York, 1968); Scholle, Rozantsev, *Russ. Chem. Rev*. **42,** 1101 (1973); J. M. McBride, *Tetrahedron* **30,** 2009 (1974).

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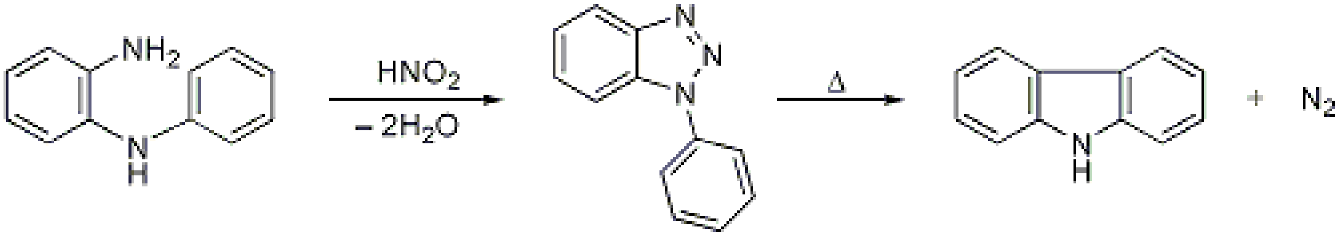
161. Graebe-Ullmann Synthesis

C. Graebe, F. Ullmann, *Ann.* **291,** 16 (1896); F. Ullmann, *ibid.* **332,** 82 (1904).

Formation of carbazoles by the action of nitrous acid on 2-aminodiphenylamines, followed by thermal decomposition of the resulting benzotriazoles:



O. Bremer, *Ann.* **514,** 279 (1934); S. H. Tucker *et al., J. Chem. Soc.* **1942,** 500; N. Campbell, B. Barclay, *Chem. Rev.* **40,** 360 (1947); C. C. Colser *et al., J. Chem. Soc.* **1951,** 110; B. W. Ashton, H. Suschitzky, *ibid.* **1957,** 4559; R. A. Abramovitch, I. D. Spenser, *Advan. Heterocyclic Chem.* **3,** 128 (1964). Photo-decomposition: L. K. Mehta *et al., J. Chem. Soc. Perkin Trans. I* **1993,** 1261. Synthetic applications: A. Molina *et al., J. Org. Chem.* **61,** 5587 (1996); D. J. Hagan *et al., J. Chem. Soc. Perkin Trans. I* **1998,** 915.

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162. Griess Diazo Reaction; Witt and Knoevenagel Diazotization Methods

P. Griess, *Ann.* **106,** 123 (1858); **121,** 257 (1862); E. Knoevenagel, *Ber.* **23,** 2994 (1890); O. N. Witt, *ibid.* **42,** 2953 (1909).

Formation of aromatic diazonium salts from primary aromatic amines and nitrous acid or other nitrosating agents:

$$\mathrm{ArNH_2 + NaNO_2 + 2HX \longrightarrow Ar\overset{+}{N}_2\,\overset{-}{X} + NaX + 2H_2O}$$

$$\mathrm{2ArNH_2 + N_2O_3 + 2HNO_3 + H_2O \longrightarrow 2Ar\overset{+}{N}_2\,NO_3^- + 4H_2O}\quad \text{(Griess reaction)}$$

$$\mathrm{2ArNH_2 + Na_2S_2O_5 + 4HNO_3 \longrightarrow 2Ar\overset{+}{N}_2\,NO_3^- + Na_2S_2O_7 + 4H_2O}\quad \text{(Witt method)}$$

$$\mathrm{ArNH_2 + RONO + HX \longrightarrow Ar\overset{+}{N}_2\,\overset{-}{X} + ROH + H_2O}\quad \text{(Knoevenagel method)}$$

N. Kornblum, *Org. React.* **2,** 264 (1944); W. A. Cowdry, D. S. Davies, *Quart. Rev.* **6,** 358 (1952); Ridd, *ibid.* **15,** 418 (1961); B. I. Belov, V. V. Kozlov, *Russ. Chem. Rev.* **32,** 59 (1963); K. Schank in *The Chemistry of Diazonium and Diazo Groups*, S. Patai, Ed. (Wiley, New York, 1978) p 645; J. B. Fox, Jr., *Anal. Chem.* **51,** 1493 (1979). Evaluation in determination of biological nitrogen: I. Guevara *et al.*, *Clin. Chim. Acta* **274,** 177 (1998); K. Schulz *et al.*, *Nitric Oxide: Biology & Chemistry* **3,** 225 (1999).

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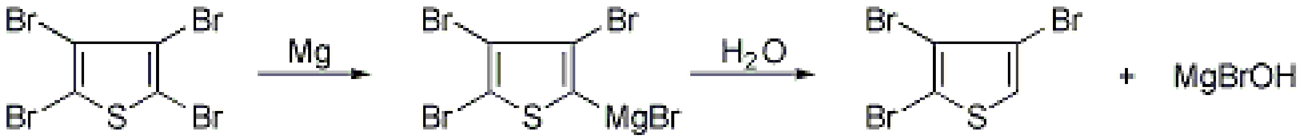
163. Grignard Degradation

W. Steinkopf *et al., Ann.* **512,** 136 (1934); **543,** 128 (1940).

Stepwise dehalogenation of a polyhalo compound through its Grignard reagent which on treatment with water yields a product containing one halogen atom less:



V. Grignard, *Compt. Rend.* **130,** 1322 (1900); F. F. Blicke, *Heterocyclic Compounds* **1,** 222 (1950); K. Nützel, *Houben-Weyl* **13/2a,** 128 (1973).

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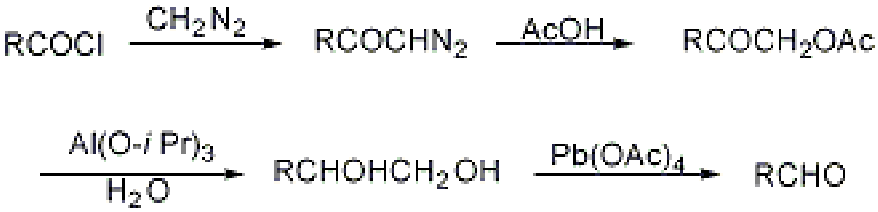
166. Grundmann Aldehyde Synthesis

C. Grundmann, *Ann.* **524,** 31 (1936).

Transformation of an acid into an aldehyde of the same chain length by conversion of the acid chloride, *via* the diazo ketone, to the acetoxy ketone, reduction with aluminum isopropoxide and hydrolysis to the glycol, and cleavage with lead tetraacetete:



$$RCOCl \xrightarrow{CH_2N_2} RCOCHN_2 \xrightarrow{AcOH} RCOCH_2OAc$$

$$\xrightarrow[H_2O]{Al(O\text{-}i\ Pr)_3} RCHOHCH_2OH \xrightarrow{Pb(OAc)_4} RCHO$$

E. Mosetting, *Org. React.* **8,** 225 (1954); O. Bayer, *Houben-Weyl* **7/1,** 239 (1954); H. K. Mangold, *J. Org. Chem.* **24,** 405 (1959). *Cf.* Sonn-Müller Method; Stephen Aldehyde Synthesis.

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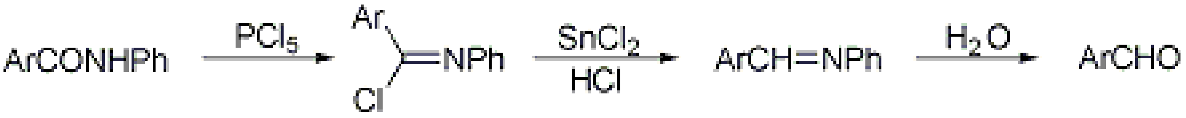
374. Sonn-Müller Method

A. Sonn, E. Müller, *Ber*. **52,** 1927 (1919).

Reaction sequence employed to convert aromatic anilides to aldehydes. Treatment of the anilide with phosphorus pentachloride generates the imidoyl chloride, which is reduced to the imine with a mixture of stannous chloride and hydrochloric acid. Subsequent hydrolysis yields the aldehyde:



T. Reichstein, H. Zschokke, *Helv. Chim. Acta* **15,** 1105 (1932); W. E. Bachmann, *J. Am. Chem. Soc.* **57,** 1381 (1935); T. S. Work, *J. Chem. Soc.* **1942,** 429; L. N. Ferguson, *Chem. Rev*. **38,** 244 (1946); E. Mosettig, *Org. React.* **8,** 240 (1954); L. F. Fieser, M. Fieser, *Advanced Organic Chemistry* (New York, 1961) p 832. *Cf.* Grundmann Aldehyde Synthesis; Stephen Aldehyde Synthesis.

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376. Stephen Aldehyde Synthesis

H. Stephen, *J. Chem. Soc.* **127,** 1874 (1925); T. Stephen, H. Stephen, *ibid.* **1956,** 4695.

Reaction sequence employed to convert nitriles to aldehydes. Treatment of the nitrile with a mixture of stannous chloride and hydrochloric acid yields the imine salt complex which is subsequently hydrolyzed to the aldehyde. Practically applied only to aromatic aldehydes:

L. N. Ferguson, *Chem. Rev.* **38,** 243 (1946); E. Mosettig, *Org. React.* **8,** 246 (1954); O. Bayer, *Houben-Weyl* **7/1,** 299 (1954); E. N. Zilberman, P. S. Pyryalova, *J. Gen. Chem. U.S.S.R.* (Engl. trans.) **33,** 3348 (1963); C. G. Stuckwisch, *J. Org. Chem.* **37,** 318 (1972). *Cf.* Grundmann Aldehyde Synthesis; Sonn-Müller Method.

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168. Guerbet Reaction

M. Guerbet, *Compt. Rend.* **128,** 511 (1899).

Condensation of 1° or 2° alcohols at high temperature and pressure in the presence of alkali metal hydroxide or alkoxide by a dehydrogenation, aldol condensation, *q.v.*, and hydrogenation sequence:

$$2\ RCH_2CH_2OH \xrightarrow{NaOEt} 2\ RCH_2CHO \longrightarrow RCH_2CHOHCHRCHO \xrightarrow{-\ H_2O}$$

$$RCH_2CH{=}CRCHO \xrightarrow{H_2} RCH_2CH_2CHRCH_2OH$$

H. Machemer, *Angew. Chem.* **64,** 213 (1952); S. Veibel, J. T. Nielsen, *Tetrahedron* **23,** 1723 (1967); G. Gregorio *et al., J. Organometal. Chem.* **37,** 385 (1972); E. Klein, *et al., Ann.* **1973,** 1004. Rhodium-promoted reaction: P. L. Burk *et al., J. Mol. Catal.* **33,** 1 (1985).

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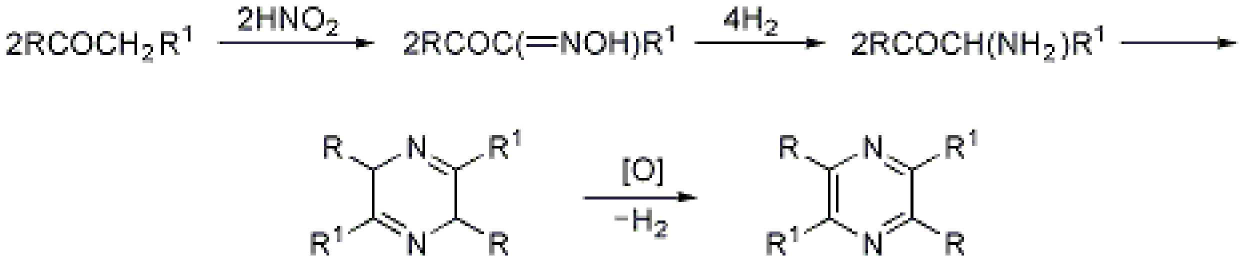
169. Gutknecht Pyrazine Synthesis

H. Gutknecht, *Ber.* **12,** 2290 (1879); **13,** 1116 (1880).

Cyclization of α-amino ketones, produced by reduction of isonitroso ketones to yield the dihydropyrazines which are dehydrogenated with mercury(I) oxide or copper(II) sulfate, or sometimes with atmospheric oxygen:



I. J. Krems, P. E. Spoerri, *Chem. Rev.* **40,** 291 (1947); Y. T. Pratt, *Heterocyclic Compounds* **6,** 379, 385 (1957).

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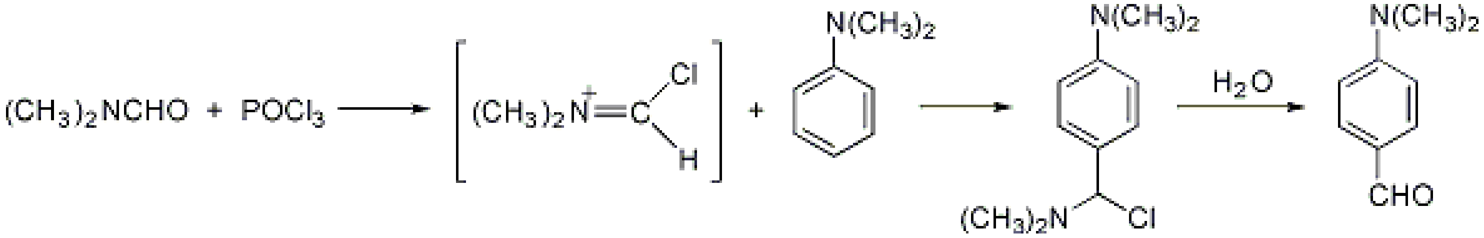
407. Vilsmeier-Haack Reaction

A. Vilsmeier, A. Haack, *Ber.* **60,** 119 (1927).

Formylation of activated aromatic or heterocyclic compounds with disubstituted formamides and phosphorus oxychloride:

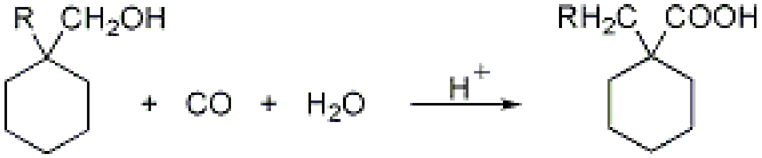


Reviews: M. R. de Maheas, *Bull. Soc. Chim. France* **1962,** 1989; W. G. Jackson *et al., J. Am. Chem. Soc.* **103,** 533 (1981); C. Jutz, *Advan. Org. Chem.* **9,** 225-342 (1976); O. Meth-Cohn, S. P. Stanforth, *Comp. Org. Syn.* **2,** 777-794 (1991).

218. Koch-Haaf Carboxylations

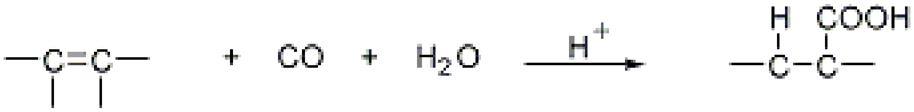
H. Koch, *Brennstoff Chem.* **36,** 321 (1955); H. Koch, W. Haaf, *Ann.* **618,** 251 (1958).

Formation of tertiary carboxylic acids by treating alcohols with carbon monoxide in strong acid:



H. Langhals *et al., Tetrahedron Letters* **22,** 2365 (1981); R. R. Rao, J. Bhattacharya, *Indian J. Chem.* **20B,** 207 (1981); *eidem, ibid.* **21B,** 405 (1982); O. Farooq *et al., J. Am. Chem. Soc.* **110,** 864 (1988). *Reviews:* K. E. Möller, *Brennstoff Chem.* **47,** 10 (1966); Y. T. Eidus, *et al., Russ. Chem. Rev.* **42,** 199 (1973); H. Bahrmann, "Koch Reactions" in *New Syntheses with Carbon Monoxide,* J. Falbe, Ed. (Springer-Verlag, New York, 1980) pp 372-413.

Extension to olefins:



G. Olah, J. Olah in *Friedel-Crafts and Related Reactions* **vol. 3,** Part 2, G. A. Olah, Ed. (Interscience, New York, 1964) pp 1272-1296; C. W. Bird, *Chem. Rev.* **62,** 283 (1962). Extension to amides: C. Leonte, E. Carp, *Rev. Roum. Chim.* **34,** 1241 (1989).

236. Lieben Iodoform Reaction (Haloform Reaction)

A. Lieben, *Ann.* (Suppl.) **7,** 218 (1870).

Cleavage of methyl ketones with halogens (mostly iodine) and base to carboxylic acids and haloform:

$$RCOCH_3 + NaOI \longrightarrow RCOI_3 \xrightarrow{NaOH} CH_3I + RCOO^- Na^+$$

R. C. Fuson, B. A. Bull, *Chem. Rev.* **15,** 275 (1934); R. N. Seelye, T. A. Turney, *J Chem. Ed.* **36,** 572 (1959); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 464-465; J. March, *Advanced Organic Chemistry* (Wiley-Interscience, New York, 4th ed., 1992) p 632.

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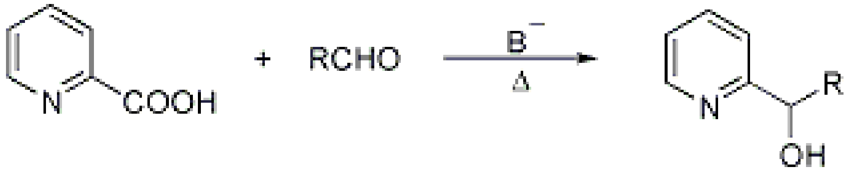
171. Hammick Reaction

P. Dyson, D. L. Hammick, *J. Chem. Soc.* **1937,** 1724.

Decarboxylation of α-picolinic or related acids in the presence of carbonyl compounds accompanied by the formation of a new carbon-carbon bond:



D. L. Hammick *et al., J. Chem. Soc.* **1939,** 809; **1949,** 659; N. H. Cantwell, E. V. Brown, *J. Am. Chem. Soc.* **75,** 1489 (1953); M. J. Betts, B. R. Brown, *J. Chem. Soc.* **1967,** 1730; E. V. Brown, M. B. Shambhu, *J. Org. Chem.* **36,** 2002 (1971). Effect of conditions on yield and products: V. P. Karandikar *et al., Indian J. Technol.* **23,** 28 (1985). Mechanism: R. Grigg *et al., J. Chem. Soc. Perkin Trans. II* **1990,** 51; B. Bohn *et al., Heterocycles* **37,** 1731 (1994).

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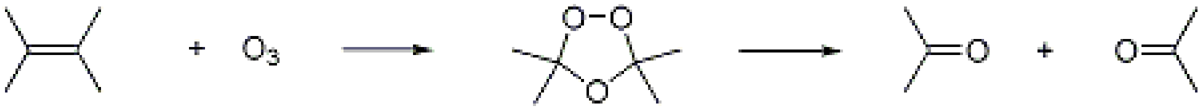
174. Harries Ozonide Reaction (Ozonolysis)

C. Harries, *Ann.* **343,** 311 (1905).

Treatment of olefins with ozone as a method of cleaving olefinic linkages. On hydrolysis or catalytic hydrogenation the initially formed ozonide yields two molecules of carbonyl compounds:



Reviews: P. S. Bailey, *Chem. Rev.* **58,** 925 (1958); L. J. Chinn, *Selection of Oxidants in Synthesis: Oxidation at the Carbon Atom* (Dekker, New York, 1971) pp 151-160; P. S. Bailey, *Ozonation in Organic Chemistry* **vols. 1 and 2** (Academic Press, New York, 1978, 1982). Mechanism: R. Criegee, *Record Chem. Progr.* **18,** 111 (1957); R. W. Murray, *Accts. Chem. Res.* **1,** 313 (1968); M. Miura *et al., J. Org. Chem.* **50,** 1504 (1985). Applications: J. Z. Gillies *et al., J. Am. Chem. Soc.* **110,** 7991 (1988); K. Griesbaum, V. Ball, *Tetrahedron Letters* **35,** 1163 (1994).

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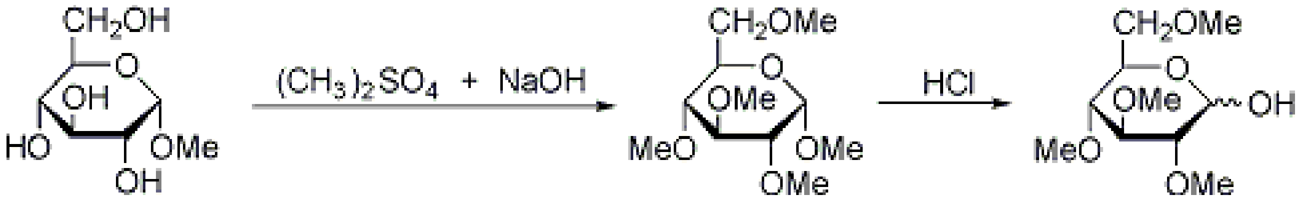
175. Haworth Methylation

W. N. Haworth, *J. Chem. Soc.* **107,** 13 (1915).

Formation of methylated methyl glycosides from monosaccharides with dimethyl sulfate and 30% sodium hydroxide. The glycosidic methyl group is hydrolyzed with acid to yield the free methylated sugar:



W. N. Haworth, H. Machemer, *J. Chem. Soc.* **1932,** 2270; C. C. Barker *et al., ibid.* **1946,** 783; E. J. Bourne, S. Peat, *Advan. Carbohyd. Chem.* **5,** 146 (1950); W. Pigman, *The Carbohydrates* **1957,** 369. *Cf.* Purdie Methylation.

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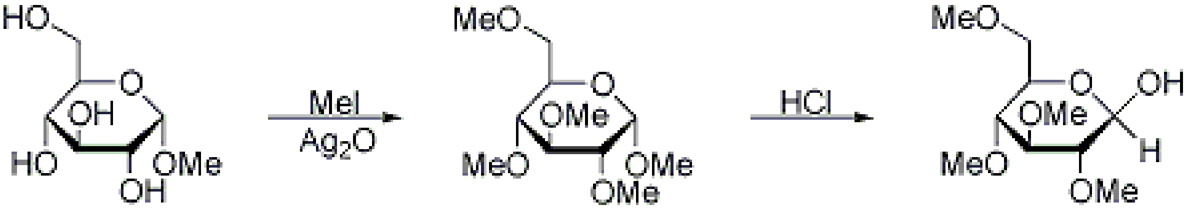
325. Purdie Methylation (Irvine-Purdie Methylation)

T. Purdie, J. C. Irvine, *J. Chem. Soc.* **83,** 1021 (1903).

Exhaustive methylation of a methyl glycoside by repeated treatment with methyl iodide and silver oxide, followed by hydrolysis of the pentamethyl ether with dilute acid to yield the anomeric hydroxyl group:



C. C. Barker, *et al., ibid.* **1946,** 753; E. J. Bourne, S. Peat, *Advan. Carbohyd. Chem.* **5,** 146 (1950); W. Pigman, *The Carbohydrates* (New York, 1957) p 370; P. V. Kovac *et al., Carbohyd. Res.* **58,** 327 (1977). *Cf.* Haworth Methylation.

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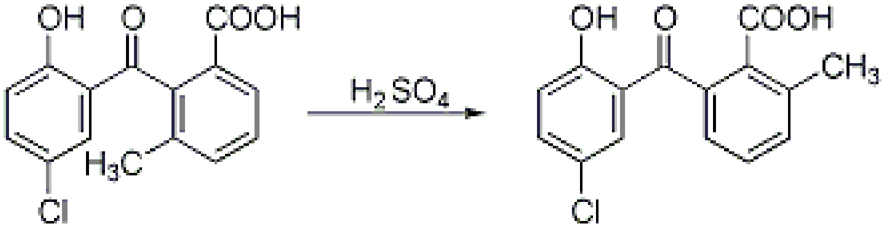
177. Hayashi Rearrangement

M. Hayashi, *J. Chem. Soc.* **1927,** 2516; **1930,** 1513, 1520, 1524.

Rearrangement of *o*-benzoylbenzoic acids in the presence of sulfuric acids or phosphorous pentoxide:



J. W. Cook, *J. Chem. Soc.* **1932,** 1472; M. Hayashi *et al., Bull. Chem. Soc. Japan* **11,** 184 (1936); R. B. Sandin, L. F. Fieser, *J. Am. Chem. Soc.* **62,** 3098 (1940); R. B. Sandin *et al., ibid.* **78,** 3817 (1956); R. Goncalves *et al., J. Org. Chem.* **17,** 705 (1952); S. Cristol, M. L. Caspar, *ibid.* **33,** 2020 (1968); M. Cushman *et al., ibid.* **45,** 5067 (1980).

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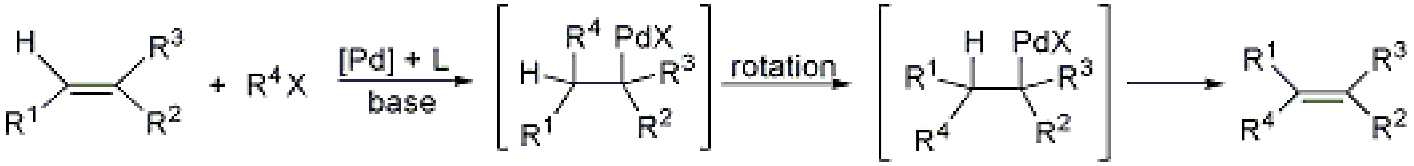
178. Heck Reaction

R. F. Heck, J. P. Nolley, Jr., *J. Org. Chem.* **37,** 2320 (1972).

Stereospecific palladium-catalyzed coupling of alkenes with organic halides or triflates lacking *sp*^{3}-hybridized β-hydrogens:



R^4 = aryl, alkenyl, benzyl
X = I, Br, OSO_2CF_3
[Pd] = $Pd(OCOCH_3)_2$, $PdCl_2$, $Pd(dba)_3$, $Pd(PPh_3)_4$
L = PAr_3, dppp, binap
base = $N(CH_2CH_3)_3$, K_2CO_3, $NaOCOCH_3$

Variation of reaction parameters in the context of the asymmetric synthesis of (+)-vernolepin: K. Ohrai *et al.*, *J. Am. Chem. Soc.* **116,** 11737 (1994). Review of intramolecular reactions: L. E. Overman, *Pure Appl. Chem.* **66,** 1423-1430 (1994); S. E. Gibson *et al.*, *Contemp. Org. Syn.* **3,** 447-471 (1996); J. T. Link, L. E. Overman, *Met.-Catal. Cross-Coupling React.* **1998,** 231-269. *Reviews:* R. F. Heck, *Org. React.* **27,** 345-390 (1982); A. de Meijere, F. E. Meyer, *Angew. Chem. Int. Ed.* **33,** 2379-2411 (1994); W. Cabri, I. Candiani, *Accts. Chem. Res.* **28,** 2-7 (1995). Review of mechanism: G. T. Crisp, *Chem. Soc. Rev.* **27,** 427-436 (1998); of enantioselective syntheses: M. Shibasaki, E. M. Vogl, *J. Organometal. Chem.* **576,** 1-15 (1999); O. Loiseleur *et al.*, *ibid.* 16-22; U. Iserloh, D. P. Curran, *Chemtracts* **12,** 289-296 (1999). *Cf.* Stille Coupling; Suzuki Coupling.

379. Stille Coupling

M. Kosugi *et al.*, *Chem. Letters* **1977,** 301 (1977); D. Milstein, J. K. Stille, *J. Am. Chem. Soc.* **100,** 3636 (1978).

Palladium-catalyzed cross coupling reaction of organostannanes with organic halides, acetates or perfluorinated sulfonates lacking a *sp*^{3}-hybridized β-hydrogen:

$$R_3Sn{-}R^1 \quad + \quad R^2{-}X \xrightarrow{[Pd]} R^1{-}R^2 \quad + \quad R_3SnX$$

$[Pd] = Pd(PPh_3)_4$, $PhCH_2Pd(PPh_3)_2Cl$

R^1 = alkynyl, alkenyl, aryl, allyl, benzyl, alkyl

R^2 = acyl, alkenyl, allyl, benzyl, aryl

X = Cl, Br, I, $OCOCH_3$, $OSO_2(C_nF_{2n+1})$, n = 0,1,4

Allylic acetates as substrates: L. Del Valle *et al., J. Org. Chem.* **55,** 3019 (1990). Effect of additives: S. Gronowitz *et al., J. Organometal. Chem.* **460,** 127 (1993); V. Farina *et al., J. Org. Chem.* **59,** 5905 (1994). Synthesis of α-methylene lactones: R. M. Adlington *et al., J. Chem. Soc. Perkin Trans. I* **1994,** 1697. Solid-phase synthesis of 1,4-benzodiazepines: M. J. Plunkett, J. A. Ellman, *J. Am. Chem. Soc.* **117,** 3306 (1995). *Reviews:* J. K. Stille, *Angew. Chem. Int. Ed.* **25,** 508-524 (1986); M. Pereyre *et al., Tin in Organic Synthesis* (Butterworths, Boston, 1987) pp 185-207 *passim*. Review of synthetic applications: T. N. Mitchell, *Synthesis* **1992,** 803-815. *Cf.* Heck Reaction; Suzuki Coupling.

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388. Suzuki Coupling

N. Miyaura *et al., Tetrahedron Letters* **1979,** 3437; N. Miyaura, A. Suzuki, *Chem. Commun.* **1979,** 866.

Palladium-catalyzed cross coupling of organic halides or perfluorinated sulfonates with organoboron derivatives proceeding with high stereo- and regioselectivity:

$$R^1{-}BY_2 \quad + \quad R^2{-}X \quad \xrightarrow[\text{base}]{[Pd]} \quad R^1{-}R^2$$

BY_2 = $B(OR)_2$, 9–BBN, $B(CHCH_3CH(CH_3)_2)_2$
X = I, Br, Cl, $OSO_2(C_nF_{2n+1})$, n = 0,1,4
R^1 = aryl, alkenyl, alkyl
R^2 = aryl, alkenyl, alkynyl, benzyl, allyl, alkyl
[Pd] = $Pd(PPh_3)_4$, $Pd(dppf)Cl_2$
base = Na_2CO_3, $NaOCH_2CH_3$, TlOH, $N(CH_2CH_3)_3$, K_3PO_4

Competition with Heck reaction, *q.v.*, when using an alkenyl boronate ester: A. R. Hunt *et al., Tetrahedron Letters* **34,** 3599 (1993). Alternative palladium catalysts: G. Marck *et al., ibid.* **35,** 3277 (1994); T. I. Wallow, B. M. Novak, *J. Org. Chem.* **59,** 5034 (1994). *Reviews:* A. Suzuki, *Pure Appl. Chem.* **63,** 419-422 (1991); A. R. Martin, Y. Yang, *Acta Chem. Scand.* **47,** 221-230 (1993). *Cf.* Hydroboration Reaction; Stille Coupling.

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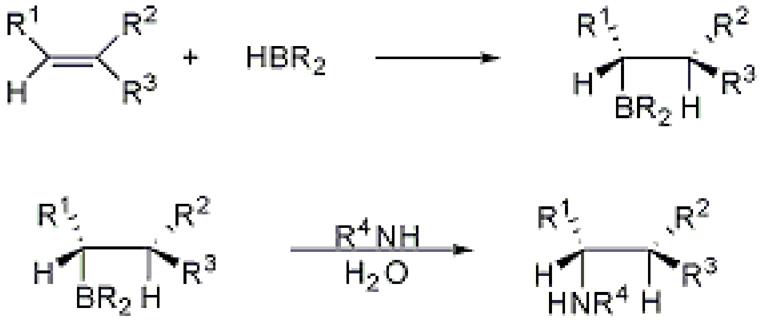
201. Hydroboration Reaction

H. C. Brown, B. C. Subba Rao, *J. Am. Chem. Soc.* **78,** 5694 (1956); *J. Org. Chem.* **22,** 1135, 1136 (1957).

Addition of boron hydrides to alkenes, allenes, and alkynes to form organoboranes, such that boron adds to the less substituted carbon. Attack usually takes place on the less hindered side in a *cis* fashion:

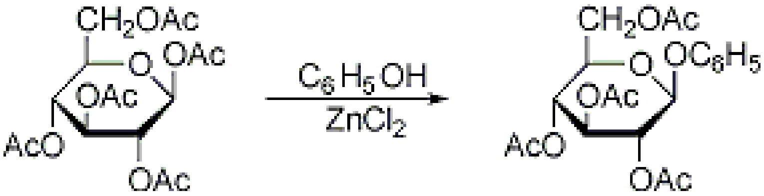


Diastereofacial and regioselectivity study: B. W. Gung *et al., Synth. Commun.* **24,** 167 (1994). Methods development for asymmetric synthesis: U. P. Dhokte, H. C. Brown, *Tetrahedron Letters* **35,** 4715 (1994). Application to hydration: G. Zweifel, H. C. Brown, *Org. React.* **13,** 1-54 (1963). General reviews: H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 106-130; K. Smith, A. Pelter, *Comp. Org. Syn.* **8,** 703-731 (1991). Reviews of asymmetric synthesis: H. C. Brown, *Tetrahedron* **37,** 3547-3587 (1981); K. Burgess, M. J. Ohlmeyer, *Adv. Chem. Ser.* **230,** 163-177 (1992). *Cf.* Suzuki Coupling.

179. Helferich Method

B. Helferich, E. Schmitz-Hillebrecht, *Ber.* **66,** 378 (1933).

Glycosidation of an acetylated sugar by heating with a phenol in the presence of a metal halide ($ZnCl_2$, $FeCl_3$) or *p*-toluenesulfonic acid as catalyst:



W. W. Pigman, R. M. Goepp, *Chemistry of the Carbohydrates* (New York, 1948) p 194; W. W. Pigman, *The Carbohydrates* (New York, 1957) p 198; B. Helferich, J. Zirner, *Ber.* **96,** 385 (1963); A. Piskala *et al., Nucleic Acid Chem.* **1,** 455 (1978). Applications: R. Polt *et al., J. Am. Chem. Soc.* **114,** 10249 (1992); P. Kosma *et al., Carbohydr. Res.* **254,** 105 (1994); D. A. Leigh *et al., ibid.* **276,** 417 (1995); V. K•en *et al., J. Chem. Soc. Perkin Trans. I* **1997,** 2467.

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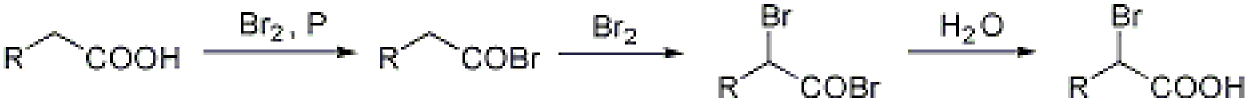
180. Hell-Volhard-Zelinsky Reaction

C. Hell, *Ber.* **14,** 891 (1881); J. Volhard, *Ann.* **242,** 141 (1887); N. Zelinsky, *Ber.* **20,** 2026 (1887).

α-Halogenation of carboxylic acids in the presence of catalytic phosphorus, presumably involving the enol form of the intermediate acyl halide:



N. O. V. Sonntag, *Chem. Rev.* **52,** 237 (1953); H. J. Harwood, *ibid.* **62,** 102 (1962); H. Kwart, E. V. Scalzi, *ibid.* **86,** 5496 (1964); A. R. Sexton *et al., J. Am. Chem. Soc.* **91,** 7098 (1969); G. L. Lange, J. A. Otulakowski, *J. Org. Chem.* **47,** 5093 (1982); R. J. Crawford, *ibid.* **48,** 1364 (1983); H.-J. Liu, W. Luo, *Synth. Commun.* **21,** 2097 (1991).

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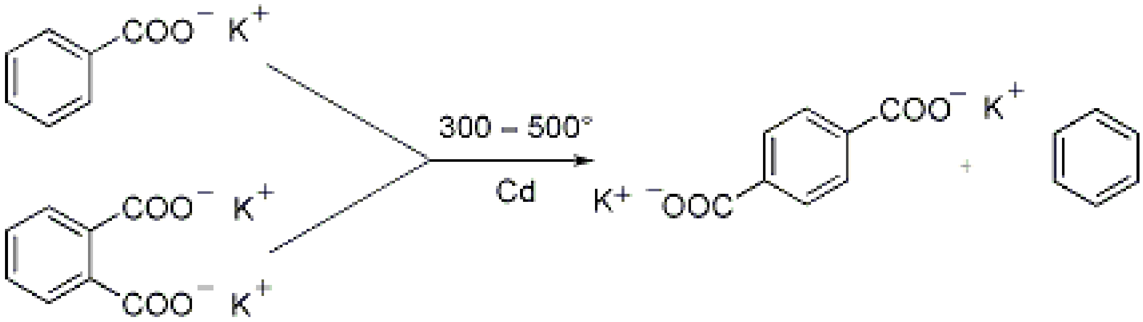
181. **Henkel Reaction** (Raecke Process, Henkel Process)

B. Raecke, **DE 936036** (1952) and **DE 958920** (1952) to Henkel & Co.

Industrial scale thermal rearrangement or disproportionation of alkaline salts of aromatic acids to symmetrical diacids in the presence of cadmium or other metallic salts:



Review: B. Raecke, *Angew. Chem.* **70,** 1 (1958); Y. Ogata *et al.*, *J. Org. Chem.* **25,** 2082 (1960); E. McNelis, *ibid.* **30,** 1209 (1965); J. Szammer, L. Otvos, *Radiochem. Radioanal. Lett.* **45,** 359 (1980).

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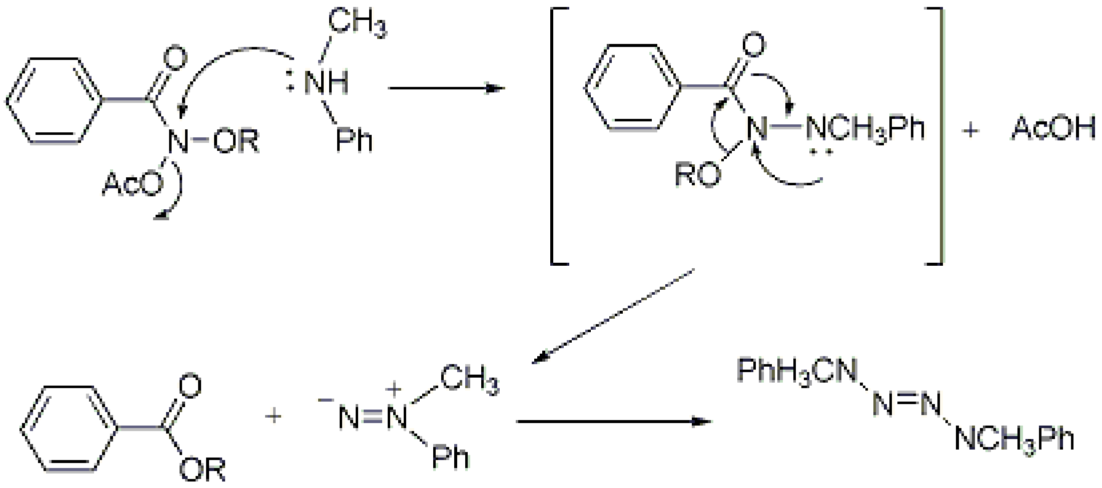
183. HERON Rearrangement (Heteroatom Rearrangements on Nitrogen)

J. M. Buccigross *et al., Aust. J. Chem.* **48,** 353 (1995); J. M. Buccigross, S. A. Glover, *J. Chem. Soc. Perkin Trans. II* **1995,** 595.

Rearrangement of bisheteroatom substituted amides to esters and 1,1-diazenes via migration of oxygen from the nitrogen to the carbonyl carbon. Analogues of *N*,*N′*-diacyl-*N*, *N′*-dialkoxyhydrazines thermally decompose to esters and N_2 through two consecutive rearrangements:

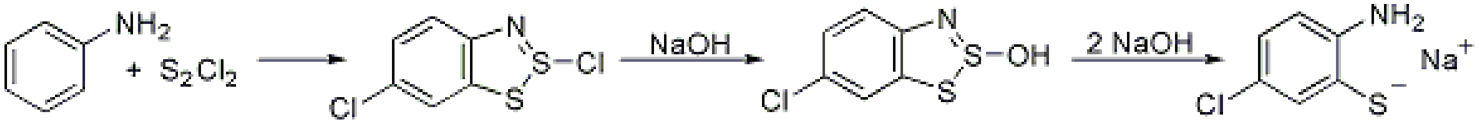


Application to *N*,*N′*-diacyl-*N*,*N′*-dialkoxyhydrazines: S. A. Glover *et al., J. Chem. Soc. Perkin Trans. II* **1999,** 2053; to mutagenic *N*-acyloxy-*N*-alkoxybenzamides: *J. Chem. Res.* **1999,** 474. Stereochemistry and computational studies: A. Rauk, S. A. Glover, *J. Org. Chem.* **61,** 2337 (1999); *eidem, ibid.* **64,** 2340. *Review:* S. A. Glover, *Tetrahedron* **54,** 7229-7272 (1998).

184. Herz Reaction

R. Herz, **DE 360690** (1914 to Cassella & Co.); **US 1637023** (1928); **US 1699432** (1929).

Formation of *o*-aminothiophenols by heating aromatic amines with excess sulfur monochloride. The initial products are thiazothionium halides (Herz compounds) which will undergo chlorination if the position *para* to the amino group is unsubstituted:



W. K. Warburton, *Chem. Rev.* **57,** 1011 (1957); L. D. Huestis *et al., J. Org. Chem.* **30,** 2763 (1965); P. Hope, L. A. Wiles, *J. Chem. Soc. C* **1967,** 1642; B. K. Strelets, L. S. Efros, *Zh. Org. Khim.* **1969,** 153; S. W. Schneller, *Int. J. Sulfur Chem.* **8,** 579 (1976); B. L. Chenard, *J. Org. Chem.* **49,** 1224 (1984).

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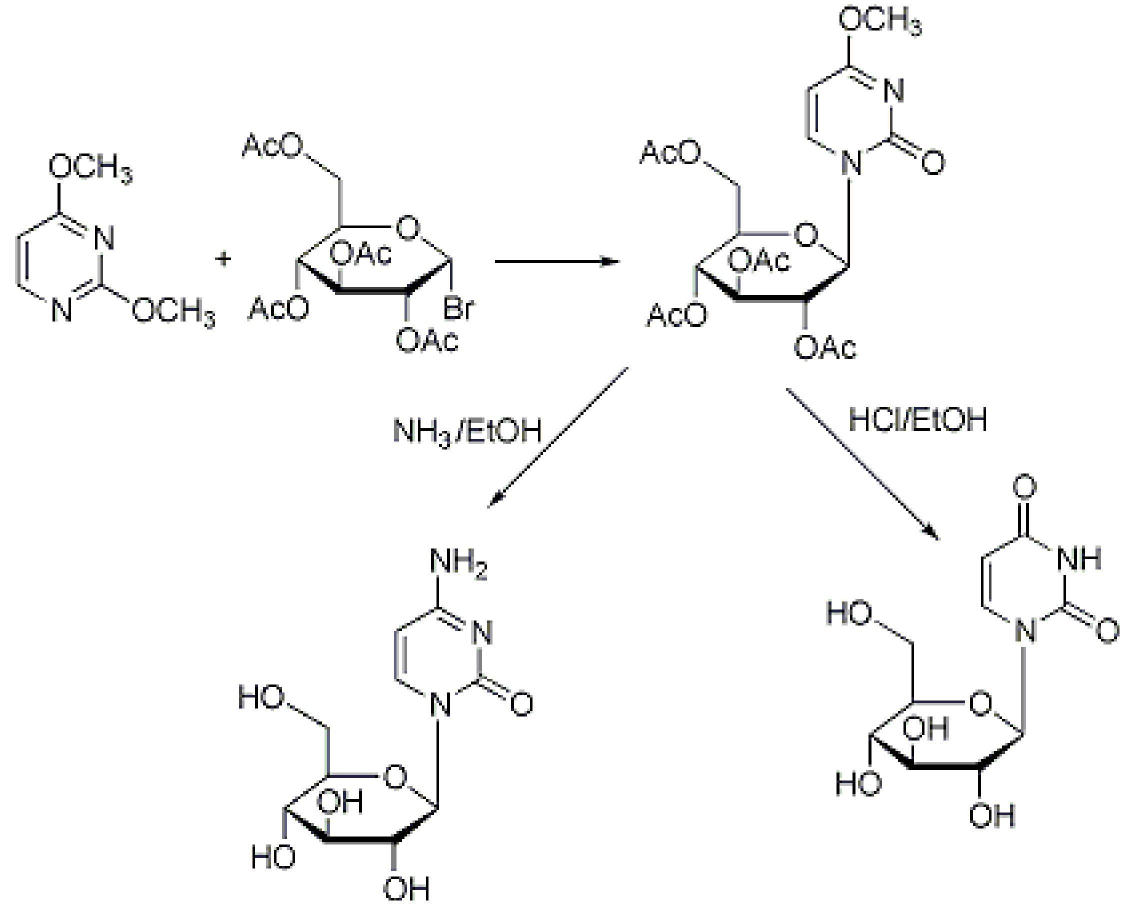
185. Hilbert-Johnson Reaction

T. B. Johnson, G. E. Hilbert, *Science* **69,** 579 (1929); G. E. Hilbert, T. B. Johnson, *J. Am. Chem. Soc.* **52,** 2001, 4489 (1930).

Reaction of 2,4-dialkoxypyrimidines with halogenated sugar to yield pyrimidine nucleosides:

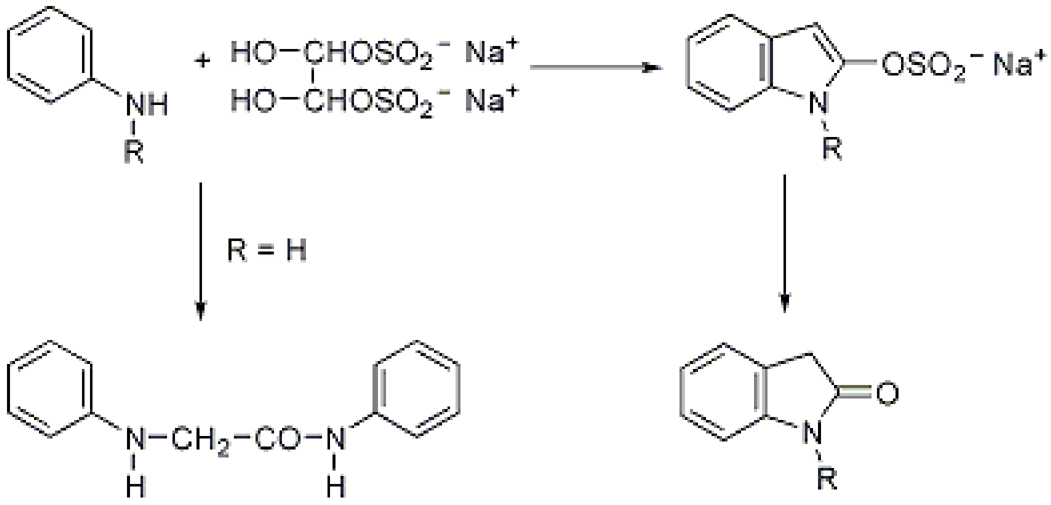


W. Zorbach, *Methods Carbohyd. Chem.* **6,** 445 (1972); T. Ueda, H. Ohtsuka, *Chem. Pharm. Bull.* **21,** 1451, 1530 (1973); C.-H. Kim *et al., J. Med. Chem.* **29,** 1374 (1986); A. A. Mourabit, *Tetrahedron Asymmetry* **7,** 3455 (1996). Modified conditions: U. Neidballa, H. Vorbrüggen, *Angew. Chem. Int. Ed.* **9,** 469 (1970); H. Vorbrüggen, *et al., Ber.* **114,** 1279 (1981); H. Kristinsson *et al., Tetrahedron* **50,** 6825 (1994); G. Liu *et al., Synth. Comm.* **26,** 2681 (1996). Review of early studies: J. Pliml, M. Prystas, *Advan. Heterocyclic Chem.* **8,** 115 (1967).

186. Hinsberg Oxindole and Oxiquinoline Synthesis

O. Hinsberg, *Ber*. **21,** 110 (1888); **25,** 2545 (1892); **41,** 1367 (1908).

Formation of oxindoles from secondary aryl amines and the acid addition compound of glyoxal; primary aryl amines give glycine or glycinamide derivatives:



O. Hinsberg, J. Rosenzweig, *ibid*. **27,** 3253 (1894); C. Hollins, *Synthesis of Nitrogen Ring Compounds* (London, 1924) p 112; H. Burton, *J. Chem. Soc*. **1932,** 546; P. L. Julian *et al*., *Heterocyclic Compounds* **3,** 139 (1952). Mechanistic study: M. I. Abasolo *et al*., *J. Heterocyclic Chem*. **29,** 1279 (1992). Applications: M. I. Abasolo *et al*., *ibid*. **27,** 157 (1990); G. A. Rodrigo *et al*., *ibid*. **34,** 505 (1997). *Cf*. Stollé Synthesis.

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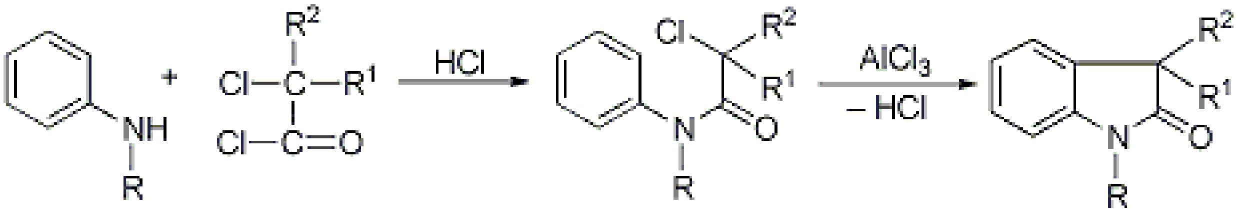
381. StolléSynthesis

R. Stollé, *Ber.* **46,** 3915 (1913); **47,** 2120 (1914); *J. Prakt. Chem.* **105,** 137 (1923); **128,** 1 (1930).

Formation of indole derivatives by the reaction of arylamines with α-haloacid chlorides or oxalyl chloride, followed by cyclization of the resulting amides with aluminum chloride:



W. C. Sumpter, *Chem. Rev.* **34,** 396 (1944); **37,** 446 (1945); P. L. Julian *et al., Heterocyclic Compounds* **3,** 142, 209 (1952); A. H. Beckett *et al., Tetrahedron* **24,** 6093 (1968). *Cf.* Hinsberg Oxindole Synthesis.

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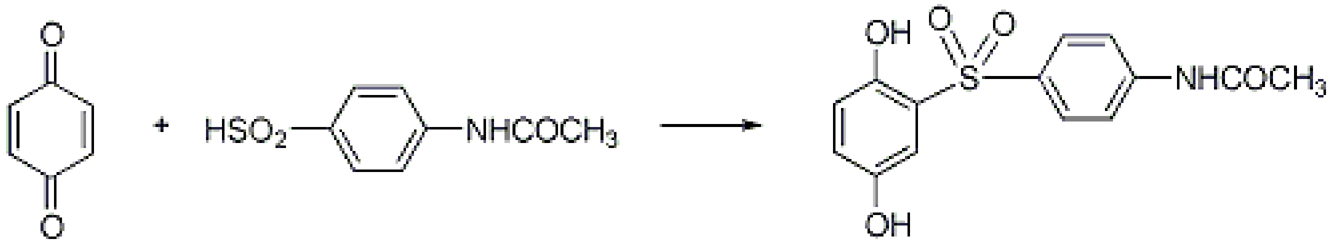
187. Hinsberg Sulfone Synthesis

O. Hinsberg, *Ber*. **27,** 3259 (1894); **28,** 1315 (1895).

Formation of sulfonylquinol derivatives by addition of quinones to cold dilute aqueous solutions of sulfinic acids:



R. M. Scribner, *J. Org. Chem.* **31,** 3671 (1966); H. Ulrich *et al., Houben-Weyl* **7/3a,** 661 (1977). *Cf.* Thiele Reaction.

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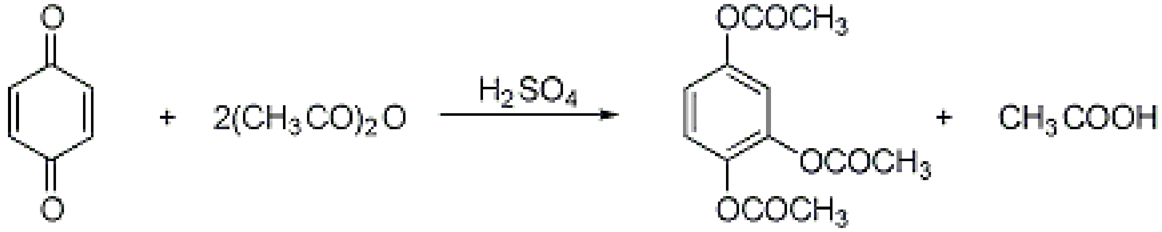
393. Thiele Reaction (Thiele-Winter Acetoxylation)

J. Thiele, *Ber.* **31,** 1247 (1898).

Formation of triacetoxy aromatic compounds by the reaction of quinones with acetic anhydride catalyzed by sulfuric acid or boron trifluoride:

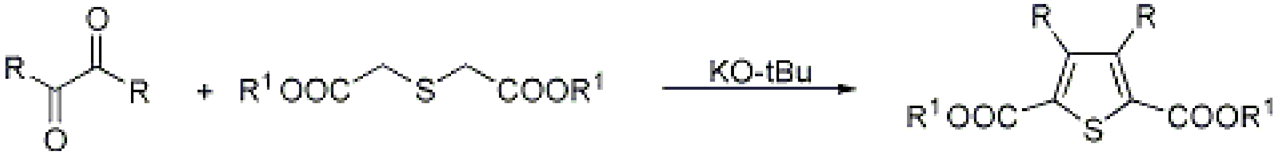


Review: J. F. W. McOmie, J. N. Blatchly, *Org. React.* **19,** 199 (1972). J. M. Blatchly *et al.*, *J. Chem. Soc. Perkin Trans. I* **1972,** 2286; J. F. W. McOmie, S. A. Saleh, *ibid.* **1974,** 384; M. Hirama, S. Ito, *Chem. Letters* **1977,** 627. *Cf.* Hinsberg Sulfone Synthesis.

188. Hinsberg Synthesis of Thiophene Derivatives

O. Hinsberg, *Ber*. **43,** 901 (1910).

Formation of thiophene carboxylic acids from α-diketones and dialkyl thiodiacetates:



H. Wynberg, D. J. Zwanenburg, *J. Org. Chem.* **29,** 1919 (1964); H. Wynberg, H. J. Kooreman, *J. Am. Chem. Soc.* **87,** 1739 (1965); A. Birch, D. A. Crombie, *Chem. Ind.* **1971,** 177; D. J. Chadwick *et al.*, *J. Chem. Soc. Perkin Trans. I* **1972,** 2079.

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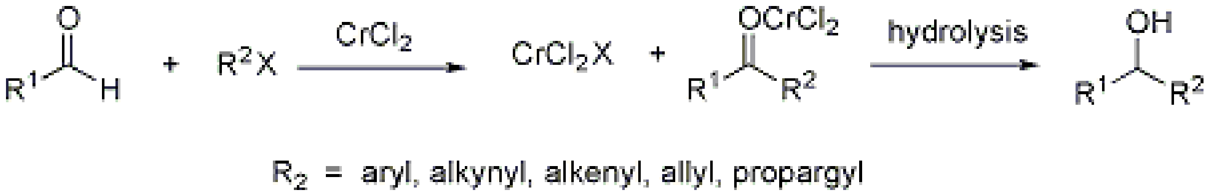
284. **Nozaki-Hiyama Coupling Reaction** (Nozaki-Hiyama-Kishi Reaction)

Y. Okude *et al., J. Am. Chem. Soc.* **99,** 3179 (1977); K. Takai *et al., Tetrahedron Letters* **24,** 5281 (1983).

Chromium chloride catalyzed redox additions or organic halides to aldehydes:



Use of nickel salts as catalyst: H. Jin *et al., J. Am. Chem. Soc.* **108,** 5644 (1986); K. Takai *et al., ibid.* 6048; of chromium: A. Furstner, N. Shi, *ibid.* **118,** 12349 (1996). Enantioselectivity: K. Sugimoto *et al., J. Org. Chem.* **62,** 2322 (1997); M. Bandini *et al., Angew. Chem. Int. Ed.* **38,** 3357 (1999). Synthetic applications: Y. Kishi, *Pure Appl. Chem.* **64,** 354 (1992); D. P. Stamos *et al., J. Org. Chem.* **62,** 7552 (1997). *Review:* N. A. Saccomano, *Comp. Org. Syn.* **1,** 173-207 (1991).

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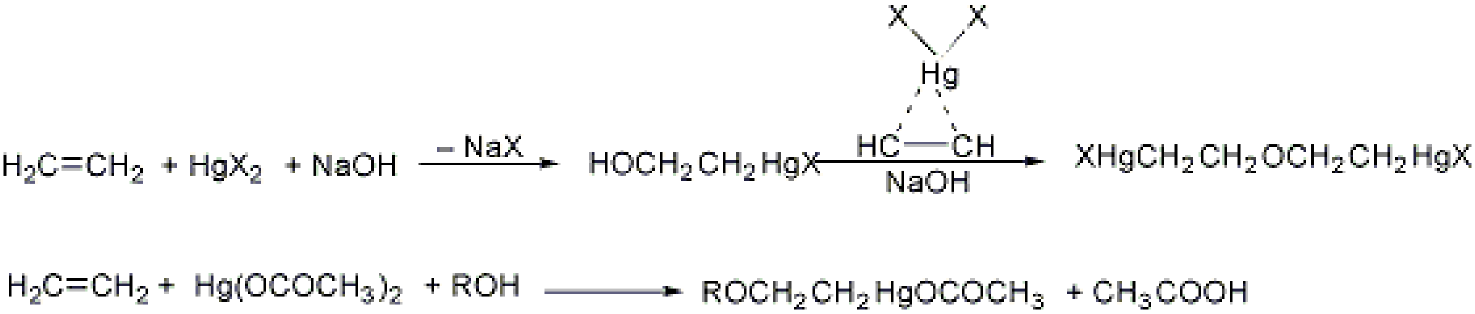
195. Hofmann-Sand Reactions

K. A. Hofmann, J. Sand, *Ber.* **33,** 1340, 1353 (1900).

Olefin mercuration with mercuric salts (halides, acetates, nitrates, or sulfates) in aqueous solution. In alcoholic solutions the accelerated reaction produces alkoxyalkyl compounds:



$$H_2C{=}CH_2 + HgX_2 + NaOH \xrightarrow{-\,NaX} HOCH_2CH_2HgX \xrightarrow[NaOH]{HC{-}CH \text{ (with } HgX_2)} XHgCH_2CH_2OCH_2CH_2HgX$$

$$H_2C{=}CH_2 + Hg(OCOCH_3)_2 + ROH \longrightarrow ROCH_2CH_2HgOCOCH_3 + CH_3COOH$$

J. Sand, *Ber.* **34,** 1385, 2906, 2910 (1901); *Ann.* **329,** 135 (1903); J. Chatt, *Chem. Rev.* **48,** 7 (1951); E. R. Rochow *et al., Chemistry of Organometallic Compounds* (New York, 1957) p 109; W. Kitching, *Organomet. Chem. Rev.* **3,** 35 (1968); K. P. Geller, H. Straub, *Houben-Weyl* **13/2b,** 130 (1974).

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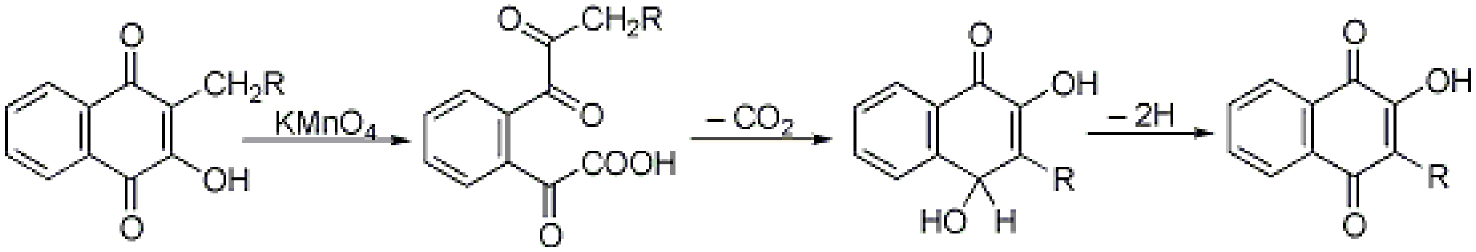
196. Hooker Reaction

S. C. Hooker, *J. Am. Chem. Soc.* **58,** 1174 (1936).

Oxidation of 2-hydroxy-3-alkyl-1,4-quinones with dilute alkaline permanganate with shortening of the alkyl side chain by a methylene group and simultaneous exchange of hydroxyl and alkyl or alkenyl group positions:



S. C. Hooker, A. Steyermark, *J. Am. Chem. Soc.* **58,** 1179 (1936); L. F. Fieser, M. Fieser, *ibid.* **70,** 3215 (1948); L. F. Fieser, A. R. Bader, *ibid.* **73,** 681 (1951); L. F. Fieser, M. Fieser, *Advanced Organic Chemistry* (New York, 1961) p 870.

352. **Sakurai Reaction** (Hosomi-Sakurai Reaction)

A. Hosomi, H. Sakurai, *Tetrahedron Letters* **1976,** 1295; A. Hosomi *et al., Chem. Letters* **1976,** 941.

Lewis acid-promoted nucleophilic addition of allylic silanes to carbon electrophiles accompanied by regiospecific transposition of the allylic moiety:

E = aldehydes, ketones, enones, acid chlorides, acetals, ketals, epoxides, iminium salts
Lewis acid = $TiCl_4$, $AlCl_3$, $BF_3 \cdot O(CH_2CH_3)_2$, $SnCl_4$, $(CH_3CH_2)_2AlCl$, cat $(CH_3)_3SiOSO_2CF_3$

Synthetic applications: I. E. Markó, D. J. Bayston, *Tetrahedron Letters* **34,** 6595 (1993); H. Hioki *et al., ibid.* 6131. $[TiCp_2(OSO_2CF_3)_2]$ as catalyst: T. K. Hollis *et al., ibid.* 4309. *Reviews:* I. Fleming *et al., Org. React.* **37,** 57-575 (1989); Y. Yamamoto, N. Sasaki, “The Stereochemistry of the Sakurai Reaction” in *Stereochemistry of Organometallic and Inorganic Compounds* **vol. 3,** I. Bernal, Ed. (Elsevier, New York, 1989) pp 363-437; I. Fleming, *Comp. Org. Syn.* **2,** 563-593 (1991).

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199. Houdry Cracking Process

E. Houdry, **US 1957648** and **US 1957649** (1934).

Decomposition of petroleum or heavy petroleum fractions into more useful lower boiling materials by heating at 500° and 30 psi, over a silica-alumina-magnanese oxide catalyst.

E. Houdry *et al., Oil Gas J.* **37,** 40 (1938); A. N. Sachanen, *Chemical Constituents of Petroleum* (New York, 1945) p 260; V. Haensel, M. J. Sterba, *Ind. Eng. Chem.* **40,** 1662 (1948); *Kirk-Othmer Encyclopedia of Chemical Technology* **4,** 323, 357 (New York, 1979); E. Boye, *Chemiker-Ztg.* **81,** 341 (1957); S. Gussow *et al., Oil Gas J.* **78,** 96 (1980); C. G. Mosley, *J. Chem. Ed.* **61,** 655 (1984); G. A. Mills, *Chemtech* **1986,** 72; Y. Nishimura, *Petrotech* **21,** 605 (1998).

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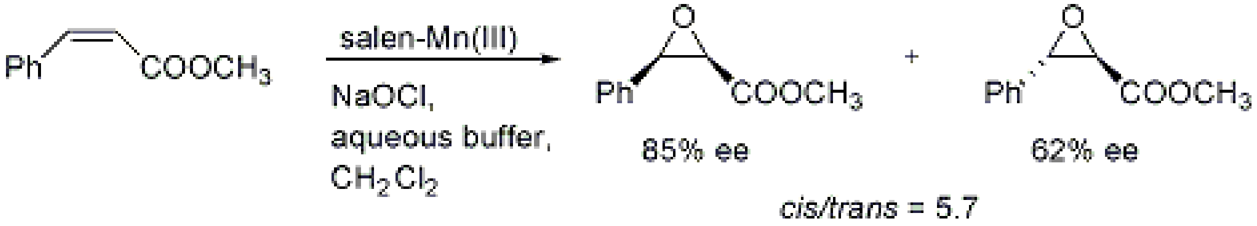
203. Jacobsen Epoxidation

W. Zhang *et al., J. Am. Chem. Soc.* **112,** 2801 (1990); E. N. Jacobsen *et al. ibid.* **113,** 7063 (1991).

Chiral (salen)manganese(III)-catalyzed asymmetric epoxidation of alkenes. Enantio- and diastereo- selectivity depend strongly on the nature of the substrate:



Methods development: E. N. Jacobsen *et al., Tetrahedron* **50,** 4323 (1994); S. Chang *et al., J. Am. Chem. Soc.* **116,** 6937 (1994); B. D. Brandes, E. N. Jacobsen, *J. Org. Chem.* **59,** 4378 (1994). Large-scale preparation of ligand: J. F. Larrow *et al., ibid.* 1939. *Review:* E. N. Jacobsen, “Asymmetric Catalytic Epoxidation of Unfunctionalized Olefins” in *Catalytic Asymmetric Synthesis*, I. Ojima, Ed. (VCH, New York, 1993) pp 159-202. For parallel studies, *see* N. Hosoya *et al., Synlett* **1993,** 641; H. Sasaki *et al., ibid.* **1994,** 356. Mechanistic study: D. L. Hughes *et al., J. Org. Chem.* **62,** 2222 (1997). Application: P. S. Savle *et al., Tetrahedron Asymmetry* **9,** 1843 (1998). *Review:* T. Flessner *et al., J. Prakt. Chem.* **341,** 436-444 (1999).

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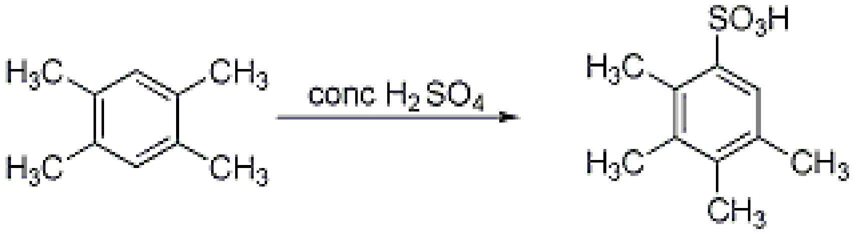
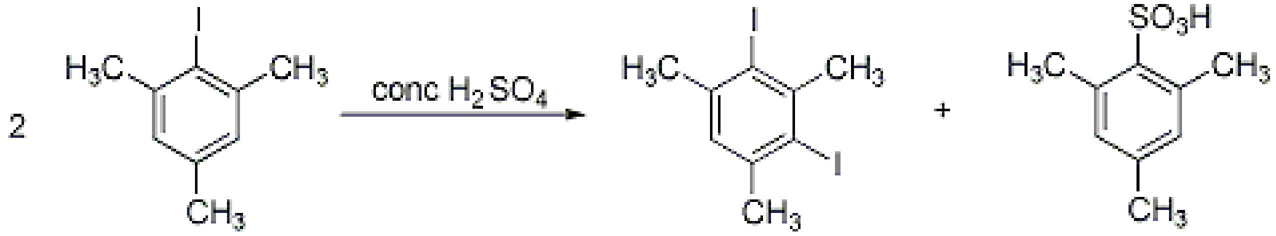
204. Jacobsen Rearrangement

O. Jacobsen, *Ber.* **19,** 1209 (1886); **20,** 901 (1887).

Reaction of polymethylbenzenes with concentrated sulfuric acid to give rearranged polymethylbenzenesulfonic acids. Under identical conditions halogenated polymethylbenzenes undergo disproportionation:



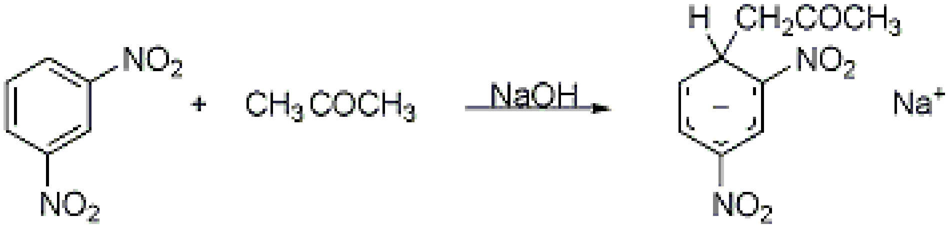


L. I. Smith, *Org. React.* **1,** 370 (1942); H. Suzuki *et al.*, *Bull. Chem. Soc. Japan* **36,** 1642 (1963); A. Koeberg-Telder, H. Cerfontain, *J. Chem. Soc. Perkin Trans. II* **1977,** 717; M. Nakada *et al.*, *Bull. Chem. Soc. Japan* **52,** 3671 (1979). Mechanism: J. L. Norula, R. P. Gupta, *Chem. Era* **10,** 7 (1974). $ZrCl_4$ catalysis: E. Solari *et al.*, *Angew. Chem. Int. Ed.* **34,** 1510 (1995).

205. Janovsky Reaction

J. V. Janovsky, L. Erb, *Ber.* **19,** 2155 (1886).

Reaction of aldehydes and ketones containing α-methylene groups with *m*-dinitrobenzenes in the presence of a strong base resulting in the formation of an intense purple coloration, used for the detection of carbonyl compounds:



Reviews: Akatsuka, *J. Pharm. Soc. Japan* **80,** 389 (1960); Foster, Mackie, *Tetrahedron* **18,** 1131 (1962); Pollitt, Saunders, *J. Chem. Soc.* **1965,** 4615; M. Kimura *et al., Chem. Pharm. Bull. Japan* **17,** 531 (1969); K. Kohashi *et al., ibid.* **25,** 50 (1977). Applications: R. G. Sutherland *et al., Can. J. Chem.* **64,** 2031 (1986); J. D. Artiss *et al., Microchem. J.* **65,** 277 (2000). *Cf.* Zimmermann Reaction.

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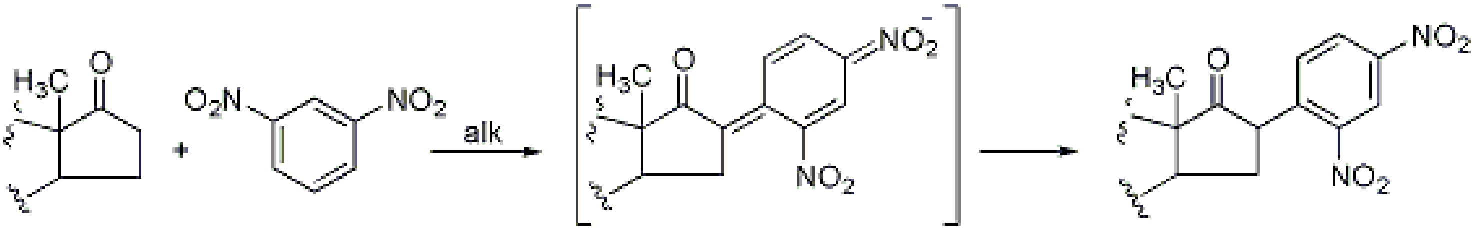
443. Zimmermann Reaction

W. Zimmermann, *Z. Physiol. Chem.* **233,** 257 (1935).

The reaction that occurs between methylene ketones and aromatic polynitro compounds in the presence of alkali. When applied to 17-oxosteroids, the colored compounds formed can be used for the quantitative determination of 17-oxosteroids:



W. Zimmerman *et al., ibid.* **289,** 91 (1952); *idem. ibid.* **300,** 141 (1955). Studies on mechanism: Neunhoffer *et al., ibid.* **323,** 116 (1961); Foster, Mackie, *Tetrahedron* **18,** 1131 (1962); H. Hoffmeister, C. Rufer, *Ber.* **98,** 2376 (1965); B. T. Rudd, O. M. Galal, *Proc. Assoc. Clin. Biochem.* **4,** 175 (1967); C. S. Feldkamp *et al., Microchem. J.* **22,** 201 (1977). *Cf.* Janovsky Reaction.

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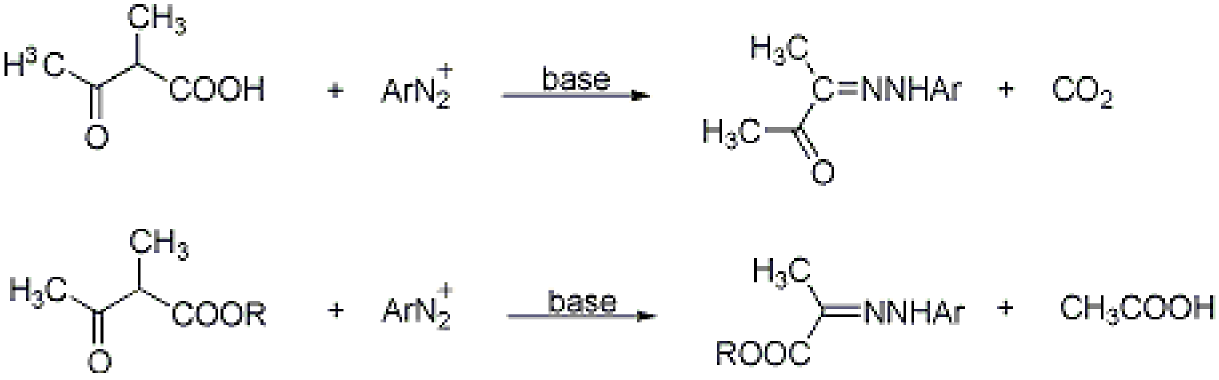
206. Japp-Klingemann Reaction

F. R. Japp, F. Klingemann, *Ann.* **247,** 190 (1888); *Ber.* **20,** 2942, 3284, 3398 (1887).

Formation of hydrazones by coupling of aryldiazonium salts with active methylene compounds in which at least one of the activating groups is acyl or carboxyl. This group usually cleaves during the process:



Review: R. R. Phillips, *Org. React.* **10,** 143 (1959); H. C. Yao, P. Resnick, *J. Am. Chem. Soc.* **84,** 3504 (1962); M. O. Lozinskii, A. A. Gershkovich, *ibid.* **8,** 785 (1972); A. Kozikowski, W. C. Floyd, *Tetrahedron Letters* **1978,** 19. Use of brominium ion as leaving group: G. Cirrincione *et al., J. Heterocyclic Chem.* **27,** 983 (1990). Synthetic applications: F. Chetoni *et al., ibid.* **30,** 1481 (1993); B. Loubinoux *et al., J. Org. Chem.* **60,** 953 (1995); B. Pete *et al., Heterocycles* **53,** 665 (2000).

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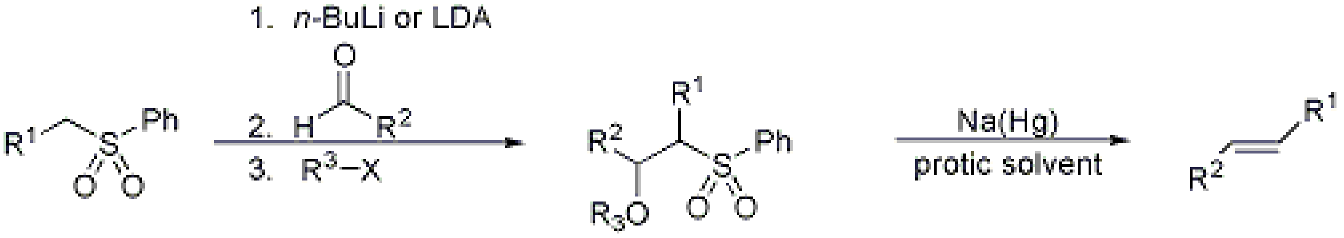
209. **Julia Olefination** (Julia-Lythgoe Olefination)

M. Julia, M.-M. Paris, *Tetrahedron Letters* **1973,** 4833.

The formation of predominantly *trans*-olefins *via* the addition of phenyl sulfones to aldehydes or ketones, followed by alcohol functionalization and subsequent reductive elimination with sodium amalgam:



$R^3 = COCH_3$, $X = OCOCH_3$; $R^3 = COPh$, SO_2CH_3, $X = Cl$

Reviews: P. Kocienski, *Phosphorus and Sulfur* **24,** 97-127 (1985); S. E. Kelly, *Comp. Org. Syn.* **1,** 792-806. Synthetic applications: R. Bellingham *et al.*, *Synthesis* **1996,** 285; I. E. Markú *et al.*, *Tetrahedron Letters* **37,** 2089 (1996); T. Satoh *et al.*, *ibid.* **39,** 6935 (1998); C. Charrier *et al.*, *ibid.* **40,** 5705 (1999). Modified conditions: P. R. Blakemore *et al.*, *Synthesis* **7,** 1209 (1999); P. J. Kocienski *et al.*, *Synlett* **2000,** 365.

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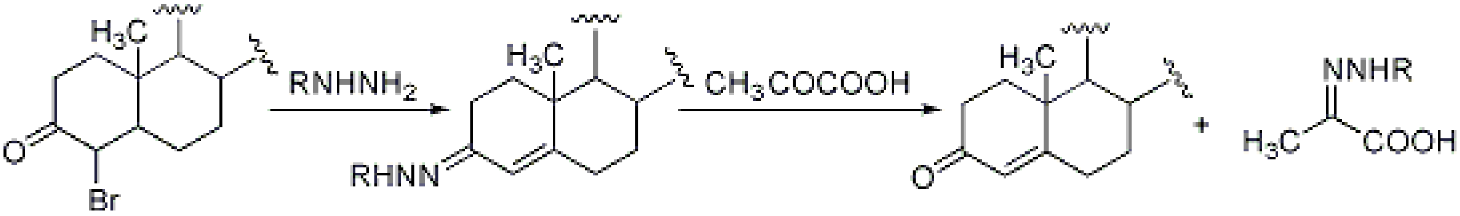
210. Kendall-Mattox Reaction

V. R. Mattox, E. C. Kendall, *J. Am. Chem. Soc.* **70,** 882 (1948); **72,** 2290 (1950); *J. Biol. Chem.* **188,** 287 (1951); E. C. Kendall, W. F. McGuckin, *J. Am. Chem. Soc.* **74,** 5811 (1952).

Formation of a conjugated ketone from an α-bromoketone *via* a phenylhydrazone or semicarbazone:



C. Djerassi, *J. Am. Chem. Soc.* **71,** 1003 (1949); B. A. Koechlin *et al., J. Biol. Chem.* **184,** 393 (1950); N. L. Wendler *et al., J. Am. Chem. Soc.* **73,** 3818 (1951); J. J. Beereboom *et al., ibid.* **75,** 3500 (1953); C. R. Engel, *ibid.* **78,** 4727 (1956); E. W. Warnhoff, *J. Org. Chem.* **28,** 887 (1963).

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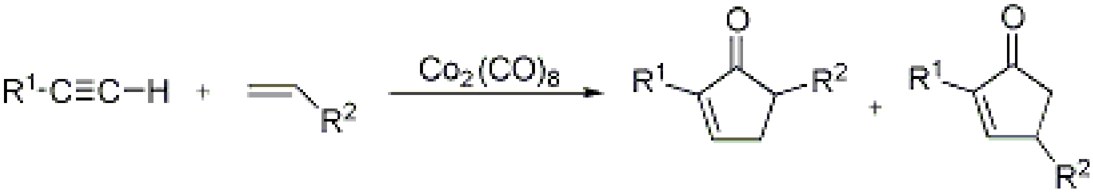
293. Pauson-Khand Reaction

I. U. Khand *et al., J. Chem. Soc. Perkin Trans. I* **1973,** 977.

The formal [2+2+1] cycloaddition of an alkene, alkyne, and carbon monoxide to form cyclopentenones:



Use of a chiral auxillary: X. Verdaguer *et al., J. Am. Chem. Soc.* **116,** 2153 (1994); V. Bernardes *et al., J. Org. Chem.* **60,** 6670 (1995); J. Adrio, J. C. Carretero, *J. Am. Chem. Soc.* **121,** 7411 (1999). Catalytic version: N. Jeong *et al., ibid.* **116,** 3159 (1994). Intramolecular cyclizations: Y.-T. Shiu *et al., ibid.* **121,** 4066 (1999); F. A. Hicks *et al., ibid.* 5881; P. M. Breczinski *et al., Tetrahedron* **55,** 6797 (1999). *Reviews:* N. E. Schore, *Org. React.* **40,** 1-90 (1991); *idem, Comp. Org. Syn.* **5,** 1037-1064 (1991); S. T. Ingate, J. Marco-Contelles, *Org. Prep. Proced. Int.* **30,** 123-143 (1998); O. Geis, H.-G. Schmalz, *Angew. Chem. Int. Ed.* **37,** 911-914 (1998).

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428. Willgerodt-Kindler Reaction

C. Willgerodt, *Ber.* **20,** 2467 (1887); **21,** 534 (1888); K. Kindler, *Ann.* **431,** 193 (1923).

Conversion of aryl alkyl ketones to amides and/or the ammonium salts of the corresponding acids by aqueous ammonium polysulfide or by sulfur and a primary or secondary amine:

$$ArCO(CH_2)_nCH_3 \xrightarrow[H_2O]{(NH_4)_2S_x} Ar(CH_2)_{n+1}{-}CONH_2 + Ar(CH_2)_{n+1}{-}COO^- \; NH_4^+$$

Reviews: M. Carmack, M. A. Spielman, *Org. React.* **3,** 83 (1946); R. Wegler *et al.*, *Newer Methods of Preparative Organic Chemistry* **vol. 3** (Academic Press, New York, 1964) pp 1-51; E. E. Campaigne in *The Chemistry of the Carbonyl Group,* S. Patai, Ed. (Wiley, New York, 1966) p 954; A. L. J. Beckwith, *The Chemistry of Amides,* J. Zabicky, Ed. (Interscience, London, 1970) pp 145-147; S. W. Schneller, *Int. J. Sulfur Chem.* **8,** 591 (1976).

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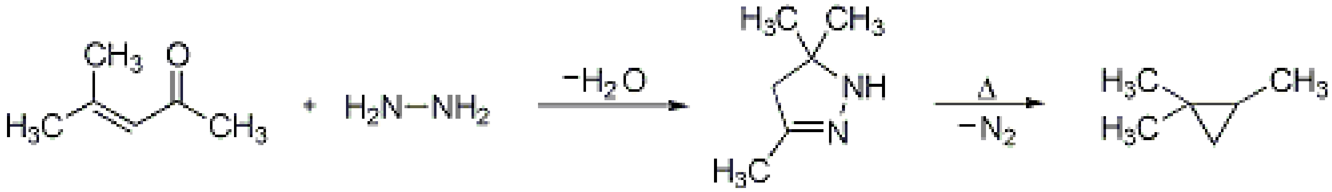
212. Kishner Cyclopropane Synthesis

N. M. Kishner, A. Zavadovskii, *J. Russ. Phys. Chem. Soc.* **43,** 1132 (1911).

Formation of cyclopropane derivatives by decomposition of pyrazolines formed by reacting α,β-unsaturated ketones or aldehydes with hydrazine:



L. I. Smith, E. R. Rogier, *J. Am. Chem. Soc.* **73,** 3840 (1951); G. S. Hammond, R. W. Todd, *ibid.* **76,** 4081 (1954); T. L. Jacobs, *Heterocyclic Compounds* **5,** 109 (1957). Mechanistic aspects of pyrazoline decomposition to cyclopropanes: R. G. Bergman in *Free Radicals* **vol. 1,** J. Kochi, Ed. (Wiley, New York, 1973) p 191; R. J. Crawford, M. Ohno, *Can. J. Chem.* **52,** 3134 (1974); R. J. Crawford, H. Tokunaga, *ibid.* 4033; J. A. Berson in *Rearrangements in Ground and Excited States* **vol. 1,** P. de Mayo, Ed. (Academic Press, New York, 1980) p 326.

214. Knoop-Oesterlin Amino Acid Synthesis

F. Knoop, H. Oesterlin, *Z. Physiol. Chem.* **148,** 294 (1925).

Preparation of α-amino acids by catalytic hydrogenation of α-oxo acids in aqueous ammonia in the presence of platinum, palladium or Raney nickel catalysts, probably *via* an unstable iminocarboxylate ion intermediate:

$$\mathrm{RCOCOO^-} + \mathrm{NH_3} \longrightarrow \mathrm{R\overset{NH}{\overset{\|}{C}}COO^-} \xrightarrow[\mathrm{Pd}]{\mathrm{H_2}} \mathrm{R\overset{NH_2}{\overset{|}{C}}HCOOH}$$

H. R. V. Arnstein, R. Bentley, *Quart. Rev.* **4,** 186 (1950); S. Nakamura, K. Ashida, *J. Agr. Chem. Soc. Japan* **24,** 185 (1950-1951); T. Wieland, *et al., Houben-Weyl* **11/2,** 311, 482 (1958); C. W. Huffman, W. G. Skelly, *Chem. Rev.* **63,** 632 (1963).

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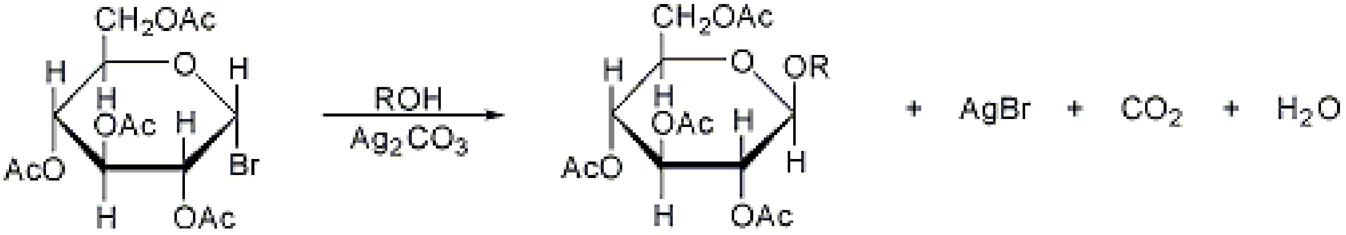
220. Koenigs-Knorr Synthesis

W. Koenigs, E. Knorr, *Ber.* **34,** 957 (1901).

Formation of glycosides from acetylated glycosyl halides and alcohols or phenols in the presence of silver salts. The reaction proceeds with inversion of configuration:



Reviews: Evans *et al., Advan. Carbohyd. Chem.* **6,** 41-52 (1951); K. Igarashi, *ibid.* **34,** 243 (1977); H. M. Flowers, *Methods Carbohyd. Chem.* **6,** 474-480 (1972); R. R. Schmidt, *Comp. Org. Syn.* **6,** 33-64 (1991). Stereoselectivity: J.-I. Tamaru *et al., J. Carbohyd. Chem.* **12,** 893 (1993). Applications: A. Milius *et al., New J. Chem.* **15,** 337 (1991); F. W. Lichtenthaler, T. W. Metz, *Tetrahedron Letters* **38,** 5477 (1997); S. Laszlo *et al., Chem. Commun.* **1999,** 591.

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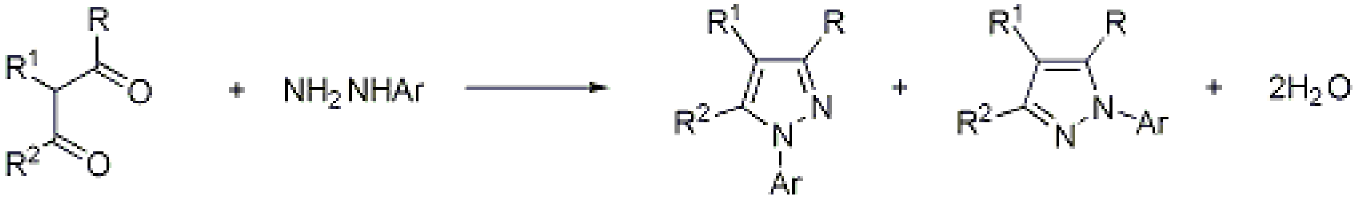
215. Knorr Pyrazole Synthesis

L. Knorr, *Ber*. **16,** 2587 (1883).

Formation of pyrazole derivatives from hydrazines, hydrazides, semicarbazides, and aminoguanidines by condensation with 1,3-dicarbonyl compounds; substituted hydrazines yield two structurally isomeric pyrazoles:



T. J. Jacobs, *Heterocyclic Compounds* **5,** 46 (1957); M. H. Palmer, *Structure and Reactions of Heterocyclic Compounds* (Arnold, London, 1967) pp 378-385. *Cf.* Pechmann Pyrazole Synthesis.

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296. Pechmann Pyrazole Synthesis

H. v. Pechmann, *Ber.* **31,** 2950 (1898).

Formation of pyrazoles from acetylenes and diazomethane. The analogous addition of diazoacetic esters to the triple bond yields pyrazolecarboxylic acid derivatives:

R. A. Raphael, *Acetylenic Compounds in Organic Synthesis* (London, 1955) p 179; T. L. Jacobs, *Heterocyclic Compounds* **5,** 70 (1957); B. Eistert *et al.*, *Houben-Weyl* **10/4,** 840 (1968). *Cf.* Knorr Pyrazole Synthesis.

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222. Kolbe-Schmitt Reaction

H. Kolbe, *Ann.* **113,** 125 (1860); R. Schmitt, *J. Prakt. Chem.* [2] **31,** 397 (1885).

Formation of aromatic hydroxy acids by carboxylation of phenolates, mostly in the *ortho* position, by carbon dioxide:

Reviews: A. S. Lindsey, H. Jeskey, *Chem. Rev.* **57,** 583 (1957); D. C. Ayres, *Carbanions in Synthesis* **1966,** 168-173; J. L. Hales *et al., J. Chem. Soc.* **1954,** 3145; J. March, *Advanced Organic Chemistry* (Wiley-Interscience, New York, 4th ed., 1992) p 546.

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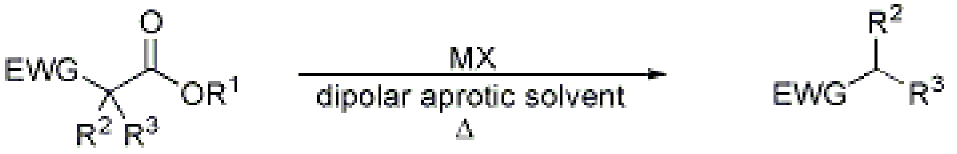
225. Krapcho Decarbalkoxylation

A. P. Krapcho *et al., Tetrahedron Letters* **1967,** 215.

The decarbalkoxylation of malonate esters, β-keto esters, α-cyano esters and α-sulfonyl esters in dipolar aprotic solvents, at high temperatures, in the presence of water and/or salt, to yield esters, ketones, nitriles and sulfonyl derivatives, respectively:



R^1 = CH_3, CH_2CH_3
EWG = COOR, COR, CN, SO_2R
solvent (possibly wet) = DMSO, DMF, HMPT
MX = LiCl, NaCl, LiI, NaCN, KCN, *n*-Bu_4NOAc

Scope and limitations: A. P. Krapcho *et al., J. Org. Chem.* **43,** 138 (1978). Mechanistic studies: A. M. Bernard *et al., Tetrahedron* **46,** 3929 (1990); P. J. Gilligan, P. J. Krenitsky, *Tetrahedron Letters* **35,** 3441 (1994). Review of synthetic applications: A. P. Krapcho, *Synthesis* **1982,** 805-822, 893-914.

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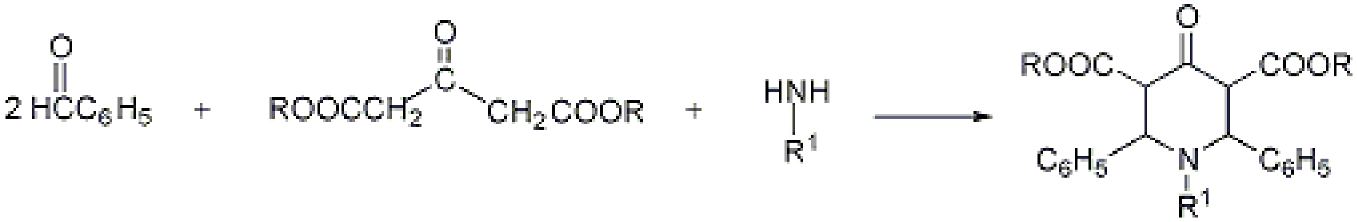
304. Petrenko-Kritschenko Piperidone Synthesis

P. Petrenko-Kritschenko *et al., Ber.* **39,** 1358 (1906); **40,** 2882 (1907); **41,** 1692 (1908); **42,** 2020, 3683 (1909).

Formation of piperidones *via* cyclization of two moles of aldehyde and one mole each of acetonedicarboxylic ester and ammonia or a primary amine:



R. Robinson, *J. Chem. Soc.* **111,** 762, 876, (1917); C. Mannich, O. Hieronimus, *Ber.* **75,** 49 (1942); H. S. Mosher, *Heterocyclic Compounds* **1,** 659 (New York, 1950). *Cf.* Robinson-Schöpf Reaction.

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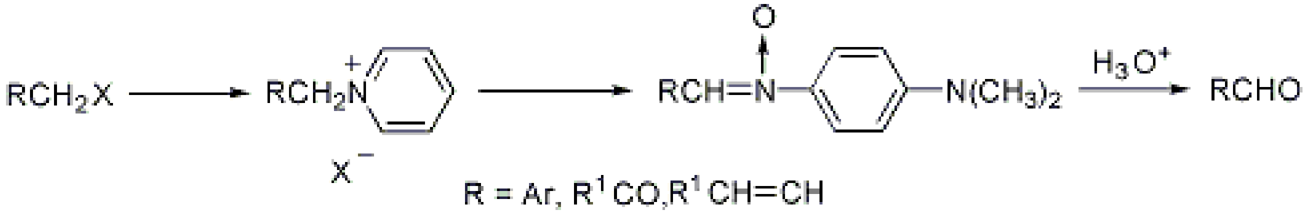
226. Kröhnke Oxidation

F. Kröhnke *et al.*, *Ber.* **69,** 2006 (1936); **71,** 2583 (1938); **72,** 440 (1939).

Transformation of activated halides into aldehydes *via* their pyridinium salts, which yield nitrones upon treatment with *p*-nitrosodimethylaniline. Aldehydes or ketones are generated upon hydrolysis:



A. A. Goldberg, H. A. Walker, *J. Chem. Soc.* **1954,** 2540; F. Kröhnke, *Angew. Chem. Int. Ed.* **2,** 380 (1963); A. Markovac *et al., Heterocyclic Chem.* **14,** 19 (1977); I. Maeba *et al., J. Chem. Soc. Perkin Trans. I* **1991,** 939; S. N. Kilenyi, *Comp. Org. Syn.* **7,** 657-659 (1991). *Cf.* Sommelet Reaction.

373. Sommelet Reaction

M. Sommelet, *Compt. Rend.* **157,** 852 (1913); *Bull. Soc. Chim. France* [4] **23,** 95 (1918).

Preparation of aldehydes from aralkyl halides by treatment with hexamethylenetetramine to yield the quaternary salt, followed by mild hydrolysis:

$$ArCH_2X + C_6H_{12}N_4 \longrightarrow [ArCH_2-C_6H_{12}N_4]^+ X^- \xrightarrow[H_2O]{\Delta} ArCHO$$

Early reviews: S. J. Angyal, *Org. React.* **8,** 197-217 (1954); Bayer, *Houben-Weyl* **7/1,** 194 (1954). Synthetic applications: S. Miyano *et al.*, *Bull. Chem. Soc. Japan* **59,** 3285 (1986); D. Evans *et al.*, *Heterocycles* **26,** 1569 (1987). *Cf.* Kröhnke Oxidation.

228. Kucherov Reaction

M. Kucherov, *Ber.* **14,** 1540 (1881).

Hydration of acetylenic hydrocarbons with dilute sulfuric acid in the presence of mercuric sulfate or boron trifluoride as catalyst:

Reviews: A. D. Petrov. *Usp. Khim.* **21,** 250 (1952); M. Miocque *et al.*, *Ann. Chim. (Paris)* **8,** 157 (1963); M. M. Khan, A. E. Martell, *Homogeneous Catalysis by Metal Complexes* **vol. 2** (Academic Press, New York, 1974) p 1974; B. S. Krupin, A. A. Petrov, *J. Gen. Chem. USSR* **33,** 3799 (1963); W. L. Budde, R. E. Dessy, *Tetrahedron Letters* **1963,** 651; *J. Am. Chem. Soc.* **85,** 3964 (1963); K. G. Golodova, S. I. Yakimovich, *Zh. Org. Khim.* **8,** 2015 (1972). Extension to allenes: A. V. Fedorova, A. A. Petrov, *J. Gen. Chem. USSR* **32,** 1740 (1962).

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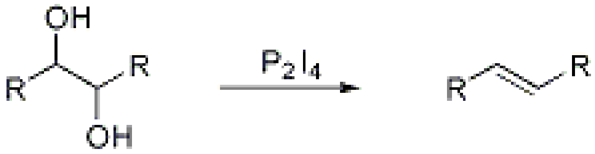
229. Kuhn-Winterstein Reaction

R. Kuhn, A. Winterstein, *Helv. Chim. Acta* **11,** 87 (1928).

Conversion of 1,2-glycols into *trans* olefins by reaction with diphosphotetraiodide (P_2I_4) or other halogenated reagents. This reaction is useful in the preparation of polyenes:

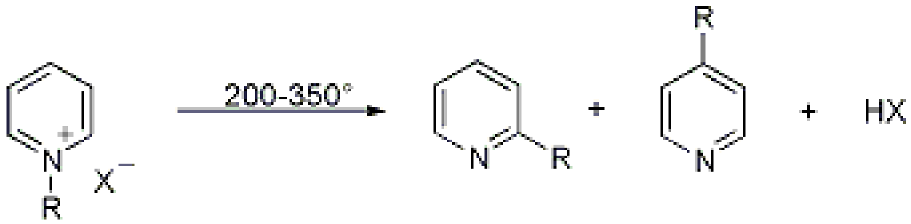


Kuhn *et al., Ber.* **71,** 1510 (1938); **84,** 566 (1961); **88,** 309 (1965); Inhoffen *et al., Ann.* **684,** 24 (1965); H. Kessler, W. Ott, *Tetrahedron Letters* **1974,** 1383; W. W. Win *et al., J. Org. Chem.* **59,** 2803 (1994).

230. Ladenburg Rearrangement

A. Ladenburg, *Ber.* **16,** 410 (1883); *Ann.* **247,** 1 (1888).

Thermal rearrangement of an alkyl- or benzylpyridinium halide to an alkyl- or benzylpyridine:



J. H. Brewster, E. L. Eliel, *Org. React.* **7,** 135 (1953); L. E. Tenenbau in *Pyridine and Its Derivatives,* Pt. 2, E. Klingsberg, Ed. (Interscience, New York, 1961) p 163.

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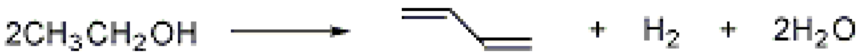
231. Lebedev Process

S. V. Lebedev, *Zh. Obshch. Khim.* **3,** 698 (1933).

Formation of butadiene from ethanol by catalytic pyrolysis. The catalysts used are mixtures of sililcates and aluminum and zinc oxides:

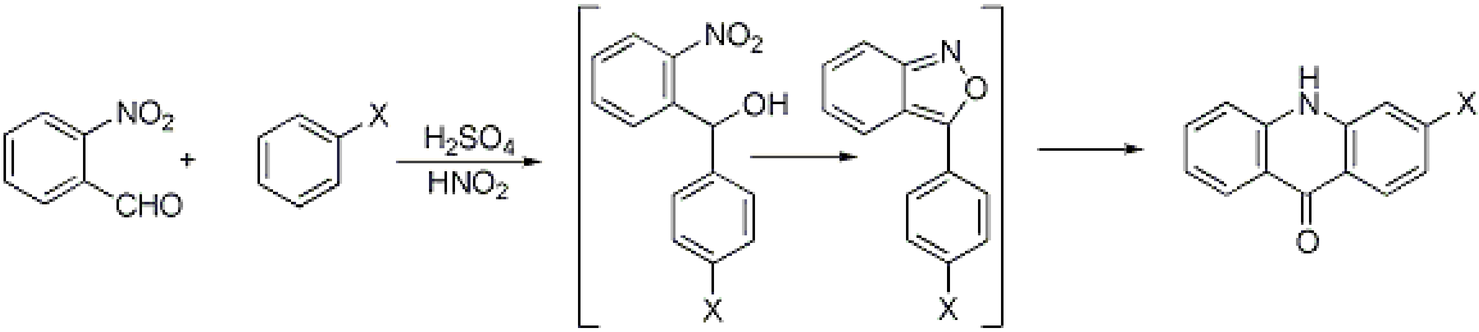


S. V. Lebedev, **FR 665917** (1928); **GB 331482** (1929); **RU 24393** (1931); C. Ellis, *The Chemistry of Petroleum Derivatives* **II** (New York, 1937) p 173; G. Egloff, G. Hulla, *Chem. Rev.* **36,** 67 (1945); Y. A. Gorin, *Zh. Obshch. Khim.* **20,** 1596 (1950); *Kirk-Othmer Encyclopedia of Chemical Technology* **vol. 4** (New York, 3rd ed., 1978) p 322.

232. Lehmstedt-Tanasescu Reaction

K. Lehmstedt, *Ber.* **65,** 834 (1932); I. Tanasescu, *Bull. Soc. Chim. France* **41,** 528 (1927).

Preparation of acridones (and 10-hydroxyacridones) from *o*-nitrobenzaldehyde and a halobenzene in the presence of concentrated sulfuric acid containing nitrous acid as catalyst:



I. Tanasescu, Z. Frenkel, *ibid.* **1960,** 693. Mechanism: Silberg, Frenkel, *Rev. Roumaine Chim.* **10,** 1035 (1965).

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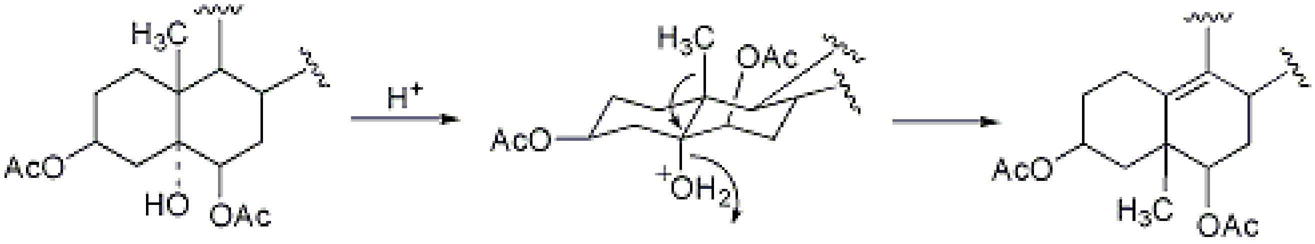
423. Westphalen-LettréRearrangement

T. Westphalen, *Ber.* **48,** 1064 (1915); H. Lettré, M. Müller, *ibid.* **70,** 1947 (1937).

Dehydration of 5-hydroxycholesterol derivatives accompanied by C-10 to C-5 methyl migration in compounds with a β-substituent at C-6:



Early review: N. L. Wendler in *Molecular Rearrangements* Part 2, P. de Mayo, Ed. (Wiley-Interscience, New York, 1964) p 1027. A. T. Rowland, *J. Org. Chem.* **29,** 222 (1964); J. W. Blunt *et al., Tetrahedron* **21,** 1567 (1965); K. Kieslich, G. Schulz, *Ann.* **726,** 152 (1969); B. Marples, J. G. L. Jones, *J. Chem. Soc. C* **1970,** 2273; J. Wicha, *Tetrahedron Letters* **1972,** 2877; P. Kocovsky, *et al., Coll. Czech. Chem. Commun.* **44,** 234 (1979).

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233. Letts Nitrile Synthesis

E. A. Letts, *Ber*. **5,** 669 (1872).

Formation of nitriles by heating aromatic carboxylic acids with metal thiocyanates:

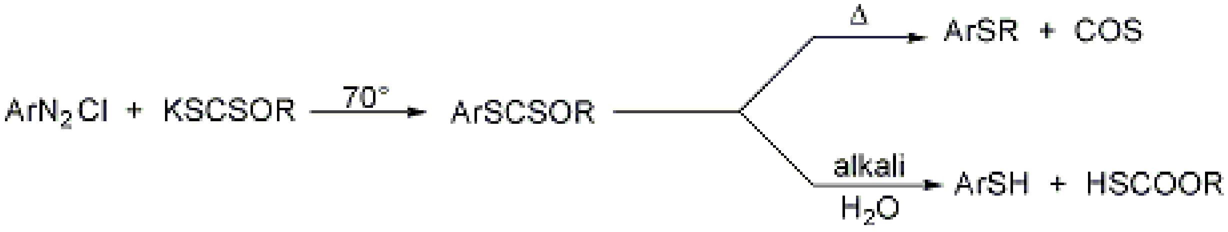
$$\mathrm{RCOOH} + \mathrm{KSCN} \xrightarrow{\Delta} \mathrm{RCN} + \mathrm{CO_2} + \mathrm{KHS}$$

G. Krüss, *Ber*. **17,** 1766 (1884); E. E. Reid, *Am. Chem. J*. **43,** 162 (1910); G. D. van Epps, E. E. Reid, *J. Am. Chem. Soc*. **38,** 2120 (1916); D. T. Mowry, *Chem. Rev*. **42,** 264 (1948); F. Klages, *Lehrbuch der organischen Chemie* **I** (Berlin, 1959) p 362.

235. Leuckart Thiophenol Reaction

R. Leuckart, *J. Prakt. Chem.* [2] **41,** 179 (1890).

Decomposition of diazoxanthates, by warming gently in faintly acidic cuprous media, to the corresponding aryl xanthates which afford aryl thiols on alkaline hydrolysis and aryl thioethers on warming:



D. S. Tarbell, D. K. Fukushima, *Org. Syn.* **coll. vol. III,** 809 (1955); K. H. Saunders, *The Aromatic Diazo-Compounds and Their Technical Applications* (London, 1949) p 325; D. S. Tarbell, M. A. McCall, *J. Am. Chem. Soc.* **74,** 48 (1952); A. R. Forrester, J. L. Wardell, *Rodd's Chemistry of Carbon Compounds* **IIIA,** 422 (1971); A. Schöberl, A. Wagner, *Houben-Weyl* **9,** 12 (1955).

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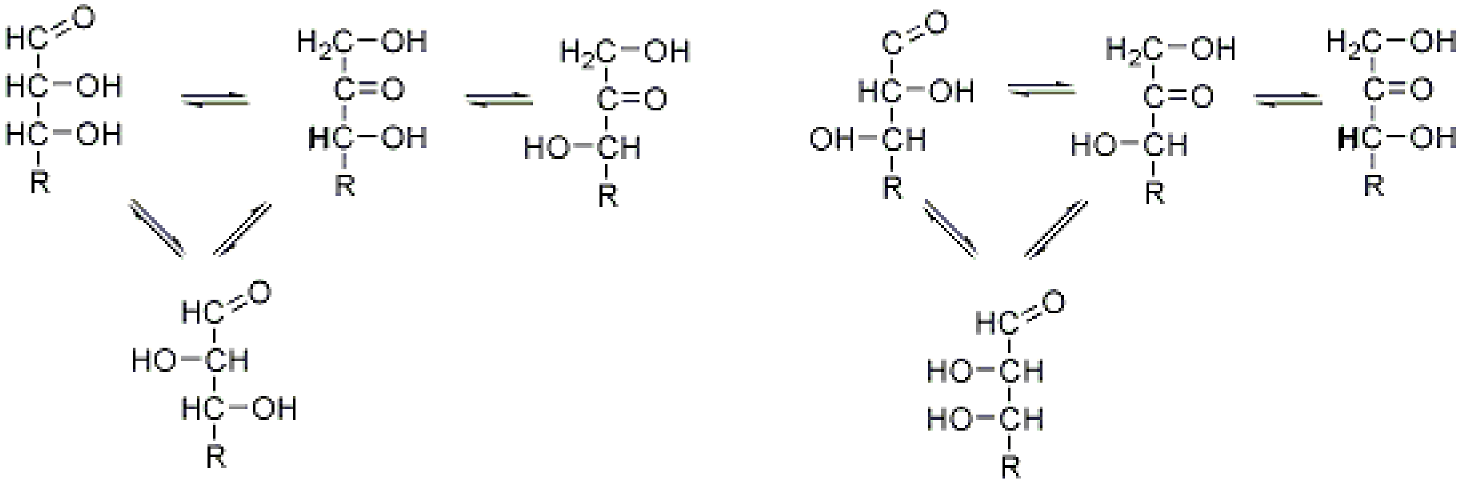
237. Lobry de Bruyn-van Ekenstein Transformation

C. A. Lobry de Bruyn, *Rec. Trav. Chim.* **14,** 150 (1895); C. A. Lobry de Bruyn, W. A. van Ekenstein, *ibid.* 195, 203; **16,** 262 (1897).

Isomerization of carbohydrates in alkaline media, considered to embrace both epimerization of aldoses and ketoses and aldose-ketose interconversion:



Reviews: Evans, *Chem. Rev.* **31,** 544 (1942); Sattler, *Advan. Carbohyd. Chem.* **3,** 113 (1948); Pigman, *The Carbohydrates* (Academic Press, New York, 1957) p 60; Speck, *Advan. Carbohyd. Chem.* **13,** 63 (1958); Schaffer, *J. Org. Chem.* **29,** 1473 (1964); M. H. Johansson, O. Samuelson, *Chem. Scr.* **9,** 151 (1976). Synthetic applications: P Köll, G. Papert, *Ann.* **1986,** 1568; B. Sauerbrei *et al., Carbohydr. Res.* **280,** 223 (1996); P. Sedmera *et al., J. Carbohydr. Chem.* **17,** 1351 (1998). Mechanistic study: B. M. Kabyemela *et al., Ind. Eng. Chem. Res.* **38,** 2888 (1999).

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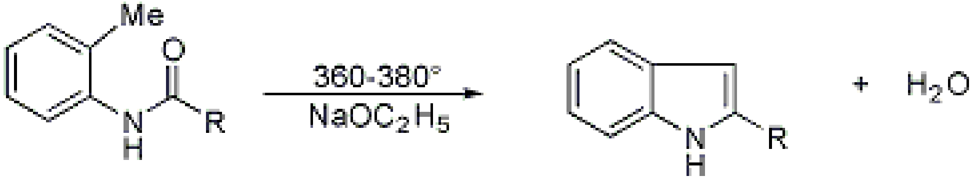
242. Madelung Synthesis

W. Madelung, *Ber.* **45,** 1128 (1912).

Formation of indole derivatives by intramolecular cyclization of an *N*-(2-alkylphenyl) alkanamide by a strong base at high temperature:



R. K. Brown in *The Chemistry of Heterocyclic Compounds,* A. Weissberger, Ed., *Indoles, Part I,* W. J. Houlihan, Ed. (Wiley, New York, 1972) pp 385-396; W. J. Houlihan *et al., J. Org. Chem.* **46,** 4511, 4515 (1981). Under mild conditions: W. Verboom *et al., Tetrahedron Letters* **26,** 685 (1985); *eidem, Tetrahedron* **42,** 5053 (1986); E. O. M. Orlemans *et al., ibid.* **43,** 3817 (1987).

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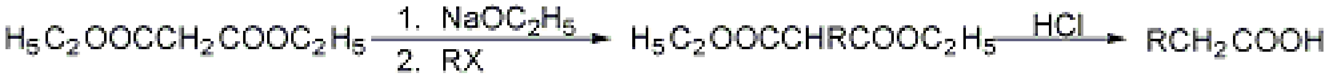
245. Malonic Ester Syntheses

Syntheses based on the strongly activated methylene group of malonic esters which on reaction with sodium ethoxide form a resonance-stabilized ion that can be alkylated or acylated. After hydrolysis, the free alkylmalonic acids readily decarboxylate to mono- or disubstituted monocarboxylic acids:



$$H_5C_2OOCCH_2COOC_2H_5 \xrightarrow[2.\ RX]{1.\ NaOC_2H_5} H_5C_2OOCCHRCOOC_2H_5 \xrightarrow{HCl} RCH_2COOH$$

H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 510-518, 756-761. Use of crown ethers as catalysts: D. H. Hunter, *et al., Synthesis* **1977,** 37. Modified conditions: M. A. Casadei *et al., J. Org. Chem.* **46,** 3127 (1981); B. K. Wilk, *Synth. Commun.* **26,** 3859 (1996). Stereoselectivity: T. Sato, J. Otera, *J. Org. Chem.* **60,** 2627 (1995); B. Klotz-Berendes *et al., Tetrahedron Asymmetry* **8,** 1821 (1997). *Cf.* Perkin Alicyclic Synthesis.

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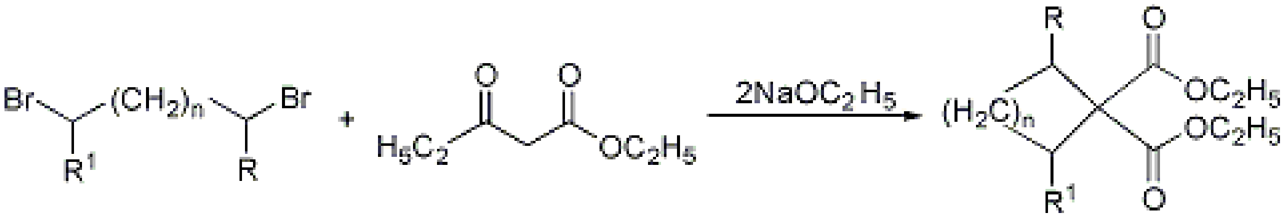
299. Perkin Alicyclic Synthesis

W. H. Perkin, Jr., *Ber.* **16,** 1793 (1883).

Synthesis of alicyclic compounds from α,ω-dihaloalkanes and compounds containing active methylene groups in the presence of sodium ethoxide:



H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Inc., Menlo Park, California, 2nd ed, 1972) pp 492-570. *Cf.* Malonic Ester Syntheses.

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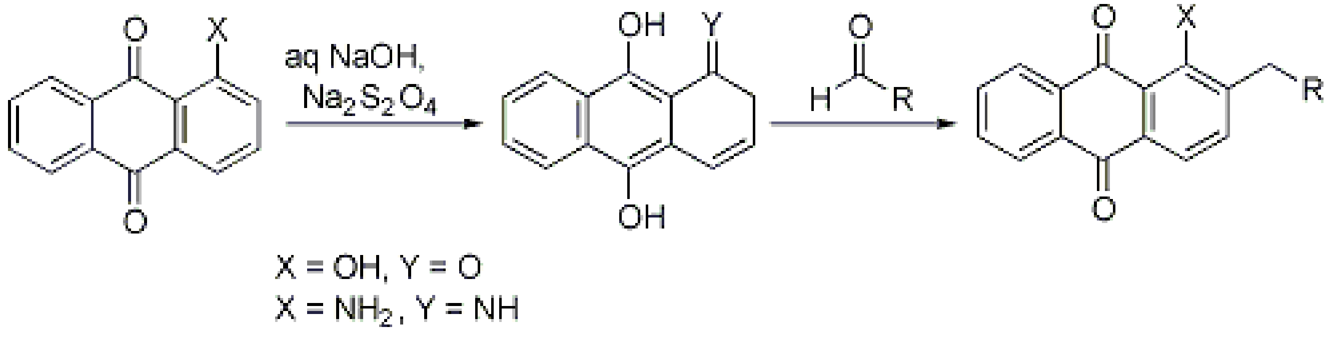
247. Marschalk Reaction

C. Marschalk *et al., Bull. Soc. Chim. France* **3,** 1545 (1936).

Sodium dithionite reduction of 1-hydroxy- or aminoanthraquinones to their leuco-forms, followed by condensation with aldehydes to yield the 2-alkylated anthraquinones. 2-Hydroxyanthraquinones yield 1-alkylated products:



Scope and limitations: K. Krohn, W. Baltus, *Tetrahedron* **44,** 49 (1988). Synthetic applications: F. Suzuki, *et al., J. Am. Chem. Soc.* **100,** 2272 (1978); L. M. Harwood *et al., Can. J. Chem.* **62,** 1922 (1984); M. T. Furlong *et al., Synth. Commun.* **20,** 2691 (1990); N. R. Ayyangar *et al., Indian J. Chem.* **31B,** 3 (1992); K. Krohn, S. Bernhard, *J. Prakt. Chem.* **340,** 26 (1998).

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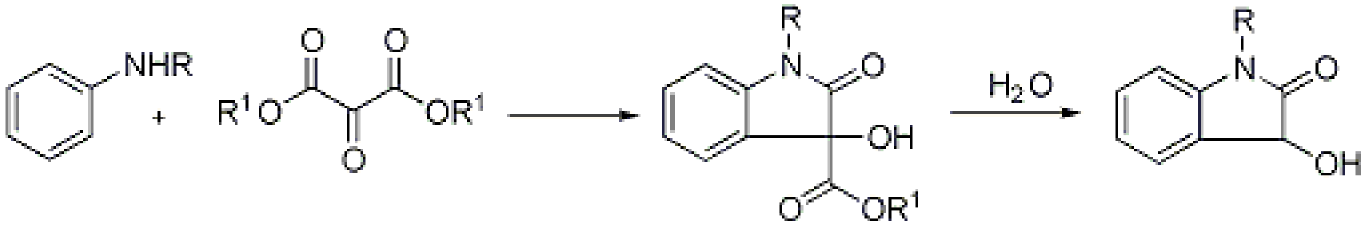
248. Martinet Dioxindole Synthesis

A. Guyot, J. Martinet, *Compt. Rend.* **156,** 1625 (1913).

Formation of derivatives of dioxindole from esters of mesoxalic acid and aromatic amines or amino quinolines:



J. Martinet, *ibid.* **166,** 851, 998 (1918); *Ann. Chim.* [9] **11,** 85 (1919); W. Langenbeck *et al., Ann.* **499,** 201 (1932); **512,** 276 (1934); W. C. Sumpter, *Chem. Rev.* **37,** 472 (1945); P. L. Julian *et al., Heterocyclic Compounds* **3,** 239 (1952).

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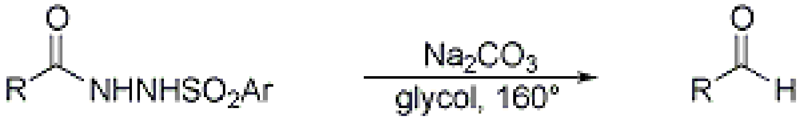
239. McFadyen-Stevens Reaction

J. S. McFadyen, T. S. Stevens, *J. Chem. Soc.* **1936,** 584.

Base-catalyzed thermal decomposition of acylbenzenesulfonylhydrazines to aldehydes:



E. Mosettig, *Org. React.* **8,** 232-240 (1954); S. Siddappa, G. A. Bhat, *J. Chem. Soc. C* **1971,** 178; S. B. Matin *et al., J. Org. Chem.* **39,** 2285 (1974); M. Nair, H. Shechter, *Chem. Commun.* **1978,** 793. Alternative hydrazide reagent: C. C. Dudman *et al., Tetrahedron Letters* **1980,** 4645. Synthetic applications: H. Graboyes *et al., J. Heterocyclic Chem.* **12,** 1225 (1975); R. K. Manna *et al., Synth. Commun.* **28,** 9 (1998).

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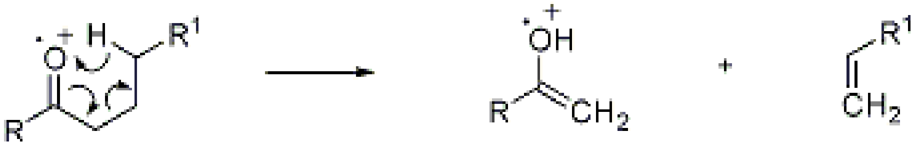
240. McLafferty Rearrangement

F. W. McLafferty, *Anal. Chem.* **31,** 82 (1959).

Electron-impact-induced cleavage of carbonyl compounds having a hydrogen in the γ-position, to an enolic fragment and an olefin:



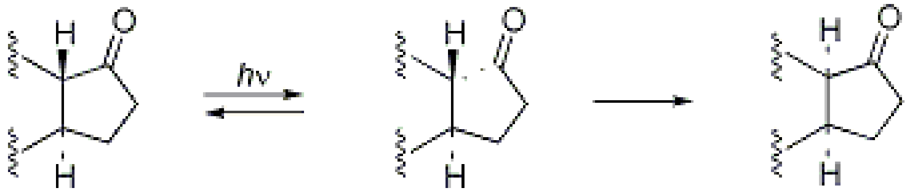
D. G. I. Kingston *et al.*, *Chem. Rev.* **74,** 215 (1974); K. Biemann, *Mass Spectrometry* (New York, 1962) p 119; Djerassi *et al.*, *J. Am. Chem. Soc.* **87,** 817 (1965); **91,** 2069 (1969); **94,** 473 (1972); M. J. Lacey *et al.*, *Org. Mass Spectrom.* **5,** 1391 (1971); G. Eadon, *J. Am. Chem. Soc.* **94,** 8938 (1972); F. Turecek, V. Hanus, *Org. Mass Spectrom.* **15,** 8 (1980). *Cf.* Norrish Type Cleavage.

282. Norrish Type Cleavage

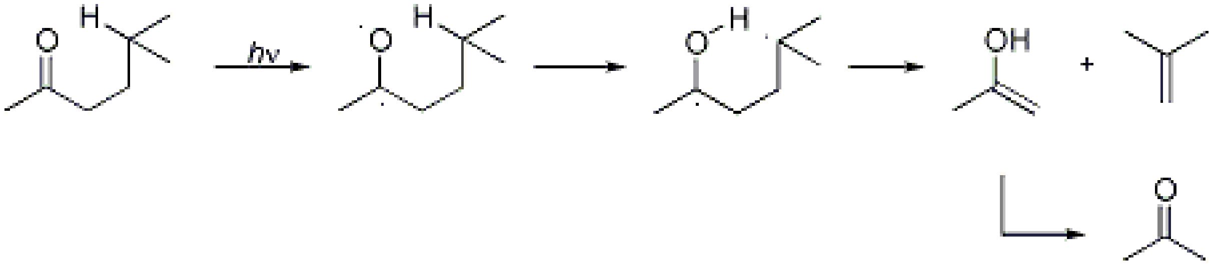
R. G. W. Norrish, C. H. Bamford, *Nature* **138,** 1016 (1936); **140,** 195 (1937).

Norrish Type I Cleavage: Homolytic cleavage of aldehydes and ketones originating from their excited nπ* state. Synthetically useful for the ring cleavage of cyclic ketones:

$$R^1-\underset{\overset{\|}{O}}{C}-R \xrightarrow{h\nu} R^1-\underset{\overset{\|}{O}}{C}^{\cdot} + R^{\cdot}$$



Norrish Type II Cleavage: Reaction originating from the nπ* excited state of aldehydes and ketones that involves intramolecular γ-hydrogen abstraction followed by cleavage of the resulting diradical to an olefin and an enol which tautomerizes to the carbonyl compound:



Norrish Type I: D. H. R. Barton *et al., J. Am. Chem. Soc.* **107,** 3607 (1985); J. R. Hwu *et al., Chem. Commun.* **1990,** 161. Norrish Type II: J. M. Nuss, M. M. Murphy, *Tetrahedron Letters* **35,** 37 (1994); F. Hénin *et al., Tetrahedron* **50,** 2849 (1994). *Reviews:* J. D. Coyle, H. A. J. Carless, *Chem. Soc. Rev.* **1,** 465 (1972); O. L. Chapman, D. S. Weiss, *Org. Photochem.* **3,** 197-277 (1973); J. March, *Advanced Organic Chemistry* (Wiley-Interscience, New York, 4th ed., 1992) p 242; W. M. Horspool, *Photochemistry* **25,** 67-100 (1994). *Cf.* McLafferty Rearrangement.

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252. Menschutkin Reaction

N. Menschutkin, *Z. Physik. Chem.* **5,** 589 (1890); **6,** 41 (1890).

Reaction of tertiary amines with alkyl halides to form quaternary salts:

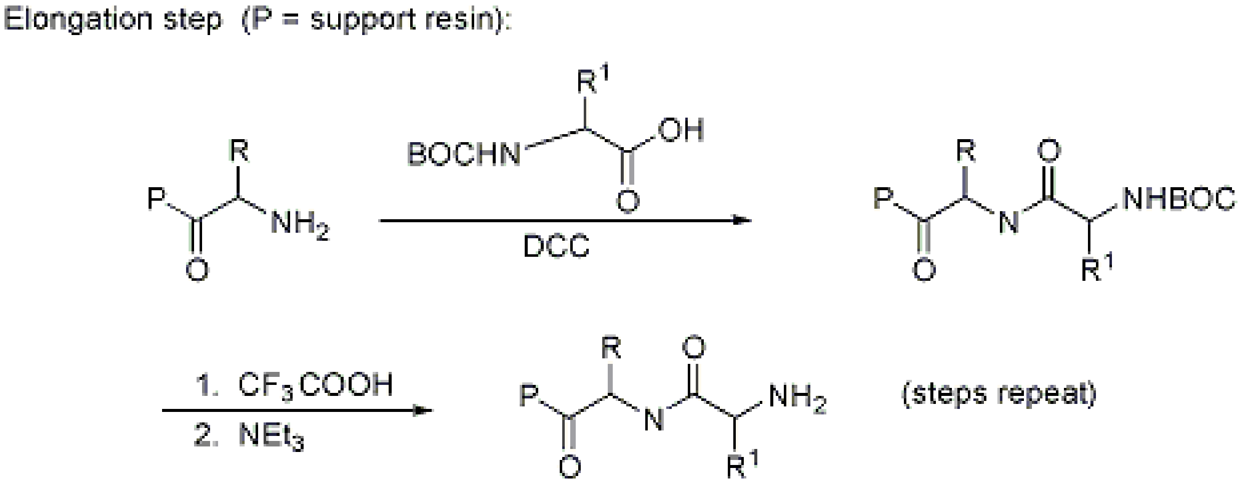
$$R_3{}^1N + RX \longrightarrow R_3{}^1RN^+ X^-$$

Mechanistic studies: C. K. Ingold, *Structure and Mechanism in Organic Chemistry* (Cornell Univ. Press, New York, 2nd ed., 1969) p 435; M. H. Abraham, *Progr. Phys. Org. Chem.* **11,** 1 (1974); E. M. Arnett, R. Reich, *J. Am. Chem. Soc.* **102,** 5892 (1980); S. Shaik *et al., ibid.* **116,** 262 (1994); S. H. Kim *et al., J. Phys. Org. Chem.* **11,** 254 (1998). Solvent effects: J.-L. M. Abboud *et al., J. Phys. Chem.* **93,** 214 (1989); S.-G. Kang *et al., Bull. Chem. Soc. Japan.* **66,** 972 (1993).

253. Merrifield Solid-Phase Peptide Synthesis (SPPS)

R. B. Merrifield, *J. Am. Chem. Soc.* **85,** 2149 (1963).

Synthesis of long peptides involving the following steps: (1) attachment of the C-terminal amino acid to an insoluble polymeric support resin, (2) elongation of the peptide chain, and (3) cleavage of the peptide from the resin:



Method for monitoring synthesis: B. D. Larsen *et al., J. Am. Chem. Soc.* **115,** 6247 (1993). Synthetic applications: D. D. Smith *et al., J. Peptide Protein Res.* **44,** 183 (1994); M. J. O'Donnell *et al., J. Am. Chem. Soc.* **118,** 6070 (1996); R. Léger *et al., Tetrahedron Letters* **39,** 4171 (1998). *Review:* C. Birr, *Aspects of Merrifield Peptide Synthesis,* K. Hafner *et al.,* Eds. (Springer-Verlag, New York, 1978) pp 102; B. Merrifield, *Science* **232,** 341-347 (1986); G. B. Wisdom *et al., Peptide Antigens* (Oxford University Press, 1994) pp 27-81. Autobiographical account: B. Merrifield, *Life During a Golden Age of Peptide Chemistry,* J. I. Seeman, Ed. (ACS, Washington, D.C., 1993) pp 54-118.

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254. Meyer Reaction

G. Meyer, *Ber.* **16,** 1439 (1883).

Preparation of alkylstannonic acids by reacting alkali stannite with an alkyl iodide. When applied to alkali arsenites or plumbites the reaction yields alkylarsonic and alkylplumbonic acids, respectively:

$$Na_2SnO_2 + RX \longrightarrow RSnO_2Na + NaX$$

$$Na_3AsO_3 + RX \longrightarrow RAsO_3Na_2 + NaX$$

W. R. Cullen, *Advan. Organometal. Chem.* **4,** 148 (1966).

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256. **Meyer Synthesis** (Victor Meyer Synthesis)

V. Meyer, O. Stuber, *Ber.* **5,** 203 (1872).

Formation of aliphatic nitrites and nitro derivatives by the reaction of aliphatic halides with metal nitrites:

$$RX + MNO_2 \longrightarrow RONO + RNO_2 + MX$$

R. B. Reynolds, H. Adkins, *J. Am. Chem. Soc.* **51,** 279 (1929). *Reviews:* H. B. Hass, E. F. Riley, *Chem. Rev.* **32,** 373 (1943); N. Kornblum, *Org. React.* **12,** 101-156 (1962). Application to the synthesis of α,ω-dinitroalkanes: J. K. Stille, E. D. Vessel, *J. Org. Chem.* **25,** 478 (1960); G. Leston, *Org. Syn.* **4,** 368 (1963).

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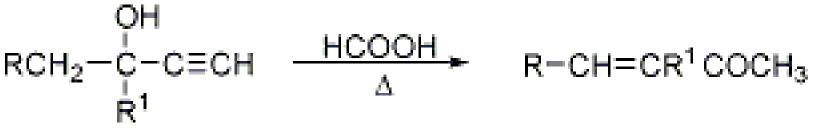
255. **Meyer-Schuster Rearrangement;** Rupe Rearrangement

K. H. Meyer, K. Schuster, *Ber.* **55,** 819 (1922); H. Rupe, E. Kambli, *Helv. Chim. Acta* **9,** 672 (1926).

Acid-catalyzed rearrangement of secondary and tertiary α-acetylenic alcohols to α,β-unsaturated carbonyl compounds: aldehydes result when the acetylenic group is terminal, ketones when it is internal:

$$R_2\overset{OH}{\overset{|}{C}}C\equiv CR^1 \xrightarrow{H^+} R_2C{=}CHCOR^1$$

The conversion of tertiary alkylacetylenic carbinols with a terminal acetylenic group to predominantly α,β-unsaturated ketones and not the expected aldehydes, is referred to as the **Rupe rearrangement:**



$$RCH_2-\underset{R^1}{\overset{OH}{C}}-C\equiv CH \xrightarrow[\Delta]{HCOOH} R-CH{=}CR^1COCH_3$$

Metal-based catalysis: P. Chabardes, *Tetrahedron Letters* **29,** 6253 (1988); C. Y. Lorber, J. A. Osborn, *ibid.* **37,** 853 (1996). Mechanism studies: M. Edens *et al., J. Org. Chem.* **42,** 3403 (1977); J. Andres *et al., J. Am. Chem. Soc.* **110,** 666 (1988). Applications: E. A. Omar *et al., J. Heterocyclic Chem.* **29,** 947 (1992); M. Yoshimatsu *et al., J. Org. Chem.* **60,** 4798 (1995). Early reviews: R. Heilmann, R. Glenat, *Ann. Chim. (Paris)* **8,** 178 (1963); S. Swaminathan, K. V. Narayanan, *Chem. Rev.* **71,** 429 (1971).

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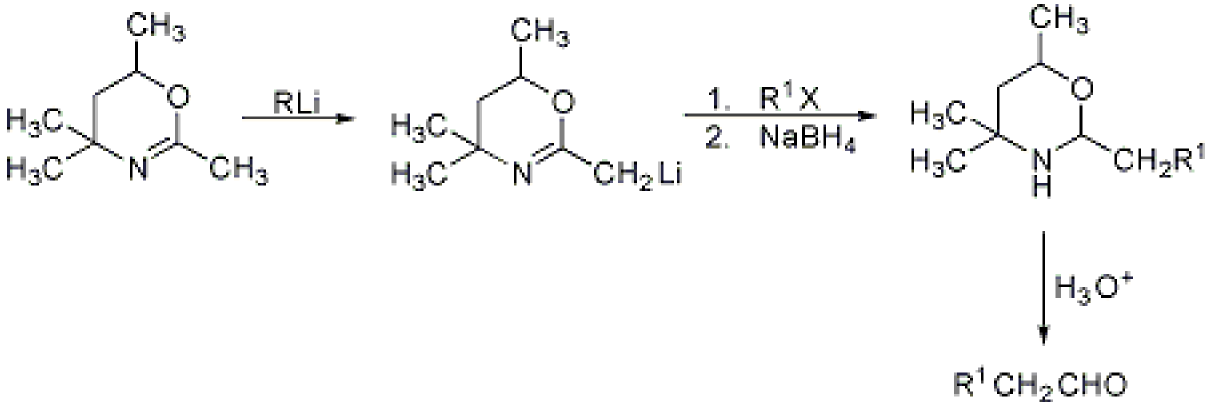
257. Meyers Aldehyde Synthesis

A. I. Meyers *et al., J. Am. Chem. Soc.* **91,** 763 (1969); *eidem, J. Org. Chem.* **38,** 36 (1973).

Synthesis of aldehydes from alkylhalides and 2-lithiomethyltetrahydro-3-oxazine:



J. March, *Advanced Organic Chemistry* (Wiley-Interscience, New York, 4th ed., 1992) pp 478-479; A. I. Meyers *et al., J. Org. Chem.* **46,** 783 (1981).

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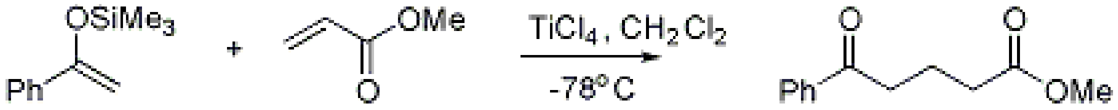
267. Mukaiyama-Michael Reaction

K. Narasaka *et al., Bull. Chem. Soc. Japan* **49,** 779 (1976).

Formation of 1,5-dicarbonyl compounds by reaction of ketene silyl acetals with α,β-unsaturated ketones and esters:



T. Mukaiyama, S. Kobayashi, *Heterocycles* **25,** 245 (1987). Enhanced diasteroselectivity: J. Otera *et al., Tetrahedron* **52,** 9409 (1996); in tandem-aldol reaction: N. Giuseppone *et al., Tetrahedron Letters* **39,** 7874 (1998). Synthetic application: H. Paulsen *et al., Angew. Chem. Int. Ed.* **38,** 3373 (1999).

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261. Mignonac Reaction

G. Mignonac, *Compt. Rend.* **172,** 223 (1921).

Formation of amines by catalytic hydrogenation of aldehydes or ketones in liquid ammonia and absolute ethanol in the presence of a nickel catalyst:

$$RCOR^1 + NH_3 + H_2 \xrightarrow{Ni} RR^1CHNH_2 + H_2O$$

F. Randvere, *Anales farm. bioquim. (Buenos Aires)* **18,** 81 (1948); *Houben-Weyl* **4/2,** 51 (1955).

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262. Milas Hydroxylation of Olefins

N. A. Milas *et al., J. Am. Chem. Soc.* **58,** 1302 (1936); **59,** 543, 2342, 2345 (1937); **61,** 1844 (1939); **62,** 1841 (1940).

Formation of *cis*-glycols by reaction of alkenes with hydrogen peroxide and either ultraviolet light or a catalytic amount of osmium, vanadium, or chromium oxide:

F. D. Gunstone, *Advan. Org. Chem.* **1,** 115 (1960); P. N. Rylander, *Organic Syntheses with Noble Metal Catalysts* (Academic Press, New York, 1973) p 60. *Cf.* Sharpless Dihydroxylation.

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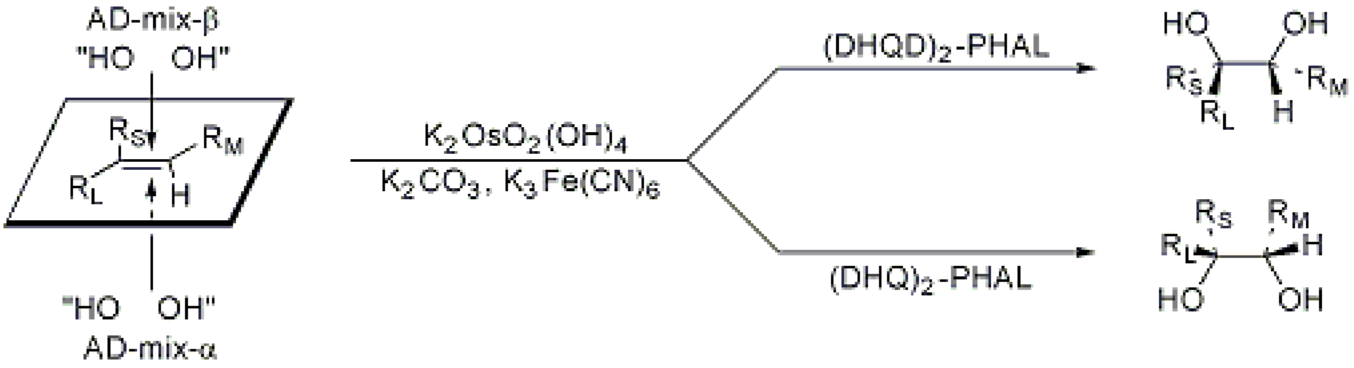
364. Sharpless Dihydroxylation

E. N. Jacobsen *et al.*, *J. Am. Chem. Soc.* **110,** 1968 (1988).

Osmium-catalyzed asymmetric *cis*-dihydroxylation of olefins:



A premix of the four reagent components is commercially available. The composition containing $(DHQD)_2$-PHAL is termed AD-mix-β; the composition containing $(DHQ)_2$-PHAL is termed AD-mix-α.
$(DHQD)_2$-PHAL = 1,4-bis(9-O-dihydroquinidine)phthalazine; $(DHQ)_2$-PHAL =1,4-bis(9-O-dihydroquinine)phthalazine.
R_L = largest substituent; R_M = medium-sized substituent; R_S = smallest substituent.

Note: The scheme shown is an empirical mnemonic indicating olefin orientation and face selectivity. It is not to be considered an absolute predictor of new diol configurations.

Allyl and vinyl silanes as substrates: A. R. Bassindale *et al.*, *J. Chem. Soc. Perkin Trans. I* **1994,** 1061. Chemoselective dihydroxylation of a polyene: S. C. Sinha, E. Keinan, *J. Org. Chem.* **59,** 949 (1994). *Reviews:* R. A. Johnson, K. B. Sharpless, “Catalytic Asymmetric Dihydroxylation” in *Catalytic Asymmetric Synthesis*, I. Ojima, Ed. (VCH, New York, 1993) pp 227-272; H. C. Kolb *et al.*, *Chem. Rev.* **94,** 2483-2547 (1994). *Cf.* Milas Hydroxylation of Olefins.

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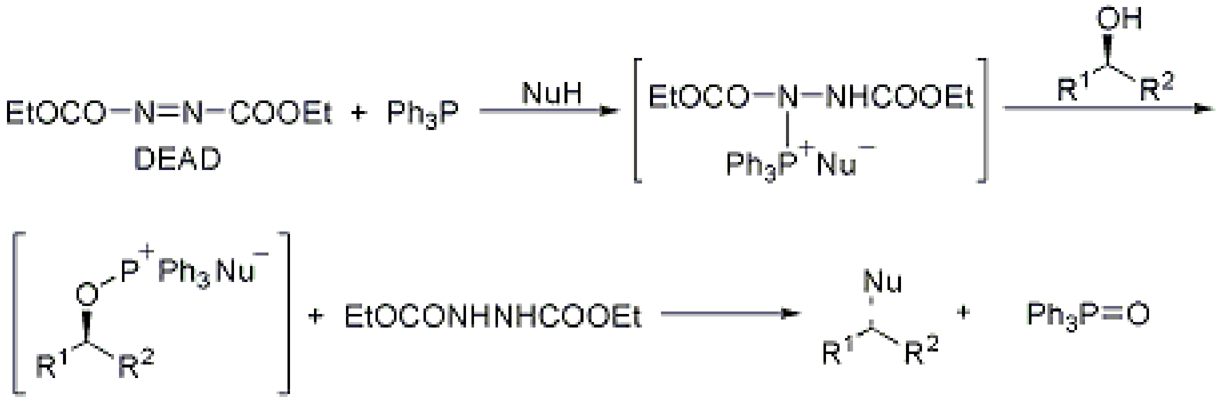
264. Mitsunobu Reaction

O. Mitsunobu *et al., Bull. Chem. Soc. Japan* **40,** 935 (1967); O. Mitsunobu, Y. Yamada, *ibid.* 2380.

Condensation of alcohols and acidic components (NuH) on treatment with dialkyl azodicarboxylates and trialkyl- or triarylphosphines occurring primarily with inversion of configuration *via* the proposed intermediary oxyphosphonium salts:



NuH = phosphoric mono- and diesters, carboxylic acids, phenols, imides, oximes, hydroxymates, heterocycles, thiols, thioamides, β-keto esters

Methods development: R. F. C. Brown *et al., Tetrahedron* **50,** 5469 (1994); T. Tsunoda *et al., Tetrahedron Letters* **40,** 7355 (1999); J. C. Pelletier, S. Kincaid, *ibid.* **41,** 797 (2000). Synthetic applications: M. A. Poelert *et al., Rec. Trav. Chim.* **113,** 355 (1994); A. Viso *et al., Tetrahedron Letters* **41,** 407 (2000); H. Schedel *et al., Tetrahedron Asymmetry* **11,** 2125 (2000). Solid-phase synthesis: S. R. Chhabra *et al., Tetrahedron Letters* **41,** 1099 (2000); F. Zaragoza, H. Stephensen, *ibid.* 2015; P.-P. Kung, E. Swayze, *ibid.* **40,** 5651 (1999). Mechanism: T. Watanabe *et al., Chirality* **12,** 346 (2000). *Reviews:* O. Mitsunobu, *Synthesis* **1981,** 1-28; D. L. Hughes, *Org. React.* **29,** 1-162 (1983); D. L. Hughes, *Organic Preparations and Procedures Int.* **28,** 127-164 (1996); J. A. Dodge, S. A. Jones, *Recent Res. Dev. Org. Chem.* **1,** 273-283 (1997).

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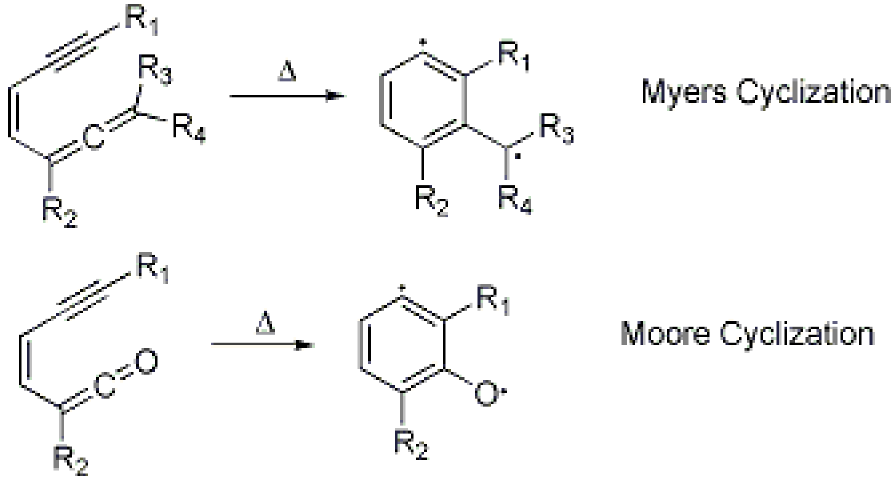
265. **Moore Myers Cyclization;** Moore Cyclization**;** Myers Cyclization

J. O. Karlsson *et al., J. Am. Chem. Soc.* **107,** 3392 (1985); A. G. Myers *et al., ibid.* **111,** 8057 (1989); R. Nagata *et al., Tetrahedron Letters* **30,** 4995 (1989).

Thermal generation of a biradical by cyclization of enyne-ketenes (Moore) or of enyene-allenes (Myers):



A. Rahm, W. D. Wulff, *J. Am. Chem. Soc*. **118,** 1807 (1996). *Reviews:* H. W. Moore, B. R. Yerxa, *Chemtracts* **1992,** 273-313; M. E. Maier, *Synlett* **1995,** 13-26; K. K. Wang, *Chem. Rev*. **96,** 207-222 (1996). *Cf.* Bergman Reaction.

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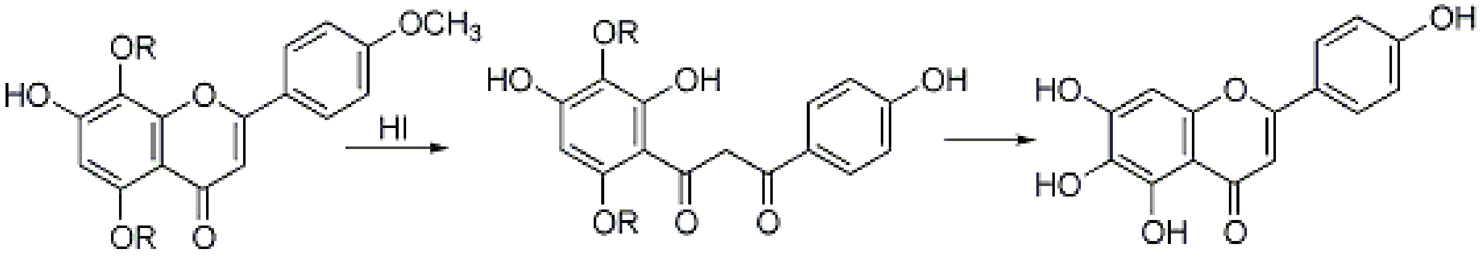
422. Wessely-Moser Rearrangement

F. Wessely, G. H. Moser, *Monatsh.* **56,** 97 (1930).

Rearrangement of flavones and flavanones possessing a 5-hydroxyl group, through fission of the heterocyclic ring and reclosure of the intermediate diaroylmethanes in the alternate direction:



alternate substrates: chromones, isoflavones, flavonols, xanthones, furanochromones

Reviews: Wheeler, *Record Chem. Progr.* **18,** 133 (1957); T. R. Seshadri, *Tetrahedron* **6,** 169 (1959); H. D. Locksley, *Fortschr. Chem. Org. Naturst.* **30,** 292 (1973).

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442. Ziegler-Natta Polymerization

K. Ziegler *et al., Angew. Chem.* **67,** 426, 541 (1955); G. Natta, *ibid.* **68,** 393 (1956).

Polymerization of vinyl monomers under mild conditions using Lewis acid catalysts to give a stereoregulated, or tactic, polymer.

K. Ziegler, *ibid.* **71,** 623 (1959); **72,** 829 (1960); C. L. Arcus in *Progress in Stereochemistry* **vol. 3,** P. B. D. de la Mare, W. Klyne, Eds. (Butterworth Inc., Washington, D.C., 1962) pp 269-288; M. N. Berger *et al., Adv. Catalysis* **19,** 211 (1969); T. Keii, *Kinetics of Ziegler-Natta Polymerization* (Halsted Press, New York, 1973) pp 129-162; *Developments in Polymerization* **vol. 2,** R. N. Haward, Ed. (Burgess-Intl., Philadelphia, 1979) pp 81-148; H. J. Sinn, W. Kaminsky, *Advan. Organomet. Chem.* **18,** 207 (1980); D. M. P. Mingos, *Comp. Organometal. Chem.* **3,** 72-75 (1982); P. D. Gavens *et al., ibid.* 475-547.

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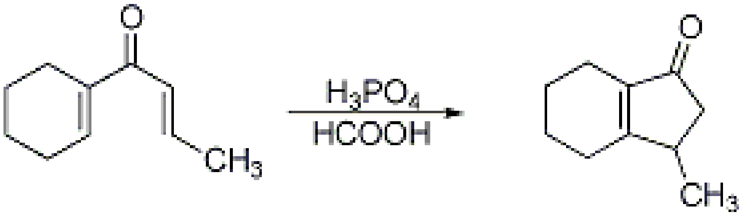
270. Nazarov Cyclization Reaction

I. N. Nazarov *et al., Izv. Akad. Nauk S.S.S.R., Otd. Khim. Nauk* **1942,** 200.

Protic or Lewis acid-catalyzed electrocyclic ring closure of divinyl ketones, or their equivalents, to yield 2-cyclopentenones:



Silicon-directed cyclizations to α-methylenecyclopentanones: H. T. Kang *et al., Tetrahedron Letters* **33,** 3495 (1992). Diastereoselectivity of interrupted reaction: J. A. Bender *et al., J. Org. Chem.* **63,** 2430 (1998); *idem et al., J. Am. Chem. Soc.* **121,** 7443 (1999); H. Hu *et al., ibid.* **121,** 9895 (1999). Lewis acid catalyzed reactions: C. Kuroda *et al., Chem. Commun.* **1997,** 1177; H. A. Buchholz, A. de Meijere, *Eur. J. Org. Chem.* **1998,** 2301. *Reviews:* S. E. Denmark, *Comp. Org. Syn.* **5,** 751-784 (1991); K. L. Habermas *et al., Org. React.* **45,** 1-158 (1994); S. Giese, F. G. West, *Tetrahedron Letters* **39,** 8393 (1998); of interrupted reaction: D. Zuev, L. A. Paquette, *Chemtracts* **12,** 1019-1025 (1999).

271. Neber Rearrangement

P. W. Neber, A. v. Friedolsheim, *Ann.* **449,** 109 (1926); P. W. Neber, G. Huh, *ibid.* **515,** 283 (1935).

Formation of α-amino ketones by treatment of sulfonic esters of ketoximes with potassium ethoxide, followed by hydrolysis:

Reviews: C. O'Brien, *Chem. Rev.* **64,** 81 (1964); C. G. McCarty in *The Chemistry of the Carbon-Nitrogen Double Bond,* S. Patai, Ed. (Interscience, New York, 1970) p 447; Y. Tamura *et al., Synthesis* **1973,** 215; R. F. Parcell, J. C. Sanchez, *J. Org. Chem.* **46,** 5229 (1981); K. Maruoka, H. Yamamoto, *Comp. Org. Syn.* **6,** 786-789 (1991). Synthetic applications: I. Moldvai *et al., Heterocycles* **43,** 2377 (1996); M. J. Mphahlele, T. A. Modro, *Phosphorus, Sulfur, Silicon Relat. Elem.* **127,** 131 (1997); J. Y. L. Chung *et al., Tetrahedron Letters* **40,** 6739 (1999).

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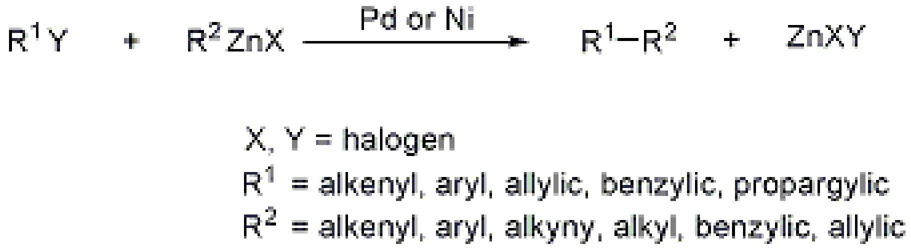
274. Negishi Cross Coupling

E. Negishi *et al., J. Org. Chem.* **42,** 1821 (1977).

Formation of unsymmetric biaryls by cross coupling arylhalides with arylzinc reagents in presence of catalytic Ni or Pd:



Synthetic application: S. Superchi *et al., Tetrahedron Letters* **37,** 6057 (1996); J. A. Miller, R. P. Farrell, *ibid.* **39,** 6441 (1998). Extension to additional functional groups: E. Negishi, *Acc. Chem. Res.* **15,** 340 (1982). *Review:* P. Knochel, R. D. Singer, *Chem. Rev.* **93,** 2117-2188 (1993); *idem et al., Ber.* **130,** 1021-1027 (1997).

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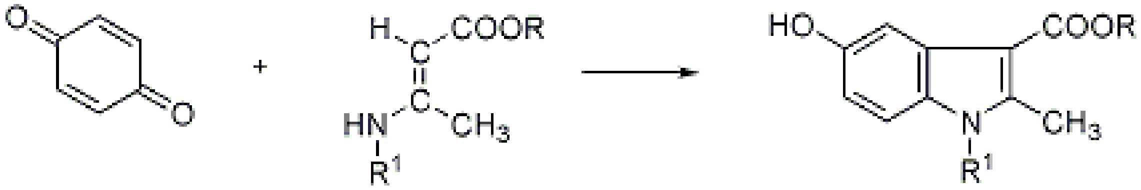
276. Nenitzescu Indole Synthesis

C. D. Nenitzescu, *Bull. Soc. Chim. Romania* **11,** 37 (1929).

Synthesis of 5-hydroxyindole derivatives by condensation of *p*-benzoquinone with β-aminocrotonic esters:



Reviews: R. K. Brown in *The Chemistry of Heterocyclic Compounds*, W. J. Houlihan, Ed. (Wiley, New York, 1972) p 413; G. R. Allen, Jr., *Org. React.* **20,** 337 (1973). Synthetic applications: U. Kuecklander, W. Huehnermann, *Arch. Pharm.* **312,** 515 (1979); J. L. Bernier, J. P., Henichart, *J. Org. Chem.* **46,** 4197 (1981). M. Kinugawa *et al., J. Chem. Soc. Perkin Trans. I* **1995,** 2677; J. M. Pawlak *et al., J. Org. Chem.* **61,** 9055 (1996).

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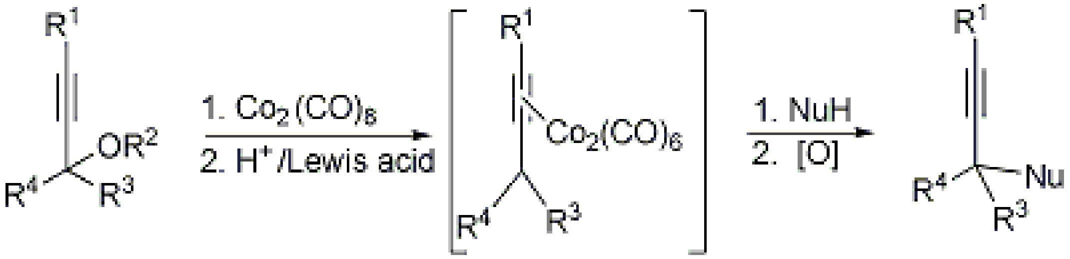
278. Nicholas Reaction

R. F. Lockwood, K. M. Nicholas, *Tetrahedron Letters* **1977,** 4163.

The reaction of dicobalthexacarbonyl-stabilized propargyl cations with nucleophiles, followed by oxidative demetalation to yield propargylated products:



R^1 = H, SiR_3, alkyl, aryl; R^2 = H, CH_3
R^3 = H, Ph, alkyl, substituted alkyl; R^4 = alkyl, substituted alkyl
H^+ = $HBF_4 \cdot O(CH_3)_2$, CF_3COOH;
Lewis acid = $BF_3 \cdot OEt_2$, $EtAlCl_2$, $TiCl_4$, $Bu_2BOSO_2CF_3$
NuH = electron rich aromatics, β-dicarbonyl compounds, ketones, enolates, allyl silanes, hydride, amines, enamines
[O] = $Fe(NO_3)_3$, $Ce(NH_4)_2(NO_3)_6$, $(CH_3)_3NO$

Stereochemistry: S. L. Schreiber *et al., J. Am. Chem. Soc.* **109,** 5749 (1987); A. V. Muehldorf *et al., Tetrahedron Letters* **35,** 8755 (1994). Scope and limitations: K. D. Roth, *Synlett* **1992,** 435; K. D. Roth, U. Müller, *Tetrahedron Letters* **34,** 2919 (1993). Synthetic applications: P. A. Jacobi, W. Zheng, *ibid.* 2581, 2585; E. Tyrrell *et al., Synlett* **1993,** 769. Diastereoselective applications: J. Berge *et al., Tetrahedron Letters* **38,** 685 (1997); A. Mann *et al., J. Chem. Soc. Perkin Trans. I* **1998,** 1427. Enantioselective applications: S. Tanaka *et al., Tetrahedron* **50,** 12883 (1994); A. M. Montana *et al., Tetrahedron Letters* **40,** 6499 (1999). *Review:* K. M. Nicholas, *Accts. Chem. Res.* **20,** 207-214 (1987).

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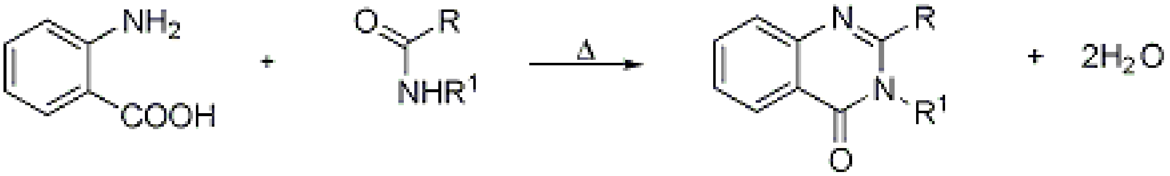
279. Niementowski Quinazoline Synthesis

S. v. Niementowski, *J. Prakt. Chem.* [2] **51,** 564 (1895).

Formation of 4-oxo-3,4-dihydroquinazolines by cyclization of the reaction products of anthranilic acid and amides:



Reviews: T. A. Williamson, *Heterocyclic Compounds* **6,** 331 (1957); W. L. F. Armarego, *Advan. Heterocyclic Chem.* **1,** 253 (1963); E. Cuny *et al.*, *Tetrahedron Letters* **21,** 3029 (1980).

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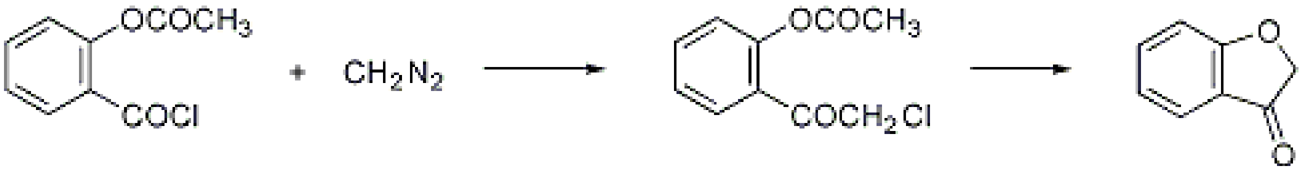
281. Nierenstein Reaction

D. A. Clibbens, M. Nierenstein, *J. Chem. Soc.* **107,** 1491 (1915).

Formation of ω-chloroacetophenones by reaction of diazomethane in dry ether with aroyl chlorides. Coumaranonones are obtained if an *ortho*-hydroxy group is present:

$$\mathrm{ArCOCl} + \mathrm{CH_2N_2} \longrightarrow \mathrm{ArCOCH_2Cl} + \mathrm{N_2}$$



W. E. Bachman, W. S. Struve, *Org. React.* **1,** 38 (1942); Y. Miyahara, *J. Heterocycl. Chem.* **16,** 1147 (1979).

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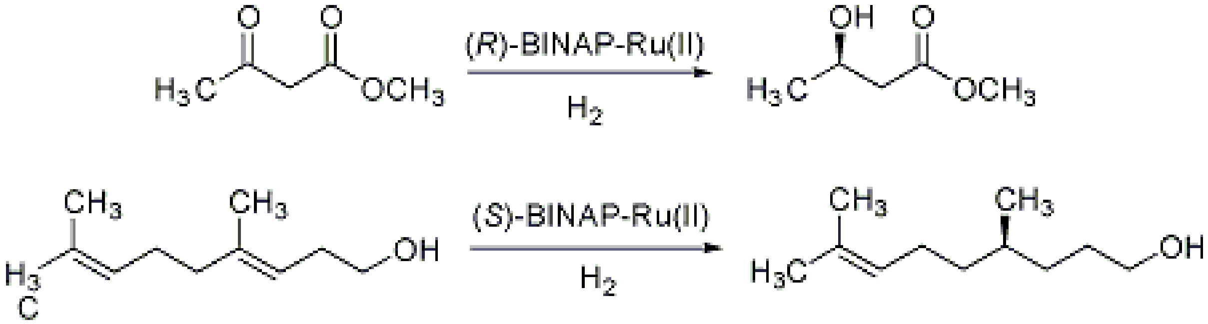
283. Noyori Hydrogenation

T. Ikariya *et al., Chem. Commun.* **1985,** 922; R. Noyori *et al., J. Am. Chem. Soc.* **108,** 7117 (1986).

Homogeneous asymmetric catalytic hydrogenation of olefinic and carbonyl bonds mediated by enantiopure ruthenium(II) BINAP complexes. The substrates must have coordinating functionalities in neighboring positions which serve as directing groups during the transformation:



Detailed experimental procedure: M. Kitamura *et al., Org. Syn.* **71,** 1 (1993). Methods development for enamide substrates: *idem et al., J. Org. Chem.* **59,** 297 (1994); E. Vedejs *et al., ibid.* **64,** 6724 (1999). Development and use of arene substituted BINAP catalysts: K. Mashima *et al., ibid.* **59,** 3064 (1994). *Reviews:* H. Takaya *et al., Adv. Chem. Ser.* **230,** 123-142 (1992); R. Noyori, *Asymmetric Catalysis in Organic Synthesis* (John Wiley & Sons, New York, 1994) pp 16-94.

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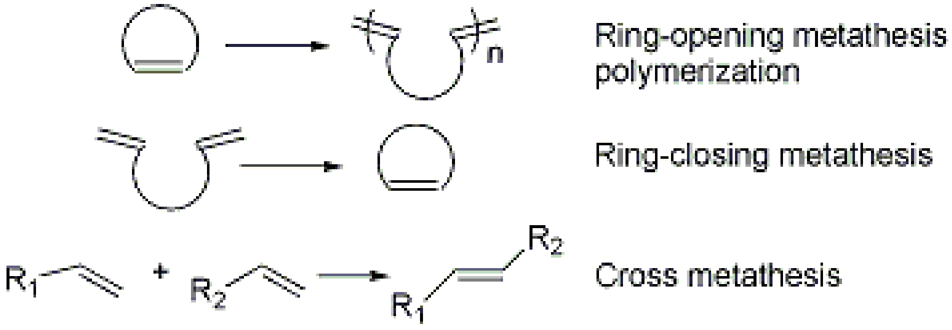
285. Olefin Metathesis

Carbon-carbon bond rearrangements in presence of metal carbene catalyst complexes especially those of molybdenum and ruthenium:



Comprehensive accounts: R. H. Grubbs, *Comp. Organometal. Chem.* **8,** 499 (1982); *idem*, S. Chang, *Tetrahedron* **54,** 4413 (1998). Synthetic applications: A. K. Chatterjee *et al., J. Am. Chem. Soc.* **122,** 3728 (2000); C. W. Lee, R. H. Grubbs, *Organic Letters* **2,** 2145 (2000). Series of articles on syntheses, polymerizations and catalysts: *J. Molec. Catal. A.* **133,** 1-274 (1998). *Review:* A. Furstner, *Angew. Chem. Int. Ed.* **39,** 3012-3043 (2000). *See monograph* Grubbs' Catalyst.

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290. Parham Cyclization

W. E. Parham *et al., J. Org. Chem.* **40,** 2394 (1975).

Four- to seven-membered ring annulation of aryl bromides bearing *ortho* side chains having an electrophilic moiety, accomplished by halogen-metal exchange and subsequent nucleophilic ring closure:

E = COOH, $CONR_2$, epoxide, CH_2Br, CH_2Cl, $OCONR_2$, NCHArCONRCOCH$_2$R, $POPh_2$

Synthetic application: M. R. Paleo *et al., J. Org. Chem.* **40,** 2029 (1975); A. Couture *et al., Chem. Commun.* **1994;** 1329; M. I. Collado *et al., Tetrahedron Letters* **37,** 6193 (1996); S. D. Larsen, *Synlett* **1997;** 1013; A. Ardeo *et al., Tetrahedron Letters* **41,** 5211 (2000). *Review:* W. E. Parham, C. K. Bradsher, *Accts. Chem. Res.* **15,** 300-305 (1982).

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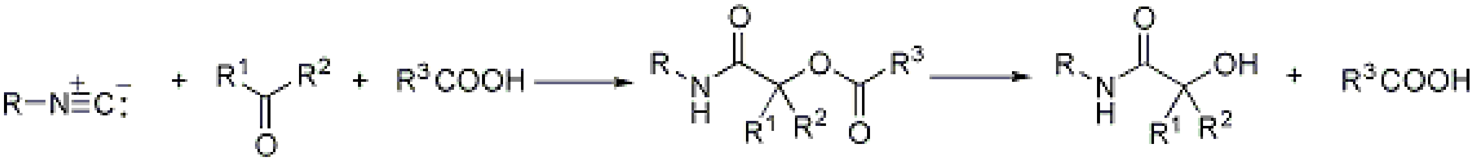
291. Passerini Reaction

M. Passerini, *Gazz. Chim. Ital.* **51,** 126, 181 (1921).

Formation of α-hydroxycarboxamides on treatment of an isonitrile with a carboxylic acid and an aldehyde or ketone:



Synthetic applications: J. R. Falck, S. Manna, *Tetrahedron Letters* **22,** 619 (1981); R. Bossio *et al.*, *Synthesis* **1993,** 783. Modifications: W. E. Lumma, *J. Org. Chem.* **46,** 3668 (1981); T. Carofiglio *et al.*, *Organometallics* **12,** 2726 (1993); for stereoselectivity: H. Bock, I. Ugi, *J. Prakt. Chem.* **339,** 385 (1997); for combinatorial chemistry; H. Bienaymé, *Tetrahedron Letters* **39,** 4255 (1998); S. W. Kim *Tetrahedron Letters* **39,** 7031 (1998). *Reviews:* I. Ugi, *Angew. Chem. Int. Ed.* **1,** 8 (1962); I. Ugi *et al.*, in *Isonitrile Chemistry* (Academic Press, New York, 1971) pp 133-143; I. Ugi, *et al.*, *Comp. Org. Syn.* **2,** 1083-1087 (1991).

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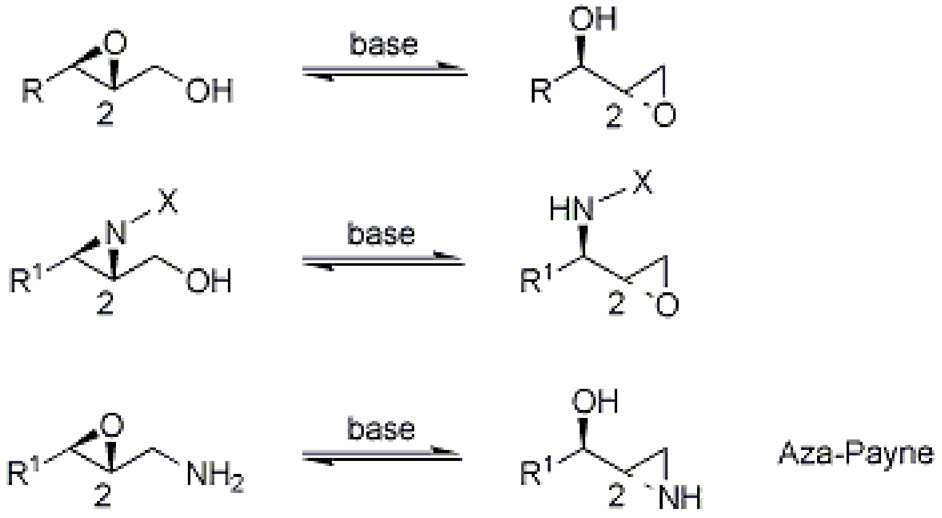
294. Payne Rearrangement

G. B. Payne, *J. Org. Chem.* **27,** 3819 (1962).

Base-promoted isomerization of 2,3-epoxyalcohols. Configuration at C-2 is inverted:



R^1 = alkyl or aryl X = H, mesyl, tosyl, etc.

In conjunction with nucleophilic ring opening: T. Katsuki *et al., ibid.* **47,** 1373 (1982); C. H. Behrens *et al., ibid.* **50,** 5687 (1985); P. C. B. Page *et al., J. Chem. Soc. Perkin Trans. I* **1990,** 1375; T. Konosu *et al., Chem. Pharm. Bull.* **40,** 562 (1992). *Aza-Payne rearrangements:* T. Ibuka *et al., J. Org. Chem.* **60,** 2044 (1995); K. Nakai *et al., Tetrahedron Letters* **36,** 6247 (1995). Enhanced stereoselectivity: W. C. Frank, *Tetrahedron Asymmetry* **9,** 3745 (1998). Review of aza-Payne: T. Ibuka *et al., Chem. Soc. Rev.* **27,** 145-154 (1998).

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298. Pelouze Synthesis

J. Pelouze, *Ann.* **10,** 249 (1834).

Formation of nitriles from alkali cyanides by alkylation with alkyl sulfates or alkyl phosphates:

$$ROSO_2OK + KCN \longrightarrow RCN + K_2SO_4$$

V. Migrdichian, *Chemistry of Organic Cyanogen Compounds* (New York, 1947) p 6; D. T. Mowry, *Chem. Rev.* **42,** 192 (1948); P. Kurtz, *Houben-Weyl* **8,** 306 (1952).

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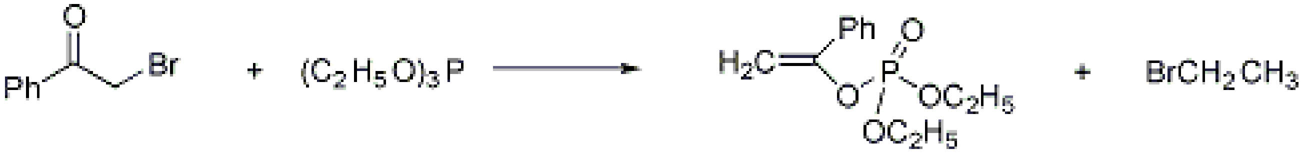
302. Perkow Reaction

W. Perkow *et al.*, *Naturwiss.* **39,** 353 (1952).

Formation of enol phosphates on treatment of α-halocarbonyl compounds with trialkyl phosphites:



F. W. Lichtenthaler, *Chem. Rev.* **61,** 607 (1961); B. Miller in *Topics in Phosphorus Chemistry* **vol. 2,** M. Grayson, E. J. Griffith, Eds. (John Wiley, New York, 1965) p 178; K. Sasse, *Houben-Weyl* **12/1,** 423 (1963); A. J. Kirby, S. G. Warren, *The Organic Chemistry of Phosphorus* (Elsevier, Amsterdam, 1967) p 123; B. A. Arbuzow, *Pure Appl. Chem.* **9,** 306 (1964); I. J. Borowitz *et al.*, *J. Org. Chem.* **38,** 1713 (1973); T. Winkler, W. L. Bencze, *Helv. Chim. Acta* **63,** 402 (1980); M. Sekine *et al.*, *J. Org. Chem.* **46,** 4030 (1981).

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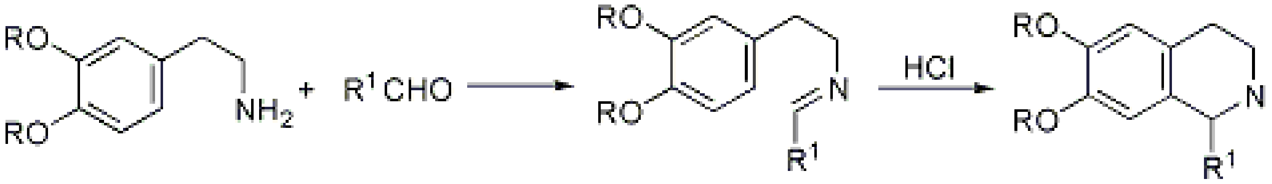
310. Pictet-Spengler Isoquinoline Synthesis

A. Pictet, T. Spengler, *Ber.* **44,** 2030 (1911).

Formation of tetrahydroisoquinoline derivatives by condensation of β-arylethylamines with carbonyl compounds and cyclization of the Schiff bases formed:



Reviews: W. M. Whaley, T. R. Govindachari, *Org. React.* **6,** 151 (1951); R. A. Abramovitch, I. D. Spenser, *Advan. Heterocyclic Chem.* **3,** 79 (1964); K. Stuart, R. Woo-Ming, *Heterocycles* **3,** 223 (1975); D. Soerens *et al., J. Org. Chem.* **44,** 535 (1979); H. Ernst *et al., Ber.* **114,** 1894 (1981). Stereochemical study: E. Dominguez *et al., Tetrahedron* **43,** 1943 (1987). Review of enantioselective modifications: M. D. Rozwadowski, *Hetereocycles* **39,** 903-931 (1994).

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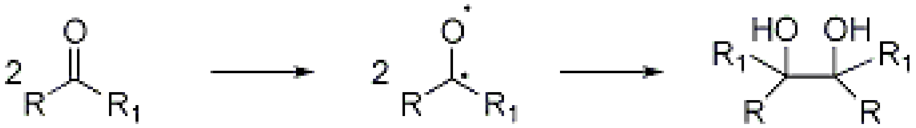
312. Pinacol Coupling Reaction

R. Fittig, *Ann.* **110,** 17 (1859).

Formation of pinacols by a reductive radical-radical coupling of carbonyl compounds, especially ketones:

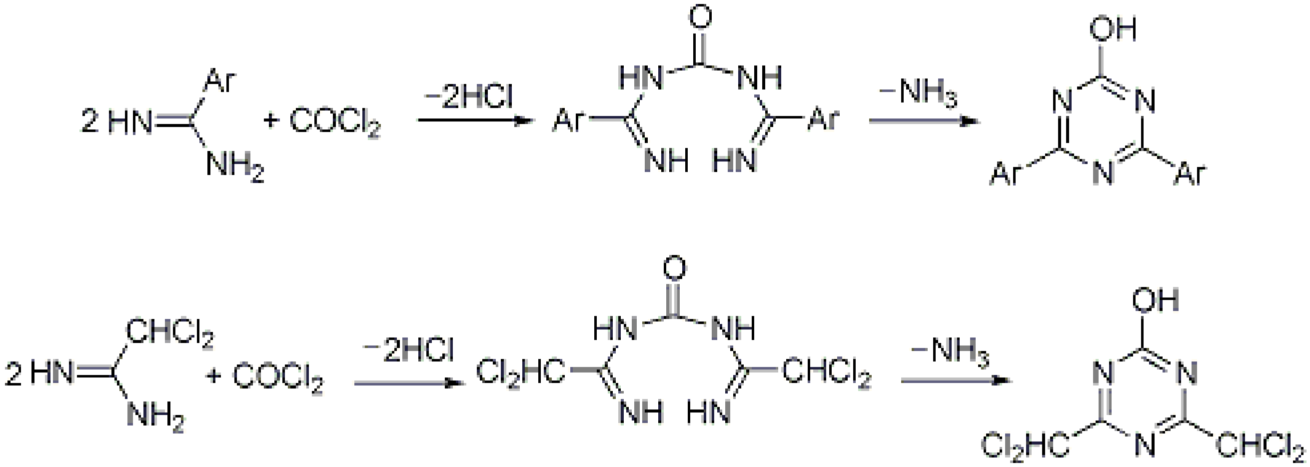


Reviews: G. M. Robertson, *Comp. Org. Syn.* **3,** 563 (1991); H. Jendralla *et al.*, in *Transition Metals for Organic Synthesis* (Wiley-VCH, Weinheim, 1998) pp. 403-417. *Cf.* McMurry Reaction.

315. Pinner Triazine Synthesis

A. Pinner, *Ber.* **23,** 2919 (1890).

Preparation of 2-hydroxy-4,6-diaryl-*s*-triazines by reaction of aryl amidines and phosgene. The reaction may be extended to halogenated aliphatic amidines:



A. Pinner, *Ber.* **25,** 1414 (1892); **28,** 483 (1895); J. Ephraim, *ibid.* **26,** 2226 (1893); P. Flatow, *ibid.* **30,** 2006 (1897); T. Rappaport, *ibid.* **34,** 1990 (1901); H. Schroeder, C. Grundmann, *J. Am. Chem. Soc.* **78,** 2447 (1956); E. M. Smolin, L. Rapoport, *The Chemistry of Heterocyclic Compounds,* A. Weissberger, Ed., *s-Triazines and Derivatives* (Interscience, New York, 1959) p 186.

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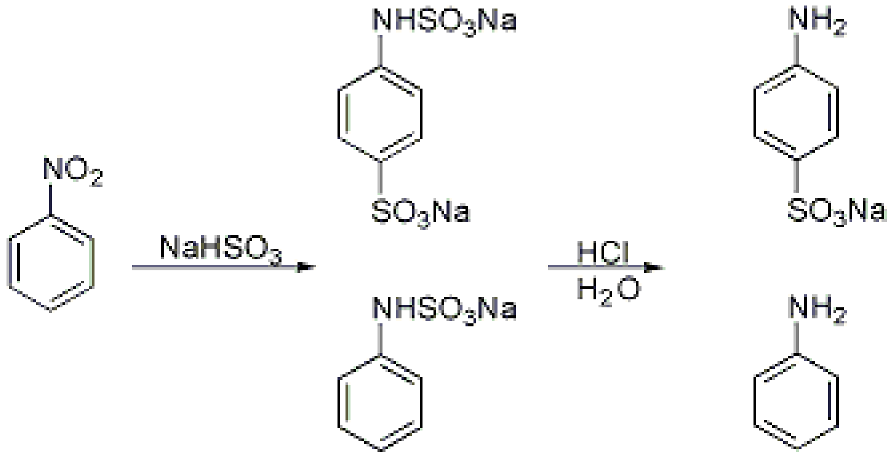
316. Piria Reaction

R. Piria, *Ann.* **78,** 31 (1851).

Formation of arylsulfamic acids or sulfonation products or both by refluxing aromatic nitro compounds with a metal sulfite and boiling the mixture with dilute acid to yield the amines and sulfamic acids:



J. F. Bunnett, R. E. Zahler, *Chem. Rev.* **49,** 398 (1951); R. Schroter, *Houben-Weyl* **11/1,** 457 (1957); R. Budziarek, *Chem. & Ind. (London)* **1978,** 583.

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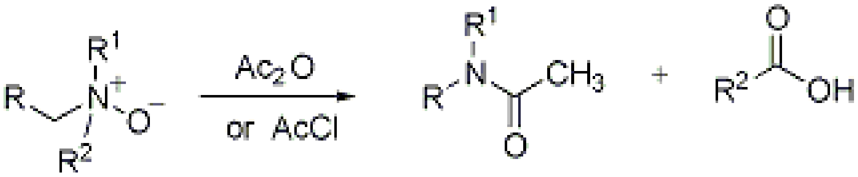
317. **Polonovski Reaction;** Potier-Polonovski Reaction

M. Polonovski, M. Polonovski, *Bull. Soc. Chim. France* **41,** 1190 (1927).

Rearrangement of tertiary amine oxides upon treatment with acetic anhydride or acetyl chloride, in which one of the alkyl groups attached to the nitrogen is cleaved, generating the *N,N*-disubstituted acetamide and aldehyde:



Reviews: A. R. Katritzky, J. N. Lagowski, *Chemistry of Heterocyclic N-Oxides* (Academic Press, New York, 1971) p 279, 362; D. Grierson, *Org. React.* **39,** 85-295 (1990); D. S. Grierson, H.-P. Husson, *Comp. Org. Syn.* **6,** 909-924 (1991).

The reaction proceeds *via* an iminium ion intermediate which becomes the stable reaction product when trifluoroacetic anhydride is employed. This modified procedure is commonly referred to as the **Potier-Polonovski reaction:** A. Cave *et al., Tetrahedron* **23,** 4681 (1967); T. Tamminen *et al., ibid.* **45,** 2683 (1989); R. J. Sundberg, *et al., ibid.* **48,** 277 (1992).

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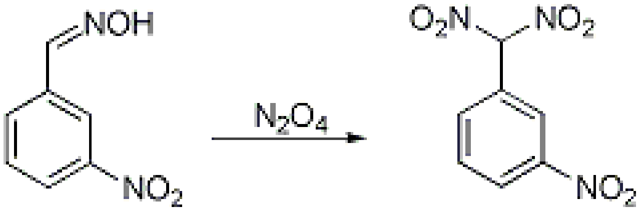
319. Ponzio Reaction

G. Ponzio, *Gazz. Chim. Ital.* **27, I,** 171 (1897).

Formation of dinitrophenylmethanes from benzaldoximes by oxidation with nitrogen dioxide in ether:

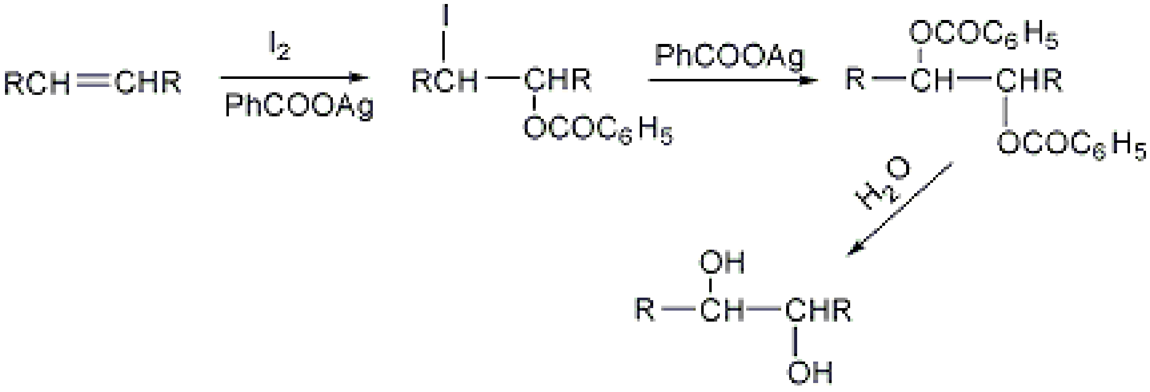


J. L. Riebsomer, *Chem. Rev.* **36,** 183 (1945); L. F. Fieser, W. von E. Doering, *J. Am. Chem. Soc.* **68,** 2252 (1946); L. F. Fieser, M. Fieser, *Reagents for Organic Synthesis* (New York, 1967) p 325; H. G. Padeken *et al., Houben-Weyl* **10/1,** 113 (1971). Improved procedure: H. Suzuki *et al., Bull. Chem. Soc. Japan* **61,** 2929 (1988).

320. Prévost Reaction

C. Prévost, *Compt. Rend.* **196,** 1129 (1933), *C.A.* **27,** 3195 (1933).

Hydroxylation of olefins with iodine and silver benzoate in an anhydrous solvent to give *trans*-glycols:



Reviews: C. V. Wilson, *Org. React.* **9,** 350 (1957); F. D. Gunstone, *Advan. Org. Chem.* **1,** 117 (1960); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) p 438; S. Amin *et al.*, *J. Org. Chem.* **46,** 2573 (1981). *Cf.* Woodward *cis*-Hydroxylation.

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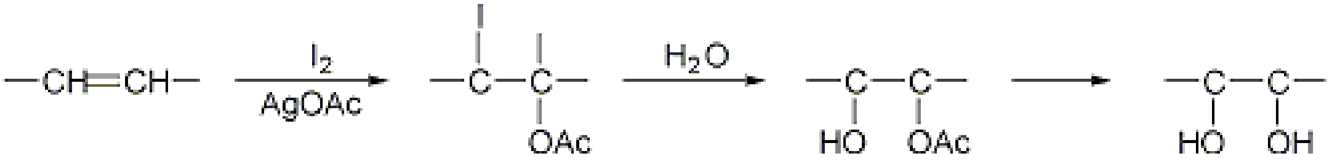
438. Woodward*cis*-Hydroxylation

R. B. Woodward, **US 2687435** (1954); R. B. Woodward, F. V. Brutcher, *J. Am. Chem. Soc.* **80,** 209 (1958).

The hydroxylation of an olefin with iodine and silver acetate in wet acetic acid to give *cis*-glycols:



L. B. Barkley, M. W. Farrar, *J. Am. Chem. Soc.* **76,** 5014, (1954); W. S. Knowles, Q. E. Thompson, *ibid.* **79,** 3212 (1957); W. F. Forbes, R. Shelton, *J. Org. Chem.* **24,** 436 (1959); F. D. Gunstone, *Advan. Org. Chem.* **1,** 117 (1960). Application to steroids: L. Mangoni, V. Dovinola, *Tetrahedron Letters* **1969,** 5235; P. Kocovsky, V. Cerny, *Coll. Czech. Chem. Commun.* **42,** 163 (1977). Modification: L. Mangoni *et al., Gazz. Chim. Ital.* **105,** 377 (1975). *Cf.* Prévost Reaction.

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321. Prilezhaev (Prileschajew) Reaction

N. Prilezhaev, *Ber.* **42,** 4811 (1909).

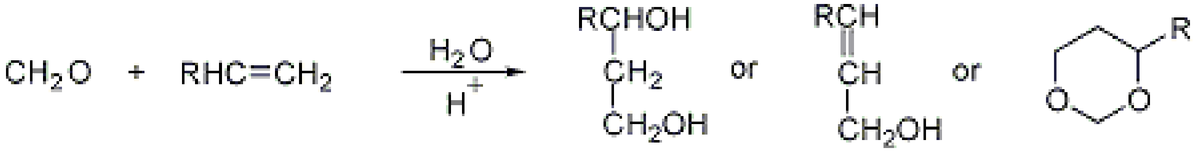
Formation of epoxides by the reaction of alkenes with peracids:

Reviews: D. Swern, *Chem. Rev.* **45,** 16 (1949); *Org. React.* **7,** 378 (1953); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 302-319; D. I. Metelitra, *Russ. Chem. Rev.* **41,** 807 (1972); D. Schnurgfeil, *Z. Chem.* **20,** 445 (1980).

322. Prins Reaction

H. J. Prins, *Chem. Weekblad* **16,** 64, 1072, 1510 (1919), *C.A.* **13,** 3155 (1919).

Acid-catalyzed addition of olefins to formaldehyde to give 1,3-diols, allylic alcohols or *meta*-dioxanes:



Reviews: R. Arundale, L. A. Mikeska, *Chem. Rev.* **51,** 505 (1952); V. I. Isagulyants *et al., Russ. Chem. Rev.* **1968,** 17; C. W. Roberts in *Friedel-Crafts and Related Reactions* **vol. 2,** Part 2, G. A. Olah, Ed. (Interscience, 1964) pp 1175-1210; D. R. Adams, S. P. Bhatnagar, *Synthesis* **1977,** 661; K. H. Schulte-Elte *et al., Helv. Chim. Acta* **62,** 2673 (1979); R. El Gharbi *et al., Synthesis* **1981,** 361; B. B. Snider, *Comp. Org. Syn.* **2,** 527-561 (1991).

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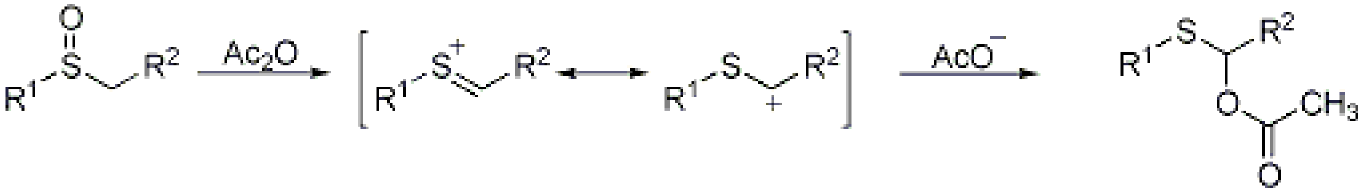
324. Pummerer Rearrangement

R. Pummerer, *Ber.* **43,** 1401 (1910).

Rearrangement of sulfoxides to α-acyloxythioethers in the presence of acyclic anhydrides. When nucleophiles other than those derived from the anhydride are present, different functionalization is achieved:



Diastereoselectivity in the preparation of 4-phenyl-4-butanolides: H. Su *et al., Bull. Chem. Soc. Japan* **66,** 2603 (1993). Application to vinyl sulfoxides (the additive Pummerer reaction): D. Craig, K. Daniels, *Tetrahedron* **49,** 11263 (1993). Regiospecific cyclization: G. Majumdar, D. Mal, *Indian J. Chem.* **33B,** 700 (1994). Asymmetric synthesis: Y. Kita *et al., Tetrahedron Letters* **35,** 3575 (1994). *Reviews:* O. DeLucchi *et al., Org. React.* **40,** 157-405 (1991); D. S. Grierson, H.-P. Husson, *Comp. Org. Syn.* **6,** 924-937 (1991).

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328. Raschig Phenol Process

F. Raschig, **FR 698341** (1930), *C.A.* **25,** 3012 (1931).

Commercial process for the production of phenol by the hydrolysis of chlorobenzene, produced by the chlorination of benzene with hydrochloric acid and air:

$$C_6H_6 + HCl \xrightarrow[\text{Cu -Fe}]{230°/\text{air}} C_6H_5Cl + H_2O \xrightarrow[SiO_2]{425°} C_6H_5OH + HCl$$

W. H. Prahl, **US 1963761** (1934); **US 2156402** (1939); J. A. Kent, *Riegel's Industrial Chemistry* (New York, 1962) p 339; W. L. Faith, D. B. Keyes, R. L. Clark, *Industrial Chemistry* (New York, 3rd ed., 1965) p 586; R. N. Shreve, *Chemical Process Industries* (New York, 3rd ed., 1967) p 105; *Kirk-Othmer Encyclopedia of Chemical Technology* **vol. 17** (New York, 1982) p 378.

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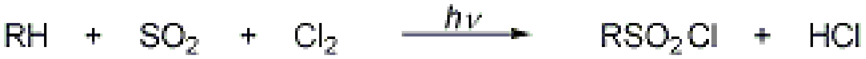
329. Reed Reaction

C. F. Reed, **US 2046090** (1933); **US 2174110** (1934); **US 2174492** (1938).

Photochemical sulfonation of paraffins and cycloparaffins by sulfur dioxide and chlorine under irradiation with ultraviolet light:



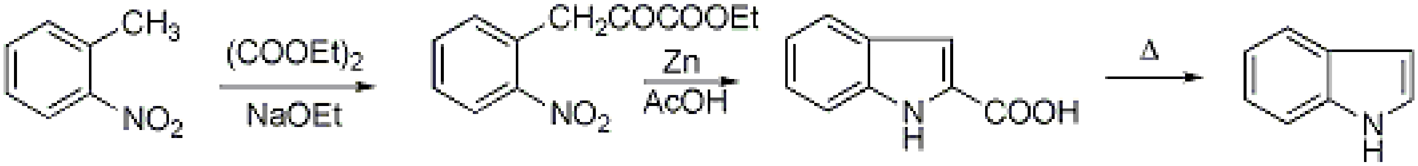
$$RH + SO_2 + Cl_2 \xrightarrow{h\nu} RSO_2Cl + HCl$$

F. Asinger *et al.*, *Ber.* **75,** 34, 42, 344 (1942); J. H. Helberger *et al.*, *Ann.* **562,** 23 (1949); H. Eckoldt, *Houben-Weyl* **9,** 407-427 (1955); A. Schönberg, *Präparative Organische Photochemie* (Berlin, 1958) p 201; G. Sosnovsky, *Free Radical Reactions in Preparative Organic Chemistry* (New York, 1964) p 105.

332. Reissert Indole Synthesis

A. Reissert, *Ber.* **30,** 1030 (1897).

Condensation of an *o*-nitrotoluene with oxalic ester, reduction to the amine, and cyclization to the indole:



W. O. Kermack *et al., J. Chem. Soc.* **119,** 1602 (1921); P. C. Julian *et al., Heterocyclic Compounds* **3,** 18 (1962); J. G. Cannon *et al., J. Med. Chem.* **24,** 238 (1981).

334. Reppe Chemistry

The term designates that phase of acetylene chemistry involving the use of acetylene at high pressures in the presence of suitable catalysts to carry out the fundamental reactions of vinylation, ethynylation, cyclopolymerization and carbonylation as developed from 1928 onward by Walter Reppe and associates in the I. G. Farbenindustrie laboratories in Ludwigshafen:

$$H_2C{=}CHOR \xleftarrow{ROH} HC{\equiv}CH \xrightarrow{RSH} H_2C{=}CHSR$$

$$RR^1CO + HC{\equiv}CH \longrightarrow RR^1C(OH)C{\equiv}CH \xrightarrow{RR^1CO} RR^1C(OH)C{\equiv}CC(OH)RR^1$$

$$4HC{\equiv}CH \longrightarrow \text{cyclooctatetraene}$$

$$4HC{\equiv}CH + 4C_2H_4OH + Ni(CO)_4 + 2HCl \longrightarrow 4H_2C{=}CHCOOC_2H_5 + NiCl_2 + H_2$$

J. W. Copenhaver, M. H. Bigelow, *Acetylene and Carbon Monoxide Chemistry* (New York, 1949) p 246; W. Reppe, *Acetylene Chemistry*, U.S. Dept. Commerce PB 18852-S (1949); *Neue Entwicklungen auf dem Gebiet des Acetylens und Kohlenoxyds* (Berlin 1949); H. Kröper, *Houben-Weyl* **4/II,** 413-422 (1955); D. W. F. Hardie, *Acetylene, Manufacture and Uses* (New York, 1965) p 67; L. F. Fieser, M. Fieser, *Reagents for Organic Synthesis* (New York, 1967) pp 61, 183, 185, 190, 519, 720, 722, 723. Review of carbonylations: A. Mullen, “Carbonylations Catalyzed by Metal Carbonyls-Reppe Reactions” in *New Syntheses with Carbon Monoxide*, J. Falbe, Ed. (Springer-Verlag, Berlin, 1980) pp 243-308. Mechanistic study of cyclooctatetraene synthesis: R. E. Colborn, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **108,** 5470 (1986); C. J. Lawrie *et al.*, *Organometallics* **8,** 2274 (1989).

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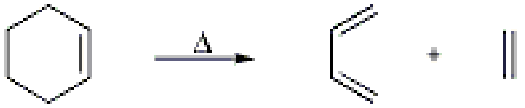
335. Retro-Diels-Alder Reaction

Thermal dissociation of Diels-Alder adducts, occurring most readily when one or both fragments are particularly stable:



Early review: H. Kwart, K. King, *Chem. Rev.* **68,** 415-447 (1968). Acceleration by alkoxide substituent: O. Papies, W. Grimme, *Tetrahedron Letters* **21,** 2799 (1980). Application to the synthesis of enethiols: Y. Vallée *et al.*, *Synth. Commun.* **23,** 1267 (1993); of cyclopentadienyl ligands: B. Y. Lee *et al.*, *J. Am. Chem. Soc.* **116,** 2163 (1994). Role in structure elucidation *via* mass spectrometry: F. Turecek, V. Hanus, *Mass Spectrom. Rev.* **3,** 85-152 (1984). Application to natural product synthesis: A. Ichihara, *Synthesis* **1987,** 207-222; R. W. Sweger, A. W. Czarnik, *Comp. Org. Syn.* **5,** 551-592 (1991).

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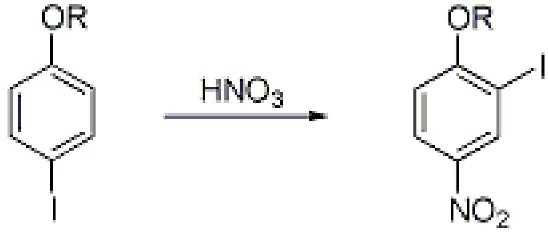
337. Reverdin Reaction

F. Reverdin, *Ber.* **29,** 997, 2595 (1896).

Migration of iodine during nitration of iodophenolic ethers:



F. Reverdin, *Bull. Soc. Chim. France* [4] **1,** 618 (1907); G. M. Robinson, *J. Chem. Soc.* **109,** 1078 (1916); D. V. Nightingale, *Chem. Rev.* **40,** 128 (1947); M. J. S. Dewar, *Electronic Theory of Organic Chemistry* (Oxford, 1949) p 232.

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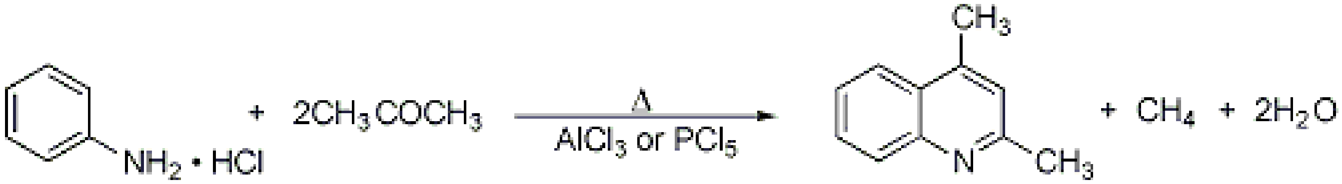
338. Riehm Quinoline Synthesis

P. Riehm *et al., Ber.* **18,** 2245 (1885); **19,** 1394 (1886); *idem, Ann.* **238,** 9 (1887).

Formation of quinoline derivatives by prolonged heating of arylamine hydrochlorides with ketones with or without use of aluminum chloride or phosphorus pentachloride:

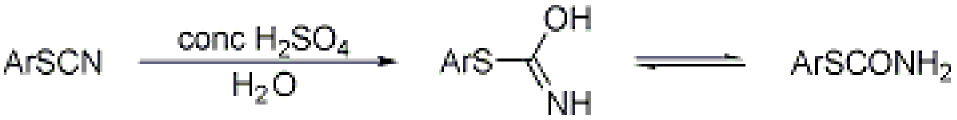


E. Knoevenagel *et al., Ann.* **55,** 1923, 1934 (1922); **56,** 2414 (1923); C. Hollins, *The Synthesis of Nitrogen Ring Compounds* (London, 1924) p 263; D. J. Craig, *J. Am. Chem. Soc.* **60,** 1458 (1938); R. C. Elderfield, J. R. McCarthy, *ibid.* **73,** 975 (1951); R. C. Elderfield, *Heterocyclic Compounds* **4,** 16 (1952).

339. Riemschneider Thiocarbamate Synthesis

R. Riemschneider, F. Wojahn, *Pharmazie* **4,** 460 (1949); *Chim. Ind. (Paris)* **64,** 99 (1950); *Pharm. Zentralhalle* **89,** 118 (1950).

The action of concentrated sulfuric acid followed by treatment with ice-water serves to transform arylthiocyanates into the corresponding thiocarbamates:



R. Riemschneider, *Chim. Ind. (Milan)* **33,** 483 (1951); *idem et al., J. Am. Chem. Soc.* **73,** 5905 (1951); R. Riemschneider, G. Orlick, *Angew. Chem.* **64,** 420 (1952); R. Riemschneider, *Chim. Ind. (Milan)* **34,** 353 (1952); *idem, Z. Naturforsch.* **7b,** 277 (1952); R. Riemschneider, G. Orlick, *Monatsh.* **84,** 316 (1953); K. Schmidt, P. Kolleck-Bös, *J. Am. Chem. Soc.* **75,** 6067 (1953).

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340. **Riley Oxidations** (Selenium Dioxide Oxidation)

H. L. Riley *et al., J. Chem. Soc.* **1932,** 1875.

Oxidations of organic compounds with selenium dioxide; *e.g.,* the oxidation of active methylene groups to carbonyl groups:

$$CH_3CH_2CHO + SeO_2 \longrightarrow CH_3COCHO + H_2O + Se$$

N. Rabjohn, *Org. React.* **5,** 331 (1949); *Oxidation*, E. N. Trachtenberg, R. L. Augustine, Eds. (Marcel Dekker, New York, 1969) pp 119-187; H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 407-411.

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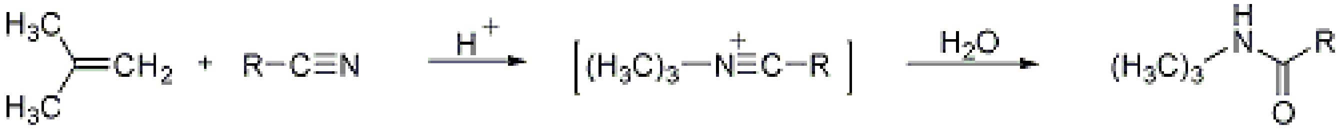
341. Ritter Reaction

J. J. Ritter, P. P. Minieri, *J. Am. Chem. Soc.* **70,** 4045 (1948); J. J. Ritter, J. Kalish, *ibid.* 4048.

Synthesis of amides from nitriles and alcohols or alkenes in strongly acidic media:



Reviews: L. I. Krimen, D. J. Cota, *Org. React.* **17,** 213-325 (1969); R. C. Larock, W. W. Leong, *Comp. Org. Syn.* **4,** 292-294 (1991); R. Bishop, *ibid.* **6,** 261-300 (1991). Synthetic applications: S. Top, G. Jaouen, *J. Org. Chem.* **46,** 78 (1981); D. M. Fink, R. C. Effland, *Synth. Commun.* **24,** 2793 (1994); W. M. Samaniego *et al.*, *Tetrahedron Letters* **35,** 6967 (1994).

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344. Rosenmund Reduction

K. W. Rosenmund, *Ber.* **51,** 585 (1918); K. W. Rosenmund, F. Zetzsche, *ibid.* **54,** 425 (1921).

Catalytic reduction of acid chlorides to aldehydes. To prevent further hydrogenation a poison is added to the catalyst:

$$RCOCl + H_2 \xrightarrow{Pd\text{-}BaSO_4} RCHO + HCl$$

Reviews: E. Mosettig, R. Mozingo, *Org. React.* **4,** 362 (1948); A. Rachlin *et al., Org. Syn.* **51,** 8 (1971); J. A. Peters, H. Van Bekkum, *Rec. Trav. Chim.* **100,** 21 (1981). Investigation of reaction parameters: W. F. Maier *et al., J. Am. Chem. Soc.* **108,** 2608 (1986). Modified procedure applied to the synthesis of esters: V. V. Grushin, H. Alper, *J. Org. Chem.* **56,** 5159 (1991).

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345. Rosenmund-von Braun Synthesis

K. W. Rosenmund, E. Struck, *Ber*. **52,** 1749 (1916); J. von Braun, G. Manz, *Ann.* **488,** 111 (1931).

Conversion of aryl halides to aromatic nitriles in the presence of cuprous cyanide:

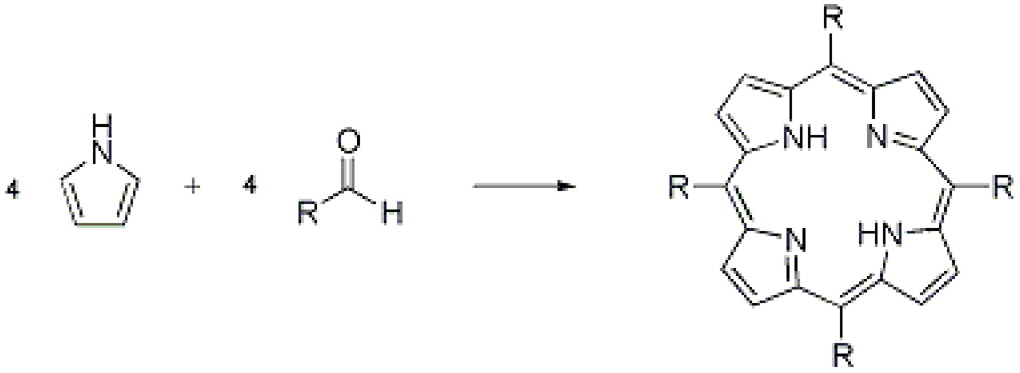
$$\mathrm{ArX} + \mathrm{CuCN} \xrightarrow{\Delta} \mathrm{ArCN} + \mathrm{CuX}$$

Reviews: D. T. Moury, *Chem. Rev.* **42,** 207 (1948); J. E. Callen *et al., Org. Syn.* **3,** 212 (1955); M. S. Newman, *ibid.* 631; K. Takagi *et al., Bull. Chem. Soc. Japan* **48,** 3298 (1975); P. Bouyssou *et al., J. Heterocyclic Chem.* **29,** 895 (1992).

346. Rothemund Reaction

P. Rothemund, *J. Am. Chem. Soc.* **57,** 2010 (1935); **61,** 2912 (1939).

Preparation of *meso*-tetrasubstituted porphyrins by condensation of pyrrole with an aldehyde:



Ball *et al., J. Am. Chem. Soc.* **68,** 2278 (1946); Thomas, Martell, *ibid.* **78,** 1335 (1956). Mechanism: Badger *et al., Aust. J. Chem.* **17,** 1028 (1964); R. G. Little, *J. Heterocyclic Chem.* **18,** 833 (1981).

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347. Rubottom Oxidation

A. G. Brook, D. M. Macrae, *J. Organometal. Chem.* **77,** C19 (1974); A. Hassner *et al., J. Org. Chem.* **40,** 3427 (1975); G. M. Rubottom *et al., Tetrahedron Letters* **1974,** 4319.

Oxidation of enolsilanes with *m*-chloroperbenzoic acid (*m*-CPBA) to afford α-hydroxy ketones:

Synthetic applications: R. Gleiter *et al., J. Org. Chem.* **57,** 252 (1992); C. R. Johnson *et al., J. Am. Chem. Soc.* **114,** 9414 (1992); M. T. Crimmins *et al., ibid.* **115,** 3146 (1993).

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350. Sabatier-Senderens Reduction

P. Sabatier, J. B. Senderens, *Compt. Rend.* **128,** 1173 (1899).

Catalytic hydrogenation of organic compounds in the vapor phase by passage over hot, finely divided nickel (the oldest of all hydrogenation methods).

E. B. Maxted in *Handbuch der Katalyse* **vol. 7,** G. M. Schwab, Ed. (Vienna, 1943) p 624; H. Roth *et al.*, *Houben-Weyl* **2,** 288 (1953); G. Schiller, *ibid.* **IV/2,** 284 (1955); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) Chapter 1.

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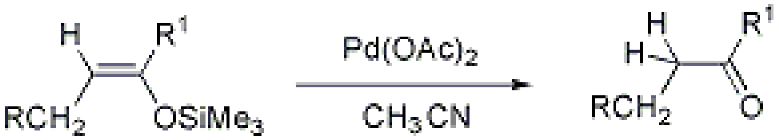
351. Saegusa Oxidation

Y. Ito *et al., J. Org. Chem.* **43,** 1011 (1978).

Conversion of silyl enol ethers into corresponding α,β-eneones using stoichiometric amounts of palladium acetate:

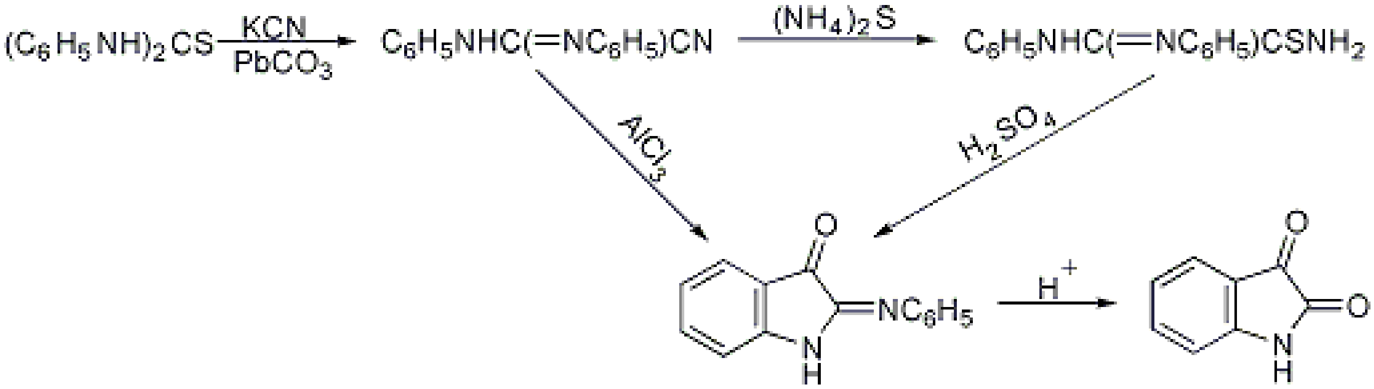


Application: M. Kim *et al., Synth. Commun.* **20,** 989 (1990). Mechanism: S. Porth *et al., Angew. Chem. Int. Ed.* **38,** 2015 (1999).

353. Sandmeyer Diphenylurea Isatin Synthesis

T. Sandmeyer, *Z. Farb. Textile Chem.* **2,** 129 (1903).

Formation of a cyanoformamidine by treatment of a symmetrical diphenylthiourea with potassium cyanide in alcohol containing lead carbonate, reduction with ammonium sulfide and ring-closure with concentrated sulfuric acid to isatin-2-anil; also formed smoothly by ring closure of the cyanoformamidine with aluminum chloride in benzene or carbon disulfide:

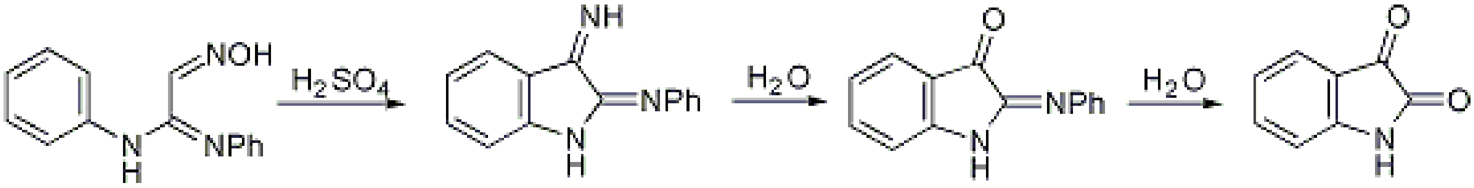


DE 115169, **DE 116563** (both 1900 to J. R. Geigy & Co.); *Friedländer* **6,** 574, 575 (1900-1902); A. Reissert, *Ber*. **37,** 3708 (1904); G. Schultz *et al., J. Prakt. Chem.* [2] **74,** 74, 76 (1906); C. Hollins, *The Synthesis of Nitrogen Ring Compounds* (London, 1924) p 102; C. S. Marvel, G. S. Hiers, *Org. Syn.* **coll. vol. I,** 327 (1943); P. L. Julian *et al.*, *Heterocyclic Compounds* **3,** 207 (1952); O. Bayer, W. Eckert, *Houben-Weyl* **7/4,** 11 (1968). *Cf.* Sandmeyer Isonitrosoacetanilide Isatin Synthesis.

354. Sandmeyer Isonitrosoacetanilide Isatin Synthesis

T. Sandmeyer, *Helv. Chim. Acta* **2,** 234 (1919).

Formation of isonitrosoacetodiphenylamidine by condensation of chloral hydrate, hydroxylamine and aniline, cyclization with concentrated sulfuric acid, and quantitative hydrolysis to isatin on dilution:



J. Martinet, P. Cousset, *Compt. Rend.* **172,** 1234 (1921); C. Hollins, *The Synthesis of Nitrogen Ring Compounds* (London, 1924) p 103; C. S. Marvel, G. S. Hiers, *Org. Syn.* **coll. vol. I,** 327 (1943); P. L. Julian *et al.*, *Heterocyclic Compounds* **3,** 208 (1952); F. E. Sheibley, J. S. McNulty, *J. Org. Chem.* **21,** 171 (1956); O. Bayer, W. Eckert, *Houben-Weyl* **7/4,** 14 (1968); S. J. Garden *et al.*, *Tetrahedron Letters* **38,** 1501 (1997). *Cf.* Sandmeyer Diphenylurea Isatin Synthesis.

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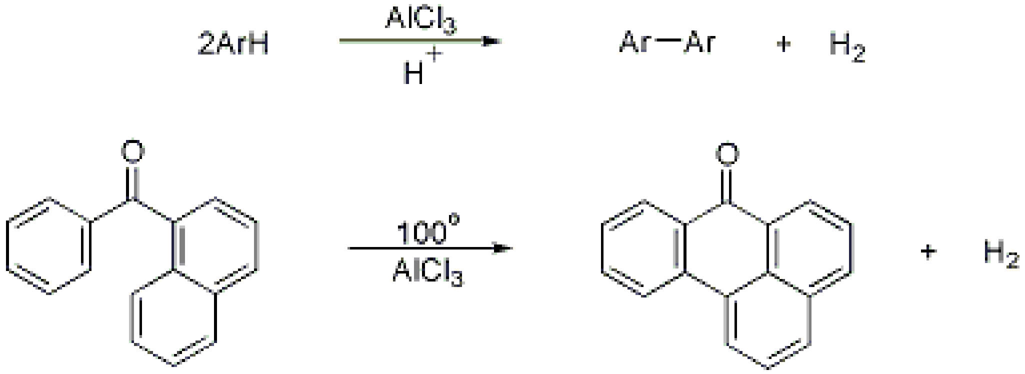
359. Scholl Reaction

R. Scholl, C. Seer, *Ann.* **394,** 111 (1912).

Coupling of aromatic molecules by treatment with Lewis acid catalysts:

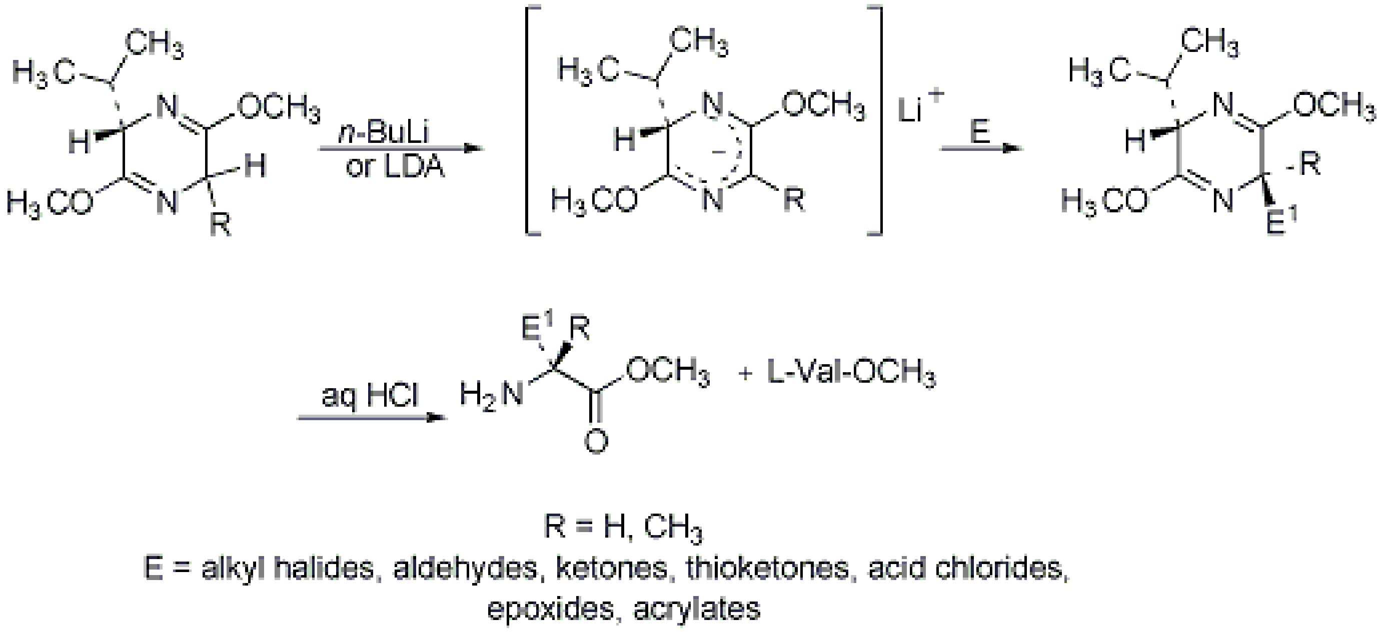


Review: C. D. Nenitzescu, A. T. Balaban in *Friedel-Crafts and Related Reactions,* **vol. 2,** part 2, G. Olah, Ed. (Wiley, New York, 1964) pp 979-1048; G. A. Clowes, *J. Chem. Soc. C* **1968,** 2519; A. C. Buchanan *et al., J. Am. Chem. Soc.* **102,** 5262 (1980).

360. Schöllkopf Bis-Lactim Amino Acid Synthesis

U. Schöllkopf *et al., Angew. Chem. Int. Ed.* **18,** 863 (1979); **20,** 798 (1981).

Asymmetric amino acid synthesis *via* diastereoselective alkylation of the lithiated bis-lactim ether (derived from L-Val and Gly or Ala) by an electrophile. Subsequent acid hydrolysis liberates L-Val-OCH_3 and the *(R)*-α-substituted amino acid ester. When the bis-lactim is generated from D-Val, the *(S)*-enantiomer forms:



Synthetic applications: S. Kotha, A. Kuki, *Chem. Commun.* **1992,** 404; M. S. Allen *et al., Synth. Commun.* **22,** 2077 (1992). Isotopic labeling: N. R. Thomas, D. Gani, *Tetrahedron* **47,** 497 (1991). *Reviews:* U. Schöllkopf, *Top. Curr. Chem.* **109,** 65-84 (1983); *idem, Pure Appl. Chem.* **55,** 1799-1806 (1983); R. M. Williams, *Synthesis of Optically Active* α-*Amino Acids* (Pergamon, New York, 1989) pp 1-33.

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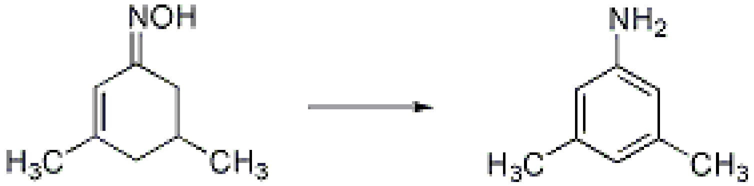
362. **Semmler-Wolff Reaction** (Wolff-Semmler Aromatization, Wolff Aromatization)

W. Semmler, *Ber.* **25,** 3352 (1892); L. Wolff, *Ann.* **322,** 351 (1902).

Rearrangement of α,β-unsaturated cyclohexenyl ketoximes into aromatic amines under acidic conditions:



Review: R. T. Conley, S. Ghosh in *Mechanisms of Molecular Migrations* **vol. 4,** B. S. Thyagarajan, Ed., (Interscience, New York, 1971) p 251; M. I. El-Sheikh, J. M. Cook, *J. Org. Chem.* **45,** 2585 (1980); Y. Tamura *et al.*, *Synthesis* **1980,** 483.

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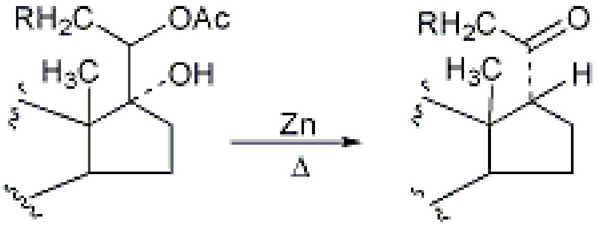
363. Serini Reaction

A. Serini *et al.*, *Ber.* **72,** 391 (1939).

Zinc-promoted rearrangement of 17-hydroxy-20-acetoxysterol derivatives into C-20 ketones; the reaction is applicable to other cyclic, as well as open-chain alcohols:



Reviews: C. W. Shoppe, *Chimia* **4,** 418 (1948); L. F. Fieser, M. Fieser, *Steroids* (Reinhold Publishing Corp., New York, 1959) p 628; N. L. Wendler in *Molecular Rearrangements* Part 2, P. de Mayo, Ed. (Wiley-Interscience, New York, 1964) p 1038; E. Ghera, *Chem. Commun.* **1968,** 1639; *J. Org. Chem.* **35,** 660 (1970).

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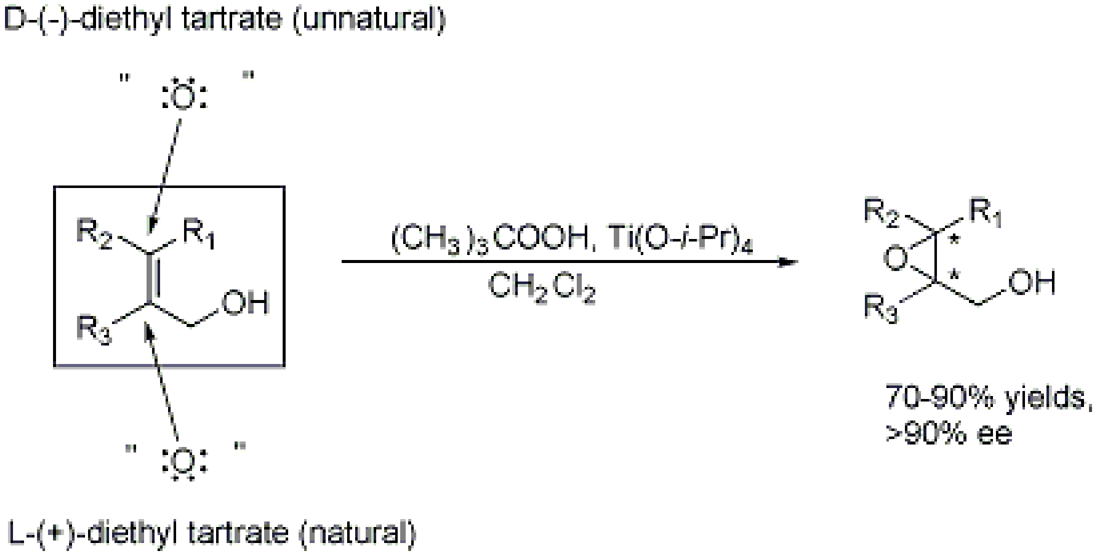
365. Sharpless Epoxidation

T. Katsuki, K. B. Sharpless, *J. Am. Chem. Soc.* **102,** 5974 (1980).

Titanium-catalyzed asymmetric epoxidation of allylic alcohols employing titanium alkoxide, an optically active tartrate ester and an alkyl hydroperoxide. A high degree of enantiomeric purity is attainable having predictable absolute stereochemistry:



Note: The asterisk at a chiral center denotes a preponderance of either the *R* or *S* configuration.

Mechanistic studies: S. S. Woodward *et al., J. Am. Chem. Soc.* **113,** 106 (1991); M. G. Finn, K. B. Sharpless, *ibid.* 113. Methods development for the synthesis of enantiopure allylic alcohols: D. C. Dittmer *et al., J. Org. Chem.* **58,** 718 (1993). Alkenylsilanols as substrates: T. H. Chan *et al., Can. J. Chem.* **71,** 60 (1993). *Reviews:* R. A. Johnson, K. B. Sharpless, *Comp. Org. Syn.* **7,** 389-436 (1991); E. Höft, *Top. Curr. Chem.* **164,** 63-77 (1993).

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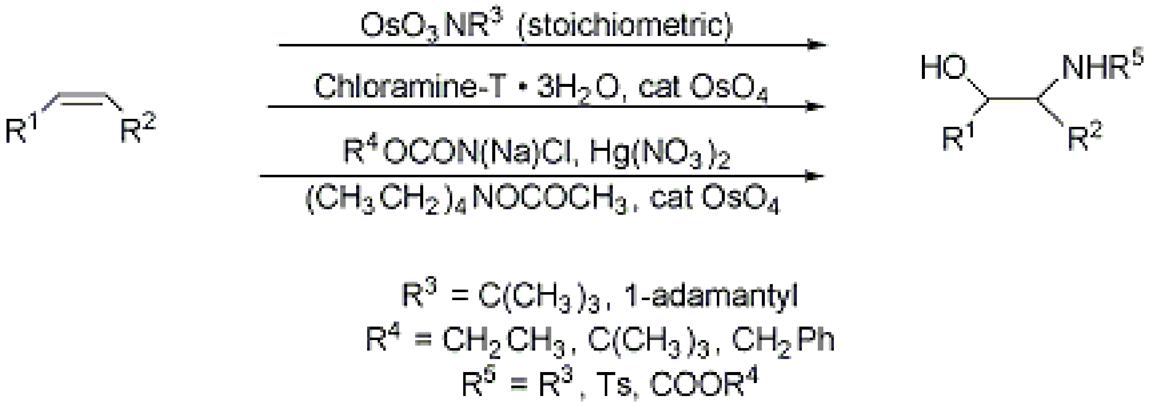
366. Sharpless Oxyamination

K. B. Sharpless *et al.*, *J. Am. Chem. Soc.* **97,** 2305 (1975).

Osmium-mediated *cis*-addition of nitrogen and oxygen moieties to mono-, di- and tri-substituted olefins to yield vicinal amino or amido alcohols:



Methods development in the context of taxol synthesis: L. Mangatal *et al.*, *Tetrahedron* **45,** 4177 (1989). Synthetic applications: S. K. Dubey, E. E. Knaus, *Can. J. Chem.* **61,** 565 (1983); M. Lemaire *et al.*, *Synlett* **1990,** 615. Brief review: *Organic Syntheses by Oxidation with Metal Compounds*, W. J. Mijs, C. R. H. I. de Jonge, Eds. (Plenum Press, New York, 1986) pp 642-645.

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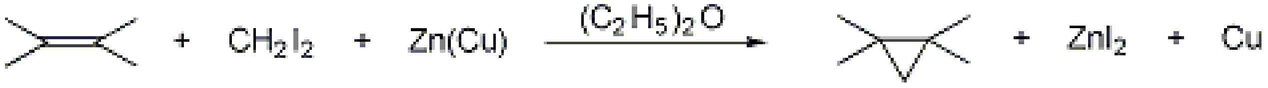
367. Simmons-Smith Reaction

H. E. Simmons, R. D. Smith, *J. Am. Chem. Soc.* **80,** 5323 (1958).

Stereospecific synthesis of cyclopropanes by treatment of olefins with methylene iodide and zinc-copper couple:

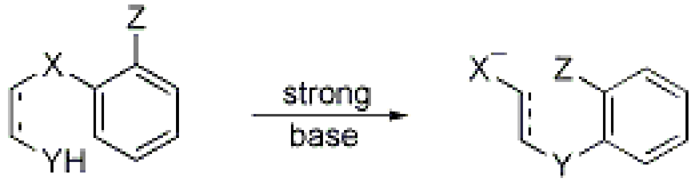


Reviews: H. E. Simmons *et al., Org. React.* **20,** 1 (1973); C. Girard, J. M. Conia, *J. Chem. Res. (S)* **1978,** 182; W. Ratier *et al., ibid.* 179; A. Sele *et al., Helv. Chim. Acta* **62,** 866 (1979); J. Joska, J. Fajkos, *Coll. Czech. Chem. Commun.* **46,** 2751 (1981).

371. **Smiles Rearrangement;** Truce-Smiles Rearrangement

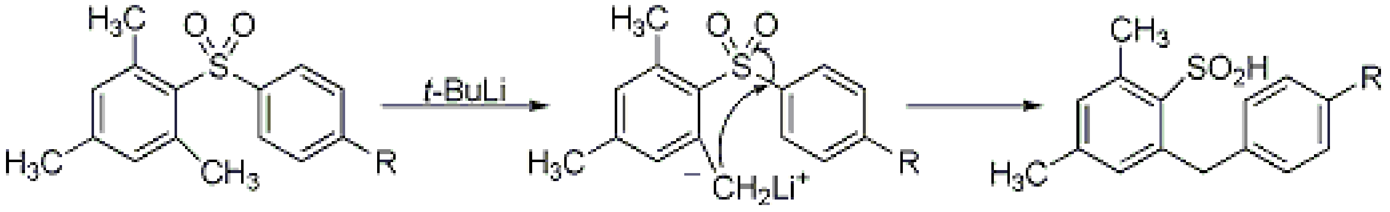
A. A. Levi *et al., J. Chem. Soc.* **1931,** 3264; W. J. Evans, S. Smiles, *ibid.* **1935,** 181; **1936,** 329.

Intramolecular nucleophilic aromatic substitution in alkaline solution resulting in the migration of an aromatic system from one heteroatom to another. The two-carbon unit joining X and Y is usually part of an aromatic ring but may also be aliphatic:



X = S, SO, SO_2, O, COO YH = OH, NHR, SH, CH_2R, CONHR
Z = NO_2, SO_2R

The conversion of *o*-methyldiaryl sulfones to *o*-benzylbenzenesulfinic acids is referred to as the **Truce-Smiles rearrangement:** W. E. Truce *et al., J. Am. Chem. Soc.* **80,** 3625 (1958); G. P. Crowther, C. R. Hauser, *J. Org. Chem.* **33,** 2228 (1968).



Early reviews: J. F. Bunnett, R. E. Zahler, *Chem. Rev.* **49,** 362 (1951); H. J. Shine, *Aromatic Rearrangements* (Elsevier, New York, 1967) pp 307-316; W. E. Truce *et al., Org. React.* **18,** 99-215 (1970). Conversion of phenols to anilines: I. G. C. Coutts, M. R. Southcott, *J. Chem. Soc. Perkin Trans. I* **1990,** 767. Kinetic study: K. Bowden, P. R. Williams, *J. Chem. Soc. Perkins Trans. II* **1991,** 215. Methods development for aliphatic substrates: M. Sako *et al., Chem. Pharm. Bull.* **42,** 806 (1994). Application to the synthesis of phenothiazines: S. K. Mukherjee *et al., Pharmazie* **49,** 453 (1994); J. Mukesh *et al., ibid.* 689.

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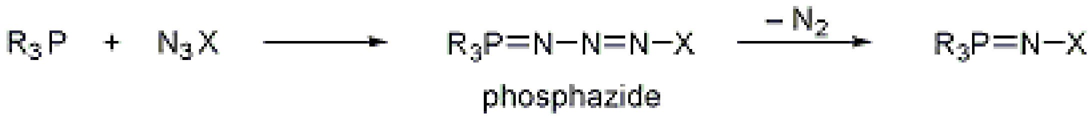
375. Staudinger Reaction

H. Staudinger, J. Meyer, *Helv. Chim. Acta* **2,** 635 (1919).

Synthesis of phosphazo compounds by the reaction of tertiary phosphines with organic azides:



Review: Y. G. Gololobov *et al., Tetrahedron* **37,** 437 (1981). Synthetic applications: M. Taillefer *et al., Chem. Commun.* **6,** 565 (1999); M. D. Velasco *et al., Tetrahedron* **56,** 4079 (2000); P. Vanek, P. Klán, *Synth. Commun.* **30,** 1503 (2000). Cell surface engineering: E. Saxon, C. R. Bertozzi, *Science* **287,** 2007 (2000).

378. Stieglitz Rearrangement

J. Stieglitz, P. N. Leech, *Ber.* **46,** 2147 (1913); *J. Am. Chem. Soc.* **36,** 272 (1914).

Rearrangement of trityl hydroxylamines to Schiff bases on treatment with phosphorus pentachloride:

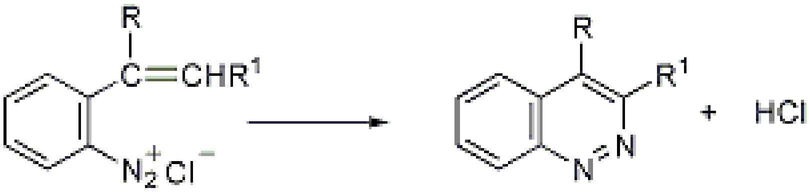
$$Ar_3CNHOH \xrightarrow{PCl_5} Ar_2C{=}NAr + POCl_3 + 2HCl$$

Reviews: P. A. S. Smith in *Molecular Rearrangements* Part 1, P. de Mayo, Ed. (Wiley-Interscience, New York, 1963) p 479; *Trans. N.Y. Acad. Sci.* **31,** 504 (1969); N. Koga, J. P. Anselme, *Tetrahedron Letters* **1969,** 4773; R. V. Hoffman, D. J. Poelker, *J. Org. Chem.* **44,** 2364 (1979).

427. Widman-Stoermer Synthesis

O. Widman, *Ber*. **17,** 722 (1884); R. Stoermer, H. Fincke, *Ber*. **42,** 3115 (1909).

Synthesis of cinnolines by cyclization of diazotized *o*-aminoarylethylenes at room temperature:



N. J. Leonard, *Chem. Rev*. **37,** 270 (1945); J. C. E. Simpson, *Condensed Pyridazine and Pyrazine Rings* (New York, 1953) p 6; T. L. Jacobs, *Heterocyclic Compounds* **6,** 137 (1957); G. R. Ramage, J. K. Landquist, *Chemistry of Carbon Compounds* **IVB,** 1217 (1959). *Cf.* von Richter (Cinnoline) Synthesis.

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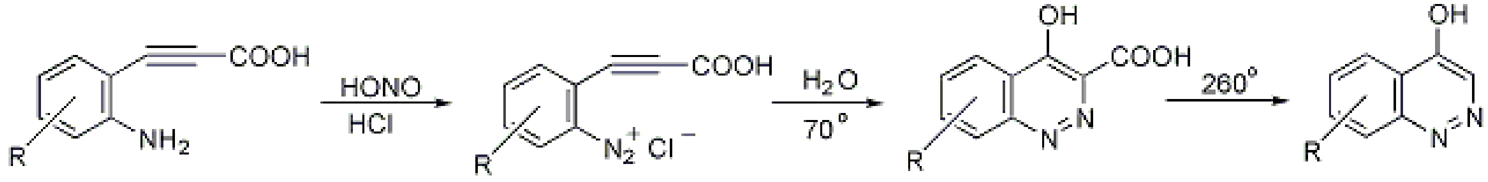
412. von Richter (Cinnoline) Synthesis

V. von Richter, *Ber.* **16,** 677 (1883).

Formation of cinnoline derivatives by diazotization of *o*-aminoarylpropiolic acids or *o*-aminoarylacetylenes followed by hydration and cyclization:



M. Busch, M. Klett, *Ber.* **25,** 2847 (1892); N. J. Leonard, *Chem. Rev.* **37,** 270 (1945); K. Schofield, J. C. E. Simpson, *J. Chem. Soc.* **1945,** 512, K. Schofield, T. Swain, *ibid.* **1949,** 2393; J. C. E. Simpson, *Condensed Pyridazine and Pyrazine Rings* (New York, 1953) p 16; G. R. Ramage, J. K. Landquist, *Chemistry of Carbon Compounds* **IVB,** 1217 (1959); G. T. Rogere *et al.*, *Tetrahedron Letters* **9,** 1028 (1968); A. C. Ellis *et al.*, *J. Chem. Soc. Chem. Comm.* **1977,** 152. *Cf.* Widman-Stoermer Synthesis.

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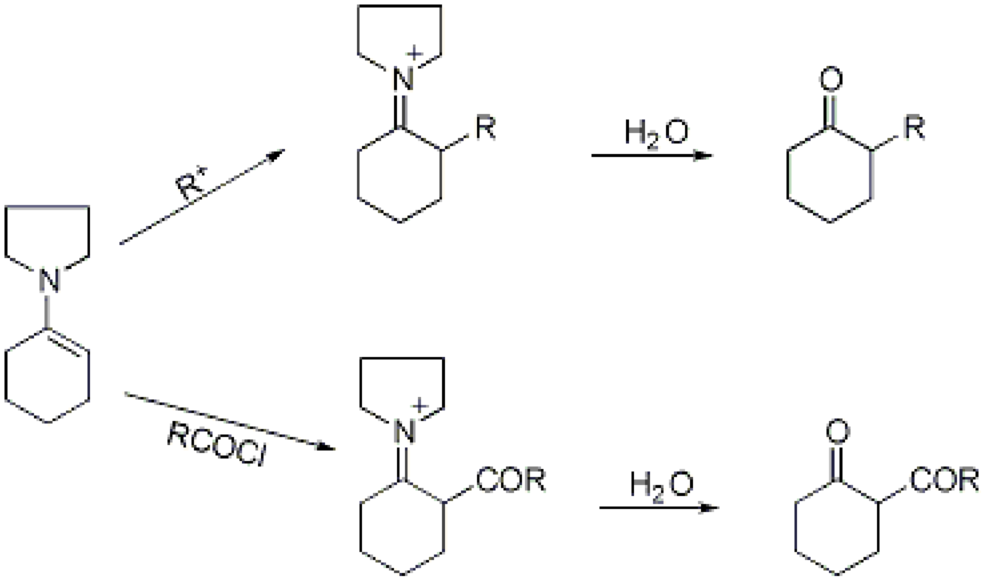
382. Stork Enamine Reaction

G. Stork *et al., J. Am. Chem. Soc.* **76,** 2029 (1954); G. Stork, H. Landesman, *ibid.* **78,** 5128 (1956).

Synthesis of α-alkyl or α-acyl carbonyl compounds from enamines and alkyl or acyl halides:



Reviews: J. Szmuszkovicz, *Adv. Org. Chem.* **4,** 1 (1963); A. G. Cook, Ed., *Enamines* (Marcel Dekker, New York, 1969); H. O. House, *Modern Synthetic Reactions* (W. A. Benjamin, Menlo Park, California, 2nd ed., 1972) pp 570-580, 766-772; S. F. Dyke, *Chemistry of Enamines* (Cambridge University Press, New York, 1973); P. W. Hickmott, *Tetrahedron* **38,** 1975 (1982). Synthetic applications: C. F. Bridge, D. O'Hagan, *J. Fluorine Chem.* **82,** 21 (1997); J. J. Li *et al., Tetrahedron Letters* **39,** 6111 (1998).

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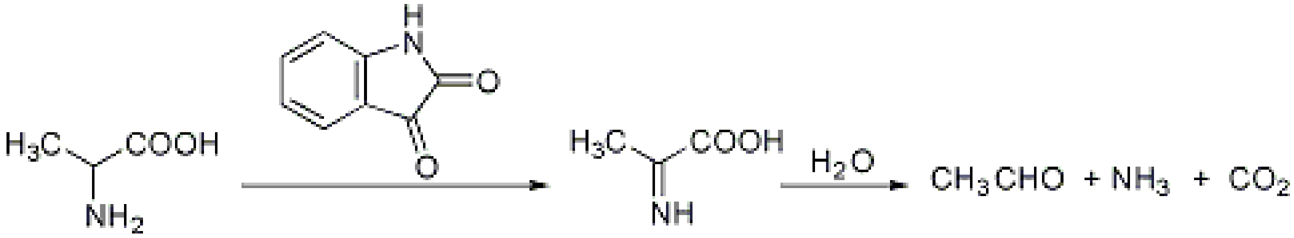
384. Strecker Degradation

A. Strecker, *Ann.* **123,** 363 (1862).

Interaction of an α-amino acid with a carbonyl compound in aqueous solution or suspension to give carbon dioxide and an aldehyde or ketone containing one less carbon atom. Inorganic oxidizing agents can also be used to bring about the reaction:



Early review: A. Schönberg, R. Moubacher, *Chem. Rev.* **50,** 261 (1952). Photo-promoted oxidation: Y. Ogata *et al., Bull. Chem. Soc. Japan* **54,** 2057 (1981). Synthetic studies: A. Schönberg *et al., J. Chem. Soc.* **1948,** 176; C.-T. Ho, G. J. Hartman, *J. Agric. Food Chem.* **1982,** 793; A. F. Ghiron *et al., ibid.* **36,** 677 (1988); J. Koch *et al., Carbohydr. Res.* **313,** 117 (1998).

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385. Strecker Sulfite Alkylation

A. Strecker, *Ann.* **148,** 90 (1868).

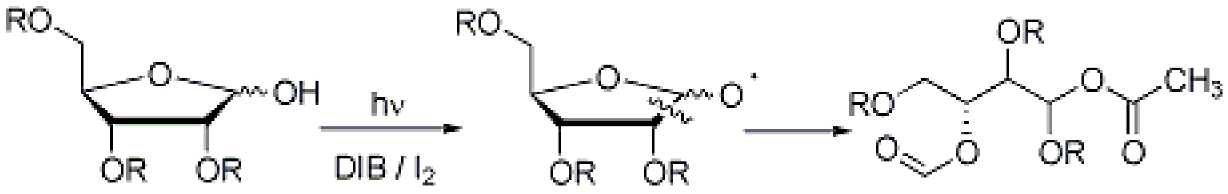
Formation of alkyl sulfonates by reaction of alkyl halides with alkali or ammonium sulfites in aqueous solution in the presence of iodide:

A. Collmann, *ibid.* 101; W. Hemilian, *ibid.* **168,** 145 (1873); *Ber.* **6,** 562 (1873); **CH 105845**; **CH 104907** (both 1925); F. C. Wagner, E. E. Reid, *J. Am. Chem. Soc.* **53,** 3409 (1931); C. Weygand, *Organic Preparations* (New York, 1945) p 306; M. Quaedvlieg, *Houben-Weyl* **9,** 372 (1955).

386. **Suarez Reaction** (Suarez Fragmentation)

J. I. Concepion *et al., Tetrahedron Letters* **25,** 1953 (1984); *eidem, J. Org. Chem.* **51,** 402 (1986).

Photoinduced conversion of hydroxyl-containing substrates with hypervalent iodine I(III) I_2 to the corresponding oxygen-centered radical:



DIB = (diacetoxyiodo)benzene

P. De Armas *et al., Angew. Chem. Int. Ed.* **31,** 772 (1992). Mechanistic studies: J. L. Courtneidge *et al., Tetrahedron Letters* **35,** 1003 (1994); T. Muraki *et al., J. Chem. Soc. Perkin Trans. I* **1999,** 1713. Synthetic applications: C. M. Hayward *et al., Tetrahedron Letters* **34,** 3989 (1993); A. Kittaka *et al., Tetrahedron* **55,** 5319 (1999).

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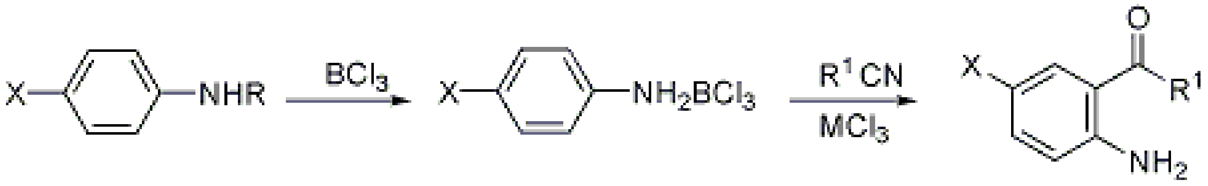
387. Sugasawa Reaction

T. Sugasawa *et al., J. Am. Chem. Soc.* **100,** 4842 (1978); M. Adachi *et al., Chem. Pharm. Bull.* **33,** 1826 (1985).

Ortho acylation of anilines by nitriles in the presence of BCl_3 and an auxillary Lewis acid:



Mechanistic study: A. W. Douglas *et al., Tetrahedron Letters* **35,** 6807 (1994). Synthetic application: J. N. Houpis *et al., ibid.* 6811.

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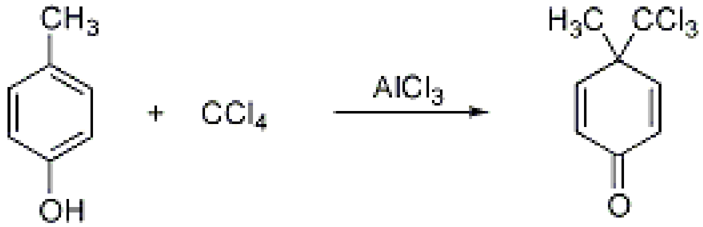
446. Zincke-Suhl Reaction

T. Zincke, R. Suhl, *Ber.* **39,** 4148 (1906).

Phenol-dienone rearrangement of *p*-cresols by addition of carbon tetrachloride in the presence of aluminum chloride with formation of 4-methyl-4-trichloromethylcyclohexa-2,5-dienone:



M. S. Newman, A. G. Pinkus, *J. Org. Chem.* **19,** 978, 985, 992, 997 (1954); M. S. Newman, L. L. Wood, Jr., *J. Am. Chem. Soc.* **81,** 6450 (1959); G. A. Olah, *Friedel-Crafts and Related Reactions* **vol. I** (Interscience, New York, 1963) p 128.

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389. Swarts Reaction

F. Swartx, *Bull. Acad. Roy. Belg.* **24,** 309 (1892).

Fluorination of organic polyhalides with antimony trifluoride (or zinc and mercury fluorides) in the presence of a trace of a pentavalent antimony salt:

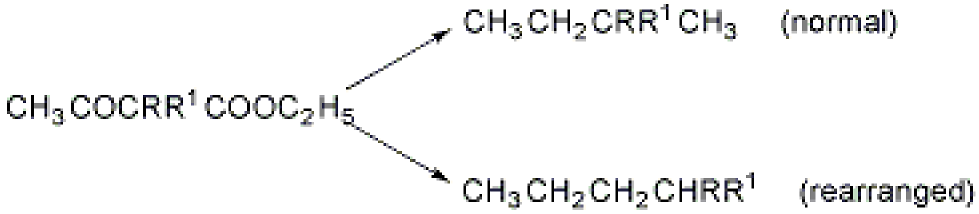
$$\mathrm{ClHC{=}CClCHCl_2} \quad + \quad \mathrm{SbF_3} \quad \xrightarrow{\mathrm{SbCl_5}} \quad \mathrm{ClHC{=}CClCF_3} \quad + \quad \mathrm{SbCl_3}$$

A. L. Henne, *Org. React.* **2,** 49 (1944); M. Hudlicky, *Chemistry of Organic Fluorine Compounds* (MacMillan, New York, 1962) pp 93-98.

391. Tafel Rearrangement

J. Tafel, H. Hahl, *Ber.* **40,** 3312 (1907).

Rearrangement of the carbon skeleton of substituted acetoacetic esters to hydrocarbons with the same number of carbon atoms by electrolytic reduction at a lead cathode in alcoholic sulfuric acid:



J. Tafel, W. Jürgen, *ibid.* **42,** 2548 (1909); J. Tafel, *ibid.* **45,** 437 (1912); C. J. Brockman, *Electro-organic Chemistry* (New York, 1926) p 321; H. Stenzl, F. Fichter, *Helv. Chim. Acta* **17,** 669 (1934); **19,** 392 (1936); **20,** 846 (1937); F. Asinger, H. H. Vogel, *Houben-Weyl* **5/1a,** 280, 471 (1970).

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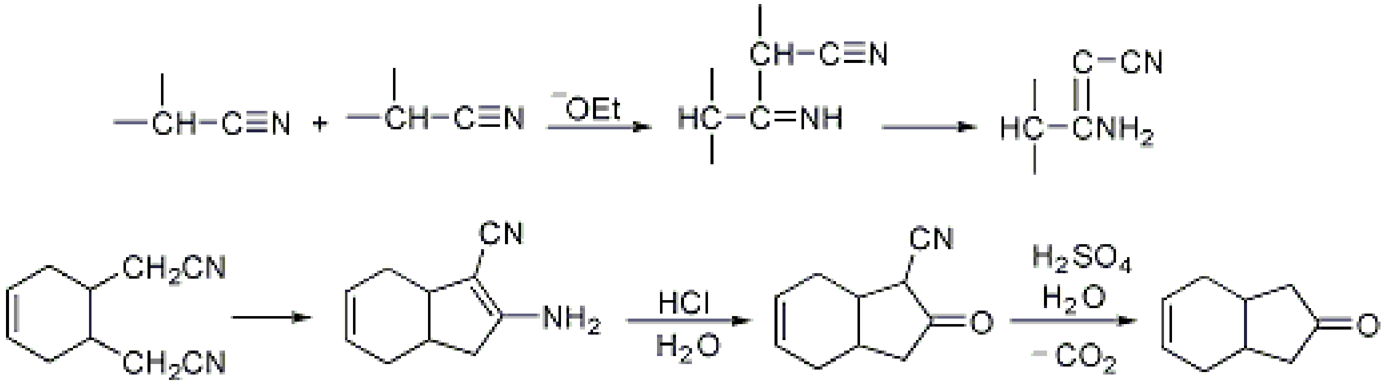
394. Thorpe Reaction

H. Baron, *et al., J. Chem. Soc.* **85,** 1726 (1904); K. Ziegler *et al., Ann.* **504,** 94 (1933).

Base-catalyzed self-condensation of nitriles to yield imines which tautomerize to enamines:



Reviews: J. P. Schaefer, J. J. Bloomfield, *Org. React.* **15,** 1 (1967); H. O. House, *Modern Synthetic Reactions* (W. Benjamin, Menlo Park, California, 2nd ed., 1972) p 742; E. C. Taylor, A. McKillop, *Chemistry of Enaminonitriles and o-Aminonitriles* (Wiley-Interscience, N.Y., 1970) pp 1-58; *eidem, Advan. Org. Chem.* **7,** 1 (1970). *Cf.* Ziegler Method.

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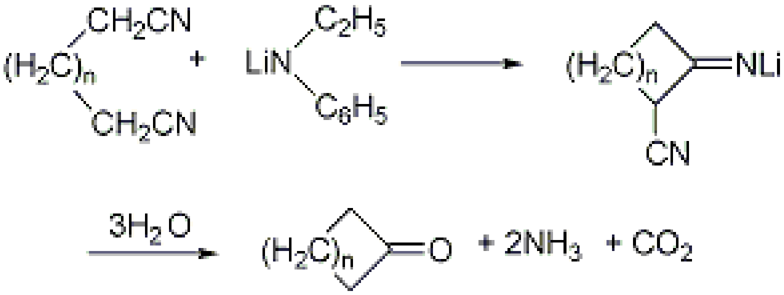
441. **Ziegler Method** (Thorpe-Ziegler Method)

K. Ziegler *et al., Ann.* **504,** 94 (1933).

Cyclization of dinitriles at high dilution in dialkyl ether in the presence of ether-soluble metal alkylanilide and hydrolysis of the resultant imino-nitrile with formation of macrocyclic ketones (yield is dependent on ring size):

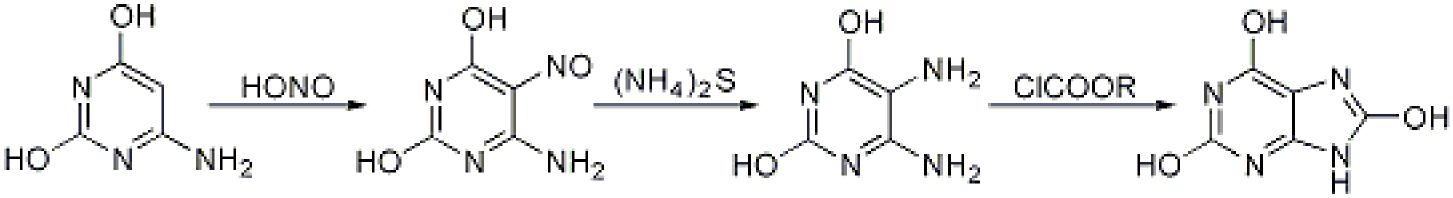


K. Ziegler *et al., ibid.* **511,** 1 (1933) **512,** 164; **513,** 43 (1934); *idem, Ber.* **67,** 139 (1934); *idem, et al., Ann.* **528,** 114, 143 (1937); R. C. Fuson in *Organic Chemistry* **vol. I,** H. Gilman, Ed. (New York, 1943) p 89; V. Migrdichian, *The Chemistry of Organic Cyanogen Compounds* (New York, 1947) p 288; K. Ziegler, *Houben-Weyl* **4/2,** 758 (1955). *Review:* J. P. Schaefer, J. J. Bloomfield, *Org. React.* **15,** 1-203 (1967). *Cf.* Thorpe Reaction.

398. Traube Purine Synthesis

W. Traube, *Ber.* **33,** 1371, 3035 (1900).

Preparation of 4,5-diaminopyrimidines by introduction of the amino group into the 5-position of 4-amino-6-hydroxy- or 4,6-diaminopyrimidines by nitrosation and ammonium sulfide reduction, followed by ring closure with formic acid or chlorocarbonic ester:



J. H. Davidson, *The Nucleic Acids* **I** (New York, 1955) p 131; A. R. Katritzky, *Quart. Rev.* **10,** 397 (1956); *idem, Rev. Pure Appl. Chem.* **11,** 178 (1961); J. H. Lister, *Purines* (Wiley, New York, 1971) pp 31-90.

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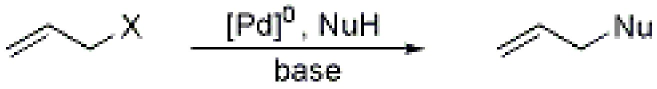
399. **Trost Allylation** (Tsuji-Trost Reaction)

J. Tsuji *et al., Tetrahedron Letters* **1965,** 4387; B. M. Trost, T. J. Fullerton, *J. Am. Chem. Soc.* **95,** 292 (1973).

Palladium-catalyzed allylation of nucleophiles proceeding in an SN2 or SN2′ fashion depending on the catalyst, nucleophile, and substituents on the substrate:



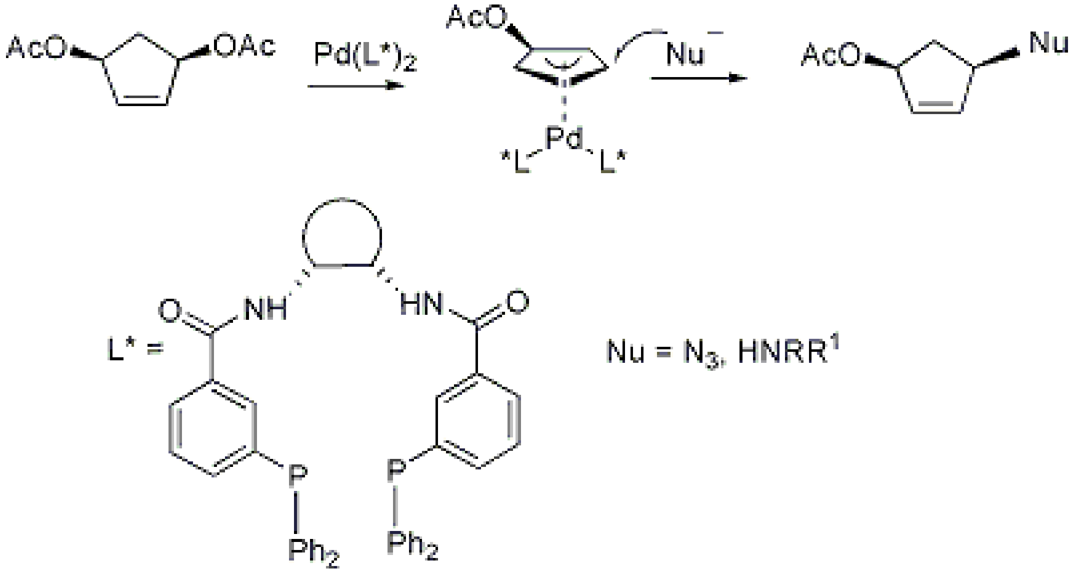
NuH = malonates, β-diketones, β-keto esters, enamines, β-keto sulfones, bis-sulfones
X = Br, Cl, OCOOR, SO_2R, OCOR, $OCONR_2$, $OPO(OR)_2$, NO_2
$[Pd]^0$ = $Pd(PPh_3)_4$, $Pd_2(dba)_3 \cdot CHCl_3$, + PPh_3, $Pd(OCOCH_3)_2$ + PPh_3
base = NaH, if necessary

Scope and limitations under neutral conditions: J. Tsuji *et al., J. Org. Chem.* **50,** 1523 (1985); in biphasic media: C. de Bellefon *et al., J. Molec. Catal. A.* **145,** 121 (1999). Application to the synthesis of polyprenoids: E. Keinan, D. Eren, *Pure Appl. Chem.* **60,** 89 (1988). Review of intramolecular applications: B. M. Trost, *Adv. Chem. Ser.* **230,** 463-478 (1992). *Review:* C. G. Frost *et al., Tetrahedron Asymmetry* **3,** 1089-1122 (1992).

400. Trost Desymmetrization

B. M. Trost *et al., J. Am. Chem. Soc.* **114,** 9333 (1992).

Formation of an enantiomerically pure, azide or amine containing, five or six membered ring by a pallidium catalyzed desymmetrization using a nitrogen nucleophile, where the palladium complex is derived from a chiral ligand and π-allylpalladium chloride:



S. R. Pulley, B. M. Trost, *J. Am. Chem. Soc.* **117,** 10143 (1995).

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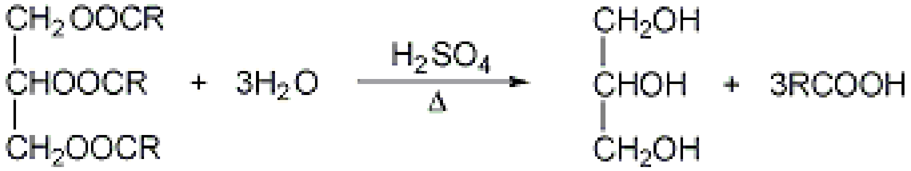
402. Twitchell Process

E. Twitchell, **US 601603; US 628503** (1898); **DE 365522; DE 385074.**

Commercial process for splitting fats to glycerol and fatty acids by heating the sulfuric-acid-washed fat 20-48 hours in an open tank with steam in a mixture of 25-50% water, 0.5% sulfuric acid and 0.75-1.25% Twitchell reagent (sulfonated petroleum products):



E. Twitchell, *J. Am. Chem. Soc.* **22,** 22 (1900); **28,** 196 (1906); J. W. Lawrie, *Glycerol and the Glycols* (New York, 1928) p 32; R. B. Trusler, *J. Oil & Fat Ind.* **8,** 141 (1931); A. F. Bailey, *Industrial Oil and Fat Products* (New York, 1945) p 668; C. J. Marsel, H. D. Allen, *Chem. Eng.* **54**(6), 104 (1947); V. Mills, H. K. McClain, *Ind. Eng. Chem.* **41,** 1982 (1949); L. Lascaray, *J. Am. Oil Chemists Soc.* **29,** 362 (1952); *Faith, Keyes & Clark's Industrial Chemicals* (Wiley-Interscience, New York, 4th ed., 1975) p 431.

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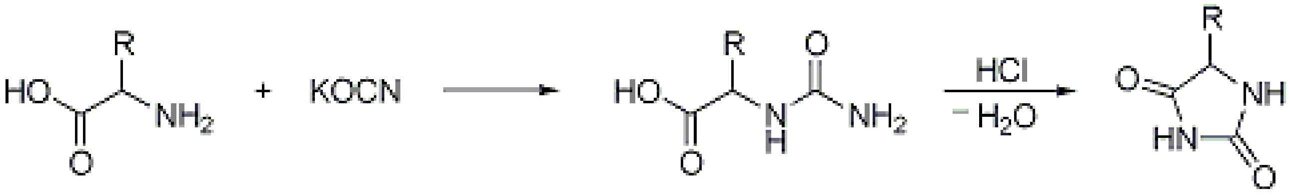
406. Urech Hydantoin Synthesis

F. Urech, *Ann.* **165,** 99 (1873).

Formation of hydantoins from α-amino acids by treatment with potassium cyanate in aqueous solution and heating the salt of the intermediate hydantoic acid with 25% hydrochloric acid:



H. D. Dakin, *Am. Chem. J.* **44,** 48 (1910); T. B. Johnson, *J. Am. Chem. Soc.* **35,** 780 (1913); W. J. Boyd, W. Robson, *Biochem. J.* **29,** 542, 546, 2256 (1935); E. Ware, *Chem. Rev.* **46,** 407 (1950); M. Sainsbury, R. S. Theobald, *Rodd's Chemistry of Carbon Compounds* **IVC,** 185 (1986).

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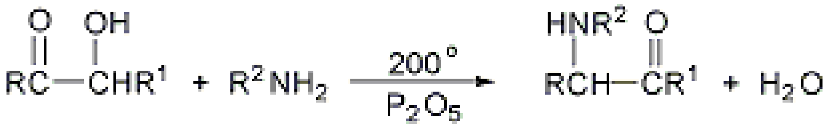
408. Voight Amination

K. Voight, *J. Prakt. Chem.* [2] **34,** 1 (1886).

Amination of benzoins with amines in the presence of phosphorus pentoxide or hydrochloric acid:



H. H. Strain, *J. Am. Chem. Soc.* **51,** 269 (1929); R. M. Cowper, T. S. Stevens, *J. Chem. Soc.* **1940,** 347; P. L. Julian *et al., J. Am. Chem. Soc.* **67,** 1203 (1945); R. E. Lutz *et al., ibid.* **70,** 2016 (1948); I. A. Kaye *et al., ibid.* **75,** 746 (1953); J. Iwao *et al., J. Pharm. Soc. Japan* **74,** 551 (1954); R. E. Lutz, J. W. Baker, *J. Org. Chem.* **21,** 49 (1956).

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410. von Braun Amide Degradation

H. von Pechmann, *Ber.* **33,** 611 (1900); J. von Braun, *ibid.* **37,** 3210 (1904).

$$RCONHR^1 \xrightarrow{PCl_5} RCN + R^1Cl$$

Mechanistic study: B. A. Phillips *et al.*, *Tetrahedron* **29,** 3309 (1973). Application to *N*-*t*-butylamides: R. B. Perni, G. W. Gribble, *Org. Prep. Proced. Int.* **15,** 297 (1983).

411. von Braun Reaction

J. von Braun, *Ber.* **40,** 3914 (1907); **42,** 2219 (1909); **44,** 1250 (1911).

Reaction of tertiary amines with cyanogen bromide to form disubstituted cyanamides and an alkyl halide:

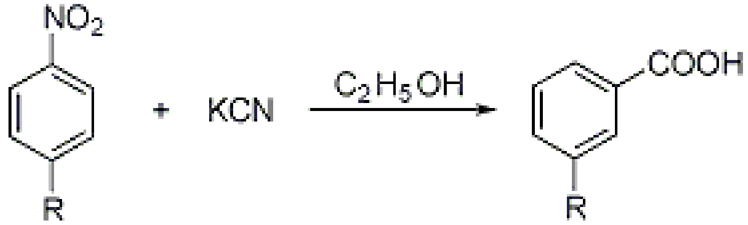
$$R_2NR^1 + BrCN \longrightarrow R_2NCN + R^1Br$$

Mechanistic correlation with Ritter, Bischler-Napieralski, Beckmann and Schmidt reactions, *q.q.v.:* G. Fodor, S. Nagubandi, *Tetrahedron* **36,** 1279 (1980). Synthetic applications: S. Siddiqui *et al., Z. Naturforsch.* **37b,** 1481 (1982); *idem et al., Pakistan J. Sci. Ind. Res.* **30,** 163 (1987). *Reviews:* H. A. Hageman, *Org. React.* **7,** 198-262 (1953); J. H. Cooley, E. J. Evain, *Synthesis* **1989,** 1-7.

413. von Richter Rearrangement

V. von Richter, *Ber.* **4,** 21, 459, 553 (1871).

Carboxylation of *para*- or *meta*-substituted aromatic nitro compounds with cyanate at 120-270°. The carboxyl group enters with cine substitution in a position *ortho* to the eliminated nitro group:



J. F. Bunnett, *Quart. Rev.* **12,** 15 (1958); D. Samuel, *J. Chem. Soc.* **1960,** 1318; J. Sauer, R. Huisgen, *Angew. Chem.* **72,** 314 (1960); M. Rosenblum, *J. Am. Chem. Soc.* **82,** 3796 (1960); E. Cullen, P. L'Ecuyer, *Can. J. Chem.* **39,** 144, 154, 382, 862 (1961); E. F. Ullman, E. A. Bartkus, *Chem. & Ind. (London)* **1962,** 93; K. M. Ibne-Rasa, E. Koubak, *J. Org. Chem.* **28,** 3240 (1963); G. T. Rogers, T. L. V. Ulbricht, *Tetrahedron Letters* **9,** 1028 (1968); A. C. Ellis, I. D. Rae, *Chem. Commun.* **1977,** 152; E. Tomitori *et al.*, *Yakugaku Zasshi* **103,** 601 (1983).

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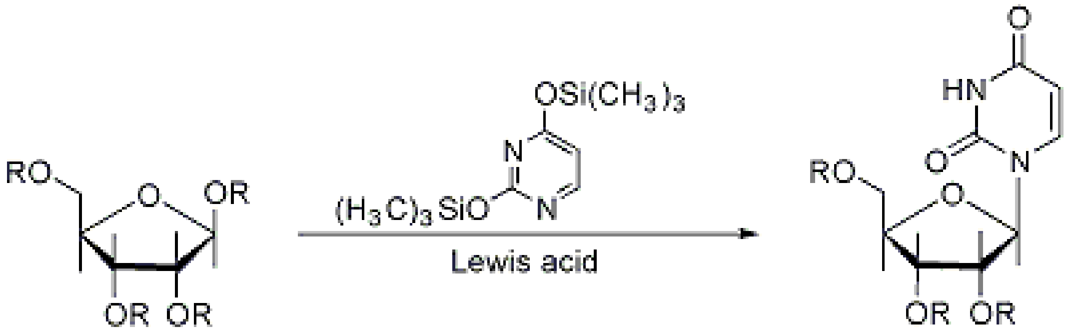
414. Vorbrüggen Glycosylation

U. Niedballa, H. Vorbrüggen, *Angew. Chem. Int. Ed.* **9,** 461 (1970).

The reaction of silylated heterocyclic bases with peracylated sugars in the presence of Lewis acids to yield natural β-nucleosides. If the sugar lacks a 2α-acyloxy substituent, an anomeric mixture forms:



R = $COCH_3$, COPh
Lewis acid = $BF_3 \cdot O(CH_2CH_3)_2$, $SnCl_4$, $(CH_3)_3SiOSO_2CF_3$, $(CH_3)_3SiClO_4$, $TiCl_4$, $AlCl_3$

Scope and limitations: H. Vorbrüggen *et al., Ber.* **114,** 1234 (1981). Mechanistic study: H. Vorbrüggen, G. Höfle, *ibid.* 1256. Synthetic applications: U. Niedballa, H. Vorbrüggen, *J. Org. Chem.* **39,** 3654, 3660, 3664, 3668, 3672 (1974); R. O. Dempcy, E. B. Skibo, *ibid.* **56,** 776 (1991); S. H. Kawai, G. Just, *Nucleosides Nucleotides* **10,** 1485 (1991). *Cf.* Hilbert-Johnson Reaction.

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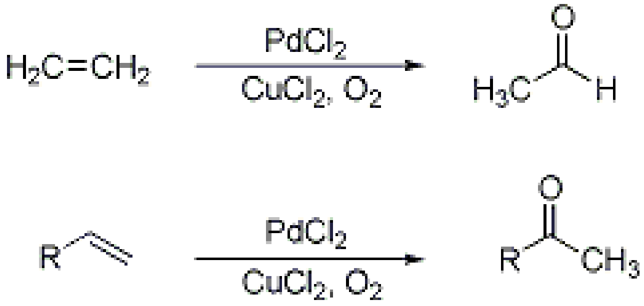
415. Wacker Oxidation

J. Smidt *et al.*, *Angew. Chem. Int. Ed.* **1,** 176 (1959).

The oxidation of ethylene to acetaldehyde employing palladium chloride and cupric chloride as catalysts and molecular oxygen as oxidant. The reaction has been extensively developed for the oxidation of terminal alkenes to methyl ketones:



Application to hydroxy-α,β-unsaturated esters: S. X. Auclair *et al.*, *Tetrahedron Letters* **33,** 7739 (1992). Use of a multicomponent catalytic system: E. Monflier *et al.*, *ibid.* **36,** 387 (1995). Synthetic applications: M. Romero *et al.*, *ibid.* **35,** 3255 (1994); L. A. Paquette, X. Wang, *J. Org. Chem.* **59,** 2052 (1994). *Reviews:* L. S. Hegedus, *Comp. Org. Syn.* **4,** 552-559 (1991); J. Tsuji, *ibid.* **6,** 449-468.

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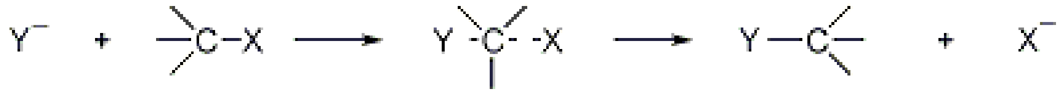
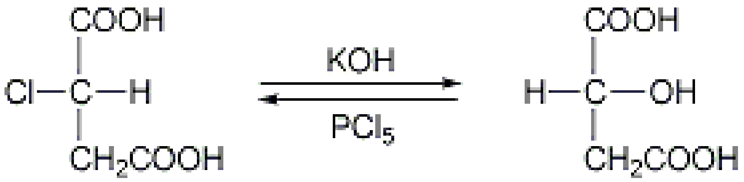
418. Walden Inversion

P. Walden, *Ber.* **28,** 1287, 2766 (1895).

Inversion of configuration of a chiral center in bimolecular nucleophilic substitution (SN2) reactions:





H. A. Bent, *Chem. Rev.* **68,** 587 (1968); D. P. G. Harmon, *J. Chem. Ed.* **47,** 398 (1970); L. Kryger *et al.*, *Acta Chem. Scand.* **26,** 2339, 2349 (1972); C. W. Shoppee, J. Nemorin, *J. Chem. Soc. Perkin Trans. I* **1973,** 542; K.-C. To *et al.*, *J. Chem. Phys.* **74,** 1499 (1981).

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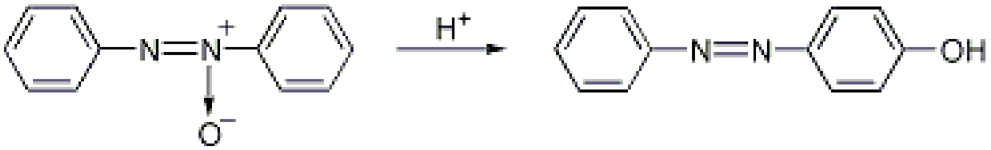
419. Wallach Rearrangement

O. Wallach, L. Belli, *Ber.* **13,** 525 (1880).

Acid-catalyzed rearrangement of azoxybenzenes to *p*-hydroxyazobenzenes:



Reviews: K. H. Schündehütte, *Houben-Weyl* **10/3,** 771-773 (1965); E. Buncel in *Mechanisms of Molecular Migrations* **vol. 1,** B. S. Thyagarajan, Ed. (Interscience, New York, 1968) p 61; R. A. Cox, E. Buncel in *The Chemistry of Hydrazo, Azo and Azoxy Groups*, pt. 2, S. Patai, Ed. (Wiley, New York, 1975) pp 808-837; J. Yamamoto *et al.*, *Tetrahedron* **36,** 3177 (1980).

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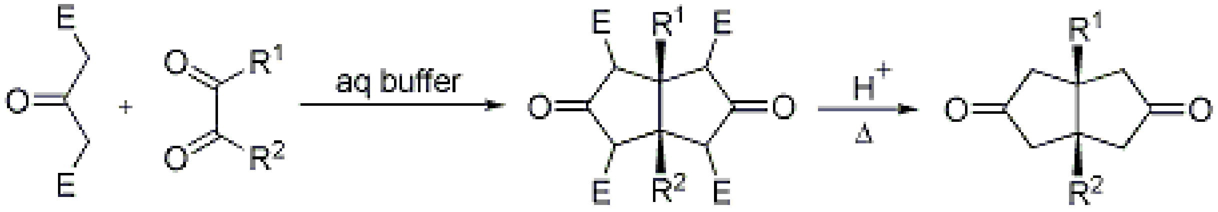
421. Weiss Reaction

U. Weiss, J. M. Edwards, *Tetrahedron Letters* **1968,** 4885.

Reaction of 1,2-dicarbonyl compounds with 3-oxoglutarates to yield *cis*-bicyclo[3.3.0] octane-3,7-dione or [n.3.3]propellanedione (n > 2) tetracarboxylates. Subsequent acid-catalyzed hydrolysis and decarboxylation yield the respective 2,4,6,8-unsubstituted diones:



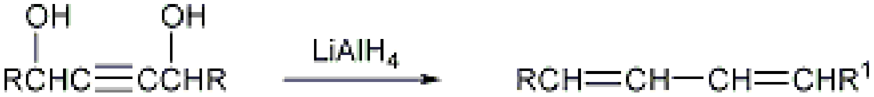
$E = COOCH_3$; R^1 or R^2 = H, alkyl, aryl or $R^1—R^2 = (CH_2)_n$, $n > 2$

Experimental procedure: S. H. Bertz *et al., Org. Syn.* **coll. vol. VII,** 50 (1990). Review of synthetic applications: A. K. Gupta *et al.*, *Tetrahedron* **47,** 3665-3710 (1991). *Review:* H.-U. Reissig, “The Weiss Reaction” in *Organic Synthesis Highlights,* J. Mulzer *et al.*, Eds. (VCH, New York, 1991) pp 121-125.

425. Whiting Reaction

P. Nayler, M. C. Whiting, *J. Chem. Soc.* **1954,** 4006.

Alkynediols are reduced by lithium aluminum hydride in ether or tertiary amines to dienes:



R. A. Raphael, *Acetylene Compounds in Organic Synthesis* (New York, 1955) p 114; O. Isler, *et al.*, *Helv. Chim. Acta* **39,** 454 (1956); L. F. Fieser, M. Fieser, *Reagents for Organic Synthesis* (New York, 1967) p 385.

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429. Williamson Synthesis

A. W. Williamson, *J. Chem. Soc.* **4,** 229 (1852).

Synthesis of ethers by alkylation of alkoxides with alkyl halides or alkyl sulfates:

$$RO^- \; Na^+ + R^1X \longrightarrow ROR^1 + NaX$$

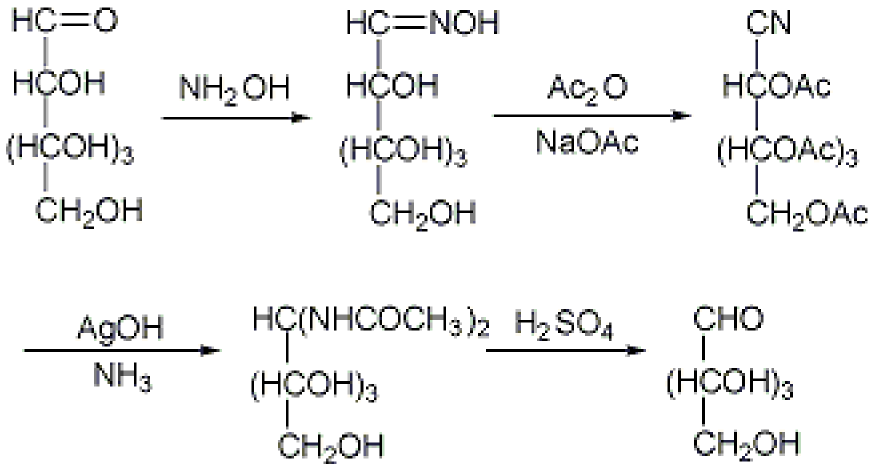
$$RO^- \; Na^+ + R^1 2SO_4 \longrightarrow ROR^1 + R^1SO_4 \; Na^+$$

Reviews: O. C. Dermer, *Chem. Rev.* **14,** 409 (1934); H. Feuer, J. Hooz in *The Chemistry of the Ether Linkage,* S. Patai, Ed. (Wiley, New York, 1967) pp 446-460; H. O. Kalinowski *et al., Ber.* **114,** 477 (1981); J. March, *Advanced Organic Chemistry* (Wiley-Interscience, New York, 4th ed., 1992) p 386.

433. **Wohl Degradation;** Zemplén Modification

A. Wohl, *Ber.* **26,** 730 (1893); **32,** 3666 (1899); G. Zemplén, *Ber.* **59,** 1254, 2402 (1926).

Method for the conversion of an aldose into an aldose with one less carbon atom by the reversal of the cyanohydrin synthesis. In the Wohl method the nitrile group is eliminated by treatment with ammoniacal silver oxide; in the **Zemplén modification** sodium alkoxide is used in the elimination of the nitrile:



Reviews: V. Deulofeu, *Advan. Carbohyd. Chem.* **4,** 129, 138 (1949); R. Bognár *et al.*, *Ann.* **680,** 118 (1964); W. W. Wendall, *Tetrahedron Letters* **1970,** 3439; L. Hough, A. C. Richardson, *The Carbohydrates* **1A,** 128 (1972).

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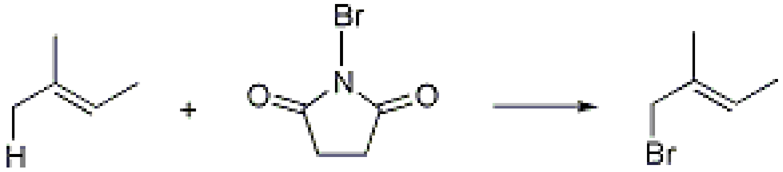
434. Wohl-Ziegler Reaction

A. Wohl, *Ber.* **52,** 51 (1919); K. Ziegler *et al., Ann.* **551,** 30 (1942).

Allylic bromination of olefins with *N*-bromosuccinimide. Peroxides or ultraviolet light are used as initiators:



Reviews: C. Djerassi, *Chem. Rev.* **43,** 271 (1948); L. Horner, E. M. Winkelman, *Angew. Chem.* **71,** 349 (1959); S. S. Novikov, *et al., Russ. Chem. Rev.* **31,** 671 (1962); A. Nechvatal, *Adv. Free-Radical Chem.* **4,** 175-201 (1972).

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440. Wurtz Reaction

A. Wurtz, *Ann. Chim. Phys.* [3] **44,** 275 (1855); *Ann.* **96,** 364 (1855).

Coupling of two alkyl radicals by treating two moles of alkyl halides with two moles of sodium:

$$2RX + 2Na \longrightarrow R{-}R + 2NaX$$

J. L. Wardell, *Comp. Organometal. Chem.* **1,** 52 (1982); W. E. Lindsell, *ibid.* 193; B. J. Wakefield, *ibid.* **7,** 45; D. C. Billington, *Comp. Org. Syn.* **3,** 413-423 (1991).

444. Zincke Disulfide Cleavage

T. Zincke, *Ber.* **44,** 769 (1911).

Formation of sulfenyl halides by three essentially similar methods involving the action of chlorine or bromine on aryl disulfides, thiophenols, or arylbenzyl sulfides:

$$\mathrm{ArSSAr} + X_2 \longrightarrow 2\mathrm{ArSX}$$

$$\mathrm{ArSH} + X_2 \longrightarrow \mathrm{ArSX} + \mathrm{HX}$$

$$\mathrm{ArSCH_2C_6H_5} + 2X_2 \longrightarrow \mathrm{ArSX} + \mathrm{C_6H_5CHX_2} + \mathrm{HX}$$

T. Zincke *et al., ibid.* **45,** 471 (1912); **51,** 751 (1918); *Ann.* **391,** 55 (1912); **400,** 1 (1913); **406,** 103 (1914); **416,** 86 (1918); M. H. Hubacher, *Org. Syn.* **coll. II,** 455 (1943); N. Kharasch *et al., Chem. Rev.* **39,** 283 (1946); A. Schöberl, A. Wagner, *Houben-Weyl* **9,** 268 (1955); E. Kühle, *Synthesis* **1970,** 561.

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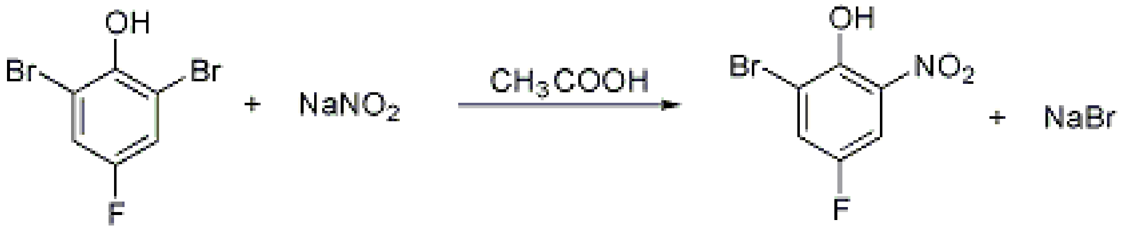
445. Zincke Nitration

T. Zincke, *J. Prakt. Chem.* **61,** 561 (1900).

Replacement of *ortho*- or *para*-bromine or iodine atoms (but not fluorine or chlorine atoms) in phenols by a nitro group on treatment with nitrous acid or a nitrite in acetic acid:



L. C. Raiford, W. Heyl, *Am. Chem. J.* **43,** 393 (1910); **44,** 209 (1911); H. H. Hodgson, J. Nixon, *J. Chem. Soc.* **1932,** 273; L. C. Raiford, G. R. Miller, *J. Am. Chem. Soc.* **55,** 2125 (1933); L. C. Raiford, A. L. LeRosen, *ibid.* **66,** 1872 (1944); W. Seidenfaden, D. Pawellek, *Houben-Weyl* **10/1,** 821 (1971).
