Organic nitrogen compounds: amines, amides, amino acids and proteins

There are many important organic compounds, including the amides and the amines. Probably the best known and most widely occurring organic nitrogen compounds are the amino acids – the fundamental building blocks of the proteins making up a considerable part of every living organism. We are going to be looking at organic nitrogen compounds in some detail in this chapter.

Ammonia – building block of the organic nitrogen compounds

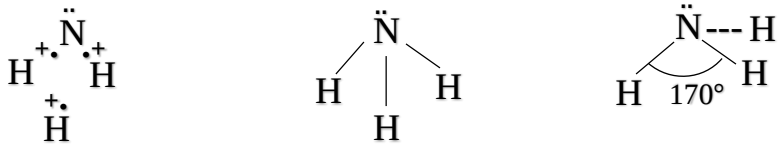


Figure: Different ways of showing the electronic arrangement and shape of the ammonia molecule.

The most important feature of an ammonia molecule is the lone pair of electrons on the nitrogen atom. This accounts for the proton-acceptor property of ammonia that makes it a base.

The amines

The amines are organic compounds based on ammonia, where one or more of the three hydrogen atoms have been substituted by an alkyl or an aryl group. They do not occur in the free state widely in the living world, except in putrefying and decaying flesh-they are formed by the action of bacteria on amino acids when proteins break down. Amines also account for some of the body odors detected from humans who do not wash frequently-bacteria on the skin digest amino acids from the sweat of the groin and armpits.

Organic Nitrogen Compounds (Amines, amides, amino acids and protein)

1. Amines:

Preparing amines: If ammonia is heated under pressure with a halogenoalkane, the ammonia's hydrogen atoms can be replaced by alkyl groups and the resulting products are amines. e.g.

$CH_3Cl(g) + NH_3(g) \longrightarrow CH_3NH_2(g) + HCl(g)$

chloromethane ammonia — Methyl amine — Hydrogen chloride

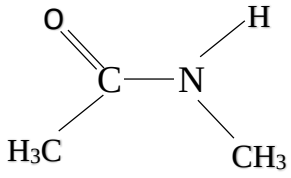
$CH_3NH_2(g) + CH_3Cl(g) \longrightarrow (CH_3)_2NH(g) + HCl(g)$

$(CH_3)_2NH(g) + CH_3Cl(g) \longrightarrow (CH_3)_3N(g) + HCl(g)$

Hydrogen atom on an electronegative atom such as **Oxygen** or **Nitrogen** could be replaced with a CH_3CO – group using ETHANOYL CHLORIDE [CH_3COCl] or **ETHANOIC ANDHYDRIDE** [$CH_3COOOCH_3$] the product is amine:-

$CH_3NH_2 + CH_3COCl \longrightarrow CH_3CONHCH_3$

Methyl amine — ethanoyl chloride — N-methyl ethanamide

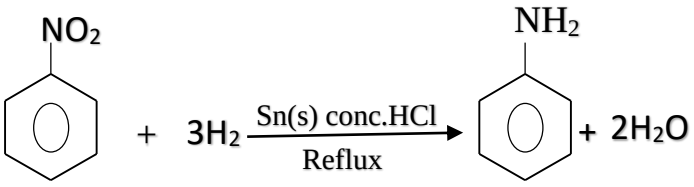


'N'- methyl indicates that the methyl group is attached to the nitrogen atom.

Reduction of aromatic nitro-compounds to form aryl amines:

Benzene and other aromatic compounds can be nitrated to form nitro compounds using a mixture of conc. HNO_3 and conc. H_2SO_4.

These nitro-compounds can produce aromatic amines. Which are very useful for making other compounds. e.g.



Phenylamine

a. $Sn(s) + 2HCl(aq) \longrightarrow Sn^{2+}(aq) + 2Cl^{-}(g) + H_2(g)$

b. $Sn^{2+}(aq) \longrightarrow Sn^{4+}(aq) + 2e^{-} \ldots\ldots\ldots \times 3$

c. $C_6H_5NO_2(l) + 6H^{+}(aq) + 6e^{-} \longrightarrow 2\,H_2O(l)$

The flask is then cooled and NaOH (aq) added to redissolve the initial precipitation of $Sn(OH)_4$ tin (IV) hydroxide. $Sn(OH)_4$ is amphoteric and with excess of alkali produces soluble $Sn(OH)_6^{2-}$ ions.

Water is then added and **steam distillation**, is used to separate the mixture of phenylamine and water.

- The initial distillate is cloudy can emulsion of phenylamine and water. When the distillate is clear, only water is distilling over.
- Powdered NaCl(s) is added now to the distillate and the mixture transferred to a separating funnel – shaken well.
- Phenylamine is sufficiently soluble in water, but very much less in NaCl solution. **This process is called salting out.**
    - Transferred to separating funnel + ethoxyethane (ether), shaken. Layers allowed to separate and lower aqueous layer is run off into a beaker. Ether layer, further extraction from aqueous layer with further portion of ether is done. The combined ether extract (obtained by solvent extraction) is heater with KOH(s) to dry ether extract and being alkaline removes traces of HCl(better than $CaCl_2$ aqueous anhydrous Na_2SO_4).

Ether is distilled off and finally phenylamine is distilled off collecting the fraction between 180 and 185℃.

Properties of amines:

The lower member of alkyl amines are gases or volatile liquids. Hydrogen bonding (because of H atoms with N atom). In tertiary amine H-bonding is not possible. Only vander waals force thus boils at a lower temperature.

Arylamines are less volatile and usually liquid at room temperature slightly soluble in water because of benzene ring over weights the tendency of NH_2 group to form hydrogen bonds. It dissolves in organic solvents.

- Like ammonia, lower members are miscible with water, because of hydrogen bonding can occur between water and amine mloecules.
- An aqueous solution of amine is alkaline. Amines are strong bases- the nitrogen atom acts as a proton acceptor.

$$CH_3CH_2NH_2(aq) + H_2O(l) = CH_3CH_2NH_3^+(aq) + OH^-(aq)$$

NH_3, being basic, can form salts with acids; e.g.

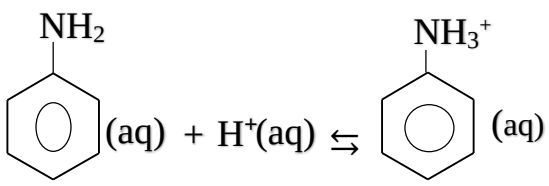
$$NH_3(aq) + HCl(aq) \longrightarrow NH_4^+Cl(aq)$$

Amines can form salts with acids in a similar way:

$$CH_3CH_2NH_2(aq) + HCl(aq) \longrightarrow CH_3CH_2NH_3^+Cl^-(aq)$$

Ethyl amine — Ethyl ammonium Chloride

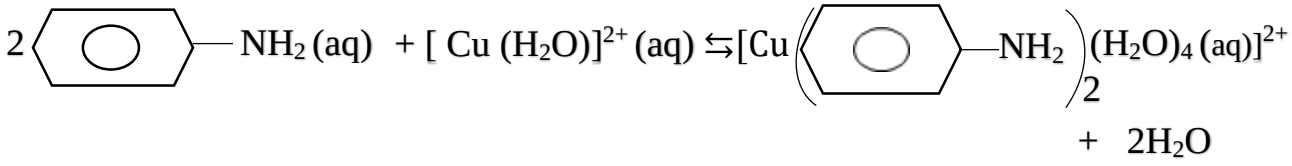
- If dil HCl(aq) is added to a solution of ethylamine, you will notice a rise in temperature(Exothermic reaction) and the loss of the fishy smell.
- Primary alkylamines are stronger bases than ammonia. This is due to a shift of electrons from alkylgroups increasing the electron density on the nitrogen atom. This means that nitrogen atom can hold a proton more strongly.
- Phenyl amine, an alkyl amine, is a weaker base than ammonia. The electrons on the nitrogen atom interact with the delocalized πelectrons in the ring and as a result, the lone pair of electrons on nitrogen atom is less available. This reduces the ease of acceptance of the proton by $–NH_2$ group. Phenylamine will form salt with strong acids, where excess of H^+ ions move the equilibrium to the right.



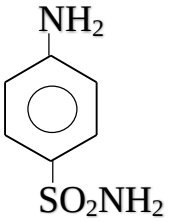
Phenylammonium ion

- Ammonia forms complex ions with transition metal cations. E.g.

  $4NH_3(aq) + [Cu(H_2O)_6]^{2+}(aq) \leftrightarrows [Cu(NH_3)_4(H_2O)]^{2+}(aq) + 4H_2O\ (l)$
  Amines form complex ins in a similar way.



- Phenylamine and the fight against bacteria the lone pair of electrons on the nitrogen atom of phenylamine has a tendency to become partly delocalized around the benzene ring. This gives a high electron density around the ring, which inturn means that phenylamine is easily oxidised and readily undergoes electrophilic substitution of the benzene ring.
  What has this to with the fight against disease causing bacteria?
- **4-aminobenzene sulphonamide** is a derivative of phenylamine that can be synthesized as a result of the ease of this substitution.This compound and other similar ones derived from it form a class of drugs known as **SULPHONAMIDES.**



4- Aminobenzene Sulphonamide give rise to a whole family of antibacterial drug.

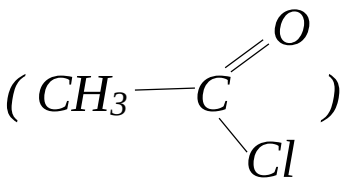
These were some of the earliest drugs to be really effective in destroying bacteria. They have played a major part in reducing the number of deaths from pneumonia, from tuberculosis and from infections after child birth and many more. They are still in use today.

➢ *AMINES AS NEUROTRANSMITTER:-*

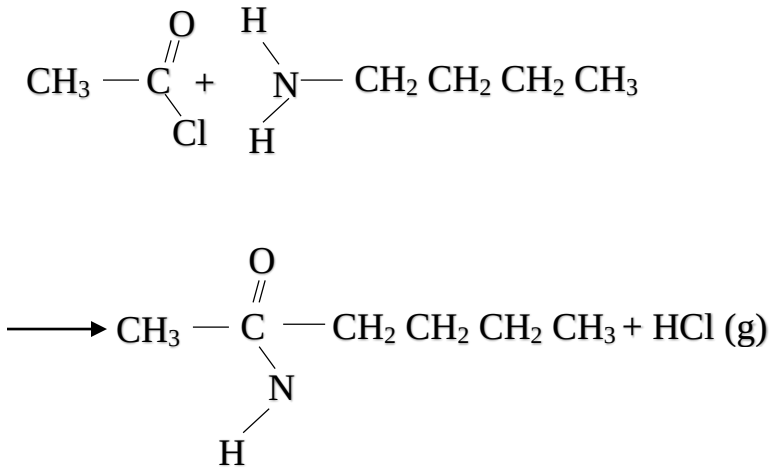
'Ecatasy' the illegal drug, is an amine. It's full name is 3,4-methylenedioxymethamphetamine (or MDMA). It produces feeling of energy, euphoria, empathy and love.This is because it causes the release of **SEROTONIN** and **DOPAMINE** in the brain. These **NEUROTRANSMITTERS** are involved in the regulation of mood – high levels are associated with positive feelings. The exact mechanism by which the drug causes the release of NEUROTRANSMITTERS remains unclear.

The drug also interferes with the normal temperature regulation mechanism of the body. This can lead to dangerous, and even fatal, overheating. Some people drink excessive amounts of water to try to prevent over heating. This can also prove fatal because the water can cause swelling of the brain, which can turn lead to coma and death.

Reaction of an amine with ethanoyl chloride



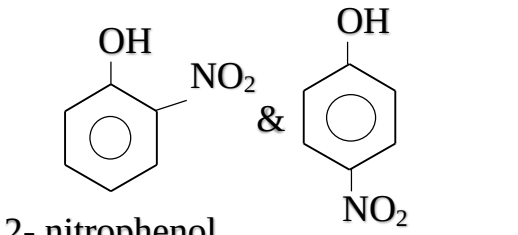
If butylamine is mixed with ethanol chloride, smoky white fumes of HCl(g) are seen to indicate that a reaction is taking place. HCl (g) that is formed reacts with any remaining butylamine, and even the product of the reaction, N-butylethanamide.



(N- Butyl ethanamide)

Paracetamol:

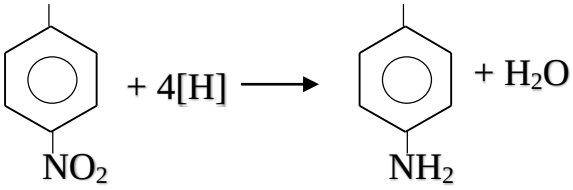
Step1: Phenol is nitrated using H_2SO_4 and $NaNO_3$ unlike nitration of benzene using conc.H_2SO_4 and conc.HNO_3. This is because the benzene ring is activated by the –OH group. A mixture of two isomers is produced;



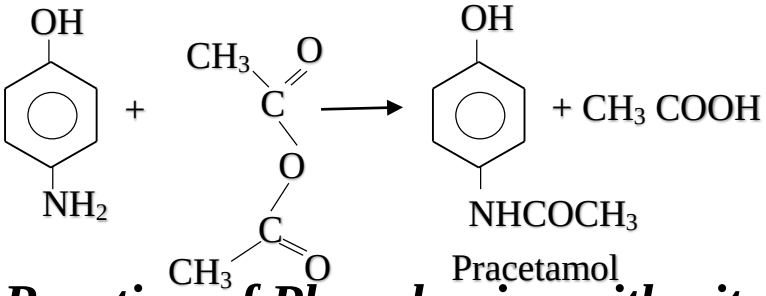
2- nitrophenol 4- nitrophenol

Step2: The two isomers are separated by fractional distillation. 4- nitrophenol has a higher boiling temperature than 2-nitrophenol, because more effective hydrogen bonding, occur between molecules in 4- nitro phenol.

Step 3: 4-nitrophenol is reduced to 4-aminophenol using reducing agent such as sodium tetrahydridoborate(III) in alkaline medium.



Step4: The 4- aminophenol is reacted with ethanoic anhydride to give paracetamol.



Reaction of Phenylamine with nitrous acid:

Nitrous acid is a very unstable compound which exists only in aqueous solution and decomposed at room temperature. That is why HNO_2 (aq) have to be prepared under very carefully controlled condition. It must be prepared as needed (in…. mixing ice-cold solution of $NaNO_2$ and dil HCl aq):

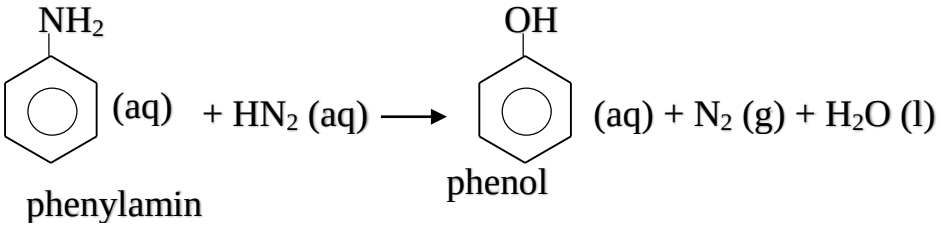
$NaNO_2$ (aq) + HCl(aq) ⟶ NaCl(aq) + HNO_2 (aq)

The reaction vessel must still be kept in an ice-water mixture, because the reaction must be carried out at 5℃ or lower.

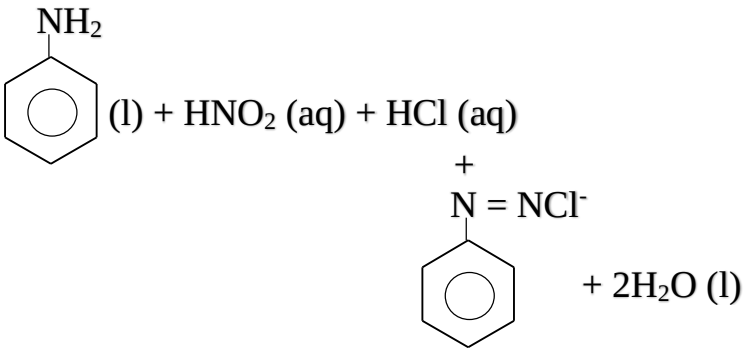
The reaction of HNO_2 with primary amine produces an alcohol:

$CH_3CH_2NH_2$(aq) + HNO_2(aq) ⟶ CH_3CH_2OH (aq) + N_2(g) + H_2O

A similar reaction takes place with an aromatic amine , such as phenylamine and nitrous acid at a temperature above 5℃ to produce a phenol.



However, if the temperature is below 5℃, an aromatic amine will form a diazonium compound with HNO_2.



Benzenediazonium chloride

If aliphatic are used, diazonium salts are not produced because they are so unstable. They decomposed almost immediate. They are formed, even at very low temperature.

The high reactivity of diazonium salts can be put to used in a wide variety of situations in organic synthesis procedures.

The use of diazonium ions is based on two aspects of their chemistry:-

Attack of the diazonium benzene ring by nucleophiles, and the ability of diazonium salts to couple with other molecules.

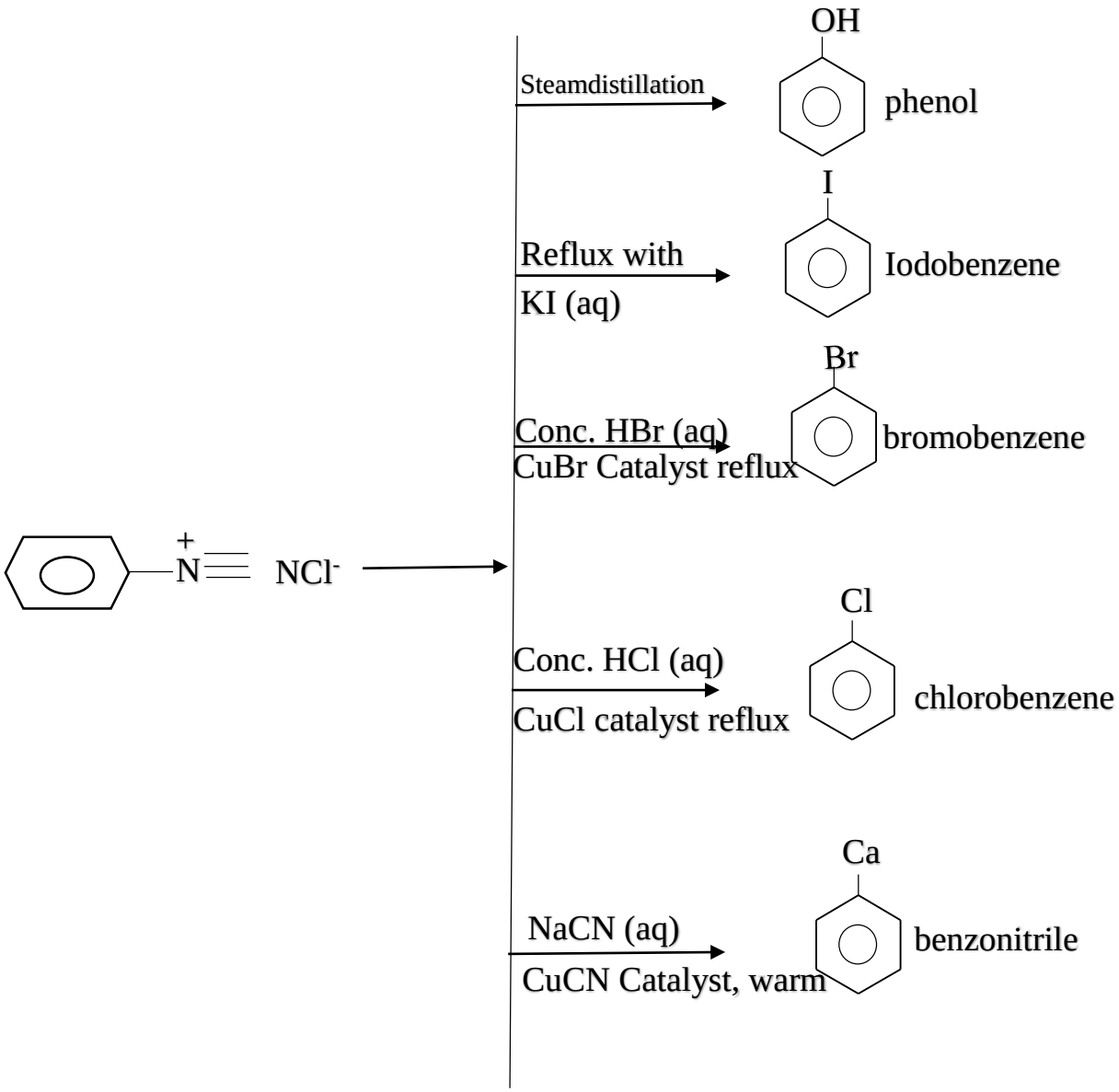
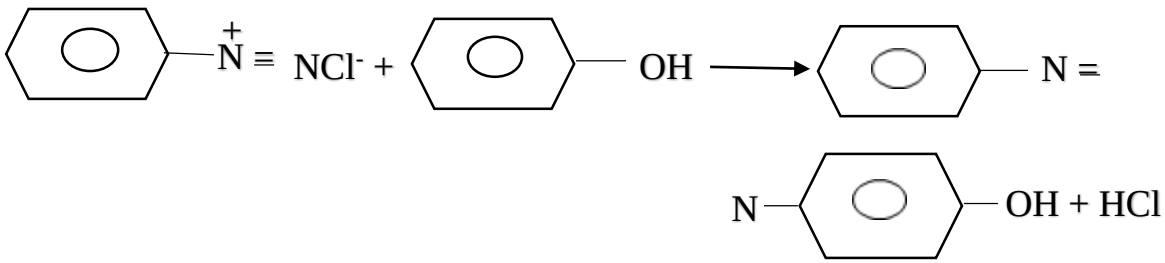


Figure: Reaction of benzenediazonium chloride with a variety of nucleophilic reagents.

Reaction of benzenediazoniumchloride (compound) as electrophiles:-



(4-hydroxyphenyl) azobenzene

Extremely stable.