بسم الله الرحمن الرحيم

BioChemistry | Lecture 7

Carbohydrates Pt.2

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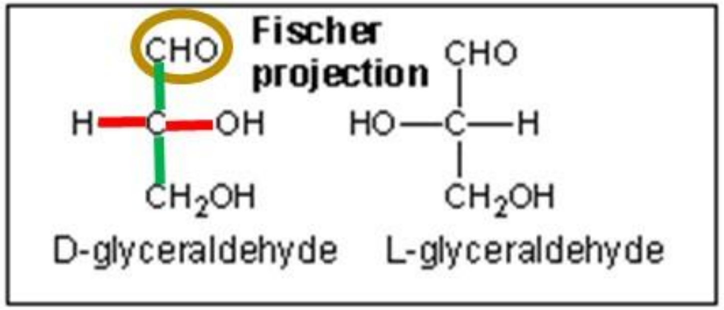
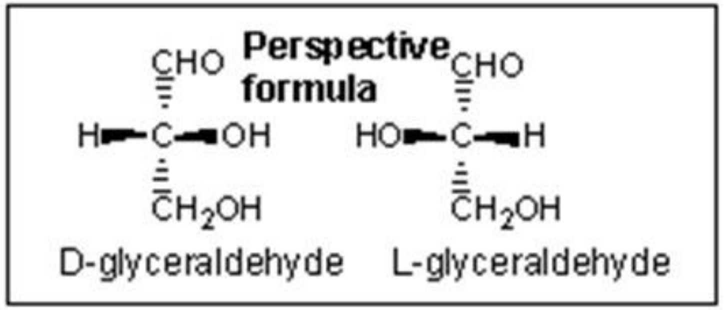
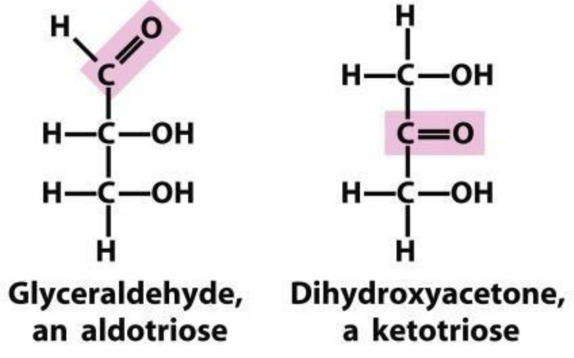
Monosaccharides

- Basic chemical formula: $(CH_2O)_n$
  N = number of carbons
- Stereocenters
- D or L
- D sugars predominate in nature
- The 2-D representation (Fischer Projections)

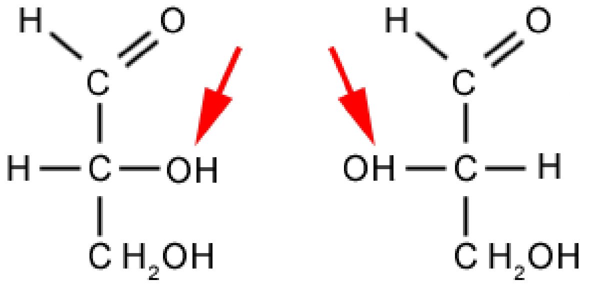




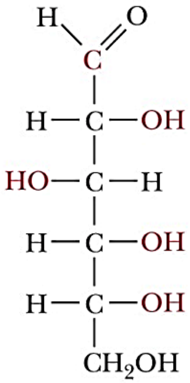
🟥 **Forward** 🟩 **Backward** ◯ **Top (C1): Most highly oxidized C**



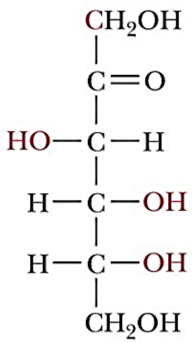
Glyceraldehyde, an aldotriose **Dihydroxyacetone, a ketotriose**



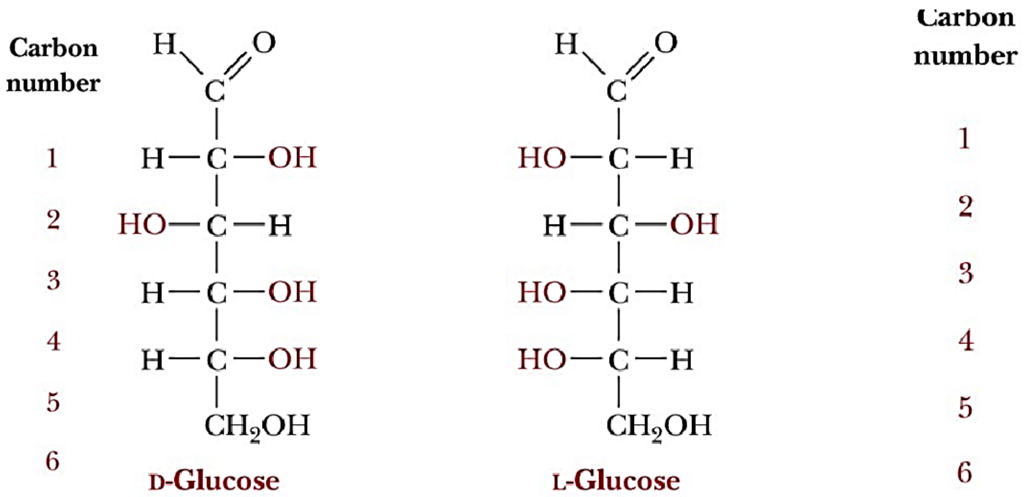
D-Glyceraldehyde L-Glyceraldehyde

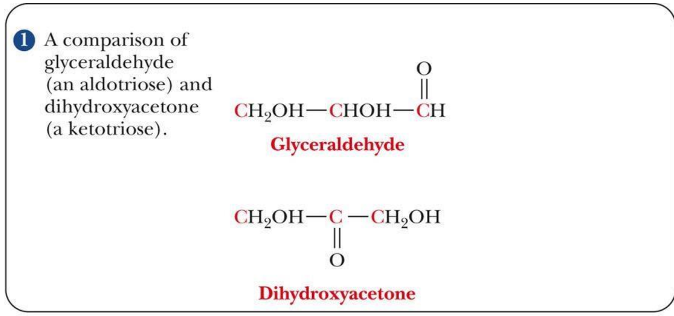


D-Glucose (an aldose)



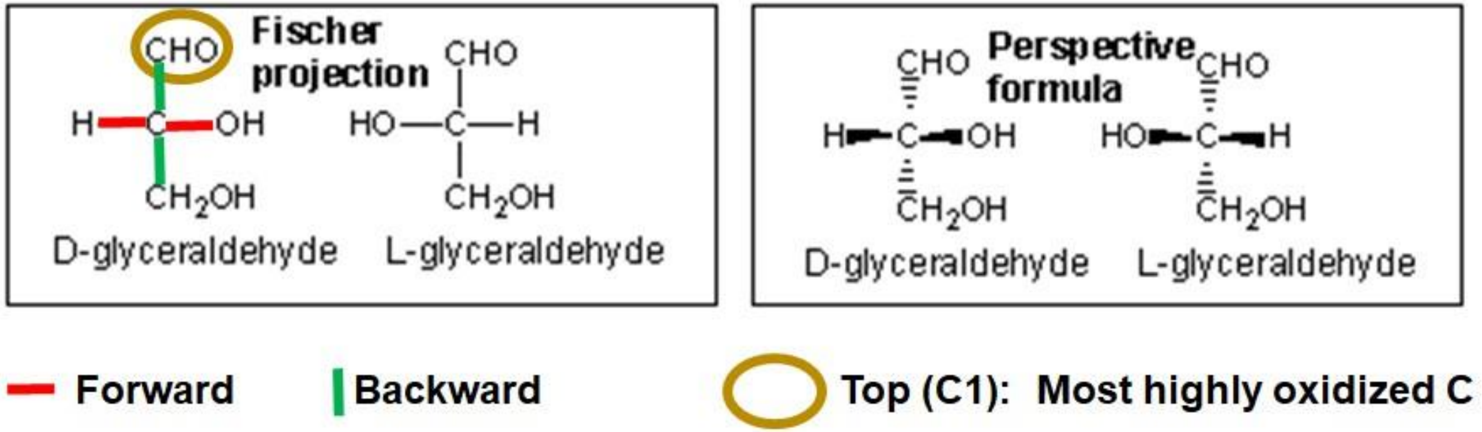
D-Fructose (a ketose)





① A comparison of glyceraldehyde (an aldotriose) and dihydroxyacetone (a ketotriose).

- **Fisher projection** : a representation used to draw the open chain structure of monosaccharides.
The first carbon is the one on the **top**.
The last carbon is one at the **bottom**.
The functional groups (which are OH and H+) are either **forward** or **backward**.
Vertical => backward.
Horizontal => forward.



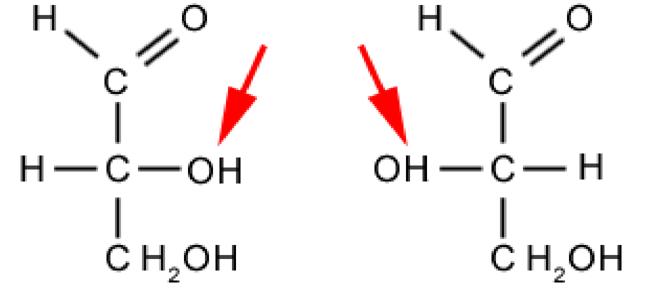
Fisher projection is used to draw a 3d structure on 2d digram.

- **Stereocenter (chiral center)** : a Carbon atom (or any atom but since we are talking about carbohydrates the chiral center can be only applied on a carbon atom) that is binding to 4 different groups.
NOTE: when you are comparing the 4 groups you should compare them to the end of the chain.

- **D or L (Dextro or Levo):** They are stereoisomers that differ only on the orientation of hydroxyl group on the last chiral carbon atom.

Last carbon is always an achira

To the **Right => Dextro** || To the **Left => Levo**



D-Glyceraldehyde L-Glyceraldehyde

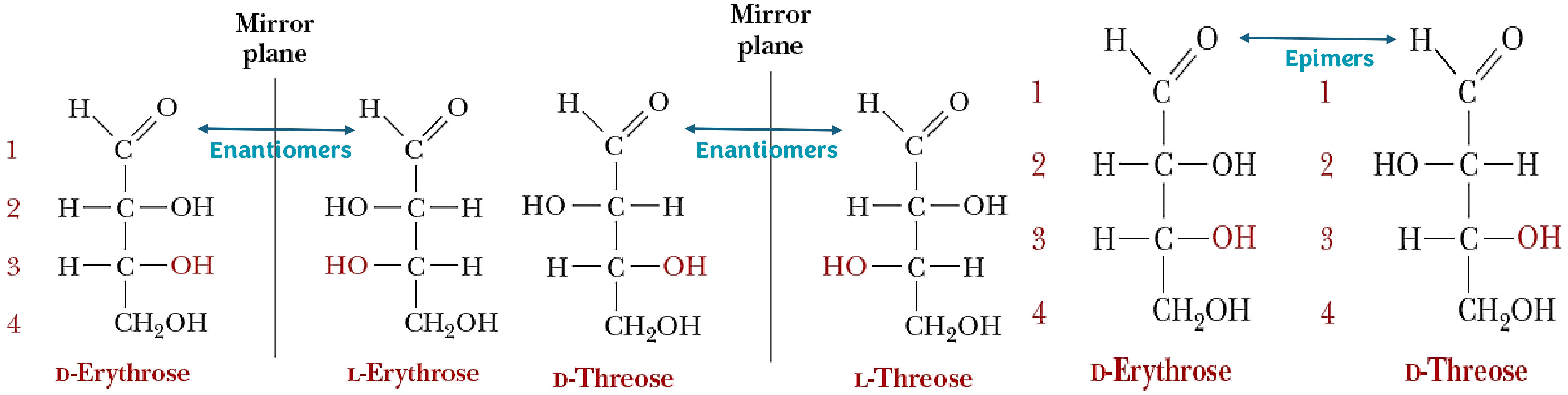
Aldotetroses

- D-erythrose & L-erythrose (enantiomers)

  Enantiomers are two molecules that have all of their chiral centers configration (OH orientation on the carbon atom) opposite to each other.
  Mirror image but not superimposable to each other.

- D-erythrose & D-threose (diastereomers)

  Diasteromers are two molecules that differ at the orientation of OH group at some chiral centers but not all of them.
  If they differ at the orientation of OH group at one chiral center only then they are called **epimers.**



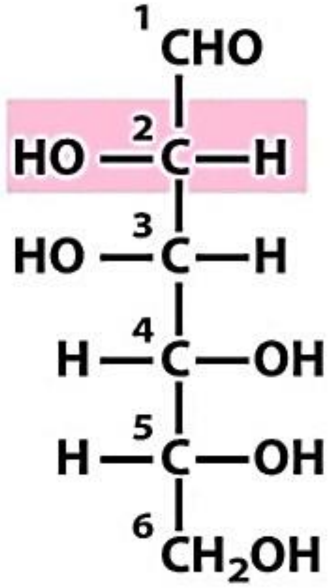
Pentoses & Hexoses

- Most of the sugars we encounter in nature, especially in foods
- Aldopentoses & Aldohexoses (how many chiral carbons? How many stereoisomers?)

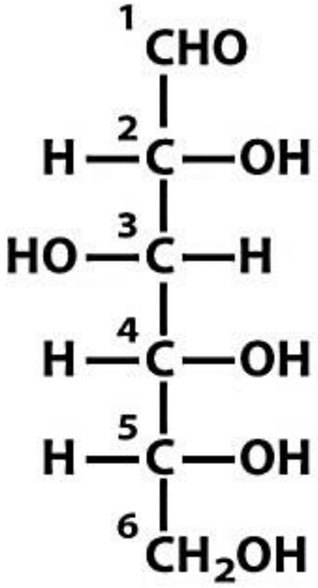
2^n Number of stereoisomers = 2^n, while n is the number of chiral centers

D-Glucose and D-Mannose are epimers at carbon number 2 since they differ in the orientation of OH at only one carbon which is carbon number 2

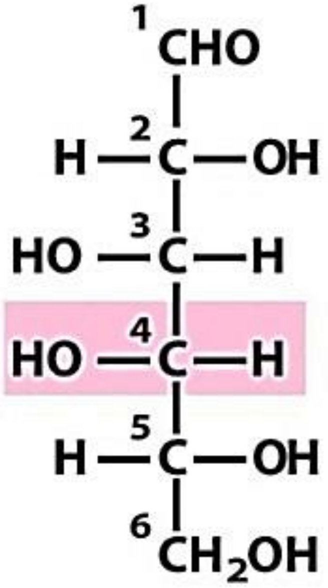
D-Glactose and D-Mannose are diastereomers since they differ in the orientation of OH at some chiral carbons but not all of them (exactly at 4 & 2)



D-Mannose
(epimer at C-2)



D-Glucose

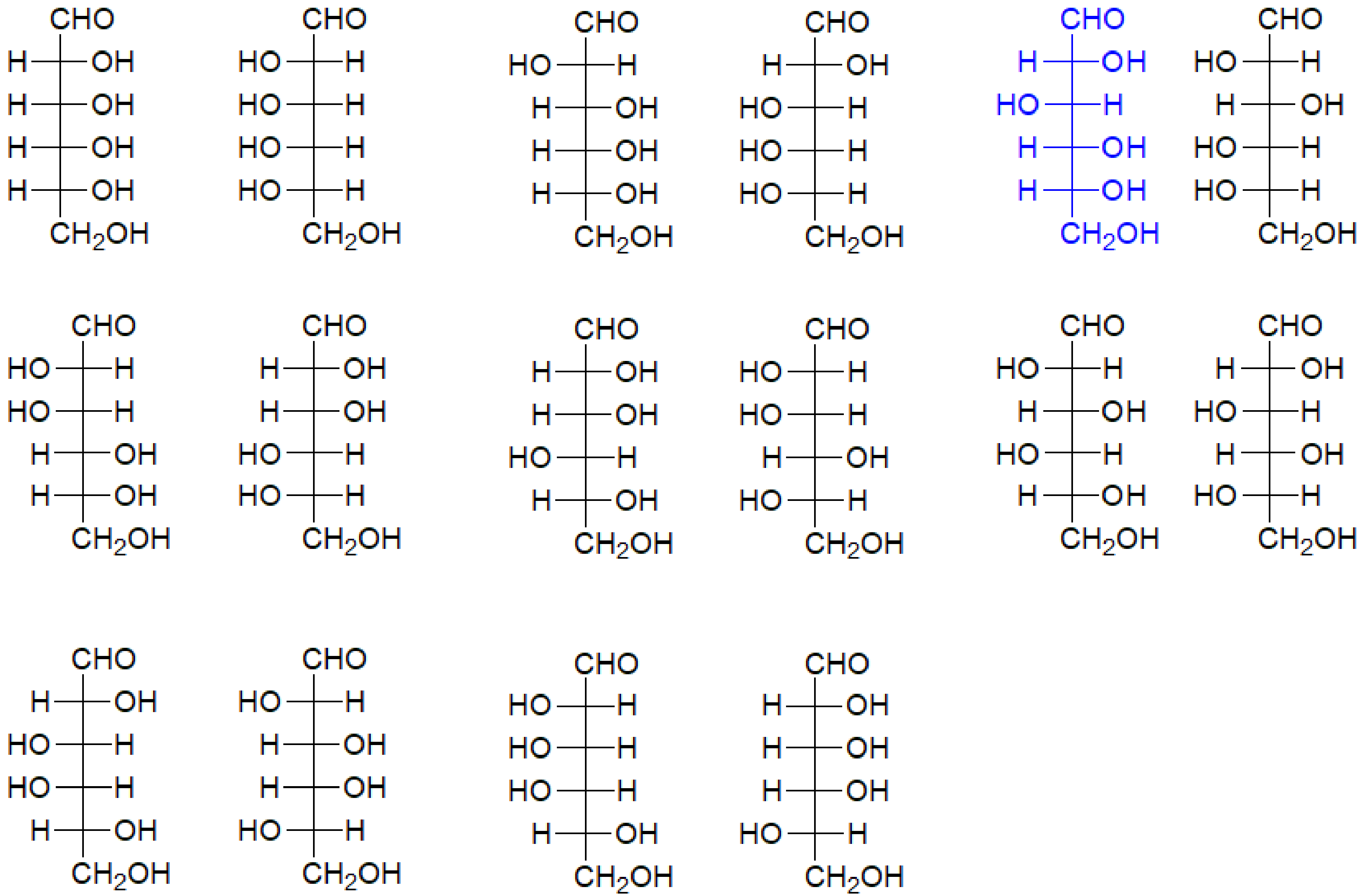


D-Galactose
(epimer at C-4)

D-Galactose and D-glucose are epimers at carbon number 4 since they differ in the orientation of OH at only one carbon which it carbon number 4

Glucose Isomers

Since you are required to memories the structures of glucose ,galactose and mannose , try findig them and mention the relation between each 2 sugar molecules (as much as you can).



Common Monosaccharides

You should be able to recognize them.

Every sugar has its own chemical and physical properties

- Glucose:
  - Mild sweet flavor
  - Known as blood sugar

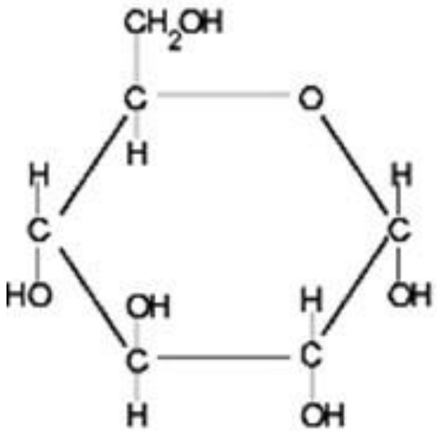
    Found in blood.
  - Essential energy source

    Found in every type of cells in our body as it is the main source for glycolysis.
  - Found in every disaccharide and polysaccharide

    Building block for other types of carbohydrates
- Galactose:
  - Hardly tastes sweet & rarely found naturally as a
  - single sugar

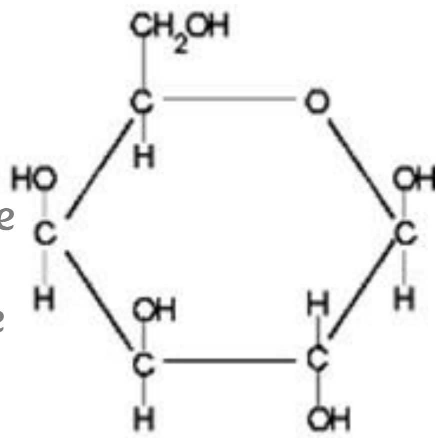
    Hard to be tasted and found in bounded form most the time
- Fructose:
  - Sweetest sugar, found in fruits and honey
  - Added to soft drinks, cereals, desserts

OH is below the plane

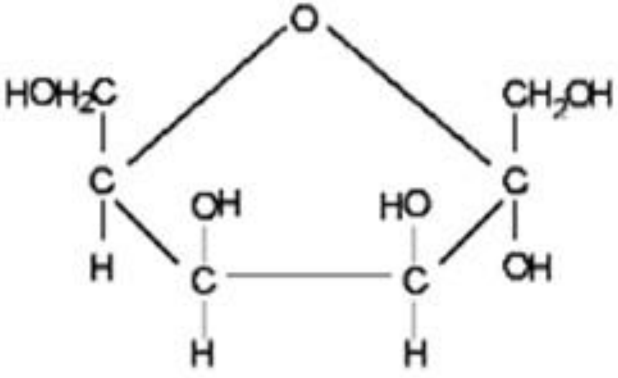


Glucose

OH is above the plane



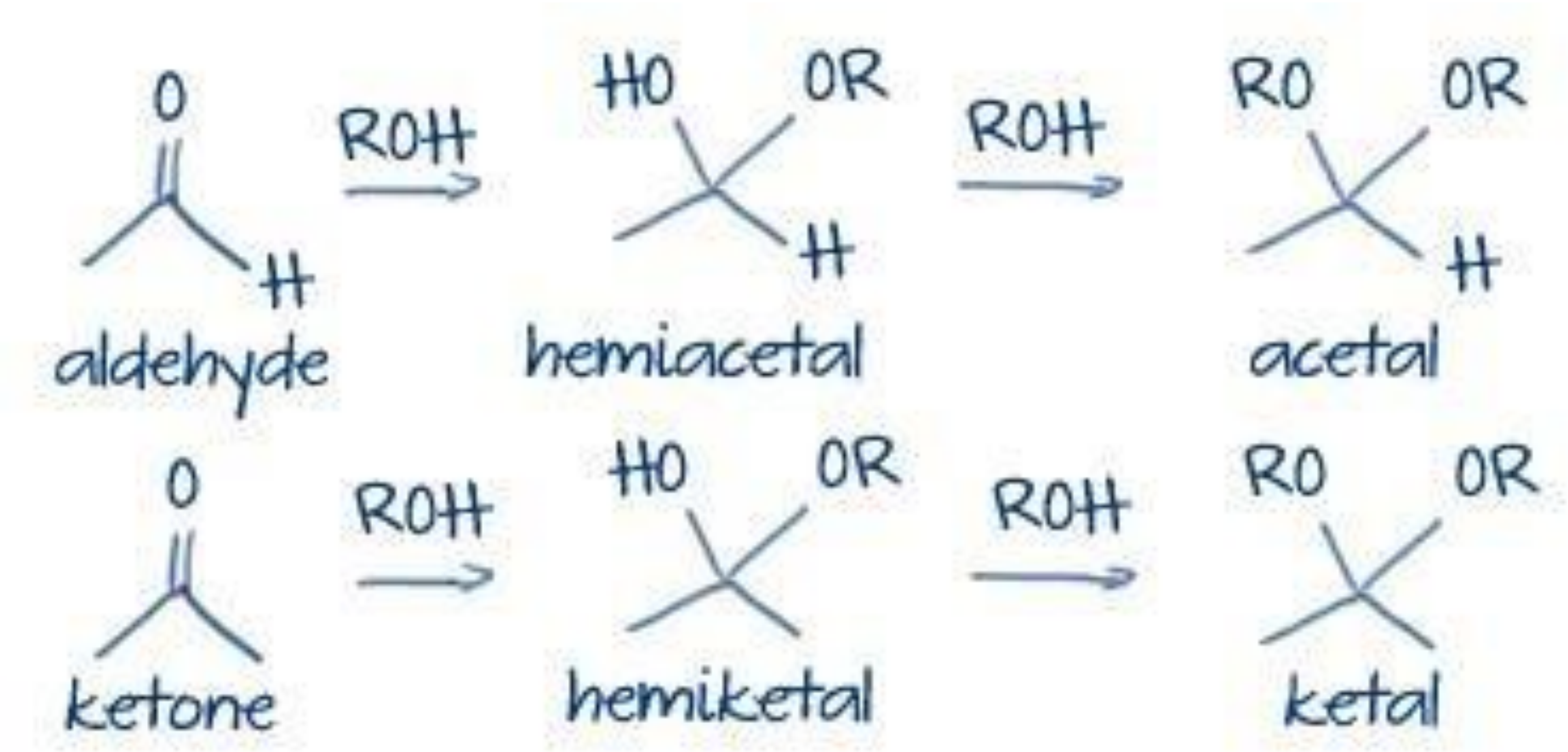
Galactose



Fructose

Cyclization of sugars

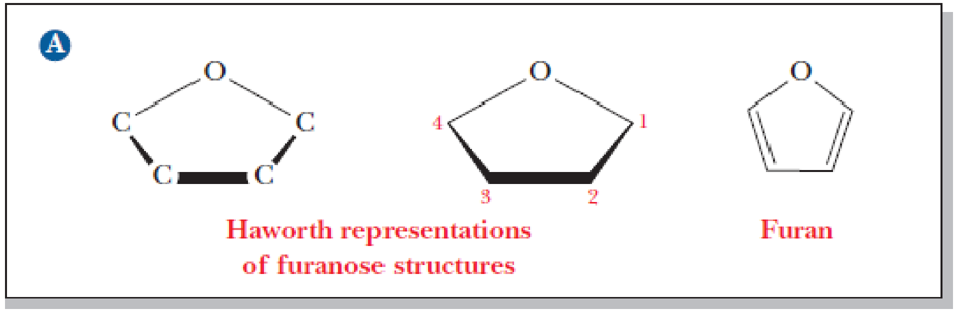
Aldehyde with alcohol –> hemiacetal || hemiacetal with other alcohol molecule –> acetal
Ketone with alcohol–> hemiketal || hemiketal with other alcohol molecule –> ketal



Cyclization of sugars

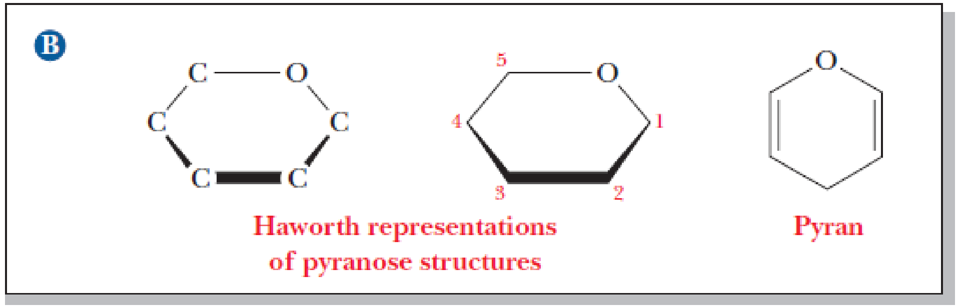
- In the cell 99% of pentoses and hexoses are in the ring form Why? Because it is more stable. Why exactly 99% ?

  Only ~1% of sugars are in the open-chain form, but this form is in equilibrium with the 99% ring form and shares the same energy level
- Haworth Projection: the carbonyl carbon is a new chiral center and becomes an <u>anomeric carbon</u>
- Anomers: differ only at their anomeric carbon, either α or β (equilibrium)



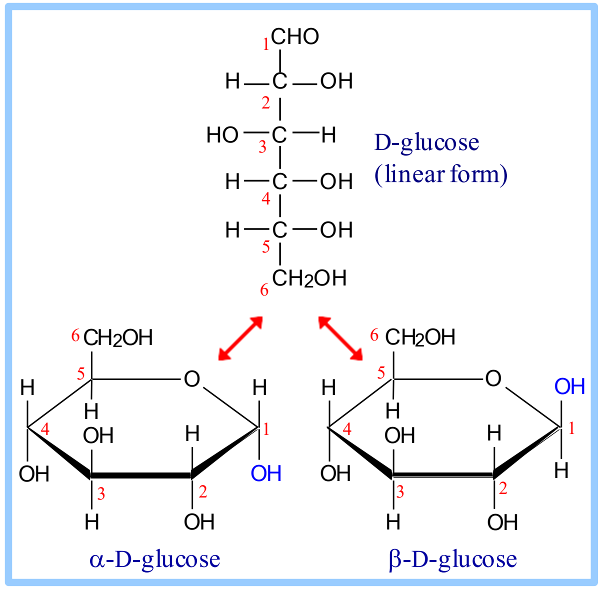
Haworth representations of furanose structures

Furan



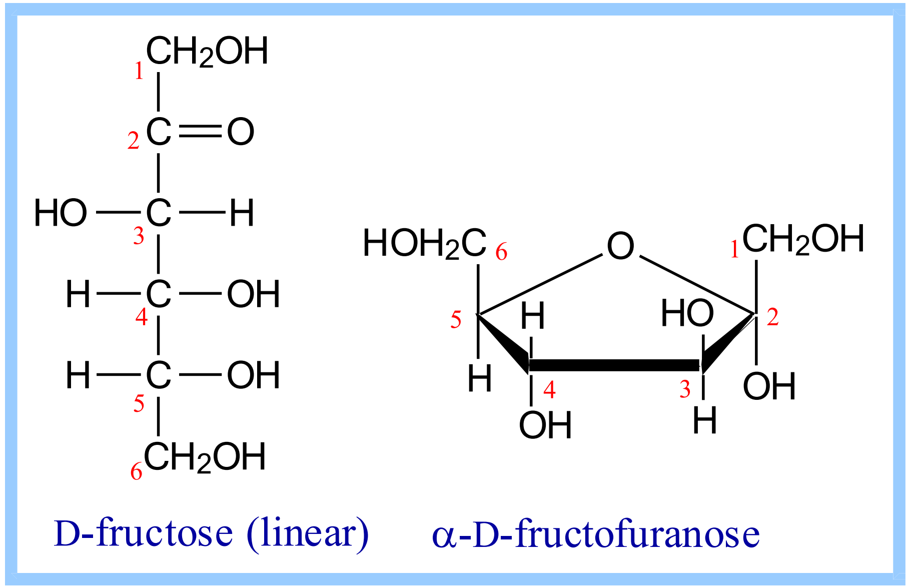
Haworth representations of pyranose structures

Pyran



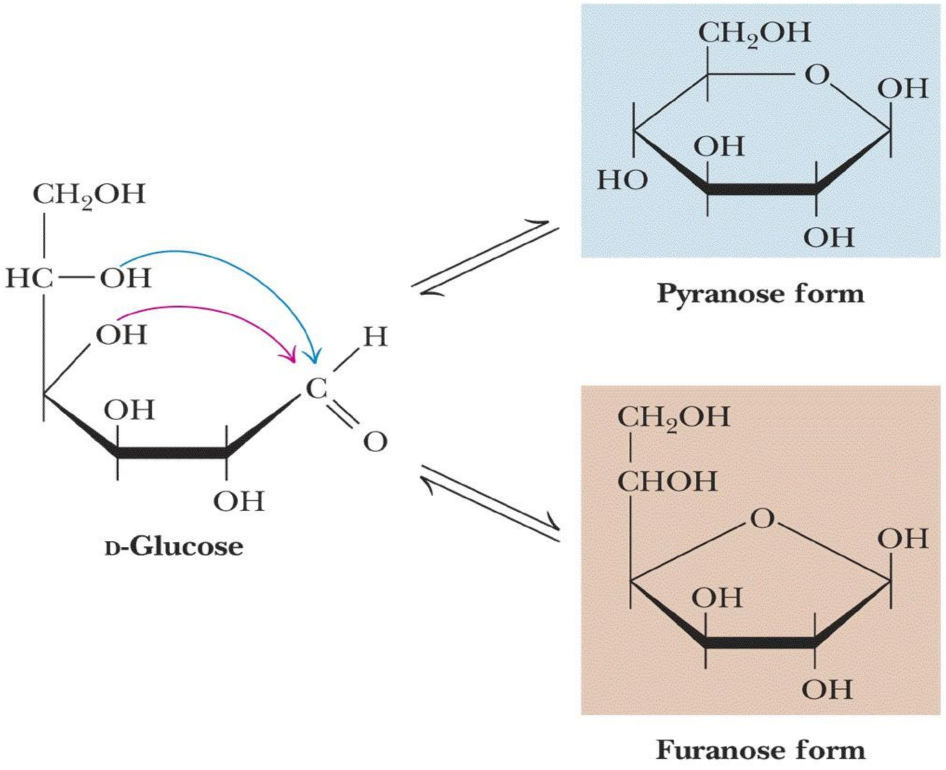
α-D-glucose

β-D-glucose



D-fructose (linear)

α-D-fructofuranose



What are the two carbons that are going to attach to each other during to form a ring?
The first one is the Carbonyl group carbon whatever it was an aldehyde or ketone
The second one is carbon:
--> number 5 --> six membered ring composed of 5 carbons and 1 oxygen.
--> number 4 --> five membered ring composed of 4 carbons and one oxygen.

What determines if the sugar will make 5 membered ring or 4 membered ring ?
- Stability of the formed ring / energy that the molecule contains.

when cyclation is happening it always going to be the right side.
All functional groups on right --> below the plane.
All functional group on the left --> above the plane.

5 membered ring --> furan --> furanose
6 membered ring --> pyran --> pyranose

If a 6 carbons sugar has been cyclized into:
6 membered ring --> one carbon will be out of the ring.
5 membered ring --> two carbons will be out of the ring.

The more the number of carbons outside the ring the less the stability of the sugar in the ring form. (doctor didn't say this but I've checked, and it is right).

The carbon number one (called the anomeric carbon) in the open chain was Achiral and in the ring form it becomes chiral.
We have two classification related to the anomeric carbon:

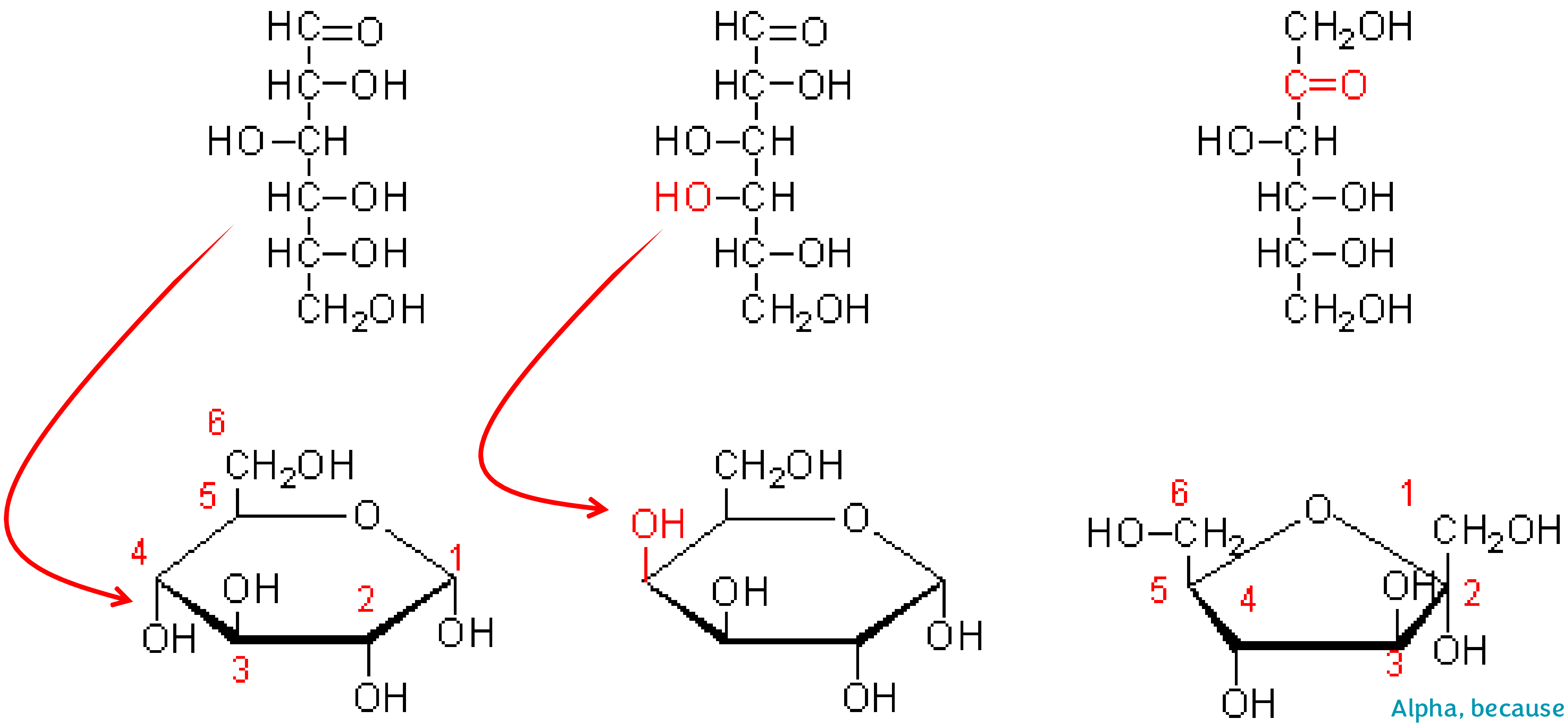
- Alpha ~> The orientation of OH (at the anoiric carbon) and CH2OH (at the last carbon) opposite to each other, ex. Above,below.

- Beta ~> The orientation of OH (at the anomric carbon) and CH2OH (at the last carbon) are the same, ex. Above,above / below,below.

alpha and beta of a specific are called anomers.

Chain to ring
Left-up, right-down

Notice how every functional group on the right has become below the plane, and every functional group on the left has become above the plane.



glucose
α

galactose
α

fructose
α

Alpha, because OH (at the anomeric carbon) and CH2OH are at opposite orientation.

Reactions of monosaccharides – modified sugars

Anomeric Carbon is the most reactive atom in a monosaccharide, formed as a new chiral center when the molecule cyclizes. In aldoses, it is located at carbon 1; in ketoses, at carbon 2. The α and β configurations are called **anomers,** as they have the same overall molecular structure, and the only difference between them is the orientation (up or down) of the hydroxyl group attached to the anomeric carbon.

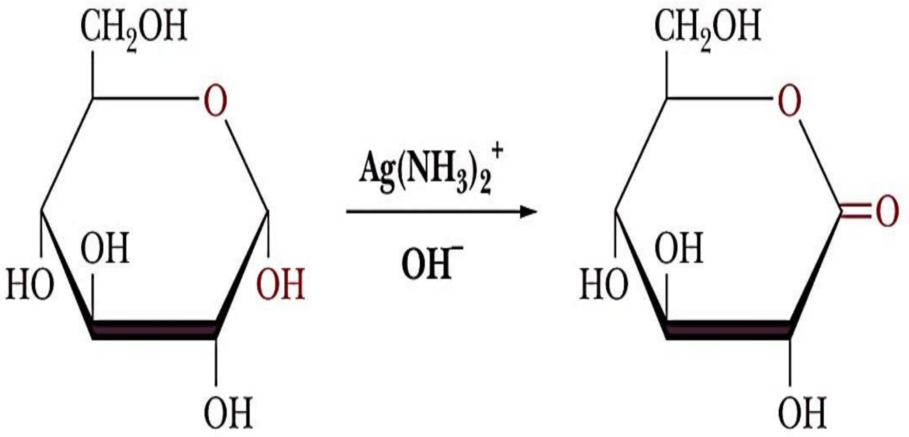
- Oxidation
- Reduction
- Esterification

  Monosaccharides are esterified with phosphate groups in many key metabolic reactions in the body, such as in glycolysis (e.g., glucose → glucose-6-phosphate).

- Glycosidic bond formation

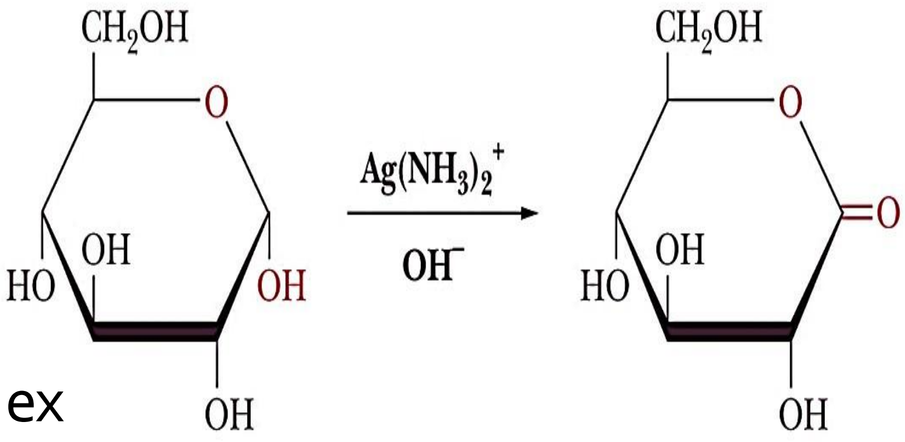
  The hemiacetal (aldose) or hemiketal (ketose) form of sugars (both in **monosaccharide ring** form, thus "hemi") reacts through the –OH group on **the anomeric carbon** to form **full acetals or ketals** (which are the basis of glycosidic bonds in **di-** and **polysaccharides)**

Oxidation



- Oxidation of a cyclic hemiacetal form gives a lactone (reforming the monosaccharide by converting the anomeric carbon's hydroxyl group into a keto group)
- Reducing sugars
- Tollens solution (oxidizing agent); silver ammonia complex ion, Ag(NH3)2+
- Specific for glucose: detection of glucose, but not other reducing sugars, is based on the use of the enzyme glucose oxidase

Oxidation



- Tollens solution (oxidizing agent); silver ammonia complex ion, Ag(NH3)2+

Tollens’ reagent is a testing method used to identify reducing sugars. It contains a silver-ammonia complex Ag(NH3)2+, which produces a silver mirror on the inner surface of the test tube. This indicates the presence of sugars that can be oxidized – i.e., reducing sugars. Carbohydrates are thus classified as reducing or non-reducing based on their ability to undergo oxidation. If the anomeric carbon is free (not involved in a glycosidic bond), it can be oxidized; if it is bonded, oxidation does not occur.

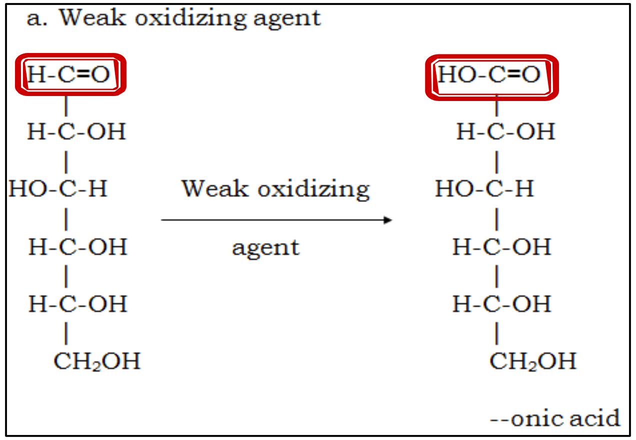
(this is for all sugars)

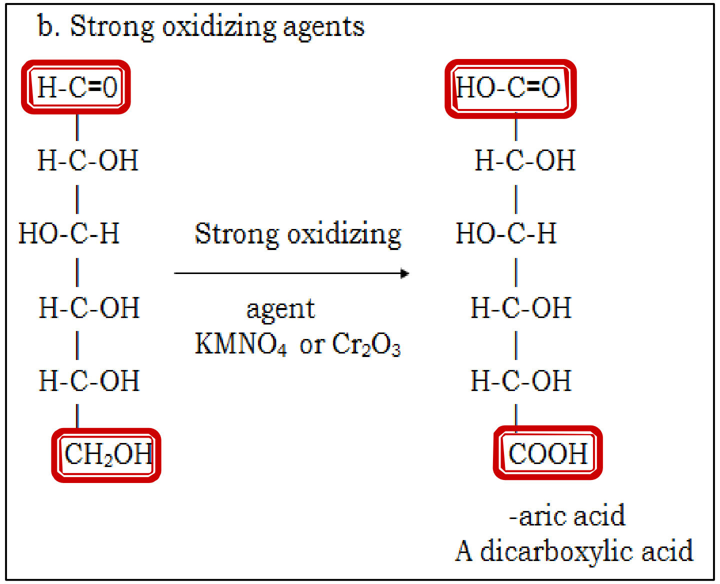
Oxidation

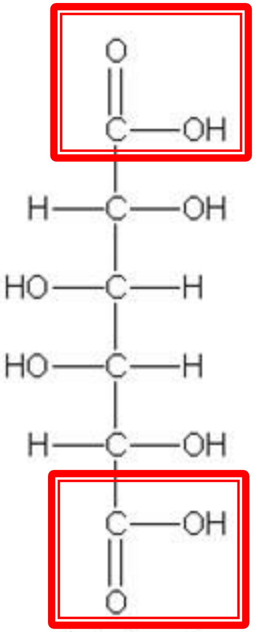
- Specific for glucose: detection of glucose, but not other reducing sugars, is based on the use of the enzyme **glucose oxidase**

In diabetes home testing devices, a drop of blood is placed onto a test strip that contains **glucose oxidase**, which specifically oxidizes glucose (not other sugars).
This oxidation reaction produces **hydrogen peroxide (H_2O_2)** as a byproduct. Since hydrogen peroxide is colorless, another enzyme – **peroxidase** – is also present on the strip. Peroxidase reacts with hydrogen peroxide and a color-producing substrate, generating a colored compound.
The intensity of the color correlates with the amount of glucose in the blood. The color depth (i.e., absorbance) is measured and compared to a reference sample with normal glucose levels to determine whether the glucose concentration is high, normal, or low.

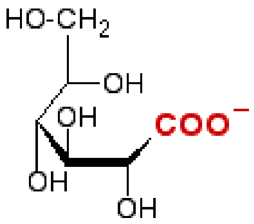
Oxidation - Naming







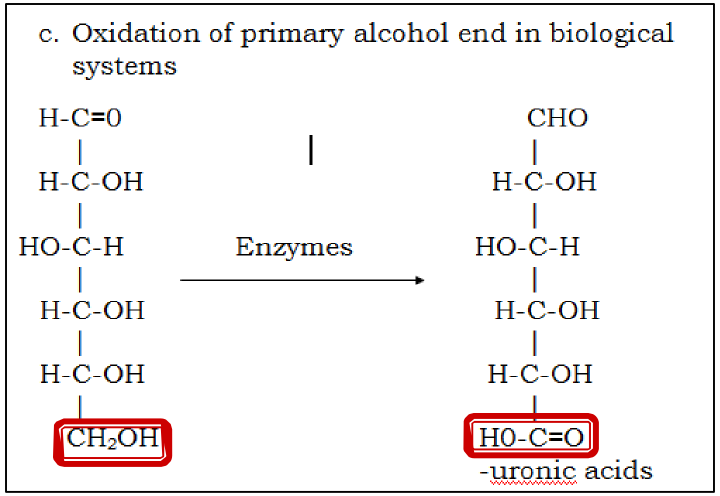
galactaric acid

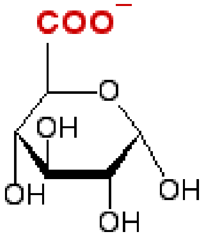


D-gluconate

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

from **oxidation of glucose C1 aldehyde)**





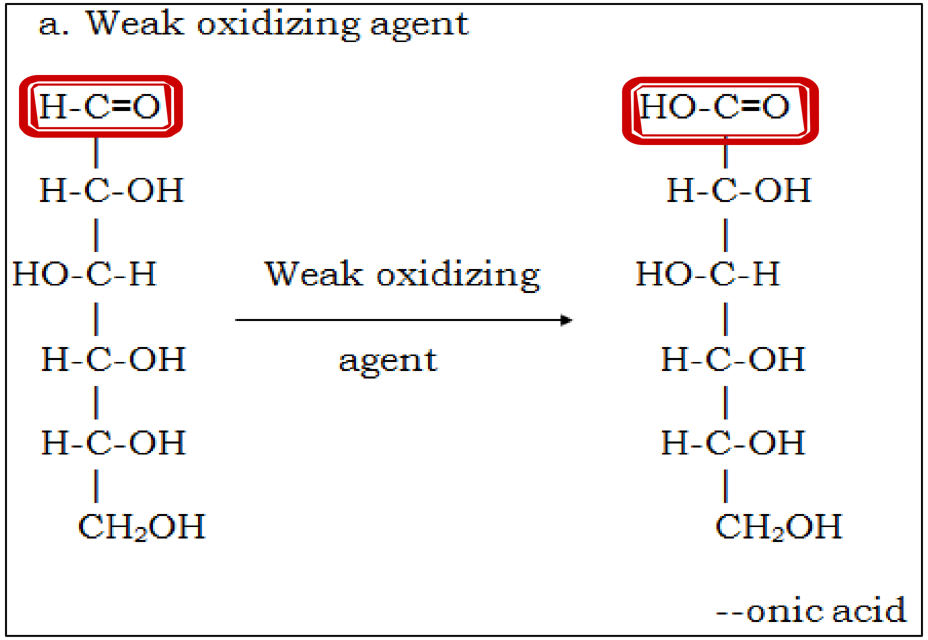
α-D-glucuronate

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

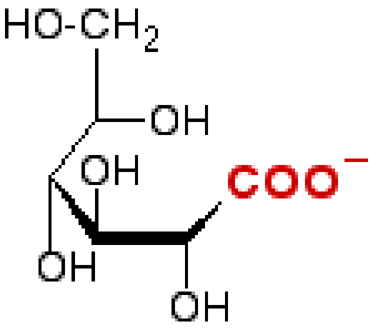
from **oxidation of glucose C6 OH**

Oxidation - Naming

- Based on the reactivity of functional groups, aldehydes are more easily oxidized than alcohols and ketones. Therefore, when a weak oxidizing agent is used, the aldehyde group reacts first, forming a carboxylic acid.



a) When glucose is oxidized using a weak oxidizing agent (e.g., Tollens' or Fehling’s), only carbon 1 (the aldehyde group) is oxidized. This produces gluconic acid, which is glucose with the C1 converted into a carboxyl group (–COOH) — now in its carboxylate form under basic conditions.

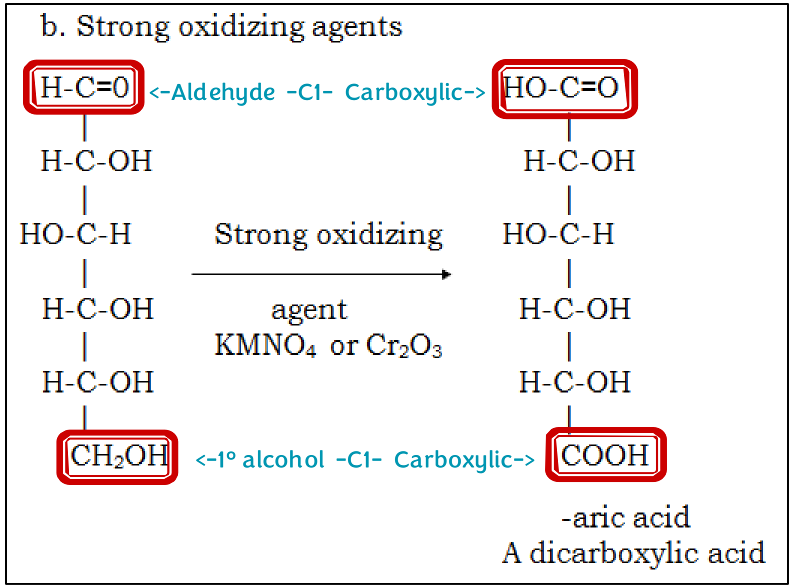


D-gluconate

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

from **oxidation of glucose C1 aldehyde)**

Oxidation - Naming

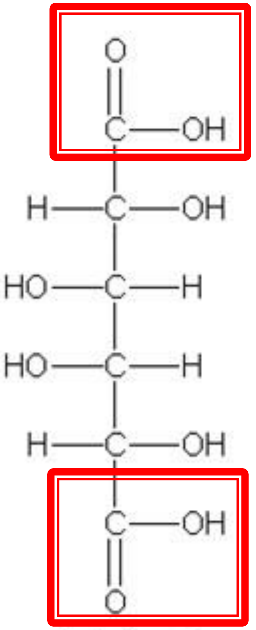


b) If a strong oxidizing agent is used, it can oxidize both terminal carbons:

·Carbon 1 (aldehyde) → oxidized to carboxylic acid

·Carbon 6 (primary alcohol) → first oxidized to aldehyde, then further to carboxylic acid

This results in a sugar with two carboxylic acid groups, one at C1 and one at C6, forming what is called a dicarboxylic acid – specifically an **aldaric acid.**



galactaric acid

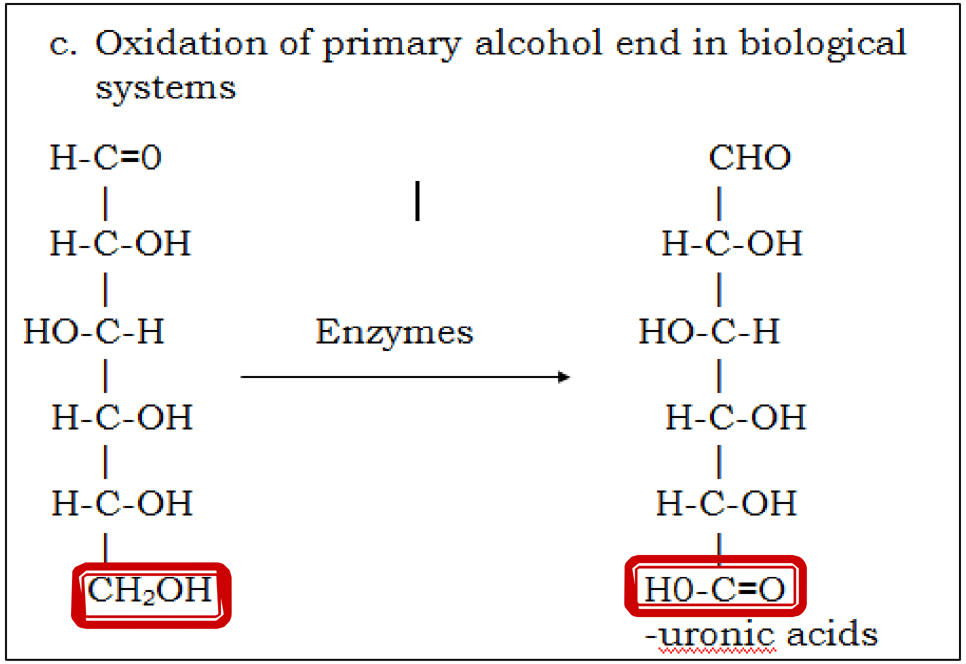
·For glucose, this becomes glucaric acid
·For galactose, this becomes galactaric acid
The naming convention reflects the parent sugar

(e.g., glucaric from glucose, galactaric from galactose).

Oxidation - Naming

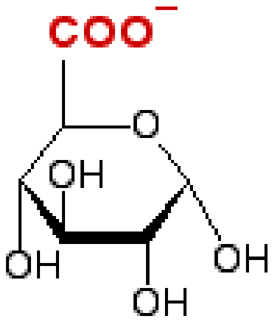
c) Enzymes, unlike chemical oxidants, can selectively oxidize just carbon 6, leaving the aldehyde at carbon 1 untouched. This produces a **uronic acid**.

- In glucose, oxidation only at C6 gives glucuronic acid
- The C6 alcohol is oxidized to a carboxylic acid, while C1 remains an aldehyde



c. Oxidation of primary alcohol end in biological systems

-uronic acids



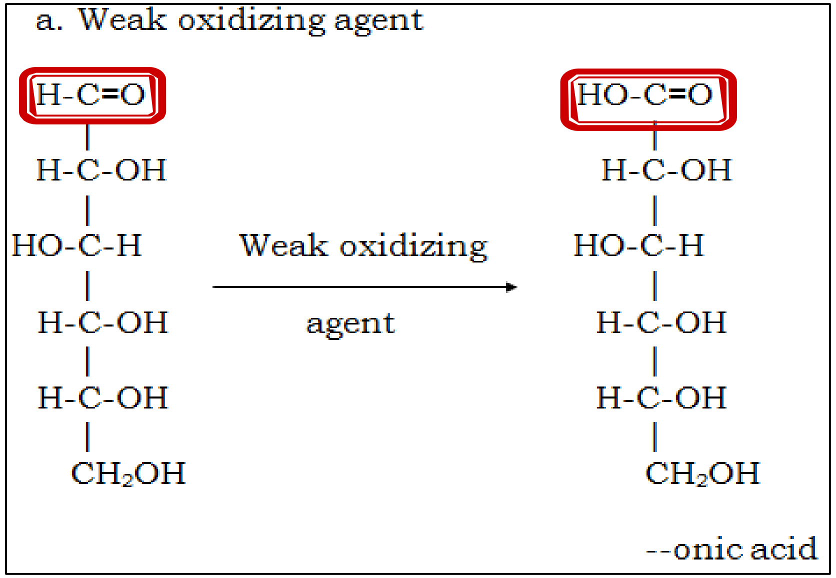
α-D-glucuronate

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

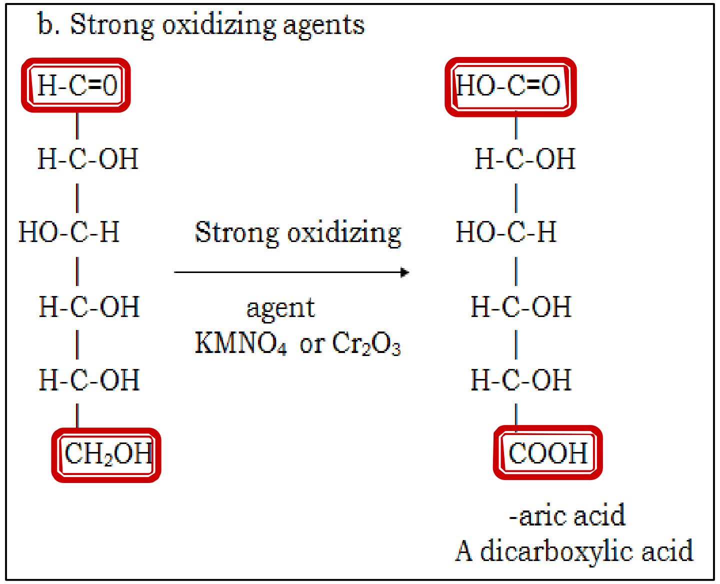
from **oxidation of glucose C6 OH**

This selectivity is possible because enzymes recognize specific positions on a molecule based on shape and fit, allowing precise oxidation.

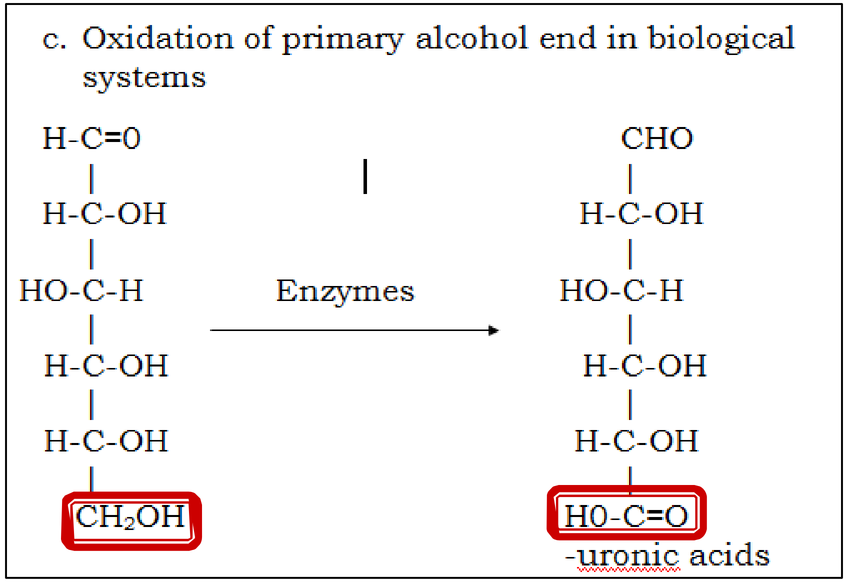
Oxidation - Naming



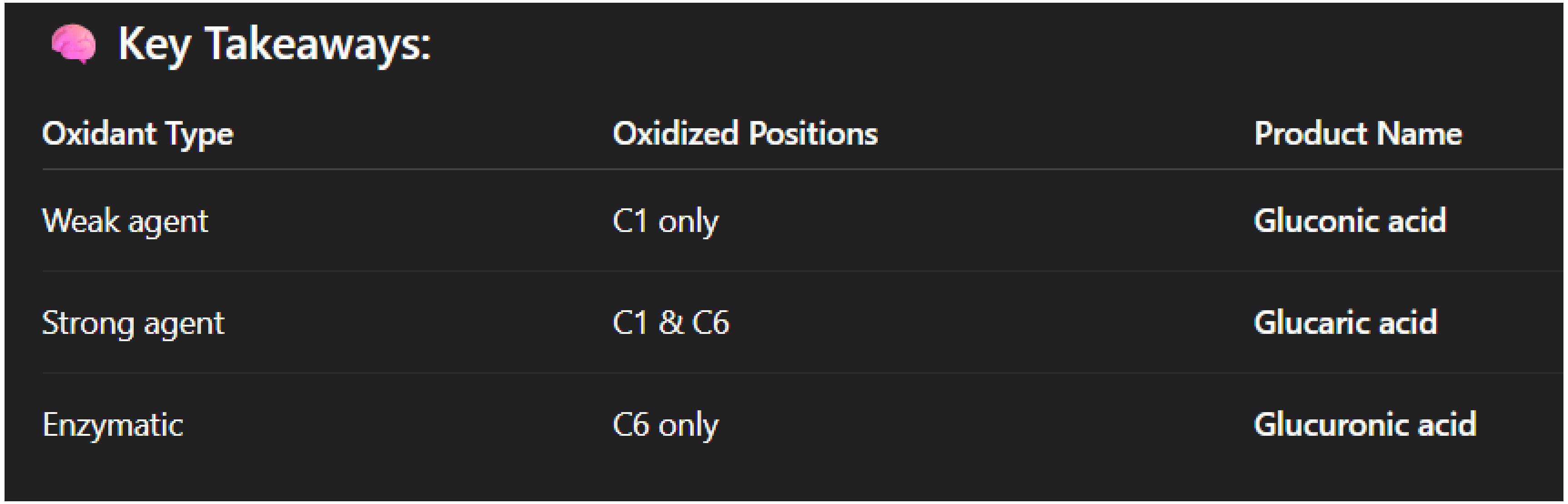
a. Weak oxidizing agent



b. Strong oxidizing agents



c. Oxidation of primary alcohol end in biological systems

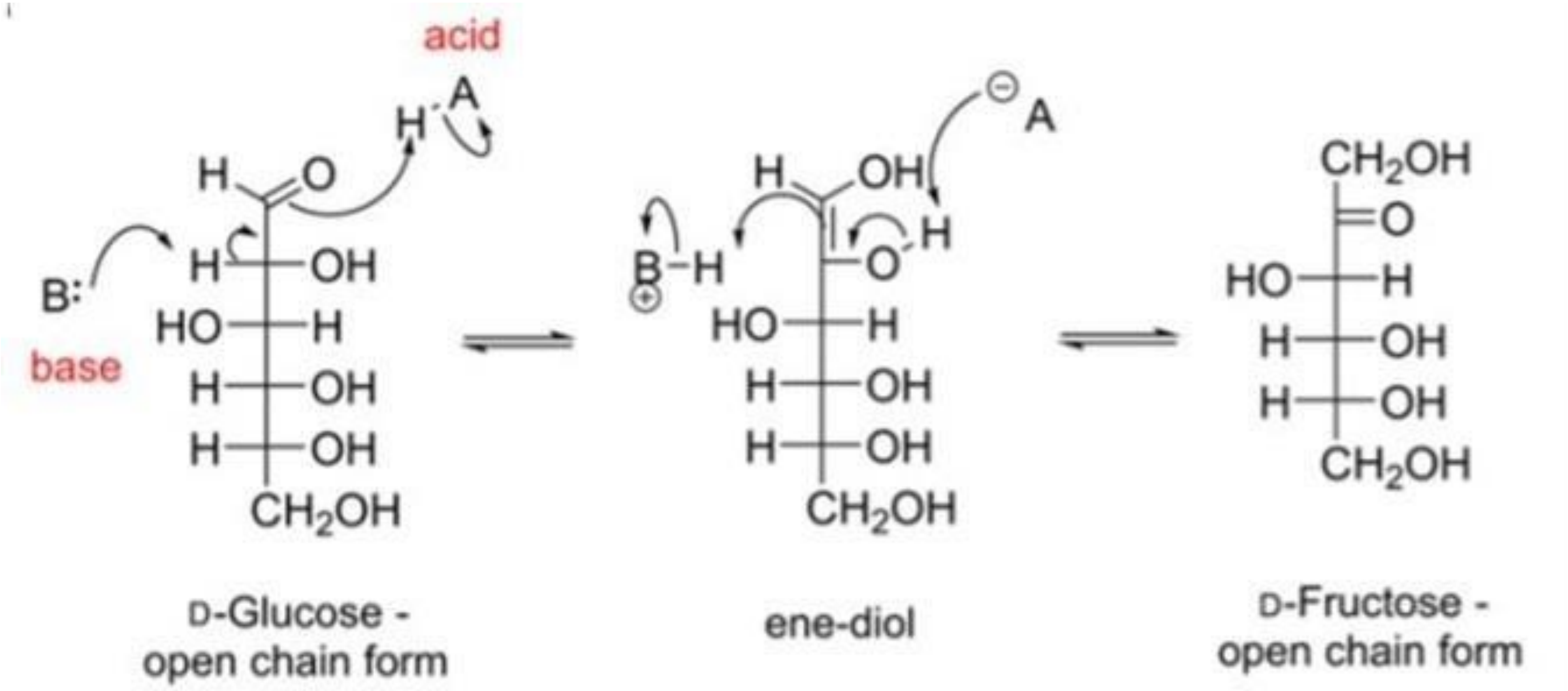


🧠 **Key Takeaways:**

Oxidant Type	Oxidized Positions	Product Name
Weak agent	C1 only	**Gluconic acid**
Strong agent	C1 & C6	**Glucaric acid**
Enzymatic	C6 only	**Glucuronic acid**

Note

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



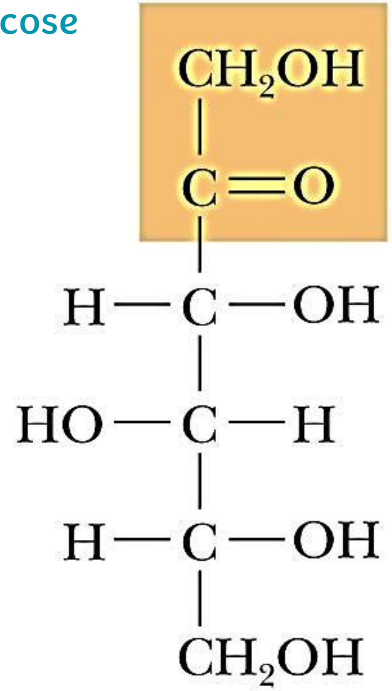
Reduction

- Monosaccharides are either aldoses or ketoses, which can be reduced to alcohols (1° or 2°) at the end

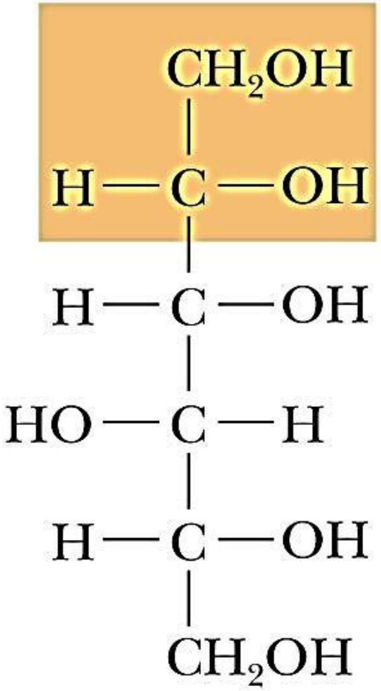
alcohols monosaccharides

- Xylitol & sorbitol: derivatives of xylulose & sorbose, have commercial importance (sweeteners in sugarless chewing gum & candy)

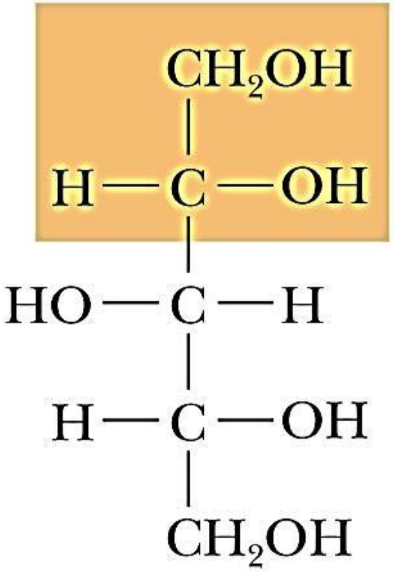
i.e. Glucitol from glucose



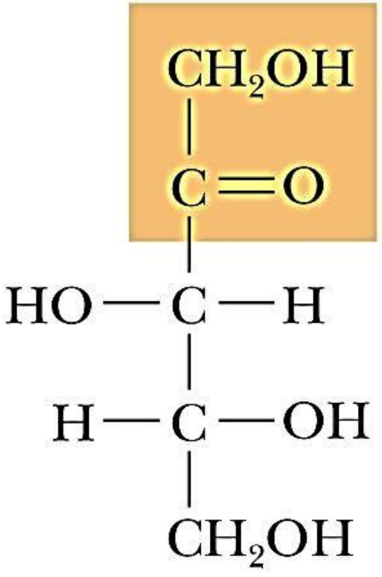
D-Sorbose



D-Sorbitol



D-Xylitol

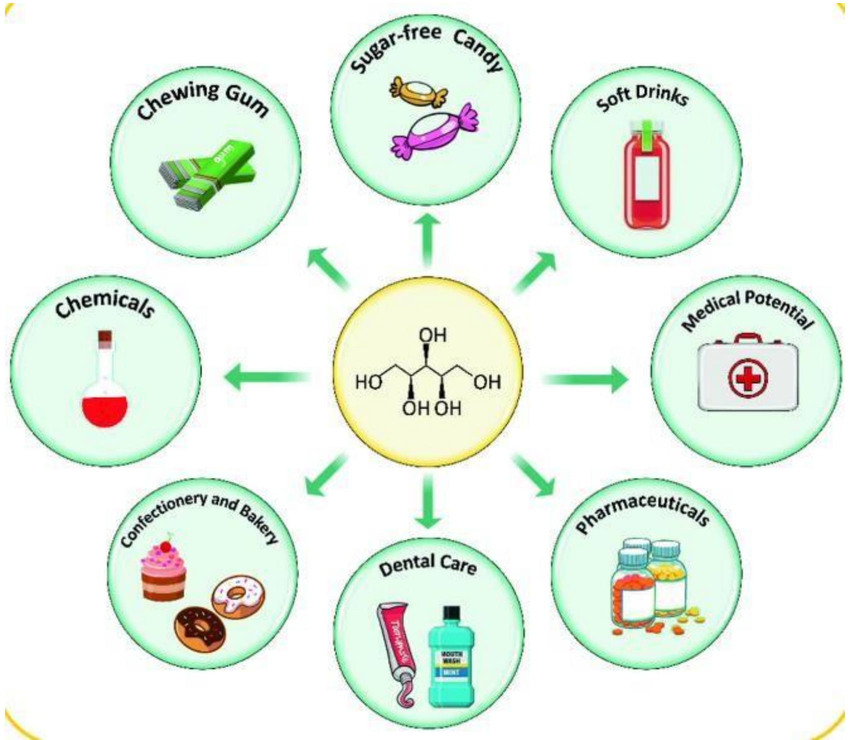


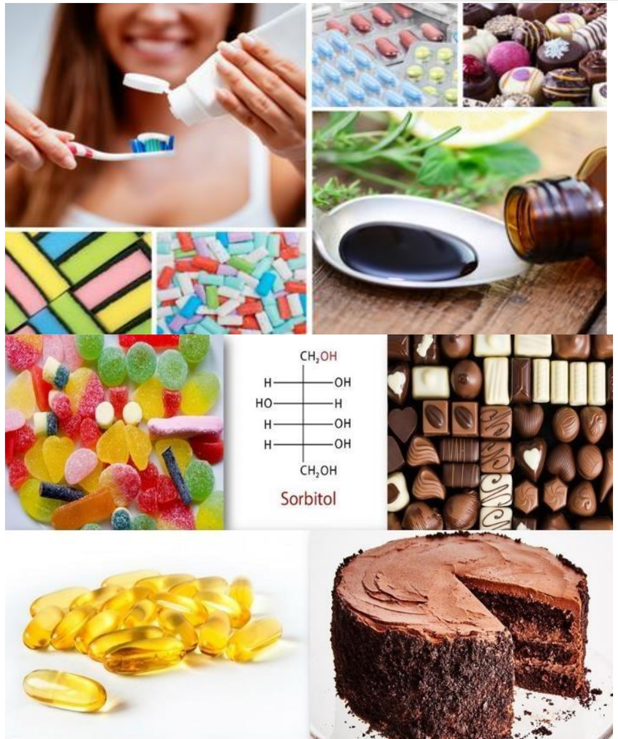
D-Xylulose

Xylitol, sorbitol, and mannitol (sugar alcohols)

more hydrogen bonding

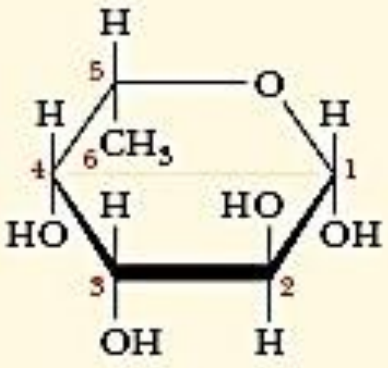
- Sweetners, cosmotics and personal care (absorb moisture), pharmaceuticals (Antihypertensive drugs, diuretics)



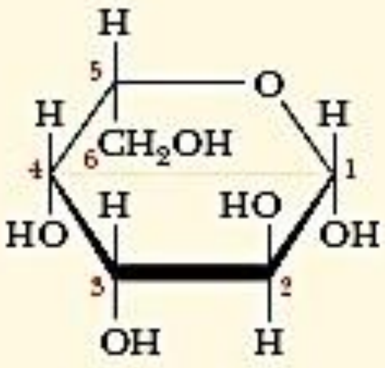


Reduction /deoxygenation : adding hydrogen or removing oxygen

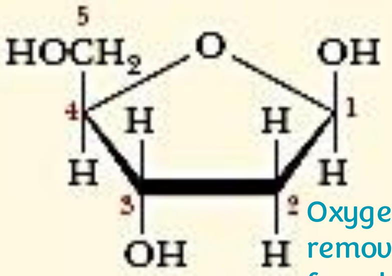
- L-fucose (L-6-deoxygalactose): some glycoproteins including the ABO blood-group antigens
- D-2-deoxyribose: in DNA (DNA is deoxygenated to be less reactive and more stable, while RNA retains its hydroxyl group, making it more reactive and easier to degrade).



β-L-Fucose
(6-Deoxy-β-L-galactose)



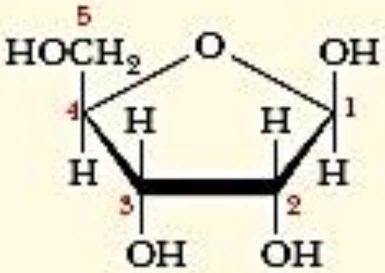
β-L-Galactose



Oxygen was removed from here

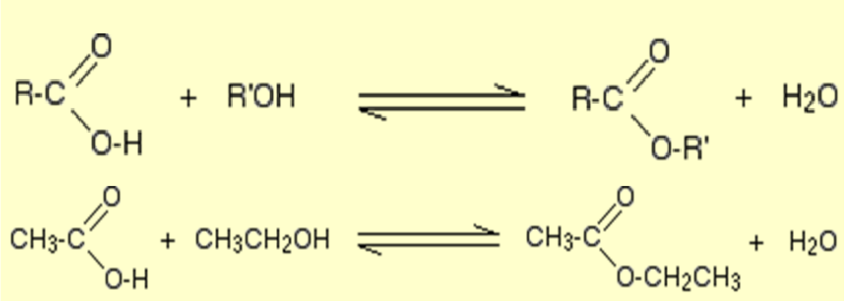
β-D-Deoxyribose
(2-Deoxy-β-D-ribose)

the backbone of DNA



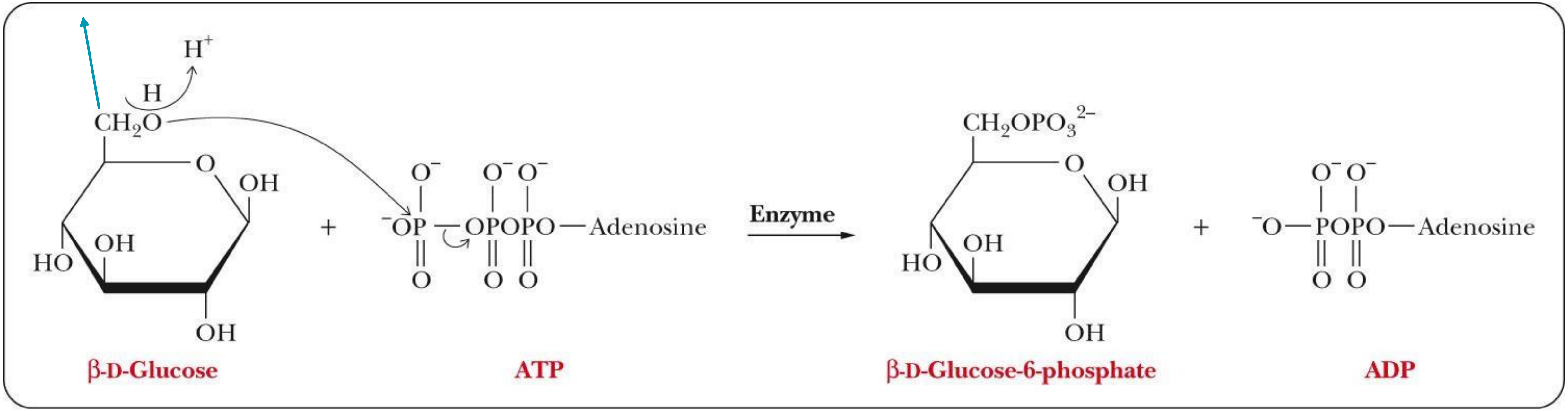
β-D-Ribose

Esterification Phosphoric Esters



- Breakdown of carbohydrates to provide energy
- Frequently formed by transfer of a phosphate group from ATP

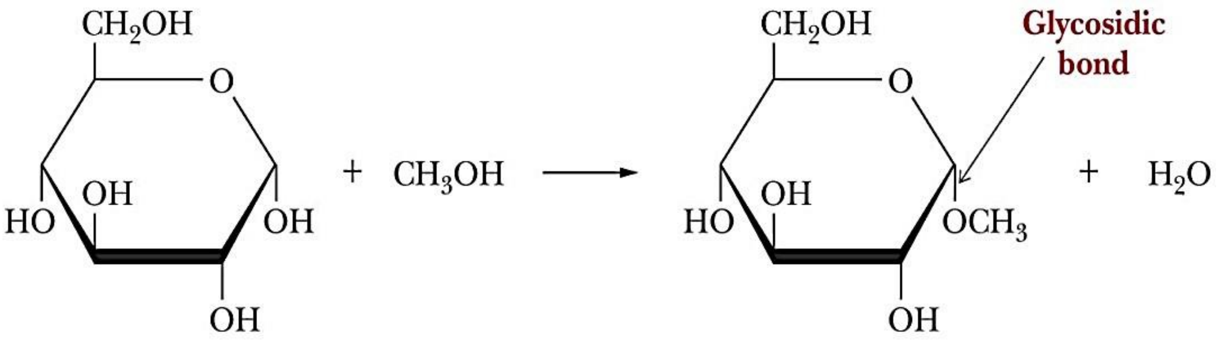
The easiest carbon to phosphorylate in glucose is carbon 6, as it lies outside the ring and is more accessible. Phosphorylation can also occur at carbon 1, but this is less common.



Glycosidic Bond Formation formation of full acetal

- The -OH of the anomeric carbon is replaced by –OR
- Glycosidic bond: bond from the anomeric carbon to the -OR group

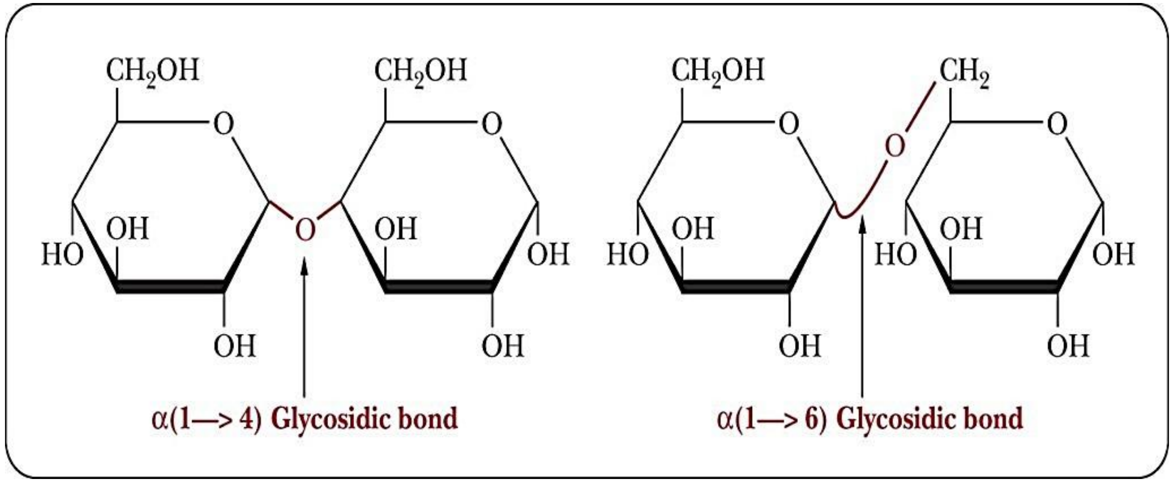
  If the glycosidic bond is formed with a nitrogen atom, it is called an N-glycosidic bond; if it is formed with a carbon atom, it is called a C-glycosidic bond, and so on.
- This type of reaction involves the anomeric carbon of the sugar in its cyclic form
- This is the basis for the formation of (di/oligo/poly)saccharides as glycosidic bonds involve the anomeric carbon and are responsible for chain lengthening



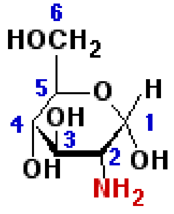
α-D-Glucopyranose (hemiacetal)

Methyl alcohol

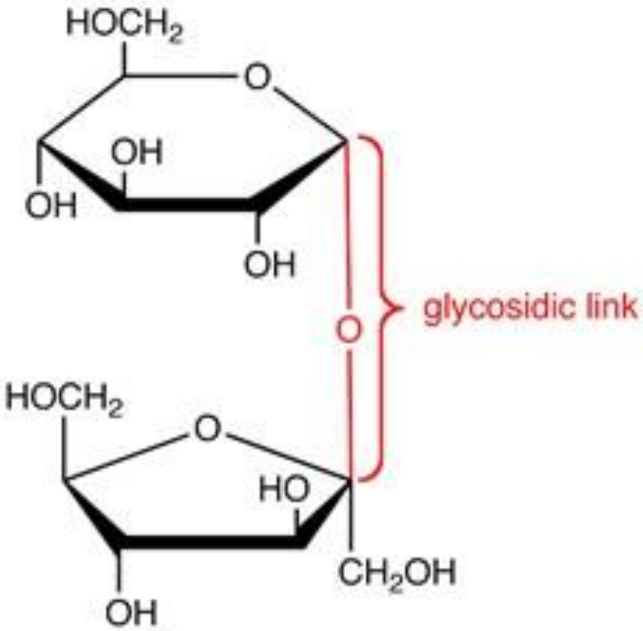
Methyl-α-D-glucopyranoside, a glycoside (full acetal)

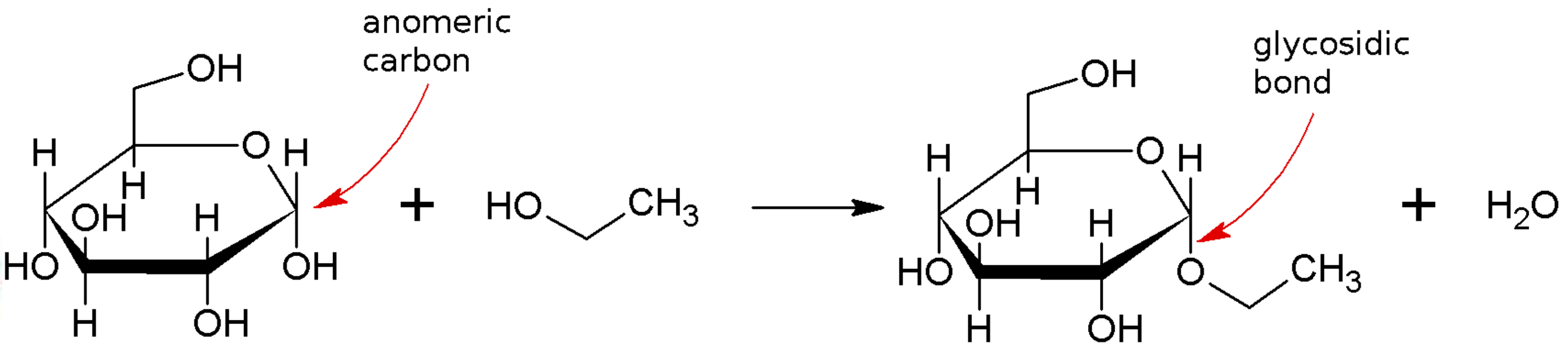


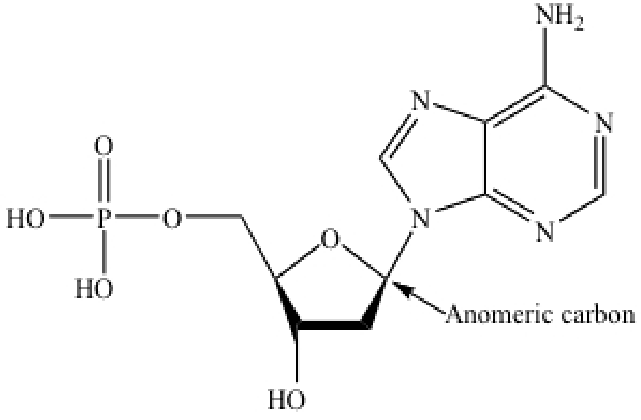
Glycosidic Bond Formation

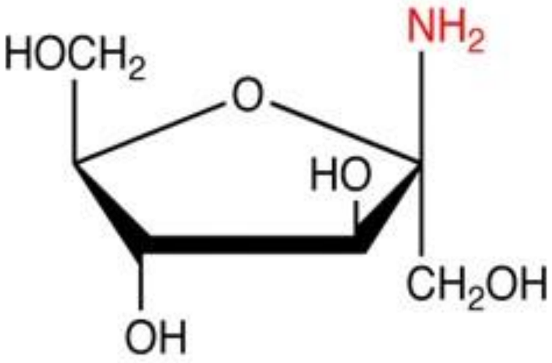


α-D-2-glucosamine
(GlcN)

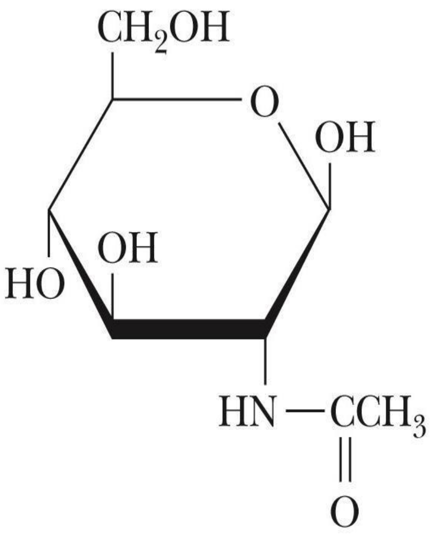




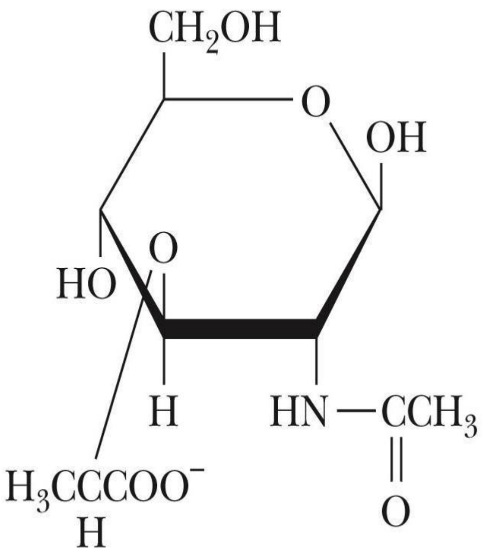




N-glycoside



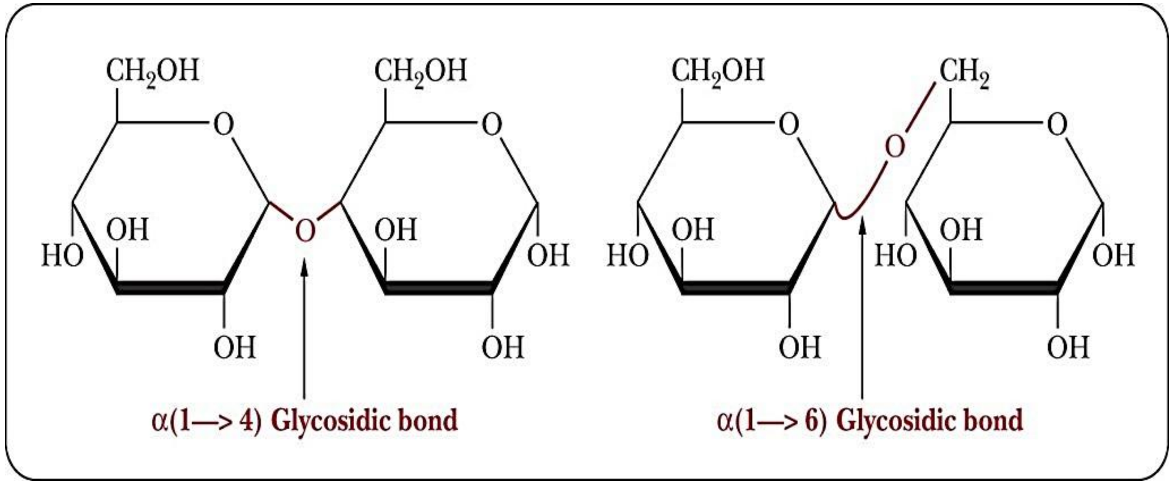
N-Acetyl-β-D-glucosamine



N-Acetylmuramic acid

Glycosidic Bond Formation

- Only one anomeric carbon needs to be involved in the linkage for a glycosidic bond to form.
- If the glycosidic bond is formed with a nitrogen atom, it is called an N-glycosidic bond; if it is formed with a carbon atom, it is called a C-glycosidic bond, and so on.
- Glycosides are defined by having a functional group attached at the anomeric carbon of a monosaccharide. If a group is attached elsewhere – like in glucosamine, where an amino group is bonded to carbon 2 – it is not considered a glycoside.



For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			

Additional Resources:

رسالة من الفريق العلمي:

﴿وَلا تَكونوا كَالَّذينَ نَسُوا اللَّهَ فَأَنساهُم أَنفُسَهُم
أُولئِكَ هُمُ الفاسِقونَ﴾

[الكلام من كتاب الوابل الصيب من الكلم الطيب لابن القيم رحمه الله]

دوامَ ذِكر الرب يُوجِب الأمان من نسيانه الذي هو سبب شقاء العبد في معاشه ومعاده؛ فإن نسيان الرب يوجب نسيان نفسه ومصالحها، قال تعالى: ﴿وَلَا تَكُونُوا كَالَّذِينَ نَسُوا اللَّهَ فَأَنْسَاهُمْ أَنْفُسَهُمْ أُولَئِكَ هُمُ الْفَاسِقُونَ (١٩)﴾ [الحشر: ١٩].

واعلم أن الحسرة كلَّ الحسرة الاشتغالُ بمن لا يُجْدِي عليك الاشتغال به إلا فوت نصيبك وحظك من الله، وانقطاعك عنه، وضياع وقتك عليك، وَشَتَاتِ قلبك عليك، وضعف عزيمتك، وتفرُّقِ همِّك.

فإذا بُلِيت بهذا - ولابُدَّ لك منه - فعامِل الله تعالى فيه، واحتسب عليه ما أمكنك، وتقرَّب إلى الله بمرضاته فيه، واجعل اجتماعك به مَتْجَرًا لك، لا تجعله خسارة، وكن معه كرجلٍ سائرٍ في طريقه عَرَضَ له رجلٌ وَقَفَهُ عن سيره، فاجْتَهِدْ أن تأخذه معك وتسير به، فَتَحْمِله ولا يحملك؛ فإن أبى ولم تَلْقَ في سيره مطمعًا، فلا تقف معه، بل اركب الدَّرْبَ ودَعْهُ ولا تلتفت إليه؛ فإنه قاطعُ طريقٍ، ولو كان من كان، فانْجُ بقلبك، وضِنَّ بيومك وليلتك، لا تغرب عليك الشمس قبل وصول المنزلة فَتُؤْخَذ، أو يطلع عليك الفجر وأنت في المنزلة فَيَسِيرَ الرِّفاقُ فتصبح وحدك، وأنَّى لك بِلَحاقهم!