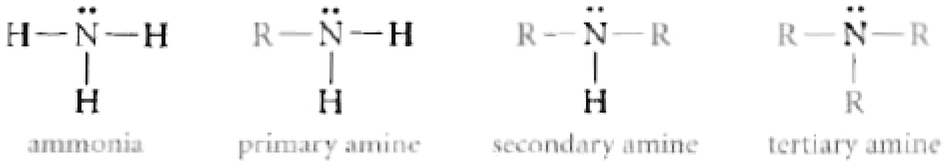
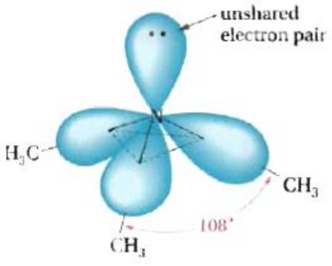
Amines

Amines may be regarded as the derivatives of ammonia in which one or more or all the hydrogen atoms are replaced by organic groups, such as alkyl or aryl

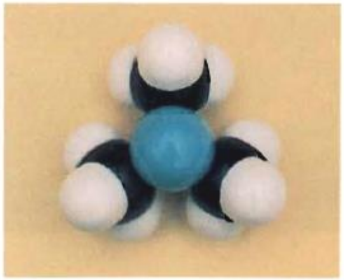
- Structure The relation between ammonia and amines is as follows:



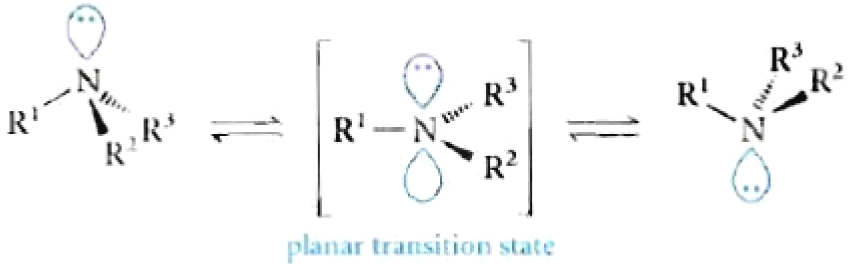
- 1º Amines have one organic group attached to the N atom
- 2º Amines have two organic groups attached to the N atom
- 3º Amines have three organic groups attached to the N atom
- In some 2º and 3º amines the N may be part of a ring
- The N atom in amines is trivalent and it carries an unshared electron pair
- The N orbitals are *sp*^{3}-hybridized, and the overall geometry is pyramidal (almost tetrahedral)



(a)



(b)

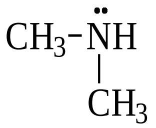
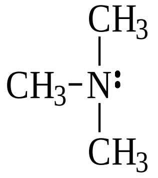


Classification of amines

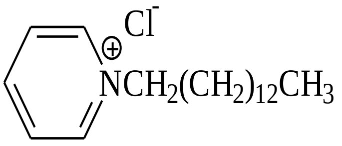
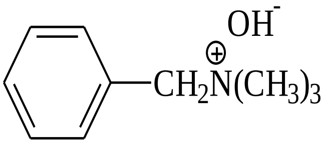
a) Primary (1°) Amines: - An amine in which one hydrogen of ammonia has been replaced by an alkyl or aryl group.

b) Secondary (2°) Amines: - An amine in which two hydrogen of ammonia have been replaced by alkyl or aryl groups.

c) Tertiary (3°) Amines: - An amine in which all three hydrogens of ammonia have been replaced by alkyl or aryl groups.

$:NH_3$	$CH_3-\ddot{N}H_2$	 $CH_3-\ddot{N}H-CH_3$	 $CH_3-\ddot{N}(CH_3)-CH_3$
Ammonia	Methylamine (1° amine)	Dimethylamine (2° amine)	Trimethylamine (3° amine)

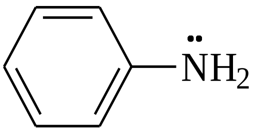
d) Quaternary (4°) ammonium ion:- An ion in which nitrogen is bonded to four carbons and bears a positive charge.

$(CH_3)_4N^+Cl^-$		
Tetramethylammonium chloride	Tetradecylpyridinium chloride (Cetylpyridinium chloride)	Benzyltrimethylammonium hydroxide

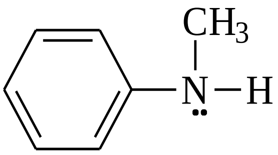
e) Aliphatic amines: - An amine in which nitrogen is bonded only to alkyl groups.

CH_3NH_2	$CH_3CH_2NH_2$	$CH_3CH_2CH_2NH_2$
methyl amine	Ethyl amine	Propyl amine

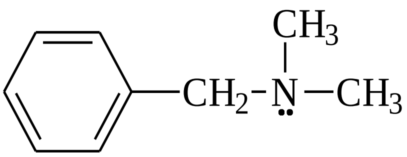
f) Aromatic amine: - An amine in which nitrogen is bonded to one or more aryl groups.



Aniline
(1° aromatic amine)

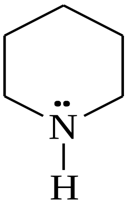


N-Methylaniline
(2° aromatic amine)

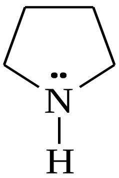


Benzyldimethylamine
(3° aliphatic amine)

g) Heterocyclic amines:-An amine in which nitrogen is one of the atoms or a ring.

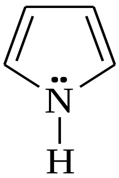


Piperidine

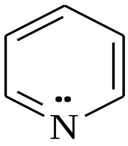


Pyrrolidine

(heterocyclic aliphatic amines)



Pyrrole



Pyridine

(heterocyclic aromatic amines)

Nomenclature of Amines

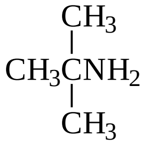
(Common Names)

Naming Simple Amines

- Are named as alkylamines.
- List the names of the alkyl groups bonded to the N atom in alphabetical order in front of amine.

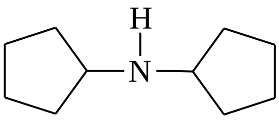
CH_3NH_2

Methylamine



$CH_3\overset{CH_3}{\underset{CH_3}{C}}NH_2$

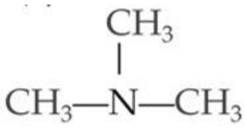
tert-Butylamine



Dicyclopentylamine

$CH_3—NH—CH_3$

Dimethylamine



$CH_3—\overset{CH_3}{N}—CH_3$

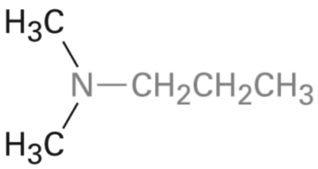
Trimethylamine

$CH_3CH_2—NH_2$

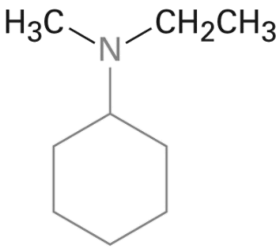
Ethylamine

$CH_3CH_2—NH—CH_3$

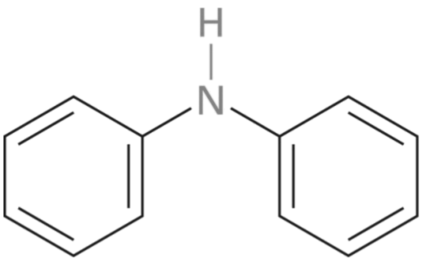
Ethylmethylamine



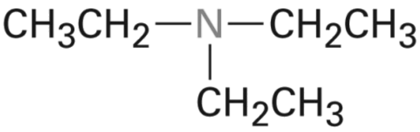
***N,N*-Dimethylpropylamine**



***N*-Ethyl-*N*-methylcyclohexylamine**



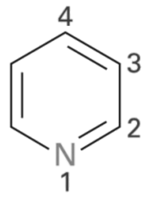
Diphenylamine



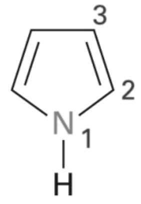
$CH_3CH_2—\underset{CH_2CH_3}{N}—CH_2CH_3$

Triethylamine

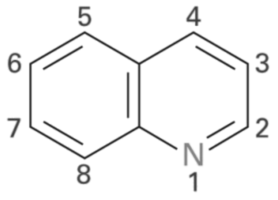
- If the nitrogen atom occurs as part of a ring, the compound is designated as being heterocyclic
- Each ring system has its own parent name



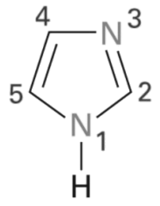
Pyridine



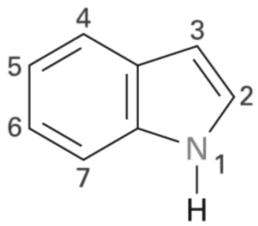
Pyrrole



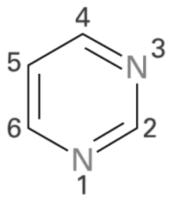
Quinoline



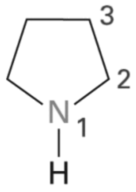
Imidazole



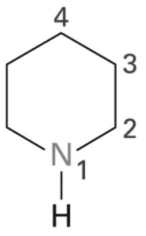
Indole



Pyrimidine



Pyrrolidine

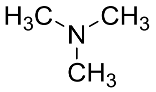


Piperidine

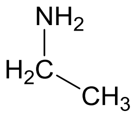
IUPAC system

- The prefix *amino* and a number designates the position of the amino group on an alkane parent chain

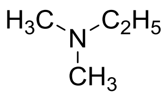
- A substituent on the N uses the –N prefix as with the systematic naming



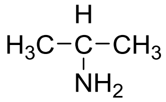
N,N-Dimethyl aminomethane



aminoethane



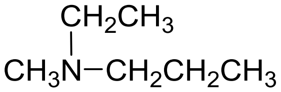
N,N-dimethyl aminoethane



2-aminopropane

$CH_3NHCH_2CH_2CH_3$

N-methylaminopropane



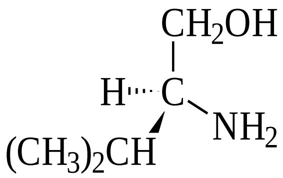
$CH_3N(CH_2CH_3)-CH_2CH_2CH_3$

N-ethyl-*N*-methylaminopropan

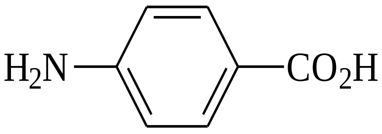
When other functional groups are present, the amino group is named as a substituent:

$H_2NCH_2CH_2OH$

2-Aminoethanol



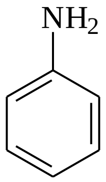
(*S*)-2-Amino-3-methyl 1-butanol



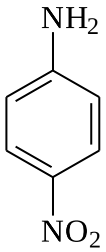
4-Aminobenzoic acid

Aromatic amine

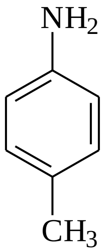
IUPAC nomenclature retains the common name aniline for $C_6H_5NH_2$, the simplest aromatic amine. Its simple derivatives are named using the prefixes *o*-, *m*-, *p*-, or numbers to locate substituents. Several derivatives of aniline have common names that are still widely used. Among those are toluidine for a methyl-substituted aniline and anisidine for a methoxy-substituted aniline.



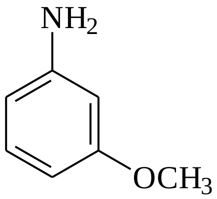
Aniline



4-Nitroaniline



4-Methylaniline
(p-Toluidine)

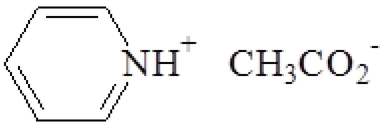


3-Methoxyaniline
(m-Anisidine)

When four atoms or groups of atoms are bonded to a nitrogen atom, the compound is named as a salt of the corresponding amine. The ending -amine (or -aniline, or pyridine, and so on) is replaced by ammonium (or anilinium, or pyridinium, etc.) and the name of the anion (chloride, acetate, etc.) is added.

$(CH_3CH_2)_3NH^+\quad Cl^-$

Triethylammonium chloride



Pyridinium acetate

Basicity of amines

Amines are the organic derivatives of ammonia, it is highly reasonable to assume that amines may be basic in character. In fact, amines, like ammonia, give an alkaline reaction in aqueous solution and form salts with acids. In aqueous solution, amine exists in the following equilibrium

$$R\ddot{N}H_2 + H_2O \rightleftharpoons R\overset{+}{N}H_3 + OH^-$$

According to this modem concept the strength of any base depends upon the simultaneous of two conditions:

(1) Availability of electrons

(2) Stability of conjugate acid formed in solution.

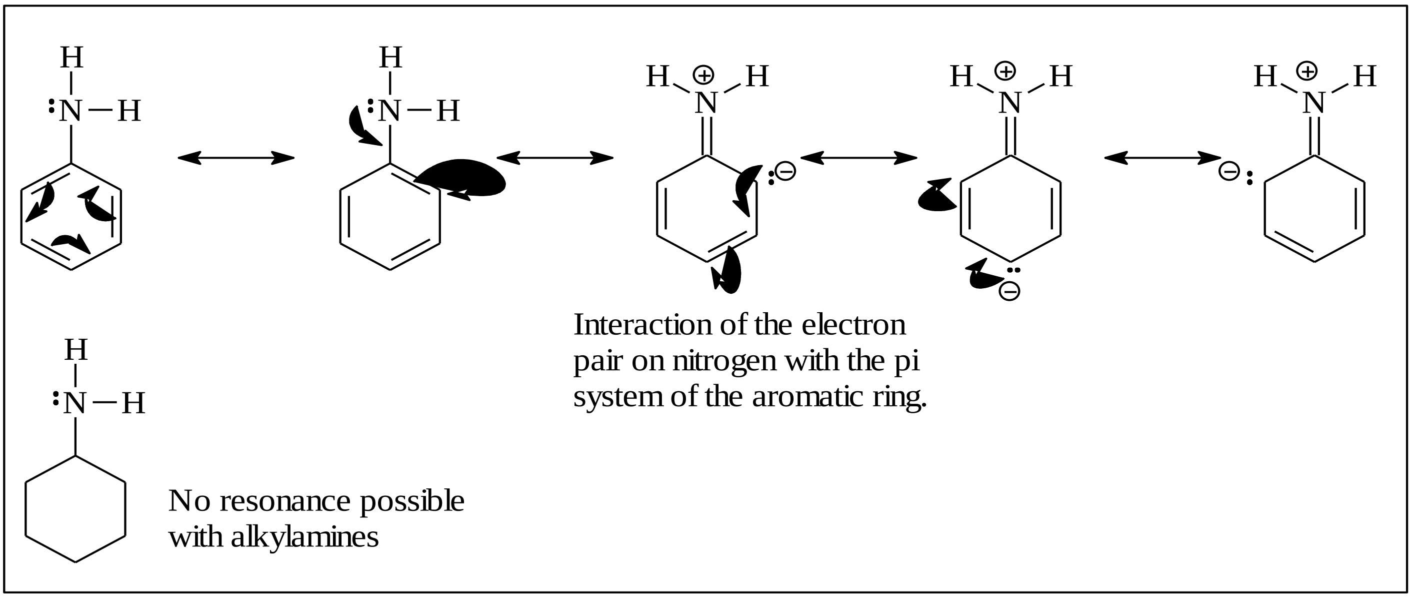
Any factor that can increase electron density of the species under consideration increases the basicity. Similarly increase in the stability of conjugate acid increases the basic strength of the compound, but both these factors are to be considered simultaneously. Based on the above concept regarding the strength of the bases the observations noted in the table may be properly rationalized It has been observed that aliphatic secondary amine is most basic among ammonia, primary, secondary and tertiary amines, i.e., the order is

$NH_3 < RNH_2 < R_2NH > R_3N > NH_3$

The greater basicity of all the three types of amines than ammonia is attributable to the electron release by alkyl groups which increases the electron density on nitrogen and at the same time the conjugate acids formed are moderately stable, as a result of which the average effect of

Both the factors are greater in these amines than in ammonia, and amines are more basic than ammonia. But among the three types of amines, average effect of these two factors is not the same.

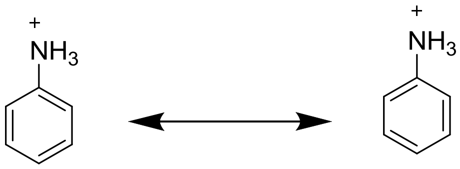
Weak basicity of aromatic amines is due to the resonance stabilization as indicated below



Interaction of the electron pair on nitrogen with the pi system of the aromatic ring.

No resonance possible with alkylamines

Owing to the above resonance, the lone pair of electrons on nitrogen is less available for coordinating with a proton and at the same time, the small charge on nitrogen atom would tend to repel a proton. Further, the conjugate acid, the anilinum ion is less stable than parent amine due to lesser number of resonating structures (only two)

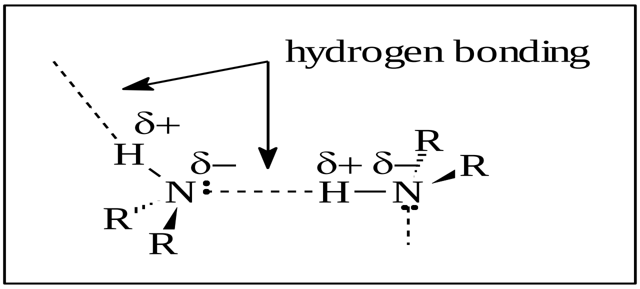


Electron releasing groups (e.g., methyl, ethyl, and other alkyl groups) increase the basicity of aromatic amines, whereas electron-withdrawing groups (halogen, nitro, and carbonyl) decrease their basicity. The decrease in basicity on halogen substitution is due to the electron withdrawing inductive effect of the electronegative halogen.

Physical properties

The lower members of the amine family are gases and soluble in water, amine containing three To eleven carbon atoms are solid.

Amines are polar compounds, and both primary and secondary amines form intermolecular hydrogen bonds. An N-H---N hydrogen bond is not as strong as an O-H---O hydrogen bond because the difference in electronegativity between nitrogen and hydrogen (0.9) is not a great as that between oxygen and hydrogen (1.4). The effect of intermolecular hydrogen bonding can be illustrated by comparing the boiling points of methylamine and methanol. Both compounds have polar molecules that interact in the pure liquid by hydrogen bonding. Hydrogen bonding is stronger in methanol than in methylamine, and, therefore, methanol has the higher boiling point. All classes of amines form hydrogen bonds with water and are more soluble in water than hydrocarbons of comparable molecular weight. Most low-molecular-weight amines are completely soluble in water. Higher molecular-weight amines are only moderately soluble or insoluble.

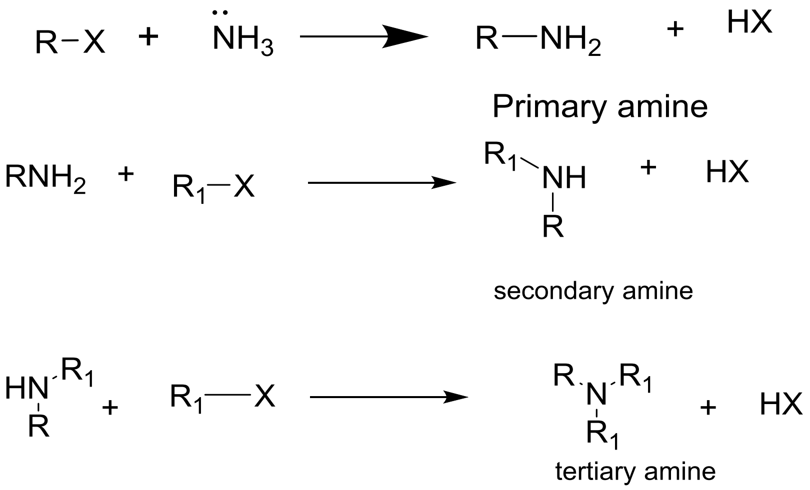


Preparation of amines

Alkylation of ammonia

Ammonia reacts as a nucleophile with alkyl halides to give primary amines in a nucleophilic substitution reaction. A yield are often poor as the product, a primary amine, RNH_2, is itself a nucleophile and can react with more alkyl halide. The result is mixtures containing primary amines, secondary amines, tertiary amines and quaternary ammonium salts.This can be avoided if a large excess of ammonia is used.

Aryl halides do not undergo simple nucleophilic substitution, they *cannot* be prepared using this method.



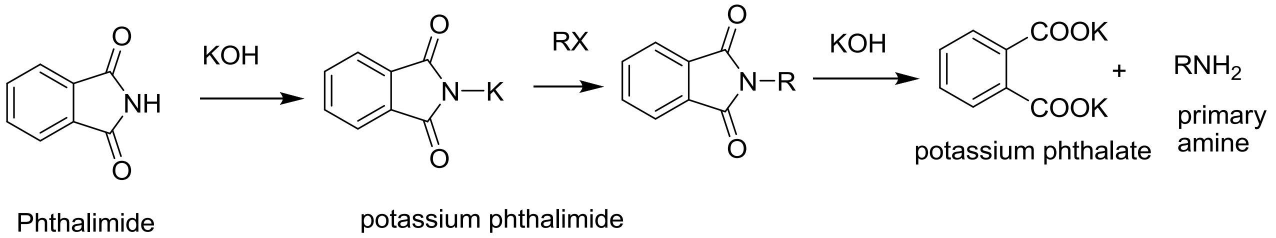
$$\underset{\text{1-bromooctane}}{CH_3(CH_2)_6CH_2Br} + NH_3 \longrightarrow \underset{\text{1-aminooctane}}{CH_3(CH_2)_6CH_2NH_2}$$

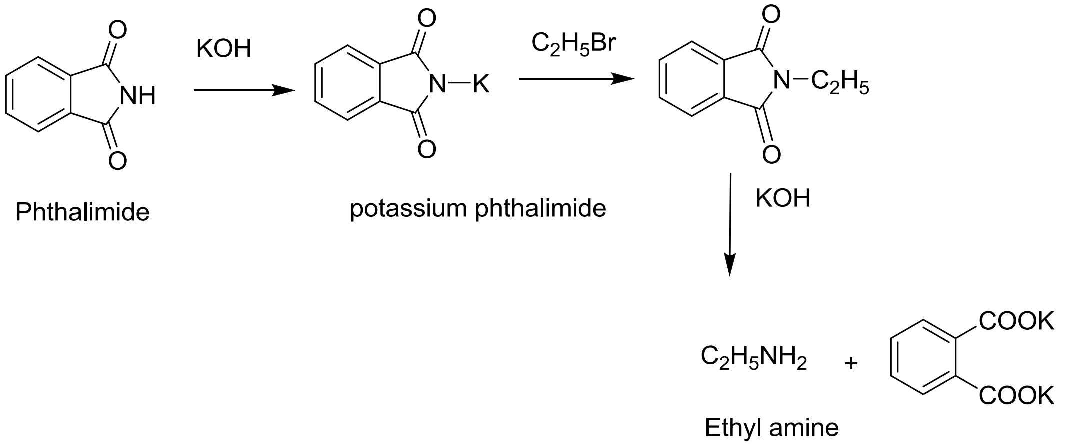
$$\underset{\text{methylbromide}}{CH_3Br} + NH_3 \longrightarrow \underset{\text{methylamine}}{CH_3NH_2} + HBr$$

$$\underset{\text{Dichloro ethane}}{ClCH_2CH_2Cl} + 2NH_3 \longrightarrow \underset{\text{Ethylene diamine}}{NH_2CH_2CH_2NH_2}$$

Gabriel Synthesis

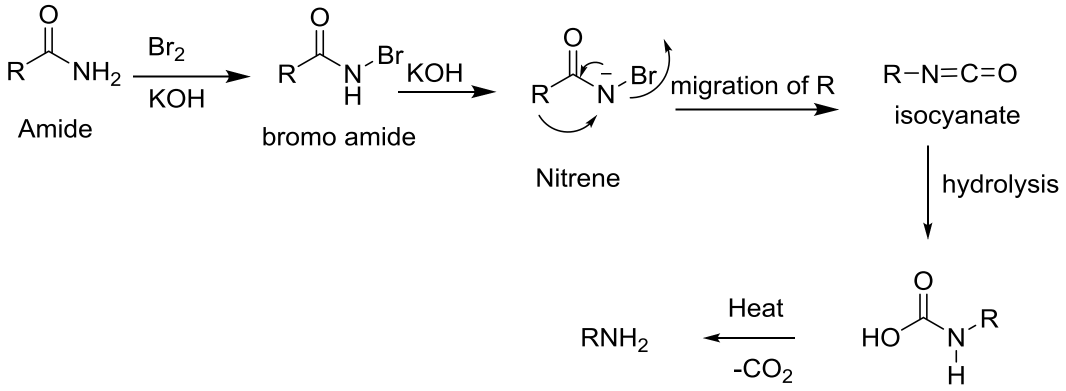
Pure primary amines can be prepared by this method by using phthalimide with alkyl halid in presence of potassium hydroxide.

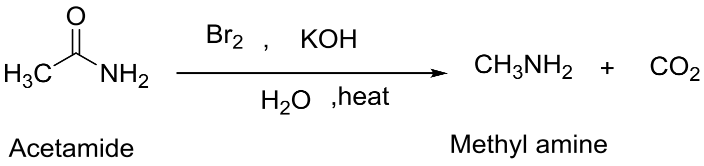


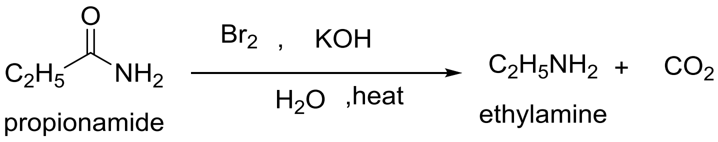


Hofmann rearrangement

Hofmann rearrangement, also known as Hofmann degradation is the reaction of a primary amide with a halogen (chlorine or bromine) in strongly basic (sodium or potassium hydroxide) aqueous medium, in this reaction the amide converts to a primary amine with one fewer carbon atoms.



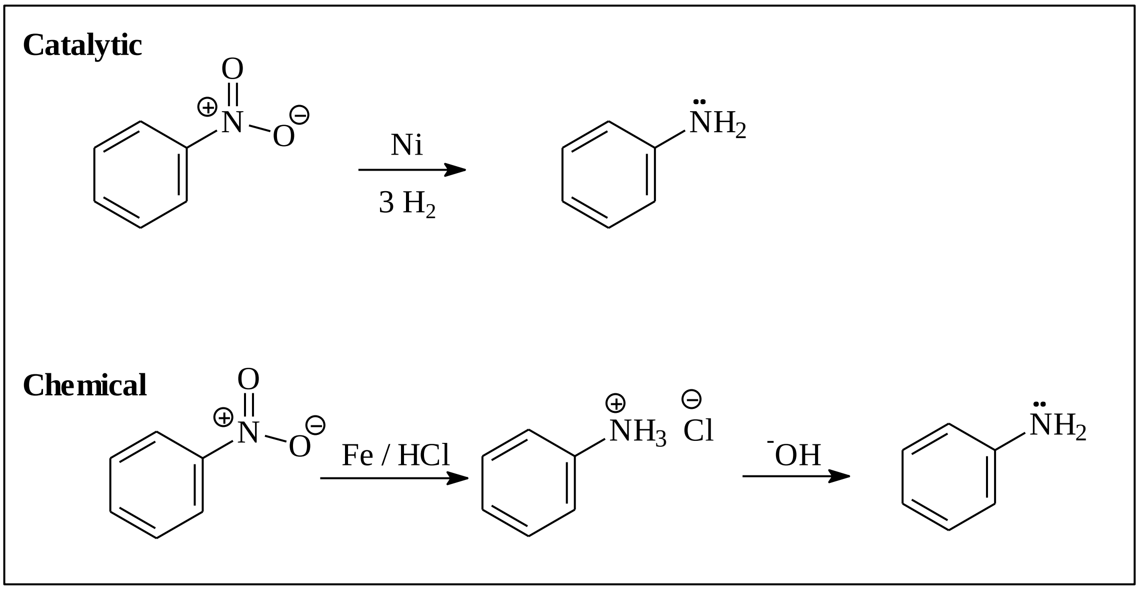




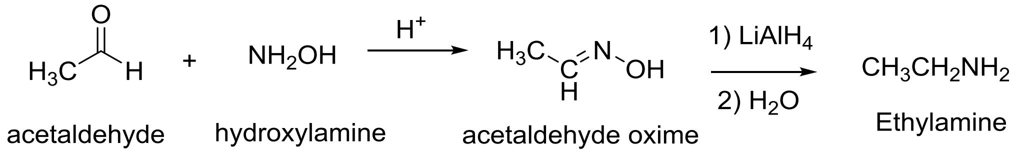
Reduction of reducible compounds

Easily reducible compounds like nitriles, oxime, amides, and nitro compounds on reduction yield amines

a) Reduction of Nitro Groups

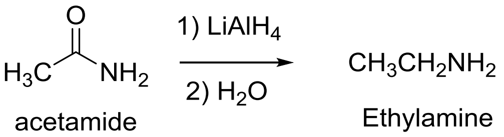


b) Reduction of Oximes, Nitriles, and Amides by Lithium Aluminum Hydride



$$H_3C-C\equiv N \xrightarrow[\text{2) } H_2O]{\text{1) } LiAlH_4} CH_3CH_2NH_2$$

acetonitrile Ethylamine

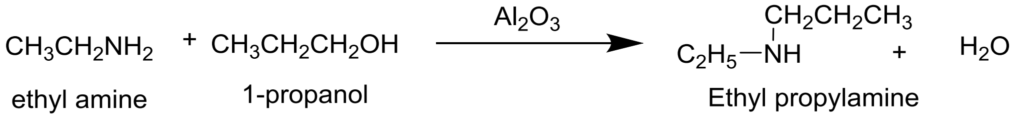


Action of ammonia on alcohols

When a mixture of alcohol and ammonia is passed over heated alumina all the three types of amines are obtained.

$$\underset{\text{ethanol}}{C_2H_5OH} + NH_3 \xrightarrow{Al_2O_3} \underset{\text{ethylamine}}{CH_3CH_2NH_2} + H_2O$$

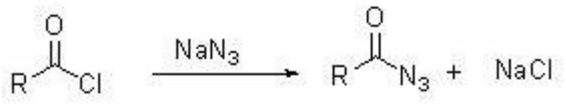
$$\underset{\text{ethyl amine}}{CH_3CH_2NH_2} \xrightarrow[Al_2O_3]{C_2H_5OH} \underset{\text{diethyl amine}}{(CH_3CH_2)_2NH} + H_2O$$

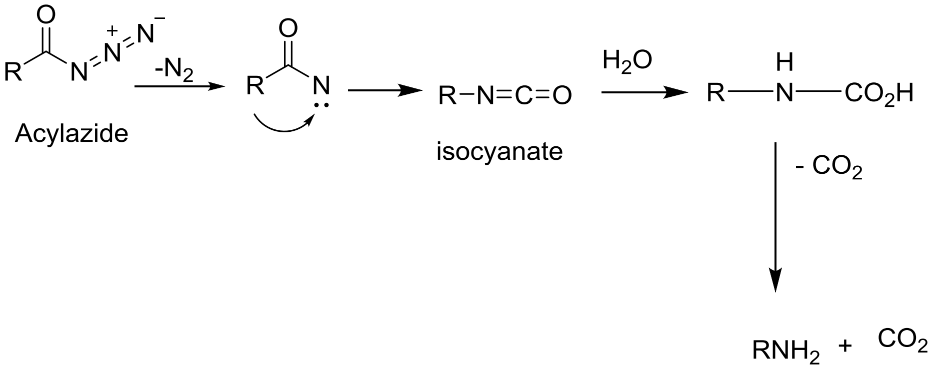


$$\underset{\text{ethyl amine}}{CH_3CH_2NH_2} + \underset{\text{1-propanol}}{CH_3CH_2CH_2OH} \xrightarrow{Al_2O_3} \underset{\text{Ethyl propylamine}}{C_2H_5-\overset{CH_2CH_2CH_3}{\overset{|}{N}H}} + H_2O$$

Curtius rearrangement

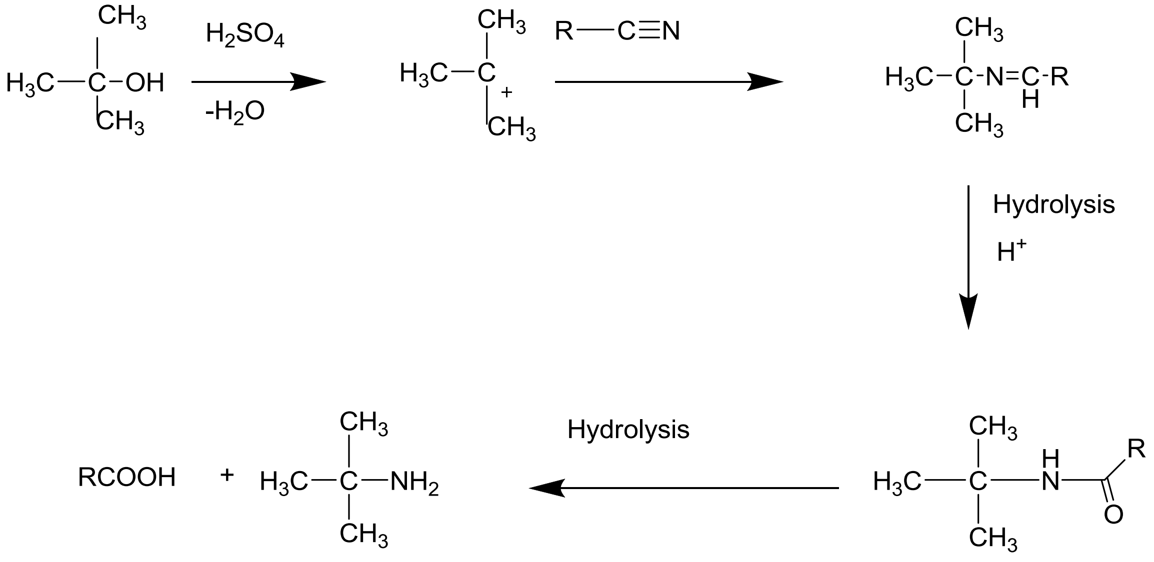
The Curtius rearrangement is an organic reaction used to convert an acyl azide to an isocyanate under thermal conditions. The mechanism consists of an alkyl shift of the R group from the carbonyl carbon to the closest nitrogen with the release of nitrogen gas. The release of gas drives the reaction forward and results in the formation of the isocyanate product which can potentially react further in the presence of nucleophiles in solution.





Ritter method

This method involves the reaction of tertiary alcohol with alkyl cyanide in presence of strong sulphuric acid.



Butyl amine

Chemical properties

a) Reactions with acids

Amines react with mineral acids to form salt .Salt formation with mineral acids is analogous to ammonium salt and is formed both in aqueous and anhydrous condition.

$$CH_3NH_2 + HCl \longrightarrow CH_3\overset{+}{N}H_3\overset{-}{Cl}$$

$$(CH_3)_2NH + HCl \longrightarrow (CH_3)_2\overset{+}{NH_2}\overset{-}{Cl}$$

$$(CH_3)_3N + HCl \longrightarrow (CH_3)_3\overset{+}{N}H\overset{-}{Cl}$$

$$CH_3CH_2\ddot{N}H_2 + HCl \xrightarrow[H_2O]{} CH_3CH_2\overset{+}{N}H_3\ Cl^-$$

Ethylaminium chloride
(an aminium salt)

$$(CH_3CH_2)_2\ddot{N}H + HBr \xrightarrow[H_2O]{} (CH_3CH_2)_2\overset{+}{N}H_2\ Br^-$$

Diethylaminium bromide

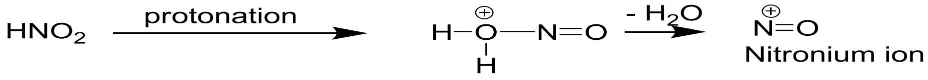
$$(CH_3CH_2)_3\ddot{N} + HI \xrightarrow[H_2O]{} (CH_3CH_2)_3\overset{+}{N}H\ I^-$$

Triethylaminium iodide

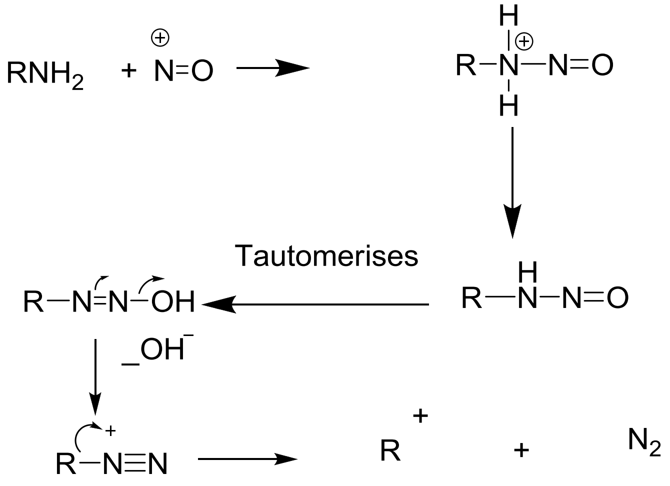
Reaction with nitrous acid

1-Primary aliphatic amine reacts with nitrous acid (HNO_2) to form initially an unstable diazonium compound which decomposes to evolve nitrogen. Nitrous acid is unstable and it is prepare d in situ by reaction of sodium nitrite with hydrochloric

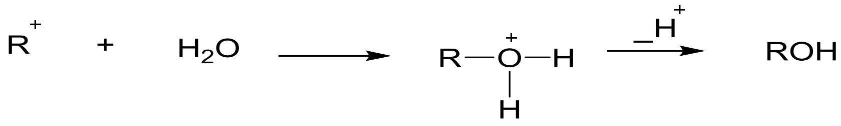
$$NaNO_2 + HCl \longrightarrow HNO_2 + NaCl$$



the nitronium ion is active electrophile and reacts with amine to form diazonium salt



The carbocation formed combines with water in aqueous solution to form alcohol



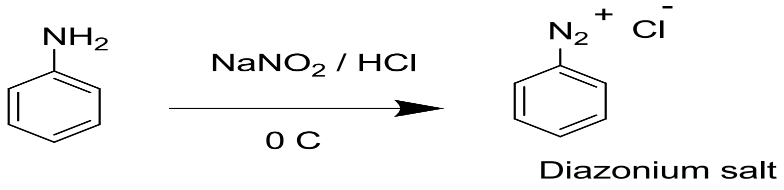
Thus primary aliphatic amines normally yield primary alcohols on reaction with nitrous acid.

$$CH_3CH_2CH_2NH_2 + HNO_2 \longrightarrow CH_3CH_2CH_2OH$$

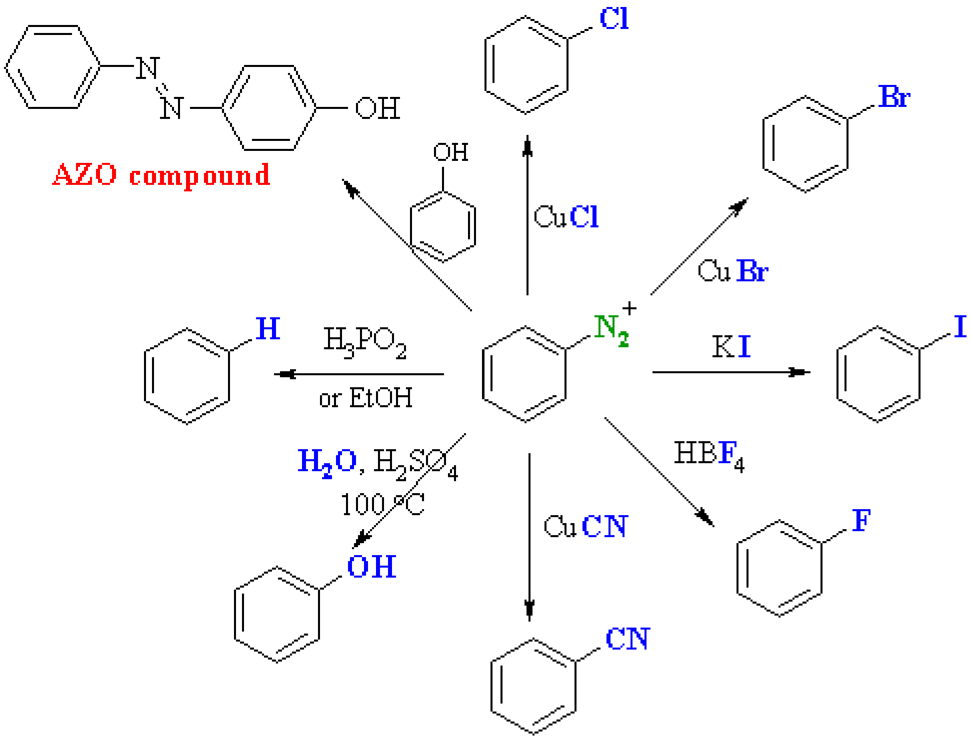
1-propanamine nitrous acid 1-Propanol

2-Primary aromatic amines

The nitrosation of primary aromatic amines with nitrous acid (generated in situ from sodium nitrite and a strong acid, such as hydrochloric acid, sulfuric acid) leads to diazonium salts.



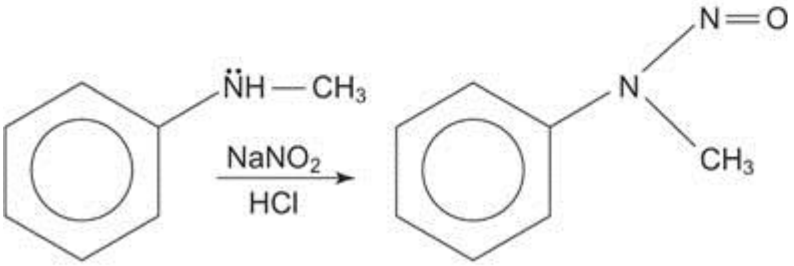
Diazonium salts are important intermediates for the preparation of halides (Sandmeyer Reaction), and azo compounds as the following.



3) Secondary aliphatic and aromatic amines form N- nitrosoamine with nitrous acid.

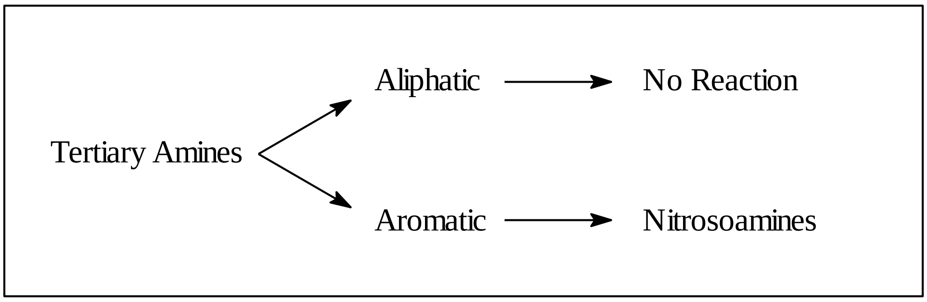
$$CH_3-NH-CH_3 \xrightarrow[HCl]{NaNO_2} (CH_3)_2-N-N{=}O$$

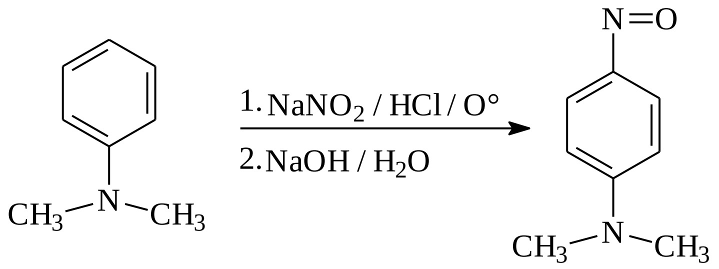
dimethylamine N,nitrosodimethylamine



N-methylaniline N-nitroso N-methylaniline

4) Tertiary Amines

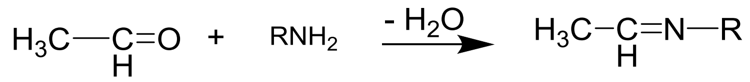




N,N-Dimethylaniline N,N-Dimethyl-4-nitrosoaniline

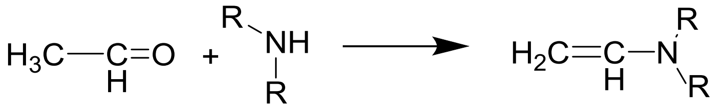
Reactions of Amines with compounds containing a carbonyl group

Amines react with compounds having carbonyl function as electron donor species(nucleophile), therefore the reaction aldehyde and primary amine produce Schiff-base ,while Secondary amines reacts with aldehydes having α-hydrogen atom produce enamines .Tertiary amines do not react with aldehyde



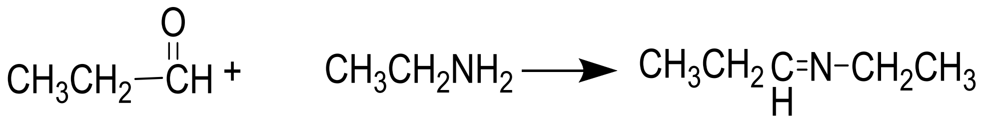
$$H_3C-\underset{H}{C}=O + RNH_2 \xrightarrow{-H_2O} H_3C-\underset{H}{C}=N-R$$

Acetaldehyde Schiff-base



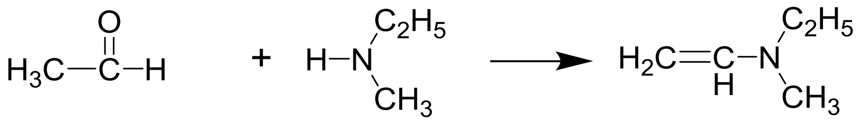
$$H_3C-\underset{H}{C}=O + R_2NH \longrightarrow H_2C=\underset{H}{C}-NR_2$$

Enamine



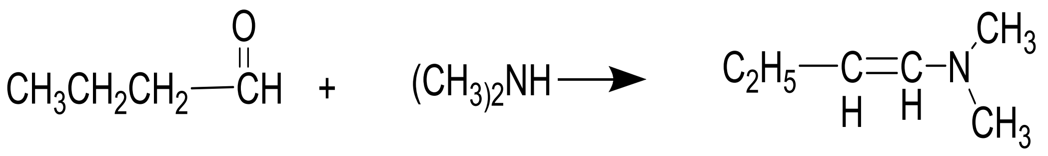
$$CH_3CH_2-\overset{O}{\overset{\|}{C}}H + CH_3CH_2NH_2 \longrightarrow CH_3CH_2\underset{H}{C}=N-CH_2CH_3$$

Propanaldehyde Ethyl amine Schiff-base



$$H_3C-\overset{O}{\overset{\|}{C}}-H + H-N(C_2H_5)(CH_3) \longrightarrow H_2C=\underset{H}{C}-N(C_2H_5)(CH_3)$$

Acetaldehyde ethyl Methyl amine *N*-ethyl-*N*-methylethenamine (Enamine)



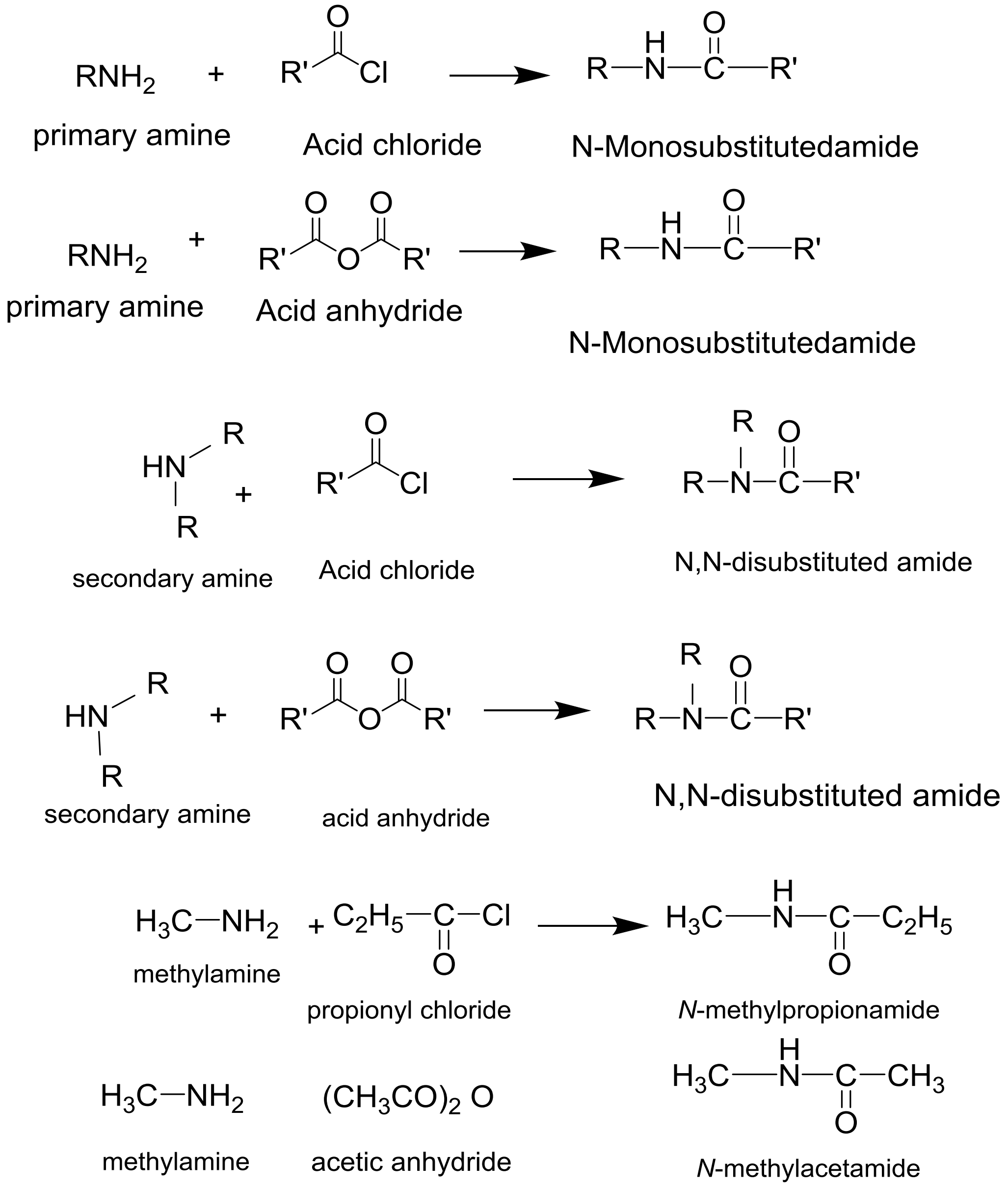
$$CH_3CH_2CH_2-\overset{O}{\overset{\|}{C}}H + (CH_3)_2NH \longrightarrow C_2H_5-\underset{H}{C}=\underset{H}{C}-N(CH_3)_2$$

Butanal Dimethyl amine *N*,*N*-dimethylbut-1-en-1-amine

(Enamine)

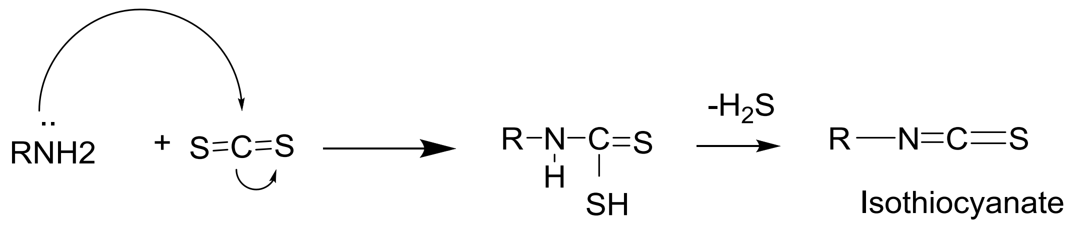
Reaction with acid-chloride and acid-anhydride

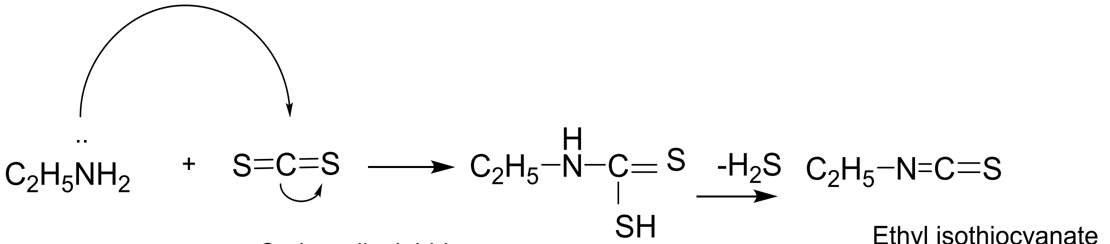
Primary and secondary amines on reaction with acid-chloride and anhydride form acyl derivatives. But tertiary amines do not form acyl derivative as they have no replaceable hydrogen atom.



Reaction with carbon disulphide

When primary amine is warmed with carbon disulphide in presence of mercuric chloride as catalyst, isothiocyanate is formed.



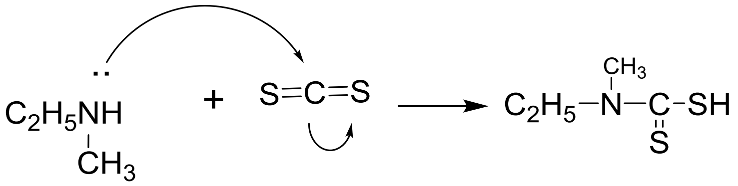


Ethyl amine

Carbon disulphide

Ethyl isothiocyanate

Secondary amines react with carbon disulphide to form dithiocarbamic acid



ethyl Methylamine

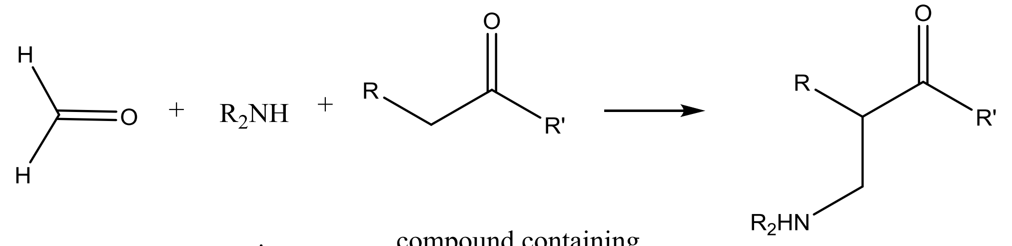
Carbon disulphide

ethyl(methyl)carbamodithioic acid

Tertiary amines don't react with carbondisulphide.

Mannich condensation reaction

Mannich condensation is a reaction of a compound containing at least one active hydrogen atom with formaldehyde and ammonia or ammonia derivatives. Only primary and secondary amines can participate in Mannich condensation reaction in this reaction active hydrogen atom is replaced by amino methyl group.



formaldehyde

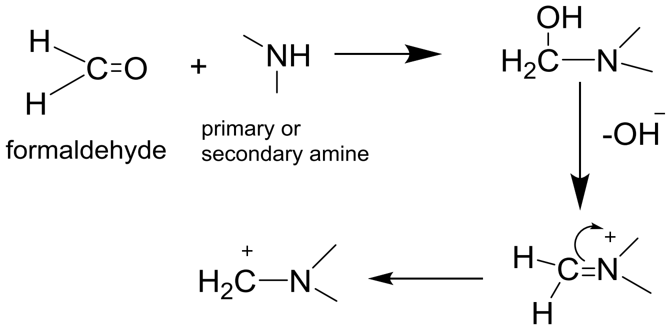
amine

compound containing
carbonyl functional group

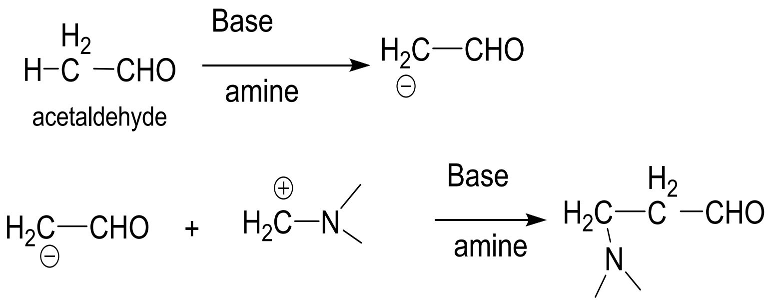
amino methylated product

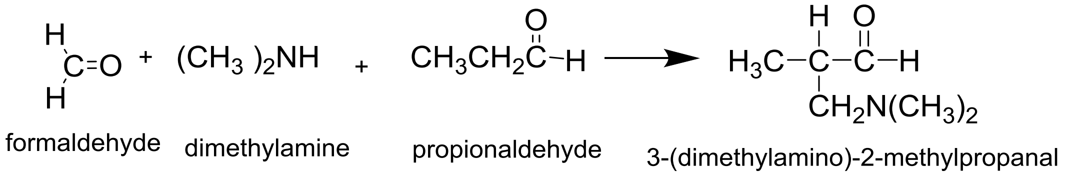
Mechanism of reaction

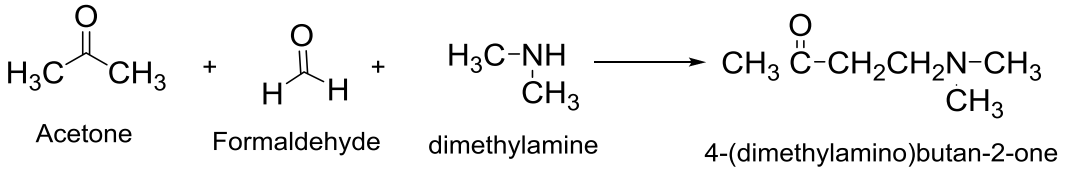
STEP1



STEP2

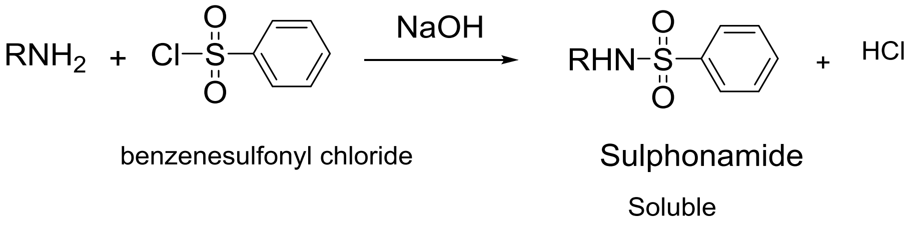


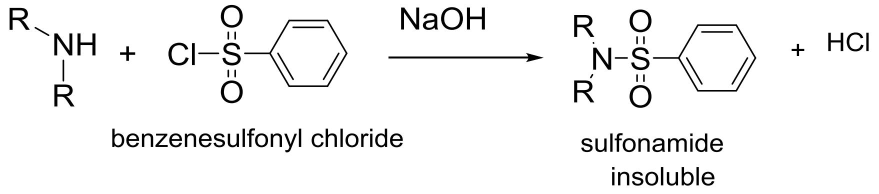


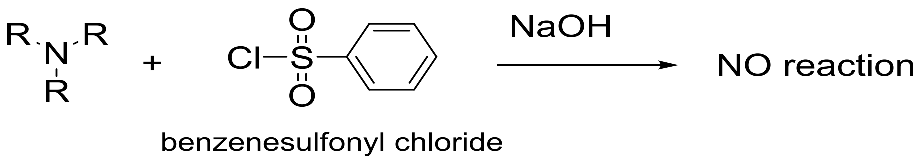


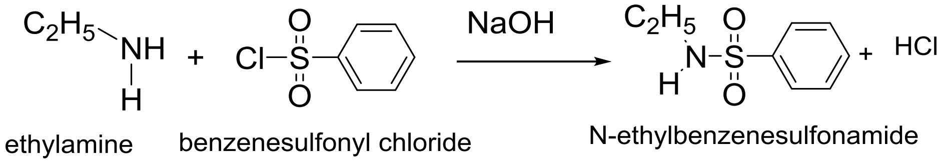
Detection of amines(**Hinsberg reaction**)

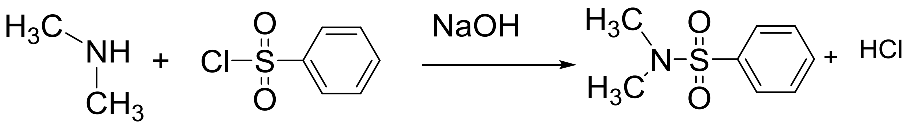
The Hinsberg reaction is a chemical test for the detection of amines. It is an excellent test for distinguishing primary, secondary and tertiary amines. In this test, the amine is shaken well with Hinsberg reagent in the presence of aqueous alkali (either KOH or NaOH). A reagent containing an aqueous sodium hydroxide solution and benzenesulfonyl chloride is added to a substrate. A primary amine will form a soluble sulfonamide salt which precipitates after addition of diluted hydrochloric acid. A secondary amine in the same reaction will directly form an insoluble sulfonamide. A tertiary amine will not react with benzensulfonyl chloride .In this way the reaction can distinguish between the three types of amines.



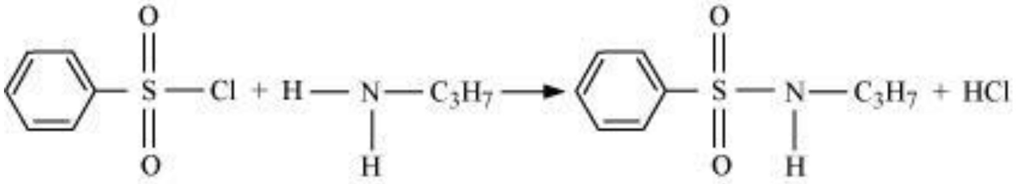








dimethylamine benzenesulfonyl chloride N,N-dimethylbenzenesulfonamide



Benzenesulphonyl chloride Propanamine *N*-Propylbenzenesulphonamide