Amines I. Preparation and Physical Properties

Amine are organic derivative of ammonia (NH_3) , amine are basic compounds & classified as primary , secondary & tertiary based on how many group are bonded to the nitrogen.

NH_3,	RNH_2,	R_2NH,	R_3N,	$R_4N^+X^-$
	1^0amine	2^0amine	3^0amine	A quaternary ammonium salt

The ion pair of electron on all amines makes them nucleophile and bases.

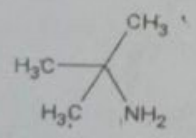
Nomenclature

Common nomenclature

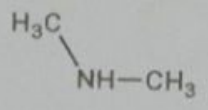
Aliphatic amine....by naming the alkyl group(s) attack to the nitrogen followed by the word amine

CH_3NH_2	$CH_3CH_2NH_2$	$CH_3NCH_2CH_3$
Methylamine	ethylamine	ethyl methylamine

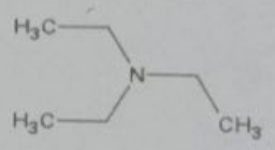
If two or three units of the same group are bonded to the nitrogen of an amine, use prefix di or tri



tert-butylamine



dimethyl amine



tri-ethylamine

Simple diamines are named by using the prefix for the the number of methylene groups in the molecule & then adding the fragment- methylene-diamine.

$NH_2CH_2CH_2CH_2CH_2NH_2$	$NH_2CH_2CH_2CH_2CH_2CH_2NH_2$
tetra methylene diamine	pentamethylenediamine

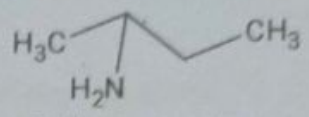
IUPAC Nomenclature

- Amine are named by dropping of the –e of corresponding alkane & adding -amine

CH_3NH_2 methanamine

$CH_3CH_2NH_2$ ethan amine

$CH_3CH_2CH_2NH_2$ 1- propanamine

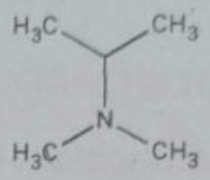


2- butanamine

- Secondary & tertiary amine are named as alkyl (aryl) substituted amine

CH_3-$NHCH_2CH_3$

N-methyl Ethan amine



2-(N,N-Dimethyl)propanamine

- **Diamine ....** Are named by numbering the two amino groups on the parent chain, separating the numbers with a comma, & then adding a dash. Finally, add the name of the corresponding hydrocarbon followed by the fragment- diamine.

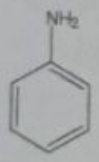
$H_2NCH_2CH_2CH_2CH_2NH_2$

1, 4-Butanediamine

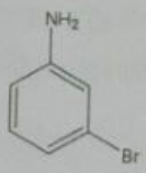
$HN_2CH_2CH_2CH_2CH_2CH_2NH_2$

1, 5- pentane diamine

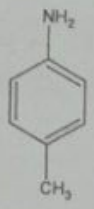
- Primary aromatic amine are named as derivatives of aniline



aniline

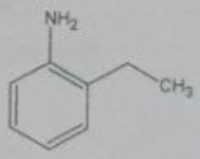


m-bromo aniline



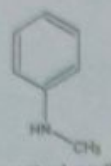
p-methyl aniline

p-Toludine



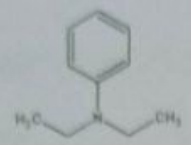
o-ethyl aniline

- Secondary & tertiary aromatic amines also can be named as derivatives of aniline. The italic capital N is used to show that the organic group(s) are bonded to the nitrogen atom. If two different alkyl groups are involved, List the groups alphabetically.



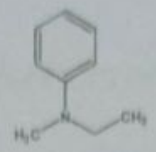
N-methyl aniline

2^0



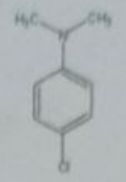
N,N-Diethyl aniline

3^0



N-Ethyl-N-methyl aniline

3^0



p- chloro-N,N-dimethyl aniline

Incorporate the amino group with functional group

$CH_2=CH-CH_2NH_2$

2-Propene 1- amine

$NH_2\overset{2}{C}H_2\overset{1}{C}H_2OH$

2- Amino ethanol

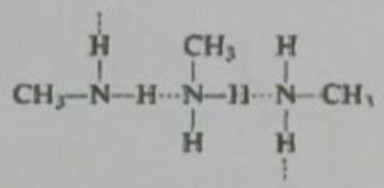
$NH_2CH_2CH_2COOH$

3-Aminopropanoic acid

Physical Properties of amines

Amine are polar compounds

- Primary & secondary amines can form intermolecular hydrogen bonds



- Where's alkanes cannot , so the 1^0 & 2^0 amine boil at higher temperature Than an alkane of about the same molecular weight

	$CH_3CH_2NH_2$	$CH_3CH_2CH_3$
Mwt	45	44
B.p	$17C^0$	$-42C^0$

- Tertiary amine and alkane of about the same molecular weight have similar boiling points (because t- amines cannot form intermolecular H.B)

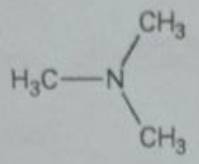
	$(C_2H_5)_3N$	$CH_3(CH_2)_5CH_3$
Mwt	101	100
B.p	$89C^0$	$98C^0$

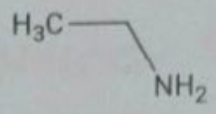
- Amine have lower B.p than alcohols or carboxylic acid

	CH_3OH	CH_3NH_2
B.p	$65C^0$	$6.5C^0$

(Electronegativity of oxygen higher than Nitrogen)

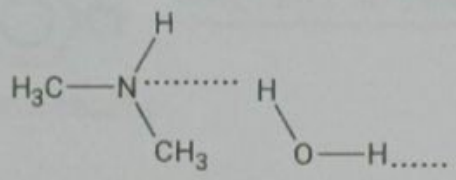
Ex;



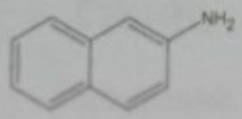


B.p	$2.9C^0$	$48.7C^0$ (H.B)

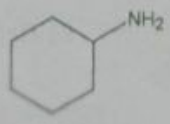
- Primary, secondary amines form hydrogen bonds with water. Thus all classes of amines, which contain up to five carbon atoms, are water- soluble.



- Amine also soluble in less polar solvent like ether, benzene, alcohol.
- Amine are readily absorbed through the skin & they are very toxic.



2- naphthyl amine



cyclohexyl amine

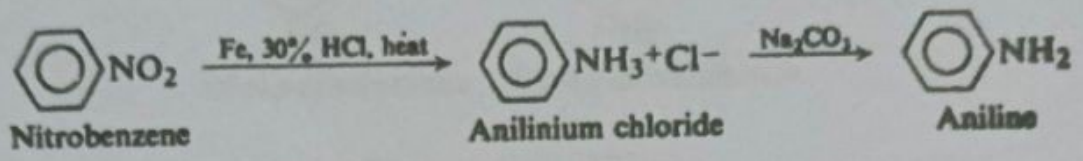
carcinogenic amines

Preparation of amine

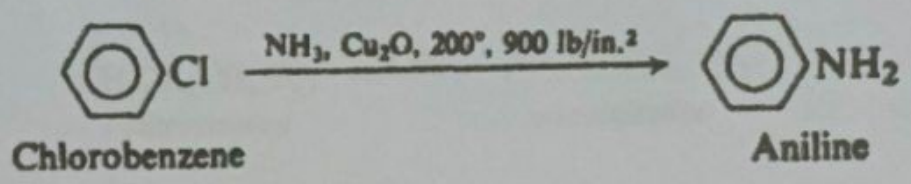
A- Industrial Sources

The most important of all amine is aniline which as prepared by several ways

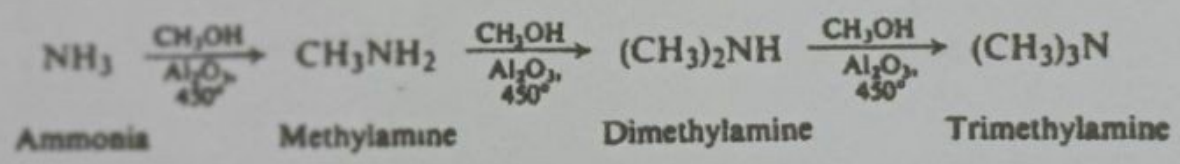
1- Reduction of nitrobenzene by Fe & dil. HCL



2- Treatment of chlorobenzene with NH_3 at high Temperature & high pressure in the presences of catalyst



- Also the following amine synthesized on the industrial scale from CH_3OH & NH_3



B- Laboratory

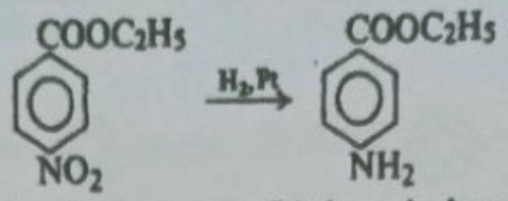
1- Reduction of Nitro , Nitriles & Amides Compounds

a- Nitro **compounds**....the reduction agent that is used for reduction are Sn or Fe in presence of HCL or H_2 with catalyst to give 1^0 amine.

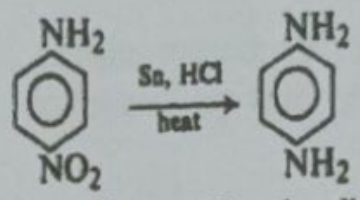
$$\underset{\text{Nitro compound}}{\begin{matrix} ArNO_2 \\ \text{or} \\ RNO_2 \end{matrix}} \xrightarrow{\text{metal, } H^+ \text{; or } H_2\text{, catalyst}} \underset{1^\circ \text{ amine}}{\begin{matrix} ArNH_2 \\ \text{or} \\ RNH_2 \end{matrix}}$$

Chiefly for aromatic amines

Examples:

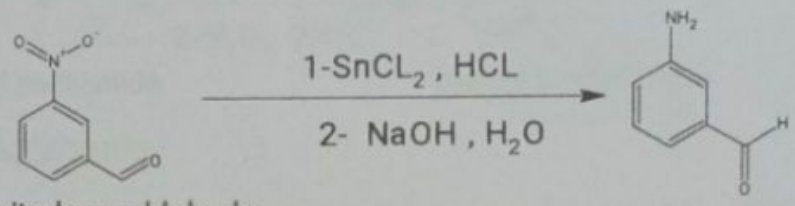


Ethyl *p*-nitrobenzoate Ethyl *p*-aminobenzoate



p-Nitroaniline *p*-Phenylenediamine

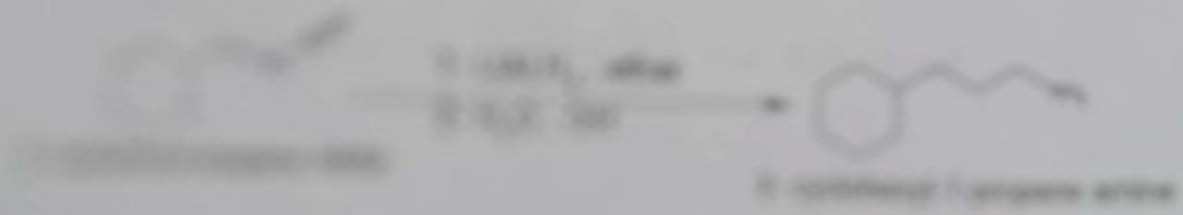
$$\underset{\text{1-Nitropropane}}{CH_3CH_2CH_2NO_2} \xrightarrow{Fe,\ HCl} \underset{n\text{-Propylamine}}{CH_3CH_2CH_2NH_2}$$

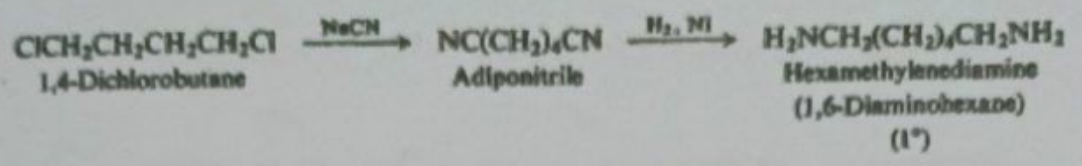


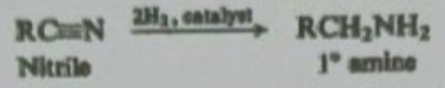
m-nitrobenzaldehyde m- aminobenzaldehyde

b- Reduction of Nitriles ... Amines are converted in good yield from Nitriles by the use of $LiALH_4$ or H_2/ Ni, followed by hydrolysis in aqueous basic solution.

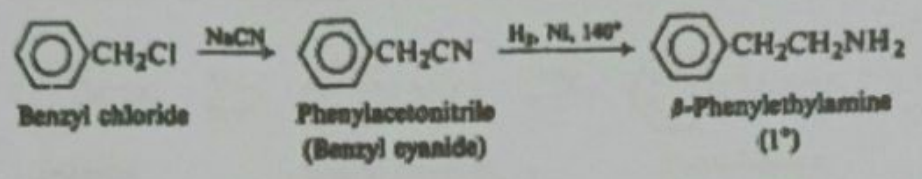
$$(R)\ +\ NaCN \longrightarrow RCN\ +\ NaX \xrightarrow[\text{2- } H_2O\text{ , } OH^-]{\text{1- } LiALH_4\text{ , ether}} \underset{1^\circ \text{ amine}}{RCH_2NH_2}$$



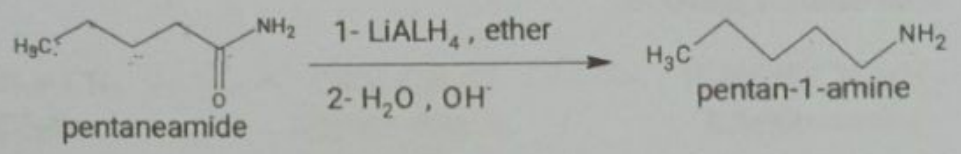


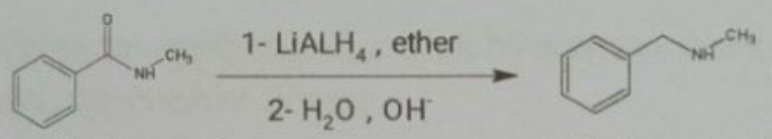


Examples:



C- Reduction of Amides.....amides are convert in good yield to amines by the use of $LiAlH_4$, followed by hydrolysis in aqueous basic solution.





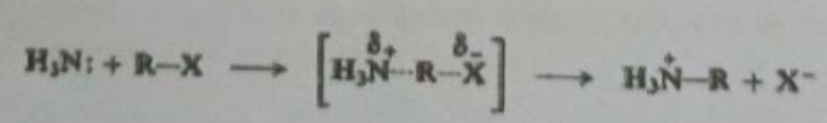
2- Alkylation of Ammonia

Displacement of halogen by NH_3 yields the amine salt, from which the free amine can be liberated by treatment with hydroxide ion.

$$RX + NH_3 \longrightarrow RN^+H_3X^-$$

$$RN^+H_3X^- + OH^- \longrightarrow RNH_2 + H_2O + X^-$$

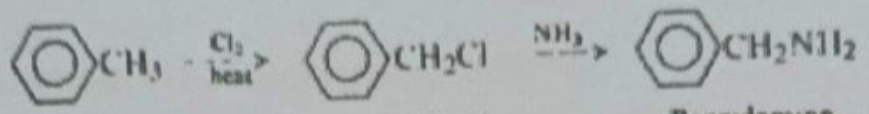
Ammonolysis of halides belongs to the class of reaction called nucleophilic substitution.



اولي $CH_3CH_2CH_2CH_2Br \xrightarrow{NH_3} CH_3CH_2CH_2CH_2NH_3^+Br^-$ *Substitution*

ثاني $CH_3-\underset{Br}{\overset{CH_3}{C}}-CH_3 \xrightarrow{NH_3} CH_3-\overset{CH_3}{C}=CH_2 + NH_4Br$ *Elimination*

Some examples of the application of ammonolysis to synthesis are:



Toluene — Benzyl chloride — Benzylamine

$$\underset{\text{Propionic acid}}{CH_3CH_2COOH} \xrightarrow[P]{Br_2} \underset{\text{α-Bromopropionic acid}}{CH_3\underset{Br}{C}HCOOH} \xrightarrow{NH_3} \underset{\text{Alanine (α-Aminopropionic acid)}}{CH_3\underset{NH_2}{C}HCOOH}$$

$$\underset{\text{Ethylene}}{CH_2=CH_2} \xrightarrow{Cl_2} \underset{\text{Ethylene chloride}}{ClCH_2CH_2Cl} \xrightarrow{2NH_3} \underset{\text{Ethylenediamine}}{H_2NCH_2CH_2NH_2}$$

Disadvantage to the synthesis of amines by ammonolysis is the formation of more than one class of amine.

$$RX + NH_3 \longrightarrow \underset{1^\circ \text{ amine salt}}{RNH_3^+X^-}$$

the initial substitution, reacts with the reagent ammonia to yield the ammonium salt and the free primary amine; the following equilibrium thus exists:

$$RNH_3^+ + NH_3 \rightleftharpoons \underset{1^\circ \text{ amine}}{RNH_2} + NH_4^+$$

The free primary amine, like the ammonia from which it was made, is a nucleophilic reagent; it too can attack the alkyl halide, to yield the salt of a secondary amine:

$$\underset{1^\circ \text{ amine}}{RNH_2} + RX \longrightarrow R_2NH_2^+X^- \rightleftharpoons \underset{2^\circ \text{ amine}}{R_2NH}$$

The secondary amine, which is in equilibrium with its salt, can in turn attack the alkyl halide to form the salt of a tertiary amine:

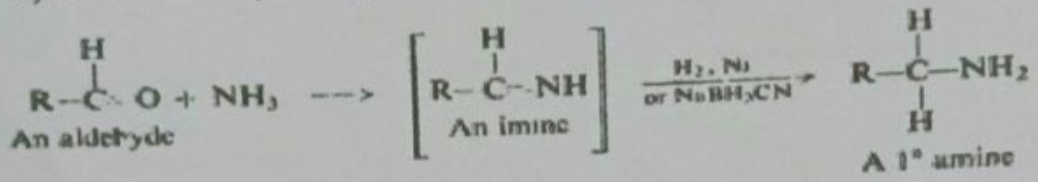
$$\underset{2^\circ \text{ amine}}{R_2NH} + RX \longrightarrow R_3NH^+X^- \underset{}{\overset{NH_3}{\rightleftharpoons}} \underset{3^\circ \text{ amine}}{R_3N}$$

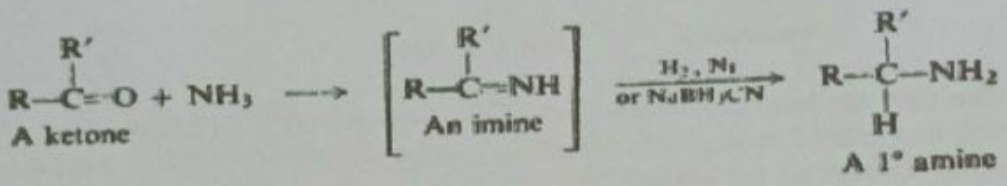
Finally, the tertiary amine can attack the alkyl halide to form a compound of the formula $R_4N^+X^-$, called a *quaternary ammonium salt* (discussed in Sec. 23.5):

$$\underset{3^\circ \text{ amine}}{R_3N} + RX \longrightarrow \underset{\text{Quaternary ammonium salt } (4^\circ)}{R_4N^+X^-}$$

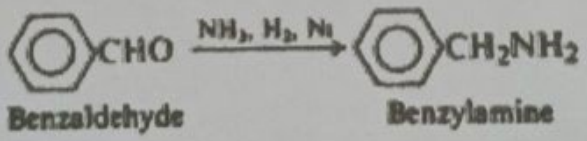
3- Reductive amination of aldehyde & ketone

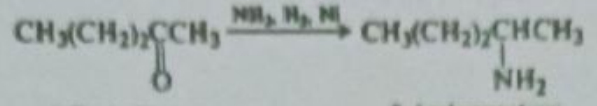
Amine can be synthesized in single step by treatment of aldehyde or ketone with NH_3 or an amine in the presence of reducing agent such as (H_2 , Ni) or sodium cyanohyridoborate ($NaBH_3CN$).



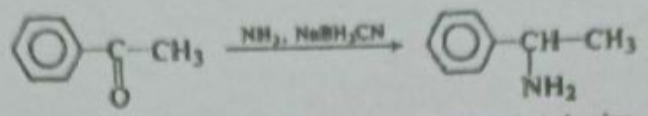


$$\underset{\text{Heptaldehyde (Heptanal)}}{CH_3(CH_2)_5CHO} \xrightarrow{NH_3,\ H_2,\ Ni} \underset{\text{n-Heptylamine (1-Aminoheptane)}}{CH_3(CH_2)_5CH_2NH_2}$$



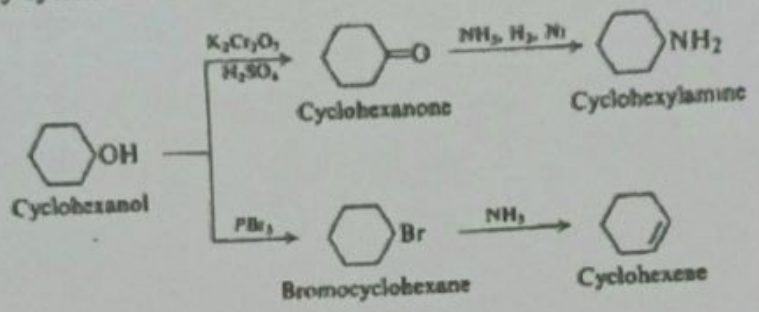


2-Pentanone (Methyl n-propyl ketone) → 2-Aminopentane



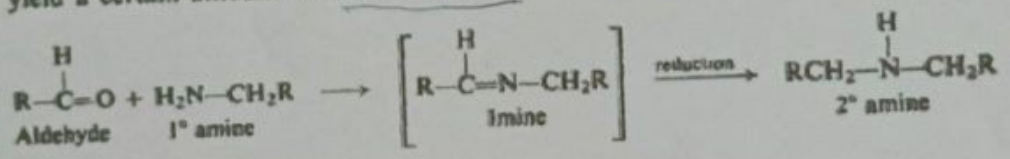
Acetophenone (Methyl phenyl ketone) → α-Phenylethylamine

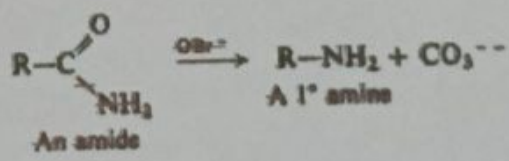
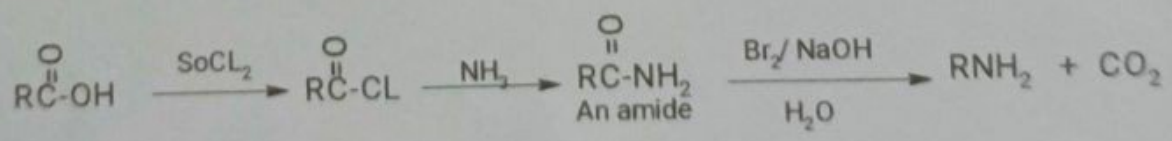
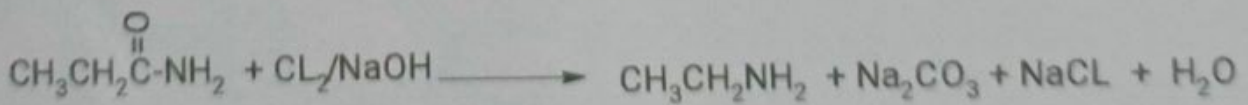
Reductive amination of ketones yields amines containing a *sec*-alkyl group; such amines are difficult to obtain by ammonolysis because of the tendency for *sec*-alkyl halides to undergo elimination. For example, cyclohexanone is converted into cyclohexylamine in good yield, whereas ammonolysis of bromocyclohexane yields only cyclohexene.



Cyclohexanol → Cyclohexanone → Cyclohexylamine; Cyclohexanol → Bromocyclohexane → Cyclohexene

During reductive amination the aldehyde or ketone can react not only with ammonia but also with the primary amine that has already been formed, and thus yield a certain amount of secondary amine. The tendency for the reaction to go



4- Hofmann rearrangement (degradation) of amide

The product in this reaction contain one carbon less than the starting material