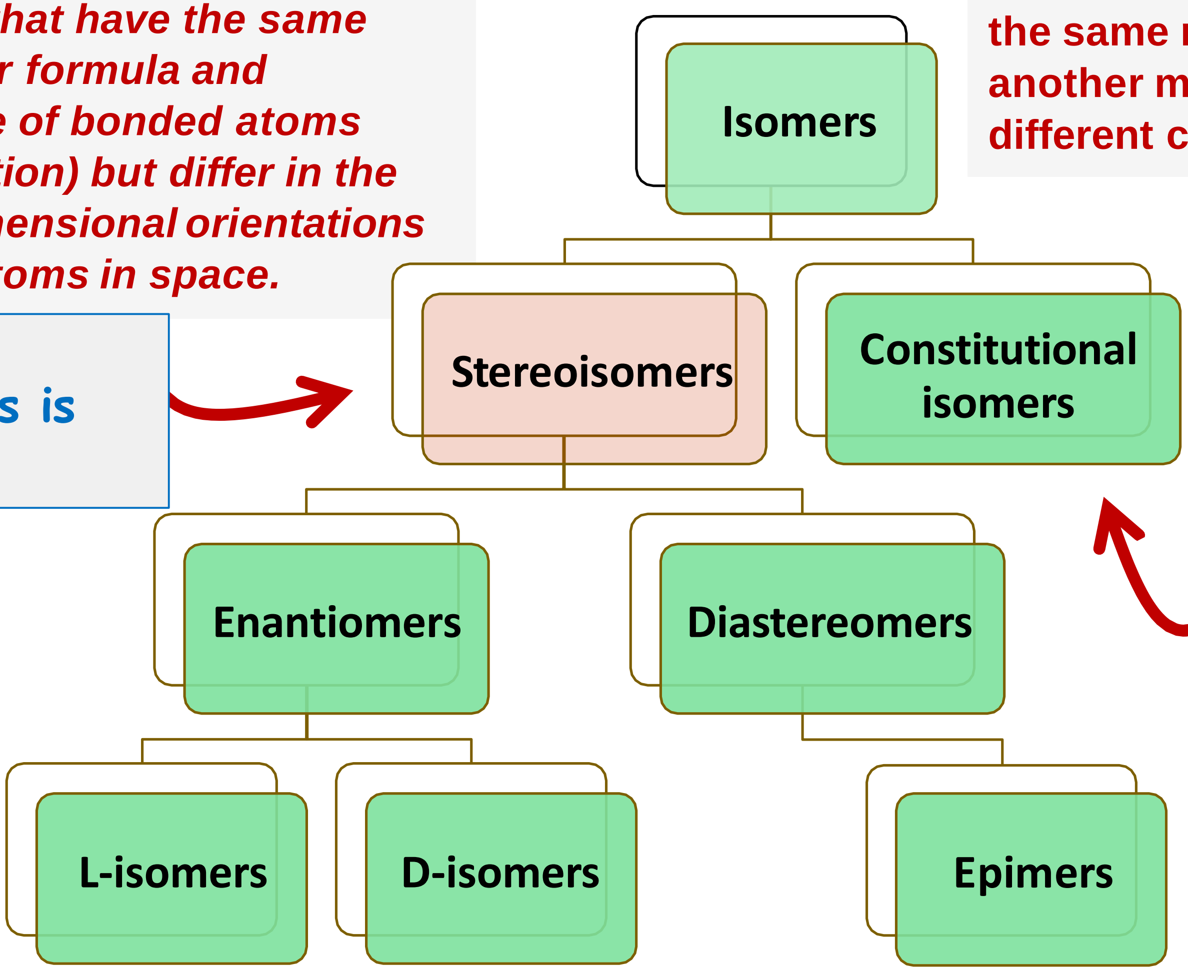
Isomerism

Isomers that have the same molecular formula and sequence of bonded atoms (constitution) but differ in the three-dimensional orientations of their atoms in space.

The main difference between stereoisomers is in shape .



- Isomers
  - Stereoisomers
    - Enantiomers
      - L-isomers
      - D-isomers
    - Diastereomers
      - Epimers
  - Constitutional isomers

An *isomer* is a molecule with the same molecular formula as another molecule, but with a different chemical structure.

Molecules with the same molecular formula but have different bonding patterns and atomic organization such as functional group

Epimers:different in one carbon (chiral) such as glucose and galactose

Glyceraldehyde has “L” and “D”isomers (the simplest aldose),that’s because it has one chiral center.

Dihydroxyacetone(the simplest ketose) has no isomers ,that’s because there is no chiral center in Dihydroxyacetone.

No body believes in you, you lost again and again and again, the lights are cut off, but you are still looking at your dreams, reviewing it every day and telling yourself it's not over until I win .

وقف هسا لو بقلك ربع ساعة للامتحان معقول تلحق؟

Isomers of glucose

2^n (n is the number of chiral carbons in a sugar molecule)

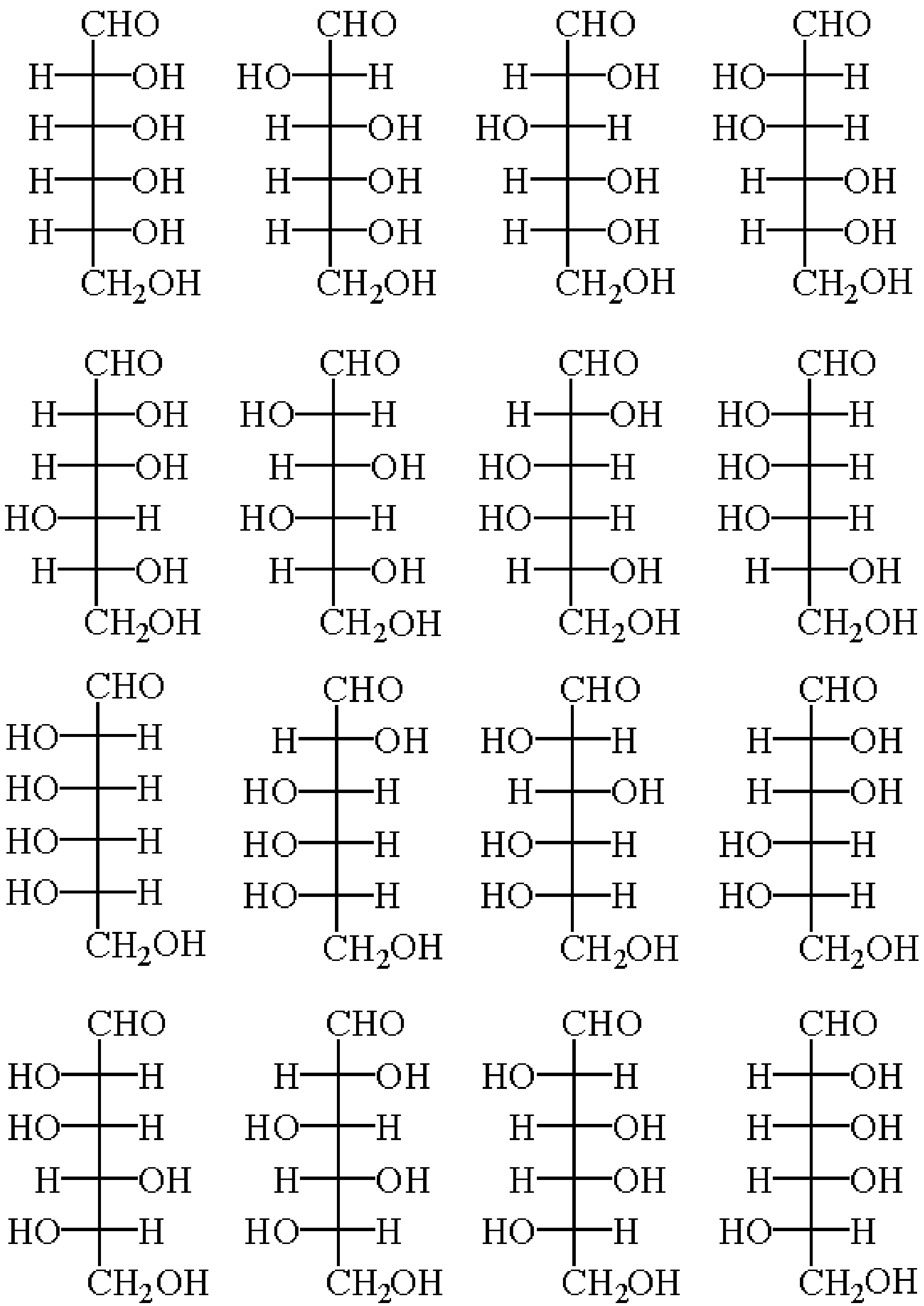
Search for:

- Glucose,
- Galactose
- Mannose

Remember: to know how many isomeres any molecule has: (2^n) n= number of chiral centers .

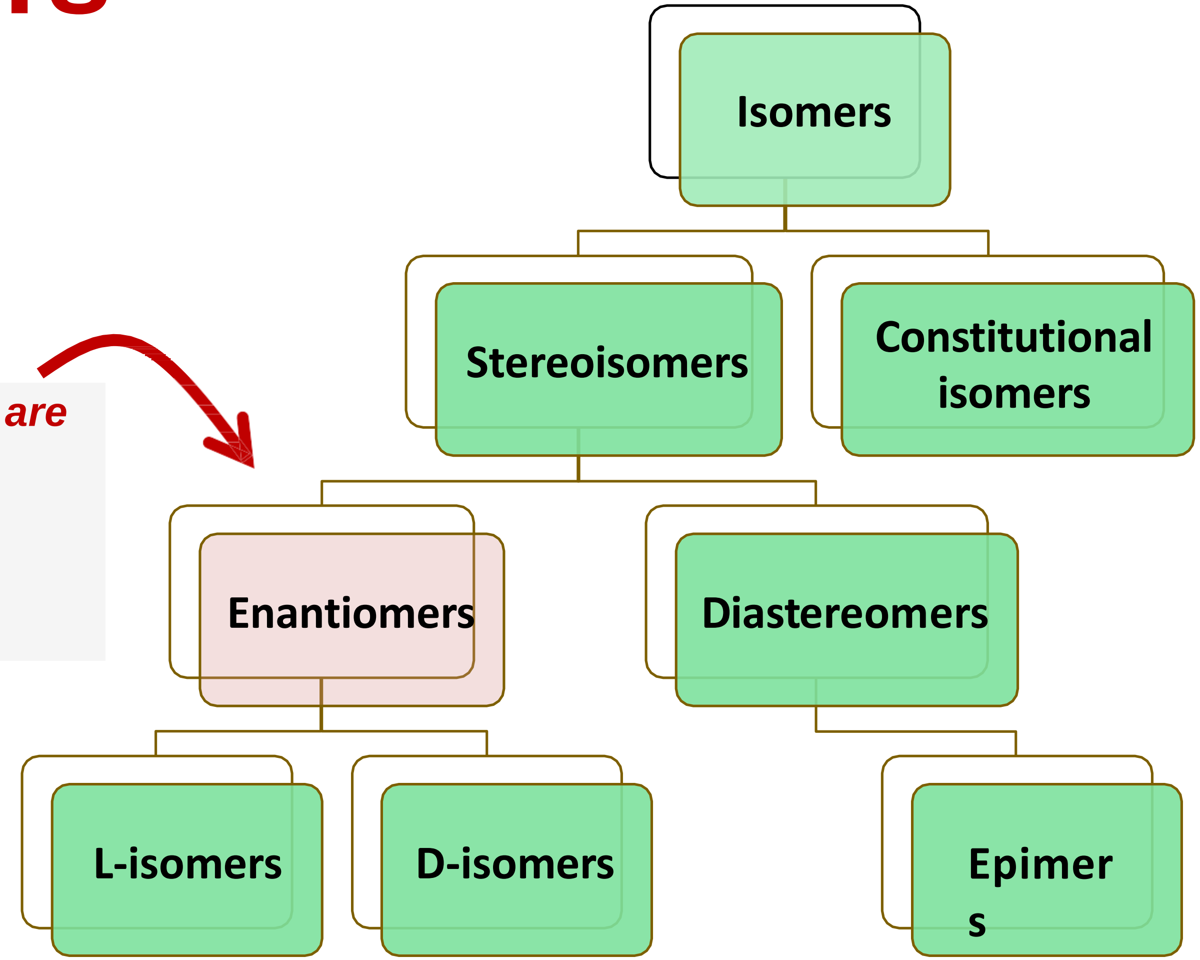
In aldohexoses we have 4 chiral carbons that's why we have 16 isomers.

16 Aldohexoses



Enantiomers

Two stereoisomers that are mirror images of each other and are non-superimposable (not identical)


Isomers

Stereoisomers

Constitutional isomers

Enantiomers

Diastereomers

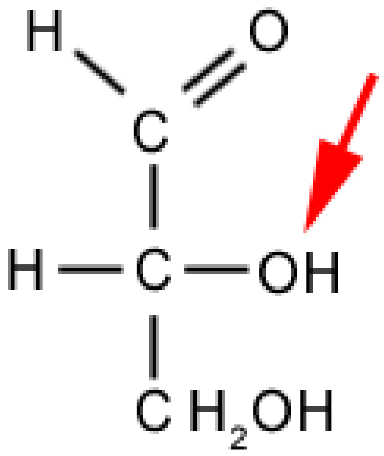
L-isomers

D-isomers

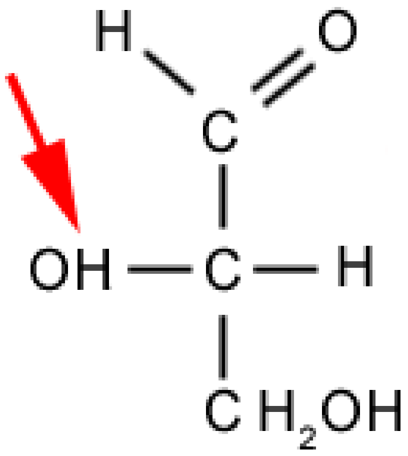
Epimers

Sugar enantiomers (D- vs. L-)

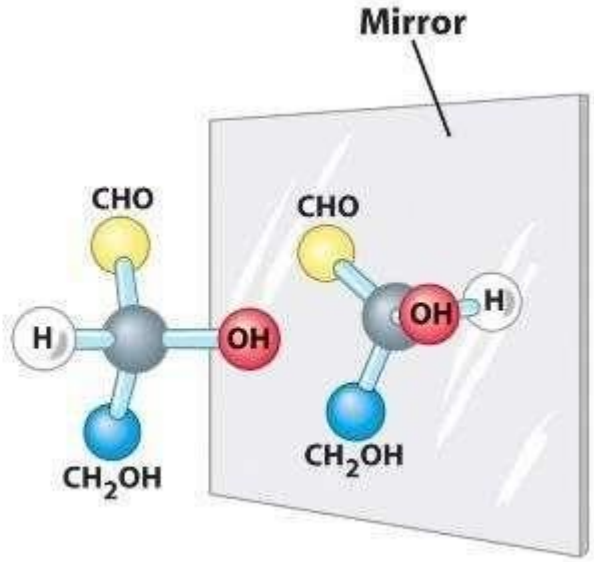
If the hydroxyl group (OH group) is to the left (linear shape),it is "L" isomer, and if it is to the right, it is "D" isomer.



D-Glyceraldehyde



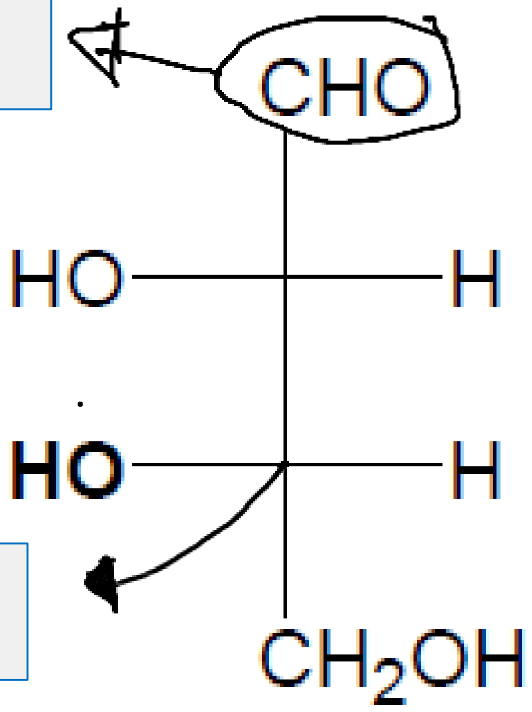
L-Glyceraldehyde



Ball-and-stick models

Which one(s) is a chiral carbon?

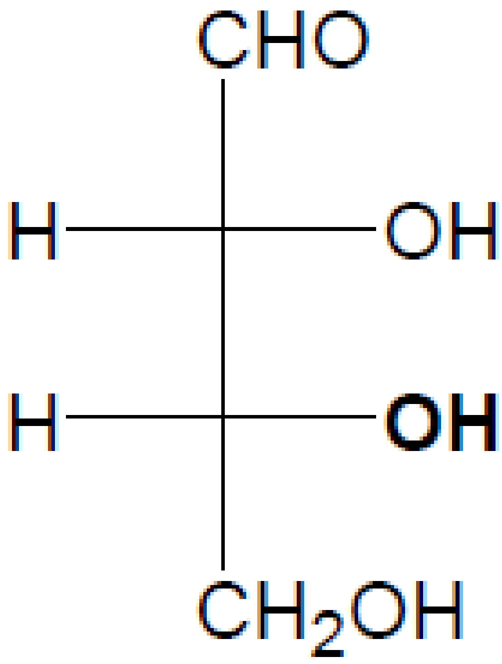
The functional group (aldehyde).



The last chiral center.

L-erythrose

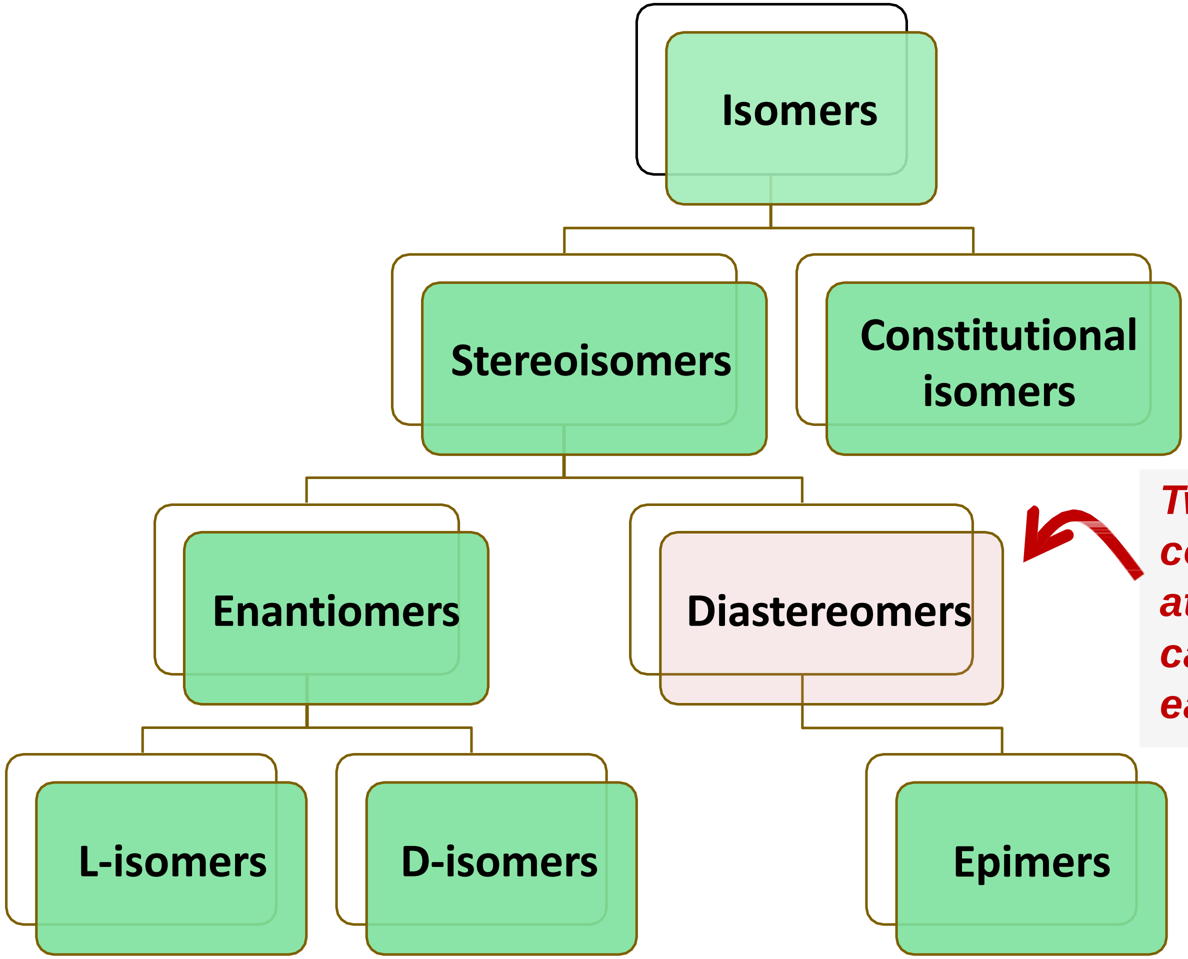
When we have more than one chiral center, we choose the farthest chiral center from the functional group (the last chiral carbon) and then check if it's “L” isomer or “D” isomer.



D-erythrose

Isomerism

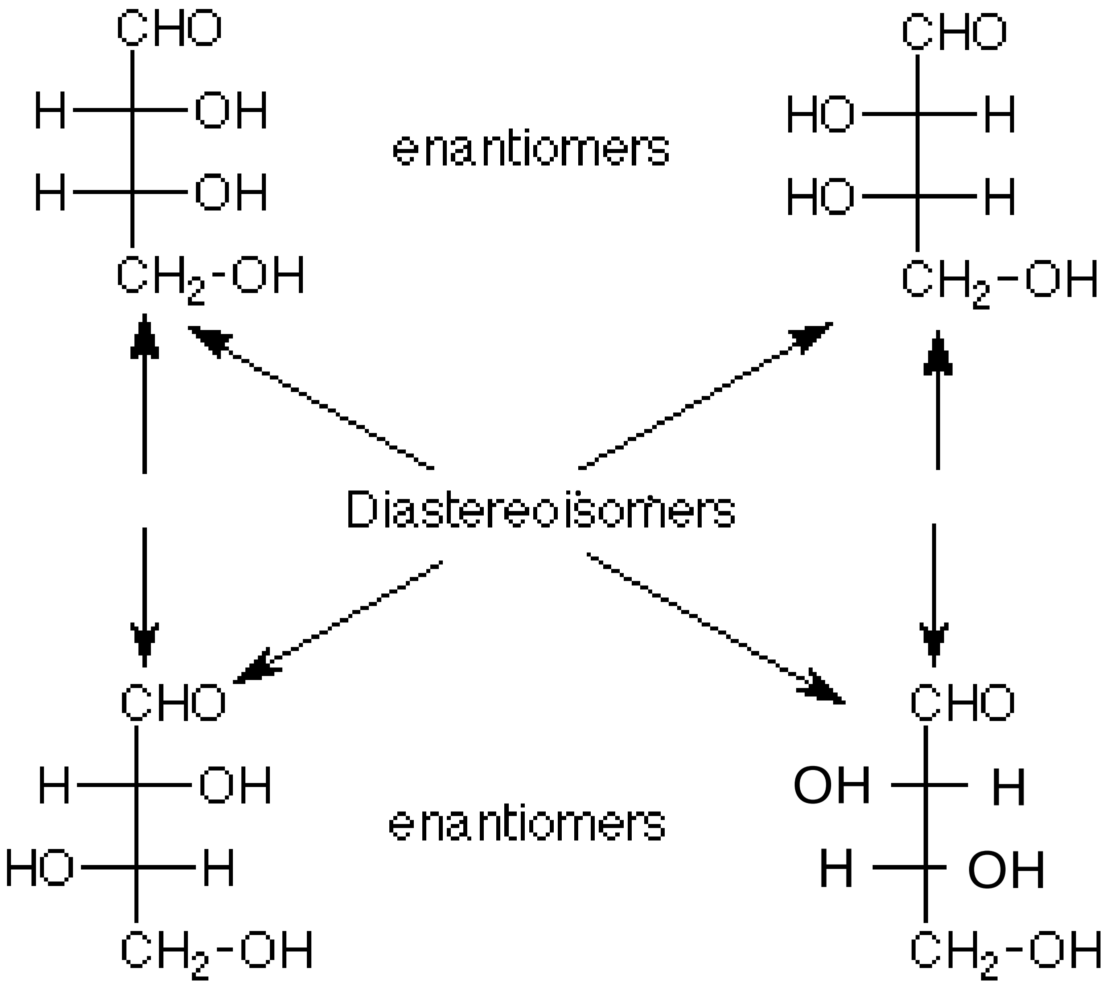
Diastereomers: Two molecules with the same formula and the same bonding and the same orientation except some groups



Two or more stereoisomers of a compound having different configurations at one or more (but not all) of the chiral carbons and are not mirror images of each other.

Stereoisomers, but non-mirror images and non-superimposable, then…diastereomers

As we notice here if the relationship is diastereomers, the names and characteristics and the reaction will be different

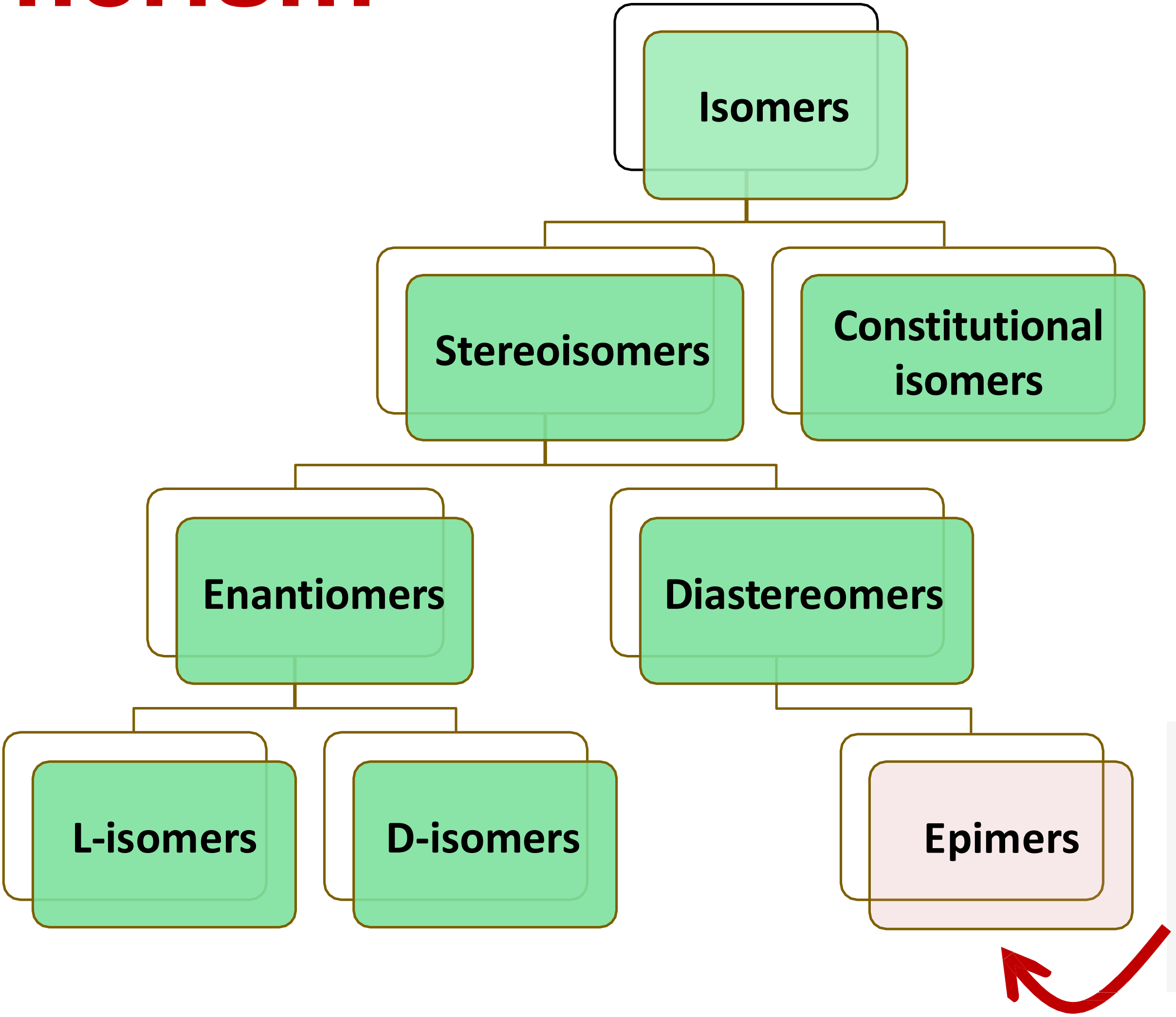


As we see here if there is a difference in just one group, the relationship will be diastereomers. But if the difference is in two groups, the relationship will be enantiomers (mirror image)

Isomerism

Epimers: A partial group of diastereomers

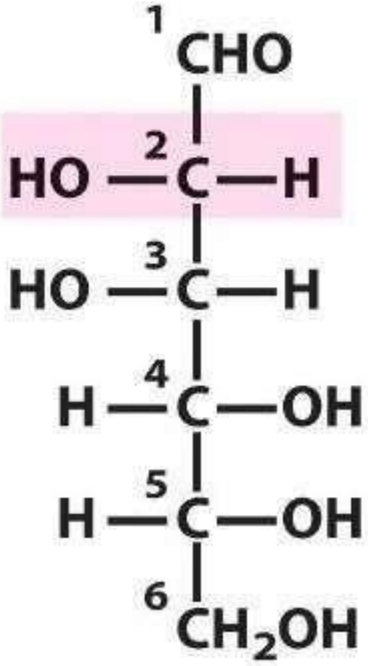
Every epimer is a diastereomer but not every diastereomer is an epimer



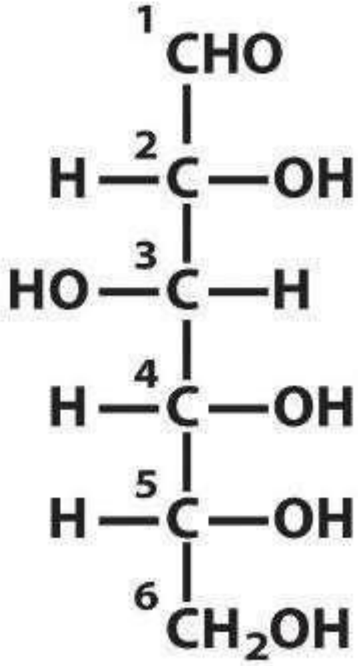
Epimer refers to one of a pair of stereoisomers whereby two isomers differ in configuration at only one chiral carbons.

Diastereomers with different orientation of one chiral carbonm then… epimers

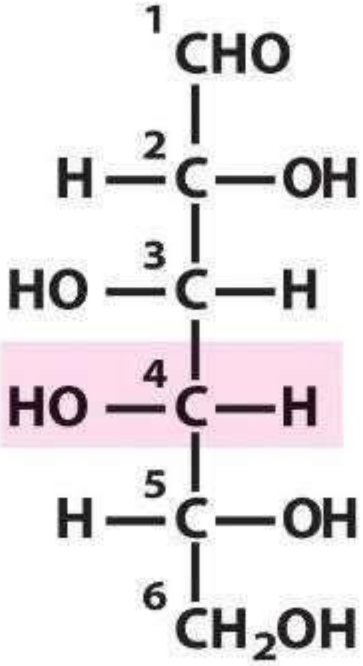
D-mannose and D- galactose are diastereomers We don't consider them epimers because of the differences in different places (More than 1 group)



D-Mannose
(epimer at C-2)



D-Glucose



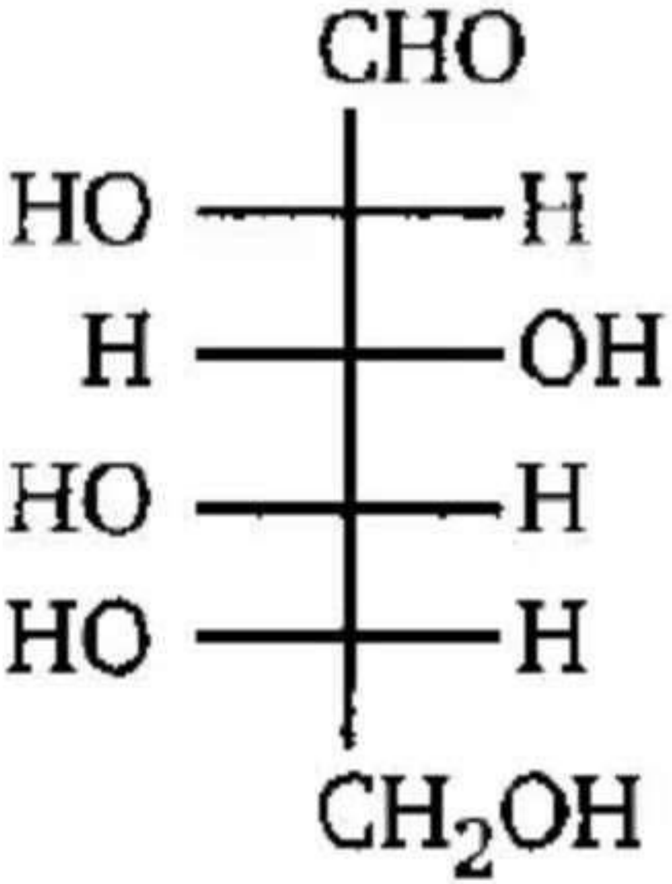
D-Galactose
(epimer at C-4)

D-glucose and the D-Mannose are epimers in carbon number 2

D-glucose and D-galactose are epimers in carbon number 4

Is L-glucose an epimer with D-mannose and D-galactose?

Notice: go to the previous slide and see the structure for D-mannose and D-galactose

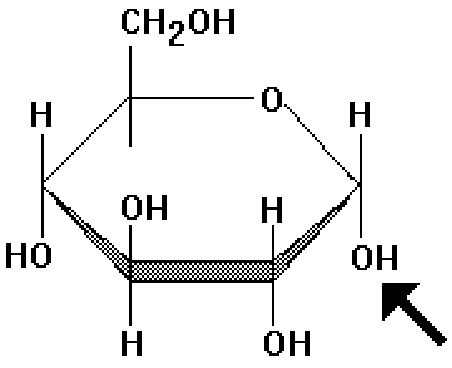


L-glucose

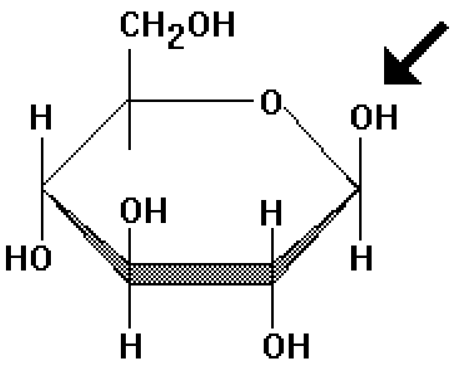
Is L-glucose an epimer with D-mannose and D-galactose ? The answer is no because they are different in 2 chiral centers

Anomers

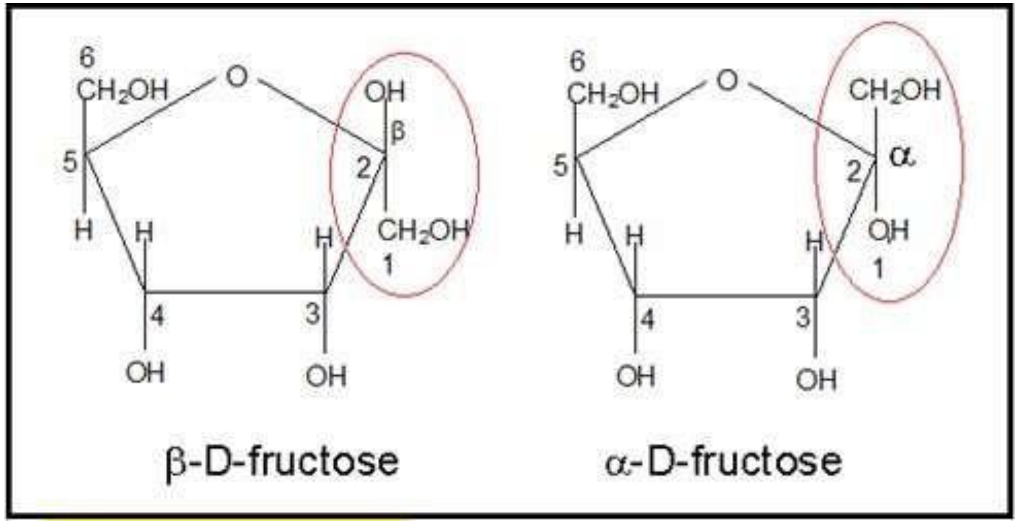
As we see in this slide in D shape
When OH is up it's beta, when OH is down it's alpha.
(In L shape, every thing is opposite)



alpha-D-glucose



beta-D-glucose



β-D-fructose

α-D-fructose

-64% of the time the glucose molecule stays as beta shape (the most stable)

-36% of the time it's in alpha shape

The liner (open chain) shape is almost zero because it only forms during reactions (some of them only not all)

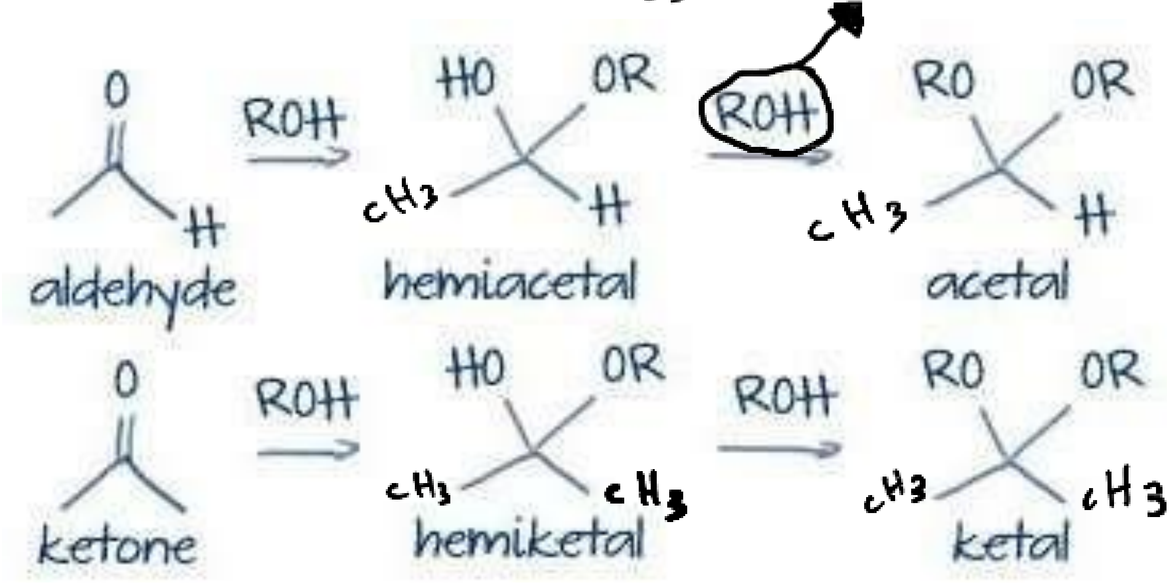
Acetal/ketal vs. hemiacetal/hemiket

Hemiacetal: A carbon that is connected with OH group and OR group.

Hemiacetal and hemiketal: ether and alcohol on same carbon
Acetal and ketal: two ethers on same carbon

مش شرط نفس النوع
من الكحول

Hemiketal: A carbon that is connected with OH group and OR group



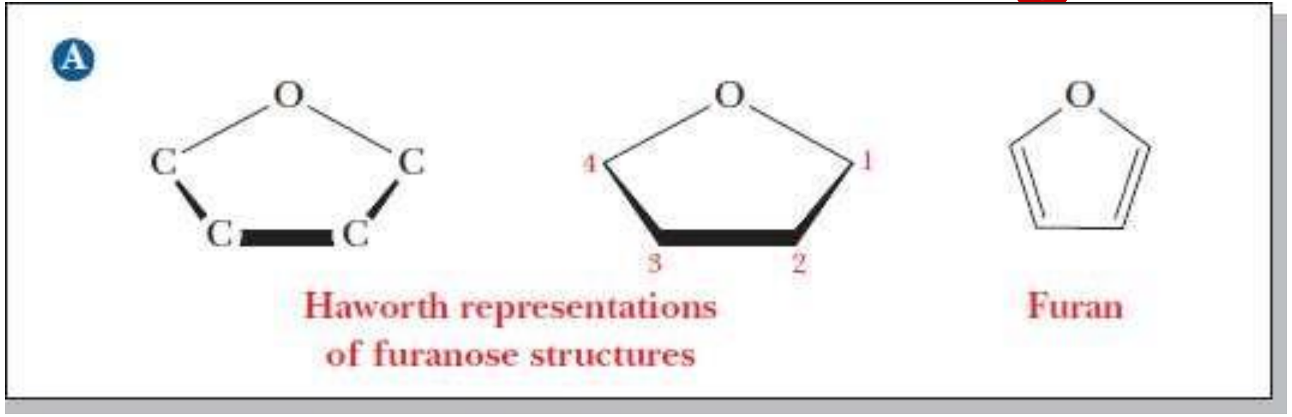
Acetal:A carbon that is connected with 2 OR groups.

Aketal:A carbon that is connected with 2 OR groups

What is the difference between hemiacetal and hemiketal and the difference between acetal and ketal?

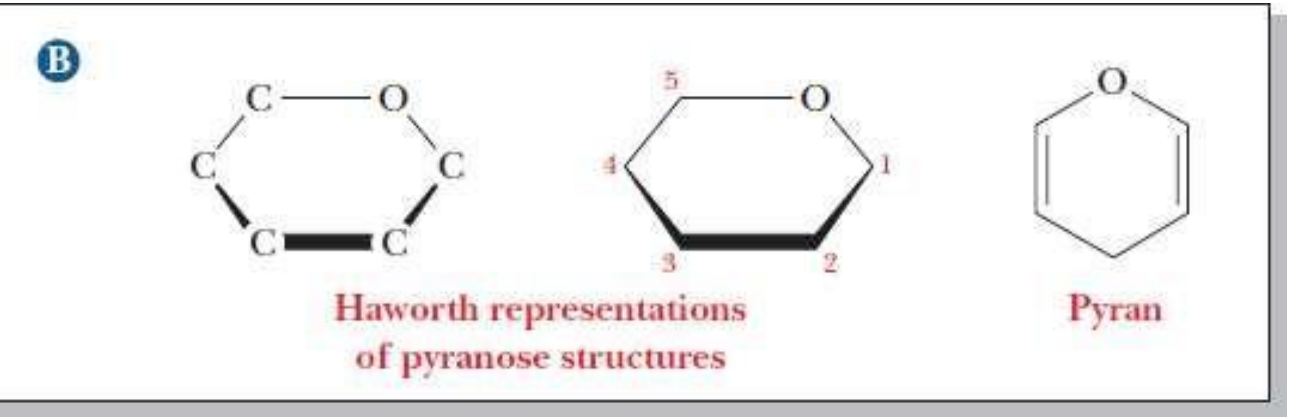
The answer is: acetal and hemiacetal are connected with a hydrogen atom. The Aketal and hemiaketal aren't connected with a hydrogen atom.

Formation of a ring structure



Haworth representations of furanose structures

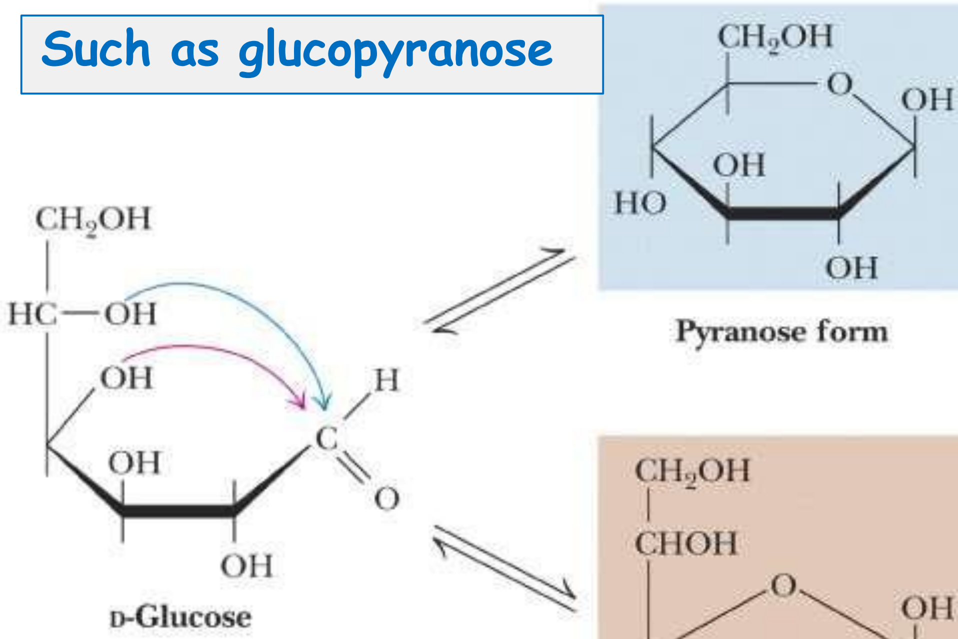
Furan



Haworth representations of pyranose structures

Pyran

Such as glucopyranose



D-Glucose

Pyranose form

Such as fructo furanose

Furanose form

When the rings form from an aldose: the reaction occurs between the first carbon and the 5th carbon making a 6-membered ring (like glucose). When the rings form from a ketose: the reaction occurs between the 2nd carbon and he 5th carbon making a 5-membered ring (like fructose).

A six-membered ring (5 Carbon and 1 Oxygen) is called a pyranose because of its resemblance to pyran.

A five-membered (4 Carbon and 1 Oxygen) ring is called a furanose because of its resemblance to furan.

Each sugar can alternate between the anomers.

What is an anomer?

-Its name comes from the anomeric carbon when it reacts with the last chiral center and closes the ring.

The anomeric carbon has no OH attached to it, it has a carbonyl group. But when the ring shape is formed it will have OH attached to which didn't exist before when the shape was liner .

While the transforming happens, the OH groups that are to the right of the liner plane will go down in the ring, while the OH groups on the left go up in the ring.

What about the new OH that's on the anomeric carbon?

An equilibrium state happens in the molecule, sometimes it puts it up, sometimes down and some times it's in a liner shape.

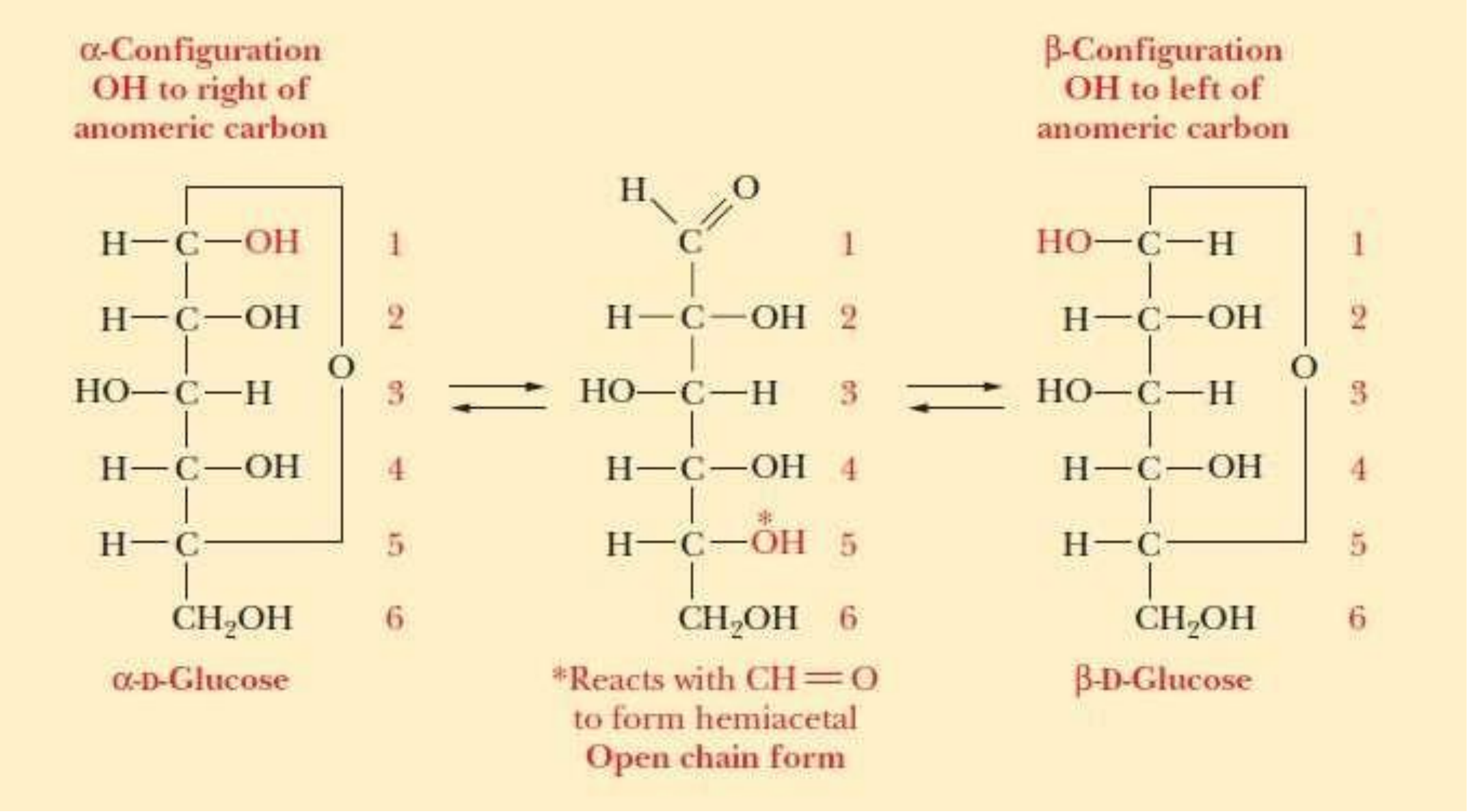
Even though it's in an equilibrium state, it's likely to be in the most stable form which is the ring.

How can we define the most stable form?

-depending on the steric strain ((كل ما زاد تباعد الجزيئات الأكبر حجما عن بعض كلما زاد الاستقرار))

Unlike anomers the molecule can't convert from D to L shape

Anomers as Fischer projection



α-Configuration
OH to right of
anomeric carbon

β-Configuration
OH to left of
anomeric carbon

α-D-Glucose

*Reacts with CH=O
to form hemiacetal
Open chain form

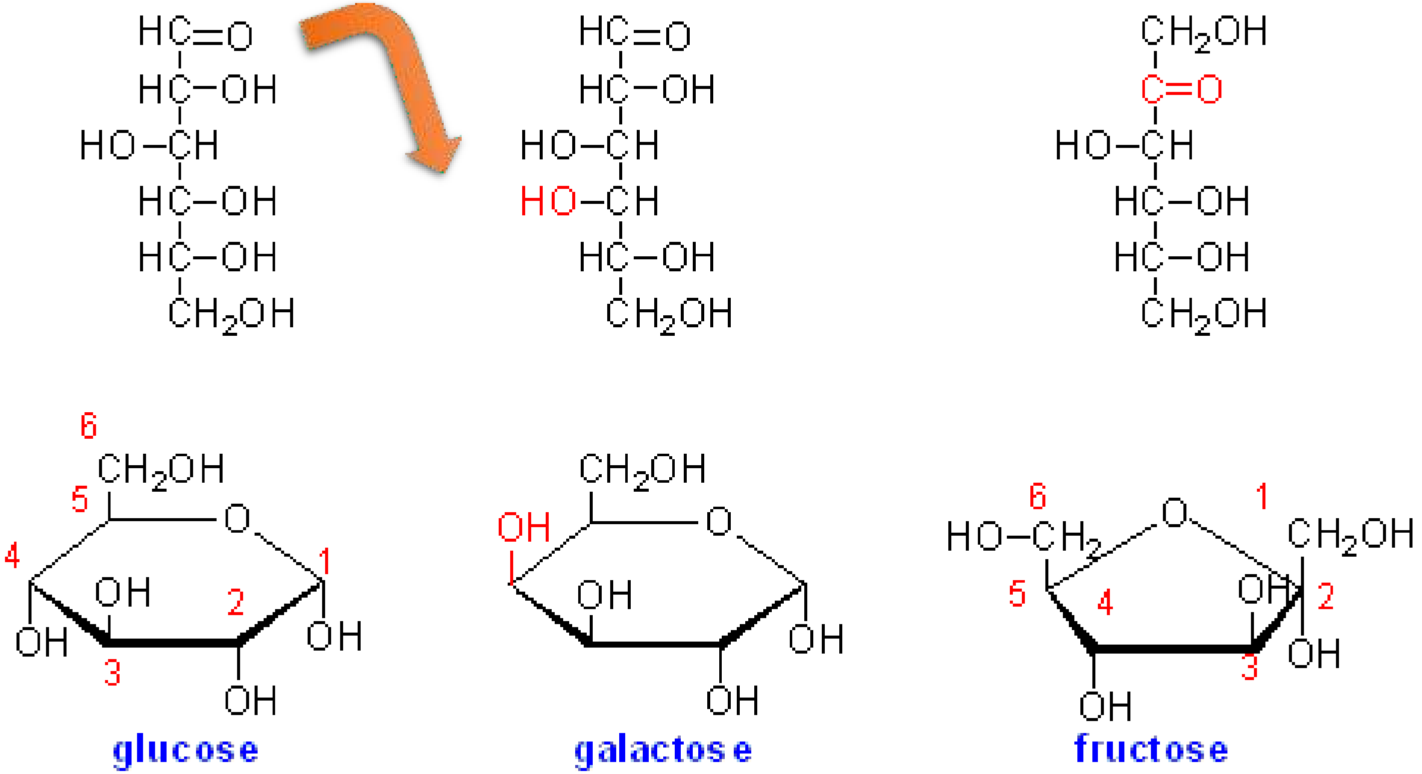
β-D-Glucose

Chain to ring
Left-up, right-down

Notice: حكت لا
تركيب لافركتوز لاكتورة
تحفظوا

Going down to [YOUR]{.underline} right

In the fructose ring shape, we define the anomeric carbon as the carbon that has CH2OH and OH



glucose

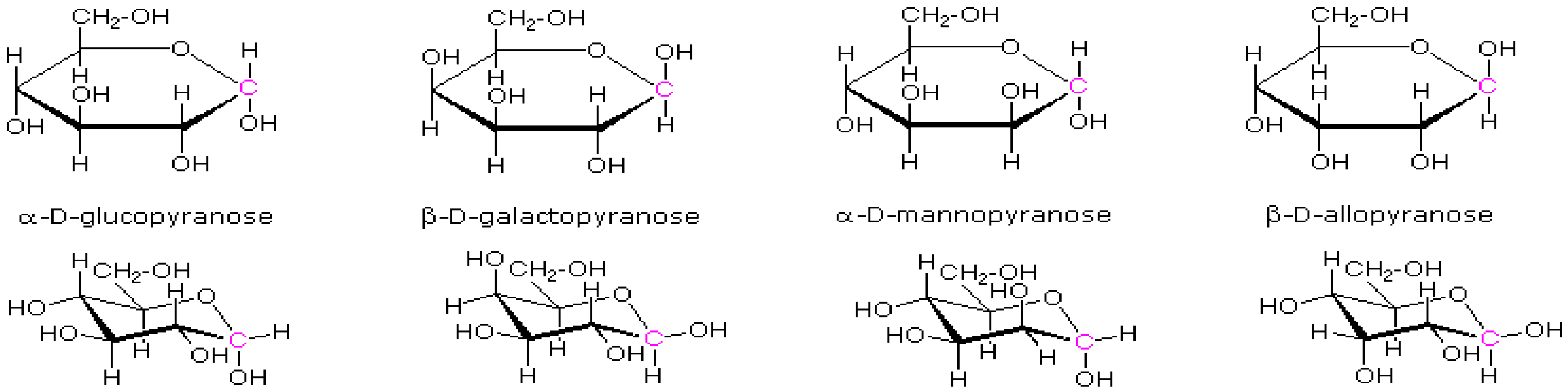
galactose

fructose

We can determine if the molecule is D or L shape by looking at the last carbon (the 6th here) in the ring shape.
If it's upwards (of the ring) -> it's D and if it's downwards ->it's L

Cyclic aldohexoses

Examples of Some Pyranose Forms of Hexoses



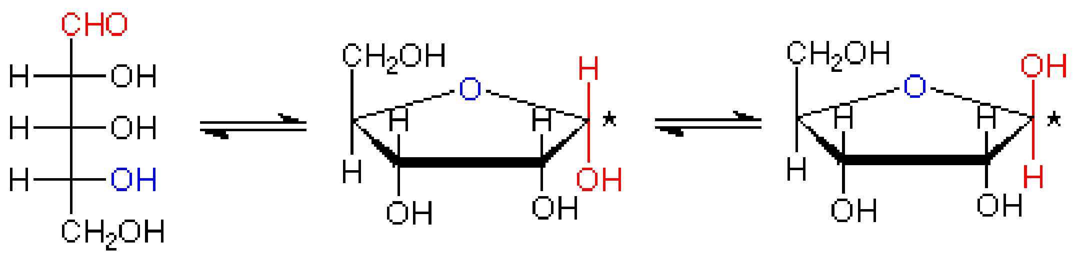
α-D-glucopyranose

β-D-galactopyranose

α-D-mannopyranose

β-D-allopyranose

Cyclic ribofuranose



* anomeric carbon

D-ribose

α-D-ribose
OH at anomeric carbon down

β-D-ribose
OH at anomeric carbon up

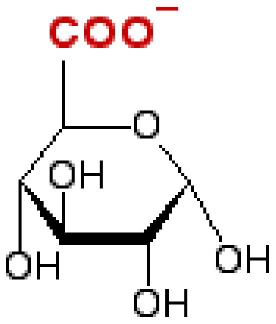
Modified sugars

Modified sugars: modifications that occurs on these sugars such as: oxidation, reduction or reactions to create certain properties

Sugar acids (oxidation)

Sugar oxidation: the process to convert sugar to carboxylic acid. This process occur on alcohol and anomeric carbon (aldehyde)

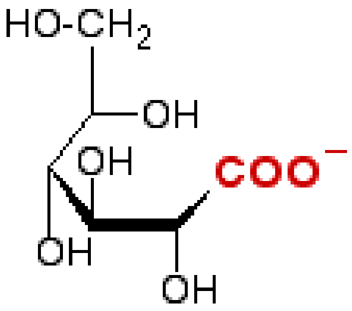
- Where is it oxidized? What does it form?



α-D-glucuronate

(D-glucuronic acid, **GlcUA**)

from **oxidation of glucose C6 OH**



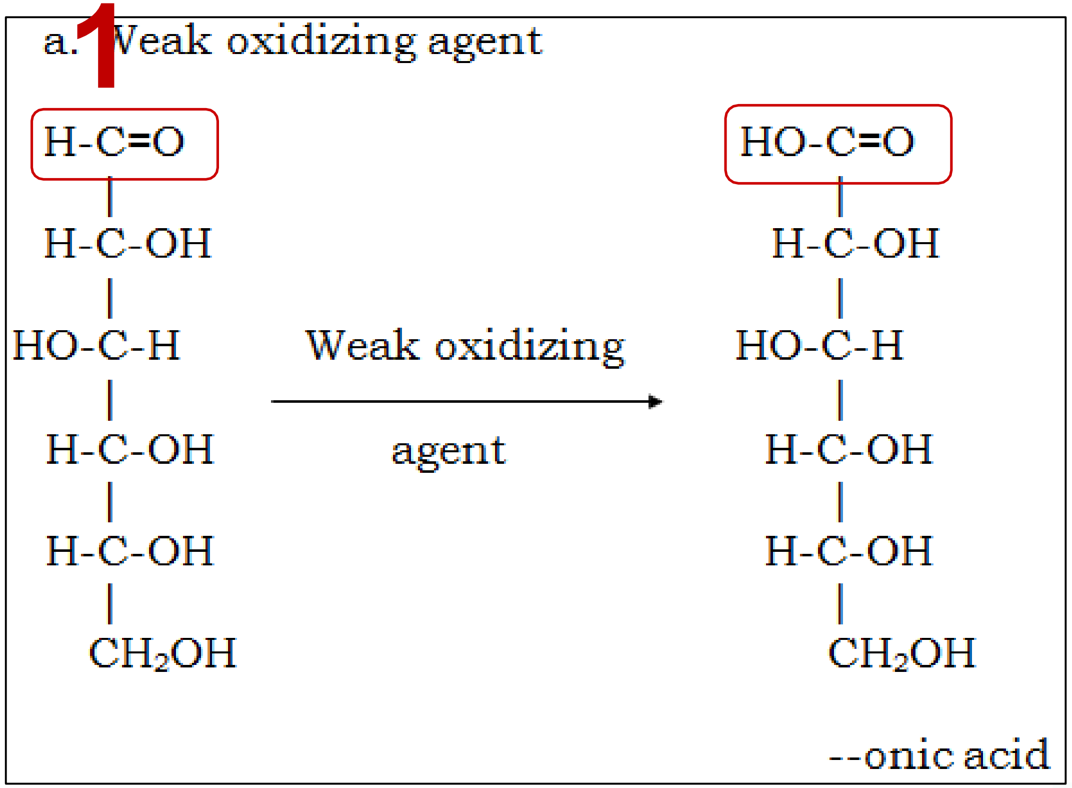
D-gluconate

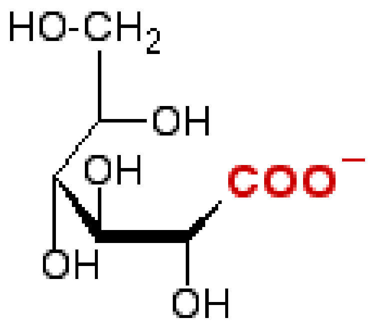
(D-gluconic acid, **GlcA**)

from **oxidation of glucose C1 aldehyde)**

The first carbon is easier to oxidize because it occurs in one step (aldehyde to carboxylic acid) Where as the 6th carbon oxidation occurs in 2 steps (alcohol to aldehyde to carboxylic acid) need strong oxidation agent

Example 1



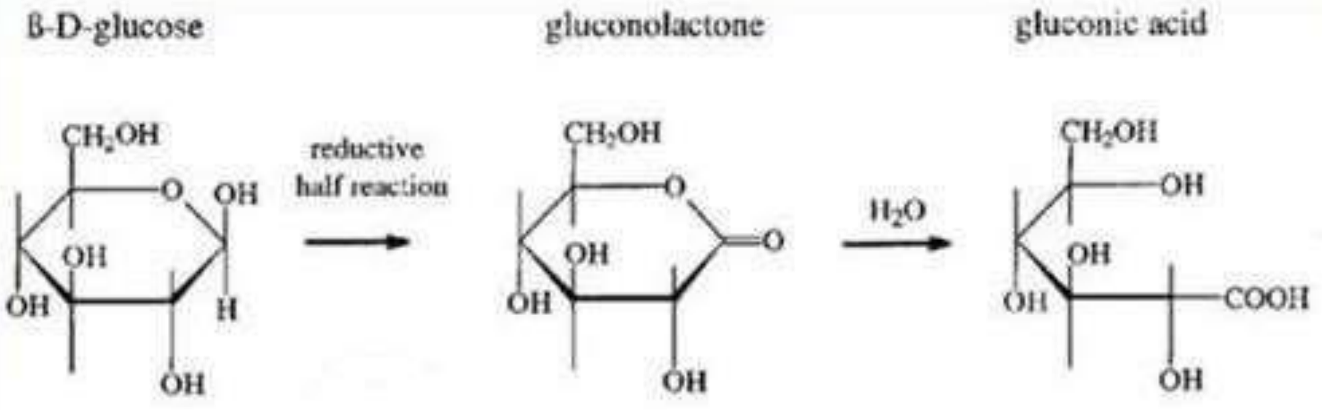


D-gluconate

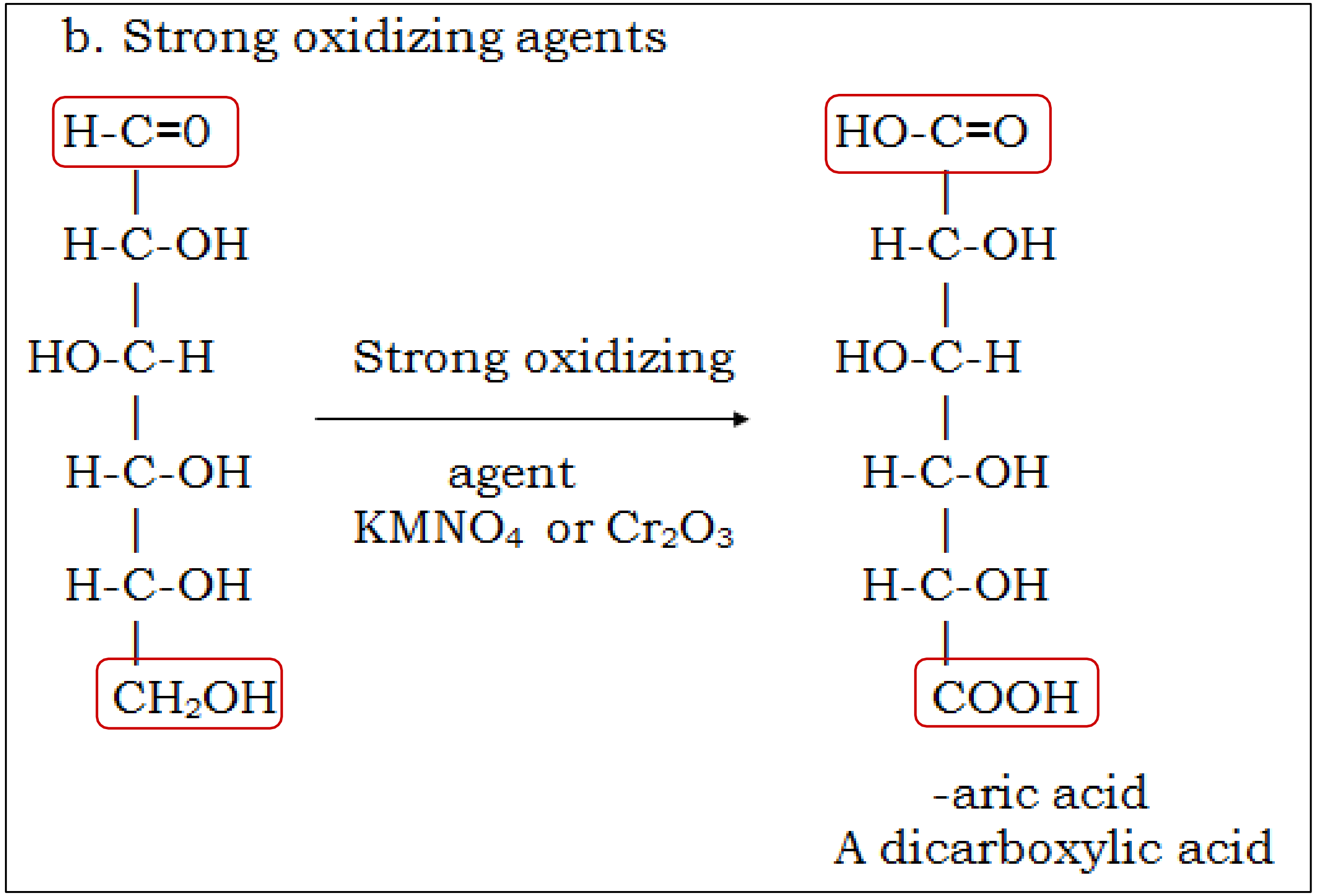
(D-gluconic acid, **GlcA**)

from **oxidation of glucose C1 aldehyde)**

The weak oxidizing agent oxidizes the first carbon(aldehyde) produced —> Onic acid such as glucose oxidation into gluconic acid



Example 2



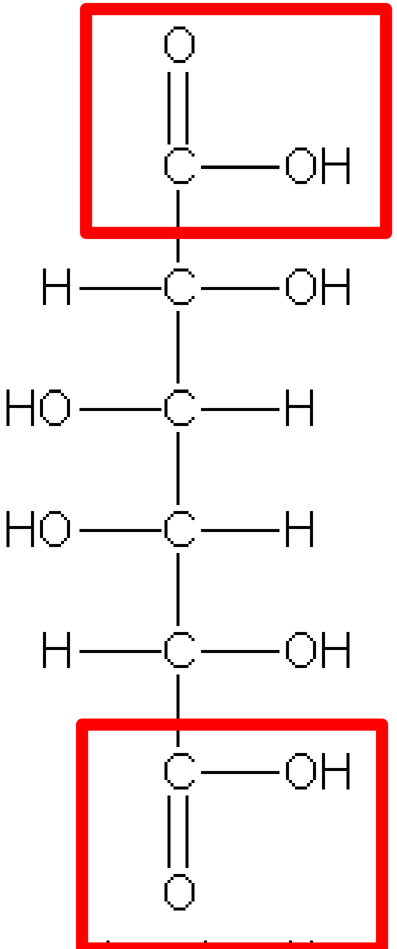
b. Strong oxidizing agents

H-C=0
H-C-OH
HO-C-H
H-C-OH
H-C-OH
CH_2OH

Strong oxidizing agent
$KMNO_4$ or Cr_2O_3

HO-C=O
H-C-OH
HO-C-H
H-C-OH
H-C-OH
COOH

-aric acid
A dicarboxylic acid

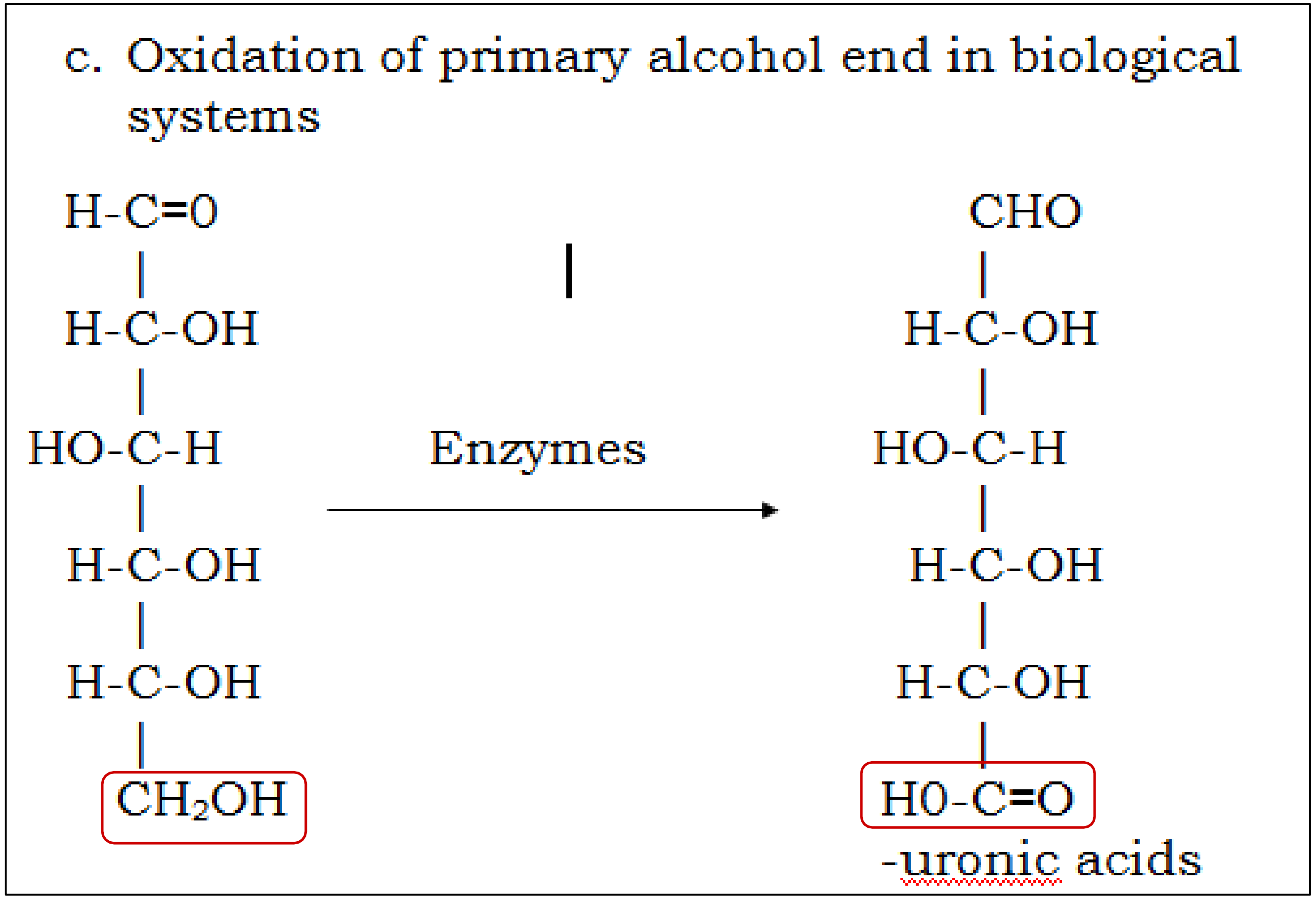


galactaric acid

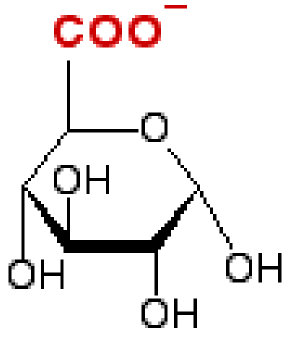
If we have a strong oxidizing agent C6 will be oxidized, also C1 will be oxidized, producing a sugar acid with two oxidized sites (C1,C6). It's called galactaric acid

Galactaric acid : a sugar acid that has 2 oxidised carbons on both sides, C1 and C6

Example 3



c. Oxidation of primary alcohol end in biological systems



α-D-glucuronate

(D-glucuronic acid, **GlcUA**)

from **oxidation of glucose C6 OH**

How can we oxidize C6 only without oxidizing C1? We need enzymes. These enzymes would specifically oxidize C6 to glucuronic, galacturonic acids, etc. • To avoid the oxidation of carbon 1 we need an enzyme that specifically oxidizes the last carbon (C6) and this occurs on glucose , galactose or any type of sugar.

Aldoses can get oxidized but ketoses cannot get oxidized directly, why? The carbonyl carbon in ketoses is connected to two carbons; so it is hard to add more oxygen or reduce hydrogen content or electrons. Whereas in aldoses, due to the presence of a hydrogen atom that's connected to the carbonyl carbon, it is easy to remove that H, replace it or add oxygen; so oxidation can occur.

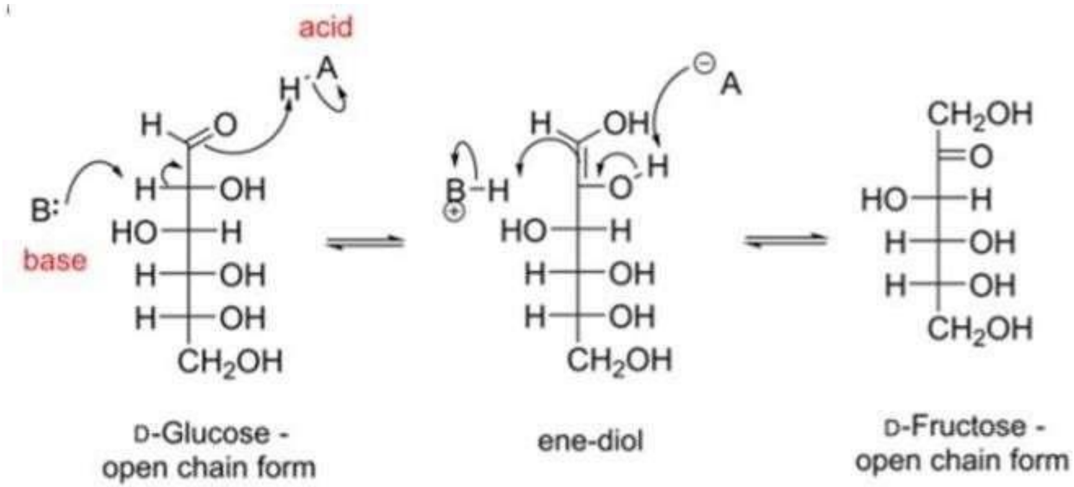
Summary

Sugar acid	Oxidation site	Oxidation agent	examples
-uronic acid	Carbon no.6	Enzymes	Glucuronic acid (glucuronate) Galacturonate
-aric acid	Carbon no.1 + no.6	Strong oxidizing agent	Galactaric acid
-onic acid	Carbon no.1	Weak oxidizing agent	Galactonic acid (Galactonate) Gluconic acid (gluconate)

This table summarizes the previous slides about sugar acids – It was taken from Legan 2020

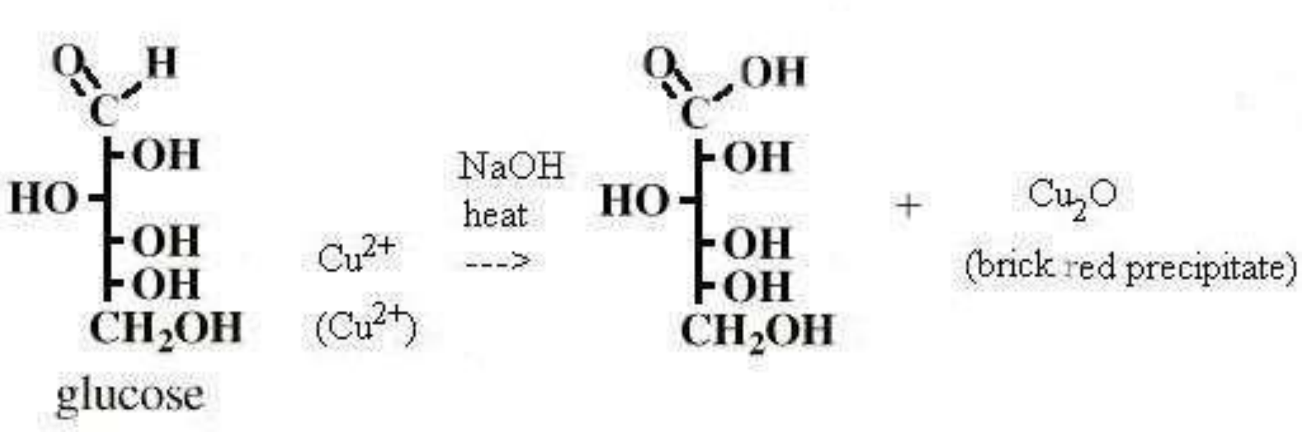
Note

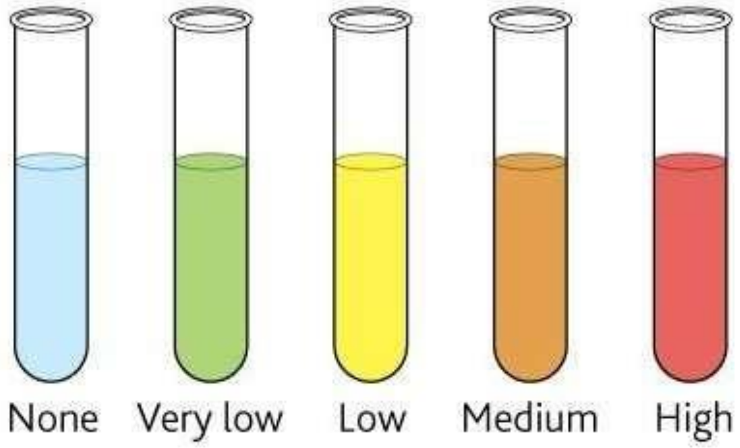
- Oxidation of ketoses to carboxylic acids does not occur, but they can be oxidized because of formation of enediol form.



•There is a way that we can oxidize ketoses indirectly. That is by converting ketose to an aldose by rearranging bonds and electrons. • So these electrons are going to move and this oxygen in carbonyl is going to be attached to a hydrogen atom, then the double bond will be transferred between the two carbons • The electrons are going to be transferred and rearranged again to produce a double bond between C1 and the oxygen removing this hydrogen. So it is like we transferred the carbonyl from position no.2 to position no.1 making the ketose an aldose so it can be oxidized this way.

Benedict’s test

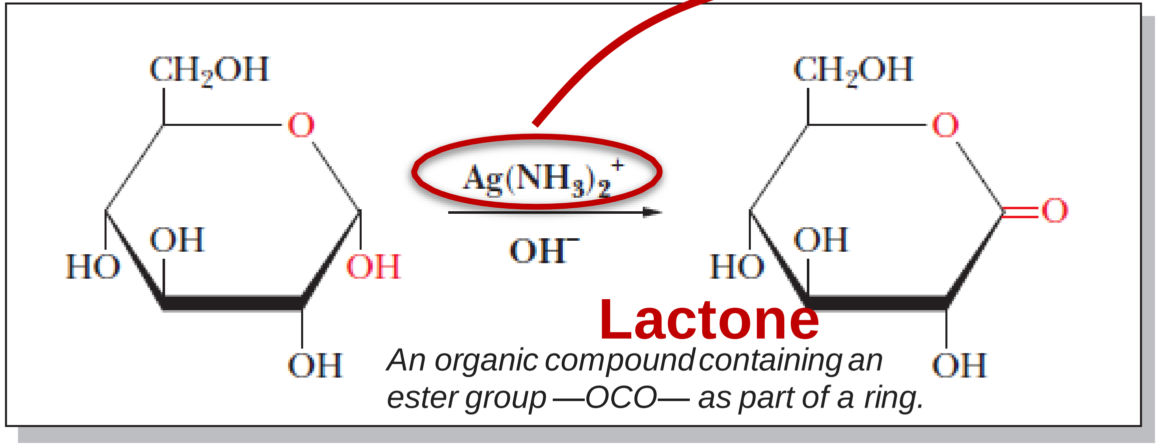




There are some biochemical tests that can be used to distinguish reducing & non-reducing . A reagent that contains copper (cu+2) will be added to an aldehyde (in this example we used glucose) so it can interact with it and oxidize it becoming a carboxylic acid, this would precipitate the Copper and the color becomes red indicating the presence of an aldehyde.

- If a ketone was added to this reagent, there will be no reaction leaving the color of the reagent as it is (it stays blue rather than turning red).

Oxidation of cyclic sugars (lactone)

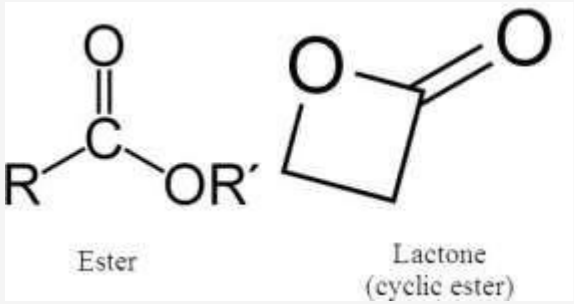


Lactone

An organic compound containing an ester group —OCO— as part of a ring.

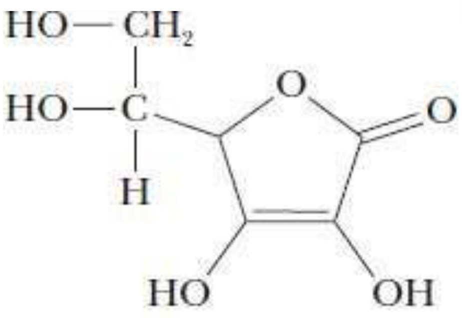
Tollen's test

Lactones are cyclic esters of organic acids.



A more recent method for the detection of glucose, but not other reducing sugars, is based on the use of the enzyme glucose oxidase.

- **Vitamin C (ascorbic acid) is an unsaturated lactone.**
- **Air oxidation of ascorbic acid, followed by hydrolysis of the ester bond, leads to loss of activity as a vitamin.**
- **A lack of fresh food can cause vitamin C deficiencies, which, in turn, can lead to scurvy.**



Ascorbic acid (Vitamin C)

Notes on the previous slide

Another test is Tollen’s test. The Tollen’s reagent contains Ag, so once the sugar interacts with it, it gets oxidized into a lactone. As you see in the highlighted group >>the (anomeric) carbon becomes =O rather than OH group (after removing hydrogen), this would precipitate Ag as a mirror on the test tube walls.

Lack of vitamin C results in :

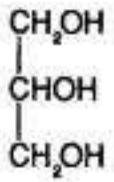
- The quality of collagen inside our bodies will be reduced due to this deficiency.
- There would be some lacerations or tears (تمزقات)in the skin, gums and other tissues. That's how the lack of vitamin C can result in a disease.

* The importance of vitamin C is that it functions as an antioxidant (neutralizesfree radical molecules, which in excess can damage cells)

Sugar alcohols (reduction)

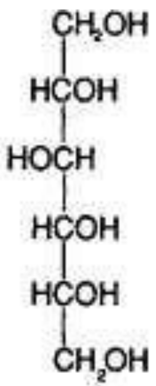
- What does it form?
- Examples include sorbitol, mannitol, and xylitol, which are used to sweeten food products

Another example of modified sugars are sugar alcohols, like sorbose (a ketose sugar with six carbons) or Xylulose (which is a kentopentose) and mannitol



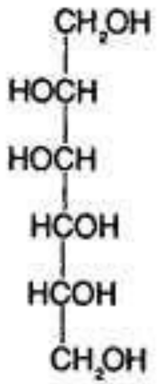
Glycerol

Obtained from the reduction of either D-glyceraldehyde or dihydroxyacetone.



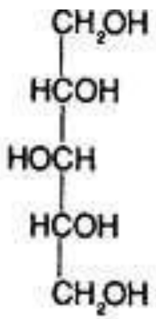
D-Sorbitol

Obtained from the reduction of either the C_1 carbonyl group of glucose or the C_2 carbonyl group of fructose.



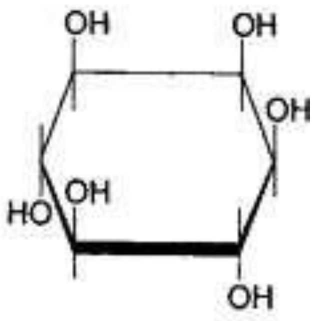
D-Mannitol

Obtained from the reduction of either the C_2 carbonyl group of D-fructose or the C_1 carbonyl group of D-mannose.



Xylitol

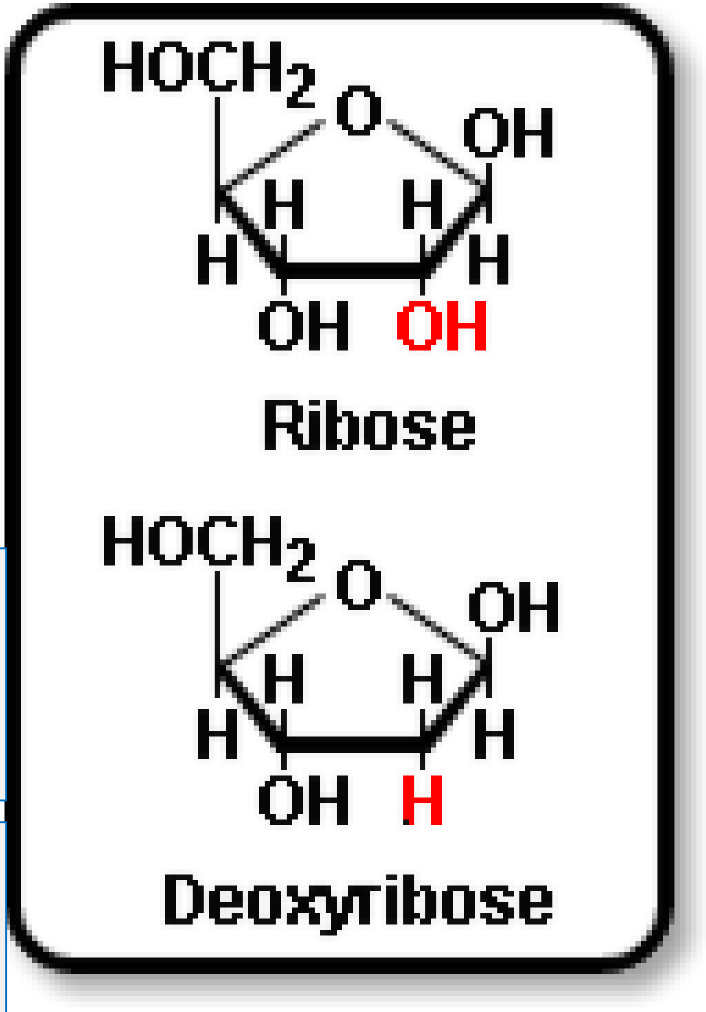
Obtained from the reduction of either the C_1 carbonyl group of D-xylose or the C_2 carbonyl group of D-xylulose.



Myo-inositol

Deoxy sugars (reduced sugars)

- One or more hydroxyl groups are replaced by hydrogens.
- An example is 2-deoxyribose, which is a constituent of DNA.



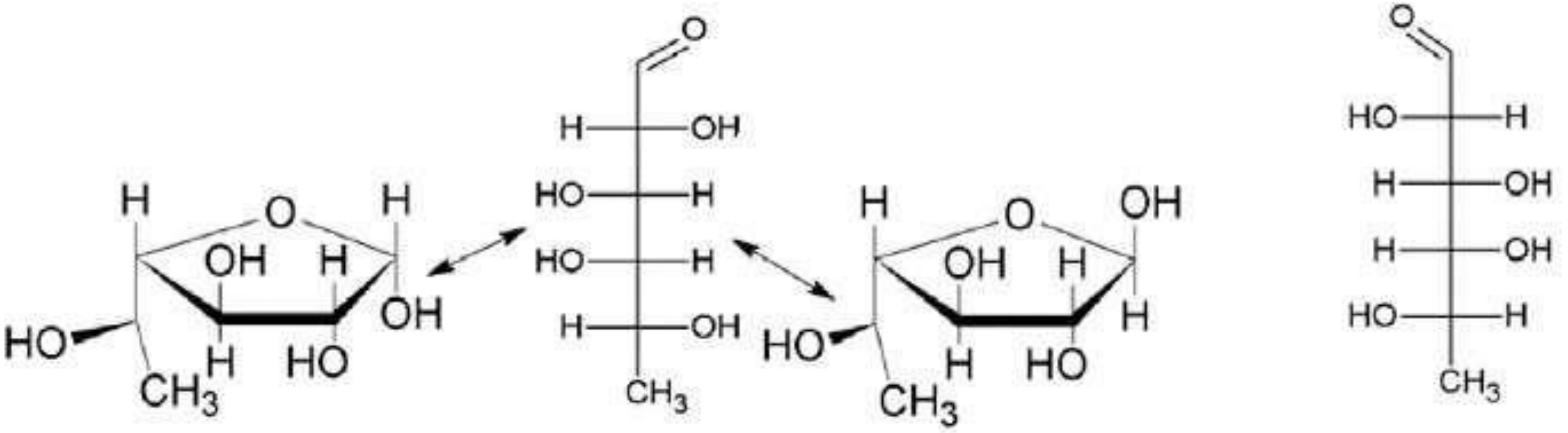
OH Group on carbon number 2 is removed and replaced with H. We lost the oxygen that's why we call it deoxyribonucleic acid (DNA). •Ribose is present in RNA• Deoxyribose is present in DNA.

There is a difference between reduced and reducing: Reduced means that the molecule got reduced. Whereas reducing means that the molecule is the one that causes another molecule to be reduced.

مثل الفرق بين الفاعل و اسم المفعول

Another one

- L-fucose (L-6-deoxygalactose)
  - found in the carbohydrate portions of some glycoproteins



6-deoxy-α-D-galactofuranose

6-deoxy-β-D-galactofuranose

L-fucose
(6-deoxy-L-galactose)

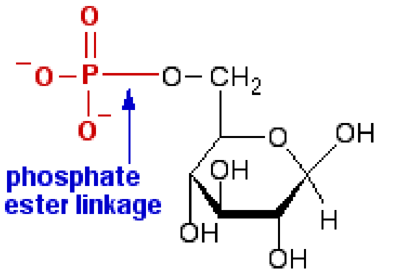
D-fucose (6-deoxy-D-galactose)

Sugar esters (esterification)

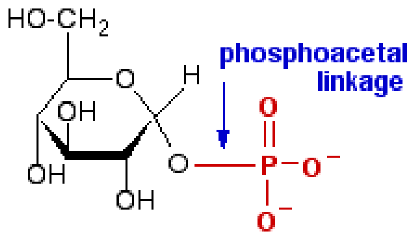
- What is the reacting functional group? Where does it react? What are the end products? Where are they used?

1) By adding a phosphate group through the OH group on carbon no.6 producing glucose-6-phosphate. Phosphate-acetal because this molecule follows the acetal formula

2) Or phosphorylation can happen on another site, on carbon no.1 through the OH group producing glucose-1-phosphate.



β-D-glucose-6-phosphate
(an ordinary **phosphate ester**)

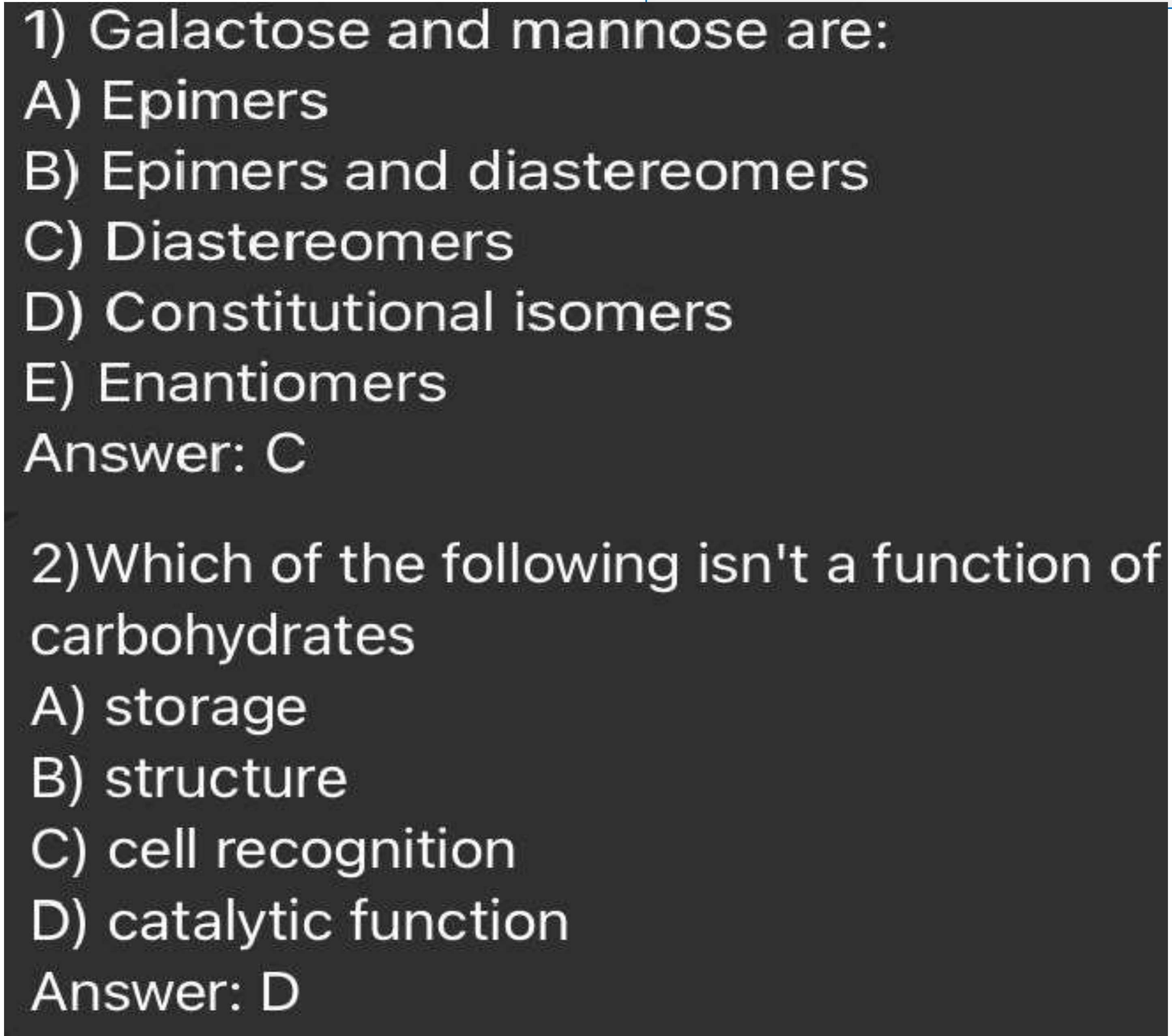


α-D-glucose-1-phosphate
(a **phosphoacetal**)

3) We call it esterification because it is very similar to the ester bond (remember the formula of esters RCOOR' but instead of carbon it's a phosphate)

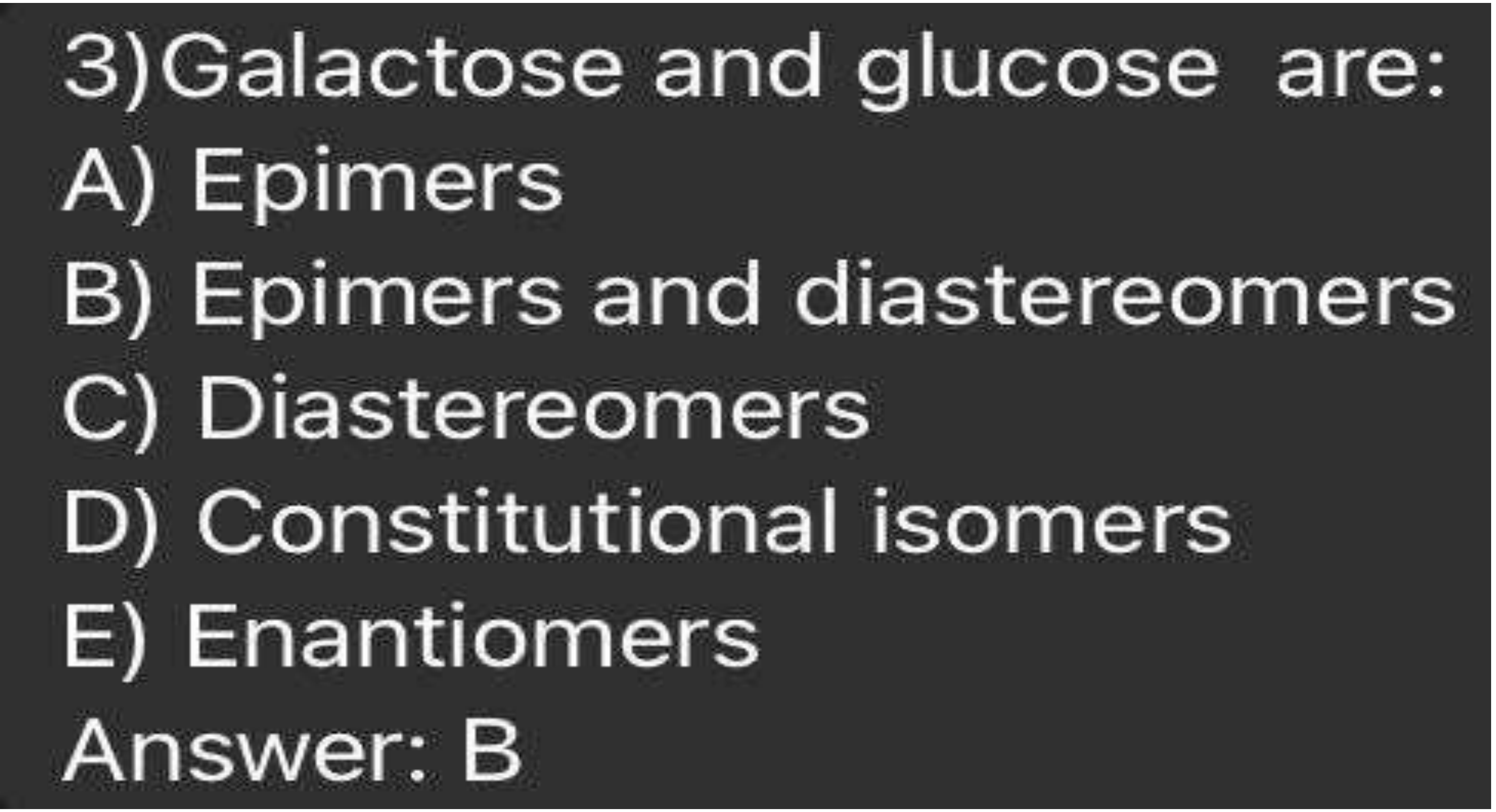
4) The importance of these reactions can be seen during metabolism, phosphorylation on carbon number 6 (producing glucose–6-phosphate) is important to mark the glucose molecule for degradation in the process of Glycolysis, glucose–6-phosphate is important for other metabolic reactions.

Extra exercises



1) Galactose and mannose are:
A) Epimers
B) Epimers and diastereomers
C) Diastereomers
D) Constitutional isomers
E) Enantiomers
Answer: C

2)Which of the following isn't a function of carbohydrates
A) storage
B) structure
C) cell recognition
D) catalytic function
Answer: D



3)Galactose and glucose are:

A) Epimers

B) Epimers and diastereomers

C) Diastereomers

D) Constitutional isomers

E) Enantiomers

Answer: B