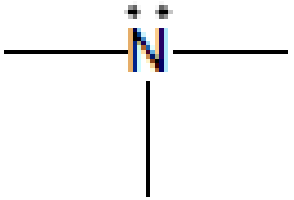
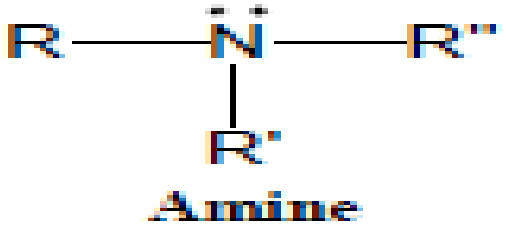
UNIT TWO
Amines

Introduction;

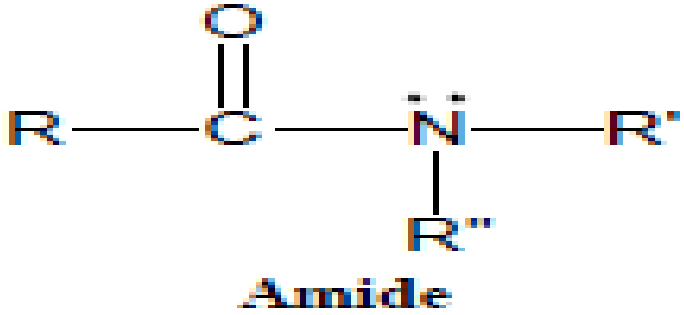
- Nitrogen is in Group V of the periodic table, and in most of its compounds, it has three single bonds and one lone pair:



- Amines and amides are abundant in nature.
- They are a major component of:
  - ✓ proteins and enzymes,
  - ✓ nucleic acids, alkaloid drugs, etc. (Alkaloids are unds)



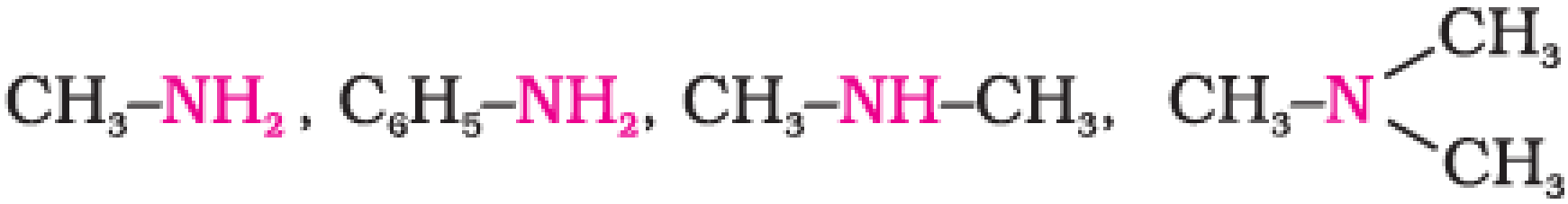
Amine



Amide

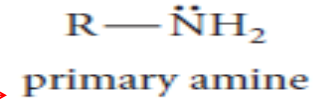
The Chemistry of Amines

- Are organic derivatives of ammonia, NH3;
- which the ammonia hydrogens are replaced by alkyl or aryl groups. For instance:

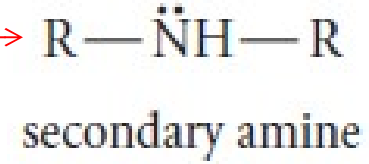


- Amines are classified by the number of alkyl or aryl substituents

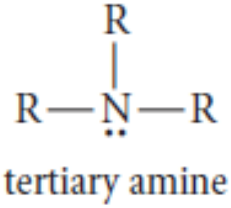
(R groups) on the amine nitrogen.



- ✓ A primary amine has one substituent;

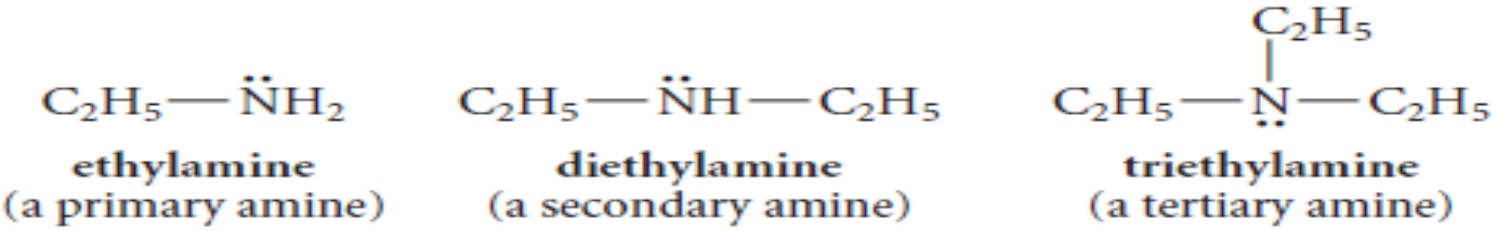


- ✓ a secondary amine has two;

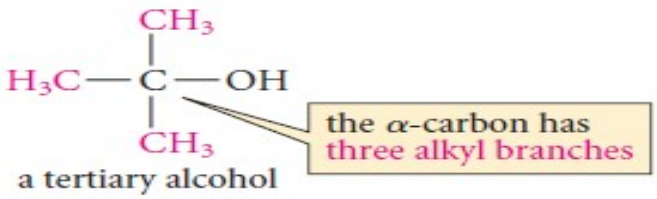


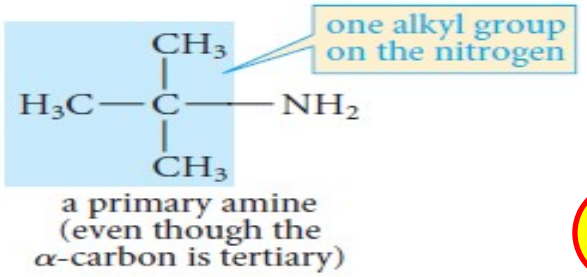
- ✓ a tertiary amine has three

For example;



- It is important to distinguish between the classifications of alcohols and amines;
- alcohols are classified according to the number of alkyl or aryl groups on the *a-carbon*,
- *but amines (like amides) are classified according* to the number of alkyl or aryl groups *on nitrogen*.



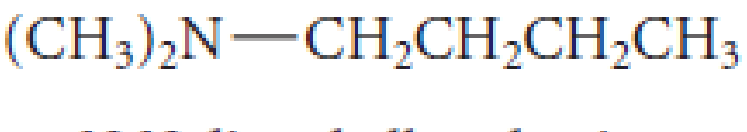


NOMENCLATURE OF AMINES

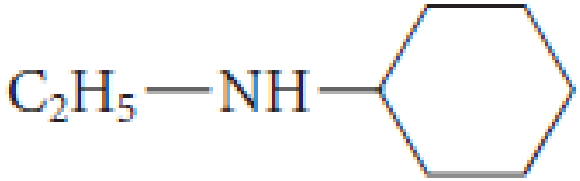
- In common system, an aliphatic amine is named by prefixing alkyl group to amine. For example; alkylamine as one word (e.g., met



- In secondary and tertiary amines, when two or more groups are the same, the prefix *di or tri* is appended before t



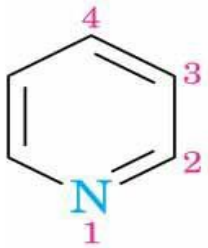
N,N-dimethylbutylamine



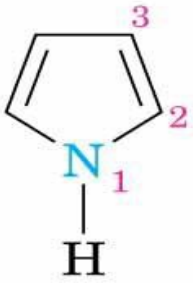
N-ethylcyclohexylamine

Common naming System...,

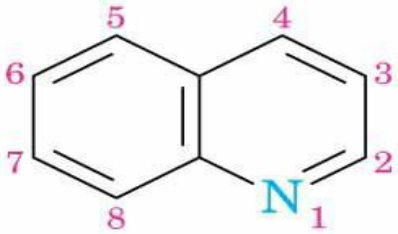
- If the nitrogen atom occurs as part of a ring, the compound is designated as being heterocyclic.



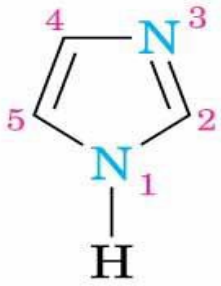
Pyridine



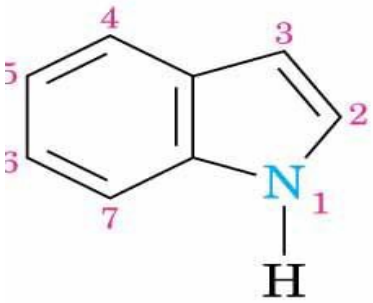
Pyrrole



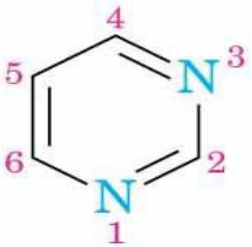
Quinoline



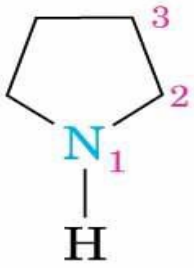
Imidazole



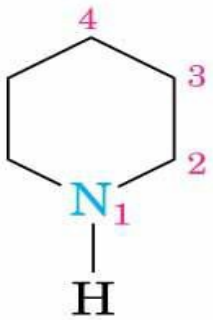
Indole



Pyrimidine



Pyrrolidine



Piperidine

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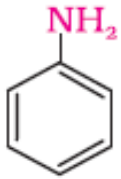
IUPAC system

- In IUPAC system, amines are named as alkanamines, derived by replacement of ‘e’ of alkane by the word amine.
- For example, CH_3NH_2 is named as methanamine.
- In case, more than one amino group is present at different positions in the parent chain, their positions are specified by giving numbers to the carbon atoms bearing $-NH_2$ groups and suitable prefix such as *di, tri*, etc. is attached to the amine.
- The letter ‘e’ of the suffix of the hydrocarbon part is retained.

NOMENCLATURE…,

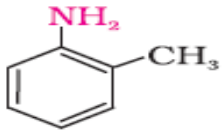
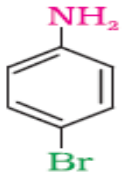
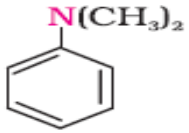
- In arylamines, $-NH_2$ group is directly attached to the benzene ring.
- $C_6H_5NH_2$ is the simplest example of arylamine and its common system is aniline.
- It is also an accepted IUPAC name. While naming arylamines according to IUPAC system, suffix ‘e’ of arene is replaced by ‘amine’.
- Thus in IUPAC system, $C_6H_5–NH_2$ is named as benzenamine.
- Common and IUPAC names of some alkylamines and

NOMENCLATURE...,

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
$C_2H_5-\underset{\displaystyle C_2H_5}{\underset{\vert}{N}}-\overset{1}{C}H_2-\overset{2}{C}H_2-\overset{3}{C}H_2-\overset{4}{C}H_3$	*N*,*N*-Diethylbutylamine	N,N-Diethylbutan-1-amine
$NH_2-\overset{1}{C}H_2-\overset{2}{C}H=\overset{3}{C}H_2$	Allylamine	Prop-2-en-1-amine
$NH_2-(CH_2)_6-NH_2$	Hexamethylenediamine	Hexane-1,6-diamine
	Aniline	Aniline or Benzenamine

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NOMENCLATURE...,

	*o*-Toluidine	2-Methylaniline
	*p*-Bromoaniline	4-Bromobenzenamine or 4-Bromoaniline
	*N*,*N*-Dimethylaniline	N,N-Dimethylbenzenamine

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PROBLEMS

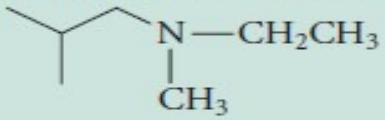
23.1 Draw the structure of each of the following compounds.

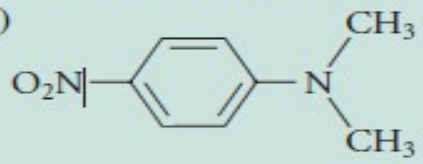
(a) *N*-isopropylaniline (b) *tert*-butylamine

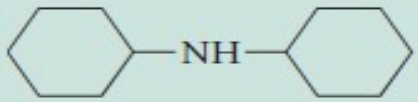
(c) 3-methoxypiperidine (d) 2,2-dimethyl-3-hexanamine

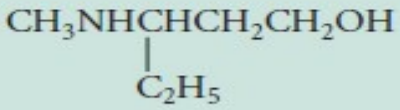
(e) ethyl 2-(diethylamino)pentanoate (f) *N*,*N*-diethyl-3-heptanamine

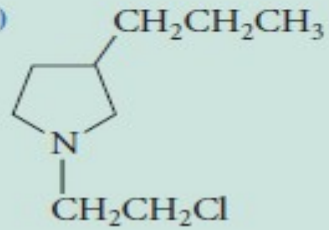
23.2 Give an acceptable name for each of the following compounds.

(a) 

(b) 

(c) 

(d) 

(e) 

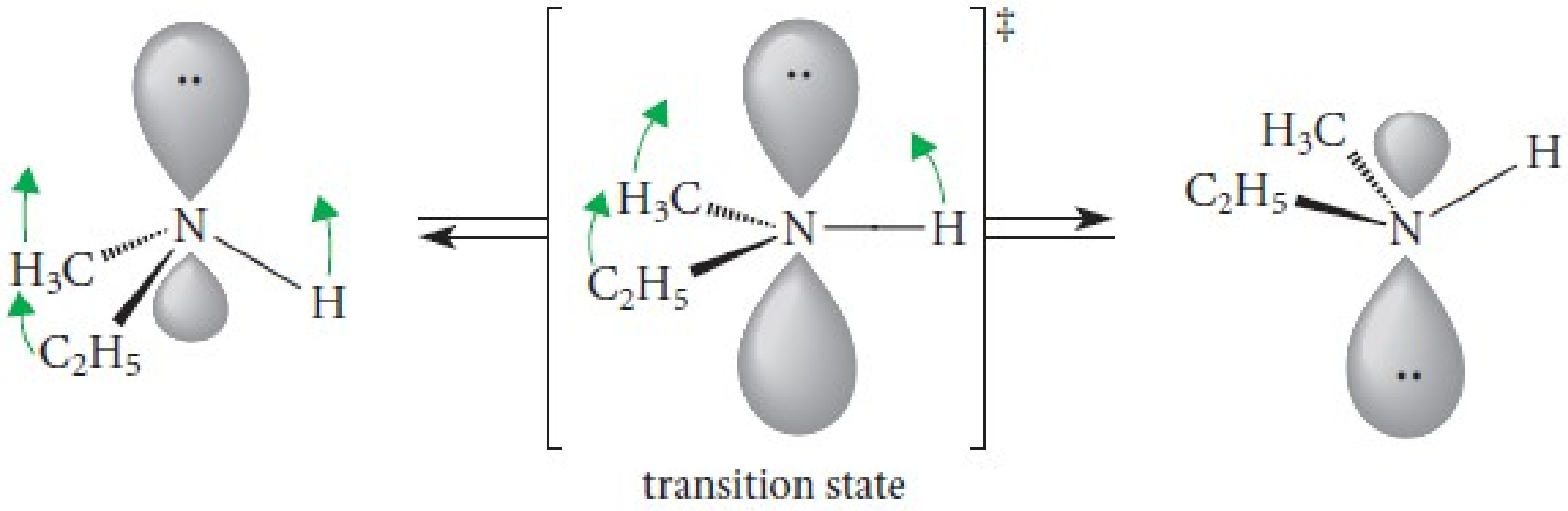
STRUCTURE OF AMINES

- The C-N bonds of aliphatic amines are longer than the C-O bonds of alcohols, but shorter than the C-C bonds of alkanes, as expected from the effect of atomic size on bond length.
- For instanc

bond:	C—C	C—N	C—O	C—F
typical length:	1.54 Å	1.47 Å	1.43 Å	1.39 Å

- Aliphatic amines have a pyramidal shape (or approximately tetrahedral shape, if the electron pair is considered to be a "group").
- Most amines undergo rapid *inversion at nitrogen, which* occurs through a planar transition state and converts a chiral amine into its mirror image. See the follo

Inversion…,



- Because of this rapid inversion, amines in which the only asymmetric atom is the amine nitrogen cannot be resolved into enantiomers and it is bonding to N is similar to that in ammonia.
- N is *sp3-hybridized,*
- C–N–C bond angles are close to 109°tetrahedral valu

Physical Properties of Amines

- ✓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.

Essay…?

- Between butan-1-ol and butan-1-amine, which will be more soluble in water and why?
- 1° and 2° amines have lower boiling points than alcohols of similar molecular weight.
- Hydrogen bonding between 1° and 2° amines is not as strong as those found in alcohols or carboxylic acids.
- Hydrogen bonds from N—H's are not as strong as those resulting from O—H's.
- 3° amines, since they do not hydrogen bond to each other,
- have similar boiling points to hydrocarbons of the s

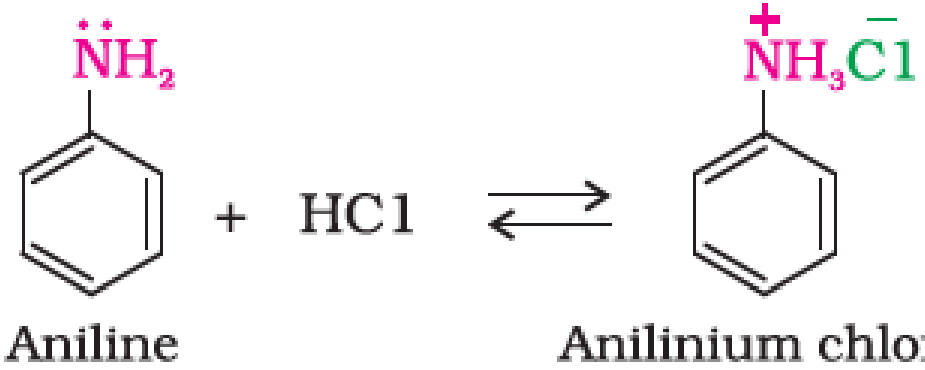
Chemical Properties of Amines

- Difference in EN between N-H atoms with 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; p ($-NH_2$), secondary $\left(\begin{array}{l}\diagup\\\diagdown\end{array}N-H\right)$ and tertiary amines $\left(\begin{array}{l}\diagup\\\diagdown\end{array}N-\right)$
- This is why primary differ in many reactions and moreover, amines behave as nucleophiles due to the presence of unshared electron pair.
- Some of the reactions of amines are described below

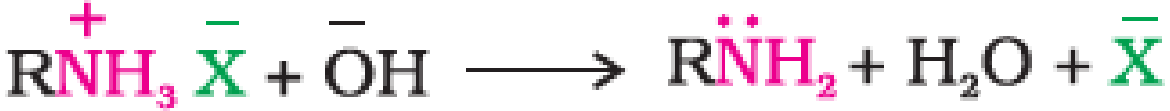
Basic character of amines

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





- And this amine salts on treatment with a base like NaOH, regenerate the parent amine



Cont'd...,

- 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.
- The reaction of amines with mineral acids to form ammonium salts shows that these are basic in nature.
- 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 *Kb* and p*Kb values as explained below:*

Hypothetical Reaction...,

$$R-NH_2 + H_2O \rightleftharpoons R-\overset{+}{N}H_3 + \overline{O}H$$

$$K = \frac{[R-\overset{+}{N}H_3][\overline{O}H]}{[R-NH_2][H_2O]}$$

$$\text{or } K[H_2O] = \frac{[R-\overset{+}{N}H_3][\overline{O}H]}{[R-NH_2]}$$

$$\text{or } \quad K_b = \frac{[R-\overset{+}{N}H_3][\overline{O}H]}{[R-NH_2]}$$

$$pK_b = -\log K_b$$

For instance:

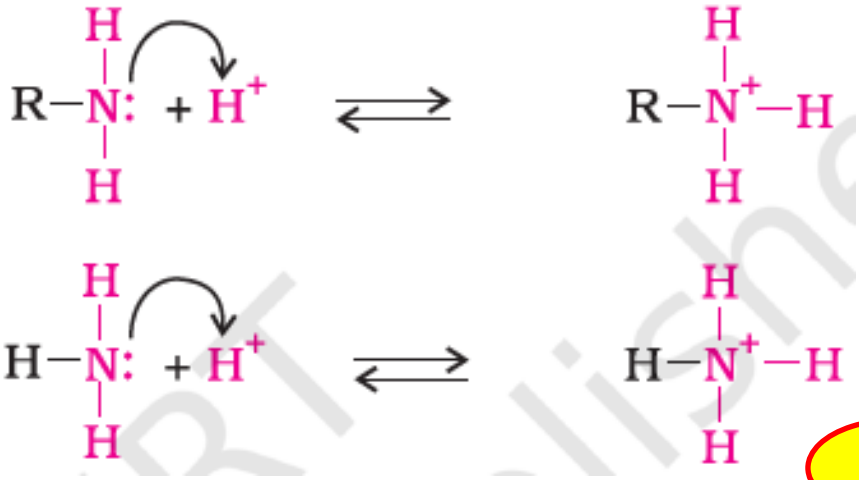
- Larger the value of *Kb or smaller the value of pKb, stronger is the* base; eg.p*Kb value of ammonia is 4.75*.
- *Aliphatic amines are stronger bases* than ammonia due to +I effect of alkyl groups leading to high electron density on the nitrogen atom.
- Their p*Kb values lie in the range of 3 to* 4.22.
- On the other hand, aromatic amines are weaker bases than ammonia due to the electron withdrawing nature of the aryl group.

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, the more basic is the amine.

i) Alkanamines versus ammonia

- consider the reaction of an alkanamine and NH_3 with a proton to compare their basicity.

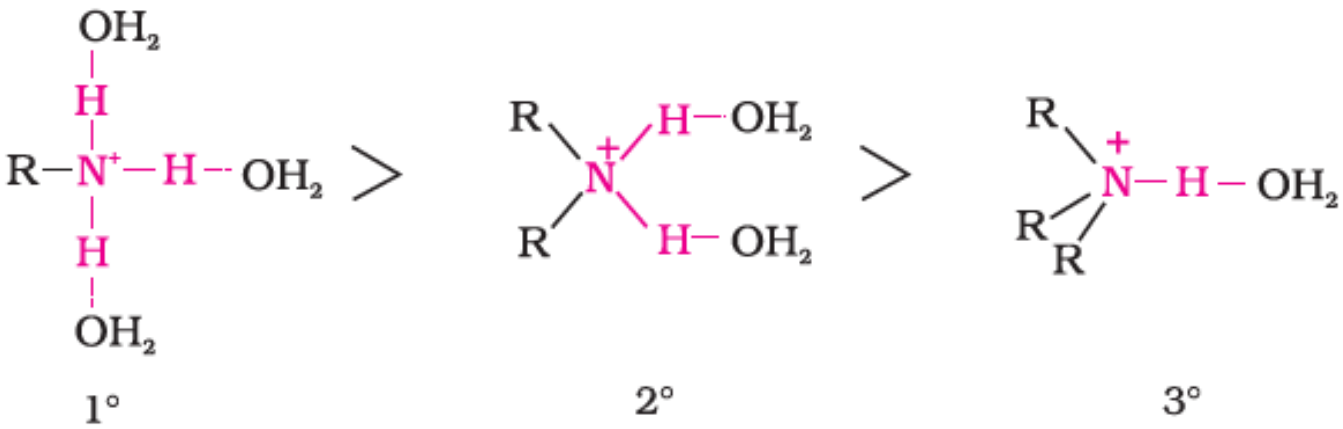


Alkanamines Vs NH_3

- Due to the electron releasing nature of alkyl group, it (R) pushes electrons towards nitrogen;
- 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;
- This is due to dispersal of the positive charge by the +I effect of the alkyl group.
- Hence, alkylamines are stronger bases than ammonia

Cont'd...,

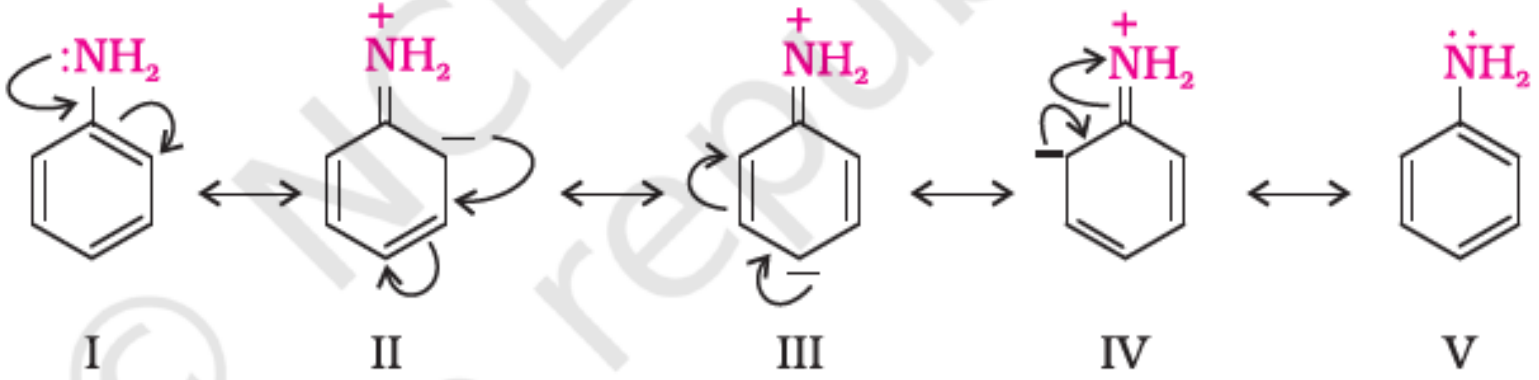
- Thus, the basic nature of aliphatic amines should increase with increase in the number of alkyl groups.
- The order of basicity of amines in the gaseous phase follows the expected order: tertiary amine > secondary amine > prima



- The greater the size of the ion, lesser will be the solvation and the less stabilised is the ion.

(ii) Arylamines versus ammonia

- p*Kb* *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;
- thus making it less available for protonation.



Example:

- Arrange the following in decreasing order of their basic strength:
- Hence, the decreasing order of basic strength of the above amines and ammonia follows the following order:

$(C_2H_5)_2NH > C_2H_5NH_2 > NH_3 > C_6H_5NH_2$.

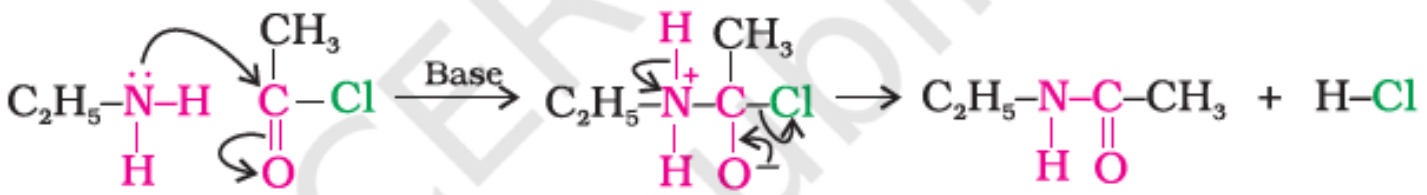
- greater the number of resonating structures, greater is the stability.
- Thus you can infer that aniline (five resonating structures) is more stable than anilinium ion.
- Hence, the proton acceptability or the basic nature of aniline or other aromatic amines would be less than th

Alkylation

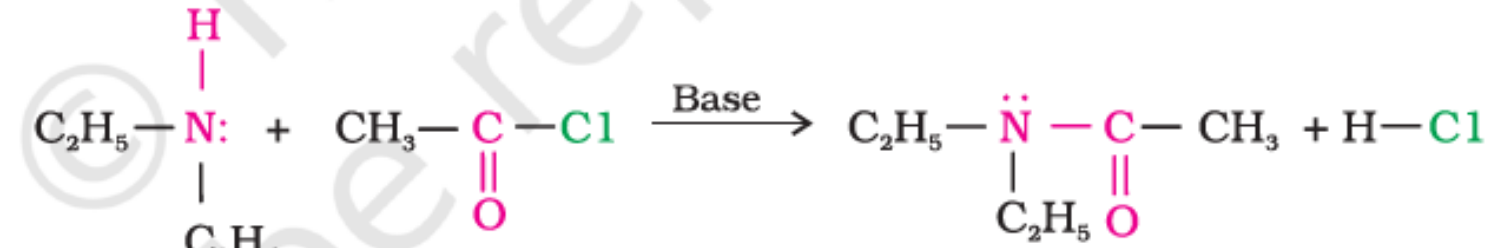
- Amines undergo alkylation on reaction with alkyl halides

Acylation

- Aliphatic and aromatic primary and secondary amines react with acid chl... ...hilic substitut... reaction



Ethanamine → N-Ethylethanamide



N-Ethylethanamine → N,N-Diethylethanamide

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Benzoylation

- Amines also react with benzoyl chloride (C_6H_5COCl).

$$CH_3NH_2 + C_6H_5COCl \rightarrow CH_3NHCOC_6H_5 + HCl$$

Methanamine Benzoyl chloride N – Methylbenzamide

Carbylamine reaction

- Aliphatic and aromatic primary amines on heating with chloroform and ethanolic potassium hydroxide form isocyanides or carbylamines; which are foul smelling substances.
- $R{-}NH_2 + CHCl_3 + 3KOH \xrightarrow{Heat} R{-}NC + 3KCl + 3H_2O$v this reaction.

Reaction with nitrous acid

- Primary aliphatic amines react with nitrous acid to form aliphatic diazonium salts which being unstable, liberate nitrogen gas quantitatively and alcohols. For instance:



- 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 compo



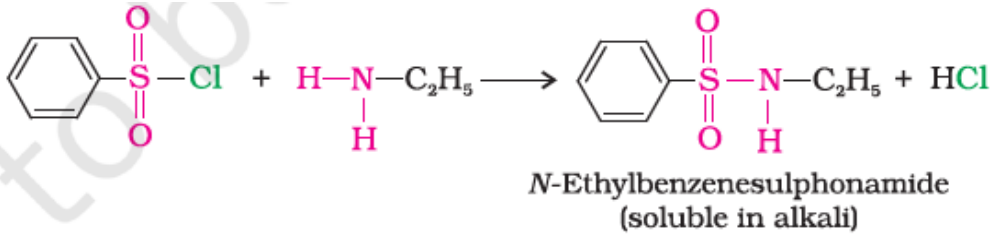
Aniline

Benzenediazonium chloride

Reaction with arylsulphonyl chloride

➢Benzenesulphonyl chloride ($C_6H_5SO_2Cl$), which is also known as Hinsberg's reagent, reacts with primary and secondary amines to form sulphonamides.

a)The reaction of benzenesulphonyl chloride with primary amine yields N-ethylbenzenesulphonyl amide.



N-Ethylbenzenesulphonamide
(soluble in alkali)

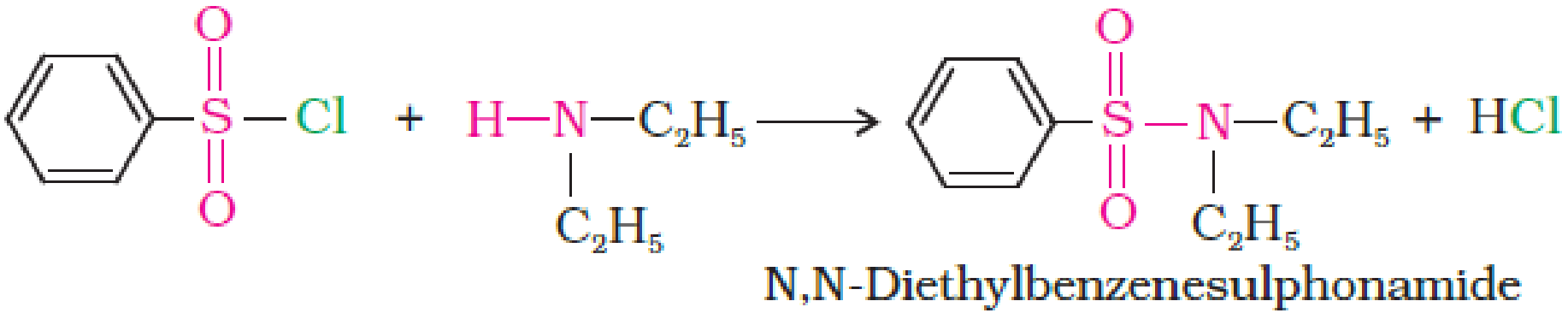
➢The hydrogen attached to nitrogen in sulphonamide is strongly

acidic due to the presence of strong electron withdrawing

Cont'd...,

b)In the reaction with secondary amine,

N,N-diethylbenzenesulphonamide is formed.



N,N-Diethylbenzenesulphonamide

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

Cont'd...,

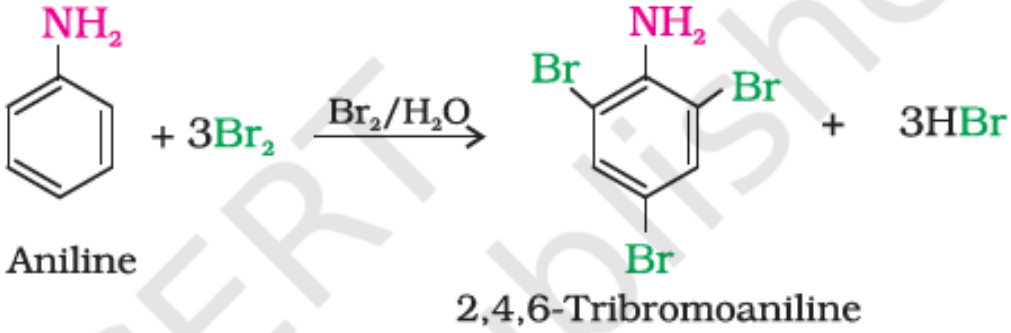
c)Tertiary amines do not react with benzenesulphonyl chloride

- This property of amines reacting with benzenesulphonyl chloride
- **Electrophilic substitution** in a different manner is used for the distinction of primary, secondary and tertiary amines;

Q. Where do you find the maximum electron density in these structures?

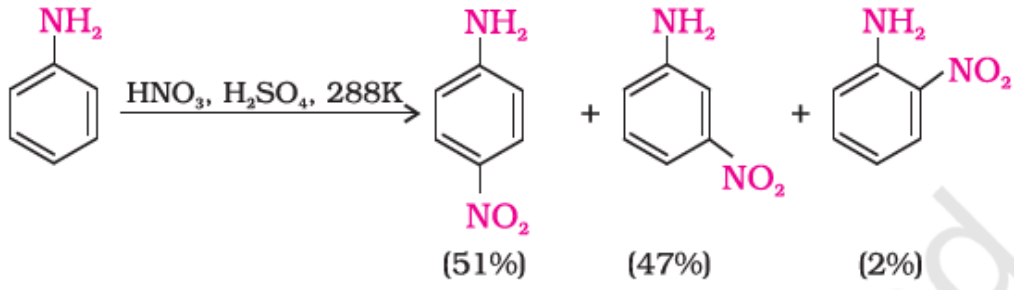
- *Ortho- and para-positions to the –NH_2 group* become centers of high electron density.
- Thus –NH_2 group is *ortho* and *para directing and a powerful activating group.*

A) Bromination



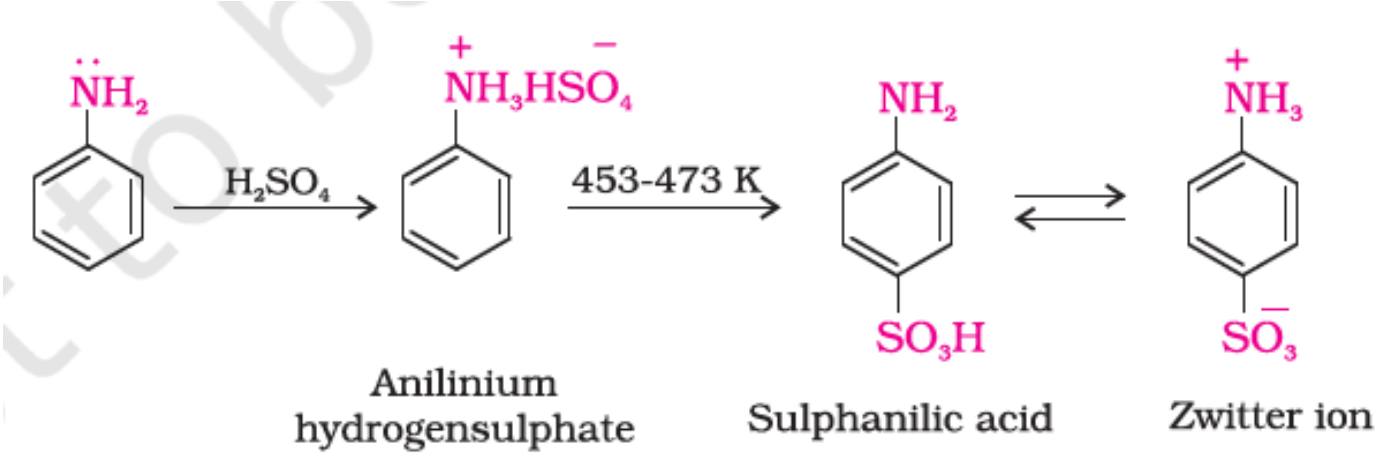
B) Nitration:

- 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

C) Sulphonation

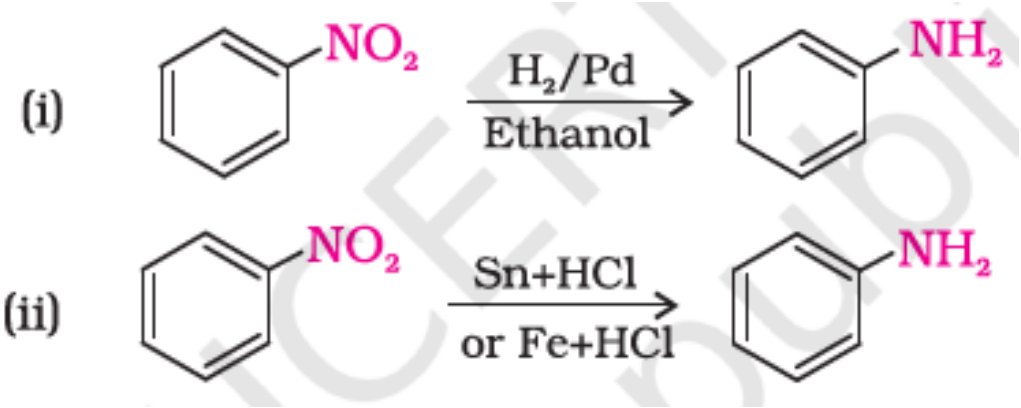


- Aniline does not undergo Friedel-Crafts reaction (alkylation and acetylation);
- This is due to salt formation with aluminium chloride, the Lewis acid, which is used as a catalyst.

Preparation of Amines

i) Reduction of nitro compounds

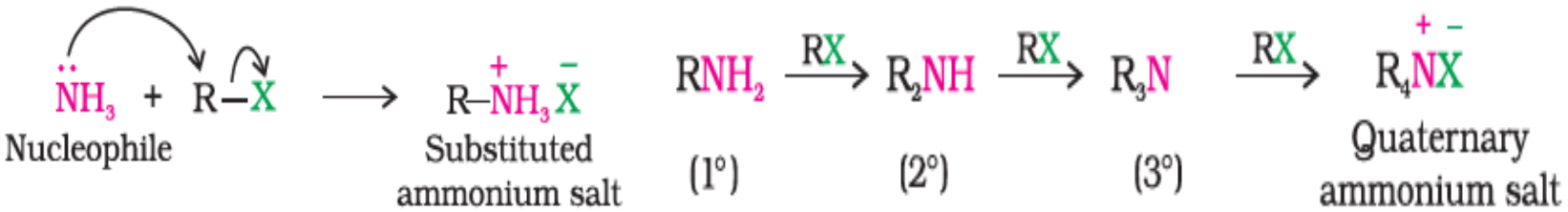
➢Nitro compounds are reduced to amines by passing hydrogen gas in the presence of finely divided nickel, palladium or platinum and also by reduction with metals in acidic m



➢Due to the formation of $FeCl_2$; use only a small amount of hydrochloric acid is required to initiate the reaction

ii) Ammonolysis of alkyl halides

- the carbon - halogen bond in alkyl or benzyl halides can be easily cleaved by a nucleophile.
- Hence, an 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 primary amino ($-NH_2$) group.
- The amine thus obtained behaves as a nucleophile and can further react with alkyl halide to form secondary and tertiary amines, and finally quaternary



iii) Reduction of nitriles

- Nitriles on reduction with lithium aluminium hydride ($LiAlH_4$) or catalytic hydrogenation produce primary amines.
- This reaction is used for ascent of amine series, i.e., for preparation of amines con

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

nore than the starting amine. For example:

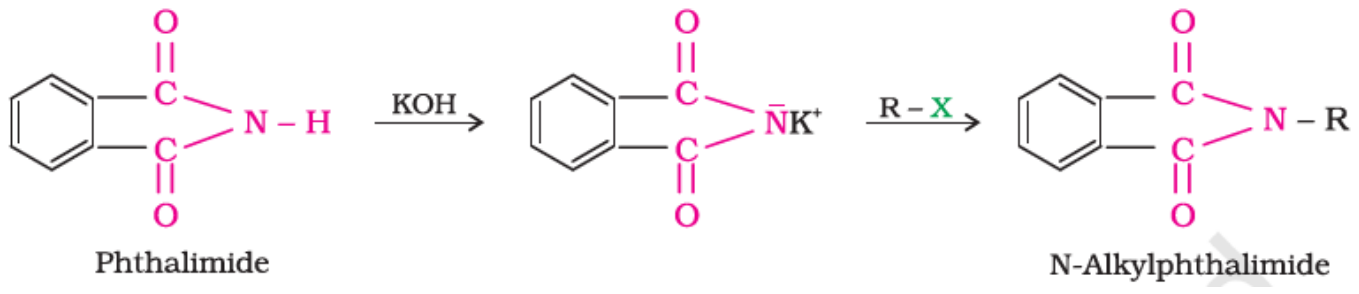
iv) Reduction of amides

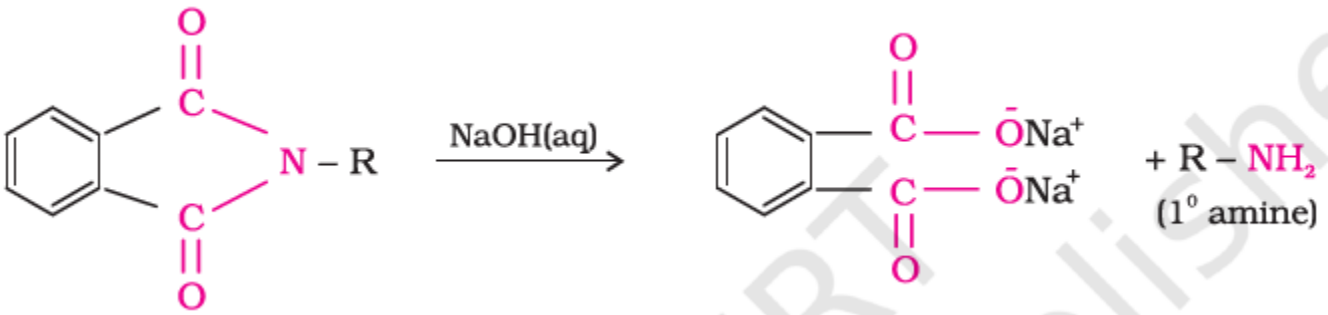
- The amides on reduction with lithium aluminium hydride yield amines. Eg.

$$R{-}\overset{\overset{O}{\|}}{C}{-}NH_2 \xrightarrow[(ii)\ H_2O]{(i)\ LiAlH_4} R{-}CH_2{-}NH_2$$

v) Gabriel phthalimide synthesis

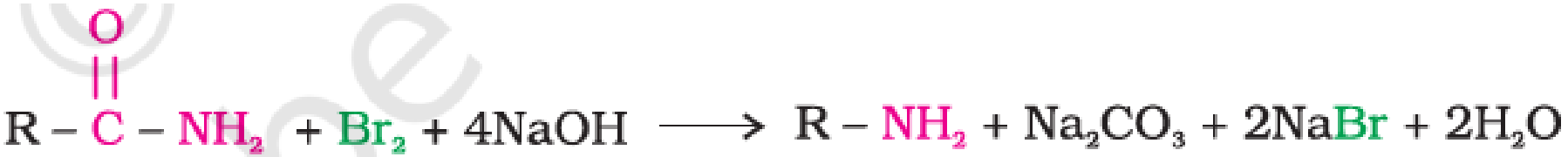
- Gabriel synthesis is used for the preparation of primary amines.
- Phthalimide on treatment with ethanolic potassium hydroxide forms potassium salt of phthalimide which on heating with a is produces the c





vi) Hoffmann bromamide degradation reaction

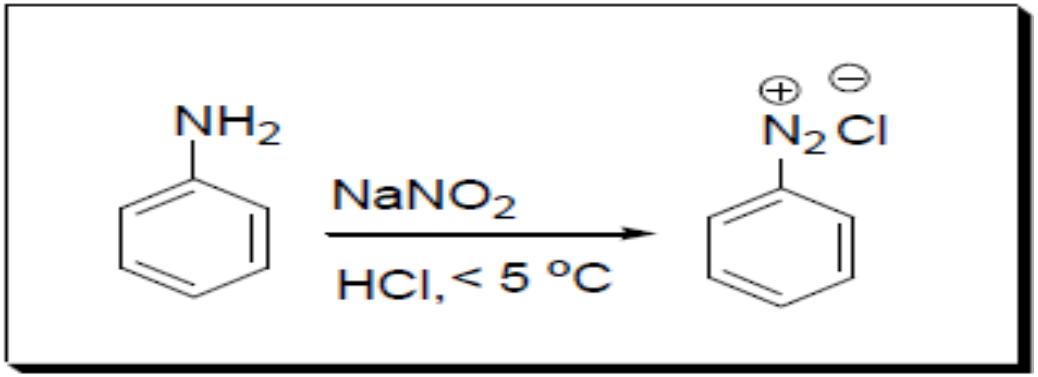
- Hoffmann developed a method for preparation of primary amines by treating an amide with bromine in an aqueous or ethanolic solution of NaOH.
- In this degradation reaction, migration of an alkyl or aryl group takes place from carbonyl carbon of the amide to the nitrogen atom.
- The amine so formed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



Reactions of Aryl Diazonium Intermediates

- Addition of aqueous solution of $NaNO_2$ to a solution of amine hydrochloride;
- The reaction is occurs in presence of excess of HCl which is cooled by an ice-bath (< 5°C),
- Then diazotization of primary aromatic amine formed.

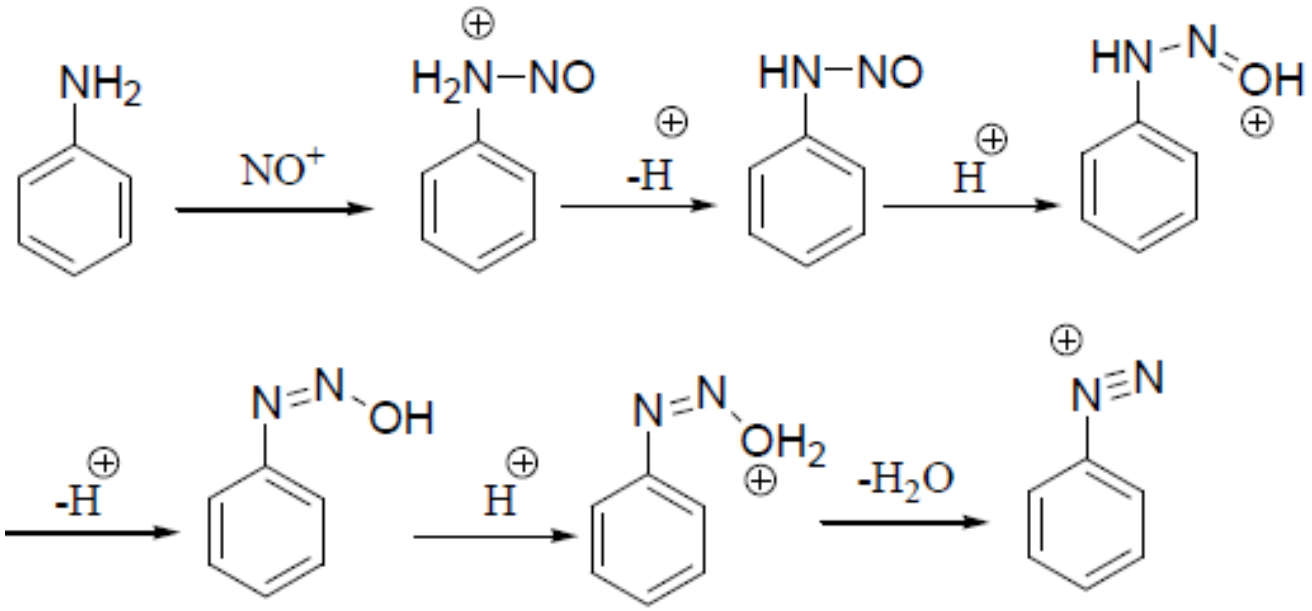
Eg.,



Mechanism, first:



Mechanism...,



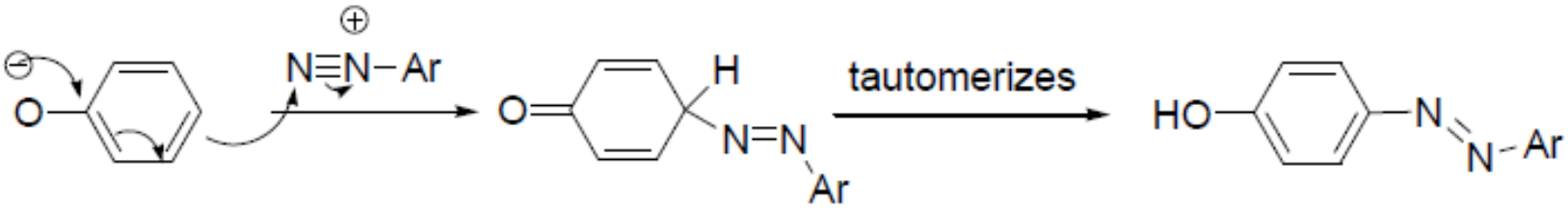
- If EWD are attached to aromatic nucleus;
- then the aromatic amines are difficult to diazotize;
- because the nucleophilicity of the amino-nitrogen;
- is reduced by the partial withdrawal of the unshared electron pair into the nucleus

The Reaction of Diazonium Salts

i) Reactions of nucleophiles at nitrogen;

✓ Nucleophiles react with diazonium ions to give covalent diazo-compounds.

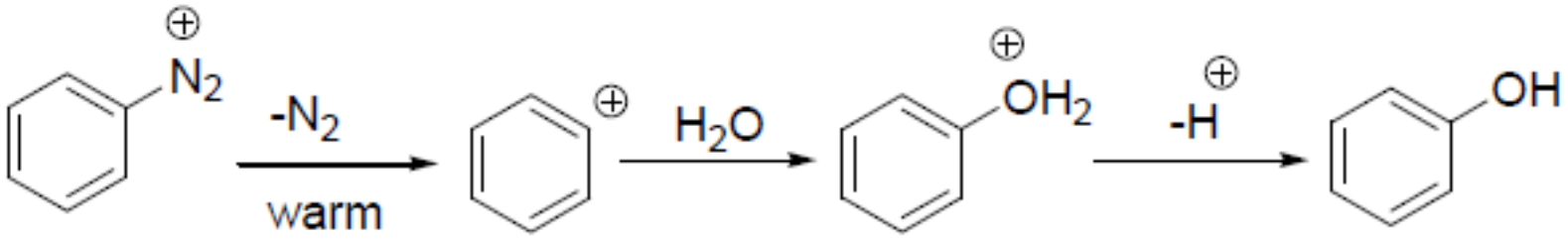
➢For example, phenol *via phenoxide ion couples with diazonium salt at pH 9-10 to afford para-azophenols in goo*



ii) SN1 Reaction;

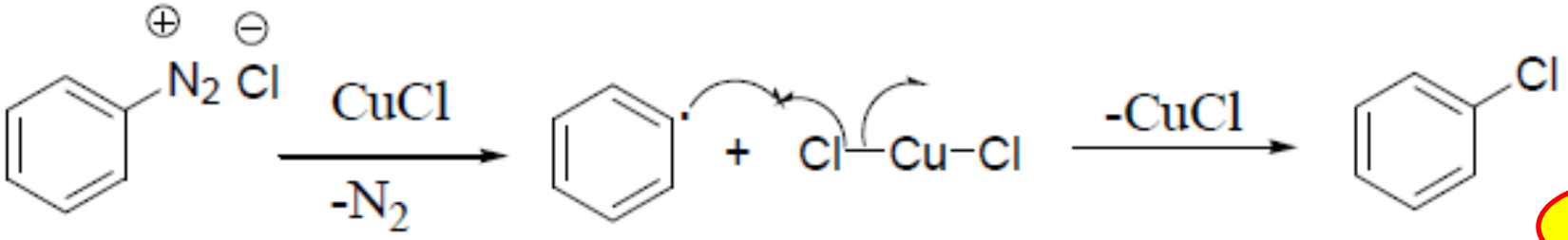
➢Diazonium salts decompose on warming into nitrogen and aryl cation which is highly reactive and could be attacked by any nucleophile in its vicinity.

For Instance…,



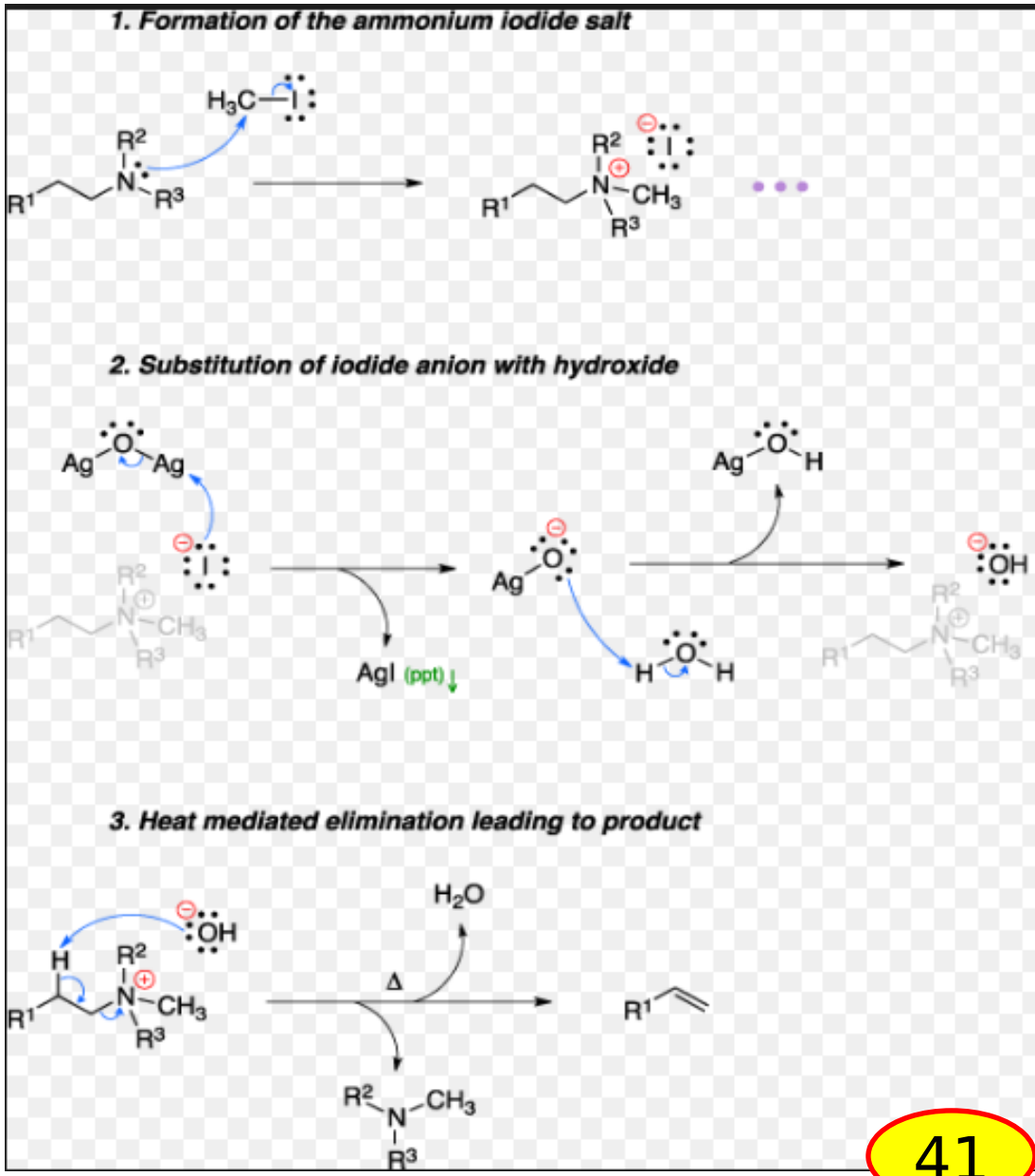
iii) One Electron Reductions;

- Diazonium ions could be reduced by single electron transfer to give an aryl radical and nitrogen.
- Copper(I) is frequently used and the aryl radical is highly reactive capable of abstracting a ligand from the transition metal ion or a hydrogen atom from a covalent bo

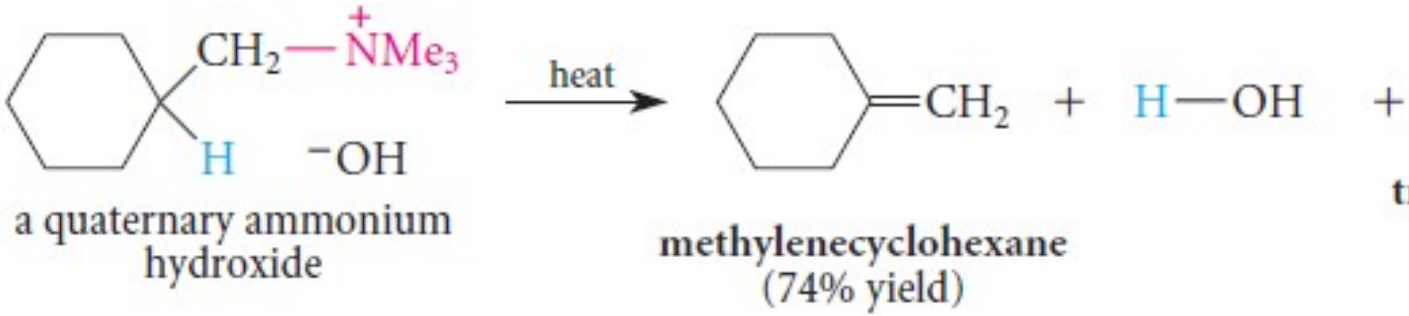


Hofmann elimination

- Is known as exhaustive methylation;
- is a process where a quaternary ammonium reacts to create a Tertiary amine and;
- an alkene by treatment with excess methyl iodide followed by treatment with silver oxide, water, and heat.



For example...,



- A quaternary ammonium hydroxide used as the starting material in Hofmann eliminations;
- is formed by treating a quaternary ammonium salt with AgOH, which is essentially a hydrated form of Ag_2O. See the above mechanism

