1. INTRODUCTION

Amines are organic derivatives of ammonia with one or more alkyl or aryl groups bonded to the nitrogen atom. Amines serve many functions in living organisms, such as bioregulation, neurotransmission, and defense against predators. Because of their high degree of biological activity, many amines are used as drugs and medicines.

The alkaloids are an important group of biologically active amines, mostly synthesized by plants to protect them from being eaten by insects and other animals. Although some alkaloids are used medicinally (chiefly as painkillers), all alkaloids are toxic and cause death if taken in large quantities.

2. CLASSIFICATION

Amines are classified as **primary** (1°) , **secondary** (2°) , or **tertiary** (3°) , corresponding to one, two or three alkyl or aryl groups bonded to nitrogen.

| Туре | Examples |
|-------------------------------------|--|
| Primary (1°) R—NH ₂ | $\begin{array}{c} \text{CH}_3 \\ \vdots \\ \text{NH}_2 \text{ , } \\ \text{H}_3\text{C} \begin{array}{c} \text{CH}_3 \\ \vdots \\ \text{CH}_3 \\ \text{CH}_3 \\ \end{array} \\ \text{Cyclohexylamine (1°)} \\ \end{array}$ |
| Secondary (2°) R ₂ NH | $\begin{array}{c c} CH_2CH_3 & \vdots \\ N: & N: \\ H & H \\ N-Ethylaniline (2^\circ) & Piperidine (2^\circ) \end{array}$ |
| Tertiary (3°) R ₃ N | $\begin{array}{c} \text{CH}_2\text{CH}_3\\ \text{N:} \\ \text{N:} \\ \text{CH}_2\text{CH}_3 \\ \text{N, N-Diethylaniline (3°)} \text{Quinuclidine (3°)} \end{array}$ |

Quaternary ammonium salts have four alkyl or aryl bonds to a nitrogen atom. The nitrogen atom bears a positive charge, just as it does in simple ammonium salts such as ammonium chloride. The following are examples of quaternary (4°) ammonium salts.

$$\begin{array}{c|c} \operatorname{CH_3CH_2} & \operatorname{I}^{\Theta} \\ \downarrow_{\bigoplus} \\ \operatorname{H_3CH_2C-N-CH_2CH_3} \\ & \operatorname{CH_2CH_3} \end{array}$$
 Tetraethylammonium Iodide

3. STRUCTURE OF AMINES

Ammonia has a slightly distorted tetrahedral shape. A lone pair of nonbonding electrons occupies one of the tetrahedral positions. This geometry is represented by sp³ hybridization of nitrogen, with the bulky lone pair compressing the H—N—H bond angles to 107° from the "ideal" sp³ bond angle of 109.5°. Trimethylamine shows less angle compression because the bulky methyl groups open the angle slightly.

A tetrahedral amine with three different substituents (and a lone pair) is non-superimposable on its mirror image. In most cases, we cannot resolve such an amine into two enantiomers, however, because the enantiomers interconvert rapidly. This interconversion takes place by **nitrogen inversion**, in which the lone pair moves from one face of the molecule to the other.

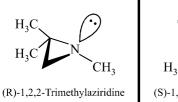
$$\begin{array}{c} sp^3 \ orbital \\ \hline \\ N \\ \hline \\ C_2H_5 \\ \hline \\ (R) \ -ethylmethylamine \end{array} \begin{array}{c} p \ orbital \\ \hline \\ H \\ \hline \\ N \\ \hline \\ C_2H_5 \\ \hline \\ (S) \ -ethylmethylamine \\ \hline \\ (S) \ -ethylmethylamine \\ \hline \end{array}$$

In case of quaternary ammonium salts with asymmetic nitrogen atoms, inversion of configuration is not possible because there is no lone pair to undergo nitrogen inversion.

$$(CH_3)_2CH_{\text{MM}} \xrightarrow{N} CH_2CH_3 H_3CH_2C \xrightarrow{N_{\text{cut}}} CH(CH_3)_2 CH_3$$

$$(R) \qquad (S)$$

Amines that cannot attain the sp²-hybrid transition state for nitrogen inversion also show chirality. If the nitrogen atom is contained in a small ring, for example, it is prevented from attaining the 120° bond angles that facilitate inversion



$$CH_3$$
 CH_3
 CH_3
(S)-1,2,2-Trimethylaziridine

4. PHYSICAL PROPERTIES

4.1 State

The lower aliphatic amines are gases with fishy odour. Primary amines with three or more carbon atoms are liquid and higher ones are solid.

Aniline and other aryl amines are usually colourless but gets coloured on storage due to atmospheric oxidation.

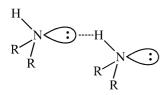
4.2 Dipole Moment

Amines are strongly polar because the large dipole moment of the lone pair of electrons adds to the dipole moments of the $C \leftarrow H$ and $H \leftarrow N$ bonds.

$$\bigcap_{\substack{N \text{ injuly} \\ \text{CH}_3}} \operatorname{CH}_2 \operatorname{CH}_3 \stackrel{\text{overall}}{\downarrow} \underset{\text{moment}}{\operatorname{dipole}}$$

4.3 Solubility

Primary and secondary amines have N—H bonds, allowing them to form hydrogen bonds. Having no N—H bonds, pure tertiary amines cannot engage in hydrogen bonding. They can, however, accept hydrogen bonds from molecules having O—H or N—H bonds.



1° or 2° Amine: Hydrogen Bond Donor and Acceptor

3° Amine: Hydrogen Bond Acceptor only

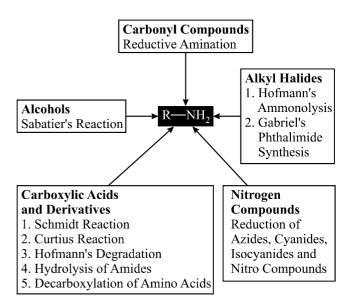
Therefore, lower aliphatic amines are soluble in water because they can form hydrogen bonds with water. However, solubility decreases with increase in molar mass of amines due to increase in size of the hydrophobic alkyl part. Higher amines are essentially insoluble in water.

4.4 Boiling Point

Because nitrogen is less electronegative than oxygen, the N—H bond is less polar than O—H bond. Therefore, amines form weaker hydrogen bonds than do alcohols of similar molecular weights. Primary and secondary amines have boiling points that are lower than those of alcohols, yet higher than those of ethers of similar molecular weights. With no hydrogen bonding, tertiary amines have lower boiling points than primary and secondary amines of similar molecular weights.

| Compound | BP(°C) | Туре | Molecular Weight |
|--|--------|--------------------|---------------------|
| (CH ₃) ₃ N: | 3 | Tertiary Amine | 59 |
| CH ₃ —O—CH ₂ —CH ₃ | 8 | Ether | 60 |
| CH ₃ —NH—CH ₂ —CH ₃ | 37 | Secondary Amine | 59 |
| CH ₃ CH ₂ CH ₂ —NH ₂ | 48 | Primary Amine | 59 |
| CH ₃ CH ₂ CH ₂ —OH | 97 | Alcohol | 60 |

5. PREPARATION OF AMINES



5.1 Alkyl Halides

5.1.1 Hofmann's Ammonolysis Method

It is an **ammonolysis**. An alkyl halide and an ethanolic solution of ammonia are heated in a sealed tube at 100°C.

- (a) The process gives a mixture of products.
- (b) Tertiary alkyl halide is not suitable as it gives an alkene.
- (c) Reaction follows bimolecular substitution (S_{N} 2).

Example - 1

$$CH_3Br + NH_3 \longrightarrow CH_3 \overset{\bigoplus}{N} H_3Br \overset{\bigoplus}{\Gamma}$$

$$CH_3NH_2 + NH_4Br$$

$$CH_{3}NH_{2} + CH_{3}Br \longrightarrow (CH_{3})NH_{2}Br^{\Theta}$$

$$NH_{3}$$

$$NH_{4}Br + (CH_{3})_{2}NH$$

$$(CH_3)_2NH + CH_3Br \longrightarrow (CH_3)_3NHBr^{\ominus}$$

$$\downarrow NH_3$$

$$(CH_3)_4NBr^{\ominus} \stackrel{CH_3Br}{\longleftarrow} NH_4Br + (CH_3)_3N$$

5.1.2 Gabriel's Phthalimide Synthesis

Phthalamide is treated with KOH first and then potassium phthalamide is heated with alkyl halide to yield alkyl phthalamide. The subsequent hydrolysis produces exclusively 1° amine.

Alkyl phthalamide is also treated with hydrazine to get a better yield of 1° amine.

Example - 2

5.1.3 Grignard Reagent

Grignard reagent or a trialkyl borane on treatment with chloramine gives the primary amine.

$$RMgX + ClNH_2 \longrightarrow R - NH_2 + MgXCl$$

5.2 Alcohols

5.2.1 Sabatier Reaction

Alcohols and ammonia are heated underpressure in the presence of a catalyst e.g., **copper chromite or alumina**. A mixture of products is obtained.

Example - 3

$$CH_{3}CH_{2} \longrightarrow OH \xrightarrow{NH_{3}} CH_{3}CH_{2} \longrightarrow NH_{2} + H_{2}O$$

$$CH_{3}CH_{2}OH$$

$$(CH_{3}CH_{2})_{3}N + H_{2}O \xrightarrow{CH_{3}CH_{2}OH} (CH_{3}CH_{2})_{2}NH + H_{2}O$$

5.3 Carbonyl Compounds

5.3.1 Reductive Amination

Several aldehydes and ketones are converted into amines by reduction in the presence of ammonia.

Reduction can be accomplished catalytically, (hydrogen (20-150 atm) over Raney nickel at 40-150°C or by use of sodium cyanohydridoborate, NaBH,CN).

Example - 4

$$CH_3(CH_2)_5CHO \xrightarrow{NH_3; H_2, Ni} CH_3(CH_2)_5CH_2NH_2$$
Heptanal 1-Aminoheptane

Example - 5

$$CH = O \xrightarrow{NH_3; H_2, Ni} CH_2NH_2$$
Benzylamine

Example - 6

$$\begin{array}{c} & & C \\ & &$$

Example - 7

$$R - C - H + CH_3CH_2NH_2 \xrightarrow{H_2, Ni} R - CH_2 - NHCH_2CH_3$$

5.4 Carboxylic Acids & Derivatives

5.4.1 Schmidt Reaction

A treatment of cold conc. H₂SO₄ to the mixture of carboxylic acid and hydrazoic acid gives 1° amine.

$$RCOOH + N_3H \xrightarrow{Cold conc.} RNH_2 + CO_2 + N_2$$

Note...

- 1. The product molecule contains one carbon atom less than that in acid.
- 2. Isocyanate is formed as an intermediate in the reaction.

Example - 8

$$\begin{array}{c|c} & & & & \\ & & & & \\ & + & N_3 H & \xrightarrow{Cold \; conc.} & & \\ & & + & CO_2 + N_2 \end{array}$$

5.4.2 Curtius Reaction

The reaction involves the pyrolysis of acyl azide to produce isocyanates. The subsequent hydrolysis gives amine.

Example - 9

$$CH_{3}(CH_{2})_{2}CH_{2}CN_{3} \xrightarrow{\Delta} CH_{3}(CH_{2})_{2}CH_{2}-N=C=O$$

$$\downarrow^{H_{2}O}$$

$$CH_{3}(CH_{2})_{2}CH_{2}NH_{2}$$

Example - 10

$$\begin{array}{c}
O \\
\parallel \\
+ \text{NaN}_3
\end{array}$$

$$NH_2 \longrightarrow N = C = O$$

5.4.3 Hofmann's Degradation of Amides

Amide is warmed with bromine and concentrated aqueous KOH or NaOH solution.

- (a) Product is 1° amine having one carbon less than amide.
- (b) Alkyl isocyanate is the intermediate and rearrangement is intramolecular.

Example - 11

$$\begin{array}{c} \text{CONH}_2 \\ + \\ \text{OBr}^{\Theta} \end{array}$$

5.4.4 Hydrolysis of Amides & Isocyanides

N-substituted amide and isocyanide on hydrolysis give 1° amine.

Example - 12

$$CH_{3}CH_{2}CNH_{2} \xrightarrow{(I) OH} CH_{3}CH_{2}CNHR$$

$$\downarrow O \\ OH$$

$$CH_{3}CH_{2}CNHR$$

$$\downarrow O$$

$$OH$$

$$CH_{3}CH_{2}CO + RNH_{2}$$

Example - 13

$$R \longrightarrow NC \xrightarrow{KOH, H_2O} R \longrightarrow NH_2 + HCOOK$$

Hydrolysis of Isocyanates also yields amines.

5.4.5 Decarboxylation of Amino Acids

Amino acids on heating with barium hydroxide gives 1° amine.

Quaternary ammonium hydroxide on heating gets decomposed into alcohol if β -hydrogen is not present in the alkyl group but if there is β -hydrogen, **Hofmann elimination** proceeds.

$$\begin{array}{c} \text{NH}_2 \\ + \text{Ba(OH)}_2 \xrightarrow{\Delta} \text{RCH}_2 \text{NH}_2 + \text{BaCO}_3 \downarrow + \text{H}_2 \text{O} \\ \text{COOH} \end{array}$$

5.5 Nitrogen Compounds

5.5.1 Reduction of Cyanides, Isocyanides, Oximes, Imines

Nitrile (—CN), oxime (—NOH), imine (—NH), enamine etc. on catalytic reduction with H₂, Ni give the corresponding amine.



- **1** 1. The reduction of nitrile by Na/C₂H₅OH is known as **Mendius reaction**.
- 2. In most of the cases $LiAlH_4$ is also effective for reduction.
- 3. Reduction of alkyl isocyanides with Na/C₂H₅OH or H₂/Pt gives 2° amine.

Example - 14

$$CH_3CH_2C = N \xrightarrow{H_2, \text{ Ni, } \Delta} CH_3CH_2CH_2NH_2$$

$$Na, C_2H_5OH$$

Example - 15

$$CH_{3} - C = NOH \xrightarrow{H_{2}, Ni} CH_{3} - CH - NH_{2}$$

$$CH_{3} - CH - NH_{2}$$

Example - 16

Ph—CH—NH
$$\xrightarrow{\text{H}_2, \text{Ni}}$$
 PhCH₂—NH₂

Example - 17

$$CH_3CH_2$$
— $\stackrel{\bigoplus}{N}$ = $\stackrel{\stackrel{\leftrightarrow}{O}}{C}$ $\stackrel{4[H]}{\longrightarrow}$ $CH_3CH_2NHCH_3$
 $\stackrel{2^{\circ}}{Amine}$

Example - 18

$$CH_{3}-CH_{2}-\overset{\oplus}{N}=\overset{\dddot{\ominus}}{C}\overset{H_{2},\ Pt}{\longrightarrow}CH_{3}CH_{2}-NH-CH_{3}$$

5.5.2 Reduction of Nitro Compounds

Nitroalkanes are usually reduced by tin and hydrochloric acid or lithium aluminium hydride into corresponding amine. $\rm H_2$ and catalyst is also used for such a reduction.

Note...

1. 1° aromatic amines are usually prepared by the reduction of corresponding nitro

compounds by tin, iron or zinc with HCl or CH3COOH.

 Aqueous ethanolic ammonium hydrogen sulphide, aqueous sodium sulphide or methanoic sodium hydrogen sulphide selectively reduce one nitro group into a polynitro compound.

Example - 19

$$CH_3CH_2NO_2 + 6[H] \xrightarrow{Sn, HCl} CH_3CH_2NH_2$$

$$CH_3CH_2NO_2 + 3H_2 \xrightarrow{Pt} CH_3CH_2NH_2$$

Example - 20

Example - 21

$$\begin{array}{c} NO_2 \\ \\ NO_2 \\ \\ \\ NH_2 \\ \\ \\ NO_2 \\ \end{array} + 3NH_4HS$$

$$\begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \\ \\ \end{array} + 3NH_3 + 3S + 2H_2O$$

Example - 22

$$\begin{array}{c|c} CH_3 & CH_3 & CH_3 \\ \hline NO_2 & NO_2 & NH_2 \\ \hline NH_2 & NO_2 & NH_2 \\ \hline \end{array}$$

Example - 23

$$\begin{array}{c|c} NH_2 & NH_2 \\ \hline \\ NHOH & NO_2 & Ethanol \\ \hline \\ NHOH & NH_2 \\ \hline \\ N-Phenyl \ Hydroxyl \ Amine & Zn + NaOH \\ \hline \\ MeOH & \\ \hline \\ Azobenzene & \\ \end{array}$$

6. REACTIONS OF AMINES

6.1 Sulphonylation – Hinsberg Test

Treatment with benzene sulphonyl chloride (**Hinsberg reagent**) or p-toluene sulphonyl chloride.

- (a) The reaction is used to separate the amine mixture.
- (b) 1° and 2° amine, due to the presence of active hydrogen react and give corresponding sulphonamide while 3° amine does not react.
- (c) 1° amine product N-alkyl benzene sulphonamide is soluble in KOH forming a water-soluble salt.

$$C_6H_5SO_2Cl + R_3N \longrightarrow No Reaction$$
3° Amine

Not soluble

6.2 Nitrous Acid Test

- (a) 1° amine on reaction with HNO₂ gives usually an alcohol. The reaction involves the formation of diazonium salt as an intermediate.
- (b) 2° amine gives nitrosoamine which is a yellow oily liquid.
- (c) 3° amine dissolves in cold HNO₂ to form an unstable salt which on heating decomposes to give nitrosoamine and an alcohol.

Example - 24

$$CH_3CH_2NH_2 \xrightarrow{HNO_2} CH_3CH_2OH + N_2 + H_2O$$

Example - 25

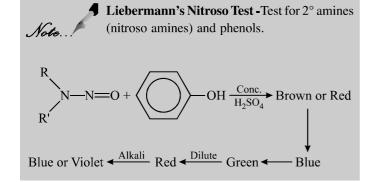
$$(CH_3)_2NH \xrightarrow{HNO_2} (CH_3)_2N \longrightarrow N = O + H_2O$$

Example - 26

$$(CH_3CH_2)_3N \xrightarrow{HNO_2} (CH_3CH_2)_3N \cdot HNO_2$$

$$\downarrow \Delta$$

$$(CH_3CH_2)_2N \xrightarrow{} N \Rightarrow O + CH_3CH_2OH$$



6.3 Carbylamine Reaction

1° amine on treatment with chloroform and alcoholic KOH gives out unpleasant or pungent vapours of alkyl carbylamine (isocyanide).

The reaction is known as a test for 1° amine.

$$CHCl_3 + OH^{\Theta} \longrightarrow :CCl_2 + H_2O$$

6.4 Treatment with CS₂/HgCl₂

- (a) 1° amine on warming with CS₂ produces dithiocarbamic acid, which is decomposed by mercuric chloride to alkyl isothiocyanate. It is called as Hofmann's Mustard Oil Reaction.
- (b) Although 2° amine gives dithiocarbamic acid but is not decomposed by mercuric chloride.
- (c) 3° amine don't react with CS_2 .

$$RNH_2 + S = C = S \xrightarrow{\Delta} R - NH - C - SH$$

$$\downarrow HgCl_2, \Delta$$

$$R - N = C = S + HgS + 2HCl$$
Pungent Smell of
Mustard Oil

$$R_2NH + S = C = S$$

$$\xrightarrow{\Delta} R_2N - C - SH$$
Dialkyl Dithiocarbamic Acid

6.5 Acylation

1° and 2° amines react with acid halide or anhydride to give N-substituted amides.

For aniline, the reaction is used to protect the ring.

Example - 27

$$\begin{array}{c}
O \\
\parallel \\
CH_3(CH_2)_4CH_2NH_2 + PhCOC1 \longrightarrow CH_3(CH_2)_4NHC \longrightarrow Ph
\end{array}$$

Example - 28

$$(CH_3CH_2)_2NH + CH_3CC1 \xrightarrow{Pyridine} (CH_3CH_2)_2NCCH_3$$

Example - 29

$$H_3C$$
 NH_2
 H_3C
 H_3C
 $NHCCH_3$
 $NHCCH_3$
 $NHCCH_3$
 $NHCCH_3$
 NH_2
 NH_2
 NH_2

6.6 Hofmann's Exhaustive Methylation and Elimination

Quarternary Ammonium Iodides are converted to hydroxides with moist Ag_2O . The hydroxide on heating undergo elimination to give 3° amines and alkenes. The important aspect of this elimination is that the least substituted alkene is the major product (**Hofmann Rule**). This is known as **Hofmann's Elimination**.

Example - 30

$$\begin{array}{c} \text{CH}_{3}\text{--}\text{CH}_{2}\text{--}\text{CH}_{3}\text{I} \stackrel{\dot{\Theta}}{\rightleftharpoons} \stackrel{\text{AgOH}}{\longrightarrow} \begin{bmatrix} \text{CH}_{3}\text{CH}_{2}\text{CH} - \text{CH}_{3} \\ & \text{N}(\text{CH}_{3})_{3} \end{bmatrix} \text{OH}^{\Theta} \\ \downarrow \text{A, 150°C} \\ \text{Hofmann Product (Major)} \qquad \begin{array}{c} \text{CH}_{3}\text{CH}_{2}\text{CH} = \text{CH}_{2} \\ & \text{Saytzeff Product (Minor)} \end{array}$$

Example - 31

$$\begin{array}{c|c} & \xrightarrow{\Delta} & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ &$$

6.7 Metal Ions

Amines form coordination compounds with metal ions.

Example - 32

$$\begin{array}{ccc} \operatorname{AgCl} & \longrightarrow [\operatorname{Ag}(\operatorname{CH_3NH_2})_2]^{\oplus} \operatorname{Cl}^{\overset{\bullet}{\Theta}} \\ & \operatorname{Soluble\ Complex} \end{array}$$

$$\operatorname{Cu}^{2\oplus} & \longrightarrow [\operatorname{Cu}(\operatorname{CH_3NH_2})_2]^{2\oplus} \\ & \operatorname{Deep\ Blue\ Complex} \end{array}$$

7. PREPARATION OF AROMATIC AMINES

Besides the methods in the preparation of aliphatic amines, following methods can also be used.

7.1 Reduction of Nitro Compounds

7.1.1 Vapour-Phase Reduction

Reducing Agents : CuO on SiO₂ or V–Pt Catalyst.

Example - 33

7.1.2 Catalytic Hydrogenation

Reducing Agents : H₂, Pd–C/Et–OH.

$$\begin{array}{c|c} NO_2 & NH_2 \\ \hline \\ CH_3 & Ethanol \end{array}$$

7.2 Ammonolysis of Aryl Halides

Note...

If deactivating groups (–NO₂ etc.) are at *ortho* or *para* position, reaction becomes quite easy to carryout.

7.3 Phenol and Ammonia

$$OH \qquad NH_2 \\ + 2NH_3 \xrightarrow{ZnCl_2} + H_2C$$

7.4 Reduction of Azo Compounds

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

8. REACTIONS OF AROMATIC AMINES

8.1 Diazonium Salt and Reactions

$$\begin{array}{c}
\ddot{N}H_{2} \\
& \stackrel{\bullet}{N} = NCI^{\Theta}
\end{array}$$

$$\begin{array}{c}
H_{2}O \\
-N_{2}
\end{array}$$

$$\begin{array}{c}
H_{3}PO_{2}
\end{array}$$

$$\begin{array}{c}
CuCI/HCI
\end{array}$$

$$\begin{array}{c}
CuBr/HBr
\end{array}$$

$$\begin{array}{c}
KI$$

$$\begin{array}{c}
HBF_{4}
\end{array}$$

$$\begin{array}{c}
KCN, Cu \text{ or} \\
K_{3}Cu(CN)_{4}
\end{array}$$

$$\begin{array}{c}
KCN, Cu \text{ or} \\
K_{3}Cu(CN)_{4}
\end{array}$$

$$\begin{array}{c}
Cu-powder \\
Ethanol
\end{array}$$

$$\begin{array}{c}
Cu-powder \\
Character
\end{array}$$

$$\begin{array}{c}
Cu-powder \\
Character$$

$$\begin{array}{c}
Cu-powder \\
Character
\end{array}$$

$$\begin{array}{c}
Cu-powder \\
Character$$

$$\begin{array}{c}
Cu-powder \\
Character
\end{array}$$

$$\begin{array}{c}
Cu-powder \\
Character$$

$$Cu-powder \\
Cu-powder \\
Cu-pow$$

8.2 Oxidation

Aromatic amines are readily oxidised to various products depending on conditions. Under controlled oxidation using Na₂Cr₂O₇ and H₂SO₄, aniline is oxidised to p-benzoquinone. In fact, on standing in air, p-benzoquinone is formed.

If oxidation is not controlled, a black dye, aniline black is formed.

$$\begin{array}{c|c} NH_2 & O \\ \hline & Na_2Cr_2O_7 \\ \hline & H_2SO_4 \end{array}$$
(Brown Colour)

8.3 Halogenation

Amine group (NH_2) is a very strong activating group and an ortho/para director. It forms 2, 4, 6-tribromo aniline on normal bromination in H_2O .

$$+ Br_2 \xrightarrow{H_2O} Br \xrightarrow{NH_2} Br$$

ortho and para derivatives can be made by decreasing the activating power of amino group by acetylation of aniline.

-NHCOCH₃ group is a mild ortho and para director.

Example - 34

$$\begin{array}{c|c} & \text{NHCOCH}_3 \\ \hline & & \\ & &$$

8.4 Nitration

The normal nitration of aniline is not done as nitrating mixture is oxidising and NH₂ is a strong activating group. Moreover, at 288 K aniline is protonated to form the anilinium ion which is meta directing. That is why besides the ortho and para derivatives, a significant amount of meta derivative is also formed.

However, by protecting the -NH₂ group by acetylation reaction with acetic anhydride, the nitration reaction can be controlled and the p-nitro derivative can be obtained as the major product.

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

8.5 Sulphonation

$$\begin{array}{c|c} NH_2 \\ \hline \\ fuming H_2SO_4 \\ 453 - 475 \ K \\ \hline \\ NH_2 \\ \hline \\ SO_3H \\ \hline \\ SUlphanilic Acid \\ \hline \\ Zwitter Ion \\ (Dipolar Ion) \\ \end{array}$$

Usually -NH₂ group attached to benzene is unable to form zwitter ion but here -SO₃H is very strongly acidic. Hence sulphanilic acid forms zwitter ion. For example when -NH₂ group is attached to benzoic acid in any position, zwitter ion is not formed.

9. ANALYSIS OF AMINES

Amines are characterized chiefly through their basicity. A water-insoluble compound that dissolves in cold dilute hydrochloric acid or a water-soluble compound whose aqueous solution turns litmus blue - must almost certainly be an amine.

Whether an amine is primary, secondary, or tertiary is best shown by the **Hinsberg test**. The amine is shaken with benzenesulfonyl chloride in the presence of aqueous potassium hydroxide. Primary and secondary amines form substituted sulfonamides; tertiary amines do not.

The monosubstituted sulfonamide from a primary amine has an acidic hydrogen attached to nitrogen. Reaction with potassium hydroxide converts this amide into a soluble salt.

The disubstituted sulfonamide from a secondary amine has no acidic hydrogen and remains insoluble in the alkaline reaction mixture.

Behaviour toward nitrous acid is of some use in determining the class of an amine. In particular, the behaviour of primary aromatic amines is quite characteristic: treatment with nitrous acid converts them into diazonium salts, which yield highly colored azo compounds upon treatment with β -naphthol.

Hinsberg test is also used for the separation of amines.

