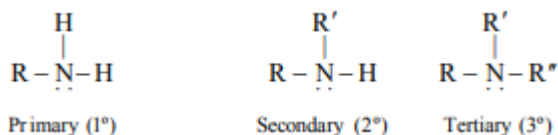


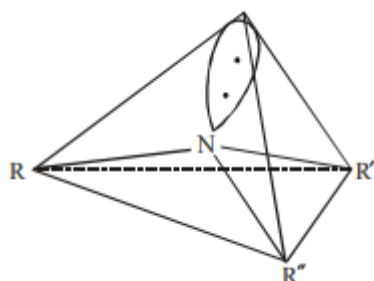
# Amines

Amines are derivatives of ammonia ( $\text{NH}_3$ ) in which one or more hydrogen atoms have been replaced by alkyl/Aryl groups.

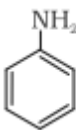
**CLASSIFICATION :** Amines are classified as primary ( $1^\circ$ ), secondary ( $2^\circ$ ) or tertiary ( $3^\circ$ ) according to the number of alkyl groups attached to the nitrogen atom.



**STRUCTURE :** The nitrogen atom in amine is  $\text{sp}^3$  hybridised. The three hybrid atomic orbitals are involved in bond formation and one hybrid atomic orbital contains the unshared pair of electrons, giving the pyramidal structure to amine



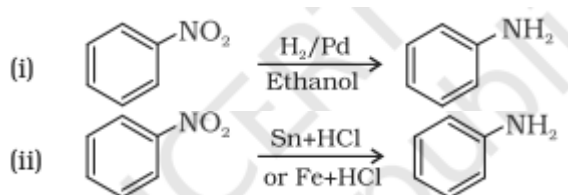
**Nomenclature:** In common system, an aliphatic amine is named by prefixing alkyl group to amine, i.e., alkylamine as one word (e.g., methylamine). In IUPAC system, amines are named as alkanamines, derived by replacement of 'e' of alkane by the word amine. For example,  $\text{CH}_3\text{NH}_2$  is named as methanamine.

Amine	Common name	IUPAC name
$\text{CH}_3\text{--CH}_2\text{--NH}_2$	Ethylamine	Ethanamine
$\text{CH}_3\text{--CH}_2\text{--CH}_2\text{--NH}_2$	<i>n</i> -Propylamine	Propan-1-amine
$\begin{array}{c} \text{CH}_3\text{--CH--CH}_3 \\   \\ \text{NH}_2 \end{array}$	Isopropylamine	Propan-2-amine
$\begin{array}{c} \text{CH}_3\text{--N--CH}_2\text{--CH}_3 \\   \\ \text{H} \end{array}$	Ethylmethylaniline	N-Methylethanamine
$\begin{array}{c} \text{CH}_3\text{--N--CH}_3 \\   \\ \text{CH}_3 \end{array}$	Trimethylamine	N,N-Dimethylmethanamine
	Aniline	Aniline or Benzenamine

## Preparation Preparation Preparation of Amines:

### 1. Reduction of nitro compounds:

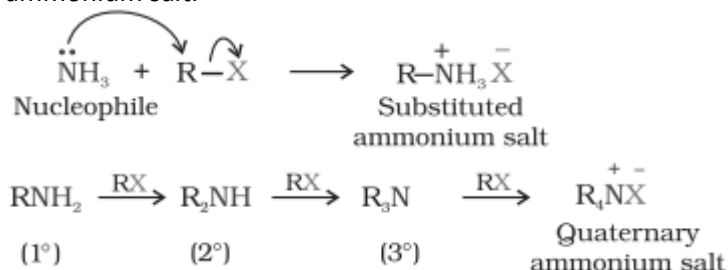
Nitro compounds are reduced to amines by passing hydrogen gas in the presence of finely divided nickel, palladium or platinum and also by reduction with metals in acidic medium. Nitroalkanes can also be similarly reduced to the corresponding alkanamines.



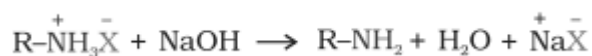
Reduction with iron scrap and hydrochloric acid is preferred because  $\text{FeCl}_2$  formed gets hydrolysed to release hydrochloric acid during the reaction. Thus, only a small amount of hydrochloric acid is required to initiate the reaction.

## 2. Ammonolysis of alkyl halides:

Alkyl or benzyl halide on reaction with an ethanolic solution of ammonia undergoes nucleophilic substitution reaction in which the halogen atom is replaced by an amino ( $-\text{NH}_2$ ) group. This process of cleavage of the  $\text{C}-\text{X}$  bond by ammonia molecule is known as ammonolysis. The reaction is carried out in a sealed tube at 373 K. The primary amine thus obtained behaves as a nucleophile and can further react with alkyl halide to form secondary and tertiary amines, and finally quaternary ammonium salt.



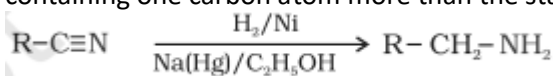
The free amine can be obtained from the ammonium salt by treatment with a strong base:



Ammonolysis has the disadvantage of yielding a mixture of primary, secondary and tertiary amines and also a quaternary ammonium salt. However, primary amine is obtained as a major product by taking large excess of ammonia. The order of reactivity of halides with amines is  $\text{RI} > \text{RBr} > \text{RCl}$

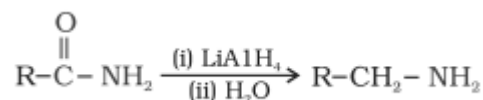
## 3. Reduction of nitriles:

Nitriles on reduction with lithium aluminium hydride ( $\text{LiAlH}_4$ ) or catalytic hydrogenation produce primary amines. This reaction is used for ascent of amine series, i.e., for preparation of amines containing one carbon atom more than the starting amine.



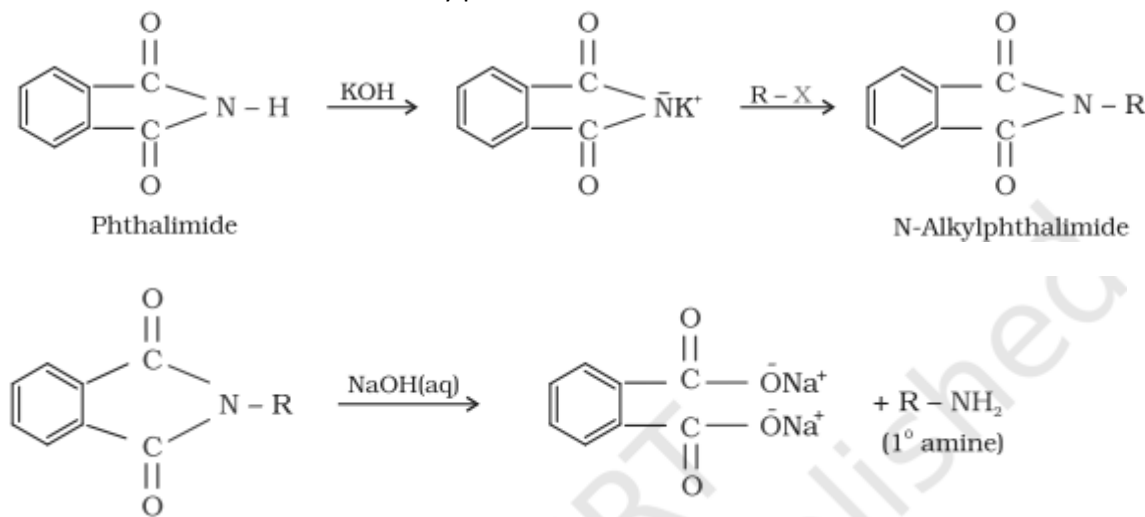
## 4. Reduction of amides:

The amides on reduction with lithium aluminium hydride yield amines



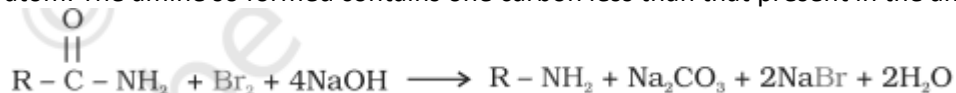
### 5. Gabriel phthalimide synthesis:

Gabriel synthesis is used for the preparation of primary amines. Phthalimide on treatment with ethanolic potassium hydroxide forms potassium salt of phthalimide which on heating with alkyl halide followed by alkaline hydrolysis produces the corresponding primary amine. Aromatic primary amines cannot be prepared by this method because aryl halides do not undergo nucleophilic substitution with the anion formed by phthalimide.

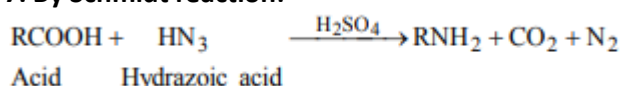


### 6. Hoffmann bromamide degradation reaction:

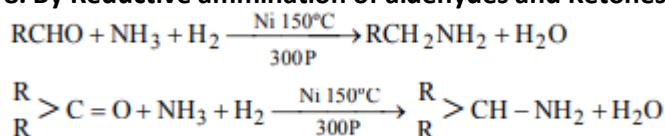
Hoffmann developed a method for preparation of primary amines by treating an amide with bromine in an aqueous or ethanolic solution of sodium hydroxide. In this degradation reaction, migration of an alkyl or aryl group takes place from carbonyl carbon of the amide to the nitrogen atom. The amine so formed contains one carbon less than that present in the amide.



### 7. By Schmidt reaction:



### 8. By Reductive amination of aldehydes and Ketones:



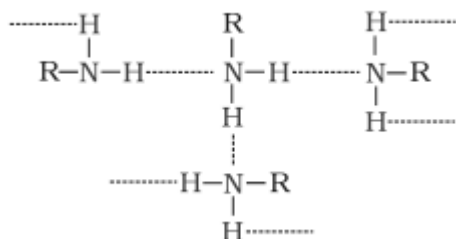
### Physical Properties:

The lower aliphatic amines are gases with fishy odour. Primary amines with three or more carbon atoms are liquid and still higher ones are solid. Aniline and other arylamines are usually colourless but get coloured on storage due to atmospheric oxidation.

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. Amines are soluble in organic solvents like alcohol, ether and benzene.

Primary and secondary amines are engaged in intermolecular association due to hydrogen bonding between nitrogen of one and hydrogen of another molecule. This intermolecular association is more in primary amines than in secondary amines as there are two hydrogen atoms available for hydrogen bond formation in it. Tertiary amines do not have intermolecular association due to the absence of

hydrogen atom available for hydrogen bond formation. Therefore, the order of boiling points of isomeric amines is as follows: Primary > Secondary > Tertiary.



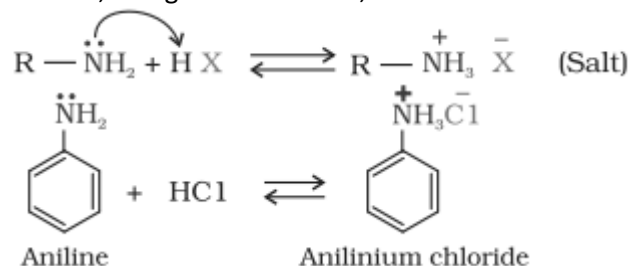
*Intermolecular hydrogen bonding in primary amines*

### Chemical Reactions:

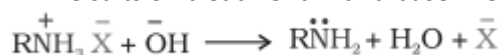
Difference in electronegativity between nitrogen and hydrogen atoms and the presence of unshared pair of electrons over the nitrogen atom makes amines reactive. The number of hydrogen atoms attached to nitrogen atom also decides the course of reaction of amines; that is why primary, secondary and tertiary amines differ in many reactions. Moreover, amines behave as nucleophiles due to the presence of unshared electron pair. Some of the reactions of amines are described below:

#### 1. Basic character of amines:

Amines, being basic in nature, react with acids to form salts,

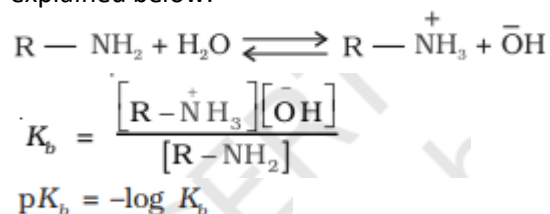


Amine salts on treatment with a base like NaOH, regenerate the parent amine.



Amine salts are soluble in water but insoluble in organic solvents like ether. This reaction is the basis for the separation of amines from the non-basic organic compounds insoluble in water.

Amines have an unshared pair of electrons on nitrogen atom due to which they behave as Lewis base. Basic character of amines can be better understood in terms of their  $K_b$  and  $pK_b$  values as explained below:



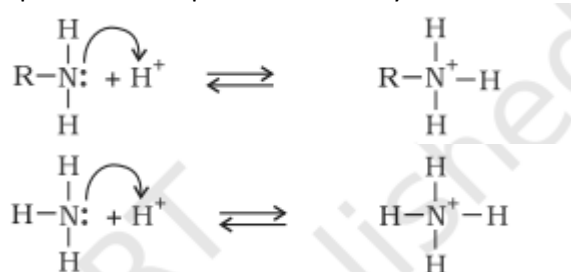
Larger the value of  $K_b$  or smaller the value of  $pK_b$ , stronger is the base.

$pK_b$  value of ammonia is 4.75. Aliphatic amines are stronger bases than ammonia due to +I effect of alkyl groups leading to high electron density on the nitrogen atom. Their  $pK_b$  values lie in the range of 3 to 4.22. On the other hand, aromatic amines are weaker bases than ammonia due to the electron withdrawing nature of the aryl group and delocalization of electron through resonance. Besides inductive effect, there are other effects like solvation effect, steric hinderance, etc., which affect the basic strength of amines.

## Structure-basicity relationship of amines:

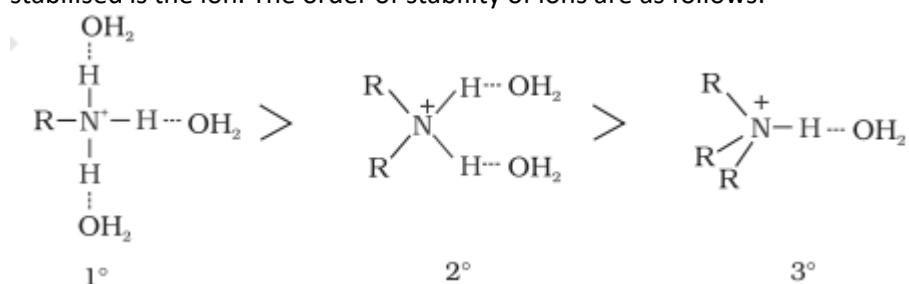
Basicity of amines is related to their structure. Basic character of an amine depends upon the ease of formation of the cation by accepting a proton from the acid. The more stable the cation is relative to the amine, more basic is the amine.

(a) **Alkanamines versus ammonia:** Let us consider the reaction of an alkanamine and ammonia with a proton to compare their basicity.



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

Thus, the basic nature of aliphatic amines should increase with increase in the number of alkyl groups. This trend is followed in the gaseous phase. The order of basicity of amines in the gaseous phase follows the expected order: tertiary amine > secondary amine > primary amine >  $\text{NH}_3$ . The trend is not regular in the aqueous state. In the aqueous phase, the substituted ammonium cations get stabilised not only by electron releasing effect of the alkyl group (+I) but also by solvation with water molecules. The greater the size of the ion, lesser will be the solvation and the less stabilised is the ion. The order of stability of ions are as follows:



Decreasing order of extent of H-bonding in water and order of stability of ions by solvation.

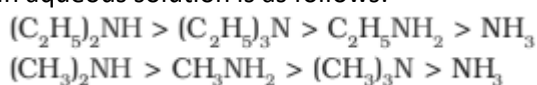
Greater is the stability of the substituted ammonium cation, stronger should be the corresponding amine as a base. Thus, the order of basicity of aliphatic amines should be:

primary > secondary > tertiary, which is opposite to the inductive effect based order.

Secondly, when the alkyl group is small, like  $-\text{CH}_3$  group, there is no steric hindrance to H-bonding. In case the alkyl group is bigger than  $\text{CH}_3$  group, there will be steric hindrance to H-bonding. Therefore, the change of nature of the alkyl group, e.g., from  $-\text{CH}_3$  to  $-\text{C}_2\text{H}_5$  results in change of the order of basic strength.

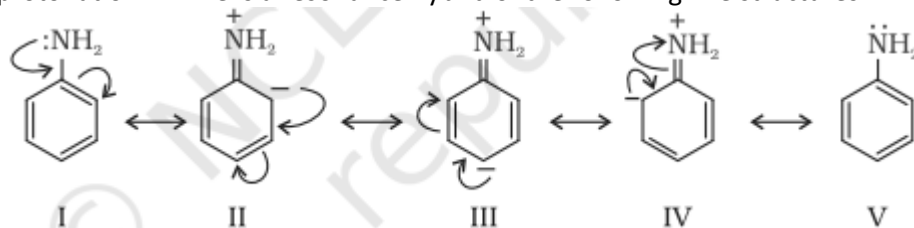
Thus, there is a subtle interplay of the inductive effect, solvation effect and steric hindrance of the alkyl group which decides the basic strength of alkyl amines in the aqueous state.

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

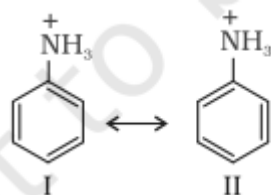


**(b) Arylamines versus ammonia:**

$pK_b$  value of aniline is quite high. Why is it so? It is because in aniline or other arylamines, the  $-NH_2$  group is attached directly to the benzene ring. It results in the unshared electron pair on nitrogen atom to be in conjugation with the benzene ring and thus making it less available for protonation. Aniline is a resonance hybrid of the following five structures.

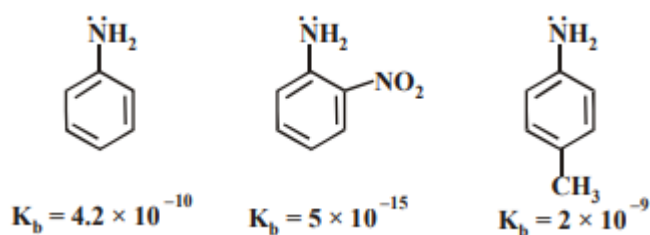


On the other hand, anilinium ion obtained by accepting a proton can have only two resonating structures (kekule).

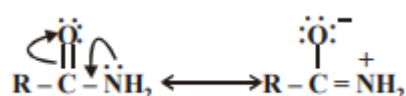


Thus, aniline (five resonating structures) is more stable than anilinium ion. Hence, the proton acceptability or the basic nature of aniline or other aromatic amines would be less than that of ammonia.

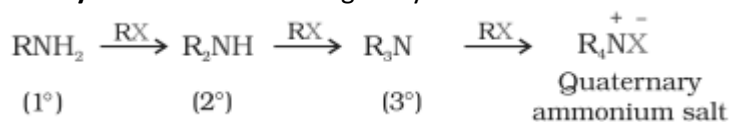
In case of substituted aniline, it is observed that electron releasing groups like  $-OCH_3$ ,  $-CH_3$  increase basic strength whereas electron withdrawing groups like  $-NO_2$ ,  $-SO_3H$ ,  $-COOH$ ,  $-X$  decrease it.



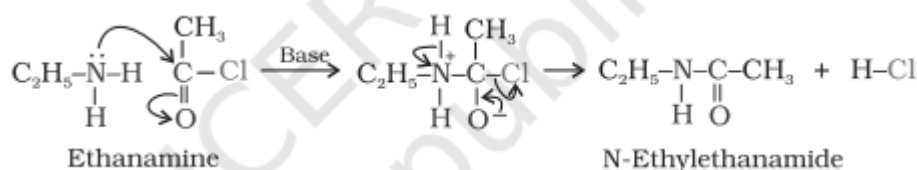
Amides are much less basic than amines due to Resonance

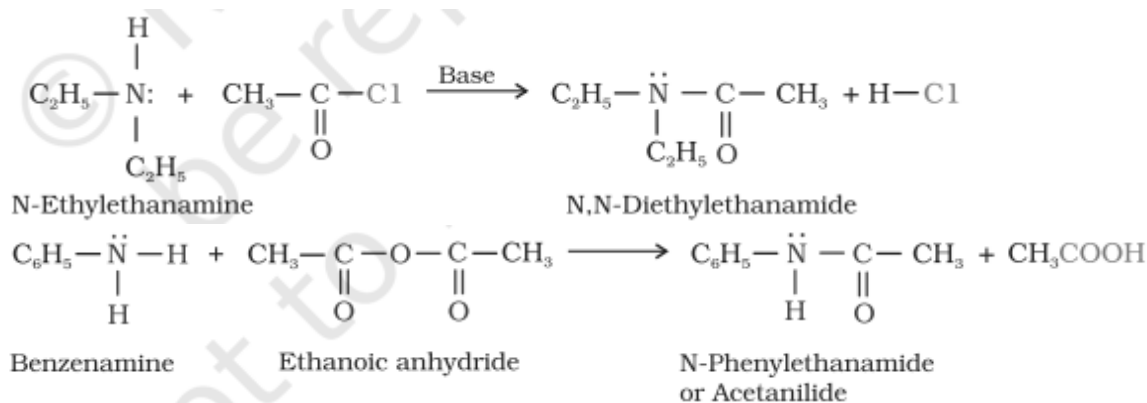


**2. Alkylation:** Amines undergo alkylation on reaction with alkyl halides



**3. Acylation:** Aliphatic and aromatic primary and secondary amines react with acid chlorides, anhydrides and esters by nucleophilic substitution reaction. This reaction is known as acylation. You can consider this reaction as the replacement of hydrogen atom of  $-NH_2$  or  $>N-H$  group by the acyl group. The products obtained by acylation reaction are known as amides. The reaction is carried out in the presence of a base stronger than the amine, like pyridine, which removes  $HCl$  so formed and shifts the equilibrium to the right hand side.

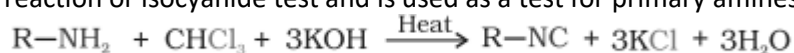




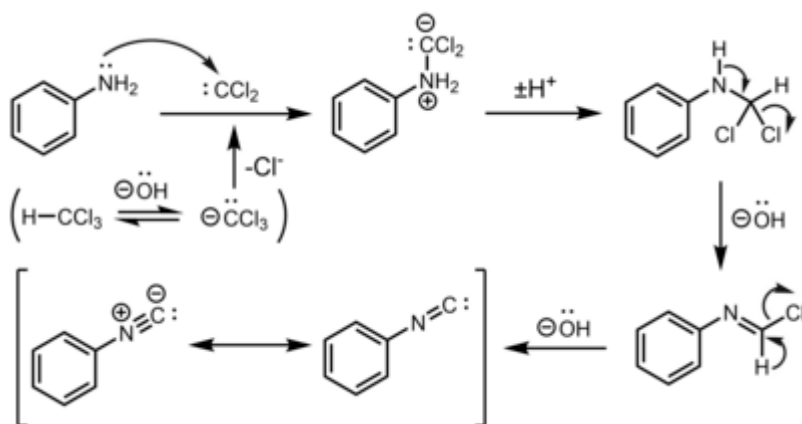
Amines also react with benzoyl chloride ( $\text{C}_6\text{H}_5\text{COCl}$ ). This reaction is known as **benzoylation**.



**4. Carbylamine reaction:** Aliphatic and aromatic primary amines on heating with chloroform and ethanolic potassium hydroxide form isocyanides or carbylamines which are foul smelling substances. Secondary and tertiary amines do not show this reaction. This reaction is known as carbylamine reaction or isocyanide test and is used as a test for primary amines.



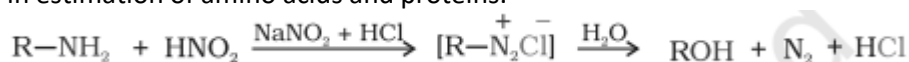
The mechanism involves the addition of amine to dichlorocarbene, a reactive intermediate generated by the dehydrohalogenation of chloroform. Two successive base-mediated dehydrochlorination steps result in formation of the isocyanide.



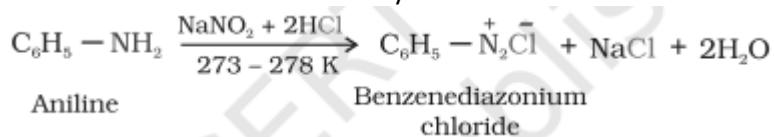
## 5. Reaction with nitrous acid:

Three classes of amines react differently with nitrous acid which is prepared in situ from a mineral acid and sodium nitrite.

(a) **Primary aliphatic amines** react with nitrous acid to form aliphatic diazonium salts which being unstable, liberate nitrogen gas quantitatively and alcohols. Quantitative evolution of nitrogen is used in estimation of amino acids and proteins.



(b) **Aromatic primary amines** react with nitrous acid at low temperatures (273-278 K) to form diazonium salts which is relatively stable.

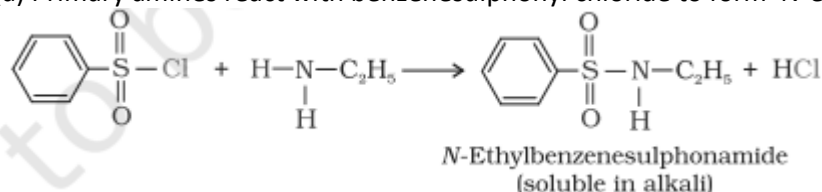


Secondary and tertiary amines react with nitrous acid in a different manner

#### 6. Reaction with arylsulphonyl chloride:

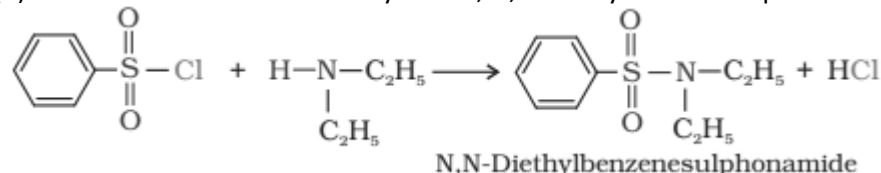
Benzenesulphonyl chloride ( $\text{C}_6\text{H}_5\text{SO}_2\text{Cl}$ ), which is also known as **Hinsberg's reagent**, reacts with primary and secondary amines to form sulphonamides.

(a) Primary amines react with benzenesulphonyl chloride to form N-ethylbenzenesulphonyl amide.



The hydrogen attached to nitrogen in sulphonamide is strongly acidic due to the presence of strong electron withdrawing sulphonyl group. Hence, it is soluble in alkali.

(b) In the reaction with secondary amine, N,N-diethylbenzenesulphonamide is formed



Since N, N-diethylbenzene sulphonamide does not contain any hydrogen atom attached to nitrogen atom, it is not acidic and hence insoluble in alkali.

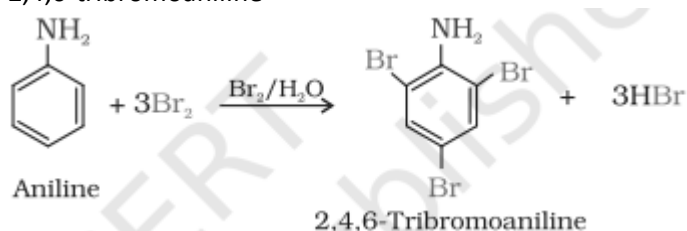
(c) Tertiary amines do not react with benzenesulphonyl chloride.

This property of amines reacting with benzenesulphonyl chloride in a different manner is used for the distinction of primary, secondary and tertiary amines and also for the separation of a mixture of amines. However, these days benzenesulphonyl chloride is replaced by p-toluenesulphonyl chloride.

#### 7. Electrophilic substitution:

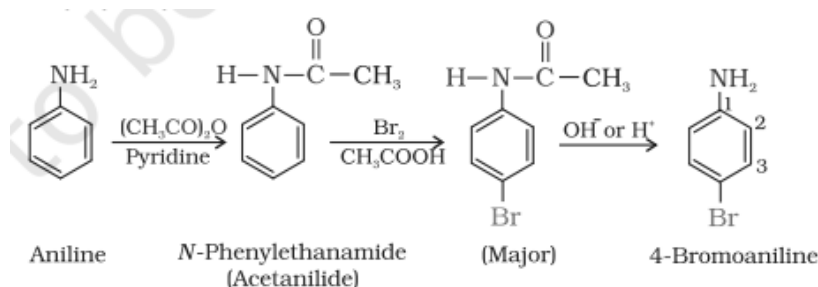
Due to resonance, Ortho- and para-positions with respect to the  $-\text{NH}_2$  group become centres of high electron density. Thus  $-\text{NH}_2$  group is ortho and para directing and a powerful activating group.

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



The main problem encountered during electrophilic substitution reactions of aromatic amines is that of their very high reactivity. Substitution tends to occur at ortho- and para-positions. If we have to prepare monosubstituted aniline derivative, how can the activating effect of  $-\text{NH}_2$  group be controlled? This can be done by protecting the  $-\text{NH}_2$  group by acetylation with acetic anhydride, then carrying out the desired substitution followed by hydrolysis of the substituted amide to the substituted amine.



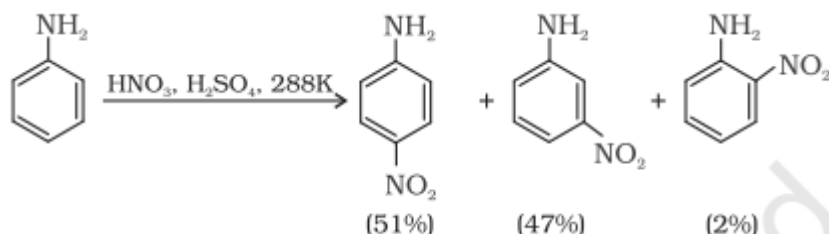


The lone pair of electrons on nitrogen of acetanilide interacts with oxygen atom due to resonance as shown below:

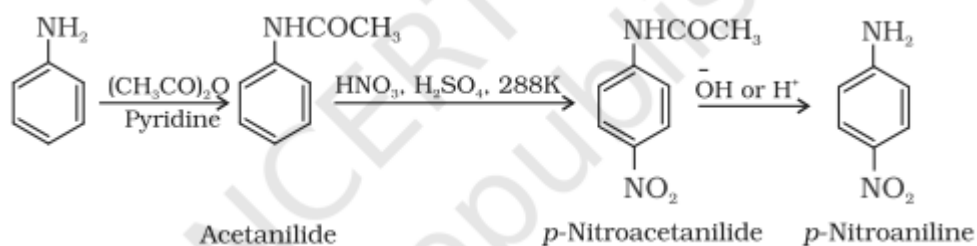


Hence, the lone pair of electrons on nitrogen is less available for donation to benzene ring by resonance. Therefore, activating effect of  $-\text{NHCOCH}_3$  group is less than that of amino group.

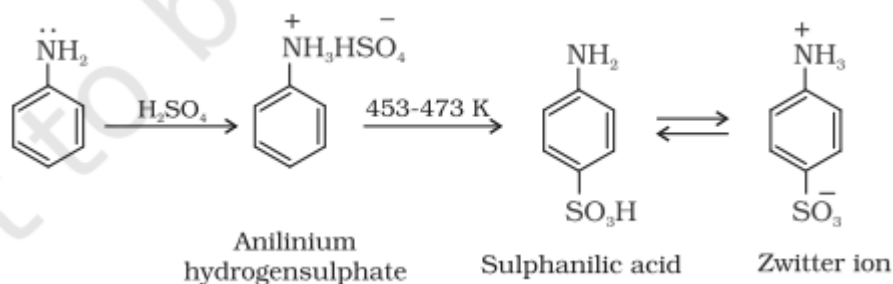
(b) **Nitration:** Direct nitration of aniline yields tarry oxidation products in addition to the nitro derivatives. Moreover, in the strongly acidic medium, aniline is protonated to form the anilinium ion which is meta directing. That is why besides the ortho and para derivatives, significant amount of meta derivative is also formed.



However, by protecting the  $-\text{NH}_2$  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.



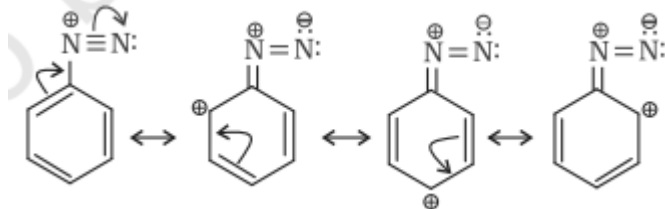
(c) **Sulphonation:** Aniline reacts with concentrated sulphuric acid to form anilinium hydrogensulphate which on heating with sulphuric acid at 453-473K produces p-aminobenzene sulphonic acid, commonly known as sulphanilic acid, as the major product.



Aniline does not undergo Friedel-Crafts reaction (alkylation and acetylation) due to salt formation with aluminium chloride, the Lewis acid, which is used as a catalyst. Due to this, nitrogen of aniline acquires positive charge and hence acts as a strong deactivating group for further reaction.

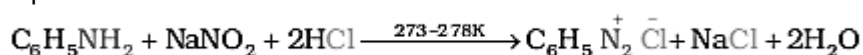
## DIAZONIUM SALTS

The diazonium salts have the general formula  $\text{Ar N}_2^+ \text{X}^-$  where Ar stands for an aryl group and  $\text{X}^-$  ion may be  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{HSO}_4^-$ ,  $\text{BF}_4^-$ , etc. Primary aromatic amines form arenediazonium salts which are stable for a short time in solution at low temperatures (273-278 K). The stability of arenediazonium ion is explained on the basis of resonance.



### Method of Preparation Preparation Preparation of Diazonium Salts:

Benzenediazonium chloride is prepared by the reaction of aniline with nitrous acid at 273-278K. Nitrous acid is produced in the reaction mixture by the reaction of sodium nitrite with hydrochloric acid. The conversion of primary aromatic amines into diazonium salts is known as **diazotisation**. Due to its instability, the diazonium salt is not generally stored and is used immediately after its preparation.



### Physical Properties:

Benzenediazonium chloride is a colourless crystalline solid. It is readily soluble in water and is stable in cold but reacts with water when warmed. It decomposes easily in the dry state.

Benzenediazonium fluoroborate is water insoluble and stable at room temperature.

### Chemical Reactions:

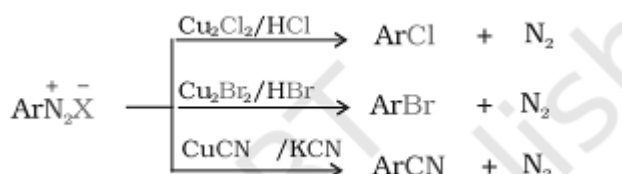
The reactions of diazonium salts can be broadly divided into two categories, namely

- (A) reactions involving displacement of nitrogen and
- (B) reactions involving retention of diazo group.

#### A. Reactions involving displacement of nitrogen

Diazonium group being a very good leaving group, is substituted by other groups such as  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{I}^-$ ,  $\text{CN}^-$  and  $\text{OH}^-$  which displace nitrogen from the aromatic ring. The nitrogen formed escapes from the reaction mixture as a gas.

**1. Replacement by halide or cyanide ion:** The  $\text{Cl}^-$ ,  $\text{Br}^-$  and  $\text{CN}^-$  nucleophiles can easily be introduced in the benzene ring in the presence of  $\text{Cu(I)}$  ion. This reaction is called Sandmeyer reaction.



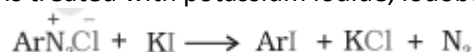
Alternatively, chlorine or bromine can also be introduced in the benzene ring by treating the diazonium salt solution with corresponding halogen acid in the presence of copper powder. This is referred as **Gatterman reaction**.



The yield in Sandmeyer reaction is found to be better than Gattermann reaction.

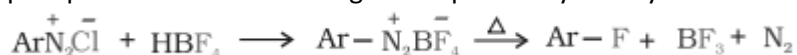
## 2. Replacement by iodide ion:

Iodine is not easily introduced into the benzene ring directly, but, when the diazonium salt solution is treated with potassium iodide, iodobenzene is formed.



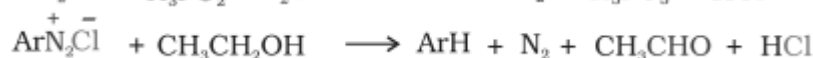
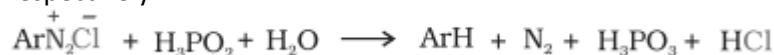
## 3. Replacement by fluoride ion:

When arenediazonium chloride is treated with fluoroboric acid, arene diazonium fluoroborate is precipitated which on heating decomposes to yield aryl fluoride.



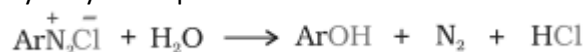
## 4. Replacement by H:

Certain mild reducing agents like hypophosphorous acid (phosphinic acid) or ethanol reduce diazonium salts to arenes and themselves get oxidised to phosphorous acid and ethanal, respectively.



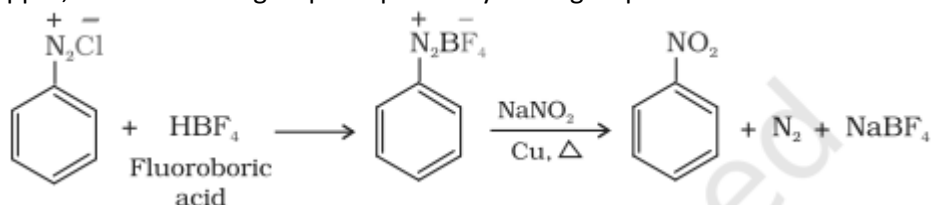
## 5. Replacement by hydroxyl group:

If the temperature of the diazonium salt solution is allowed to rise upto 283 K, the salt gets hydrolysed to phenol.



## 6. Replacement by $-\text{NO}_2$ group:

When diazonium fluoroborate is heated with aqueous sodium nitrite solution in the presence of copper, the diazonium group is replaced by  $-\text{NO}_2$  group.



## B. Reactions involving retention of diazo group :coupling reactions

The azo products obtained have an extended conjugate system having both the aromatic rings joined through the  $-\text{N}=\text{N}-$  bond. These compounds are often coloured and are used as dyes. Benzene diazonium chloride reacts with phenol in which the phenol molecule at its para position is coupled with the diazonium salt to form p-hydroxyazobenzene. This type of reaction is known as coupling reaction. Similarly the reaction of diazonium salt with aniline yields p-aminoazobenzene. This is an example of electrophilic substitution reaction where diazonium ion acts as electrophile. For this reason coupling reaction occurs only with those compounds (like phenol, aniline etc) where benzene ring highly activated and not with compounds like nitrobenzene where the ring is deactivated.

