

Carbohydrates

The most abundant class of bioorganic compounds are carbohydrates, of which glucose is most commonly found. Plants produce glucose by photosynthesis. Functions include: energy storage and production, normal lipid metabolism, part of RNA & DNA, structural support.

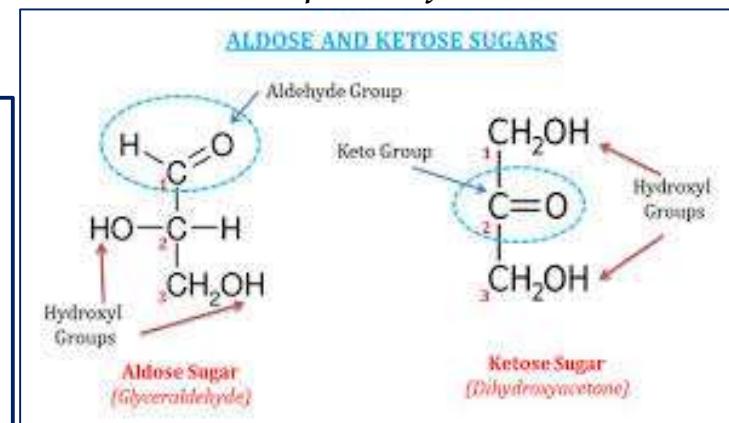
Carbohydrates are hydrates of carbon, that is on decomposition they give water molecules: glucose on complete combustion [respiration] releases CO_2 and water.

Carbohydrates are defined as polyhydroxy aldehydes [D-glucose], polyhydroxy ketones [D-fructose] or compounds that yield polyhydroxy aldehydes or polyhydroxy ketones on hydrolysis [D-sucrose]. The latter group can be hydrolyzed to polyhydroxy aldehydes or polyhydroxy ketones. **OR**
Carbohydrates are also defined as aldehyde or ketone derivatives of polyhydroxy alcohols.

They contain some number of oxydrilic groups bearing the formula $(\text{CH}_2\text{O})_n$ (only molecules with $n \geq 3$ are considered carbohydrates). However, not all carbohydrates have the empirical formula $(\text{CH}_2\text{O})_n$; some also contain nitrogen, phosphorus or sulfur.

Three major classes of carbohydrates can be defined as:

1. Monosaccharides (1 unit sugar): $C_n(\text{H}_2\text{O})_n$
2. Oligosaccharides (2-10) [Disaccharides { $n=2$: $C_n(\text{H}_2\text{O})_n$ }]
3. Polysaccharides (10 to 10^7)



Monosaccharides can be further classified as aldose or ketose depending on the type of functional group and no. of carbons present. E.g. aldohexose (6-carbon monosaccharide with $-CHO$ gp)

ketopentose (5-carbon monosaccharide with $C=O$ gp)

Monosaccharide	Oligosaccharide	Polysaccharide
Functional group	Number of carbon atoms	
Aldoses e.g Glucose	Trioses	Di-saccharide
Ketoses e.g Fructose	Tetroses	Tri-saccharide
	Pentoses	Tetra-saccharide
	Hexoses	
	Heptoses	
	Maltose	Homopoly-saccharide
	Lactose	Heteropoly-saccharide
	Sucrose	Starch
		Dextrin
		Glycogen
		Cellulose
		Inulin
		Hyaluronic acid
		Heparin
		Chondroitin sulfate
		Dermatan Sulfate
		Keratan Sulfate

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Most carbohydrates are produced photo-synthetically by bacteria, algae and plants

Carbohydrates (“hydrate of carbon”) have the empirical formula of $(CH_2O)_n$, where $n \geq 3$.

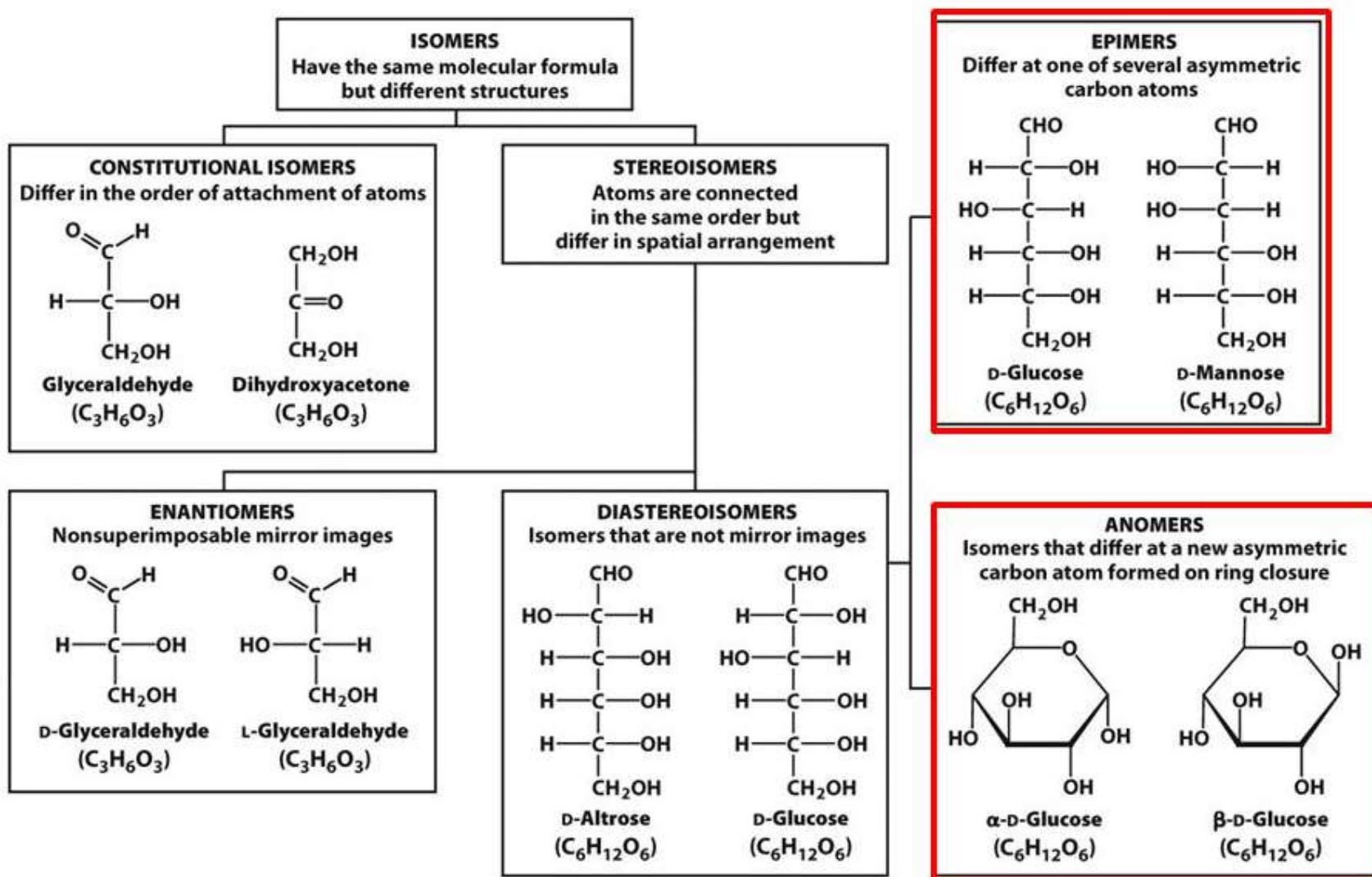
- **Monosaccharides**: one monomeric unit
- **Oligosaccharides**: ~2-20 monosaccharides
- **Polysaccharides**: > 20 monosaccharides
- **Glycoconjugates**: linkages to proteins or lipids

No. of Carbons	Category Name	Examples
3	Triose	<i>Glyceraldehyde</i>
4	Tetrose	<i>Erythrose</i> , Threose
5	Pentose	Arabinose, <i>Ribose</i> , Ribulose, Xylose, Xylulose, Lyxose
6	Hexose	Allose, Altrose, <i>Fructose</i> , Galactose, <i>Glucose</i> , Gulose, Idose, Mannose, Sorbose, Talose, Tagatose
7	Heptose	Sedoheptulose

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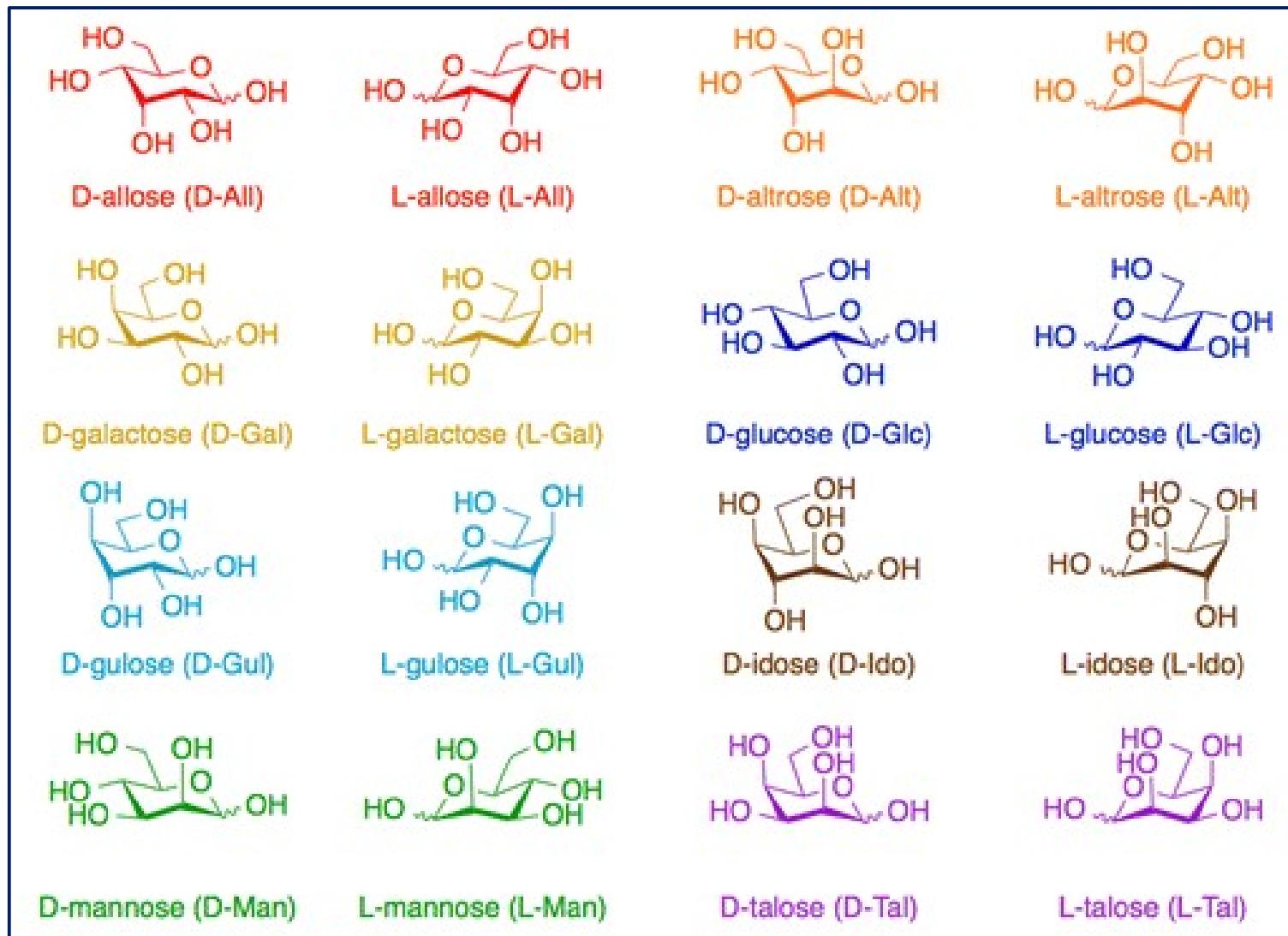
Isomeric forms of carbohydrates



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$2^4 = 16$ stereoisomers of Glucose



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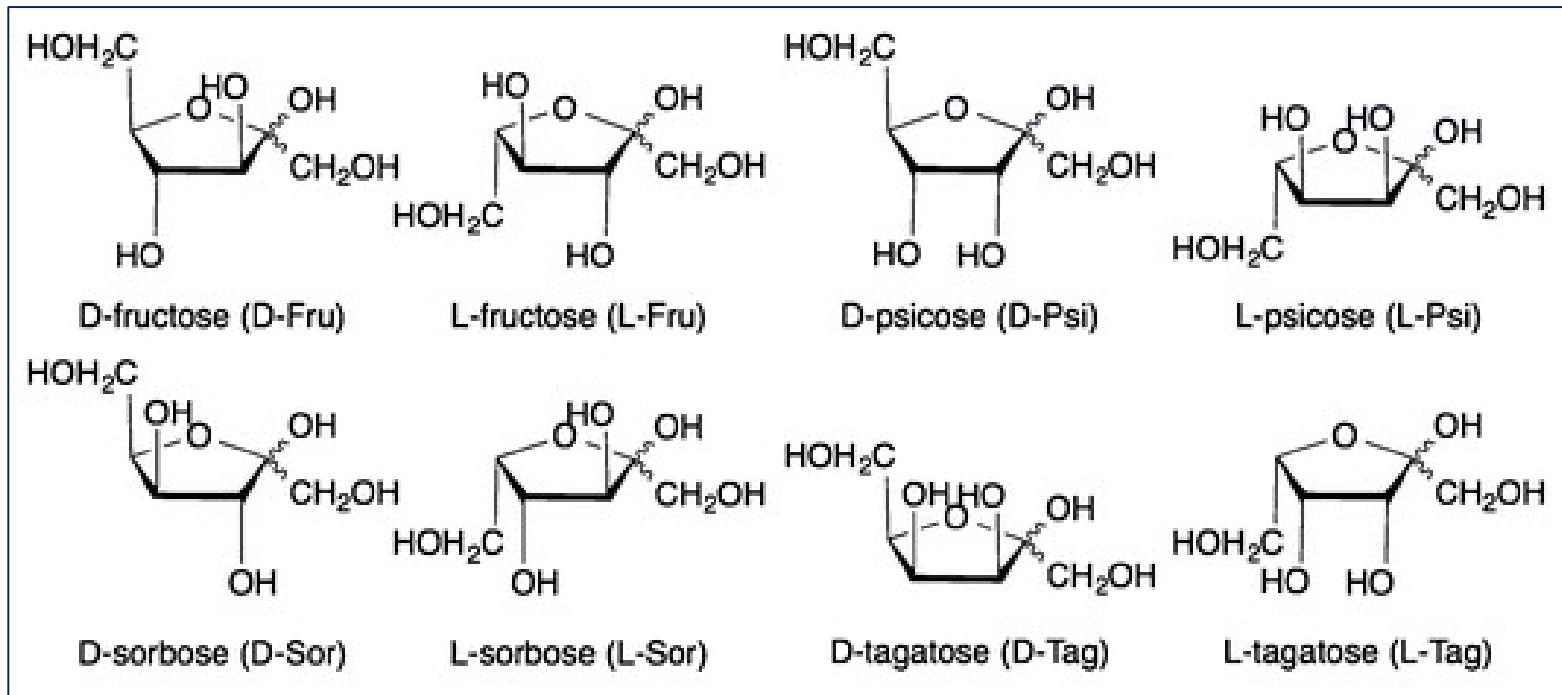
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$2^3 = 8$ stereoisomers of Fructose



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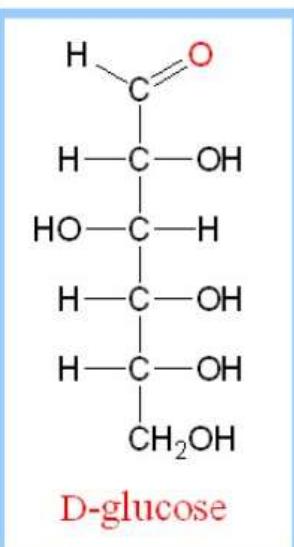
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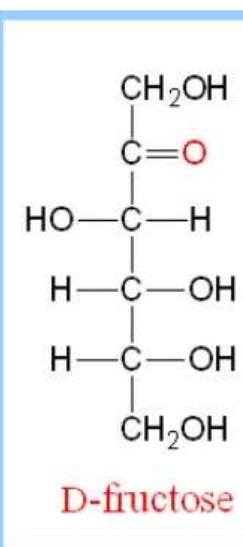
Aldose-Ketose Isomerism

Monosaccharides

Aldoses (e.g., glucose) have an aldehyde group at one end.



Ketoses (e.g., fructose) have a keto group, usually at C2.



Polyhydroxy aldehyde

Fischer projection formulae of D-glucose and D-fructose

Polyhydroxy ketone

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D-glyceraldehyde L-glyceraldehyde



D-glyceraldehyde L-glyceraldehyde

D and L Notations

In a Fischer projection, the — OH group on the

- chiral carbon *farthest from the carbonyl group* determines
- an L or D isomer
- left is assigned the letter L
- right is assigned the letter D

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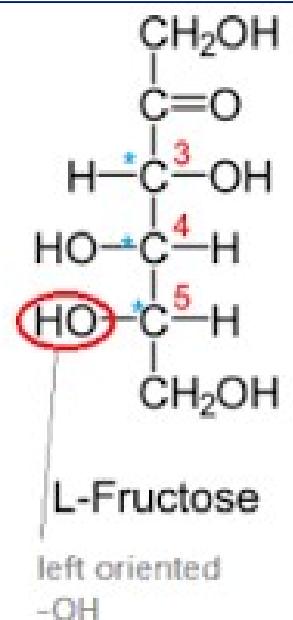
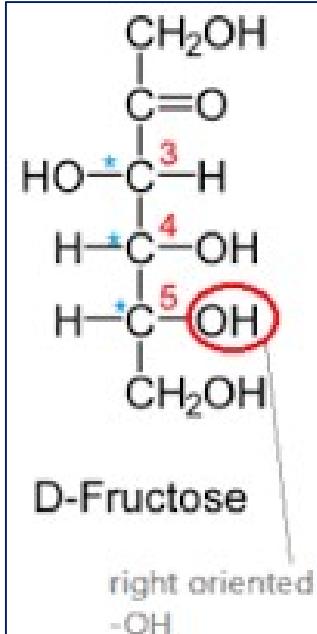
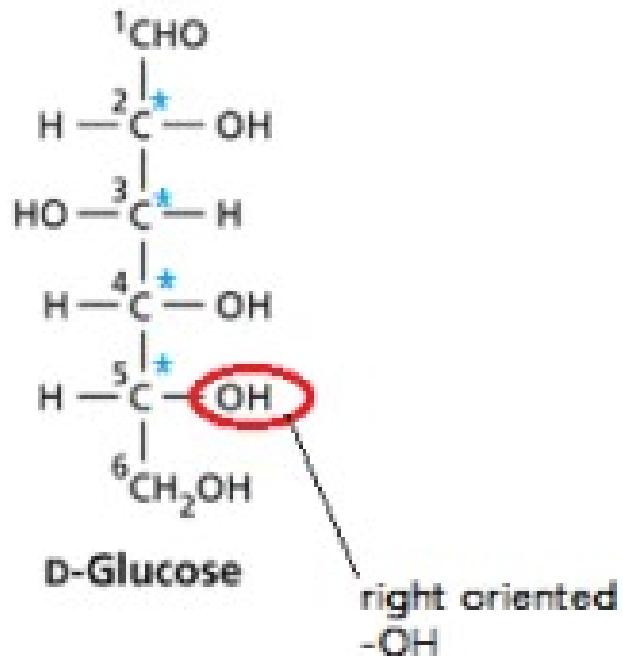
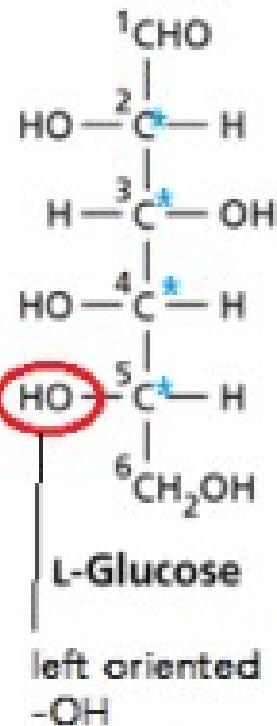
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Enantiomers/ Optical Isomers

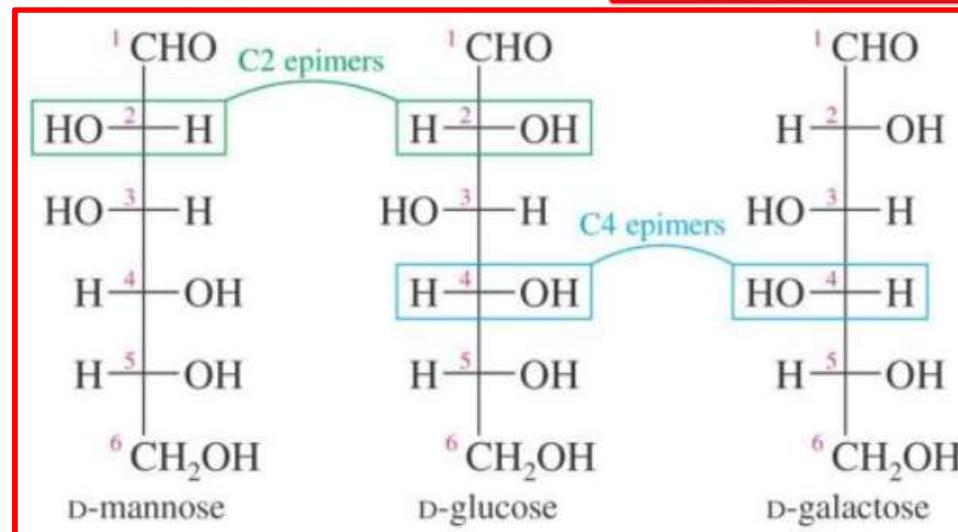
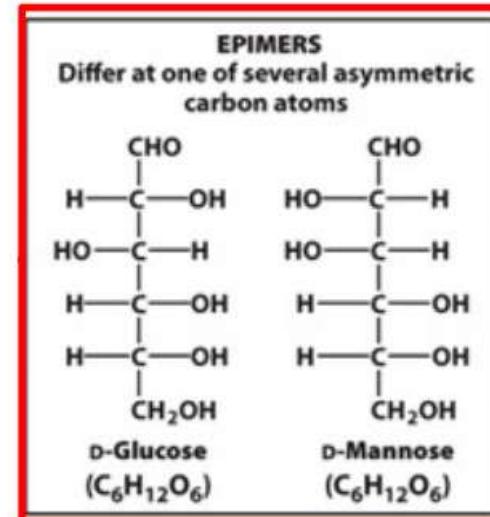
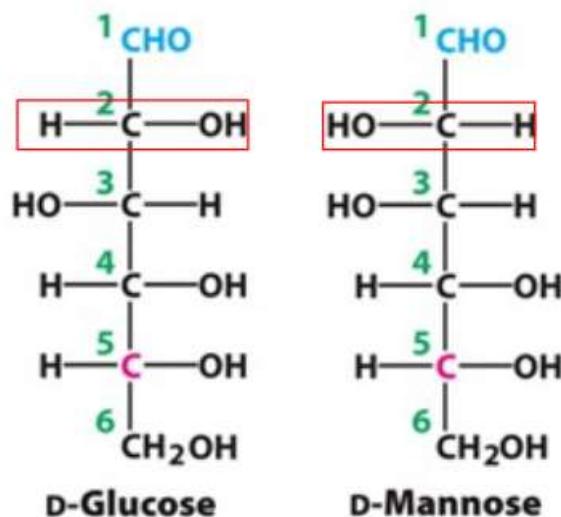


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Epimers

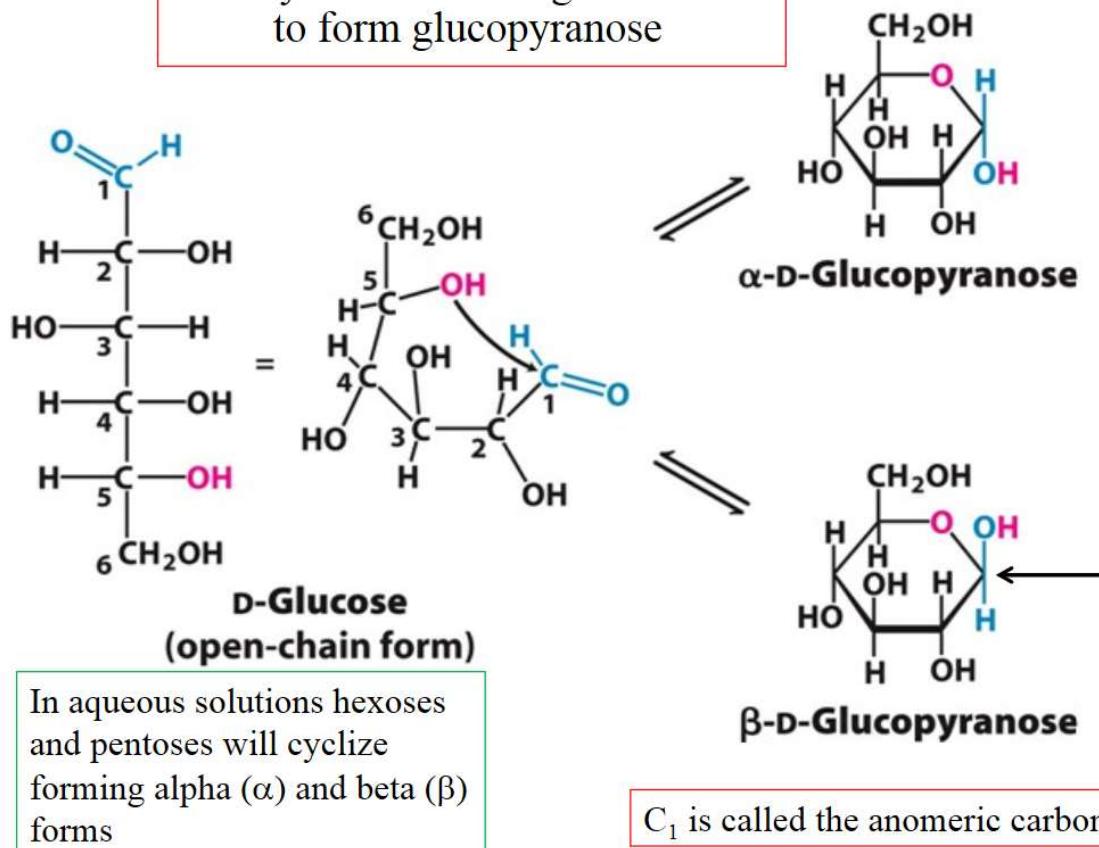
- Epimers – sugars that differ at only **one** of several chiral centers. example: D-Mannose is an epimer of D-Glucose



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Cyclization of D-glucose
to form glucopyranose



The new stereogenic center generated by hemiacetal ring closure is called the anomeric center. The two possible stereoisomers are referred to as anomers, designated as α or β according to the stereochemical relationship between the anomeric center and the configuration of the most distant stereogenic center. If the hydroxyl groups bound to this center point in the same direction (*cis*), this anomer is called the α -anomer, when they are pointing in opposite directions (*trans*), it is named β . Anomers are diastereomers.

Anomers are diastereoisomers of cyclic forms of sugars or similar molecules differing in the configuration at the anomeric carbon (C-1 atom of an aldose or the C-2 atom of a 2-ketose)

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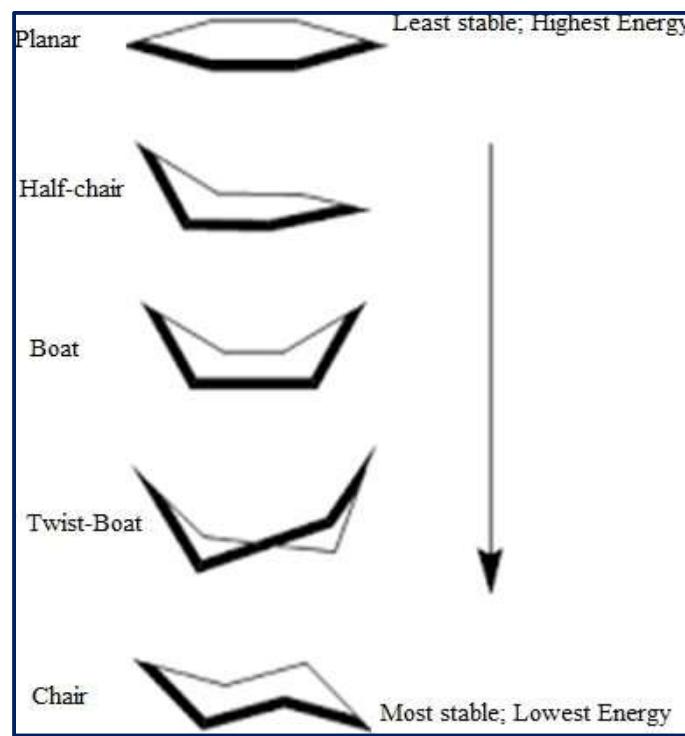
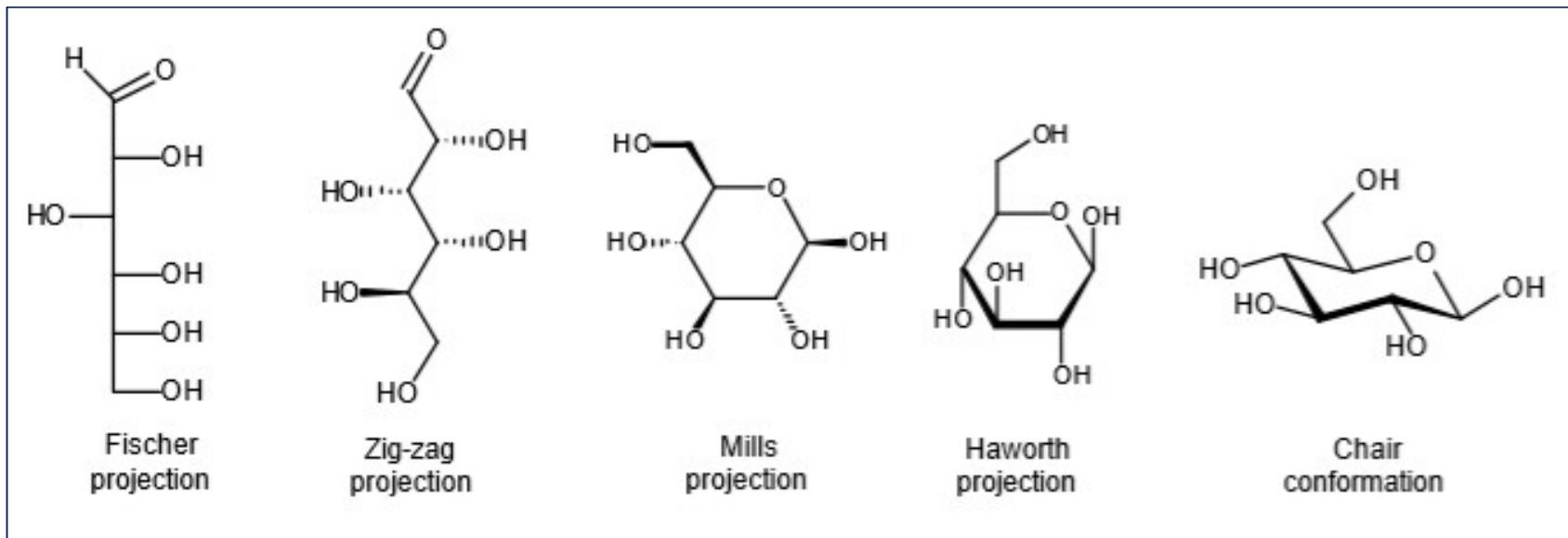
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Different Representations of Monosaccharide Structures



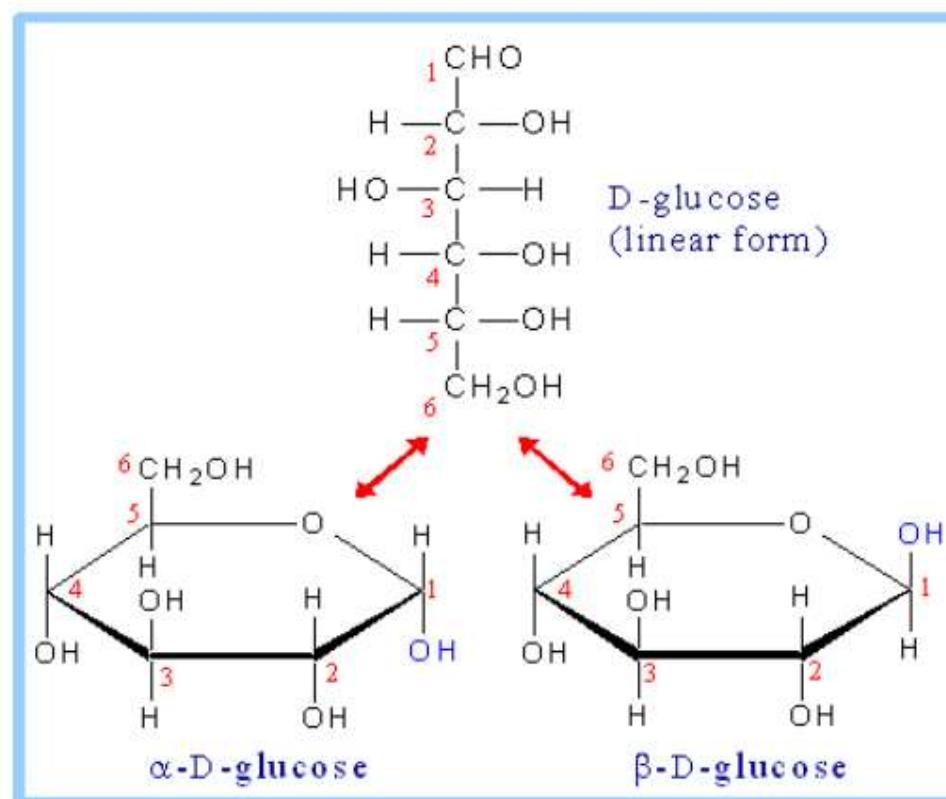
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Cyclic Structure of Glucose

Pentoses and hexoses can **cyclize** as the ketone or aldehyde reacts with a distal OH.

Glucose forms an intra-molecular hemiacetal, as the C1 aldehyde & C5 OH react, to form a 6-member pyranose ring, named after pyran.



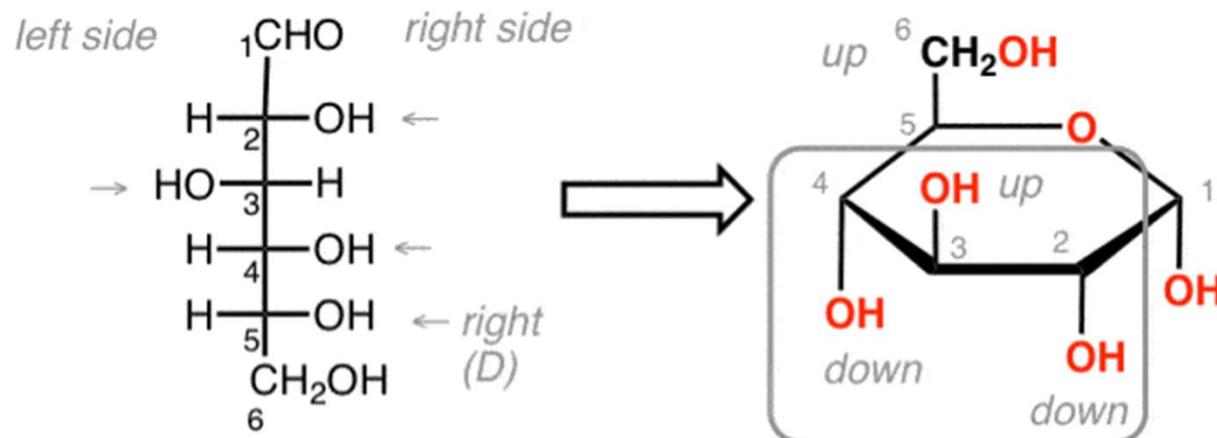
These representations of the cyclic sugars are called **Haworth projections**.

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Converting a Fischer Projection to A Haworth Projection

Shortcut: for C₂, C₃, and C₄ right side → down
left side → up

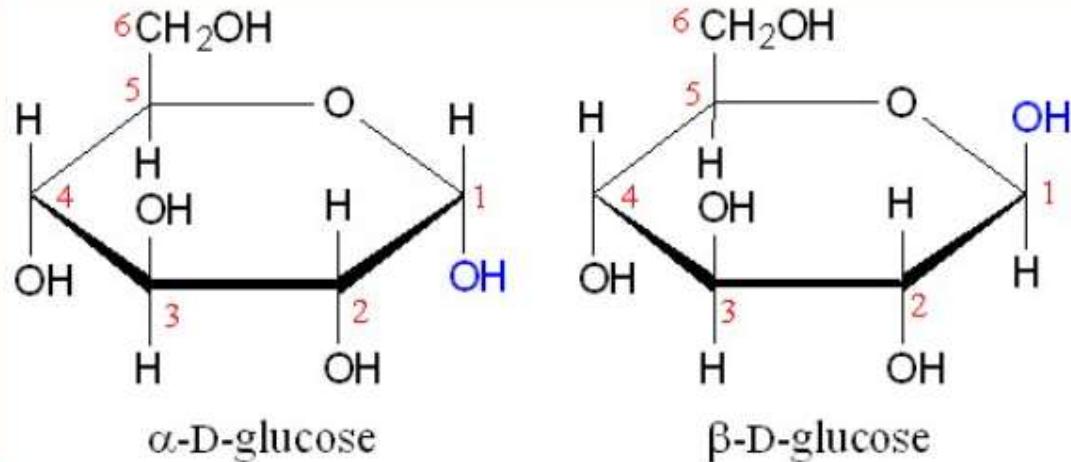


D-Glucose
(Fischer projection)

α-D-Glucopyranose
(Haworth projection)

For C₅ : if OH is on the right of the Fischer, it's a D-sugar (by definition)
This will place C₆ on the top face of the Haworth.

For C₁ : the α anomer has OH → down (for D-sugars)
the β anomer has OH → up (for D-sugars)



Cyclization of glucose produces a new **asymmetric center** at **C1**. The 2 stereoisomers are called **anomers**, α & β .

Haworth projections represent the cyclic sugars as having essentially planar rings, with the OH at the anomeric C1:

- ◆ α (OH **below** the ring)
- ◆ β (OH **above** the ring).

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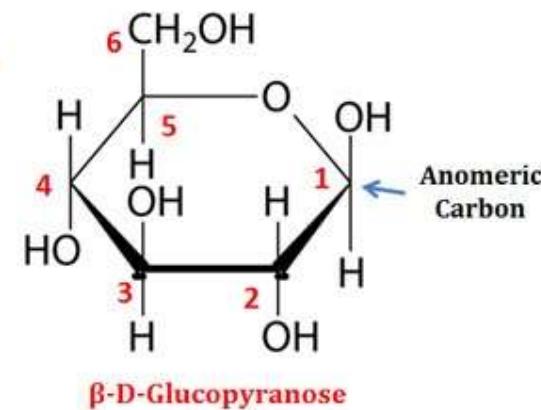
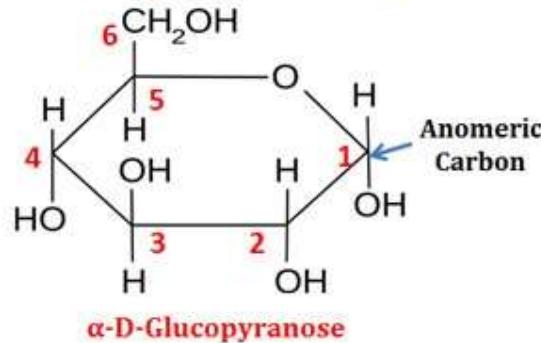
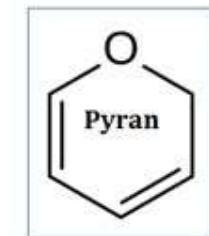
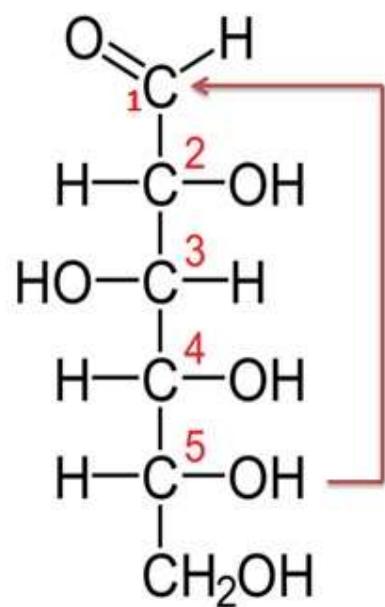
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Formation of Cyclic Structure of Glucose (Aldohexose)



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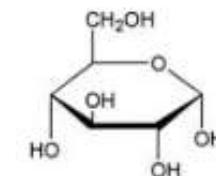
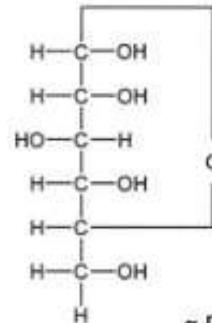
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The most common sugar ring forms

- Pyranose

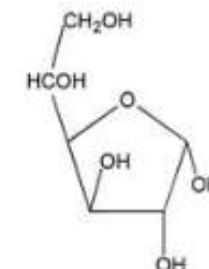
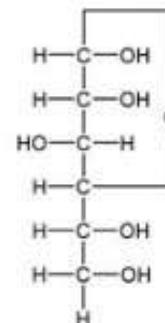
- Six-member rings
- More thermodynamically favorable
- Most common



α -D-glucopyranose

- Furanose

- Five-membered rings
- More kinetically favorable



α -D-glucofuranose

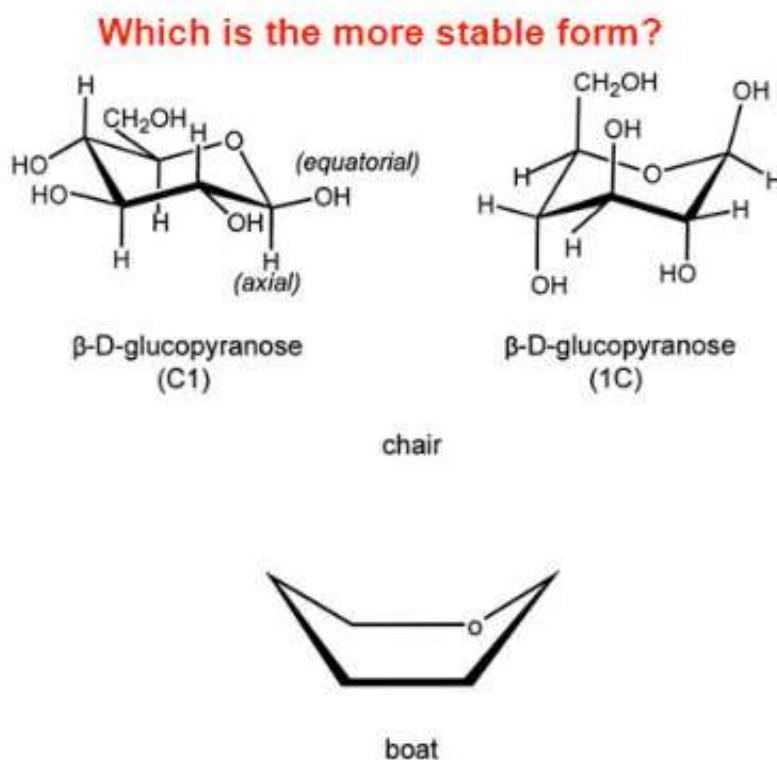
The six-membered ring compounds are called pyranoses and the five-membered ring compounds are called furanoses. The six-membered aldopyranose ring is much more stable than the aldonofuranose ring and predominates in aldohexose solution.

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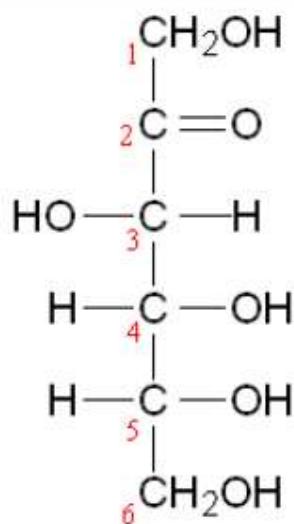
The more correct representation of the ring form

- The pyranose and furanose rings are not flat
- For pyranose rings the chair and boat forms are better representations of their actual structures
- The furanose rings are present as either envelope or twist conformations

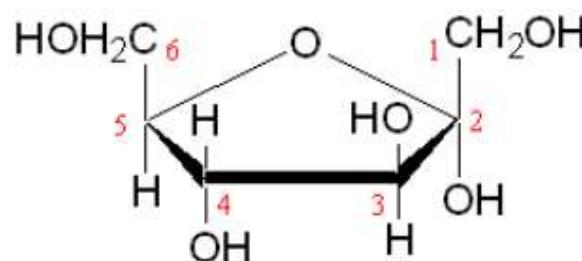


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D-fructose (linear)



α -D-fructofuranose

Fructose forms either

- ◆ a 6-member pyranose ring, by reaction of the C2 keto group with the OH on C6, or
- ◆ a 5-member furanose ring, by reaction of the C2 keto group with the OH on C5.

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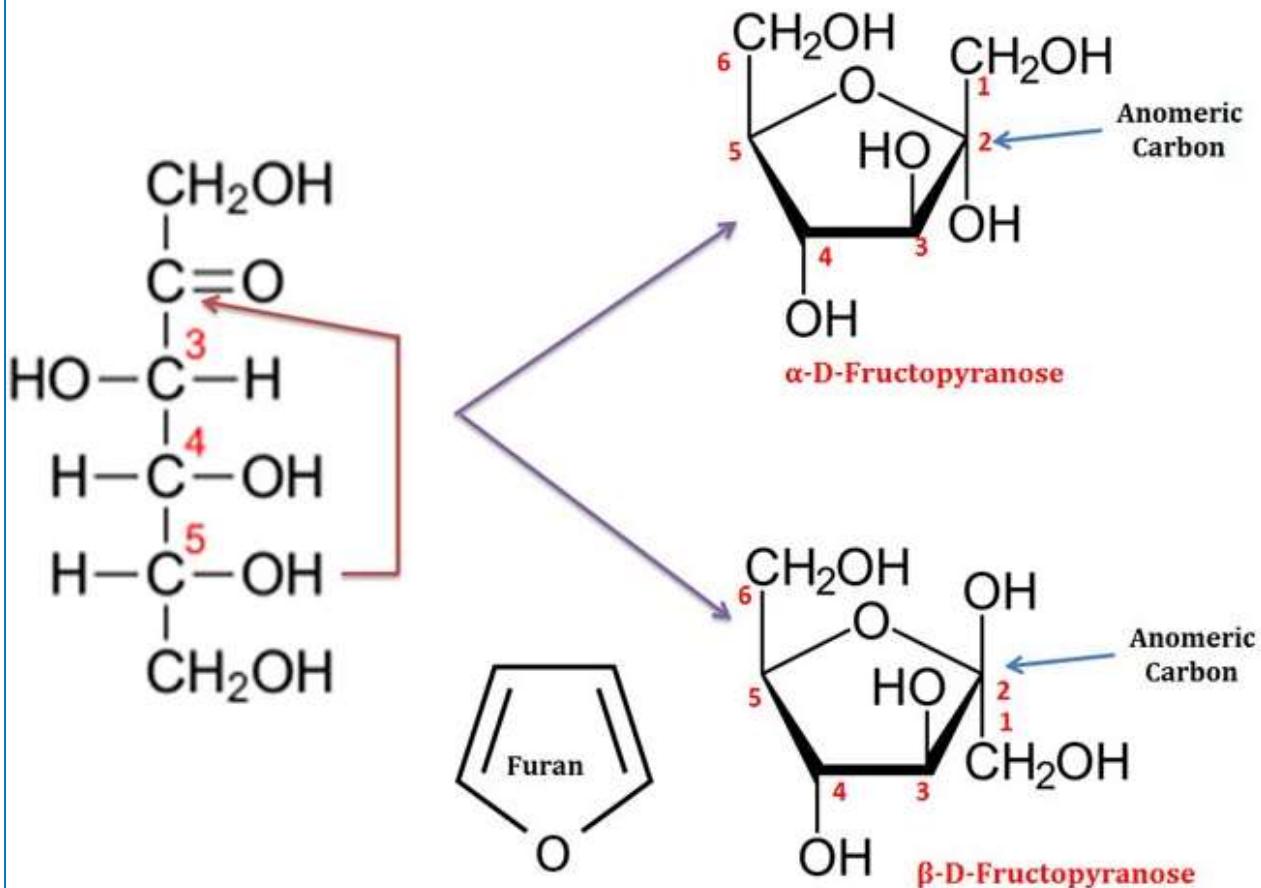
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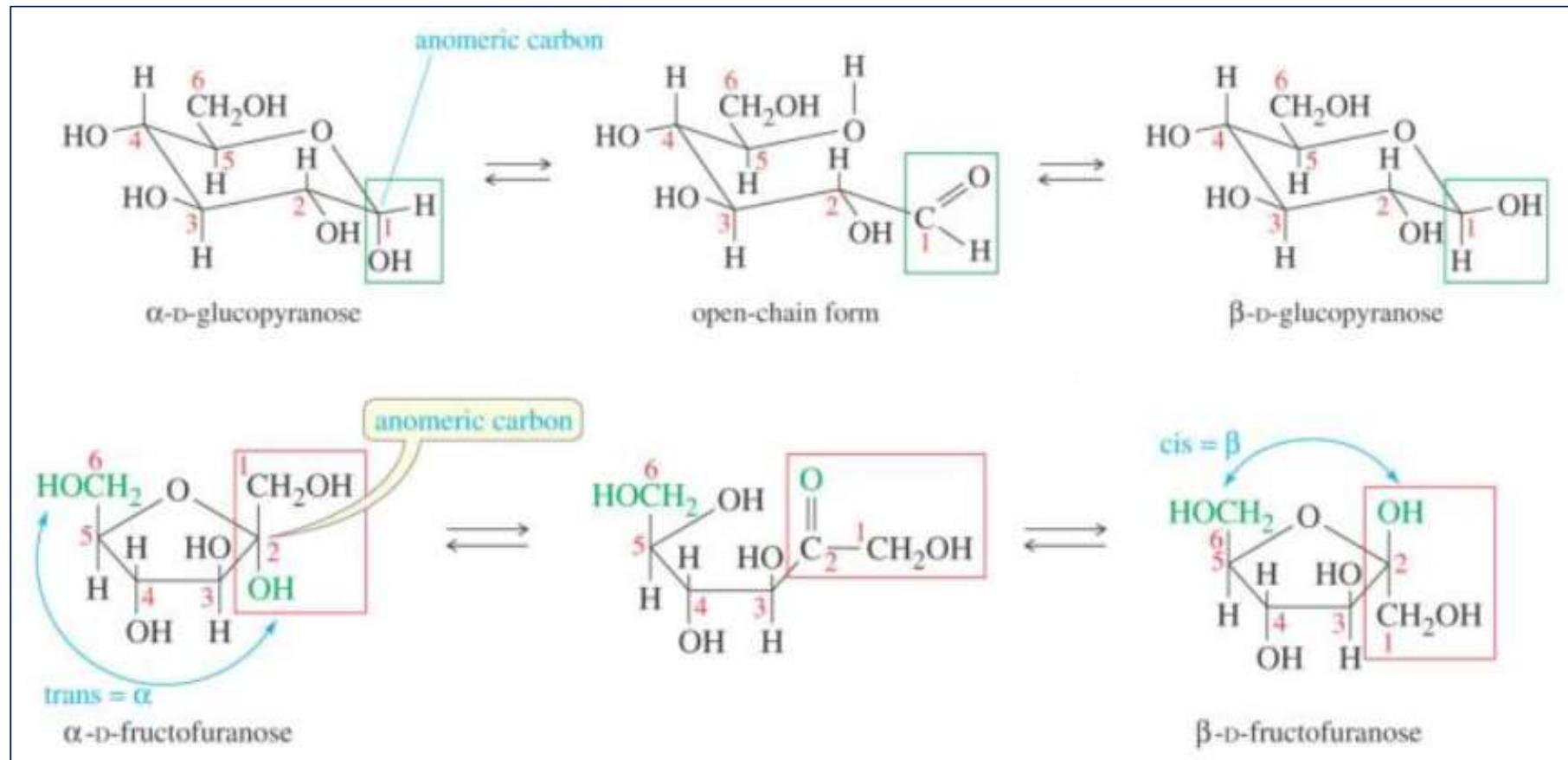
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Formation of Cyclic Structure of Fructose (Ketohexose)



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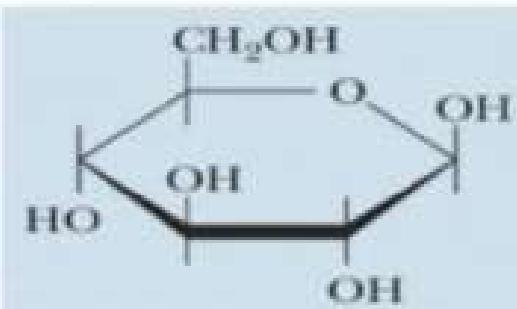
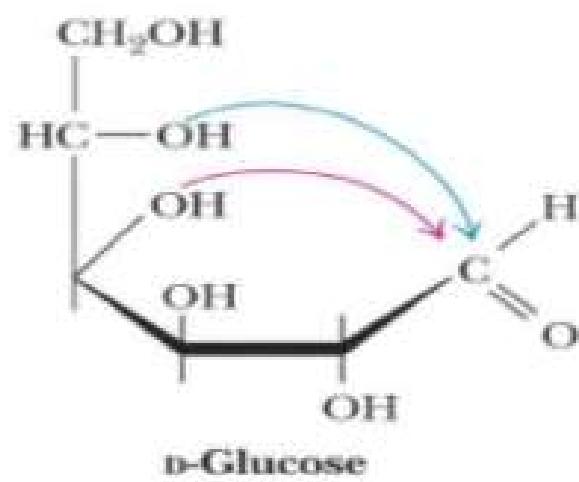
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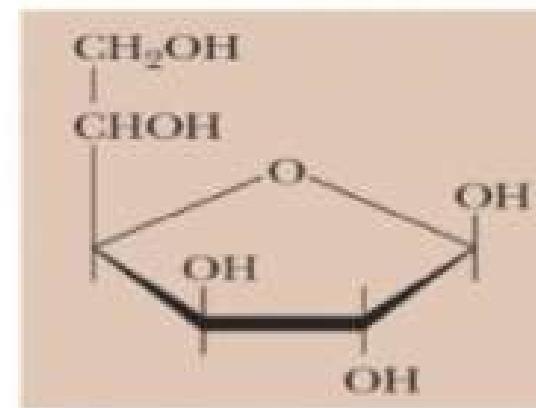
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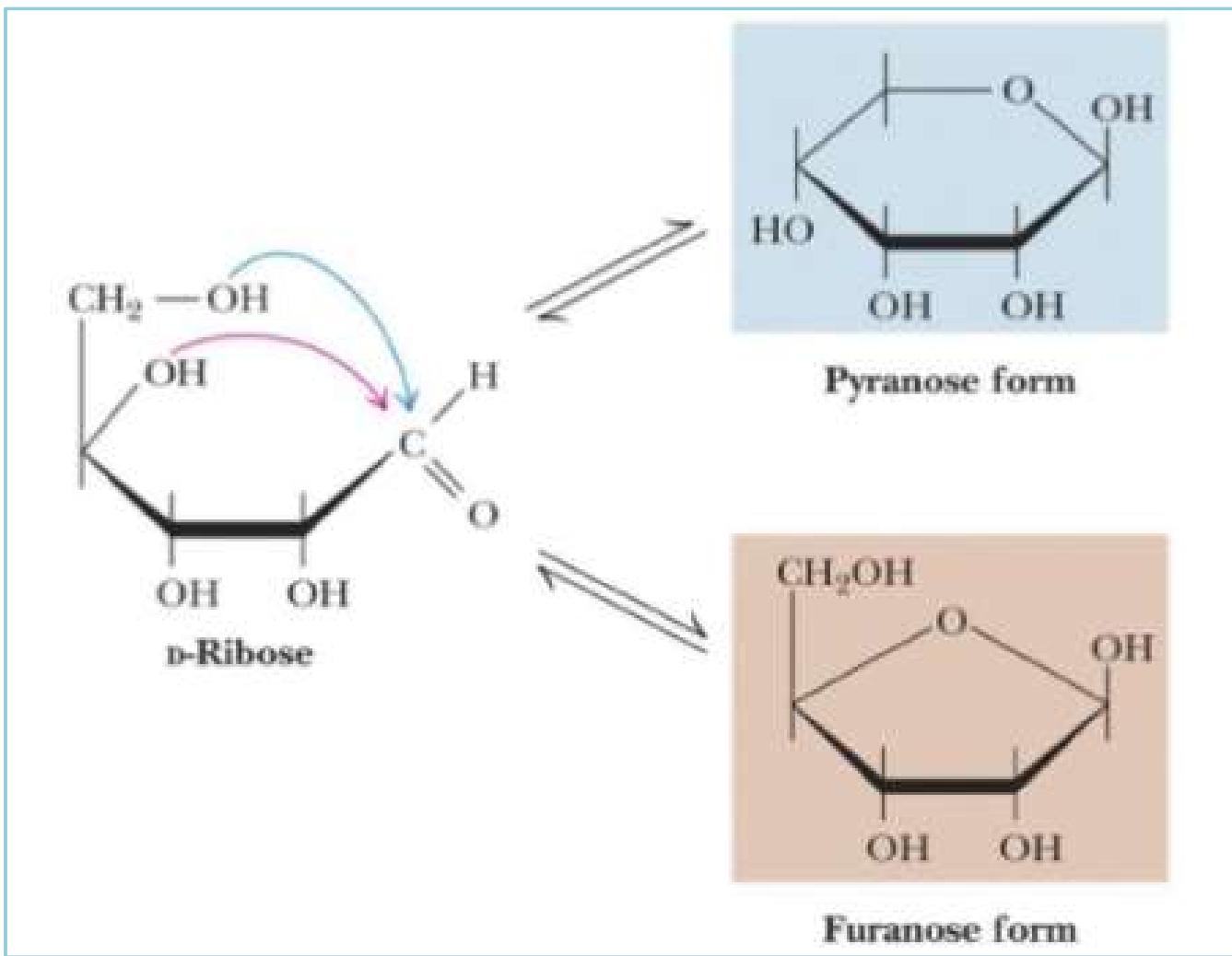
Pyranose form



Furanose form

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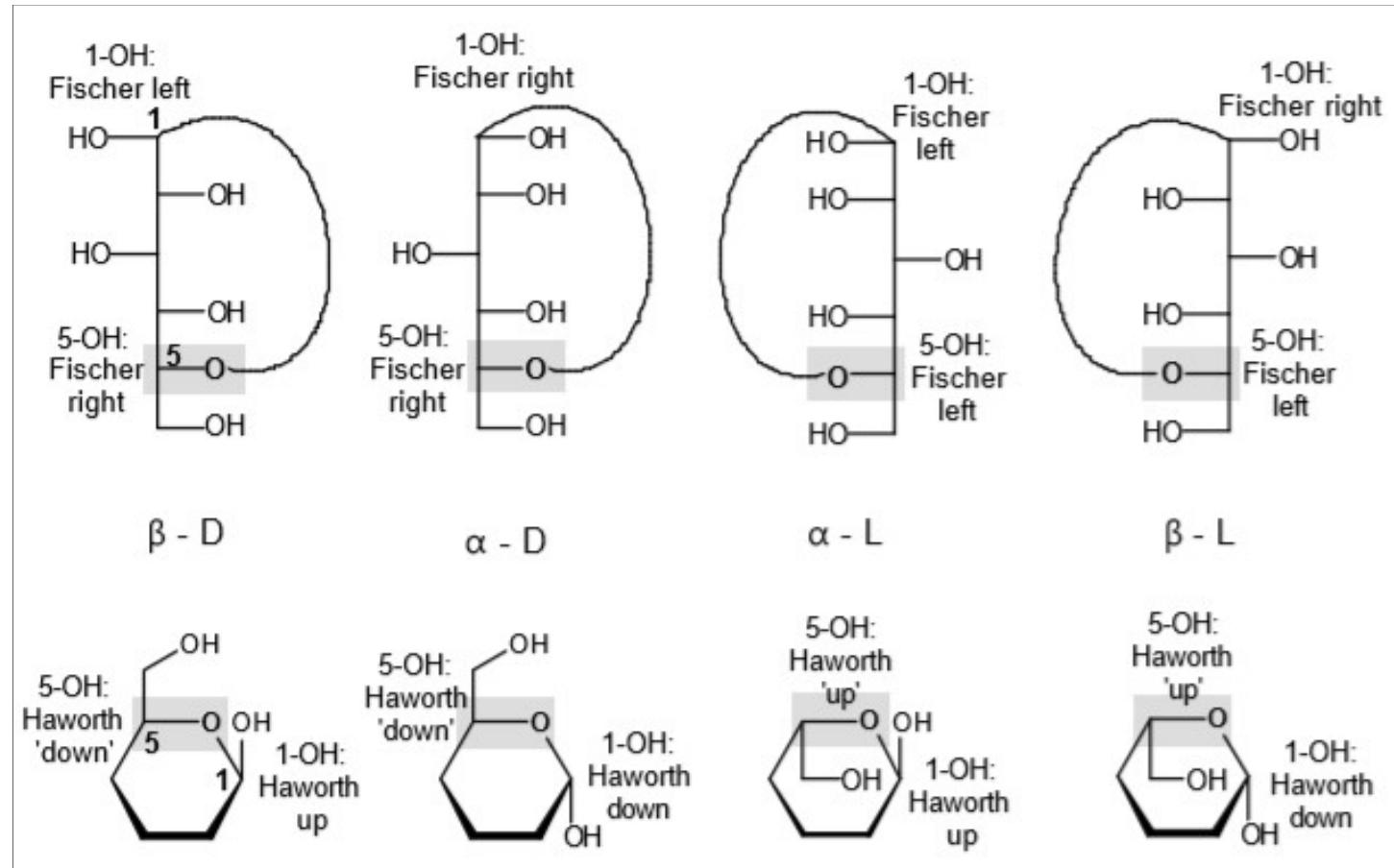
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Corresponding structures of α - and β -anomers of monosaccharide hemiacetals of the D- and L-series, represented as Fischer and Haworth projections; the correct numbering of the carbohydrate ring is indicated.



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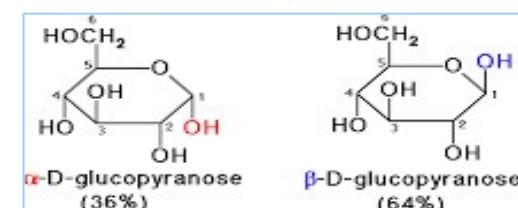
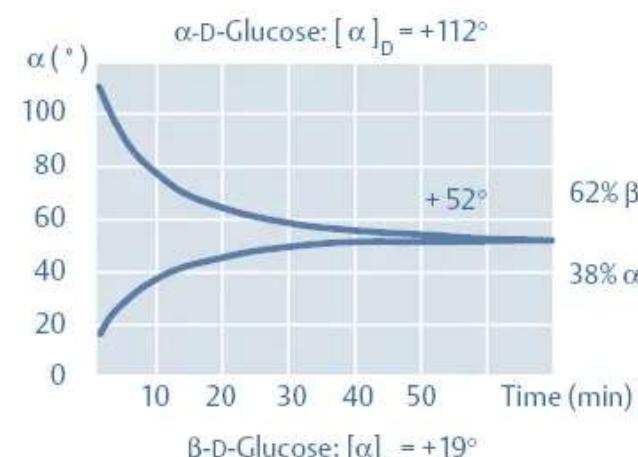
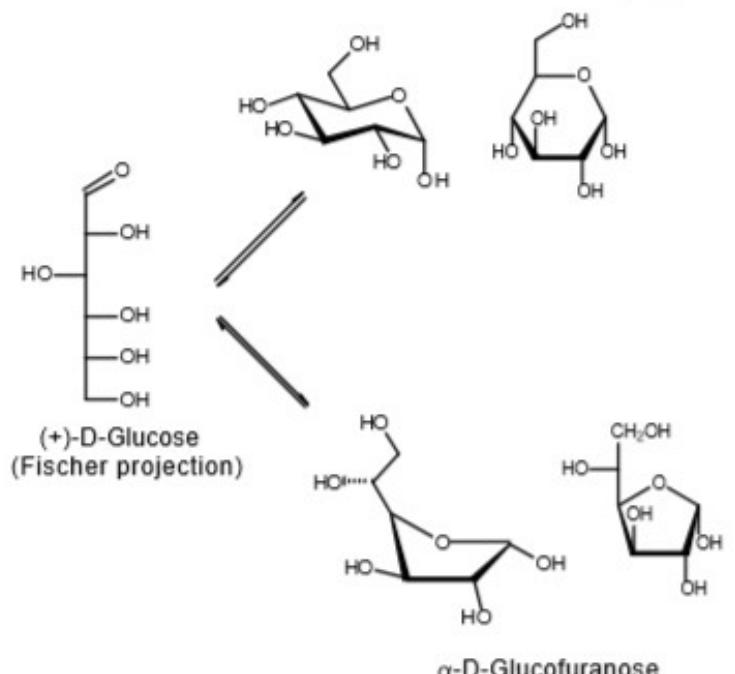
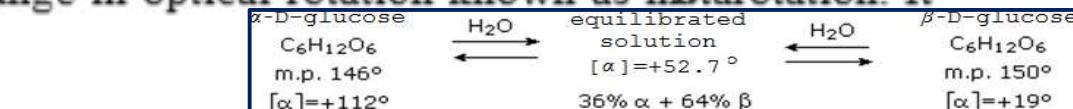
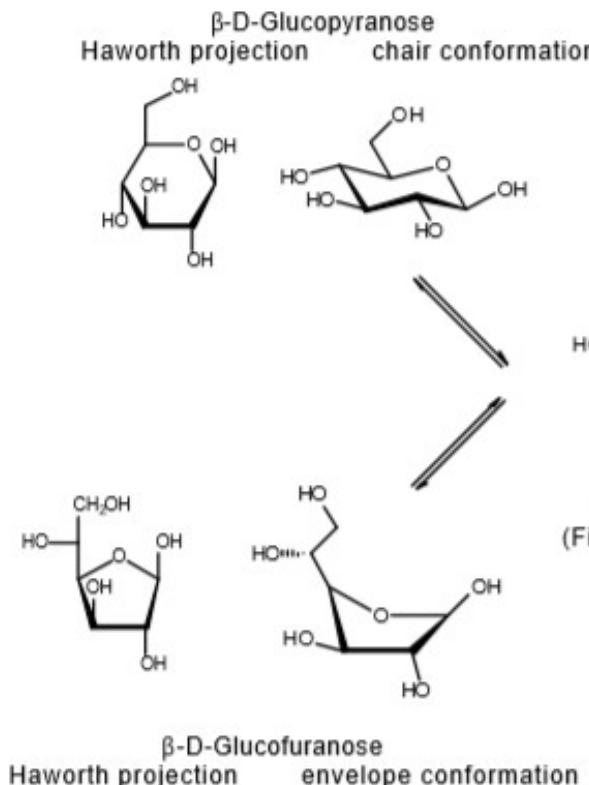
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Each crystalline free sugar is a discrete stereoisomer. On dissolution in water however, the hemiacetal ring opens and reforms to give products with different ring sizes and configurations at the anomeric center. This equilibration occurs with all reducing saccharides and is accompanied by a change in optical rotation known as mutarotation. It can be acid- and base-catalyzed.

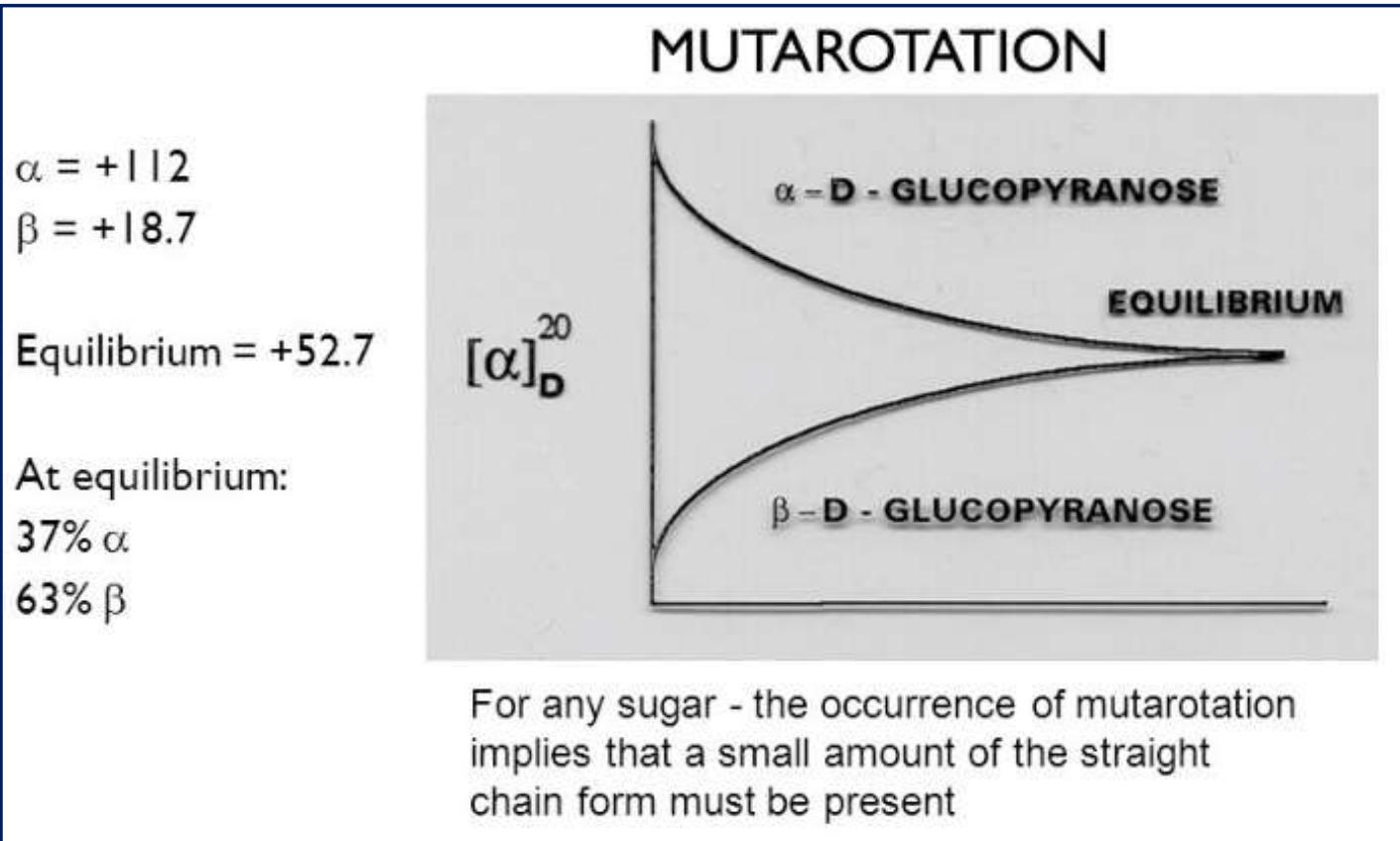


Mutarotation of D-glucose in solution leads to a mixture of α - and β -pyranoses as well as α - and β -furanoses. In addition to the structures shown, several other species can be involved in mutarotation including the acyclic hydrate and even septanoses and oxetanoses.

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Anomers of D-glucose hemiacetal



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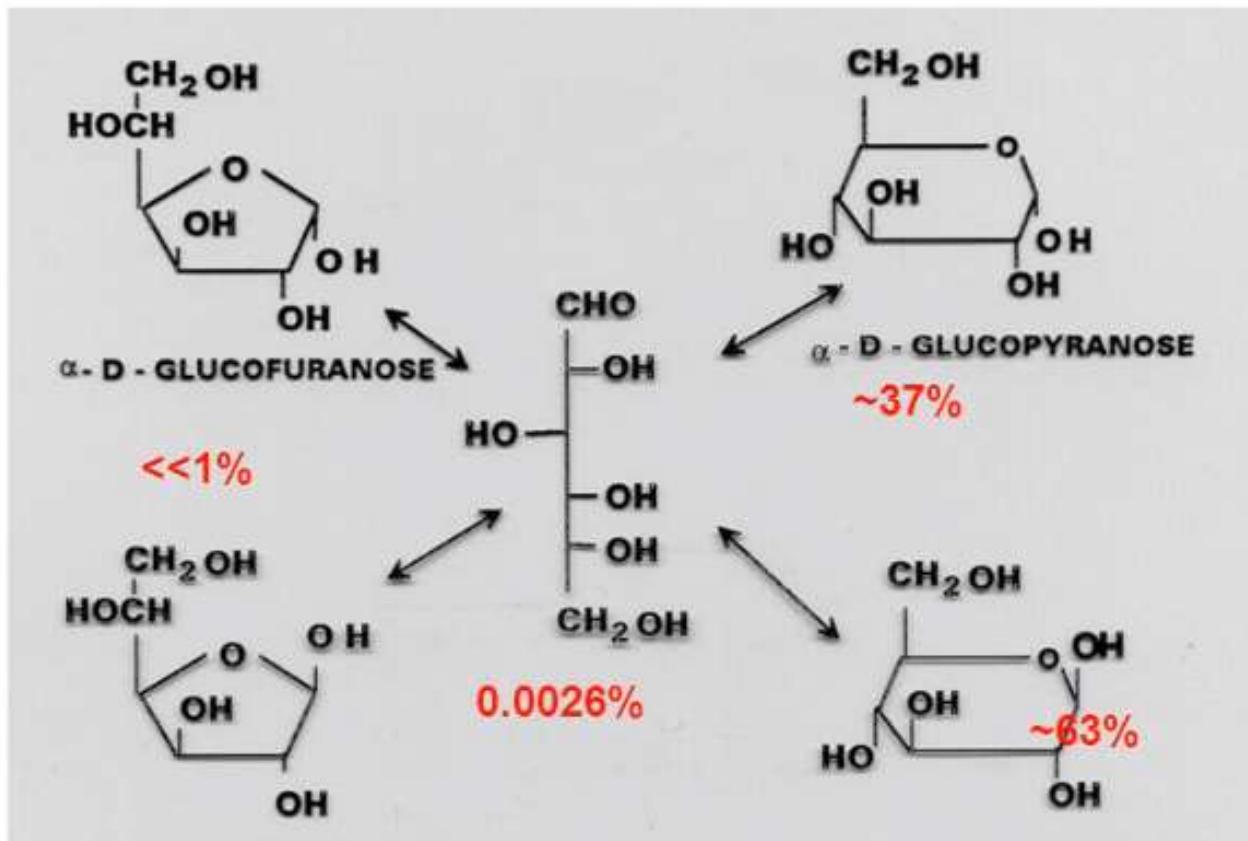
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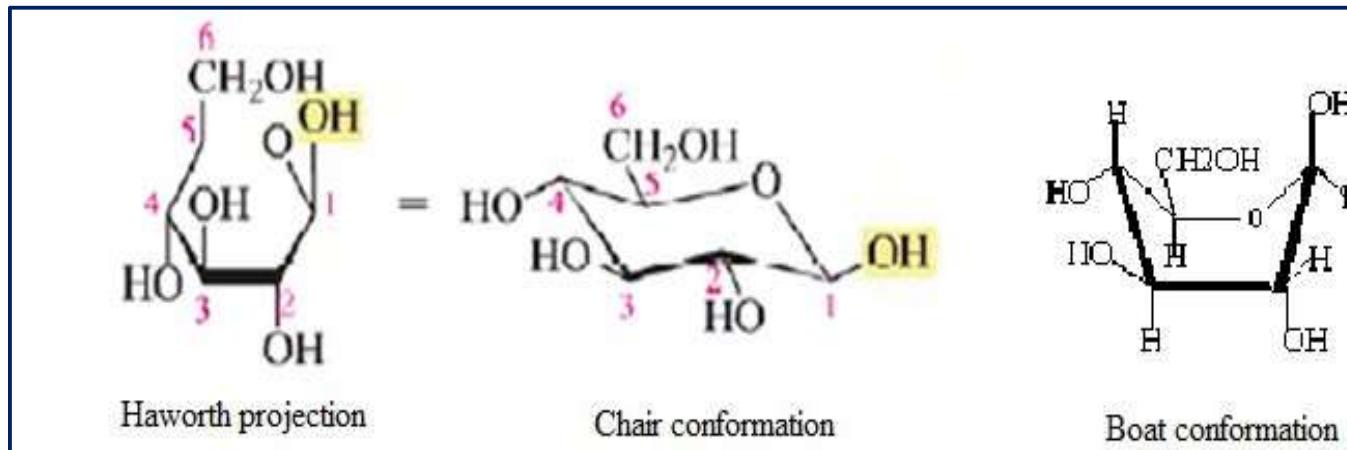
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MUTAROTATION



It is defined as "the change in the specific optical rotation representing interconversion of α and β forms of D-glucose to an equilibrium mixture."

Conformations of D-glucose (β -anomer)



In addition to intramolecular van der Waals interactions, carbohydrate conformations are determined by some other factors, such as electrostatic interactions as well as intramolecular hydrogen bond formation and especially the anomeric effect.

Chair conformation is most stable conformation.

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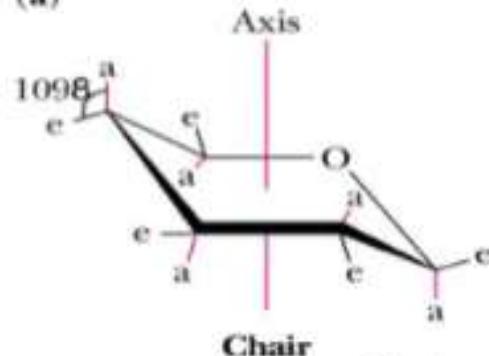
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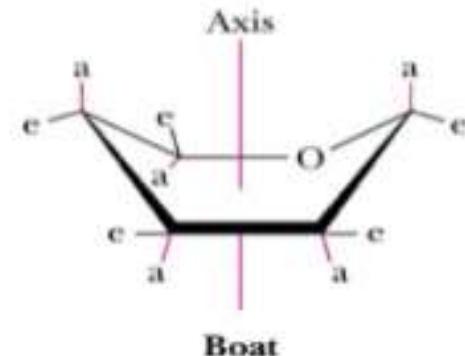
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(a)



Chair



Boat

Chair and boat conformations of a pyranose sugar

a = axial bond

e = equatorial bond

(b)



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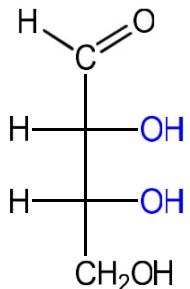
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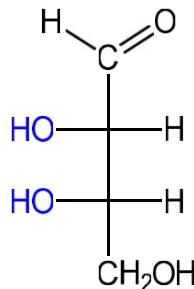
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Configurations of Aldoses

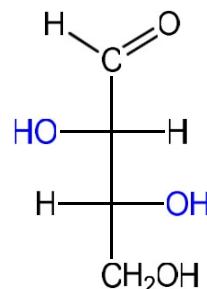
Aldotetroses: two asymmetric centres ($n=2$) and four stereoisomers ($2^n=2^2=4$)



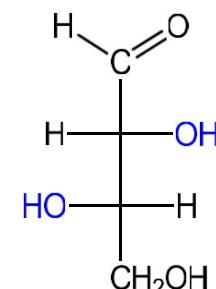
D-erythrose



L-erythrose



D-threose



L-threose

(R,R)-(+)-Erythrose (S,S)-(-)-Erythrose

(2S,3R)-(-)-Threose

(2R,3S)-(+)-Threose

Aldopentoses: three asymmetric centres ($n=3$) and eight stereoisomers ($2^3=8$)

Aldohexoses: four asymmetric centres ($n=4$) and 16 stereoisomers ($2^4=16$)

Aldoheptoses: five asymmetric centres ($n=5$) and 32 stereoisomers ($2^5=32$)

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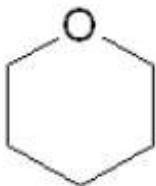
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Cyclic form of Glucose:

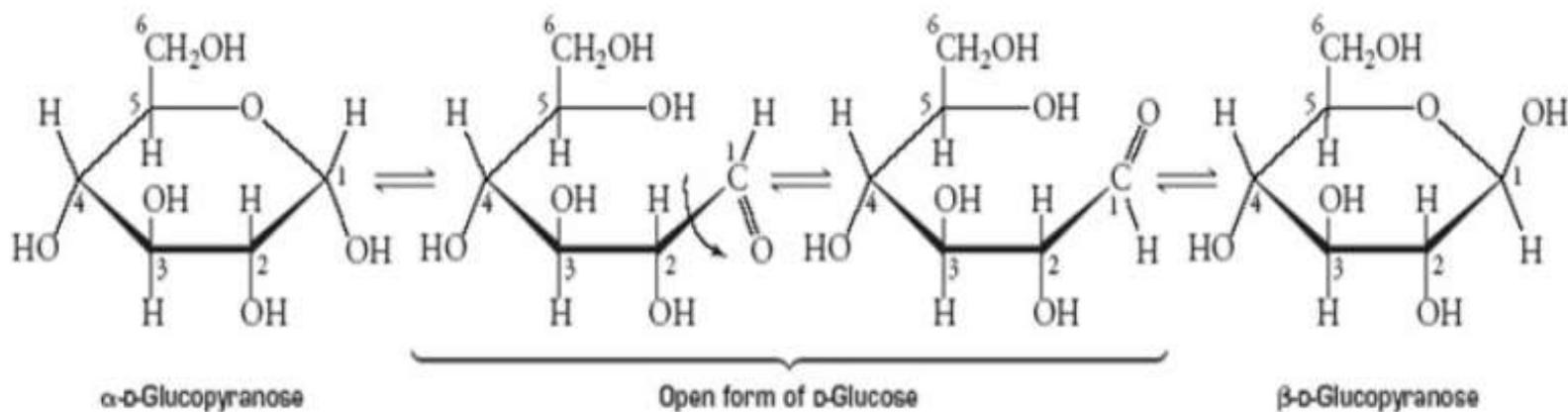


pyranose ring



furanose ring

- *Mutarotation is the interconversion of the α and β anomers.*

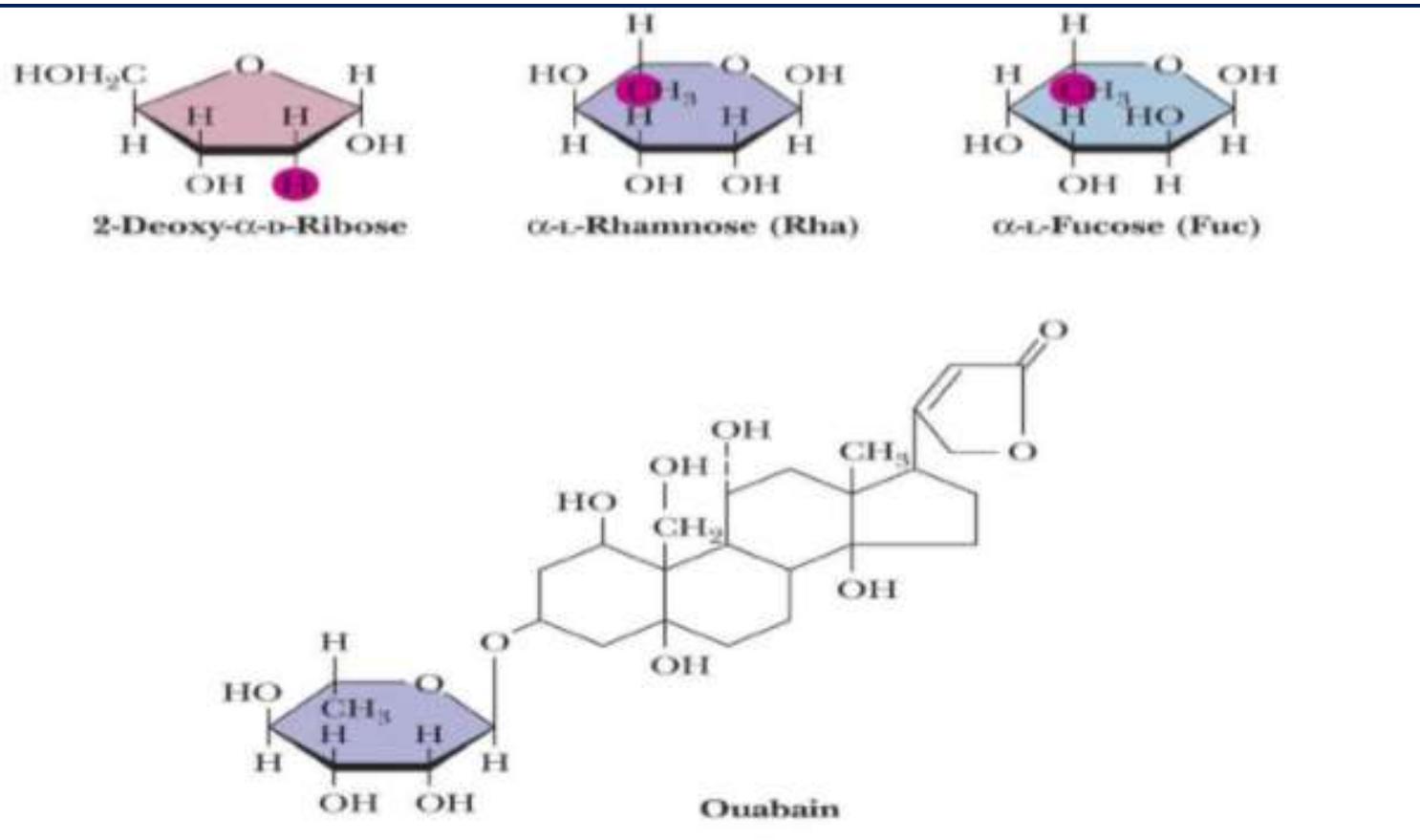


These two forms of Glucose are said to be anomers (α and β anomers).

D-Glucose anomers

Glucose forms a pair of cyclic hemiacetals when the $-\text{OH}$ group attached to carbon atom 5 reacts with the C=O group. The cyclic hemiacetal with the $-\text{OH}$ on carbon atom 1 pointing down is the α anomer and that with the $-\text{OH}$ pointing up is the β anomer. Monosaccharides that form anomers containing six-membered rings are called pyranoses.

Derived Sugars



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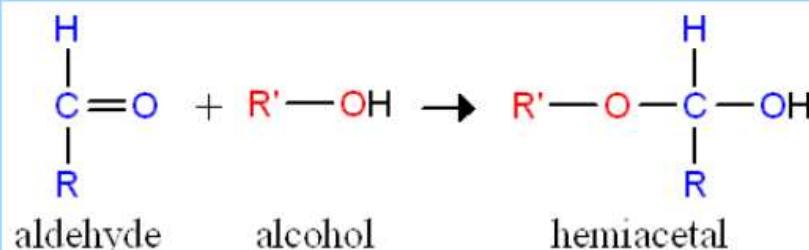
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Cyclic forms of sugars

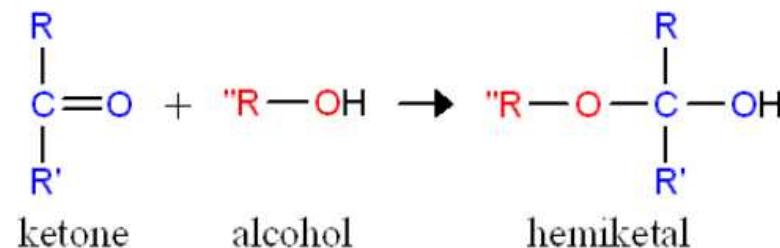
The formation of cyclic ring structures occurs due to a reaction between alcohols and aldehydes or ketones to form derivatives called hemiacetals or hemiketals which contain an additional asymmetric carbon atom and thus can exist in two stereoisomeric forms. For example, D-glucose exists in solution as an intramolecular hemiacetal in which the free hydroxyl group at C-5 has reacted with the aldehydic C-1, rendering the latter carbon asymmetric and producing two stereoisomers, designated as α and β .

Hemiacetal & hemiketal formation

An aldehyde can react with an alcohol to form a **hemiacetal**.



A ketone can react with an alcohol to form a **hemiketal**.



An aldehyde or ketone can react with an alcohol in a 1: 1 ratio to give hemiacetal or hemiketal.

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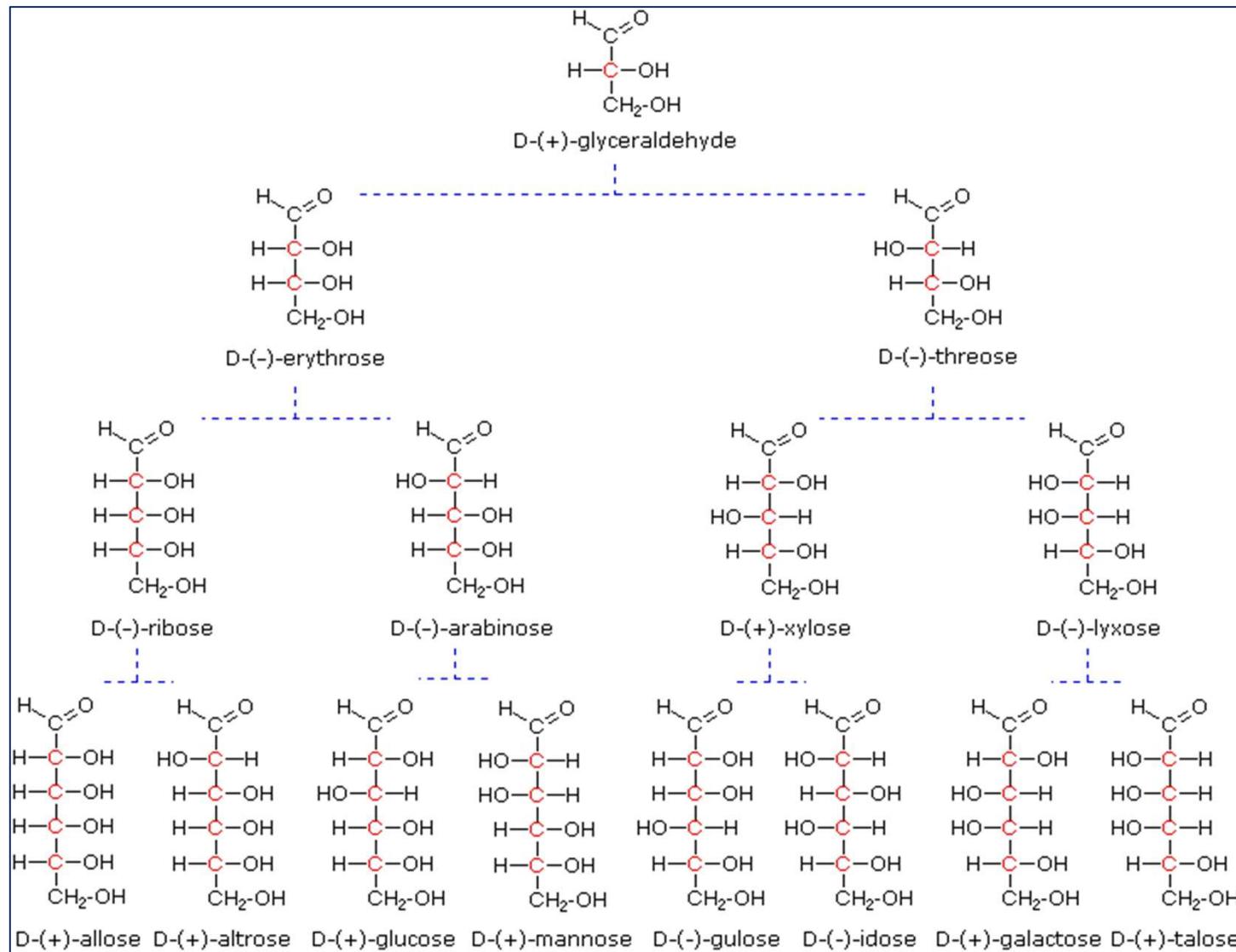
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Higher homologue carbohydrates [D-configuration] of glyceraldehyde



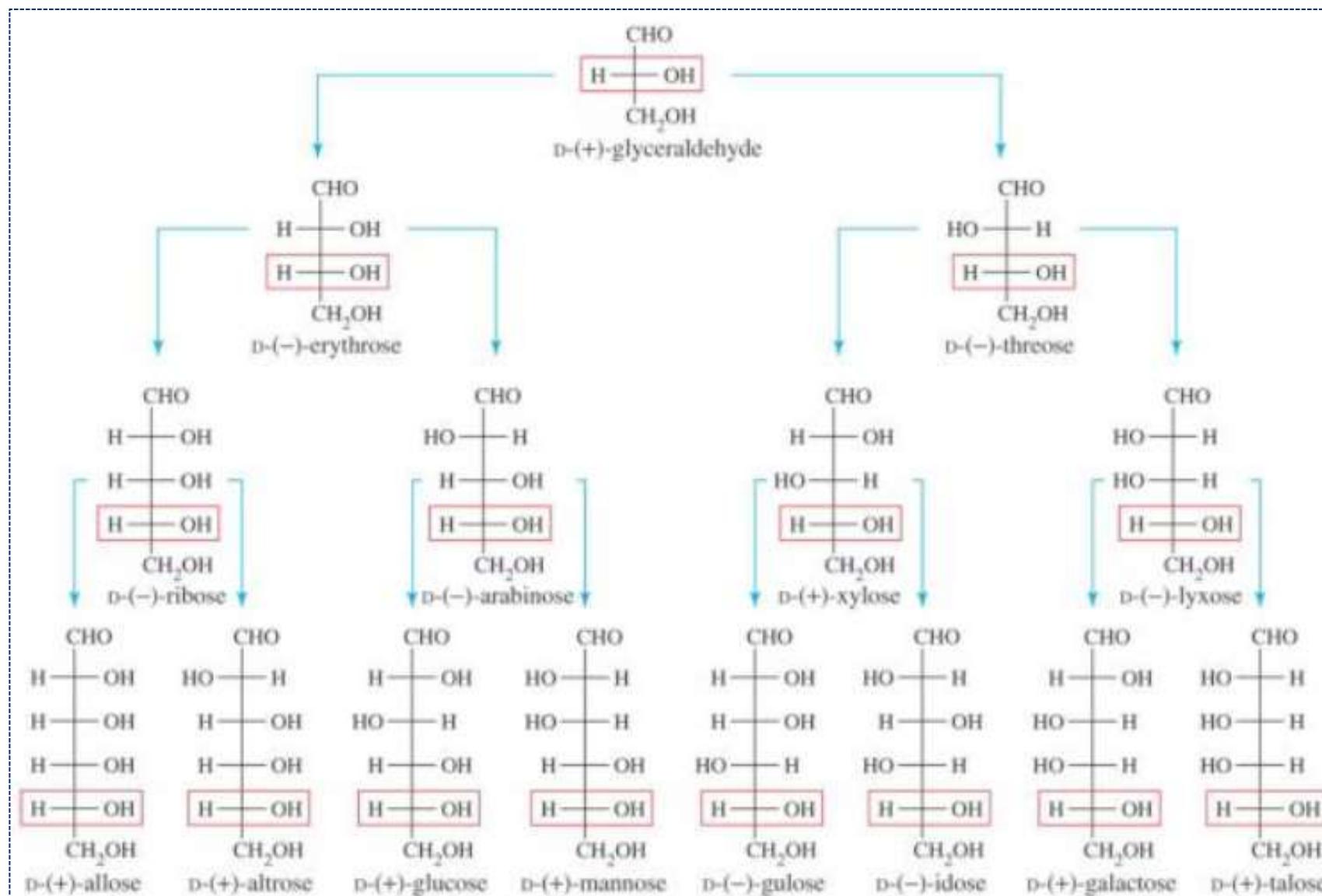
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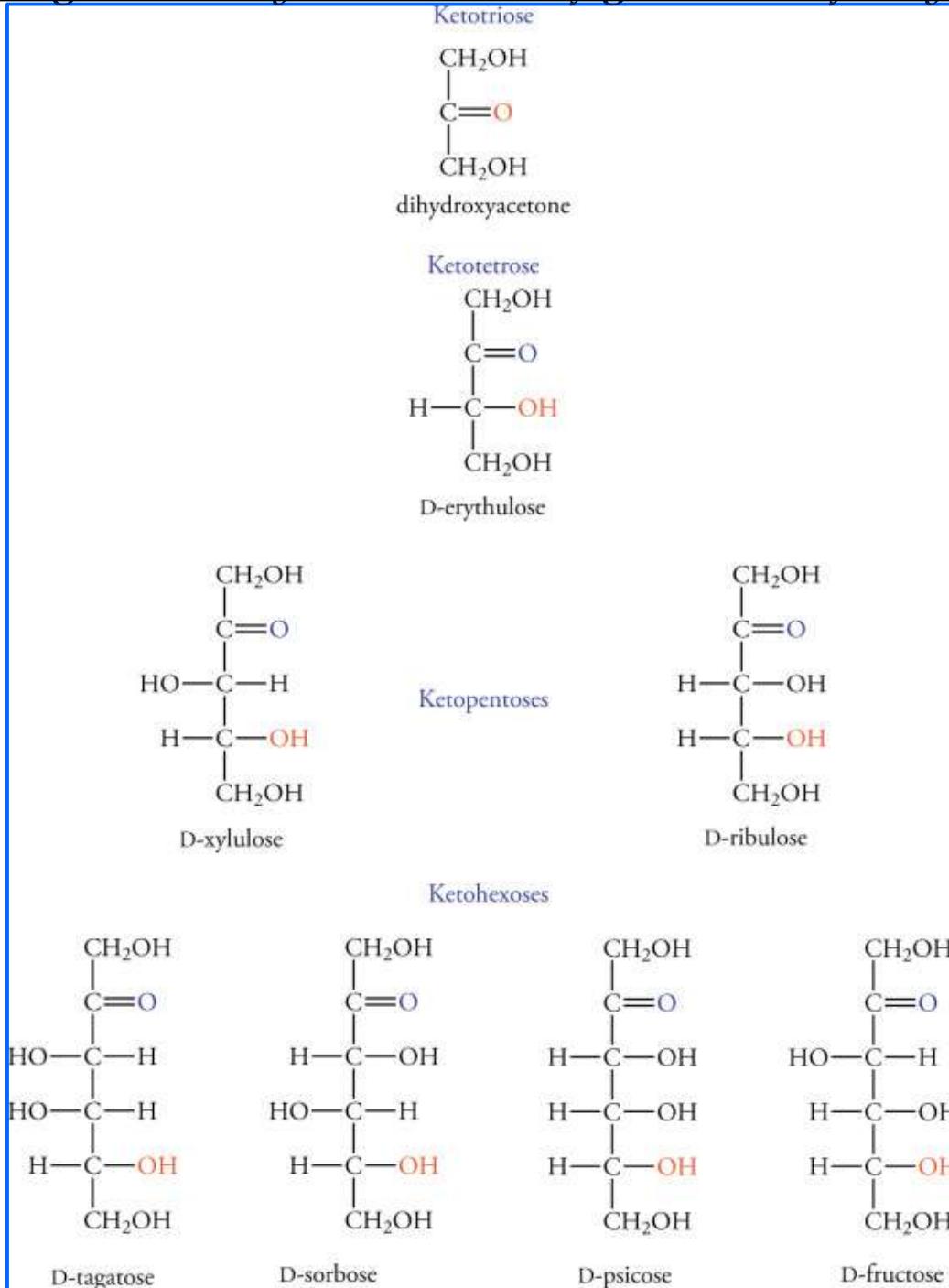
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Higher homologue carbohydrates [D-configuration] of dihydroxyacetone

Configurations of Ketoses

A ketose has one less asymmetric centre than an aldose. Thus a ketose has half the no. of stereoisomers as compared to aldoses with same no. of C-atoms. Also, D-ketoses found in nature have the C=O group in the 2-position and CH₂OH in 1-position.

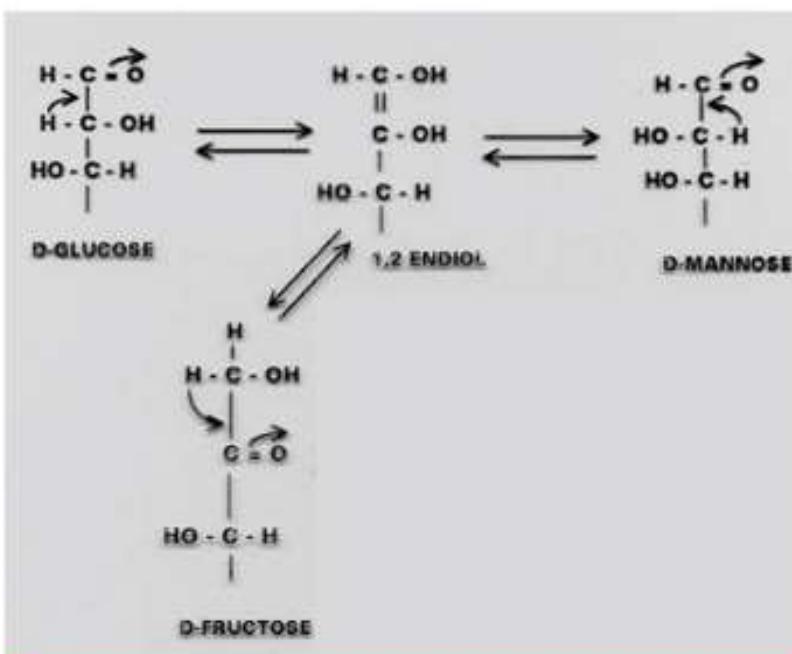


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ENOLIZATION/ISOMERIZATION

- Aldose & ketose sugars are enolized in the presence of **alkali** solutions
- Thus **glucose, mannose & fructose** can be in equilibrium with each other through a 1,2-Endiol
- Therefore, you can get isomerization (transfer of 1 sugar type to another type) of varying yield
- Can happen during storage and heating

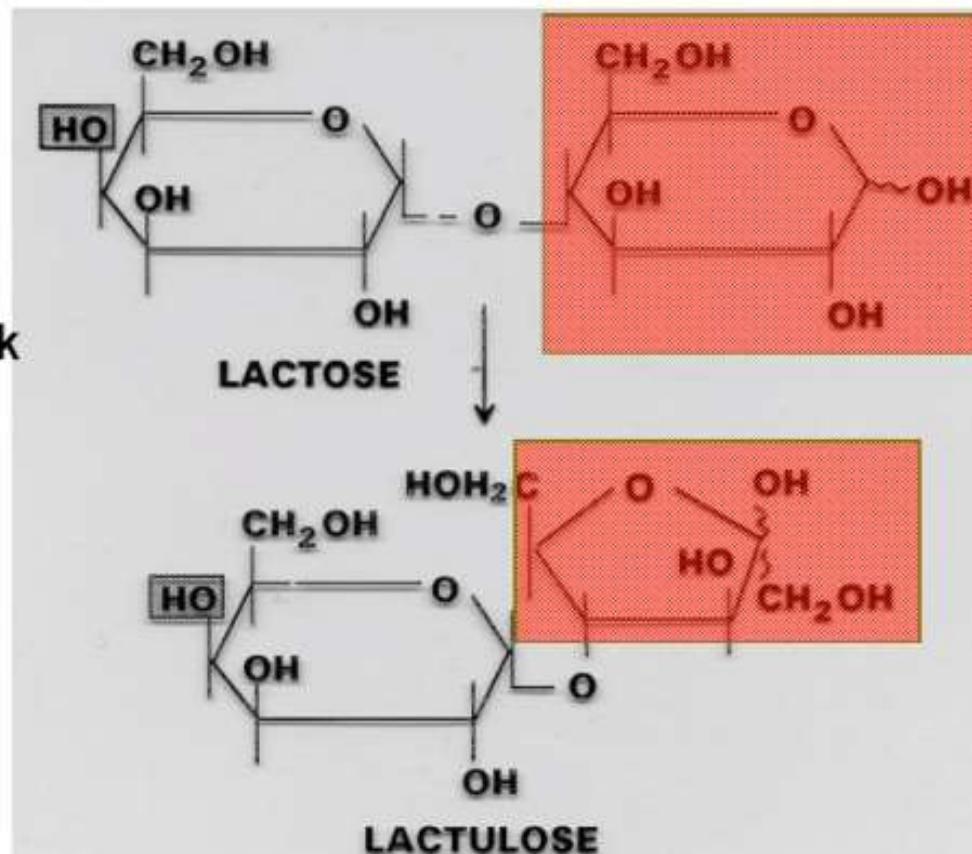


Glucose in dilute alkali after 21 days
-66% Glucose
-29% Fructose
-1% Mannose

ENOLIZATION/ISOMERIZATION

Lactulose used in infant nutrition as a bifidus factor - promotes friendly bacteria in breast milk

Not hydrolyzed by digestion
- strong laxative
- prevents constipation



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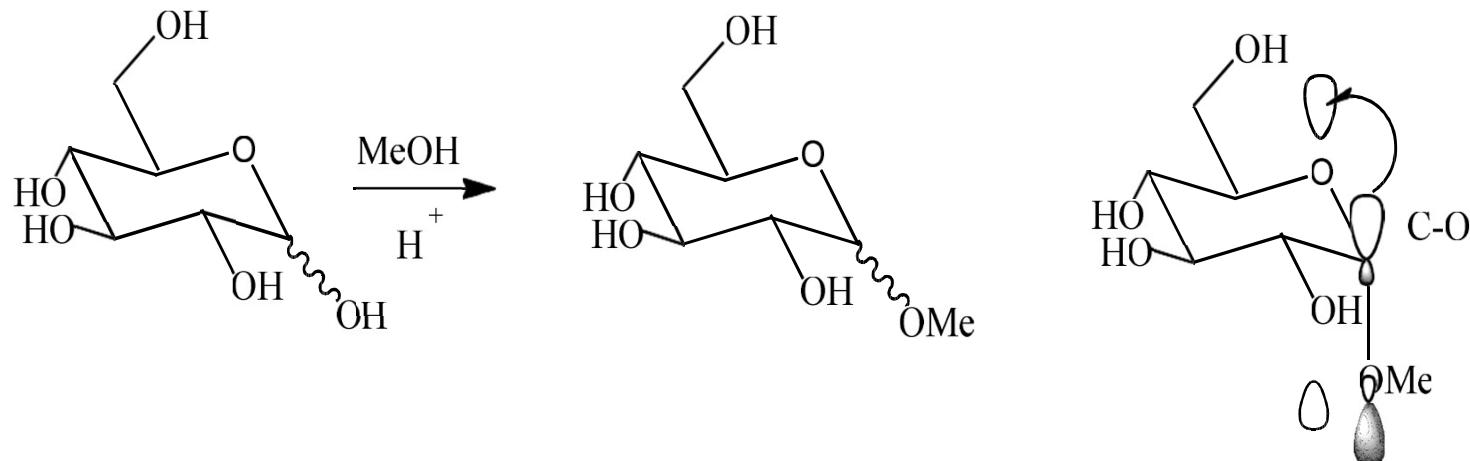
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Conformations can be stabilized by acetal formation of sugars

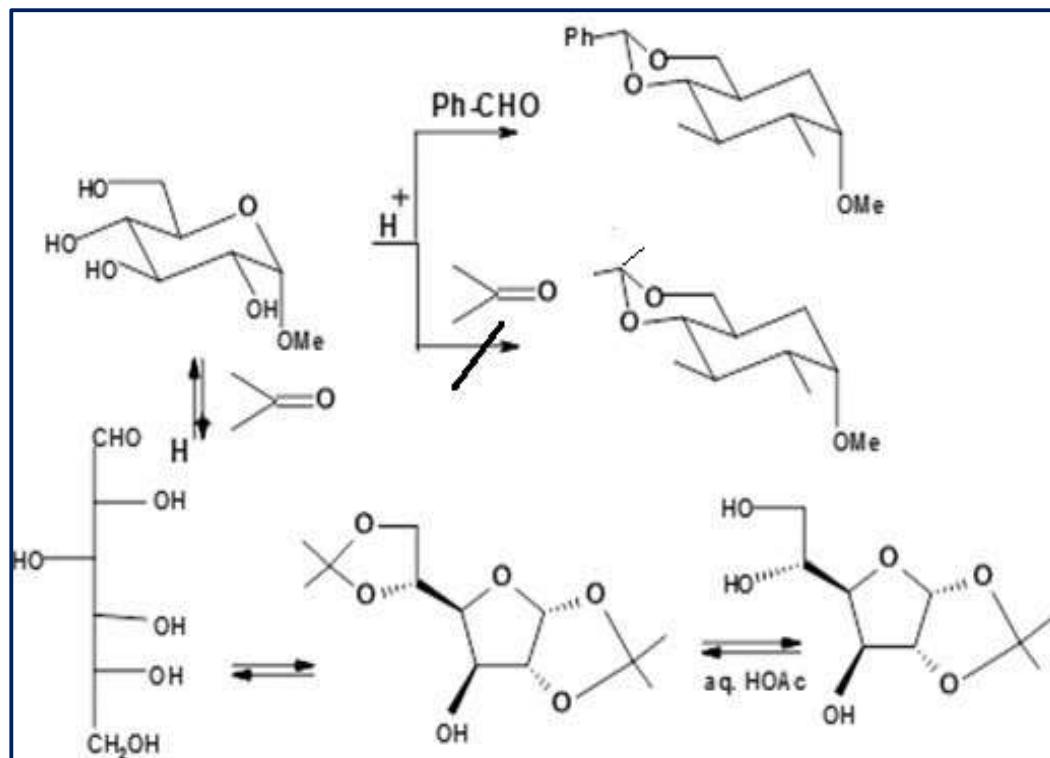


Acid-catalyzed condensation with any alcohol gives an acetal which has an axial OR group. This is because thermodynamically, there exists a bonding interaction between the axial lone pair on the ring oxygen atom and the σ* orbital of the -OCH₃ group. Cyclic acetals formed from sugars and acetone (acetonides) favour five over six-membered rings. In case of six-membered rings, each of the methyl (Me) groups of acetone would be axial and equatorial. Acetonides form from cis-1,2-diols (furanose structure of glucose).

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When benzaldehyde is added to methyl glucoside, the resulting compound is a single stereoisomer where the two six-membered rings are trans-fused to form a very stable all chair-bicyclic structure, in which the phenyl group occupies equatorial position.

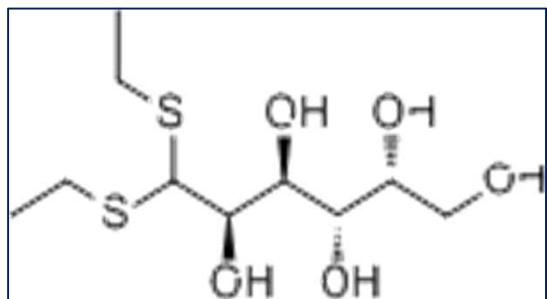


The furanose form builds a double acetal of glucose with acetone, one having two-cis-fused five membered rings, and the other being on the side chain.

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Stability of glucose in the open chain form is achieved thro.' reaction of glucose with a thiol [RSH] in place of an alcohol/ aldehyde/ ketone to yield the dithioacetal of glucose. This is more stable than acetals in pyranose or furanose form.



Many O, S and N-acetals of glucose are naturally occurring to improve solubility or movement across cellular membranes. Syndecans have a single transmembraned domain and an extracellular domain bearing three to five chains of heparin sulfate. Glypcans are attached to the membrane by a lipid anchor, a derivative of the membrane lipid phosphatidylinositol.

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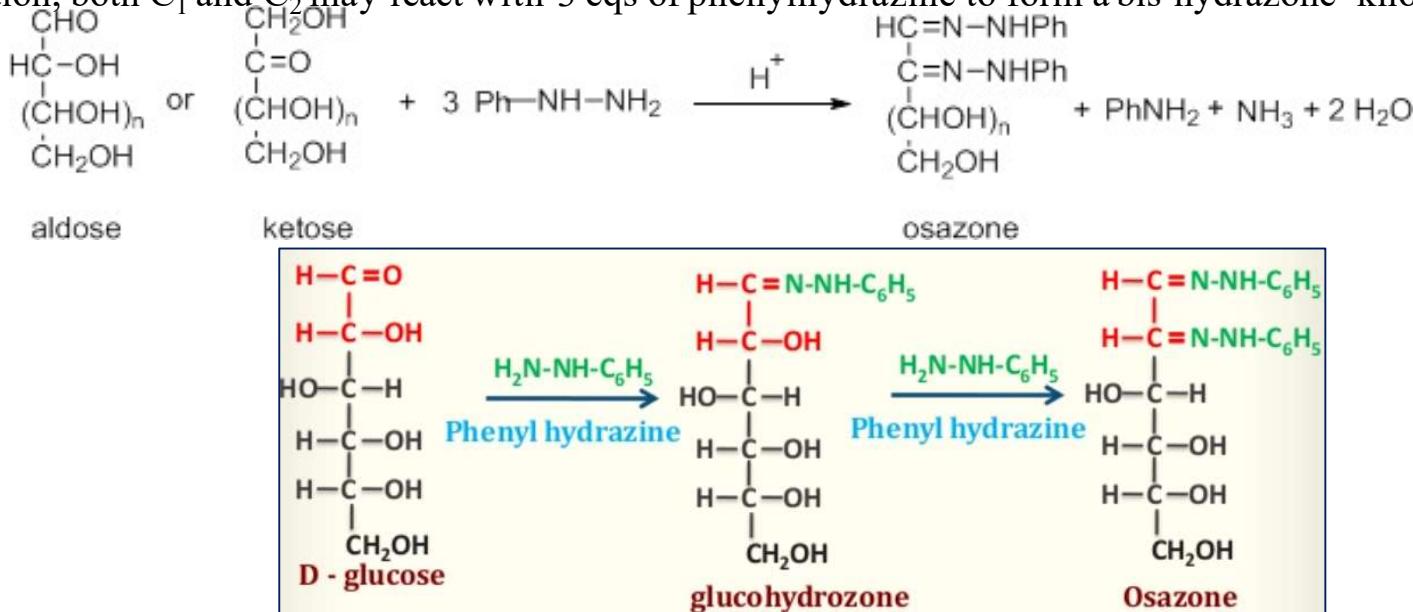
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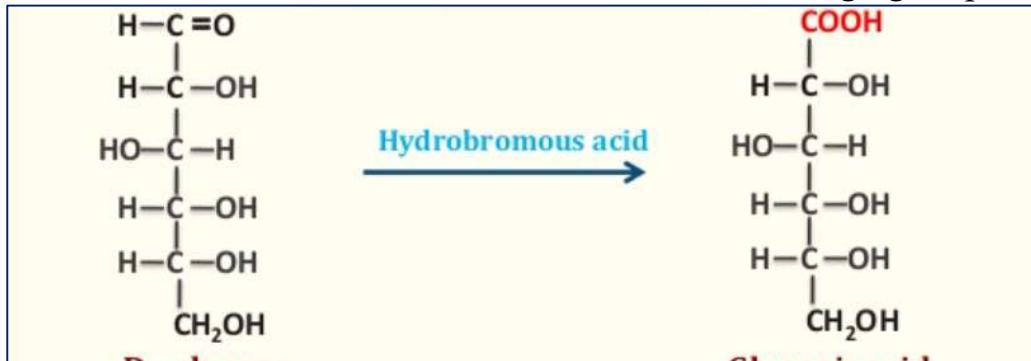
Reactions:

1. Reaction with phenylhydrazine

Aldoses and ketoses react with one equivalent each of phenylhydrazine to produce phenylhydrazone. In addition, both C₁ and C₂ may react with 3 eqs of phenylhydrazine to form a bis-hydrazone known as an osazone.



2. Reaction with Bromine water: Bromine water oxidizes aldoses but not ketoses, therefore, it is a differentiation reaction between an aldose and a ketose. It is a mild oxidizing agent producing an aldonic acid from an aldose.



Medical Importance

- Calcium gluconate (gluconic acid) used as source of calcium. These are given I.V. fluids raise the calcium levels.

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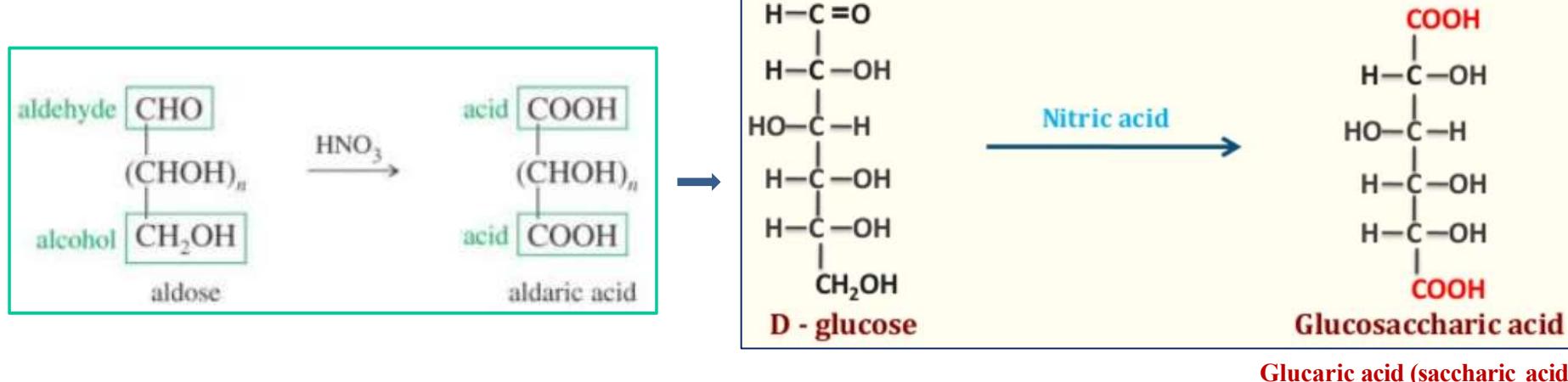
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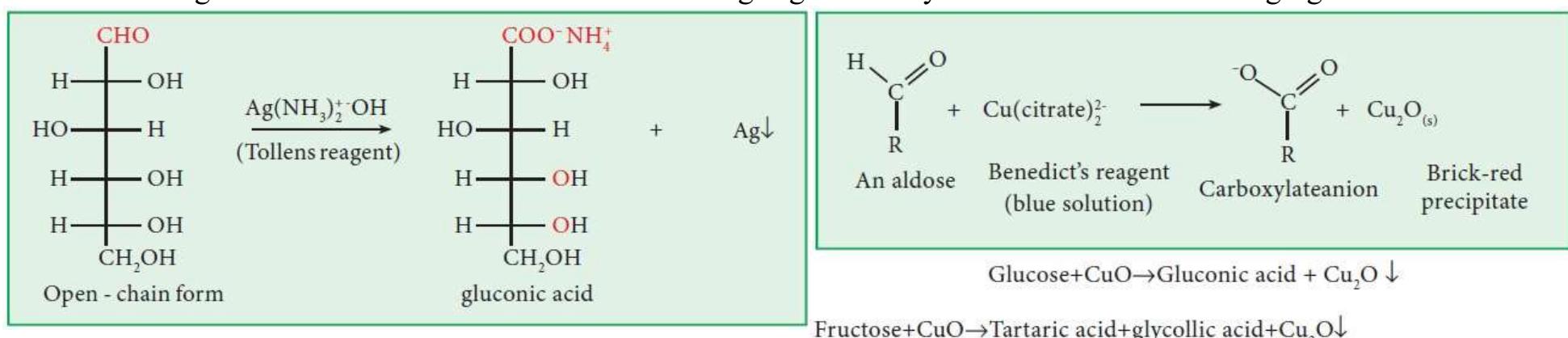
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3. Reaction with nitric acid [HNO_3]: HNO_3 is a strong oxidizing agent which oxidizes both $-\text{CHO}$ as well as $-\text{CH}_2\text{OH}$ group to form an aldaric acid (dicarboxylic acid) from an aldose.



4. Oxidation of the $-\text{CHO}$ group of an aldose to a $-\text{CO}_2\text{H}$ group can be carried out using Tollens' $[\text{Ag}(\text{NH}_3)_2\text{OH}]$, or Benedict's (alkaline solution of cupric citrate complex) solutions. 2-Ketoses are also oxidized by these reagents because 2-ketoses equilibrate with isomeric aldoses as base promotes enediol rearrangement. So all monosaccharides are reducing sugars as they can reduce these oxidizing agents.



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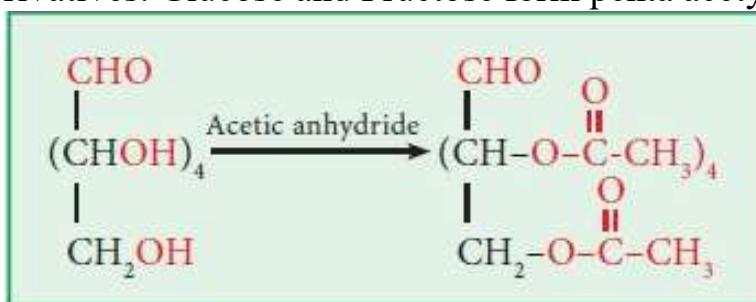
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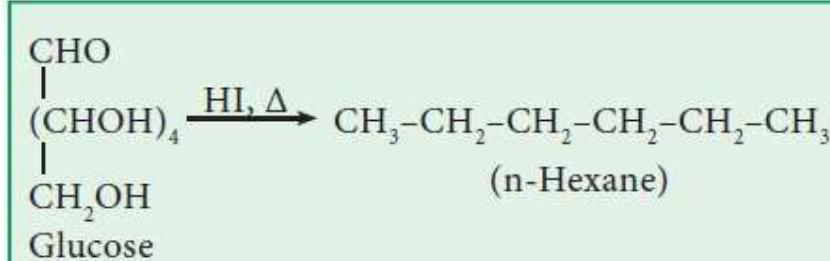
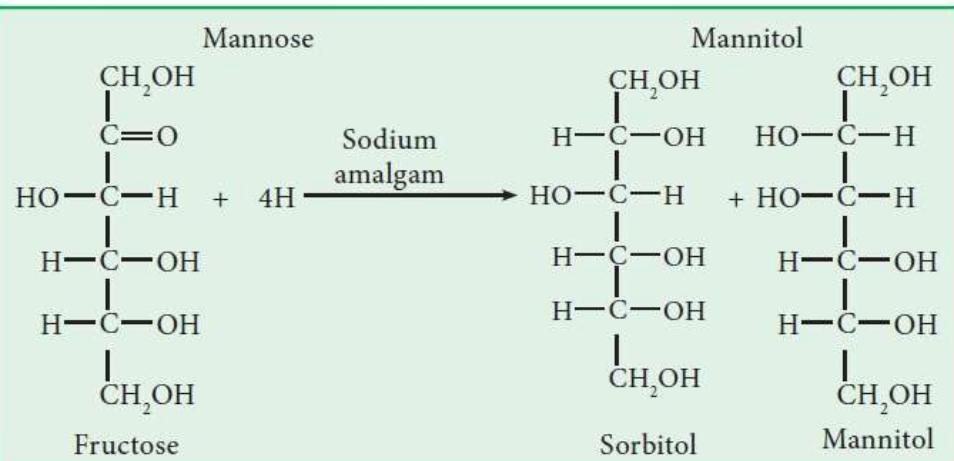
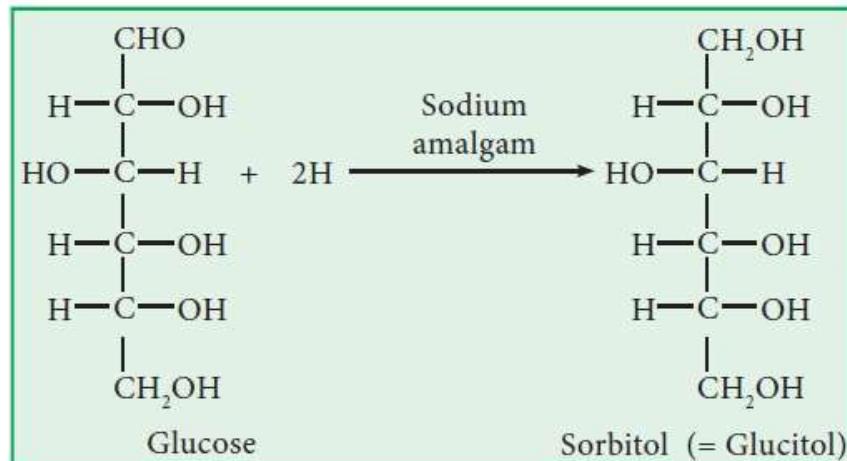
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5. Reaction with acetic anhydride: All –OH groups of aldoses and ketoses, including –CH₂OH, are acetylated to form O-acetyl derivatives. Glucose and Fructose form penta acetyl derivative when treated with acetic anhydride.



6. Reduction: Aldoses are reduced to 1° alcohols, ketoses to 2° alcohols.



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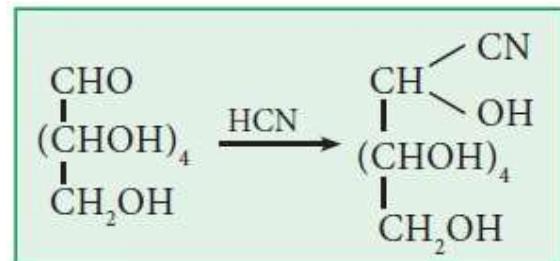
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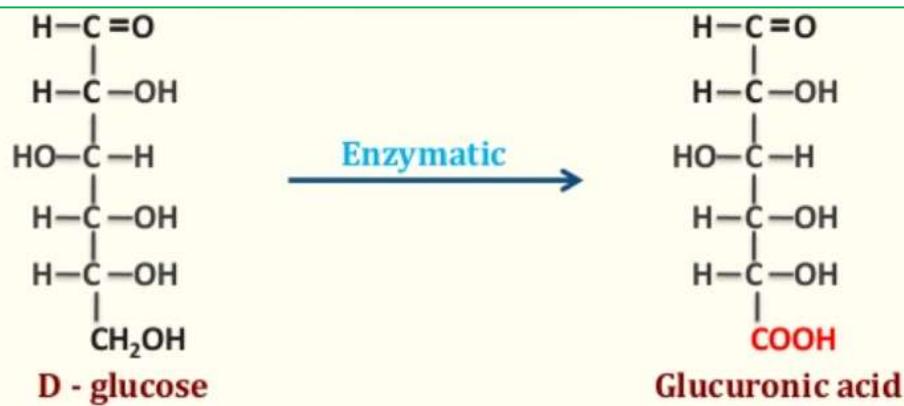
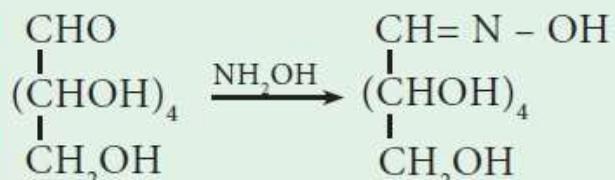
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7. Reaction with HCN: Aldoses/ketoses react with hydrogen cyanide to form cyanohydrins(epimeric).



8. Reaction with hydroxylamine: Both glucose and fructose form oximes with hydroxylamine.



Medical Importance

- These are present in the heteropolysaccharides and glycoproteins.
- Involved in detoxification of benzoic acid, bilirubin & certain drugs

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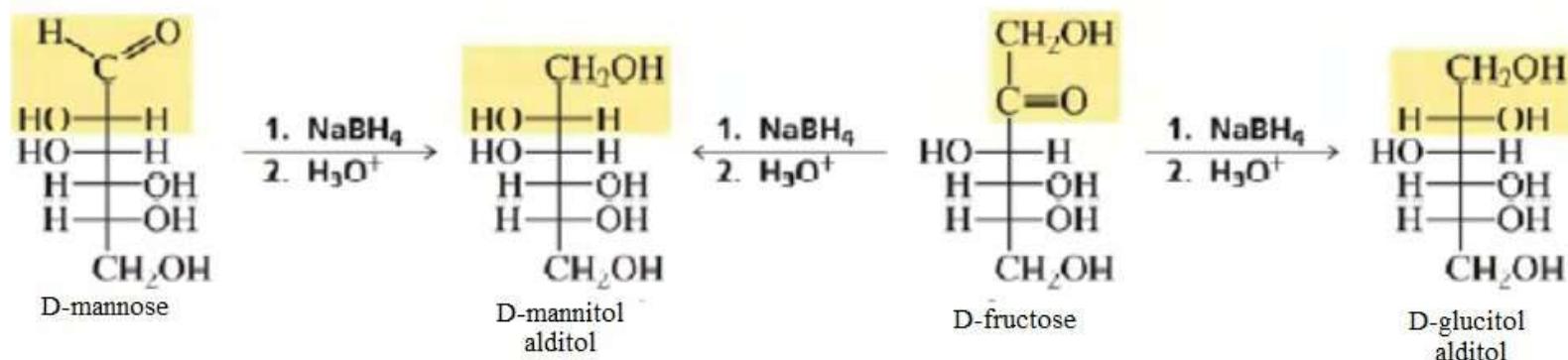
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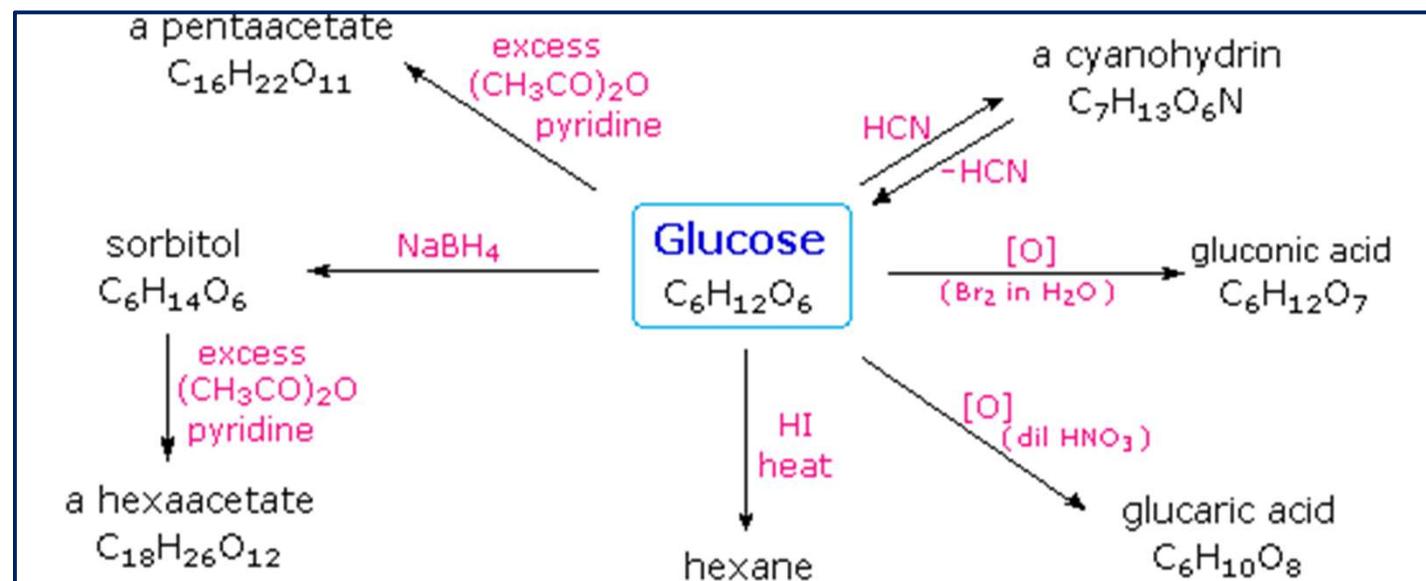
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9. Redox Reactions of Monosaccharides:



Reduction of ketoses forms 2 alditols, epimers of each other at C-2 position.



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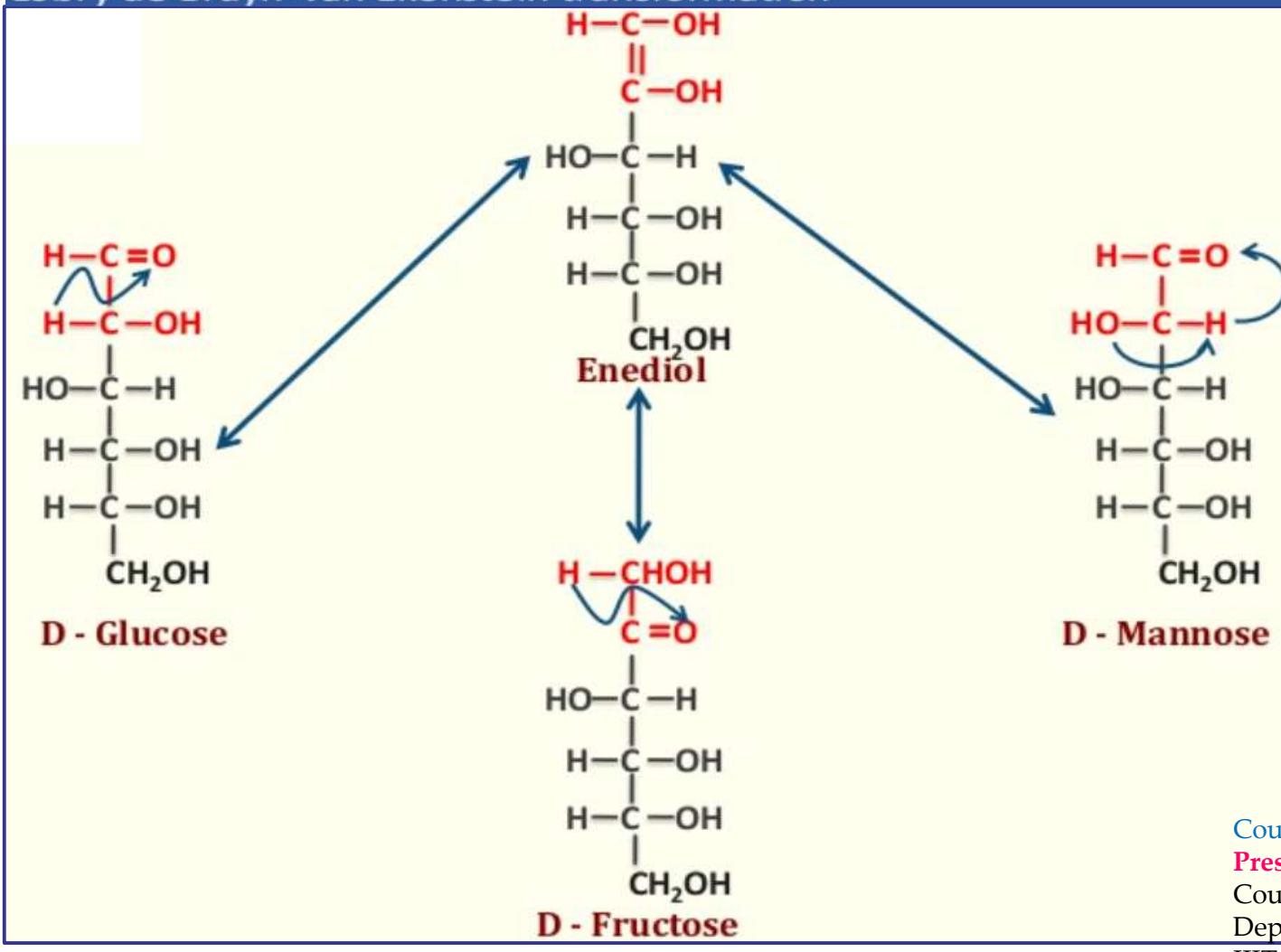
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In mild alkaline solutions, carbohydrates containing a free sugar group (aldehyde or keto) will tautomerize to form **enediols**, where two hydroxyl groups are attached to the double-bonded carbon.
 In mild alkaline conditions, **glucose is converted into fructose and mannose.**

The interconversion of sugars through a common enediol form is called **Lobry de Bruyn-Van Ekenstein transformation**



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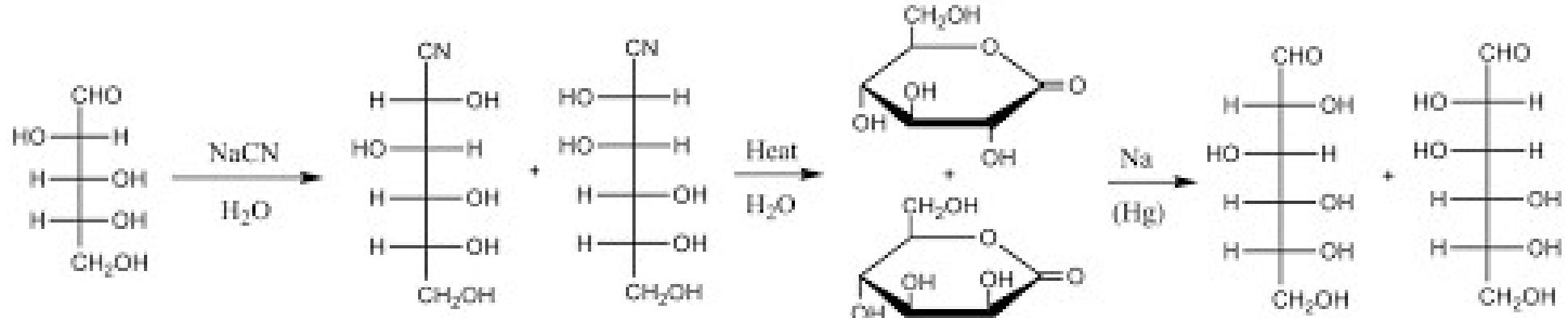
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Lengthening the chain- Kiliani Fischer synthesis

The Kiliani Fischer synthesis is a process by which we can lengthen the carbon chain on a sugar molecule by adding an additional carbon atom to it. There are two versions of this reaction - the older (original) and the modern (modified) version. The steps involved in the original version are:

1. Addition of hydrogen cyanide (sodium cyanide and HCl) to the carbonyl group ($C=O$) of aldose or ketose generating an additional asymmetric centre & forming two diastereomeric cyanohydrins.
2. The cyanohydrins are heated in water, oxidized to respective carboxylic acids called aldonic acids. The corresponding acids are also epimeric.
3. The carboxylic acids undergo lactonisation and subsequent reduction to corresponding epimeric aldoses.
4. However, the two epimers are formed in unequal amounts.

The configurations of other chiral carbons remain unchanged, because none of their bonds are broken during



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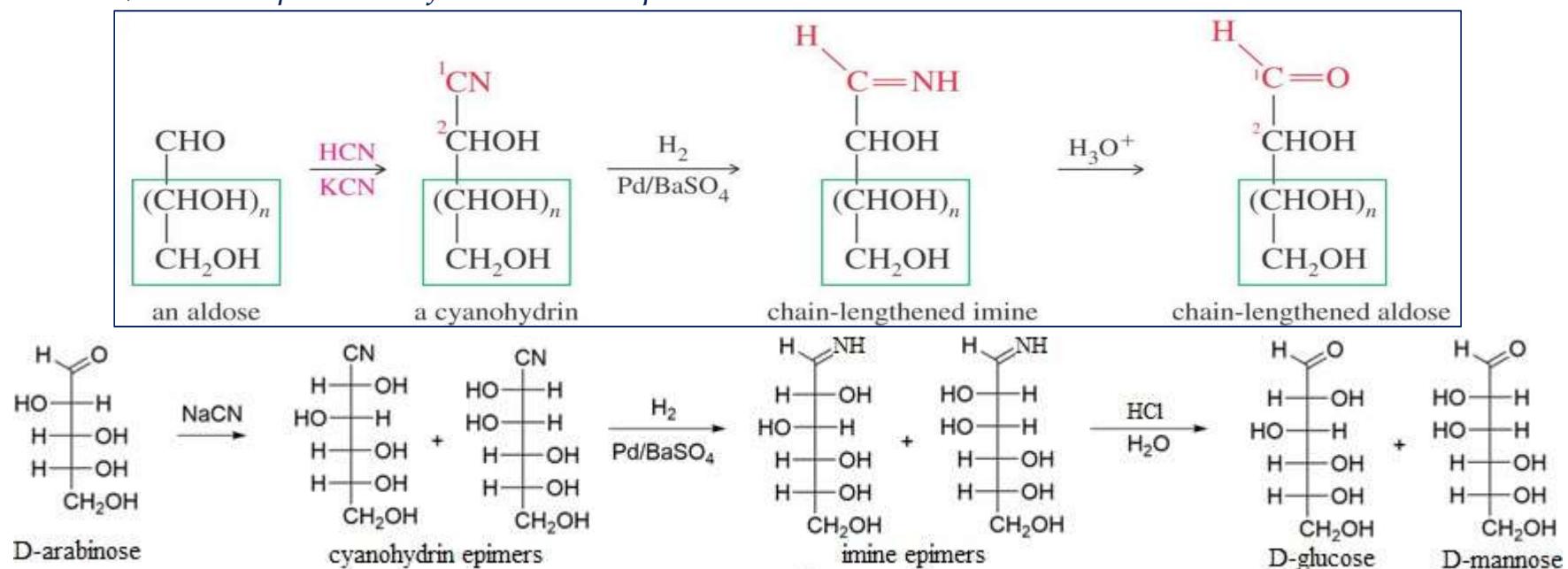
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Lengthening the chain- modified Kiliani Fischer synthesis

In 1979, Serianni and Barker developed the modified Kiliani–Fischer synthesis. The steps involved in the modified version are:

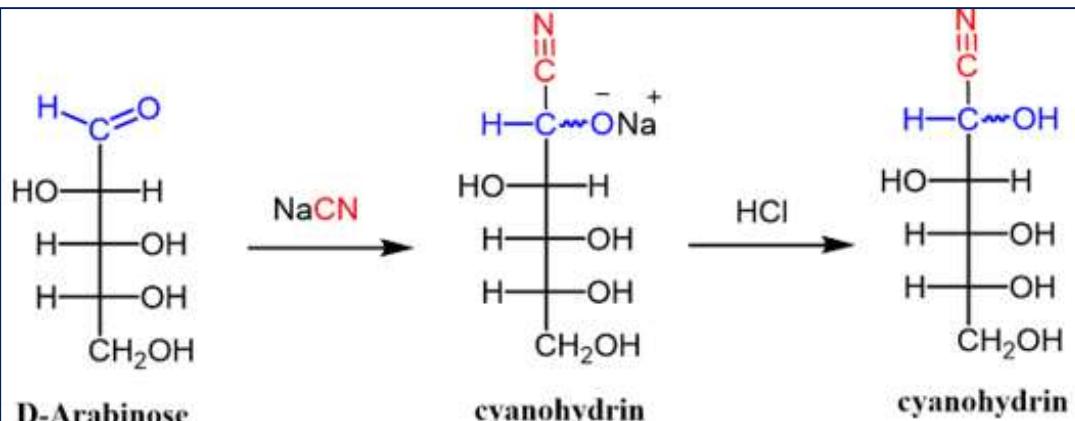
1. Hydrogen cyanide adds to the carbonyl group ($C=O$) of aldose or ketose generating an additional asymmetric centre & forming two epimeric cyanohydrins.
2. The nitrile bond is partially reduced to imine using partially deactivated palladium on barium sulfate. The corresponding imines are also epimeric.
3. The imines undergo acid hydrolysis to corresponding epimeric aldoses.
4. However, the two epimers are formed in unequal amounts.



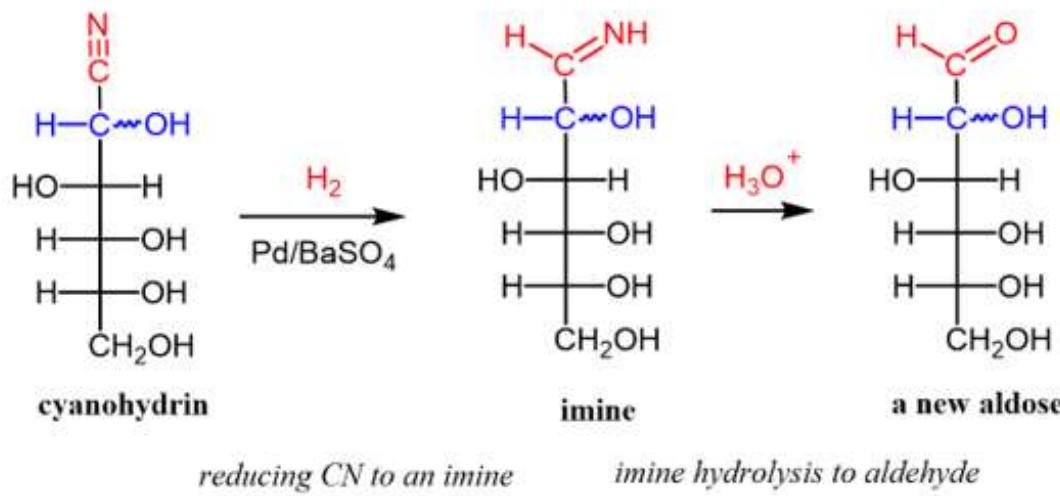
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Reduction of the nitrile group to an imine followed by a acidic hydrolysis of the imine to an aldehyde.



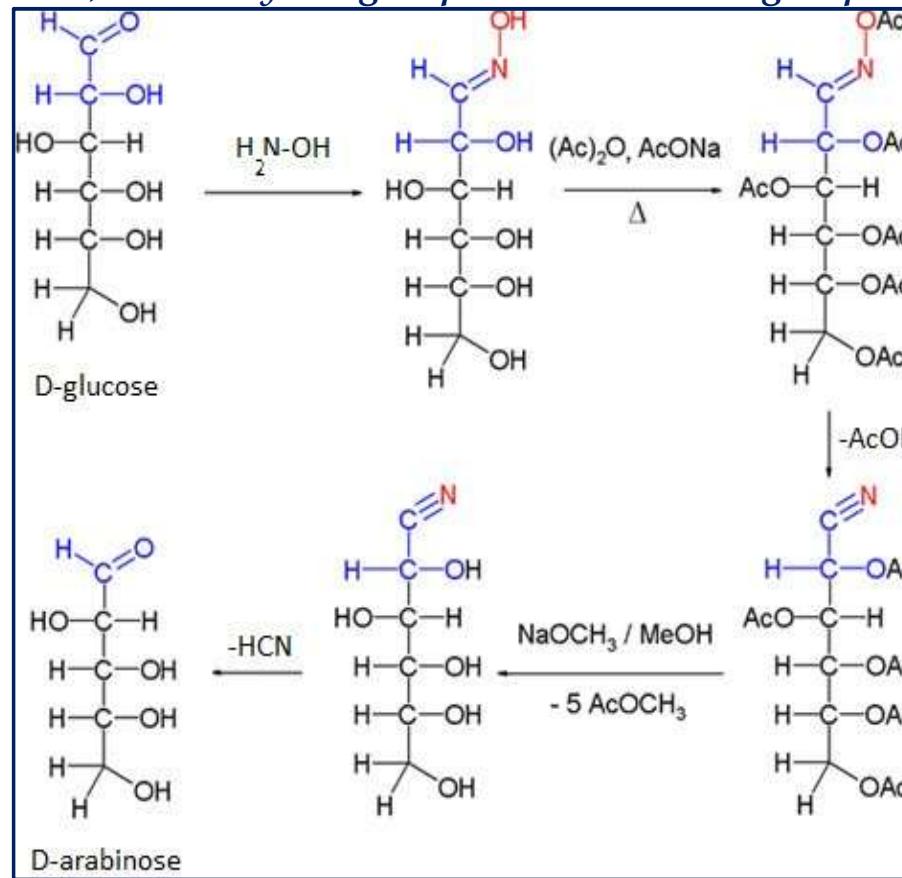
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Shortening the chain- Wohl Degradation

The length of the sugar chain is decreased by removing the first carbon along with the aldehyde group and placing the new aldehyde group with the second carbon atom. The steps involved in Wohl degradation are:

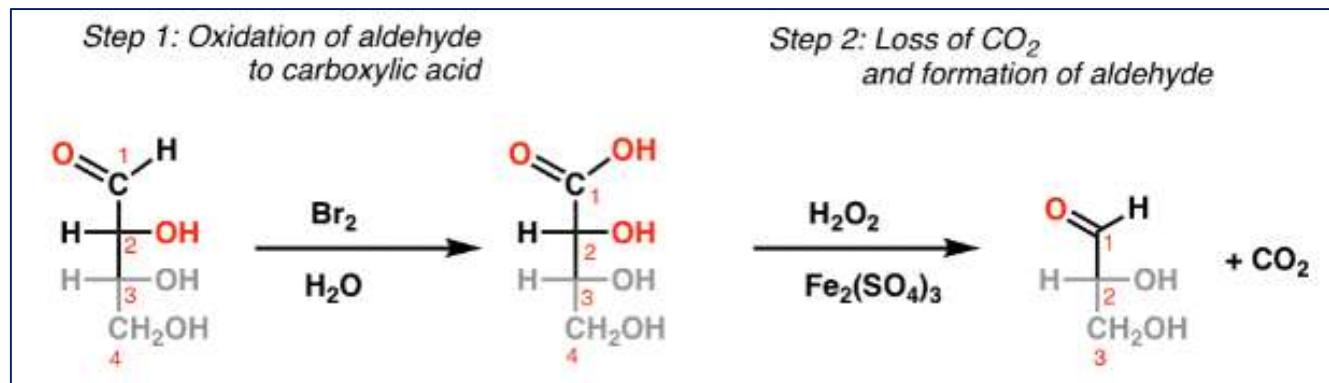
1. The aldehyde group of the aldose reacts with hydroxylamine forming an oxime.
2. Heating at 100°C with acetic anhydride results in dehydration yielding a nitrile followed by formation of acetate esters of hydroxyl groups.
3. In basic aqueous medium, nitrile/cyano group leaves and ester groups are hydrolyzed back to $-\text{OH}$.



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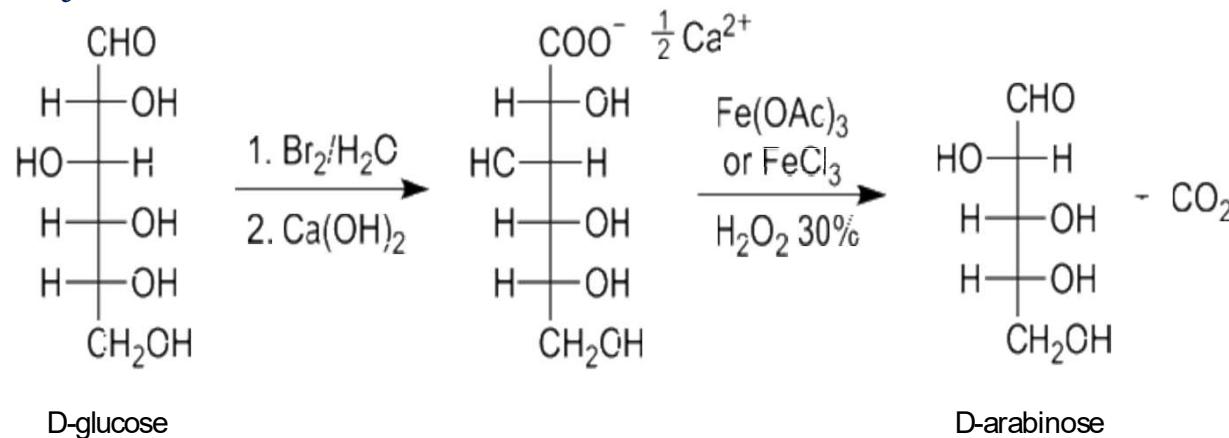
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Shortening the chain- Ruff Degradation



The steps involved in the Ruff degradation are:

1. *Oxidation of the aldose to an aldonic acid.*
2. *Synthesis of the calcium salt of the aldonic acid by adding calcium hydroxide.*
3. *The calcium salt of the aldonic acid is oxidized with hydrogen peroxide. Ferric ion catalyzes the oxidation reaction, which cleaves the bond between C₁ and C₂, forming an aldehyde and CO₂.*



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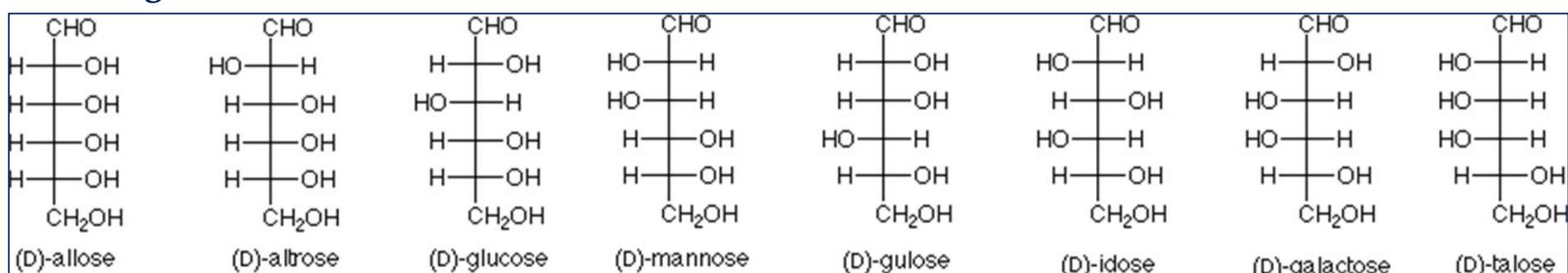
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The Fischer Proof for Stereochemistry of Glucose

Fischer knew that (+)-glucose is an aldohexose. Therefore, there are 4 stereocentres and $2^4=16$ stereoisomers (8 D-sugars and 8 L-sugars). Also, the 16 stereoisomers are eight pairs of enantiomers. He considered the 8 stereoisomers which have their C₅-OH group on the right. i.e. D-sugars.



Until 1951, one could not determine the actual configuration (D or L) of sugars (X-ray crystallography). So Fischer arbitrarily assigned D-glyceraldehyde the following structure:



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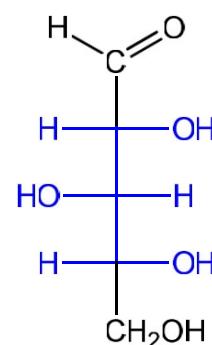
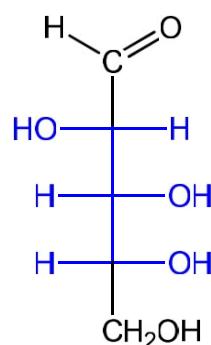
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1. Kiliani–Fischer synthesis performed on the sugar (-)-arabinose yields the two sugars known as (+)- glucose and (+)-mannose, implying that (+)-glucose and (+)-mannose are C₂ epimers, or, in other words, they have the same configuration at C₃, C₄, and C₅. Therefore, (+)-glucose and (+)-mannose can be any one of the following pairs:

sugars 1 & 2, 3 & 4, 5 & 6, or 7 & 8

2. Both (+)-glucose and (+)-mannose undergo oxidation by nitric acid and the resulting aldaric acids are optically active. However sugars 1 & 7 are optically inactive since they possess a plane of symmetry, giving a superimposable mirror image. So, the pairs of sugars must be 3 & 4 or 5 & 6.

3. Since lengthening of chain of (-)-arabinose by Kiliani–Fischer synthesis results in (+)-glucose and (+)-mannose, (-)-arabinose can have only two possible structures. If we consider the pair of sugars 3 and 4, then (-)-arabinose has the structure on the left; else, if (+)-glucose and (+)-mannose are sugars 5 and 6, then (-)-arabinose has the structure shown on the right:

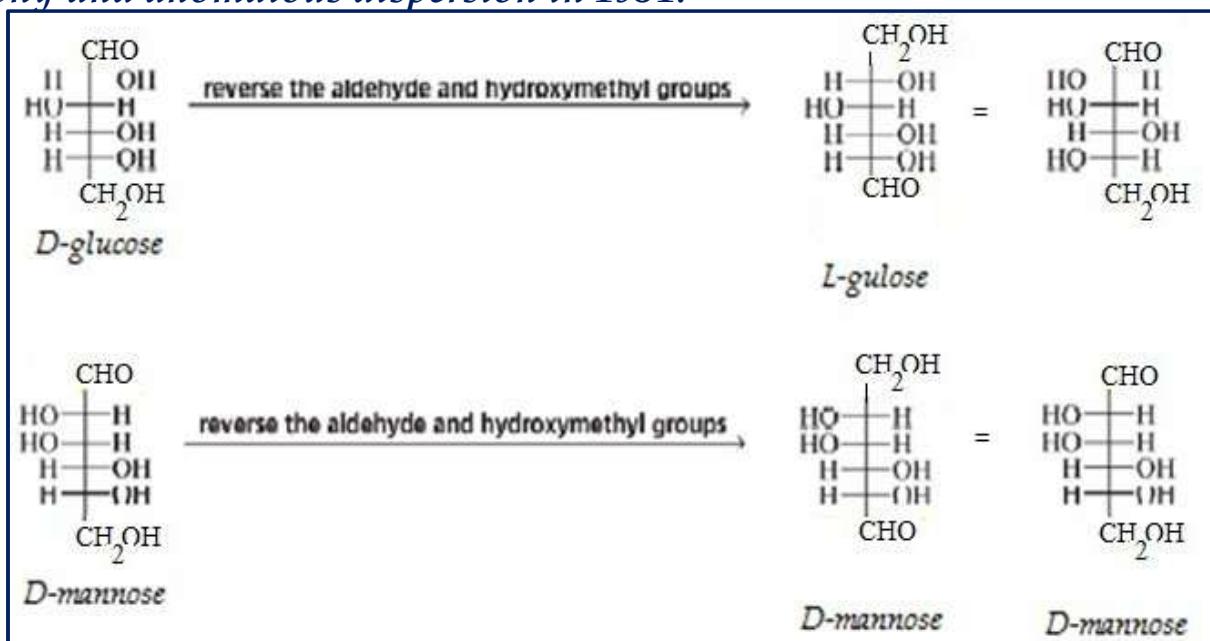


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When (-)-arabinose is oxidized with nitric acid, the corresponding aldaric acid is optically active, i.e. it lacks a plane of symmetry. Thus, (-)-arabinose must have the left-hand structure because the aldaric acid of the sugar on the right has a plane of symmetry. (+)-Glucose and (+)-mannose are then represented by sugars 3 and 4.

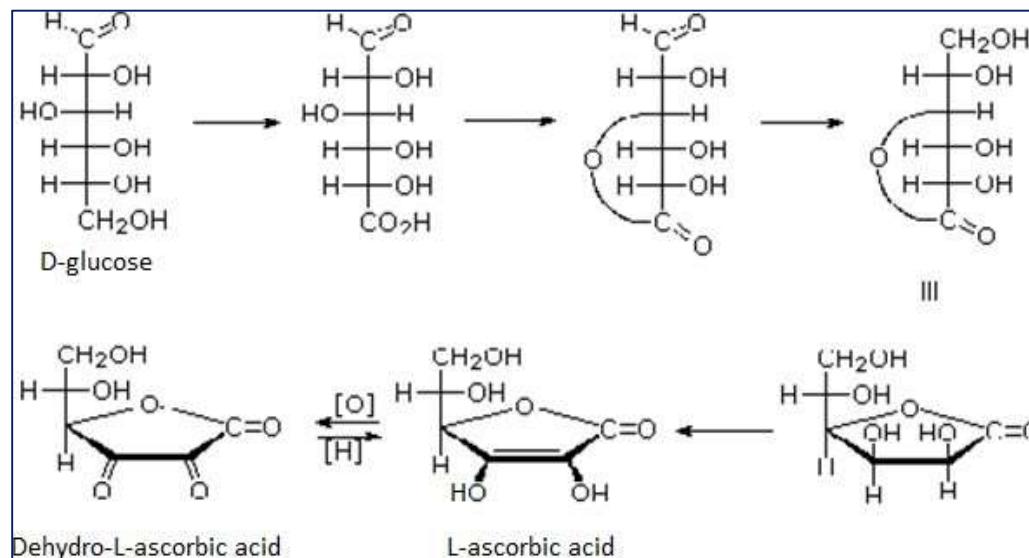
4. To determine whether (+)-glucose is 3 or 4, Fischer chemically interchanged the aldehyde and primary alcohol groups of the sugar known as (+)-glucose and he obtained an aldohexose that was different from (+)-glucose. When he chemically interchanged the aldehyde and primary alcohol groups of (+)-mannose, he still had (+)-mannose. Thus, Fischer identified sugar 3 as (+)-glucose since reversal of the aldehyde and alcohol groups of sugar 3 led to a different sugar: L-gulose. His guess that (+)-glucose is a D-sugar was later shown to be correct by X-ray crystallography and anomalous dispersion in 1951.



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Vitamin C ($C_6H_8O_6$) is derived from glucose. Ascorbic acid, or vitamin C, is an important water soluble biological antioxidant like fat soluble antioxidants such as vitamin E. Most animals synthesize this vital compound from glucose by a series of four enzymatic transformations. Unfortunately, we do not have the enzyme, L-gulonolactone oxidase, needed for the fourth step. So we must consume ascorbic acid as part of our daily diet or have chronic deficiency effects, like scurvy. Although it does not have a free carboxyl group, ascorbic acid has a pK_a of 4.17 as a result of vinylogous activation of the C-3 hydroxyl group. Vitamin C is a cofactor in many enzymatic reactions in the human body.



Biosynthesis of Vitamin C

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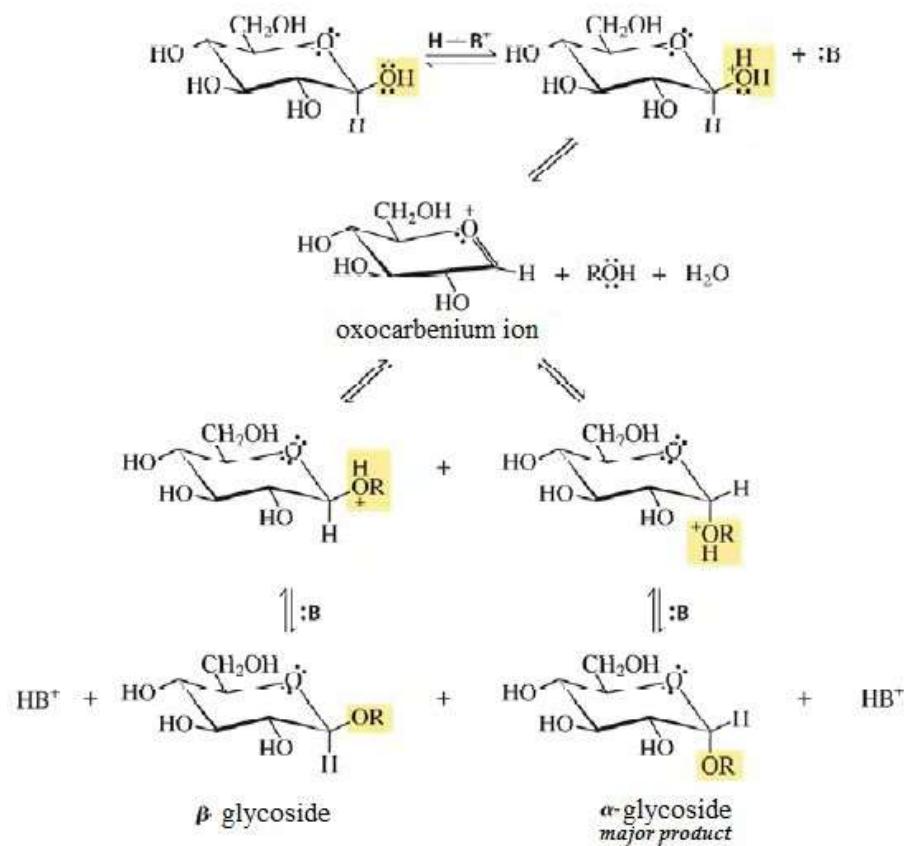
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Reducing/ Non-Reducing Sugars

The cyclic hemiacetal (or hemiketal) formed by a monosaccharide can react with an alcohol to form an acetal (or ketal), also called a glycoside. Glycosides are named by replacing the "e" of the sugar's name with "ide." The α -glucoside is the major product due to anomeric effect.



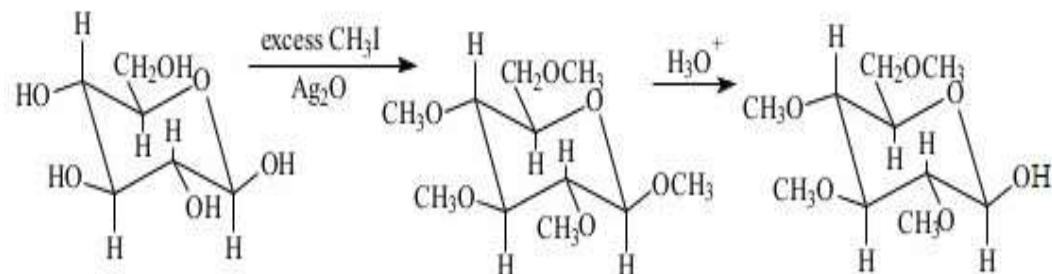
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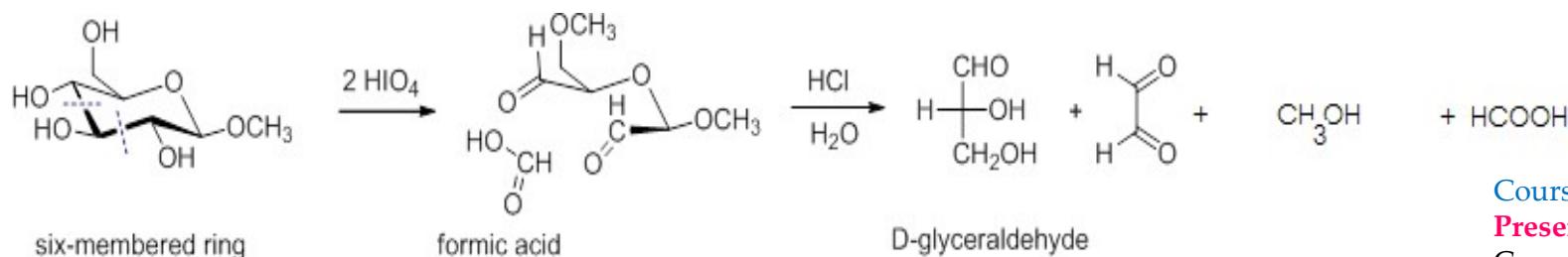
Determination of Ring Size

Two procedures can be used to determine the size of a monosaccharide's ring.

1. Treatment of the monosaccharide with excess methyl iodide and silver oxide converts all the OH groups to OCH_3 groups. Acid-catalyzed hydrolysis of the acetal then forms a hemiacetal, which is in equilibrium with its open chain form. The size of the ring can be determined from the structure of the open-chain form because the sole OH group is the one that had formed the cyclic hemiacetal (anomeric carbon).



2. An acetal of the monosaccharide is oxidized with excess periodic acid which cleaves 1,2-diols. i.e. it cleaves the C-C bond between two alcohols on adjacent C-atoms. The α -hydroxyaldehyde formed when periodic acid cleaves a 1,2,3-diol is further oxidized to formic acid and another aldehyde. 1° alcohols and aldehydes oxidise to formaldehyde (HCHO), 2° alcohols oxidise to aldehydes, ketones to carboxylic acids & carboxylic acids oxidise finally to CO_2 .



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DISACCHARIDES

each consists of **2 monosaccharides** linked by a glycosidic bond

...can be...

reducing sugar

non-reducing sugar

- Have the ability to reduce metal ions such as Cu^{2+} and Ag^+ to insoluble product
- The anomeric carbon of the second monomer is not involved in glycosidic bond
- Have the ability to form the straight chain

e.g.

1. Lactose
2. Maltose
3. Cellobiose

- Both anomeric carbon atom fixed in glycosidic linkage

e.g.

1. sucrose

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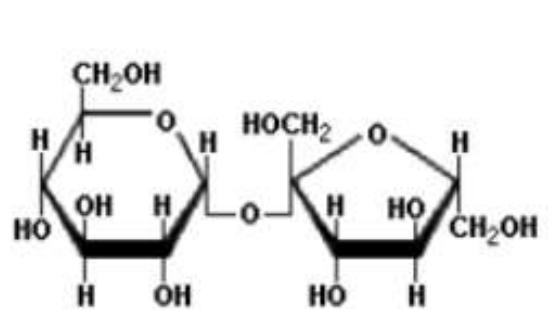
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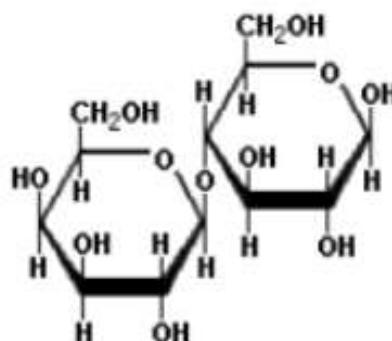
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Disachharide Combinations

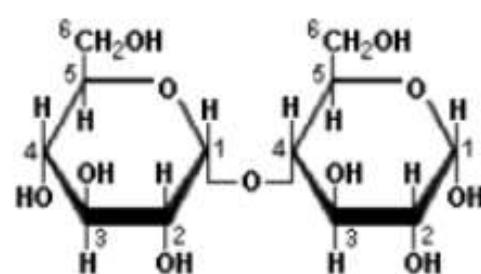
sucrose	common table sugar	glucose + fructose
lactose	main sugar in milk	galactose + glucose
maltose	product of starch hydrolysis	glucose + glucose
trehalose	found in fungi	glucose + glucose



Sucrose



Lactose

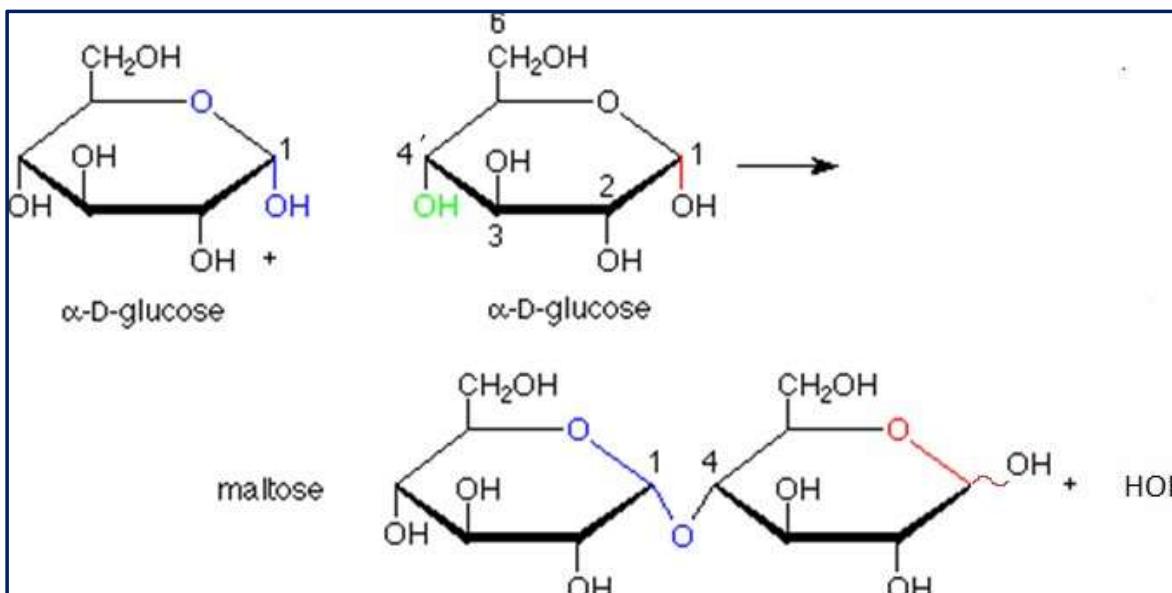


Maltose

Disaccharides

Disaccharides are compounds comprising of two units of monosaccharide (same or different) joined via a glycosidic linkage, formed by the reaction of the hemiacetal group of a monosaccharide with the alcohol group of another monosaccharide. A glycosidic linkage may be 1,4' or 1,6' or 1,1' linkage.

Starch, on hydrolysis yields a disaccharide, maltose comprising of two D-glucose subunits connected by a α - 1,4'-glycosidic linkage as the C₁ of one unit is connected to C_{4'} of the other. The α -position is axial because the oxygen bonded to the anomeric carbon is in the α -position (axial). In β - glycosidic linkage, equatorial position of oxygen of anomeric carbon is considered. Maltose can exist in both α and β anomeric forms as suggested by the wavy line of C_{1'}OH.



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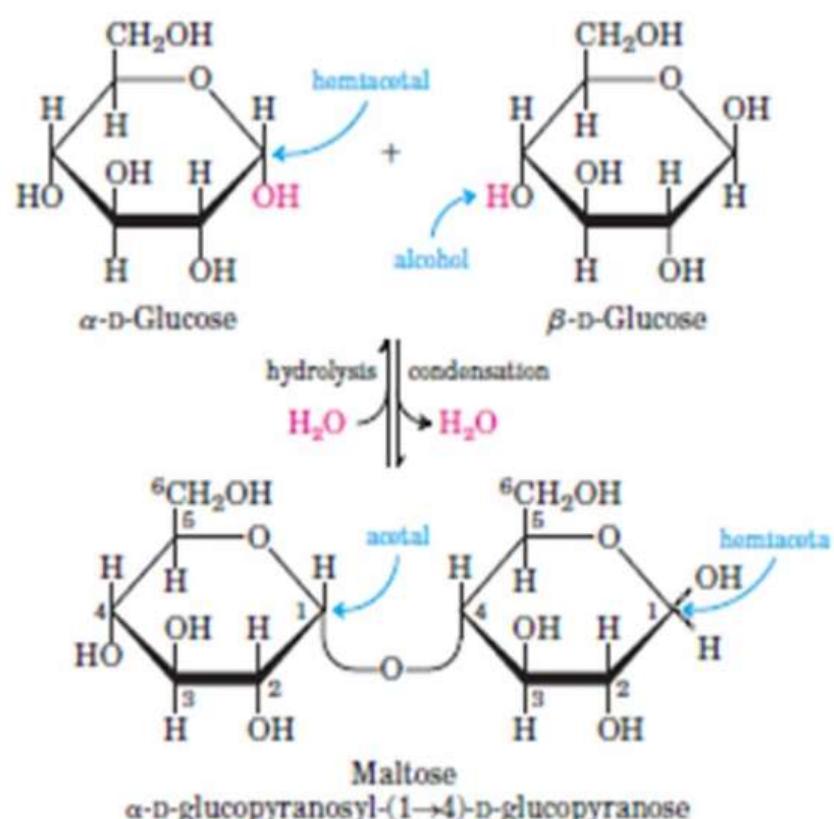
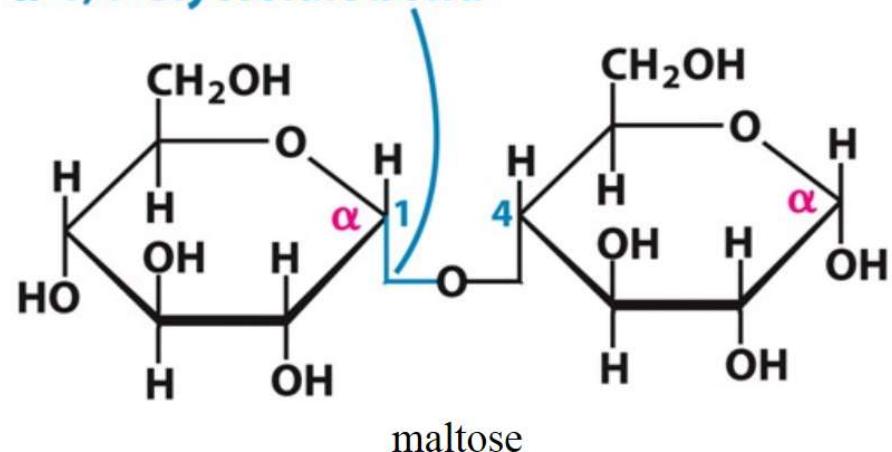
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Disaccharides and other Glycosides

Glycosidic bond – the primary structural linkage in all polymers of monosaccharides

Glycosides – glucose provides the anomeric carbon

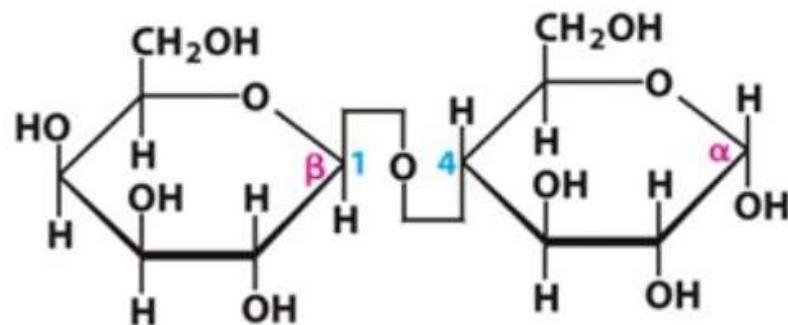
α -1,4-Glycosidic bond



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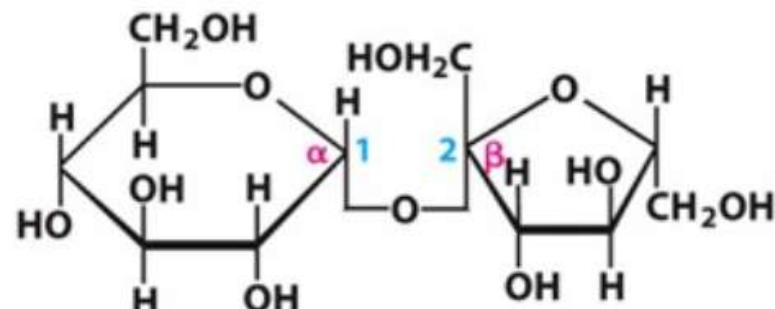
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Lactose

β -D-Galactopyranosyl-(1 → 4)- α -D-glucopyranose

Major carbohydrate
in milk

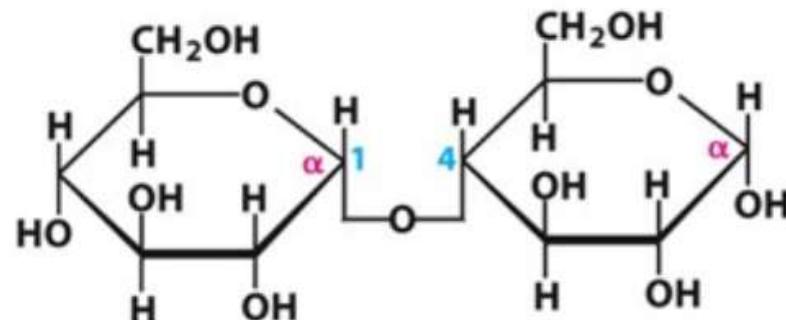


Sucrose

α -D-Glucopyranosyl- β -D-fructofuranose

Most abundant sugar

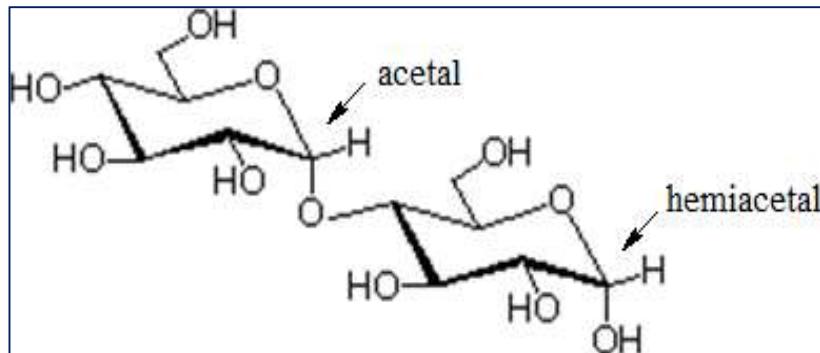
Sucrase, lactase and maltase are found on the outer surface of the epithelial cells lining the small intestine.



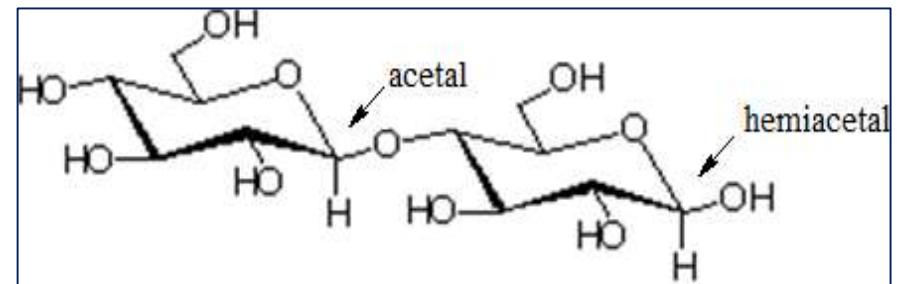
Maltose

α -D-Glucopyranosyl-(1 → 4)- α -D-glucopyranose

Comes from the breakdown of starch and glycogen



Maltose : disaccharide made from starch
 α -D-glucopyranosyl- α -D-glucopyranoside
 reducing sugar



Cellobiose
 β -D-glucopyranosyl- β -D-glucopyranoside
 reducing sugar

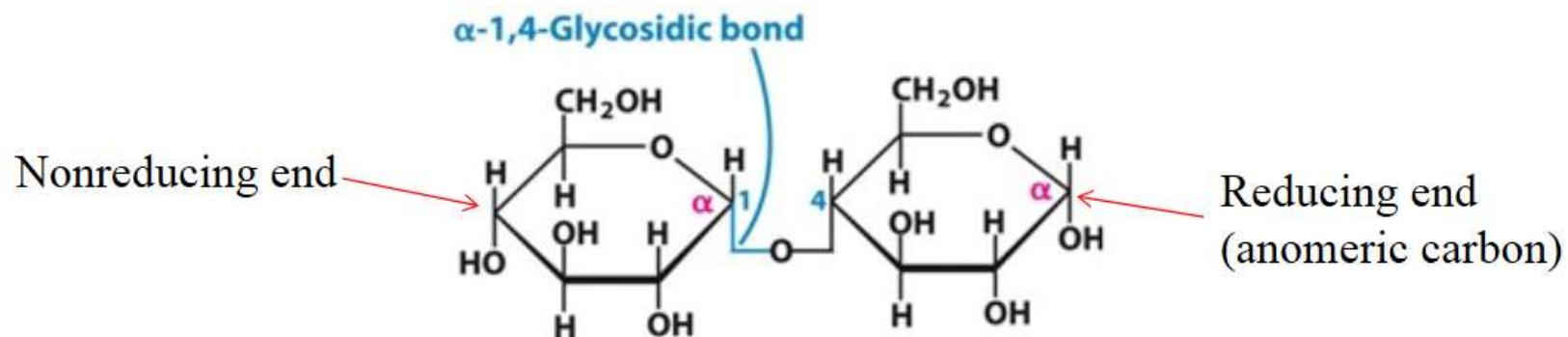
Cellobiose and maltose both contain two D-glucose units linked to each other, but cellobiose is formed by two glucose subunits linked via a β -glycosidic linkage. Cellobiose can exist in both α and β anomeric forms as the OH gp bonded to the anomeric C of the 2nd glucose subunit (not involved in formation of acetal)[C_{1'} OH] can be axial (α) or equatorial (β).

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Reducing and Nonreducing ends of sugars

- In linear polymeric chains of monosaccharides there is usually one reducing end (containing the free anomeric carbon) and one nonreducing end
- Branched polysaccharides have a number of nonreducing ends, but only one reducing end



The substituents that prefer the axial position have a lone pair on the atom (Z) bonded to the ring. The bond has a σ^ antibonding orbital. If one of the ring oxygen's lone pairs is in an orbital that is parallel to the σ^* antibonding orbital, the molecule can be stabilized by electron density from oxygen moving into the orbital. The orbital containing the axial lone pair of the ring oxygen can overlap the orbital only if the substituent is axial. If the substituent is equatorial, neither of the orbitals that contain a lone pair is aligned correctly for overlap.*

As glycosides are acetals, they are not in equilibrium with the open chain aldehyde (or ketone) in neutral or basic aqueous solutions and so cannot be oxidized by reagents such as Ag^+ or Br_2 therefore, are nonreducing sugars—they cannot reduce Ag^+ or Br_2 .

Hemiacetals (or hemiketals) are in equilibrium with the open-chain sugars in aqueous and so can reduce an oxidizing agent and therefore are classified as reducing sugars.

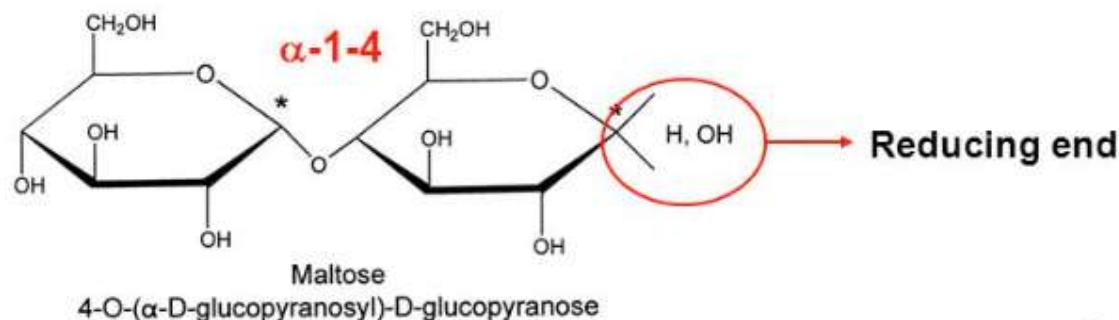
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Features of Disachharides

Maltose

- 2 units of glucose
- Forms from the breakdown of starch during malting of grains (barley) and commercially by using enzymes (β -amylase)
 - E.g. malt beverages; beer
- Used sparingly as mild sweetener in foods
- Very hygroscopic
- OH-group can be reactive and we term this as a **REDUCING SUGAR**
 - Is free to react with oxidants



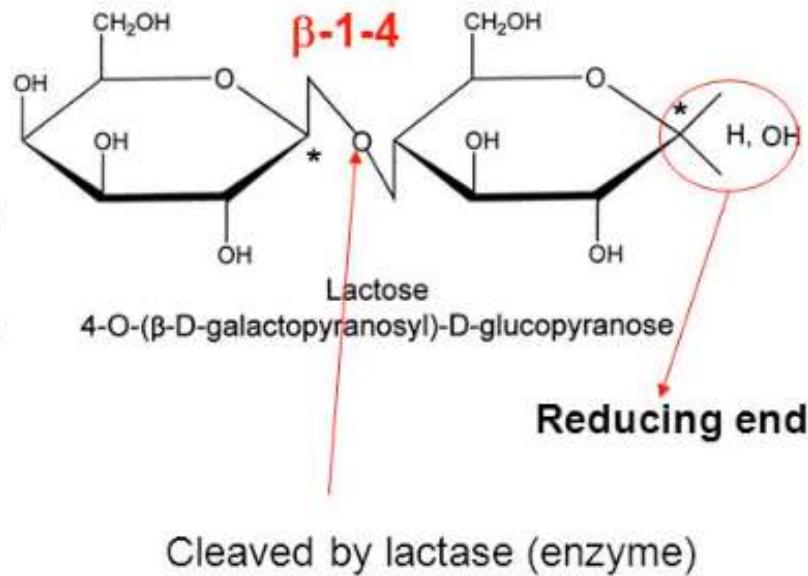
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Lactose

- Galactose and glucose
- The only sugar found in milk
 - 4.8% in cows
 - 6.7% in humans
 - The primary carbohydrate source for developing mammals
 - Stimulates uptake and retention of calcium
- Food products
 - Milk
 - Unfermented dairy products
 - Fermented dairy products
 - Contain less lactose
 - Lactose converted to lactic acid



Cleaved by lactase (enzyme)

α -D-lactose **VERY INSOLUBLE** (5 gm/100 ml)

- Causes the glass-like appearance in foods

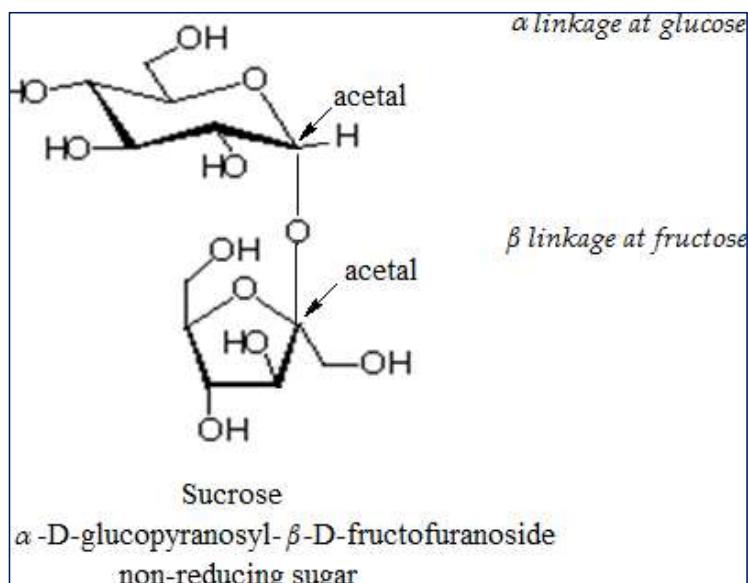
β -D-lactose **MORE SOLUBLE** (45 gm/100 ml)

If $\alpha >> \beta$ more α will form

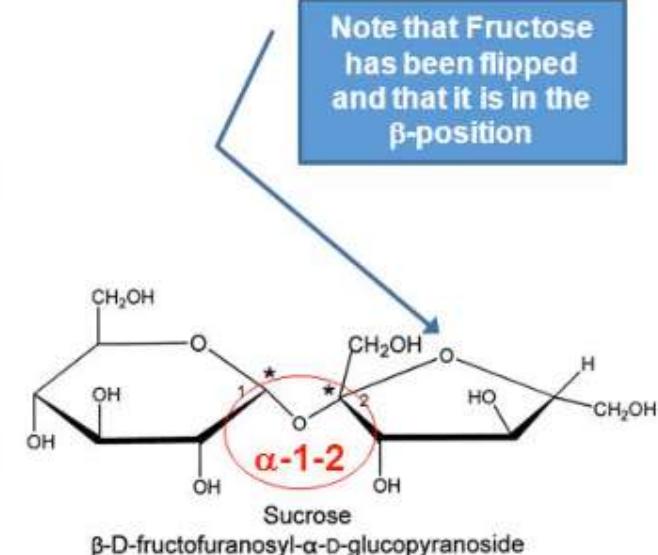
Limits amounts of milk solids one can use in formulations

- Quick drying \rightarrow get non-crystalline lactose (amorphous) \rightarrow no crystalline form
- Slow drying or concentration \rightarrow more crystalline lactose

Sucrose (table sugar)



- Naturally present
- Popular ingredient in foods (very large daily consumption)
- Used widely in fermentation
- Different commercial forms
- Composed of glucose and fructose
- The glycosidic bond is formed between the anomeric carbons of Glu and Fru
- This renders the anomeric carbons non-reactive and the sugar is therefore called a **NON-REDUCING** sugar



The bond can be broken by hydrolysis

- Enzyme (fructosidase invertase)
- Acid/heat

Product called **Invert sugar**

Sucrose, the most common disaccharide, comprises of a D-glucose unit linked to a D-fructose unit via a glycosidic linkage between C₁ of glucose (α -position) connected to C₂ of the fructose (β -posn). Crystalline sucrose has a specific rotation of +66.5, but on hydrolysis, shows a specific rotation of -22.0. Due to inversion of sign of rotation on its hydrolysis, it is also called invert sugar, and the enzyme catalyzing hydrolysis of sucrose is called invertase.

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Disaccharide	Unit 1	Unit 2	Bond
Sucrose (<i>table sugar, cane sugar, beet sugar, or saccharose</i>)	glucose	fructose	$\alpha(1 \rightarrow 2)\beta$
Lactulose	galactose	fructose	$\beta(1 \rightarrow 4)$
Lactose (<i>milk sugar</i>)	galactose	glucose	$\beta(1 \rightarrow 4)$
Maltose	glucose	glucose	$\alpha(1 \rightarrow 4)$
Trehalose	glucose	glucose	$\alpha(1 \rightarrow 1)\alpha$
Cellobiose	glucose	glucose	$\beta(1 \rightarrow 4)$

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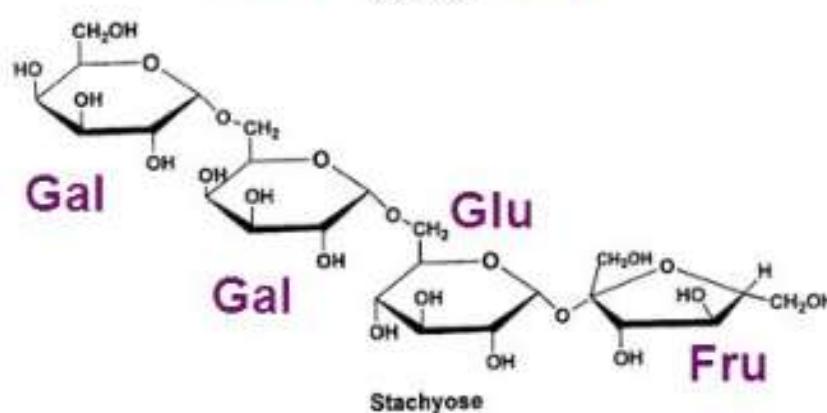
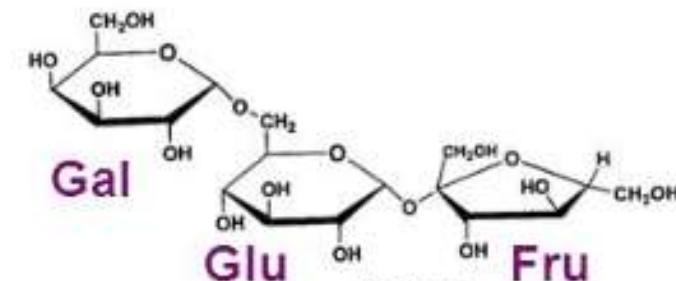
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Tri- and tetrasaccharides

Galactosylsucroses

Raffinose and Stachyose

- Found primarily in legumes



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Polysaccharides

- **Homoglycans** – homopolysaccharides containing only one type of monosaccharide.
- **Heteroglycans** – heteropolysaccharides containing residues of more than one type of monosaccharide
- The lengths and compositions of a polysaccharide may vary within a population of these molecules
 - e.g.: starch and glycogen – storage polysaccharides
 - cellulose and chitin – structural polysaccharides

Polysaccharides are compounds comprising of ten to several thousand units of monosaccharide (same or different) joined via glycosidic linkages. E.g. starch and cellulose. Starch is a mixture of two different polysaccharides- amylose [20%] and amylopectin [80%].

Amylose has unbranched chains of D-glucose linked via α -1,4'-glycosidic linkages.

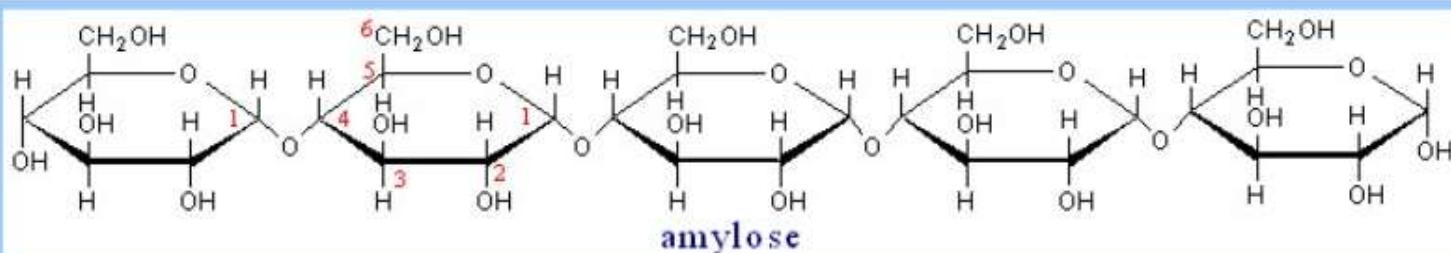
Amylopectin is unbranched: chain of D-glucose linked by α -1,4'-glycosidic linkages and branches created by 1,6'-glycosidic linkages.

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Starch

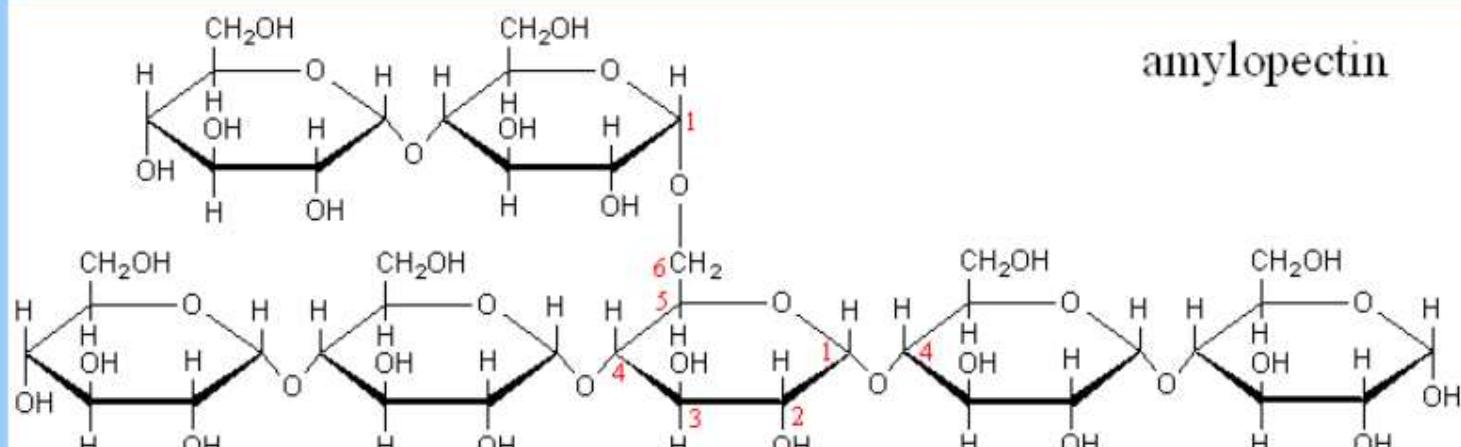
- The reserve carbohydrate of plants. Occurs as granules in the cell. Made of amylose and amylopectin.
- **Amylose** is a glucose polymer with $\alpha(1 \rightarrow 4)$ linkages.
- The end of the polysaccharide with an anomeric C1 not involved in a glycosidic bond is called the **reducing end**.



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- **Amylopectin** is a glucose polymer with mainly $\alpha(1 \rightarrow 4)$ linkages, but it also has **branches** formed by $\alpha(1 \rightarrow 6)$ linkages. Branches are generally longer than shown above.
- The branches produce a compact structure & provide multiple chain ends at which enzymatic cleavage can occur.

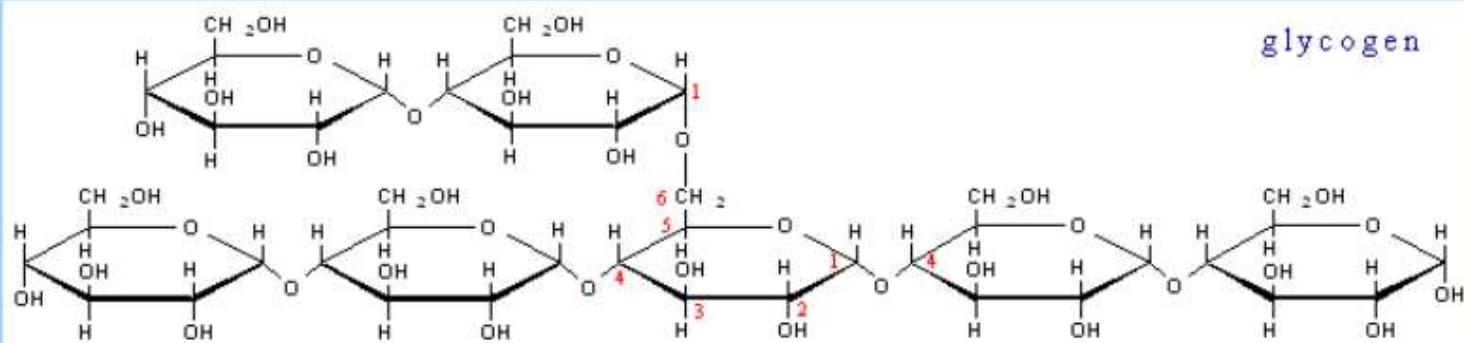


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Glycogen

- **Glycogen**, the glucose storage polymer in **animals**, is similar in structure to amylopectin.
- But glycogen has **more $\alpha(1 \rightarrow 6)$ branches**.
- The highly branched structure permits rapid glucose release from glycogen stores, e.g., in muscle during exercise.
- The ability to rapidly mobilize glucose is more essential to animals than to plants.

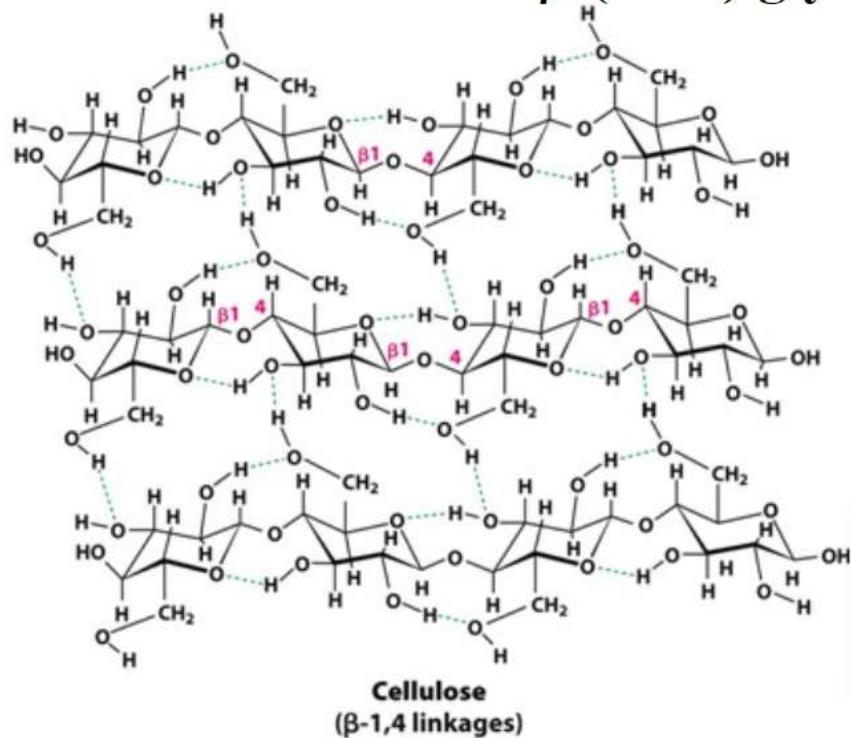


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Cellulose – a structural polysaccharide that is a Major component of cell walls of plants

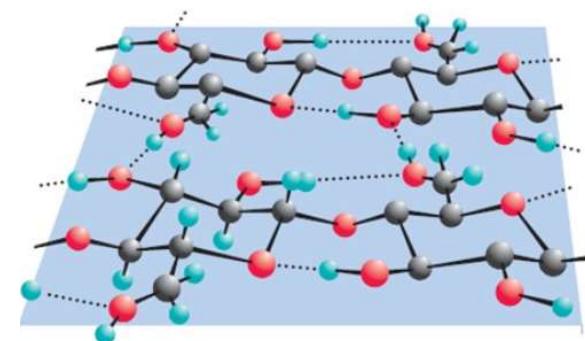
Cellulose has β -(1 \rightarrow 4) glycosidic bonds



Each glucose residue is rotated 180° relative to the next residue

Extended hydrogen bonding between chains leads to bundles or fibrils

Cellulose, present in higher plants, is comprised of unbranched chains of D-glucose, however, unlike amylose, these units are linked via β -1,4'-glycosidic linkages. These β linkages promote formation of intramolecular hydrogen bonds, thereby causing cellulose to be insoluble in aqueous medium. This lends it structural strength.



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- Humans digest starch and glycogens ingested in their diet using amylases, enzymes that hydrolyze α -(1 \rightarrow 4) glycosidic bond
- Humans cannot hydrolyze β -(1 \rightarrow 4) linkages of cellulose. Therefore cellulose is not a fuel source for humans. **It is fiber.**
- Certain microorganisms have cellulases, enzymes that hydrolyze β -(1 \rightarrow 4) linkages of cellulose.
 - cattle have these organisms in their rumen
 - termites have them in their intestinal tract

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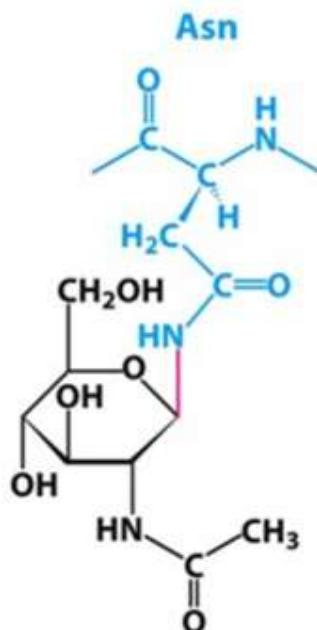
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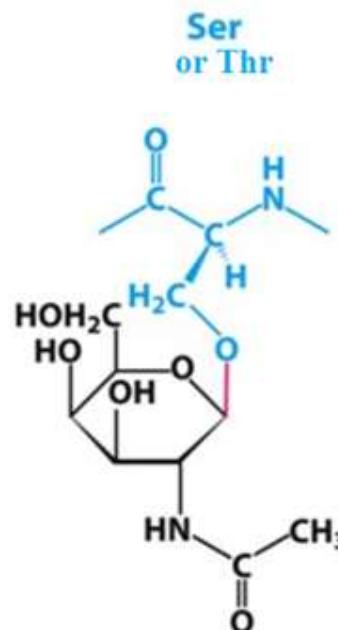
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Carbohydrates attached to proteins form **glycoproteins**

Many glycoproteins are found as components of cell membranes and take part in cell adhesion and binding.



N-linked GlcNAc



O-linked GalNAc

Ser
or Thr

Mucins or mucoproteins are proteins which has N-acetylgalactosamine attached. This glycoprotein is found in mucus and is a lubricant.

Two methods to anchor the protein to carbohydrates

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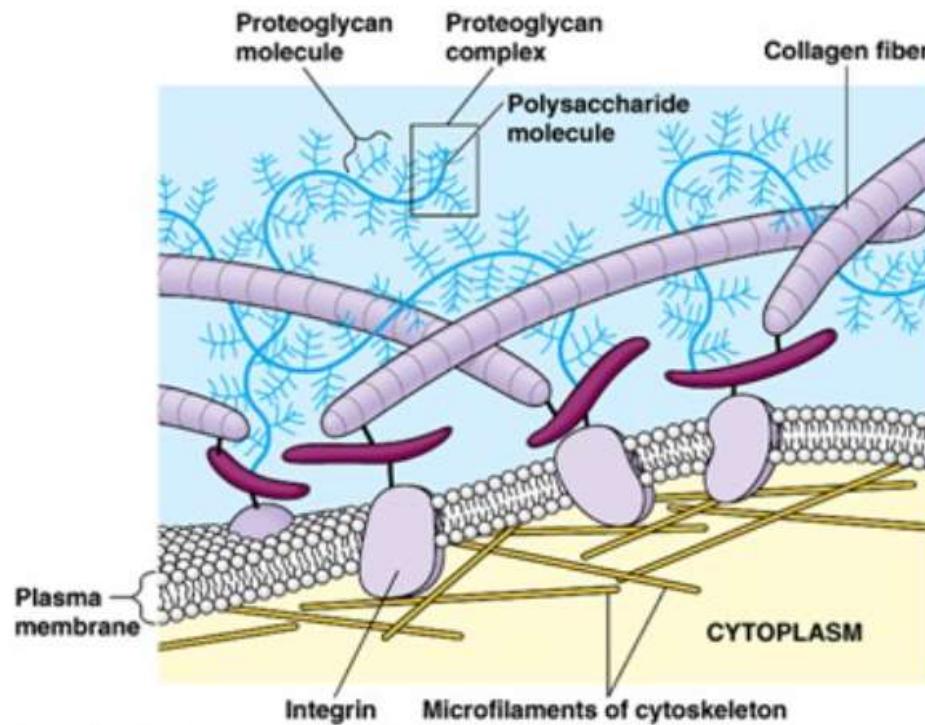
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Proteoglycans are glycoproteins where the protein is bound to a special class of polysaccharides called a glycosaminoglycan.

This class of glycoprotein are used as structural components and lubricants.

-In proteoglycans nearly 95% of the mass comes from the polysaccharide.

-Proteoglycans function as lubricants, structural components in tissue and mediate the adhesion of cells to the extracellular matrix.



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These polysaccharides, when hydrolysed will yield the constituent simple sugars.

The simple sugars can then be bioprocessed to form other products. Some of these products and applications are:

- alternative fuels such as ethanol, methane
- starch-based adhesives, agrochemicals (starch encapsulation agents for pesticides)
- cosmetics and toiletries (sorbitol in toothpaste)
- biodegradable detergents
- paper making additives
- pharmaceuticals
- glucose hydrolysates or their derivatives as fermentation substrate in order to produce several active compounds (i.e. vitamins, antibiotics and hormones)

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