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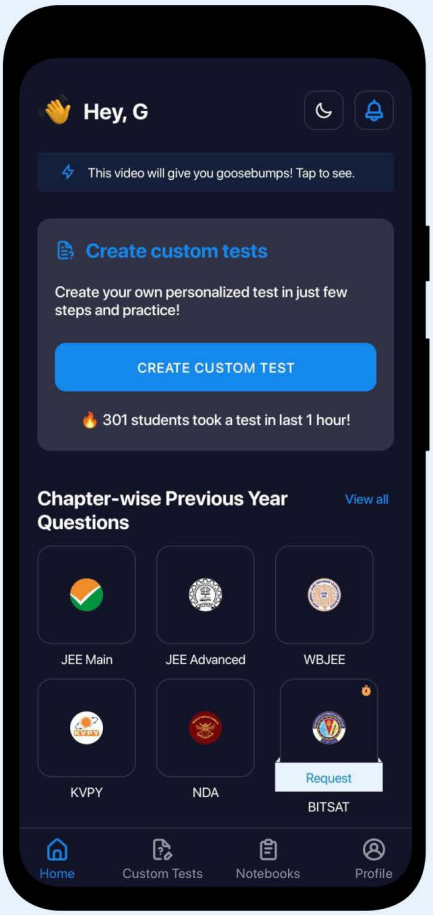

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BIOMOLECULES

BIOMOLECULES

1.1 Carbohydrate

Carbohydrates have general formula, $C_x(H_2O)_y$, and were considered as hydrates of carbon from where the name carbohydrate was derived. But this is not completely true.

For example, the molecular formula of glucose ($C_6H_{12}O_6$) fits into this general formula,$C_6(H_2O)_6$. But all the compounds which fit into this formula may not be classified as carbohydrates. Acetic acid (CH_3COOH) fits into this general formula, $C_2(H_2O)_2$ but is not a carbohydrate.

Similarly, rhamnose, $C_6H_{12}O_5$ is a carbohydrate but does not fit in this definition. A largenumber of their reactions have shown that they contain specific functional groups.

Chemically, the carbohydrates may be defined as optically active polyhydroxy aldehydes or ketones or the compounds which produce such units on hydrolysis.

1.2 Classification

Carbohydrates are classified into three groups based on the number of sugar units and upon their behaviour towards hydrolysis.

They are

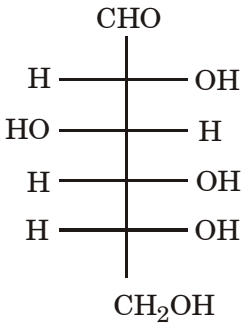
- Monosaccharides
- Oligosaccharides
- Polysaccharides.

1. **Monosaccharides :** These are simplest group of carbohydrates and are referred as simple sugars as they are sweet in taste. The cannot be further hydrolyzed to simpler compounds. They have the general formula $C_n(H_2O)_n$. Examples: Glucose and fructose.

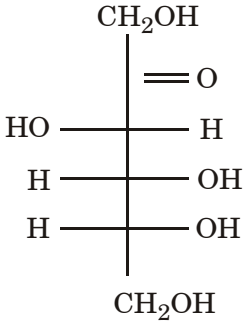
   Monosaccharides can be further classified into :

   (a) Aldose is polyhydroxy aldehyde (glucose, galactose)

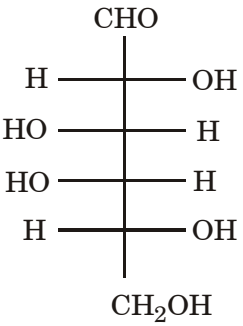
   (b) Ketose is polyhydroxy ketone (fructose)



D-glucose
aldehxose



D-fructose
ketohexose



D-galactose
aldehexose

- Glucose is also called grape sugar or blood sugar; fructose is also called fruit sugar.

2. **Oligosaccharides** : These carbohydrates liberate two to ten monosaccharide molecules on hydrolysis. They are further classified as disaccharides, trisaccharides, tetrasaccharides, etc. based on the number of monosaccharide units. For e.g., disaccharides like sucrose produce two molecules of monosaccharides on hydrolysis.

$$\text{Sucrose} \xrightarrow{\text{Hydrolysis}} \text{glucose + fructose}$$

A trisaccharide like raffinose on hydrolysis gives glucose, fructose and galactose.

3. **Polysaccharides** : This carbohydrates liberate a large number of monosaccharide molecules on hydrolysis. They are usually amorphous, insoluble in water and tasteless and are called non-sugars.

Examples : Starch, cellulose and glycogen

2. Carbohydrates may also be classified as either reducing or non-reducing sugars.

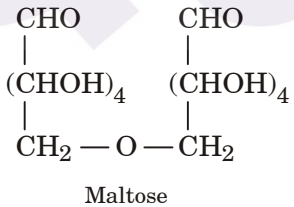
(a) Reducing Sugar

All those carbohydrates which contain free aldehyde or ketonic group and reduce Fehling's solution and Tollen's reagent referred to as reducing sugars. All monosaccharides whether aldose or ketose are reducing sugars. Their functional groups are free. Examples: Maltose and lactose.

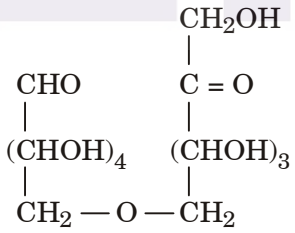
(b) Non Reducing Sugar

In disaccharides if the reducing group of monosaccharides i.e., aldehydic or ketonic groups are bonded, these are non reducing sugars e.g., sucrose, while others in which these functional groups are free are reducing sugars. They don't reduce Felling or Tollent's reagent.

Examples : Sucrose



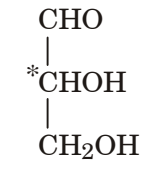
Maltose



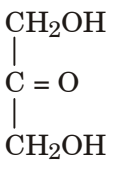
Sucrose

Trioses

D and L Terminology : The simplest of all carbohydrates that fit the definition we have given for carbohydrates are the trioses, glyceraldehydes and dihydroxyacetone. Glyceraldehyde is aldotriose, and dihydroxyacetone is a ketotriose.

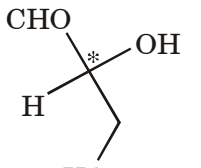


Glyceraldehyde
(an aldotriose)

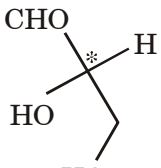


Dihydroxyacetone
(a ketotriose)

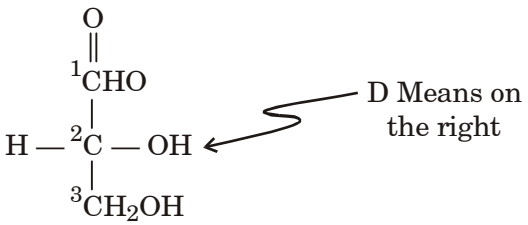
Glyceraldehyde contains one asymmetric carbon atom (marked by an asterisk) and can thus exist in two optically active forms, called the D-form and the L-form. Clearly, the two forms are mirror images that cannot be superimposed, that is they are enantiomers.



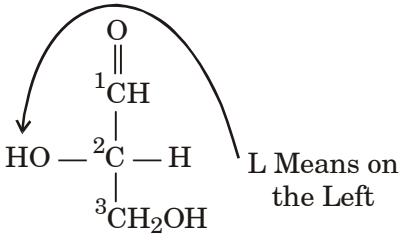
D–Glyceraldehyde



L–Glyceraldehyde



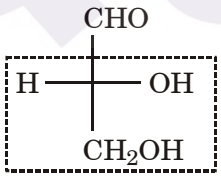
D–Glycerldehyde



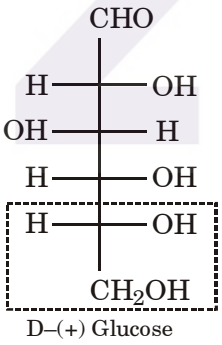
L–Glycerldehyde

The letters 'D' or 'L' before the name of any compound indicate the relative configuration of a particular stereoisomer. This refers to their relation with a particular isomer of glyceraldehydes. Glyceraldehyde contains one asymmetric carbon atom and exists in two enantiomeric forms

For assigning the configuration of monosaccharides, it is the lowest asymmetric carbon atom (as shown below) which is compared. As in glucose,—OH on the lowest asymmetric carbon is on the right side which is comparable to glyceraldehydes, so it is assigned D-configuration. For this comparison, the structure is written in a way that most oxidized carbon is at the top



D–(+) – Glyceraldehyde



D–(+) Glucose

D and L have nothing to take with direction of rotation of light. The maximum number of optical isomers of a sugar is related to the number of asymmetric carbon atoms in the molecule and may be calculated by the following simple equation.

Maximum Number of Optical Isomors = 2^n, where n = the number of asymmetric carbon atoms. Since glyceraldehydes contains only one asymmetric carbon atom, the number of optical isomer is 2^1. We know that 2^1 is = 2, and we have seen that there are indeed two different glyceraldehydes.

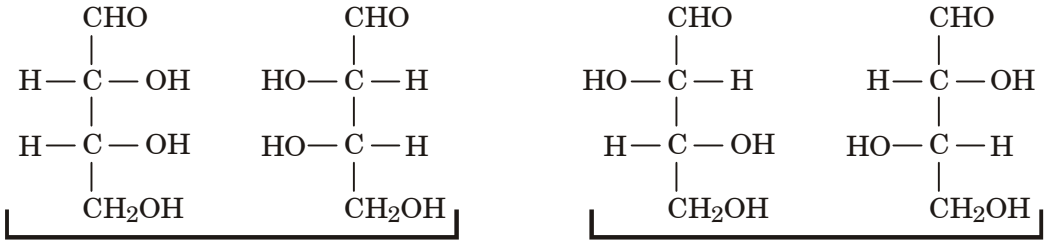
Aldotetroses

If we examine the general formula of an aldotetrose, we see that they contain two asymmetric carbon atoms (marked by asterisks).

This means that 2^2 or 4 optical isomers are possible. They may be represented as the following two pairs :

1. CHO
2. *CHOH
3. *CHOH
4. CH_2OH

an aldotetrose



Mirror images (racemic pair) Mirror images (racemic pair)

D (–)-erythrose L (+)-erythrose D (–)-threose L (+)-threose

All four isomers have been prepared synthetically. The D- and L-erythrose are mirror images, that is, they are enantiomers. They have exactly the same degree of rotation but in opposite directions. Equal amounts of the two would constitute a racemic mixture, that is, a mixture that would allow a plane-polarised light to pass through the solution unchanged but could be separated into dextrorotatory and laevorotatory isomers. The same comments hold for D- and L-threose. However, D-erythrose and L-threose are not images, that is, they are diastereomers (optical isomers that are not mirror images are called diastereomers), and the degree of rotation of each would probably differ.

Aldopentoses

If we examine the general formula of an aldopentose, we see that they contain three asymmetric carbon atoms.

This means that 2^3 or 8 optical isomers are possible. These are : D(–) lyxose, L(+)-lyxose, D(–) xylose, L(+) xylose, D(–) arabinose, L(+)-arabinose, D(–)-ribose, L(+)-ribose

1. CHO
2. *CHOH
3. *CHOH
4. *CHOH
5. CH_2OH

an aldopentose

Aldohexoses

If we examine the general formula of aldohexose, we see that it contains four asymmetric carbon atoms. This means that 2^4 or 16 optical isomers are possible. D and L forms of altrose, allose glucose, mannose, galactose, talose, arabinose and idose.

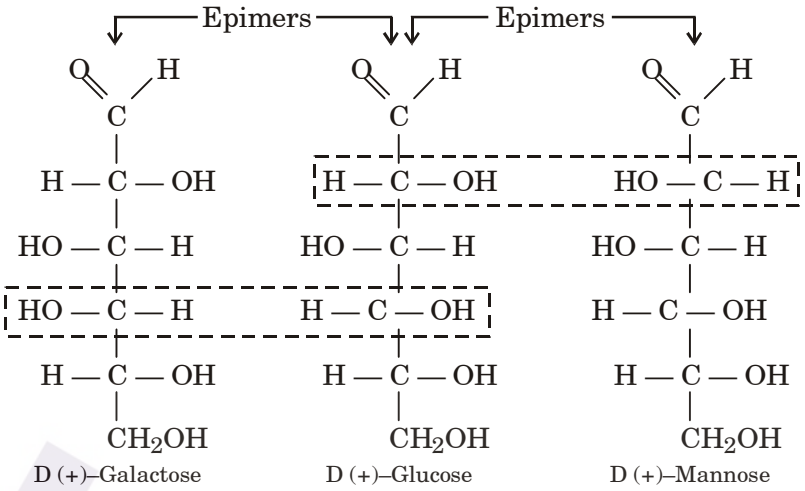
Only three of the sixteen possible aldohexoses are found in nature (all sixteen isomers have been prepared synthetically). They are D-glucose, D- mannose, and D-galactose. No one of these three optical isomers is a mirror image of any of the others, so all three are diastereomers of each other.

1. CHO
2. *CHOH
3. *CHOH
4. *CHOH
5. *CHOH
6. CH_2OH

an aldohexose

Epimers

A pair of diastereomers that differ only in the configuration about of a single carbon atom are said to be epimers. e.g D(+)- glucose is empimeric with D(+)-mannose and D(+) –galactose as shown below :

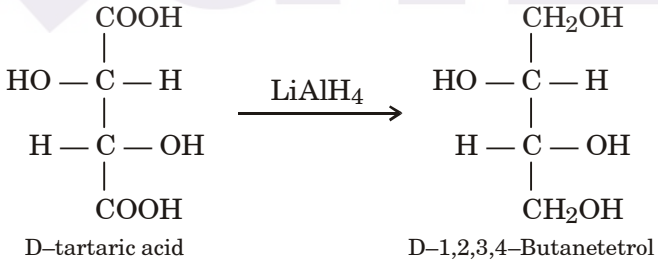


Example 1

Why are optically active tartaric acid and 1,2,3,4-butanetetrol called D?

Solution :

Since the configuration of asymmetric (chiral) carbons do not change during the oxidation or reduction, the D configuration is retained.



PREPARATION OF GLUCOSE AND FRUCTOSE

- $\underset{\text{sucrose}}{C_{12}H_{22}O_{11}} + H_2O \xrightarrow{H^+} \underset{\text{glucose}}{C_6H_{12}O_6} + \underset{\text{fructose}}{C_6H_{12}O_6}$

Glucose and fructose are separated by fractional crystallisation.

- $\underset{\text{starch}}{(C_6H_{12}O_5)_n} + nH_2O \xrightarrow[120°C,\,2\text{-}3\ atm]{H^+} \underset{\text{glucose}}{nC_6H_{12}O_6}$

After neutralisation with CaCO3, and filtration, filtrate is decolourised by boiling with animal charcoal and then concentrated under reduced pressure and crystallised.

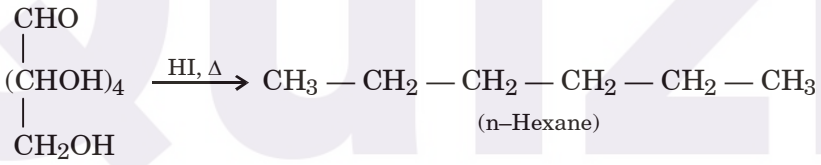
- $\underset{\text{insulin}}{(C_6H_{10}O_5)_n} + nH_2O \xrightarrow[\Delta]{H_2SO_4} \underset{\text{fructose}}{nC_6H_{12}O_6}$

Physical Properties

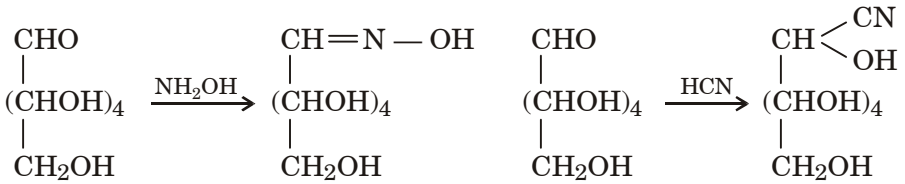
- Glucose and fructose both are soluble in H_2O, sparingly soluble in alcohol and insoluble in ether.
- Melting points : glucose : 160 C, fructose : 102.4 C
- Glucose is dextrorotatory hence, called dextrose.
- Fructose is laevorotatory hence, called laevulose.

CHEMICAL PROPERTIES

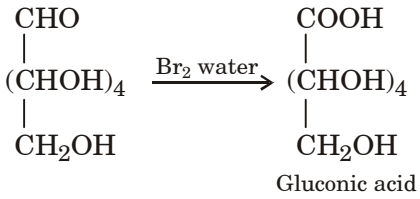
1. On prolonged heating with HI, it forms n-hexane, suggesting that all the six carbon atoms are linked in a straight chain.



2. Glucose reacts with hydroxylamine to form an oxime and adds a molecule of hydrogen cyanide to give cyanohydrin. These reactions confirm the presence of a carbonyl group (>C = 0) in glucose.

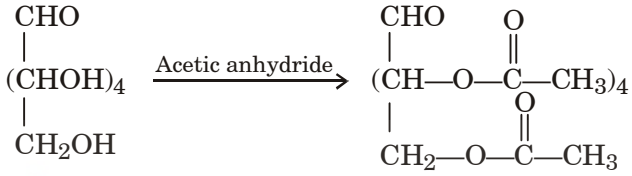


3. Glucose gets oxidized to six carbon carboxylic acid (gluconic acid) on reaction with a mild oxidising agent like bromine water. This indicates that the carbonyl group is present as an aldehydic group.

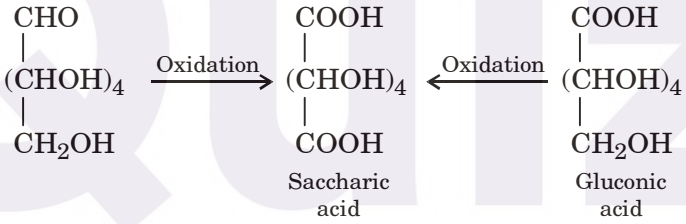


Gluconic acid

4. Acetylation of glucose with acetic anhydride gives glucose pentaacetate which confirms the presence of five –OH groups. Since it exists as a stable compound, five –OH groups should be attached to different carbon atoms.



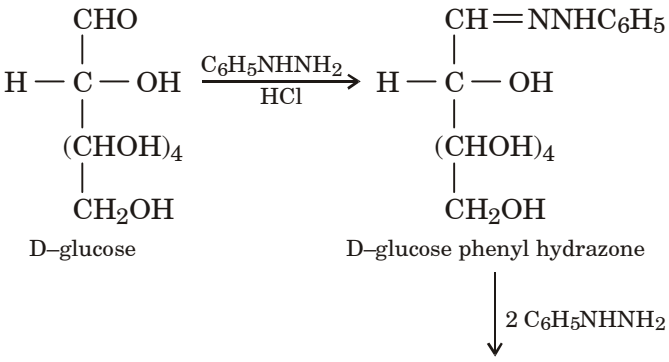
5. On oxidation with nitric acid, glucose as well as gluconic acid both yield a dicarboxylic acid, saccharic acid. This indicates the presence of a primary alcoholic (-OH) group in glucose.



Saccharic acid

Gluconic acid

6. D-glucose reacts with phenyl hydrazine to give glucose phenyl hydrazine which is soluble. If excess of phenyl hydrazine is used, a dihydrazone, known as osazone is obtained.



D–glucose

D–glucose phenyl hydrazone

$$NH_3 + C_6H_5NH_2 + \begin{array}{l} CH{=}NNHC_6H_5 \\ | \\ C{=}NNHC_6H_5 \\ | \\ (CHOH)_4 \\ | \\ CH_2OH \end{array}$$

D–Clucosazone

7. On oxidation with nitric acid, glucose as well as gluconic acid both yield a dicarboxylic acid saccharic acid. This again indicates presence of a primary alcoholic group in glucose.

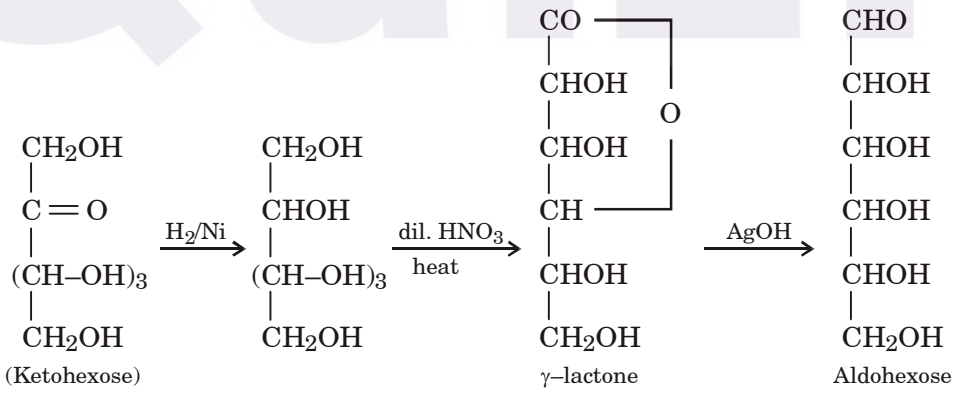
$$\underset{\text{Glucose}}{HOCH_2-(CHOH)_4-CHO} \xrightarrow{HNO_3} \underset{\text{Saccharic acid}}{HOOC-(CHOH)_4-COOH}$$

8. Glucose reduces ammoniacal silver nitrate solution (Tollent's reagent) to metallic silver and also Fehlings' solution to reddish brown cuprous oxide and itself gets oxidized to gluconic acid. This confirms the presence of an aldehydic group in Glucose.

$$\underset{\text{Glucose}}{HOCH_2-(CHOH)_4-CHO} + Ag_2O \longrightarrow \underset{\text{Gluconic acid}}{HOCH_2-(CHOH)_4-COOH} + 2Ag$$

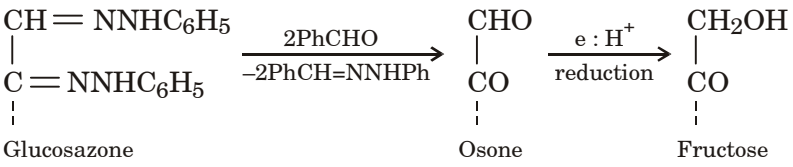
CONVERSION OF A KETOSE INTO AN ALDOSE AND VICE-VERSA

The ketoses are reduced to corresponding polyhydric alcohol, which is then oxidized to a monocarboxylic acid. On warming the acid it is converted into γ-lactone, which on reduction with Na/Hg in faintly acidic medium gives aldose.



Theoretically, two polyhydric alcohol can be formed by reduction of ketose due to the formation of the new asymmetric carbon atom. In practice, however, one isomer is obtained in great yield.

The aldose is converted into its osazone, which is then treated with PhCHO to form osone. On reduction with zinc and acetic acid, the osone is converted into the ketose.



Cyclic Structure of D-Glucose

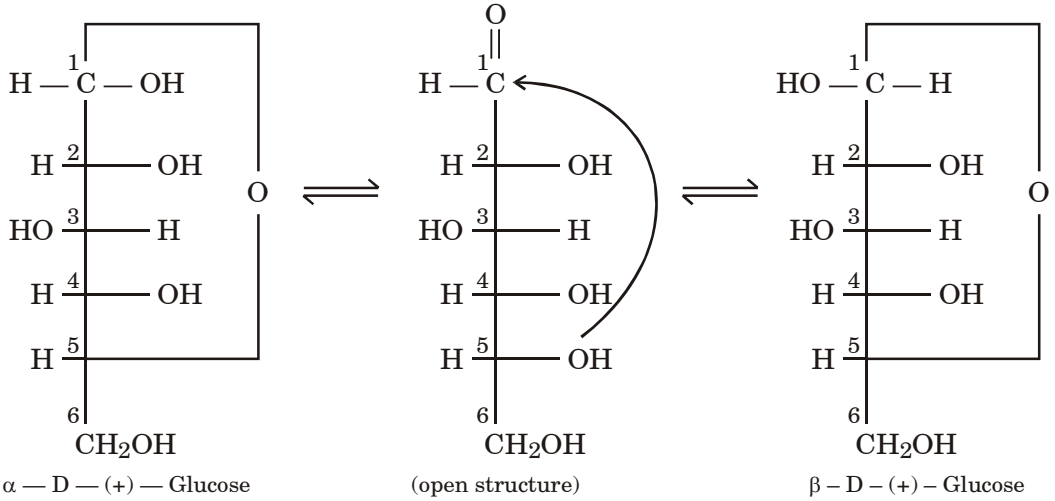
The open chain structure of glucose proposed by Baeyer explained most of its properties. However, it could not explain the following:

1. Despite having an aldehydic group, glucose does not gives Schiff's test and it does not react with sodium bi-sulphite and ammonia.
2. The penta acetate of glucose does not react with hydroxylamine indicating absence of -CHO group.
3. Mutarotation. When glucose was crystallized from a concentrated solution at 30 C it gave a form of glucose (Melting point 146 C) whose optical rotation is 111 . The β form (Melting point 150) obtained on crystallization of glucose from a hot saturated aqueous solution at a temperature above 98 C has an optical rotation of 19.2 . These two forms of glucose are called anomers.

This behaviour could not be explained by the open chain structure **(I)** for glucose. It was proposed that one of the —OH groups may add to the —CHO group and form a cyclic hemiacetal structure. It was found that glucose forms a six-membered ring in which —OH at C-5 is involved in ring formation. This explains the absence of —CHO group and also existence of glucose in two forms as shown below. These two cyclic forms exist in equilibrium with open chain structure.

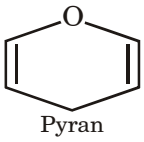
Anomeric Carbon

A pair of stereoisomers that differ in configurations around C-1 are called anomers and the C-1 carbon is called anomeric carbon. The α and β – cyclic forms of D-glucose are known as anomers. In this case, β-anomers of glucose contains the -OH group towards right at C-1 position and β-anomer of glucose contains the -OH group towards left at C-1 position. So, D-glucose exists in two stereo isomeric forms with different specific rotations and melting points. The structures of α and β anomers of carbon are shown below :

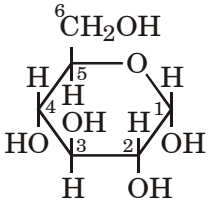


α — D — (+) — Glucose (open structure) β – D – (+) – Glucose

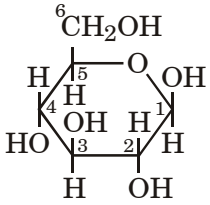
The six membered cyclic structure of glucose is called **pyranose structure,** in analogy with pyran. Pyran is a cyclic organic compound with one oxygen atom and five carbon atoms in the ring. The cyclic structure of glucose is more correctly represented by Haworth structure as given below.



Pyran



α –D – (+) – Glucopyranose



β –D – (+) – Glucopyranose

Disaccharides

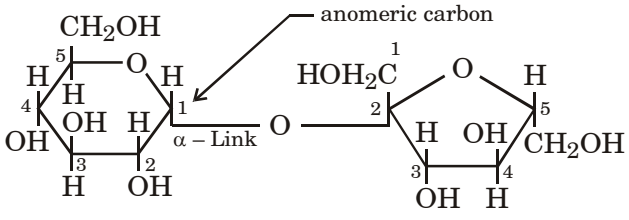
A disaccharide upon hydrolysis liberates two monosaccharide units. These two molecules are held together by a glycosidic bond. The monosaccharides liberated due to hydrolysis may be of similar or different molecules. The disaccharides are of two types. They are – Reducing sugars and non-reducing sugars.

The most common disaccharides are :

- Sucrose (cane sugar) made up of glucose + fructose
- Maltose (Malt sugar) made up of glucose + glucose

Sucrose

Sucrose is made up of α-D-Glucose and β-D-fructose held together by a glycosidic bond, between C_1 of α-glucose and C_2 of β-fructose. The reducing groups of glucose and fructose are involved in glycosidic bond, so it is a non-reducing sugar.



α – D – Glucopyranose

β –D – Fructose

Sucrose is a colourless, crystalline and sweet substance soluble in water. Sucrase is the enzyme that can hydrolyze sucrose in the body.

Sucrose is a non-reducing sugar as carbony1 group is not free

(i) Inversion of cane sugar On hydrolysis with dilute acids or enzyme invertose, canesugar gives equimolar mixture of D(+) glucose and D(-) fructose.

$$\underset{\text{Sucrose}}{C_{12}H_{22}O_{11}} + H_2O \xrightarrow{HCl} \underset{\text{D – Glucose}}{C_6H_{12}O_6} + \underset{\text{D fructose}}{H_{12}O_6}$$

$[\alpha]_D = +66.5$ $\qquad$ $[\alpha]_D = +52.5$ $\qquad$ $[\alpha]_D = -92.4$

Sucrose is dextrorotatory but after hydrolysis gives dextrorotary glucose and laevorotatory fructose. Since the laevorotation of fructose (-92.4) is more than dextrotation of glucose (+52.5) the mixture is laevorotatory. Thus hydrolysis of sucrose brings a change in the sign of rotation from dextro(+) is laevo(-) and is known as inversion and the mixture is known as invert sugar.

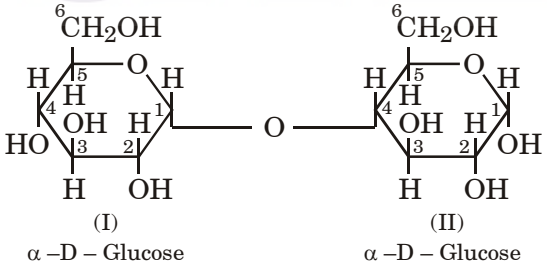
Sucrose solution is fermented by yeast when the enzyme invertase hydrolyses sucrose to glucose and fructose.

$$\underset{\text{Sucrose}}{C_{12}H_{22}O_{11}} + H_2O \xrightarrow{\text{Invertase}} \underset{\text{glucose}}{C_6H_{12}O_6} + \underset{\text{fructose}}{C_6H_{12}O_6}$$

Enzyme zymase converts these monosaccarides to ethyl alcohol.

$$\underset{\text{monosaccaride}}{C_6H_{12}O_6} \xrightarrow{\text{zymese}} 2C_2H_5OH + 2\,CO_2$$

(ii) Maltose : Another disaccharide, maltose is composed of two ⟨α-D-glucose units in which C1 of one glucose (I) is linked to C4 of another glucose unit (II). The free aldehyde group can be produced at C1 of second glucose in solution and it shows reducing properties so it is a reducing sugar.



(I) α –D – Glucose $\qquad$ (II) α –D – Glucose

Maltose

TESTS FOR CARBOHYDRATE

(i) When heated in a dry test tube, it melts, turns brown and finally black, giving a characteristic smell of burning sugar.

(ii) When warmed with a little concentrated H_2SO_4, it leaves a charred residue of carbon.

(iii) **Molisch's test :** A drop or two of alcoholic solution of α-naphthol is added to 2 ml of glucose solution and 1 ml of concentrated H_2SO_4 is added carefully along the sides of the test tube. The formation of a violet ring, at the junction of two liquids confirms the presence of a carbohydrate.

Test Of Starch

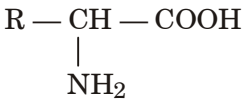
- When few drops of I_2 are added into starch solution, it turns into blue color which disappears on heating and reappears again on cooling.

AMINO ACID

Amino Acid

Amino acids are molecules which contain amino ($-NH_2$) and carboxyl (–COOH) functional groups. Depending upon the relative position of amino group with respect to carboxyl group, the amino acids can be classified as α, β, γ and so on. Only α-amino acids are obtained on hydrolysis of proteins. They

An amino acid cab be representd by :

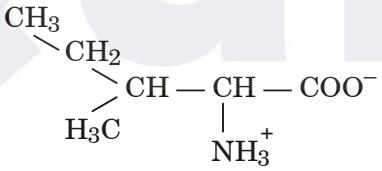


α–amino acid
(R = side chain)

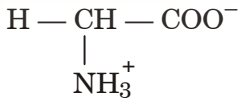
Classification of Amino

Based on Polarity Amino acids are classified into different ways based on polarity, structure, nutritional requirement, metabolic rate, etc. Generally used classification is based on polarity. Based on polarity amino acids are classified into four groups.

1. **Non-polar amino acids :** They have equal number of amino and carboxyl groups and are neutral. These amino acids are hydrophobic and have no charge on the 'R' group. The amino acids in this group are alanine, valine, leucine, isoleucine, etc.

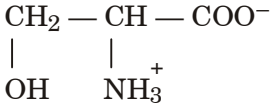


Isoleucine

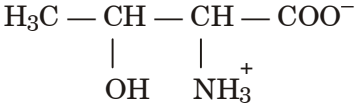


Glycine

2. **Polar amino acids with no charge :** These amino acids do not have any charge on the 'R' group. These amino acids participate in hydrogen bonding of protein structure. The amino acids in this group are - serine, threonine etc.

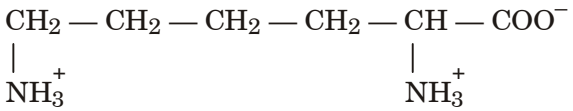


Serine



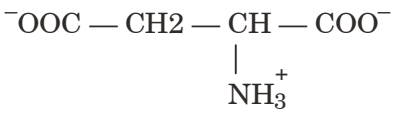
Threonine

3. **Polar amino acids with positive charge :** Polar amino acids with positive charge have more amino groups as compared to carboxyl groups making it basic. The amino acids, which have positive charge on the 'R' group are placed in this category. They are lysine, arginine etc.



Lysine

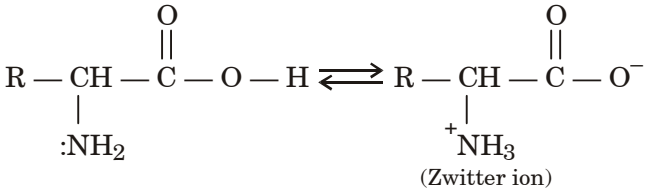
4. **Polar amino acids with negative charge :** Polar amino acids with negative charge have more carboxyl groups than amino groups making them acidic. The amino acids, which have negative charge on the 'R' group are placed in this category. They are called as dicarboxylic mono-amino acids. They are aspartic acid and glutamic acid.



Aspartic acid

Physical Properties Of Amino acids

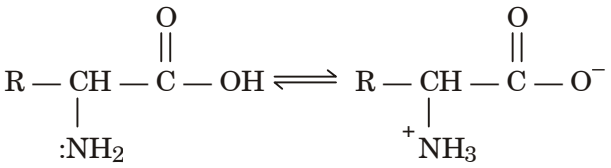
- Amino acids are usually colourless, crystalline solids.
- These are water-soluble, high melting solids and behave like salts rather than simple amines or carboxylic acids.
- This behaviour is due to the presence of both acidic (carboxyl group) and basic (amino group) groups in the same molecule, the carboxyl group can lose a proton and amino group can accept a proton, giving rise to a dipolar ion known as zwitter ion.
- This is neutral but contains both positive and negative charges.



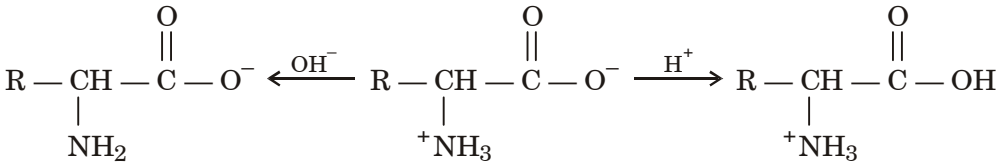
(Zwitter ion)

In zwitter ionic form, amino acids slow amphoteric behavior as they react both with acids and bases.

In acidic solution, the carboxylate function ($-COO^-$) accepts a proton and gets converted to carboxyl substituent (–COOH) while in basic solution the



ammonium substituent ($\overset{+}{N}H_3$) changes to amino group(-NH_2) by losing a proton.



Negative ion Zwitter ion Positive ion

In acidic solution, an amino acid exists as a positive ion and migrates towards the cathode in an electric field, while in alkaline solution it exists as a negative ion and migrates towards anode. At a certain hydrogen ion concentration (pH),the dipolar ion exists as a neutral ion and does not migrate to either electrode. This pH is known as the **isoelectric point** of the amino acid.

If the amino acid has amino group and one carboxyl group, it has two pK values. The isoelectric point of this amino acid has the average value of the both pK values.

We take example of glycine.

$$\underset{\text{Conjugated acid (CA)}}{H_3^+N{-}CH_2{-}COOH} \rightleftharpoons \underset{\text{Dipolar Ion(DI)}}{H_3N^+{-}CH_2{-}COO^-} + H^+ \quad ...(1)$$

At equilibrium $K_1 = \dfrac{[DI]\,[H^+]}{[CA]}$

$$\underset{\text{DI}}{H_3N^+{-}CH_2{-}COO^-} \rightleftharpoons \underset{\text{Conjugated Base (CB)}}{H_2N{-}CH_2{-}COO^-} + H^+ \quad ...(2)$$

At equilibrium $K_2 = \dfrac{[CB]\,[H^+]}{[DI]}$

$$[CA] = \frac{[DI][H^+]}{K_1}$$

$$[CB] = \frac{K_2[DI]}{[H^+]}$$

At isoelectric point [CA] = [CB]

$$\frac{[DI]\,[H_i^+]}{K_1} = \frac{K_2[DI]}{[H_i^+]} \quad \text{Where } [H_i^+] = \text{conc. of } [H^+] \text{ at isoelectric point}$$

or, $[H_i^+]^2 = K_1K_2$

or, $2\log[H_i^+] = \log K_1 + \log K_2$

or $-2\log(H_i^+] = -\log K_1 - \log K_2$

or $2pH_i = pK_1 + pK_2$

or $pH_i = \frac{pK_1 + pK_2}{2}$

The acid base properties also become understandable when it is realized that the measured Ka actually refers to the acidity of an ammonium ion, RNH_3^+

$$^+H_3NCHRCOO^- + H_2O \rightleftharpoons H_3O^+ + H_2NCHRCOO^-$$

$$K_a = \frac{[H_3O^+][H_2NCHRCOO^-]}{[^+H_3N - CH - RCOO^-]}$$

and K_b actually refers to the basicity of a carboxylate ion, $RCOO^-$

$$^+H_3N—CHR—COO^- + H_2O \rightleftharpoons {}^+H_3N — CHR—COOH + OH^-$$

$$K_b = \frac{[^3H_3N–CHR–COOH][OH^-]}{[^+H_3NCHRCOO^-]}$$

When the solution of an amino acid is made alkaline, the dipolar ion(I) is converted to the anion (II); the stronger base, hydroxide ion, removes a proton from the ammonium ion and displaces the weaker base, the amine.

$$^+H_3N—CHRCOO^- + OH^- \rightleftharpoons H_2NCHRCOO^- + H_2O$$

(I) (II)

Stronger acid — Stronger base — Weaker acid — Weaker base

When the solution of an amino acid is made acidic; the dipolar ion I is converted into the cation (III); the stronger acid H_3O^+, gives up a proton to the carboxylate ion, and displaces the weaker carboxylic acid.

$$\underset{\text{(I)}}{{}^{+}H_3N\,CHRCOO^-} + H_3O^+ \rightleftharpoons \underset{\text{(II)}}{{}^{+}H_3NCHRCOOH} + H_2O$$

Stronger base — Stronger acid — Weaker base — Weaker acid

In summary, the acidic group of a simple amino acid like glycine is $-NH_3^+$ not –COOH, and basic group is $-COO^-$ not $-NH_2$.

Example 2

What are essential and nonessential amino acids? Give the two examples of each.

Solution :

α-Amino acids which are needed for health and growth of human beings but are not synthesized by the human body are called essential amino acids. For example, valine, leucine, phenylalanine etc. On the other hand, α–amino acids which are needed for health and growth of human beings and are synthesized by the human body are called nonessential amino acids. For example, glycine, alanine, aspartic acid etc.

ELECTROPHORESIS

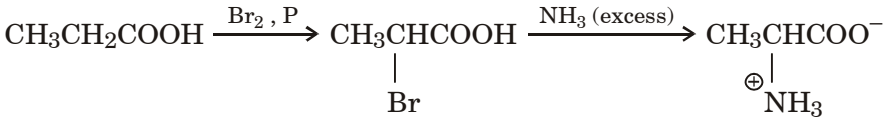
If a filter paper-strip moistened with a solution of a mixture of AA's is placed between two electrodes, the charged molecule will migrate to one electrode or the other at a rate that depends on its net charge and the applied voltage. The net charge depends on the pH. The strip is then stained with a reagent that reacts with the amino acid, thereby forming a color whose position on the strip is compared for identification with that of a known sample. This process known as electrophoresis is used for identification of amino acids.

SYNTHESIS OF AMINO ACIDS

1. AMINATION OF α-HALO ACIDS

Amination of α–halo acids of the many methods that have been developed for synthesizing amino acids, we shall take up only one: amination of α–halo acids. Considered in its various modifications, this method is probably the most generally useful, although, like any of the methods, it cannot be applied to the synthesis of all the amino acids.

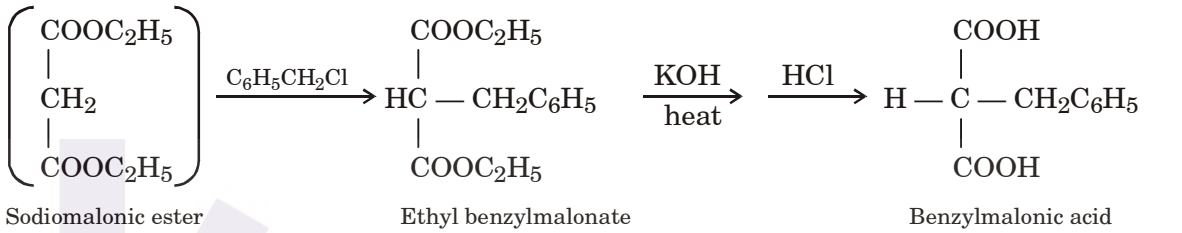
Sometimes an α–chloro or α–bromo acid is subjected to direct ammonolysis with a large excess of concentrated aqueous ammonia. For example,



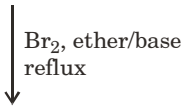
α–Bromopropionic acid — Alanine

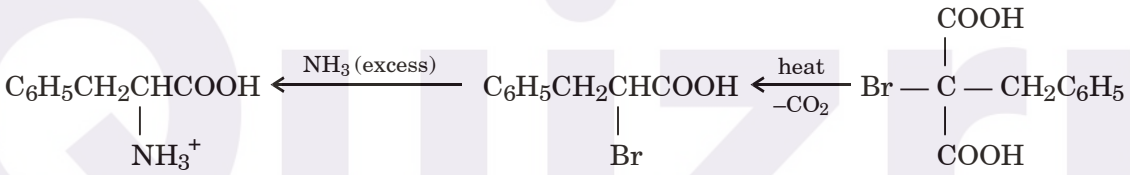
The necessary α–halo acids or esters can be prepared by the Hell–Volhard–Zelinsky halogenation of the unsubstituted acids, or by a modification of the malonic ester synthesis, the usual route to the unsubstituted acids. For example,

2. FROM DIETHYL MALONATE



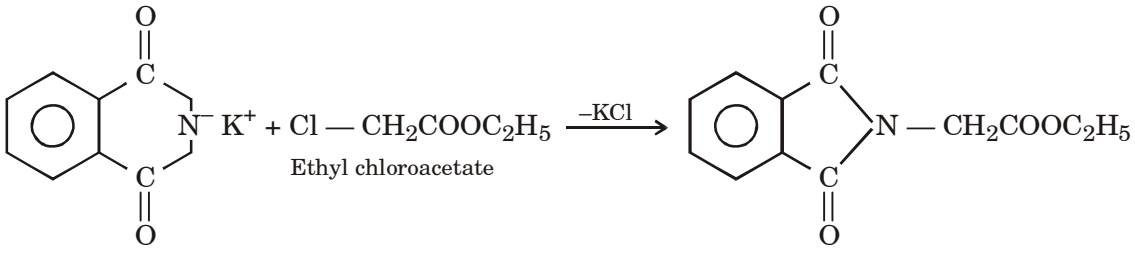
Sodiomalonic ester — Ethyl benzylmalonate — Benzylmalonic acid



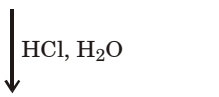


Phenylalanine
35% overall yield

3. GABRIEL PHTHALIMIDE SYNTHESIS



Potassium phthalimide — Ethyl chloroacetate



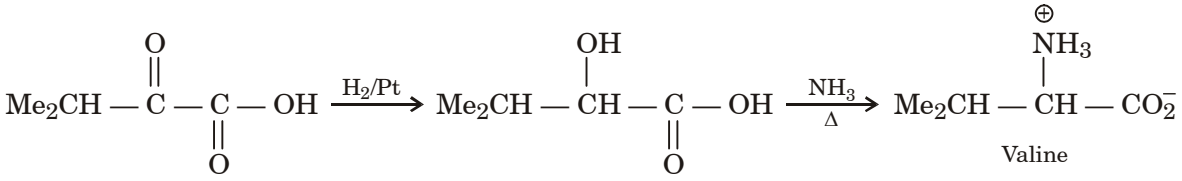
Cl⁻ ⁺H3N — CH2COOH + phthalic acid

Glycine hydrochloride

4. REDUCTIVE AMINATION

Another method of preparing α–amino acids is reductive amination of α–keto acids.

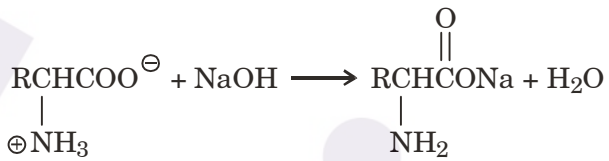
For example



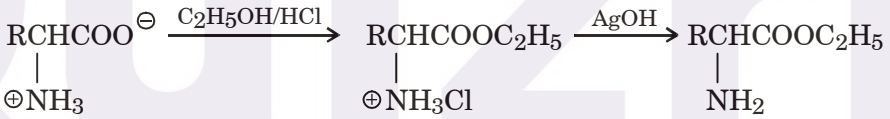
REACTIONS OF AMINO ACID

(1) REACTIONS OF THE CARBOXYL GROUP

- They form salts with base

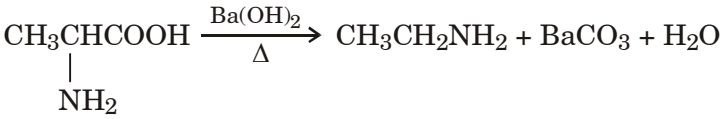


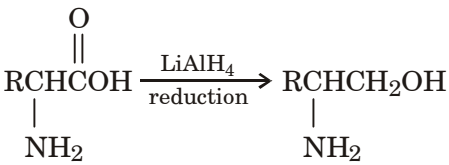
- They form ester with alcohol



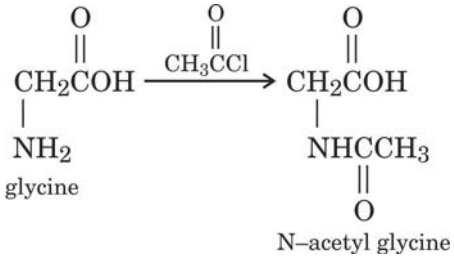
AgOH is used to obtain free ester.

- It can be decarboxylated to get amine



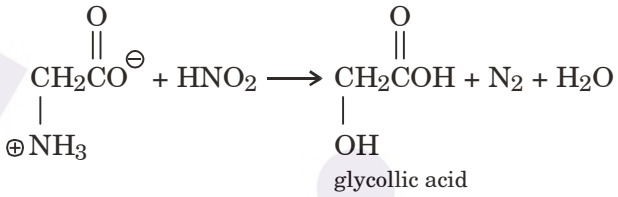
- 

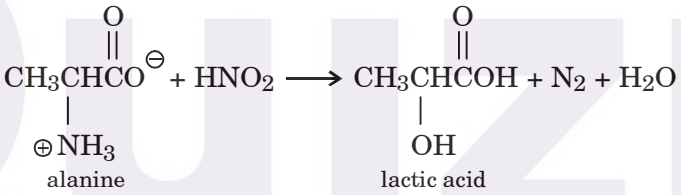
(2) REACTIONS OF THE AMINO GROUP

- 

Acylation can also be done using acetic anhydride, $\left(CH_3\overset{\overset{O}{\|}}{C}O\right)_2O$.

- HNO_2 ($NaNO_2$ +dil.HCI) converts $-NH_2$ group into –OH with liberation of N_2.

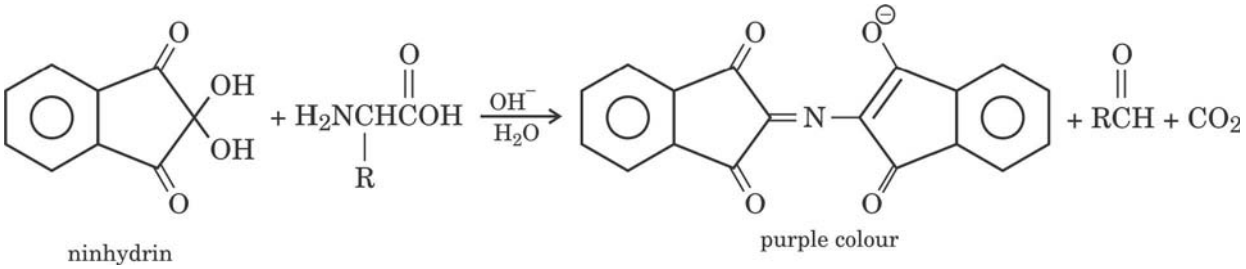




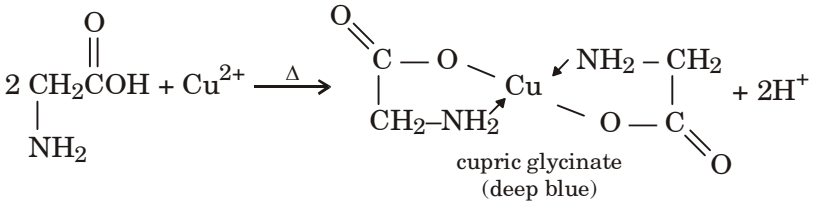
This reactions forms the basis of the **Van Slyke** method for the estimation of amino acids in which volume of N_2 gas collected is measured quantitatively.

(3) REACTIONS INVOLVING BOTH THE CARBOXYL AND AMINO GROUPS

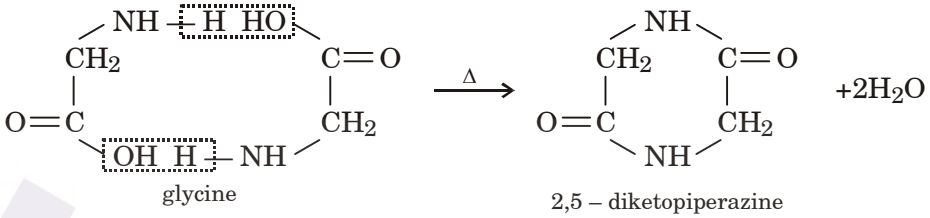
- All α-amino acids (with primary $-NH_2$ group) react with **ninhydrin** to form an intense purple coloured complex.



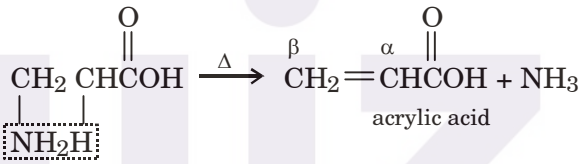
- Cu^{2+} salts form blue coloured complex with amino acids which is a bidentate legand.



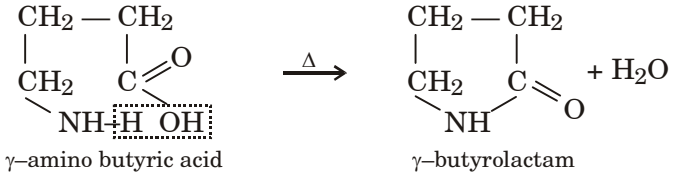
- **Effect of Heat :**
- α-amino acids undergo intermolecular dehydration on heating at about 200 C to give diketopiperazines.

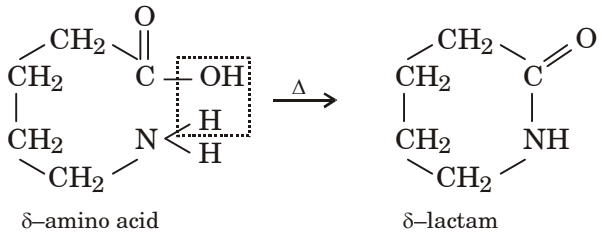


- β-amino acids undergo intramolecular deamination on heating to form α,β-unsaturated acids.

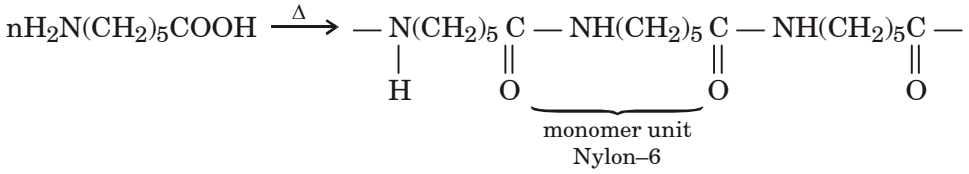


- γ-amino acids and δ-amino acids undergo intramolecular dehydration to form cyclic amides called **Lactams.**



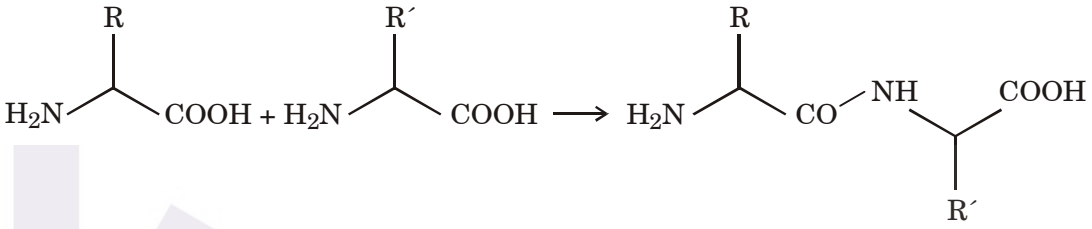


- In case of ε-amino acid, intramolecular cyclisation would give a seven-membered ring, which is formed with difficulty. Hence, there is intermolecular polymerisation forming nylon-6.



PEPTIDES

As the amino acid molecules contain both basic as well as acidic group it might be expected that an intermolecular reaction may take place between the carboxyl group of one amino acid and the amino group of another amino acid, with the elimination of a molecule of water.



Since the resulting milecule still has a free amino and a carboxyl group, it may react with other amino acids at either of the ends to give a higher molecular weight linear or condensation product. Every two amino acids are linked by means of a –CO-NH group, which is commonly referred as peptide bond. So now we can define peptides as the amides formed by interaction between amino groups and carboxyl groups of amino acids.

Depending upon the number of amino acid residues per molecule, they are known as depeptides, tripeptides and so on and finally polypeptides.

- Proteins are polypepties in which no. of repeating unit of peptide is very large. The peptide units are arrange in a uneque fashion in a partiular protein.

PROTEINS

Proteins are categorized according to (a) shape and (b) their biological function. Proteins according to shape are further classified as globular, somewhat spherical and fibrous, long fibres or planar sheets.

According to their biological action, they are classified as enzymes, hormones, antibodies, etc.

A protein has, secondary, tertiary and quaternary structures.

The primary structure is simply the amino acid sequence of the peptide chain. The secondary structure is a result of the different conformations that the chain can take. The tertiary structure is determined by any folding of the chain in on itself. A quaternary structure results when two or more peptide chains in some proteins are linked together by weak forces of attraction of their surface groups. Such proteins are called oligomers (dimers, trimers etc.).

The H–bonding in secondary structure exists between an N–H of one amino acid residue and the O=C of another properly situated amino acid residue. There are 3 types of secondary structures for protein. (1) The peptide sequence is coiled into a right–handed spiral in the α-helix, with the R groups positioned on the outside of the spiral. Each amide H–N bonds to the O=C on the next turn of the coil, four residues away by H–bonds, stabilizing this arrangement. (2) In the pleated sheet of β-structure, the peptide chains lie side–by–side in an open structure, with inter–chain amide H–bonding holding the chains together. Parallel pleated sheets have chains running in the same direction, all with their N–terminal residues starting at the same end. Antiparallel pleated sheets have their chains running in opposite directions. The α C's rotate slightly out of the plane of the sheet to minimize repulsions between their bulky R groups, giving rise to the crimps or pleats. In both cases, the R groups alternate positions above and below the sheet. (3) The random coil structure has no repeating geometric pattern; encompassed within it are sequences in a helical conformation, a pleated sheet conformation and regions that appear to have no discernible repeating structure, but are actually not random conformations.

The unique three–dimensional shape of a protein in tertiary structure is the result of the intramolecular forces of attraction that cause bending and coiling in the helical coil. These forces are a function of the nature of the amino acid side chains within the molecule. Globular proteins have their non–polar R groups pointing to the interior (the hydrophobic or non–aqueous region) and their polar side chains projecting toward the aqueous environment, somewhat like a micelle. They are slightly water soluble. Fibrous proteins are insoluble in water. Their polypeptide chains are held together by inter–chain H–bonds. The following are the attractive forces responsible for the tertiary structure :

(1) Ionic: bonding between COO^- and NH_3^+ at different sites.

(2) H–bonding: mainly between side–chain NH_2 and COOH, also involving OH's (of serine, for example) and the N–H of tryptophan.

(3) Weakly hydrophobic van der Waal's attractive forces engendered by side–chain R groups and

(4) Disulfide cross linkages between loops of the polypeptide chain.

The same kind of attractive and repulsive forces responsible for the tertiary structure operate to hold together and stabilize the subunits of the quaternary structure.

Protein found in living system with definite configuration and biological activity is termed as native protein. If a native protein is subjected to physical or chemical treatment, which may disrupt its higher structures (conformations) without affecting its primary structure, the protein is said to be denatured. During denaturation, the protein molecule uncoils from an ordered and specific conformation into a more random conformation leading to precipitation. Thus denaturation leads to increase in entropy and loss of biological activity of the protein. The denaturation may be reversible or reversible. Thus, the coagulation of egg white on boiling of egg protein is an example of irreversible protein denaturation. However, in certain cases it is found that if the

disruptive agent is removed the protein recovers its original physical and chemical properties and biological activity the reverse of denaturation is known as renaturation.

Test for Proteins

(i) Biuret test : On adding a dilute solution of $CuSO_4$ to alkaline solution of protein, a violet colour is developed.

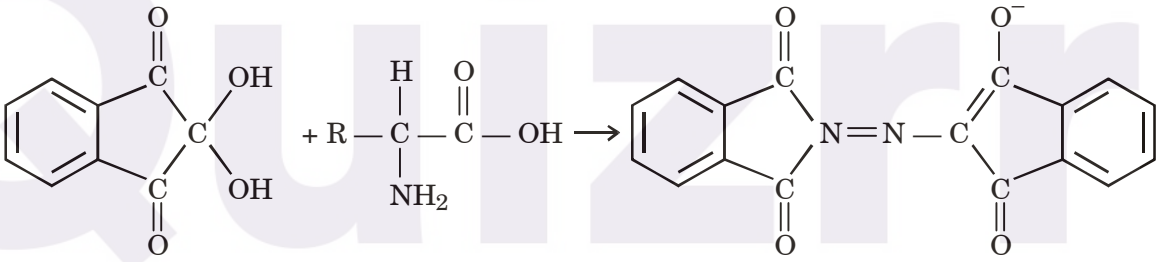
This test is due to the presence of peptide $\left(\begin{array}{c} O \quad H \\ \| \quad | \\ -C-N- \end{array}\right)$ linkage.

(ii) Millon's test : Millon's reagent consist of mercury dissolved in nitric acid (forming a mixture or mercuric and mercurous nitrates).

When Millon's reagent is added to a protein, a white precipitate forms, which turn brick red on heating.

This test is given by protein which yield tyrosine on hydrolysis (due to HCI of phenolic group).

(iii) Ninhydrin test: Given by all proteins. When protein is boiled with a dilute solution of ninhydrin, a violet colour is produced.



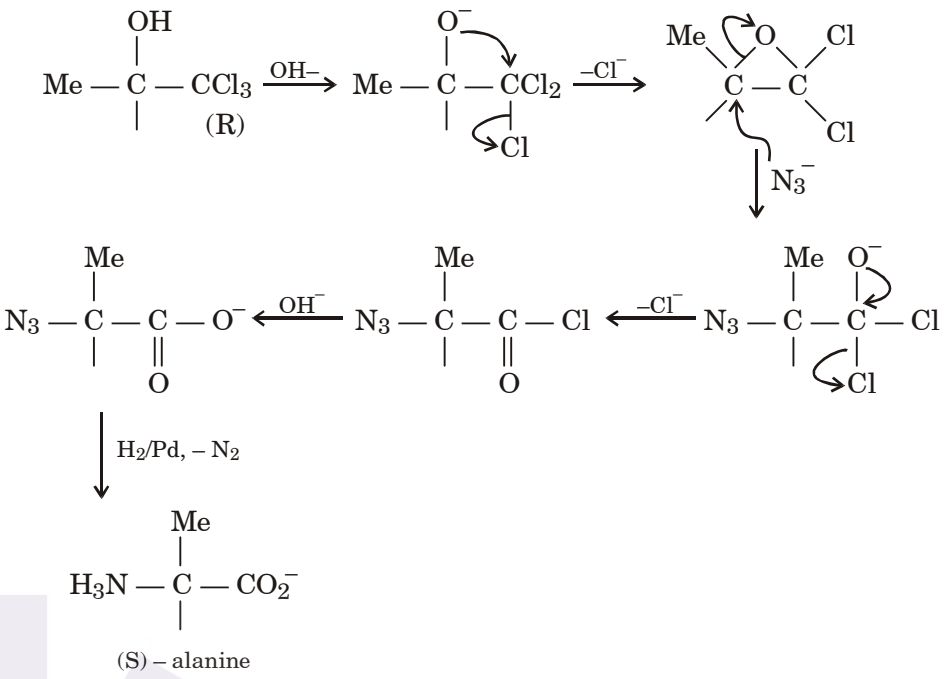
(Ninhydrin) Violet Complex

Example 3

Treatment of (R)–MeCH(OH)CCl_3, first with alkaline NaN_3 and then reducing the product with H_2/Pd yields (S)–alanine, $CH_3CH(\overset{\oplus}{N}H_3)CO_2^-$. Explain.

Solution :

In alkaline solution, the OH will be converted to O^- which displaces Cl of adacent carbon to form an oxirane ring. In the oxirane ring, the configuration of chiral carbon is still (R). The oxirane ring is then opened by nucleophilic attack of azide ion, which occurs with inversion of configuration i.e. configuration becomes (S). The acid chloride will be hydrolysed in alkaline conditions to give acid. This is followed by reduction of N_3 group to give (S)–alanine.



Example 4

Pick out incorrect statement :

(A) In an electrolysis experiment, α-amino acids migrate at the isoelectric point point towards electrodes.

(B) p-aminobenzenesulphonic acid as a dipolar ion; while p-aminobenzoic acid does not

(C) Sulphanillic acid is soluble in base, but not in acid

(D) $H_3^{\oplus}NCH_2COOH$ (pK_a = 2.4) is more acidic than RCH_2COOH (pK_a = 4 – 5)

Solution :

(A) The pH at which [Anion] = [Cation] is called isoelectric point. At isoelectric point, α-amino acids donot migrate when electric field is applied.

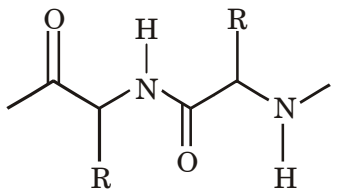
(B) $–SO_3H$ is strongly acidic and donates H^+ to weakly basic arylamino group. ArCOOH is not acidic enough to transfer H^+ to the arylamino group.

(C) in p – $H_3^{\oplus}NC_6H_4SO_3$, $H_3N^{\oplus}$ is acidic anough to transfer H^+ to bases to give the soluble anion, p-$H_2N–C_6H_4SO_3$, $–SO_3$ is too feebly basic and cannot accept H^+ from acids.

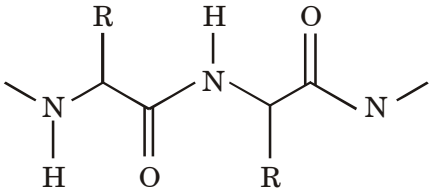
(D) α –$H_3^{\oplus}N$ group increases acidity, because of its electron – withdrawing inductive effect.

Example 5

Show the fundamental unit of structure common to all polypeptides and proteins and show how cross linking occurs between two chains by H –bonding.



Solution :



Example 6

Glycine exists as ($H_3N^+CH_2COO^-$) while anthranilic acid ($P–NH_2–C_6H_4$ – COOH) does not exist as dipolar ion.

Solution :

–COOH is too weakly acidic to transfer H^+ to the weakly basic $–NH_2$ attached to the electron withdrawing benzene ring. When attached to an aliphatic carbon, the $–NH_2$ is sufficiently basic to accept H^+ form –COOH group.

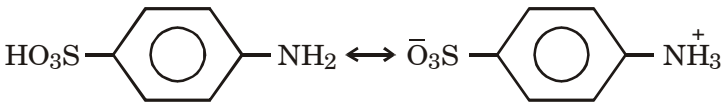
Example 7

(i) Sulphanilic acid although has acidic as well as basic group, it is soluble in alkali but insoluble in mineral acid

(i) Sulphanilic acid is not soluble in organic solvents.

Solution :

(i) Sulphanilic acid exist as Zwitterion



The weakly acidic $–{}^+NH_3$ transfers H^+ to OH^- to form a soluble salt, $P–NH_2–C_6H_4–SO_3^-Na^+$ on the other hand $–SO_3^-$ is too weakly basic to accept H^+ from strong acids.

(ii) Due to its ionic character it is insoluble in organic solvents.

Example 8

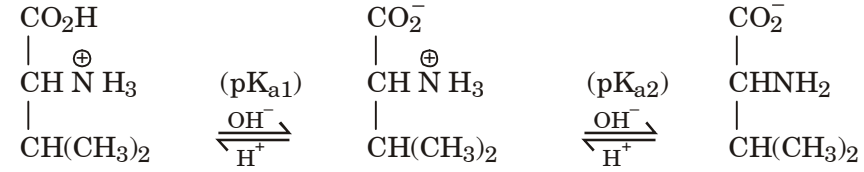
The pKa of the carboxyl group in an amino acid valine, $(CH_3)_2CHCH(NH_2)(COOH)$ is 2.31 and the pKa for the amino group of the same amino acid is 9.69. Compute the isoelectric point (pI) for valine and draw the structure of this amino acid when the pH of the solution equals to pI. Also draw the structures of valine that predominate at pH = 2 AND pOH = 2.

Solution:

The isoelectric point (pI) is the pH at which the amino acid exists only as a dipolar ion with net charge zero.

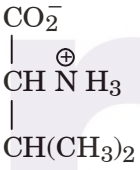
At isoelectric point, for a neutral amino acid, $pI = \frac{(pK_{a_1} + pK_{a_2}}{2}$

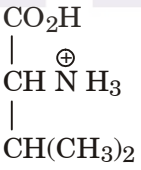
The dissociation of cationic form of valine can be represented as



The species with zero net charge exists between species with (+1) and (–1) net charges.

$$pI = \frac{(pK_{a_1} + pKa_2)}{2} = \frac{9.69 + 2.31}{2} = 6$$

When the pH of the solution equals to pI, the structure of valine is 

When the pH of the solution is two, the structure of valine is 

When the pH of the solution is 12, the structure of valine is