Biochemistry

Prepared by

Mustafa F. Aly

Chemistry department --- Faculty of Science

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Chemistry of Carbohydrates

Part_1 : Chemistry of Carbohydrates

Chapter_1

Introduction:

The carbohydrates mean such compounds that contain carbon and water, thus the empirical formula for example monosaccharides, is $C_n(H_2O)_n$, which could refer to hydrated carbon. In fact, carbohydrates are divided into three different classes: sugars, starch and cellulose. Sugars and starch are one of the main sources of energy for human beings. It is well known that cellulose is the main diet for most domestic animals. Generally, sugars are soluble in water, whereas starch and cellulose are not. However, all carbohydrates are naturally obtained compounds, and no doubt of their importance to human beings.

Carbohydrates are obtained in nature *via* photosynthesis in green plants. The chlorophyll (green pigments) catalyzes the conversion of carbon dioxide and water into carbohydrates, such process is presented in the given equation:

$$6\,CO_2 + 6\,H_2O \underset{\text{- energy, animal metabolism}}{\overset{\text{+ Light, Chlorophyll}}{\rightleftharpoons}} C_6(H_2O)_6 + 6\,O_2$$

Definition and Classification:

Carbohydrates are in fact polyhdroxy aldehydes, polyhdroxy ketones. Carbohydrates must have the following features:

(i) Contain carbon, hydrogen and oxygen and the ratio H : O is 2 : 1.

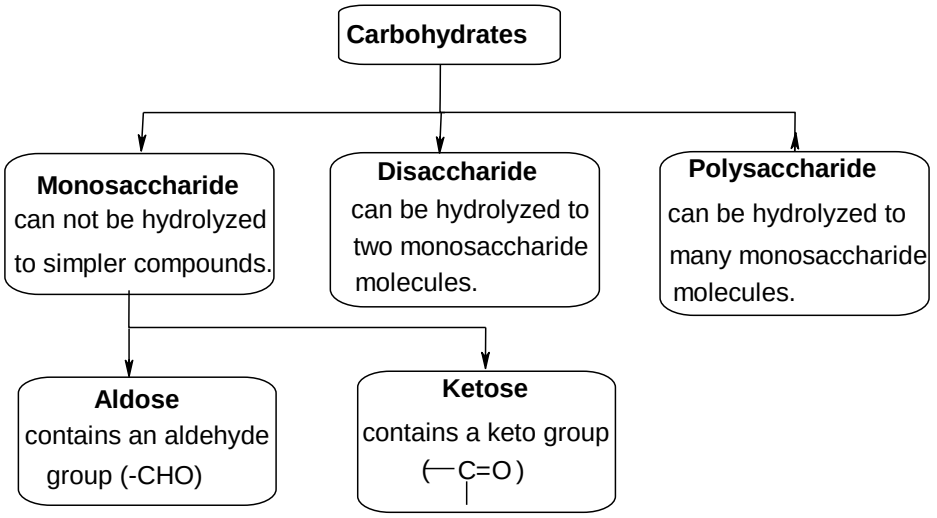
(ii) Contain primary and secondary hydroxyl groups.

(iii) Contain carbonyl group (as aldehyde or ketone), however sucrose does contain carbonyl group, both of them are involved in the glycosidic linkage.

(iv) Contain asymmetric carbon atoms (chiral centers).

(v) Carbohydrates rotate the plane of the polarized light, and each individual has its own specific rotation number, and the rotation could be to the right (+) or to the left (-).

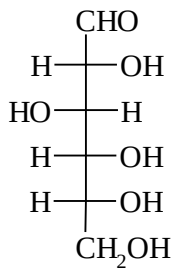
According to the number of carbon atoms, a monosaccharide contains, it is known as a triose, tetrose, pentose and hexose.



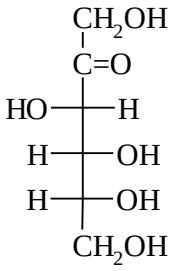
Examples of monosaccharides:

- **Glucose is a six-carbon monosaccharide containing an aldehyde group, so it can be known as aldohexose.**
- **Fructose is a six-carbon monosaccharide containing a keto group is kctohexosc.**
- **Ribose is a five-carbon monosaccharide containing an aldehyde group is aldopentose.**
- **The -ose suffix is used to designate a carbohydrate.**
- **The aldo- and keto- prefixes designate the nature of the carbonyl group (aldehyde or ketone).**

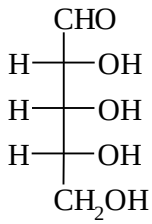
Examples:



Glucose
aldohexose



Fructose
ketohexose



Ribose
aldopentose

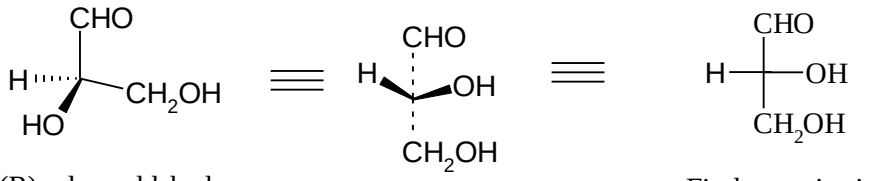
CHAPTER 2

Monosaccharides

($C_6H_{12}O_6$)

Fischer projection for drawing carbohydrates:

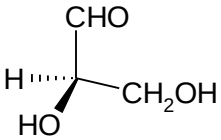
The tetrahedral carbon atom is represented in a Fischer projection by two crossed lines as shown in the following figure.



(R)- glyceraldehyde Fischer projection

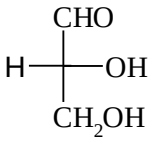
D, L-Sugars:

Three Dimensional

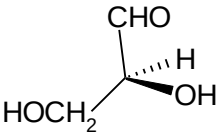


R(+)- glyceraldehyde

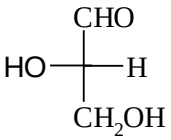
Fischer projection



D- glyceraldehyde



S(-)- glyceraldehyde



L- glyceraldehyde

In Fischer Projection:

Emil Fischer Found out that glyceraldehyde exists as a pair of enantiomers one of them rotates the plane of polarized light to the right and the other rotates the plane of polarized light to the left. He

recognized the former one as D-glyceraldehyde (D means *dextrorotatory*) and the later one as L-glyceraldehyde (L means *Leavorotatory*).

Fischer divided sugars into two main groups referred to D-glyceraldehyde and L-glyceraldehyde as follows:

- **The D-sugars are recognized by the secondary hydroxyl group at the lowest asymmetric carbon atom (chiral center) to be on the right side.**
- **The L-sugars are recognized by the secondary hydroxyl group at the lowest carbon atom (chiral center) to be on the left side.**
- **It must be noted that the D-and L-notations are given to show the difference between the two classes in the Fischer projection. In fact they have no relation to the direction in which a given sugar rotates the plane of polarized light, a D sugar may be either dextrorotatory or levorotatory, and the same with an L sugar.**
- **As sugars contain chiral centers, so the number of isomers of any given sugar depends on the number of the chiral centers. According to the following formula:**

Number of isomers = 2^n

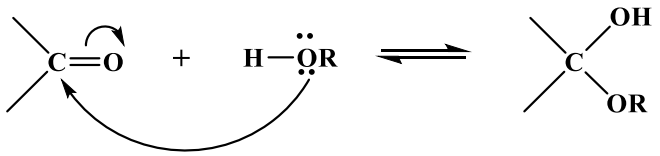
Where n is the number of chiral centers.

- **Glyceraldehyde has only one chiral center (an asymmetric carbon atom) so it has two isomers D-glyceraldehyde and L-glyceraldehyde.**

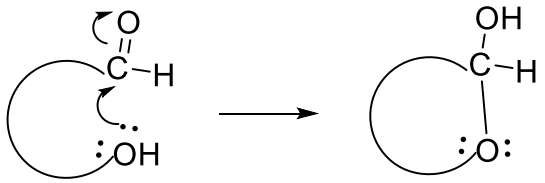
Cyclic Structures of monosaccharides:

Hemiacetal Formation:

- **Alcohols undergo a rapid and reversible nucleophilic addition reaction with aldehydes and ketones in acidic medium to form hemiacetals and hemiketals, respectively in an intermolecular fashion. Such derivatives exist in equilibrium with its related free carbonyl compounds as presented in the following equation:**



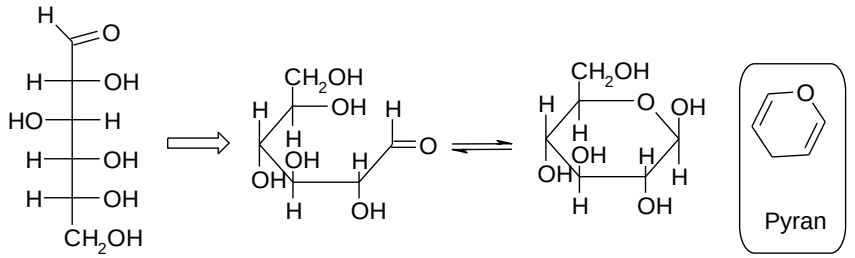
- **However, if both the hydroxyl group and the carbonyl group are exist in the same molecule: an intramolecular nucleophilic addition can take place to form a cyclic hemiacetal.**



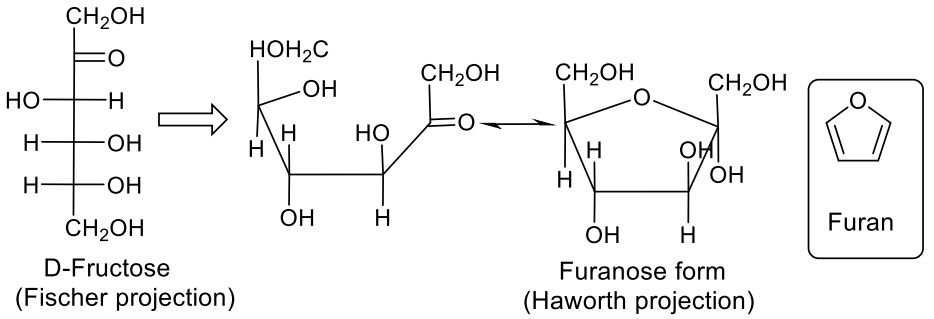
- **Five and six-membered cyclic hemiacetals are easily formed.**
- **For such reasons many carbohydrates exist in an equilibrium between the open-chain and cyclic forms.**
- **Glucose exists in aqueous solution mainly in cyclic form.**

- **Pyranose ring formed by intramolecular nucleophilic addition of the hydroxyl group at C_5 to the C_1 aldehyde group.**

So that the pyranose (referred to pyran) form of glucose can be formed by the nucleophilic attack of the hydroxyl group at C5 on the aldehydic group as shown below.



Fructose exists to the extent of about 20% as the five membered furanose ring (referred to furan), which is formed by addition of the hydroxyl group at C5 to the C2 ketone group as shown below.



However, we must consider that both hemiacetals and hemiketals react with one more molecule of alcohol to give the corresponding stable derivatives.

Haworth Projection:

The following steps explain how we can draw Haworth projection:

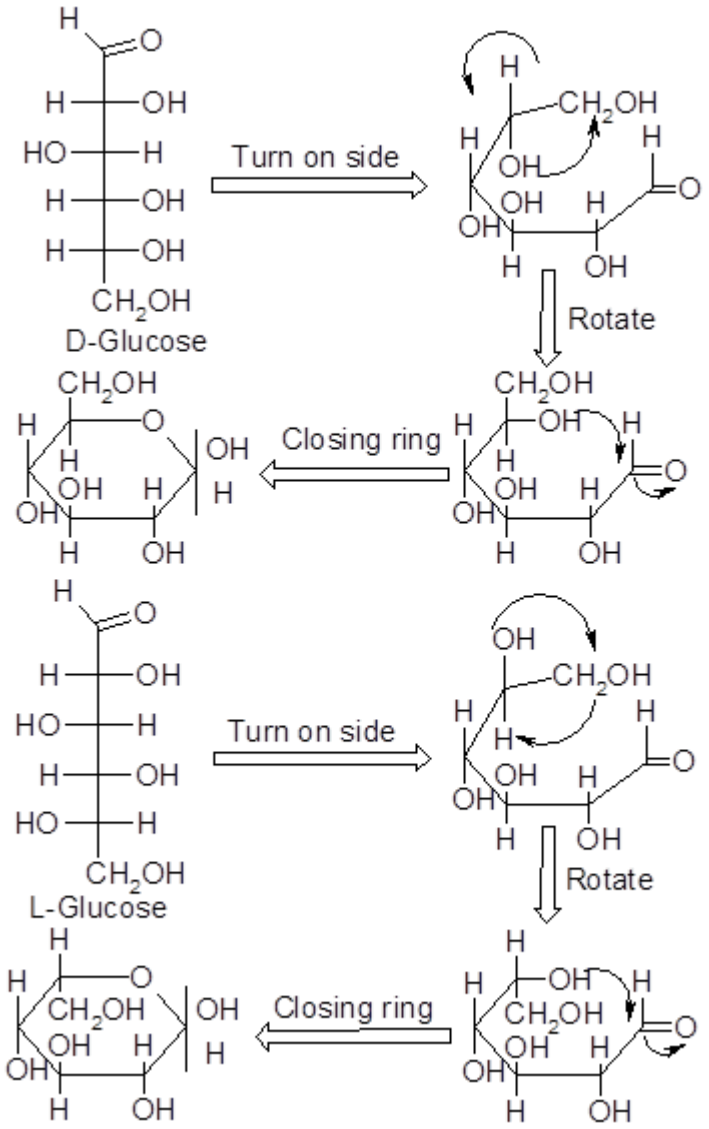
a- In such projection the cyclic hemiacetal six membered ring is drawn planar with the oxygen atom at the upper right.

b- Hydroxyl group on the right in a Fischer projection is down in a Haworth projection.

c- Hydroxyl group on the left in a Fischer projection is up in a Haworth projection.

d- For D-sugars the terminal CH_2OH group is up in Haworth projection.

e- For L-sugars the terminal CH_2OH group is down in Haworth projection.



There are two reasons to confirm the cyclic conformation of D-glucose:

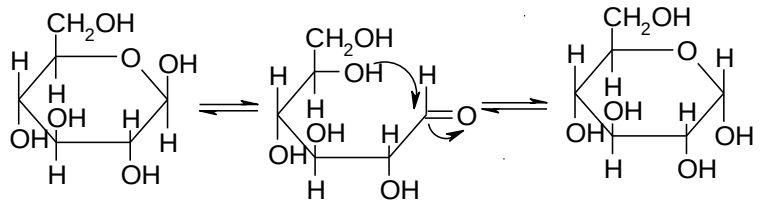
(i) Mutarotation and

(ii) D-Glucose reacts with only one molecule of methanol to give the corresponding stable acetal.

MUTAROTATION:

D-Glucose can be obtained in two crystalline forms; one melts at 150ºC and the other at 146ºC. The fact that neither form shows a carbonyl frequency in the infrared suggests that these two crystalline forms are the α- and β-hemiacetals. X-ray diffraction studies confirm such hypothesis. The crystals melt at 150ºC, are β-D-glucose with the anomeric hydroxyl group is in the equatorial position. The crystals of melt at 146ºC, are α-D-Glucose with the anomeric hydroxyl group is in the axial position. A freshly prepared solution of β-D-glucose crystals in water gives a specific rotation of + 18.7º. This value slowly rises with time to +52.5º. On the other hand, immediate determination of the α-D-glucose shows a rotation, of +112º, but this value also goes down slowly with time to + 52.5º.

The slow change of optical rotation in solution is called mutarotation, and this phenomenon is interpreted by the interconversion of hemiacetals through the aldehyde intermediate. The equilibrium mixture contains nearly 64% of the β-isomer, 36% of the α-isomer and only about 0.02% of the free aldehyde.

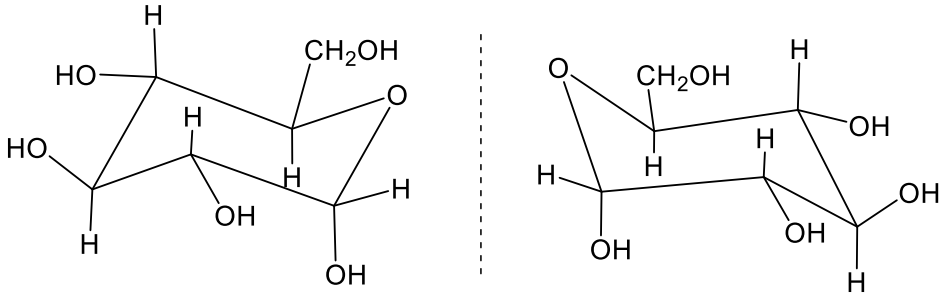


β-D-Glucopyranose **free carbonyl** **α-D-Glucopyranose**

nearly 64% **0.02%** **nearly 36%**

It should be understood that the mirror image of D is L, the mirror image of (+) is (-), but the mirror image of α is α and not β, as shown in the following example (i.e., α-implies an axial 1-hydroxyl group in both enantiomers).

Mirror images



α-D-(+) Glucopyranose α-L-(-) Glucopyranose

<u>The interconversion of Haworth projection into the conventional Conformation:</u>

Pyranose rings like cyclohexane rings have a chair like geometry with axial and equatorial substituents.

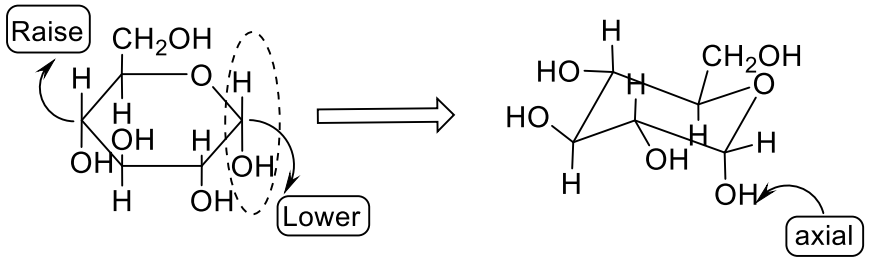
It is well known that six membered alicyclic compounds have the stable chair form, so Haworth projections must be converted into the

chair form according to the following steps: representations by the following three steps:

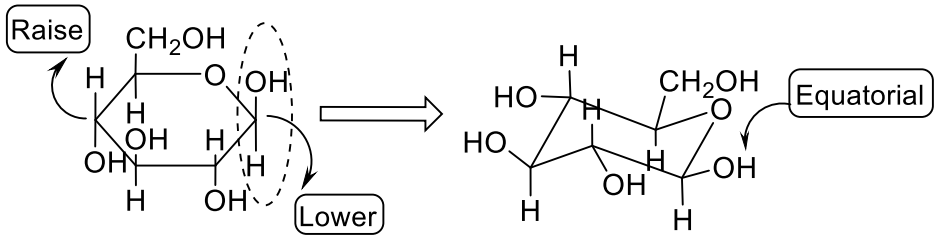
1- **Draw the Haworth projection with the ring oxygen atom at the upper right.**

2- **Raise the left most carbon atom(C_4) above the ring plane.**

3- **Lower the anomeric carbon atom (C_1) below the ring plane.**



α-D-Glucopyranose



β-D-Glucopyranose

Note that in β-D-glucopyranose all the substituents on the ring are equatorial, thus β-D-glucopyranose is less sterically hindered than α-D-glucopyranose, which suffers a 1,3-diaxial interactions.

CHAPTER 3

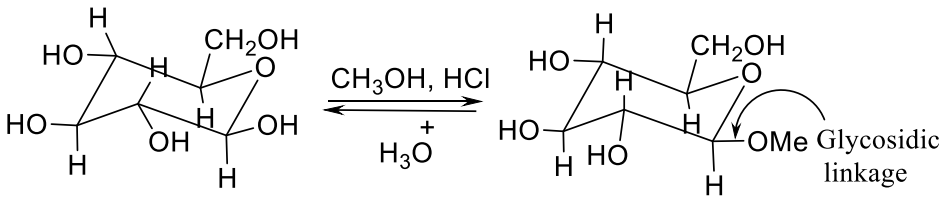
Reactions and Interconversion of Monosaccharides

1- Glycoside Formation:

Treatment of a hemiacetal with an alcohol in acidic medium yields an acetal a very stable compound.

Hemiacetal Acetal

In the same way, treatment of a monosaccharide (a hemiacetal) with methyl alcohol in acidic medium to form 1-Mehoxy-D-pyranose (an acetal derivative), in which the anomeric hydroxyl group has been replaced by the methoxy group. Thus, D-glucopyranose reacts with methanol in acidic medium to give the corresponding methyl-D-glucopyranoside (an acetal).



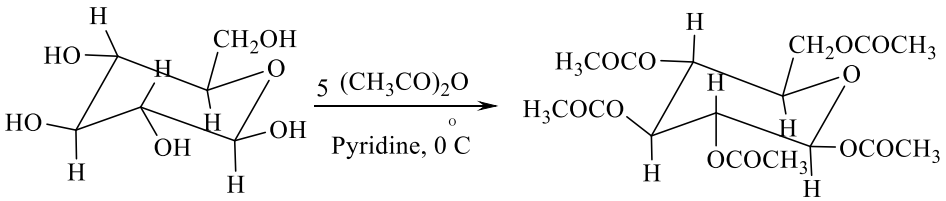
β-D-Glucopyranose Methyl-β-D-Glucopyranoside (an acetal)

In general carbohydrate acetals are called glycosides. They are named by citing the alkyl group and adding the -oside suffix to the name of the specific sugar.

However, glycosides are stable to water, and can be converted back to the free monosaccharide by hydrolysis with aqueous acid.

2- Ester Formation:

Esterification is normally carried out by treating the carbohydrate with acid anhydride (or acid chloride) in the presence of a base at 0°C to give the corresponding penta-O-acetyl-D-glucopyranose. All the hydroxyl groups react, including the anomeric one to produce the corresponding penta-*O*-acetyl derivative.

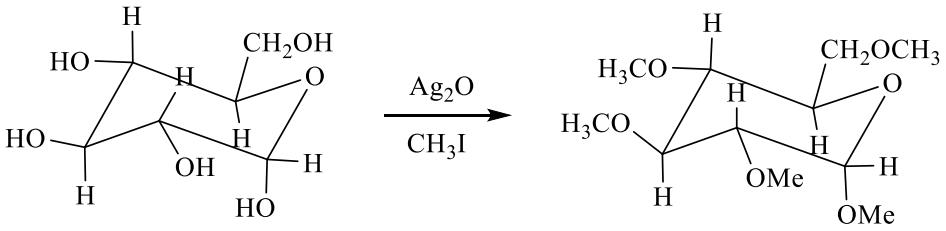


β-D-Glucopyranose

Penta-*O*-acetyl-β-D-Glucopyranose-91 %

3-Ether Formation:

Carbohydrates can be converted into their ether derivatives by treatment with an alkyl halide in the presence of a base (the Williamson ether synthesis). Normal Williamson conditions using a strong base, which tends to degrade the sensitive sugar molecules. In 1903 Purdie showed that silver oxide works particularly well and high yields of ethers are obtained. For example, reacting α-D-glucopyranose with a mixture of iodomethane and silver oxide gives an 85% yield of the corresponding pentamethyl ether.

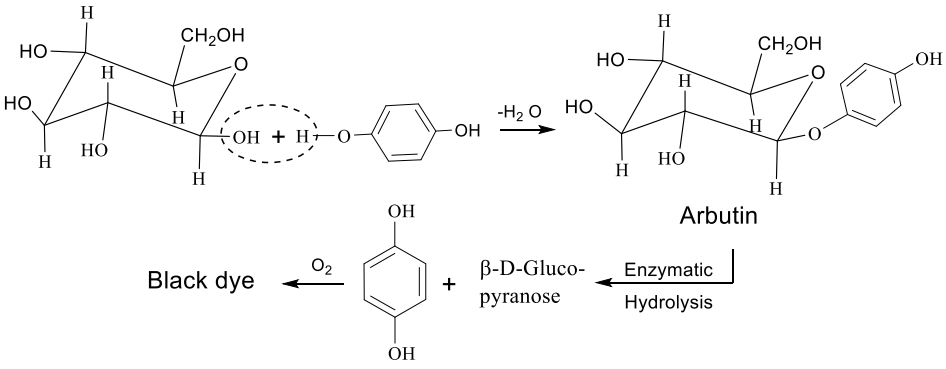


β-D-Glucopyranose

Penta-*O*-acetyl-β-D-Glucopyranose 85 %

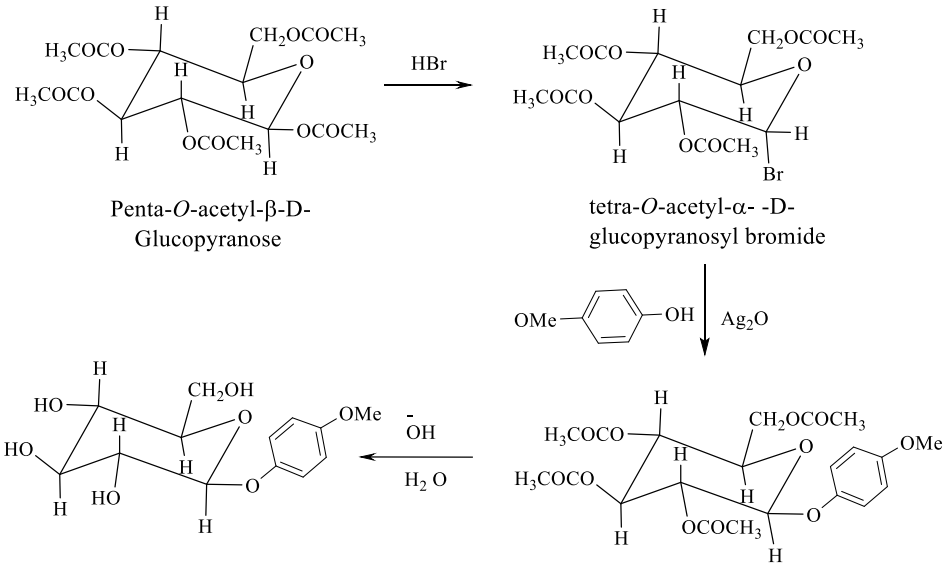
Sugar Derivatives in Nature:

Many natural products contain sugars attached to some other types of chemical residues. In arbutin, the sugar is attached to a substituted phenyl derivative. Arbutin is hydroquinone β-D-glucoside, and it exists in many plants. In the autumn, the falllen leaves from certain pear trees turn black instead of yellow and red. Such black colour is obtained due to the presence of high concentration of arbutin, which on enzymatic hydrolysis librates hydroquinone, which is readily oxidized by air to give a black dye named_quinone, Scheme. The moiety attached to the glucpyranose is known as aglycone, which is responsible for the colourful flowers.



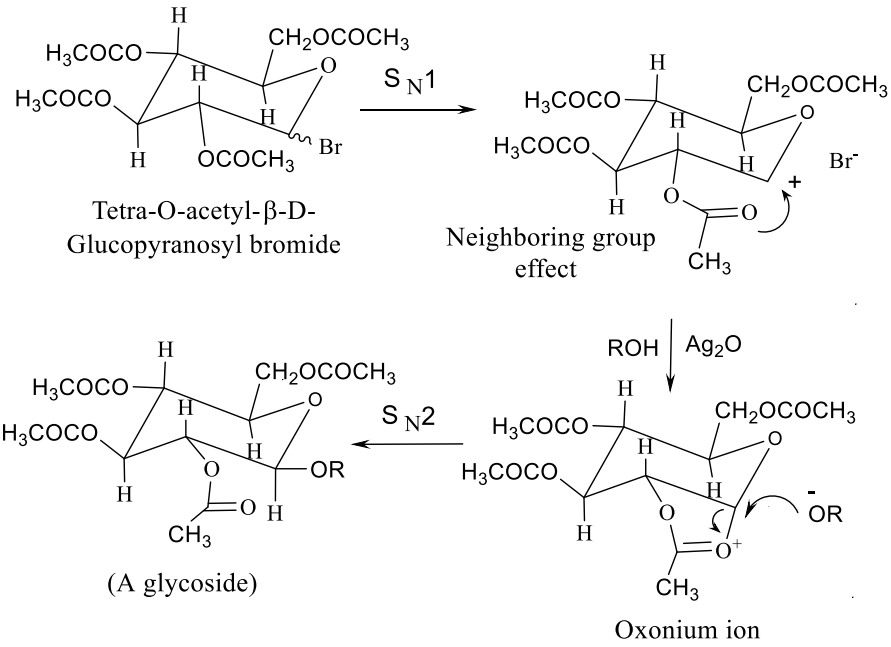
Koenigs Knorr reaction:

This reaction is specific for obtaining only the β-anomer from both α (alpha) and β (beta) anomers.



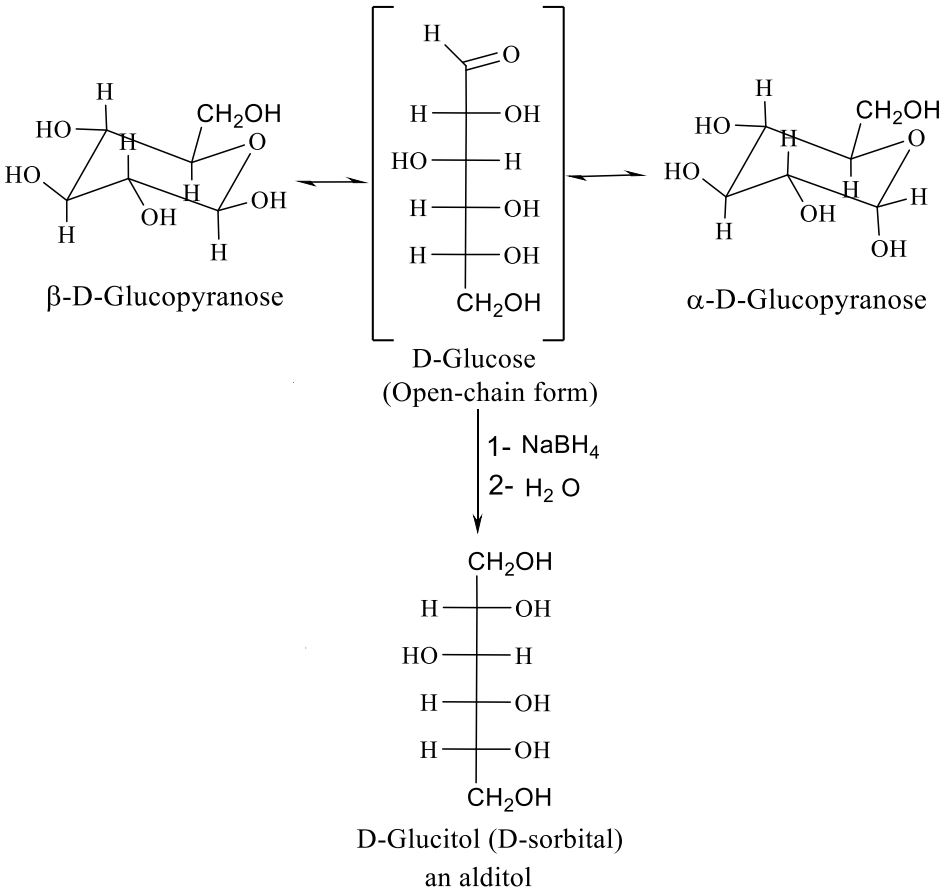
The mechanism of Koenigs Knorr reaction is as follows:

Both alpha and beta anomers of tetraacetyl-D-glycopyranosyl bromide give the same β-glycoside product. It is obvious means that both anomers react by the same mechanism.



3- Reduction of Monosaccharides:

Treatment of an aldose or a ketose with $NaBH_4$ reduces it to a polyalcohol.



4-Oxidation of Monosaccharides:

Like other aldehydes. aldoses are easily oxidized to yield carboxylic acids. Aldoses reacts with oxidizing reagents to yield the oxidized sugar and a reduced metallic.

Oxidizing reagents like:

1- **Tollen's reagent (Ag^+ in aqueous ammonia) produce silver metal (Ag) as a mirror.**

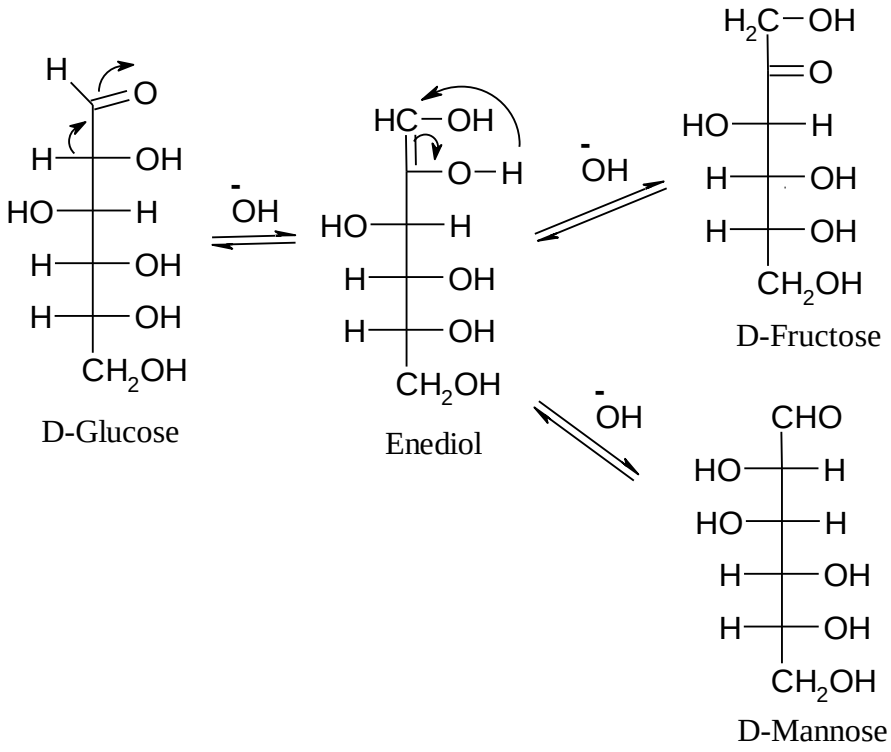
2- **Fehling's reagent (Cu^{++} in aqueous sod. tartrate) produce reddish precipitate of cuprous oxide (Cu_2O).**

3- **Benedict's reagent (Cu^{++} in aqueous sod. citrate) produce reddish precipitate of cuprous oxide (Cu_2O).**

All aldoses are reducing sugars because the hemiacetals are in equilibrium with the free aldehydes, which are known as good reducing compounds. However, some ketoses (hemiketals) are reducing sugars, too. In fact D-fructose is a good example, which reduces Tollen's, Fehling's and Benedict's reagents. It is believed that fructose is smoothly isomerized to an aldose in the basic solution through a series of keto-enol tautomeric steps. The obtained aldose would be readily oxidized.

ALKALINE ISOMERIZATION OF MONOSACCHARIDES:

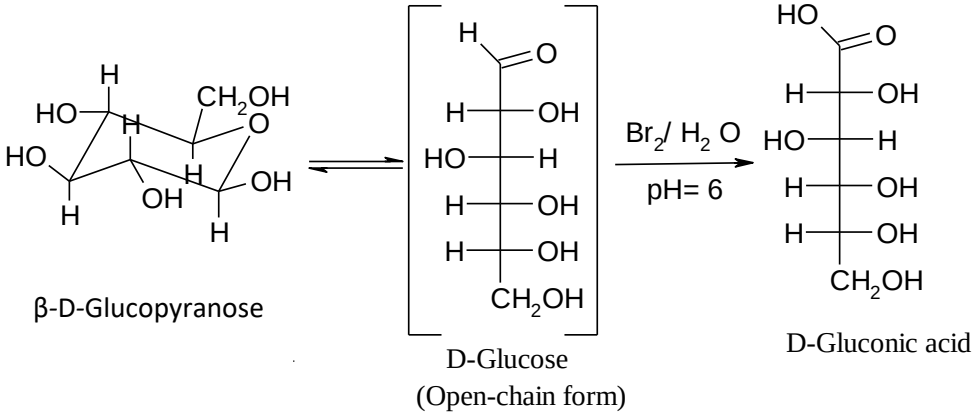
The isomerization of glucose to fructose can be achieved by alkaline treatment, but a variety of other isomeric and decomposition products can be obtained. Thus, treating D-glucose with NaOH, the unstable enediol is formed. In the obtained intermediate the stereochemistry of C-2 is no longer exist. The enediol can then revert back to any of the three more stable hydroxy carbonyl compounds, Scheme.



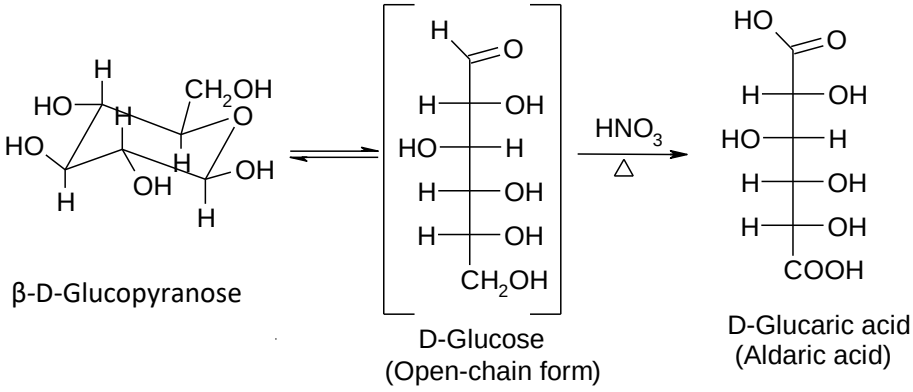
Scheme

However, the interconversion of glucose and fructose in *vivo* is an enzyme catalyzed process, which plays a key role in carbohydrate metabolism in living organisms.

A buffered solution of aqueous bromine oxidizes aldoses to monocarboxydic acids called aldonic acids. The reaction is specific for aldoses, whereas ketoses cannot be oxidized by bromine water.



On the other hand, using more powerful oxidizing agent e.g. warm dilute nitric acid, aldoses are oxidized to dicarboxylic acids called aldaric acids. In this reaction both the aldehyde group CHO and the primary hydroxyl group CH_2OH are oxidized.



5-Synthesis and interconversion of the monosaccarides:

A- Conversion of an aldose into the next higher aldose (Chain Lengthening).

1- The Kiliani-Fischer synthesis:

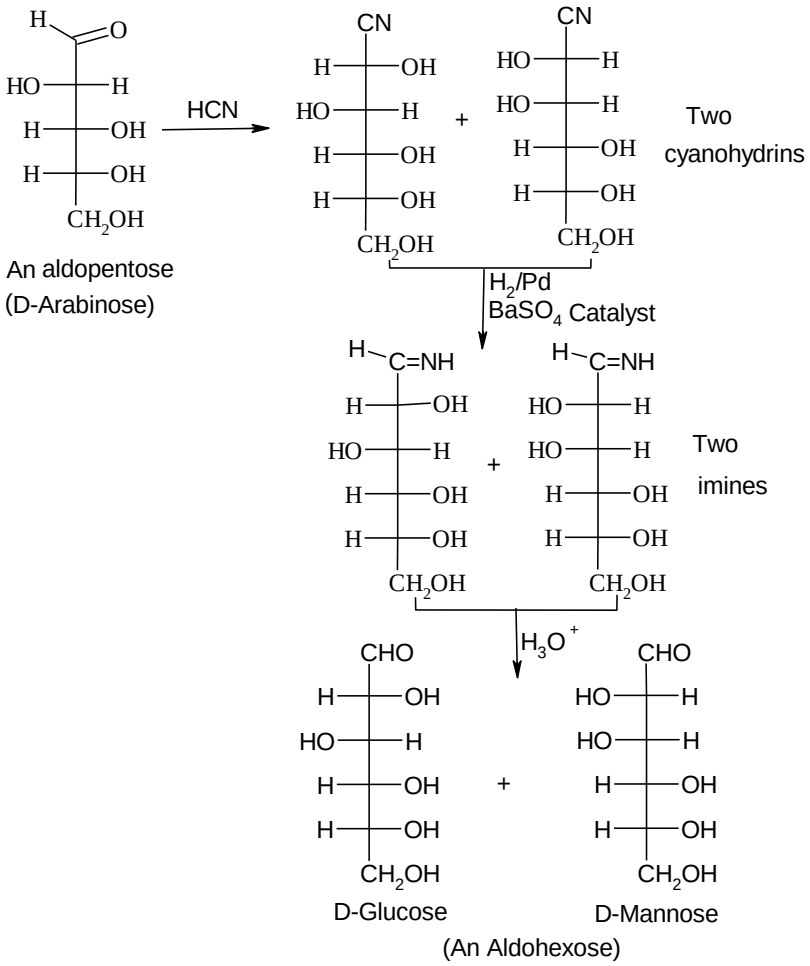
This method is carried out as follows:

a- Aldose reacts with HCN to form two anomers of cyanohydrins (the new obtained carbon is named anomeric atom).

b- Conversion of the nitrile into an imine intermediate by catalytic hydrogenation over a palladium catalyst.

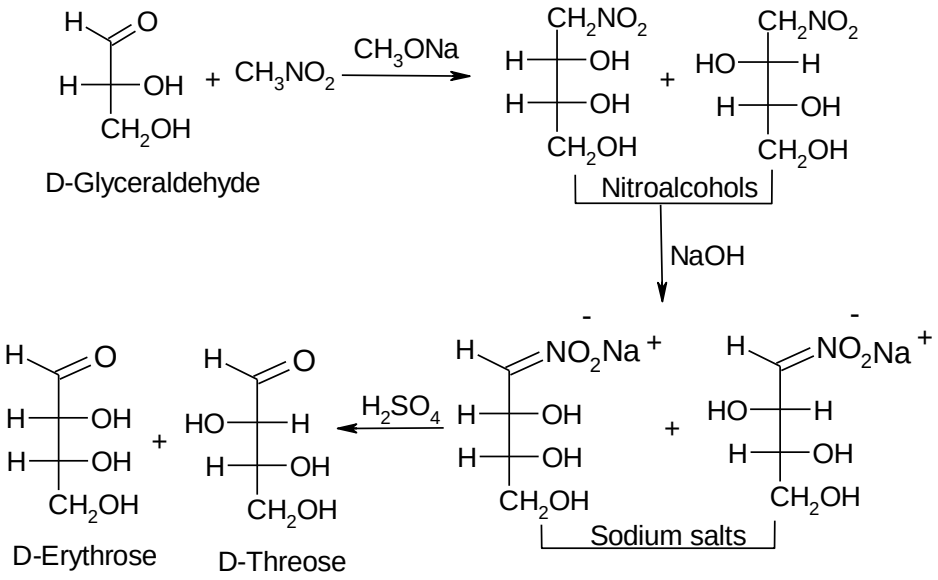
c- Hydrolysis of the intermediate yields an aldehydic group.

Kiliani-Fischer synthesis lengthens an aldose chain by one more carbon. Note that two aldohexoses are obtained with anomeric carbon atom (two anomers).



2- Sowden-Fischer Nitromethane Synthesis:

This is a quite new method, in which an aldose reacts with nitromethane in the presence of a base to produce two different nitroalcohols which can be separated by fractional crystallization. Treating both of the separated nitroalcohols with sodium hydroxide solution form the corresponding sodium salts which after some steps give the higher aldoses.



B) Conversion of an aldose into the next lower aldose (Chain Shortening):

1- The Wohl Degradation:

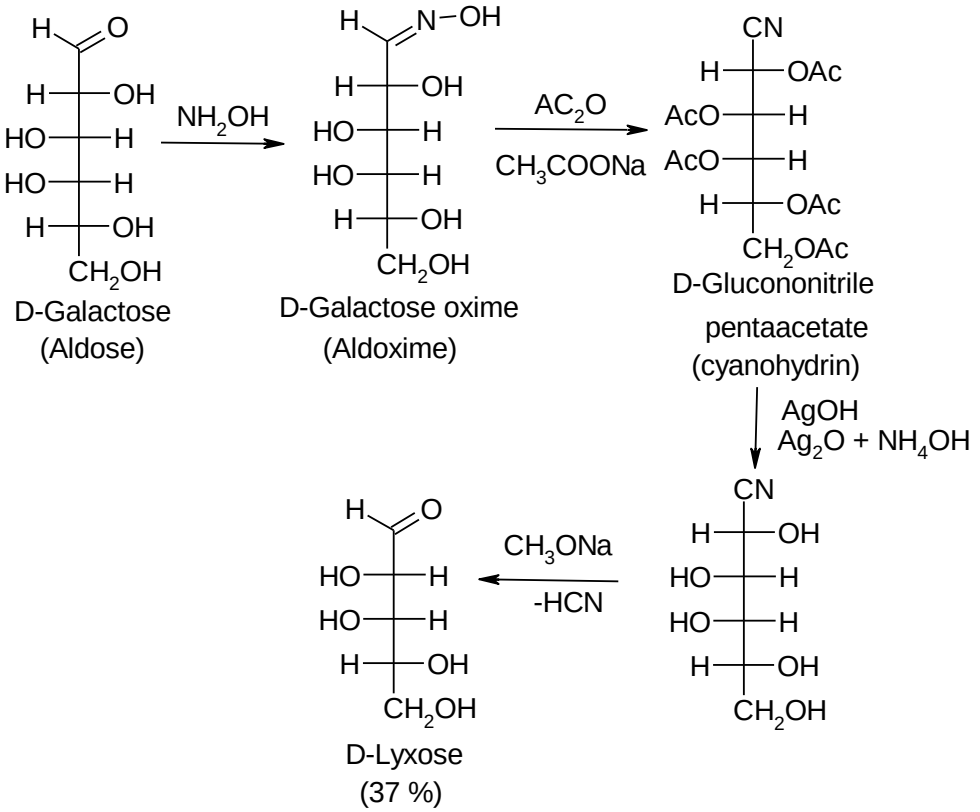
This degradation occurs as follows:

a- An aldehydose reacts with hydroxylamine to give an oxime.

b- The obtained oxime reacted with Ac_2O in the presence of a base (CH_3COONa) to give the cyanide derivative, which, on the treatment with a mixture of $Ag_2O + NH_4OH$ yields a cyanohydrin derivative.

c- The resulting cyanohydrin loses HCN under basic conditions (a retro nucleophilic addition reaction) to give an aldehyde with one carbon atom less.

So that Wohl degradation shortens an aldose chain by one carbon atom. It must be clear that only one aldose is obtained. The stereogenic center is lost and the rest of the chiral centers stayed unchanged.



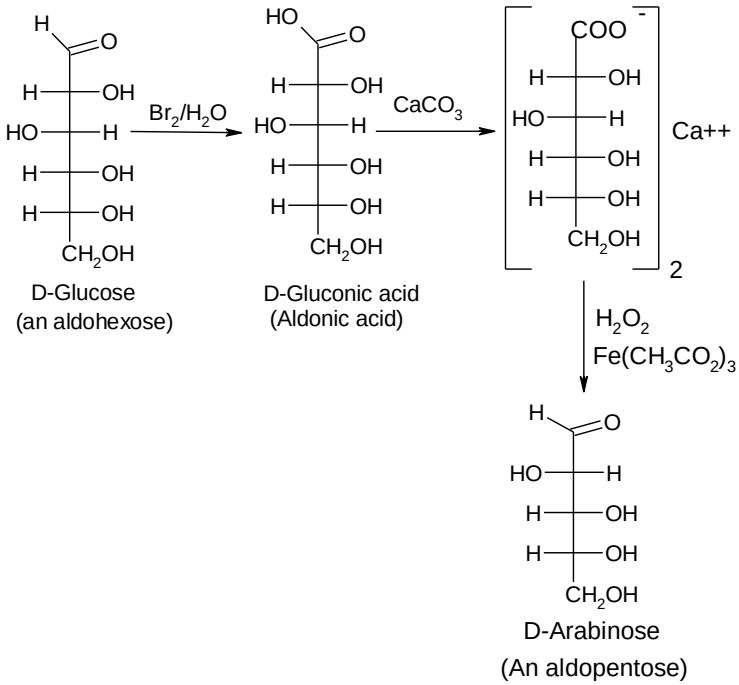
2- Ruff's Method:

In this method:

1- The aldose is oxidized with bromine water to give the corresponding aldonic acid.

2- The aldonic acid is next treated with calcium carbonate to give the calcium salt.

3- The obtained calcium salt is then treated with hydrogen peroxide and ferric acetate (Fenton's reagent), by which CO_2 and H_2O are eliminated to give the lower aldose.



C) Conversion of an aldose into the next higher ketose:

Wolfrom's method:

In this method:

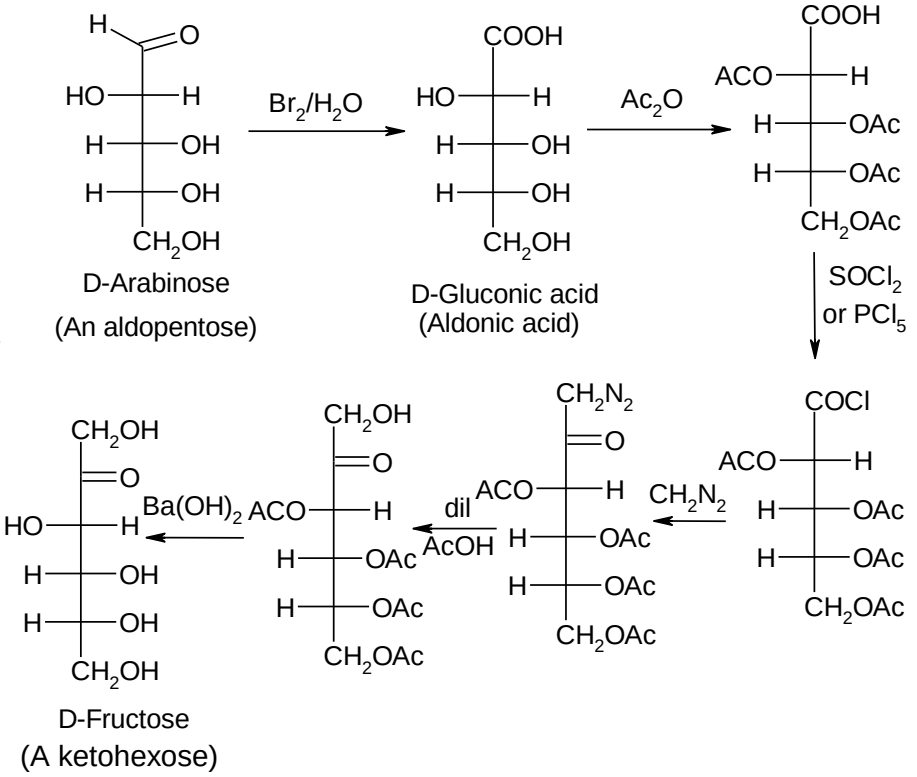
1- **Aldose reacts with Br_2/H_2O to give aldonic acid.**

2- **Acetylating the aldonic with acetic anhydnide to form the acetylated compound.**

3- The acetylated aldonic acid is treated with $SOCl_2$ or PCl_5 to give the corresponding acid chloride.

4- Treatment of the obtained acid chloride with diazomethane followed by heating with aqueous acetic acid.

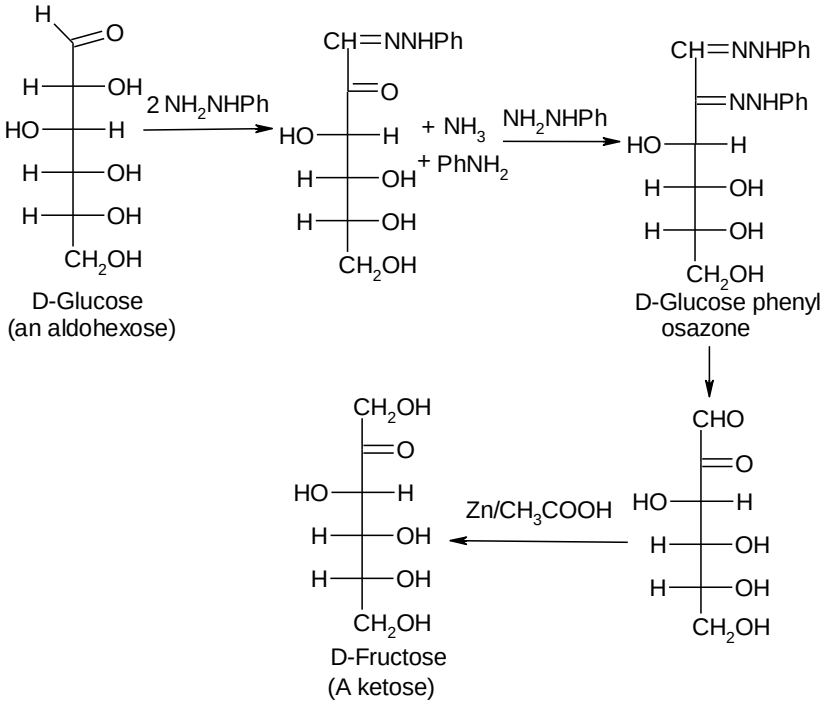
5- Deacetylation by alkaline hydrolysis gives the next higher ketose.



D) Conversion of an aldose into the corresponding ketose:

This conversion can be done by the following.

a- The aldose reacted with excess of phenyl hydrazine to give the corresponding osazone.



b- Hydrolysis with HCI to give the osonzonee which is then reduced with zinc and glacial acetic acid to give the corresponding ketose

<u>E) Conversion of the ketose into the corresponding aldose:</u>

This conversion can be done by the following procedure:

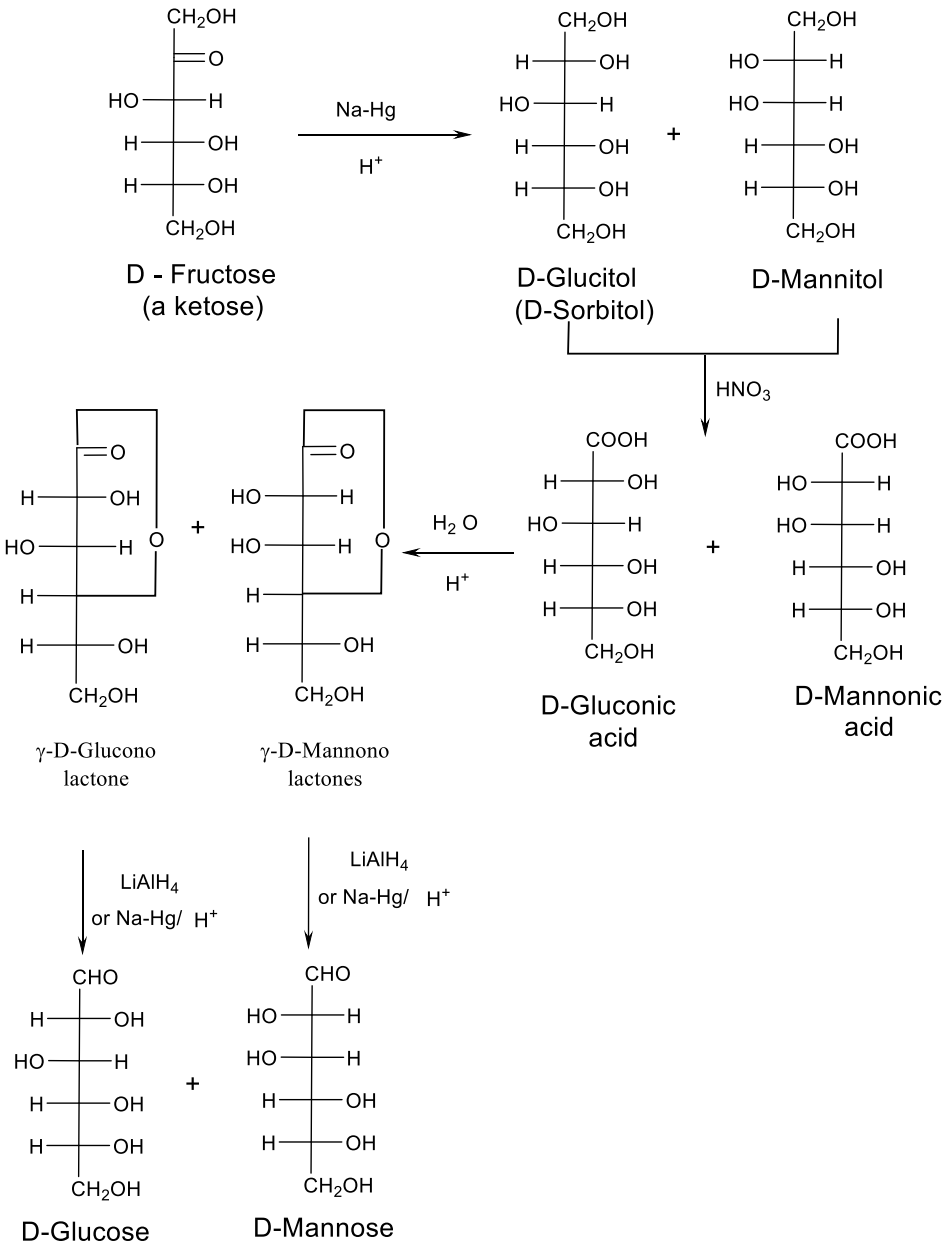
1- Reducing a ketose with sodium amalgam in the presence of a trace of acid forms two anomers of polyhydric alcohol.

2- Oxidation of the obtained alcohols by nitric acid gives monobasic aldonic acids.

3- Treating the aldonic acids with dilute HCI gives γ-lactones.

4- Fractional crystallization of the obtained γ-lactones afforded the pure isomers.

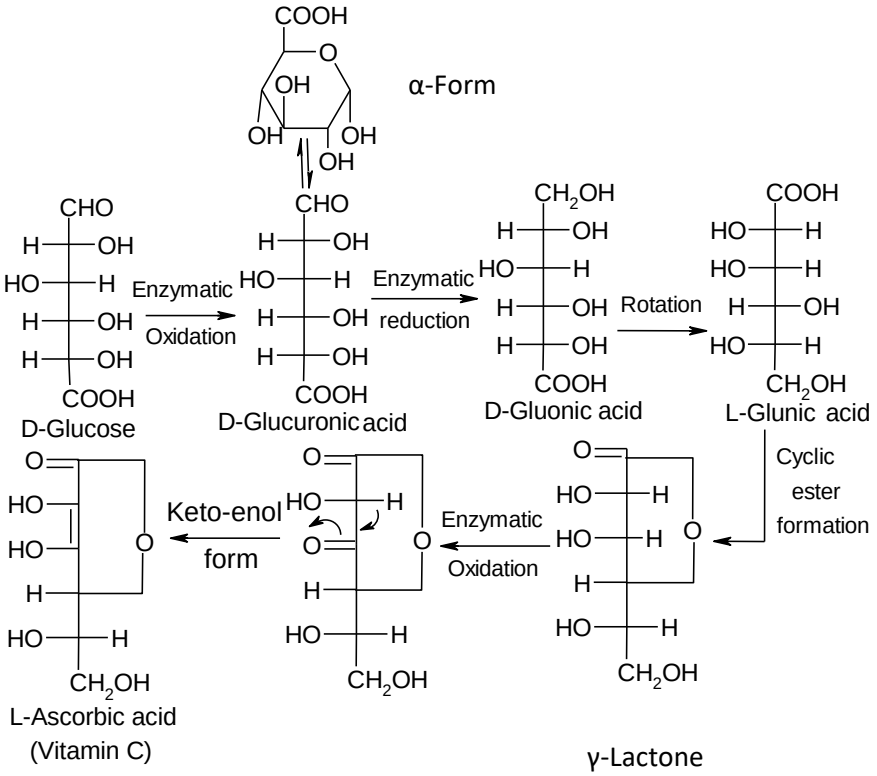
5- The pure individual γ-lactones are then reduced with lithium aluminum hydride or sodium amalgam in a solution of a weak acid to yield two aldoses which are isomeric with the original ketose.


Na-Hg
H+
D - Fructose
(a ketose)
D-Glucitol
(D-Sorbitol)
D-Mannitol
HNO3
H2 O
H+
D-Gluconic
acid
D-Mannonic
acid
γ-D-Glucono
lactone
γ-D-Mannono
lactones
LiAlH4
or Na-Hg/ H+
LiAlH4
or Na-Hg/ H+
D-Glucose
D-Mannose

OPTIONAL MATERIAL

The bio synthesis of vitamin C:

Ascorbic and glucuronic acids are very important for human beings. Ascorbic acid is commercially named Vitamin C, which is widely distributed in nature, especially, in green plants. It functions as a biological oxidation-reduction reagent, and acts as a hydrogen carrier.



Enzyme oxidation of D-glucose gives glucuronic acid, in which the primary hydroxyl group of glucose has been oxidized to a carboxylic acid while the aldehyde group remains intact. Glucuronic is a major building block in many naturally occurring polysaccharides.

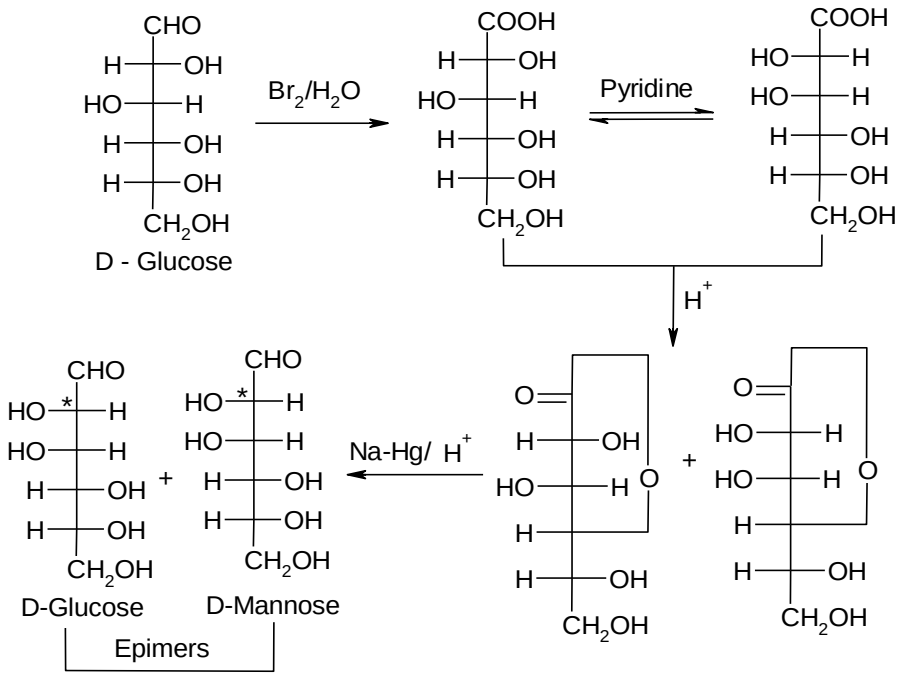
F) Conversion of an aldose into its epimeric aldose (Epimerisation):

This conversion can be done by the following steps:

a- Oxidation of an aldose by Br_2-H_2O gives an aldonic acid.

b- The obtained aldonic acid is heated in pyridine or quinoline to give an equilibrium mixture of the original acid and its isomer at C_2.

c- The obtained aldonic acids are converted into lactones, which then seprated. The pure lactones are reduced to give an aldose and its epimer at C_2.

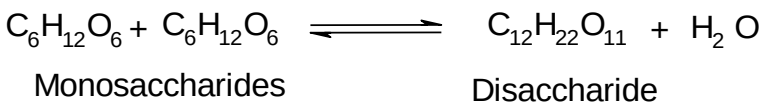


Such change of configuration at one asymmetric carbon atom in a compound containing two or more asymmetric carbon atom is know as epimerization.

Chapter 4

Disaccharides

The di sacchareaction are formed from two primarsaccharides. A reaction occurs between the hydroxyl group of one monosaccharide molecule, which acts as alcohol, with the hemiacetal group of a second monosaccharide, yields a glycoside compound, called a disaccharide. The obtained compound is in fact acetal, formed from two molecules of monosaccharides by the elimination of one molecule of water. On the other way round, hydrolysis of a disaccharide by water in the presence of an acid or by enzymes or under acidic conditions yields two molecules of monosaccharides.



The disaccharides are carbohydrates that are made of two units of monosaccharides. As mentioned above hydrolysis a molecule of disaccharide yields two molecules of monosaccharides. The general formula of disaccharides is $C_nH_{2n-2}O_{n-1}$.

The most common disaccharides are:

1- (+) – Sucrose (Can or beet sugar)

2- (+) – Lactose (Milk sugar)

3- (+) – Maltose (Malt sugar)

4- (+) - Cellobiose.

During this study we will focus our attention on the structure of the disaccharides, and how the monosaccharides are attached to each other, as well as studying the properties of the disaccharides.

Sucrose

(Cane sugar or Beet sugar $C_{12}H_{22}O_{11}$)

The most important disaccharide, which is known as the table sugar and it is part of the diet of human beings in every single day.

Occurrence:

Sugar cane (16 - 20%) Sugar beets (10 - I5%)

Pineapples (10 - 12%)

Maple sap (2 - 4%)

It is present in apricot, banana, mango. Almonds, Café, and honey.

Structure Determination of Sucrose:

The structure of sucrose has been deduced according to the following steps:

1- **Elemental analysis and molecular weight determination showed that the molecular formula of sucrose $C_{12}H_{22}O_{11}$.**

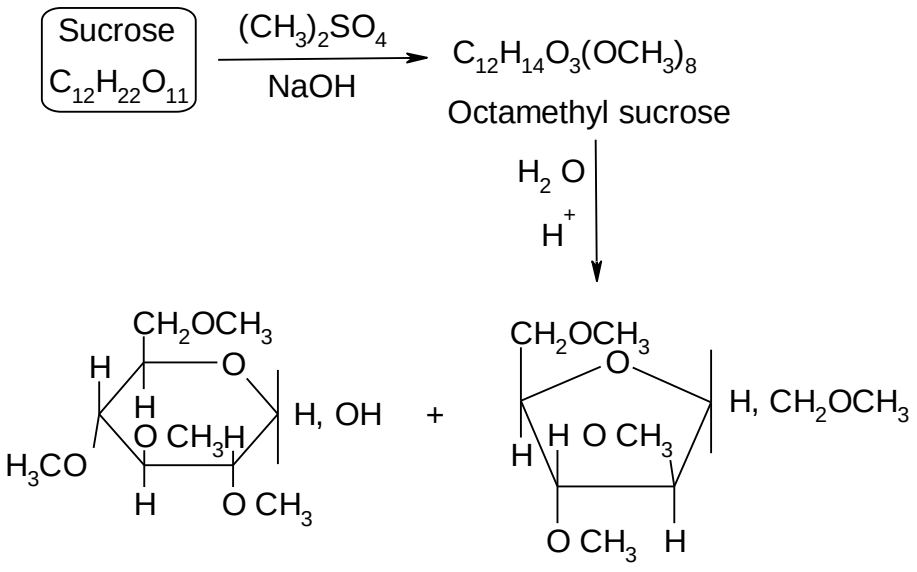
2- **Sucrose reacts with acetic anhydride in the presence of sodium acetate to form sucrose octaacetate. This indicates the presence of eight hydroxyl groups in a sucrose molecule.**

3- **Hydrolysis of sucrose under acidic conditions gives an equimolecular mixture of D-glucose and D-fructose, which**

indicates that sucrose molecule is made up of one unit of D-glucose and one unit D-fructose.

4- Sucrose is a reducing sugar as it does not reduce Tollen's reagent or Fehling's solution. It does not also form an osazone (except on boiling for a prolonged time, in fact sucrose would be acid hydrolyzed to give the two units of monosaccharides, which form the corresponding osazones). It does not react with methyl alcohol to form methyl glycosides. Moreover, it does not undergo mutarotation. Such observations indicate that the cyclic forms of glucose and fructose are joined together through a glycosidic linkage between the two hemiacetalic groups at C-1 in D-glucose and C-2 in D-fructose.

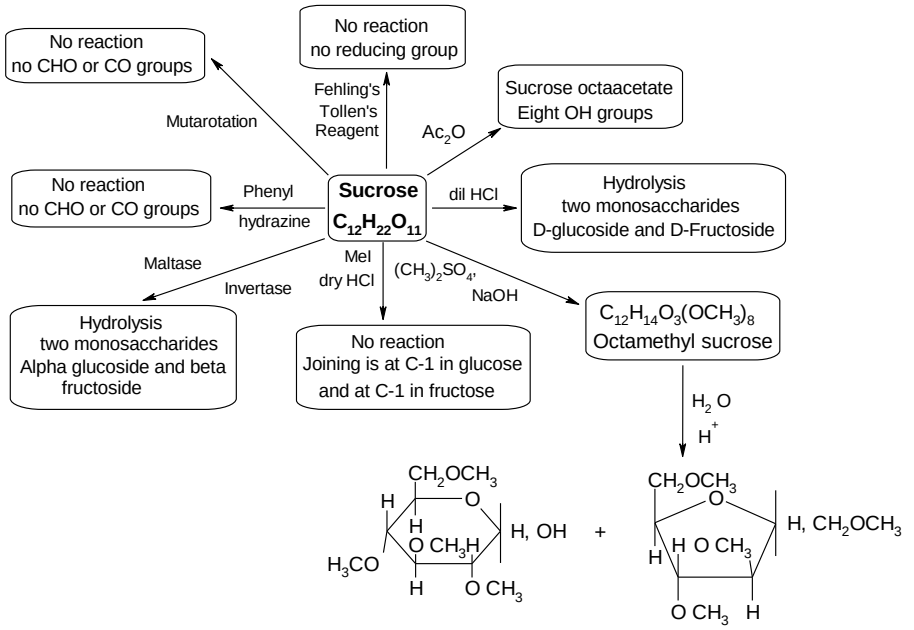
5- The reaction of sucrose with dimethyl sulphate in an alkaline medium formed octamethyl sucrose which on hydrolysis yields a mixture of 2, 3, 4, 6-tetramethyl-D-glucopyranose and 1, 3, 4, 6-tetramethyl-D-fructofuranose. The formation of such compounds indicates that the D-glucose unit in sucrose has a pyranose form (6-membered ring), and the D-fructose unit has the furanose form (5-membered ring).



2,3,4,6-Tetramethyl-D-Glucopyranose (α-and β-forms)

1,3,4,6-Tetramethyl-D-fructofuranose furanose (α-and β-forms)

6- Enzymatic hydrolysis of sucrose by maltase, an enzyme that hydrolyses only α-glycosides. Whereas, on the hydrolysis by invertase, an enzyme that hydrolyses β- but not α-fructofuranosides. These observations indicate that sucrose is both an α-glucoside and a β-fructoside.



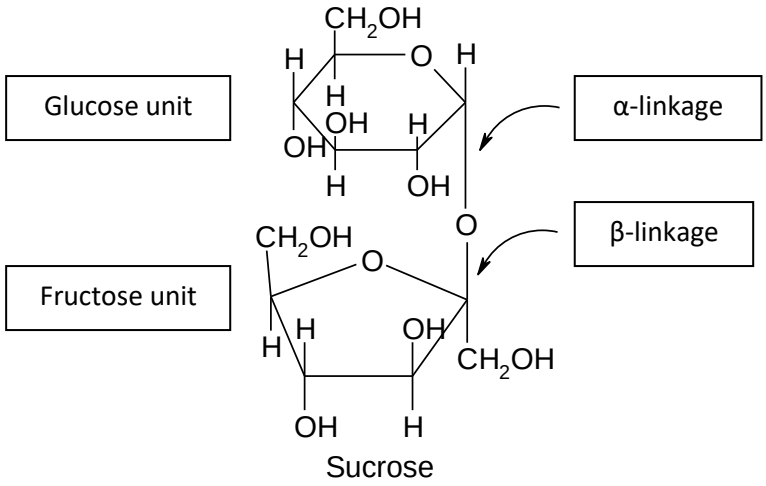
2,3,4,6-Tetra methyl-D-Glucopyranose

(α and β- forms)

1,3,4,6-Tetra methyl-D-fructofuranose

furanose (α and β- forms)

This evidence clearly indicates that (+)-sucrose is made up of a D-glucose unit and a D-fructose unit and has the following structure.



Physical Properties of Sucrose:

Sucrose is a colourless and odourless, crystalline solid, m.p. 184-5 ºC. It is very soluble in water, whereas slightly soluble in ethyl alcohol. The aqueous solution of sucrose is dextrorotatory ([α] = +66.5º) and does not exhibit mutarotation.

Chemical properties of Sucrose:

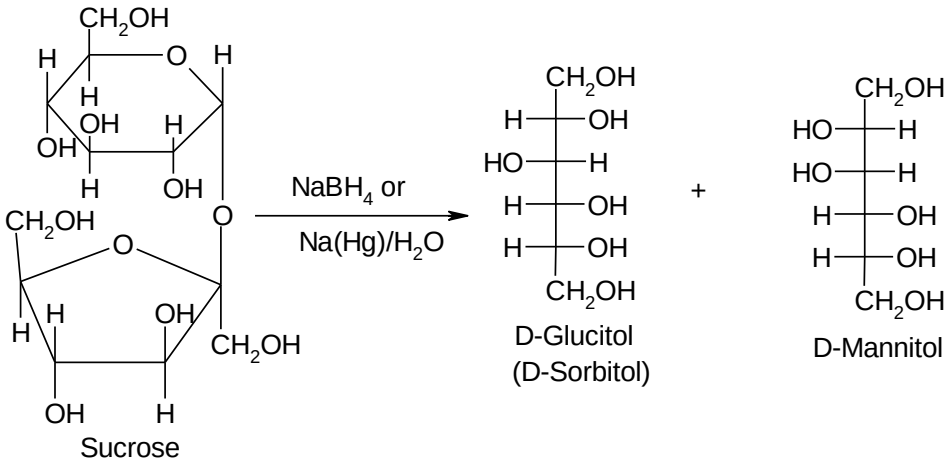
Ssucrose is not a reducing sugar due the absence of a free carbonyl group, and for this reason it does not react with TolIen's reagent and Fehling's solution, hydrogen cyanide, hydroxylamine or phenyl hydrazine. However, it gives the following reactions.

(1) Effect of Heat:

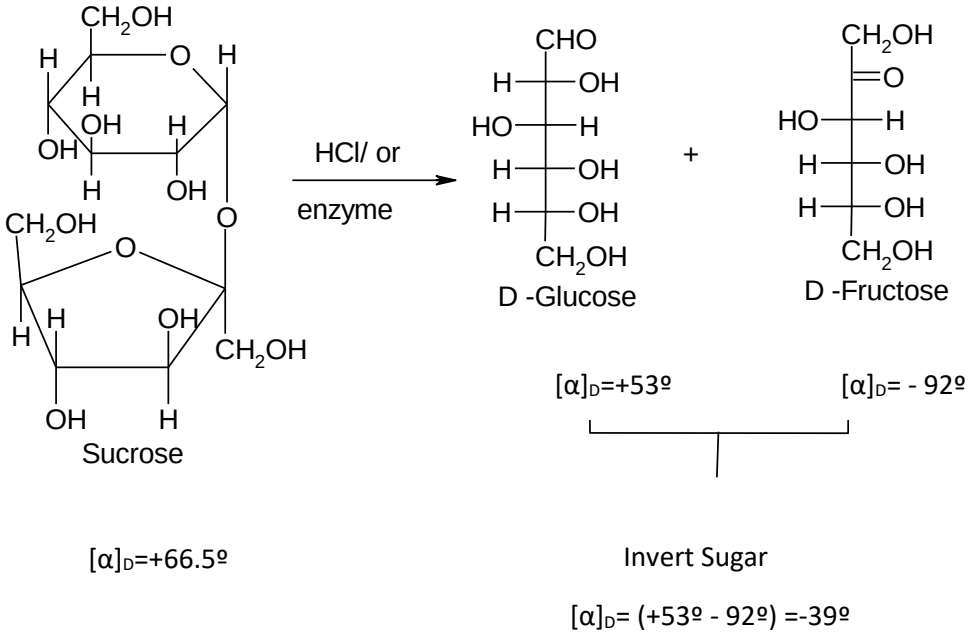
When sucrose is heated to 210ºC it forms a brown mass known as Caramel. Caramel has a characteristic colour and flavour, and it is used as colouring and flavouring material in foods and candies. At higher temperatures sucrose chars to almost pure carbon and gives vapours of many different decomposition products, e.g. carbon dioxide, carbon monoxide methane, ethylene, acetylene, acetone, formic acid, acetic acid, ethanal, and acrolein.

(2) Oxidation: reacting sucrose with concentrated nitric acid forms a mixture of oxalic acid, tartaric acid and D-glucanic acid.

(3) Reduction (Hydrogenation): sucrose reacts with sodium borohydride or sodium amalgam in water under controlled conditions affords a mixture of D-sorbitol and D-mannitol.



(4) <u>Acid Hydrolysis</u> (Invert Sugar or Invertose): reacting sucrose with hot dilute acid gives D-glucose and D-fructose.

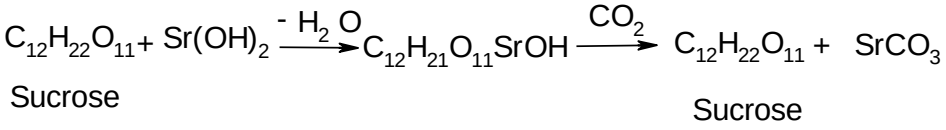


Sucrose is dextrorotatory, its specific rotation is + 66.5º and D-glucose is also dextrorotatory, $[\alpha]_D$ = +53º but D-fructose has a large negative

rotation, $[\alpha]_D$ = - 92º. Since D-fructose has a greater specific rotation than D-glucose, so the resulting mixture is laevorotatory (- 39º).

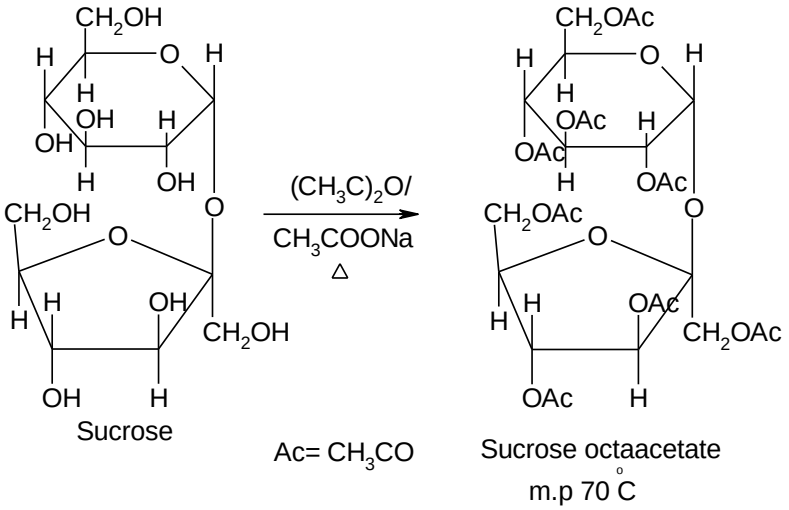
Since sucrose under acid hydrolysis gives equimolecular ratio mixture of glucose and fructose, and the sum of their specific rotation of the plane of polarized light seems to be a levorotatory. Because of this phenomenon sucrose is known as invert sugar or invertose. However, such inversion (hydrolysis) of sucrose can also be done by *invertase* enzyme, which is found in yeast.

(5) <u>Reaction with metallic hydroxides</u> (Formation of sucrosates). Sucrose in aqueous solution reacts with hydroxides of calcium strontium, and barium to yield insoluble products called sucrosates. These compounds are readily decomposed when carbon dioxide is passed into their aqueous suspensions. The strontium compound in particular is used for isolating pure sucrose from crude molasses, as presented in the following equation:



(6) <u>Reaction with acetic anhydride in basic medium (acetylation):</u>

Sucrose reacts with acetic anhydride in the presence of sodium acetate to form sucrose octaacetate. However, it also reacts readily with a mixture of acetic anhydride and pyridine to afford the same product.



(7) <u>Fermentation.</u>

Invertase enzyme (present in yeast) causes fermentation of an aqueous solution of sucrose to yield ethyl alcohol. The process occurs in two steps, in the first step invertase enzyme converts sucrose into mono saccharides (glucose and fructose). Such obtained monosaccharides are then decomposed by zymase enzyme (also present in yeast) to give ethyl alcohol and carbon dioxide according to the following equation:

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

$$\underset{\text{Glucose or Fructose}}{C_6H_{12}O_6} \xrightarrow{\text{zymase}} 2\,C_2H_5OH + 2\,CO_2$$

Lactose

(milk sugar $C_{12}H_{22}O_{11}$)

Occurrence:

Lactose is produced in the milk of mammals, for example:

Caw's milk contains 4 to 6%.

Human milk contains 5 to 8%.

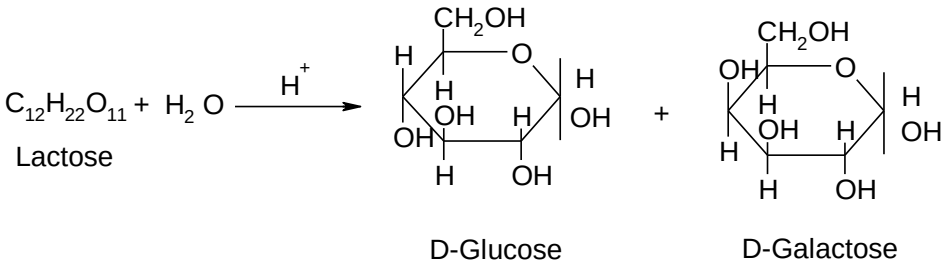
Structure deternination of lactose:

The structure of lactose can be derived as follows:

1- **Elemental analysis and molecular weight determination show that the molecular formula of lactose is $C_{12}H_{22}O_{11}$.**

2- **Reacting lactose with a mixture of acetic anhydride and sodium acetate gives lactose octaacetate, This result means the presence of eight hydroxyl groups in the lactose molecule.**

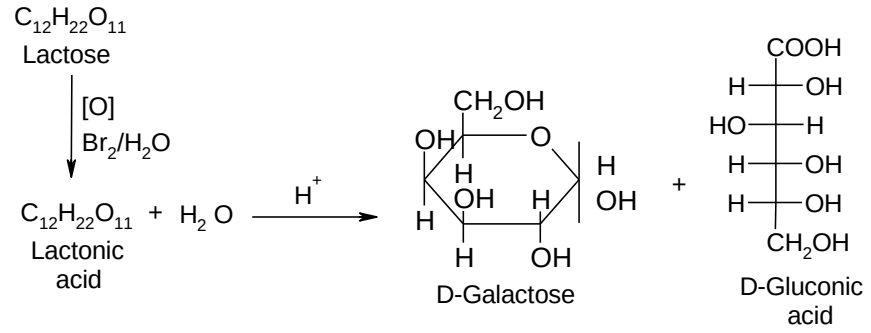
3- **Acid hydrolysis of lactose yields an equimolecular mixture of D-glucose and D-galactose, which indicates that the lactose molecule is made up of those two monosaccharides.**



4- **Lactose is a reducing sugar, as it reacts with Tollen's reagent and Fehling's solution to give the corresponding results. It also reacts with hydrogen cyanide and forms the corresponding osazone. All of these reactions indicate that at least one free hemiacetal group must be present, and this is in equilibrium with the free aldehyde (the open form).**

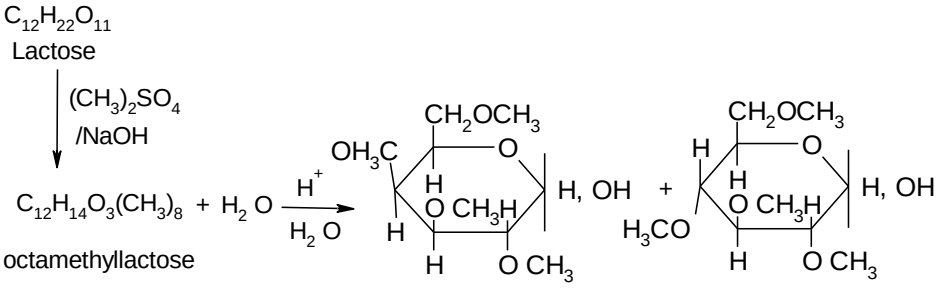
5- **Depending on the way of crystallization Lactose can be isolated in two crystalline forms. If it is recrystallised from a concentrated aqueous solution at ordinary temperatures, the □-form of the sugar is obtained. Its melting point is 223ºC and the specific rotation is +90º. However, if lactose is crystallized from water at temperatures higher than 95ºC, the β-form is isolated: its melting point is 252ºC and the specific rotation is +35º, both α- and β-forms exhibit mutarotatlon until an equilibrium value of +55º is reached. These results confirm the presence of the equilibrium between the two hemiacetal groups and the free aldehyde.**

6- **Furthermore, oxidation of lactose with bromine water gives lactonic acid, which on hydrolysis yields a mixture of D galactose and D gluconic acid. This result confirms that the glucose unit contains the hemiacetal-aldehyde group.**



Galactose (α and β-forms)

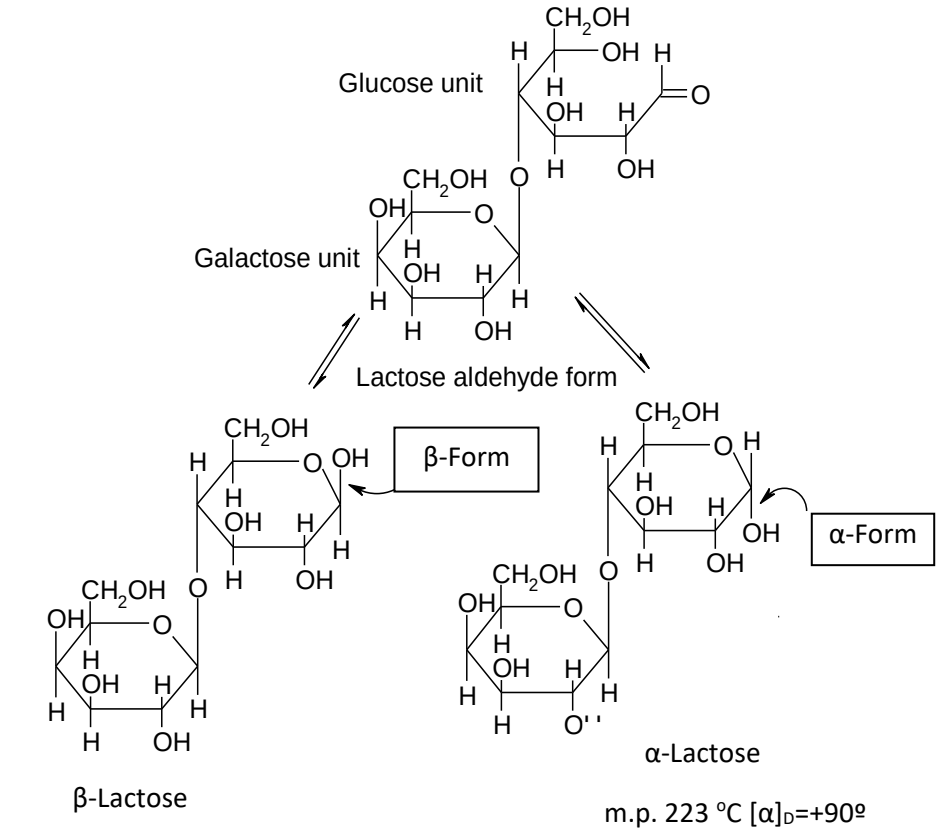
7- Lactose reacts with dimethyl sulphate in the presence of NaOH to form octamethyl lactose, which on hydrolysis gives 2,3,4,6-tetramethyl-D- galacose (α and β-forms) and 1,2,3,6-tetramethyl-D- glucose (α and β-forms).



2,3,4,6-Tetramethyl-D-Galactose (α and β-forms)

1,2,3,6-Tetramethyl-D-Glucose (α-and β-forms)

8- Lactose is also hydrolyzed by an enzyme that hydrolyses only β-glycoside linkage. This result confirms that the the two units are connected through the hemiacetalic hydroxyl group in β-galactose and the hydroxyl group at C4 in the glucose unit. According to the above results lactose must have the following structure.



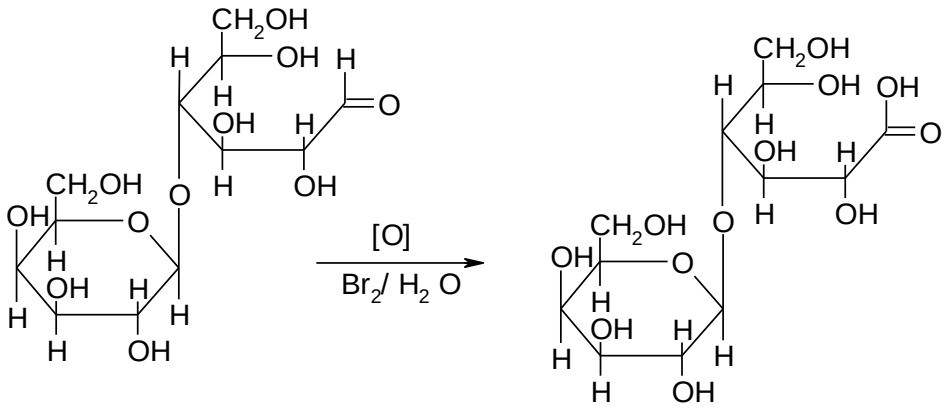
Properties of Lactose:

Physical properties: Lactose (α-form, [α] = +35º) is a colourless, odourless, crystalline solid melts at 223ºC (with decomposition). It is soluble in water, but insoluble in alcohol and ether, whereas (β-form, [α] = +90º) melts at 252ºC. However, an aqueous solution of lactose is dextrorotatory and exhibits mutarotation.

Chemical properties:

Lactose is a reducing sugar, as it reduces Fehling's solution and Tollen's reagent. Its reactivity is mainly attributed to the presence of the hemiacetal function in the glucose unit, which would be in equilibrium with the free aldehyde. Some of the chemical reactions of lactose are summarized as follows:

(1) Oxidation: lactose is oxidized by bromine water to yield a monocarboxylic acid called lactonic acid.

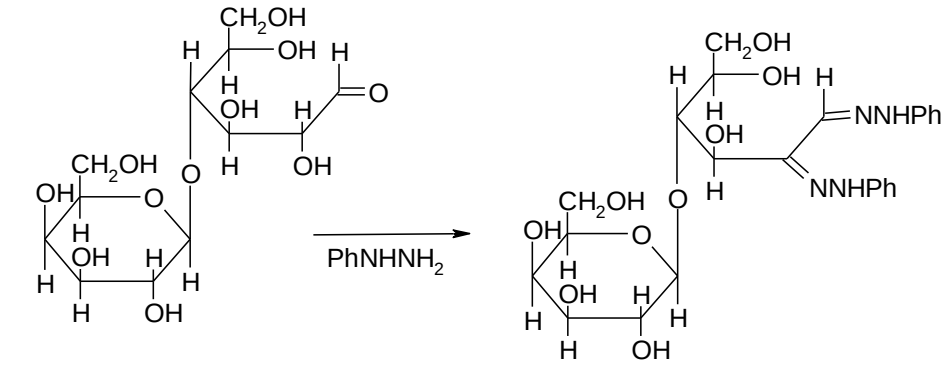


Lactose aldehyde form

Lactonic acid

2- Hydrolysis: lactose reacts readily with hot dilute acid or by the enzyme emulsion, yields an equimolar mixture of D-galactose and D-glucose.

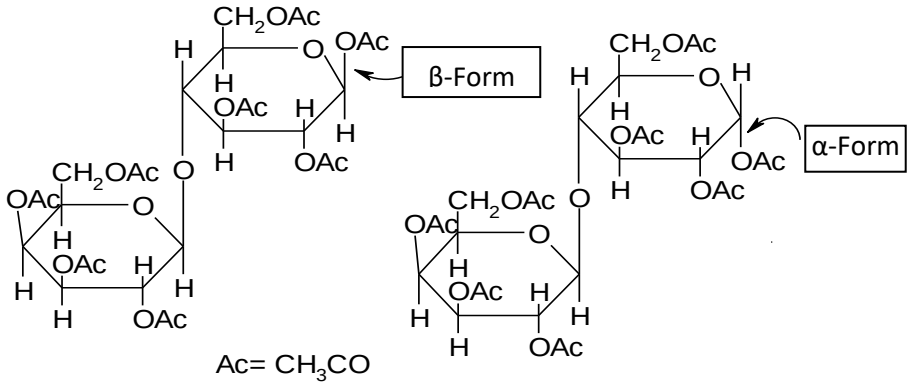
(2) Reaction with phenyl hydrazine: (Osazone formation) Heating lactose with excess of phenyl hydrazine in the presence of acetic acid affords the corresponding osazone.



Lactose aldehyde form

Lactosazone
(Lactose phenylosazone)

(3) <u>Acetylation</u>: Lactose reacts with acetic anhydride in the presence of sodium acetate to form two isomenic octaacetates. In solution, both α- and β-forms of lactose are in equilibrium and each reacts in turn to yield the corresponding two different isomers.



β-Lactose octaacetate

m.p. 90°C; $[\alpha]_D$=-4º

α-Lactose octaacetate

(4) Fermentation.

Some bacteria affect lactose is to produce actic acid, which is responsible for the sour taste of the fermented milk. However, lactose can be also fermented by yeast.

Maltose

(Malt Sugar $C_{12}H_{22}O_{11}$)

Maltose is not obtained naturally in great quantities. It is usually obtained via partial hydrolysis of starch by diastase enzyme (present in malt).

$$\underset{\text{Starch}}{(C_6H_{10}O_5)n} + H_2O \xrightarrow{\text{diastase}} \underset{\text{Maltose}}{C_{12}H_{22}O_{11}}$$

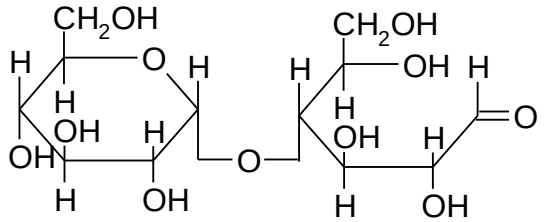
Structure Determination of Maltose:

(1) However, acid hydrolysis of maltose affords D-glucose as a sole product. This result showed that the maltose molecule is made up of two D-glucose units.

(2) Structural studies show that the two glucose units are joined by an α-glycosidic linkage between C-1 of one unit and C-4 of the other one. Maltose also exists as an isomeric mixture of two hemiacetals (*α*- and β- forms). The two hemiacetals are in equilibrium through the free aldehyde and both exhibit, mutarotation. The individual values of specific rotation are:

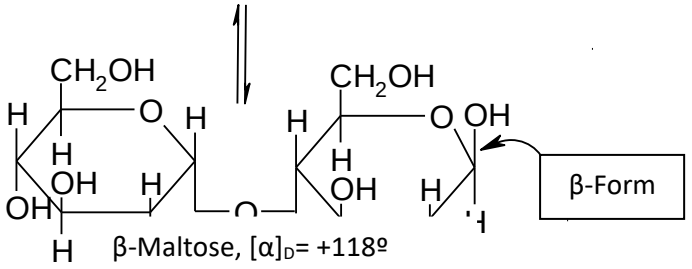
α-Maltose = +168º, β-Maltose = +118º

For equilibrium mixture = +136º

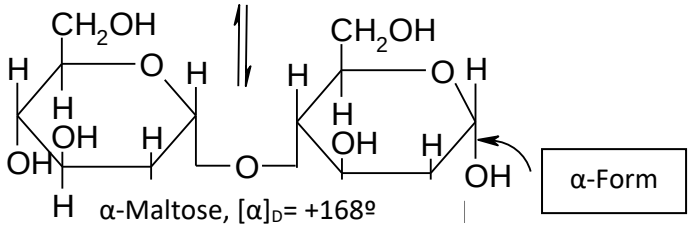


Glucose unit Glucose unit

Maltose aldehyde form



Glucose unit Glucose unit



Glucose unit Glucose unit

Properties of Maltose:

Physical properties: Maltose (β-form) is colourless crystalline solid mp l60-165ºC. It is soluble in water, but insoluble in alcohol or ether. An

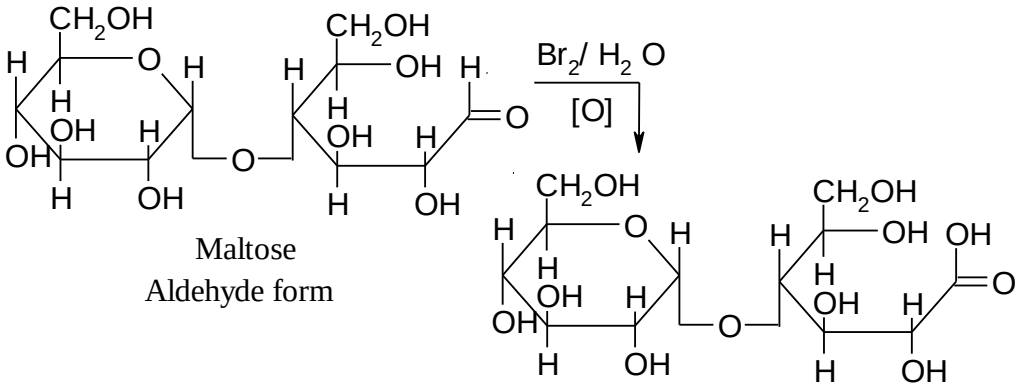
aqueous solution of β-maltose is dextrorotatory $[\alpha]_D$ = +118º and exhibits mutarotation. Whereas α-maltose melts at 240ºC and its aqueous solution is dextrorotatory $[\alpha]_D$ = +168º and also shows mutarotation.

Chemical properties.

Maltose is a reducing sugar due to the presence of a hemiacetal group in one of the glucose units.

(1) Oxidation:

Maltose is readily oxidized by bromine water to afford the monocarboxylic acid called maltonic acid.

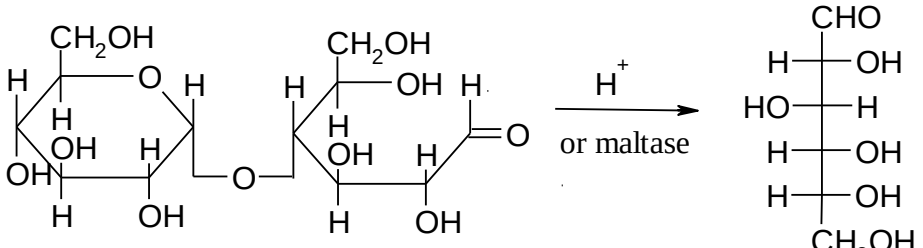


Maltose
Aldehyde form

Maltonic acid
or Maltobionic acid

(2) Hydrolysis:

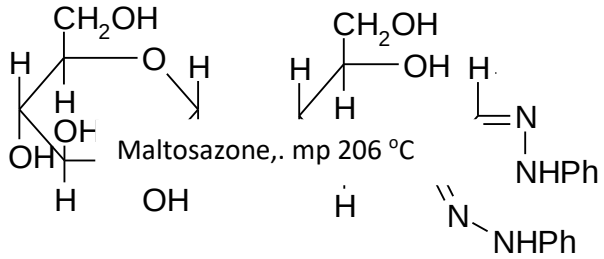
Heating maltose with dilute acids or by maltase enzyme gives D-g]ucose as the only product.



Maltose
aldehyde form

D-Glucose

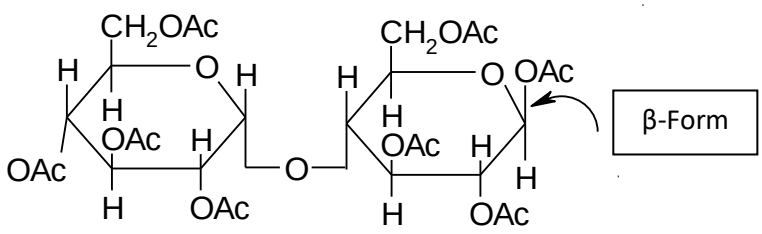
3- Heating an aqueous solution of maltose with excess of phenyl hydrazine in the presence of acetic acid to affords maltosazone, mp 206ºC.



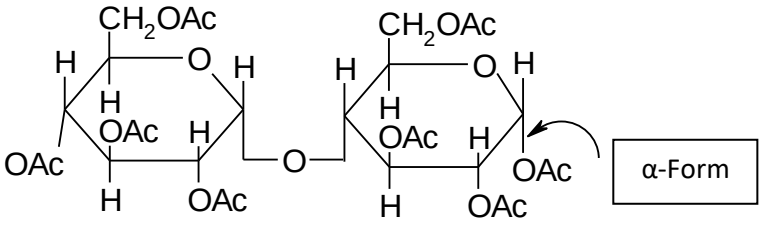
Maltosazone,. mp 206 ºC

3- Acetylation:

Reacting maltose with acetic anhydride in the presence of sodium acetate yields α-maltose octaacetate (mp 125 ºC, [α]D = + 123º) and β-maltose octaacetate (mp 160ºC, [α]D = + 63º).



β-Maltose octaacetate, mp 160°C. [α]D=+63°.



α-Maltose octaacetate, mp 125 °C, [α]D=+123°.

4- **Fermentation.**

Maltose is fermented in the normal way by yeast to give ethyl alcohol and carbon dioxide.

Cellobiose

($C_{12}H_{22}O_{11}$)

Cellobiose is obtainedin from cellulose in two steps: (i) The acetylation of cellulose by acetic anhydride in the presence of sulphuric acid yields cellobiose octaacetate. (ii) Hydrolysis of the obtained cellobiose octaacetate by potassium hydroxide or sodium methoxide affords cellobiose.

Structure Determination of celloblose:

(1) Hydrolysis.

Acid hydrolysis of cellobiose yields only D-glucose, which means that the cellobiose molecule contains two D-glucose units.

(2) Structural studies (cf. sucrose and lactose) confirm that the two D-glucose units are joined through a β-glycosidic linkage between C-1 of one unit and C-4 of the other one. Cellobiose exists in α- and β- forms due to the presence of a hemiacetalic group, which is in equilibrium with the other isomer through the free aldehyde. The two forms are dextrorotatory and both exhibit mutarotation, and the values of specific rotation are:

α-cellobiose = +72° β-cellobiose = +16°

For equilibrium mixture = +35°

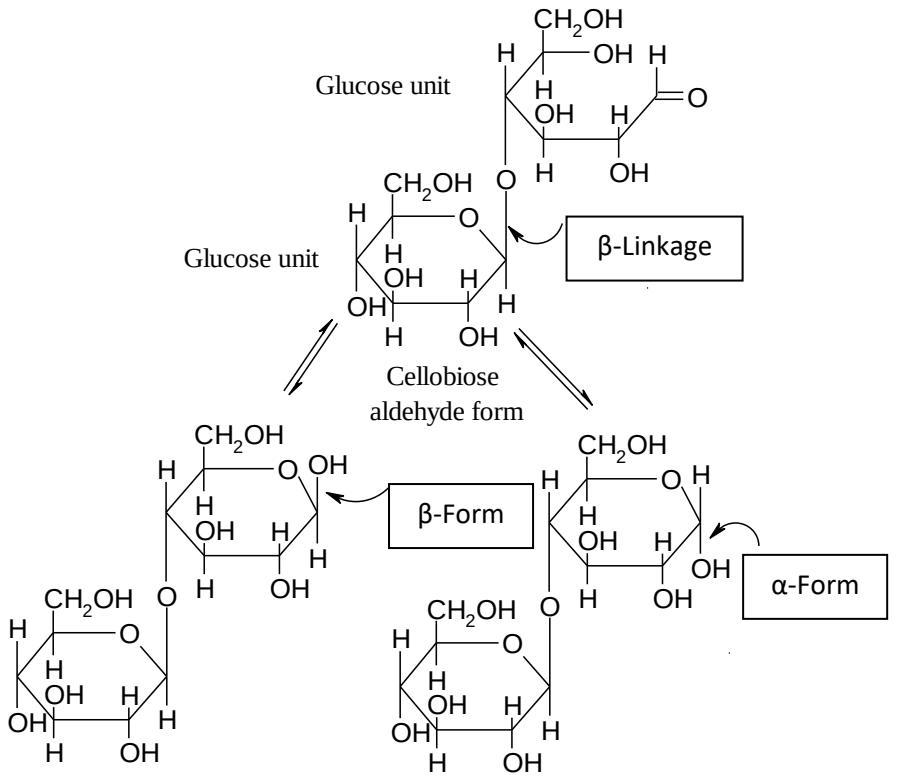
Properties of Cellobiose:

Physical properties:

Cellobiose (β-form) is a colourless, odourless crystalline solid, mp 225ºC. It is soluble in water, but insoluble in ether.

Chemical propertie:

Cellobiose is a reducing sugar, and its reactivity is mainly due to the presence of a hemiacetal group in one of the D-glucose units.



β-Cellobiose, $[\alpha]_D$= +16º

α-Cellobiose, $[\alpha]_D$= +72º

CHAPTER 5

Polysaccharides

Polysaccharides are naturally occurring compounds, in which each molecule consists of many-hundreds or even thousands of monosaccharide units, which are connected together by glycosidic likages. They can be obtained *via* polymerization of aldoses or ketoses. However, polysaccharides are not reducing sugars and do not exhibit mutarotation. Polysaccharides derived from hexoses have the general formula $(C_6H_{10}O_5)_n$.

Starch and cellulose are the most common and important polysaccharides and both are produced in plants from CO_2 and H_2O by the photosynthesis process. Both are made up of units of D-(+)-glucose.

Starch is considered as the food reservoir and is obtained only in seeds. Starch is more easily hydrolyzed than cellulose so they are more readily digested.

The enormous existence of cellulose in nature encouraged chemists to make a very much use of it for the benefit of human beings e.g. the viscose textile industry.

However, both cellulose and starch are highly important.

Starch:

Starch contains about 20% of water-soluble fraction called amylose, and 80% of water insoluble fraction called amylopectin. Starch is readily hydrolyzed under acicdic conditions. Hydrolysis of starch is

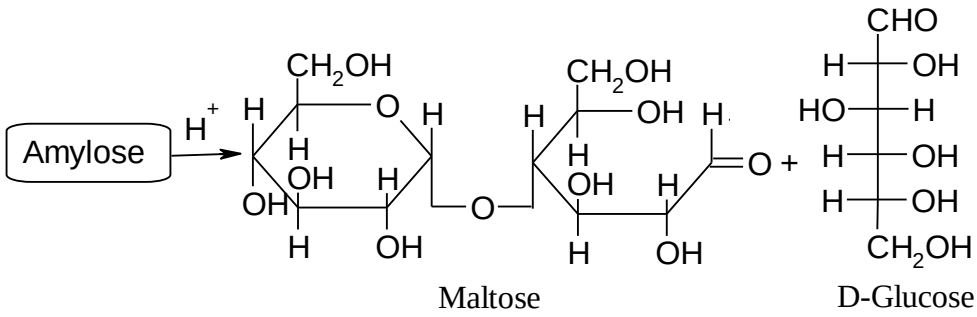
also occurred by the effect of enzymes. It is hydrolyzed first to dextrin (a mixture of low molecular weight polysaccharides), and then (+)-maltose, and fina1ly D-(+)-glucose. Both amylose and amylopectin consist of only D-(+)-glucose units, but the molecular size and shape are different from one another.

Structure of Amylose:

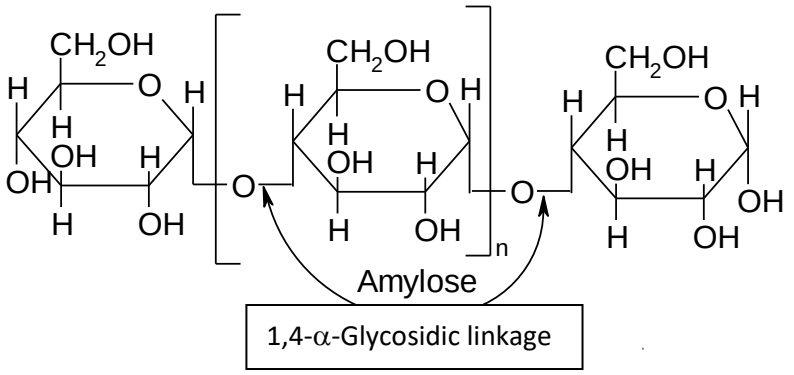
On hydrolysis of amylose yields:

1- (+)-Maltose (the only disaccharide), and

2- (+)-Glucose (the only monosaccharide).

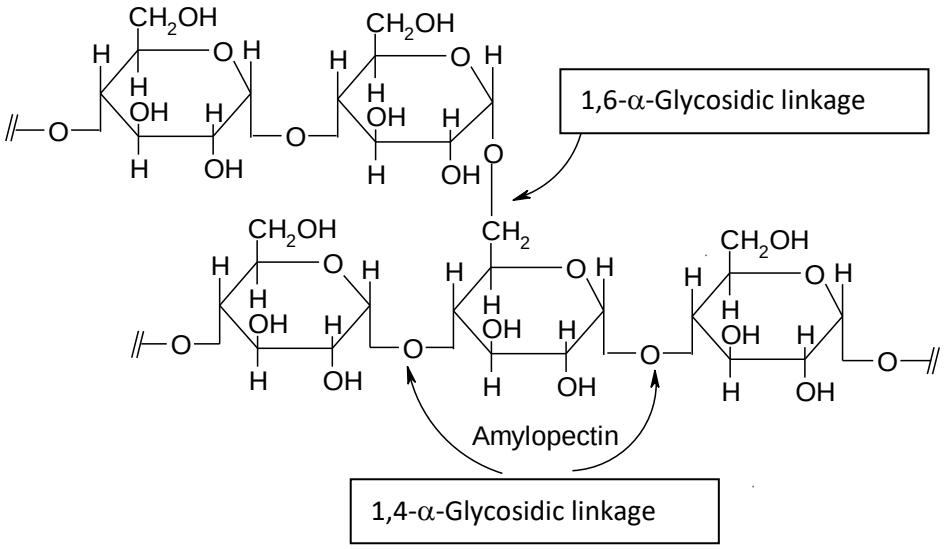


This result shows that D-(+)-glucose units in amylose are connected together by an alpha-glycoside linkage of one unit to C-4 of the next one (cf. maltose).



Structure of Amylopectin:

Amylopectin is a branched chain polysaccharide, which on hydrolysis gives D- (+)-glucose. It is composed of chains of 24 to 30 D-glucose units joined by α-glycosidic linkages between C-1 of one glucose unit and C-4 of the next glucose unit. At the end of each of these chains a glyccosidic linkage is obtained through C-1 to a C-6 on the next chain.

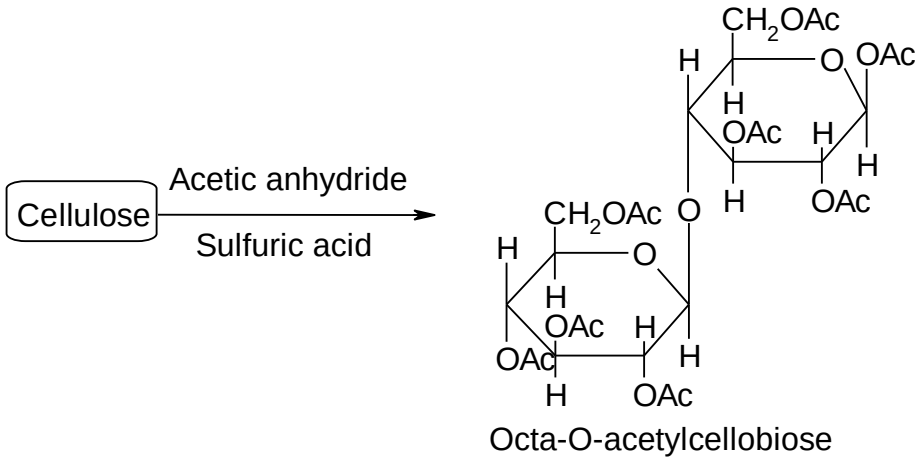


Cellulose

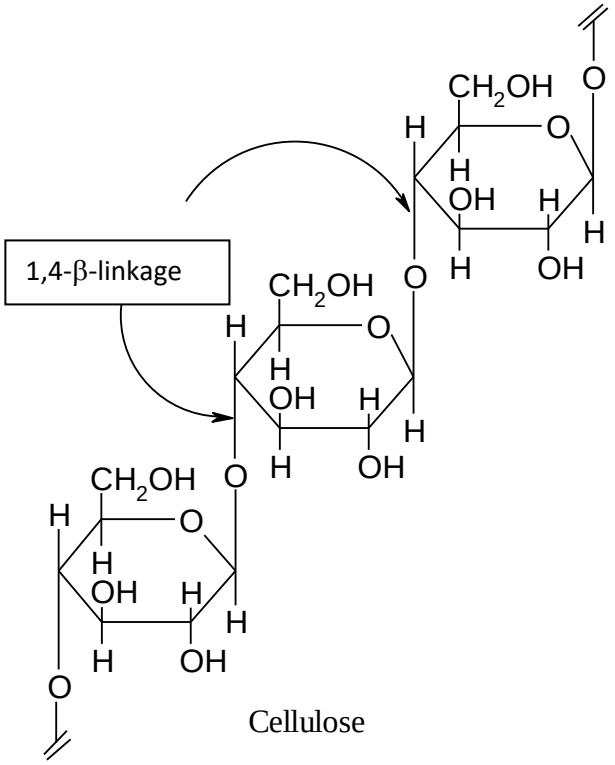
$(C_6H_{10}O_5)_n$

Structure of cellulose:

The glycoside linkage between D-glucose units in cellulose has the β-glycosidic confugration, whereas the glycoside linkage between D-glucose units in starch has the α-gycosidic confugration. Thus, treating cellulose with acetic anhydride in the presence of sulfuric acid, gives only octa-*O*-acetylcellobiose, to confirm that all glycosidic linkages in cellulose are beta linkages.



Octa-O-acetylcellobiose



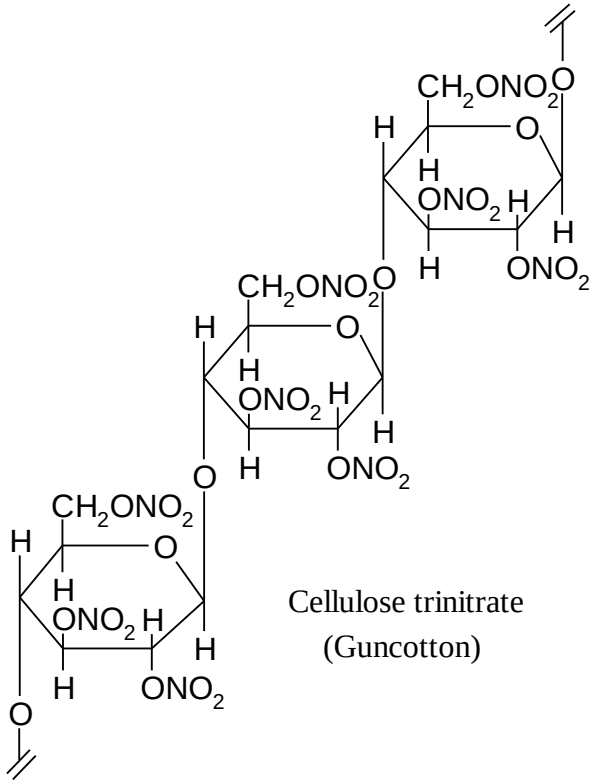
Reactions of Cellulose:

We have seen that the glycoside linkages of cellulose are broken by the action of acid, each cellulose molecule yielding many molecules of D-(+)-glucose. Now let us look briefly at reactions of cellulose in which the chain remains essentally intact. Each D-glucose unit in cellulose contains three free hydroxyl groups (3 OH); these are the positions at which a chemical reaction occurs. These reactions of cellulose are highly important industrialwise.

1- Cellulose nitrate:

Like alcohol, cellulose forms esters. However, treatment with a mixture of nitric acid and sulfuric acid converts cellulose into cellulose nitrate, great precautious must be given for such reaction. It must be noticed that the properties and uses of the product depend upon the extent of nitration. The nitration process is highly dangerous and they cannot be carried out in an ordinary laboratory. In general nitration reactions are highly dangerous and great precautions must be taken in any nitration process.

Guncotton, in which of the -OH groups are replaced by -ONO_2 groups, i.e. each D-glucose unit contains three -ONO_2 groups, and is often named cellulose trinitrate. Guncotton looks something like ordinary cotton but is highly explosive.



Cellulose trinitrate
(Guncotton)

2- Cellulose acetate.

Cellulose is converted into cellulose triacetate by treatment with acetic acid, acetic anhydride and a little amount sulfuric acid.

Part_2

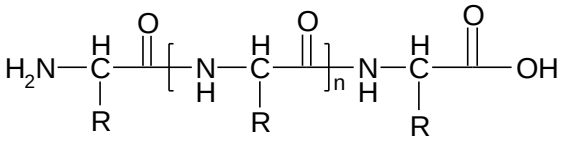
Amino Acids, Peptides and Enzymes

Part_2: Amino Acids, Peptides and Enzymes

1. INTRODUCTION:

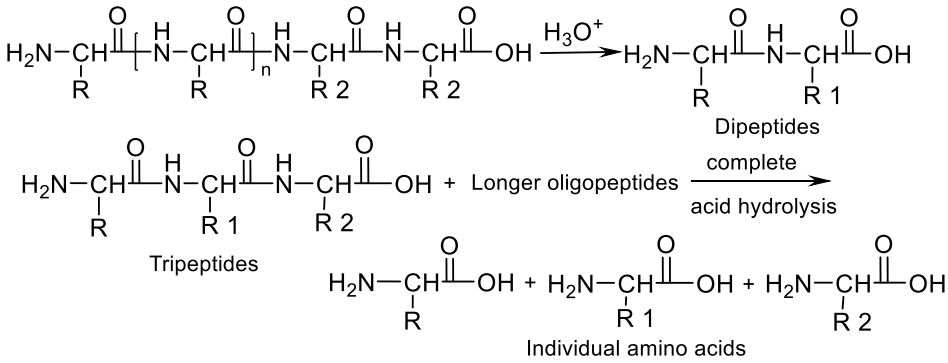
Proteins are naturally occurring organic polymers, which are very essential for living organisms. These are polymers of α-amino acids. Skin, hair, and muscle fiber and enzymes, which are known as biocatalysts are made up of such polymers. Some other proteins also play an important role in living systems such as hormones and antibodies. However, some proteins are different from one species to another, and even differ from one individual to another.

The α-amino acids in proteins are joined together through amide bonds, which are called peptide linkages, proteins are called polypeptides:



These peptide linkages in proteins are easily cleaved by partial hydrolysis of proteins to yield smaller polyamides, whereas, complete hydrolysis would give the individual amino acid components.

The sequence of amino acids in proteins is responsible for the biological functions of each individual.



2. NATURALLY OCCURRING AMINO ACIDS:

In general, in the α-amino acids the amino group is attached to the α-carbon atom with respect to the carboxylic group. There is also a side chain group attached to this α-carbon. Thus, most of the naturally occurring α-amino acids the only difference between them is in the structure of the side chain group. All α-amino acids isolated from proteins of different species have the L-configuration at the α-carbon. However, some other α-amino acids have been isolated from microorganisms have the D-configuration.

L-Configuration

D-Configuration

There are nearly about 20 α-amino acids have been isolated from living systems. Human beings are able to synthesize some of the α-amino acids and cannot synthesize some others due to deficient in their ability to synthesize them within their own metabolic system. It is well known that all α-amino acids are necessary for human's life. Those eight α-amino acids, which cannot be obtained by human beings are called essential α-amino acids and must be part of his diet (Table 1).

The other 12 amino acids (Table 2) found in the human beings can be synthesized from substrates that contain carbon, hydrogen, oxygen and nitrogen.

Table 1: Essential Amino Acids:

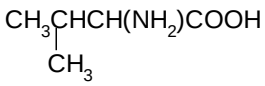
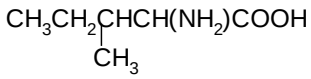
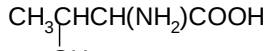
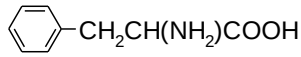
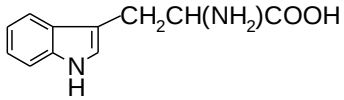
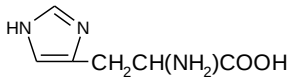
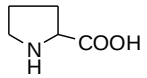
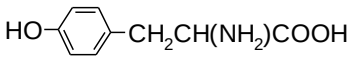
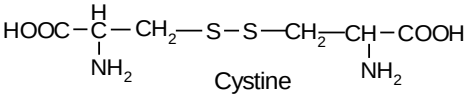
Structure	Name	Abbreviation
	L-(+)- Valine	Val
$(CH_3)_2CHCH_2CH(NH_2)COOH$	L-(-)- Leucine	Leu
	L-(+)- Isoleucine	Ile
	L-(-)- Threonine	Thr
$CH_3S(CH_2)_2CH(NH_2)COOH$	L-(-)- Methionine	Met
	L-(-)- Phenlyalanine	Phe
	L-(-)- Tryptophan	Trp
$NH_2(CH_2)_4CH(NH_2)COOH$	L-(+)- Lysline	Lys

Table 2: Other Common Amino Acids[a]:

Structure	Name	Abbreviation
$CH_3CH(NH_2)COOH$	alanine	Ala
$HN{=}C(NH_2)NH(CH_2)_3CH(NH_2)COOH$	Arginine	Arg
$HOOCCH_2CH(NH_2)COOH$	Aspartic acid	Asp
$HSCH_2CH(NH_2)COOH$	Cysteine	CySH
$HOOC(CH_2)_2CH(NH_2)COOH$	Glutamic acid	Glu
H_2NCH_2COOH	Glycine	Gly
	Histidine	His
	Proline	Pro
$HOCH_2CH(NH_2)COOH$	Serine	Ser
	Tyrosine	Tyr
$NH_2COCH_2CH(NH_2)COOH$	Asparagine	Asn
$NH_2CO(CH_2)_2CH(NH_2)COOH$	Glutamine	Gln

[a]One of the α-amino acids commonly found in protein has the name cystine, and has the following structure:



Cystine (CyS-SCy)

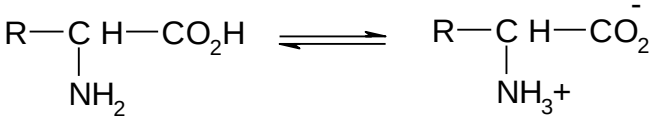
It is in fact a dimer of two cysteine units, where the two thiol groups are oxidized to form a disulfide linkage.

EXERCISE 5.1

Glycylalanine is a dipeptide composed of one molecule of glycine and another molecule of alanine. Write its structure.

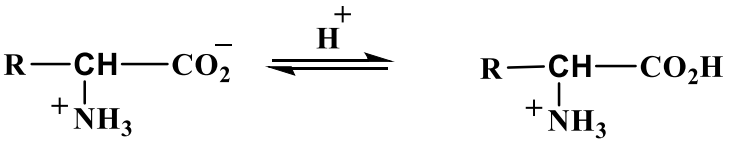
3. CHEMICAL AND PHYSICAL PROPERTIES OF α-AMINO ACIDS:

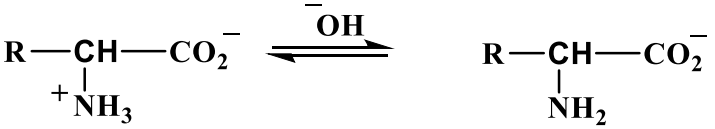
α-Amino acids are solids and melt at high temperatures with decomposition. they are soluble in water and insoluble in organic solvents, due to the presence of their two polar groups (-NH_2 and -COOH). Due to the presence of both the acidic function and the basic function, the α-amino acids in aqueous solution normally exist as dipolar ions called zwitterions.



Zwitterion

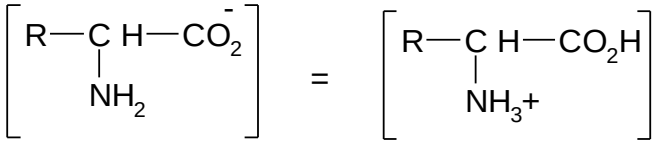
The α-Amino acids for such reason react with both acids and bases:





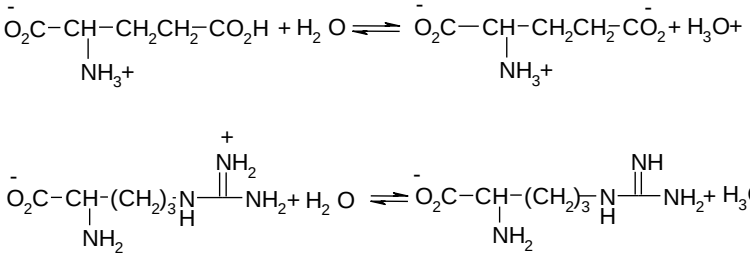
However if a solution of α-amino acid is placed in an electrical cell, the α-amino acid will migrate to either the anode or the cathode, depending upon the pH value. Thus at certain pH, called the isoelectric

point, there is no *net* migration of the α-amino acid because the concentration' anion is the same as the concentration of the cation:



The isoelectric point is characteristic for each individual α-amino acid; for example, it is pH 6.0 for glycine, pH 5.5 for phenylalanine, pH 11.2 for arginine …*etc*.

The α-amino acids with ionizable functional groups would have characteristic ionization constants related to those functional groups. For example. the side chain of glutamic acid has a pK_a of 4.3 and that of arginine has a pK_a of 13.2.

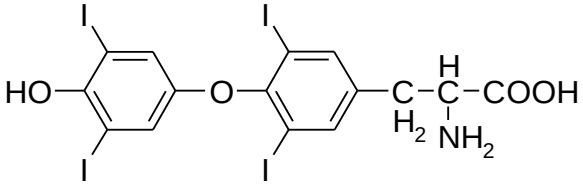


As mentioned above the α-amino acids can react by ways as carboxylic acids and aliphatic amines. However, amino α-acid esters are relatively unstable, and they are usually obtained as hydrochloride salts.

4. Structure of polypeptides:

In all proteins the α-amino acids must be in a precise order. The main target for scientists is to find out the sequence of α-amino acids in the given protein. In following pages, we shall put some light on the relationship between the sequence of α-amino acids and the biological activity of some polypeptides.

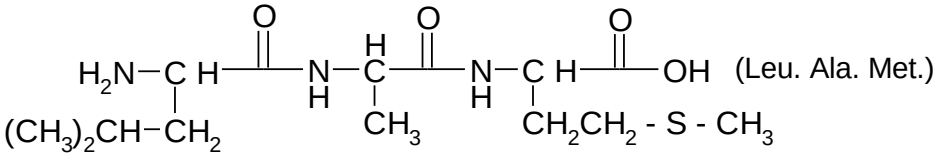
Even a single amino acid may exhibit potent biological activity: for example, Thyroxine is a hormone produced by thyroid gland, which controls the metabolism of nearly every single cell in the body.



Thyroxine

<u>Nomenclature:</u>

Any peptide has α-amino acid with the free amino group at the far left end, named N-terminal α-amino acid, and α-amino acid with the free carboxyl group at the far right end called C-terminal α-amino acid.



(Leu. Ala. Met.)

Leucylalanylmethionine

If the above peptide is written as follows: Leu. Ala. Met(NH_2) it means that the free carboxylic group of the C-terminal α-amino acid is converted into an amide. On the other hand, writing the peptide as follows: (Ac)Leu. Ala. Met, means that the free amino group of N-terminal α-amino acid is acetylated.

EXERCISE 5.2:

Write out the full structures that correspond to the following formulas:

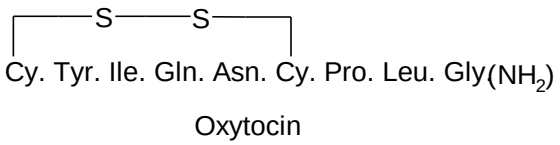
(a) Pro.Val. Glu(NH_2)

(b) (Ac)Arg. Gly. Phe. Ser

(c) Ser. Tyr. Arg. Asp

The effect of the sequence of α-amino acids in peptides:

Oxytocin and bradvkinin are both polypeptides consisted of nine α-amino acids, however some of the α-amino acids are different with different sequences. They biological functions are amazing different.



Oxytocin

Oxytocin is responsible for uterine contractions during childbirth and stimulates the ejection of milk. Interestingly that such phenomenon is only specific for the female of the species. Such specific chemical compound is also effective in causing a chicken to lay an egg or a cow to give down her milk.

Bradykinin is released by blood plasma globulins in response to a wasp sting, which causes a potent pain. The two examples show that any change of the □-amino acids sequence would change dramatically the biological activity of the peptide.

Arg. Pro. Pro. Gly. Phe. Ser. Pro. Phe. Arg

Bradykinin

However, many naturally polypeptides may function similarly in different species even though they are not identical in the primary structure. However, the difference in arrangement of α-amino acids in many polypeptides does not greatly affect their biological function. For example, the arrangement of 4 of its 51 α-amino acids in insulin (a hormone that controls carbohydrate metabolism) is different in many species. Thus, bovine insulin may be used to compensate for the insulin deficiency of human beings suffering from diabetes.

It is noteworthy to mention that proteins of more than 100 α-amino acids are transferred between species with difficulty due to immunological problems.

A more dramatic example of the importance of the α-amino acid sequence in polypeptides is provided by the polypeptide globin, the protein moiety of hemoglobin. It provides another example, thus globin has 146 α-amino acid residues in a very specific order, any change in the number of even one α-amino acid or change its sequence might lead to a very serious disease or may be death. The disease called sickle-cell anemia, which is suffered by people whose globin differs

from normal only in the sixth α-amino acid, valine instead of glutamic acid. Victims of this disease are unable to utilize oxygen at the normal rate. The formula below shows the substitution that distinguishes the globin of a normal human from one who has sickle-cell anemia.

Normal Globin:

VaL. His. Leu. Thr. Pro. Glu. Glu. Lys.

Sickle-Cell Globin:

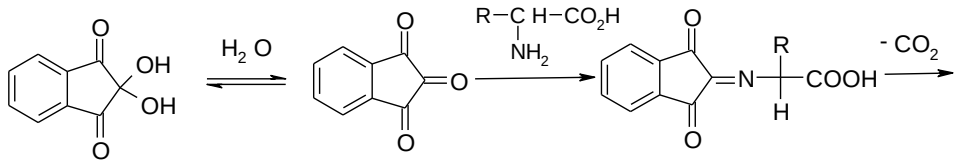
Val. His. Leu. Thr. Pro. Val. Glu. Lys

Enzymes are even more complex polypeptide materials. Every living cell contains thousands of enzymes, which are considered as bio catalysts for catalyzing the biochemical reactions specifically.

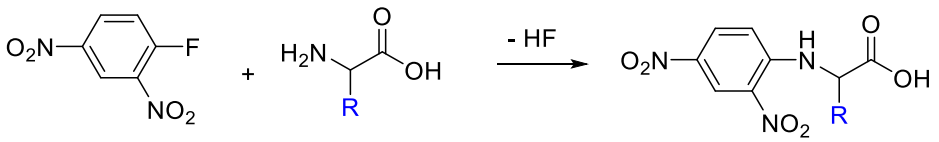
OPTIONAL MATERIAL:

Some chemical reactions of α-amino acids:

(1) The reagent ninhydrin produces a blue color with primary α-amino acids by the following series of reactions:

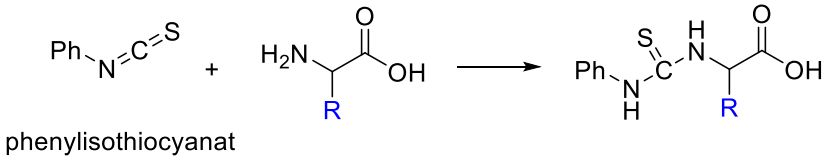


(2) α-Amino acids react with 2,4-dinitro fluorobenzene to give the corresponding N-(2,4-dinitrophenyl) derivatives:

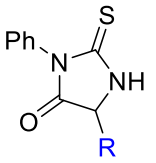


(3) α-Amino acids react with phenyl isothiocyanate:

An alternative procedure for determination of the N-terminal amino acid, which does not hydrolyze the peptide, is called Edman degradation. An N-phenylthiocarbamyl derivative is prepared with phenyl isothiocyanate.

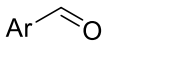


phenylisothiocyanat

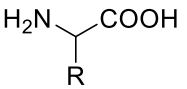


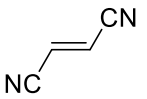
Thiohydantoin

(4) α-amino acids react with aromatic aldehyde and fumaronitrile to form pyrrolidine derivatives.

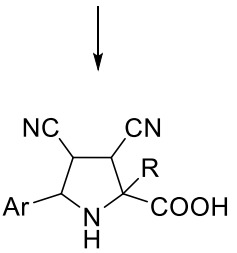


Aromatic aldehyde

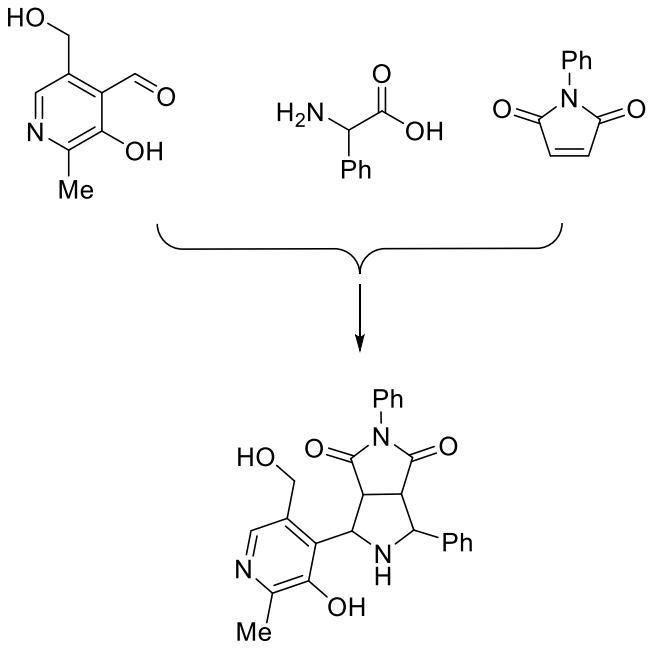




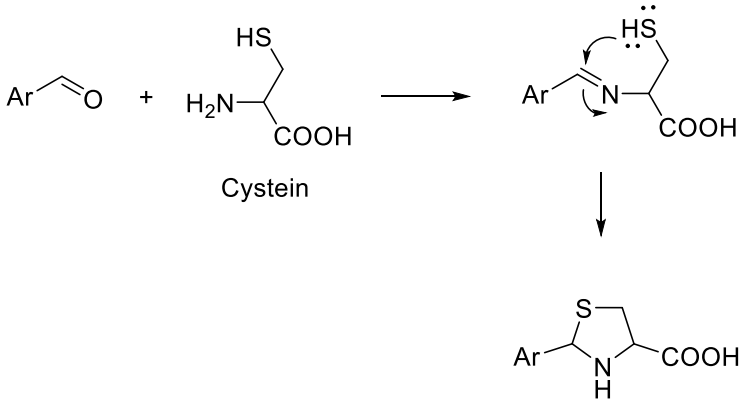
fumaronitrile



(5) Treating α-amino acids with pyridoxal in the presence of N-phenylmaliemide gives the corresponding cycloadduct.



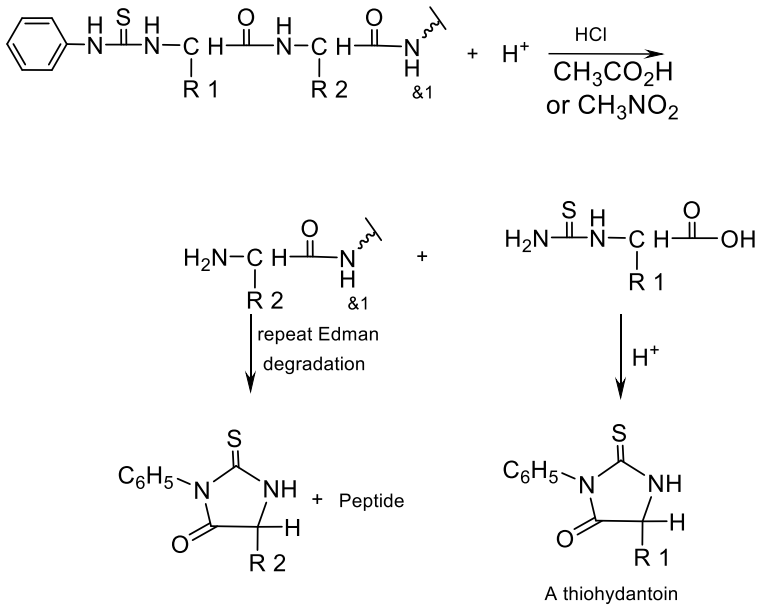
(6) Cysteine in particular reacts with aryl aldehydes to form the corresponding 2-arylthiazolidine-4-carboxylic acid.



Thiazolidine-4-carboxylic acid

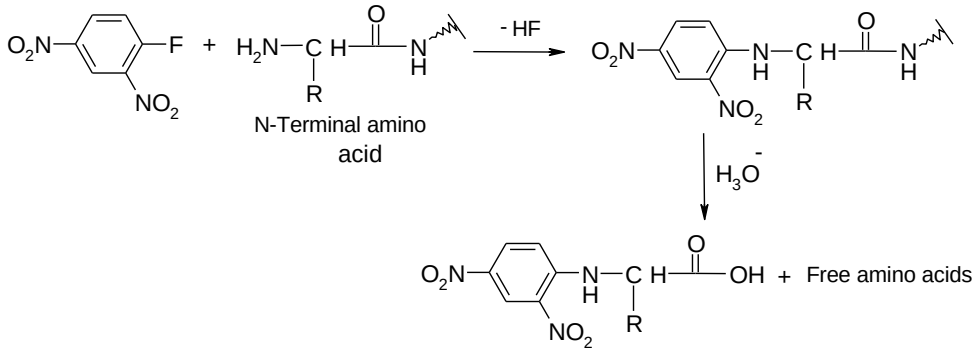
Determination of the sequence of a-amino acids in poly peptides:

(1) Acid hydrolysis of a poly peptide gives the individual α-amino acids.

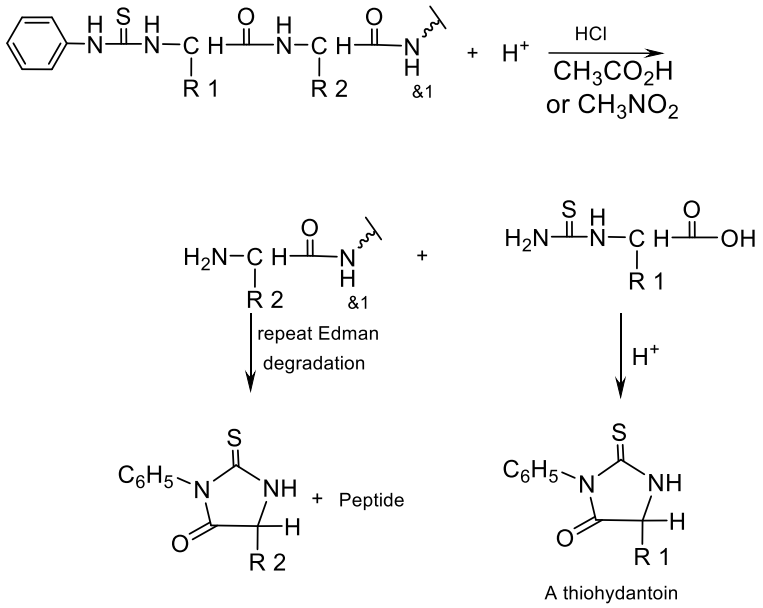


(2) Detrmination of the N-terminal α-amino acid:

a- Reacting the polypeptide with 2,4-dinitro fluorobenzene, and then acid hydrolysis would give corresponding N-(2,4-dinitrophenyl) derivative of the N-terminal α-amino acid:



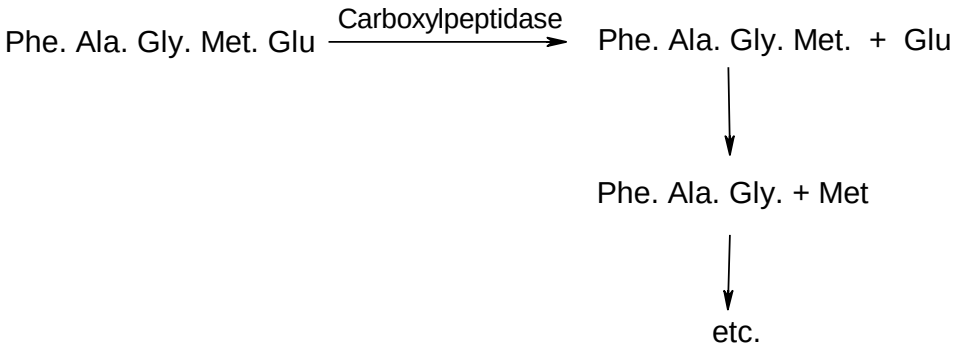
b- Reacting the polypeptide with isothiocyanate, and then acid hydrolysis would yield the corresponding thiohydantoin:



(3) Determination of the C-terminal α-amino acid:

a- Heating the polypeptide with anhydrous hydrazine would afford the hydrazide derivatives of all α-amino acids and only the C-terminal α-amino acid would be left as free □-amino acid.

b- The effect of carboxypeptidase enzymes obtained from the pancreas, such enzymes affect the peptide linkage of the C-terminal α-amino acid:



The action of the enzyme cannot be stopped after it has released Glu. The enzyme proceeds to attack the tetrapeptide and release Met, and then to attack the tripeptide, and so on. Such process is only used successfully in limited peptides.

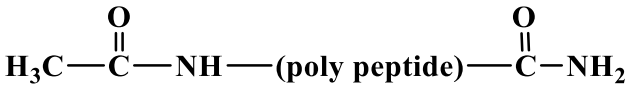
(4) The effect of chymotrypsin enzyme, this enzyme affects the peptide linkage in which the carbonyl group comes from □-amino acid whose side chain contain aryl residue.

Sample problem:

A melanocyte-stimulating hormone from pituitary glands, with the molecular formula: (Arg, Glu, Gly, His, Lys, Met, Phe, Pro, Ser_2, Trp, Tyr, Val.NH_2). It must be noticed that the commas between the abbreviations mean that the sequence of the α-amino acids is unknown. The α-amino acids are present in equimolar quantities, and serine it is present in two fold excess.

The experimental results show that no N-terminal α-amino acid was found in the Edman degradation or dinitrophenylation reaction and the C-terminal α-amino acid was not liberated by the effect of carboxypeptidase enzyme. These results indicate that the N-

terminal α-amino acid exists as the N-acetyl derivative, whereas the C-terminal α-amino acid is present as the amide:



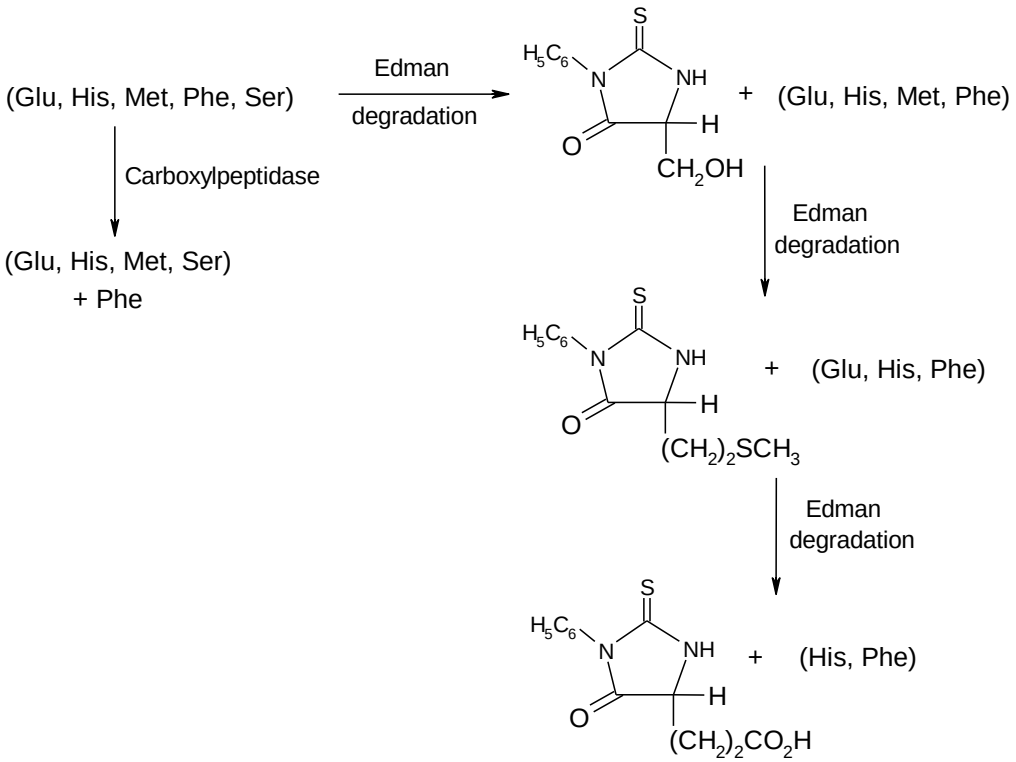
The hydrolysis by chymotrjpsin enzyme, which preferentially attacks peptide linkage whose carbonyl group comes from an aromatic α-amino acid, produces three peptide fragments:

(Arg, Gly, Gly, His, Lys, Met, Phe, Pro, Ser_2, Tyr, Val, NH_3)
chymotrypsin
⟶
(Ser, Tyr) + (Glu, His, Met, Phe, Ser) + (Arg, Gly, Lys, Pro, Trp, val)

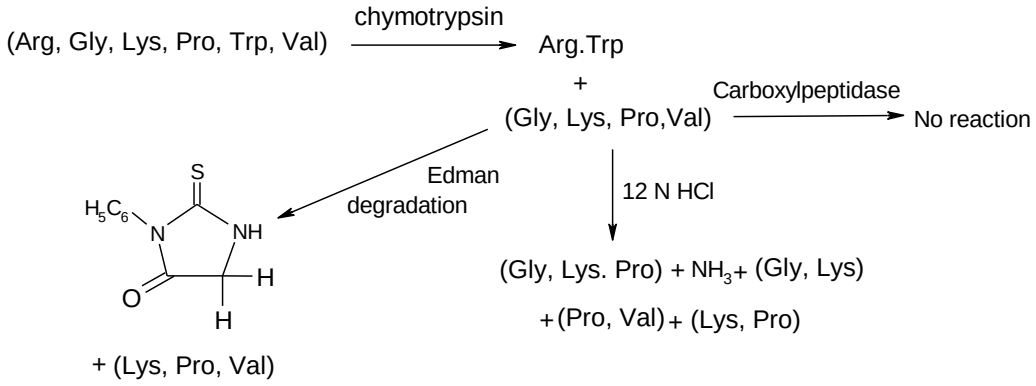
The analysis results showed that serine in the dipeptide (Ser.Tyr) exists as the N-acetyl derivative. Thus, (Ac)Ser. Tyr is the N-terminal end of α-MSH, and a partial structure of α-MSH is

(Ac) Ser. Tyr. { **(Glu, His, Met, Phe, Ser)** / **(Arg, Gly, Lys, Pro, Trp, Val)** } **–NH_2**

The carboxypeptidase action upon the pentapeptide fragment gave phenylalanine as the C-terminal α-amino acid, leading to the partial structure (Glu, His, Met, Ser). Phe. Edman degradation showed that serine is N-terminal: Ser. (Glu, His, Met). Phe. Two more Edman degradations gave, first, methionine, and second, glutamic acid:



Accordingly the pentapeptide is (Ac)Ser. Met. Glu. His. Phe. His.



However the hexapentpeptide (Arg, Gly, Lys, Pro, Trp, Val) was inert to carboxypeptidase, which means that it contains the C-terminal end of in such hexapeptide. Further chymotryptic hydrolysis of this hexapeptide yielded (Arg, Trp) and (Gly, Lvs, Pro, Val). The dipeptide must have the sequence Arg. Trp as chymotrypsin enzyme attacks only the carbonyl function of tryptophan:

The tetrapeptide (Gly, Lys, Pro, Val) was subjected to the Edman degradation, and glycine was found to be the N-terminal amino acid. It was partially hydrolyzed in 12N HC1 at 37 ºC for 120 hours. The following peptides were obtained, along with ammonia: (Gly, Lys, Pro) + (Gly, Lys) + (Pro, Val) + (Lys, Pro) + NH_3. The ammonia is obtained because the C-terminal end is in the amide form. Since the Edman reaction established Gly as the N-terminal residue of this peptide, the isolation of the dipeptides (Gly, Lys), (Lys, Pro), and (Pro, Val) establishes the obligatory sequence Gly. Lys. Pro. Val(NH_2). The presence of tripeptide containing Gly, Lys, and Pro adds strength to the sequence assignment. The complete hexapeptide must be: Arg. Trp. Gly. Lys. Pro. Val(NH_2).

At this point, the information known about α-MSH is

(Ac)Ser. Tyr + Ser. Met. Glu. His. Phe + Arg. Trp. Gly. Lys. Pro. Val (NH_2).

EXERCISE 5.3

A hexapeptide gave upon hydrolysis the following amino acids: Glu, Gly, Glv, Lvs, Ser, Tvr. However partial hydrolysis gave two

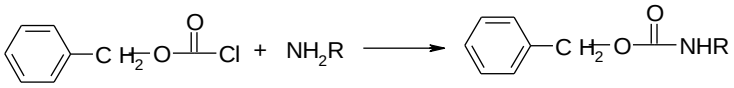
dipeptides and a tripeptide with the following structures: (Gly. Ser), (Tyr. Lys), and (Gly. Glu. Gly). The results showed that tyrosine occupied the N-terminal position by an appropriate test. What is the structure of the hexapeptide?

PEPTIDE SYNTHESIS:

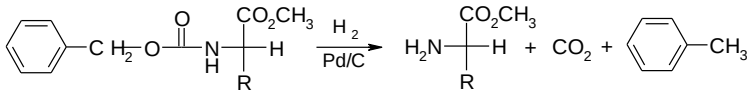
Peptide synthesis has been a great secret area of organic chemistry, mainly due to the specific sequence of a-amino acids in the peptide chain. However, two major problems are facing organic chemists to sort out the sequence problems in the peptide synthesis. They are: (1) protecting the α-amino group of one α-amino acid and activating its acid group; and (2) protecting the acid group of the other α-amino acid and leaving its α-amino group free to react. It must be taken in account that the protecting group must be: (a) very easy to introduce, (b) very stable during the reactions and (c) very easy to get rid of.

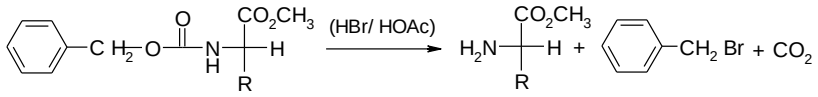
However, first let us see how to protect the α-amino group. It is well known that benzoxycarbonyl and *t*-butoxycarbonyl groups are usefully used as good amino protecting groups.

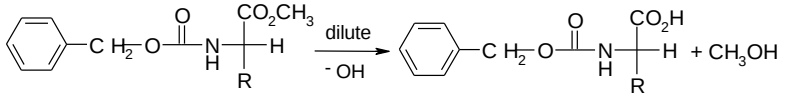
1- **The N- benzoxycarbonyl: Treating the □-amino acid with benzyl chloroformate affords the corresponding (N-benzoxycarbonyl).**



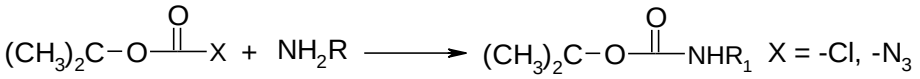
However, such protecting group can be easily removed by catalytic hydrogenation or by acid hydrolysis, to regenerate the free the α-amino group. However such protecting group is relatively stable to dilute alkalies.





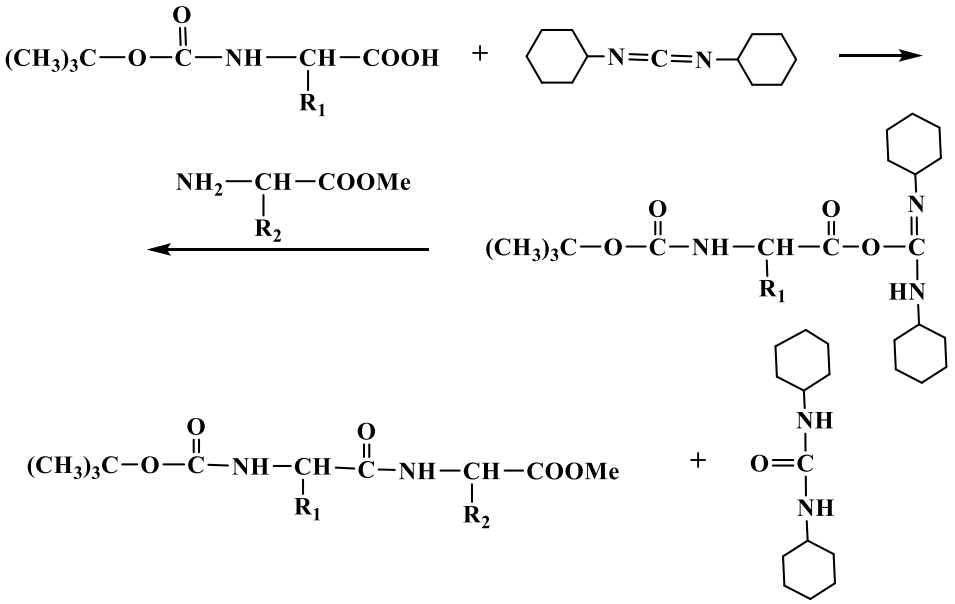


2- N-*t*-butoxycarbonyl is often known as N-Boc group is formed by reacting the amino acid with *t*-butyl chloroformate at 0 °C or by gently heating the amino acid with the more stable *t*-butoxycarbonyl azide.

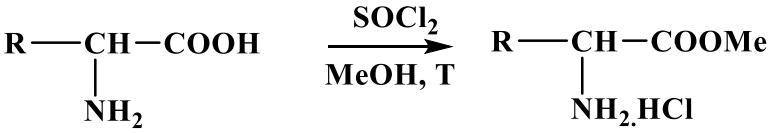


The N-*t*-butoxycarbonyl (N-Boc) group can be readily removed by acid hydrolysis to yield the free a-amino group, however such protecting group is not affected by catalytic hydrogenation or a dilute base.

Dicyclohexylcarbodiimide a reagent that can easily react with N-Boc α-amino acid, and then the formed compound reacts with another α-amino acid ester with a free α-amino group to finally give a dipeptide, in which the amino group and the carboxyl group are both protected:



Now let us see, how to protect the carboxylic group of the α-amino acid. The ester formation is the best way for such purpose:



It seems possible to build up a chain of any length with α-amino acids with the required sequence by choosing the proper protecting groups. However, in the laboratory, small peptides (two-, three-, or four-unit) are formed and then coupled together. Such methodology was used by Du Vigneaud in his remarkable synthesis of oxytocin in 1954. However, racemization of the obtained peptides is the only synthetic problem in this approach.

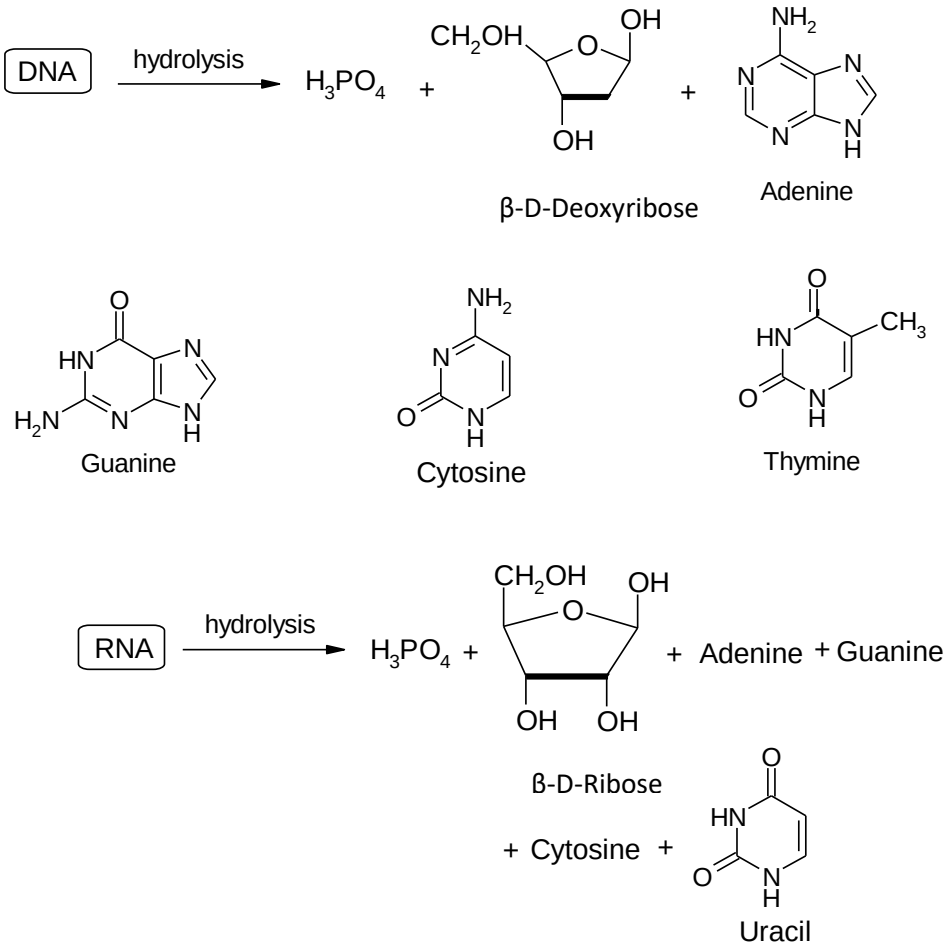
EXERCISE:

Draw the structure of the material which would he obtained by a1lowing methyl alanine ester to react with BOC-glycine in the presence of dicyclohexyl-carbodiimide.

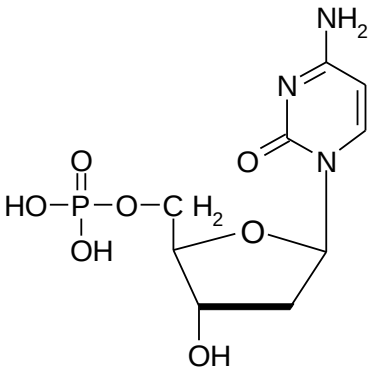
THE NUCLEIC ACIDS:

The nucleic acids are considered as one of the most important biopolymers. The found nucleic acids in cells are: (i) ribonucleic acids (RNA) and (ii) deoxyribonucleic acids (DNA). Both RNA and DNA are essential for the biosynthesis of proteins. However, DNA constitutes the genetic material of cells. Like polysaccharides and proteins RNA and DNA are very large molecules.

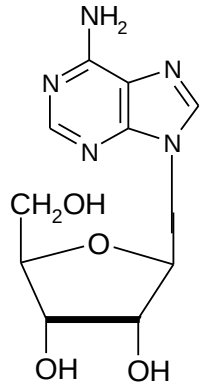
On hydrolysis, both types of nucleic acids yield phosphoric acid, pentose and a mixture of heteroaryl bases. Thus, hydrolysis of DNA produces phosphoric acid (H_3PO_4), β-D-deoxyribose and the heteroaryl bases such as adenine, guanine, cytosine and thymine. However, the hydrolysis of RNA gives phosphoric acid (H_3PO_4), □-D-ribose, and heteroaryl bases e.g. adenine, guanine, cytosine and uracil.



Mild degradation of a nucleic acid yields a mixture of acids known as nucleotides. Each nucleotide contains the elements of one heteroaryl base unit, one phosphate unit and one pentose unit. However, careful hydrolysis would easily remove the phosphate unit and convert a nucleotide into a nucleoside, a molecule that contains only two units (a pentose joined to a heteroaryl base). In a nucleotide, C-l of the pentose is joined to N-l of a pyrimidine derivative or N-9 of a purine derivative and the phosphoric acid unit exists as an ester at C-5 of the pentose.

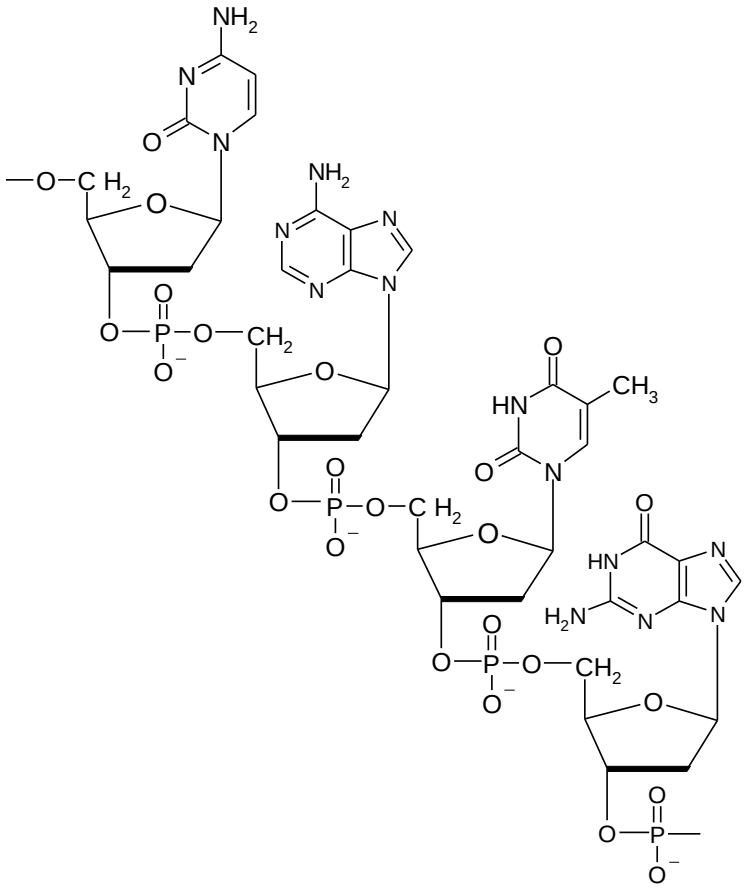


Deoxycytidylic acid
(a nucleotide)



Adenosine
(a nucleoside)
(A)

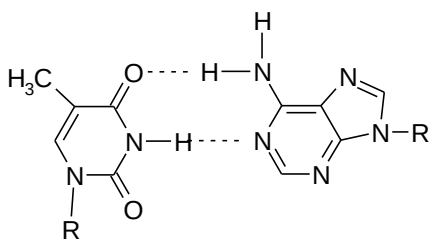
In a nucleic acid chain the phosphoric acid exists as an ester bridge to join C-5 of the pentose of one nucleoside and C-3 of the pentose of another nueleoside. The regular intervals of the heteroayl bases are the only different from one living organism to another. A typical segment of a DNA chain is shown:



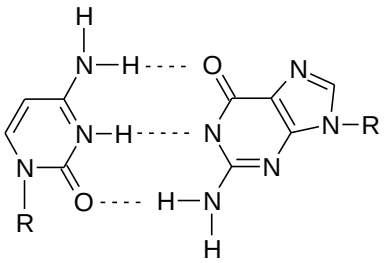
DNA

The hydrogen bonding between the heteroaryl bases keeps each two hydrogen bonded chains chains in a double-helical structure.

The double-helical structure of DNA is shown schematically in Figure 5.4. Interestingly, a molecule of DNA reproduces itself by an outstanding simple mechanism. Thus, the two chains of a DNA



Thymine-adenine
(T to A)
hydrogen bonding



Cytosine-guanine
(C to G)
hydrogen bonding

molecule dissociate into free nucleotides. An enzyme catalyzes the polymerization of these free nucleotides in an order complementary to that of the original strands, producing two new double-stranded DNA molecules identical to the original one. It has been said that this

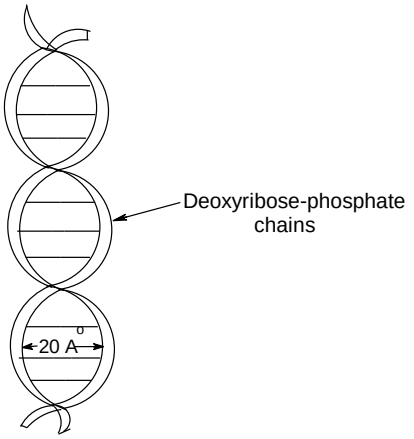


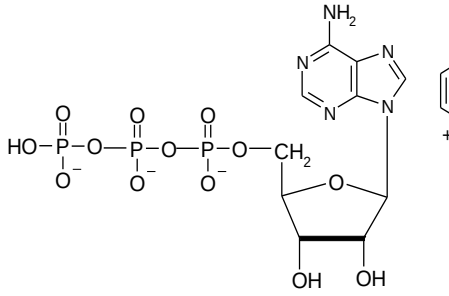
Figure 5.4: Double-helix structure of DNA

simple process is the "secret of life", that is why children look much more like their relatives.

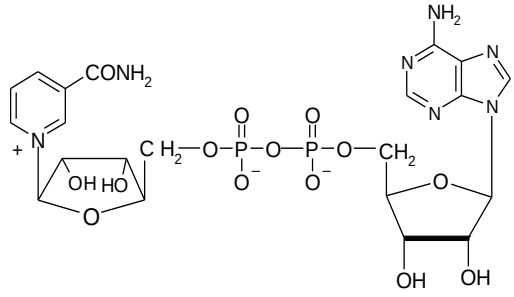
The DNA has two important functions: (i) it is the reference material or "book of instructions" to explain how a given plant or animal is to be constructed, and it reproduces itself. (ii) The second function is to act as a template in producing RNA. In fact RNA is the material that carries out the synthesis of proteins.

Nucleosides and nucleotides serve as coenzymes. Numerous enzymes require coenzymes, which are small nonprotein moieties bound to the protein for high performance of catalytic function.

Examples of such nucleotides are nicotinamide adenine dinucleotide (NAD), and adenosine triphosphate (ATP), which functions as a pool for chemical energy in cells because of its energy-rich triphosphate unit.

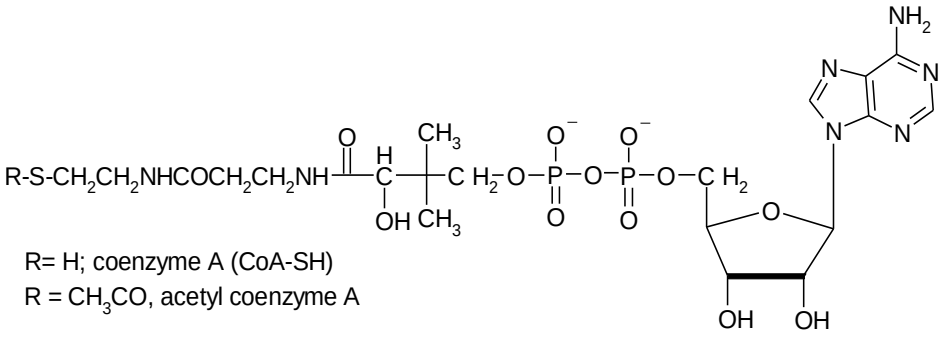


Adenosine triphosphate
(ATP)



Nicotinamide adenine dinucleotide
(NAD)

A third very important adenine nucleotide derivative is coenzyme A (CoA-SH), that plays a very significant role in acyl group-transfer reactions. Acyl derivatives of CoA-SH are effective acylating agents.



PROBLEMS

1- Name the three types of natural organic polymers that are essential to life processes.

2- Give a definition and example of:

(a) An essential amino acid

(b) The peptide bond

(c) Polypeptide

(d) Tripeptide

(e) Enzyme

3- Define the isoelectric point of an amino acid and explain why arginine has an isoelectric point 5 pH units higher than does glycine, and glutamic acid has one about 3 pH units lower than that of glycine.

4- Write the structures that correspond to the following formulas:

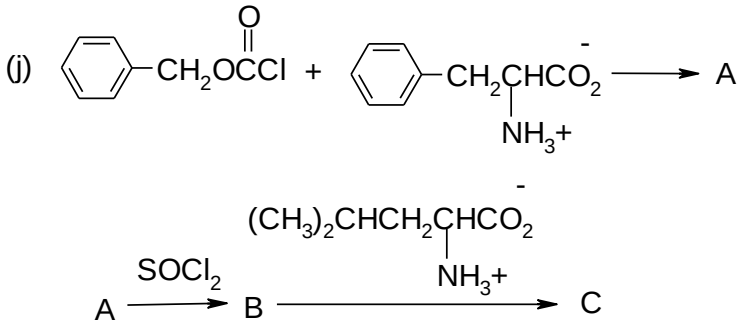
(a) Val. Trp. Lys. (NH_2).

(b) (Ac) HiS. Gly. CySH. Gln.

5- Describe by formula two N-terminal amino acid determinations.

6- Octapeptide upon hydrolysis gave the following amino acids: Met. Asn, CySH. Lys. Pro. Thr, Thr, and Val. Partial hydrolysis gave a mixture from which it was possible to isolate four dipeptides and two tripeptides. which had the following structures: Met, Lys. Val. Thr. Asn. Val. Thr. Met. Pro. Thr. Asn. and Lys. CySH. Pro. What is the structure of the ecta-peptide?

7- Complete:



8- Suggest a synthesis for Ala. Pro. Val.

9- Cells contain two types of nucleic acids. commonly referred to as RNA and DNA.

(a) What do the abbreviations RNA and DNA stand for?

(b) What are the similarities between RNA and DNA?

(c) What are the differences between RNA and DNA?

10- Show the mechanism of peptide coupling by dicyclohexylcarbodiimide.

11- A certain tetrapeptide is found to yield on hydrolysis 2 mol of alanine, 1 mol of glycine. and 1 mol of valine. Write the formula for each possible structurally isomeric tetrapeptide that could give this result.

Enzymes

The word enzyme means "in yeast." Even without any knowledge of their structures or functions, humans have used enzymes since prehistoric times in the production of wine, vinegar, and cheese. Pasteur thought that living yeast cells were necessary for fermentation processes. However, we know by now that no need for living cells, it is believed that what we need for an enzymatic reaction is the proper enzyme and optimum reaction conditions.

Enzymes are biological catalysts. Mammals, the higher animals contain thousands of enzymes, and in fact every biochemical reaction is catalyzed by an enzyme. Even the equilibrium:

$$CO_2 + H_2O \leftrightarrows H_2CO_3$$

It is an enzyme-catalyzed process, as the rate of the uncatalyzed is enzyme-catalyzed, as the rate of the uncatalyzed equilibration does not offer carbonic acid fast enough for an animal's needs.

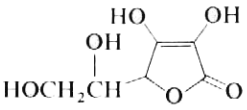
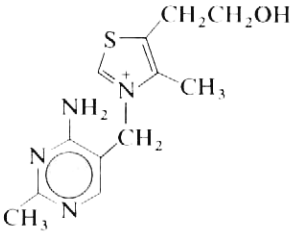
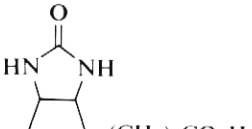
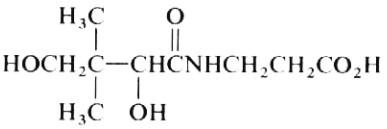
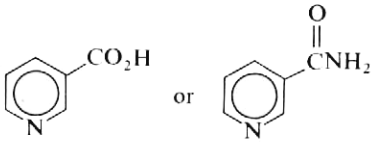
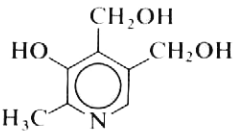
General features of enzymes: (i) are biocatalysts proteins, (ii) are more efficient catalysts compared to most laboratory or industrial catalysts (such as Pd in a hydrogenation reaction), (iii) are working well in

humans in aqueous media at 37^0C and (iv) are working in an enantioselective manner. However, for biological activity numerous enzymes require coenzymes. Such coenzymes may be a simple metal ion; for example, copper ion is the cofactor for the enzyme ascorbic acid oxidase. Other enzymes contain small nonprotein organic molecules as coenzymes. Some enzymes are relatively simple in structure however, most of them are complex. The structures of many enzymes are still unknown.

If an organism cannot synthesize a necessary cofactor required for its biological activity, such cofactor must be present in small amounts in its diet. The active units of many cofactors are vitamins. Table 3 shows a few cofactors and the corresponding vitamins.

Table 3. Some cofactors that contain vitamins

Name of cofactor	**Vitamin needed**	**Structure of vitamin**
Vitamin C (ascorbic acid)	Vitamin C	
Vitamin B_1 (Thiamine)	Vitamin B_1	
biotin	Biotin	

Coenzyme A	Pabtothenic acid	
NAD^{+a}	Nicotinic acid (niacin) or nicotinamide (niacinamide)	
Pyridoxyl phosphate	Pyridoxyl	   

a: Nicotinamide adenine dinucleotide, a biological oxidizing agent.

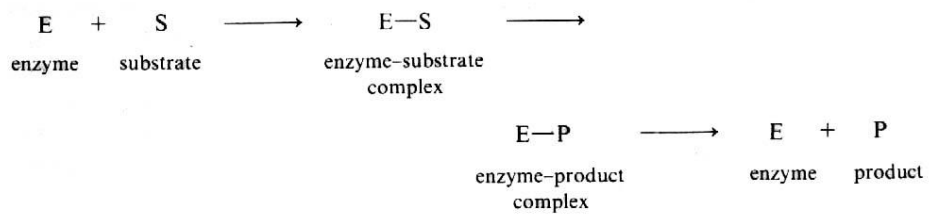
A. NAMING ENZYMES:

Most of enzymes are named after the catalyzed reactions they catalyze, *e.g.* decarboxylase, dehydrogenase, transaminase, invertase ……*etc*. The name of chemical process plus a -ase suffix and then adding the word enzyme: for example the enzyme, which is used for dehydrogenation is named dehydrogenase enzyme, for the hydrolysis of sucrose (invert sugar) is named invertase enzyme and so on. Sometimes the enzyme name may refer to a specific enzyme, for example the enzyme that catalyzes the oxidation of ascorbic acid is named ascorbic acid oxidase.

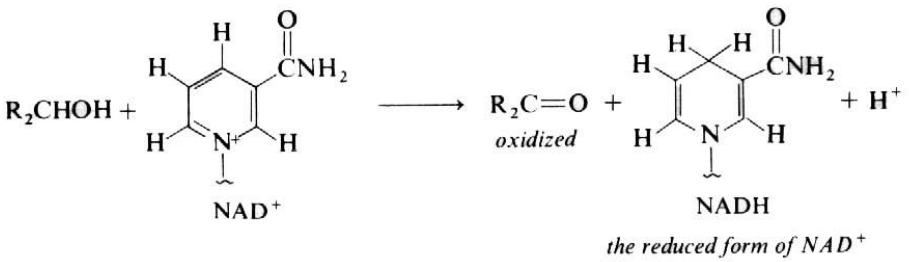
B. How enzymes work:

Some enzymes have been studied in detail, yet there is still much to learn about even the well-known enzymes. It is believed that an enzyme fits itself around the substrate (the molecule to be acted upon) to form an enzyme-substrate complex. There is some sort of bonding between the substrate and the enzyme to produce an enzyme-product complex.

In many cases, the product is not the same shape as the reacting substrate; thus the fit between the product and the enzyme is no longer perfect. The altered shape of the product causes a dissociation of the enzyme-product complex. Then the enzyme surface is ready to accept another molecule of substrate, and so on. This theory of enzyme activity is called the induced-fit theory.



Enzymes have molecular weights of 12,000 and higher. Most substrates (for example, an amino acid or a unit of glucose) are much smaller molecules. There is specific location of the large enzyme structure at where the reaction occurs is called the active site. This site is where the prosthetic group (if any) is located. Metallic prosthetic groups are thought to serve as electrophilic agents and, in this way, catalyze the desired reactions. In NAD^+, the active site is the nicotinamide end of the cofactor. NAD^+ is readily reduced and therefore catalyzes oxidation reactions such as oxidation of secondary alcohols into Ketones:



However, the rest of the enzyme molecule recognizes its substrate and holds it in place. It was suggested in the 1890's by Emil Fischer that enzymes are chiral molecules and that reactants must complement this chirality in order to undergo reaction. Fischer compared the fitting

together of the substrate structure and the enzyme structure to a key fitting into a lock (see Figure 6.6).

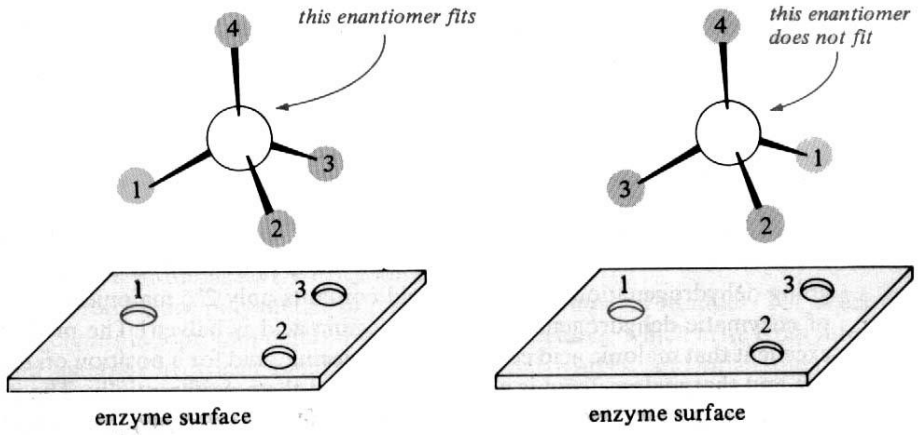
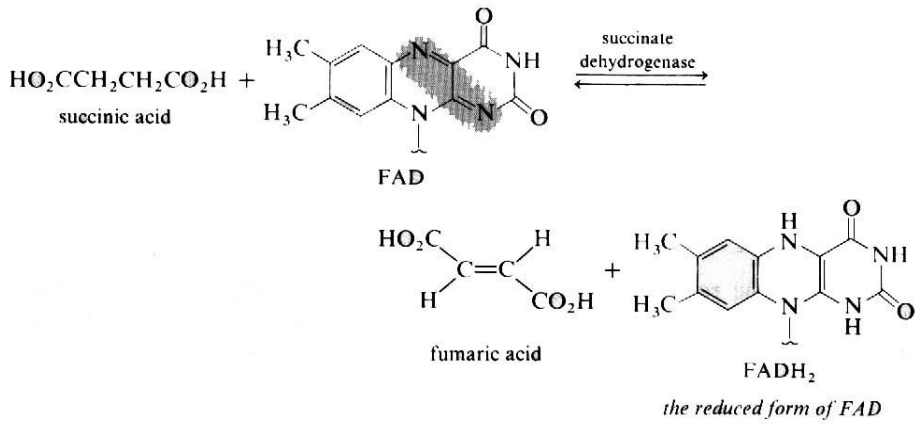


FIGURE 6.6. One enantiomer fits on the enzyme surface; its mirror image does not.

Both the active site and the rest of an enzyme are important in the **enzyme activity. Let us look at one reaction in which the active site seems to be the more important factor in substrate recognition. The enzyme succinate dehydrogenase catalyzes the dehydrogenation of succinic acid to the fumaric acid (*trans*-diacid). (The *cis*-isomer, maleic acid, is not produced in this reaction.) The oxidizing agent in this reaction is flavin adenine dinucleotide (FAD), which is reduced by a 1,4-addition of two hydrogen atoms (plus two electrons). (We show only the functional portion of FAD here.)**



Inhibitors of succinate dehydrogenase:

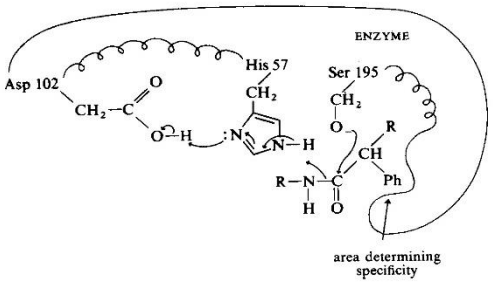
Other diacids, such as oxalic acid, malonic acid, and glutaric acid, inhibit the dehydrogenation of succinic acid.

$HO_2C—CO_2H$	$HO_2CCH_2CO_2H$	$HO_2C\text{-}CH_2CH_2\ CH_2\text{-}CO_2H$
oxalic acid	malonic acid	glutaric acid

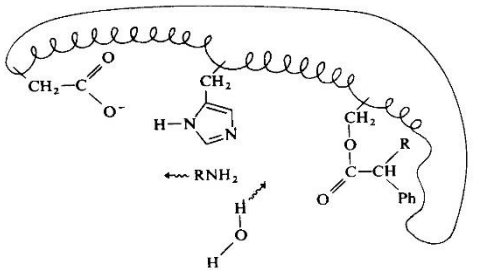
Of these diacids, malonic acid has the greatest inhibiting effect. Malonic acid is very similar in structure to succinic acid, but is structurally incapable of undergoing dehydrogenation. If succinic acid contains only 2% malonic acid, the rate of enzymatic dehydrogenation of the succinic acid is halved! The probability is excellent that malonic acid competes with succinic acid for a position on the active site and that malonic acid is attracted and held there preferentially. The presence of malonic acid on the active site thus blocks the approach of succinic acid.

The hydrolysis process of a protein that contains an aryl side chain by chymotrypsin enzyme is a magnificent example to show how the rest of the enzyme molecule is folded to form a hydrophobic pocket that holds a nonpolar portion (the aryl side chain) of the substrate in the right place. The whole process seems to be worthwhile studied.

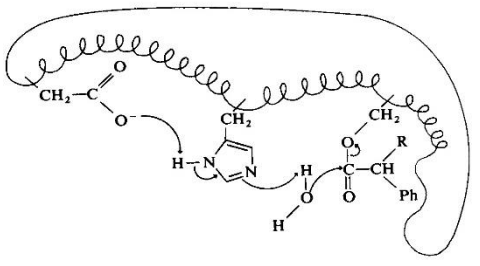
1. Initial Binding of the Substrate (after proton transfer from Ser to Asp via His)



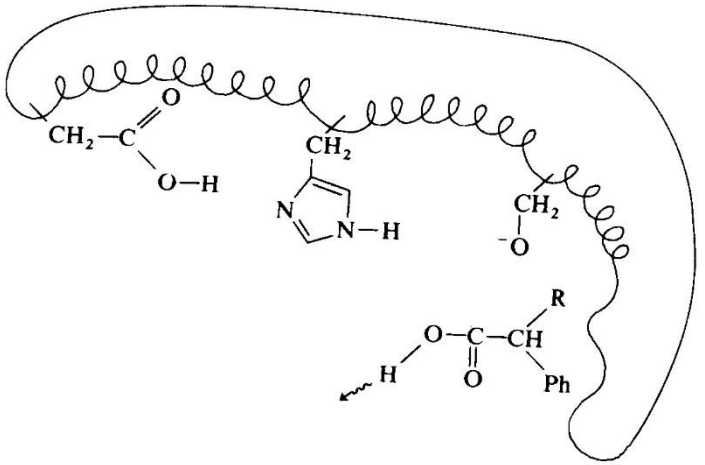
2. Formation of an Acyl Enzyme Intermediate and Release of Amine



3. Deacylation

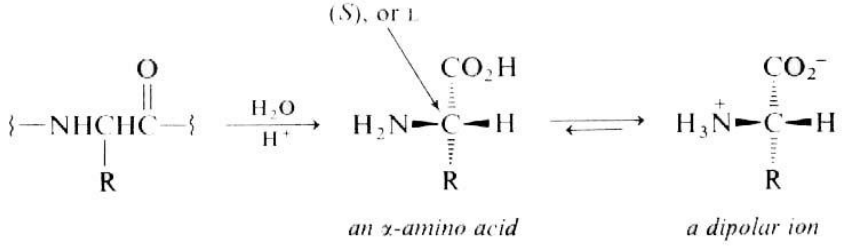


4. Release of Carboxylic Acid



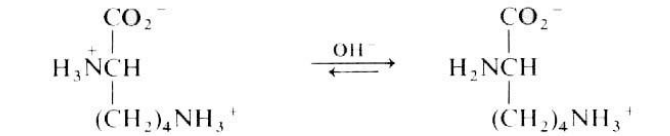
Summary:

A protein is a polypeptide, which on hydrolysis yields α-amino acids of (S)-configuration at the α carbon. Amino acids undergo an internal acid-base reaction to form zwitter ions.



Essential amino acids are those that cannot be synthesized by human being and must be present in his diet. Acidic amino acids are those with a carboxyl group in the side chain (R = COOH). Basic amino acids contain an amino group in the side chain. Neutral amino acids contain neither -CO_2H nor -NH_2 in the side chain. Some □-

amino acids may contain polar group (OH, SH …..). Cross-linking in proteins may be provided by the SH group in cysteine, which can link with another SH in an oxidation reaction: 2 RSH → RS-SR + 2 H. The isoelectric point of an amino acid is the pH at which the dipolar ion is electrically neutral and does not migrate toward an anode or cathode. The iso-electric point depends on the acidity or basicity of the side chain.



Racemic amino acids may be synthesized by a variety of routes.

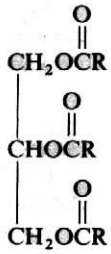
A peptide is a polyamide of fewer than 50 amino acid residues. The N-terminal α-amino acid is the amino acid with a free α-amino group, while the C-terminal amino acid has a free carboxyl group at carbon 1. Analytical processes to determine the C- and N-terminals and partial hydrolysis to smaller peptides both are techniques for peptide structure-determination. In the synthesis of a peptide, the undesired reactive groups must be protected. In general the amino group is protected as Boc-N or BnOCO-N. The biosynthesis of proteins is accomplished by RNA. Enzymes are proteins that catalyze biochemical reactions. Enzymes are efficient and specific in their catalytic action. Some enzymes work in conjunction with a nonprotein cofactor, which may be metal ion or organic residue.

Part_3

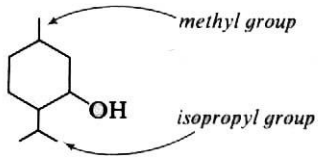
Lipids and Related Natural Products

Lipids and Related Natural Products

Lipids are known as naturally occurring organic compounds, which are insoluble in water, but soluble in nonpolar organic solvents *e.g.* hydrocarbons or ethers. Such compounds in fact include many types of compounds. All various classes of lipids are sharing such physical property. However, they are different in their chemical properties, functional groups, and structural relationships, and each class has its own biological function. Fats and oils, terpenes, steroids, are considered as good examples of lipids.

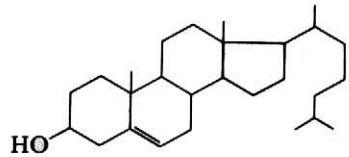


a fat, or triglyceride



menthol

a terpene



cholesterol

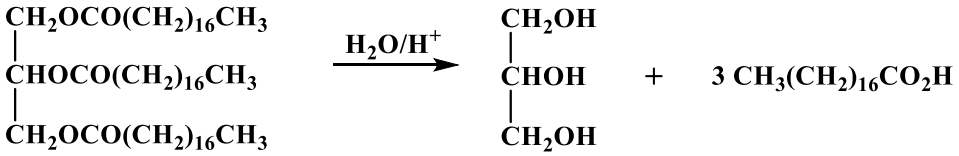
a steroid

Fats and Oils:

Fats and oils are triglycerides, a term meaning "triesters of glycerol." Fats are solids at room temperature, whereas oils are liquids. In general glycerides obtained from animals are fats, while those from plants are oils.

Fatty acids are obtained by the hydrolysis of fats and oils. They have long, unbranched hydrocarbon chains However,. Fats and oils are considered as derivatives of these fatty acids, thus the tristearate of

glycerol is named tristearin, and the tripalmitate of glycerol is named tripalmitin.



Tristearin (glyceryl tristearate) a typical fat | **glycerol** | **stearic acid (a fatty acid)**

Fatty acids are also obtained in waxes, such as beeswax. In these cases, the fatty acids are esterified with a simple long-chain alcohol.

$C_{25}H_{51}CO_2C_{28}H_{57}$	$C_{27}H_{55}CO_2C_{32}H_{65}$	$C_{15}H_{31}CO_2C_{16}H_{33}$
in beeswax	in carnauba wax	cetyl palmitate in spermaceti

Most naturally occurring fats and oils are mixed triglycerides, thus, the three fatty-acid portions of the glyceride are not the same. Table 1 lists Some representative fatty acids are listed in Table 7.1, whereas Table 2 shows the fatty-acid composition of some plant and animal triglycerides.

Table 1 Selected fatty acids and their sources:

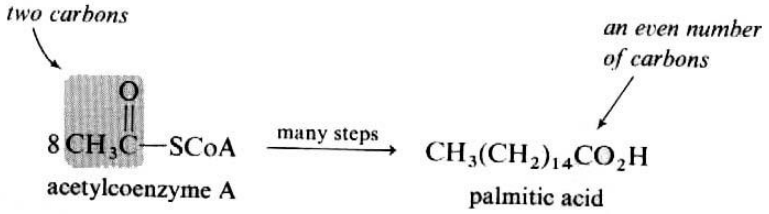
Name of acid	Structure	Source
Saturated:		
butyric	$CH_3(CH_2)_2CO_2H$	**milk fat**
Palmitic	$CH_3(CH_2)_{14}CO_2H$	**animal and plant *fat***
Stearic	$CH_3(CH_2)_{16}CO_2H$	**animal and plant fat**
Unsaturated:		
Palmitoleic	$CH_3(CH_2)_5CH=CH(CH_2)_7CO_2H$	**animal and plant fat**
Oleic	$CH_3(CH)_7CH=CH(CH_2)_7CO_2H$	**animal and plant fat**
Linoleic	$CH_3(CH_2)_4CH=CHCH_2CH=CH(CH)_7CO_2H$	**plant oils**
Linolenic	$CH_3CH_2CH=CHCH_2CH=CHCH_2CH=CH(CH_2)_7CP_2H$	**Linseed oil**

Table2 Approximate fatty-acid composition of some common fats and oils

Composition (%)[a]

Source	*Palmitic*	*Stearic*	*Oleic*	*Linoleic*
corn oil	***10***	***5***	***45***	***38***
soybean oil	***10***	***--***	***25***	***55***
Lard	***30***	***15***	***45***	***5***
Butter	***25***	***10***	***35***	***--***
human fat	***25***	***8***	***46***	***10***
a: other fatty acids are also found in lesser amounts.				

Generally, all naturally occurring fatty acids have an *even* number of carbon atoms because they are biosynthesized from the two-carbon acetyl groups in acetylcoenzyme A (CH3CO-SCoA.



It is well known that the hydrocarbon chains in fatty acids could be saturated or containing double bonds. Oleic acid (olive oil), contains one double bond. Fatty acids with more than one double bond are uncommon, particularly in vegetable oils.

The configuration around the double bond in a naturally occurring fatty acid is *cis,* such configuration causes the low melting points of oils. In the triglycerides of the saturated fatty acids would have zigzag chains that can be fit compactly together, leading to high van der Waals attractions; therefore, saturated fats are solids at room temperature. In the case of oils, the unsaturated fatty acids contain a few *cis*-double bonds present in the chains. According to the stereo configuration of these *cis*-double bonds the chains of molecules would be partially far apart, and no more full van der Waals attractions exist; polyunsaturated triglycerides tend to be oils at room temperature. Figure 1 shows models of the two types of chains in fats and oils, respectively.

Triglycerides are one of the three principal foodstuffs (the other two are carbohydrates and proteins). The comparison between the three as energy sources is: (i) triglycerides are the most efficient as they provide 9.5 kcal/gram (ii) proteins provide 4.4 kcal/gram and (iii) carbohydrates provide 4.2 kcal/gram.

Fats can be converted *in vivo* by enzymatic hydrolysis into mono-glycerides, di-glycerides, fatty acids, and glycerol, which would be absorbed through the intestinal wall. Thus organism can use such products: (i) to synthesize its own fats; (ii) converts the fatty acids into carbohydrates or cholesterol or (iii) converts the fatty acids to energy.

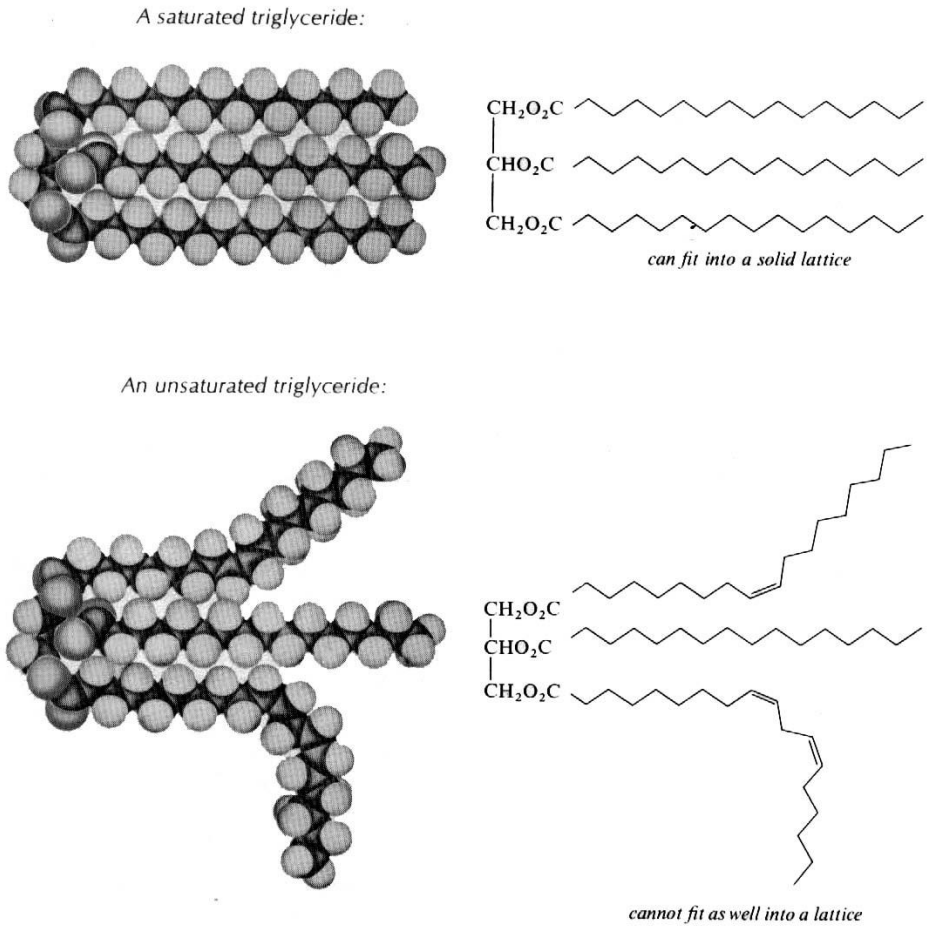
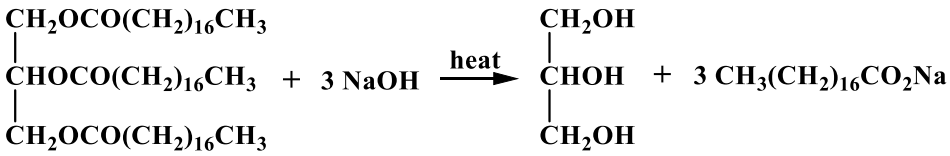


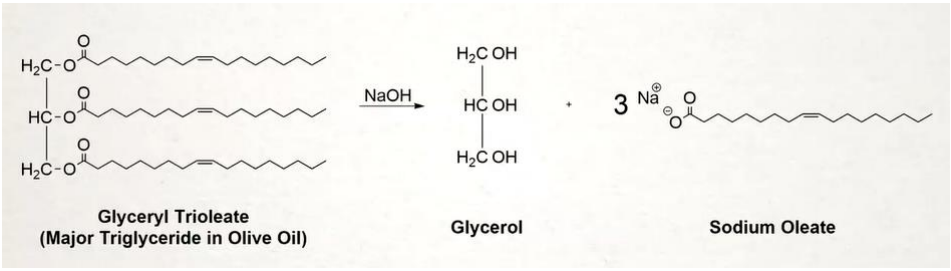
Figure 1 The shapes of saturated and unsaturated triglycerides.

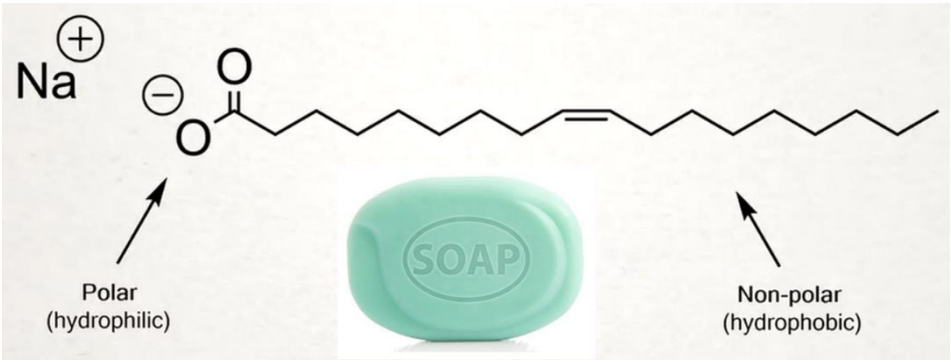
Soaps and Detergents:

The word *saponjfy* means "make soap." Saponification of an ester with aqueous NaOH yields the sodium salt of a carboxylic acid. Saponification of triglyceride yields the sodium salt of a long-chain fatty acid, which is known as soap. American pioneers used beef or pork fat and wood ashes (which contain alkaline salts, such as K_2CO_3) to make soap.



Tristearin **glycerol** **a soap**





A molecule of soap contains a long hydrocarbon chain with an ionic end (COO^-Na^+). The hydrocarbon portion of the molecule is

hydrophobic (water non-soluble) is named hydrophobic tail, which is only soluble in nonpolar substances, while the ionic end is hydrophilic (water-soluble). In fact the long hydrophobic hydrocarbon chain makes soap molecule as a whole not truly soluble in water, and it rather suspends in water. However, the suspension of soap in water forms micelles, (clusters of the hydrocarbon chains with their ionic ends facing water, *cf*. Figure 2). The soap can emulsify oily dirt, which could be easily rinsed away. This ability to act as an emulsifying agent arises from two properties of the soap.

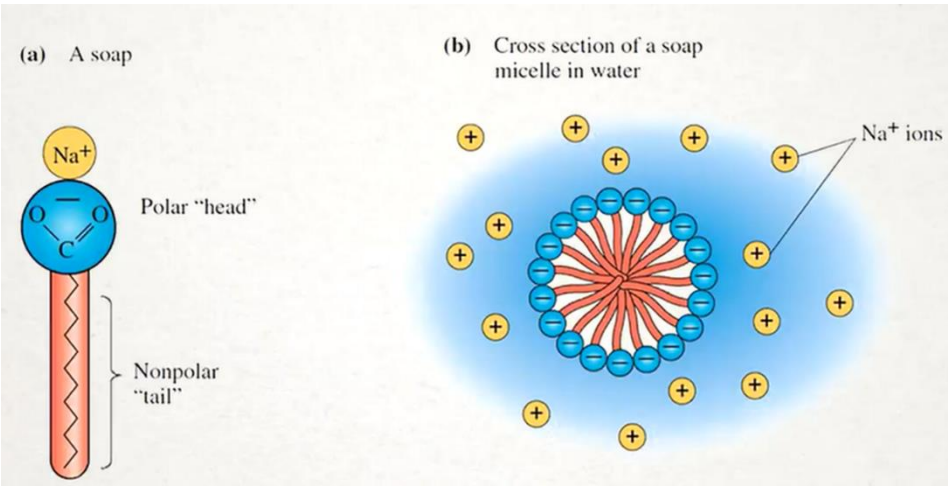
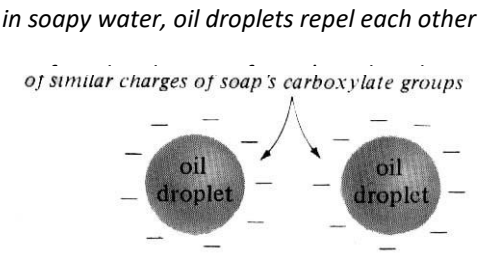


Figure 2 A micelle of the alkylcarboxylate ions of a soap

HOW SOAP WORKS:

Such process occurs in steps: (i) The mechanical action would divide the oily dirt into small oily droplets. (ii) The hydrophobic hydrocarbon chains would surround each oily droplet with their electrophilic ionic ends facing water. Accordingly, the oily droplets would exist as isolated small balls covered with the same negative charges. Due to

repulsions between the soap-oil droplets, the oil cannot come together again, but remains suspended. (iii) The final emulsion could be then easily rinsed away.



There are some disadvantages of soap:

(i) It does not work in hard water, but forms insoluble salts with Ca^{2+}, Mg^{2+} and other ions found in hard water. ("Softening" water involves exchanging these ions for Na^{+}).

$$2\ CH_3(CH_2)_{16}CO_2Na + Ca^{2+} \longrightarrow [CH_3(CH_2)_{16}CO_2]_2Ca + 2\ Na^{+}$$

sodium stearate calcium stearate insoluble

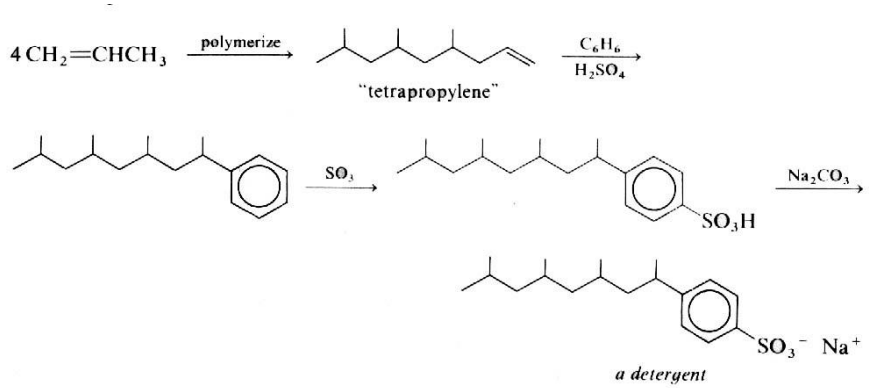
(ii) Soap affects both skin and clothes.

(iii) The economic cost is quite high.

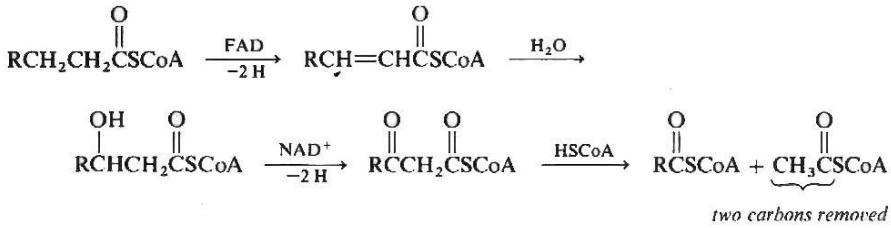
For these reasons, organic chemists started to think of making the synthetic soaps named detergents. In fact that most laundry products and many toilet "soaps" and shampoos are not soaps, but detergents. A detergent is a compound with a hydrophobic hydrocarbon tail with a sulfonate or sulfate ionic end, nearly the same properties of a soap molecule. Because of this structure, a detergent has the same

emulsifying properties as soap. The advantage of a detergent is that most metal alkylsulfonates and sulfates are water-soluble; detergents do not precipitate with the metal ions found in hard water.

One of the first detergents in common use was a highly branched alkylbenzenesulfonate. The alkyl portion of this compound is synthesized by the polymerization of 4 propylene molecules, which is then attached to the benzene ring by a Friedel-Crafts alkylation reaction. Sulfonation is the final step, followed by treatment with base, yields the detergent.



The produced detergent has a major disadvantage that they build up in rivers and lakes. It is well known that microorganisms can break down continuous-chain alkyl groups into smaller organic molecules according to the following equations: However, such microorganisms cannot biodegrade branched chains as branching interferes with the formation of the ketone group, and thus blocks the entire sequence. (FAD, NAD^+ and HSCoA, as shown in the following equation:



Organic chemists have overcome such problems and they easily obtain detergents with continuous alkyl chains.

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