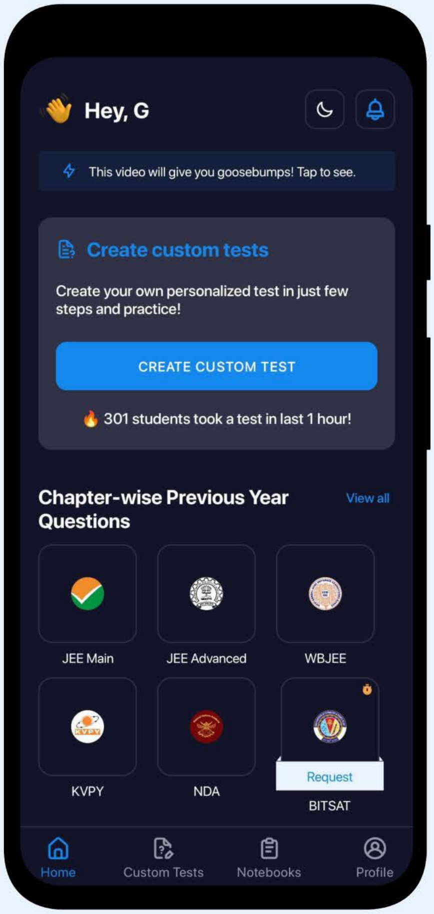


AMINES

AMINES

1. Amines

Amines are organic compounds and functional groups that contain a basic nitrogen atom with a lone pair. Amines are derivatives of ammonia, wherein one or more hydrogen atoms have replaced a substituent such as an alkyl or aryl group. Important amines include amino acids, biogenic amines, trimethylamine and aniline.

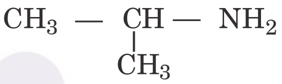
1.1 Aliphatic Amines

As displayed in the images below, primary amines arise when one of three hydrogen atoms in ammonia is replaced by an organic substituent. Secondary amines have two organic substituent bound to N together with one H. In tertiary amines all three hydrogen atoms are replaced by organic substituents.

(a) Primary amines

$CH_3\ CH_2\ NH_2$

1-ethanamine



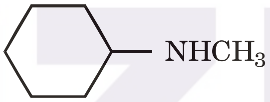
$$CH_3 - \underset{\displaystyle CH_3}{\underset{|}{CH}} - NH_2$$

1-methyl-1-ethanamine

(b) Secondary amines

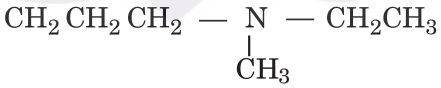
$CH_3\ CH_2\ NHCH_3$

N-methyl ethanamine



N-methyl cyclohexanamine

(C) Tertiary amines



$$CH_2\,CH_2\,CH_2 - \underset{\displaystyle CH_3}{\underset{|}{N}} - CH_2CH_3$$

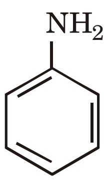
N-ethyl-N-methyl-1-1propanamine

$(CH_3)_3N$

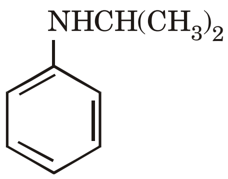
N-N-dimethyl methanamine

1.2 Aromatic amine

An aromatic amine is an amine with an aromatic substituent – that is $–NH_2$, –NH– or nitrogen group(s) attached to an aromatic hydrocarbon, whose structure usually contains one or more benzene rings. Aniline is an example.



Benzenamine (Aniline)

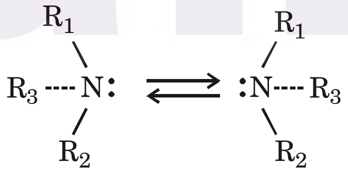


N-isopropyl benzenamine

1.3 Physical properties

1.3.1 General properties

1. Hydrogen bonding significantly influences the properties of primary and secondary amines as well as the protonated derivatives of all amines. Thus the boiling point of amines is higher than those of the corresponding phosphines, but generally lower than those of the corresponding alcohols. Alcohols, or alkanols, resemble amines but feature an OH group in place of NR_2. Since oxygen is more electronegative than nitrogen, RO-H is typically more acidic than the related $R_2N\text{-}H$ compound.
2. Methyl, dimethyl, trimethyl and ethylamine are gases under standard conditions, whereas diethylamine and triethylamine are liquids. Most other common alkyl amines are liquids; high-molecular-weight amine are solids.
3. Most aliphatic amines display some solubility in water, reflecting their ability to form hydrogen bonds. Solubility decreases with the increase in the number of carbon atoms, especially when the carbon atom number is greater than 6.
4. The aromatic amines, such as aniline, have their lone pair electrons conjugated into the benzene ring, thus their tendency to engage in hydrogen bonding is diminished. Otherwise they display the following properties :
   - Their boiling points are usually still high due to their larger size.
   - Diminished solubility in water, although they retain their solubility in suitable organic solvents only.
   - They are toxic and are easily absorbed through the skin : thus hazardous.



1.3.2 Chirality

Tertiary amines of the type NHRR´ and NRR´R´´ are chiral : the nitrogen atom bears four distinct substituents counting the lone pair. The interconversion of the stereoisomers has been compared to the inversion of an open umbrella into a strong wind. Quaternary ammonium salts with four distinct groups on the nitrogen are capable of exhibiting optical activity.

1.3.3 Properties as bases

Like ammonia, amines act as bases but are reasonably weak. The basicity of amines depends on :

1. The electronic properties of the substituents (alkyl groups enhance the basicity, aryl groups diminish it).
2. Steric hindrance offered by the groups on nitrogen.
3. The degree of solvation of the protonated amine.

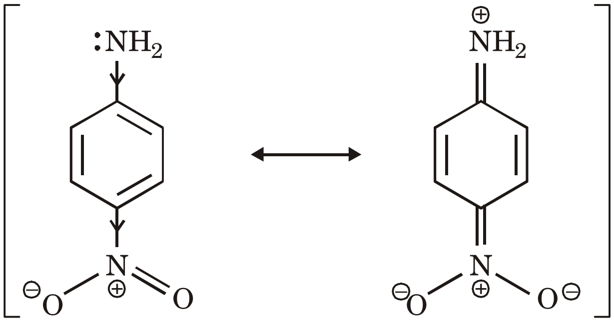
The nitrogen atom features a lone electron pair that can bind H^+ to form an ammonium ion R_3NH^+. The water solubility of simple amines is largely due to hydrogen bonding between protons on the water molecules and these lone electrons pairs.

1. Inductive effects of alkyl group : + I effect of alkyl groups raises the energy of the lone pair of electrons, thus elevating the basicity. Thus the basicity of an amine may be expected to increase with the number of alkyl groups on the amine. However, there is no strict trend in this regard, as basicity is also governed by other factors. The increase in K_b from methylamine to dimethylamine may be attributed to + I effect; however, there is a decrease from dimethylamine to trimethyl amine due to the predominance of steric hindrance offered by the three methyl groups to the approaching Lewis acid.
2. Mesomeric effect of aromatic systems : – M effect of aromatic ring delocalises the lone pair of electrons on nitrogen into the ring, resulting in decreased basicity. Substituents on the aromatic ring, and their positions relative to the amine group may also considerably alter basicity.
3. The degree of solvation of protonated amines : The degree of solvation of the protonated amine depends on the approachability of solvent molecules. If the molecule is sterically hindered (as in the case of trimethylamine), the protonated form is not well-solvated, thereby reducing basicity. This also explains the oroder of basicity of the methyl amines.

The major determinant of basic strength in alkyl-substituted anilines remain mesomeric stabilisation of the aniline molecule with respect to the cation; born out by the irregular effect of introducing Me groups into the o-, m- and p-positions in aniline.

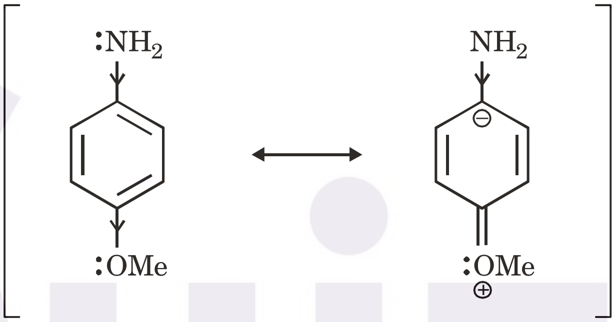
A group with a more powerful (electron-withdrawing) inductive effect, e.g. NO_2 is found to have rather more influence. Electron withdrawal is intensified when the nitro group is in the o- or p-position, for the interaction of the unshared pair of the amino nitrogen with the delocalised π orbital system of the benzene nucleus is then enhanced. The neutral molecule is thus stabilised even further respect to the cation, resulting in further weakening as a base. Thus the nitro-amines are found to have related pK_a values.

$PhNh_2$	$NO_2C_6H_4NH_2$
4.62	o – 0.28
	m – 2.45
	p – 0.95



The extra base-weakening effect, when the substituent is in the o-position, is due in part to the short distance over which its inductive effect is operating, and also to direct interaction, both steric and by hydrogen bonding with the NH_2 group. o-Nitroaniline is such a weak base that its salts are largely hydrolysed in aqueous solution, while 2, 4-dinitroaniline is insoluble in aqueous acids, and 2, 4, 6-trinitroaniline resembles an amide; it readily undergoes hydrolysis to picric acid (2, 4, 6-trinitrophenol).

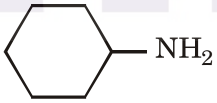
With substituents such as OH and OMe that have unshared electron pairs, an electron-donating, i.e. base-strengthening, mesomeric effect can be exerted from the o- and p-, but not from the m-position, with the result that the p-substituted aniline is a stronger base than the corresponding m-compound. The m-compound is a weaker base than aniline itself, due to the electron-withdrawing inductive effect exerted by the oxygen atom in each case. As so often, the effect of the o-substituent remains somewhat anomalous, due to the interaction with the NH_2 group by both steric and polar effects.



Example 1

Compare the basicities of

$PhNH_2$ **Ph_2NH**



I **II** **III**

Solution :

III > I > II

In structure III, lone pair electron of Nitrogen does not participate in resonance.

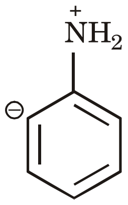
Example 2

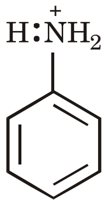
Arrange the following compound according to their basic strength (with suitable explanation) : $C_6H_5NH_2$, C_6H_5NHMe, $C_6H_5NMe_2$, o-$MeC_6H_4NH_2$

Solution :

$C_6H_5NH_2$	C_6H_5NHMe	$C_6H_5NMe_2$	o-$MeC_6H_4NH_2$
$pK_a = 4.62$	$pK_a = 4.84$	$pK_a = 5.15$	$pK_a = 4.38$

The major determinant of basic strength in alkyl substituted anilines remains mesomeric stabilization of aniline molecule (A) w.r.t. to the cation (B). Where (A) and (B) are


(A)


(B)

1.4. Preparation of Amines

1.4.1 Alkylation of Ammonia

$$R-X + 2NH_3 \longrightarrow R-NH_2 + \overset{+}{N}H_4X^-$$

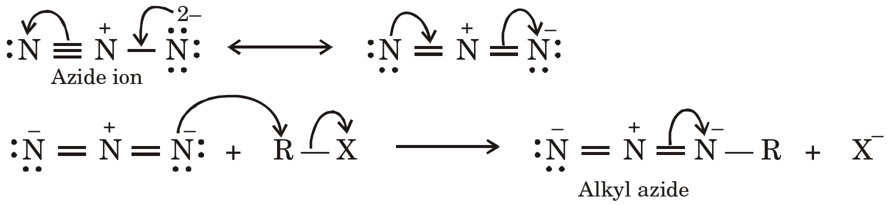
- Ammonia reacts as a nucleophile with alkyl halides to give primary amines in a nucleophilic substitution reaction.
- Yields are often poor as the product, a primary amine, RNH_2, is itself a nucleophile and can react with more alkyl halide.
- The result are mixtures containing primary amines, secondary amines, tertiary amines and quaternary ammonium salts.

$$\underset{\text{primary}}{R\ddot{N}H_2} \xrightarrow{R'CH_2X} \underset{\text{secondary}}{R\ddot{N}H(CH_2R')} \xrightarrow{R'CH_2X} \underset{\text{tertiary}}{R\ddot{N}(CH_2R')_2} \xrightarrow{R'CH_2X} \underset{\text{quaternary}}{R\overset{+}{N}(CH_2R')_3X^-}$$

- As aryl halides do not undergo simple nucleophilic substitution, they cannot be prepared using this method.

1.4.2 Alkylation of Azide ion and Reduction

A much better method for preparing a primary amine from alkyl halide first to convert the alkyl halide to an alkyl azide (RN_3) by a nucleophilic substitution reaction with sodium azide (NaN_3).

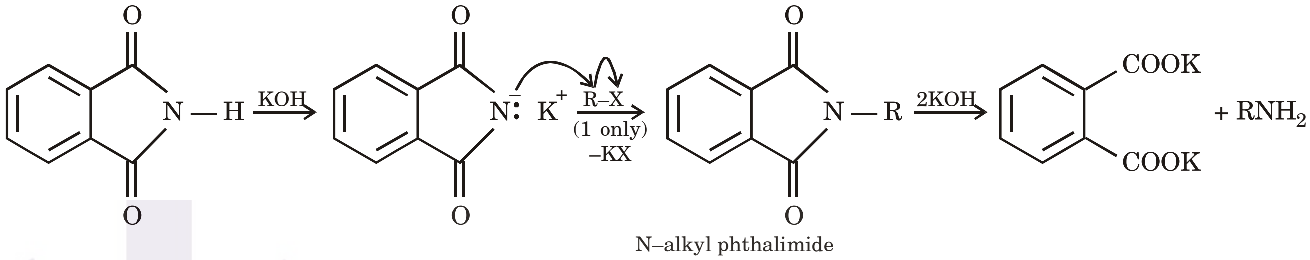


The alkyl azide is then reduced to a primary amine with Na/C_2H_5OH or $LiAlH_4$.

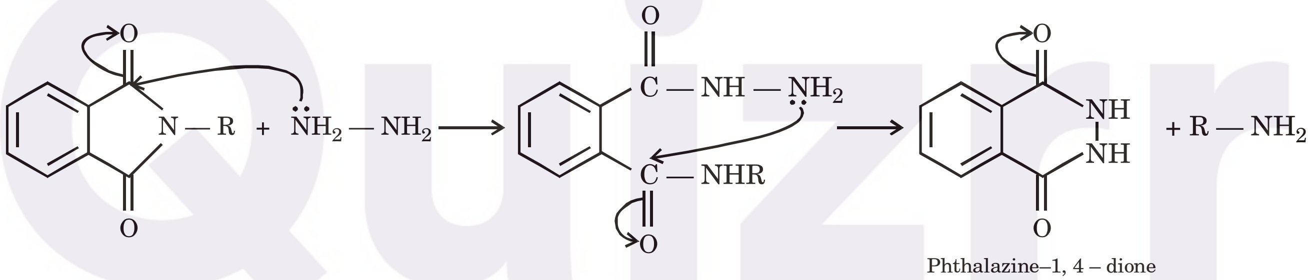
$$R-N=\overset{+}{N}=\overset{-}{\ddot{N}}: \xrightarrow[\text{or } LiAlH_4]{Na/C_2H_5OH} R-NH_2 + N_2$$

1.4.3 Gabriel Phthalimide Synthesis

Another method used for the preparation of primary aliphatic amines only is the Gabriel Phthalimide synthesis. Phthalimide ($pK_a = 9$) is quite acidic in nature. It can be converted to potassium phthalimide by its reaction with KOH. The phthalimide anion is a strong nucleophile. It reacts with alkyl halide, preferably methyl halide and primary alkyl halide only, by an S_N2 mechanism to give N–alkylphthalimide. The secondary and tertiary alkyl halides are not employed because they undergo elimination reactions also. The N–alkyl phthalimide is hydrolysed with dilute HCl or KOH solution to give primary aliphatic amine.



N–alkylphthalimide can also be converted to primary amine and phthalazine–1, 4–dione by treating it with hydrazine.



This method is not suitable for preparing aromatic primary amines as aryl halides are not good substrates for nucleophilic substitution.

1.4.4 Reduction of Nitro Compounds

Aliphatic primary amines can be synthesised by reducing nitroalkanes with metal and acid or with H_2 in presence of nickel as a catalyst.

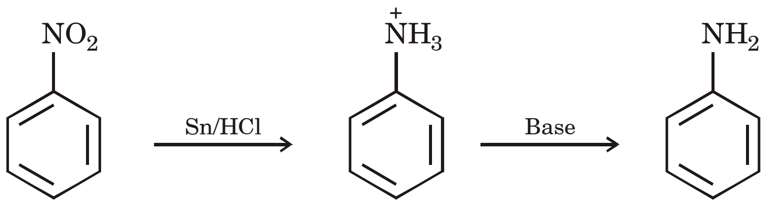
$$R - NO_2 + 3H_2 \xrightarrow{Ni} R - NH_2 + 2H_2O$$

$$R - NO_2 \xrightarrow{Sn/HCl} R - \overset{+}{N}H_3 \xrightarrow{Base} R - NH_2$$

For example :

$$\underset{\text{2-nitro ethanol}}{O_2N - CH_2CH_2 - OH} \xrightarrow{H_2/Ni} \underset{\text{2-amino ethanol}}{H_2N - CH_2CH_2 - OH}$$

Primary aromatic amines are also prepared by the reduction of corresponding nitro compounds.



Other reducing agents such as $LiAlH_4$ and H_2/Pt also reduce nitrobenzene to aniline.

Reduction in neutral medium

1. With Fe and steam, a nitro group gets reduced to nitroso group.

$$C_6H_5 - NO_2 \xrightarrow{\text{Fe/steam}} C_6H_5 - NO$$

2. Zn/NH_4Cl H_2O or $Zn/CaCl_2/H_2O$ reduces nitro group to hydroxylamine.

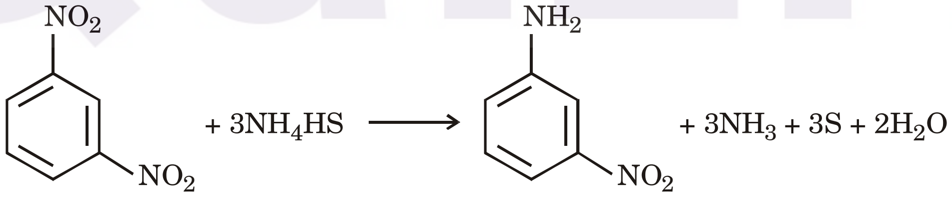
$$C_6H_5 - NO_2 \xrightarrow[\text{50-50°C}]{Zn/NH_4Cl/H_2O} C_6H_5 - NHOH$$

Reduction in alkaline medium

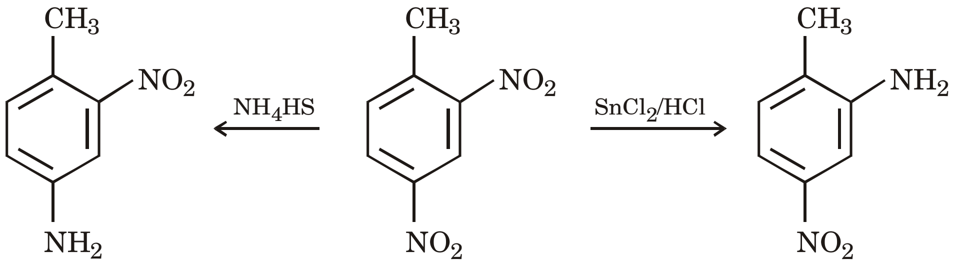
Nitro benzene when reduced with $Zn/NaOH/C_2H_5OH$ gives hydroazobenzene.

$$2C_6H_5 - NO_2 \xrightarrow{Zn/NaOH/C_2H_5OH} C_6H_5 - NH - NH - C_6H_5$$

By means of aqueous ethanolic NH_4HS, aqueous Na_2S or $SnCl_2$ in HCl, nitro groups in a polynitro compound can be reduced one at a time. For example, m-dinitrobenzene can be reduced to m-nitroaniline.

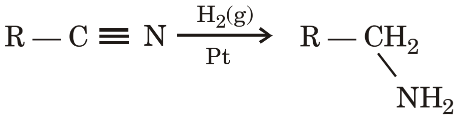


It is not always possible to predict that which nitro group will be reduced first. For instance, 2, 4–dinitrotoluene when treated with NH_4HS, the 4–nitro group is reduced whereas treatment with $SnCl_2/HCl$ results in the reduction of 2–nitro group.



2,4–dinitrotoluene

1.4.5 Reduction of nitriles, isonitriles & oximes

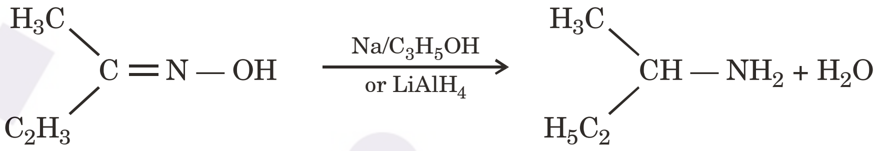


$$R - C \equiv N \xrightarrow[Pt]{H_2(g)} R - CH_2 - NH_2$$

Nitriles are reduced to amines using hydrogen in the presence of a nickel catalyst, although acidic or alkaline conditions should be avoided to avoid hydrolysis of -CN group. $LiAlH_4$ is more commonly employed for the reduction of nitriles on the laboratory scale. Both aliphatic & aromatic amines can be synthesised by reduction.

$$C_6H_6 - \overset{+}{N} \equiv C^- \xrightarrow[LiAlH_4]{H_2/Ni} C_6H_5 - NH - CH_3$$

(2 amine)

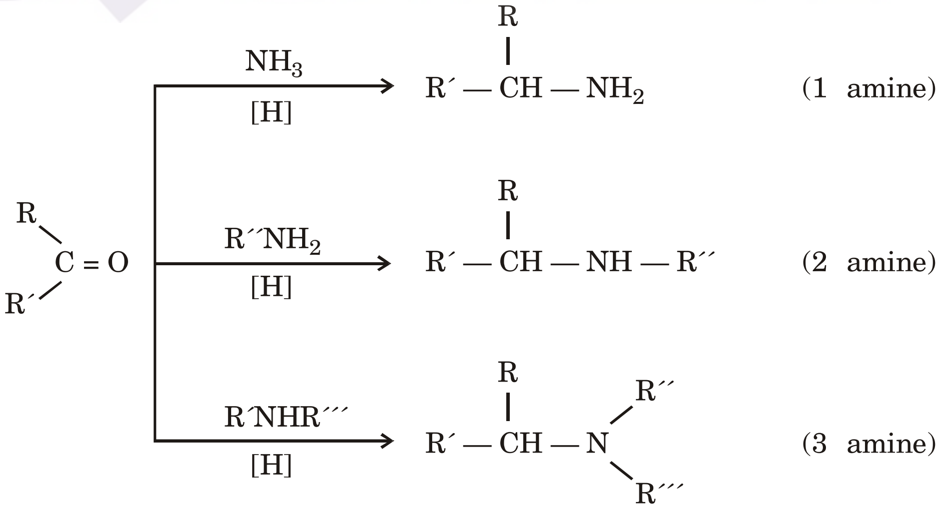


(oxime)

(1 amine)

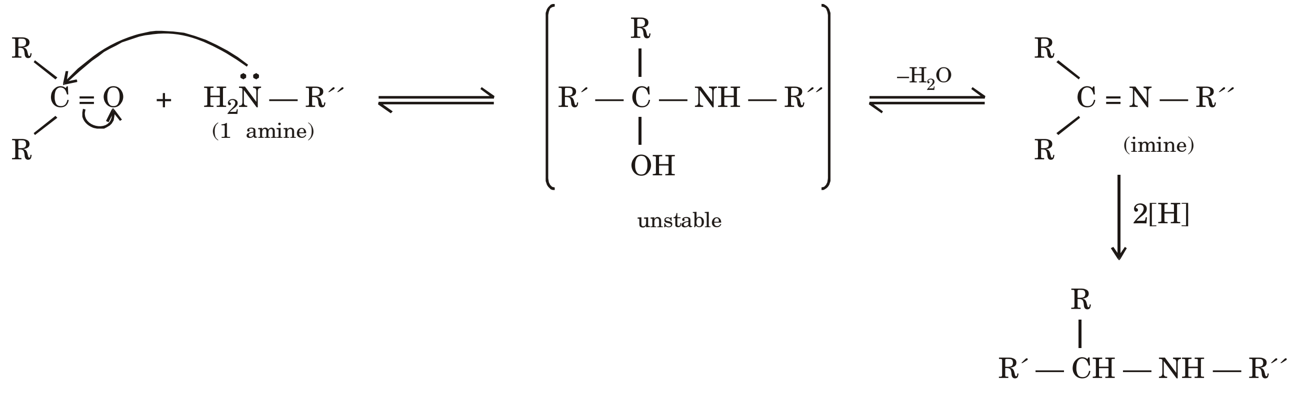
1.4.6 Reductive Amination of Carbonyl Compounds

Aldehydes and ketones are converted to amines through catalytic or chemical reduction in the presence of ammonia or amine. Primary, secondary and tertiary amines can be prepared this method.

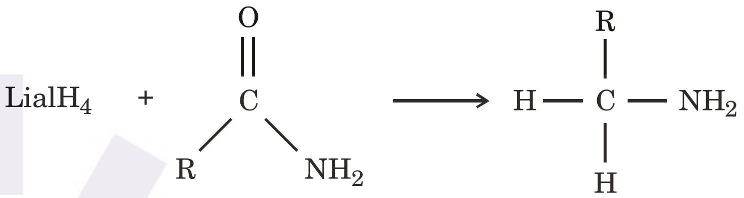


(R´ may be hydrogen or an alkyl group)

The above process appears to proceed through the following mechanism.

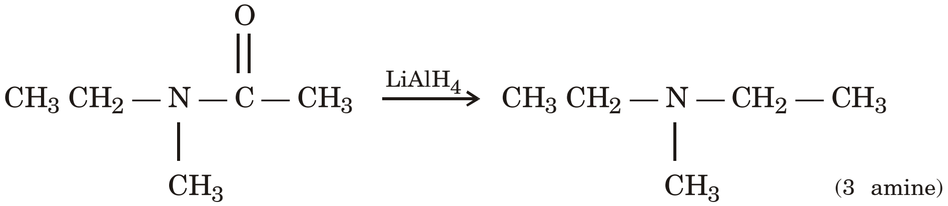


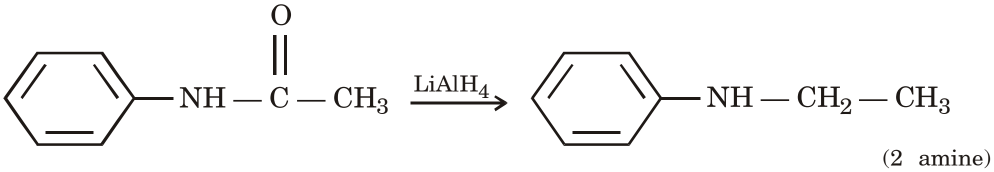
1.4.7 Reduction of Amides



Reactions usually in Et_2O or THF followed by H_3O^+ work-ups.

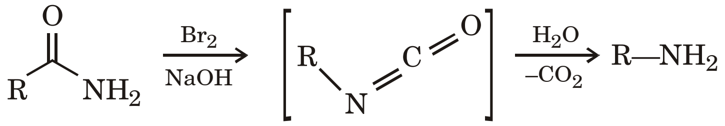
- Amides $RCONR'_2$, can be reduced to the amine, $RCH_2NR'_2$ by conversion of the C = O to $-CH_2^-$
- Amides can be reduced by $LiAlH_4$ but not by the less reactive $NaBH_4$.
- Typical reagents : $LiAlH_4$/ether solvent, followed by aqueous work-up.
- Note that this reaction is different to that of other C = O compounds which reduce to alcohols.
- The nature of the amine obtained depends on the substituents present on the original amide.





1.4.8 Hofmann rearrangement

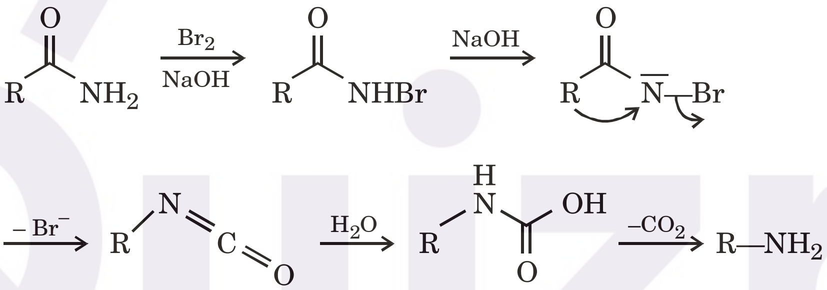
Hofmann rearrangement is the organic reaction of a primary amide to a primary amine with one fewer carbon atom.



The reaction of bromine with sodium hydroxide forms sodium hypobromite in situ, which transforms the primary amide into an intermediate isocyanate. The intermediate isocyanate is hydrolyzed to a primary amine giving off carbon dioxide.

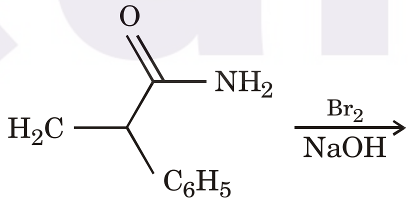
The reaction is also sometimes called the Hofmann degradation, and should not be confused with the Hofmann elimination.

Mechanism :



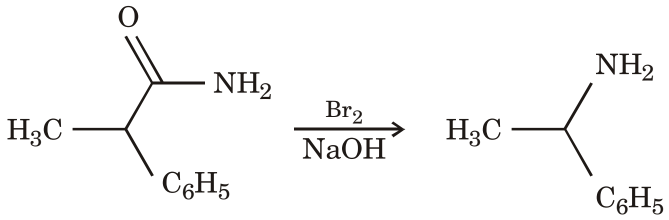
Example 3

Identify the product :



Product

Solution :



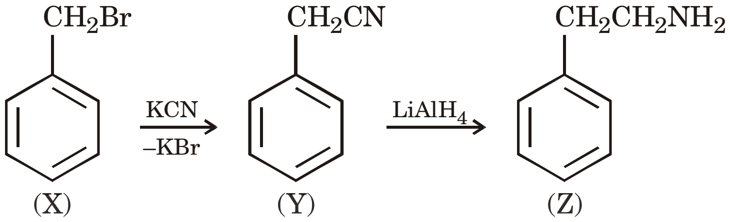
This is a example of Hofmann bromide reaction.

Example 4

A compound X (C_7H_7Br) reacts with KCN to give Y (C_8H_7N). Reduction of Y with $LiAlH_4$ yields Z ($C_8H_{11}N$). Z gives carbylamine reaction, reacts with Hinsberg's reagent in the presence of aq. KOH to give a clear solution. With $NaNO_2$ and HCl at 0 C (Z) gives a neutral compound which gives red colour. What are X, Y and Z ?

Solution :

$$\underset{(X)}{C_7H_7Br} \xrightarrow[\text{-KBr}]{\text{KCN}} \underset{(Y)}{C_8H_7N} \xrightarrow{LiAlH_4} \underset{(Z)}{C_8H_{11}N}$$

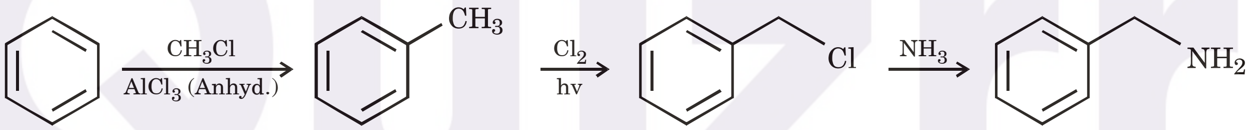


Example 5

Convert Benzene to benzylamine.

Solution :

Friedel-crafts alkylation, can easily obtain Toluene from benzene. The sequence of reaction is thus

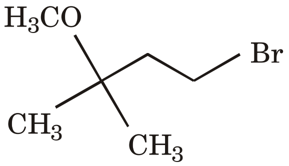


Example 6

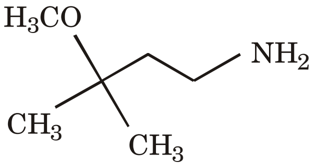
One mole of each of bromo derivative (A) and NH_3 react to give one mole of an organic compound (B). (B) reacts with CH_3I to give (C). Both (B) and (C) react with HNO_2 to give compounds (D) and (E), respectively. (D) on oxidation and subsequent decarboxylation gives 2-methoxy-2-methyl propane. Give structures of (A) to (E) with proper reasoning.

Solution :

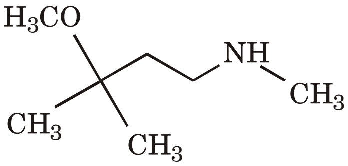
A



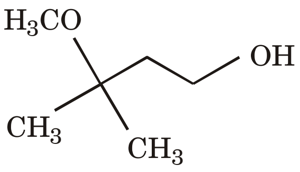
B



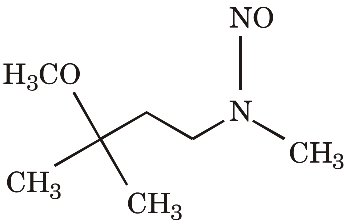
C



D

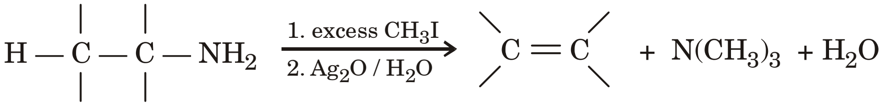


E



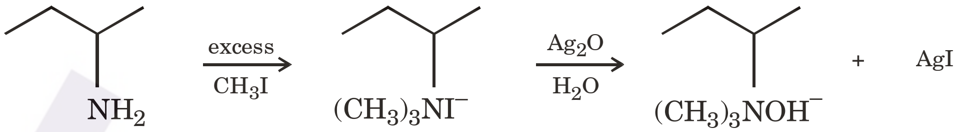
REACTIONS OF AMINES

1.5.1 Hofmann Elimination

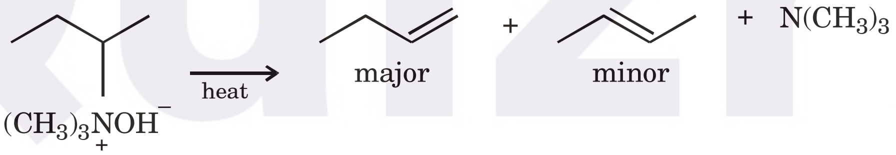


$$H-C-C-NH_2 \xrightarrow[2.\ Ag_2O / H_2O]{1.\ excess\ CH_3I} C=C + N(CH_3)_3 + H_2O$$

- Like alcohols, amines can undergo elimination reactions.
- Quaternary ammonium salts undergo an E2 elimination when heated with silver oxide Ag_2O, in water.
- Amines can readily be converted into quaternary ammonium iodides by treating them with excess methyl iodide.
- Ag_2O/H_2O reacts giving the quaternary ammonium hydroxide, silver iodide precipitates.



- When heated the hydroxide induces a base promoted 1, 2- or β-elimination giving an amine and alkene.
- The addition is opposite to that predicted by Saytzeff's rule in that it leads to the less highly substituted alkene.
- The less highly substituted alkene is sometimes referred to as the Hofmann product.

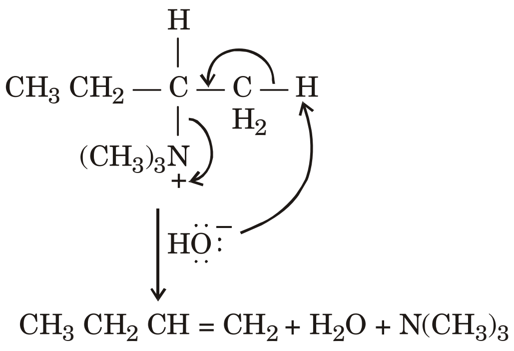


- The outcome is dictated by steric effects of the large leaving group and the alkyl chain.
- NH_2^- and NR_2^- are very poor leaving groups (both anionic), but NR_3 is much better (neutral).

Mechanism of the Hofmann Elimination

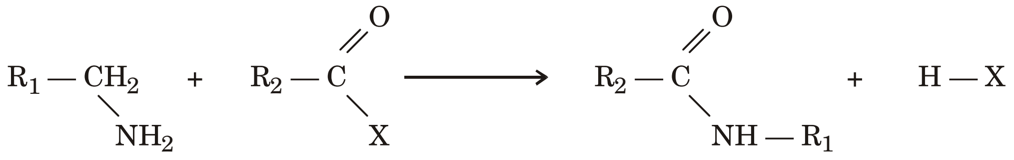
The initial steps are an example of the alkylation of an amine by methyl iodide. The mechanism of the elimination step is shown.

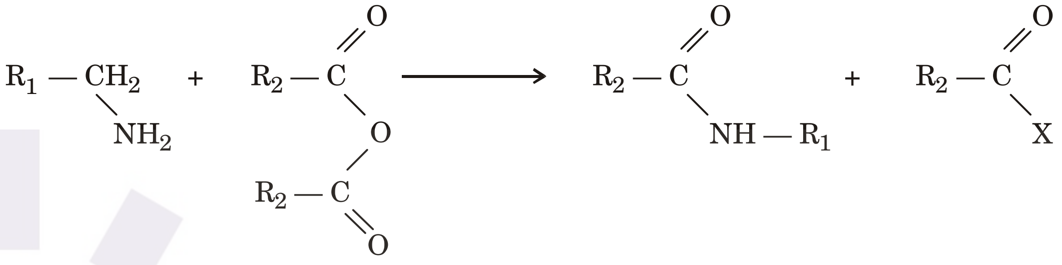
When heated, the hydroxide removes the more accessible proton, the π bond of the alkene C = C forms and the leaving group, a neutral amine departs.



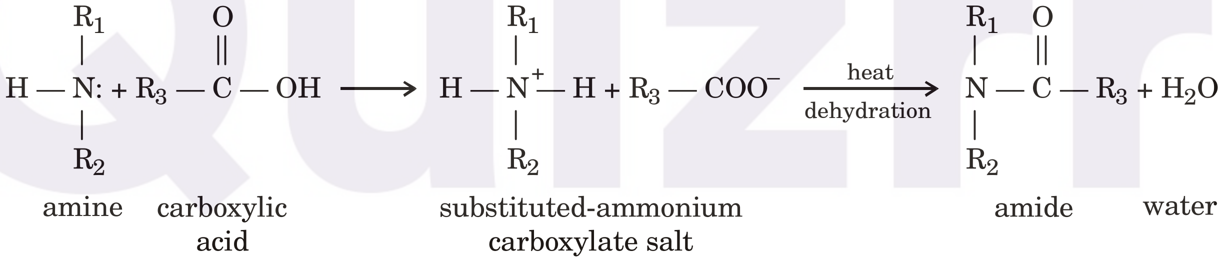
1.5.2 Nucleophilic acyl substitution

Acyl chlorides and acid anhydrides react with primary and secondary amines in cold to form amides in the Schotten-Baumann reaction. Tertiary amines cannot be acylated due to the absence of a replaceable hydrogen atom. With the much less active benzoyl chloride, acylation can still be performed by the use of excess aqueous alkali to facilitate the reaction.





Because amines are basic, they neutralize carboxylic acid to form the corresponding ammonium carboxylate salts. Upon heating to 200 C, the primary and secondary amine salts dehydrate to form the corresponding amides.

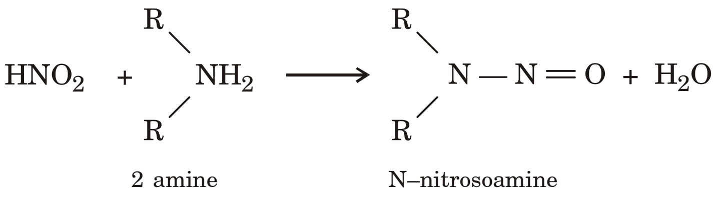


$$H-\underset{R_2}{\overset{R_1}{N}}: + R_3-\overset{O}{\overset{\|}{C}}-OH \longrightarrow H-\underset{R_2}{\overset{R_1}{N^+}}-H + R_3-COO^- \xrightarrow[\text{dehydration}]{\text{heat}} \underset{R_2}{\overset{R_1}{N}}-\overset{O}{\overset{\|}{C}}-R_3 + H_2O$$

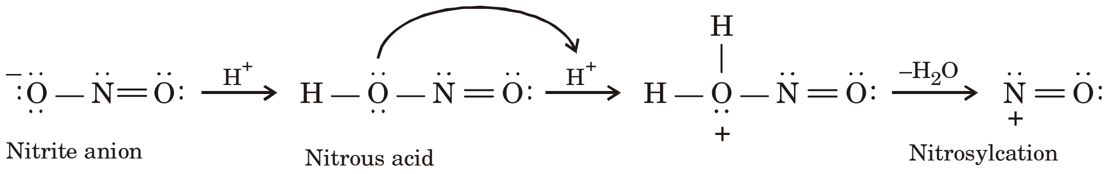
1.5.3 Nitrosation of Amines

$$HNO_2 + R-NH_2 \longrightarrow R-\overset{\oplus}{N}\equiv N + 2\,H_2O$$

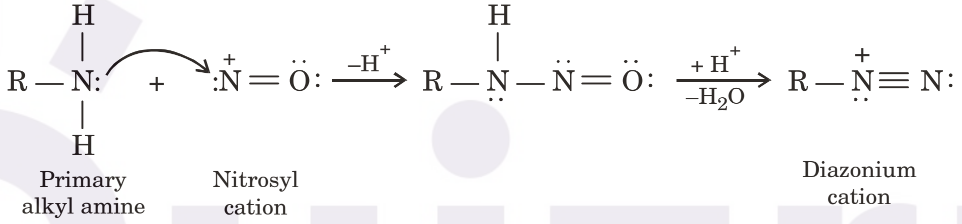
1 amine diazoniumion



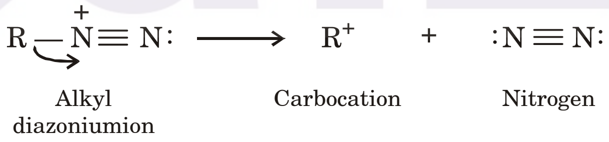
- Typical reagents : sodium nitrite and aq. HCl or H_2SO_4 (this mixture yields nitrous acid, HNO_2)
- The most useful reactions are probably those of primary aryl amines, Ar-NH_2, which give aryl diazonium salts, Ar-N_2^+ which can then be used to prepare substituted benzenes.
- The actual nitrosation reagent is the nitrosyl cation, NO^+ which is formed in situ :



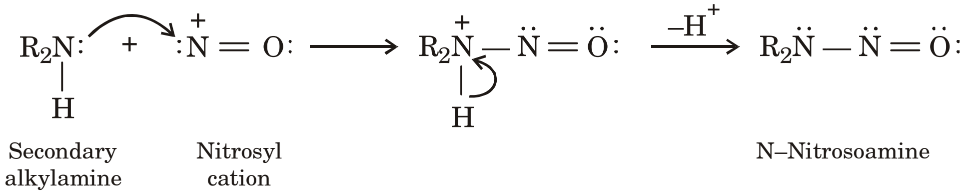
- The nature of the product depends on the nature of the initial amine
- Primary alkyl or aryl amines yield diazonium salts (hence the diazotisation reaction).



- Alkyl diazonium salts are very unstable and yield carbocation-derived products by loss of the very good leaving group, N_2.

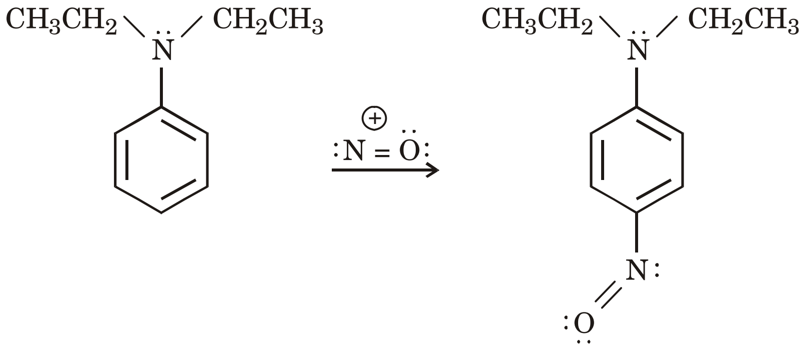


- **Secondary alkyl or aryl amines** yield N-nitrosoamines :

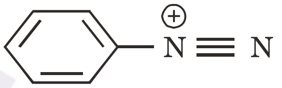


- **Tertiary alkyl amines** do not react in a useful fashion.

- **Tertiary aryl amines** undergo nitrosation of the ring (an electrophilic aromatic substitution reaction).

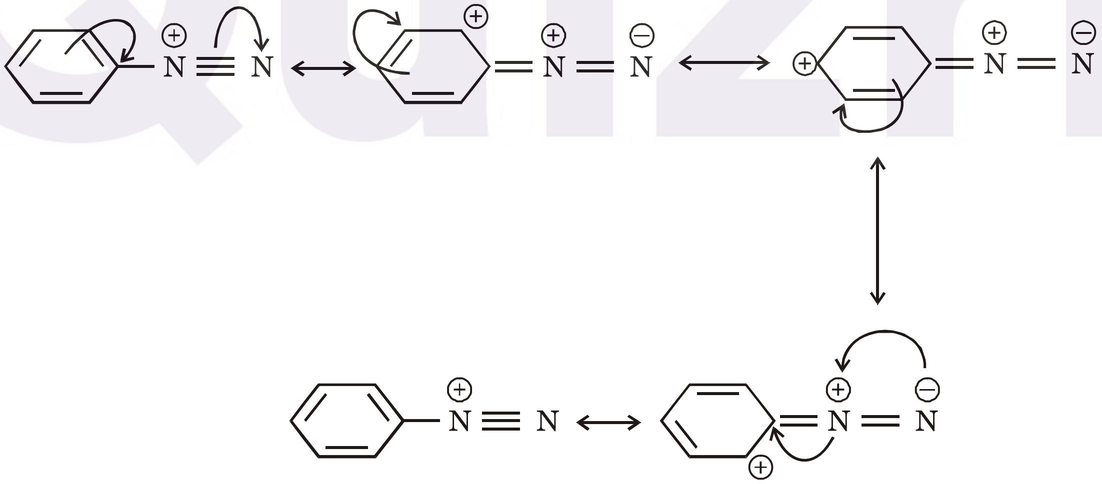


Diazonium Compound



{phenyldiazonium compound}

Aromatic diazonium chlorides, sulphates, nitrates etc. are reasonably stable in aqueous solution at room temperature or below but cannot be readily isolated without decomposition. The π-orbital system of benzene ring stabilizes the diazonium cation by resonance.



The diazonium salts are very important synthetic reagents, being the starting point in the preparation of various aromatic compounds. Their reactions may be divided into two groups, those which involve the liberation of N_2 gas and the displacement of the diazo group N_2^+ by another univalent group and those in which the two N-atoms are retained (coupling reactions).

1.5.4 Replacement Reactions :

$$C_6H_5-\overset{+}{N}\equiv N^-$$

$$\xrightarrow{H_2O,\,\Delta} C_6H_5-OH + N_2 + H^+$$

$$\xrightarrow{H_3PO_2O/\,H_2O\ \Delta} C_6H_6 + N_2 + H_3PO_3 + H^+$$

$$\left.\begin{array}{l}\xrightarrow{CuCl/HCl,\,\Delta} C_6H_5Cl + N_2 + H^+\\ \xrightarrow{CuBr/HCl,\,\Delta} C_6H_5Br + N_2 + H^+\end{array}\right\}\text{Sandmeyer reaction}$$

$$\xrightarrow{KI,\,\Delta} C_6H_5-I + N_2 + K^+$$

$$\xrightarrow{HBF_4,\,\Delta} C_6H_5N_2^+\,BF_4^- \xrightarrow{\Delta} C_6H_5F + N_2 + BF_3\}\ \text{Baltz Scheimann reaction}$$

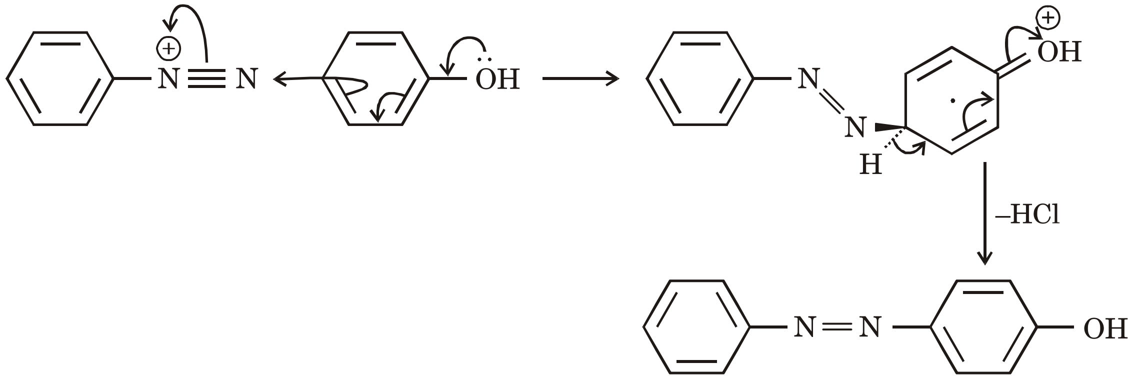
$$\xrightarrow[\Delta]{Cu/KCN} C_6H_5-CN + N_2 + K^+$$

$$\xrightarrow[\Delta]{NaNO_2/Cu} C_6H_5-NO_2 + N_2 + Na^+$$

$$\xrightarrow[\Delta]{C_6H_6/NaOH} C_6H_5-C_6H_5 + N_2 + H_2O$$

1.5.5 Azo coupling

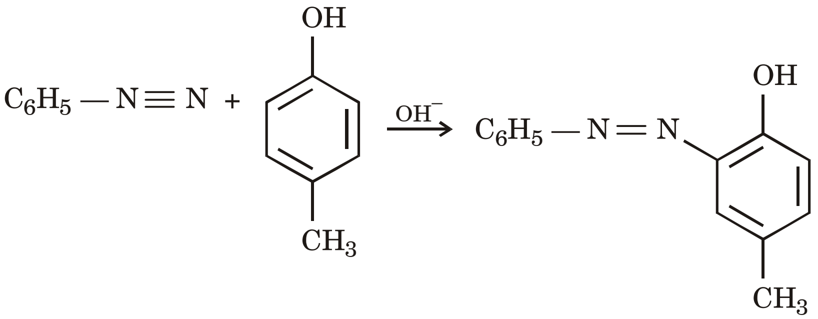
An azo coupling is an organic reaction between a diazonium compound and an aniline, phenol or other aromatic compound which produces an azo compound. In this reaction the diazonium salts is an electrophile and the activated arene is a nucleophile in an electrophilic aromatic substitution. In most cases, including the example below, the diazodium compound is also aromatic.



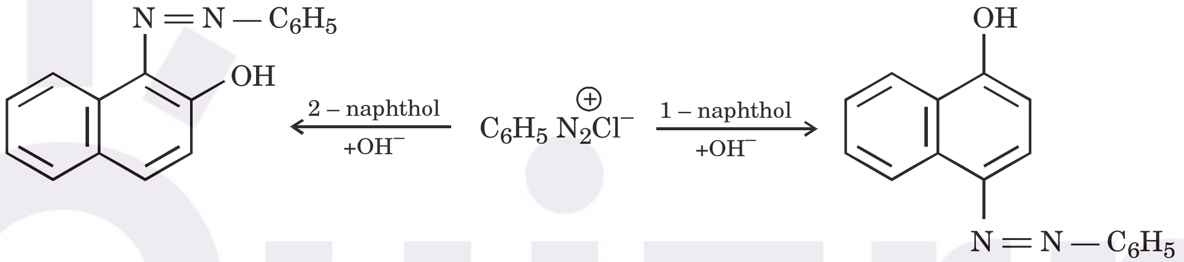
(coupling)

Azo couplings are important in the production of dyes and pH indicators such as methyl red.

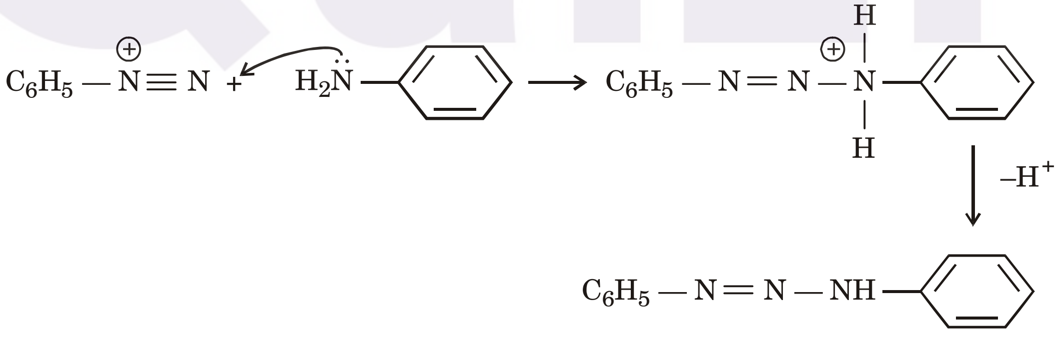
Coupling with benzene substrates occurs preferentially in the para position to the hydroxyl group. But if this position is blocked, then the coupling occurs at the ortho position.



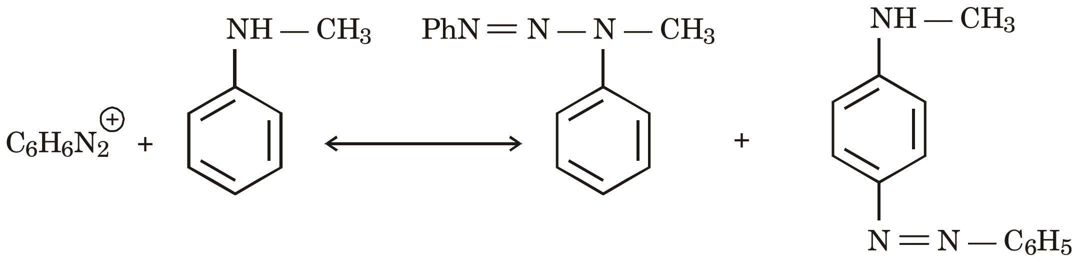
Example : 1 and 2 naphthols in alkaline soln. couple with diazonium salt in the 4 and 1-position respectively.



Note : With aromatic amines, there is the possibility of attack on either nitrogen or carbon. In the case of primary amines, the attack of diazonium ion mainly takes place at the nitrogen forming diazo-amino compound (A).



In secondary amines two products will be formed.



1.5.6 Oxidation Reactions

Both the primary and secondary amines undergo oxidation. The oxidation products obtained depend on the oxidising agent used and on the nature of alkyl group.

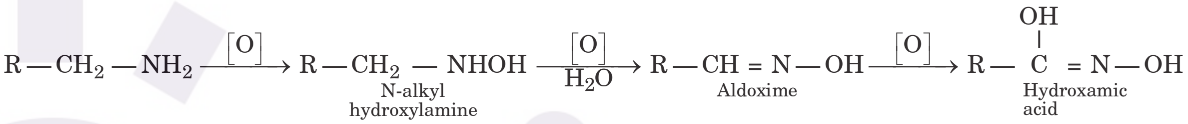
Primary amines :

(i) With $KMnO_4$:

$$R-CH_2-NH_2 \xrightarrow{[O]} \underset{\text{Aldimine}}{R-CH=NH} \xrightarrow{H_2O} R-CHO+NH_3$$

$$R_2CH-NH_2 \xrightarrow{[O]} \underset{\text{Ketimine}}{R_2C=NH} \xrightarrow{H_2O} R_2C=O+NH_3$$

(ii) With Caro's acid $(H_2SO_5)/H_2O_2$/Peroxy carboxylic acid :

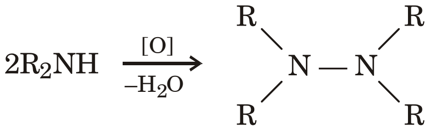


$$R-CH_2-NH_2 \xrightarrow{[O]} \underset{\substack{\text{N-alkyl}\\ \text{hydroxylamine}}}{R-CH_2-NHOH} \xrightarrow[H_2O]{[O]} \underset{\text{Aldoxime}}{R-CH=N-OH} \xrightarrow{[O]} \underset{\substack{\text{Hydroxamic}\\ \text{acid}}}{R-\overset{\overset{OH}{|}}{C}=N-OH}$$

$$R_2CH-NH_2 \xrightarrow{[O]} R_2CH-NHOH \xrightarrow[-H_2O]{[O]} \underset{\text{Ketoxime}}{R_2C=N-OH}$$

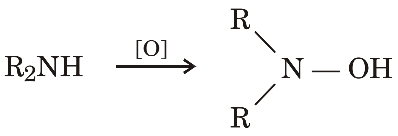
Secondary amines :

(i) With $KMnO_4$:



Tetraalkyl hydrazine

(ii) With Caro's acid $(H_2SO_5)/H_2O_2$/Peroxy carboxylic acid :



N,N–dialkyl hydroxylamine

Tertiary amines

(i) With H_2O_2/Peroxy carboxylic acid $\left(R_3N \xrightarrow{[O]} R_3\overset{\oplus}{N} — \overset{-}{O}\right)$

Tertiary amines are oxidised to amine oxide, $R_3\overset{\oplus}{N} — \overset{-}{O}$ (a dipolar ion or Zwitterion).

1.5.7 Reactions of Quaternary Ammonium Salts

(1) Formation of 4 Ammonium Hydroxides

$$2R_4N^+X^- + Ag_2O + H_2O \longrightarrow 2R_4N^+\ OH^- + 2AgX$$

very strong bases like NaOH

(2) **Hofmann Elimination of Quaternary Ammonium Hydroxides**

When a quaternary ammonium hydroxide is heated strongly it decomposes to yield water, a tertiary amine and alkene.

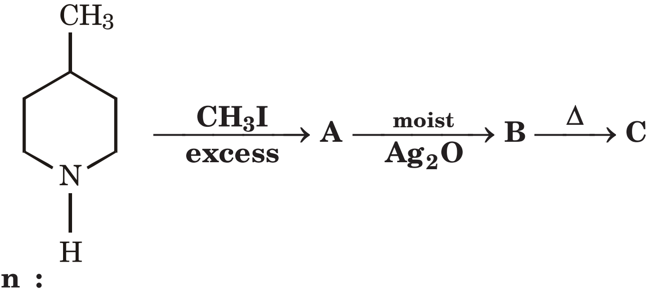
$$[(CH_3)_3\ NCH(CH_3)CH_2CH_3]^+\ OH^- \longrightarrow (CH_3)_3N + H_2C = CHCH_2CH_3 + H_2O$$

s-Butyltrimethylammonium hydroxide 1-Butene

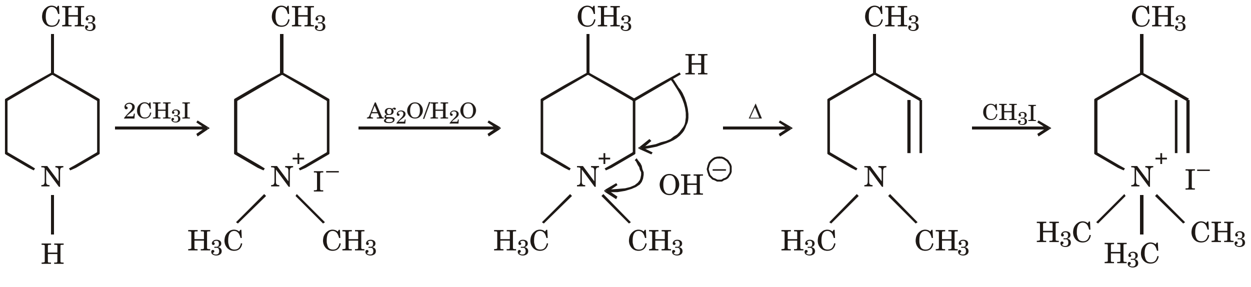
This E_2 elimination gives the less substituted alkene (Hofmann product) rather than the more substituted alkene (Saytzeff product).

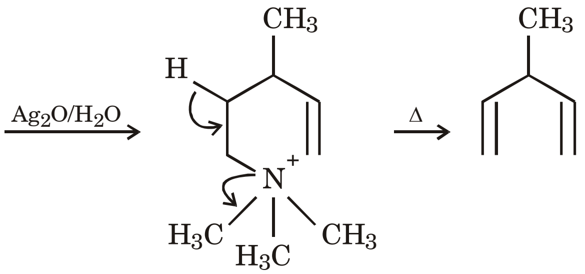
Example 7

Identify the end product (C).



Solution :



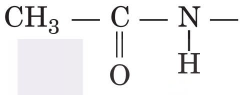


1.5.8 Ring Reactions of Aromatic Amines

NH_2, – NHR and – NR_2 strongly activate the benzene ring towards electrophilic substitution.

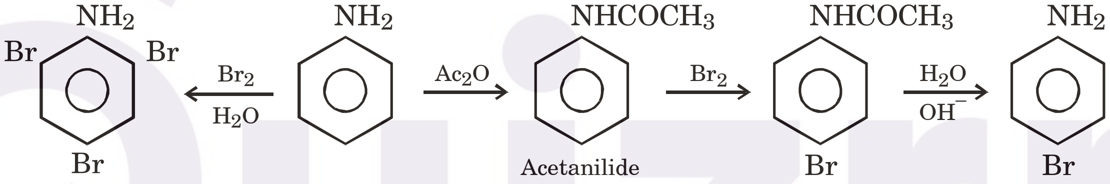
(1) Halogenation

For monohalogenation, – NH_2 is first acetylated, because

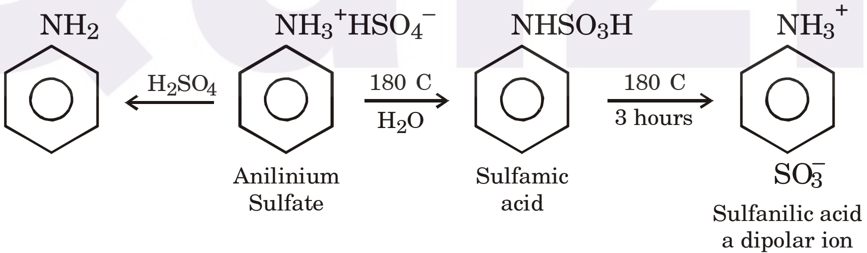


$CH_3 - \underset{\underset{O}{\|}}{C} - \underset{\underset{H}{|}}{N} -$

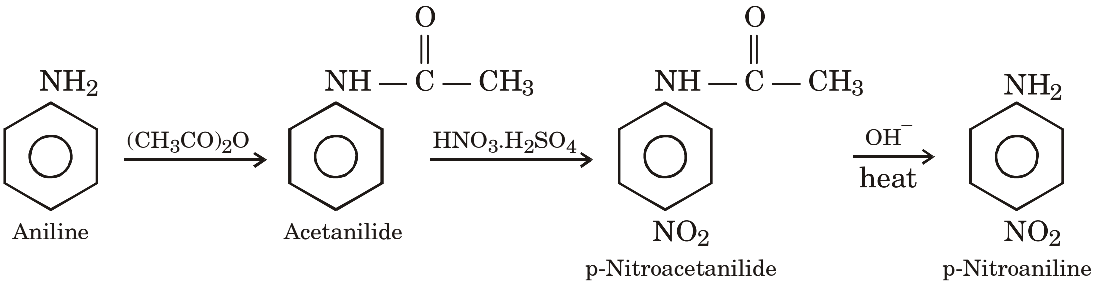
is only moderately activating



(2) Sulfonation



(3) Nitration

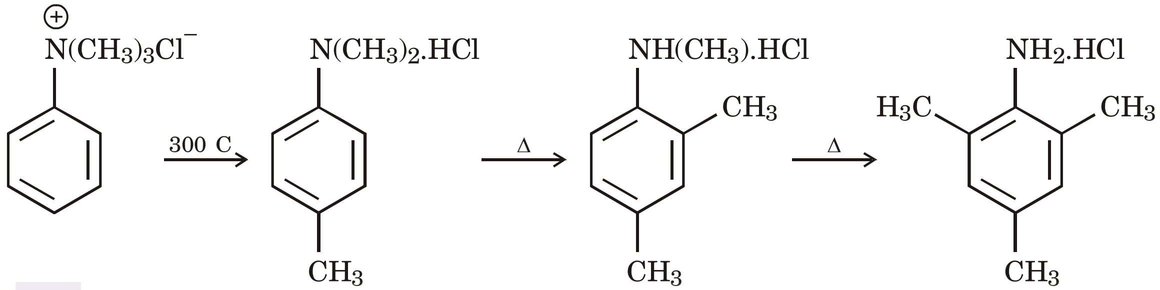


To prevent oxidation by HNO_3 and meta substitution of $C_6H_5NH_3^+$, amines are first acetylated.

1.5.9. Rearrangement Reactions

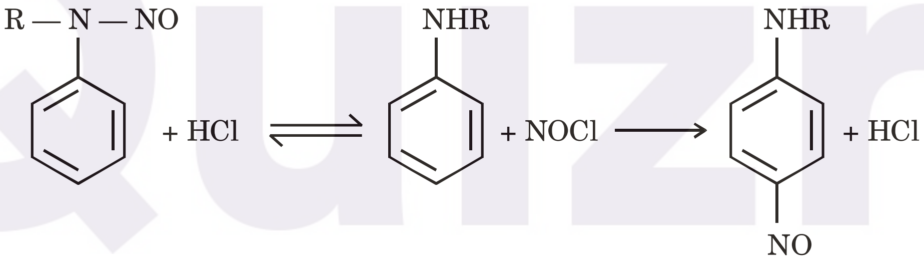
A remarkable property of mono–, di–, and trialkyl anilinium chlorides (or bromides) is their ability to undergo rearrangement on strong heating, an alkyl group migrating from the N–atom and entering preferentially the p–position. If this position is occupied, then the alkyl group migrates to the o–position. For example, when trimethyl anilinium chloride is heated under pressure, the following rearrangement takes place.

(1)

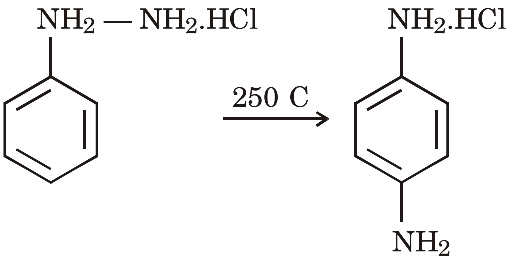


This reaction is known as the **Hofmann–Martius rearrangement.**

(2) Rearrangements of this kind have been observed to take place with aniline derivatives of the type $C_6H_5 - NH - Z$ where Z is R, X, NH_2, OH, NO or NO_2. For example,

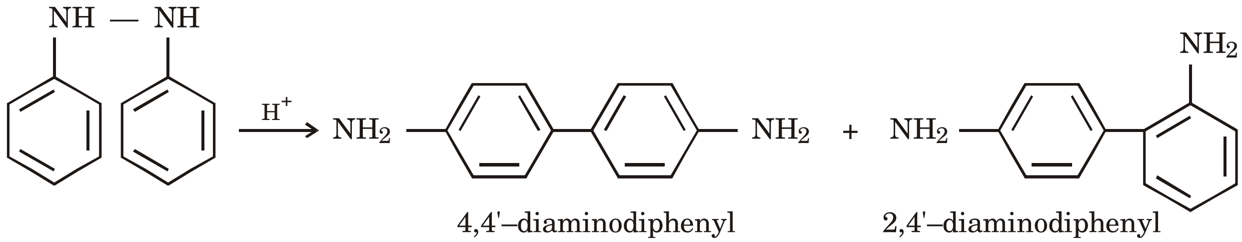


This reaction is called **Fischer–Hepp rearrangement.**

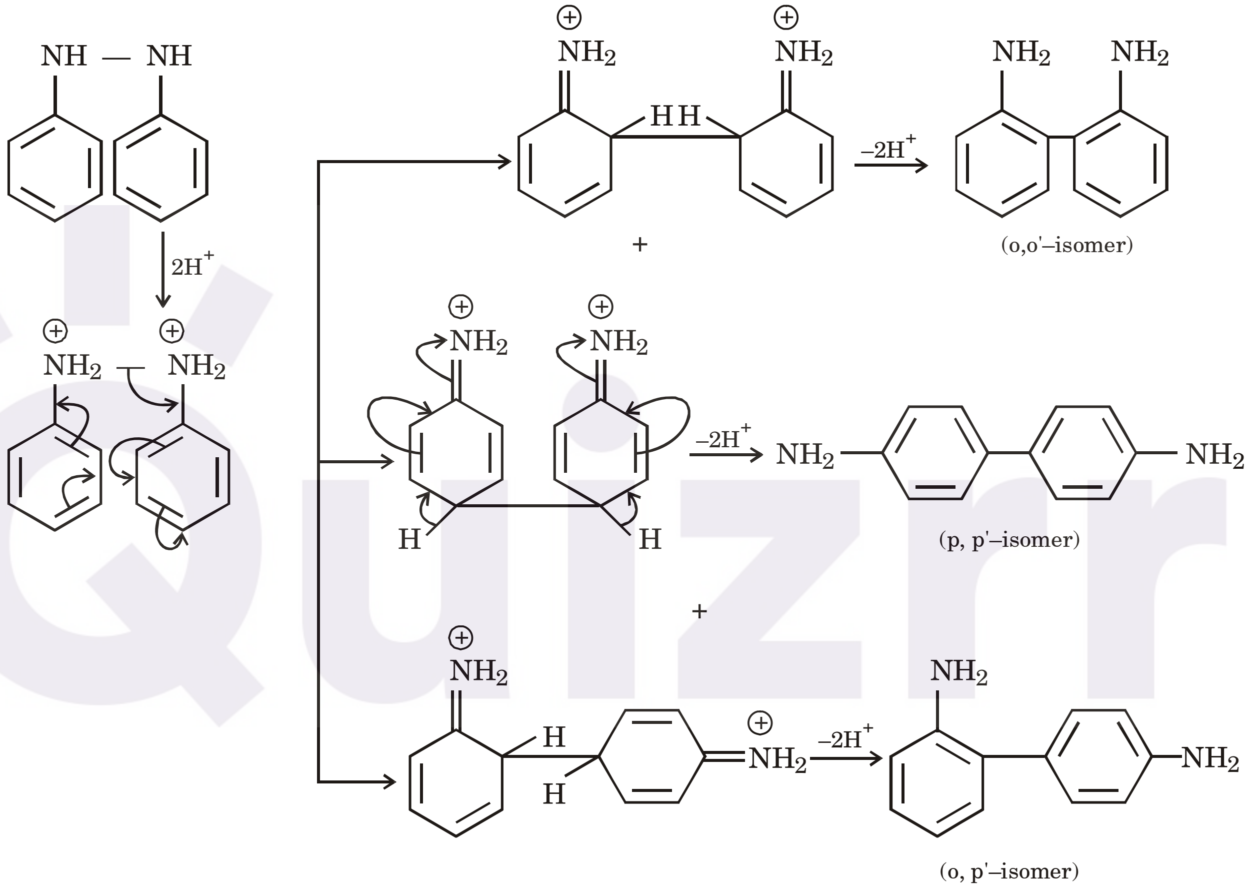


(3) Benzidine Rearrangement

Hydroazobenzene, $C_6H_5NH - NHC_6H_5$ undergoes rearrangement when heated in the presence of acid to yield benzidine (4, 4´–diamino diphenyl).



This is known as benzidine rearrangement. The p, p´–isomer is the major product (70%) and the rest is o, p´ and o, o´–isomer. The reaction probably follows the given mechanism.



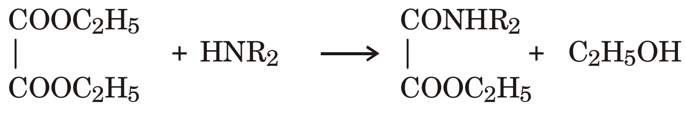
1.5.10 Reaction with Diethyl Oxalate

1 , 2 and 3 amines can be distinguished by their reaction with diethyl oxalate. Primary (1) amines react with diethyl oxalate forming N, N–oxamide, which is a solid.

$$\begin{array}{l} COOC_2H_5 \\ | \\ COOC_2H_5 \end{array} + \begin{array}{l} H–NH–R \\ \\ H–NH–R \end{array} \longrightarrow \begin{array}{l} CONHR \\ | \\ CONHR \end{array} + 2C_2H_5OH$$

N, N´–dialkyl
oxamide (solid)

Secondary (2) amines react with diethyl oxalate forming oxamic ester, which is a liquid.



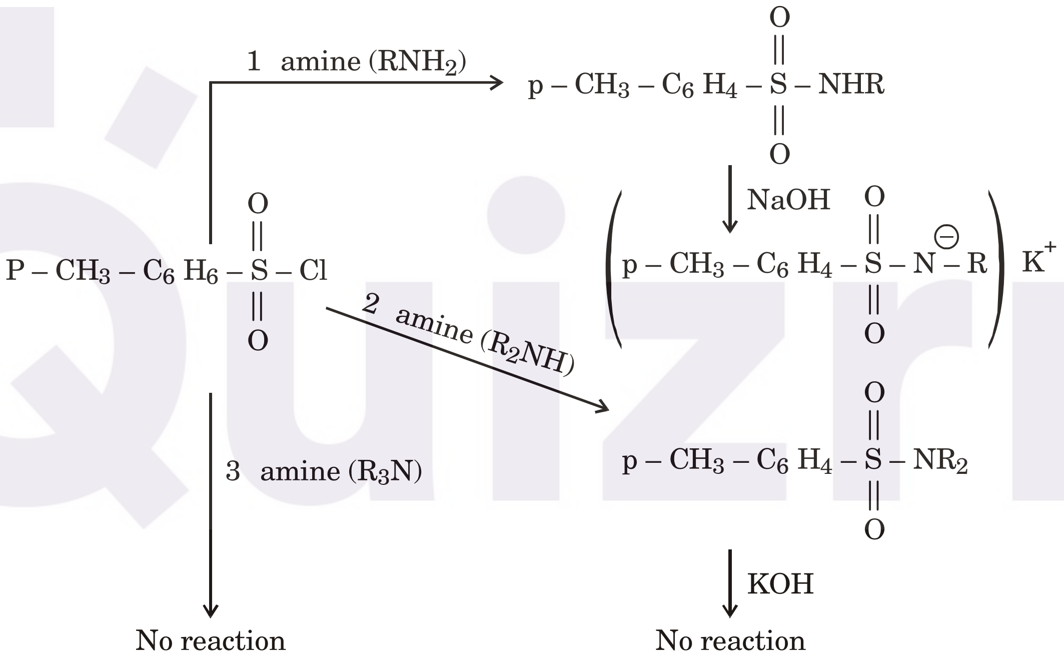
$$\begin{matrix} COOC_2H_5 \\ | \\ COOC_2H_5 \end{matrix} + HNR_2 \longrightarrow \begin{matrix} CONHR_2 \\ | \\ COOC_2H_5 \end{matrix} + C_2H_5OH$$

oxamic ester
(liquid)

Tertiary (3) amines do not react with diethyl oxalate.

Test for Amines

(1) Hinsberg Test : This reaction is used for the separation of amines from a mixture. The mixture containing primary, secondary and tertiary amines is treated with an aromatic sulphonyl chloride.

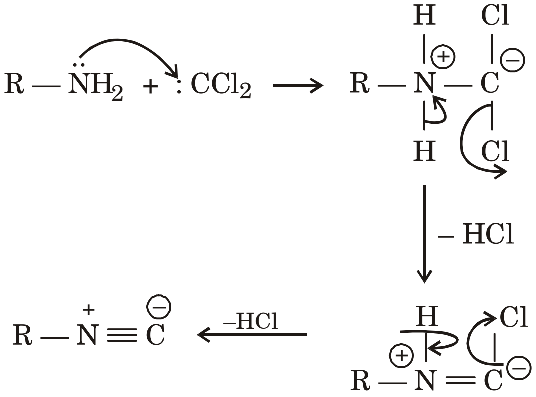


(2) Carbylamine Reaction : This is a chemical test for the detection of primary amines. Both aliphatic and aromatic primary amines when heated with chloroform and ethanolic KOH form isocyanide, also called carbylamine, a foul smelling compound.

$$\begin{matrix} R-NH_2 \\ \text{or} \\ Ar-NH_2 \end{matrix} + CHCl_3 + 3KOH \longrightarrow \begin{matrix} R-N\equiv C \\ \text{or} \\ Ar-N\equiv C \end{matrix} + 3KCL + H_2O$$

Mechanism :

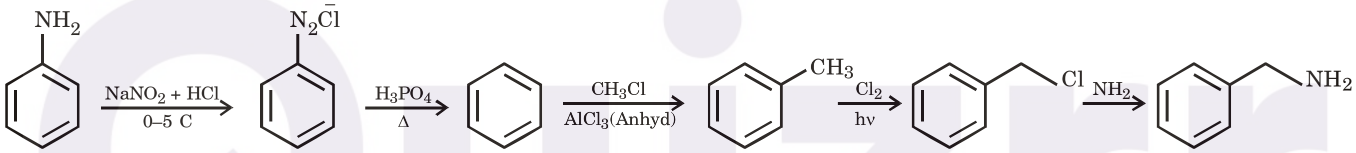
$$CHCl_3 \xrightarrow[-Cl^{-}\\ -H_2O]{\overset{\ominus}{O}H} :CCl_2$$



Example 8

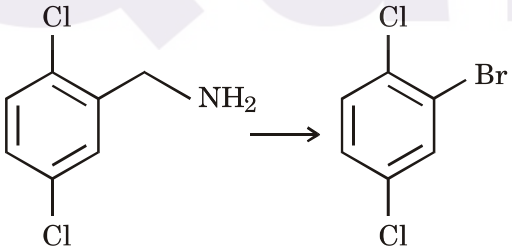
How will you bring about the following conversion ? Aniline → Benzylamine

Solution :

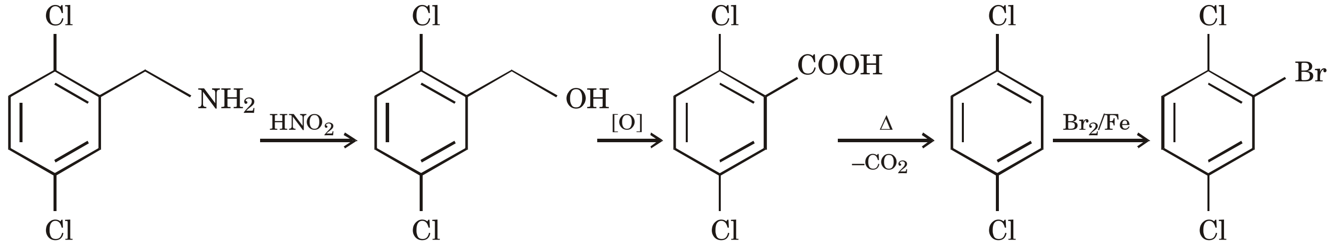


Example 9

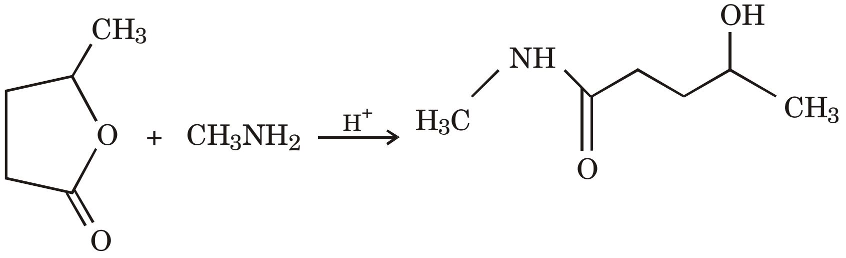
Convert :



Solution :

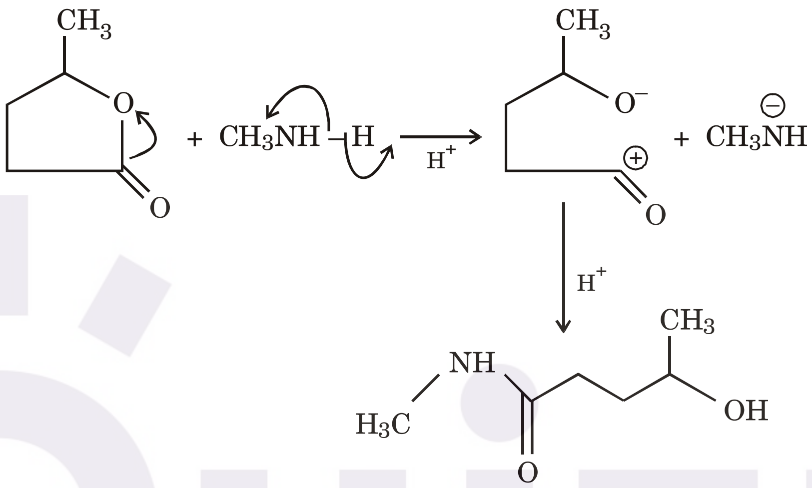


Example 10



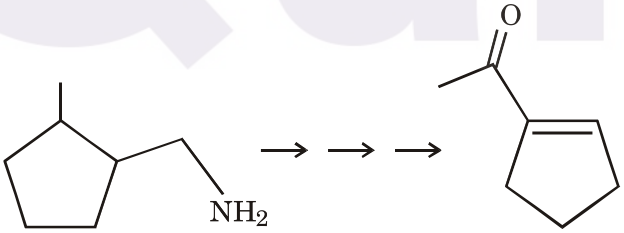
Predict the mechanism of above conversion.

Solution :

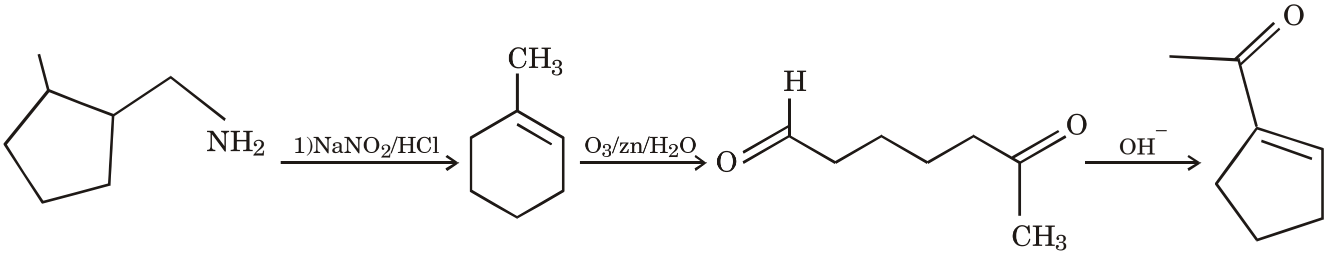


Example 11

Bring out the following conversion.



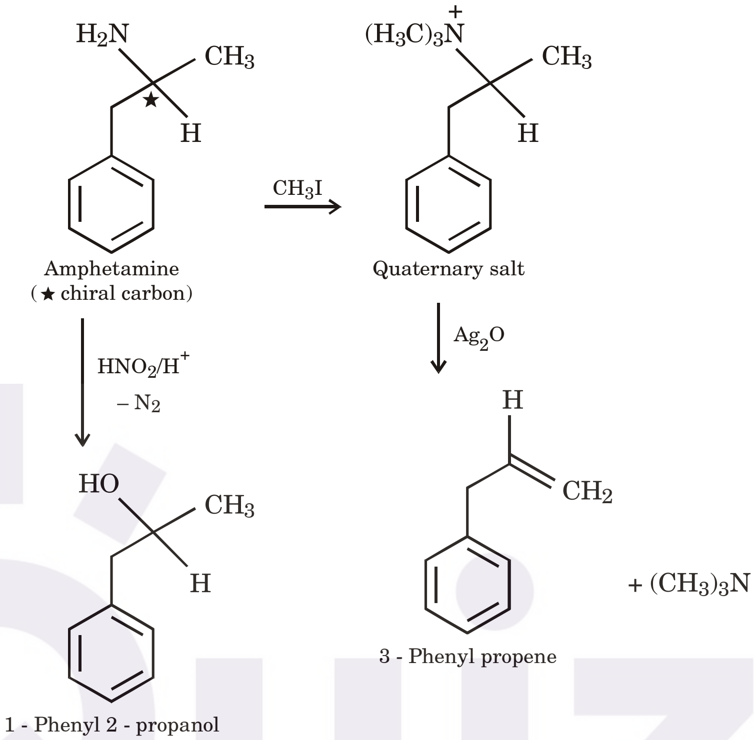
Solution :



Example 12

Amphetamine is a liquid that is nearly insoluble in water, but quite soluble in aqueous acid. It can be resolved into enantiomers and liberates nitrogen spontaneously when reacted with nitrous acid. When amphetamine is quarternised with CH_3I, heated with Ag_2O and heated, 3–phenyl–1–propene is the major product. Deduce the structure of amphetamine.

Solution :



Example 13

$\underset{(X)}{C_5H_{13}N} \xrightarrow[-N_2]{NaNO_2/HCl} \underset{3° \text{ alcohol}}{(Y)}$ **+ other products. (X) is optically active. Identify the structure of (X) and (Y). Explain the formation of (Y) from (X). Will (Y) also be optically active ? Justify your answer. Draw the structure of important intermediates, if any.**

Solution :