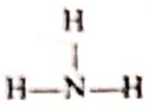
9

AMINES

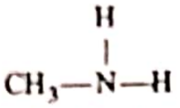
9.1. INTRODUCTION

Amines are the organic derivatives of ammonia in which one, two or all the three hydrogen atoms have been replaced by alkyl, aryl or aralkyl groups. For example,



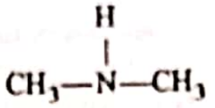
$$\begin{array}{c}\mathrm{H}\\ | \\ \mathrm{H-N-H}\end{array}$$

Ammonia



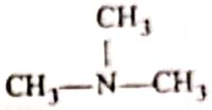
$$\begin{array}{c}\mathrm{H}\\ | \\ \mathrm{CH_3-N-H}\end{array}$$

Methylamine



$$\begin{array}{c}\mathrm{H}\\ | \\ \mathrm{CH_3-N-CH_3}\end{array}$$

Dimethylamine



$$\begin{array}{c}\mathrm{CH_3}\\ | \\ \mathrm{CH_3-N-CH_3}\end{array}$$

Triethylamine

Amines from an important class of organic compounds since they not only serve as starting materials for the synthesis of other classes of organic compounds but many of them also possess profound physiological activity. In this unit, we shall briefly discuss the chemistry of aliphatic and aromatic amines.

9.2. CLASSIFICATION OF AMINES

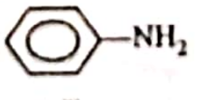
Amines are classified as **primary (1°) secondary (2°) and tertiary (3°)*** according as *one, two* or all the *three* hydrogen atoms of ammonia are replaced by alkyl or aryl or aralkyl groups as described below :

(*i*) **Primary (1°) amines.** Primary amines are derivatives of ammonia in which one hydrogen atom of ammonia has been replaced by alkyl, aryl or aralkyl group. Therefore, *their functional group is the* **amino group (—NH_2).**

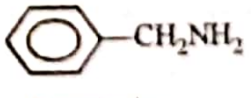
Depending upon whether the group directly attached to the nitrogen atom is an alkyl, aryl or aralkyl group they are called **aliphatic amines (or alkylamines) aromatic amines (or arylamines)** and **aralkylamines** respectively. For example,

$CH_3—NH_2$

Methylamine
(*Aliphatic amine*)



Aniline
(*Arylamine*)



Benzylamine
(*Aralkylamine*)

(*ii*) **Secondary (2°) amines.** These are derivatives of ammonia in which two hydrogen atoms of ammonia have been replaced by alkyl, aryl or aralkyl groups. Therefore, their functional group is the **imino group**

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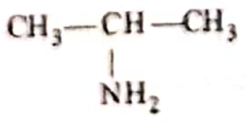
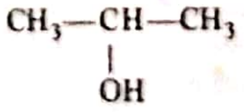
*It may be noted here that the terms primary, secondary and tertiary used here have different meanings than those used in case of alcohols. In alcohols, 1°, 2° and 3° alcohols refer to the type of carbon to which OH is attached. Thus, 2-propanamine is a primary amine but 2-propanol is secondary alcohol.



$$\begin{array}{c}\mathrm{CH_3-CH-CH_3}\\ | \\ \mathrm{NH_2}\end{array}$$

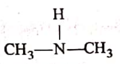
1° Amine



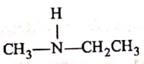
$$\begin{array}{c}\mathrm{CH_3-CH-CH_3}\\ | \\ \mathrm{OH}\end{array}$$

2° Alcohol

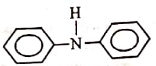
(>NH). Depending upon whether the two groups attached to the N-atom are same or different, 2° amines are further classifed as simple or mixed. Further, the 2° amines may be purely aliphatic or purely aromatic or mixed aliphatic-aromatic depending upon the nature of the two groups attached to the nitrogen atom. For example,


$CH_3-\overset{\overset{H}{|}}{N}-CH_3$

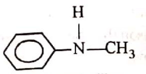
Dimethylamine
(*Simple : aliphatic*)


$CH_3-\overset{\overset{H}{|}}{N}-CH_2CH_3$

Ethylmethylamine
(*Mixed : aliphatic*)

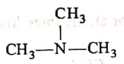


Diphenylamine
(*Simple aromatic*)

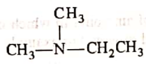


N-Methylaniline
(*Mixed : aliphatic-aromatic*)

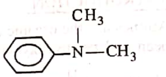
Tertiary (3°) amines. These are ammonia derivatives in which all the three hydrogen atoms of ammonia have been replaced by alkyl, aryl or aralkyl groups. Therefore, they contain **tertiary nitrogen** (>*N*—) *as the functional group*. Like secondary amines, they may also be purely aliphatic, purely aromatic or mixed aliphatic aromatic. For example,


$CH_3-\overset{\overset{CH_3}{|}}{N}-CH_3$

Trimethylamine
(*Simple : aliphatic*)


$CH_3-\overset{\overset{CH_3}{|}}{N}-CH_2CH_3$

Ethyldimethylamine
(*Mixed : aliphatic*)



N, N-Dimethylaniline
(*Mixed : aliphatic-aromatic*)

Quaternary ammonium compounds or salts. Apart from three types of amines, there is another class of compounds called **quaternary ammonium salts.** These compounds may be regarded as derivatives of ammonium salts in which all the four H-atoms of the ammonium ion have been replaced by alkyl or aryl or aralkyl groups.

$NH_4^+X^-$ Ammonium salt

$R_4N^+X^-$ Quaternary ammonium salt

(*where X is halogen, hydroxide ion etc.*)

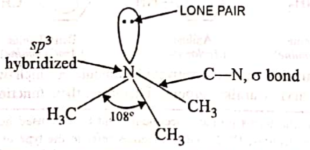
e.g. $[(CH_3)_4N]^- I^-$ Tetramethylammonium iodide

$[(CH_3CH_2)_4N]^+ OH^-$ Tetraethylammonium hydroxide

$C_6H_5\overset{+}{N}(CH_3)_3Br^-$ Trimethylphenylammonium bromide

9.3. STRUCTURE OF AMINES

The structure of amines is similar to that of ammonia. Like in ammonia, N of amines is also sp^3-hybridized. Three of the sp^3-orbitals, which contain one electron each, form σ-bonds either with H-atoms or the alkyl or aryl groups while the fourth one contains a lone pair of electrons. For example, the structure of trimethylamine is shown below :



Since lone-pair-bond pair repulsions are much greater than bond pair-bond pair repulsions, therefore, the bond angles between any two adjacent H-atoms or alkyl groups decreases from the tetrahedral angle of 109·28′ to 107° in 1° and 2° amines. However, in case of 3° amines, due to steric hindrance between the three bulky alkyl groups, the bond angle increases from 107° in ammonia to 108° in trimethylamine. Thus, *all the three amines (1°, 2° or 3°) like NH_3 have pyramidal shape.*

9.4. STEREOCHEMISTRY OF AMINES

A tertiary amine like NH_3 has a **pyramidal shape** with its lone pair of electrons present in a sp^3-orbital. If this orbital containing the lone pair of electrons is considered as the fourth different substituent, then the tertiary amines of the type $R^1R^2R^3N$ because of their pyramidal shapes should be chiral and hence resolvable. But, in actual practice, such type of tertiary amines have never been resolved. This is due to the reason that the energy difference between the enantiomers of such type of amines is very small (25 kJ mol^{-1}) and hence they rapidly interconvert into one another by a process called **nitrogen inversion or amine inversion.**

During this nitrogen inversion, the state of hybridization of N changes from sp^3 to sp^2 to give a planar transition state which, in turn, can either revert to the starting amine (I) or to its enantiomer (II) as shown in Fig. 9.1.

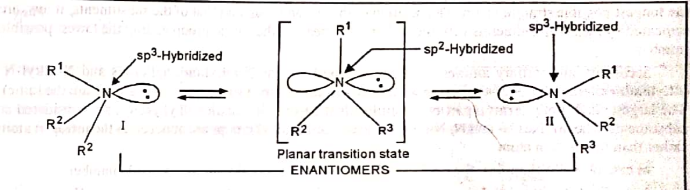


FIGURE 9.1. Racemization of tertiary amines via nitrogen inversion.

Since the rate of this inversion is very high (2·3 × 10^{10} sec^{-1}), therefore, *tertiary amines of the type $R^1R^2R^3N$ though chiral exist as racemic mixtures which cannot be resolved.*

Optical activity of quaternary ammonium salts of the type $R^1R^2R^3R^4\overset{+}{N}X^-$. The lone pairs of electrons on the N-atom is involved in nitrogen inversion and hence racemization of tertiary amines with different substituents occurs. However, if the lone pair of electrons on nitrogen is bonded to fourth different substituent, then racemization due to nitrogen inversion will not be possible and hence such quaternary ammonium salts should exhibit optical activity. This prediction has been found to be true. For example, allylbenzylmethylphenylammonium iodide has been resolved into two optically active forms **(Fig. 9.2).**

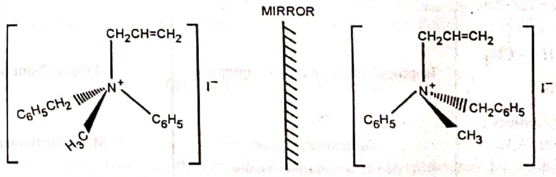


FIGURE 9.2. Enantiomers of allylbenzylmethylphenylammonium iodide.

9.5. NOMENCLATURE OF AMINES

1. Aliphatic amines. *In the common system*, aliphatic amines are named by the following two methods.

(*i*) According to one method, aliphatic amines are called **alkylamines.** The common names of aliphatic primary amines are then obtained by adding the suffix **amine** to the name of the alkyl group attached to the nitrogen atom. In case of mixed secondary and tertiary amines, the names of the alkyl groups are arranged in alphabetical order and the suffix **amine** is then added. However, for simple secondary and tertiary amines respectively, the prefixes **di** and **tri** are used before the name of the alkyl group.

Similarly, the names of **aralkylamines** are derived by adding the suffix **amine** to the name of the aralkyl group (or groups arranged in alphabetical order).

(*ii*) According to the second system, aliphatic amines are called **aminoalkanes.** In this system, the primary amines are named by adding the prefix **amino** to the name of the parent alkane corresponding to the longest possible straight chain. The position of the amino group and that of the substituents, if any, are indicated by the arabic numerals with the carbon atom bearing the amino group getting the lowest possible number.

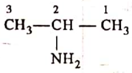
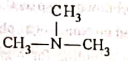
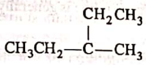
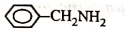
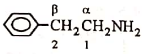
Secondary and tertiary amines are named respectively as **N-alkylaminoalkanes** and **N-alkyl-N-alkylaminoalkanes (or N, N-dialkylaminoalkanes** in case the two substituent alkyl groups are the same). The largest alkyl group forms a part of the aminoalkane while the smaller alkyl groups are considered as substituents. The prefixes N- and N, N-simply mean that the alkyl groups are attached to the nitrogen atom rather than to a carbon atom.

In case of aralkaylamines, the position of the aryl group is indicated by a suitable number.

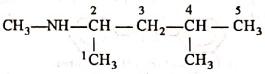
In the IUPAC system, aliphatic amines are called **alkanamines.** These names are obtained by removing the final *'e'* from the name of the corresponding alkane and adding the suffix **amine.**

It may be noted here that regardless of the system of nomenclature, the complete name of an amine is always written as one word.

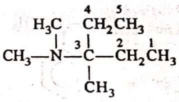
The common and IUPAC names of some aliphatic amines are given below :

AMINE	COMMON NAME	IUPAC NAME
Primary amines :		
CH_3NH_2	Methylamine or Aminomethane	Methanamine
$CH_3CH_2NH_2$	Ethylamine or Aminoethane	Ethanamine
$\overset{3}{CH_3}\overset{2}{CH_2}\overset{1}{CH_2}NH_2$	*n*-Propylamine or 1-Aminopropane	1-Propanamine or Propan-1-amine
 $\overset{3}{CH_3}-\underset{\underset{NH_2}{\vert}}{\overset{2}{CH}}-\overset{1}{CH_3}$	Isopropylamine or 2-Aminopropane	Propan-2-amine
Secondary amines :		
$CH_3-NH-CH_3$	Dimethylamine or N-Methylaminomethane	N-Methylmethanamine
$CH_3CH_2-NH-CH_3$	Ethylmethylamine or N-Methylaminoethane	N-Methylethanamine
Tertiary amines :		
 $CH_3-\overset{\overset{CH_3}{\vert}}{N}-CH_3$	Trimethylamine	N, N-Dimethylmethanamine
 $CH_3CH_2-\overset{\overset{CH_2CH_3}{\vert}}{C}-CH_3$	N, N-Diethyl-N-methylamine	N-Ethyl-N-methylethanamine
Aralkylamines :		
	Benzylamine or Phenylaminomethane	Phenylmethanamine
	β-Phenylethylamine or 2-Phenylaminoethane	2-Phenylethanamine

In case of mixed secondary and tertiary amines in which one of the alkyl groups has three or more carbon atoms and hence can exhibit position isomerism, the position of carbon atom of the chain to which the nitrogen is attached is included in the name of the amine. For example,



$$CH_3-NH-\overset{2}{\underset{\underset{^1CH_3}{\vert}}{CH}}-\overset{3}{CH_2}-\overset{4}{\underset{\underset{CH_3}{\vert}}{CH}}-\overset{5}{CH_3}$$



$$CH_3-\overset{\overset{H_3C}{\vert}}{N}-\overset{\overset{\overset{4\quad 5}{CH_2CH_3}}{\vert}}{\underset{\underset{CH_3}{\vert}}{\overset{3}{C}}}-\overset{2}{CH_2}\overset{1}{CH_3}$$

Common : 2-(N-Methylamino)-4-methylpentane 3-(N, N-Dimethylamino)-3-methylpentane

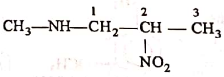
IUPAC : N, 4-Dimethylpentan-2-amine 3, N, N-Trimethyl-3-pentanamine

In case of polyfunctional compounds, the amine is named as a derivative of the principal functional group. For example,

$$H_2N-\overset{2}{CH_2}\overset{1}{CH_2}-OH \qquad NH_2-\overset{4}{CH_2}\overset{3}{CH_2}\overset{2}{CH_2}-\overset{1}{COOH}$$

2-Aminoethanol 4-Aminobutanoic acid

If, however, all the functional groups are substituent functional groups, the compound is named as a derivative of the compound containing the functional group which comes first in the alphabetical order. For example,



$$CH_3-NH-\overset{1}{CH_2}-\underset{\underset{NO_2}{\vert}}{\overset{2}{CH}}-\overset{3}{CH_3}$$

N-Methyl-2-nitropentanamine

In case of unsaturated amines, the double/triple bond is given the preference. For example,

$$CH_3CH=CHNH_2 \qquad \overset{1}{CH_2}=\overset{2}{CH}-\overset{3}{CH_2}NH_2$$

1-Propenamine Prop-1-en-3-amine

2. Aromatic amines. *In the common system*, aromatic amines are called **arylamines.** The name of an individual amine is then obtained by adding the suffix **amine** to the name of the aryl group.

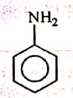
More often they are named as derivatives of the simplest aromatic amine called **aniline.**

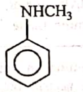
However, in some cases, special names are also used. For example, *o/m/p*-toluidine for *o/m/p*-methylaniline and *o/m/p*-anisidine for *o/m/p*-methoxyaniline. Even N-phenyl derivative of aniline is generally called diphenylamine.

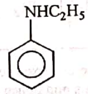
In the IUPAC system, the simplest aromatic amine is called **benzenamine** and other amines are named as derivatives of this amine.

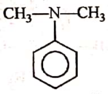
It may be noted here again that the *complete name of an amine is always written as one word.*

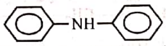
The common and IUPAC names of some arylamines are given below :

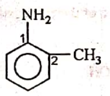

Aniline or
Benzenamine

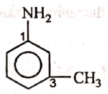

N–Methylaniline
or N–Methylbenzenamine

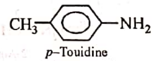

N–Ethylaniline
N–Ethylbenzenamine

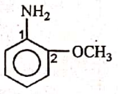

N,N–Dimethylaniline
or N,N–Dimethylbenzenamine

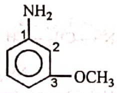

N–Phenylaniline or Diphenylamine
or N–Phenylbenzenamine

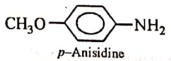

o-Toluidine
or 2–Methylaniline
or 2–Methylbenzenamine


m-Toluidine
or 3–Methylaniline
or 3–Methylbenzenamine


p–Touidine
or 4–Methylaniline
or 4–Methylbenzenamine


o-Anisidine
or 2–Methoxyaniline
or 2–Methoxybenzenamine


m-Anisidine
or 3–Methoxyaniline
or 3–Methoxybenzenamine

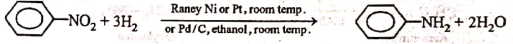

p–Anisidine
or 4-Methoxyaniline
4-Methoxybenzenamine

Since amines are better known by their common names, therefore, in this unit, we shall be using common names more frequently though here and there some IUPAC names have also been given.

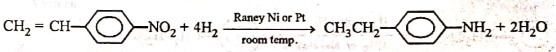
9.6. PREPARATION OF AMINES

Amines are generally prepared by the following methods :

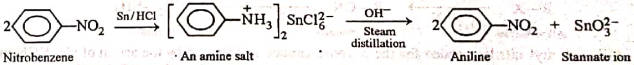
1. Reduction of nitro compounds. The nitro compounds can be easily reduced to the corresponding primary amines either by **catalytic hydrogenation** or by combination of an **active metal and a mineral acid.** This method is particularly useful for the preparation of *aromatic primary amines* since aromatic nitro compounds can be easily prepared by nitration of arenes. In recent years, this method has become increasingly important even for the preparation of aliphatic primary amines since aliphatic nitro compounds are now being prepared commercially by vapour phase nitration of alkanes.


Nitrobenzene Aniline

One disadvantage of catalytic hydrogenation is that other reducible groups such as ethylenic double bond if present in the nitro compound, also gets reduced. For example,


p-Nitrostyrene *p*-Ethylaniline

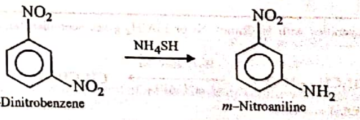
(ii) *Reduction with an active metal such as Fe, Sn, Zn etc. and concentrated hydrochloric acid.* For example, reduction of nitrobenzene with Sn/HCl first gives a chlorostannate salt from which free amine is recovered by the addition of alkali followed by steam distillation.


Nitrobenzene An amine salt Aniline Stannate ion

Lithium aluminium hydride ($LiAlH_4$) can also be used for the reduction of aliphatic (but not aromatic) nitro compounds.

$$\underset{\text{Nitroethane}}{CH_3CH_2—NO_2 + 3H_2} \xrightarrow[\text{room temp.}]{\text{Raney Ni or Pt}} \underset{\text{Ethylamine}}{CH_3CH_2—NH_2 + 2H_2O}$$

In case of di or trinitro compounds, *selective reduction* of one nitro group can also be achieved by using ammonium hydrogen sulphide as a reducing agent. Thus,

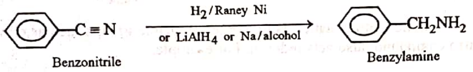

m–Dinitrobenzene *m*–Nitroaniline

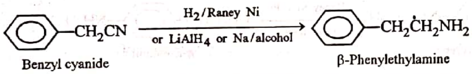
2. By the reduction of nitriles*. *Aliphatic and aralkyl primary amines* can be easily prepared by the reduction of the corresponding nitriles either catalytically with H_2 and Raney nickel or chemically with lithium aluminium hydride or sodium and alcohol (reduction with sodium and alcohol is called **Mendius reduction**)

$$\underset{\text{Alkyl nitrile}}{R{-}C\equiv N} \xrightarrow[\text{or LiAlH}_4\text{ or Na/alcohol}]{H_2/\text{Raney Ni}} \underset{1^\circ\text{ Amine}}{R{-}CH_2NH_2}$$

e.g.

$$\underset{\text{Acetonitrile}}{CH_3C\equiv N} \xrightarrow[\text{or LiAlH}_4\text{ or Na/alcohol}]{H_2/\text{Raney Ni}} \underset{\text{Ethylamine}}{CH_3CH_2{-}NH_2}$$


Benzonitrile Benzylamine


Benzyl cyanide β-Phenylethylamine

Synthetic importance. Since alkyl/aralkyl nitriles can be easily prepared by the action of alcoholic NaCN or KCN on the corresponding alkyl/aralkyl halides, this gives us *an excellent method for converting alkyl halides into primary amines having one carbon atom more than the parent alkyl halide.* Thus,

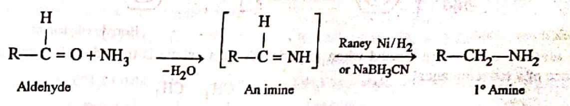
$$\underset{\text{Alkyl halide}}{R{-}X} \xrightarrow[-KX]{KCN\ (alc)} \underset{\text{Alkyl cyanide}}{R{-}CN} \xrightarrow{LiAlH_4/\text{Ether}} \underset{1^\circ\text{ Amine}}{RCH_2{-}NH_2}$$

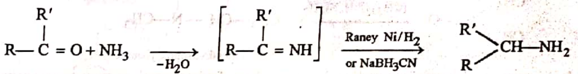
Although aryl nitriles needed for the purpose cannot be prepared by the action of alc. KCN on the corresponding aryl halides, yet they can be easily prepared by the action of aq. KCN on the corresponding arenediazonium salts.

$$\underset{\text{Benzenediazonium chloride}}{C_6H_5\overset{+}{N}\equiv NCl^-} \xrightarrow[\text{Cu catalyst}]{\text{Aq. KCN}} \underset{\text{Benzonitrile}}{C_6H_5{-}CN} + N_2 + KCl$$

3. Reductive amination. *Primary, secondary and tertiary amines* can be prepared from aldehydes and ketones by **reductive amination.** *It involves the treatment of an aldehyde or a ketone with ammonia or an amine in presence of a reducing agent.* The reaction occurs through the intermediate formation of an imine which upon reduction gives the corresponding amine. The reduction of the imine is achieved eith catalytically with Raney Ni/H_2 at 373 K and 150 atm. pressure or chemically with sodium cyanoborohydri ($NaBH_3CN$). *Sodium cyanoborohydride being less reactive than $NaBH_4$, reduces the imine but not t carbonyl compound.*

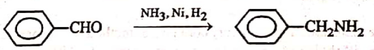
Primary amines are formed by treatment of an aldehyde or ketone with ammonia in presence of reducing agent,

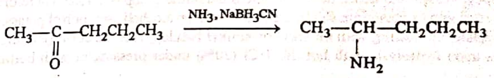

Aldehyde An imine 1° Amine


A ketone An imine 1° Amine

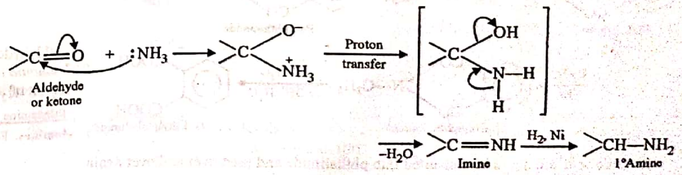
e.g.

$$\underset{n\text{-Butyraldehyde}}{CH_3CH_2CH_2CHO} \xrightarrow{NH_3,\ Ni,\ H_2} \underset{n\text{-Butylamine}}{CH_3CH_2CH_2CH_2NH_2}$$


Benzaldehyde Benzylamine


$$\underset{\text{2-Pentanone}}{CH_3{-}\underset{\underset{O}{\|}}{C}{-}CH_2CH_2CH_3} \xrightarrow{NH_3,\ NaBH_3CN} \underset{\text{2-Pentanamine}}{CH_3{-}\underset{\underset{NH_2}{|}}{CH}{-}CH_2CH_2CH_3}$$

Mechanism. Reductive amination occurs through intermediate formation of an imine and occurs through the following steps.



Secondary amines are formed by treatment of an aldehyde or ketone with a primary amine in presence of a reducing agent :

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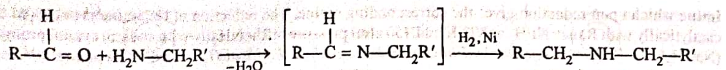
*Reduction of isocyanides with H_2/Raney Ni or $LiAlH_4$ gives secondary amines, *i.e.*, **N-methylamines.** For example,

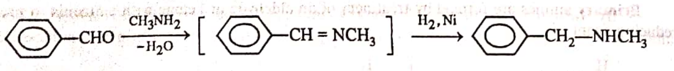
$$\underset{\text{Ethyl isocyanide}}{CH_3CH_2{-}N\rightleftarrows C} \xrightarrow[\text{or LiAlH}_4]{H_2/\text{Raney Ni}} \underset{\text{Ethylmethylamine}}{CH_3CH_2{-}NH{-}CH_3}$$

$$\underset{\text{Phenyl isocyanide}}{C_6H_5{-}N\rightleftarrows C} \xrightarrow[\text{or LiAlH}_4]{H_2/\text{Raney Ni}} \underset{\text{N-Methylaniline}}{C_6H_5{-}NH{-}CH_3}$$



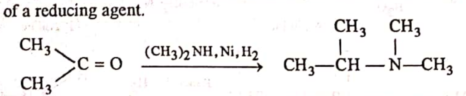
$$R{-}\overset{\overset{\large H}{|}}{C}{=}O + H_2N{-}CH_2R' \xrightarrow[-H_2O]{} \left[R{-}\overset{\overset{\large H}{|}}{C}{=}N{-}CH_2R'\right] \xrightarrow{H_2,\,Ni} R{-}CH_2{-}NH{-}CH_2{-}R'$$

Aldehyde 1° Amine An imine 2° Amine



Benzaldehyde Benzylmethylamine

Similarly, **tertiary amines** are formed when an aldehyde or a ketone is treated with a secondary amine in presence of a reducing agent.

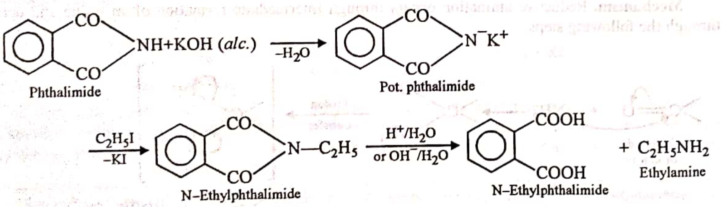


Acetone N, N-Dimethylisopropylamine

Merits. It is a particularly useful method for the preparation of primary amines containing a secondary alkyl group (*i.e.*, 2-pentanamine). Recall these amines are difficult to prepare by *Hofmann ammonolysis of alkyl halides* because of the tendency of *sec*-alkyl halides to undergo elimination.

Limitations. The primary amines formed during reductive amination can react further with the aldehyde or ketone to form a certain amount of the secondary amine. This can, however, be avoided by using desired proportions of the reactants.

4. Gabriel phthalimide reaction. This is a very convenient method for the preparation o pure *aliphatic and aralkyl primary amines.* Phthalimide contains an imino group (—NH—) flanked by two electron-withdrawing carbonyl groups and hence the hydrogen of the imino group is *acidic.* Therefore, phthalimide can be easily converted into its potassium salt by treatment with an alcoholic solution of potassium hydroxide. Potassium phthalimide, on heating with an alkyl or aralkyl halide, gives the corresponding N-substituted phthalimide. This upon hydrolysis with hot dil. HCl (20%) under pressure or with boiling alkali gives primary amine.



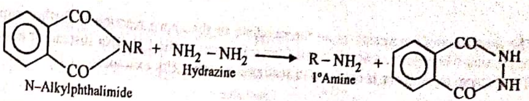
Phthalimide Pot. phthalimide

N–Ethylphthalimide N–Ethylphthalimide Ethylamine

Phthalic acid can again be converted into phthalimide and used over and over again.

Similarly benzylamine can be prepared by using benzyl chloride and glycine (NH_2CH_2COOH) by using chloroacetic acid in place of ethyl iodide in the above reaction.

Hydrazinolysis (*Cleavage by hydrazine*) **of N-alkylphthalimides** is a more convenient and efficient meth[illegible] compared to acidic/basic hydrolysis for obtaining 1° amines using **Gabriel synthesis.** For example,

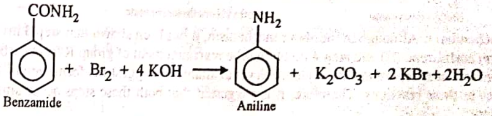


N–Alkylphthalimide Hydrazine 1°Amine Phthalhydrazide

5. By Hofmann degradation of primary amides. (*Hofmann bromamide reaction*). When a primary amide is treated with bromine or chlorine in aqueous alkali, it gives a primary amine containing *one carbon atom less than the original amide.*

$$\underset{1^\circ\text{ Amide}}{R{-}CONH_2} + Br_2 + 4KOH \longrightarrow \underset{1^\circ\text{ Amine}}{R{-}NH_2} + K_2CO_3 + 2KBr + 2H_2O$$

e.g., $\underset{\text{Propionamide}}{CH_3CH_2CONH_2} + Br_2 + 4KOH \longrightarrow \underset{\text{Ethylamine}}{CH_3CH_2{-}NH_2} + K_2CO_3 + 2KBr + 2H_2O$

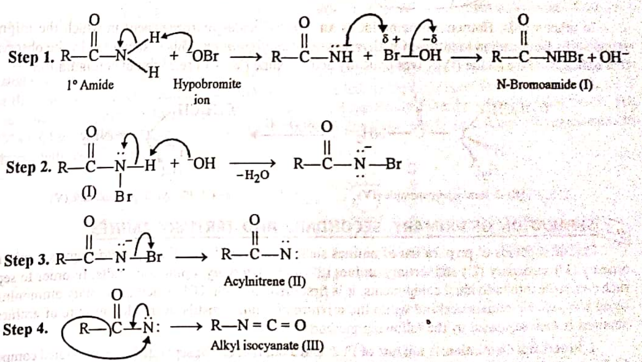


Benzamide Aniline

Mechanism. Br_2 reacts with alkali to form hypobromite ion (BrO^-) which initiates the reaction. The

$$Br_2 + 2OH^- \longrightarrow OBr^- + Br^- + H_2O$$

reaction is believed to occur through the following steps :



Step 1.

1° Amide Hypobromite ion N-Bromoamide (I)

Step 2.

Step 3.

Acylnitrene (II)

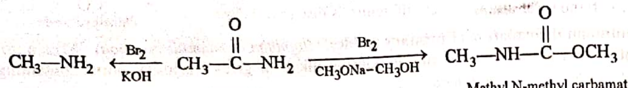
Step 4.

Alkyl isocyanate (III)

Step 5. $R{-}N{=}C{=}O + 2KOH \xrightarrow{\text{Hydrolysis}} \underset{1^\circ\text{ Amine}}{R{-}NH_2} + K_2CO_3$

Evidence is support of the mechanism. This mechanism has been supported by the observation that N-bromoamide (I) and alkyl isocyanates (III) have actually been isolated as intermediates in the above reaction. These intermediates yield the expected amine when treated with KOH.

The formation of isocyanate as an intermediate in the above reaction is further supported by the observation that when this reaction is carried out with methanolic CH_3ONa instead of aqueous NaOH, a methyl carbamate or urethane is obtained instead of the amine. For example,



$$CH_3{-}NH_2 \xleftarrow[KOH]{Br_2} CH_3{-}\overset{O}{\overset{\|}{C}}{-}NH_2 \xrightarrow[CH_3ONa-CH_3OH]{Br_2} CH_3{-}NH{-}\overset{O}{\overset{\|}{C}}{-}OCH_3$$

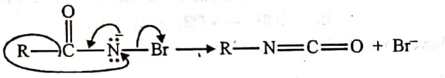
Methylamine Acetamide Methyl N-methyl carbamate

(*A urethane*)

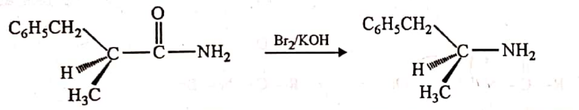
The methyl N-methyl carbamate is actually formed by addition of CH_3OH to methyl isocyanate formed as an intermediate in the above reaction.

$$\underset{\text{Methyl isocyanate}}{CH_3{-}N=C=O} + CH_3OH \longrightarrow \underset{\text{Methyl N-methylcarbamate}}{CH_3{-}NH{-}COOCH_3}$$

Stereochemistry. Although in the above mechanism, it has been shown that **step 3** involving the loss of Br^- to form acylnitrene (II) and **step 4** involving the rearrangement of group R from carbon to electron-deficient N-atom occur separately, no evidence is yet available to suggest the formation of acylnitrenes as intermediates in these reactions. Therefore, it is suggested that both these steps occur simultaneously as depicted below :



In other words, Hofmann bromomide is an *intramolecular rearrangement* in which the migrating group shifts from carbon to nitrogen with *retention of configuration*. This is supported by the observation that optically active amide (IV) gives optically active amine (V) with retention of configuration.



(S)-2-Benzylpropanamide (IV) (S)-1-Phenyl-2-propanamine (V)

9.7. SEPARATION OF PRIMARY, SECONDARY AND TERTIARY AMINES

Certain methods of preparation of amines such as *ammonolysis of alkyl halides* gives a mixture of primary (1°) secondary (2°) and tertiary amines (3°) and quaternary ammonium salts. In order to separate such a mixture into individual components, it is first distilled with KOH when quaternary ammonium salt being *non-volatile* remains behind while the mixture of amines distils over. The mixture of amines thus obtained is then separated by the following methods.

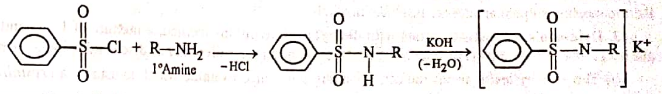
1. Fractional distillation. A mixture of 1°, 2° and 3° amines can be separated into individual components by fractional distillation since their boiling points are fairly apart. For example,

$CH_3CH_2NH_2$	$(CH_3CH_2)_2NH$	$(CH_3CH_2)_3N$
1° Amine (290K)	2° Amine (329K)	3° Amine (371K)

This is the most satisfactory method and is now used industrially because of the availability of highly efficient fractionating columns which can separate a mixture of amines even if their boiling are quite close.

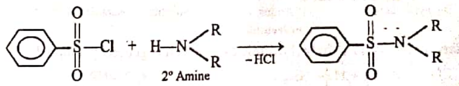
2. Hinsberg's method—Reaction with benzenesulphonyl chloride. This is an excellent method for separating a mixture of 1°, 2° and 3° amines. In this method, a mixture of 1°, 2° and 3° amines is treated with benzenesulphonyl chloride (*Hinsberg's reagent*) and the resulting reaction mixture is basified with aq. KOH solution when the three amines react differently as discussed below :

(*i*) *A primary amine forms N-alkylbenzenesulphonamide which because of the presence of an acidic hydrogen on the N-atom dissolves in KOH.*



Benzenesulphonyl chloride (*Hinsberg's reagent*) N-Alkylbenzenesulphonamide Potassium salt (*soluble in KOH*)

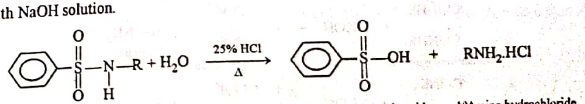
(*ii*) *A secondary amine forms N, N-dialkylbenzenesulphonamide which due to the absence of acidic hydrogen on N-atom does not dissolve in KOH.*



Benzenesulphonyl chloride N, N-Dialkylbenzenesulphonamide (*Insoluble in KOH*)

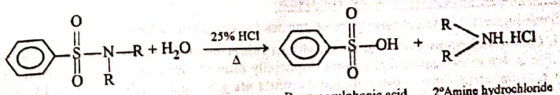
(*iii*) *The tertiary amine under these conditions does not react at all since it does not contain a replaceable hydrogen on the nitrogen atom.*

The reaction mixture obtained after treatment with benzenesulphonyl chloride in presence of alkali is distilled when tertiary amine distils over. The remaining mixture is filtered and the filtrate on acidification gives the sulphonamide of 1° amine while the solid residue left on the filter paper is the sulphonamide of 2° amine. The two sulphonamides thus isolated are hydrolysed separately either by refluxing with 70% H_2SO_4 or 25% HCl to form the corresponding amine hydrochlorides from which the amines are regenerated on treatment with NaOH solution.



N-Alkylbenzenesulphonamide Benzenesulphonic acid 1°Amine hydrochloride

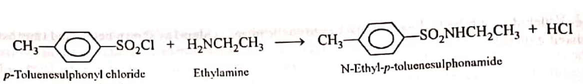
$$RNH_2.HCl + NaOH \longrightarrow \underset{\text{1°Amine}}{RNH_2} + NaCl + H_2O$$



N, N-Dialkylbenzenesulphonamide Benzenesulphonic acid 2°Amine hydrochloride

$$R_2NH.HCl + NaOH \longrightarrow \underset{\text{2°Amine}}{R_2NH} + NaCl + H_2O$$

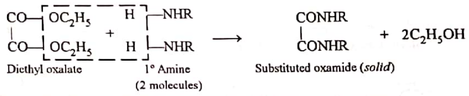
Recently benzenesulphonyl chloride is replaced by *p*-toluenesulphonyl chloride (*tosyl chloride*) since



the substituted sulphonamides thus formed are stable solids which can be easily purified by crystallization. Unfortunately, the *Hinsberg's* method is not suitable for higher primary amines, *i.e. n*-heptylamine because their monoalkyl sulphonamides are insoluble in alkali.

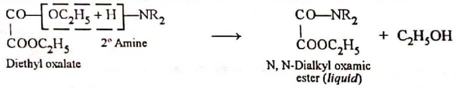
3. Hofmann's method—Reaction with diethyl oxalate. In this method, a mixture of 1°, 2° and 3° amines is treated with diethyl oxalate when the three amines react differently as discussed below:

(*i*) The *primary amine* forms the corresponding substituted oxamide which is usually a *crystalline solid.*



$$\underset{\text{Diethyl oxalate}}{\begin{matrix}\text{CO}-\text{OC}_2\text{H}_5\\ | \\ \text{CO}-\text{OC}_2\text{H}_5\end{matrix}} + \underset{\substack{1^\circ\text{ Amine}\\ (2\text{ molecules})}}{\begin{matrix}\text{H}-\text{NHR}\\ \\ \text{H}-\text{NHR}\end{matrix}} \longrightarrow \underset{\text{Substituted oxamide }(solid)}{\begin{matrix}\text{CONHR}\\ | \\ \text{CONHR}\end{matrix}} + 2\text{C}_2\text{H}_5\text{OH}$$

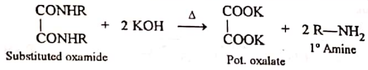
(*ii*) The secondary amine forms a diethyl oxamic ester which is generally a *liquid.*



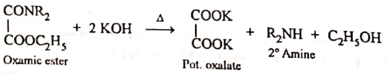
$$\underset{\text{Diethyl oxalate}}{\begin{matrix}\text{CO}-\text{OC}_2\text{H}_5\\ | \\ \text{COOC}_2\text{H}_5\end{matrix}} + \underset{2^\circ\text{ Amine}}{\text{H}-\text{NR}_2} \longrightarrow \underset{\substack{\text{N, N-Dialkyl oxamic}\\ \text{ester }(liquid)}}{\begin{matrix}\text{CO}-\text{NR}_2\\ | \\ \text{COOC}_2\text{H}_5\end{matrix}} + \text{C}_2\text{H}_5\text{OH}$$

(*iii*) The *tertiary amine* under these conditions does not react at all since it does not contain a replaceable hydrogen atom.

The reaction mixture containing the substituted oxamide, oxamic ester and unreacted tertiary amine is distilled when the tertiary amine distils over. The residual mixture containing the substituted oxamide (*solid*) and the oxamic ester (*liquid*) is separated by simple filtration. Both the oxamide and the oxamic ester when boiled separately with a strong base, regenerate the corresponding amines. Thus.



$$\underset{\text{Substituted oxamide}}{\begin{matrix}\text{CONHR}\\ | \\ \text{CONHR}\end{matrix}} + 2\,\text{KOH} \xrightarrow{\Delta} \underset{\text{Pot. oxalate}}{\begin{matrix}\text{COOK}\\ | \\ \text{COOK}\end{matrix}} + \underset{1^\circ\text{ Amine}}{2\,\text{R}-\text{NH}_2}$$



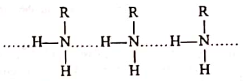
$$\underset{\text{Oxamic ester}}{\begin{matrix}\text{CONR}_2\\ | \\ \text{COOC}_2\text{H}_5\end{matrix}} + 2\,\text{KOH} \xrightarrow{\Delta} \underset{\text{Pot. oxalate}}{\begin{matrix}\text{COOK}\\ | \\ \text{COOK}\end{matrix}} + \underset{2^\circ\text{ Amine}}{\text{R}_2\text{NH}} + \text{C}_2\text{H}_5\text{OH}$$

9.8. PHYSICAL PROPERTIES OF AMINES

Some important physical properties of amines are discussed below :

1. Colour and odour. Pure amines are almost colourless but develop colour on keeping in air for long time. This is due to the reason that amines, especially aromatic amines, are readily oxidised in air to form coloured oxidation products. Lower aliphatic amines are gases and smell very much like ammonia but the higher amines are liquids with fishy odours. Lower aromatic amines are liquids having characteristic unpleasant odours but the higher ones are low melting solids which are almost odourless. Aromatic amines, in general, are toxic.

2. Boiling points. Amines have higher boiling points than hydrocarbons of comparable molecular masses. This is due to the reason that amines being polar, form intermolecular H-bonds (except tertiary amines which do not have hydrogen atoms linked to the nitrogen atom) as shown below and thus exist as associated molecules.



(*where R is any alkyl or aryl group*)

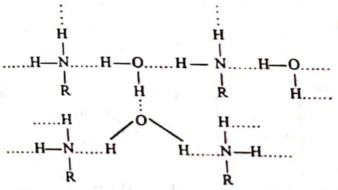
The degree of association, however, depends upon the extent of H- bonding. Since 1° amines have *two*, 2° amines have *one* while 3° amines have no hydrogen linked to nitrogen, therefore, among isomeric amines, *1° amines have the highest, while 3° amines have the lowest boiling point.* For example,

Compound	Molar mass	b.p. (K)
n-$C_4H_9NH_2$	73	350·8
$(C_2H_5)_2NH$	73	329·3
$C_2H_5N(CH_3)_2$	73	310·5
$CH_3(CH_2)_3CH_3$	72	309·0
$C_2H_5CH(CH_3)_2$	72	300·8

Further, since the electronegativity of nitrogen is lower than that of oxygen, therefore, *amines form weaker H-bonds as compared to alcohols and carboxylic acids.* As a result, amines are not associated to the extent of alcohols and carboxylic acids and hence the boiling points of amines are lower than those of alcohols and carboxylic acids of comparable molecular masses. For example, ethylamine (mol. mass 45) boils at 292 K while ethyl alcohol (mol. mass 46) and formic acid (mol. mass 46) boil at 351 K and 374 K respectively.

Compound	Molar mass	b.p. (K)
$C_2H_5NH_2$	45	292
C_3H_8	44	231
C_2H_5OH	46	351
$HCOOH$	46	374

3. Solubility. All the three classes of aliphatic amines (1°, 2° and 3°) form H-bonds with water. *As a result, lower aliphatic amines are soluble in water.*



Methylamine and ethylamine are gases but they are highly soluble in water. That is why they are sold in the market as their 34% aqueous solutions. However, as the size of the alkyl group increases (with increase in molecular mass), the solubility decreases due to a corresponding increase in the hydrocarbon part (*hydrophobic part*) of the molecule. The borderline solubility is reached with amines of about six carbon atoms in the molecule. However, amines are quite soluble in organic solvents such as benzene, ether, alcohol etc.

Aromatic amines, on the other hand, are insoluble in water. This is due to the larger hydrocarbon part which tends to retard the formation of H-bonds. Thus, aniline is almost insoluble in water. However, it is quite soluble in benzene, ether, alcohol etc.

9.9. BASICITY OF AMINES

Like ammonia, all the three classes of amines contain a pair of unshared electrons on the nitrogen atom. Therefore, they have a strong tendency to donate this electron pair to a proton (H^+) or any other electron deficient species. As a result, all the three classes of amines, like ammonia, are basic in nature.

The basicity of an amine can be easily expressed either in terms of its basicity constant (K_b) or pK_b value.

Basicity constant (K_b). When an amine is dissolved or suspended in water, the following equilibrium is established.

$$RNH_2 + H_2O \rightleftharpoons R\overset{+}{N}H_3 + \overset{-}{O}H$$

The equilibrium constant for this reaction is

$$K_{eq} = \frac{[R\overset{+}{N}H_3]\,[OH^-]}{[RNH_2]\,[H_2O]}$$

Since water is present in large excess, its concentration is taken to be constant. Rewritting the above expression, we have,

$$K_{eq}\,[H_2O] = K_b = \frac{[R\overset{+}{N}H_3]\,[OH^-]}{[RNH_2]}$$

This new *equilibrium constant, K_b, which gives a measure of the extent to which an amine accepts a proton from water is called the* **basicity constant.** In other words, K_b is the index of the basicity of an amine. *The greater the numerical value of K_b, the stronger is the amine.*

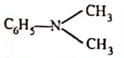
pK_b values. Since the values of K_b vary by many orders of magnitude, it is more convenient to express the basicity of an amine in terms of its **pK_b value** *i.e. negative logarithm of K_b*

$$pK_b = -\log K_b$$

Evidently, *smaller the numerical value of pK_b more basic is the amine.*

The K_b and pK_b values of some amines are given in Table 9.1.

TABLE 9.1. K_b and pK_b values of some Amines

AMINE	K_b	pK_b	AMINE	K_b	pK_b
NH_3	$1{\cdot}8 \times 10^{-5}$	4·75	$(CH_3CH_2)_3N$	$5{\cdot}6 \times 10^{-4}$	3·25
CH_3NH_2	$4{\cdot}5 \times 10^{-4}$	3·38	$C_6H_5NH_2$	$4{\cdot}2 \times 10^{-10}$	9·38
$(CH_3)_2NH$	$5{\cdot}4 \times 10^{-4}$	3·27	$C_6H_5NHCH_3$	$5{\cdot}0 \times 10^{-10}$	9·30
$(CH_3)_3N$	$0{\cdot}6 \times 10^{-4}$	4·22	 $C_6H_5-N(CH_3)_2$	$11{\cdot}5 \times 10^{-10}$	8·92
$CH_3CH_2NH_2$	$5{\cdot}1 \times 10^{-4}$	3·29	$C_6H_5-NH-C_6H_5$	$7{\cdot}1 \times 10^{-14}$	13·15
$(CH_3CH_2)_2NH$	$10{\cdot}0 \times 10^{-4}$	3·00	$C_6H_5-CH_2NH_2$	$2{\cdot}0 \times 10^{-5}$	4·70

9.9.1. STRUCTURE-BASICITY RELATIONSHIP OF AMINES

From Table 9.1, the following conclusions can be drawn :

(*i*) *All classes of aliphatic amines are stronger bases than ammonia (pK_b = 4·75)*

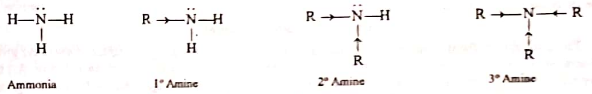
(*ii*) *Aromatic amines are much weaker bases than ammonia.*

(*iii*) *Mixed secondary and tertiary amines are slightly more basic than purely aromatic amines. For example, N-methylaniline and N, N-dimethylaniline are stronger bases than aniline or diphenylamine.*

Let us now discuss the effect of structure on the basicity of aliphatic and aromatic amines.

I. Basicity of Aliphatic Amines

As stated above *all the three classes of aliphatic amines are stronger bases than ammonia.* This is due to the reason that alkyl groups are electron-donating groups. As a result, *the electron density on the nitrogen atom increases and thus they can donate the lone pair of electrons more easily than ammonia.*



Thus, the basicity of amines should decrease in the order :

3° amine > 2° amine > 1° amine > NH_3

However, it has been found that in aqueous solutions, 2° amines are invariably found to be stronger bases than 1° amines while 3° amines are found to be weaker bases than 2° amines and sometimes even weaker than 1° amines. The actual basicity order of methyl and ethylamines is as under :

Basicity order : $(CH_3)_2NH > CH_3NH_2 > (CH_3)_3N > NH_3$

: $(CH_3CH_2)_2NH > (CH_3CH_2)_3N > CH_3CH_2NH_2 > NH_3$

The reason why the actual order is different from the expected order can be explained as follows :

The basicity of an amine in aqueous solution primarily depends upon the stability of the ammonium cation or the conjugate acid formed by accepting a proton from water. The stability of the ammonium cation, in turn, depends upon a combination of the following three factors :

(*i*) *+ I-Effect of the alkyl groups.*

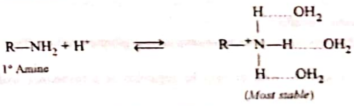
(*ii*) *Extent of H-bonding with water molecules.*

(*iii*) *Steric effects of the alkyl groups.*

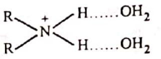
Let us now discuss these factors one by one. As the number of alkyl groups increases, the dispersal of the +ve charge on the ammonium cation by the + I-effect of the alkyl groups increases accordingly. Thus, on the basis of + I-effect alone, *the basicity of amines should decrease in the order :*

3° amine > 2° amine > 1° amine

The stability of the ammonium cation due to H-bonding depends upon the number of H-atoms present on the N-atom. Obviously, greater the number of H-atoms on N-atom, more stable is the ammonium cation. Thus, the ammonium cation derived from a 1° amine is the *most stable* since it has *three H-atoms* which can form *H- bonds* with H_2O ; the ammonium cation-derived from the 2° amine is *less stable* since it has *two H-atoms* while that of the 3° amines is the *least stable* since it has only *one H-atom* which can form H-bonds with H_2O as shown below :



$R_2NH + H^+ \rightleftharpoons$



2° Amine

(*Less stable*)

$$R_3N + H^+ \rightleftharpoons R_3\overset{+}{N}—H......OH_2$$

3° Amine

(*Less stable*)

However, in case of ammonium cation derived from tertiary amines, there is some steric repulsion to H-bonding and hence stability further decreases. Thus, on the basis of H-bonding and steric factors, the basicity of amines should decrease in the order :

1° amine > 2° amine > 3° amine.

From the above discussion, we may conclude that *it is a combination of + I-effect of the alkyl groups, H-bonding and steric factors which determine the stability of the ammonium cations in solution.* All these three factors are favourable for 2° amines and hence *2° amines are the strongest bases.* If the alkyl group is small, *i.e.*, CH_3 then there is no steric *hindrance to H-bonding. In other words, the stability due to hydrogen bonding predominates over the stability due to + I-effect the CH_3 group and hence 1° amine, i.e., CH_3NH_2 is a stronger base than 3° amine, i.e., $(CH_3)_3N$.* In other words, the overall decreasing strength of methylamines is $(CH_3)_2NH > CH_3NH_2 > (CH_3)_3N$.

If, however, the alkyl group is bigger than CH_3 group, *i.e.*, ethyl, propyl etc. *there will be some steric hindrance to H-bonding. As a result, stability due to* + I-effect predominates over the stability due to *H-bonding and hence 3° amines become more basic than 1° amines,* In other words, the overall decreasing strength of ethylamines follows the sequence :

$$(CH_3CH_2)_2NH > (CH_3CH_2)_3N > CH_3CH_2NH_2$$

It is interesting to note that in gas phase or in non-aqueous solvents such as chlorobenzene etc., the **solvation effects**, *i.e.*, *the stabilization of the conjugate acid due to H-bonding are absent* and hence in these media the basicity of amines depends only on the + I-effect of the alkyl groups. Thus, the basicity of 1°, 2° and 3° amines in the gas phase or in non-aqueous solvents follows the order :

3° Amine > 2° Amine > 1°Amine > NH_3

II. Basicity of Ararkylamines

Aralkylamines ($ArCH_2NH_2$) are essentially aryl substituted alkylamines. Due to the **electron withdrawing inductive effect (or –I-effect)** of the aryl group, the unshared electron pair of nitrogen in these amines is less easily available (than in alkylamines) for sharing with a proton. As a result, *simple aralkylamines are weaker bases than alkylamines.* For example,

$C_6H_6CH_2NH_2$	CH_3NH_2
$pK_b = 4{\cdot}70$	$pK_b = 3{\cdot}36$

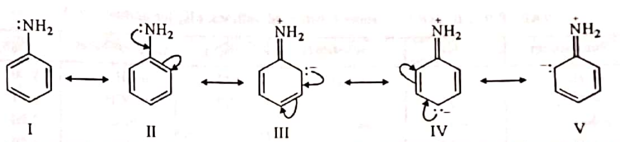
Further as the distance between the aryl group and the amino group increases, the –I-effect decreases and hence the basicity increases accordingly. For example,

$C_6H_5CH_2CH_2CH_2NH_2$ >	$C_6H_5CH_2CH_2NH_2$ >	$C_6H_5CH_2NH_2$
γ-Phenyl-*n*-propylamine	β-Phenylethylamine	Benzylamine

III. Basicity of Aromatic amines

Aromatic amines are far less basic than ammonia and aliphatic amines. This may be explained as follows :

(*i*) *Due to resonance in aniline.* Aniline may be regarded as a resonance hydrid of the following structures :



I II III IV V

As a result of resonance, the lone pair of electrons on the nitrogen atom gets delocalized over the benzene ring and thus is less easily available for protonation. Therefore, aromatic amines are weaker bases than ammonia.

(*ii*) *Lower stability of anilinium ion than aniline.* If we compare the relative stabilities of aniline and the anilinium ion, which aniline forms by accepting a proton, we find that whereas aniline is a resonance hybrid of five structure. *i.e.* I—V, anilinium ion is a resonance hybrid of only two structures, *i.e.* VI and VII. Structures analogous to III, IV and V are not possible in this case due to localization of the lone pair of electrons on nitrogen because of the formation of an additional nitrogen-hydrogen bond.

VI VII

In other words, aniline is more stable than anilinium ion. Hence, aniline has very little tendency to combine with a proton to form anilinium ion. On the other hand, in case of ammonia and aliphatic amines, delocalization of the lone pair of electrons on the nitrogen atom by resonance is not possible. Furthermore, the electron density on the nitrogen atom is increased by electron-donating inductive effect of the alkyl groups. As a result, *ammonia and aliphatic amines are much stronger bases than aniline and other aromatic amines.*

Effect of substituents on the basicity of aromatic amines.

Let us now discuss the effect of substituents on the basicity of aromatic amines.

(*i*) **Effect of substituents on the nitrogen atom.** When the hydrogen atoms of the amino group in primary arylamines ($ArNH_2$) are replaced by electron donating alkyl groups, the basicity of the resultant arylamine increases. For example, N-methylaniline and N, N-dimethylaniline are stronger bases than aniline.

	$C_6H_5NH_2$	$C_6H_5NHCH_3$	$C_6H_5N(CH_3)_2$
pK_b	9·38	9·15	8·92

Conversely, if the hydrogen atoms of the amino group are replaced by electron withdrawing groups, the basicity decreases. For example, diphenylamine is a much weaker base than aniline and triphenylamine is too weak a base to measure its pK_b.

	$C_6H_5NH_2$	$(C_6H_5)_2NH$	$(C_6H_5)_3N$
pK_b	9·38	13·2	—

(*ii*) **Effect of nuclear substituents on the basicity of arylamines**

Table 9.2 lists the basicities of some substituted anilines.

TABLE 9.2. Basicities of some substituted anilines, pK_b for aniline = 9·38.

Substituent	pK_b	Substituent	pK_b	Substituent	pK_b
o-CH_3	9·62	m-CH_3	9·33	p-CH_3	9·00
o-OCH_3	9·51	m-OCH_3	9·80	p-OCH_3	8·71
o-NH_2	9·52	m-NH_2	9·00	p-NH_2	7·86
o-OH	9·28	m-OH	9·83	p-OH	8·50
o-NO_2	14·28	m-NO_2	11·55	p-NO_2	13·02
o-Cl	13·30	m-Cl	11·52	p-Cl	10·00

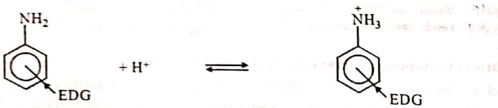
From the above table following points emerge :

(i) Electron-donating substituents tend to increase and electron withdrawing substituents tend to decrease the basicity of anilines and arylamines.

(ii) The base-weakening effect of the electron withdrawing substituents and base strengthening effect of the electron donating substituents is more marked at p-positions than at m-positions.

(iii) o-Substituted anilines are usually weaker bases than aniline regardless of the nature (electron donating or electron-withdrawing) of the substituent. This is called **ortho-effect** *and is probably due to a combination of steric and electronic factors.*

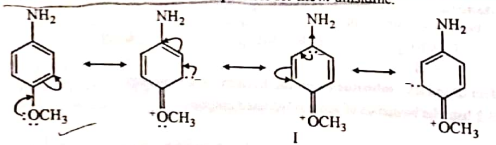
Explanation. Electron-donating substituents (*e.g.* $-CH_3$, $-OH$, $-NH_2$, $-OCH_3$ etc.) tend to increase the electron density on the nitrogen atom. As a result, the lone pair of electrons on the nitrogen atom is more easily available for protonation. At the same time, electron-donating substituents tend to disperse the positive charge of the substituted anilinium ion and thus increase their stability relative to the parent amines. The combined effect is that electron-donating substituents increase the basicity of aromatic amines relative to the parent amine.



EDG donates electrons, increases the electron density on N-atom, increases the basicity

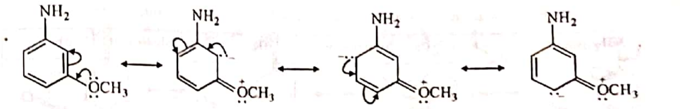
EDG donates electrons, stabilizes the substituted anilinium ion, increases the basicity

The base strengthening effect of the electron-donating substituents is more pronounced at *p*-position than at *m*-position. For example, *p*-anisidine ($pK_b = 8·71$) is more basic than *m*-anisidine ($pK_b = 9·80$). The reason being that in *p*-anisidine, one of the resonance structures *i.e.* (I), carries the negative charge on the carbon to which the amino group is attached. This structure directly increases the electron density on the nitrogen atom but no such resonance structure is possible for the *m*-anisidine.



I

Resonance structures of p-anisidine



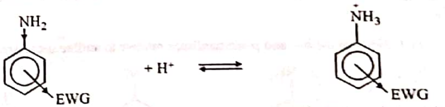
Resonance structures of m-anisidine

In other words, *p*-methoxy group increases the electron density more on the nitrogen atom than the *m*-methoxy group. Therefore, *p*-anisidine is a stronger base than *m*-anisidine.

It may be noted here that groups like OCH_3, OH etc. have both *electron-withdrawing inductive effect* **(–I-effect)** and electron-donating reaonsnace **(+ R–effect).** When such a group in present at *p*-position +R-effect outweights the –I-effect and thus the *overall effect is electron donating. As a result, p-methoxy-aniline is a stronger base than aniline.*

However, when $-OCH_3$ group is present at *m*-position, it can exert only –I-effect since resonance effect does not operate at *m*-position. This decreases the electron density on nitrogen atom and hence *m-methoxyaniline is a weaker base than aniline.*

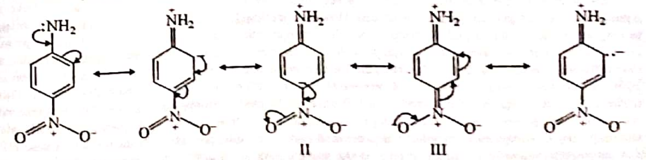
Conversely, the electron withdrawing substituents (*e.g.*, $-NO_2$, $-Cl$, $-\overset{+}{N}R_3$, $-COOH$ etc.) tend to decrease the electron density on the nitrogen atom. As a result, the lone pair of electrons on the nitrogen atom becomes less easily available for protonation and the basicity decreases. At the same time, electron-withdrawing substituents tend to intensify the positive charge of the substituted anilinium ion and thus decrease their stability relative to the parent amines. *The combined effect is that electron-withdrawing substituents decrease the basicity of aromatic amines relative to the parent amines.*



EWG withdraws electrons, decreases electron density on N-atom, decreases basicity

EWG withdraws electrons, destablizes the anilinium ion, decreases the basicity

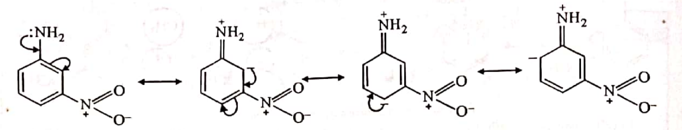
Here again, the base weakening effect of the electron-withdrawing substituents is more marked at *p*-position tham at *m*-position. For example, *p*-nitroaniline ($pK_b = 13·02$) is a weaker base than *m*-nitroaniline ($pK_b = 11·55$). The reason being that in *p*-nitroaniline, one of the resonating structures, *e.g.*, (II), carries the negative charge on the carbon to which $-NO_2$ group is attached. This structure directly decreases the electron density on the nitrogen atom by pushing the electrons from the $—NH_2$ group to the $—NO_2$ group



II

III

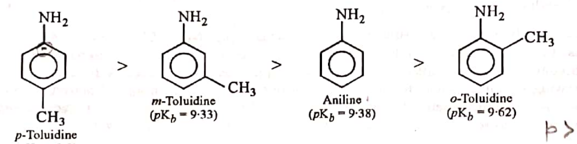
Resonance structures of p-nitroaniline



Resonance structures of m-nitroaniline

(II ↔ III). But no such resonance form is possible for the *m*-nitroaniline. In other words, *p*-nitro group decreases the electron density on nitrogen more than the *m*-nitro group. Therefore *p-nitroaniline is a weaker base than m-nitroaniline.*

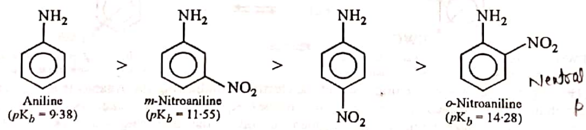
In the light of the above discussion, basicity of *o*-, *m*-, and *p*-toluidines relative to aniline decreases in the order :



p-Toluidine (pK_b = 9·0) > *m*-Toluidine (pK_b = 9·33) > Aniline (pK_b = 9·38) > *o*-Toluidine (pK_b = 9·62)

p > m > neutral > ortho

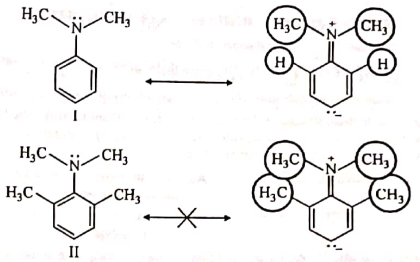
Similarly, the basicity of *o*-, *m*-, and *p*-nitroanilines relative to aniline decreases in the order :



Aniline (pK_b = 9·38) > *m*-Nitroaniline (pK_b = 11·55) > *p*-Nitroaniline (pK_b = 13·02) > *o*-Nitroaniline (pK_b = 14·28)

Neutral > meta > para > ortho

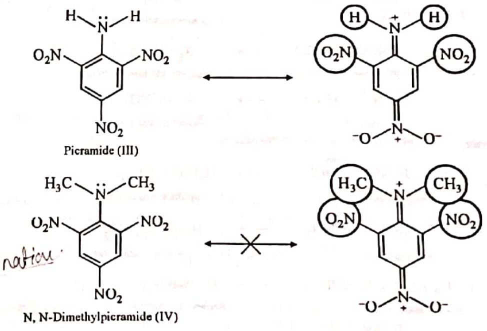
Steric effects. Since a proton occupies a very small volume, therefore, steric effects do not have any significant effect on proton-transfer reactions. However, steric effects may indirectly affect the base strength by interfering in resonance stabilization. Since for resonance to occur, it is essential that all the atoms must lie in a plane, therefore, any factor which prevents atoms from assuming coplanarity reduces resonance and thus influences the availability of electrons on the nitrogen atom. For example, *steric inhibition of resonance increases the base strength of N, N, 2, 6-tetramethylaniline (II) relative to N, N-dimethylaniline (I).* This is because the bulky *o*-methyl groups in amine (II) push the N-methyl groups out of plane of the benzene ring. As a result, the *p*-orbital on N containing the lone pair of electrons is no longer parallel to *p*-orbitals of benzene ring. Consequently resonance is prevented and hence lone pair of electrons on N in amine (II) is not contributed towards the benzene ring to the same extent as in amine (I). Therefore, the lone pair of electrons on N in amine (II) is more easily available for protonation than in amine (I) and hence *amine (II) is a stronger base than amine (I).*



I

II

On similar lines, we can explain that N, N-dimethylpicramide (IV) is a stronger base than picramide (III).



Picramide (III)

N, N-Dimethylpicramide (IV)

Cope elimination.
Curtius.

9.10. CHEMICAL PROPERTIES OF AMINES

The chemical properties of amines largely depend upon the presence of lone pairs of electrons on the nitrogen atom. Some important properties of amines are discussed below :

1. Basic character. As discussed above all the three classes of amines (1°, 2° and 3°) because of the presence of a lone pair of electrons on the nitrogen atom behave as bases. Their basic character is shown by the following reactions.

(*i*) Reaction with water. Due to the presence of a lone pair of electrons on the N-atom, amines like NH_3 are stronger bases than H_2O. Therefore, they react with water to form alkyl or arylammonium hydroxides which ionize to furnish hydroxyl ions :

$$\underset{\text{1° Amine}}{RNH_2} + H_2O \rightleftharpoons \underset{\text{Alkylamm. hydroxide}}{R\overset{+}{N}H_3OH^-} \rightleftharpoons R\overset{+}{N}H_3 + OH^-$$

$$(cf.\ NH_3 + H_2O \rightleftharpoons NH_4OH \rightleftharpoons NH_4^+ + OH^-)$$

Due to the formation of hydroxide ions, the aqueous solutions of amines are basic in nature.

The presence of the hydroxide ions in the aqueous solutions of amines is detected by the precipitation of metal hydroxides such as aluminium hydroxide (*gelatinous white ppt.*) or ferric hydroxide (*brown ppt.*) when $AlCl_3$ or $FeCl_3$ is added to their aqueous solutions.

$$AlCl_3 + 3\,OH^- \longrightarrow \underset{\text{Gelatinous white ppt.}}{Al(OH)_3} + 3\,Cl^-$$

$$FeCl_3 + 3\,OH^- \longrightarrow \underset{\text{Brown ppt.}}{Fe(OH)_3} + 3\,Cl^-$$

(ii) Reaction with acids. Being basic, all types of amines react with mineral acids such as HCl, HNO_3, H_2SO_4 etc. to form soluble salts.

$$\underset{\text{1°Amine}}{RNH_2} + HCl \longrightarrow \underset{\text{Alkylammonium chloride}}{R\overset{+}{N}H_3Cl^-}$$

$$\underset{\text{2° Amine}}{2\,R_2NH} + H_2SO_4 \longrightarrow \underset{\text{Dialkylammonium sulphate}}{[R_2\overset{+}{N}H_2]_2SO_4^{2-}}$$

$$\underset{\text{3° Amine}}{R_3N} + HNO_3 \longrightarrow \underset{\text{Trialkylammonium nitrate}}{R_3NH^+NO_3^-}$$

For example,

$$\underset{\text{Ethylamine}}{CH_3CH_2NH_2} + HCl \longrightarrow \underset{\text{Ethylammonium chloride}}{[CH_3CH_2\overset{+}{N}H_3]\bar{C}l}$$

$$\underset{\text{Dimethylamine}}{(CH_3)_2NH} + HNO_3 \longrightarrow \underset{\text{Dimethylammonium nitrate}}{[(CH_3)_2\overset{+}{N}H_2]\ NO_3^-}$$

$$\underset{\text{Aniline}}{C_6H_5NH_2} + HCl \longrightarrow \underset{\text{Anilinium chloride}}{[C_6H_5\overset{+}{N}H_3]\bar{C}l}$$

$$\underset{\text{N, N-Dimethylaniline}}{C_6H_5N(CH_3)_2} + CH_3COOH \longrightarrow \underset{\text{N, N-Dimethylanilinium acetate}}{[C_6H_5\overset{+}{N}H(CH_3)_2]^-OCOCH_3}$$

These amine salts are ionic compounds. They are non-volatile solids and generally decompose before their melting points are reached. They are soluble in water but are insoluble in non-polar solvents such as benzene, chloroform, ether etc. In contrast, higher amines are generally insoluble in water but are soluble in organic solvents. This difference in solubility behaviour of amines and their salts is often used to detect amines and separate (or purify) them from non-basic compounds.

Further, amines react with chloroplatinic acid (H_2PtCl_6) to form insoluble salts called *chloroplatinates.*

$$2RNH_2 + H_2PtCl_6 \longrightarrow \underset{\text{Chloroplatinate}}{(R\overset{+}{N}H_3)_2PtCl_6^{2-}}$$

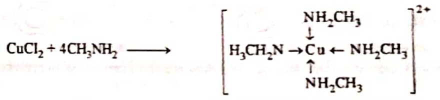
Chloroplatinates of amines are used for the determination of equivalent and molecular masses of amines.

2. Reaction with meta ions. Like ammonia, amines also form soluble *coordiination complexes* with transition metal ions such as Ag^+, Cu^{2+} ions etc. Thus, silver chloride dissolves in methylamine solution due to the formation of a soluble complex salt as shown below :

$$\underset{\substack{\text{Silver chloride}\\(\textit{Insoluble})}}{AgCl} + \underset{\text{Methylamine}}{2\,CH_3NH_2} \longrightarrow \underset{\text{Bis(methylamine)silver (I) chloride }(\textit{Soluble})}{[CH_3NH_2 \longrightarrow Ag \longleftarrow NH_2CH_3]^+\,Cl^- \text{ or } [Ag(CH_3NH_2)_2]^+Cl^-}$$

$$(cf.\ AgCl + 2\,NH_3 \longrightarrow [Ag(NH_3)_2]^+\ Cl^-)$$

Similarly like ammonia, amines such as methylamine, ethylamine etc. react with Cu^{2+} ions to form a deep blue solution due to the formation of the following soluble coordination complex.



$$\underset{\text{Methylamine}}{CuCl_2 + 4CH_3NH_2} \longrightarrow \underset{\substack{\text{Tetrakis(methylamine)copper (II) chloride}\\(\textit{Soluble})}}{\left[\begin{array}{c} NH_2CH_3 \\ \downarrow \\ H_3CH_2N \rightarrow Cu \leftarrow NH_2CH_3 \\ \uparrow \\ NH_2CH_3 \end{array}\right]^{2+}}$$

$$CuSO_4 + \underset{\text{Ethylamine}}{4\,CH_3CH_2NH_2} \longrightarrow \underset{\substack{\text{Tetrakis(ethylamine)copper (II) sulphate}\\(\textit{Soluble})}}{[Cu(CH_3CH_2NH_2)_4]^{2+}\ SO_4^{2-}}$$

$$(cf.\ CuCl_2 + 4\,NH_3 \longrightarrow [Cu(NH_3)_4]^{2+}\ (Cl^-)_2)$$

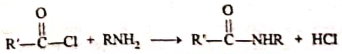
3. Alkylation. Both aliphatic and aromatic primary secondary and tertiary amines react with alkyl halides to form secondary and tertiary amines and quaternary ammonium salts respectively.

$$\underset{\text{1° Amine}}{RNH_2} \xrightarrow[-HX]{+RX} \underset{\text{2° Amine}}{R_2NH} \xrightarrow[-HX]{+RX} \underset{\text{3° Amine}}{R_3N} \xrightarrow{+RX} \underset{\text{Quaternary amm. halide}}{R\overset{+}{N}X^-}$$

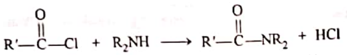
This process of introducing an alkyl group into any molecule is called **alkylation.** In case of amines alkylation occurs through nucleophilic substitution reactions on alkyl halides.

This process of converting an amine (1°, 2° or 3°) into its quaternary ammonium salt on treatment with excess of an alkyl halide is called exhaustic alkylation. However, if the alkyl halide used is methyl iodide, the process is commonly known as **exhaustive methylation.**

4. Acylation—Reaction with acid chlorides and acid anhydrides. Primary and secondary amines (but not tertiary amines because they do not contain a H-atom on the N-atom) undergo *nucleophilic acylation reactions* when treated with acid chlorides or acid anhydrides to form N-substituted amides. Thus,



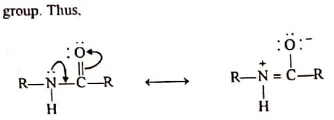
$$\underset{\text{Acid chloride}}{R'\!-\!\overset{\overset{O}{\|}}{C}\!-\!Cl} + \underset{\text{1° Amine}}{RNH_2} \longrightarrow \underset{\text{N-Substituted amide}}{R'\!-\!\overset{\overset{O}{\|}}{C}\!-\!NHR} + HCl$$



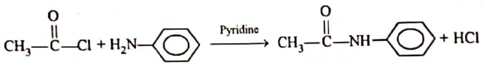
$$R'-\overset{\overset{O}{\|}}{C}-Cl + R_2NH \longrightarrow R'-\overset{\overset{O}{\|}}{C}-NR_2 + HCl$$

Acid chloride 2° Amine N, N-Disubstituted amide

Unlike alkylation reactions of amines, the amides formed here do not react further with acid chlorides/anhydrides because the amide is non-basic and a poor nucleophile due to delocalization of its lone pair of electrons on the carbonyl group. Thus,

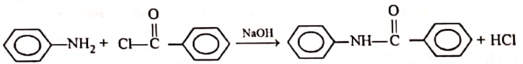


Acylation with aliphatic acid chlorides and anhydrides is usually carried out in presence of pyridine.



Acetyl chloride Aniline Acetanilide

However with aromatic acid chlorides, acylation is usually carried out in presence of aqueous NaOH solution.



Aniline Benzoyl chloride Benzanilide

This reaction is called **Schotten-Baumann reaction**

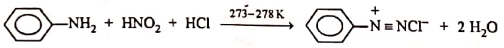
The process of acylation is often used for identification of aliphatic and aromatic 1° and 2° amines. This is because acyl derivatives particularly acetyl or benzoyl derivatives of these amines are generally crystalline solids having sharp melting points.

5. Reaction with nitrous acid. Primary, secondary and tertiary amines react differently with nitrous acid. Since nitrous acid is *unstable*, it is prepared *in situ* by the action of *dilute hydrochloric acid on sodium nitrite*.

(a) Primary amines

(*i*) *Aromatic primary amines* react with nitrous acid at 273–278 K (0–5°C) to form arenediazonium salts. Thus,

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



Aniline Benzenediazonium chloride

This reaction of converting aromatic primary amines into diazonium salts by treatment with a cold (273–278 K) solution of nitrous acid is called **diazotisation.**

(*ii*) *Primary aliphatic amines also react with cold nitrous acid to yield diazonium salts.* But aliphatic diazonium salts are **unstable** even in the cold (273–278 K) and decompose as soon as they are formed to give a complex mixture consisting of alcohols, alkenes, alkyl halides with the quantitative evolution of N_2 gas.

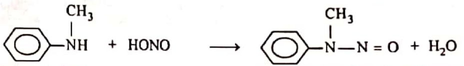
$$\underset{1^\circ \text{ Amine}}{RNH_2} \xrightarrow[273\text{-}278\,K]{NaNO_2/HCl} \underset{\substack{\text{Diazonium salt}\\(\textit{unstable even in the cold})}}{[R-\overset{+}{N}\equiv NCl^-]} \xrightarrow{\text{Decomposes}} N_2 + \text{Alcohols} + \text{Alkenes} + \text{Alkyl halides}$$

The quantitative evolution of N_2 in this reaction forms the basis of **Van Slyke method** for estimation of primary amino groups in amino acids and proteins.

Since no other class of amines liberates N_2 gas on treatment with HNO_2, *this reaction is used as a test for aliphatic primary amines.*

(*b*) **Secondary amines.** *Both aliphatic and aromatic secondary amins* react with nitrous acid to give *N-nitrosoamines* which being insoluble in dilute mineral acids separate out as yellow oily compounds :

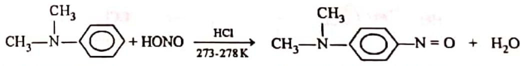
$$\underset{2^\circ \text{ Amine}}{R_2NH} + HONO \longrightarrow \underset{\text{N-Nitrosodialkylamine } (\textit{yellow oil})}{R_2N-N=O} + H_2O$$



N-Methylaniline N-Nitroso-N-methylaniline (*yellow oil*)

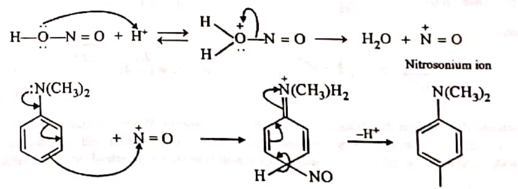
These N-nitrosoamines on warming with a crystal of phenol and a few drops of conc. H_2SO_4 form a green solution which when made alkaline with aqueous NaOH, turns deep blue and then red on dilution. This reaction is called **Liebermann's nitroso reaction** *and is used as a test for secondary amines.*

(*c*) **Aromatic tertiary amines** undergo electrophilic substitution with *nitrosonium ion* at *p*-position of the phenyl ring to form green-coloured *p-nitrosoamines.* For example,



N, N-Dimethylaniline *p*-Nitroso-N, N-dimethylaniline (*green*)

Mechanism. Protonation of nitrous acid followed by loss of water generates *nitrosonium ion* which attacks the benzene ring at the less hindered *p*-position to afford the product as shown below :



It may be emphasized here that as compared to electrophilic species involved in halogenation, nitration, sulphonation etc., nitrosonium ion is a very weak electrophile and thus reacts only with aromatic compounds containing strongly activating groups such as dialkylamino ($-NR_2$) and hydroxy ($-OH$) groups.

Aliphatic tertiary amines, on the other hand, react with nitrous acid to form *water soluble nitrite* salts

$$\underset{3^\circ\text{ Amine}}{R_3N} + HONO \longrightarrow \underset{\text{Trialkylammonium nitrite}}{R_3\overset{+}{N}HNO_2^-}$$

Sometimes these amine salts decompose to yield N-nitroso derivative of the secondary amine alongwith an aldehyde or a ketone.

$$R_3\overset{+}{N}HNO_2^- \longrightarrow R_2N{-}N{=}O + \text{Aldehyde or ketone}$$

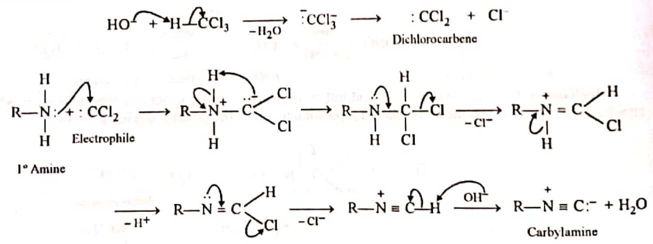
Thus, it is evident from the above discussion that *reaction with nitrous acid can be used for the distinction of 1°, 2° and 3° amines and in some cases, it is also possible to determine whether the amine is aliphatic or aromatic.*

6. Carbylamine reaction or Isocyanide test. Both aliphatic and aromatic primary amines when warmed with chloroform and an alcoholic solution of KOH produce **isocyanides** or **carbylamines** which have very unpleasant odours.

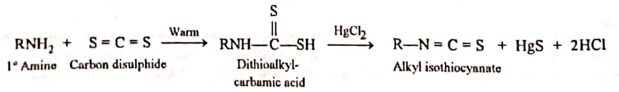
$$\underset{1^\circ\text{ Amine}}{R{-}NH_2} + \underset{\text{Chloroform}}{CHCl_3} + 3KOH\,(alc.) \xrightarrow{\Delta} \underset{\substack{\text{Alkyl isocyanide or}\\ \text{Alkyl carbylamine}}}{R{-}N\overset{\rightarrow}{=}C} + 3KCl + 3H_2O$$

In contrast, secondary and tertiary amines (both aliphatic and aromatic) do not give this test. Therefore, this test is used to *distinguish primary amines from secondary and tertiary amines.*

Mechanism. This reaction is believed to occur through intermediate formation of dichlorocarbene as shown below :



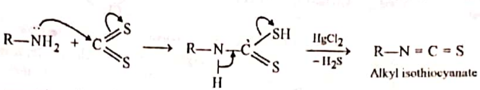
7. Reaction with carbon disulphide. (*a*) *With aliphatic amines.* When warmed with carbon disulphide, aliphatic primary amines form *dithioalkylcarbamic acids* which decompose on heating with mercuric chloride to give *alkyl isothiocyanates* having a characteristic smell like that of mustard oil. For example,



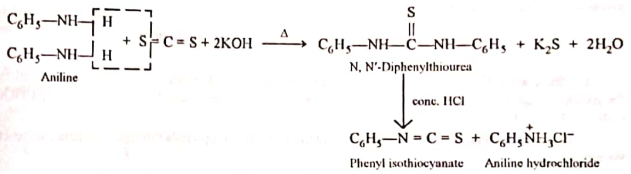
$$\underset{1^\circ\text{ Amine}}{RNH_2} + \underset{\text{Carbon disulphide}}{S{=}C{=}S} \xrightarrow{\text{Warm}} \underset{\substack{\text{Dithioalkyl-}\\ \text{carbamic acid}}}{RNH{-}\overset{\overset{S}{\|}}{C}{-}SH} \xrightarrow{HgCl_2} \underset{\text{Alkyl isothiocyanate}}{R{-}N{=}C{=}S} + HgS + 2HCl$$

This reaction is called **Hofmann mustard oil reaction** *and is used as a test for primary amines.*

Mechanism. This reaction is believed to occur through nucleophilic attack on C = S followed by loss of H_2S



(*b*) *With aromatic amines.* Aromatic primary amines, however, react in a slightly differnt manner. For example, when aniline is heated with ethanolic CS_2, and solid KOH, it gives N, N′-diphenylthiourea which upon treatment with conc. HCl gives phenyl isothiocyanate.



$$\underset{\text{Aniline}}{\begin{matrix}C_6H_5{-}NH{-}H\\ C_6H_5{-}NH{-}H\end{matrix}} + S{=}C{=}S + 2KOH \xrightarrow{\Delta} \underset{\text{N, N'-Diphenylthiourea}}{C_6H_5{-}NH{-}\overset{\overset{S}{\|}}{C}{-}NH{-}C_6H_5} + K_2S + 2H_2O$$

$$\xrightarrow{\text{conc. HCl}} \underset{\text{Phenyl isothiocyanate}}{C_6H_5{-}N{=}C{=}S} + \underset{\text{Aniline hydrochloride}}{C_6H_5\overset{+}{N}H_3Cl^-}$$

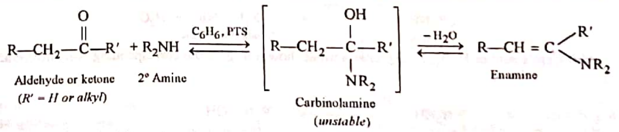
N, N-Diphenylthiourea (or thiocarbanilide or *sym*-diphenylthiourea) is used as an accelerator during vulcanization of rubber.

8. Reaction with aldehydes and ketones. *Primary amines* (both aliphatic and aromatic) react with aldehydes and ketones in presence of a trace of an acid as catalyst to produce azomethines called **Schiff's bases or anils.**

$$\underset{1^\circ\text{ Amine}}{RNH_2} + \underset{\text{Aldehyde}}{O{=}CHR} \xrightarrow{H^+} \underset{\text{Schiff's base or Anil}}{RN{=}CHR} + H_2O$$

e.g. $$\underset{\text{Benzaldehyde}}{C_6H_5CH{=}O} + \underset{\text{Aniline}}{H_2N{-}C_6H_5} \xrightarrow{H^+} \underset{\text{Benzylideneaniline}}{C_6H_5CH{=}NC_6H_5} + H_2O$$

Secondary amines also react with aldehydes and ketones containing α-hydrogen atom/s to form first *carbinolamines* which being unstable readily lose a molecule of H_2O to form stable **enamines.** Thus,

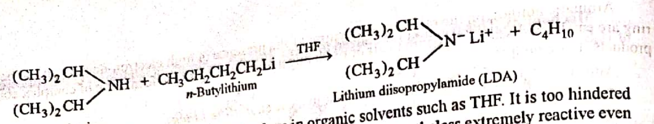


$$\underset{\substack{\text{Aldehyde or ketone}\\ (R' = H \text{ or alkyl})}}{R{-}CH_2{-}\overset{\overset{O}{\|}}{C}{-}R'} + \underset{2^\circ\text{ Amine}}{R_2NH} \xrightleftharpoons{C_6H_6,\ PTS} \underset{\substack{\text{Carbinolamine}\\ (unstable)}}{\left[R{-}CH_2{-}\underset{NR_2}{\overset{OH}{C}}{-}R'\right]} \xrightleftharpoons{-H_2O} \underset{\text{Enamine}}{R{-}CH{=}C\begin{smallmatrix}R'\\ NR_2\end{smallmatrix}}$$

9. Acidic nature. Although amines are essentially basic in nature, primary and secondary amines (but not tertiary amines since they do not a hydrogen present on nitrogen atom) can also act as weak acids when treated with strong bases such as sodium metal, *n*-butyllithium etc.

$$\underset{1^\circ\text{ Amine}}{2RNH_2} + 2Na \xrightarrow{\Delta} \underset{\text{Sodium alkyl amide}}{2RNH^-Na^+} + H_2$$

e.g.



$$(CH_3)_2CH\text{—}NH(\text{—}CH(CH_3)_2) + CH_3CH_2CH_2CH_2Li \xrightarrow{THF} ((CH_3)_2CH)_2N^-\,Li^+ + C_4H_{10}$$

Diisopropylamine n-Butylithium Lithium diisopropylamide (LDA)

LDA is an exceedingly powerful base. It dissolves in organic solvents such as THF. It is too hindered to add to the carbonyl group in nucleophilic addition reactions, but is nevertheless extremely reactive even at 199 K.

Primary and secondary amines (but not tertiary amines because they do not contain a hydrogen on the nitrogen atom) also react with Grignard reagents (strong bases) to form alkanes corresponding to the alkyl group of the Grignard reagent.

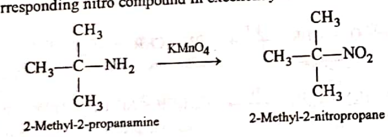
$$\underset{1°\ \text{Amine}}{R\text{—}NH_2} + \underset{\text{Alkane}}{R'\text{—}MgX} \xrightarrow{\text{Dry ether}} R'\text{—}H + Mg(NHR)X$$

10. Oxidation. Oxidation of amines gives different products depending upon the nature of amine and the oxidising agent. The oxidising agents which are commonly used are H_2O_2, peroxyacids (RCOOOH), Caro's acid (H_2SO_5) etc.

(*i*) **Primary aliphatic amines** undergo oxidation to nitro compounds through a sequence of reactions shown below :

$$\underset{1°\ \text{Amine}}{R\text{—}NH_2} \xrightarrow{[O]} \underset{\text{Hydroxylamine}}{RNHOH} \xrightarrow[-H_2O]{[O]} \underset{\text{Nitroso compound}}{R\text{—}N=O} \xrightarrow{[O]} \underset{\text{Nitro compound}}{R\text{—}NO_2}$$

Primary amines in which the —NH_2 group is attached to a tertiary carbon can be oxidised with $KMnO_4$ to the corresponding nitro compound in excellent yield



$$CH_3\text{—}C(CH_3)_2\text{—}NH_2 \xrightarrow{KMnO_4} CH_3\text{—}C(CH_3)_2\text{—}NO_2$$

2-Methyl-2-propanamine 2-Methyl-2-nitropropane (83%)

(*ii*) **Secondary aliphatic amines** on oxidation with $KMnO_4$ give tetra-alkylhydrazines.

$$\underset{2°\ \text{Amine}}{2R_2NH} \xrightarrow{KMnO_4} \underset{\text{Tetralkylhydrazine}}{R_2N\text{—}NR_2} + H_2O$$

With Caro's acid or H_2O_2, 2° aliphatic amines, however, give the corresponding N-hydroxylamines

$$\underset{2°\ \text{Amine}}{R_2NH} \xrightarrow{H_2SO_5 \text{ or } H_2O_2} \underset{\text{N-Hydroxylamine}}{R_2N\text{—}OH}$$

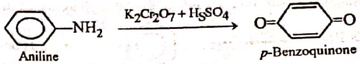
(*iii*) **Tertiary aliphatic amines** are not oxidised by $KMnO_4$ but are oxidised to the corresponding amine N-oxides by Caro's acid, ozone or H_2O_2.

$$\underset{3°\ \text{Amine}}{R_3N} + [O] \xrightarrow{RCOOH \text{ or } H_2O_2 \text{ or } H_2SO_5} \underset{3°\ \text{Amine-N-oxide}}{R_3N \rightarrow O}$$

Aromatic amines, on the other hand, because of the presence of high electron-density on the be ring are easily oxidised on exposure to air or oxidising agents leading to the formation of complex co products. For example,

Aniline + $K_2Cr_2O_7 + H_2SO_4 \longrightarrow$ A black dye called *aniline black*

Controlled oxidation of aniline with $K_2Cr_2O_7 + H_2SO_4$, however, gives *p*-benzoquinone.



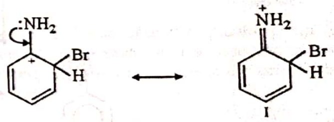
Aniline *p*-Benzoquinone

11. Electophilic substitution reactions. In addition to the reactions of the amino group, ar amines also undergo typical electrophilic substitution reactions of the aromatic ring. In all these rea the NH_2 or NHR or NR_2 group strongly activates the aromatic ring through delocalization of the lo of electrons of the N-atom over the aromatic ring (refer to structures I–V on page 343).

As a result, electron density increases more at *o*- and *p*-positions as compared to *m*-positions. The the –NH_2 group directs the incoming group to *o*- and *p*-positions, *i.e.*, –NH_2 *is an o-, p-directing*

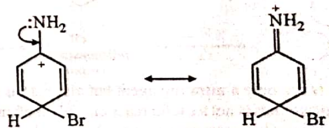
Due to the strong activating effect of the –NH_2 group, *aromatic amines undergo electrophilic subs reactions readily and it is* difficult to stop the reaction at the monosubstitution stage. Usually the proceeds to give 2, 4, 6-trisubstituted amines. The high reactivity of aromatic amines towards elect substitution reactions is due to the fact that, in addition to the usual resonating structures that stab intermediate carbocation, the following resonance structures (I and II) formed by the interaction of pair of electrons on the nitrogen atom with the positively charged carbon atom of the ring also increase the stability of the carbocation intermediate formed during attack of the Br^+ ion at *o*- positions respectively.

***o*-Bromination :**



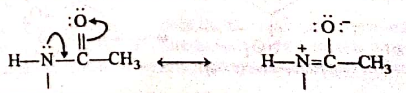
I

***p*-Bromination :**



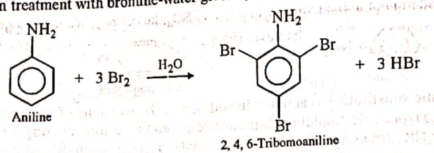
II

However, sometimes a monosubstitution product is required. In order to do so, the activat the amino group is reduced by acetylation. The acetyl group being electron-withdrawing attra pair of electrons of the N-atom towards itself. As a result, the activating effect of the ami reduced. This *method is known as* **protection** *of the amino group by acetylation and can be use the rate of substitution and to prevent the formation of di- and tri-substitution products.*

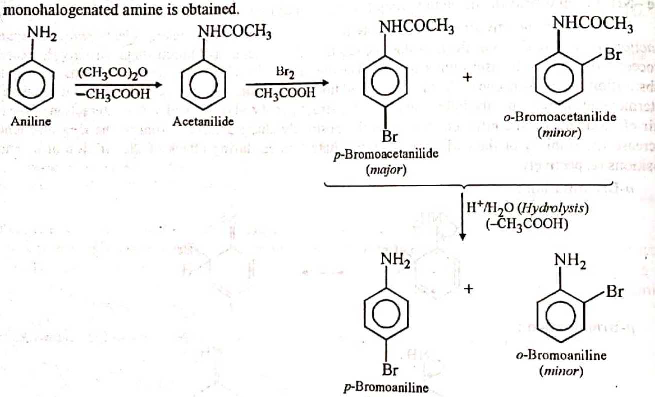


Some typical electrophilic substitution reactions of aromatic amines are discussed below :

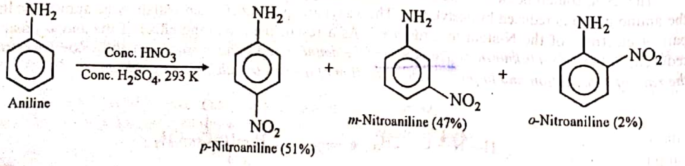
(*i*) **Halogenation.** Due to the strong activating effect of the amino group, halogenation of amines occurs very fast and the halogen enters the *p*- and both the *o*-positions even in the absence of a catalyst. For example, aniline on treatment with bromine-water gives 2, 4, 6-tribromoaniline.



If however, a monohalogenated derivative is required, the amino group is first acetylated and then halogenation of the ring is carried out. After halogenation, the acetyl group is removed by hydrolysis and the monohalogenated amine is obtained.

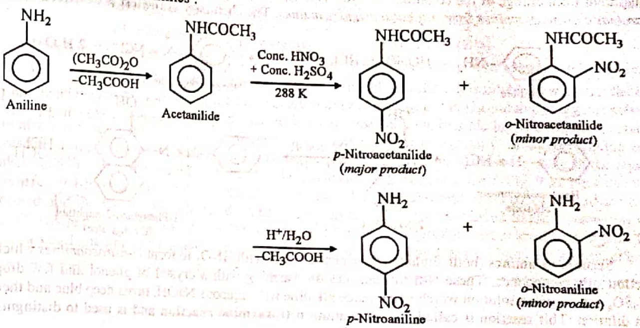


(*ii*) **Nitration.** Nitric acid is not only a nitrating agent but also acts as a strong oxidizing agent. As a result, direct nitration of aromatic amines is not a useful reaction since it often gives tarry oxidation products along with some nitration products. However, under controlled conditions, nitration of aniline gives a mixture of *p*-nitroaniline and *m*-nitroaniline in approx. 1 : 1 ratio.

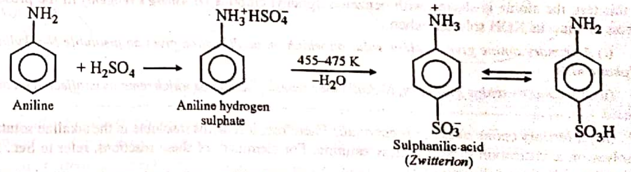


The reason for formation of larger amount of unexpected *m*-nitroaniline is that under strongly acidic conditions of nitration, most of the aniline is converted into anilinium ion and since $-\overset{+}{N}H_3$ is a *m*-directing group, therefore, an unexpectedly large amount of *m*-nitroaniline is obtained.

Therefore, to avoid these problems, the most convenient method to carry out the nitration of aniline is to first protect the amino group by acetylation. The acetyl group is finally removed by hydrolysis to give a mixture of *o*- and *p*-notroanilines :



(*iii*) **Sulphonation.** In spite of the presence of activating amino group, sulphonation of aromatic amines occurs only under drastic conditions. For example, when aniline is treated with conc. H_2SO_4 at 455–475 K, it gives *p*-aminobenzenesulphonic acid also called *sulphanilic acid.* This reaction is believed to occur through the amine salt as depicted below :



Sulphanilic acid contains both an acidic (SO_3H) as well as a basic (NH_2) group. It is, therefore, quite understandable that sulphanilic acid exists as an internal salt. During the formation of this salt, the NH_2 group has accepted the proton donated by the SO_3H group. Such types of internal salts are called *dipolar ions or zwitterions*. Due to zwitterion character, sulphanilic acid has high melting point and is practically insoluble in water and organic solvents.

Sulphanilic acid is an important intermediate in the manufacture of dyes and drugs. Sulphanilic acid and its derivatives are also used in the manufacture of well-known sulpha drugs such as sulphathiazole, sulphadiazine, sulphapyridine etc. which are widely used against bacterial infections.