METHOD OF PREPARATION

Preparation Methods of Amines

(1) Ammonolysis of Alkyl Halides and Alcohol:

(a) From Ammonolysis of Alkyl Halides [Hofmann's ammonolysis]

Upon heating an aqueous ammonia solution in the presence of an alkyl halide, a mixture of the three amine types and quaternary ammonium salt is generated.

$$R—X \xrightarrow[-HX]{NH_2} R—NH_2 \xrightarrow[-HX]{R-X} R_2—NH \xrightarrow[-HX]{R-X} R_3N \xrightarrow{R-X} R_4\overset{\oplus}{N}\,X^{\ominus}$$

(Quaternary ammonium salt)

If ammonia is taken in excess, 1° amine is the main product.

(b) Ammonolysis of Alcohols

When ROH and NH_3 are passed over Al_2O_3 or ThO_2 at 350° C all the three types of amines are formed.

$$R—OH \xrightarrow[Al_3O_3/400^oC]{NH_3} R—NH_2 \xrightarrow[Al_2O_2]{R-OH} R_2—NH \xrightarrow[Al_2O_3]{R-OH} R_3N$$

Note: **(i)** Quaternary ammonium hydroxide is not formed due to steric hindrance.

(ii) If excess of ammonia is used, then main product will be primary amine.

(2) By Reduction

(a) With $RCONH_2$: $RCONH_2 \xrightarrow[\text{or } Na/\ C_2H_2OH]{LiAlH_4} RCH_2NH_2$

(b) With RCN: $RCN + 4H \xrightarrow{Na/C_2H_2OH} RCH_2NH_2$

This chemical process is commonly known as the Mendius reaction. When alkyl isocyanides are reduced using sodium and ethanol, it results in the formation of secondary amines.

$$R — NC + 4H \xrightarrow{Na/C_2H_5\,OH} RNHCH_3$$

(c) With Oximes: $R - CH{=}N - OH + 4H \xrightarrow[Na/C_2H_5OH]{LiAlH_4} RCH_2 - NH_2 + H_2O$

(d) With RNO_2 : $RNO_2 + 6H \xrightarrow[\Delta]{Sn/HCl} RNH_2 + 2H_2O$

In lab method we use Sn/HCl while in industrial method we use Fe/ HCl.

(3) By Hydrolysis of

(a) R—NC: Alkyl isocyanide undergoes hydrolysis with mineral acid and forms alkyl amine.

$$R—NC + 2H_2O\ HCl \rightarrow RNH_2 + HCOOH$$

(b) RNCO: Alkyl isocyanate undergoes hydrolysis on heating with KOH.

$$R—N{=}CO + 2\ KOH \quad RNH_2 + K_2CO_3$$

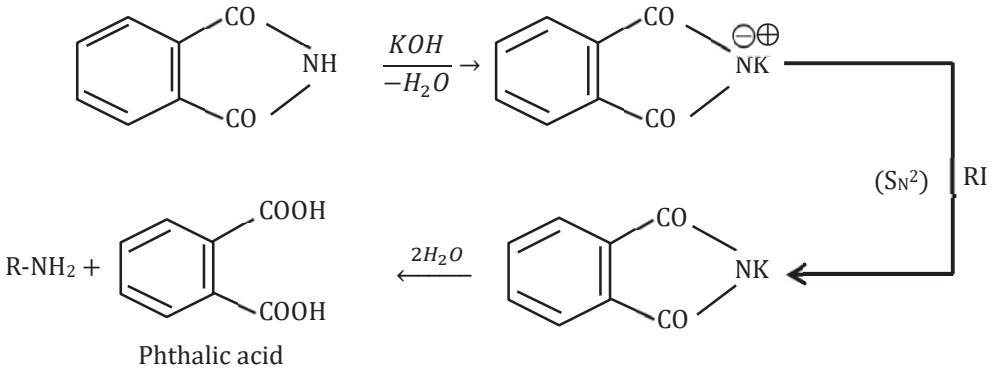
(4) From Grignard Reagent

Alkyl magnesium iodide reacts with chloramine to yield alkyl amine.

$$R - Mg - I + Cl - NH_2 \rightarrow R - NH_2 + Mg\begin{matrix} I \\ \diagup \\ \diagdown \\ Cl \end{matrix}$$

(5) Gabriel Phthalimide Synthesis

The process begins with the treatment of phthalimide with KOH to produce potassium phthalimide, which is subsequently subjected to alkyl iodide. Upon hydrolysis, alkyl phthalimide transforms into alkyl amine. This technique finds application in the production of highly pure aliphatic primary amines.



Phthalic acid

(6) By Hofmann's Bromamide Reaction (Hofmann's Hypobromite Reaction)

This method serves as a general approach to transform alkane amides into primary amines with one less carbon atom. The procedure involves heating ethanamide with an excess of KOH and bromine.

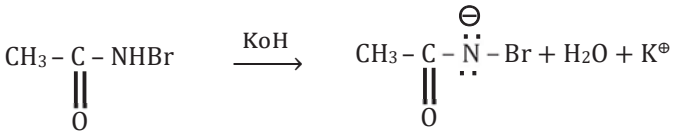
$$CH_3CONH_2 + Br_2 + 4KOH \longrightarrow CH_3NH_2 + K_2CO_3 + 2KBr + 2H_2O$$

Mechanism:

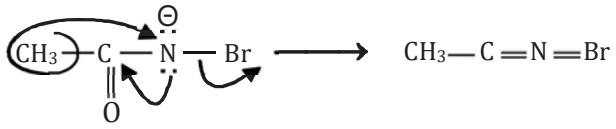
Step 1 $CH_3—CONH_2 + Br_2 + KOH \longrightarrow CH_3CONHBr + KBr + H_2O$

N–bromo ethanamide

Step 2



Step 3



(Methyl isocyanate)

Step 4 $CH_3 — N = C = O + 2KOH \longrightarrow CH_3NH_2 + K_2CO_3$

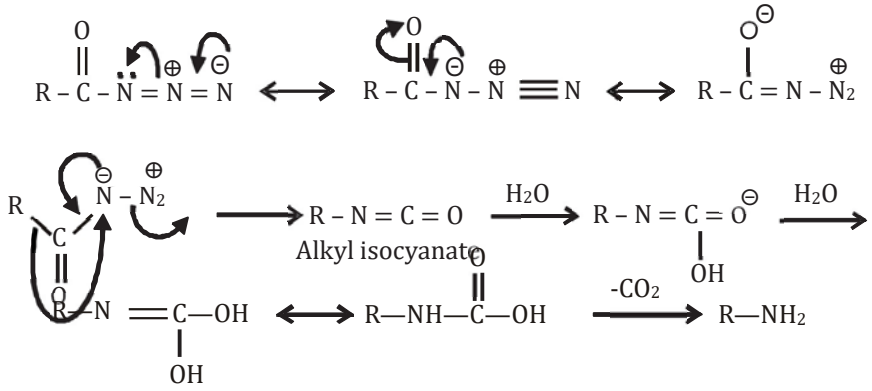
(7) Curtius Reaction

Acid chloride on treatment with sodium aside give acid asides which on pyrolysis gives isocyanates which on hydrolysis gives corresponding amines.

$$RCON_3 \xrightarrow[\Delta]{-N_2} \underset{\text{A cylaside}}{RCON_3} \xrightarrow[\Delta]{-N_2} \underset{\text{Alkyl isocyanate}}{R-N=C=O} \xrightarrow[\Delta]{-N_2} \underset{\text{Alkyl amide}}{R-NH_2}$$

Mechanism:

$$RCOCl + NaN_3 \; RCON_3 + NaCl$$

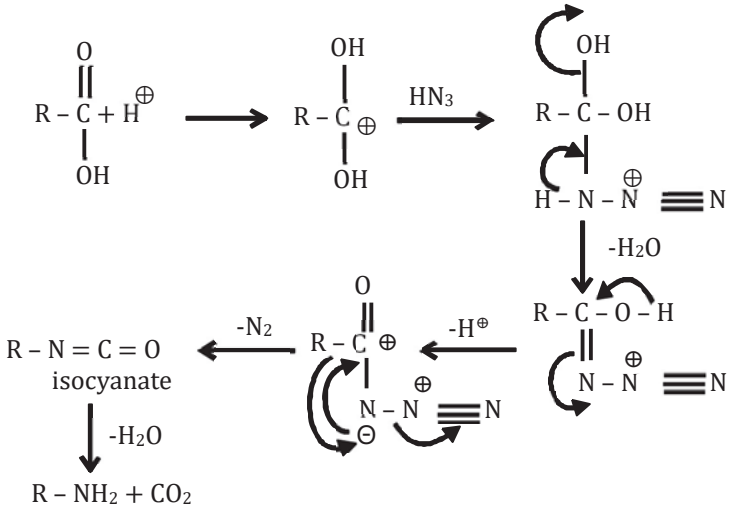


(8) Schmidt Reaction

In presence of conc. H_2SO_4 alkanoic acid reacts with hydrazoic acid (N_3H) to yield alkylamine.

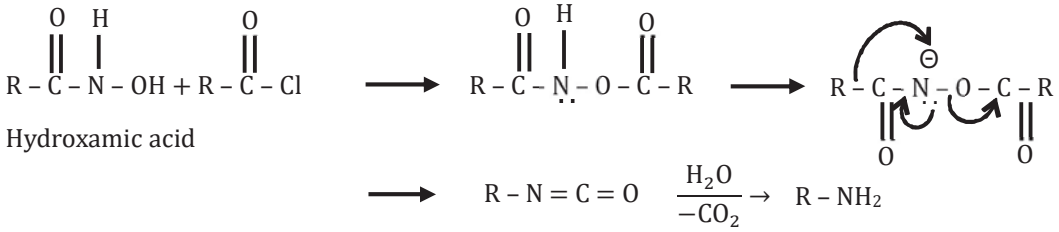
$$R—COOH + N_3H \xrightarrow{conc.H_2SO_4} R\text{-}NH_2 + NH_2 + N_2 + CO_2$$

Mechanism



(9) Lossen Rearrangement Reaction

In this reaction hydroxamic acid undergoes rearrangement and gives alkyl amine.



(10) Reductive Amination of Aldehyde and Ketone

$$>C{=}O + NH_3 + H_2 \xrightarrow[\Delta]{Ni} >CH - NH_2 + H_2O \ 1^o \text{ amine}$$

$$>C{=}O + RNH_2 + H_2 \xrightarrow[\Delta]{Ni} >CH - NHR + H_2O \ 2^o \text{ amine}$$

$$>C{=}O + R_2NH + H_2 \xrightarrow[\Delta]{Ni} >CH - NH_2 + H_2O \ 3^o \text{ amine}$$