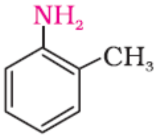
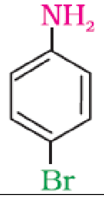
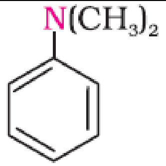
9. AMINES

Amines are the derivatives of ammonia. Like ammonia, the nitrogen atom in amines is also sp^3 hybridised with an unpaired electron in one of the sp^3 hybridised orbitals. So the shape of amines is also pyramidal.

Amines are classified into three types – primary (1^0), secondary (2^0) and tertiary (3^0) amines. If one hydrogen atom of ammonia is replaced by R (alkyl) or aryl (Ar) group, we get 1^0 amine. Their general formula is $R\text{-}NH_2$. If two hydrogen atoms of ammonia are replaced by two alkyl (R) or aryl (Ar) groups, we get 2^0amine. Their general formula is R_2NH. If three hydrogen atoms of ammonia are replaced by R or Ar groups we get 3^0amine. Their general formula is R_3NH.

If all the alkyl or aryl groups are the same, that amine is called simple amine and if they are different, it is called mixed amine.

Nomenclature: In common system, amines are named by prefixing alkyl group to amine, i.e. alkyl amine. In secondary and tertiary amines, when the alkyl groups are same, the prefix di or tri is used before the name of the alkyl group. In IUPAC system, amines are named by replacing of 'e' of alkane by the word amine, i.e. alkanamine. In the case of secondary and tertiary amines, the alkyl group containing the maximum number of carbon atom is taken as the parent chain and the other alkyl groups are taken as substituents. While naming aryl amines according to IUPAC system, the suffix 'e' of arene is replaced by 'amine', i.e. arenamine. E.g. benzenamine.

Amine	Common name	IUPAC name
$CH\text{-}NH_2$	Methyl amine	Methanamine
$CH_3\text{-}CH_2\text{-}NH_2$	Ethylamine	Ethanamine
$CH_3–CH_2–CH_2–NH_2$	n-Propylamine	Propan-1-amine
$(CH_3)_2CH\text{-}NH_2$	Isopropylamine	Propan-2-amine
$CH_3\text{-}NH\text{-}CH_2\text{-}CH_3$	Ethylmethylamine	N-Methylethanamine
$(CH_3)_3N$	Trimethylamine	N,N-Dimethylmethanamine
$CH_3\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}N(C_2H_5)_2$	n-Butyldiethylamine	N,N-Diethylbutan-1-amine
$CH_2{=}CH\text{-}CH_2\text{-}NH_2$	Allylamine	Prop-2-en-1-amine
$H_2N–CH_2–CH_2–NH_2$	Ethylene diamine	Ethane-1,2-diamine
$H_2N\text{-}(CH_2)_6\text{-}NH_2$	Hexamethylenediamine	Hexane-1,6-diamine
$C_6H_5\text{-}NH_2$	Aniline	Aniline or Benzenamine
$(C_6H_5)_2NH$	Diphenyl amine	N-phenylbenzenanamine
	o-Toluidine	2-Aminotoluene
	p-Bromoaniline	4-Bromobenzenamine Or, 4-Bromoaniline
	N,N-Dimethylaniline	N,N-Dimethylbenzenamine

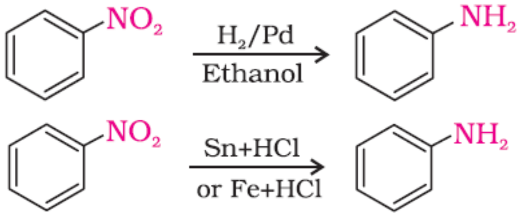
Preparation of Amines

1. ***Reduction of nitro compounds***:

   Nitro compounds when reduced by passing hydrogen gas in the presence of finely divided nickel, palladium or platinum or by reduction with metals in acidic medium, we get amines.

   $$R\text{-}NO_2 + H_2 \xrightarrow{\text{Pd/ethanol}} R\text{-}NH_2$$

   Nitrobenzene when reduced using H_2 in presence of Ni, Pd or Pt Or, by using iron or tin and HCl, we get aniline.



Reduction with iron and hydrochloric acid is preferred because $FeCl_2$ formed gets hydrolysed to release hydrochloric acid during the reaction. Thus, only a small amount of hydrochloric acid is required to initiate the reaction.

2. ***Ammonolysis of alkyl halides:***

   Alkyl halides when treated with alcoholic solution of ammonia at 373 K, undergo nucleophilic substitution reaction to give a mixture of primary, secondary and tertiary amines and quaternary ammonium salt ($R_4N^+X^-$). This process of cleavage of C-X bond by ammonia is called ***ammonolysis*** (Hofmann's Ammonolysis).

   $$R\text{-}X + NH_3\ (\text{alc.}) \longrightarrow R\text{-}NH_2 + R_2NH + R_3N + R_4N^+X^-$$

   If large excess of ammonia is used, primary amine is formed as the major product. The order of reactivity of alkyl halides with amines is RI > RBr >RCl.

3. ***Reduction of Nitriles:***

   Nitriles on reduction with lithium aluminium hydride ($LiAlH_4$) or catalytic hydrogenation to give primary amines. This reaction is used for ascending in amine series, i.e., for preparation of amines containing one carbon atom more than the starting amine.

   $$R\text{-}CN \xrightarrow[\text{ii) } H_2O]{\text{i) } LiAlH_4} R\text{-}CH_2\text{-}NH_2$$

4. ***Reduction of amides:***

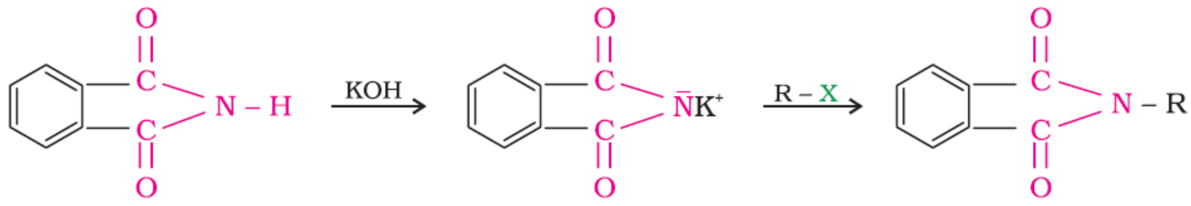
   Acid amides on reduction with lithium aluminium hydride give amines.

   $$R\text{-}CO\text{-}NH_2 \xrightarrow[\text{ii) } H_2O]{\text{i) } LiAlH_4} R\text{-}CH_2\text{-}NH_2$$

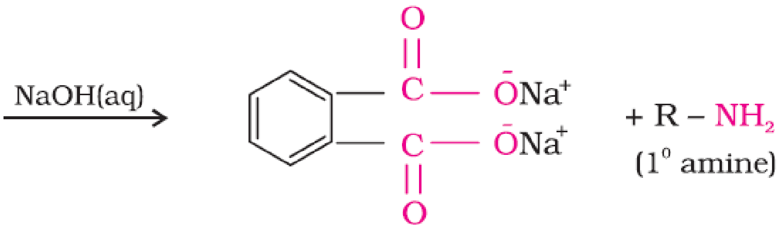
   $$\underset{\text{Ethanamide (acetamide)}}{CH_3\text{-}CO\text{-}NH_2} \xrightarrow{LiAlH_4/H_2O} \underset{\text{Ethanamine}}{CH_3\text{-}CH_2\text{-}NH_2}$$

5. ***Gabriel phthalimide synthesis:***

   This method is used for the preparation of aliphatic primary amines only. Phthalimide when treated with ethanolic solution of potassium hydroxide to form potassium salt of phthalimide which on heating with alkyl halide followed by alkaline hydrolysis produces the corresponding primary amine.



Phthalimide potassium salt of phthalimide N-alkyl phthalimide



Aromatic primary amines cannot be prepared by this method because aryl halides do not undergo nucleophilic substitution with the anion formed by phthalimide.

6. <u>Hoffmann bromamide degradation reaction:</u>

When an amide is treated with bromine and ethanolic solution of NaOH, we get a 1^0 amine. This reaction is called Hoffmann bromamide degradation reaction. It is used for the conversion of an amide to a primary amine with one carbon atom less than that present in the amide.

$R\text{-}CO\text{-}NH_2 + Br_2 + 4\ NaOH \longrightarrow R\text{-}NH_2 + Na_2CO_3 + 2\ NaBr + 2\ H_2O$

$CH_3\text{-}CO\text{-}NH_2 + Br_2 + 4\ NaOH \longrightarrow CH_3\text{-}NH_2 + Na_2CO_3 + 2\ NaBr + 2\ H_2O$

Ethanamide (acetamide) Methanamine

<u>Physical Properties</u>: Lower amines have fishy smell.

1. **Solubility**: Lower aliphatic amines are soluble in water because they can form hydrogen bonds with water molecules. However, solubility decreases with increase in molar mass of amines due to increase in size of the hydrophobic alkyl part. Higher amines are insoluble in water. Amines are soluble in organic solvents like alcohol, ether and benzene.
2. **Boiling point:** Primary and secondary amines are associated through intermolecular hydrogen bonding. This intermolecular association is more in primary amines than in secondary amines. Tertiary amines do not have intermolecular association due to the absence of hydrogen atom. Therefore, the order of boiling points of isomeric amines is as follows: Primary > Secondary > Tertiary

<u>Chemical Reactions</u>

1. **<u>Basic character of amines</u>:** Amines react with acids to form salts. This reaction shows that they are basic in nature.

$R\text{-}NH_2 + HX \rightleftharpoons R\text{-}NH_3^+X^-$

$C_6H_5\text{-}NH_2 + HCl \rightleftharpoons C_6H_5NH_3^+Cl^-$

Aniline Anilinium chloride

In amine, there is an unshared pair of electrons on nitrogen atom and hence it can donate this electron pair. So it acts as a Lewis base. Basic character of amines can be expressed in terms of K_b and pK_b. ($pK_b = -\log K_b$)

Greater the value of K_b, smaller will be the pK_b value and stronger will be the base.

Aliphatic amines are stronger bases than ammonia. This is due to the +I effect of alkyl groups leading to greater electron density on the nitrogen atom. But aromatic amines are weaker bases than ammonia. This is due to the electron withdrawing nature of the aryl group.

Besides inductive effect, there are some other effects like solvation effect, steric hindrance etc. affect the basic strength of amines.

Structure-basicity relationship of amines

Basicity of amines is related to their structure. Basic character of an amine depends upon the ease of formation of the cation by accepting a proton from the acid. As the stability of the cation increases, the basicity also increases.

a) Comparison of basicity of alkyl amines (alkanamines) and ammonia

Due to the electron releasing nature of alkyl group (R) in alkyl amines, it (the alkyl group) pushes electrons towards nitrogen and thus makes the unshared electron pair more available for sharing with the proton of the acid. Also the substituted ammonium ion formed from the amine gets stabilized charge by the +I effect of the alkyl group. Hence, *alkyl amines are stronger bases than ammonia.*

The basic nature of aliphatic amines should increase with increase in the number of alkyl groups. But this trend is followed only in gas phase. The order of basicity of amines in the gaseous phase is:

Tertiary amine > Secondary amine > Primary amine > NH_3.

In the aqueous solution, in addition to inductive effect, there are some other effects like solvation effect and steric hindrance determine the basicity. The greater the size of the ion, lesser will be the solvation and the less stabilised is the ion. So the basicity also decreses. Thus, the order of basicity of aliphatic amines should be: primary > secondary > tertiary, which is opposite to the inductive effect based order.

When the alkyl group is small, there is no steric hindrance to H-bonding. In case the alkyl group is bigger than CH_3 group, there will be steric hindrance to H-bonding. Therefore, the size of the alkyl group also determines the order of basic strength. Thus inductive effect, solvation effect and steric hindrance of the alkyl group decide the basic strength of alkyl amines in the aqueous state.

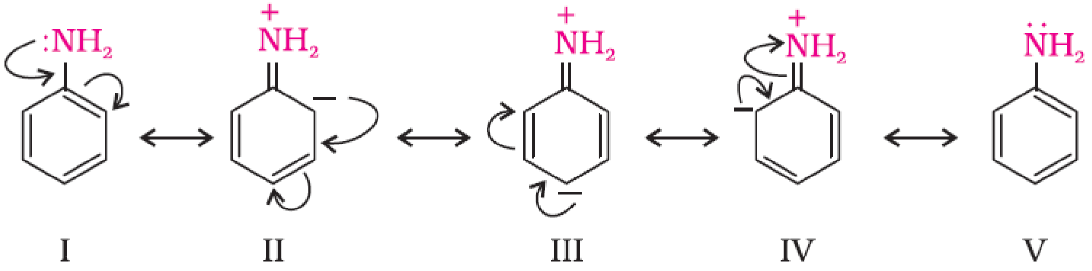
The order of basic strength in case of methyl substituted amines and ethyl substituted amines in aqueous solution is as follows:

$$\underset{2^0}{(C_2H_5)_2NH} > \underset{3^0}{(C_2H_5)_3N} > \underset{1^0}{C_2H_5NH_2} > NH_3$$

$$\underset{2^0}{(CH_3)_2NH} > \underset{1^0}{CH_3NH_2} > \underset{3^0}{(CH_3)_3N} > NH_3$$

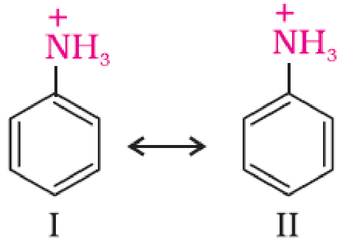
b) ***Comparison of basicity aryl amines and ammonia***

Aryl amines are less basic than ammonia. This is because in aryl amines, the $-NH_2$ group is attached directly to the benzene ring. So the lone pair electrons present in the nitrogen atom enter into the benzene ring and the following resonating structures are formed.



So the electron pairs are less available for protonation and hence aryl amines are less basic.

Also the anilinium ion formed by accepting a proton can have only two resonating structures as follows:



So it is less stable and hence aniline does not easily accept proton. So it is less basic.

In the case of substituted aniline, the electron releasing groups like $-OCH_3$, $-CH_3$ increase basic strength while electron withdrawing groups like $-NO_2$, $-SO_3$, $-COOH$, $-X$ etc. decrease the basic strength.

2. ***Alkylation***:
   Amines react with alkyl halides undergo nucleophilic substitution reaction to form a mixture of secondary and tertiary amines and quaternary ammonium salt. (Hofmann's Ammonolysis)
   $$R\text{-}X + R\text{-}NH_2\ (alc.) \longrightarrow R_2NH + R_3N + R_4N^+X^-$$

3. ***Acylation***: Aliphatic and aromatic primary and secondary amines react with acid chlorides, anhydrides and esters in presence of base like pyridine to form substituted amides. This reaction is known as ***acylation***.
   $$CH_3\text{-}NH_2 + CH_3\text{-}CO\text{-}Cl \xrightarrow{base} CH_3\text{-}NH\text{-}CO\text{-}CH_3 + HCl$$
   Methanamine — N-methylethanamide (N-methyl acetamide)
   $$(C_2H_5)_2NH + CH_3\text{-}CO\text{-}Cl \xrightarrow{base} (C_2H_5)_2N\text{-}CO\text{-}CH_3 + HCl$$
   N-Ethylethanamine — N,N-Diethylethanamide
   $$C_6H_5\text{-}NH_2 + CH_3\text{-}CO\text{-}O\text{-}CO\text{-}CH_3 \longrightarrow C_6H_5\text{-}NH\text{-}CO\text{-}CH_3 + CH_3\text{-}COOH$$
   Aniline — ethanoic anhydride — N-Phenylethanamide (Acetanilide)

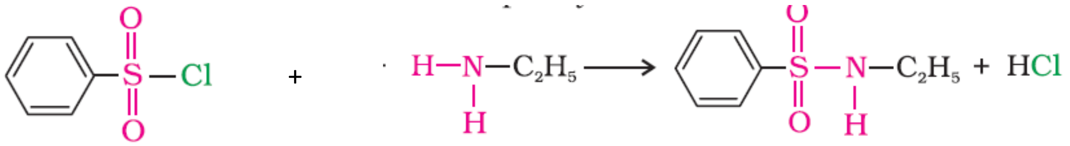
   Amines react with benzoyl chloride (C_6H_5COCl) to form N-alkyl benzamide. This reaction is known as ***benzoylation***.
   $$CH_3\text{-}NH_2 + C_6H_5\text{-}CO\text{-}Cl \longrightarrow CH_3\text{-}NH\text{-}CO\text{-}C_6H_5 + HCl$$
   Methanamine — Benzoyl chloride — N-Methylbenzamide

4. ***Carbylamine reaction (isocyanide test):*** Test for primary amines.
   Aliphatic and aromatic primary amines on heating with chloroform and alcoholic potassium hydroxide form foul smelling isocyanides or carbylamines. This reaction is known as **carbylamines reaction or isocyanide test** and is used as ***a test for primary amines***. Secondary and tertiary amines do not give this reaction.
   $$R\text{-}NH_2 + CHCl_3 + 3\ KOH \xrightarrow{heat} R\text{-}NC + 3\ KCl + 3\ H_2O$$
   $$CH_3\text{-}NH_2 + CHCl_3 + 3\ KOH \xrightarrow{heat} CH_3\text{-}NC + 3\ KCl + 3\ H_2O$$
   Methanamine — methyl carbylamine
   $$C_6H_5\text{-}NH_2 + CHCl_3 + 3\ KOH \xrightarrow{heat} C_6H_5\text{-}NC + 3\ KCl + 3\ H_2O$$
   Aniline — phenyl carbylamine

5. ***Reaction with nitrous acid***:
   Aliphatic 1^0 amines react with nitrous acid (prepared by mixing sodium nitrite and HCl) to form alcohols with the liberation of nitrogen gas. From the amount of nitrogen evolved, we can estimate amino acids and proteins.
   $$R\text{-}NH_2 + HNO_2 \xrightarrow{NaNO_2 + HCl} [R\text{-}N_2^+Cl^-] \xrightarrow{H_2O} R\text{-}OH + N_2 + HCl$$
   Aromatic primary amines react with nitrous acid at 0 to 5^0C (273-278 K) to form aromatic diazonium salts [Diazotisation].
   $$C_6H_5\text{-}NH_2 \xrightarrow{NaNO_2 + HCl} C_6H_5N_2^+Cl^- + NaCl + 2H_2O$$
   Aniline — Benzenediazoniumchloride

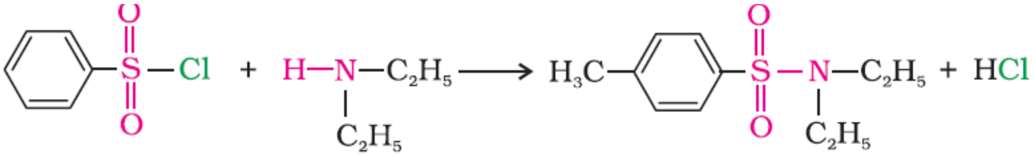
6. ***Reaction with benzene sulphonyl chloride [Hinsberg's Test]:***
   Benzenesulphonyl chloride ($C_6H_5SO_2Cl$) is known as Hinsberg's reagent. It is used to distinguish primary, secondary and tertiary amines and also for the separation of a mixture of amines.

a) Primary amines react with benzenesulphonyl chloride to form a precipitate of N-alkyl benzenesulphonamide, which is soluble in alkail.



Benzene sulphonyl chloride ethanamine N-ethylbenzenesulphonamide

b) Secondary amines react with benzene sulphonyl chloride to give a precipitate of N,N-dialkylbenzene sulphonamide, which is insoluble in alkali.



Benzene sulphonyl chloride N-ethylethanamine N,N-diethylbenzenesulphonamide

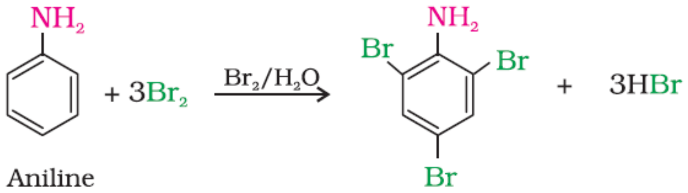
c) Tertiary amines do not react with benzenesulphonyl chloride.

Nowadays, *Benzenesulphonyl chloride is replaced by p-toluenesulphonyl chloride.*

7. *Electrophilic substitution Reactions:*

–NH_2 group is ortho and para directing and a powerful activating group. So the reactions are very vigorous.

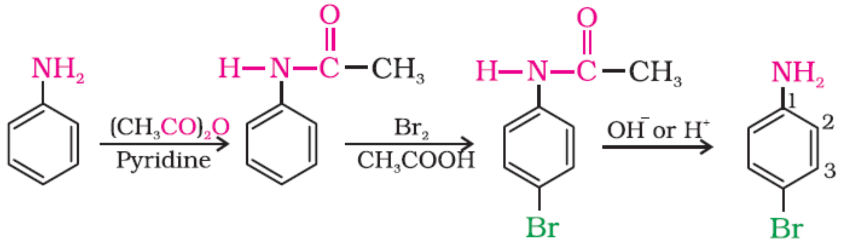
a) Bromination: Aniline reacts with bromine water at room temperature to give a white precipitate of 2,4,6-tribromoaniline.



Aniline

2,4,6-Tribromoaniline

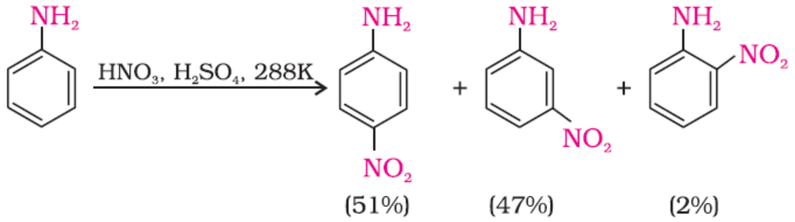
In order to prepare o-bromoaniline and p-bromoaniline, first reduce the activating power of –NH_2 group by protecting it through acetylation with acetyl chloride or acetic anhydride. Then the resulting acetanilide is brominated by Br_2 in acetic acid followed by hydrolysis, we get p-bromoaniline as the major product.



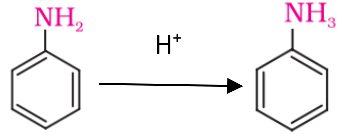
Aniline Acetanilide p-Bromoacetanilide p-Bromoaniline

b) Nitration

Direct nitration of aniline with conc. HNO_3 and conc. H_2SO_4 gives a mixture of ortho, meta and para nitroanilines and some tarry (tar-like) products.

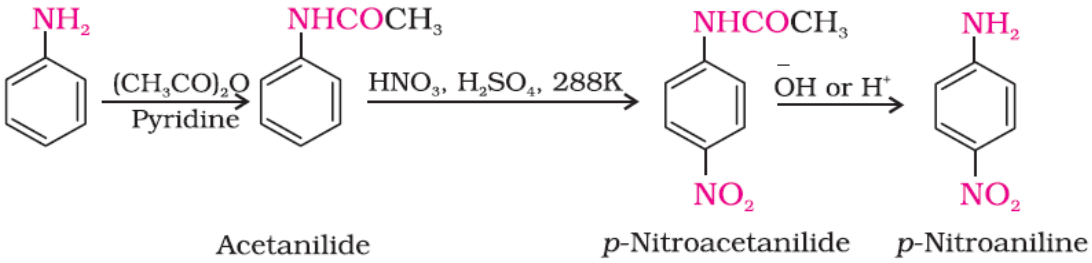


A large amount of meta-isomer is formed, eventhough -NH_2 is ortho-para directing. This is because in strongly acidic medium, aniline is protonated to form the anilinium ion which is meta directing.



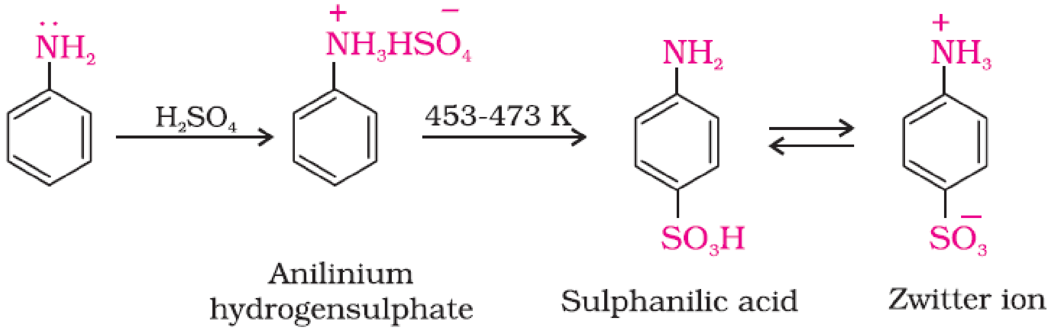
Aniline Anilinium ion

For the preparation of p-nitroaniline, the –NH_2 group is first deactivated by acetylation. The acetanilide thus formed is nitrated followed by hydrolysed.



c) Sulphonation:

Aniline reacts with concentrated sulphuric acid to form anilinium hydrogensulphate which on heating with sulphuric acid at 453-473K produces p-aminobenzene sulphonic acid, commonly known as sulphanilic acid, as the major product. Sulphanilic acid contains both acidic and basic groups and so it forms internal salts called zwitter ions.



Aniline does not undergo Friedel-Crafts reaction (alkylation and acylation) since it form salt with anhydrous aluminium chloride, which is used as catalyst in the reaction.

AROMATIC DIAZONIUM SALTS

They have the general formula $ArN_2^+ X^-$ where Ar is an aryl group and X^- may be Cl^-, Br^-, HSO_4^- , BF_4^- , etc. The N_2^+ group is called diazonium group. They are named by suffixing diazonium to the name of the parent hydrocarbon followed by the name of anion such as chloride, hydrogensulphate, flouroborate etc. Some examples are:

1. $C_6H_5N_2^+Cl^-$ Benzenediazoniumchloride
2. $C_6H_5N_2^+HSO_4^-$ Benzenediazoniumhydrogensulphate
3. $C_6H_5N_2^+BF_4^-$ Benzenediazoniumfluoroborate

Preparation – Diazotisation: Aromatic diazonium salts are prepared by treating an aromatic primary amine with Nitrous acid (which is prepared by mixing $NaNO_2$ and HCl) at 273 – 278K (0-5^{0}C). *The conversion of primary aromatic amines into diazonium salts is known as **diazotisation**.*

E.g. benzenediazonium chloride is prepared by the reaction of aniline with nitrous acid at 273-278K.

$$C_6H_5NH_2 + NaNO_2 + 2HCl \xrightarrow{273 - 278\ K} C_6H_5N_2^+Cl^- + NaCl + 2H_2O$$

Aromatic diazonium salts are stable only at low temperatures. So it is produced in situ (in site).

Chemical reactions

The reactions of diazonium salts can be broadly divided into two categories – Reactions involving displacement of nitrogen and reactions involving retention of diazo group.

A) Reactions involving displacement of nitrogen

1. ***Replacement by halide or cyanide ion***: When a diazonium salt is treated with hydrogen halide in presence of cuprous halide, we get halobenzene. This reaction is called ***Sandmeyer's reaction***. For the preparation of cyanobenzene, benzenediazonium salt is treated with KCN in presence of cuprous cyanide.

   $C_6H_5N_2^+Cl^- + HX \xrightarrow{CuX} C_6H_5\text{-}X + N_2 + HCl$ [where X = Cl or Br]

   $C_6H_5N_2^+Cl^- + KCN \xrightarrow{CuCN} C_6H_5\text{-}CN + N_2 + HCl$

   If cuprous halide is replaced by copper powder, the reaction is called ***Gattemann's reaction***.

   $C_6H_5N_2^+Cl^- + HX \xrightarrow{Cu} C_6H_5\text{-}X + N_2 + CuCl$

2. ***Replacement by iodide ion***: When the diazonium salt solution is treated with potassium iodide, iodobenzene is formed.

   $C_6H_5N_2^+Cl^- + KI \longrightarrow C_6H_5\text{-}I + N_2 + KCl$

3. ***Replacement by fluoride ion***: When benzenediazonium chloride is treated with fluoroboric acid (HBF_4), benzene diazonium fluoroborate is formed which on heating decomposes to give flourobenzene. This reaction is called ***Balz-Schiemann reaction***.

   $C_6H_5N_2^+Cl^- + HBF_4 \longrightarrow C_6H_5\text{-} N_2^+BF_4^- \xrightarrow{\Delta} C_6H_5\text{-}F + BF_3 + N_2$

4. ***Replacement by H***: When benzenediazonium chloride is treated with reducing agents like hypophosphorous acid (phosphinic acid) or ethanol, we get benzene.

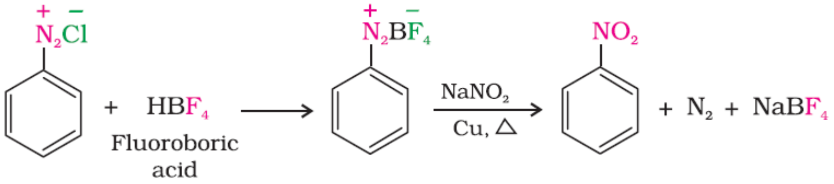
   $C_6H_5N_2^+Cl^- + H_3PO_2 + H_2O \longrightarrow C_6H_6 + N_2 + H_3PO_3 + HCl$

   $C_6H_5N_2+Cl- + CH_3CH_2OH \longrightarrow C_6H_6 + N_2 + CH_3\text{-}CHO + HCl$

5. ***Replacement by hydroxyl group***: When benzenediazoniumchloride is warmed with water, we get phenol.

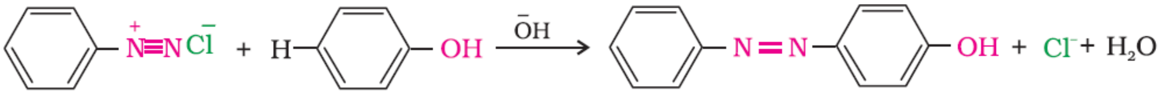
   $C_6H_5N_2^+Cl^- + H_2O \longrightarrow C_6H_5\text{-}OH + N_2 + HCl$

6. ***Replacement by –NO₂ group***: When benzenediazonium fluoroborate is heated with aqueous sodium nitrite solution in the presence of copper, the diazonium group is replaced by $-NO_2$ group.

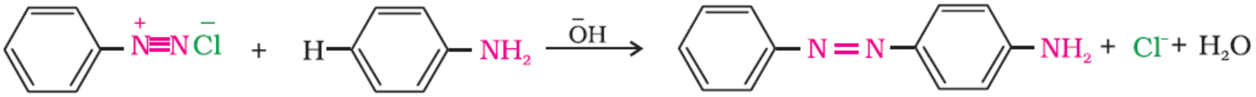


B) Reactions involving retention of diazo group

Coupling reactions: When benzene diazonium chloride is treated with phenol or aniline, the para position of is coupled with the diazonium salt to form p-hydroxyazobenzene or p-aminoazobenzene. This type of reaction is known as ***coupling reaction***. This is an example of electrophilic substitution reaction.



Benzenediazonium chloride Phenol p-hydroxyazobenzene



Benzenediazonium chloride Aniline p-aminoazobenzene