[39] Murray and Ronzio, *J. Am. Chem. Soc.*, 71, 2245 (1949).
[40] Lamchen, *J. Chem. Soc.*, 748 (1950).
[41] Kurzer, *Org. Syntheses*, 31, 8 (1951) including note 5.
[43] Kurzer, *Org. Syntheses*, 31, 11 (1951) including note 5.

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Amines

CONTENTS

CONTENTS *(continued)*

425. Reduction of Nitro Compounds

$$ArNO_2 \xrightarrow{(H)} ArNH_2$$

This method has had limited application for making aliphatic amines[2] although it assumes increasing importance in view of the commercial availability of the nitroparaffins and the development of processes for their ready conversion to nitro olefins,[31, 487, 518] nitro alcohols,[1] nitro ethers,[518] nitro amines,[487] and nitro cyanides,[519] all of which have been reduced to the corresponding amino compounds.

Aromatic primary amines are commonly prepared from nitro compounds by the action of one of several reducing agents; the reaction has been discussed.[535] Reduction with a metal-acid combination like granulated iron and a small quantity of acid gives excellent results. By this procedure, many aromatic amines have been prepared, including aniline (86%), o-toluidine (73%), 4-aminobiphenyl (93%), and α-naphthylamine (96%).[4, 6] Another common combination is tin and hydrochloric acid, but reduction may be accompanied by nuclear halogenation, particularly in the treatment of o-substituted nitrobenzenes. The action of zinc dust and aqueous alcohol in the presence of calcium chloride, essentially neutral conditions, is sufficient to convert 2-nitrofluorene to 2-aminofluorene (82%).[21] Aluminum amalgam and aqueous alcohol, still another neutral combination, has been successfully applied in the formation of 3-aminoacenaphthene (85%)[22] and the isomeric aminoacridines (70–75%).[30] Lithium aluminum hydride is an effective reductant for certain nitroölefins in the thiophene series.[31, 559]

Catalytic hydrogenation is performed in alcohol solution over Raney nickel at 25° to 100° and 30 atm.[14] or over platinum oxide at room temperature and 1 to 2 atm.[16] The reaction is highly exothermic; therefore, precautions should be taken against excessive reaction temperatures. Typical illustrations are found in the preparations of 2-amino-*p*-cymene (90%)[15] and 3,4-diethylaniline (90%).[13] Heterocyclic nitro compounds in the quinoline[25] and dibenzothiophene[35] series also respond favorably to catalytic hydrogenation.

In addition to these procedures, electrolytic reduction of the nitro group has been accomplished, as illustrated by the preparation of o-aminocyclohexylbenzene (85%); however, the procedure is rarely employed. An apparatus for large-scale runs has been described,[17] and a comprehensive review of electrolytic reactions has been given.[201]

Often under the non-acidic conditions, the reduction stops at the hydroxylamine stage.[26, 526] Thus phenylhydroxylamine, C_6H_5NHOH, is synthesized in 68% yield by the action of zinc dust and water on nitrobenzene.[527]

Certain aliphatic *diamines* have been prepared by reduction of nitro amines with hydrogen[40, 487] or aluminum amalgam.[39] The starting materials are readily obtained by the reaction of nitroparaffins with formaldehyde and amines (method 444).

Aromatic diamines and other polyfunctional aromatic amino compounds are prepared by the above general procedures. In the hydrogenation of polynitro compounds in the presence of Raney nickel catalyst, ethyl acetate has been found to be a better solvent than aliphatic alcohols.[42] The synthesis of 2,4-diaminotoluene is accomplished by reduction of the corresponding dinitro compound with iron filings and hydrochloric acid (89%).[43] Alkaline reducing agents, including ammonium sulfide, sodium sulfide, zinc and alcoholic alkali, etc., have also been employed. For example, o-phenylenediamine is synthesized in 85% to 90% yield by reducing o-nitroaniline with zinc and alcoholic alkali.[41]

Certain *unsaturated amino* compounds like the *cis*- and *trans*-*p*,*p*′-diaminostilbenes and *p*,*p*′-diaminotolane are prepared by selective hydrogenation of the corresponding dinitro compounds using Raney nickel catalyst (60–89%).[45, 47] The reduction has also been accomplished with hydrazine hydrate in the presence of alkali.[46]

Haloanilines are obtained from halonitrobenzenes preferably by the iron-acid reduction procedure.[4, 51] Nuclear halogenation occurs during the reduction of nitrobenzene by stannous chloride in the presence of acetic anhydride; a quantitative yield of *p*-chloroacetanilide is obtained.[49] Hydrogenation of halonitrobenzenes over Raney nickel catalyst is possible provided that the temperature is kept below 150°, at which point

dehalogenation occurs.[50, 52] The iodine atom is the most susceptible of the halogens to replacement during catalytic hydrogenation of the nitro group; however reduction by stannous chloride and hydrochloric acid has been successful, e.g., *m*-iodoaniline (83%).[53]

Aliphatic nitro alcohols, conveniently derived by the condensation of nitroparaffins with aldehydes,[54] are reduced to *amino alcohols* in almost quantitative yields by the action of iron powder and mineral acid.[1] Best results are obtained when an excess of acid is present. The procedure is illustrated by the synthesis of 2-amino-1-butanol (90%).[1]

$$CH_3CH_2CH_2NO_2 + H_2CO \xrightarrow{OH^-} CH_3CH_2CH(NO_2)CH_2OH \xrightarrow[Ca(OH)_2]{Fe - H_2SO_4;} CH_3CH_2CH(NH_2)CH_2OH$$

This same reducing agent has been successfully employed in the synthesis of 2-amino-1-phenyl-1-propanol (70%).[55] The formation of amino alcohols by catalytic hydrogenation over Raney nickel catalyst has been accomplished. However, because of the instability of the nitro alcohols in basic media, lower amines are also formed.

$$RCHOHCH(NO_2)CH_3 \rightleftharpoons RCHO + C_2H_5NO_2$$

$$C_2H_5NO_2 + H_2 \xrightarrow{Ni} C_2H_5NH_2$$

$$RCHO + C_2H_5NH_2 + H_2 \xrightarrow{Ni} RCH_2NHC_2H_5$$

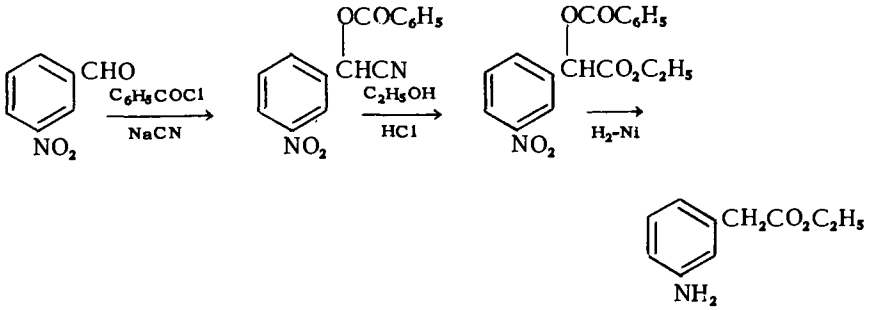
These by-products are suppressed by hydrogenating in an acid medium, e.g., in the presence of carbonic, acetic, or oxalic acids.[55, 56, 529]

The acid-sensitive *amino phenols* can be obtained by the reduction of nitro phenols with sodium sulfide or sodium hydrogen sulfite[58] or by treatment of the *p*-tolylsulfonic esters with iron and acetic acid.[59] Also, hydrogenation over Raney nickel at 100° gives excellent results.[14]

Aromatic nitro alcohols are converted by hydrogenation[60] or by the action of metals and acids. Various combinations have been compared in the preparation of β-(4-aminophenyl)-ethanol.[62]

Other functional groups may be present during reduction. Aromatic *amino ethers* are prepared by the same general procedures described above, e.g., *m*-aminoanisole (80%)[63] and 2-aminodiphenyl ether (94%).[65] The reduction of *o*-nitrobenzaldehyde to the sensitive *o-aminobenzaldehyde* is successfully accomplished by the action of ferrous sulfate and ammonia (75%).[67] *m*-Dimethylaminobenzaldehyde is formed by reduction of the nitro acetal in aqueous solution with sodium sulfide followed by methylation (74% over-all)[68] or by catalytic reduction of *m*-nitrobenzaldehyde in

the presence of formaldehyde (27%)[530] (cf. method 431). Reduction of the nitroacetophenones has been accomplished by metal-acid combinations and by selective hydrogenations over Raney nickel and platinum oxide catalysts; a comparison of these procedures has been made in the preparation of *o*- and *m-aminoacetophenones*.[69, 70] Other methods of preparation for *o*-amino ketones have been summarized.[72] *p-Aminophenylacetic acid* is best obtained by reduction of the nitro compound with ammonium sulfide (84%).[73] *Amino esters* are readily obtained by catalytic reduction of nitro esters over platinum oxide, e.g., ethyl *p*-aminobenzoate (100%).[75] A novel synthesis of ethyl *m*-aminophenylacetate from *m*-nitrobenzaldehyde consists in converting this substance to *m*-nitro-O-benzoylmandelonitrile by the action of benzoyl chloride and sodium cyanide, followed by alcoholysis and hydrogenation with simultaneous hydrogenolysis (69% over-all).[77]



3-Aminobenzonitrile is prepared by reduction of 3-nitrobenzonitrile by sodium disulfide in aqueous suspension (63%). This reagent causes some hydrolysis of the cyano group.[79] A selective hydrogenation of the more reactive nitro group in the presence of the cyano group can also be done, e.g., in the preparation of *p*-aminobenzyl *cyanide* (79%).[78]

Partial reduction of aromatic polynitro compounds leads to *nitro amines*. The most successful reagents are the alkali metal or ammonium sulfides in aqueous alcohol.[80] In some instances, sodium bicarbonate combined with sodium sulfide gives better results because of the formation of sodium hydrosulfide, which is believed to be the main reducing agent. Also, aqueous methanol is preferred to aqueous ethanol.[81] Nitro compounds that are sparingly soluble in alcohol solutions may be reduced by hydrogen sulfide in pyridine solution.[82]

Very often reduction of an aromatic nitro compound is carried out in the presence of acetic anhydride, whereby the corresponding acetamido compound is formed.[49] *Amino amides* are prepared by catalytic hydrogenation of nitro amides, e.g., 2-aminoacetanilide (90%).[83]

426. Reduction of Oximes

$$R_2C{=}NOH \xrightarrow{(H)} R_2CHNH_2$$

Reduction of oximes to primary amines proceeds readily and can be accomplished with hydrogen and Raney nickel catalyst with or without high pressures (50–90%).[174, 206, 308, 346–349] Primary amines formed from aldoximes are accompanied by secondary amines, $(RCH_2)_2NH$. The reduction may also be carried out with sodium and absolute ethanol, as illustrated by the synthesis of *n*-heptylamine (73%).[350] The action of zinc dust and acetic acid is effective in the formation of 9-fluorylamine (74%).[351] Lithium aluminum hydride is a good reagent, as shown by the reduction of 2,2-diphenylcyclohexanone oxime to 2,2-diphenylcyclohexylamine (80%).[545]

Aliphatic *diamines* are made by reduction of amino oximes by these same general procedures.[352, 353] Sometimes catalytic hydrogenation gives low-boiling cleavage products.[219]

The reduction of isonitroso ketones with hydrogen and platinum in the presence of hydrochloric acid gives *amino ketones* or *amino alcohols*, e.g., 1-phenyl-2-amino-1-propanol (98%)[356] and α-aminopropiophenone (88%).[357]

The reduction of α-oximino acids to *α-amino acids* is accomplished by catalytic hydrogenation with a Raney nickel[361] or palladium-charcoal[362, 363] catalyst or by the action of sodium or aluminum amalgam.[314, 364–367]

Several procedures involving the formation of α-oximino acid intermediates for the synthesis of α-amino acids have been described[103, 360] (cf. method 385). One outstanding synthesis consists in the production of α-oximino acids or esters by the action of a nitrite on a substituted acetoacetic or malonic ester.[360, 361]

$$\left.\begin{matrix} CH_3COCH(R)CO_2R' \\ RCH(CO_2R')_2 \end{matrix}\right\rangle \xrightarrow[\text{Acid or Base}]{(HONO)} HON{=}C(R)COOH \xrightarrow{(H)} RCH(NH_2)COOH$$

Oximes carrying a second group like a hydroxyl, carbonyl, or carbalkoxyl may form cyclic products, such as pyrazines from α-keto oximes and pyrrolidones from γ-oximino esters, upon reduction.[341]

427. Reduction of Nitriles

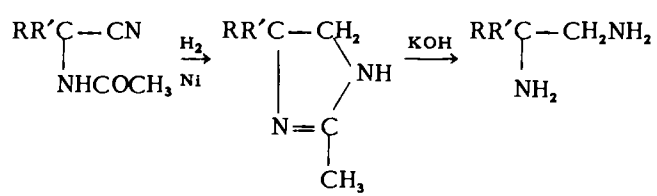
$$RCN + H_2 \xrightarrow{Ni} RCH{=}NH \xrightarrow{H_2} RCH_2NH_2$$

$$RCH{=}NH + RCH_2NH_2 \longrightarrow RCH(NH_2)NHCH_2R \xrightarrow{H_2} (RCH_2)_2NH + NH_3$$

Catalytic hydrogenation of aliphatic and aromatic nitriles yields primary and secondary amines.[215, 309] Formation of the secondary products can be suppressed (1) by carrying out the reduction in acetic anhydride, which acetylates the primary amine and prevents its reaction with the intermediate aldimine (platinum catalyst);[307] (2) by reducing in the presence of ammonia (nickel catalyst);[203, 310] or (3) by simply hydrogenating as rapidly as possible with a relatively large amount of catalyst.[14] Temperatures above 150° during hydrogenation favor the formation of the secondary amine by the elimination of ammonia from the primary amine, viz., $2RNH_2 \longrightarrow R_2NH + NH_3$.[215] A typical procedure employing high-pressure equipment and ammonia is illustrated by the synthesis of β-phenylethylamine (87%).[310] If hydrogenation of the nitrile is performed in the presence of an amine like methylamine or dimethylamine, then the corresponding N-mono- or N,N-di-alkylamine is formed.[342] A Raney nickel catalyst that is useful for hydrogenation at room temperature and low pressure has been described.[308]

Reduction may also be brought about by sodium and alcohol, although extensive cleavage of the cyanide group may occur, viz., $RCN \longrightarrow RH + NaCN$.[303–306] Lithium aluminum hydride has been successfully employed for the reduction of aliphatic and aromatic nitriles[302, 559] as well as several cyanides in the thiophene series.[314, 544]

A large number of aliphatic *diamines* have been made by the reduction of amino nitriles. Dialkylaminoacetonitriles, R_2NCH_2CN, are reduced with hydrogen in the presence of ammonia (Raney nickel catalyst)[316, 317, 320] or with sodium and alcohol (40–80%).[304, 320] Unsubstituted α-amino nitriles lose hydrogen cyanide on attempted hydrogenation and poison the catalyst; consequently, the stable acetyl derivatives are reduced in acetic anhydride to give the diacetyl diamine.[318] Also, the acetamido nitriles may be converted to 1,2-diamines through the dihydroimidazoles with subsequent hydrolysis, as illustrated by the preparation of 2-methyl-1,2-diaminobutane (53% over-all).[322]



The addition of primary or secondary amines to acrylonitriles, followed by catalytic reduction of the β-amino cyanides, constitutes a good synthesis of γ-aminopropylamines. The yields in the first step are usually in the range of 60% to 95% and in the second about 50% to 75%.[195, 319, 320]

$$RNH_2 + H_2C{=}CHCN \longrightarrow RNHCH_2CH_2CN \xrightarrow[Ni]{H_2,NH_3} RNH(CH_2)_3NH_2$$

In a similar manner, higher amino nitriles are reduced.[321]

Amines containing *other functional groups* have been prepared. Amino ethers are readily made by catalytic hydrogenation or sodium-alcohol reduction of the corresponding cyanides.[328–331] β-Hydroxy amines may be prepared by reduction of α-hydroxy or α-keto nitriles. Best results are obtained when the reduction is carried out with hydrogen and platinum or palladium catalyst in the presence of mineral acid. In this manner, substituted mandelonitriles, ArCHOHCN,[332] and aroyl cyanides, ArCOCN,[333] yield β-hydroxy-β-arylethylamines (24–94%). Reduction of β-keto nitriles gives keto amines or amino alcohols; however, the yields are poor.[334] Amino acids and amino esters are similarly prepared in good yields.[336–340]

Cyanides bearing a second group in a suitable position may undergo ring closure on hydrogenation, as illustrated by the formation of piperidine from trimethylene cyanide and pyrrolidines from β-cyano esters[341] (cf. method 574).

428. Reduction of Amides

$$RCONH_2 \xrightarrow{(H)} RCH_2NH_2$$

Catalytic hydrogenation of amides to amines requires drastic conditions: in general, a temperature of 250° to 265° and a pressure of 200 to 300 atm. over copper-chromium oxide catalyst using dioxane as the solvent.[14] The yields of primary amines from unsubstituted amides are lowered mainly by the formation of secondary amines, viz., $2RNH_2 \longrightarrow R_2NH + NH_3$. N-Mono- and di-substituted amides yield secondary and tertiary amines, respectively; however, considerable cleavage of the carbon-nitrogen bonds occurs.[343]

Amides are more conveniently reduced with lithium aluminum hydride in ether solution to yield amines with the same carbon content, e.g., triethylamine from N,N-diethylacetamide (50%) and ethyl-*n*-propylamine from N-ethylpropionamide (53%).[330, 344, 559] The same conversion has been accomplished by an electrolytic reduction.[201, 345]

429. Reduction of Schiff Bases

$$RCH{=}NR' \xrightarrow[Catalyst]{H_2} RCH_2NHR'$$

Unsymmetrical secondary amines are readily prepared in good yields by the catalytic reduction of Schiff bases at moderate temperatures in high- or low-pressure equipment. Many examples have been cited.[202] The intermediate imines are prepared from primary amines and aldehydes—very seldom from ketones—and may be used without isolation (cf. method 431). For the preparation of aliphatic amines, e.g., ethyl-*n*-propylamine and *n*-butylisoamylamine, a prereduced platinum oxide catalyst is preferred with alcohol as the solvent.[368, 369] Schiff bases from the condensation of aromatic aldehydes with either aromatic[215, 372] or aliphatic[138, 373] amines are more readily prepared and are reduced over a nickel catalyst. In this manner, a large number of N-alkylbenzylamines having halo,[138] hydroxyl,[374] or methoxyl[138, 374] groups on the nucleus have been made. Reductions by means of sodium and alcohol[370] and lithium aluminum hydride[302, 559] have also been described.

430. Reduction of Aromatic Amines

$$C_6H_5NH_2 \xrightarrow{(H)} C_6H_{11}NH_2$$

Certain amines are readily prepared by the reduction of aromatic, aryl aliphatic, and heterocyclic amines. For example, aniline is reduced to cyclohexylamine by high-pressure hydrogenation in the presence of Raney nickel catalyst or a cobalt oxide-calcium oxide catalyst. The reaction occurs at a temperature above 200°, where condensation of the primary amine also takes place, viz., $2C_6H_{11}NH_2 \longrightarrow (C_6H_{11})_2NH + NH_3$. If this side reaction is repressed by the presence of dicyclohexylamine at the start of the reaction, a 94% yield of cyclohexylamine is obtained.[377] Hydrogenation of aryl aliphatic amines proceeds more readily, occurring at moderate temperatures and pressures over platinum catalyst in glacial acetic acid.[378, 379] Other reductions using this catalyst are best performed on the amines in the form of their hydrochlorides.[523]

The reduction of N-alkyl-*p*-nitroanilines to the corresponding cyclohexanediamines has been carried out with hydrogen over cobalt-on-alumina and ruthenium catalysts.[198] Sometimes a nuclear-substituted aniline is acetylated before reduction in order to avoid side reactions. Thus, catalytic hydrogenation of *p*-acetaminophenol[381] and ethyl *p*-acetaminophenylacetate[382] has been successfully accomplished with platinum catalyst at 50–60° in the presence of acetic acid.

Other conditions for the reduction of the aromatic nucleus are discussed in method 4. The hydrogenation of heterocyclic nuclei is treated in method 554.

431. Reductive Alkylation (or Reductive Amination)

$$RCOR' + NH_3 + H_2 \xrightarrow{Ni} RR'CHNH_2 + H_2O \quad (R' = H \text{ or alkyl})$$

Alkyl groups may be introduced into ammonia, a primary amine, or a secondary amine by means of an aldehyde or ketone in the presence of a reducing agent, such as molecular hydrogen and a catalyst, active metals and acids, or formic acid or one of its derivatives. When the reducing agent is formic acid or a derivative, the reaction is known as the Leuckart reaction and is discussed elsewhere (method 432). An excellent review of the preparation of amines by reductive alkylation has been presented. This article includes a discussion of the scope and utility of the reaction, a selection of experimental conditions, illustrative preparations, and a tabulation of primary, secondary, and tertiary amines prepared thereby.[202]

Reductive alkylation of ammonia has been proved an effective and highly versatile method for obtaining *primary amines*. The most satisfactory conditions have been catalytic hydrogenation (Raney nickel) of the carbonyl compound in an ethanolic solution of ammonia under pressure ranging from 20 to 150 atm. and at temperatures in the range of 40° to 150°.[203–206] Typical amines prepared in this manner include benzylamine (89%)[204] and 2-aminoheptane (80%).[206] With liquid ammonia and no solvent, a higher pressure (330 atm.) at the higher temperature (150°) is required, as illustrated by the synthesis of α-phenylethylamine from acetophenone (52%).[208] More recently, improved procedures for hydrogenation at lower pressures over platinum oxide or Raney nickel have been described.[205, 207] Treatment of benzalacetone and furfuralacetone under these conditions leads to saturation of the α,β-olefinic linkage as well as to reductive alkylation.[205] In general, the method is particularly successful for obtaining aliphatic amines having five or more carbon atoms. In all these reactions for making a primary amine, ammonia is present in excess to minimize the formation of a secondary amine.

Secondary amines are prepared by several procedures of reductive alkylation. A procedure similar to that described for primary amines may be employed; the ratio of reactants must be changed to at least two moles of the carbonyl compound to one of ammonia. The procedure leads to symmetrical secondary amines and is most successful starting with aromatic aldehydes, as in the formation of dibenzylamine (67%).[204]

$$2ArCHO + NH_3 + H_2 \xrightarrow{Ni} ArCH_2NHCH_2Ar + 2H_2O$$

Symmetrical and unsymmetrical secondary amines are made by substituting a primary amine for the ammonia. In this reduction, the higher aliphatic aldehydes (above C_3) and simple ketones[215] respond best, usually over a platinum catalyst.

$$RCOR' + R''NH_2 + H_2 \xrightarrow{Pt} RR'CHNHR'' + H_2O$$

Aromatic amines like aniline, α- and β-naphthylamines, etc., are readily converted to the N-alkylamines by using aldehydes in the presence of Raney nickel, hydrogen, and sodium acetate (24–88%).[210,213] Since many aromatic amines are prepared under similar conditions by the reduction of nitro compounds, it is possible to combine both reductions in a single operation and convert nitro compounds to secondary amines (31–96%).[211]

Tertiary amines are formed if the reduction of the nitro compound and aldehyde is carried out with hydrogen and platinum in the presence of acetic acid. Nitroparaffins as well as aromatic nitro compounds react (34–92%).[212] Reductive dimethylation of amines of the type $ArCH(CH_3)CH_2NH_2$ and $ArCH_2CH(CH_3)NH_2$ with formaldehyde and hydrogen over Raney nickel catalyst occurs in 48–97% yields.[214] N-Monoalkylated anilines are methylated in good yields by the action of formaldehyde in the presence of zinc and mineral acid.[217] Many tertiary aliphatic amines have been prepared by reductive alkylation of secondary amines with aldehydes and ketones, the aldehydes giving better results.[216]

Difunctional compounds are formed by these procedures. *Diamines* are prepared by reductive amination of amino ketones[205] or by reductive alkylation of diamines.[219] A few aromatic *halo amines*[50, 221] and *amino ethers*[213] have been made. *Hydroxy amines* are conveniently formed by the reductive alkylation of amino alcohols[160, 222–227] as illustrated by the synthesis of 2-isopropylaminoethanol (95%).[223] N-Alkyl derivatives of 5-amino-1-pentanol are readily obtained by the reductive amination of 5-hydroxypentanal.[228–230] Several α-diketones have been treated under these conditions giving *amino ketones* or *amino alcohols*, only one carbonyl group undergoing reductive amination and the other being unaffected or reduced to a hydroxyl group.[231] Aliphatic and aromatic *amino acids* can be converted to their N,N-dimethyl derivatives in excellent yields with formaldehyde and hydrogen over palladium-charcoal catalyst.[232] Aromatic nitro acids may be reduced and methylated in one operation. Reductive amination of α-keto acids yields α-amino acids.[233] Sometimes a considerable quantity of the corresponding hydroxy acid is also formed; β- and γ-keto acids give little or no amino acids.[233]

432. Reductive Alkylation of Amines (Leuckart)

$$R_2CO \xrightarrow[\text{Heat}]{HCO_2NH_4} R_2CHNHCHO \xrightarrow{H_2O} R_2CHNH_2$$

Reductive amination of carbonyl compounds with ammonia or amines in the presence of a reducing agent has been discussed (method 431). When the reducing agent is formic acid or a derivative, the products are the formyl derivatives of primary or secondary amines or the formates of tertiary amines. These intermediates readily furnish the amines. A critical discussion of the reaction along with experimental conditions and procedures and a tabular survey of compounds has been presented.[397]

Many water-insoluble ketones, aliphatic, aryl aliphatic, and heterocyclic, respond favorably to treatment with ammonium formate or formamide to form with subsequent hydrolysis the primary amines. A typical procedure for the synthesis of α-phenylethylamine (66%) from acetophenone and ammonium formate has been applied to many other ketones (65–84%).[399] Nuclear alkoxyl, halo, and nitro groups are not disturbed.[399, 401] The reaction with formamide as the reducing agent is catalyzed by ammonium formate, ammonium sulfate, or magnesium chloride.[405]

If the ammonium formate is substituted by N-alkylformamide, then the formyl derivative of a secondary amine is formed.

$$R_2CO + 2HCONHR' \xrightarrow{\text{Heat}} R_2CHN(R')CHO + R'NH_2$$

In a similar manner, treatment with an N,N-dialkylformamide leads to tertiary amines; moreover, magnesium chloride, or better still calcium chloride, catalyzes the reaction.[402] Other factors have been studied.[403]

The method is employed extensively for the methylation of primary and secondary to the corresponding tertiary amines by the action of formaldehyde and formic acid.

$$RNH_2 + 2CH_2O + 2HCO_2H \xrightarrow{\text{Heat}} RN(CH_3)_2 + 2CO_2 + 2H_2O$$

In this manner, N,N-dimethyl-*n*-butylamine[123] and N,N-dimethylphenethylamine[400] are obtained in yields over 80% from the corresponding primary amines. Higher aliphatic aldehydes do not respond as satisfactorily as formaldehyde.

By means of a modification of the procedure, aromatic aldehydes may be converted by the action of ammonium formate to primary amines, e.g., benzylamine (60%) and *p*-methoxybenzylamine (23%).[547]

Methylation of *diamines* with formaldehyde and formic acid yields the tetramethyl derivatives, e.g., tetramethyldiaminobutane (92%).[123] In most instances, alkylation of *amino acids* by this same combination gives complex products, although α-dimethylaminobutyric acid can be made from the corresponding α-amino acid in 80% yield.[123] Reaction of the readily available *amino alcohols* like N-methylethanolamine and 2-isopropylaminoethanol gives the N,N-dialkyl derivatives.[408]

433. Reductive Cleavage of Azo Compounds

$$HOC_6H_4N{=}NC_6H_4SO_3Na \xrightarrow{Na_2S_2O_4} HOC_6H_4NH_2$$

The introduction of amino groups into phenols and ethers can be accomplished by the formation and reductive cleavage of their azo compounds. The diazotizing agent may be prepared from sulfanilic acid, and the reduction can be performed with sodium hydrosulfite. Excellent examples are found in the synthesis of 1-amino-2-naphthol (85%) and 4-amino-1-naphthol (75%).[554]

434. Catalytic Debenzylation of N-Benzyldialkylamines

$$C_6H_5CH_2NR_2 \xrightarrow[\text{Catalyst}]{H_2} R_2NH + C_6H_5CH_3$$

The reductive debenzylation of N-benzyldialkylamines with hydrogen in the presence of a platinum or palladium catalyst affords an excellent synthesis for symmetrical and unsymmetrical secondary amines.[122, 125, 444] The starting materials are readily available by dialkylation of benzylamine or by the monoalkylation of alkylbenzylamines, which in turn are prepared by the reduction of Schiff bases (method 429). The method has been extended to the formation of hydroxy amines,[446] amino esters,[447] and amino acids.[447]

435. Ammonolysis of Halogen Compounds

$$RCl + NH_3 \longrightarrow RNH_2 \cdot HCl$$

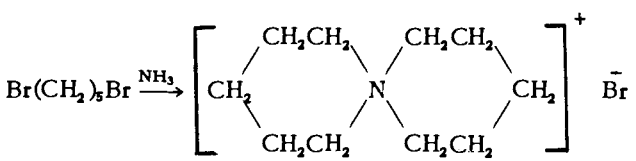
The direct conversion of halides to primary amines is discussed here. However, it is usually much more desirable to use one of the indirect methods such as method 437 or 452.

The reaction of ammonia with primary alkyl halides generally forms a mixture of primary, secondary, and tertiary amines and even a certain amount of the quaternary ammonium halide. Still, the method may be profitable for obtaining primary amines if the halogen compound is above C_3 and excess ammonia is employed, for then polyalkylation is less likely and the products, having widely different boiling points, are more readily separated. Thus *n*-butyl bromide and a large excess of ammonia in alcohol solution at room temperature give a 47% yield of *n*-butylamine.[84] In general, primary alkyl halides react better than secondary; tertiary halides undergo dehydrohalogenation. High-molecular-weight alkyl halides are slow to react and must be heated with alcoholic ammonia.[85] Anhydrous liquid ammonia favors the formation of primary amines.[96] Aryl-

substituted aliphatic halides such as the arylchloropropanes give 21–51% yields of the corresponding amines.[86]

Aryl halides react to form largely primary amines. High-pressure ammonolysis at an elevated temperature (100–200°) in the presence of a copper catalyst is required.[87,88] The 9-halofluorenes take an anomalous course.[89] Heterocyclic amines are quite often prepared by ammonolysis of the halides over a copper catalyst.[90–94] The halogen atom in 9-chloroacridine is easily replaced by an amino group by heating to 120° with ammonium carbonate and phenol.[92] Similarly, 2-chlorolepidine is converted to 2-aminolepidine (2-amino-4-methylquinoline) (78%).[95] Aryl halides in which the halogen atom is activated by nitro groups are easily converted to the amines without catalyst, as in the preparation of 2,4-dinitroaniline (76%).[113]

Preparation of the simplest *diamine*, ethylene diamine, by ammonolysis of the dihalide is accompanied by the formation of diethylenediamine and triethylenetetramine;[98] other methods for its preparation are more suitable. Only the higher homologs of β-dialkylaminoethyl bromide respond favorably to this treatment. Thus, di-*n*-butylaminoethyl bromide is converted to the diamine in 55% yield whereas the dimethylaminoethyl bromide undergoes extensive dimerization.[97] Trimethylene bromide reacts with liquid ammonia to form trimethylenediamine (50%);[96] however, experimental details are lacking. When the two halogens in the dihalide approach one another in space as in tetra- and penta-methylene dibromides, then nitrogen spiranes are the main products.[96]



The exchange of halogen for the amino group is important in the formation of other polyfunctional compounds, particularly the *amino acids*. In several of these transformations with aqueous or liquid ammonia, it has been shown that the presence of ammonium salts minimizes the formation of secondary and tertiary amines.[100,102] Excellent directions for the synthesis of α-amino acids (C_2–C_6) from α-halo acids and ammonia are given.[104–110] The methods have been reviewed.[102,103] Long-chain amino acids are prepared by this and other procedures.[112]

Other aspects of the ammonolysis process have been discussed.[536,555]

436. Alkylation of Amines

$$RNH_2 \xrightarrow{R'X} RR'NH \xrightarrow{R'X} RR'_2N \cdot HX$$

The direct alkylation of a primary amine with an alkyl halide results in the formation of secondary and tertiary amines in varying amounts, depending on the conditions of the reaction. Quite often, these products are accompanied by unchanged amine and quaternary ammonium salt. As in the ammonolysis of halides, formation of a particular product is favored by employing a large excess of one reactant: excess alkylating agent for the tertiary amine or excess amine for the secondary amine. The reaction is important in the synthesis of aromatic secondary and tertiary amines as well as some aliphatic tertiary amines. Thus, in the synthesis of N-phenylbenzylamine, an unusually high yield of this secondary amine (96%) is obtained with a 4 : 1 molar ratio of aniline to benzyl chloride.[114] Other N-monoalkylated anilines are obtained in a similar manner (75–85%).[119] Also, certain β-arylethylamines, $ArCH_2CH_2NHR$, are prepared from β-arylethyl bromides and primary amines by using a large excess of the latter.[118] Very often, alkylations of this nature which are carried out in aqueous ethanol are accompanied by hydrolysis and alcoholysis of the halide.[86] Some N-alkylated aryl amines like N-ethyl-*m*-toluidine may be synthesized in fair yields from reactants which are present in equimolar quantities (66%).[115] Conditions for the exclusive formation of N-methylaniline from chlorobenzene and methylamine have been found.[117]

$$C_6H_5Cl + 2CH_3NH_2 \xrightarrow[\text{Heat}]{Cu} C_6H_5NHCH_3 + CH_3NH_2 \cdot HCl$$

Such a process parallels that for making aniline from chlorobenzene and ammonia and involves a copper catalyst which promotes the reaction of the aryl halogen atom.

Sometimes the degree of alkylation can be controlled more carefully by employing other alkylating agents. Thus, primary amines may be alkylated to secondary amines free from tertiary amines by the action of aluminum alkoxides at 250–350° in a sealed tube. The procedure is illustrated by the treatment of aniline with aluminum ethoxide at 275° to form N-ethylaniline (94%).[116] On the other hand, alkylation with alkyl phosphates leads to tertiary amines, e.g., N,N-diethylaniline (99%) and N,N-di-*n*-butylaniline (79%).[131,132] These reagents afford a simple and convenient procedure furnishing yields in the range of 53% to 95%. Other alkylating agents for the formation of dialkylarylamines include the esters of sulfuric, sulfurous, and *p*-toluenesulfonic acids.[131] It has been noted that pyridine acts as a catalyst in the production of N,N-dimethyl-α-naphthylamine from α-naphthylamine and dimethyl sulfate.[134]

Commercial processes for obtaining the N-alkylated anilines are based on the reaction of aniline salts with alcohol in an autoclave at about 200°. A laboratory adaptation of this application of an alcohol as the alkylating

agent consists in heating the alcohol and aniline with a small amount of iodine in an autoclave for 10 hours at 220° to 230°. In this manner, either mono- or di-alkylated anilines are prepared (60–90%).[135] Other catalysts include copper and sodium halides.[200] The mono- and di-alkylated amines may be separated by treatment with acetic anhydride and distillation.[395]

Aliphatic tertiary amines are prepared by the interaction of secondary amines and alkyl bromides. Equimolar quantities of the reactants are treated in alcohol solution in the presence of an inorganic base for 2 to 6 days at room temperature or more quickly in an autoclave at a higher temperature. Many compounds have been characterized; however, the yields are not always stated.[121, 124] N-Alkylated benzylamines are commonly prepared by this procedure;[122, 125, 138] these compounds are important intermediates in the synthesis of pure secondary amines (method 434). Alkylation of diethylamine with isopropyl bromide has been accomplished, after many unsuccessful attempts, by heating the reactants under reflux in glycerol solution for 72 hours (60%).[126]

Preparation of aromatic secondary and tertiary amines like diphenyl- and triphenyl-amine is catalyzed by copper powder.[136]

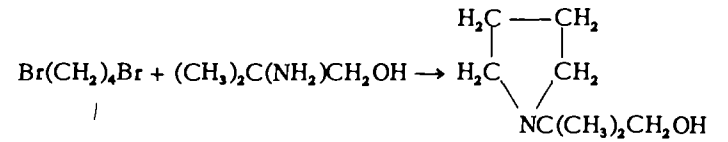
Further alkylation of tertiary amines yields quaternary ammonium salts. These compounds are numerous and are readily prepared by heating the alkyl halide and tertiary amine in the absence of a solvent or in the presence of alcohol.[139–141] Methylation of tertiary amines to quaternary ammonium salts can be accomplished with methyl halides[142, 537] or dimethyl sulfate.[143]

Monoalkylation of *ethylenediamine* with high-molecular-weight alkyl chlorides and bromides (C_6 to C_{18}) can be successfully carried out when a highly concentrated solution (95%) of the diamine is employed. The yields are in the range of 83% to 98%.[144] N,N-Dialkylethylenediamines, $R_2NCH_2CH_2NH_2$, are prepared by other methods (methods 427, 435, and 452). *sym*-N,N′-Dialkylethylenediamines, $RNHCH_2CH_2NHR$, may be obtained either by the treatment of ethylenediamine with two moles of halide (84–90%)[145] or by the reaction of ethylene chloride with an excess of the primary amine in an autoclave, as in the preparation of N,N′-di-*n*-butylethylenediamine (50%).[146] Other alkylated diamines are formed by the amination of dialkylaminoethyl chloride.[147, 148] In some instances, a copper-bronze catalyst has been employed;[148, 149] the yield of diethylaminoethylaniline from the alkylation of aniline by diethylaminoethyl chloride is increased from 72% to 88% with this catalyst.[149] A copper-bronze or cuprous chloride catalyst is more frequently employed in the condensation of aryl halides with amines.[150]

Alkylation with allyl halides gives *olefinic amines*.[151]

Halo amines are formed by these procedures. Partial amination of trimethylene chlorobromide with diethylamine yields 1-diethylamino-3-chloropropane (70%) accompanied by the formation of diethylamine hydrobromide.[153] Halo anilines respond to the usual treatment with dimethyl sulfate,[130, 155] alkyl halides,[154] or alkyl phosphates.[132]

Amino alcohols are commonly made by the amination of halo alcohols or by alkylation of amino alcohols. Thus β-diethylaminoethyl alcohol is synthesized from diethylamine and ethylene chlorohydrin (70%).[156] Higher amino alcohols are made in a similar manner.[152, 165–168] No isomerization through the formation of an ethylene oxide intermediate occurs during the reaction of a 1,2-chlorohydrin.[165] Several series of alkylaminoalkylcarbinols, $RNHCH_2(CH_2)_nOH$, have been prepared by alkylations of ethanolamine (16–53%),[157] 2-amino-2-methyl-1-propanol, and 2-amino-1-butanol.[162] For the preparation of mixed N,N-dialkyl derivatives, better yields are obtained when the larger alkyl group is introduced first.[160, 161] Aliphatic tertiary amino alcohols of the type $(CH_3)_2COH(CH_2)_nN(CH_3)_2$, $n = 1$ to 4, have been prepared by amination of the corresponding bromohydrins (52%).[163] The latter compounds are readily obtained by the action of methylmagnesium bromide on bromo esters (method 91). The alkylation of 2-amino-2-methylpropanol with tetramethylene bromide leads to 2-(1-pyrrolidyl)-2-methylpropanol (76%).[169]



Amino ethers are obtained by the same reactions employed for amino alcohols.[152, 170–174]

Aliphatic and aryl aliphatic *amino ketones* are made by the amination of the halogenated carbonyl compounds,[176–185] e.g., dimethylaminoacetone (74%),[176] 1-diethylamino-2-pentanone (79%),[538] and α-methylaminopropiophenone (57%).[185] It is noteworthy that this system may undergo a rearrangement, viz., $ArCOCH_2Br + (C_2H_5)_2NH \longrightarrow ArCH_2CON(C_2H_5)_2$ (45%).[539] The reaction of α-halo ketones with arylamines is even more complex.[540] Examples of the formation of α-aminoaldehydes by this method are few.[175] However, the same results may be achieved by the amination of the halo acetals with subsequent hydrolysis.[68, 176, 177]

Amination of halogenated *acids* or *esters* is possible.[187–191] When circumstances are favorable, dehydrohalogenation occurs, as in the treatment of ethyl α-bromoisovalerate with diethylamine; the product is predominantly the α,β-unsaturated ester.[191] The amination of aliphatic chloro and bromo *nitriles* is facilitated by the presence of potassium iodide.[193–196] Halogen atoms in the *o*- and *p*-nitrohalobenzenes are readily

replaced by the dialkylamino group, as in the preparation of *p-nitrodimethylaniline* (97%).[197, 198]

437. Interaction of Hexamine and Halogen Compounds

$$RX + (CH_2)_6N_4 \longrightarrow (CH_2)_6N_4 \cdot RX \xrightarrow{HCl} RNH_2 \cdot HCl + NH_4Cl$$

The interaction of alkyl halides, preferably iodides or bromides, with hexamine in chloroform or alcohol solution forms quaternary ammonium salts which on heating with hydrochloric acid are readily converted to primary amines.[234, 235, 237] The procedure has been employed successfully in the reaction of primary, but not secondary or tertiary, aliphatic halides,[235, 236] certain benzyl halides,[234, 237] halo ketones,[238] halo acids,[239, 240] and halo esters.[240, 241] The yields range from 40% to 85%.

Certain quaternary ammonium salts, particularly the hexaminebenzyl halides, form aldehydes when heated with water (method 147).

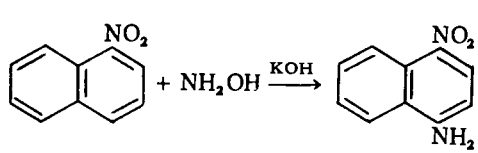
438. Replacement of Hydroxyl Groups by Amino Groups

$$C_{10}H_7OH + NH_3 \underset{}{\overset{(NH_4)_2SO_3}{\rightleftharpoons}} C_{10}H_7NH_2 + H_2O$$

This equilibrium reaction in the presence of sulfites is important for the preparation of certain polyfunctional benzenes and naphthalene derivatives bearing hydroxyl or amino groups (cf. method 94) (Bucherer). A review of the literature to 1942 has been made.[389] The hydroxy compounds are converted to the corresponding primary amines by treatment with aqueous ammonia and ammonium sulfite at 90–150°, good mixing being essential, as illustrated by the preparation of 2-naphthylamine (96%) and 7-methyl-1-naphthylamine (90%).[389] In a similar manner, resorcinol and its alkylated derivatives have been changed to the corresponding amino phenols (50–80%).[390, 391] Benzene derivatives containing one hydroxyl or one amino group are much less reactive. Hydroxyquinolines undergo this reaction (65–88%).[392, 393, 546]

Sometimes, replacement can be effected by heating with ammonia under pressure in the presence of zinc chloride, e.g., 3-amino-2-naphthoic acid from 3-hydroxy-2-naphthoic acid (70%).[524]

439. Amination of Aromatic Nuclei



Certain aromatic and heterocyclic compounds having reactive nuclear positions undergo direct amination. Thus α-nitronaphthalene on treatment with hydroxylamine in methanolic potassium hydroxide yields 4-nitro-1-naphthylamine (60%),[507] following the rules of orientation for substitution by a nucleophilic reagent rather than an electrophilic reagent.

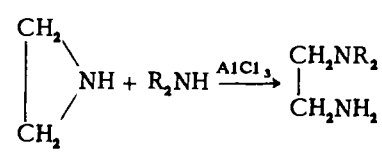
The amination of heterocyclic bases such as pyridine, quinoline, and their derivatives by alkali amides furnishes a good method for obtaining the 2-amino compounds (50–100%). The scope and limitations of the reaction have been reviewed; the procedure is illustrated by the preparation of 2-aminopyridine (76%).[508]

440. Rearrangement of N-Alkylanilines

$$C_6H_5NHR \xrightarrow[Heat]{CoCl_2} p\text{-}RC_6H_4NH_2$$

Treatment of N-monoalkylanilines with anhydrous cobalt chloride at about 220° for 13 hours causes a nitrogen-to-carbon rearrangement to form *p*-alkylanilines.[359, 396] Normal alkyl groups migrate without apparent isomerization within the group to give good yields (60–85%); however, *s*- and *t*-alkylanilines undergo extensive decomposition to give olefins and aniline. Similar treatment of the aniline salts gives the rearrangement, viz., N-isobutylaniline · HCl ⟶ *p*-amino-*t*-butylbenzene. In this case, isomerization occurs within the alkyl group.

441. Amination of Cyclic Imines



N-Alkyl- and N,N-dialkyl-ethylenediamines are prepared in a single step (cf. methods 427, 435, and 452) by the addition of gaseous ethylenimine to primary or secondary amines in the presence of anhydrous aluminum chloride (77–89%).[451] Primary amines react at about 90° with benzene as solvent, whereas secondary amines react at 180° with tetralin or biphenyl as solvent. In a similar manner, homologs of ethylenimine and ammonia (or amines) react in high-pressure equipment at 100° in the presence of ammonium chloride.[452]

442. Amination of Oxides

$$\underset{\diagdown\,\diagup}{\overset{O}{}}\!\!\text{CH}_2\text{—CH}_2 + \text{R}_2\text{NH} \longrightarrow \text{R}_2\text{NCH}_2\text{CH}_2\text{OH}$$

Ammonia and amines open oxide rings to form amino alcohols;[461–469] the yields are markedly higher when amines are employed (55–90% vs. 18–40%).[464,467,468] The ready availability of ethylene and propylene oxides makes this procedure attractive for preparing 2-dialkylaminoethanols[461] and 1-dialkylamino-2-propanols.[464] Thus β-diethylaminoethanol is conveniently prepared by the addition of ethylene oxide to diethylamine in methanol at 45° to 60° or by a combination of the two reactants in an autoclave at 100° (81%).[461] Isopropylamine reacts with ethylene oxide in the presence of water and a small amount of hydrochloric acid to form β-isopropylaminoethanol (76%).[463] The reaction is general and is shown by higher oxides like isobutylene oxide,[465] styrene oxide,[468] and stilbene oxide.[469]

443. Amination of Unsaturated Compounds

$$\text{HC}\equiv\text{CH} \xrightarrow[\text{Catalyst}]{\text{R}_2\text{NH}} [\text{R}_2\text{NCH}=\text{CH}_2] \xrightarrow{\text{HC}\equiv\text{CH}} \text{R}_2\text{NCH(CH}_3\text{)C}\equiv\text{CH}$$

Acetylene and either primary or secondary aliphatic amines react under pressure at 80° to 100° in the presence of a copper catalyst to form N-mono- and N-di-substituted 3-aminobutynes, e.g., 3-diethylamino-1-butyne (65%).[472] Although benzylamine responds favorably, aniline and acetylene furnish only a 25% yield of 3-anilino-1-butyne.

The treatment of allyl alcohol with amines in the presence of an equimolar quantity of alkali in an autoclave at about 115° represents a general method for the preparation of N-alkyl-3-aminopropanols, e.g., 3-dimethylamino-1-propanol (65%).[473]

$$\text{CH}_2=\text{CHCH}_2\text{OH} \xrightarrow[\text{NaOH}]{\text{R}_2\text{NH}} \text{R}_2\text{NCH}_2\text{CH}_2\text{CH}_2\text{OH}$$

Ammonia and amines add more easily to a double bond which is conjugated with a carbonyl or carbalkoxyl group to form β-amino compounds. Thus, mesityl oxide and aqueous ammonia react under mild conditions to form diacetonamine (70%).[474]

$$\text{CH}_3\text{COCH}=\text{C(CH}_3\text{)}_2 \xrightarrow{\text{NH}_3} \text{CH}_3\text{COCH}_2\text{C(CH}_3\text{)}_2\text{NH}_2$$

The addition of aliphatic and aromatic amines to other unsaturated ketones has been discussed.[475] α,β-Unsaturated aldehydes like acrolein and crotonaldehyde combine with two moles of amine to form unsaturated 1,3-diamines, $\text{RCH(NR}_2\text{)CH}=\text{CHNR}_2$.[453] The addition of primary or secondary amines to acrylic esters has provided a good route to the N-alkyl-β-aminopropionic esters.[477–480] The product may add a second molecule of ester to furnish alkyl di-(carbalkoxyethyl)-amines;[481] however, the course of the reaction can be controlled in many instances to provide largely the secondary or tertiary amine.

$$\text{RNH}_2 \xrightarrow{\text{CH}_2=\text{CHCO}_2\text{R}'} \text{RNHCH}_2\text{CH}_2\text{CO}_2\text{R}' \xrightarrow{\text{CH}_2=\text{CHCO}_2\text{R}'}$$

$$\text{RN(CH}_2\text{CH}_2\text{CO}_2\text{R}')_2$$

Other α,β-unsaturated esters including methyl methacrylate,[169] ethyl crotonate,[482] and ethyl cinnamate[483] respond to this treatment. Ammonia adds to ethyl crotonate to form a 55% yield of ethyl β-aminobutyrate; on the other hand, the interaction of ammonia and ethyl acrylate produces only di- and tri-substituted products.[484]

Amination of α,β-unsaturated acids is brought about by treatment with two moles of hydroxylamine in alcohol solution, as illustrated by the synthesis of *dl*-β-amino-β-phenylpropionic acid (34%).[485,486]

$$\text{C}_6\text{H}_5\text{CH}=\text{CHCO}_2\text{H} \xrightarrow{\text{NH}_2\text{OH}} \text{C}_6\text{H}_5\text{CH(NHOH)CH}_2\text{CO}_2\text{H} \xrightarrow{\text{NH}_2\text{OH}}$$

$$\text{C}_6\text{H}_5\text{CH(NH}_2\text{)CH}_2\text{CO}_2\text{H}$$

The interaction of ammonia or amines with α-nitro olefins, $\text{RCH}=\text{CHNO}_2$, in alcoholic solution at 0° forms nitroamines, e.g., 1-nitro-2-aminopropane (55%) and 2-nitro-3-aminobutane (60%). The reaction is general and is applied to numerous nitro olefins readily obtained by the dehydration of aldehyde-nitroparaffin condensation products.[487,488]

$$\text{RCH}=\text{CHNO}_2 + \text{NH}_3 \longrightarrow \text{RCH(NH}_2\text{)CH}_2\text{NO}_2$$

444. Aminomethylation (Mannich)

$$\text{RCOCH}_3 + \text{CH}_2\text{O} + \text{(CH}_3\text{)}_2\text{NH}\cdot\text{HCl} \xrightarrow{-\text{H}_2\text{O}} \text{RCOCH}_2\text{CH}_2\text{N(CH}_3\text{)}_2\cdot\text{HCl}$$

Compounds possessing labile hydrogen atoms readily condense with formaldehyde and an amine (primary or secondary) or ammonia, thereby placing an aminomethyl or substituted aminomethyl group at the location

of the reactive hydrogen atom. The reactive hydrogen may be present in the *alpha* position of an aldehyde,[416] ketone,[417–423] acid,[424] ester, or nitroparaffin;[39,40,425,426] or it may be in the *ortho* or *para* position of a phenol[415] or in certain heterocyclic compounds.[409–412]

Secondary products are often formed by the replacement of a second active hydrogen with an aminomethyl group.

$$RCOCH_2CH_2N(CH_3)_2 \cdot HCl \xrightarrow[(CH_3)_2NH \cdot HCl]{CH_2O} RCOCH[CH_2N(CH_3)_2 \cdot HCl]_2$$

Also, Mannich bases which are themselves primary or secondary amines may undergo further condensation to yield tertiary amines.

$$RCOCH_2CH_2NHR \cdot HCl \xrightarrow[RCOCH_3]{CH_2O} (RCOCH_2CH_2)_2NR \cdot HCl + H_2O$$

The literature of this reaction to 1942 has been reviewed.[427] Later observations have been made.[414,422,514] The synthesis of β-dimethylaminopropiophenone (72%) exhibits a typical procedure.[420]

445. Aminomethylation of Alcohols

$$R_2NH + CH_2O + R'OH \longrightarrow R_2NCH_2OR'$$

The interaction of paraformaldehyde, a secondary amine, and an alcohol occurs vigorously to form in good yields an aminomethyl alkyl ether. The method is general and has been applied to the formation of many amino ethers.[513]

446. Degradation of Amides (Hofmann)

$$RCONH_2 \xrightarrow{NaOBr} RNCO \xrightarrow{H_2O} RNH_2$$

Amides react with alkaline hypochlorite or hypobromite solutions to form primary amines having one less carbon atom. The reaction involves the hydrolysis of an isocyanate, which is seldom isolated. Isocyanates are also intermediates in the Curtius and Lossen rearrangements (methods 447 and 448). Although these methods have a common mechanism and intermediate, they involve three separate and distinct types of starting materials and are, therefore, treated individually. A comparison of these reactions has been made.[270] A detailed discussion of the Hofmann reaction, which includes conditions, typical procedures, and compounds prepared thereby, has been presented.[244]

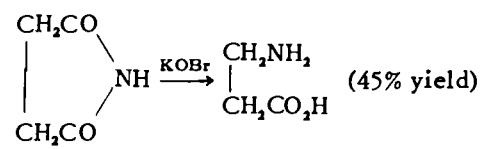
The method has been used for the preparation of aliphatic, aryl aliphatic,[254–258] aromatic,[252,253] and heterocyclic[24,260,261,522,542] amines. Yields for the lower aliphatic amines (C_1–C_8) are about 70–90% but are

poor for the higher amines because of the formation of the corresponding nitriles and acyl alkyl ureas.[245–248] In order to overcome this difficulty, the high-molecular-weight aliphatic amides are treated with bromine and sodium methoxide with subsequent hydrolysis of the resulting urethanes.[349]

$$RCONH_2 + Br_2 + 2NaOCH_3 \longrightarrow RNHCO_2CH_3 + 2NaBr + CH_3OH$$

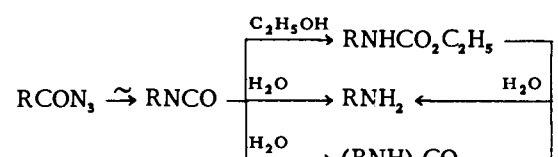
Alicyclic amines have been produced by the same modification.[250,251]

A few diamides have been converted to diamines.[220,252,253] For the most part, the conversion of unsaturated amides is unsatisfactory; however, α-allylphenylacetamide is transformed to α-allylbenzylamine in a 90% yield.[254] Aromatic amides having free or methylated phenolic groups are treated preferably with sodium hypochlorite rather than hypobromite in order to avoid excessive ring halogenation.[256,265,266] Certain amino acids like anthranilic acid and β-alanine have been synthesized from the appropriate imides.[268]



(45% yield)

447. Degradation of Acyl Azides (Curtius)

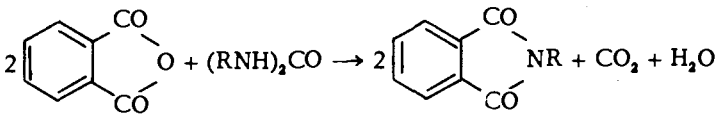


The conversion of an acid to an amine of one less carbon may be conveniently accomplished by way of the azide and rearrangement to the isocyanate. The azide may be obtained either from the acyl chloride and sodium azide or from an ester by treatment with hydrazine and subsequent diazotization. An excellent review including scope and limitations of the reactions, selection of experimental conditions and procedures, and a tabulation of compounds prepared thereby has been presented.[270]

The acyl azide undergoes a rearrangement similar to the Hofmann rearrangement (method 446) and to the Lossen rearrangement (method 448). This step is carried out in inert solvents like benzene and chloroform to give the isocyanate directly or in solvents like alcohol and water which will react with the isocyanate to form urethanes and ureas.

The amines are obtained by hydrolysis of any of these three intermediates. When hydrolysis is impracticable, the alkylureas or urethanes

may be converted with phthalic anhydride to alkylphthalimides which are formed in excellent yields. These compounds are then readily decomposed by hydrazine according to the usual Gabriel synthesis (method 452).[272]

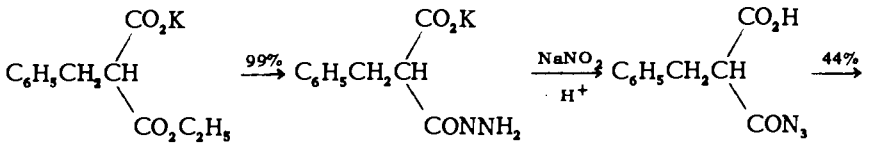


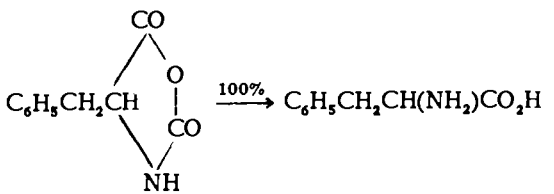
The Curtius reaction can be performed on aliphatic,[271] alicyclic,[273,278,279] aromatic,[274–278] or heterocyclic[281–283] azides.

The application of the procedure to azides containing *other functional groups* has also been described.[270] Diamines (from dicarboxylic acids),[278–280] arylhaloamines,[285,286] and nitroarylamines[285,286] have been successfully prepared, whereas certain groups like the double bond, hydroxyl, carbonyl, and amino often cause the formation of products other than the anticipated amine. For the synthesis of α-amino acids, the readily accessible alkylcyanoacetic esters may be employed as starting materials. Their azides rearrange to cyano isocyanates, which can be easily hydrolyzed.[287,288]

$$NCCH(R)CON_3 \xrightarrow{\sim} NCCH(R)NCO \xrightarrow{H_2O} HOOCCH(R)NH_2$$

α-Amino acids may also be obtained by applying the Curtius reaction to substituted malonic acid esters as in the preparation of β-phenylalanine (44% over-all).[278,289,290]





448. Degradation of Hydroxamic Acids (Lossen)

$$RCONHOH \xrightarrow[Heat]{KOH} RNCO \xrightarrow{H_2O} RNH_2 + CO_2$$

Alkali salts of hydroxamic acids and their derivatives undergo a rearrangement to give isocyanates. The method has had little synthetic application; it has been reviewed.[291]

449. Interaction of Hydrazoic Acid and Carbonyl Compounds (Schmidt)

(*a*) $$RCO_2H + HN_3 \xrightarrow{H_2SO_4} RNH_2 + CO_2 + N_2$$

(*b*) $$RCOR + HN_3 \xrightarrow{H_2SO_4} RCONHR \longrightarrow RNH_2$$

The reaction of equimolar quantities of hydrazoic acid with an acid or ketone affords a convenient method for preparing certain amines. The reaction is carried out by treating the organic compound in an inert solvent in the presence of sulfuric acid with gaseous hydrogen azide,[299] hydrazoic acid in solution, or sodium azide directly.[292] An excess of hydrazoic acid should be avoided in the reaction of ketones, for then tetrazoles are formed. It should be recalled that hydrazoic acid is toxic and explosive. A discussion of the method including scope and limitations, experimental conditions and procedures, and compounds prepared thereby has been presented.[292]

Aliphatic,[293] alicyclic,[294] and aromatic acids[294–298] which are stable to concentrated sulfuric acid undergo the reaction in good yields, although detailed directions are frequently lacking. Amines prepared by this single-step process are often obtained in higher yields than when prepared by either the Hofmann or Curtius degradation.*

Benzoic acids substituted with alkyl, halo, hydroxyl, alkoxyl, cyano, or nitro groups react to give the corresponding substituted anilines in 41–80% yields.[295] The carboxyl group in an α-amino acid does not react with hydrazoic acid; the reaction proceeds, however, if the amino group is further removed. This difference in reactivity is shown by the conversion of α-aminoadipic acid to *dl*-ornithine (75%).[300]

$$HO_2C(CH_2)_3CH(NH_2)CO_2H + HN_3 \xrightarrow{H_2SO_4} H_2N(CH_2)_3CH(NH_2)CO_2H$$

The conversion of ketones to amides by the Schmidt reaction has been mentioned elsewhere (method 362). Since the hydrolysis of the amides so obtained proceeds readily, the two steps provide a convenient synthesis of amines from ketones. The yields are often higher than those obtained from the Beckmann rearrangement with subsequent hydrolysis (method

*For a comparison of the Schmidt, Hofmann, and Curtius reactions, see ref. 270, p. 363.

451).[297-299] The procedure is convenient for the synthesis of α-amino acids from mono- or di-substituted acetoacetic esters (80–98%).[301]

$$CH_3COC(R)_2CO_2C_2H_5 + HN_3 \xrightarrow[C_6H_6]{H_2SO_4} CH_3CONHC(R)_2CO_2C_2H_5 \xrightarrow{H_2O} H_2NCR_2CO_2H + C_2H_5OH + CH_3CO_2H$$

450. Hydrolysis of Isocyanates, Isothiocyanates, Urethanes, and Ureas

$$RNCO + H_2O \longrightarrow RNH_2 + CO_2$$

Many important amines have been obtained by the hydrolysis of one of these substances. Thus, *t*-butylamine is formed by alkaline hydrolysis of *t*-butylurea (78%)[454] or by treatment of *t*-butylisothiocyanate with formic acid (79%).[455] Allylamine is synthesized by hydrolysis of allyl isocyanate with dilute hydrochloric acid (73%).[456] The hydrolysis of isocyanates, urethanes, and ureas, which occur as intermediates in the degradation of amides and azides, has been discussed under methods 446 and 447, where many examples have been cited.

β-Arylaminoethanols are made by the condensation of arylamines with chloroethyl chloroformate followed by treatment of the resulting carbamates with excess alkali. The reaction proceeds by way of an intermediate oxazolidone which need not be isolated.[458]

$$ArNH_2 \xrightarrow[80\%]{ClCO_2CH_2CH_2Cl} ArNHCO_2CH_2CH_2Cl \longrightarrow ArNCO_2CH_2CH_2 \xrightarrow[(80\%-100\%)]{KOH} ArNHCH_2CH_2OH$$

In a similar manner, γ-chloropropyl arylcarbamates formed from aromatic amines and γ-chloropropyl chloroformate are converted to γ-arylaminopropanols.[459]

451. Hydrolysis of N-Substituted Amides

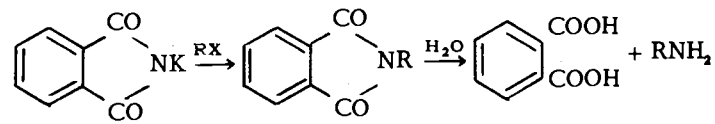
$$RCONHR \xrightarrow[Na]{R'X} RCONRR' \xrightarrow{H_2O} RR'NH$$

The N-alkylation of amides followed by hydrolysis furnishes a good route for making secondary amines. The formyl,[494] acetyl,[375] and arylsulfonyl[492,550] derivatives of amines are best suited for alkylation (method 358). Hydrolysis is accomplished by refluxing concentrated hydrochloric acid alone[35,375,494,497] or in acetic acid.[492,502,503] N-Alkylformamides prepared by the addition of olefins to nitriles (method 355) are hydrolyzed with aqueous alkali.[506] Similar hydrolytic procedures

have been employed for obtaining diamines,[387,497] unsaturated amines,[495,496] and amino acids.[498-500] The deacylation of *p*- and *o*-nitroacetanilides is carried out with sodium ethoxide in boiling alcohol.[501]

Certain amines are conveniently prepared by the hydrolysis of N-substituted amides which are made by the Beckmann rearrangement (method 359) and the Schmidt reaction (method 362).

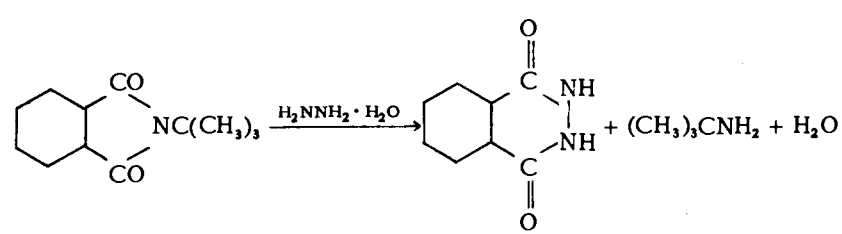
452. Hydrolysis of N-Substituted Phthalimides (Gabriel)



The facile alkylation of phthalimide and subsequent hydrolysis of the N-substituted derivatives furnishes a convenient synthesis for primary amines. The substituted phthalimide was originally prepared by heating a mixture of phthalimide, potassium carbonate, and organic halide in a non-polar solvent for 2 to 24 hours at 100° to 150°.[428] An improved procedure consists in performing this initial step in a polar solvent like dimethylformamide, in which potassium phthalimide is appreciably soluble; the reaction occurs at room temperature within 10 minutes.[429] Various esters of *p*-toluenesulfonic acid may be substituted for the organic halides as alkylating agents.[437]

Tertiary alkyl halides lose hydrogen halide in their reaction with potassium phthalimide. However, the *t*-alkylphthalimides are readily prepared by heating the corresponding *t*-alkylureas and phthalic anhydride to 200° to 240°.[430]

Hydrolysis may be carried out directly by refluxing the alkylated phthalimide in basic or acidic solutions or by the action of hydrazine hydrate followed by acidification.[428] This procedure is illustrated by the synthesis of *t*-butylamine (67% over-all).[430]



Alkylation with organic halides carrying a second functional group affords a good synthesis of some difficultly obtained difunctional compounds including diamines,[353,432-436] amino halides,[438] hydroxy amines,[556] amino ketones,[429,440] amino acids,[429,441-443] amino cyanides,[441,445] and

nitro amines.[426] Also the stability of the N-substituted phthalimide allows further changes to be made, for example, (*a*) amination of γ-bromopropylphthalimide with various secondary amines (60–80%),[433] (*b*) catalytic reduction of N-(*m*-nitrobenzyl)-phthalimide,[38] (*c*) oxidation of β-hydroxyethylphthalimide,[443] and (*d*) the action of halogen acids on epihydrinphthalimide.[439]

453. Hydrolysis of Nitrosoanilines

$$C_6H_5NRR' \xrightarrow{(HONO)} p\text{-}RR'NC_6H_4NO \xrightarrow{H_2O} RR'NH + p\text{-}HOC_6H_4NO$$

This classical method for preparing secondary amines is rarely used. It has been applied in the preparation of some α-dialkylamino-ω-methylaminoalkanes (65–70%).[158] Higher yields have been obtained by hydrolyzing with sodium bisulfite rather than with sodium hydroxide, which is the common reagent.

454. Hydrolysis of Quaternary Imine Salts

$$ArCH{=}NR \xrightarrow{R'X} [ArCH{=}NRR']^+X^- \xrightarrow{H_2O} RRNH$$

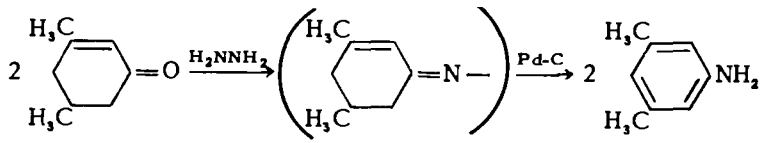
The alkylation of Schiff bases and hydrolysis of the resulting quaternary salts is an excellent method for obtaining certain secondary amines, RR'NH, particularly where R' = CH_3.[214] The procedure is less satisfactory for the introduction of large alkyl groups. The Schiff base is usually a derivative of benzaldehyde. It is readily prepared, and, without isolation, is alkylated; furthermore, the salt is seldom isolated. An example is the treatment of the Schiff base from allylamine and benzaldehyde. Methylation is accomplished by the action of methyl iodide at 80° for 16 hours; subsequent hydrolysis furnishes methylallylamine in 71% yield.[553]

455. Hydrolysis of Cyanamides

$$2RBr \xrightarrow{Na_2NCN} R_2NCN \xrightarrow{H_2O} R_2NH + CO_2 + NH_3$$

Examples include the synthesis of diallylamine (88%) and di-*n*-butylamine (75%).[460]

456. Ring Dehydrogenation



Azines of certain carbonyl compounds like 3-methyl-5-alkyl-2-cyclohexen-1-ones and the alkylated 1-tetralones have been aromatized to the corresponding 3-methyl-5-alkylanilines and 1-aminonaphthalenes by boiling with a palladium-carbon catalyst in triethylbenzene.[449] The yields in the first step are in the range 24% to 74% and in the second 20% to 55%.

The nuclear amino group is stable during the sulfur dehydrogenation of 2-amino-9,10-dihydrophenanthrene (cf. method 2).[450] In another instance, it is protected by acetylation before dehydrogenation.[491]

457. Condensation of Grignard Reagents and O-Methylhydroxylamine

$$CH_3ONH_2 \xrightarrow{2RMgX} RNHMgX \xrightarrow{H_2O} RNH_2$$

A general method for the preparation of primary amines, free from secondary and tertiary amines, involves the interaction of Grignard reagents and O-methylhydroxylamine. The yields range from 45% to 90% for many amines including ethylamine (81%), *t*-butylamine (70%), *n*-amylamine (65%), and β-phenylethylamine (68%).[512]

Grignard reagents which have been prepared from polymethylene halides and magnesium *in the presence of 0.1% water in the ether* react readily with O-methylhydroxylamine to form the corresponding polymethylene diamines (50–68%).[512]

458. Addition of Grignard Reagents to Schiff Bases

$$ArCHO \xrightarrow{RNH_2} ArCH{=}NR \xrightarrow{R'MgX} ArCH(R')NHR$$

This method is particularly desirable when the stable and readily available Schiff bases from substituted benzaldehydes are employed. It furnishes a good synthesis for amines of the type ArCH(R')NHR where the two R groups may be widely varied to include those from many Grignard reagents and primary aliphatic amines, e.g., N-methyl-1,2-diphenylethylamine (95%)[470] and 1-ethylamino-1-phenylbutane (90%).[471] The reaction of aliphatic aldimines and Grignard reagents has been found to proceed less readily.[370]

459. Interaction of Grignard Reagents and Halo amines[376]

$$RMgX + NH_2Cl \longrightarrow RNH_2 + MgXCl \text{ or } RCl + MgXNH_2$$

460. Reduction of Unsaturated Amines[367,453] (cf. methods 431 and 443)

$$RCH{=}CHCHO \xrightarrow{2HNR_2} RCH(NR_2)CH{=}CHNR_2 \xrightarrow[70\text{–}93\%]{H_2,Pt} RCH(NR_2)CH_2CH_2NR_2$$

461. Interaction of Sodium Amide and Halogen Compounds[384-387]

$$RX + NaNH_2 \xrightarrow[\text{Ammonia}]{\text{Liquid}} RNH_2 + NaX$$

R = *n*-hexyl (74%);[384] R = 2-pyridyl (67%).[387]

462. Rearrangement of Hydrazobenzenes[489,490]

$$C_6H_5NHNHC_6H_5 \xrightarrow{H^+} H_2NC_6H_4C_6H_4NH_2$$

463. Interaction of Amines and β-Keto Esters[511]

$$RCOCH_2CO_2C_2H_5 \xrightarrow{R'NH_2} RC(NHR')=CHCO_2C_2H_5$$

464. Condensation of Unsaturated Amines and Aromatic Compounds[496]

$$CH_2=CHCH_2NH_2 + ArH \xrightarrow{AlCl_3} ArCH(CH_3)CH_2NH_2$$

TABLE 81. AMINES

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic Amines				
C_1	Methylamine	437	72	24[235]	−6.5*
		431	51	24[128]	
		446	78	24[247]	
		447	60†	24[271]	
C_2	Ethylamine	437	83	24[235]	16.6*, 160HBr*
		446	90	24[245]	
	Dimethylamine	431	95	24[129]	171HCl*
C_3	*n*-Propylamine	446	90	24[245]	48, 158HCl*
	Isopropylamine	446	70	24[245]	32
		426	89	24[347]	34
	Trimethylamine	431	90	24[127]	3.5*, 275HCl*
C_4	*n*-Butylamine	426	60	24[350]	75-80, 195HCl*
		435	47	24[84]	76.5/742, 1.4008
		457	63	24[512]	78, 151Pi*
	s-Butylamine	426	54	24[174]	63/745, 1.3939
		426	60	24[350]	59-65
		431	80	24[209]	66
	Isobutylamine	426	52	24[174]	68/745, 1.3969
		446	90	24[245]	67
		447	71†	24[271]	164HCl
		457	90	24[512]	69, 150Pi
	t-Butylamine	429	82	24[371]	44.5, 1.3770
		450	78	24[454]	46, 1.3800
		451	78	24[506]	310HCl
		452	67†	24[480]	46, 198Pi*
		457	70	24[512]	45, 1.3789, 134Bz
	Methylisopropylamine	431	65	24[220]	50, 74HCl
		431	59	24[212]	45-55, 135Pi
	Tetramethylammonium chloride	436	95	24[537]	
C_5	*n*-Amylamine	426	62	24[346]	100-104
		427	95	24[203]	
		427	68	24[303]	105
		446	88	24[245]	96
		449	75	24[293]	138Pi
		457	65	24[512]	104, 139Pi
	2-Aminopentane	431	66	24[227]	89
	3-Aminopentane	431	60	24[227]	92
	Isoamylamine	446	88	24[245]	78
		457	71	24[512]	96, 138Pi
	t-Amylamine	452	63†	24[480]	78
		457	48	24[512]	78, 183Pi
	Neopentylamine hydrochloride	446	94	24[248]	(273d)

For explanations and symbols see pp. xi-xii.

TABLE 81 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic Amines *(continued)*				
C_5	Methyl-*n*-butylamine	429	26†	24[369]	91/750, 1.4011
	Ethyl-*n*-propylamine	428	53	24[344]	78, 223HCl
		429	43†	24[368]	80/738, 1.3966, 224HCl
	N,N-Diethylmethylamine	431	92	24[212]	185Pi
C_6	*n*-Hexylamine	427	70	24[310]	130
		446	70	24[245]	128
		449	75	24[293]	126Pi
		461	74	24[384]	
	2-Methyl-4-aminopentane	431	55	24[207]	109, 1.4063[25], 139HCl*
	2,2-Dimethyl-3-aminobutane	431	51	24[208]	102, 297HCl
	Ethyl-*n*-butylamine	429	52†	24[368]	109/737, 1.4056, 197HCl
	Dimethyl-*n*-butylamine	432	80	24[123]	94
	Triethylamine	428	50	24[344]	89
C_7	*n*-Heptylamine	426	64	24[347]	153
		426	73	24[350]	152–157
		427	95	24[203]	
		431	63	24[208]	58/23, 122Pi*
		446	65	24[246]	156
		449	75	24[293]	119Pi
	2-Aminoheptane	426	80	24[206]	142.5
		431	80	24[206]	142, 1.4150[24], 83HCl
		432	55	24[206]	142.5
	n-Propyl-*n*-butylamine	429	54†	24[368]	93/200, 1.4112, 268HCl
	Isopropyl-*n*-butylamine	429	52†	24[369]	125/748, 1.4050
	Diethylisopropylamine	436	60	24[126]	108
	n-Butyltrimethylammonium bromide	436	93	24[139]	(198)
C_8	Ethyl-*n*-hexylamine	434	76	24[135]	158/743, 191HCl
	Di-*n*-butylamine	455	75	24[460]	160
C_{12}	Di-*n*-hexylamine	434	100	24[557]	122/15, 270HCl
	Alicyclic Amines				
C_3	Cyclopropylamine	446	50†	24[250]	50/750, 149Pi
C_5	Cyclopentylamine	426	80	24[14]	
C_6	Cyclohexylamine	426	60	24[350]	135
		426	90	24[308]	48–52/30, 1.4569[25], 206HCl
		430	94	24[377]	
		431	50	24[207]	
		432	75	24[547]	
		449	82	24[294]	
C_7	2-Methyl-1-aminocyclohexane	446	77†	24[251]	150, 1.4575[16], 147Bz

TABLE 81 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
	Alicyclic Amines *(continued)*				
C_7	3-Methyl-1-aminocyclohexane	446	66†	24[251]	150/747, 1.4488[22], 163Bz
	4-Methyl-1-aminocyclohexane	446	90	24[251]	150/743, 1.4535[15], 260HCl
C_8	β-Cyclohexylethylamine	430	79	24[378]	85/25, 1.4656, 256HCl
	trans-2-Ethylcyclohexylamine	426	80	24[348]	151/745, 65/17, 198Pi
	N-Ethylcyclohexylamine	430	91	24[309]	165/745
C_9	1-Cyclohexyl-2-aminopropane	430	77	24[378]	87/21, 1.4615, 192HCl
	β-Methyl-β-cyclohexylethylamine	430	86	24[378]	91/17, 1.4718, 196HCl
	N-Methyl-β-cyclohexylethylamine	430	85	24[378]	78/9, 1.4586, 172HCl
C_{10}	9-Aminodecalin	425	73	24[3]	92/12, 148Bz
C_{12}	Dicyclohexylamine	430	95	24[14]	145/30
		431	70	24[215]	115–120/10, 333HCl
	Aromatic Amines				
C_6	Aniline	425	86	24[5]	184, 195HCl
		447	76	24[271]	115Ac
		449	85	24[294]	
C_7	Benzylamine	426	73	24[346]	74/15
		427	72	24[302]	
		427	69	24[307]	85/24
		431	89	24[204]	80/8
		432	60	24[547]	182/680, 198Pi
		435	53	24[96]	75/14, 105Bz*
		437	84	24[234]	184
		446	85	24[254]	184, 258HCl
		447	94†	24[278]	257HCl
		449	75	24[294]	
		451	81	24[375]	84/20, 60Ac
		452	75†	24[428]	187, 60Ac
		457	57	24[512]	90/12, 194Pi
	N-Methylaniline	431	50	24[211]	196*
		436	90	24[117]	
		436	73	24[135]	101Ac
	o-Toluidine	425	73	24[4]	199*, 111Ac
	m-Toluidine	425	25†	24[528]	201/756, 65Ac
	p-Toluidine	425	91	24[4]	200*, 149Ac
C_8	α-Phenylethylamine	426	97	24[347]	76/13, 158HCl
		431	52	24[208]	81/18

For explanations and symbols see pp. xi–xii.

TABLE 81 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
		Aromatic Amines *(continued)*			
C_8	α-Phenylethylamine *(continued)*	431	69	24[207]	
		432	66	24[399]	186
		446	60	24[255]	73/14, 104Ac
		447	68†	24[275]	70/12, 104Ac
	β-Phenylethylamine	427	87	24[310]	93/15, 219HCl
		427	72	24[308]	107/37, 1.5306, 174Pi
		437	54	24[235]	
		446	60	24[254]	
		449	70	24[294]	
		452	95	24[428]	205
		457	68	24[512]	78/10, 167Pi
	o-Methylbenzylamine	427	69	24[309]	105/20
		427	88	24[302]	134/85, 1.5412
		431	83	24[204]	
	p-Methylbenzylamine	427	88	24[307]	108/54, 234HCl
		432	62	24[547]	200/680, 205Pi
	p-Ethylaniline	425	90	24[7]	
		440	83	24[395]	216, 94Ac*
	3-Amino-1,2-dimethylbenzene	425	92	24[11]	119/25, 134Ac
	4-Amino-1,2-dimethylbenzene	425	69	24[12]	
		435	66	24[87]	118/25, (49)
		449	21†	24[297]	(51)
	1,3-Dimethyl-5-aminobenzene	438	75	24[12]	218/760, (10), 1.5581
	N-Ethylaniline	431	63	24[211]	205*, 135Pi
		436	75	24[135]	
	N-Methylbenzylamine	429	72	24[373]	186
	N,N-Dimethylaniline	431	79	24[217]	195
		436	86	24[138]	
		436	68	24[131]	
C_9	1-Phenyl-1-aminopropane	431	65	24[207]	
	2-Phenyl-1-aminopropane	435	51	24[86]	83/10, 145HCl
		446	60	24[257]	92/12, 147HCl
		464	94	24[496]	98/19, 1.5255, 144HCl
	1-Phenyl-2-aminopropane	426	55	24[349]	
		431	85	24[205]	80/10, 146HCl
		435	51	24[86]	82/11, 149HCl
		446	42	24[256]	104/22, 152HCl
		449	73	24[296]	146HCl
	α,α-Dimethylbenzylamine	446	84	24[258]	73/8, 1.5175-85[25], 241HCl
	p-n-Propylaniline	440	67	24[395]	220-225, 96Ac
	p-Isopropylaniline (p-cumidine)	425	58	24[8]	105/20, 102Ac
	N-Methyl-α-phenethylamine	432	60	24[401]	179HCl

TABLE 81 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
		Aromatic Amines *(continued)*			
C_9	N-Ethyl m-toluidine	436	66	24[115]	112/20
	Benzyldimethylamine	436	80	24[123]	176-180
	N-Methyl-N-ethylaniline	431	88	24[217]	209, 129Pi
	N,N-dimethyl-m-toluidine	436	60	24[132]	206/740
	N,N-Dimethyl-p-toluidine	436	53	24[132]	206/740
	Phenyltrimethylammonium sulfate	436	90	24[143]	(126), 124Pi
	5-Aminohydrindene	451	92	24[505]	247, (34)
C_{10}	1-Phenyl-3-aminobutane	431	67	24[205]	80/4, 148HCl
	2-Amino-3-phenylbutane	447	96†	24[274]	111/14
	o-Amino-t-butylbenzene	425	85	24[10]	161Ac
	p-Amino-t-butylbenzene	425	73	24[9]	93/3, (16), 170Ac
	2-Amino-p-cymene	425	90	24[15]	242/760, 110/10
	3,4-Diethylaniline	425	99	24[13]	117/10, 1.5458[29], 119Ac
	1-Methylamino-1-phenylpropane	458	75	24[471]	
	1-Methylamino-2-phenylpropane	436	44	24[86]	100/20, 133HCl
		454	80	24[214]	98/18, 159HCl
		464	47	24[496]	87/10, 1.5112, 146HCl
	2-Methylamino-1-phenylpropane	454	93	24[214]	80/6, 136HCl
	N-Ethyl-α-phenethylamine	432	70	24[401]	200HCl
	N,N-Dimethylphenethylamine	432	83	24[400]	98/22
	Benzylmethylethylamine	436	100	24[122]	80/16, 152HCl
	N,N-Diethylaniline	431	70	24[212]	140Pi
		436	87	24[138]	216
		436	99	24[131]	
	p-Dimethylaminoethylbenzene	436	27	24[395]	104/16
	1-Naphthylamine	425	96	24[4]	(50), 159Ac*
		449	70†	24[298]	
	2-Naphthylamine	438	96	24[389]	(112), 132Ac*
	1,2,3,4-Tetrahydro-2-naphthylamine	430	57	24[383]	118/8, 140/20
C_{11}	1-Ethylamino-2-phenylpropane	431	94	24[214]	127/30, 160HCl
		464	77	24[496]	93/10, 1.5032, 159HCl
	1-Dimethylamino-2-phenylpropane	464	62	24[496]	80/10, 1.4983, 222HCl
	2-Dimethylamino-1-phenylpropane	431	67	24[214]	100/12, 161HCl
	7-Methyl-1-naphthylamine	438	90	24[389]	140/3, (59)
	α-Aminomethylnaphthalene	435	72	24[96]	135/0.3

For explanations and symbols see pp. xi-xii.

TABLE 81 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aromatic Amines *(continued)*				
C_{11}	N-Methylnaphthylamine	437	73	24[343]	200–205/30, 262HCl
		451	70	24[492]	170/12
C_{12}	β-(α-Naphthyl)-ethylamine	447	45†	24[276]	170/12, 245HCl
	α-(β-Naphthyl)-ethylamine	432	84	24[399]	199HCl
	N-Ethyl-α-naphthylamine	431	88	24[213]	190/20*
	N-Ethyl-β-naphthylamine	431	64	24[213]	316*
	N,N-Dimethyl-α-naphthylamine	436	70	24[133]	272*
	N,N-Dimethyl-β-naphthylamine	436	64	24[131]	305*
	2-Aminobiphenyl	425	93	24[18]	182/30, (49)
	3-Aminobiphenyl	425	99	24[19]	178/18, (31)
	4-Aminobiphenyl	425	93	24[4]	211/30, (54)*, 171Ac
	o-Aminocyclohexylbenzene	425	85	24[17]	134/3, 106/0.5
	3-Aminoacenaphthene	425	85	24[22]	(81.5), 193Ac
C_{13}	Benzhydrylamine	426	87	24[347]	171/16, 270HCl
		432	96	24[405]	
	o-Phenylbenzylamine	427	60	24[312]	168/15, 179/12, 217HCl
	N-Phenyl benzylamine (benzylaniline)	429	97	24[215]	146/1
		436	87	24[114]	180/12, (36)
	N-Phenyl-p-toluidine	451	40†	24[493]	
	Methyldiphenylamine	431	65	24[216]	148/13
	2-Aminofluorene	425	82	24[21]	(127)
	9-Aminofluorene	426	74	24[351]	(65), 255HCl
		432	75	24[404]	
		452	87†	24[431]	(62)
C_{14}	β,β-Diphenylethylamine	427	76	24[311]	134/2, (43.5)
	Dibenzylamine	429	50	24[375]	150–155/4–5
	m-Tolylbenzylamine	429	94	24[372]	157/4, 199HCl
	Ethyldiphenylamine	431	80	24[216]	150/13
	2-Dimethylaminobiphenyl	436	94	24[130]	145/11
	N,N-Diethyl-α-naphthylamine	431	40	24[212]	155–165/30, 1.5961, 154Pi
		436	60	24[131]	
	1-Aminophenanthrene	451	72†	24[304]	(146), 220Ac
		456	60	24[491]	(147), 204Pi*
	2-Aminophenanthrene	449	88†	24[298]	(84)
		451	86†	24[503]	(86)
		456	68	24[450]	(86)
	3-Aminophenanthrene	449	80†	24[298]	(86)
		451	70†	24[503]	(87)
	9-Aminophenanthrene	447	81†	24[277]	(137.5)
		449	73†	24[296]	(137)
		451	60†	24[502]	(130)

TABLE 81 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aromatic Amines *(continued)*				
C_{14}	9-Aminoanthracene	425	91	24[20]	(135–140), 274Ac
C_{15}	β,γ-Diphenylpropylamine	427	88	24[311]	171/6
	γ,γ-Diphenylpropylamine	427	81	24[311]	150/2, 218HCl
	N-Methyl-1,2-diphenylethylamine	458	95	24[470]	186HCl
	9-Aminomethylphenanthrene	427	100	24[313]	(108.5), 294HCl
		435	70	24[96]	165/0.15
C_{18}	Triphenylamine	436	85	24[136]	(126)
C_{24}	p-Aminotetraphenylmethane	1	74	24[552]	(250)
	Heterocyclic Amines				
C_4	2-Aminofuran	447	54†	24[282]	124Bz
C_5	Furfurylamine	431	79	24[204]	146*
	2-Methyl-3-aminofuran	447	54†	24[281]	52/4, 137Bz
	2-Methylaminofuran	427	84	24[321]	50/10
	2-Thenylamine	444	45	24[411]	65/4, 1.5628, 189HCl
	α-Thienylaminomethane	437	84	24[248]	75/11, 194HCl
	2-Aminopyridine	435	70	24[93]	(57)
		439	76	24[506]	120/36
	3-Aminopyridine	425	93	24[23]	(64)
		435	80	24[93]	(64), 133Ac
		435	60	24[532]	109/3, (61)
		446	89	24[542]	(64)
	4-Aminopyridine	435	30	24[532]	(159)
		446	74	24[532]	(159)
	2-Aminopiperidine	430	78	24[380]	68/17, (57), 197Bz
		554	90	39[120]	68/17, (57), 225HCl
C_6	N-Methylfurfurylamine	436	50	24[120]	149/761, 1.4729, 146HCl
	1-(α-Thienyl)-1-aminoethane	432	51	24[242]	84/16, 142HCl
	β-(2-Thienyl)-ethylamine	425	63	24[91]	78/7.0, 202HCl
		427	34	24[314]	74/3, 203HCl
		446	63	24[522]	201/750, 202HCl
	2-Methyl-5-aminopyridine	446	55	24[260]	(96), 123Ac*
		447	93	24[360]	(96), 218HCl
	6-Amino-2-picoline	439	61	24[509]	125/20, (40)
	2-Aminomethylpyridine	427	38	24[315]	93/3, 76/3, 138NBz
	3-Aminomethylpyridine	427	60	24[315]	98/3, 116/3, 191NBz
	4-Aminomethylpyridine	427	60	24[315]	117/5, 112/4, 180Pi*
	2-Aminomethylpiperidine	554	61	39[126]	81/18
C_7	1-Furyl-2-aminopropane	426	90	24[349]	

For explanations and symbols see pp. xi–xii.

TABLE 81 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Heterocyclic Amines *(continued)*				
C_7	N-Ethylfurfurylamine	429	49	24[138]	75/25, 121HCl
		436	58	24[120]	167/761, 1.4688, 128HCl
	N,N-Dimethylfurfurylamine	432	60	24[397]	146
		432	85	24[141]	145, 103Pi
	2-Dimethylaminomethyl-pyrrole	444	77	24[409]	94/19, 137Pi
	α-(Ethylamino)-pyridine	451	81	24[404]	82/4
C_8	1-(α-Furyl)-3-aminobutane	431	50	24[203]	190/760, 102/25
	N-Ethyl-5-methylfurfuryl-amine	444	45	24[410]	76/17, 1.4689[25], 139HCl
	N,N-Dimethyl-5-methyl-furfurylamine	444	65	24[410]	70/25, 1.4620[25], 158HCl
	β-(3-Pyridyl)-isopropyl-amine	432	36	24[406]	88/1, 187Pi
	γ-Piperidinopropylamine	427	69	24[195]	205/730, 1.4750, 210Pi
	3-Aminothianaphthene	425	67	24[34]	168Ac
	5-Aminothianaphthene	425	65	24[32]	(72)
C_9	N,N-Diethylfurfurylamine	432	68	24[141]	172, 85Pi
	δ-Piperidinobutylamine	427	54	24[195]	120/25, 1.4756, 160Pi
	2-Aminoquinoline	435	50	24[94]	(129)
	3-Aminoquinoline	425	97	24[24]	(83), 172Ac
		435	60	24[94]	(84)
		435	73	24[164]	(83), 172Ac
	4-Aminoquinoline	435	70	24[332]	(154)
		446	90	24[24]	(69), (156), 178Ac
		446	90	39[164]	(156), 178Ac
		575	43†	39[163]	(153)
	5-Aminoquinoline	425	80	24[25]	181/7, (110), 240HCl
	6-Aminoquinoline	425	85	24[29]	187-200/10-13, (114)
	7-Aminoquinoline	425	95	24[28]	(75), (93)
	8-Aminoquinoline	425	95	24[26]	141/7, (65)
		438	88	24[393]	(65.5)
	1-Aminoisoquinoline	439	70	24[810]	(123)*
	4-Aminoisoquinoline	435	70	24[33]	(108.5), 168Ac
	5-Aminoisoquinoline	425	80	24[33]	(129), 166Ac
		438	65	24[392]	(132)
	6-Aminoisoquinoline	438	85	24[546]	(218)
	cis-trans-Decahydro-quinoline	430	95	24[309]	206
C_{10}	β-3-Thianaphthylethyl-amine	427	32	24[544]	125/1, 177Pi
	1-(β-Diethylaminoethyl)-pyrrole	436	66	24[388]	80/4

TABLE 81 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Heterocyclic Amines *(continued)*				
C_{10}	N,N-Diethyl-β-pyridyl-methylamine	428	55	24[344]	100/12, 170Pi
	2-Aminolepidine	435	78	24[95]	(133), 232Ac
C_{11}	3-Dimethylaminomethyl-indole	444	100	24[412]	(134), 142Pi
	2-Dimethylaminoquinoline	436	91	24[137]	(71)
C_{12}	1-Aminodibenzofuran	435	24	24[90]	(74), 205Ac
	3-Aminodibenzofuran	425	91	24[551]	(94)*
	4-Aminodibenzofuran	438	45	24[394]	(85)*
		446	55	24[261]	
	2-Aminodibenzothiophene	425	91	24[35]	(133)
		435	62	24[91]	(129), 178Ac
		451	72	24[35]	(131)
	3-Aminodibenzothiophene	461	50	24[385]	(122), 200Ac
	4-Aminodibenzothiophene	435	37†	24[91]	(110), 198Ac
		....	64	24[36]	(110)
C_{13}	2-Aminoacridine	....	60	39[219]	(216)
	9-Aminoacridine	435	89	39[217]	(233)

For explanations and symbols see pp. xi-xii.

TABLE 82. DIAMINES

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic Diamines				
C_2	Ethylenediamine	447	75†	24[280]	172Ac
		452	60	24[432]	116, 172Ac
C_3	1,2-Diaminopropane	425	52	24[487]	221HCl
	Trimethylenediamine	427	23	24[195]	138/735, 1.4600, 178Pi
		446	54	24[220]	131/760*, 250Pi
		449	65	24[220]	250Pi
		452	90	24[432]	136, 140Bz*
	N-Methylethylenediamine	427	66	24[341]	111, 112Bz*
		451	33†	24[497]	116/757, 220Pi
C_4	1,2-Butylenediamine	441	55	24[452]	140, 1.4490, 187Bz
	Tetramethylenediamine	446	60	24[262]	177Bz
		447	48†	24[280]	
		449	80	24[294]	
		452	74	24[434]	159/760

For explanations and symbols see pp. xi-xii.

TABLE 82 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic Diamines *(continued)*				
C_4	2,3-Diaminobutane	425	40	24[487]	3 12HCl
	Isobutylenediamine	427	80	24[318]	115/754*, 100Ac
	γ-Methylaminopropylamine	427	70	24[319]	141, 1.4479, 226Pi
	N-Monoethylethylenediamine	451	20†	24[497]	131/759, 195Pi
	β-Dimethylaminoethylamine	427	47	24[316]	108
	N,N′-Dimethylethylenediamine	436	50	24[147]	150–160, 160Pi
C_5	Pentamethylenediamine (cadaverine)	457	68	24[512]	180, 237Pi
	2-Methyl-1,2-diaminobutane	427	61†	24[322]	143/752, 1.4483, 229Pi
	2-Methyl-1,4-diaminobutane	446	72	24[263]	154Bz
	2,2-Dimethyl-1,3-propanediamine	425	90	24[1]	78/50, (29), 257HCl*
		425	67	24[37]	153/737, 1.4566, 240Pi
	γ-Ethylaminopropylamine	427	74	24[195]	156/735, 1.4441, 193Pi
	1-Dimethylamino-2-aminopropane	431	40	24[178]	113, 1.4177[25]
C_6	Hexamethylenediamine	452	86†	24[435]	258HCl
		457	51	24[512]	204, 220Pi
	1-Ethylamino-2-aminobutane	441	20	24[452]	157, 1.4431, 116Bz
	2-Methyl-2-methylamino-1-aminobutane	427	66†	24[322]	155/737, 1.4502, 203Pi
	3-Ethylamino-2-methyl-2-aminopropane	441	42	24[452]	141, 1.4300, 108Bz
	β-Diethylaminoethylamine	427	53	24[304]	145/760, 99/13, 207Pi
		427	62	24[317]	144–150, 211Pi
		441	89	24[451]	
		452	57	24[353]	145–149
C_7	1-Diethylamino-2-aminopropane	431	62	24[218]	153, 182Pi
		431	65	24[205]	154/760, 70/20
	γ-Diethylaminopropylamine	427	72	24[195]	168/735, 1.4355, 194Pi
		452	60	24[433]	170, 1.4437
	1-Dimethylamino-3-methylaminobutane	436	100	24[146]	56/14, 186Pi
	1,3-*bis*-Dimethylaminopropane	460	78	24[453]	145, 207Pi
	β-Diethylaminoethylmethylamine	436	40	24[147]	160

TABLE 82 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic Diamines *(continued)*				
C_8	1-Diethylamino-2-aminobutane	425	55	24[39]	80/16
		441	54	24[452]	173, 1.4347
	1-Diethylamino-3-aminobutane	426	60	24[353]	74/12, 1.4428[18]
		431	72	24[205]	70/10, 1.4430[18]
	4-Diethylaminobutylamine	427	97	24[321]	88/18, 1.4462*, 156Pi
		427	50	24[194]	86/16, 1.4420[25]
	1,3-*bis*-Dimethylaminobutane	436	100	24[146]	56/12
		460	74	24[453]	
	1,4-*bis*-Dimethylaminobutane	436	92	24[123]	167, 199Pi
	1-Diethylamino-3-methylaminopropane	453	65	24[158]	60/8, 1.4390[19]
C_9	1-Diethylamino-3-aminopentane	426	75	24[536]	86–95/22, 1.4421, 155Pi
	Tetraethylmethylenediamine	....	76	24[513]	167/757
C_{10}	Decamethylenediamine	427	80	24[323]	146/14, (60)
	1-Diethylamino-4-aminohexane	426	64	24[352]	105–112/20
	β-Diethylaminoethyldiethylamine	436	50	24[147]	151Pi
	Alicyclic Diamines				
C_4	*trans*-1,2-Diaminocyclobutane	447	12†	24[273]	74/50, 1.4837
		449	55†	24[273]	74/50, 1.4837
C_6	1,3-Diaminocyclohexane	430	60	24[279]	265Pi
		447	50†	24[279]	198/760, 265Pi
		450	100	24[279]	198/760, 265Pi
	1,4-Diaminocyclohexane	447	72†	24[278]	
C_8	*cis*-1,4-Diaminomethylcyclohexane	427	33†	24[324]	115/8, 350HCl
	trans-1,4-Diaminomethylcyclohexane	427	22†		118/10, (27), 380HCl
	N-Ethyl-1,4-cyclohexanediamine	430	63	24[198]	87/11, 1.4767[25]
C_{10}	N,N-Diethyl-1,4-cyclohexanediamine	430	70	24[198]	85/4, 1.4720[25]
	Aromatic Diamines				
C_6	o-Phenylenediamine	425	85	24[41]	(101)
	m-Phenylenediamine	425	95	24[14]	154/10, 70Ac
	sym-Triaminobenzene	425	76	24[42]	(84), (112), 357Bz

For explanations and symbols see pp. xi–xii.

TABLE 82 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aromatic Diamines *(continued)*				
C_7	*o*-Aminobenzylamine	425	43	24[38]	85–90/1, (59), 138Ac
	m-Aminobenzylamine	452	28†	24[38]	134/4, 1.6092, 174Bz
	2,4-Diaminotoluene	425	74	24[43]	(98)
	sym-Triaminotoluene	425	60	24[42]	(122)
C_8	Phenylethylenediamine	427	90	24[316]	159Ac
	m-Xylylendiamine	452	38†	24[436]	141/14, 135Ac
	N-Phenylaminoethylamine	441	89	24[451]	
	p-Aminodimethylaniline	....	75	24[517]	140/12, 130Ac
C_{10}	*m*-Phenylen-β,β'-diethylamine	427	79	24[325]	161/14, 302HCl
	p-Phenylen-β,β'-diethylamine	427	75	24[325]	116/0.9, (36), 210Ac
	N-(2-Dimethylaminoethyl)-aniline	436	88	24[149]	127/3, 1.5251^{25}, 124HCl
C_{12}	3,3′-Diaminobiphenyl	425	95	24[14]	
	4,4′-Diaminobiphenyl (benzidine)	425	82	24[44]	(125)
C_{13}	4,4′-Diaminodiphenylmethane	....	70	24[516]	(91), 237Ac
C_{14}	*p,p′-bis*-Aminomethylbiphenyl	427	80	24[326]	180/0.5, (145), 235Pi
C_{15}	*p,p′-bis*-Aminomethyldiphenylmethane	427	80	24[326]	(90), 224Bz

For explanations and symbols see pp. xi–xii.

TABLE 83. OLEFINIC AMINES

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
C_3	Allylamine	450	73	24[456]	57/746
C_4	Methallyl amine	435	70	24[100]	78.8, 1.431
		450	35	24[457]	62, 1.4155, 158Pi
	Allylmethylamine	451	48	24[406]	65, 1.4065
		454	71	24[553]	64
C_5	1-Amino-4-pentene	427	60	24[327]	106/767, 1.428^{16}, 116Pi
	Allyldimethylamine	436	43	24[151]	64, 1.3981^{25}, 116Pi
C_6	1-Ethylamino-3-butene	436	42	24[182]	109
	Diallylamine	455	88	24[460]	111

TABLE 83 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
C_7	1-Dimethylamino-4-pentene	29	80	2[193]	118/750, 1.4202^{18}
	Allyldiethylamine	436	84	24[151]	111, 1.4170^{25}, 91Pi
C_8	*p*-Aminostyrene	19	20	2[166]	79/2.5, 1.6070^{25}
C_9	1-Diethylamino-4-pentene	29	85	2[193]	156/746, 1.4310
	2-(*o*-Aminophenyl)-propene	19	87	2[108]	87/2, 1.5676^{25}
	N-Allylaniline	451	63	24[495]	80/2
C_{10}	α-Allylbenzylamine	446	90	24[264]	75/3.5, 1.5300, 153Pi
	p-Dimethylaminostyrene	19	30	2[455]	1.6120, (17)
C_{14}	*cis-p*-Aminostilbene	425	72	24[48]	150/0.2
	trans-p-Aminostilbene				(151)
	cis-o,o′-Diaminostilbene	30	69	2[220]	(108), 156Pi
	cis-p,p′-Diaminostilbene	30	89	2[221]	(121), 172Ac
	trans-p,p′-Diaminostilbene	425	81	24[46]	(229)
	cis-p,p′-Diaminostilbene	425	89	24[45]	(121), 172Ac
	trans-p,p′-Diaminostilbene				(231)

For explanations and symbols see pp. xi–xii.

TABLE 84. ACETYLENIC AMINES

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
C_6	3-Dimethylamino-1-butyne	443	63	24[472]	95
C_7	1-Diethylamino-2-propyne	43	83	3[55]	120, 1.4296^{25}
C_8	3-Diethylamino-1-butyne	443	65	24[472]	126, (10), 179HCl
	1-Diethylamino-2-butyne	44	74	3[55]	153, 1.4413^{25}
C_{13}	3-Diethylamino-1-phenyl-1-propyne	444	80	24[433]	137/18, 137HCl
C_{14}	*p,p′*-Diaminotolane	425	60	24[47]	(235), 281Ac

For explanations and symbols see pp. xi–xii.

TABLE 85. HALO AMINES

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic and Alicyclic Halo Amines				
C_2	β-Bromoethylamine	51	83	4[70]	
		52	72	4[138]	173HBr
		....	80	24[515]	(174)
	β-Iodoethylamine	51	77	4[573]	
	N-Tetrachloro-1,2-diaminoethane	69	92	4[656]	78/10, (4.5)

For explanations and symbols see pp. xi–xii.

TABLE 85 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic and Alicyclic Halo Amines *(continued)*				
C_3	1-Amino-2-bromopropane	52	70	4[138]	159HBr
	γ-Bromopropylamine	452	89	24[438]	163HBr
	Isopropyldichloroamine	69	76	4[656]	43/15, 1.4572[23]
C_4	2-Chloroethylethylamine	53	91	4[176]	223HCl
	β,β′-Dichlorodiethylamine	53	59	4[177]	217HCl, 136Bz
	β-Dimethylaminoethyl chloride	53	90	4[696]	203HCl
	β-Dimethylaminoethyl bromide	51	83	4[70]	
	t-Butylchloroamine	69	75	4[657]	
	n-Butyldichloroamine	69	92	4[656]	40/17, 46/30, 1.4553
	N-Chlorodiethylamine	69	94	4[655]	
C_5	1-Dimethylamino-2-chloropropane	53	68	4[171]	186HCl, 103Pi
	1-Dimethylamino-3-chloropropane	53	96	4[584]	145HCl
	2-Dimethylamino-1-chloropropane	53	41	4[171]	104HCl, 167Pi
	3-Bromopropyldimethylamine	54	75	4[376]	51/15, 1.4602
C_6	1-Dimethylamino-3-chlorobutane	53	85	4[175]	39/10, 168HCl
	β-Diethylaminoethyl chloride	53	85†	4[170]	69/50
	β-Diethylaminoethyl bromide	51	80	4[70]	
	β,β′,β″-Trichlorotriethylamine	53	66	4[178]	133HCl, 137Pi
	o-Chlorocyclohexylamine	52	80	4[137]	85/15
	o-Bromocyclohexylamine	52	70	4[137]	168HCl
	Cyclohexyldichloroamine	69	95	4[656]	90/17
C_7	1-Methylamino-6-bromohexane	54	100	4[128]	60HBr
	1-Diethylamino-2-chloropropane	53	78	4[172]	107HCl, 126Pi
	1-Diethylamino-3-chloropropane	53	57	4[173]	82/28, 171/169, 64HCl
		436	70	24[541]	86HCl
		436	70	24[153]	70/20
	2-Diethylamino-1-chloropropane	53	73	4[172]	107HCl, 113Pi
	3-Bromopropyldiethylamine	54	80	4[375]	94HBr

TABLE 85 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic and Alicyclic Halo Amines *(continued)*				
C_8	1-Bromo-6-dimethylaminohexane	54	100	4[377]	
	1-Diethylamino-3-chlorobutane	53	87	4[174]	72/17, 82HCl
		436	68	24[541]	84HCl
C_9	1-Diethylamino-3-chloropentane	53	72	4[174]	87/18
	1-Diethylamino-4-chloropentane	73	90	4[204]	67/5
C_{10}	1-Bromo-6-diethylaminohexane	54	98	4[377]	
	1-Diethylamino-4-methyl-4-chloropentane	73	75	4[204]	65/3, 1.4459
	Aromatic Halo Amines				
C_6	o-Chloroaniline	425	97	24[50]	95–100/8, 235HCl
		425	92	24[4]	209*, 86Ac
	o-Bromoaniline	425	82	24[6]	229, (32)*, 99Ac*
	o-Iodoaniline	425	83	24[53]	(61), 110Ac*
	m-Fluoroaniline	425	90	24[558]	187/770
	m-Chloroaniline	425	90	24[50]	95–100/9, 119Bz
	m-Bromoaniline	425	80	24[51]	124/10, (17), 120Bz*
		446	87	24[253]	250, 88Ac
	m-Iodoaniline	425	83	24[53]	146/15, (33)*, 119Ac*
	p-Fluoroaniline	425	95	24[52]	99/33, 152Ac*
		425	91	24[558]	188/762, 185Bz*
	p-Chloroaniline	425	100	24[49]	(71), 173Ac
		425	97	24[50]	100–110/8, 188Bz
	p-Bromoaniline	425	97	24[4]	(66)*, 168Ac
		425	83	24[50]	(60), 202Bz
	p-Iodoaniline	64	84	4[290]	(63)
C_7	o-Chlorobenzylamine	426	81	24[50]	95–100/9, 116Bz
		431	88	24[50]	90–95/8, 116Bz
	p-Chlorobenzylamine	427	64	24[50]	98–102/10, 240HCl
		447	100	24[285]	215/734, 259HCl
	o-Aminobenzyl chloride	51	84	4[69]	
	o-Aminobenzyl bromide	51	91	4[208]	
	4-Amino-3-chlorotoluene	64	60	4[291]	225
C_8	1-Phenyl-1-amino-2-chloroethane	52	76	4[138]	190HCl
	N,N-Dimethyl-o-chloroaniline	436	90	24[132]	206/740
	N,N-Dimethyl-o-bromoaniline	436	70	24[155]	101/12

For explanations and symbols see pp. xi–xii.

TABLE 85 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aromatic Halo Amines *(continued)*				
C_8	N,N-Dimethyl-*m*-chloroaniline	436	75	24[132]	232/740
	N,N-Dimethyl-*m*-bromoaniline	436	54	24[155]	119/8, 135Pi
	N,N-Dimethyl-*p*-fluoroaniline	436	45	24[154]	(35)
	N,N-Dimethyl-*p*-chloroaniline	56	80	4[336]	(33.5)
		436	70	24[154]	(35.5)
		436	72	24[132]	236/740, (33)
	N,N-Dimethyl-*p*-iodoaniline	59	48	4[601]	(81)
C_{10}	N,N-Diethyl-o-chloroaniline	436	91	24[132]	221/740, 164Pi
	N,N-Diethyl-*m*-chloroaniline	436	95	24[132]	250/740
	N,N-Diethyl-*p*-chloroaniline	436	95	24[132]	253/740, (46)
C_{12}	3,3′-Dibromobenzidene	462	75	24[489]	(129)

For explanations and symbols see pp. xi–xii.

TABLE 86. HYDROXY AMINES

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic Hydroxy Amines				
C_3	2-Amino-1-propanol	84	80	5[15]	80/18, 1.4502, 114Pi
		425	74	24[57]	78/15
		434	95	24[446]	73/11
	1-Amino-2-hydroxypropane	442	25	24[467]	65/4, 158/738
	3-Hydroxypropylamine	452	85	24[556]	186
	2-Amino-1,3-propanediol	84	80	5[15]	116/1, 1.4891, 97HCl
	2-(N-Methylamino)-1-ethanol	84	63	5[15]	56/11, 1.4385, 148Pi
	Dimethylaminomethanol	....	70	24[514]	1.4050
C_4	2-Amino-1-butanol	425	90	24[1]	173*
		434	100	24[446]	80/11
	1-Amino-2-butanol (as oxalate)	425	83	24[529]	(200d), 113Bz
	3-Amino-2-butanol	435	49	24[467]	162/742, 1.4482
	2-Amino-2-methyl-1-propanol	84	80	5[15]	69/10, 1.4486, 205HCl
		425	90	24[1]	

TABLE 86 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic Hydroxy Amines *(continued)*				
C_4	1-Amino-2-methyl-2-propanol	.442	30	24[468]	145–155
	β-Ethylaminoethanol	436	35	24[156]	169, 1.4440
		442	55	24[462]	169
	2-Amino-1,3-butanediol	84	80	5[15]	113/2, 1.4833^{21}
	2-Amino-2-methyl-1,3-propanediol	425	96	24[1]	
C_5	4-Amino-1-pentanol	426	80	24[354]	119/25, 100Bz
	5-Amino-1-pentanol	431	77	24[228]	81/1, (39)
		452	60	24[556]	271
	3-Amino-2-pentanol	425	92	24[54]	100/10, 1.4419
	1-Amino-4-pentanol	436	32	24[152]	$81/1, 1.4551^{25}$
	2-Methyl-2-amino-1-butanol	425	86	24[54]	98/10, 1.4468
	2-Amino-3-methyl-1-butanol (valinol)	84		5[62]	(119)
	2-Methyl-3-amino-2-butanol	91	66	5[438]	117HCl
	3-Methylamino-2-methyl-2-propanol	436	52	24[164]	143, 1.4338, 138Pi
	2-Isopropylaminoethanol	431	95	24[223]	87/23
		442	76	24[463]	171
	2-Dimethylamino-1-propanol	436	82	24[57]	65/37
	3-Dimethylamino-1-propanol	443	65	24[473]	113/150
	1-Dimethylamino-2-propanol	442	70	24[464]	126/758
	2-Amino-2-ethyl-1,3-propanediol	425	92	24[1]	
C_6	2-Amino-1-hexanol	84	65	5[84]	104/13, 114Pi
	2-Hydroxy-3-aminohexane	97	45	5[292]	95/20, 207Db
	2-Amino-4-methyl-1-pentanol	84	55	5[84]	95/11, (44), 163HCl
		434	90	24[446]	99/11
	4-Methyl-4-amino-2-pentanol	79	34	5[170]	75/15
	5-Methylamino-1-pentanol	431	50†	24[229]	97/3
	2,2-Dimethyl-3-methylamino-1-propanol	79	72	5[675]	70–82/12
		436	57	24[166]	71/14, (46), 173HCl
	1-Isopropylamino-2-propanol	431	97	24[224]	$76/22, 1.4322^{25}$, 131Pi
	3-Ethylamino-2-methyl-2-propanol	436	56	24[164]	153, 1.4344, 133Pi
	3-Dimethylamino-1-butanol	79	35	5[185]	78/14, 105BzHCl

For explanations and symbols see pp. xi–xii.

TABLE 86 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic Hydroxy Amines *(continued)*				
C_6	4-Dimethylamino-2-butanol	79	85	5[172]	
	3-Dimethylamino-2-methyl-1-propanol	84	50	5[85]	164
	3-Dimethylamino-2-methyl-2-propanol	436	40†	24[163]	130/743, 1.4215, 115HCl
	β-Diethylaminoethanol	436	70	24[156]	65/18, 1.4389[25]
		442	81	24[461]	160/741, 1.4389[25]
C_7	2-Amino-2,4-dimethyl-1-pentanol	84	80	5[15]	98/12, 1.4563
	1-Ethylamino-4-pentanol	436	32	24[152]	81/1.0, 1.4551[25], 148HBr
	5-Dimethylamino-1-pentanol	431	59†	24[229]	114/23
	4-Dimethylamino-2-methyl-2-butanol	436	34†	24[163]	160/743, 1.4295, 141HCl
	2-Diethylamino-1-propanol	84	63	5[83]	66/18, 1.4332
	3-Diethylamino-1-propanol	436	91	24[158]	95/28
	2,2-Dimethyl-3-dimethylamino-1-propanol	436	64	24[166]	63/15, 132HCl
	1-Diethylamino-2-propanol	442	88	24[464]	63/22, 1.4265*, 139HCl*
C_8	5-Isopropylamino-1-pentanol	431	71†	24[230]	98HCl
	5-Dimethylamino-2-methyl-2-pentanol	436	34†	24[163]	99/30, 1.4400, 154HCl
	3-Diethylamino-1-butanol	79	45	5[185]	85/13, 161BzHCl
	4-Diethylamino-1-butanol	84	52	5[86]	92/9, 1.4474
	1-Diethylamino-3-butanol	79	40	5[168]	73/20, 116HCl
		436	60	24[165]	82/18, 1.4372[25], 116HCl
C_9	5-Diethylamino-1-pentanol	95	68	5[709]	131/23, 1.4544
	2-Diethylamino-3-methyl-1-butanol	84	44	5[86]	90/14
	2,2-Dimethyl-3-diethylamino-1-propanol	79	86	5[675]	88/12
C_{10}	1-Diethylamino-5-hexanol	80	88	5[192]	108/10, 1.4490[25]
	Alicyclic Hydroxy Amines				
C_5	*trans*-2-Aminocyclopentanol	442	40	24[466]	194HCl
C_6	2-Aminocyclohexanol	442	63	24[467]	214, (66)
	cis-2-Aminocyclohexanol	447	68	24[284]	110/15, (70), 185HCl
	trans-2-Aminocyclohexanol				108/15, (67), 175HCl
	cis-2-Aminocyclohexanol	435	50	24[99]	(73), 187HCl
	trans-2-Aminocyclohexanol	435	72	24[99]	104/7, (66), 175HCl
		442	64	24[549]	111/16, (69), 169Bz

TABLE 86 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
	Alicyclic Hydroxy Amines *(continued)*				
C_6	*cis-trans*-4-Aminocyclohexanol	430	98	24[581]	(80), (111)
	1-Amino-1-hydroxymethylcyclopentane	84	80	5[15]	69/1, 1.4899, 131HCl
	1-Aminomethyl cyclopentanol	427	50	24[543]	140/40, 190HCl
C_7	1-Aminomethylcyclohexanol	427	70	24[543]	115/20, 190HCl
	2-Aminomethylcyclohexanol	427	68	24[335]	133/17, 1.4910[25], 150HCl
	1-Amino-1-hydroxymethylcyclohexane	84	80	5[15]	118/27, 1.4970, 159HCl
C_8	2-(N-Cyclohexylamino)-1-ethanol	84	80	5[15]	97/3, 1.4862, 130Pi
C_9	2-Amino-2-cyclohexyl-1-propanol	84	80	5[15]	104/2, (80), 202HCl
	2-Amino-3-cyclohexyl-1-propanol	84	80	5[15]	108/1, 1.4989, 192HCl
	Aromatic Hydroxy Amines				
C_6	o-Aminophenol	446	72	24[266]	(171)
	m-Aminophenol	438	50	24[390]	(123), 229HCl
C_7	o-Aminobenzyl alcohol	84	78	5[81]	(81)
	m-Aminobenzyl alcohol	425	100	24[61]	(96)
C_8	β-Amino-α-phenylethyl alcohol	427	80	24[333]	(57)
		442	18	24[468]	149-155/16
	β-Amino-β-phenylethyl alcohol	84	93	5[84]	103/2, (111), 208Pi
	β-(4-Aminophenyl)-ethanol	425	88	24[62]	(108)
	m-Aminophenylmethylcarbinol	425	94	24[60]	(64)
	2-Anilinoethanol	450	75	24[458]	170/19, 1.5749
C_9	2-Amino-1-phenyl-1-propanol	425	87	24[55]	122/4-5
		426	71†	24[356]	(103), 191HCl
	2-Amino-3-phenyl-1-propanol	84	52	5[84]	156HCl
	3-Amino-1-phenyl-1-propanol	79	70	5[166]	(64), 86Bz
	α-Phenyl-β-methylaminoethanol	79	90	5[167]	(76)
	3-Anilino-1-propanol	436	68	24[159]	192/30, 1.502
		450	80	24[459]	154/5, 1.568[18]

For explanations and symbols see pp. xi-xii.

TABLE 86 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aromatic Hydroxy Amines *(continued)*				
C_9	*p*-Dimethylaminobenzyl alcohol	79	96	5[2]	1.5775[25]
		....	65	5[781]	125/1, 1.5727[14]
C_{10}	1-Amino-2-phenyl-2-butanol	89	73	5[403]	181HCl
	2-Amino-3-phenyl-3-butanol	89	63	5[403]	239HCl
	2-Methylamino-1-phenyl-1-propanol	431	81	24[55]	115–120/5
		79	90	5[167]	(77)
	β-Ethylamino-α-phenylethyl alcohol	442	56	24[468]	140–164/14, (78)
	4-Amino-1-naphthol	433	75	24[554]	
	1-Amino-2-naphthol	433	85	24[554]	
C_{11}	2-Amino-3-phenyl-3-pentanol	89	93	5[403]	222HCl
	1-Phenyl-2-methylamino-1-butanol	79	60	5[169]	202HCl, 168Pi
		79	90	5[167]	(90)
	2-Methylamino-3-phenyl-3-butanol	89	75	5[403]	235HCl
	5-Anilino-1-pentanol	436	45	24[167]	164/1.4
	2-Diethylaminomethylphenol	444	69	24[415]	67/2, 1.5108[25]
C_{12}	Phenyl-γ-dimethylaminopropylcarbinol	89	70	5[402]	107/0.07, (48)
	β-Diethylamino-α-phenylethyl alcohol	436	66	24[468]	145/14, 1.5101[25]
	6-Anilino-1-hexanol	436	74	24[167]	138/0.05, (42)

For explanations and symbols see pp. xi–xii.

TABLE 87. AMINO ETHERS

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic Amino Ethers				
C_4	γ-Methoxy-*n*-propylamine	427	50	24[329]	118/733, 1.4182
C_5	γ-Ethoxy-*n*-propylamine	427	50	24[329]	136/732, 1.4201
	β-Methoxyisobutylamine	428	42	24[330]	121, 1.4204
	γ-Methoxyisobutylamine	427	59	24[330]	128, 1.4192[23]
C_6	β-Ethoxy-*n*-butyl amine	435	42	24[101]	140, 1.4190
	Diethylaminomethyl methyl ether	445	40	24[513]	116/755
	Di-(γ-aminopropyl) ether	427	77	24[328]	59/1.5, 1.4605, 152Pi
C_7	2-Methoxy-3-aminohexane	432	34	24[407]	98/100

TABLE 87 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic Amino Ethers *(continued)*				
C_7	β-Ethoxy-*n*-amyl amine	435	44	24[101]	56/15, 1.4220
	Diethylaminomethyl ethyl ether	445	69	24[513]	134/756
C_8	β-Ethoxy-*n*-hexyl amine	435	60	24[101]	69/13, 1.4271
	1-Methylamino-6-methoxyhexane	436	79	24[152]	84/15
C_9	1-Ethylamino-6-methoxyhexane	436	73	24[173]	90/2, 1.4269[27]
	1-Methoxy-4-ethylaminohexane	436	60	24[152]	89/16
	1-Dimethylamino-6-methoxyhexane	436	78	24[173]	78/11
C_{10}	1-Diethylamino-5-methoxypentane	436	91	24[132]	77/18, 1.2490
C_{12}	β,β′,β″-Triethoxytriethylamine	115	66	6[61]	137/12, 195HCl
	Aromatic Amino Ethers				
C_7	*m*-Aminoanisole (*m*-anisidine)	425	80	24[63]	125/13
C_8	β-Phenoxyethylamine	428	80	24[344]	104/12, 168Pi
		435	65	24[96]	115/12
	p-Aminophenetole	425	78	24[6]	254*, 138Ac*
	3,4-Dimethoxyaniline (4-aminoveratrole)	446	82	24[265]	174/24, (88)
C_9	γ-Phenoxypropyl amine	435	71	24[96]	126/15, (13)
	2-Phenoxyisopropylamine	426	65	24[355]	120/13, 1.5237, 148HCl
	N-Ethyl-*p*-anisidine	431	51	24[213]	135–140/20, 1.5444
	p-Methoxydimethylaminobenzene	436	55	24[132]	234/740, (38.5)
C_{10}	δ-Phenoxy-*n*-butylamine	427	87	24[331]	148/17
	3-Phenoxypropylmethylamine	436	61	24[172]	133–138/23, 1.5255, 151HCl
	β-Ethoxy-β-phenylethyl amine	435	62	24[101]	109/12, 1.5102
C_{11}	3-Phenoxypropylethylamine	436	66	24[172]	148/26, 1.5127, 155HCl
	3-Phenoxypropyldimethylamine	436	82	24[171]	132/20
	p-Methoxydiethylaminobenzene	436	74	24[132]	247/740
C_{12}	2-Aminodiphenyl ether	425	94	24[65]	173/14, (47), 81Ac

For explanations and symbols see pp. xi–xii.

TABLE 87 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
	Aromatic Amino Ethers *(continued)*				
C_{12}	3-Aminodiphenyl ether	115	57	6[14]	191/14, (37)
		425	84	24[64]	148/1, 141HCl
	4-Aminodiphenyl ether	115	65	6[14]	(83.5)
		425	100	24[66]	189/14, (83.5)
C_{13}	3-Phenoxypropyldiethylamine	436	94	24[170]	150/20, 1.4987, 102HCl
C_{14}	1-Phenoxy-6-ethylaminohexane	436	90	24[174]	148/3, 1.5010, 135HCl

For explanations and symbols see pp. xi–xii.

TABLE 88. AMINO ALDEHYDES

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
C_6	α-Dimethylaminoisobutyraldehyde	436	32	24[175]	129
C_7	α,α-Dimethyl-β-dimethylaminopropionaldehyde	444	80	24[416]	144, 153HCl
	o-Aminobenzaldehyde	425	75	24[67]	(40)*
	m-Aminobenzaldehyde	149	52	9[127]	162Ph
	p-Aminobenzaldehyde	155	52	9[136]	
		425	50	24[560]	(70)
C_9	*m*-Dimethylaminobenzaldehyde	425	74†	24[68]	112/7, 229Se
		431	27	24[530]	114/3, 76-Ox*
	p-Dimethylaminobenzaldehyde	142	80	9[103]	166/15, (73)
		144	45	9[99]	180/20, (73), 148Ph
		150	59	9[187]	(73), 144-Ox*
C_{10}	*p*-Formylphenyltrimethylammonium iodide	148	68	9[261]	(152d)
C_{11}	*m*-Diethylaminobenzaldehyde	436	48†	24[177]	138/7, 165Se
	p-Diethylaminobenzaldehyde	144	45	9[99]	(41), 121Ph
		150	50	9[188]	(41), 93-Ox*

For explanations and symbols see pp. xi–xii.

TABLE 89. AMINO KETONES

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic and Alicyclic Amino Ketones				
C_3	Aminoacetone	426	96	24[358]	75HCl
	Diaminoacetone	426	83	24[359]	
C_5	Dimethylaminoacetone	436	74	24[178]	36/25, 1.4128, 137Se*
C_6	1-Dimethylamino-3-butanone	444	45	24[417]	70/40, 1.4213[25]
	Diacetonamine (as acid oxalate)	443	70	24[474]	(127)
C_7	Diethylaminoacetone	436	72	24[179]	70/32, 1.4249, 143Se
C_8	1-Diethylamino-3-butanone	444	59	24[417]	70/11, 1.4333[24]
	Diacetonethylamine	443	42	24[476]	191
C_9	1-Dimethylamino-3-methyl-5-hexanone	184	46	10[308]	83/11
	1-Diethylamino-2-pentanone	436	79	24[538]	91/24, 104Se
	1-Diethylamino-3-pentanone	436	55	24[180]	84/13, 1.4368[15]
		443	37	24[538]	96/36, 102Se
	2-Dimethylaminomethylcyclohexanone	444	71	24[419]	97/11.5, 146HCl
C_{10}	5-Diethylamino-2-hexanone	184	42	10[309]	95/16, 1.4337[25]
	1-Diethylamino-4-hexanone	184	44†	10[306]	108/20
	1-Diethylamino-5-hexanone	184	60†	10[307]	98/11, 1.4380[25]
	2-Diethylaminomethylcyclopentanone	444	85	24[418]	103/13
	Aromatic Amino Ketones				
C_8	ω-Aminoacetophenone hydrochloride	437	75	24[238]	(187)
	o-Aminoacetophenone	425	78	24[69]	113/6, 75Ac
	m-Aminoacetophenone	425	71	24[70]	(99), 128Ac
	p-Acetylaniline	178	19	10[26]	168/6, (106), 166Ac
	N,N-Dimethyl-*p*-bromoaniline	431	88	24[221]	145/22, (53)
C_9	α-Aminopropiophenone	426	88	24[357]	114HCl
	β-Aminopropiophenone	452	80	24[440]	127HCl
	o-Aminopropiophenone	425	76	24[81]	146/17, 74Ac
	m-Aminopropiophenone	425	96	24[71]	169/15, (42), 93Ac
C_{10}	2-Phenylamino-3-butanone	436	80	24[182]	121/4, (52)

For explanations and symbols see pp. xi–xii.

TABLE 89 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
	Aromatic Amino Ketones *(continued)*				
C_{10}	α-Methylamino-propiophenone	436	57	24[185]	177HCl
	o-Dimethylamino-acetophenone	436	56	24[186]	94/1.5, 184Pi
C_{11}	3-Phenylamino-2-pentanone	436	72	24[181]	120/1
	α-Methylaminobutyr-ophenone	436	70	24[185]	194HCl
	1-Phenyl-3-dimethyl-amino-2-propanone	187	53	10[676]	141/26, 127Pi
	β-Dimethylaminopro-piophenone	444	72	24[420]	156HCl
C_{12}	1-Dimethylamino-4-phenyl-2-butanone	436	43	24[184]	107/3.5, 1.5070
	β-Dimethylamino-α-methylpropiophenone	444	74	24[421]	82/1, 1.5162^{25}, 154HCl
C_{13}	2-Aminobenzophenone	446	92	24[259]	(107)
	4,4′-Diaminobenzophenone	183	70†	10[248]	(245), 241Ph
	1-Aminofluorenone	446	56	24[267]	(118.5), 138Ac
	4-Aminofluorenone	446	74	24[267]	(139)
C_{15}	1-Phenyl-1-phenylamino-propanone	436	74	24[183]	(91.5)
C_{16}	*p*-Dimethylaminobenzil	179	90	10[199]	(116)

For explanations and symbols see pp. xi-xii.

TABLE 90. AMINO ACIDS

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
C_2	Aminoacetic acid (glycine)	247	92	13[519]	(263), 67Am*
		247	87	13[518]	(246), 62An*
		435	77	24[104]	(236d)
		447	54†	24[278]	
		452	85†	24[443]	
C_3	α-Aminopropionic acid (alanine)	247	72†	13[519]	(295), 62Am*
		247	60	13[520]	(295)
		253	44†	13[526]	163Bz
		435	70	24[105]	(295d)
		451	71	24[500]	
	β-Aminopropionic acid (β-alanine)	247	90	13[523]	(198), 123HCl*
		247	86	13[521]	

TABLE 90 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
C_3	β-Aminopropionic acid (β-alanine) *(continued)*	247	90	13[522]	(198)
		247	75†	13[524]	(200)
		247	69†	13[525]	(197)
		248	70	13[201]	
		249	72	13[527]	(195)
		427	75	24[336]	(195)
		437	85	24[239]	(200d)
		446	45	24[268]	(198d)
	α-Amino-β-hydroxypro-pionic acid (serine)	97	40†	5[542]	
		247	51†	13[528]	(244), 150Bz
C_4	α-Amino-*n*-butyric acid	247	61†	13[519]	(304), 75Am*
		253	50†	13[529]	140Bz
		278	82	13[548]	142Bz
		431	58	24[233]	
		435	60	24[102]	
		447	21†	24[290]	182HCl
	γ-Aminobutyric acid	452	62	24[441]	
	α-Aminoisobutyric acid	247	70	13[530]	
		247	33	13[531]	
		247	73†	13[519]	
		253	77†	13[529]	198Bz
		280	76	13[530]	127Am*
	α-Methyl-β-alanine	427	73	24[339]	(182)
	N-Methylalanine	451	81	24[499]	(317d), 129Bz
	N-Ethylglycine	451	70	24[499]	(182d)
	N,N-Dimethylglycine	431	100	24[232]	(183)
	α-Aminosuccinic (*dl*-aspartic) acid	278	43	13[643]	162Bz
		451	95	24[498]	(280d)
	α,γ-Diaminobutyric acid	449	41	24[500]	(215d), 181Pi
	meso-α,β-Diamino-succinic acid	434	90	24[448]	(306d)
	α-Amino-β-hydroxy-butyric acid	97	90	5[543]	(235)
C_5	α-Aminovaleric acid (norvaline)	247	68†	13[519]	(291), 188HCl*
		278	86	13[537]	117Ac
		447	43	24[289]	188HCl
		447	31	24[287]	152Bz
	γ-Aminovaleric acid	425	99	24[531]	(197)
	δ-Aminovaleric acid	248	71	13[533]	(158)*, 90Bz
		248	80	13[534]	94HCl
	α-Aminoisovaleric acid (*dl*-valine)	278	85	13[644]	
		435	48	24[106]	(282d)
		447	33†	24[289]	
		447	60	24[288]	
	γ-Amino-β-methylbutyric acid	452	40	24[442]	(174)

For explanations and symbols see pp. xi-xii.

TABLE 90 (*continued*)

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
C_5	*dl*-α-Methylaminobutyric acid	431	62	24[233]	
	γ-N-Methylaminobutyric acid	248	90	13[598]	121HCl
	N-Methyl-α-aminoisobutyric acid	247	43†	13[537]	
	N,N-Dimethylalanine monohydrate	431	100	24[232]	(182), 148HCl
	α-Aminoglutaric (*dl*-glutamic) acid	247	75	13[182]	
		278	64†	13[557]	(199)*, 193HCl*
		278	75	13[535]	
		....	....	13[536]	(213), 202HCl*
	α-Amino-α-methyl-succinic acid	247	51†	13[519]	(230)
	α,δ-Diamino-*n*-valeric acid (*dl*-ornithine)	449	75	24[300]	200Pi, 187Bz
	Methyliminodiacetic acid	436	71	24[187]	(215)
	γ-Methylmercapto-α-amino-butyric acid (*dl*-methionine)	278	85	13[642]	(280), 145Bz
C_6	*dl*-α-Amino-*n*-caproic acid (norleucine)	435	67	24[108]	
	γ-Amino-*n*-caproic acid	426	47	24[366]	(181), 121HCl
	ε-Aminocaproic acid	248	100	13[540]	(202), 105HBr*
		248	92	13[541]	(203)
	dl-α-Amino-β-methyl-valeric acid	247	74†	13[519]	(318)
		435	49	24[109]	(280d)
	α-Aminoisocaproic acid (leucine)	278	64	13[557]	(295)*, 161Ac
		278	87	13[542]	(283), 141Bz
		435	45	24[107]	(292d)
		447	51	24[287]	(293)
		447	68	24[289]	(282)
	α-Amino-α-ethylbutyric acid	247	43†	13[543]	
	α-Dimethylaminoisobutyric acid	436	80	24[123]	264HCl
	α-Aminoadipic acid	253	48†	13[608]	(189)
		435	86	24[534]	(202)
		452	84	24[534]	(202)
	α,δ-Diaminoadipic acid	452	91	24[429]	(300)
	α,ε-Diaminocaproic acid (*dl*-lysine)	280	78	13[649]	253HCl
		435	69	24[110]	189HCl
		449	74	24[300]	189HCl
	dl-lysine dihydrochloride	435	62	24[533]	188HCl
	l-Cystine	....	....	13[545]	(261)*
		....	....	13[546]	

TABLE 90 (*continued*)

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
C_6	Histidine	278	45	13[542]	(272)
	l-Histidine hydrochloride	....	....	13[544]	(252)
	d-Arginine hydrochloride	....	90	13[547]	(220)
C_7	α-Aminoheptanoic acid	278	55	13[548]	(281), 135Bz
	7-Aminoheptanoic acid	427	30	24[337]	(187)
	β,β-Diethyl-β-amino-propionic acid	443	30	24[486]	(184)
	N,N-Dimethyl-*dl*-valine	431	100	24[232]	(152), 164HCl
	α-Methyl-γ-dimethyl-aminobutyric acid	249	90	13[549]	(76)
	β-Dimethylaminopivalic acid	253	74	13[436]	(99)
	β-2-Thienylalanine	426	68	24[314]	(275)
C_8	α-Aminooctanoic acid	247	47†	13[550]	
		278	82	13[548]	(270), 128Bz
	N,N-Dimethyl-*dl*-leucine	431	100	24[232]	(188)
	α-Aminophenylacetic acid	247	37†	13[551]	176Bz*
	o-Aminophenylacetic acid	425	85	24[74]	(119)
	m-Aminophenylacetic acid	248	61	13[147]	(146), 166Am*
	p-Aminophenylacetic acid	248	51	13[147]	(197), 162Am*
		425	84	24[73]	(200)
	p-Aminomethyl)-benzoic acid	427	80	24[338]	(342), 288HCl
		437	64†	24[240]	
C_9	α-Aminononanoic acid	278	55	13[548]	(273), 128Bz
		280	92	13[552]	
	α-Amino-α-phenyl-propionic acid	247	40†	13[553]	(267)
	α-Amino-β-phenyl-propionic acid	278	83	13[557]	146Ac
		278	67	13[542]	(257), 184Bz
		279	67	13[556]	(288)
	dl-α-Amino-β-phenyl-propionic acid	431	62	24[233]	
		435	62†	24[111]	(273d)
		447	50	24[288]	(265)
		447	44†	24[278]	235HCl
	β-Amino-α-phenyl-propionic acid	446	66	24[269]	(223)
	β-Amino-β-phenyl-propionic acid	264	50	13[554]	
		264	70	13[555]	(222)
		443	34	24[485]	(221d)
	p-(β-Aminoethyl)-benzoic acid	260	48†	13[558]	175Ac
	m-Dimethylaminobenzoic acid	431	100	24[232]	(150)
	p-Dimethylaminobenzoic acid	431	80	24[232]	(240)
		263	50	13[619]	(243)*

For explanations and symbols see pp. xi-xii.

TABLE 90 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
C_9	β-Anilinopropionic acid	249	65	13[265]	(60)
C_{10}	*dl*-γ-Phenyl-α-amino-butyric acid	431	62	24[233]	
C_{11}	Tryptophane	278	45†	13[560]	(282), 206Ac
		278	88	13[561]	193Bz

For explanations and symbols see pp. xi-xii.

TABLE 91. AMINO ESTERS

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic Amino Esters				
C_4	Methyl β-aminopropionate	292	67	14[301]	51/12
	Ethyl aminoacetate	293	90	14[171]	143HCl
C_5	Methyl α-aminoisobutyrate	285	64	14[73]	134, 183HCl
	Ethyl α-aminopropionate	285	95	14[7]	
	Ethyl β-aminopropionate	427	74	24[340]	56/10
		434	100	24[447]	67HCl
	Methyl β-methylamino-propionate	443	40	24[447]	50/11
C_6	Ethyl β-amino-*n*-butyrate	426	21†	24[367]	69/17, 148Pi
		443	55	24[482]	62/10, 74Am
	Ethyl β-methylamino-propionate	443	49	24[478]	68/18, 1.4218[22]
C_7	Ethyl β-amino-*n*-valerate	426	23†	24[367]	84/17
	Ethyl α-methylamino-butyrate	436	63	24[190]	65/20, 1.4174, 104Pi
	Ethyl β-methylamino-*n*-butyrate	443	89	24[482]	66/10
	Ethyl aminomalonate (as acetyl derivative)	426	44†	24[364]	(96)
C_8	Ethyl α-amino-*n*-caproate	426	86	24[361]	88/11
	Ethyl β-amino-*n*-caproate	426	48	24[367]	104/25
	Isobutyl α-aminoiso-butyrate	285	66	14[72]	61/4, 1.4210, 103HCl
	Ethyl β-ethylamino-*n*-butyrate	431	68	24[367]	75/12
	Methyl β-diethylamino-propionate	443	100	24[477]	66.5/8
	Ethyl α-aminosuccinate (*dl*-aspartic ester)	426	70	24[365]	98/1

TABLE 91 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic Amino Esters *(continued)*				
C_9	Ethyl α-methyl-γ-dimethylaminobutyrate	285	63†	14[290]	83/16
	Methyl γ-diethylamino-butyrate	436	74	24[189]	63/3, 102HCl
	Ethyl α-diethylamino-propionate	436	84	24[188]	75/13
	Diethyl dimethylamino-malonate	436	74	24[521]	117/15, 1.4320[19]
C_{10}	Ethyl γ-diethylamino-butyrate	285	70†	14[291]	105/17, 1.4342
	Aromatic Amino Esters				
C_8	Methyl o-aminobenzoate	285	85	14[1]	139/19
	Methyl *m*-aminobenzoate	321	48	14[428]	(37)
		425	95	24[76]	153/11, (37), 137Ac
	Methyl *p*-aminobenzoate	285	53	14[1]	
C_9	Ethyl *p*-aminobenzoate	425	100	24[75]	(90)
C_{10}	Ethyl α-aminophenyl-acetate	285	65	14[74]	115/5, 1.500[25], 200HCl
	Ethyl *m*-aminophenyl-acetate	425	87	24[77]	140/4, 1.5435[21], 131HCl
	Ethyl *p*-(aminomethyl)-benzoate	437	40	24[240]	148/8, 237HCl
	Methyl β-anilinopropionate	443	69	24[479]	160/14, (38)
	Methyl o-dimethylamino-benzoate	436	60	24[192]	137-142/17
C_{11}	Ethyl α-amino-β-phenyl-propionate	426	53	24[361]	142/10
	Ethyl β-amino-β-phenyl-propionate	443	35	24[483]	146/11

For explanations and symbols see pp. xi-xii.

TABLE 92. AMINO CYANIDES

C_n	Compound	Method	Yield (%)	Chapter[ref.]	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic and Alicyclic Amino Cyanides				
C_2	Aminoacetonitrile hydrochloride	391	95	20[328]	(166)
	Aminoacetonitrile hydrogen sulfate	....	81	24[525]	

For explanations and symbols see pp. xi-xii.

TABLE 92 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic and Alicyclic Amino Cyanides *(continued)*				
C_3	β-Aminopropionitrile	388	33	20[247]	89/20, 1.3496
	Methylaminoacetonitrile	391	93	20[390]	65/20
	Methyleneaminoacetonitrile	391	71	20[312]	(129)
C_4	3-Amino-*n*-propyl cyanide	452	38†	24[445]	97/20, 140HCl
	α-Aminoisobutyronitrile	391	77	20[317]	48/11
		391	80	20[327]	68/24, 1.4198
	β-Methylaminopropionitrile	388	78	20[248]	74/16, 1.4342[15]
	Ethylaminoacetonitrile	391	70	20[324]	83/29
	Dimethylaminoacetonitrile	391	83	20[313]	134–137, 1.4095[25]
	Iminodiacetonitrile	392	100	20[341]	(75)
C_5	α-Methylaminoisobutyronitrile	391	57	20[388]	54/18, 133/747, 1.4176
	β-Ethylaminopropionitrile	388	90	20[250]	95/30, 1.4322
	Isopropylaminoacetonitrile	391	89	20[389]	169HCl
		391	90	20[390]	85/20
C_6	5-Amino-*n*-amyl cyanide	452	68†	24[445]	118/14, 98Bz
	α-Aminodiethylacetonitrile	391	40	20[317]	71/11
	α-Methylamino-*n*-valeronitrile	391	85	20[390]	85/25
		392	77	20[391]	74/14, 167, 1.4362[14], 103Pi
	α-Methylaminoisovaleronitrile	391	80	20[390]	70/20
	α-Methylamino-α-methyl-*n*-butyronitrile	391	83	20[388]	68/17, 1.4282[21], 83Bz
	α-Ethylaminoisobutyronitrile	391	94	20[321]	144/761
	β-*n*-Propylaminopropionitrile	388	92	20[249]	121/30, 1.4362
	β-Isopropylaminopropionitrile	388	95	20[251]	87/17, 1.4290[25]
	α-Dimethylaminobutyronitrile	391	78	20[319]	68/23
	4-Dimethylaminobutyronitrile	387	64	20[215]	44–47/1.5
	α-Dimethylaminoisobutyronitrile	391	69	20[319]	57/25
		391	88	20[327]	50/20, 1.4215
	Diethylaminoacetonitrile	391	90	20[322]	63/14, 1.4230[25]
C_7	α-Aminomethylbutylacetonitrile	391	51	20[317]	88/10
	α-Aminomethylisobutylacetonitrile	391	53	20[317]	76/10

TABLE 92 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
	Aliphatic and Alicyclic Amino Cyanides *(continued)*				
C_7	α-Methylamino-α-ethylbutyronitrile	391	73	20[321]	167/765
	α-Dimethylamino-α-methylbutyronitrile	391	70	20[319]	63/12
	α-Methylethylaminoisobutyronitrile	391	53	20[319]	58/14
	α-Diethylaminopropionitrile	391	65	20[323]	49/7, 68/17
		391	68	20[319]	55/11
	β-Diethylaminopropionitrile	388	97	20[250]	120/70, 1.4353
		436	56	24[194]	84/13, 1.4343[25]
	1-Amino-1-cyanocyclohexane hydrochloride		77	20[315]	(204)
C_8	α-Ethylamino-α-isobutylacetonitrile	391	84	20[324]	84/12
	α-Dimethylamino-α-methyl-*n*-valeronitrile	391	49	20[319]	75/10
	α-Dimethylamino-α-methylisovaleronitrile	391	49	20[319]	63/7
	α-Dimethylamino-α-ethylbutyronitrile	391	75	20[319]	69–73/10
	γ-Diethylaminobutyronitrile	378	84	20[113]	93/14
		387	83	20[215]	89/9
		436	97	24[193]	103/21, 1.4351, 70Pi
	α-Diethylaminoisobutyronitrile	391	59	20[327]	68/14, 1.4312
		391	39	20[319]	74/14
C_9	α-Diethylamino-*n*-valeronitrile	391	44	20[319]	95/15
	α-Diethylaminoisovaleronitrile	391	39	20[319]	69/4
	β-Cyclohexylaminopropionitrile	388	92	20[249]	124/4, 1.4764
C_{10}	ε-Diethylaminocapronitrile	436	90	24[196]	102/4, 62Pi
	α-Diethylamino-α-isobutylacetonitrile	391	92	20[324]	89/11
	Aromatic Amino Cyanides				
C_7	*m*-Aminobenzonitrile	425	63	24[79]	(53), 131Ac
C_8	*o*-Aminobenzyl cyanide	425	88	24[520]	(72)
	p-Aminobenzyl cyanide	425	79	24[78]	147/1
	Anilinoacetonitrile	391	35	20[324]	(47)
C_9	Methylphenylaminoacetonitrile	391	76	20[319]	141/9

For explanations and symbols see pp. xi–xii.

TABLE 92 *(continued)*

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
	Aromatic Amino Cyanides *(continued)*				
C_{10}	β-Benzylaminopropionitrile	388	73	20[252]	185/23
	α-Dimethylaminophenylacetonitrile	391	29	20[319]	90/6
	α-Anilinoisobutyronitrile	391	93	20[327]	(94)
C_{12}	α-Diethylaminophenylacetonitrile	391	83	20[323]	112/7, 131/11
		391	56	20[319]	124/9
C_{14}	α-Aminodiphenylacetonitrile	392	77	20[339]	(102)
	γ-Diethylamino-α-phenylbutyronitrile	386	74	20[190]	122/1
	9-Amino-9-cyanofluorene	392	70	20[340]	(96)

For explanations and symbols see pp. xi–xii.

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25

Imines

CONTENTS

465. Condensation of Carbonyl Compounds with Amines

$$RCHO + R'NH_2 \rightarrow RCH{=}NR' + H_2O$$

Both aliphatic and aromatic aldehydes condense with primary amines, aliphatic and aromatic, to form N-substituted imines. The purely aliphatic imines (C_5 to C_{10}) can be obtained in 50–80% yield; however, these compounds are unstable and should be used immediately after distillation.[1] Side reactions which may occur during their formation have been studied.[2] On the other hand, Schiff bases from substituted benzaldehydes and amines, aliphatic and aromatic, are more stable and have been prepared in large numbers.[3–6] The benzaldehyde entity may carry a halo, hydroxyl, methoxyl, dialkylamino, or nitro group.[5] Usually, an immediate reaction occurs upon mixing the two reactants either without a solvent or in dilute alcohol, as illustrated by the synthesis of benzalaniline, $C_6H_5CH{=}NC_6H_5$ (87%).[3]

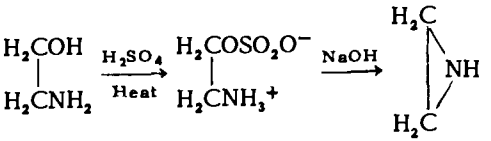
The formation of Schiff bases by the reaction of ketones with amines is more difficult. Acetophenone and other aryl alkyl ketones which are slow to react under the usual conditions will combine with aromatic amines at 160–180° in the presence of a zinc chloride-aniline salt.[21] In another procedure, 2-acetylthiophene and aniline are condensed in boiling toluene with the aid of a water separator.[26]

Ketones like acetophenone have been heated with ammonia in the presence of a dehydrating agent, but the formation of the ketimines is

poor.[7] A successful conversion of 9-fluorenone to its ketimine has been described in which anhydrous ammonia is passed through the molten ketone at 165° (66%).[8]

Invariably, the combination of ammonia and aldehydes forms other products; these reactions have been reviewed.[9] Monochloramine (NH_2Cl) reacts readily with substituted benzaldehydes to form aldchlorimines ($ArCH{=}NCl$).[10]

466. Cyclization of β-Amino Alcohols

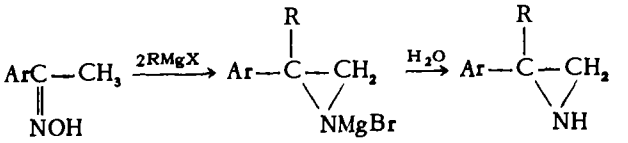


Ethylenimine is conveniently prepared from ethanolamine by heating the inner salt of the sulfate ester with aqueous alkali (37%).[11] The method has been applied to other β-amino alcohols to form the C-alkyl homologs of ethylenimine in which one to three of the four hydrogens may be substituted.[12] The general procedure is illustrated by the synthesis of 2,2-dimethylethylenimine (51%).[13] The N-alkyl analogs can be made by treating the N-alkylethanolamine hydrochlorides with chlorosulfonic acid followed by the action of base on the intermediate sulfuric acid esters, as in the preparation of N-ethylethylenimine (70%).[14]

Aryl-substituted amino alcohols fail to undergo this reaction but instead are dehydrated to vinylamines.

The reactions of ethylenimine have been studied extensively.[25]

467. Action of Grignard Reagents on Oximes



Certain substituted ethylenimines are obtained by the action of aliphatic or aromatic Grignard reagents on aryl alkyl ketoximes with subsequent non-acidic decomposition of the intermediate complex (20–60%).[15,16]

468. Action of Grignard Reagents on Nitriles

$$ArCN \xrightarrow{RMgX} ArRC{=}NMgX \xrightarrow{NH_3} ArRC{=}NH$$

The interaction of Grignard reagents and nitriles produces ketimines which may be hydrolyzed to ketones without isolation (method 187). Many of the alkyl aryl ketimines have been isolated for further study. For this purpose, the intermediate addition compound is decomposed by treatment with anhydrous hydrogen chloride or, preferably, with anhydrous ammonia.[17–19] The yields range from 50% to 86%. Often, the ketimines are non-hydrolyzable or hydrolyzed with difficulty, allowing them to be easily isolated;[18] others must be isolated and stored under anhydrous conditions.[19,20]

469. β-Iminonitriles by Condensation of Nitriles[22]

$$2CH_3CN \xrightarrow[H_2O]{NaNH_2;} CH_3C(=NH)CH_2CN$$

470. Ethylene Imino Ketones by the Action of Amines on α,β-Dibromo Ketones[23]

$$ArCH(Br)-CH(Br)-COAr \xrightarrow{RNH_2} ArCH(NR)-CHCOAr$$

TABLE 93. IMINES

C_n	Compound	Method	Yield %	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
C_2	Ethylenimine	466	37	25[11]	58, 1.4123[25]
C_3	1,2-Propylenimine	466	65	25[12]	64, 1.4095[25]
	Ethylidenemethylamine	465	55	25[1]	28/754, 1.4010[14]
C_4	1,2-Butylenimine	466	46	25[12]	89, 1.4165[25]
	trans-2,3-Butylenimine	466	47	25[12]	76, 1.4070[25]
	2,2-Dimethylethylenimine	466	51	25[13]	72, 1.4050[25]
	N-Ethylethylenimine	466	70	25[14]	222HCl
	Propylidenemethylamine	465	77	25[1]	53/758, 1.4033[13]
	Ethylidene-ethylamine	465	77	25[1]	48/774, 1.3953[13]
C_5	Propylidene-ethylamine	465	81	25[1]	74/764, 1.4053[14]
	Butylidenemethylamine	465	76	25[1]	81/764, 1.4095[13]
C_6	Butylidene-ethylamine	465	84	25[1]	102/763, 1.4105[21]
C_8	N-Benzylidenemethylamine	465	70	25[4]	185, 69/20, 1.5519
C_9	N-Benzylidene-ethylamine	465	90	25[24]	99/28, 1.5397
C_{10}	2-Phenyl-2-ethylethylenimine	467	60	25[16]	86/7, 1.5318, 191HCl
C_{12}	N-Phenyl 2-thienyl methyl ketimine	465	46	25[6]	155/5, (70)
C_{13}	Diphenylmethane imine hydrochloride	....	66	25[20]	
	Fluorenyllidenimine	465	66	25[8]	(124)
	N-Benzylideneaniline (benzalaniline)	465	87	25[3]	(52)
C_{14}	Acetophenonanil	465	42	25[21]	167/12, (99)
C_{15}	2,2-Diphenyl-3-methylethylenimine	467	70	25[15]	132/1, (75), 140HCl

For explanations and symbols see pp. xi–xii.

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26

Hydrazines

CONTENTS

These compounds are prepared in part by methods similar to those for amines; in addition, specific methods are employed including the reduction of diazonium compounds, reduction of azo compounds, and reduction of nitrosamines leading to *sym*- or *unsym*-substituted hydrazines.

471. Alkylation of Hydrazines

$$RX + NH_2NH_2 \longrightarrow RNHNH_2$$

High-molecular-weight monoalkylhydrazines (C_6 and above) can be made from anhydrous hydrazine[33] and alkyl halides in a manner similar to the alkylation of amines.[2] On the other hand, alkylation with the lower halides leads chiefly to di-, tri-, and tetra-substituted hydrazines.[2] Ethylhydrazine has been obtained by alkylation of hydrazine with ethyl sulfate (32%).[3] Methylhydrazine is synthesized by a special variation of this method (54%).[9]

If activated by nitro groups, aryl halogens are easily replaced by the hydrazino group, as illustrated by the synthesis of 2,4-dinitrophenylhydrazine (85%).[4] Other nitrophenylhydrazines may be obtained by the action of hydrazine or methylhydrazine.[5]

Alkali metal phenylhydrazines, $ArN(Na)NH_2$, which are prepared by the direct reaction of primary hydrazines with alkali amide in liquid

ammonia are readily alkylated by alkyl halides to furnish N,N-alkylarylhydrazines, $Ar(R)NNH_2$ (73–94%).[7]

sym-Hydrazines, RNHNHR, are prepared by the alkylation of dibenzoylhydrazine ($C_6H_5CONHNHCOC_6H_5$) followed by hydrolytic treatment, as shown by the synthesis of *sym*-dimethylhydrazine (73% over-all).[8] This procedure may be applied to dibenzoylalkylhydrazines which upon alkylation and hydrolysis yield *sym*-hydrazines substituted with different groups, e.g., *sym*-methylisopropylhydrazine.[10]

The interaction of hydrazine hydrate and ethyl chlorocarbonate in methanol solution yields methyl hydrazinecarboxylate, $H_2NNHCO_2CH_3$ (49%).[11]

472. Interaction of Amines and Hydroxylamine-O-Sulfonic Acid

$$RNH_2 + NH_2O \cdot SO_2OH \xrightarrow{\text{Heat}} RNHNH_2$$

Monoalkylhydrazines (C_2 to C_5) are readily prepared by heating amines with hydroxylamine-O-sulfonic acid in the presence of alkali (31–60%).[1] The products are isolated as the oxalate salts.

473. Reduction of Diazonium Compounds

$$ArN_2^+Cl^- \xrightarrow{Na_2SO_3} ArNHNH_2 \cdot HCl$$

The reduction of diazonium salts by sodium sulfite forms monosubstituted arylhydrazines. An improved procedure for the synthesis of phenylhydrazine in 84% yield is typical.[12] Arylhydrazine salts substituted in the nucleus with halo,[14] ether,[15] carboxyl,[16,19] or nitro[17,18] groups have been prepared. The free bases are liberated from the salts by the action of aqueous sodium hydroxide or sodium acetate.

474. Reduction of Nitrosoamines

$$R_2NH \xrightarrow{(HONO)} R_2NNO \xrightarrow[CH_3COOH]{Zn} R_2NNH_2$$

unsym-Disubstituted hydrazines, R_2NNH_2, are prepared by the zinc-acetic acid reduction of either aliphatic or aromatic nitrosoamines. In this manner, *unsym*-dimethylhydrazine is synthesized in 73% yield from nitrosodimethylamine.[20] Similarly, α-methyl-α-phenylhydrazine is prepared (56%).[21] Preparations of the nitrosoamines from the corresponding secondary amines are also described.

Ethylhydrazine is made from nitrosodiethylurea, $C_2H_5N(NO)CONHC_2H_5$, by the usual steps of reduction and hydrolysis.[22]

475. Reduction of Azo Compounds

$$ArNO_2 \xrightarrow{(H)} ArN{=}NAr \xrightarrow{(H)} ArNHNHAr$$

Aromatic *sym*-disubstituted hydrazines are obtained by reduction of azo compounds, which in turn are intermediates in properly controlled reductions of nitro compounds. The over-all reduction can be accomplished with zinc dust and alkali or electrolytically. For example, hydrazobenzene, the simplest member, is made by both procedures.[23,24] Chemical reduction is carried out on *o*-nitrobromobenzene to form 2,2′-dibromohydrazobenzene (57%), the halo groups remaining intact.[25] Many examples of the electrolytic procedure have been cited; the yields vary from 50% to 95%.[26] To a limited extent, a magnesium-magnesium iodide system has been employed as a reducting agent for the azobenzenes.[27]

476. Action of Grignard Reagents on Diazomethane[29]

$$CH_3(CH_2)_2CH_2MgX \xrightarrow[H_2O]{CH_2N_2;} CH_3(CH_2)_2CH_2NHNHCH_3 \quad (53\%)$$

477. Reductive Hydrazination of Carbonyl Compounds[30]

$$2R_2CO + H_2NNH_2 \xrightarrow[\text{Catalyst}]{H_2} R_2CHNHNHCHR_2$$

R = isopropyl (80%)

478. Addition of Grignard Reagents to Dialkyl-alkylidenhydrazones[31,32]

$$R_2NNH_2 \xrightarrow{H_2CO} R_2NN{=}CH_2 \xrightarrow[H_2O]{CH_3MgX;} R_2NNHCH_2CH_3$$

R = ethyl (22% over-all)

TABLE 94. HYDRAZINES

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
C_1	Methylhydrazine (as sulfate)	471	54	26[9]	(142)
C_2	Ethylhydrazine	471	32	26[3]	99.5/709, 110HCl
	Ethylhydrazine (as oxalate)	472	42	26[1]	(171)
	sym-Dimethylhydrazine (as hydrochloride)	471	78	26[8]	(167)
	unsym-Dimethylhydrazine	474	73	26[20]	65/765, 82HCl
	Methyl hydrazinocarboxylate	471	49	26[11]	108/12, (63), 160HCl
C_3	*n*-Propylhydrazine (as oxalate)	472	52	26[1]	(175)
	Isopropylhydrazine	477	90	26[30]	107/750, 114HCl
	Isopropylhydrazine (as oxalate)	472	44	26[1]	(172)
C_4	*n*-Butylhydrazine (as oxalate)	472	45	26[1]	(165)
	sym-Methylisopropylhydrazine	471	50	26[10]	79/37
	N,N-Dimethyl-N′-ethylhydrazine	478	65	26[31]	77/720, 93Pi
C_5	*n*-Amylhydrazine (as oxalate)	472	31	26[1]	(164)
	sym-Methyl-*n*-butylhydrazine	476	53	26[29]	115HCl
C_6	*n*-Hexylhydrazine	471	26	26[2]	81/14
	sym-Diisopropylhydrazine	477	100	26[30]	124/750, 1.4125^{24}
	Triethylhydrazine	478	22†	26[32]	39/37
	Phenylhydrazine	473	84	26[12]	138/18, (23)
	p-Fluorophenylhydrazine	473	74	26[14]	129/21, (39)
	o-Nitrophenylhydrazine	473	64	26[18]	(90)*, 140Ac*
	p-Nitrophenylhydrazine	473	66	26[17]	(157), 120Pi*
	2,4-Dinitrophenylhydrazine	471	85	26[4]	(192)
C_7	α-Methyl-α-phenylhydrazine	474	56	26[21]	109/13
	o-Carboxyphenylhydrazine	473	84	26[16]	(247), 190HCl
	p-Carboxyphenylhydrazine	473	76	26[19]	253HCl
C_8	N,N-Ethylphenylhydrazine	471	88	26[7]	120–7/25, 147HCl
C_{12}	2-Phenoxyphenylhydrazine	473	45	26[15]	(154)
	Hydrazobenzene	475	85	26[23]	(124)
	2,2′-Dibromohydrazobenzene	475	57	26[25]	(98)

TABLE 94 (*continued*)

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.), Deriv.
C_{13}	4,4′-Dihydrazinodiphenylmethane	473	35	26[13]	(141)
C_{24}	Tetraphenylhydrazine	....	70	26[28]	(144)

For explanations and symbols see pp. xi–xii.

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27

Oximes and Nitroso Compounds

CONTENTS

479. Oximination of Carbonyl Compounds

$$R_2CO + H_2NOH \cdot HCl + NaOH \longrightarrow R_2C{=}NOH + H_2O + NaCl$$

Oximes are commonly prepared by the interaction of ketones with hydroxylamine hydrochloride (or sulfate) in the presence of an inorganic base. The reaction is reversible, but the state of equilibrium highly favors the desired products. Preparations of large quantities for synthetic work are illustrated for methyl ethyl ketoxime,[1] cyclohexanone oxime,[2,3] heptaldoxime,[3] and benzophenone oxime,[4] the procedures varying somewhat with the nature of the carbonyl compound. In some instances, a readily available and cheap reagent like sodium hydroxylamine disulfonate, $HON(SO_3Na)_2$, is first prepared from sodium nitrite and sodium bisulfite and, without isolation, treated with the carbonyl compound,[2,6,7,15] Hydroxylamine-O-sulfonic acid, H_2NOSO_3H, is still another reagent and, like sodium hydroxylamine disulfonate, is used in the absence of a base. The preparation of hydroxylamine hydrochloride is described.[6]

The oximes of ketones with large hydrocarbon radicals like the acetylphenanthrenes are readily prepared by the action of hydroxylamine hydrochloride in the presence of pyridine.[12] Special studies have been made for the synthesis of 1,2-cyclohexanedione dioxime[14] as well as the next higher homolog.[13] Dimethylglyoxime, $CH_3C(=NOH)C(=NOH)CH_3$, is

prepared by the action of sodium hydroxylamine monosulfonate on biacetyl monoxime.[18]

480. Nitrosation of Active Methylene Compounds

$$RCOCH_2R + R'ONO \xrightarrow{HCl} RCOC(=NOH)R + R'OH$$

Compounds having active methylene groups react with nitrous acid to form oximino derivatives. The attack on the α-methylene group of ketones is illustrated by the action of ethyl nitrite on methyl ethyl ketone, and by the action of methyl nitrite on propiophenone, to form biacetyl monoxime (60%)[15] and isonitrosopropiophenone (68%),[16] respectively. Methyl and ethyl nitrites are passed in gaseous form into the ketones in the presence of hydrochloric acid. In other preparations, *n*-butyl, amyl, or octyl nitrite in liquid form is employed.[14,17,18]

Similarly, the α-methylene group of acetoacetic ester is oximinated by the action of sodium nitrite in glacial acetic acid (63%).[19] Nitrosation of alkylated malonic,[20,21] acetoacetic,[21] and benzoylacetic[22] esters with subsequent cleavage affords an excellent synthesis for α-oximino esters, $RC(=NOH)CO_2C_2H_5$. A survey of several possible procedures for this conversion has been made.[21] If a β-keto *acid* is nitrosated, then the carboxyl group is lost and an α-oximino ketone is formed, viz.,

$$CH_3COCHRCO_2H \xrightarrow{(HONO)} CH_3COC(=NOH)R + CO_2$$

The conversion of *o*- and *p*-nitroethylbenzenes with *t*-butyl nitrite and sodium *t*-butoxide into the corresponding nitroacetophenone oximes is accomplished in 67–74% yields.[25]

481. Partial Reduction of Nitro Compounds

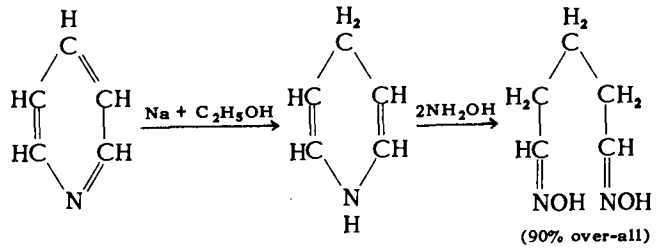
Various procedures have been developed for the production of oximes from nitroparaffins. Direct reduction with zinc dust and acetic acid has been proposed, but the yields are poor because of the simultaneous formation of amines.[26] A synthesis for cyclohexanone oxime has been demonstrated which involves the formation and selective hydrogenation of 1-chloro-1-nitrocyclohexane. The halogenated intermediate is prepared in quantitative yield by chlorination of the sodium salt of *aci*-nitrocyclohexane, and subsequent hydrogenation is performed in an 80% yield over palladium-on-charcoal,[27]

Still another scheme is concerned with the zinc-acetic acid reduction of an aliphatic nitro olefin, which is readily prepared by the condensation of an aldehyde with the nitroparaffin (method 37).[28]

$$RCH_2NO_2 \xrightarrow{R'CHO} R'CH=C(R)NO_2 \xrightarrow[CH_3COOH]{Zn} R'CH_2C(=NOH)R$$

α-Nitrostilbene, $C_6H_5CH=C(NO_2)C_6H_5$, is selectively hydrogenated over a palladium catalyst to desoxybenzoin oxime in an almost quantitative yield.[29]

482. Hydroxylamination of Dihydropyridines[30]



483. Nitrosation of Secondary Amines

$$R_2NH \cdot HCl \xrightarrow{(HONO)} R_2NNO$$

Aliphatic and aromatic amines react with nitrous acid to form N-nitroso derivatives. For example, dimethylamine hydrochloride on treatment with sodium nitrite and hydrochloric acid is converted to nitrosodimethylamine in 90% yield.[39] In like manner, N-nitrosomethylaniline is synthesized from N-methylaniline in 93% yield.[40] The ready formation of these derivatives and the easy reconversion to the amine by reduction affords an advantageous procedure for separating secondary amines from primary and tertiary amines, as shown in the synthesis of N-ethyl-*m*-toluidine and other N-alkyl derivatives by the alkylation of *m*-toluidine.[41]

Certain N-nitroso derivatives are important intermediates in the synthesis of diazomethane and homologs. One synthesis involves the nitrosation of a β-alkylaminoisobutyl methyl ketone; the corresponding N-nitrosoamine is readily decomposed to the diazoalkane and mesityl oxide by treatment with sodium isopropoxide.[42]

$$(CH_3)_2CCH_2COCH_3 \xrightarrow{(HONO)} (CH_3)_2CCH_2COCH_3 \xrightarrow{NaOR} CH_2N_2 +$$
$$\begin{matrix} | \\ CH_3NH \end{matrix} \qquad\qquad \begin{matrix} | \\ CH_3NNO \end{matrix}$$
$$(CH_3)_2C=CHCOCH_3 + H_2O$$

Other intermediates for the synthesis of diazomethane are nitrosomethylurea, $CH_3N(NO)CONH_2$,[43] and nitrosomethylurethane, $CH_3N(NO)CO_2C_2H_5$.[44]

Certain α-anilino acids like phenylglycine and α-anilinopropionic acid have been converted to their N-nitroso derivatives.[45]

484. Nitrosation of an Aromatic Nucleus

$$C_6H_5N(CH_3)_2 \xrightarrow{(HONO)} p\text{-}ONC_6H_4N(CH_3)_2$$

Aromatic tertiary amines and phenolic compounds undergo nuclear nitrosation, as illustrated by the synthesis of *p*-nitrosodimethylaniline (89%),[31] *p*-nitrosophenol (80%),[33] and 1-nitroso-2-naphthol (99%).[32] In the reaction of α-naphthol, an isomeric mixture of the nitrosonaphthols is obtained.[34] The nitrosation of phenols with nitrous acid usually produces *p*-nitroso compounds; however, *o*-nitrosophenols can be prepared by nitrosating phenols in the presence of cupric sulfate.[35]

N-Nitroso derivatives of secondary amines are transformed into *p*-nitroso derivatives by the action of hydrogen chloride in alcohol and ether solution (Fischer-Hepp). The conversion is believed to occur through the liberation of nitrosyl chloride followed by *p*-nitrosation, viz.,[38]

$$C_6H_5N(NO)CH_3 \xrightarrow{HCl} C_6H_5NHCH_3 \xrightarrow{NOCl} p\text{-}ONC_6H_4NHCH_3$$

485. Oxidation of Hydroxylamines and Amines

$$ArNO_2 \xrightarrow[NH_4Cl]{Zn} ArNHOH \xrightarrow{(O)} ArNO \xleftarrow{(O)} ArNH_2$$

Nitrosobenzene is readily synthesized by the chromic acid oxidation of β-phenylhydroxylamine, which in turn is prepared by the reduction of nitrobenzene by the action of zinc dust and ammonium chloride (53%).[46] The hydroxylamines need not be isolated. In other preparations, ferric chloride is employed as oxidant.[47,48]

Primary aromatic amines react with Caro's acid to form nitroso derivatives, as in the preparation of 5-nitro-2-nitrosotoluene from 2-amino-5-nitrotoluene (71%).[49]

TABLE 95. OXIMES (ISONITROSO COMPOUNDS)

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.)
C_2	Acetaldoxime	479	80	27[24]	114
C_3	Acetoxime	479	76	27[6]	136, (61)
	Methylglyoxime	479	62	27[23]	(154)
	α-Oximinopropionic acid	480	90	27[21]	(181d)
C_4	Methyl ethyl ketoxime	479	85	27[1]	150–155
	Biacetyl monoxime	480	60	27[15]	(76.5)
	Dimethylglyoxime	479	60	27[15]	(240)
	α-Oximinobutyric acid	480	65	27[21]	(154d)
C_5	Glutardialdoxime	482	90†	27[30]	(175)
	Cyclopentanone oxime	479	93	27[5]	97/24, (54)
C_6	Cyclohexanone oxime	479	93	27[3]	105/12, (88)
		479	65	27[2]	95–100/5, (80)
		481	80	27[27]	(88)
	2-Isonitrosocyclohexanone	480	82	27[14]	
	1,2-Cyclohexanedione dioxime	479	70	27[14]	(188)
	α-Oximinocaproic acid	480	70	27[21]	(135d)
	Ethyl α-oximinoacetoacetate	480	63	27[19]	(58)
C_7	Heptaldoxime	479	93	27[3]	107/6, (55)
	3-Heptanone oxime	481	60	27[28]	56/1, 1.4522[25]
	1,2-Cycloheptanedione dioxime	479	46	27[13]	(180)
	Ethyl α-oximinovalerate	480	75	27[22]	124/5, (48)
C_8	Acetophenone oxime	479	90	27[9]	(59)
	p-Chloroacetophenone oxime	479	94	27[10]	(98)
	o-Nitroacetophenone oxime	480	74	27[25]	(117)
	p-Nitroacetophenone oxime	480	67	27[25]	(174)
	Ethyl α-oximinocaproate	480	80	27[20]	(55)
C_9	Isonitrosopropiophenone	480	68	27[26]	(113)
	p-Methylacetophenone oxime	479	95	27[10]	(87)
	α-Oximino-β-phenylpropionic acid	480	95	27[21]	(169)
C_{12}	Methyl α-naphthyl ketoxime	479	98	27[10]	(137)
C_{13}	Benzophenone oxime	479	99	27[4]	(142)
		479	98	27[11]	(144)*
C_{14}	*p*-Phenylacetophenone oxime	479	90	27[9]	(186)
	Desoxybenzoin oxime	481	100	27[29]	(94)
C_{16}	3-Acetylphenanthrene oxime	479	100	27[12]	(72)

*For explanations and symbols see pp. xi–xii.

TABLE 96. NITROSO COMPOUNDS

C_n	Compound	Method	Yield (%)	Chapter ref.	B.p./mm., n_D^t, (M.p.)
	C-Nitroso Compounds				
C_6	Nitrosobenzene	485	53	27[46]	(67)
	p-Dinitrosobenzene	484	40†	27[37]	(180)
	o-Chloronitrosobenzene	485	40	27[47]	(56)
	o-Bromonitrosobenzene	485	35	27[47]	(97)
	p-Nitrosophenol	484	80	27[33]	(125d)
C_7	*o*-Nitrosotoluene	485	20	27[47]	(72.5)
C_8	*p*-Nitrosodimethylaniline	484	89	27[31]	
C_{10}	*p*-Nitrosodiethylaniline	484	95	27[31]	
	N-Nitroso Compounds				
C_2	Nitrosodimethylamine	483	90	27[39]	150/755
	Nitrosomethylurea	483	72	27[43]	
C_4	Nitrosomethylurethane	483	76	27[44]	61/10
C_7	N-Nitroso-β-methylamino-isobutyl methyl ketone	483	80†	27[42]	101/1.5
	N-Nitrosomethylaniline	483	93	27[40]	137/13
C_8	N-Nitrosophenylglycine	483	90	27[43]	(103d)

For explanations and symbols see pp. xi–xii.

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