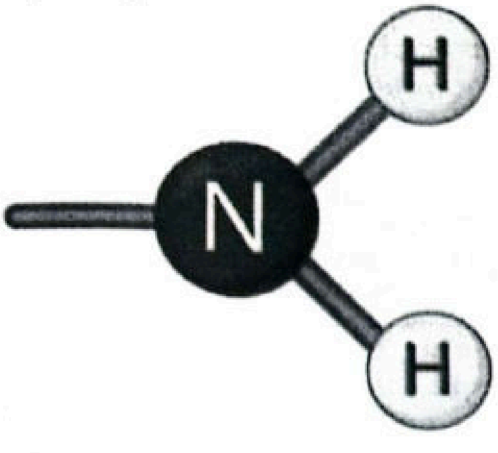
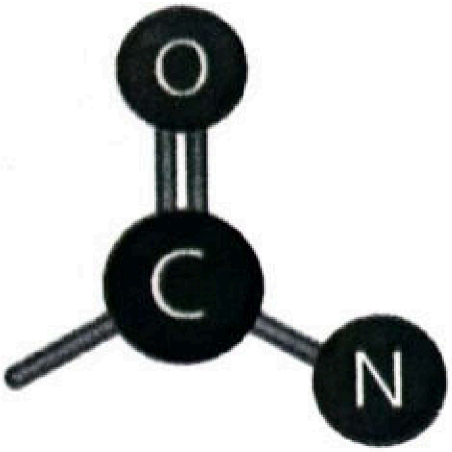
UNIT 12





NITROGEN COMPOUNDS

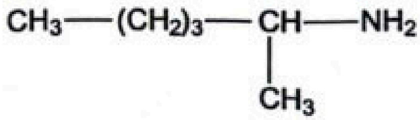
Student Learning Outcomes (SLOs)

- Recall the reactions (reagents and conditions) by which primary and secondary amines are produced.
  - (a) Reaction of halogenoalkanes with NH_3 in ethanol heated under pressure.
  - (b) Reaction of halogenoalkanes with primary amines in ethanol, heated in a sealed tube/ under pressure.
  - (c) The reaction of amides with $LiAlH_4$.
  - (d) The reduction of nitriles with $LiAlH_4$ or H_2/Ni.
- Describe the reactions by which nitriles can be produced: reaction of a halogenoalkane with KCN in ethanol and heat.
- Recall the reactions by which hydroxyl nitriles can be produced: the reaction of aldehydes and ketones with HCN, KCN as catalyst, and heat.
- Describe the hydrolysis of nitriles with dilute acid or dilute alkali followed by acidification.
- Descrbe the basicity of aqueous solutions of amides.
- Describe the reaction of phenylamine with $Br_2(aq)$ at room temperature.
- Describe the reaction of phenylamine with HNO_2 and dilute acid below 10 °C to produce the diazonium salt; further warming of the diazonium salt with water to give phenol.
- Explain the relative basicities of aqueous ammonia, ethylamine, and phenylamine.

- Identify the properties of azo compounds (some examples include: (a) describe the coupling of benzenediazonium chloride with phenol in $NaOH_{(aq)}$ to form an azo compound. (b) Identify the azo group (c) state that azo compounds are often used as dyes (d) recognize that other azo dyes can be formed via a similar route.
- Identify the reactions (reagents and conditions) by which amides are produced (some examples include; (a) the reaction between ammonia and acyl chloride at room temperature (b) the reaction between a primary amine and an acyl chloride at room temperature.
- Describe the reactions of amides (some examples include: (a) hydrolysis with aqueous alkali or aqueous acid (b) the reduction of the CO group in amides with $LiAlH_4$ to for an amine.
- Explain why amides are much weaker bases than amines.
- Describe the acid-bas properties of amino acids and the formation of zwitterions.
- Describe the formation of amide (peptide) bonds between amino acids to give di- and tripeptides.
- Predict the results of electrophoresis on mixtures of amino acids and dipeptides at varying pHs.

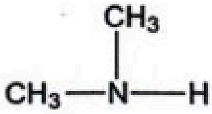
In this chapter, we are going to look at the chemistry of some nitrogen compounds such as amines, amides, and nitriles. Amides are one of the most important functional groups of organic chemistry. Amides are weak bases compared to amines, but they play an important role in many chemical reactions. Amines are the building blocks of many organic compounds. Amines are the building blocks for amino acids, which are the building blocks for proteins. Nitriles are used in the synthesis of amines and other valuable organic compounds. These compounds have a wide range applications in the formation of dyes, drugs, and other materials.

$CH_3-CH_2-NH_2$ Ethyl amine (Primary amine)



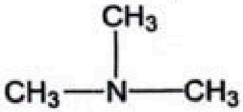
$CH_3-(CH_2)_3-CH(CH_3)-NH_2$

2-Hexyl amine (Primary amine)



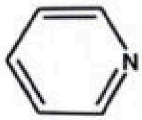
$(CH_3)_2N-H$

Dimethyl amine (a sec-amine)



$(CH_3)_3N$

Trimethly amine (a ter-amine)



Pyridine (a ter-amine)

12.1 Preparation of Amines

Recall that primary and secondary amines can be prepared by various chemical reactions, depending on the desired structure and starting materials. For example;

1. **By the reaction of Alkyl Halides with ammonia**

When an ethanolic solution of ammonia is heated with an alkyl halide in a sealed tube at 100 °C, we get a mixture of amines together with their salts. The salt formed reacts with excess ammonia to produce free amine.

$$NH_3 + CH_3CH_2Br \longrightarrow CH_3CH_2NH_3^+ + Br^-$$

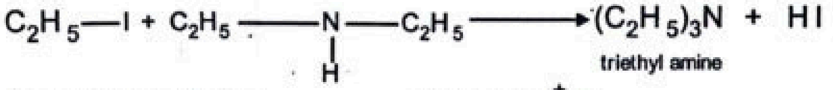
$$CH_3CH_2NH_3^+Br^- + NH_3 \longrightarrow \underset{\text{ethylamine}}{CH_3CH_2NH_2} + NH_4^+Br^-$$

The reaction does not stop at the primary amine. The ethyl amine reacts with bromoethane in the same way in two steps producing a secondary amine.

$$CH_3CH_2Br + CH_3CH_2NH_2 \longrightarrow (CH_3CH_2)_2NH_2^+Br^-$$

$$(CH_3CH_2)_2NH_2^+Br^- + NH_3 \longrightarrow \underset{\text{diethylamine}}{(CH_3CH_2)_2NH} + NH_4^+Br^-$$

Secondary amine further reacts with ammonia to give tertiary amine, which forms quaternary ammonium salt.



$$C_2H_5{-}I + C_2H_5{-}\underset{H}{\underset{|}{N}}{-}C_2H_5 \longrightarrow \underset{\text{triethyl amine}}{(C_2H_5)_3N} + HI$$

$$(C_2H_5)_3N + C_2H_5I \longrightarrow \underset{\text{quaternaryethyl amine}}{[(C_2H_5)_4\overset{+}{N}]I^-}$$

At the end of the reaction, the addition of strong alkali such as KOH liberates free amines from their salts, but the quaternary salt is unaffected. The three types of amines are separated by fractional distillation. Using excess ammonia primary amine is produced but the yield is low.

2. **By the reductions of nitrogen containing functional groups:**

Compounds containing nitrogen such as nitriles, and amides are reduced to amino group by various reducing agents.

(a) Reduction of Nitriles

Reduction of alkyl or aryl nitriles gives primary amines. The reduction may be brought about by reducing agent i.e. $LiAlH_4$, or sodium in ethanol.

$$\underset{\text{Nitrile}}{R-C\equiv N:} + 4[H] \xrightarrow[\text{Reducing agent}]{LiAlH_4} \underset{\text{Amine}}{R-CH_2-NH_2}$$

(b) Catalytic Reduction of nitriles

Nitriles on reaction with hydrogen gas in the presence of catalyst nickel give primary amines.

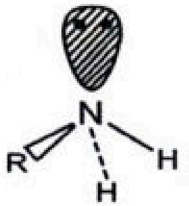
$$CH_3CH_2C\equiv N + 2H_2 \xrightarrow{Ni} CH_3CH_2CH_2\text{-}NH_2$$

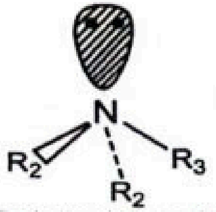
(c). Reduction of Amides

When an amide is treated with reducing agent $LiAlH_4$, $-CO$ group of amide is reduced to $-CH_2$ and the primary amine is formed.

$$CH_3CONH_2 + 2[H] \longrightarrow CH_3CH_2NH_2 + H_2O$$

12.2 Basicity of amines





(Such tertiary amine is optically active)

In amines, the nitrogen atom is sp^3-hybridized and has a nearly tetrahedral structure. It forms three sigma bonds with its three sp^3-hybrid orbitals while the fourth non-bonding sp^3-hybrid carries a pair of electrons.

The lone pair of electrons on the nitrogen atom makes them basic in nature. The lone pair in amines behaves in the same way as in ammonia. When an amine is dissolved in water, the nitrogen lone pair accepts protons from water molecules to produce alkyl ammonium ions and hydroxide ions. The formation of hydroxide ions makes the solution alkaline. So the aqueous solutions of amines are alkaline. However, amines are more basic than ammonia.

$$RNH_2 + H\text{-}OH \longrightarrow [RNH_3]^+ + OH^-$$

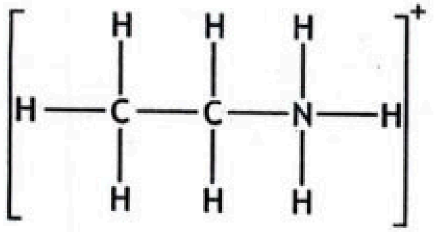
12.2.1 Relative basicities of aqueous ammonia, ethyl amine and phenylamine

The relative strengths of weak bases are determined from their pK_b values. pK_b values of these bases are as follows;

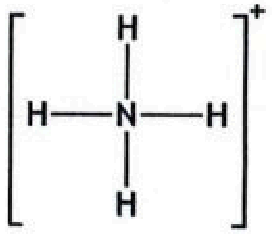
Base	pK_b
Ammonia	4.75
Ethyl amine	3.27
Phenylamine	9.36

The lower the pKb value the stronger the base. Thus, ethylamine is a stronger base than ammonia, which in turns is stronger than phenylamine. Two factors determine the basic strength of the substrate.

- The ease with which its lone pair can capture the hydrogen ion H^+.
- Stability of the ion formed after receiving the H^+ ion. Ethylamine and ammonia have the following structure.



$$[CH_3CH_2NH_3]^+$$



$$[NH_4]^+$$

An ethyl group is an electron-donating group. This increases the electron density of the nitrogen atoms. This makes the nitrogen lone pair more electron-rich and more attractive to hydrogen ions. The ethyl ammonium ion formed which is more stable than the simple ammonium ion formed from *ammonia*. This is because the ethyl group reduces its positive charge.

Both reasons make ethyl amine more basic than ammonia.

Phenyl amine is an aromatic primary amine. The lone pair of electrons on nitrogen is involved in resonance and delocalizing over the ring. So this lone pair can no longer combine with proton, H^+. Thus the intensity of negative charge around the nitrogen atom is much less than in ammonia. Hence, phenylamine is a much weaker base than ammonia. The order of basic ability of these compounds is as follows;

phenylamine < ammonia < ethyl amine

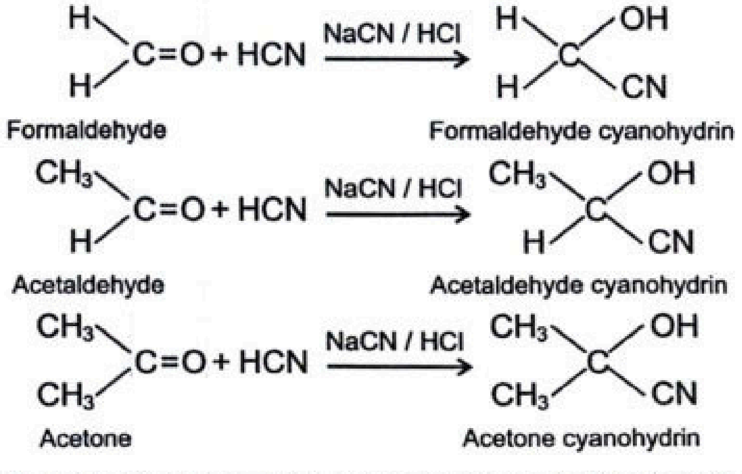
12.3 Formation of Nitriles

1. Recall that nitriles are prepared by heating halogenoalkane and potassium cyanide in ethanol.
   Halogenoalkanes on heating with KCN in ethanol produce alkyl cyanides or nitriles.

$$CH_3Br + KCN \longrightarrow \underset{\text{Cyano methane}}{CH_3CN} + KBr$$

$$CH_3CH_2Br + KCN \longrightarrow \underset{\text{Cyano ethane}}{CH_3CH_2CN} + KBr$$

2. Recall that aldehydes and ketones add hydrogen cyanide across the carbon-oxygen double bond forming compounds known as cyanohydrins. Since, HCN is a highly toxic gas, the aldehyde or ketone is mixed with a solution of KCN in water containing a little HCl. The KCN catalyses this reaction. It reacts with HCl to produce HCN, but the solution still contains some free cyanide ions which catalyze the reaction.



Note that the formation of nitriles results in an increase in the length of the carbon chain because of the extra carbon in the CN group. This reaction is often used in organic synthesis to increase the carbon chain.

12.4 Hydrolysis of nitriles

Hydrolysis of nitriles can occur with both dilute acid or dilute alkali.

Acid hydrolysis of nitriles

When a nitrile is heated with a dilute acid such as dilute hydrochloric acid or dilute sulphuric acid, a carboxylic acid is formed.

$$\underset{\text{ethanenitrile}}{CH_3CN_{(aq)}} + 2H_2O_{(l)} + HCl_{(aq)} \longrightarrow \underset{\text{ethanoic acid}}{CH_3COOH_{(aq)}} + NH_4Cl_{(aq)}$$

Alkaline hydrolysis of nitriles

When a nitrile is heated with a dilute sodium hydroxide solution, a salt of carboxylic acid is produced, which on acidification with dilute hydrochloric acid gives free carboxylic acid.

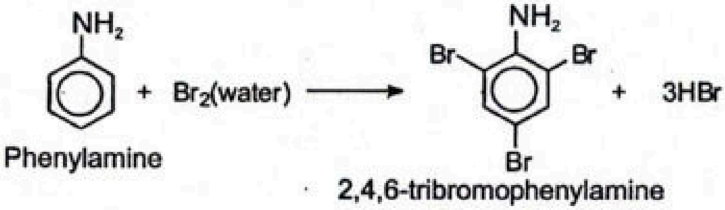
$$CH_3CN_{(aq)} + H_2O_{(l)} + NaOH_{(aq)} \longrightarrow CH_3COONa_{(aq)} + NH_{3(g)}$$

$$CH_3COONa_{(aq)} + HCl_{(aq)} \longrightarrow CH_3COOH_{(aq)} + NaCl_{(aq)}$$

12.5 Phenylamine and Azo Compounds

(a) Reaction of phenylamine with bromine water

When bromine water is added to an aqueous solution of phenylamine at room temperature, the reddish-brown colour of bromine is decolourized and a white precipitate of 2,4,6-tribromophenylamine is produced.



(b) Reaction of phenylamine with HNO₂ or NaNO₂

(Preparation of Diazonium Salts)

The solution of phenylamine in hydrochloric acid is cooled in ice (below 5 °C). The sodium or potassium nitrite solution is also ice-cooled. The ice-cooled solution of nitrite is slowly added to the phenylamine solution. A solution containing phenyl diazonium chloride is produced. It is also known as benzene diazonium chloride. The temperature of the reaction mixture should never go above 5 °C. Diazonium salts are highly unstable and tend to decompose readily above 10 °C.

Warming its aqueous solution decomposes it to phenol.

$$C_6H_5NH_2 + HNO_2 \xrightarrow{HCl} \underset{\text{Benzene diazonium chloride}}{C_6H_5{-}\overset{+}{N}{\equiv}N\overset{-}{Cl}} + 2H_2O$$

12.6 Reactions of benzene diazonium chloride

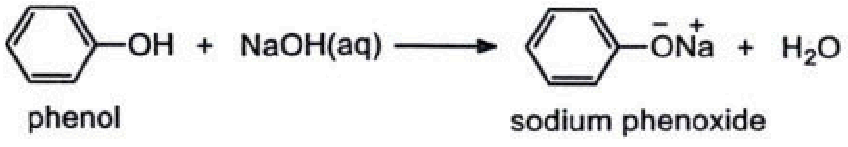
1. **Reaction of benzene diazonium chloride with water**

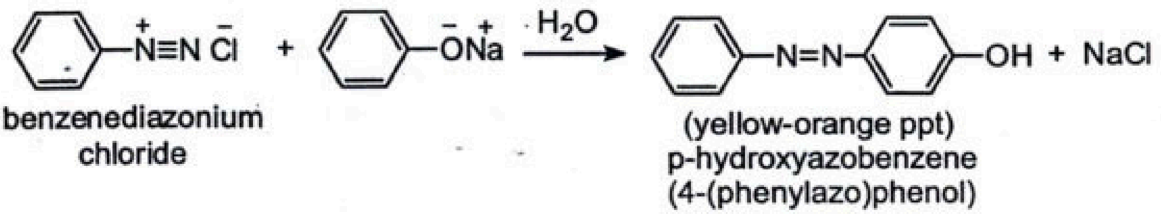
Warming of diazonium salt reacts with water to give phenol.

$$C_6H_5\overset{+}{N}\equiv N\overset{-}{Cl} + H_2O \longrightarrow C_6H_5OH + N_2 + HCl$$

2. **Reaction of benzene diazonium chloride with phenol**

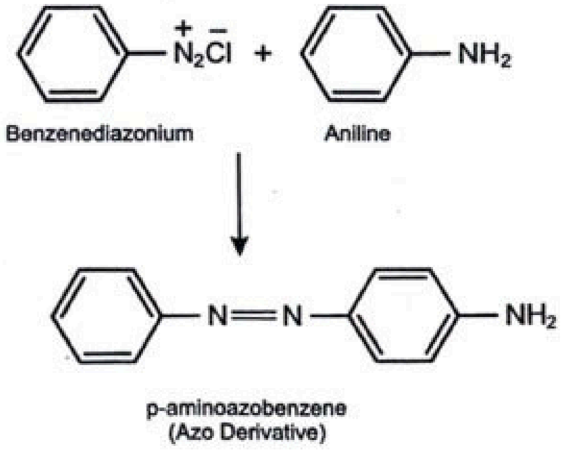
Recall when phenol is dissolved in sodium hydroxide solution and its ice-cold solution is mixed with ice-cold solution of diazonium chloride. A coupling reaction between phenoxide and diazonium ion takes place producing a yellow-orange solution or precipitate. The product is one of the simplest compounds called azo compounds. These are strongly coloured compounds and are known as azo-dyes. Azo compounds are used as dyes.





Azo-dyes make up more than 60% of the total dyes. About 70% of all industrial dyes are azo compounds. The -N = N- unit is called an azo group. Compounds containing this functional group are called azo dyes. In azo-dyes, two benzene rings are linked by a nitrogen bridge.

Other dyes can also be produced from diazonium salts via a similar route. For example, when ice cold solution of benzene diazonium chloride is shaken with phenylamine. A yellow solid dye is produced, which is known as aniline yellow.



For more examples see unit 10

12.7 Preparation of Amides

1. By the reaction of acyl chloride with ammonia

Acyl halides react with ammonia at room temperature to produce amides. The hydroge chloride produced reacts with excess ammonia to give ammonium chloride.

$$CH_3COCl \quad + \quad NH_3 \quad \longrightarrow \quad CH_3CONH_2 \quad + \quad HCl$$

ethanamide

$$HCl \quad + \quad NH_3 \quad \longrightarrow \quad NH_4Cl$$

2. By the reaction of acyl chloride with primary amines

Primary amines react in a similar way as ammonia at room temperature to produce N-substituted amides. The hydrogen chloride reacts with excess amine to give ammonium salt.

$$CH_3COCl \quad + \quad CH_3NH_2 \quad \longrightarrow \quad CH_3CONHCH_3 \quad + \quad HCl$$

ethanoyl chloride methanamide N-methylmethanamide

12.7.1 Reactions of amides

1. Reduction of Amides

When an amide is treated with reducing agent $LiAlH_4$, $-CO$ of amide is reduced to $-CH_2$ and a primary amine is formed. The carbon chain remains intact in this reaction

$$CH_3CONH_2 \quad + \quad 2[H] \quad \longrightarrow \quad CH_3CH_2NH_2 \quad + \quad H_2O$$

2. Hydrolysis of amides

Hydrolysis of amide can occur in both acidic and basic mediums.

(a) Acid hydrolysis of amides

When an amide is heated with dilute acids such as dilute hydrochloric acid or dilute sulphuric acid, a carboxylic is formed.

$$CH_3CONH_{2(aq)} + H_2O_{(l)} + HCl_{(aq)} \longrightarrow CH_3COOH_{(aq)} + NH_4Cl_{(aq)}$$

ethanenitrile ethanoic acid

(b) Alkaline hydrolysis of amides

When an amide is heated with a dilute sodium hydroxide solution, a salt of carboxylic acid is produced with the liberation of ammonia gas. Carboxylic salt on acidification with dilute hydrochloric acid gives free carboxylic acid.

$$CH_3CONH_{2(aq)} + NaOH_{(aq)} \longrightarrow CH_3COONa_{(aq)} + NH_{3(g)}$$

$$CH_3COONa_{(aq)} + HCl_{(aq)} \longrightarrow CH_3COOH_{(aq)} + NaCl_{(aq)}$$

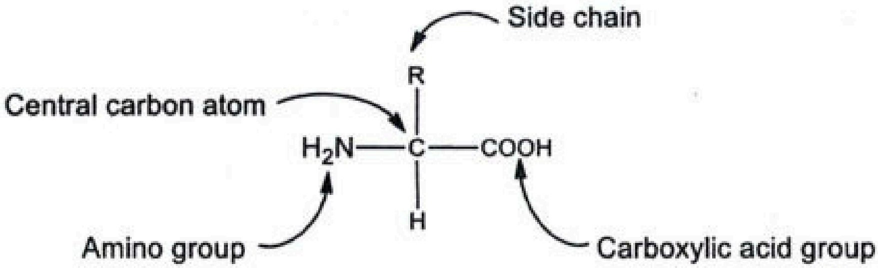
12.7.2 Basicity of amides

Amides are much weaker bases than amines. The amido group has a carbonyl group which is extremely electronegative. It pulls electrons towards it by resonance as well as inductive effect. So, its NH_2 group has little protonation ability. In amines, the lone pair of electrons on nitrogen is not delocalized. Moreover, alkyl group tends to increase electron density around nitrogen atoms. So amines have a strong ability to attract proton (H^+).

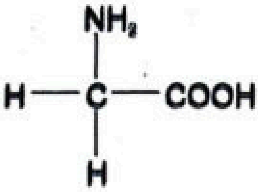
12.8 Amino Acids

The compounds containing an amino group, -NH_2, and a carboxylic acid group, -COOH are called *amino acids*

An amino acid has two functional groups. What are those? Amino acids are the building blocks of protein synthesis. Twenty different amino acids are involved in protein synthesis. Out of twenty amino acids, our bodies can synthesize only ten amino acids. Such amino acids are called **non-essential amino acids.** The remaining ten are called **essential amino acids.** Essential amino acids must be present in our diet. Why? The general formula for an amino acid is:

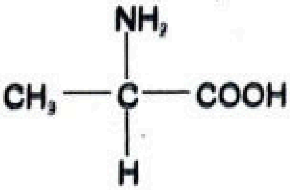


The amino acids generally have the amino group attached to the carbon atom next to the –COOH group. They are known as 2-amino acids or alpha-amino acids.



$$H-\overset{\displaystyle NH_2}{\underset{\displaystyle H}{C}}-COOH$$

2-aminoethanoic acid



$$CH_3-\overset{\displaystyle NH_2}{\underset{\displaystyle H}{C}}-COOH$$

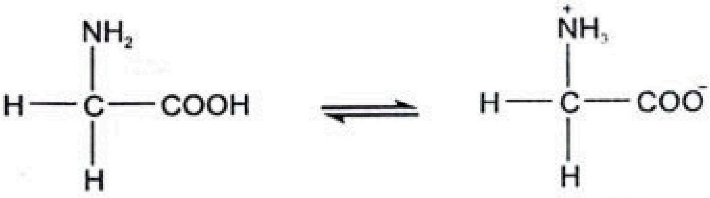
2-aminopropanoic acid.

12.8.1 Physical properties of amino acids

An amino acid has both a basic amine group and an acidic carboxylic acid group.

There is an internal transfer of a hydrogen ion from the –COOH group to the –NH_2 group to leave an ion with both a negative and a positive charge. This is called a ***zwitter ion.***

A zwitterion has no overall electrical charge but contains separate parts which are positively and negatively charged.



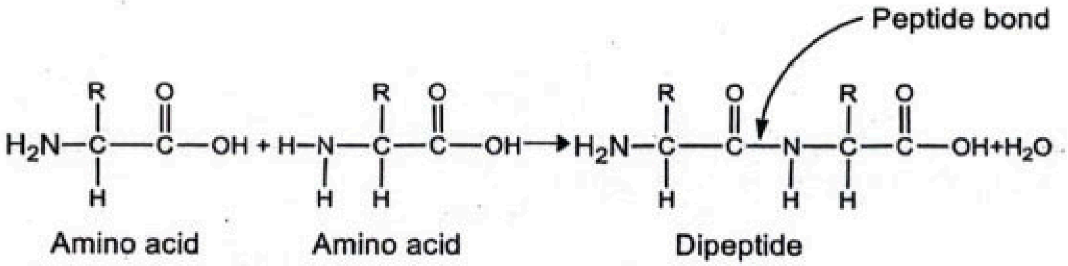
$$H-\overset{\displaystyle NH_2}{\underset{\displaystyle H}{C}}-COOH \rightleftharpoons H-\overset{\displaystyle \overset{+}{N}H_3}{\underset{\displaystyle H}{C}}-COO^-$$

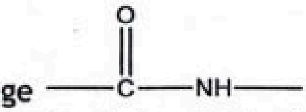
zwitter ion

This is the form that amino acids exist in even in the solid state. In amino acids, the intermolecular forces are much stronger ionic attractions between one ion and its neighbours. These ionic attractions need more energy to break and so the amino acids have high melting points.

12.8.2 Formation of peptide bond

Molecules of amino acids join through the amino (-NH_2) group of one molecule and the carboxyl (-COOH) group of another molecule by eliminating a water molecule.



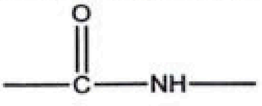
The linkage  $-\overset{O}{\overset{\|}{C}}-NH-$ which joins two amino acid units is called a **peptide bond.** The resulting molecule is called a dipeptide. There is still an amino group on the left and a carboxyl group on the right. Each of these groups can react further to join more amino acid units. When a dipeptide combines with another amino acid molecule, the resulting molecule is called a tripeptide. In this way, thousands of amino acid units join to form a giant protein molecule.

12.8.3 Behaviour of amino acids and dipeptides in an electric field

Electrophoresis is a technique that can be used to separate charged molecules, such as amino acids and peptides. This method takes advantage of the movement of these molecules in the presence of an electric field. The speed at which these molecules move in the electric field is influenced by the pH of the medium. With the pH of the medium, the degree of ionization of amino acids changes. At the cathode, amino acids usually exist in the protonated state (as $-NH_3^+$) and move towards it at low pH. When the pH is high, amino acids exist in their deprotonated state (COO^-). As a result, they migrate towards the positive anode. The movement of dipeptides in an electric field depends on the net charge on the molecules, similarly. Altering the pH changes the charge on amino acid and dipeptide molecules.

KEY POINTS

- When an ethanolic solution of ammonia is heated with an alkyl halide in a sealed tube at 100°C, we get a mixture of amines together with their salts.
- The reduction of alkyl or aryl nitriles gives primary amines.
- When an amide is treated with reducing agent $LiAlH_4$, $-CO$ group g of amide is reduced to $-CH_2$, and a primary amine is formed.
- The lower the pKb value the stronger the base
- Halogenoalkanes on heating with KCN in ethanol produce alkyl cyanides or nitriles
- When a nitrile is heated with dilute acids such as dilute hydrochloric acid or dilute sulphuric acid, a carboxylic is formed.
- Acyl halides react with ammonia at room temperature to produce amides.

- When an amide is treated with reducing agent $LiAlH_4$, $-CO$ of amide is reduced to $-CH_2$ and primary amine is formed.
- When an amide is heated with a dilute sodium hydroxide solution, a salt of carboxylic *acid* is produced with the liberation of ammonia gas.
- The compounds containing an amino group, $-NH_2$, and a carboxylic acid group, $-COOH$ are called amino acids.
- A zwitterion has no overall electrical charge but contains separate parts which are positively and negatively charged.
- The linkage  $-\overset{\overset{O}{\|}}{C}-NH-$ which joins two amino acid units is called a **peptide bond.**

EXERCISE

1. Multiple Choice Questions (MCQs)

i. What is the reagent and condition used to convert halogenoalkanes to primary amines?
   - a) NH_3 in ethanol, heated under pressure
   - b) H_2SO_4 in water, room temperature
   - c) $LiAlH_4$ in dry ether, reflux
   - d) KOH in ethanol, heated under pressure

ii. Which of the following produces hydroxyl nitriles from aldehydes and ketones?
   - a) H_2O, H_2SO_4, heat
   - b) HCN, KCN as a catalyst, heat
   - c) NH_3 in ethanol, heated under pressure
   - d) Br_2, light, room temperature

iii. Which reaction is used to produce secondary amines from halogenoalkanes?
   - a) Reaction with ammonia in ethanol
   - b) Reaction with primary amines in ethanol
   - c) Reaction with $LiAlH_4$
   - d) Reaction with HCN and KCN

iv. Which reagent is used to convert nitriles to primary amines?
   - a) H_2O, HCl, reflux
   - b) H_2/Pt, room temperature
   - c) H_2/Ni or $LiAlH_4$
   - d) Br_2, room temperature

v. What is the final product of the hydrolysis of nitriles with dilute acid?
   - a) Alcohol
   - b) Ketone
   - c) Carboxylic acid
   - d) Aldehyde

vi. What is the structure of the azo group in azo compounds?
   - a) $R_1\text{-}N{=}N\text{-}R_2$
   - b) $R_1\text{-}C{\equiv}N\text{-}R_2$
   - c) $R_1\text{-}NH_2\text{-}R_2$
   - d) $R_1\text{-}O\text{-}R_2$

vii. What product is formed when phenylamine reacts with $Br_{2(aq)}$ at room temperature?
   - a) Phenol
   - b) Phenylamine bromide
   - c) 2,4,6-tribromophenylamine
   - d) An azo compound

viii. What is the basicity order among aqueous ammonia, ethylamine, and phenylamine?
  a) Ethylamine > Aqueous ammonia > Phenylamine
  b) Phenylamine > Ethylamine > Aqueous ammonia
  c) Aqueous ammonia > Ethylamine > Phenylamine
  d) Aqueous ammonia > Phenylamine > Ethylamine

ix. What happens when benzenediazonium chloride reacts with phenol in $NaOH_{(aq)}$?
  a) Formation of phenylhydrazine
  b) Formation of an azo compound
  c) Formation of a nitro compound
  d) Formation of an ester

x. What is the role of peptide bonds in proteins?
  a) Provide structural support b) Store energy
  c) Link amino acids d) Bind with DNA

xi. Hydrolysis of nitriles with dilute acid produces:
  a) Amides b) Carboxylic acids c) Alcohols d) Amines

xii. Phenylamine reacts with $Br_{2(aq)}$ at room temperature to give:
  a) Trihalogenated product b) Monohalogenated product
  c) Dihalogenated product d) No reaction

2. Short Answer Questions

i. Explain the conditions and reagents required for the reaction between a halogenoalkane and KCN to form a nitrile.

ii. Describe the hydrolysis of amides using aqueous acid or aqueous alkali. What is the final product of this reaction?

iii. Discuss the reaction of phenylamine with HNO_2 and dilute acid below 5°C. What is the major product formed?

iv. Describe the acid-base properties of amino acids and how they can form zwitterions.

v. Explain why amides are much weaker bases than amines. What structural aspect contributes to this difference?

vi. Compare the basicity of aqueous ammonia, ethylamine, and phenylamine, and explain the observed trends

  i. Outline the steps and conditions required to hydrolyze a nitrile to a carboxylic acid using dilute acid.

  ii. Describe the hydrolysis of an amide under acidic and basic conditions.

vii. Predict the results of electrophoresis on mixtures of amino acids at pH 3 and pH 11.

  i. Compare the reduction of nitriles and amides using $LiAlH_4$.

  ii. Analyse the significance of diazonium salts in synthetic organic chemistry.

3. Long Answer Questions

i. Describe the steps and conditions involved in the hydrolysis of nitriles with dilute acid or alkali followed by acidification. What is the final product of this reaction?

ii. Explain the relative basicities of aqueous ammonia, ethylamine, and phenylamine. What factors contribute to these differences in basicity?

iii. Discuss the formation of amide (peptide) bonds between amino acids to give di- and tripeptides. What role do these bonds play in biological systems?

iv. Describe the reaction of phenylamine with HNO_2 and dilute acid below 1°C to produce the diazonium salt. What is the significance of this reaction in organic chemistry?

v. Predict the results of electrophoresis on mixtures of amino acids and dipeptides at different pH. What changes might you observe at different pH, and why?

vi. Describe the acid-base properties of amino acids and the formation of zwitterions. Discuss the significance of zwitterions in the behavior of amino acids in different pH environments.

vii. Describe the formation of amide (peptide) bonds between amino acids to give di- and tripeptides

viii. Predict and explain the results of electrophoresis on mixtures of amino acids and dipeptides at different pH. Discuss how the charge and size of the molecules affect their migration during electrophoresis.