Amines.
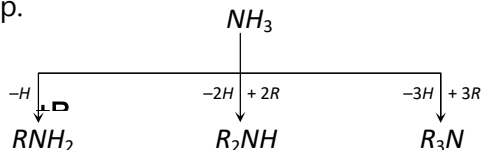
Amines are regarded as derivatives of ammonia in which one, two or all three hydrogen atoms are replaced by alkyl or aryl group.

$$NH_3$$

$-H$ $-2H$ | $+2R$ $-3H$ | $+3R$
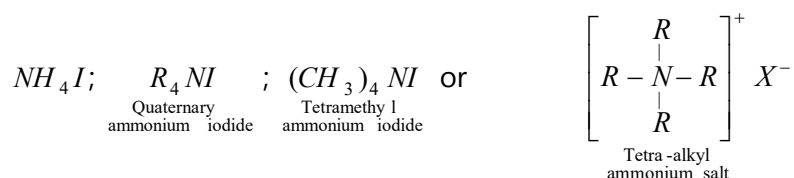
$$RNH_2 \qquad R_2NH \qquad R_3N$$

Amines are classified as primary, secondary or tertiary depending on the number of alkyl groups attached to nitrogen atom.
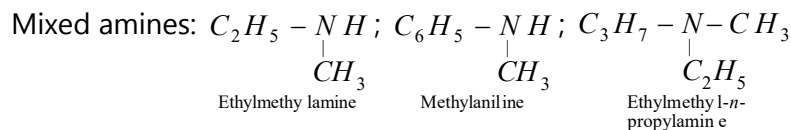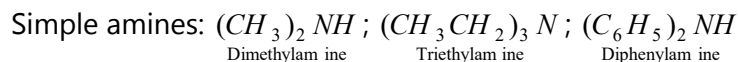
The characteristic groups in primary, secondary and tertiary amines are: $-NH_2$; $-\overset{|}{NH}$;
(amino)   (imino)

$$-\overset{\displaystyle |}{\underset{\displaystyle |}{N}}$$
($tert-$nitrogen)
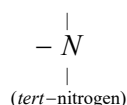
In addition to above amines, tetra-alkyl derivatives similar to ammonium salts also exist which are called quaternary ammonium compounds.

NH_4I; R_4NI ; $(CH_3)_4NI$ or $\left[R-\overset{\displaystyle R}{\underset{\displaystyle R}{N}}-R \right]^+ X^-$
         Quaternary   Tetramethy l
    ammonium iodide   ammonium iodide   Tetra -alkyl
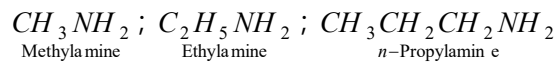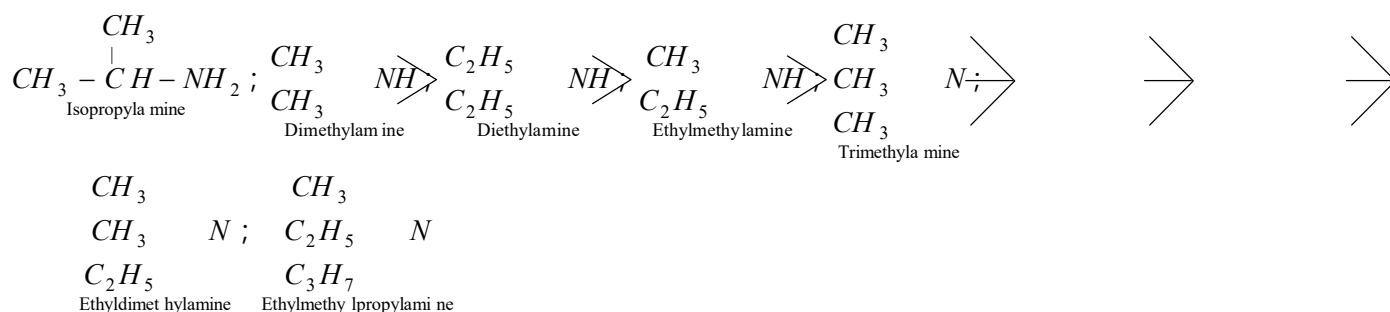   ammonium salt

(1) Simple and mixed amines : Secondary and tertiary amines may be classified as simple or mixed amines according as all the alkyl or aryl groups attached to the nitrogen atom are same or different. For example,

Simple amines: $(CH_3)_2NH$; $(CH_3CH_2)_3N$; $(C_6H_5)_2NH$
             Dimethylam ine   Triethylam ine   Diphenylam ine

Mixed amines: $C_2H_5-\overset{\displaystyle |}{\underset{\displaystyle CH_3}{N}}H$; $C_6H_5-\overset{\displaystyle |}{\underset{\displaystyle CH_3}{N}}H$; $C_3H_7-\overset{\displaystyle |}{\underset{\displaystyle C_2H_5}{N}}-CH_3$
        Ethylmethy lamine   Methylanil ine   Ethylmethy l-n-
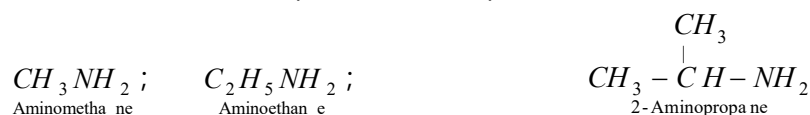   propylamin e

The aliphatic amines have pyramidal shape with one electron pair. In amines, N undergoes sp^3hybridisation.

(2) Nomenclature: In common system, amines are named by naming the alkyl groups attached to nitrogen atom followed by suffix-amine.
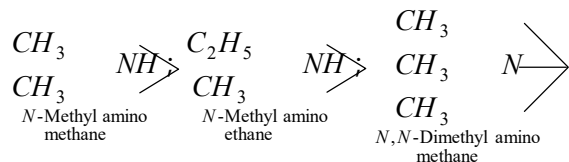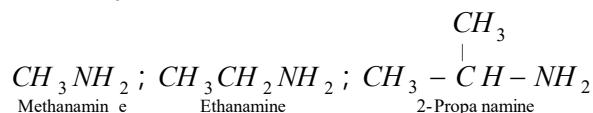
CH_3NH_2 ; $C_2H_5NH_2$; $CH_3CH_2CH_2NH_2$
  Methyla mine   Ethyla mine $n-$Propylamin e

$$CH_3 - \underset{\substack{| \\ CH_3}}{\overset{\substack{CH_3 \\ |}}{C}H} - NH_2 \; ;$$
Isopropylamine

$$\underset{CH_3}{\overset{CH_3}{>}}NH$$
Dimethylamine

$$\underset{C_2H_5}{\overset{C_2H_5}{>}}NH$$
Diethylamine

$$\underset{C_2H_5}{\overset{CH_3}{>}}NH$$
Ethylmethylamine

$$\underset{\substack{CH_3 \\ CH_3}}{\overset{\substack{CH_3 \\ CH_3}}{>}}N\div$$
Trimethylamine

$$\underset{\substack{C_2H_5 \\ }}{\overset{\substack{CH_3 \\ CH_3}}{}}N \; ;$$
Ethyldimethylamine

$$\underset{\substack{C_3H_7 \\ }}{\overset{\substack{CH_3 \\ C_2H_5}}{}}N$$
Ethylmethylpropylamine

In IUPAC system, amino group is considered as substituent and amines are named as amino derivatives of alkanes (Amino alkanes).

$$CH_3NH_2 \; ;$$
Aminomethane

$$C_2H_5NH_2 \; ;$$
Aminoethane

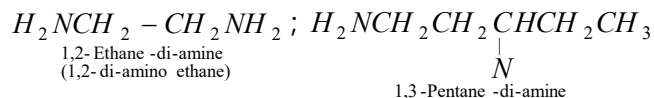$$CH_3 - \underset{\substack{| \\ }}{\overset{\substack{CH_3 \\ |}}{C}H} - NH_2$$
2-Aminopropane

Secondary amines are named as alkyl aminoalkanes and tertiary as dialkyl amino alkanes with highest rank to the amino alkane (primary amine).

$$\underset{CH_3}{\overset{CH_3}{>}}NH\div$$
N-Methyl amino methane

$$\underset{CH_3}{\overset{C_2H_5}{>}}NH$$
N-Methyl amino ethane

$$\underset{\substack{CH_3 \\ CH_3}}{\overset{\substack{CH_3 \\ }}{}}N$$
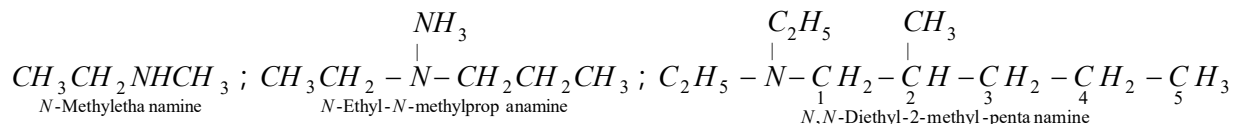N,N-Dimethyl amino methane

Alternatively, in IUPAC system, primary amines are named by replacing the final-e of the parent alkane by   -amine (Alkanamine). A number is added to indicate the position of $– NH_2$ group.

$$CH_3NH_2 \; ;$$
Methanamine

$$CH_3CH_2NH_2 \; ;$$
Ethanamine

$$CH_3 - \underset{\substack{| \\ }}{\overset{\substack{CH_3 \\ |}}{C}H} - NH_2$$
2-Propanamine

When two or more amino groups are present, words di, tri- etc., are used with position numbers.

$$H_2NCH_2 - CH_2NH_2 \; ;$$
1,2-Ethane-di-amine
(1,2-di-amino ethane)

$$H_2NCH_2CH_2\underset{\substack{| \\ N}}{C}HCH_2CH_3$$
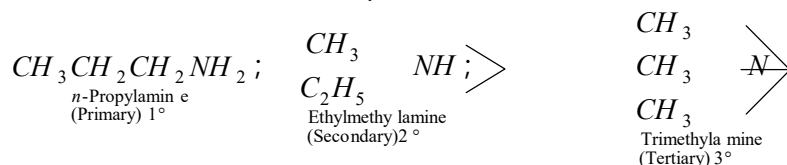1,3-Pentane-di-amine

Secondary or tertiary amines are named as N-substituted derivatives of primary amines. The largest group attached to nitrogen is taken as the alkyl group of the primary amine.
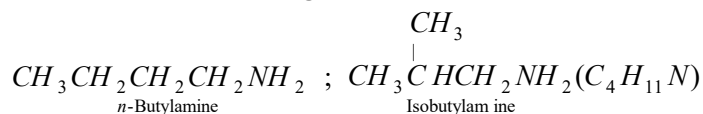
$$CH_3CH_2NHCH_3 \; ; \; \overset{\overset{\displaystyle NH_3}{|}}{CH_3CH_2-N-CH_2CH_2CH_3} \; ; \; \overset{\overset{\displaystyle C_2H_5}{|}}{C_2H_5-N}-\underset{1}{C}H_2-\overset{\overset{\displaystyle CH_3}{|}}{\underset{2}{C}H}-\underset{3}{C}H_2-\underset{4}{C}H_2-\underset{5}{C}H_3$$

N-Methyletha namine   N-Ethyl-N-methylprop anamine   N,N-Diethyl-2-methyl-penta namine

(3) Isomerism: Amines are represented by a general formula, $C_nH_{2n+3}N$ and exhibit following types of isomerism,
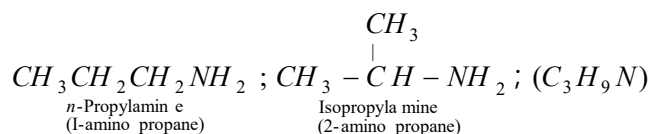
(i) Functional isomerism: This is due to the presence of different functional groups. Molecular formula C_3H_9N represents three functional isomers.

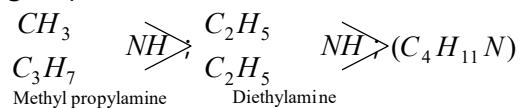$$CH_3CH_2CH_2NH_2 \; ; \; \overset{\displaystyle CH_3}{\underset{\displaystyle C_2H_5}{}}NH \; ; \; \overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{CH_3}}\!\!-\!\!N$$

n-Propylamin e
(Primary) 1°

Ethylmethy lamine
(Secondary)2 °

Trimethyla mine
(Tertiary) 3°

(ii) Chain isomerism: This is due to the difference in the carbon skeleton of the alkyl group attached to the amino group.

$$CH_3CH_2CH_2CH_2NH_2 \; ; \; \overset{\overset{\displaystyle CH_3}{|}}{CH_3\overset{}{C}HCH_2NH_2}\,(C_4H_{11}N)$$

n-Butylamine   Isobutylam ine

(iii) Position isomerism: This is due to the difference in the position of amino group in the carbon chain.

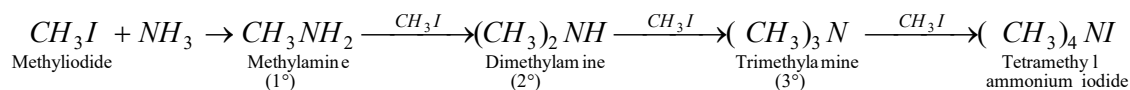$$CH_3CH_2CH_2NH_2 \; ; \; CH_3-\overset{\overset{\displaystyle CH_3}{|}}{C}H-NH_2 \; ; \; (C_3H_9N)$$

n-Propylamin e
(I-amino propane)

Isopropyla mine
(2-amino propane)

(iv) Metamerism: This is due to different alkyl groups attached to the same polyvalent functional group.

$$\overset{\displaystyle CH_3}{\underset{\displaystyle C_3H_7}{}}NH \; ; \; \overset{\displaystyle C_2H_5}{\underset{\displaystyle C_2H_5}{}}NH\,(C_4H_{11}N)$$

Methyl propylamine   Diethylamine

(4) General methods of preparation

(i) Methods yielding mixture of amines (Primary, secondary and tertiary)

(a) Hofmann's method:The mixture of amines (1°, 2° and 3°) is formed by the alkylation of ammonia with alkyl halides.

$$CH_3I + NH_3 \rightarrow CH_3NH_2 \xrightarrow{CH_3I} (CH_3)_2NH \xrightarrow{CH_3I} (CH_3)_3N \xrightarrow{CH_3I} (CH_3)_4NI$$

Methyliodide Methylamine (1°) Dimethylamine (2°) Trimethylamine (3°) Tetramethyl ammonium iodide

The primary amine may be obtained in a good yield by using a large excess of ammonia. The process is also termed as ammonolysis of alkyl halides. It is a nucleophilic substitution reaction.
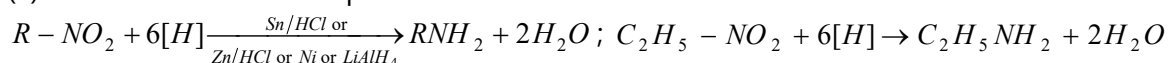
(b) Ammonolysis of alcohols:

$$CH_3OH + NH_3 \xrightarrow[350\,°C]{Al_2O_3} CH_3NH_2 \xrightarrow{CH_3OH} (CH_3)_2NH \xrightarrow{CH_3OH} (CH_3)_3N$$
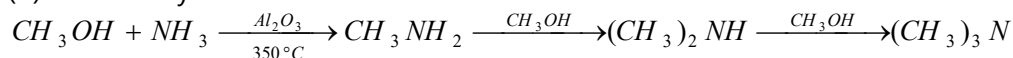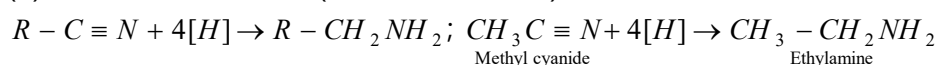
Primary amine may be obtained in a good yield by using a large excess of ammonia.

(ii) Methods yielding primary amines

(a) Reduction of nitro compounds
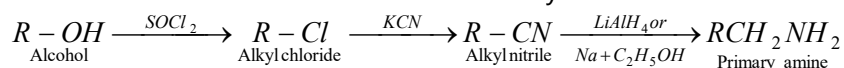
$$R-NO_2 + 6[H] \xrightarrow[Zn/HCl \text{ or } Ni \text{ or } LiAlH_4]{Sn/HCl \text{ or}} RNH_2 + 2H_2O ;\ C_2H_5 - NO_2 + 6[H] \rightarrow C_2H_5NH_2 + 2H_2O$$

(b) Reduction of nitriles (Mendius reaction)

$$R-C \equiv N + 4[H] \rightarrow R-CH_2NH_2 ;\ CH_3C \equiv N + 4[H] \rightarrow CH_3 - CH_2NH_2$$

Methyl cyanide   Ethylamine

The start can be made from alcohol or alkyl halide.

$$R-OH \xrightarrow{SOCl_2} R-Cl \xrightarrow{KCN} R-CN \xrightarrow[Na+C_2H_5OH]{LiAlH_4 or} RCH_2NH_2$$
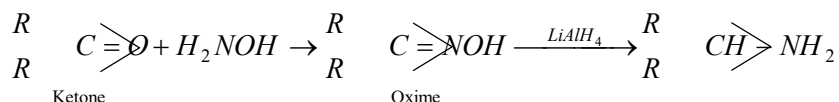
Alcohol   Alkyl chloride   Alkyl nitrile   Primary amine

This sequence gives an amine containing one more carbon atom than alcohol.

(c) By reduction of amides with LiAlH$_4$

$$RCONH_2 \xrightarrow{LiAlH_4} RCH_2NH_2 ;\ CH_3CONH_2 \xrightarrow{LiAlH_4} CH_3CH_2NH_2$$

Acetamide   Ethylamine
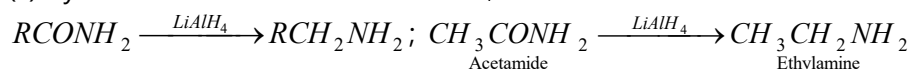
(d) By reduction of oximes: The start can be made from an aldehyde or ketone.

$$RCHO \xrightarrow{H_2NOH} RCH=NOH \xrightarrow[or H_2/Ni]{LiAlH_4} RCH_2NH_2$$

Aldehyde   Oxime   Primary amine

$$\begin{matrix} R \\ R \end{matrix} C=O + H_2NOH \rightarrow \begin{matrix} R \\ R \end{matrix} C=NOH \xrightarrow{LiAlH_4} \begin{matrix} R \\ R \end{matrix} CH-NH_2$$

Ketone   Oxime
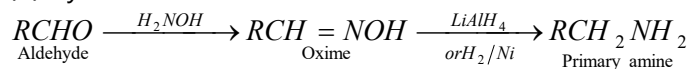
(e) Hofmann's bromamide reaction or degradation (Laboratory method) : By this method the amide (–CONH₂) group is converted into primary amino (– NH₂) group.

$$R-CO-NH_2 + Br_2 + 4KOH \rightarrow R-NH_2 + 2KBr + K_2CO_3 + 2H_2O$$

Amide   Pri-amine
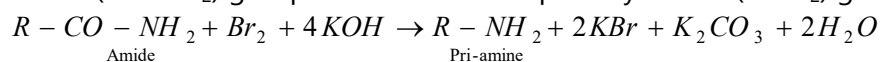
This is the most convenient method for preparing primary amines.
This method gives an amine containing one carbon atom less than amide.

(f) Gabriel phthalimide synthesis: This method involves the following three steps.
•Phthalimide is reacted with KOH to form potassium phthalimide.
• The potassium salt is treated with an alkyl halide.

• The product N-alkyl phthalimide is put to hydrolysis with hydrochloric acid when primary amine is formed.

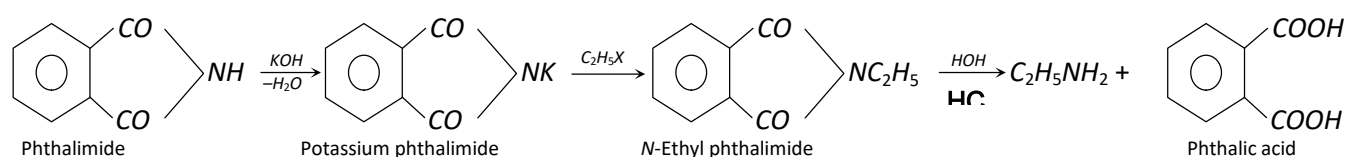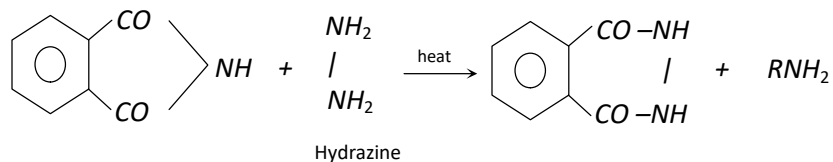| Phthalimide | Potassium phthalimide | N-Ethyl phthalimide | Phthalic acid |

When hydrolysis is difficult, the N-alkyl phthalimide can be treated with hydrazine to give the required amine.

Hydrazine

(g) By decarboxylation of α-amino acids

$$R \underset{\underset{NH_2}{|}}{C} HC\,OOH \xrightarrow[heat]{Ba(OH)_2} RCH_2NH_2; \quad \underset{\underset{NH_2}{|}}{CH_2}-COOH \xrightarrow[heat]{Ba(OH)_2} \underset{Methyl\,amine}{CH_3NH_2}$$

α-amino acetic acid
(Glycine)
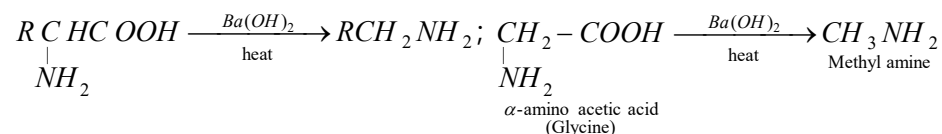
(h) By means of a Grignard regent and chloramine: $RMgX + ClNH_2 \rightarrow RNH_2 + MgXCl$

(i) By hydrolysis of Isocyanides or Isocyanates

$$\underset{Alkylisocyanide}{R-\underset{\underset{H\quad OH}{}}{N}\equiv\overset{H\quad OH|}{C}}+2H_2O \xrightarrow{(HCl)} \underset{Alkylamine}{R-NH_2}+HCOOH \;;$$

$$\underset{Aceto\,isonitile}{CH_3-NC}+2HOH \xrightarrow{H^+} CH_3-NH_2+HCOOH$$

$$\underset{Methyl\,isocyanate}{CH_3-\overset{H\quad OH|}{\underset{H\quad OH|}{N}}=C}=O+2KOH \rightarrow CH_3-NH_2+K_2CO_3; \quad \underset{Alkyl\,isocyanate}{R-NCO}+2KOH \rightarrow R-NH_2+K_2CO_3$$

(j) By Schmidt reaction: $R-COOH + \underset{\substack{\text{Hydrazoic}\\\text{acid}}}{N_3H} \xrightarrow{Conc.H_2SO_4} \underset{\substack{\text{Alkyl}\\\text{amine}}}{R-NH_2} + N_2 + CO_2$

In this reaction the acyl azide (R – CON$_3$) and alkyl isocyanate (R – NCO) are formed as an intermediate.

$R-COOH + N_3H \rightarrow \underset{\text{Acyl azide}}{RCON_3} + H_2O$; $\underset{\text{Acyl azide}}{RCON_3} \rightarrow \underset{\text{Alkyl isocyanate}}{R-N=C=O} + N_2$

$R-N=C=O + H_2O \rightarrow \underset{\text{Alkyl amine}}{R-NH_2} + CO_2$

The overall reaction which proceeds by the elimination of nitrogen from acyl azide followed by acidic or alkaline hydrolysis to yield primary amine containing one carbonless, is called **Curtius Degradation**.

The method uses acid chloride to prepare primary amine through acyl azide.

$\underset{}{R-\overset{\overset{O}{||}}{C}-OH} \xrightarrow{SOCl_2} \underset{\text{Acyl chloride}}{R-\overset{\overset{O}{||}}{C}-Cl} \xrightarrow{NaN_3} \underset{\text{Acyl azide}}{R-\overset{\overset{O}{||}}{C}-N_3}$

$R-\overset{\overset{O}{||}}{C}-N_3 \xrightarrow{-N_2} R-N=C=O \xrightarrow[heat]{2NaOH} R-NH_2 + Na_2CO_3$

The mechanism of **curtius rearrangement** is very similar to Hofmann degradation.

Schmidt reaction converts $R-\overset{\overset{||}{}}{COOH}$ to R–NH$_2$, which is a modification of curtius degradation. In this reaction a carboxylic acid is warmed with sodium azide (Na$^+$N$_3^-$) and conc. H$_2$SO$_4$. The carboxylic acid is directly converted to the primary amine without the necessity of isolating alkyl azide.

$R-\overset{\overset{O}{||}}{C}-OH \xrightarrow[heat]{NaN_3 + H_2SO_4(conc.)} RNH_2 + N_2 + CO_2$

$(NaN_3 + H_2SO_4 \rightarrow N_3H + NaHSO_4)$

(k) By Ritter reaction: It is a good method for preparing primary amines having α-tertiary alkyl group.

$\underset{\text{Tert-butyl alcohol}}{(CH_3)_3C-OH} + H_2SO_4 + HCN \rightarrow \underset{\substack{\text{Tert−butylamine}\\\text{(1°amine)}}}{(CH_3)_3C-NH_2}$

$\left[R_3C-OH \xrightarrow{H^+} H_2O + \underset{\text{Tert-carbonium ion}}{R_3C^+} \xrightarrow{HCN} R_3C\overset{+}{N}\equiv CH \xrightarrow{H_2O} \right.$

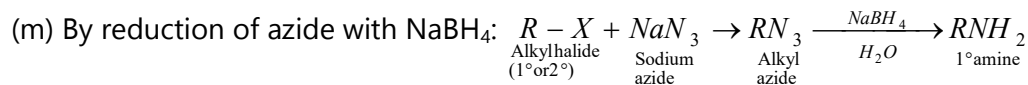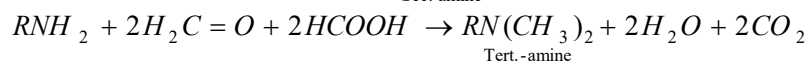$$CHO - R_3CNH \xrightarrow{OH^-} R_3C - NH_2 + HCOO^-]$$
<div align="center">Pri-amine</div>

(l) Reductive amination of aldehydes and ketones:

$$R - \overset{\overset{O}{\underset{||}{}}}{C} - H + NH_3 + H_2 \xrightarrow[300\,atm]{Ni,150°C} R - CH_2 - NH_2 + H_2O$$
<div>Aldehyde   Primary amine</div>

$$\left[R - \overset{H}{\underset{|}{C}} = O + H_2HN \xrightarrow{(-H_2O)} [R - \overset{H}{\underset{|}{C}} = NH] \xrightarrow[Ni]{H_2} RCH_2 - NH_2 \right]$$
<div>Imine</div>

$$R - \overset{\overset{O}{\underset{||}{}}}{C} - CH_3 + NH_3 + H_2 \xrightarrow[300\,atm]{Ni,150°C} R - \overset{\overset{CH_3}{\underset{|}{}}}{CH} - NH_2$$
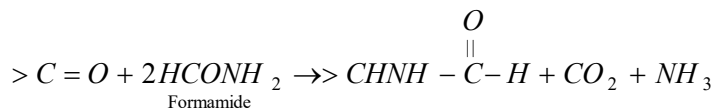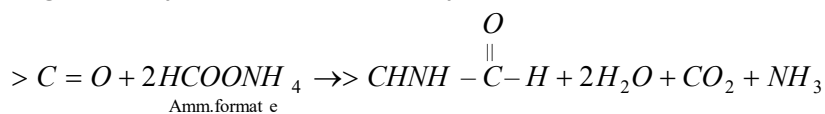<div>Ketone</div>

This reaction probably takes place through the formation of an imine (Schiff's base).
The primary amine can also be converted into sec. or tert. amines by the following steps
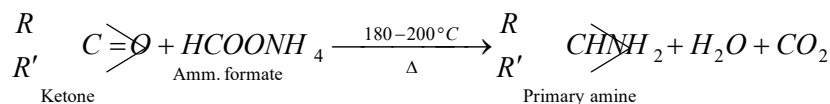
$$R - CHO + R'NH_2 \xrightarrow{H_2/Ni} RCH_2NHR'\,;$$
<div align="center">Sec. amine</div>

$$RNH_2 + 2H_2C = O + 2HCOOH \rightarrow RN(CH_3)_2 + 2H_2O + 2CO_2$$
<div align="center">Tert.-amine</div>

(m) By reduction of azide with NaBH$_4$: $R - X + NaN_3 \rightarrow RN_3 \xrightarrow[H_2O]{NaBH_4} RNH_2$

<div>Alkylhalide   Sodium   Alkyl   1°amine
(1°or2°)   azide   azide</div>
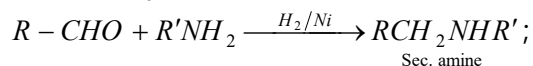
(n) By Leuckart reaction: Aldehydes or ketones react with ammonium formate or with formamide to give formyl derivative of primary amine.

$$> C = O + 2HCOONH_4 \rightarrow> CHNH - \overset{\overset{O}{\underset{||}{}}}{C} - H + 2H_2O + CO_2 + NH_3$$
<div>Amm.format e</div>

$$> C = O + 2HCONH_2 \rightarrow> CHNH - \overset{\overset{O}{\underset{||}{}}}{C} - H + CO_2 + NH_3$$
<div>Formamide</div>

These formyl derivatives are readily hydrolysed by acid to yield primary amine.

$$\overset{R}{\underset{R}{}} CHNH - \overset{\overset{O}{\underset{||}{}}}{C} - H + HOH \xrightarrow{H^+} \overset{R}{\underset{R}{}} CHNH_2 + H_2O + CO_2$$
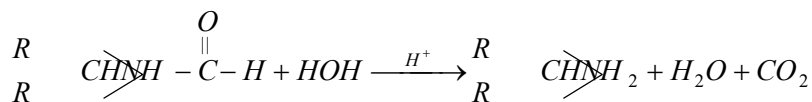
This is called Leuckart reaction, i.e.,

$$\overset{R}{\underset{R'}{}} C = O + HCOONH_4 \xrightarrow[\Delta]{180-200°C} \overset{R}{\underset{R'}{}} CHNH_2 + H_2O + CO_2$$
<div>Ketone   Amm. formate   Primary amine</div>

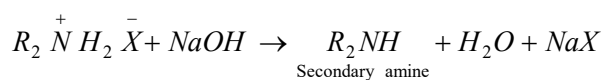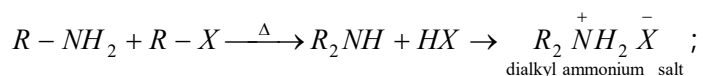Note: On commercial scale, ethylamine is obtained by heating a mixture of ethylene and ammonia at 450°C under 20 atmospheric pressure in presence of cobalt catalyst.

$$CH_2 = CH_2 + NH_3 \xrightarrow[450\,°C, 20\,atm]{Cobalt\ catalyst} CH_3CH_2NH_2$$
$$\underset{Ethylene}{}$$
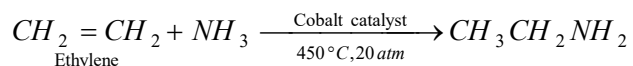
(iii) Methods yielding secondary amines

(a) Reaction of primary amines with alkyl halides

$$R-NH_2 + R-X \xrightarrow{\Delta} R_2NH + HX \rightarrow \underset{dialkyl\ ammonium\ salt}{R_2 \overset{+}{N}H_2 \overset{-}{X}} \ ;$$

$$R_2 \overset{+}{N} H_2 \overset{-}{X} + NaOH \rightarrow \underset{Secondary\ amine}{R_2NH} + H_2O + NaX$$

(b) Reduction of isonitriles: $\underset{Alkyl\ isnitrile}{R-NC} + 4[H] \xrightarrow{Pt} \underset{Sec.\ amine}{RNHCH_3}$
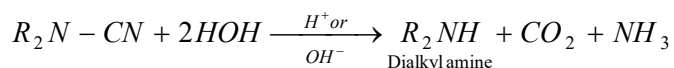
Secondary amine formed by this method always possesses one –CH_3 group linked directly to nitorgen.

(c) Reaction of p-nitroso-dialkyl aniline with strong alkali solution:

Aniline → Dialkyl aniline → p-Nitroso-dialkyl aniline → p-Nitroso phenol +R_2NH
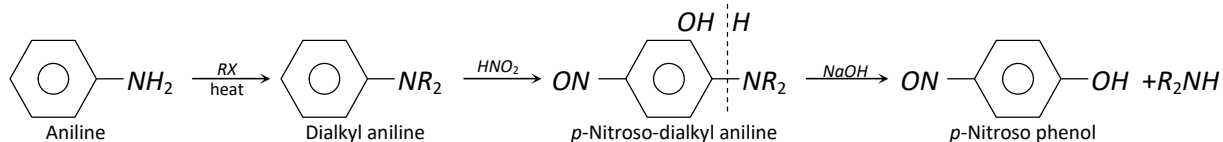
This is one of the best method for preparing pure secondary amines.

(d) Hydrolysis of dialkylcyanamide:
$$\left[\underset{\substack{Calcium\\cyanamide}}{CaN-CN} \xrightarrow{2NaOH} \underset{\substack{Sodium\\cyanamide}}{Na_2N-CN} \xrightarrow{2RX} \underset{\substack{Dialkyl\\cyanamide}}{R_2N-CN} \right]$$

$$R_2N-CN + 2HOH \xrightarrow[OH^-]{H^+ or} \underset{Dialkyl\ amine}{R_2NH} + CO_2 + NH_3$$

(e) Reduction of N-substituted amides: Reduction of N-substituted amides with $LiAlH_4$ yields secondary amines.

Alkyl β-amino ketones are formed by the action of ketone with formaldehyde and NH_3 (or primry or secondary amines).

The product is referred to as Mannich base and the reaction is called **Mannich Reaction.**

$$CH_3COCH_3 + HCHO + RNH_2 \xrightarrow{heat} CH_3COCH_2CH_2NHR$$
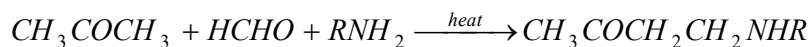
Which can be reduced to alkyl amines.

$$\underset{N\text{-Alkyl acid amide}}{R-CONHR'} + 4[H] \xrightarrow{LiAlH_4} \underset{Sec.amine}{RCH_2NHR'} + H_2O$$
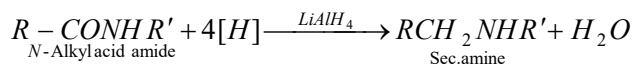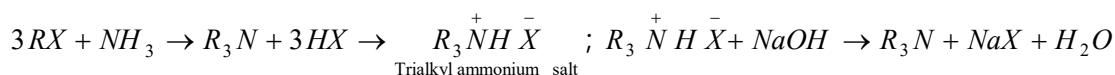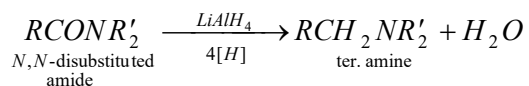
(iv) **Methods yielding tertiary amines**

(a)Reaction of alkylhalides with ammonia

$$3RX + NH_3 \rightarrow R_3N + 3HX \rightarrow \underset{\text{Trialkyl ammonium salt}}{R_3\overset{+}{N}H\overset{-}{X}} ; \ R_3\overset{+}{N}H\overset{-}{X} + NaOH \rightarrow R_3N + NaX + H_2O$$

(b) Reduction of N, N-disubstituted amides: The carbonyl group is converted into $-CH_2$ group.

$$\underset{\substack{N,N\text{-disubstituted}\\amide}}{RCONR'_2} \xrightarrow[4[H]]{LiAlH_4} \underset{\text{ter. amine}}{RCH_2NR'_2} + H_2O$$

(c) Decomposition of tetra-ammonium hydroxides: The tetra-alkyl ammonium hydroxides are formed when corresponding halides are treated with moist silver oxide.

$$R_4\overset{+}{N}\overset{-}{I} + AgOH \rightarrow R_4\overset{+}{N}O\overset{-}{H} + AgI$$
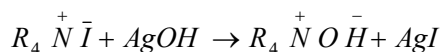
The hydroxides thus formed on heating decompose into tertiary amines. Tetramethyl ammonium hydroxide gives methyl alcohol as one of the products while all other tetra-alkyl ammonium hydroxides give an olefin and water besides tertiary amines.

$$(CH_3)_4NOH \rightarrow (CH_3)_3N + CH_3OH ; \ (R)_4NOH \rightarrow (R)_3N + \text{olefin} + H_2O$$
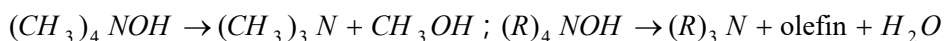
(5)**Separation of mixture of amines:** When the mixture consists of salts of primary, secondary and tertiary amines along with quaternary salt, **it is first distilled with KOH solution**. The mixture of three amines distils over leaving behind non-volatile quaternary salt.

$$RNH_2.HI \text{ or } \underset{\substack{\text{Primary amine}\\(\text{Volatile), Distillate}}}{RN\overset{+}{H}_3 - \overset{-}{I}} + \overset{+}{K}O\overset{-}{H} \rightarrow RNH_2 + KI + H_2O$$

$$R_2NH.HI \text{ or } R_2N\overset{+}{H}_2 - \overset{-}{I} + \overset{+}{K}O\overset{-}{H} \rightarrow R_2NH + KI + H_2O$$

$R_3N.HI$ or $R_3N \overset{+}{H} - \bar{I} + \overset{+}{K} O \overset{-}{H} \rightarrow R_3N + KI + H_2O$
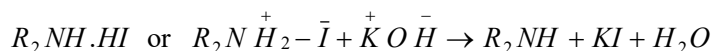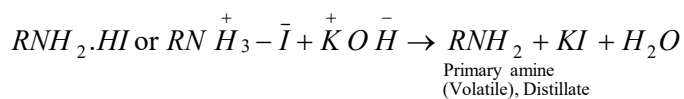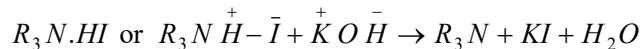
$R_4 \overset{+}{N} \bar{I}$ (non-volatile tetra-alkyl ammonium salt) has no reaction with KOH, however remains as residue.

This mixture is separated into primary, secondary and tertiary amines by the application of following methods.

(i) **Fractional distillation :** The boiling points of primary, secondary and tertiary amines are quite different, i.e., the boiling point of $C_2H_5NH_2$ is 17°C, $(C_2H_5)_2NH$ is 56°C and $(C_2H_5)_3N$ is 95°C and thus, these can be separated by fractional distillation. This method is used satisfactorily in industry.

(ii) **Hofmann's method :** The mixture of three amines is treated with diethyl oxalate. The primary amine forms a soildoxamide, a secondary amine gives a liquid oxamic ester while tertiary amine does not react.

$$\begin{array}{l} CO\ OC_2H_5 \quad\quad H\ NHR \\ | \quad\quad\quad\quad + \\ CO\ OC_2H_5 \quad\quad H\ NHR \\ \scriptstyle\text{Diethyl oxa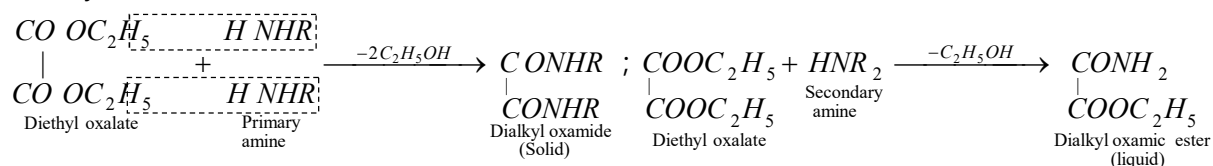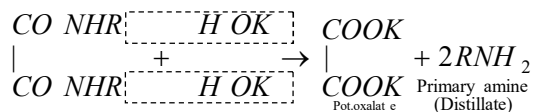late} \quad\quad \text{Primary} \\ \scriptstyle\text{amine} \end{array} \xrightarrow{-2C_2H_5OH} \begin{array}{l} C\ ONHR \\ | \\ CONHR \\ \scriptstyle\text{Dialkyl oxamide} \\ \scriptstyle\text{(Solid)} \end{array} ; \begin{array}{l} COOC_2H_5 + HNR_2 \\ | \quad\quad\quad\quad \scriptstyle\text{Secondary} \\ COOC_2H_5 \quad\quad \scriptstyle\text{amine} \\ \scriptstyle\text{Diethyl oxalate} \end{array} \xrightarrow{-C_2H_5OH} \begin{array}{l} CONH_2 \\ | \\ COOC_2H_5 \\ \scriptstyle\text{Dialkyl oxamic ester} \\ \scriptstyle\text{(liquid)} \end{array}$$

Primary amine is recovered when solid oxamide is heated with caustic potash solution and collected as distillate on distilling the reaction mixture.

$$\begin{array}{l} CO\ NHR \quad\quad H\ \overline{O}K \\ | \quad\quad\quad + \\ CO\ NHR \quad\quad H\ \overline{O}K \end{array} \rightarrow \begin{array}{l} COOK \\ | \quad\quad + 2RNH_2 \\ COOK \quad \scriptstyle\text{Primary amine} \\ \scriptstyle\text{Pot.oxalat e} \quad\quad \scriptstyle\text{(Distillate)} \end{array}$$

The liquid (mixture of oxamic ester+ tertiary amine) is subjected to fractional distillation when tertiary amine distils over.

The remaining liquid is distilled with KOH to recover secondary amine.

$$\begin{array}{l} CONR_2 \quad\quad HOK \\ | \quad\quad\quad + \\ COOC_2H_5 \quad\quad HOK \end{array} \rightarrow R_2NH + \begin{array}{l} COOK \\ | \quad\quad + C_2H_5OH \\ COOK \\ \scriptstyle\text{Pot. oxalate} \end{array}$$
$\scriptstyle\text{Secondary amine}$
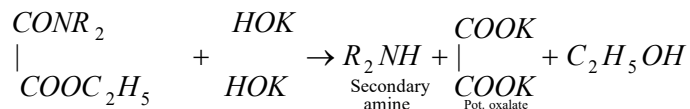
(iii) **Hinsberg's method:** It involves the treatment of the mixture with benzene sulphonyl chloride, i.e., **Hinsberg's reagent** $(C_6H_5SO_2Cl)$. The solution is then made alkaline with aqueous alkali to form sodium or potassium salt of monoalkyl benzene sulphonamide (soluble in water).

$$C_6H_5SO_2Cl + HNHR \rightarrow C_6H_5SO_2NHR \xrightarrow{NaOH} C_6H_5SO_2N(Na)R$$

Primary amine · N-Alkyl benzene sulphonami de · Soluble salt
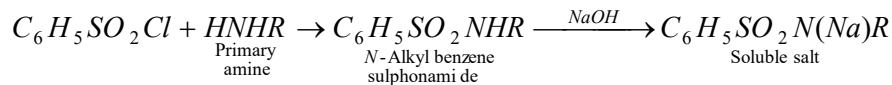
The secondary amine forms N,N-dialkyl benzene sulphonamide which does not form any salt with NaOH and remains as insoluble in alkali solution.

$$C_6H_5SO_2Cl + HNR_2 \rightarrow C_6H_5SO_2NR_2 \xrightarrow{NaOH} \text{No reaction}$$

Sec. amine · (Insoluble in water, soluble in ether)
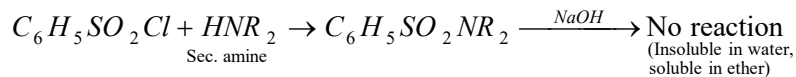
Tertiary amine does not react.

The above alkaline mixture of the amines is extracted with ether.

Two distinct layers are formed. Lower layer, the aqueous layer consists of sodium salt of N-alkyl benzene sulphonamide (primary amine) and upper layer, the ether layer consists of N,N-dialkyl benzene sulphonamide (secondary amine) and tertiary amine.

Two layers are separated. The upper layer is fractionally distilled. One fraction obtained is tertiary amine and the other fraction is treated with concentrated HCl to recover secondary amine hydrochloride which gives free secondary amine on distillation with NaOH.

$$C_6H_5SO_2NR_2 + HCl + H_2O \rightarrow C_6H_5SO_2.OH + R_2NH.HCl \; ;$$

$$R_2NH.HCl + NaOH \rightarrow R_2NH + NaCl + H_2O$$

Sec. amine

The aqueous layer is acidified and hydrolysed with dilute HCl. The hydrochloride formed is then distilled with NaOH when primary amine distils over.

$$C_6H_5SO_2N(Na)R + HCl \rightarrow C_6H_5SO_2NHR + NaCl$$

Sulphonami de of primary amine

$$C_6H_5SO_2NHR + HCl + H_2O \rightarrow C_6H_5SO_2.OH + RNH_2.HCl \; ;$$

Primary amine hydrochlor ide

$$RNH_2.HCl + NaOH \rightarrow RNH_2 + NaCl + H_2O$$

(6) **Physical properties**

(i) Lower amines are gases or low boiling point liquids and possess a **characteristic ammonia like smell (fishy odour).** Higher members are solids.

(ii) The boiling points rise gradually with increase of molecular mass. Amines are polar compounds like NH_3 and have comparatively higher boiling points than non-polar compounds of similar molecular masses. This due to the presence of **intermolecular hydrogen bonding.**

$$H - \overset{\overset{H}{|}}{\underset{\underset{R}{|}}{N}}:---H - \overset{\overset{H}{|}}{\underset{\underset{R}{|}}{N}}:----H - \overset{\overset{H}{|}}{\underset{\underset{R}{|}}{N}}:---$$

Hydrogen bonding in amines

(iii) Amines are soluble in water. This is due to hydrogen bonding between amine and water molecules. Amines are also soluble in benzene and ether.

$$H - \overset{..}{\underset{\underset{H}{|}}{O}}:---H - \overset{\overset{H}{|}}{\underset{\underset{R}{|}}{N}}:---H - \overset{..}{\underset{\underset{H}{|}}{O}}:---H - \overset{\overset{H}{|}}{\underset{\underset{R}{|}}{N}}:---$$

Hydrogen bonding between amine and water molecules

Solubility decreases with increase of molecular mass.

(7) **Chemical properties:** The main reactions of amines are due to the presence of a lone pair of electrons on nitrogen atom. Amines are **electrophilic reagents** as the lone pair of electrons can be donated to electron seeking reagents, (i.e., electrophiles).

(i) **Basic nature of aliphatic amines:** Amines like ammonia are basic in nature. The basic nature is due to the presence of an unshared pair (lone pair) of electrons on nitrogen atom. This lone pair of electrons is available for the formation of a new bond with a proton or Lewis acids.

$$H - \overset{..}{\underset{\underset{H}{|}}{N}} - H \ ; \ R - \overset{..}{\underset{\underset{H}{|}}{N}} - H ; \ R - \overset{..}{\underset{\underset{R}{|}}{N}} - H \ ; R - \overset{..}{\underset{\underset{R}{|}}{N}} - R$$

Ammonia   Primary amine   Secondary amine   Tertiary amine

Amines are weak bases as they combine partially with the water to form hydroxyl ions.

$$R - NH_2 + H_2O \rightleftharpoons R - \overset{+}{N}H_3 + OH^-$$

Alkylammonium ion

Applying law of mass action.

$$K_b = \frac{[R - \overset{+}{N}H_3][OH^-]}{[R - NH_2]}$$ (Where K_b is dissociation constant of the base)

[Concentration of water is considered constant as it is present in large amounts.]
The value of K_b describes the relative strength of the bases. Strong bases have higher value of K_b while weak bases have low values.

$$NH_3 \ ; CH_3NH_2 ;(CH_3)_2NH;(CH_3)_3N$$
$K_b; \ 1.8\times10^{-5} \quad 37\times10^{-5} \quad\quad 54\times10^{-5} \quad\quad 6.7\times10^{-5}$

Except the amines containing tertiary butyl group, all lower aliphatic amines are stronger bases than ammonia because of $+ I$ (inductive) effect. The alkyl groups, which are electron releasing groups, increase the electron density around the nitrogen thereby increasing the availability of

the lone pair of electrons to proton or Lewis acids and making the amine more basic (larger K_b). Thus, it is expected that the basic nature or amines should be in the order tertiary > secondary > primary, but the observed order in the case of lower members is found to be as **secondary > primary > tertiary.** This anomalous behavior of tertiary amines is **due to steric factors,** i.e., crowding of alkyl groups cover nitrogen atom from all sides and thus makes the approach and bonding by a proton relatively difficult which results the maximum steric strain in tertiary amines. The electrons are there but the path is blocked, resulting the reduced in its basicity.

The order of basic nature of various amines has been found **to vary with nature of alkyl groups.**

Alkyl group	Relative strength
$CH_3 -$	$R_2NH > RNH_2 > R_3N > NH_3$
$C_2H_5 -$	$R_2NH > RNH_2 > NH_3 > R_3N$
$(CH_3)_2CH -$	$RNH_2 > NH_3 > R_2NH > R_3N$
$(CH_3)_3C -$	$NH_3 > RNH_2 > R_2NH > R_3N$

(ii) **Basic nature of aromatic amines:** In aniline or other aromatic amines, the **non-bonding electron pair** is delocalized into benzene ring by resonance.
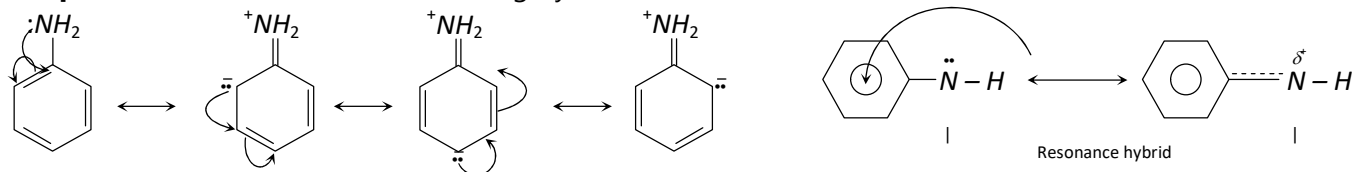

But anilinium ion is less resonance stabilized than aniline.

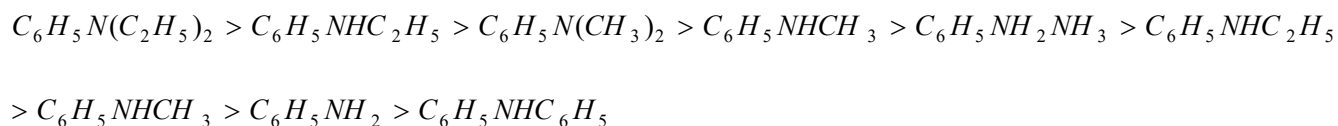No other resonating structure possible
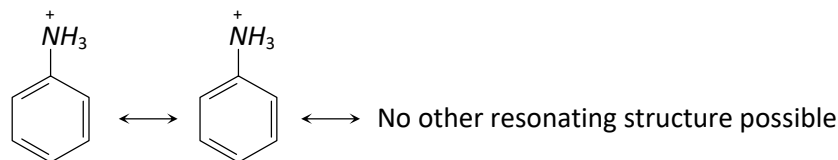
Thus, electron density is less on N atom due to which aniline or other aromatic amines are less basic than aliphatic amines.

However, any group which when present on benzene ring has electron withdrawing effect (– NO_2, – CN, – SO_3H, – COOHT – Cl, C_6H_5, etc.) decreases basicity of aniline(Nitroaniline is less basic than aniline as nitro group is electron withdrawing group (– I group) and aniline is more basic than diphenyl amine), while a group which has electron repelling effect (– NH_2, – OR, R –, etc.) increases basicity of aniline. Toluidine is more basic than aniline as – CH_3 group is electron repelling group (+ I group).

Further greater the value of K_b or lower the value of pK_b, stronger will be the base. The basic character of some amines have the following order,

$$R_2NH > RNH_2 > C_6H_5CH_2NH_2 > NH_3 > C_6H_5NH_2$$
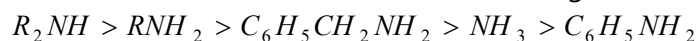
N-alkylated anilines are stronger bases than aniline because of steric effect. Ethyl group being bigger than methyl has more steric effect, so N-ethyl aniline is stronger base than N-methyl aniline. Thus, basic character is,

$$C_6H_5N(C_2H_5)_2 > C_6H_5NHC_2H_5 > C_6H_5N(CH_3)_2 > C_6H_5NHCH_3 > C_6H_5NH_2 NH_3 > C_6H_5NHC_2H_5$$

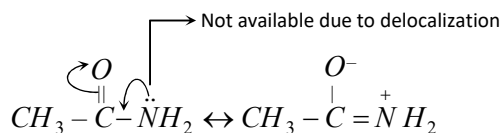$$> C_6H_5NHCH_3 > C_6H_5NH_2 > C_6H_5NHC_6H_5$$

In Toluidines –p-isomer > m- > o-

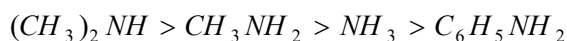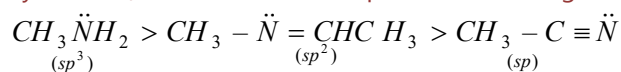Chloroanilines–p-isomer>m-> o-

Phenylenediamines –p-isomer > m- > o-

Nitroanilines–m-isomer > p- > o-

Note: Aniline is less basic than ammonia. The phenyl group exerts –I (inductive) effect, i.e., it withdraws electrons. This results to the lower availability of electrons on nitrogen for protonation.

❑Ethylamine and acetamide both contain an amino group but acetamide does not show basic nature. This is because lone pair of electrons on nitrogen is delocalised by resonance with the carbonyl group which makes it less available for protonation.

→ Not available due to delocalization

$$CH_3 - \overset{O}{\overset{\|}{C}} - \ddot{N}H_2 \leftrightarrow CH_3 - \overset{O^-}{\overset{|}{C}} = \overset{+}{N}H_2$$

❑The compounds with least 's' character (sp^3-hybridized) is most basic and with more 's' character (sp-hybridized) is least basic. Examples in decreasing order of basicity are,

$$\underset{(sp^3)}{CH_3\ddot{N}H_2} > \underset{(sp^2)}{CH_3 - \ddot{N} = CHCH_3} > \underset{(sp)}{CH_3 - C \equiv \ddot{N}}$$

$$CH_3CH_2CH_2NH_2 > H_2C = CHCH_2NH_2 > HC \equiv CCH_2NH_2$$

$$(CH_3)_2NH > CH_3NH_2 > NH_3 > C_6H_5NH_2$$

❑Electron withdrawing (C_6H_5 –) groups decrease electron density on nitrogen atom and thereby decreasing basicity.
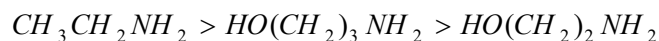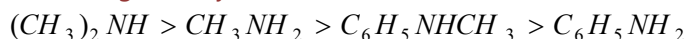
$$(CH_3)_2NH > CH_3NH_2 > C_6H_5NHCH_3 > C_6H_5NH_2$$

$$CH_3CH_2NH_2 > HO(CH_2)_3NH_2 > HO(CH_2)_2NH_2$$

❑Electron withdrawing inductive effect of the –OH group decreases the electron density on nitrogen. This effect diminishes with distance from the amino group.

$$CH_3CH_2NH_2 > C_6H_5CONH_2 > CH_3CONH_2$$

(iii) **Salt formation:** Amines being basic in nature, combine with mineral acids to form salts.

$$R-NH_2 + HCl \rightarrow R\overset{+}{N}H_3\overline{C}l \ ; \ 2R-NH_2 + H_2SO_4 \rightarrow (R\overset{+}{N}H_3)_2 SO_4^-$$
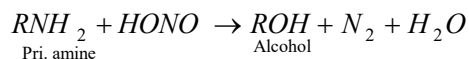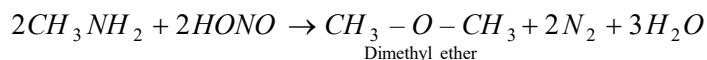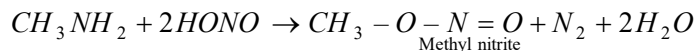$$\underset{\substack{\text{Alkylammon ium}\\ \text{chloride}}}{} \qquad\qquad\qquad\qquad \underset{\text{Alkylammon ium sulphate}}{}$$

(iv) **Nature of aqueous solution:** Solutions of amines are alkaline in nature.

$$RNH_2 + HOH \rightleftharpoons R\overset{+}{N}H_3OH^- \rightleftharpoons [RNH_3]^+ + OH^-$$

$$R_2NH + HOH \rightleftharpoons R_2\overset{+}{N}H_2OH^- \rightleftharpoons [R_2NH_2]^+ + OH^-$$

$$R_3N + HOH \rightleftharpoons R_3\overset{+}{N}HOH^- \rightleftharpoons [R_3NH]^+ + OH^-$$

The aqueous solutions of amines behaves like NH_4OH and give ferric hydroxide precipitate with ferric chloride and blue solution with copper sulphate.

$$3RNH_3OH + FeCl_3 \rightarrow Fe(OH)_3 + 3RNH_3Cl$$

(v) **Reaction with alkyl halides (Alkylation)**

$$\underset{\text{Pri.amine}}{RNH_2} \xrightarrow[-HX]{R'X} \underset{\text{Sec.amine}}{RNHR'} \xrightarrow[-HX]{R'X} \underset{\text{Tert. amine}}{R-NR'_2} \xrightarrow{R'X} \underset{\text{Quaternary salt}}{(R-\overset{+}{N}R'_3)X^-}$$

(vi) **Reaction with acetyl chloride (Acylation**

$$\underset{\text{Pri. amine}}{RNH_2} + ClOCCH_3 \xrightarrow{-HCl} \underset{N\text{-Alkyl acetamide}}{RNHOCCH_3} \ ; \ \underset{\text{Sec. amine}}{R_2NH} + ClOCCH_3 \xrightarrow{-HCl} \underset{N,N\text{-Dialkyl acetamide}}{R_2NOCCH_3}$$

Tertiary amines do not react since they do not have replaceable hydrogen on nitrogen. Therefore, all these above reactions are used to distinguish between P,S and T-amines.

(vii) **Action of sodium**

$$2RNH_2 + 2Na \xrightarrow{\Delta} \underset{\text{Sod. salt}}{2[RNH]^- Na^+} + H_2 \uparrow \ ; \ 2R_2NH + 2Na \xrightarrow{\Delta} \underset{\text{Sod.sa lt}}{2[R_2N]^- Na^+} + H_2 \uparrow$$

(viii) **Action of halogens**

$$\underset{\text{Alkylamine}}{RNH_2} \xrightarrow[NaOH]{X_2} RNHX \xrightarrow[NaOH]{X_2} \underset{\substack{\text{Dihalo-alkyl}\\ \text{amine}}}{RNX_2} \ ; \ \underset{\text{Dialkyl amine}}{R_2NH} \xrightarrow[NaOH]{X_2} \underset{\substack{\text{Halo-dialkyl}\\ \text{amine}}}{R_2NX}$$

(ix) **Reaction with Grignard reagent**

$$RNH_2 + Mg \overset{CH_3}{\underset{I}{<}} \rightarrow CH_4 + RNH-Mg-I \ ; \ R_2NH + CH_3-Mg-I \rightarrow CH_4 + R_2N-Mg-I$$

(x) **Carbylamine reaction:** This reaction is shown by only **primary amines.** This is a test of primary amines and is used to distinguish primary amines from secondary and tertiary amines.

$$RNH_2 + CHCl_3 + 3KOH \underset{\text{(Alc.)}}{\rightarrow} \underset{\substack{\text{Alkylisocyanide}\\ \text{(carbyl amine)}}}{RNC} + 3KCl + 3H_2O$$

Isocyanides are bad smelling compounds and can be easily detected.

(xi) **Reaction with nitrous acid**

(a) Primary amines form alcohols with nitrous acid (NaNO$_2$+ HCl). Nitrogen is eliminated.

$$RNH_2 + HONO \rightarrow ROH + N_2 + H_2O$$
$\underset{\text{Pri. amine}}{}$ $\underset{\text{Alcohol}}{}$

Methyl amine is an exception to this reaction, i.e.,

$$CH_3NH_2 + 2HONO \rightarrow CH_3 - O - N = O + N_2 + 2H_2O$$
$\underset{\text{Methyl nitrite}}{}$

$$2CH_3NH_2 + 2HONO \rightarrow CH_3 - O - CH_3 + 2N_2 + 3H_2O$$
$\underset{\text{Dimethyl ether}}{}$

(b) Secondary amines form nitrosoamines which are water insoluble yellow oily liquids.

$$R_2NH + HONO \rightarrow R_2NNO + H_2O$$
$\underset{\text{Sec. amine}}{}$ $\underset{\substack{\text{Dialkyl} \\ \text{nitrosoami ne}}}{}$
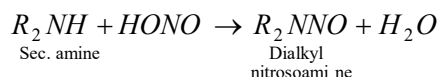
Nitrosoamine on warming with phenol and conc. H$_2$SO$_4$ give a brown or red colour which soon changes to blue green. The colour changes to red on dilution and further changes to blue or violet with alkali. This colour change is referred to **Liebermann's nitroso reaction** and is used for the test of secondary amines.

(c) Tertiary amines react nitrous acid to form nitrite salts which are soluble in water. These salts on heating give alcohols and nitrosoamines.

$$R_3N + HONO \rightarrow [R_3NH]^+ NO_2^- \xrightarrow{heat} R - OH + R_2N - N = O$$
$\underset{\text{Tert.amine}}{}$ $\underset{\text{Trialkyl ammoniumni trite}}{}$ $\underset{\text{Alcohol}}{}$ $\underset{\text{Nitrosoami ne}}{}$
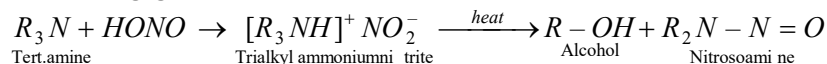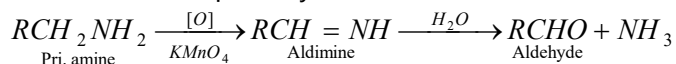
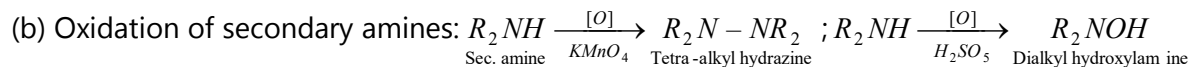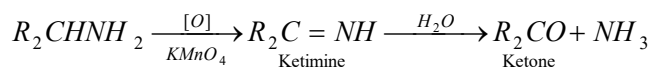This reaction (nitrous acid test) is used to make distinction between primary, secondary and tertiary amines.

(xii) **Reaction with carbon di sulphide:** This **Hofmann's mustard oil reaction** and is used as a **test for primary amines**.

$$RNH_2 \xrightarrow[\text{heat}]{S=C=S} S = C \underset{SH}{\overset{NHR}{<}} \xrightarrow{HgCl_2} RNC = S + HgS + 2HCl$$
$\underset{1°}{}$ $\underset{\text{Alkyldithiocarb amic acid}}{}$ $\underset{\substack{\text{Alkylisothiocya nate} \\ \text{(Mustard oil smell)}}}{}$ $\underset{\text{Black ppt.}}{}$

$$R_{2NH} \xrightarrow{S=C=S} S = C \underset{SH}{\overset{NR_2}{<}} \xrightarrow{HgCl_2} \text{No reaction}$$
$\underset{2°}{}$ $\underset{\text{Dialkyl dithiocarb amic acid}}{}$
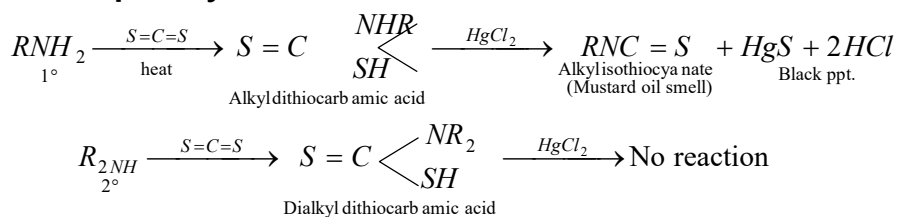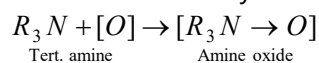
(xiii) **Oxidation:** All the three types of amines undergo oxidation. The product depends upon the nature of oxidising agent, class of amine and the nature of the alkyl group.
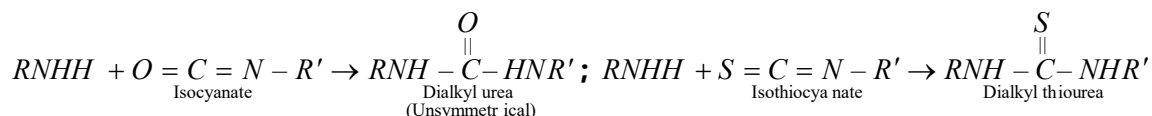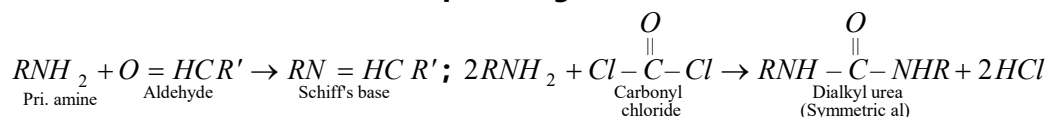
(a) Oxidation of primary amines

$$RCH_2NH_2 \xrightarrow[KMnO_4]{[O]} RCH = NH \xrightarrow{H_2O} RCHO + NH_3$$
$\underset{\text{Pri. amine}}{}$ $\underset{\text{Aldimine}}{}$ $\underset{\text{Aldehyde}}{}$

$$R_2CHNH_2 \xrightarrow[KMnO_4]{[O]} \underset{\text{Ketimine}}{R_2C = NH} \xrightarrow{H_2O} \underset{\text{Ketone}}{R_2CO + NH_3}$$

(b) Oxidation of secondary amines: $\underset{\text{Sec. amine}}{R_2NH} \xrightarrow[KMnO_4]{[O]} \underset{\text{Tetra-alkyl hydrazine}}{R_2N - NR_2}$; $\underset{}{R_2NH} \xrightarrow[H_2SO_5]{[O]} \underset{\text{Dialkyl hydroxylam ine}}{R_2NOH}$

(c) Oxidation of tertiary amines: Tertiary amines are not oxidised by potassium permanganate but are oxidised by Caro's acid or Fenton's reagent to amine oxides.

$$\underset{\text{Tert. amine}}{R_3N} + [O] \rightarrow \underset{\text{Amine oxide}}{[R_3N \rightarrow O]}$$

(xiv) **Reaction with other electrophilic regents**

$$\underset{\text{Pri. amine}}{RNH_2} + \underset{\text{Aldehyde}}{O = HCR'} \rightarrow \underset{\text{Schiff's base}}{RN = HC\,R'} \textbf{;} \quad 2RNH_2 + \underset{\substack{\text{Carbonyl} \\ \text{chloride}}}{Cl - \overset{\overset{O}{\|}}{C} - Cl} \rightarrow \underset{\substack{\text{Dialkyl urea} \\ \text{(Symmetric al)}}}{RNH - \overset{\overset{O}{\|}}{C} - NHR} + 2HCl$$

$$RNHH + O = C = N - R' \rightarrow \underset{\substack{\text{Dialkyl urea} \\ \text{(Unsymmetr ical)}}}{RNH - \overset{\overset{O}{\|}}{C} - HNR'} \textbf{;} \quad RNHH + \underset{\text{Isothiocya nate}}{S = C = N - R'} \rightarrow \underset{\text{Dialkyl th iourea}}{RNH - \overset{\overset{S}{\|}}{C} - NHR'}$$
$$\underset{\text{Isocyanate}}{}$$

(xv) **Ring substitution in aromatic amines:** Aniline is more reactive than benzene. The presence of amino group activates the aromatic ring and directs the incoming group preferably to ortho and para positions.

(a) Halogenation

2, 4, 6-Tri
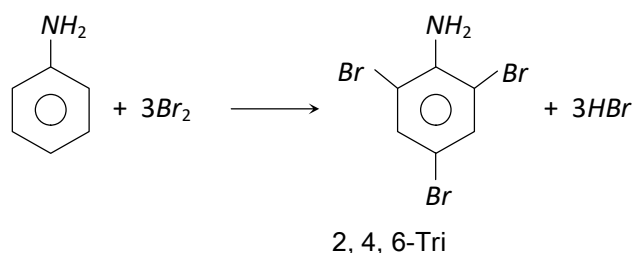
This reaction is used as a test for aniline.

However, if monosubstituted derivative is desired, aniline is first acetylated with acetic anhydride and then halogenation is carried out. After halogenation, the acetyl group is removed by hydrolysis and only monosubstituted halogen derivative is obtained.

It may be noted that – NH_2 group directs the attacking group at o- and p-positions and therefore, both o- and p-derivatives are obtained.
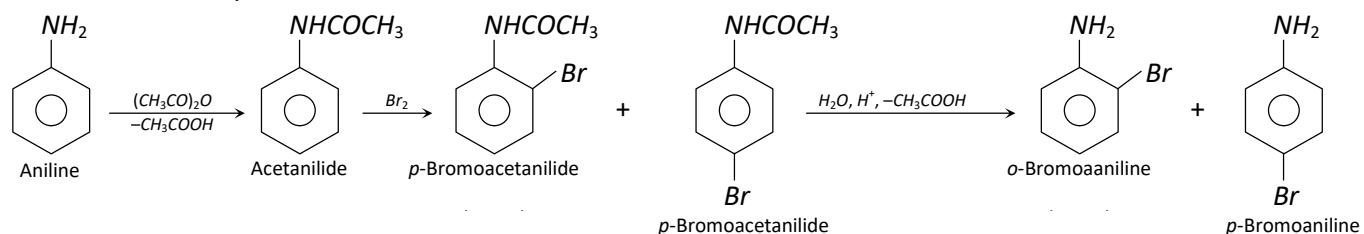
Acetylation deactivates the ring and controls the reaction to monosubstitution stage only because acetyl group is electron withdrawing group and therefore, the electron pair of N-atom is withdrawn towards the carbonyl group.

(b) Nitration: Aromatic amines cannot be nitrated directly because they are readily oxidized. This is because, HNO_3 is a strong oxidising agent and results in partial oxidation of the ring to form a black mass.

Therefore, to solve this problem, nitration is carried out by protecting the $-NH_2$ group by acetylation. The acetylation deactivates the ring and therefore, controls the reaction.
The hydrolysis of nitroacetanilides removes the protecting acyl group and gives back amines.
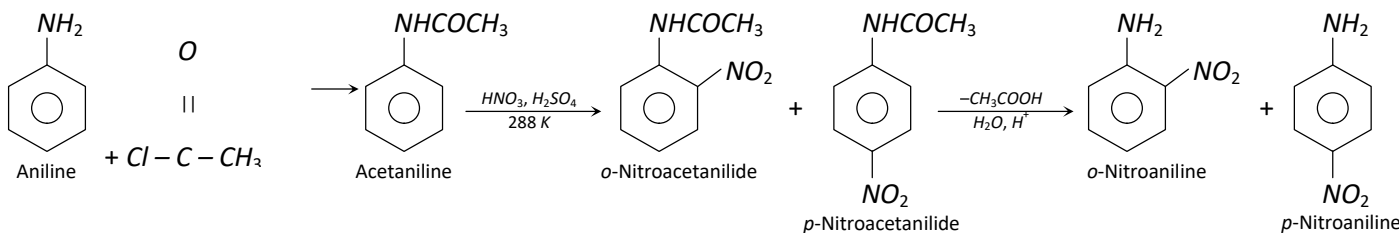
(c) Sulphonation
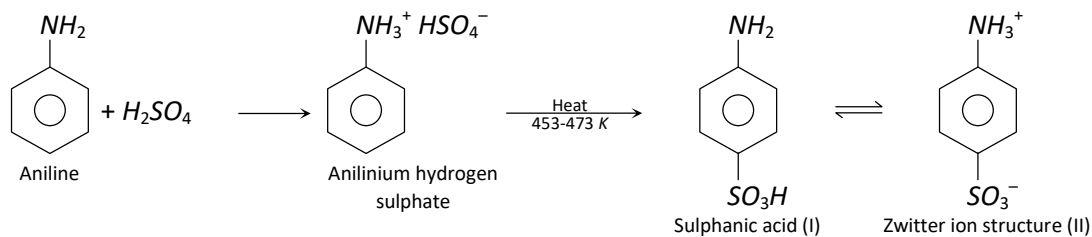
The sulphanilic acid exists as a dipolar ion (structure II) which has acidic and basic groups in the same molecule. Such ions are called **Zwitter ions or inner salts.**

(8) **Uses:**

(i) Ethylamine is used in solvent extraction processes in **petroleum refining** and as a **stabilizer** for **rubber latex.**

(ii) The quaternary ammonium salts derived from long chain aliphatic tertiary amines are widely used as detergents.

(iii) Aliphatic amines of low molecular mass are used as solvents.

Distinction between primary, secondary and tertiary amines

Test	Primary amine	Secondary amine	Tertiary amine
Action of $CHCl_3$ and alcoholic KOH. (Carbylamine test)	Bad smelling carbylamine (Isocyanide) is formed.	No action.	No action.
Action of CS_2 and $HgCl_2$. (Mustard oil test)	Alkyl isothiocyanate is formed which has pungent smell like mustard oil.	No action.	No action
Action of nitrous acid.	Alcohol is formed with evolution of nitogen.	Forms nitrosoamine which gives green colour with phenol and conc. H_2SO_4 (Liebermann's test).	Forms nitrite in cold which on heating gives nitrosoa- mine which responds to Liebermann's test.
Action of acetyl chloride.	Acetyl derivative is formed.	Acetyl derivative is formed.	No action.
Action of Hinsberg's reagent.	Monoalkylsulphonamide is formed which is soluble in KOH.	Dialkylsulphonamide is formed which is insoluble in KOH.	No action.
Action of methyl iodide.	3 molecules (moles) of CH_3I to form quaternary salt with one mole of primary amine.	2 moles of CH_3I to form quaternary salt with one mole of secondary amine.	One mole of CH_3I to form quaternary salt with one mole of tertiary amine.

Note: Aniline does not form alcohol with nitrous acid but it forms benzene diazonium chloride which **shows dye test.**