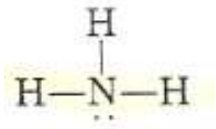
CHEM 241
Organic Chemistry II

PRE-REQUISITES COURSE; CHEM 240
CREDIT HOURS; 2 (2+0)

Amines

Structure and Classification of Amines

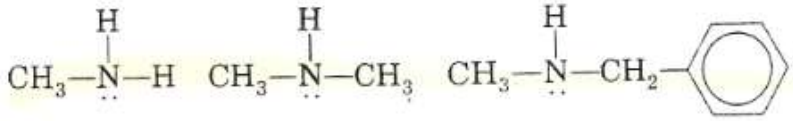
- **Amines** can be considered as derivatives of ammonia, obtained by replacement of one, two or all the three hydrogen atoms by alkyl and/or aryl groups.



Ammonia

$CH_3–NH_2$, $C_6H_5–NH_2$, $CH_3–NH–CH_3$, $CH_3–N(CH_3)_2$

- **Aliphatic amines** contain only alkyl groups bonded directly to the nitrogen atom.



Aliphatic amines

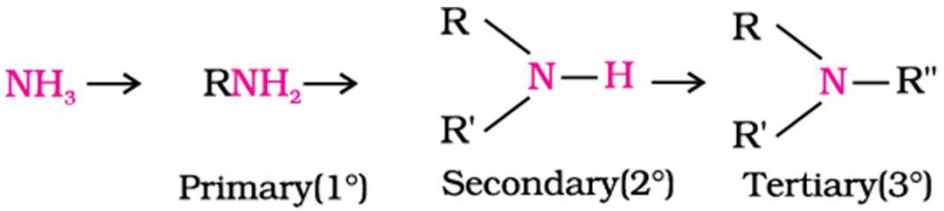
- **Aromatic amines** are those in which one or more aryl groups are bonded directly to nitrogen.

Aromatic amines

- **Amines** are said to be 'simple' when all the alkyl or aryl groups are the same, and 'mixed' when they are different.

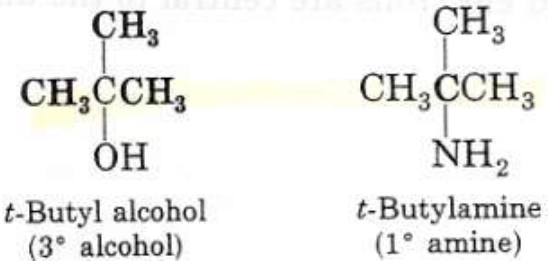
Structure and Classification of Amines

- **Amines** are classified as *primary (1^o)*, *secondary (2^o)* and *tertiary (3^o)* depending upon the number of hydrogen atoms replaced by alkyl or aryl groups in ammonia molecule.



NOTE

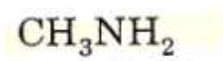
- ***t*-butyl alcohol** is a **tertiary alcohol** (because three carbons are attached to the carbinol carbon),
- ***t*-butyl amine** is a **primary alcohol** (because only one carbon is attached directly to the nitrogen atom),



Nomenclature of Amines

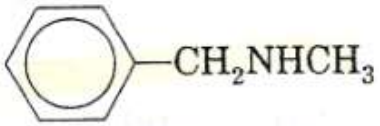
A) Common names

- An **aliphatic amine** is named by prefixing alkyl group to amine, i.e., ***alkylamine*** as one word.
- In **secondary and tertiary amines**, when two or more groups are the same, the prefix di or tri is appended before the name of alkyl group.



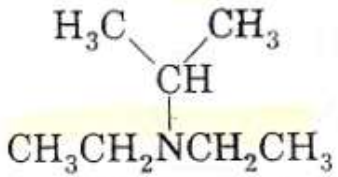
Methylamine

Ethylmethylamine



Benzylmethylamine

Dimethylamine

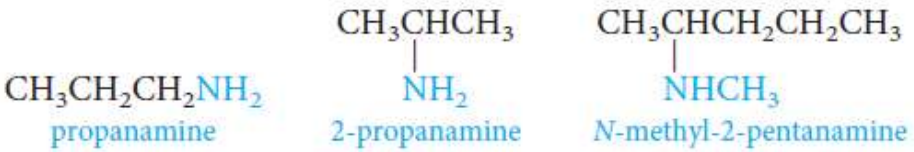


Diethylisopropylamine

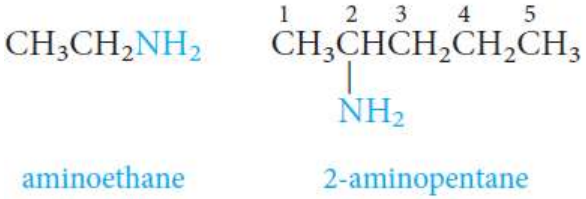
Nomenclature of Amines

B) IUPAC System

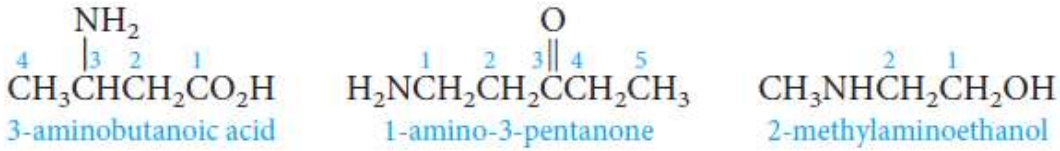
- Amines are named as "**alkanamine**", derived by replacement of 'e' of alkane by the word amine.
- For example, CH_3NH_2 is named as methanamine.



- The amino group, $-NH_2$, is named as a **substituent**.



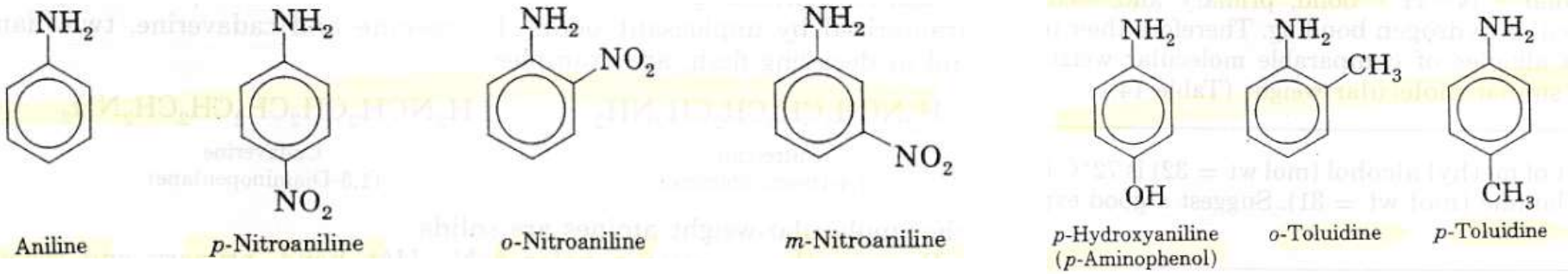
- When **other functional groups are present**, the amino group, $-NH_2$, is named as a substituent.



Nomenclature of Amines

B) IUPAC System

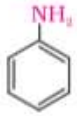
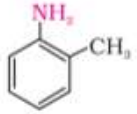
- In **arylamines**, $-NH_2$ group is directly attached to the benzene ring.
- $C_6H_5NH_2$ is the simplest example of arylamine; In common system, it is known as **aniline** and is also an accepted IUPAC name.
- While naming arylamines according to IUPAC system, suffix 'e' of arene is replaced by 'amine'.
- Thus in IUPAC system, $C_6H_5NH_2$ is named as benzenamine.



Aniline | *p*-Nitroaniline | *o*-Nitroaniline | *m*-Nitroaniline | *p*-Hydroxyaniline (*p*-Aminophenol) | *o*-Toluidine | *p*-Toluidine

Nomenclature of Amines

Nomenclature of Some Alkylamines and Arylamines

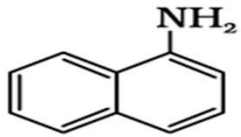
Amine	Common name	IUPAC name
$CH_3-CH_2-NH_2$	Ethylamine	Ethanamine
$CH_3-CH_2-CH_2-NH_2$	*n*-Propylamine	Propan-1-amine
$CH_3-\underset{\displaystyle NH_2}{\underset{\vert}{CH}}-CH_3$	Isopropylamine	Propan-2-amine
$CH_3-\underset{\displaystyle H}{\underset{\vert}{N}}-CH_2-CH_3$	Ethylmethylamine	N-Methylethanamine
$CH_3-\underset{\displaystyle CH_3}{\underset{\vert}{N}}-CH_3$	Trimethylamine	N,N-Dimethylmethanamine
$C_2H_5-\underset{\displaystyle C_2H_5}{\underset{\vert}{N}}-\overset{1}{CH_2}-\overset{2}{CH_2}-\overset{3}{CH_2}-\overset{4}{CH_3}$	*N,N*-Diethylbutylamine	N,N-Diethylbutan-1-amine
$NH_2-\overset{1}{CH_2}-\overset{2}{CH}=\overset{3}{CH_2}$	Allylamine	Prop-2-en-1-amine
$NH_2-(CH_2)_6-NH_2$	Hexamethylenediamine	Hexane-1,6-diamine
	Aniline	Aniline or Benzenamine
	*o*-Toluidine	2-Methylaniline
	*p*-Bromoaniline	4-Bromobenzenamine or 4-Bromoaniline
	*N,N*-Dimethylaniline	N,N-Dimethylbenzenamine

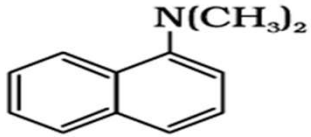
Nomenclature of Amines

Questions

Question one:

Classify the following amines as primary, secondary or tertiary:

(i) 

(ii) 

(iii) $(C_2H_5)_2CHNH_2$

(iv) $(C_2H_5)_2NH$

Question two:

(i)Write structures of different isomeric amines corresponding to the molecular formula, $C_4H_{11}N$.

(ii) Write IUPAC names of all the isomers.

(iii) What type of isomerism is exhibited by different pairs of amines?

Physical Properties of Amines

Physical State

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

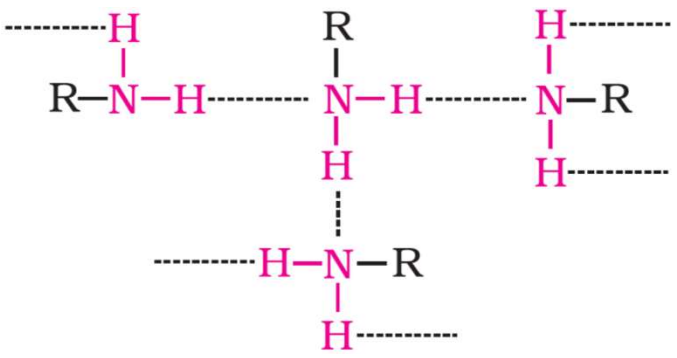
Solubility in Water

- **Lower aliphatic amines** are soluble in water because they can form *hydrogen bonds* with water molecules.
- **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.
- Amines are **soluble in organic solvents** like alcohol, ether and benzene.

Physical Properties of Amines

Boiling Points

- You may remember that **alcohols are more polar than amines** and **form stronger intermolecular hydrogen bonds than amines**.
- **Primary and secondary amines** are engaged in intermolecular association due to hydrogen bonding between nitrogen of one and hydrogen of another molecule.
- **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

Physical Properties of Amines

Boiling Points

- **Primary amines** boil well above alkanes with comparable molecular weights, but below comparable alcohols.

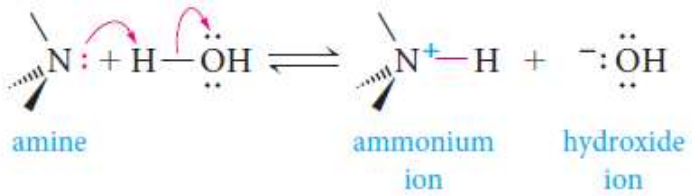
  Intermolecular N-H· · ·N hydrogen bonds are important and raise the boiling points of primary and secondary amines but are not as strong as the O-H · · · O bonds of alcohols.

  The reason for this is that nitrogen is not as electronegative as oxygen.

alkane	CH_3CH_3 (30) bp −88.6°C	$CH_3CH_2CH_3$ (44) bp −42.1°C
amine	CH_3NH_2 (31) bp −6.3°C	$CH_3CH_2NH_2$ (45) bp +16.6°C
alcohol	CH_3OH (32) bp +65.0°C	CH_3CH_2OH (46) bp +78.5°C

The Basicity of Amines

- The unshared pair of electrons on the nitrogen atom dominates the chemistry of amines.
- **Because of this electron pair, amines are both basic and nucleophilic.**
- Aqueous solutions of amines are basic because of the following equilibrium:



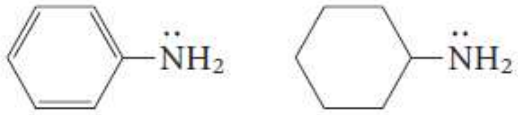
  - Electron-donating groups increase the basicity of amines.
  - Electron-withdrawing groups decrease their basicity.

- **Alkylamines** are stronger bases than ammonia.
- Thus, the basic nature of aliphatic amines should increase with increase in the number of alkyl groups.
- **The order of basicity of amines** follows the expected order:

  tertiary amine > secondary amine > primary amine > NH_3.

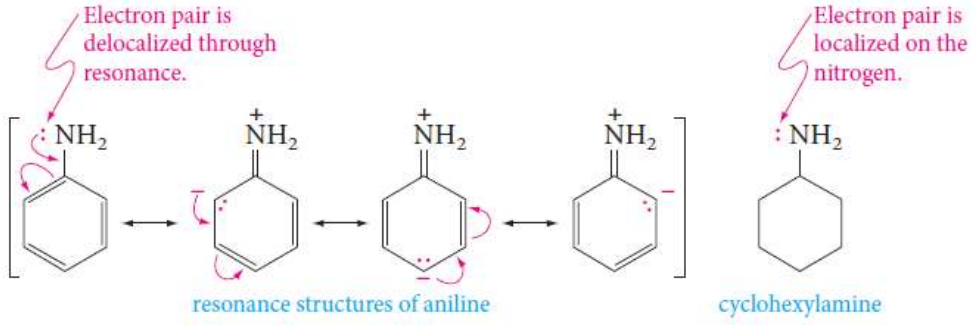
The Basicity of Amines

- **Aromatic amines** are much weaker than aliphatic amines or ammonia.
  - Example: aniline is less basic than cyclohexylamine.

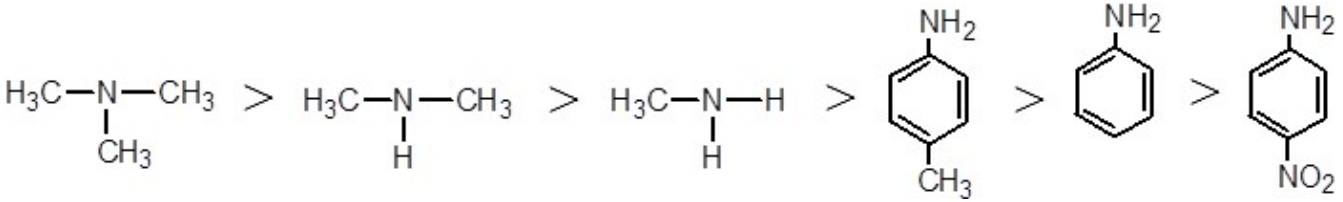


aniline cyclohexylamine

The reason is the resonance delocalization of the unshared electron pair that is possible in aniline, but not in cyclohexylamine:



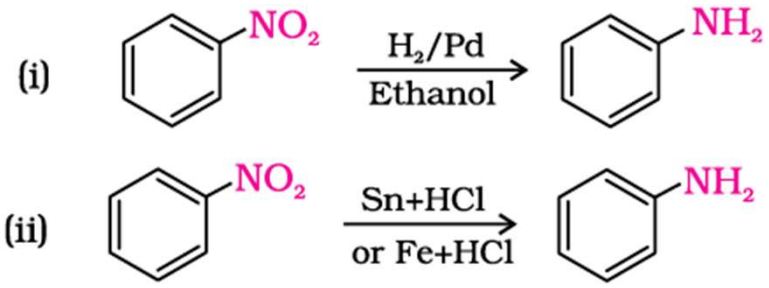
resonance structures of aniline cyclohexylamine



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.



$$CH_3CH_2NO_2 \xrightarrow{H_2/Pt} CH_3CH_2NH_2$$

Preparation of Amines

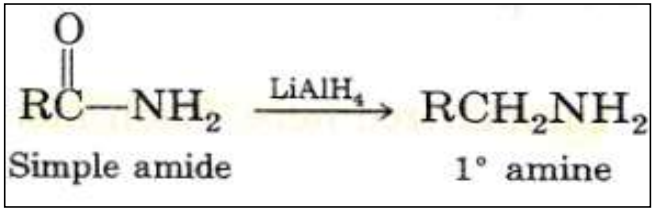
2. Reduction of Nitriles

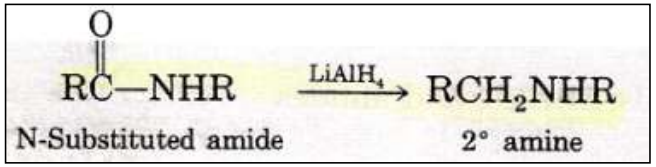
- **Nitriles** on reduction with lithium aluminum hydride ($LiAlH_4$) or catalytic hydrogenation produce primary amines.
- This reaction is used for preparation of **amines containing one carbon atom more** than the starting amine.

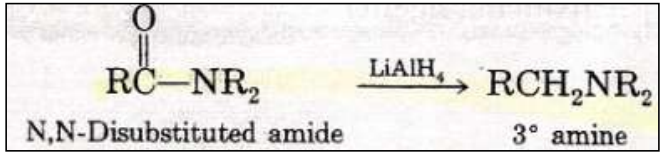
$$R{-}C{\equiv}N \xrightarrow[Na(Hg)/C_2H_5OH]{H_2/Ni} R{-}CH_2{-}NH_2$$

3. Reduction of Amides

- The **amides** on reduction with lithium aluminium hydride yield amines.



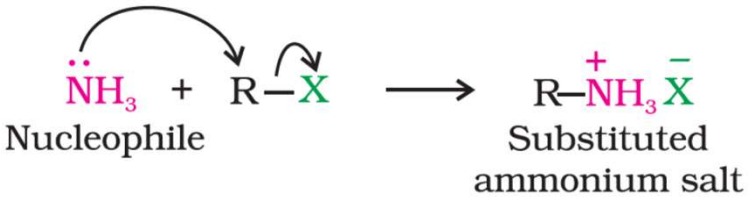




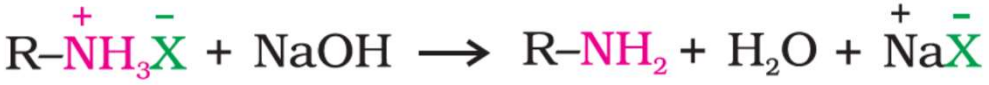
Preparation of Amines

4. Ammonolysis of alkyl halides

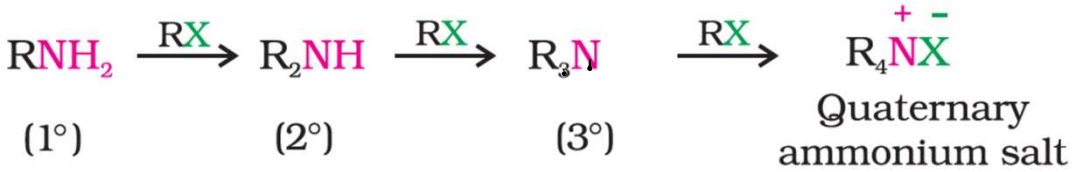
- Alkyl or benzyl halide on reaction with an ethanolic solution of ammonia undergoes nucleophilic substitution reaction in which the halogen atom is replaced by an amino ($-NH_2$) group.
- This process of **cleavage of the C–X bond by ammonia molecule is known as ammonolysis**.



- Treatment of the alkylammonium salt with a strong base (NaOH) liberates the free amine.



- Ammonolysis has the **disadvantage of yielding a mixture** of primary, secondary and tertiary amines and also a quaternary ammonium salt.



Questions

Write chemical equations for the following reactions:
(i) Reaction of ethanolic NH_3 with C_2H_5Cl.
(ii) Ammonolysis of benzyl chloride and reaction of amine so formed with two moles of CH_3Cl.

Solution

(i) $C_2H_5–Cl \xrightarrow{NH_3} C_2H_5–NH_2 \xrightarrow{C_2H_5-Cl} C_2H_5–\underset{H}{N}–C_2H_5 \xrightarrow{C_2H_5-Cl} C_2H_5–\underset{C_2H_5}{\underset{|}{N}}–C_2H_5 \xrightarrow{C_2H_5Cl} (C_2H_5)_3\overset{+}{N}\,\overset{-}{Cl}$

Chloroethane — Ethanamine — N-Ethylethanamine — N,N-Diethylethanamine — Quaternary ammonium Salt

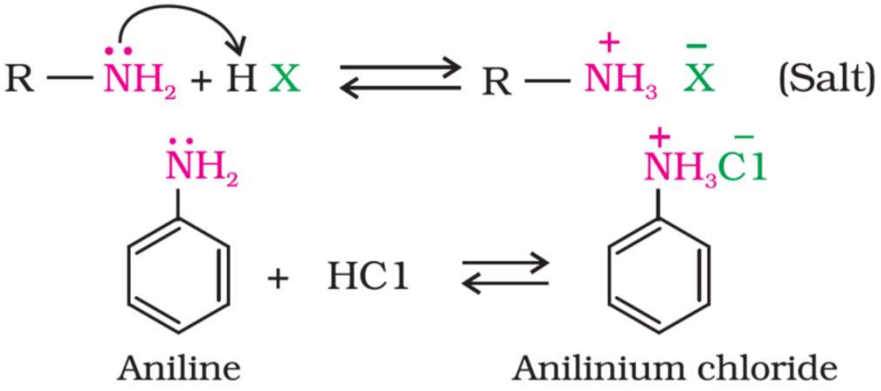
(ii) $C_6H_5–CH_2–Cl \xrightarrow{NH_3} C_6H_5–CH_2NH_2 \xrightarrow{2CH_3Cl} C_6H_5–CH_2–\underset{CH_3}{\underset{|}{N}}–CH_3$

Benzylchloride — Benzylamine — N,N-Dimethylphenylmethanamine

Chemical Reactions of Amines

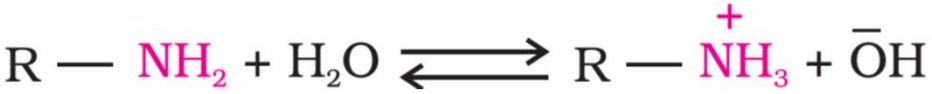
1. Basic character of amines

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



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

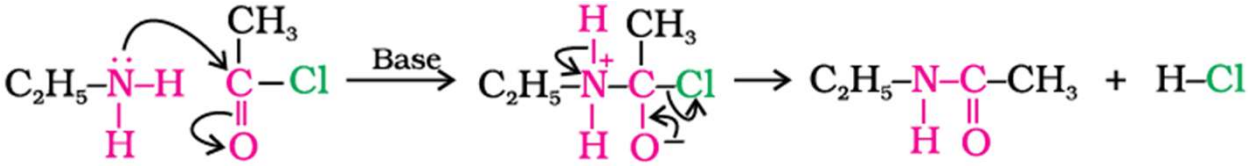
- Amines have an unshared pair of electrons on nitrogen atom due to which they behave as **Lewis base**.



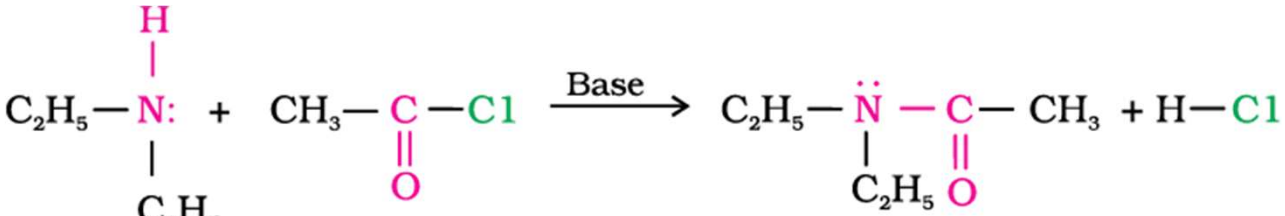
Chemical Reactions of Amines

2. Acylation

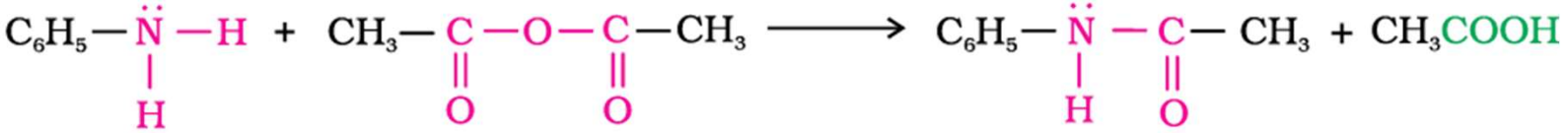
- **Aliphatic and aromatic primary and secondary amines** react with acid chlorides, anhydrides and esters by nucleophilic substitution reaction.
- The products obtained by acylation reaction are known as **amides**.



Ethanamine — N-Ethylethanamide



N-Ethylethanamine — N,N-Diethylethanamide



Benzenamine — Ethanoic anhydride — N-Phenylethanamide or Acetanilide

Chemical Reactions of Amines

2. Acylation

- Amines also **react with benzoyl chloride** (C_6H_5COCl). This reaction is known as **benzoylation.**

$$\underset{\text{Methanamine}}{CH_3NH_2} + \underset{\text{Benzoyl chloride}}{C_6H_5COCl} \rightarrow \underset{\text{N – Methylbenzamide}}{CH_3NHCOC_6H_5} + HCl$$

- What do you think is the product of the reaction of amines with carboxylic acids ?
  They form salts with amines at room temperature.

3. 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.

$$R{-}NH_2 + CHCl_3 + 3KOH \xrightarrow{\text{Heat}} R{-}NC + 3KCl + 3H_2O$$

Chemical Reactions of Amines

4. Reaction with nitrous acid

(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.

$$R{-}NH_2 + HNO_2 \xrightarrow{NaNO_2 + HCl} [R{-}\overset{+}{N}_2\overset{-}{Cl}] \xrightarrow{H_2O} ROH + N_2 + HCl$$

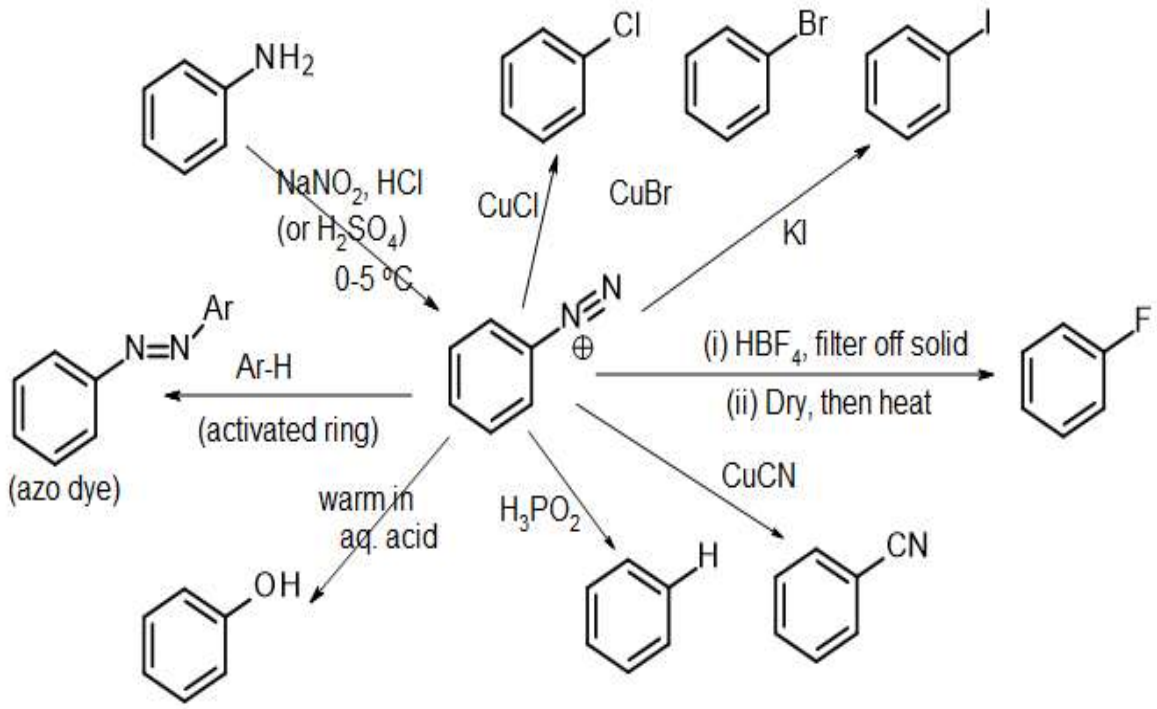
(b) Aromatic amines react with nitrous acid at low temperatures (273-278 K) to form diazonium salts, a very important class of compounds used for synthesis of a variety of aromatic compounds.

$$\underset{\text{Aniline}}{C_6H_5{-}NH_2} \xrightarrow[273-278\ K]{NaNO_2 + 2HCl} \underset{\text{Benzenediazonium chloride}}{C_6H_5{-}\overset{+}{N}_2\overset{-}{Cl}} + NaCl + 2H_2O$$

Chemical Reactions of Amines

4. Reaction with nitrous acid

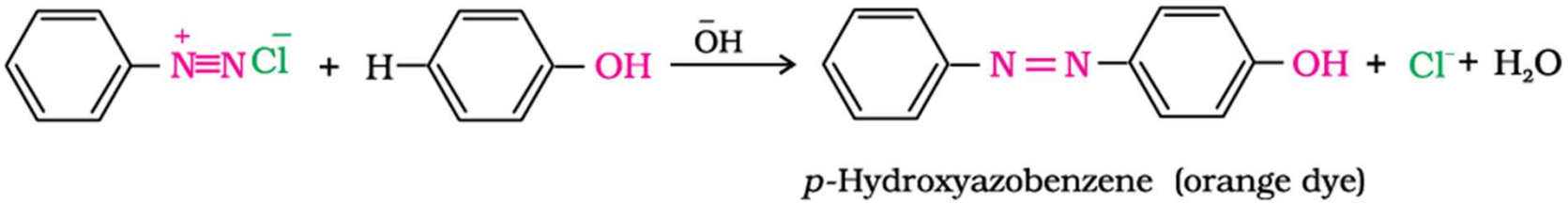
- They are useful in synthesis because the **diazonio groum ($-N_2^+$) can be replaced by nucleophiles**; the other product is nitrogen gas.



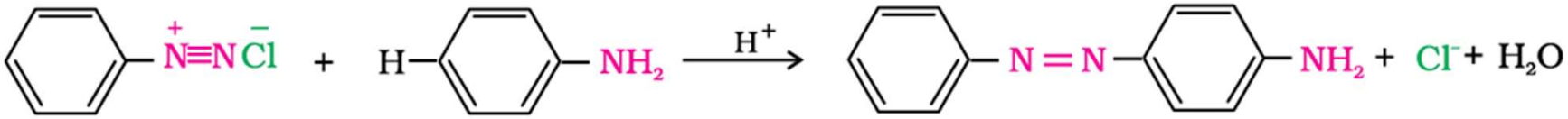
Chemical Reactions of Amines

4. Reaction with nitrous acid

- ***Reactions involving retention of diazo group coupling reactions***
  - 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.
  - Similarly the reaction of diazonium salt **with aniline** yields *p*-aminoazobenzene.



p-Hydroxyazobenzene (orange dye)



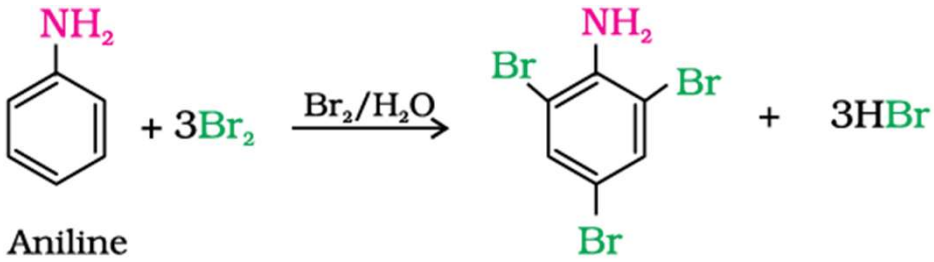
p-Aminoazobenzene
(yellow dye)

Chemical Reactions of Amines

5. Electrophilic substitution

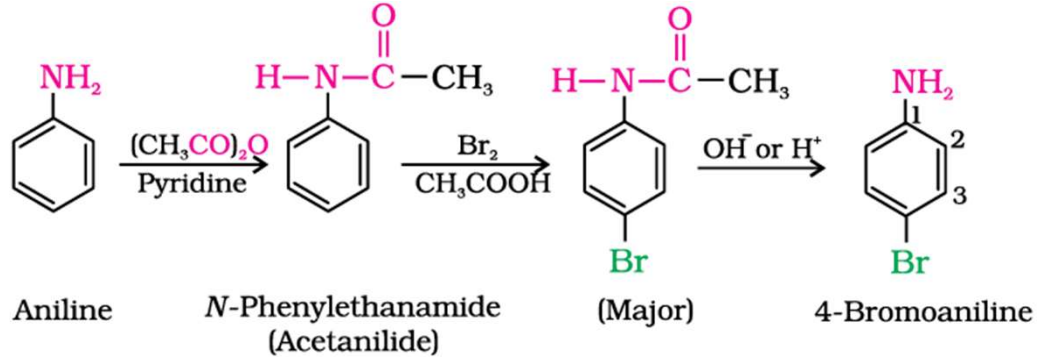
(a) Bromination:

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



If we have to prepare monosubstituted aniline derivative, how can the activating effect of $-NH_2$ group be controlled ?

This can be done by protecting the $-NH_2$ group by acetylation with acetic anhydride, then carrying out the desired substitution followed by hydrolysis of the substituted amide to the substituted amine.

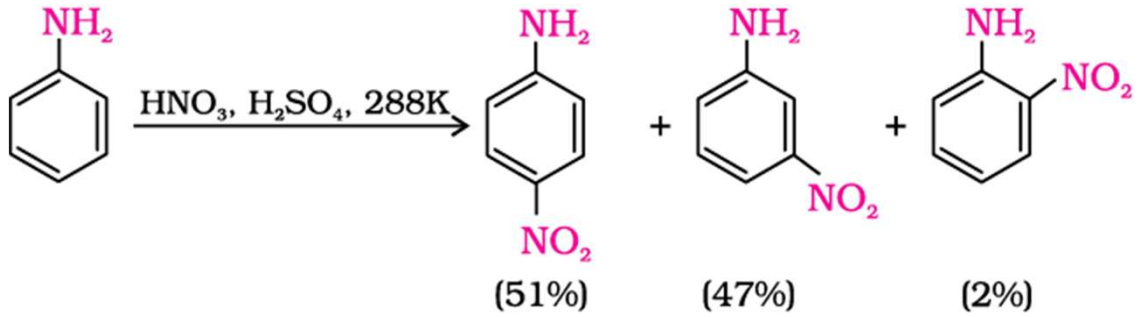


Chemical Reactions of Amines

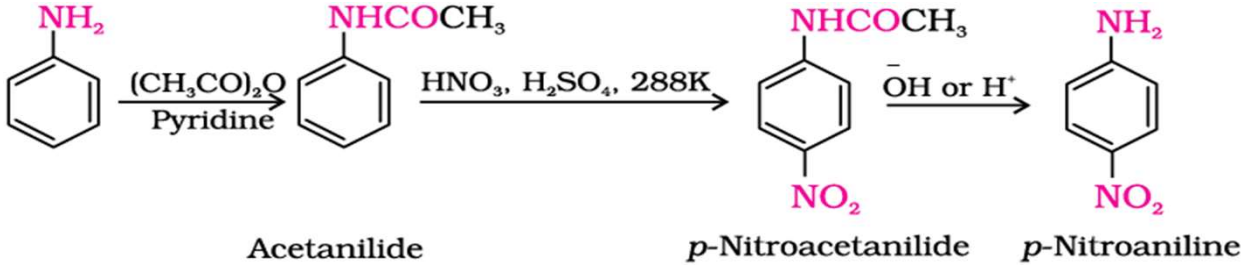
5. Electrophilic substitution

(b) Nitration:

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 –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.

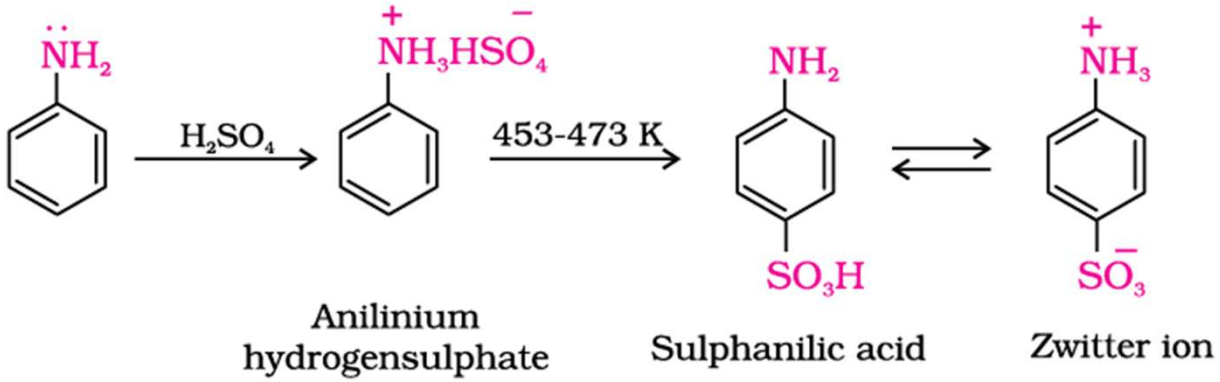


Chemical Reactions of Amines

5. Electrophilic substitution

(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.



(d) Friedel-Crafts reaction (alkylation and acetylation):

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.

Chemical Reactions of Amines

Questions

1) Arrange the following in increasing order of their basic strength:

(i) $C_2H_5NH_2$, $C_6H_5NH_2$, NH_3, $C_6H_5CH_2NH_2$ and $(C_2H_5)_2NH$

(ii) $C_2H_5NH_2$, $(C_2H_5)_2NH$, $(C_2H_5)_3N$, $C_6H_5NH_2$

(iii) CH_3NH_2, $(CH_3)_2NH$, $(CH_3)_3N$, $C_6H_5NH_2$, $C_6H_5CH_2NH_2$.

2) Complete the following acid-base reactions and name the products:

(i) $CH_3CH_2CH_2NH_2 + HCl \rightarrow$ (ii) $(C_2H_5)_3N + HCl \rightarrow$

3) Write reactions of the final alkylation product of aniline with excess of methyl iodide in the presence of sodium carbonate solution.

4) Write chemical reaction of aniline with benzoyl chloride and write the name of the product obtained.

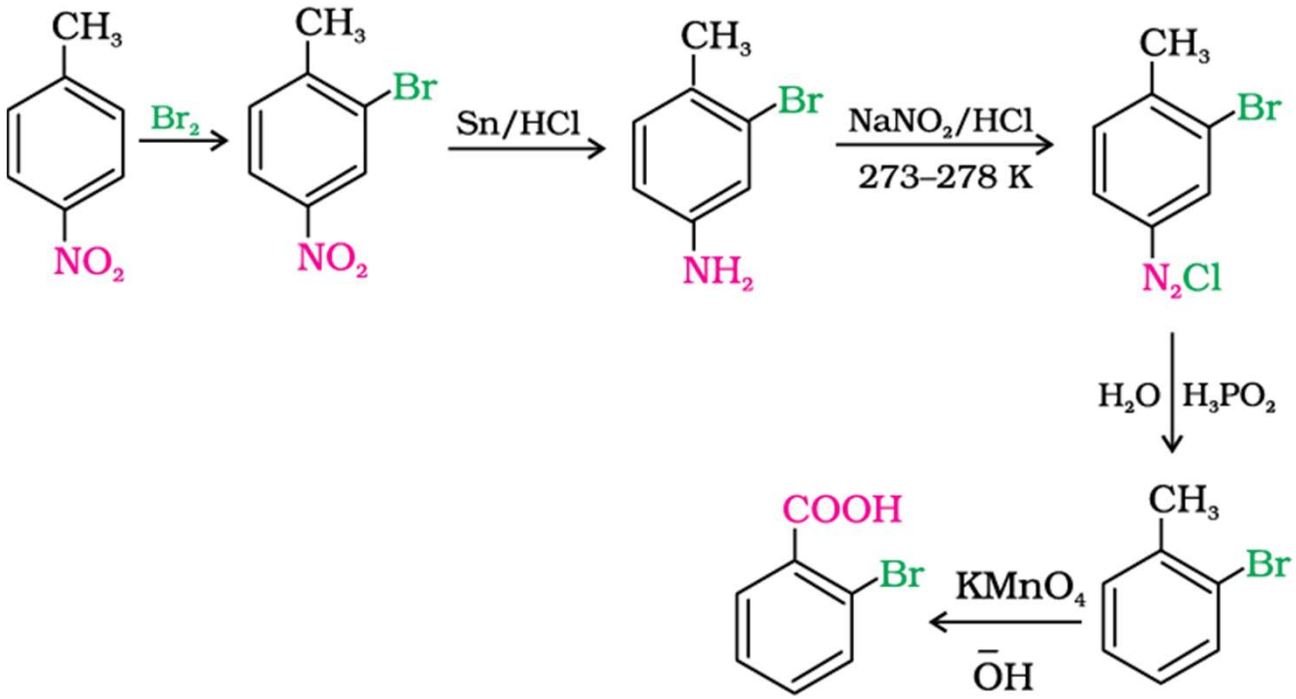
5) Write structures of different isomers corresponding to the molecular formula, C_3H_9N. Write IUPAC names of the isomers which will liberate nitrogen gas on treatment with nitrous acid.

Chemical Reactions of Amines

Question:

How will you convert 4-nitrotoluene to 2-bromobenzoic acid ?

Solution



Uses of Amines

- In nature, they occur among proteins, vitamins, alkaloids and hormones.
- Synthetic examples include polymers, dyestuffs and drugs.
- Two biologically active compounds, namely adrenaline and ephedrine, both containing secondary amino group, are used to increase blood pressure.
- Novocain, a synthetic amino compound, is used as an anesthetic in dentistry.
- Benadryl, a well known antihistaminic drug also contains tertiary amino group.
- Quaternary ammonium salts are used as surfactants.
- Diazonium salts are intermediates in the preparation of a variety of aromatic compounds including dyes.