7

BIOCHEMISTRY
faculty of medicine - JU2017

● Sheet ○ Slides

DONE BY

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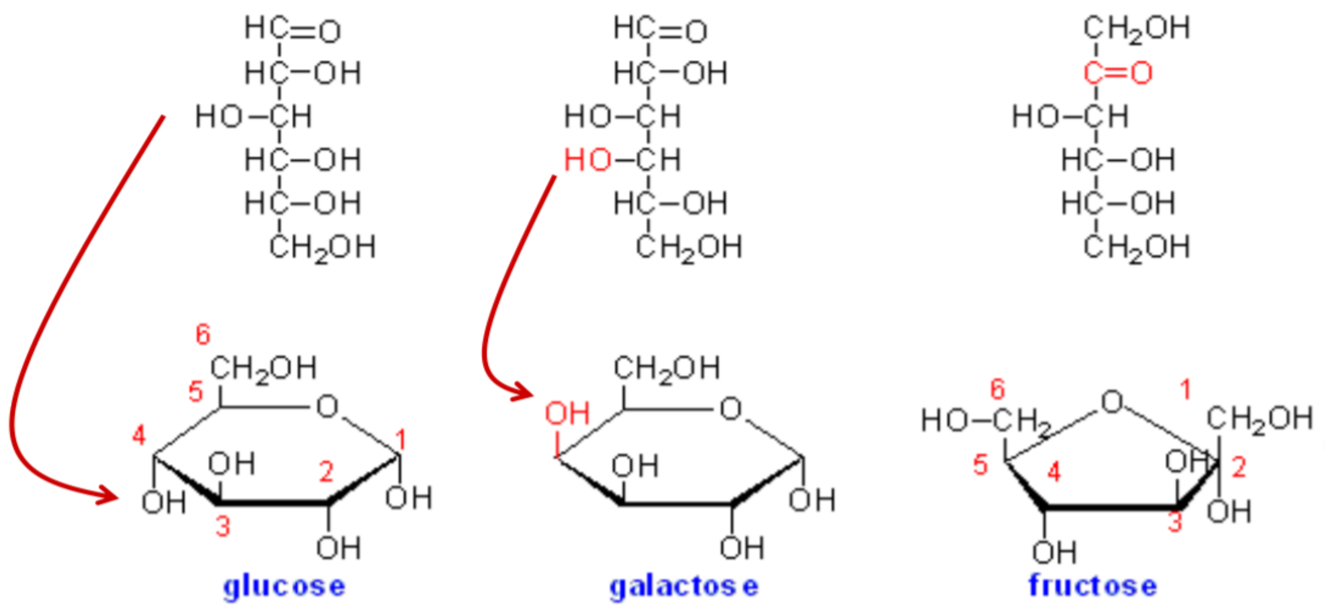
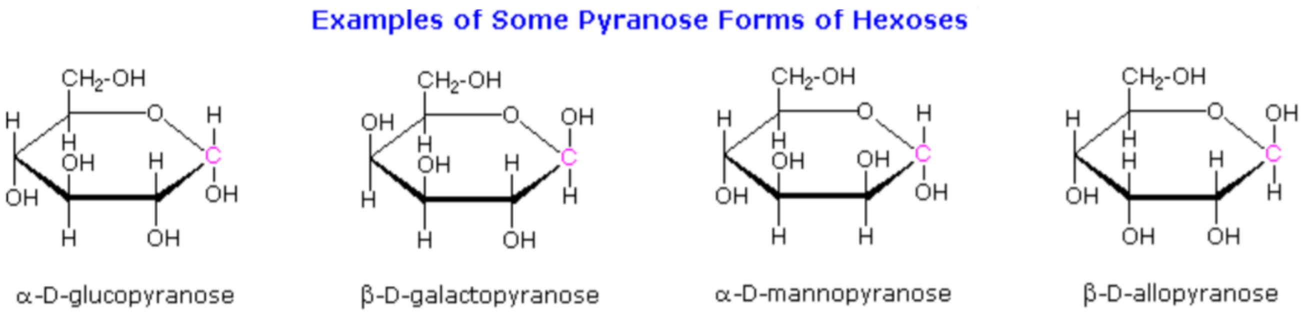
In this lecture we are going to talk about modified sugars.

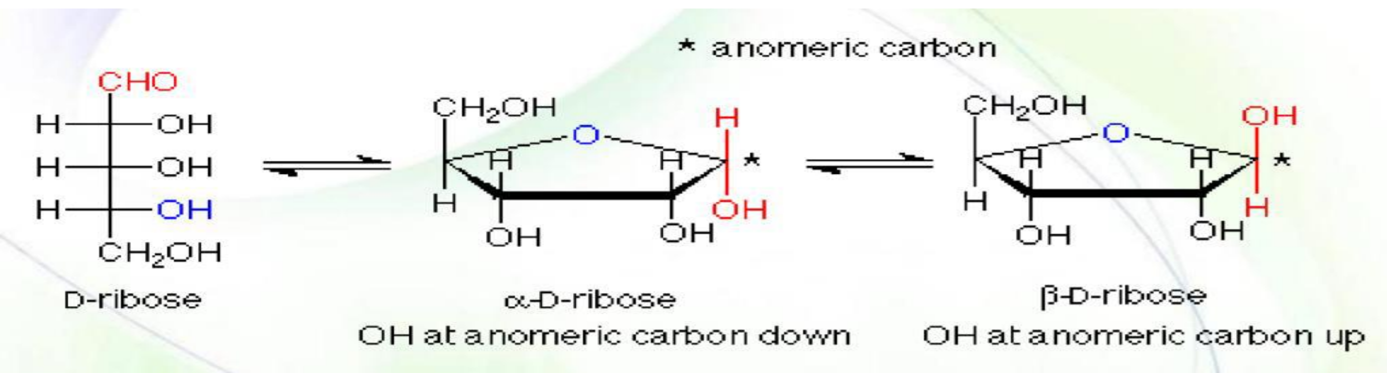
Remember: The Fischer projection can be turned into a ring structure *(which is known as the Haworth projection)* by a simple rule: **right = down, left = up.** Any hydroxyl groups on the **right** will be **below** the ring, and any on the **left** will be **above** the ring. As observed in the figure below

Note: in physiological conditions, carbohydrates almost always exist in the ring structure because it's more stable





Note:



Note:

- Once the ring is formed, hydroxyl groups' positions are fixed, they don't interconvert or change position, this is true for (C-2, C-3, C-4 of glucose).
  But the hydroxyl group that is attached to the *anomeric* carbon (C-1 of glucose), it interconverts in a process called mutarotation to form either an alpha (when the hydroxyl group is below the ring) or a beta sugar (when the hydroxyl group is above the ring), in this way we name the molecule depending on the anomeric carbon.
- the doctor advised us not to confuse ourselves by trying to integrate D and L with the left-right/up-down rule. Most of compounds in the biological conditions are D-compounds. It's worth mentioning that we cannot metabolize L-compounds.

- Epimers: they are diastereomers that differ in the orientation of **one chiral carbon**, examples:
  D-Glucose and D-Mannose are carbon-2 epimers.
  D-Glucose and D-Galactose are carbon-4 epimers.
  You can go back to the previous slides (slide 3-page #21) and check it

- **Reducing and Non-reducing sugars:** If the hydroxyl group on the anomeric carbon of a cyclized sugar is not linked to another compound by a *glycosidic bond* (free anomeric carbon), then the ring can open, and we call it a reducing sugar.

Modified Sugars

1-Oxidation (sugar acids)

→ 2-Sugar alcohols + deoxysugars (reduction)

3-Sugar esters

1-Oxidation of sugars (sugar acids)

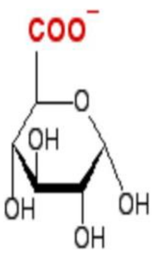
- Oxidation and reduction reactions of sugars play a very important role in terms of providing energy for organisms to carry out their life processes, as carbohydrates give the highest yield of energy when they are oxidized completely to CO_2 and H_2O

Primary alcohol→aldehyde→carboxylic acid

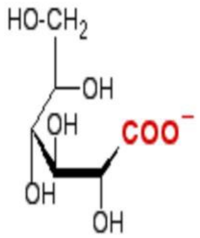
Secondary alcohol →ketone

Oxidation of glucose:

The oxidation of C#6 → **Glucuronate**
The oxidation of C#1 → **Gluconate**
**(Gluconate is the ionic form of gluconic acid)*

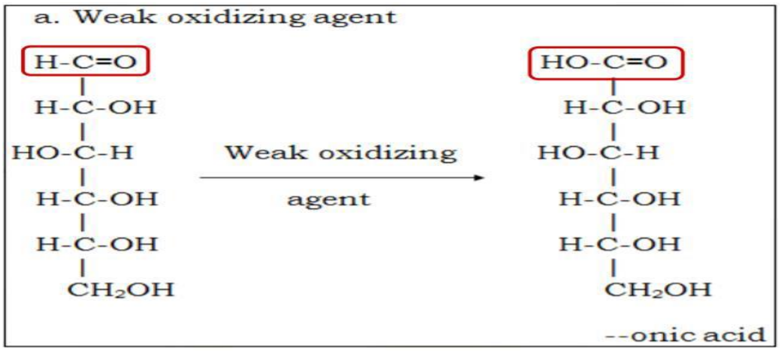


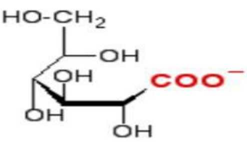
α-D-glucuronate
(D-glucuronic acid, GlcUA)
from oxidation of glucose C6 OH



D-gluconate
(D-gluconic acid, GlcA)
from oxidation of glucose C1 aldehyde)

Example 1:





D-gluconate
(D-gluconic acid, GlcA)
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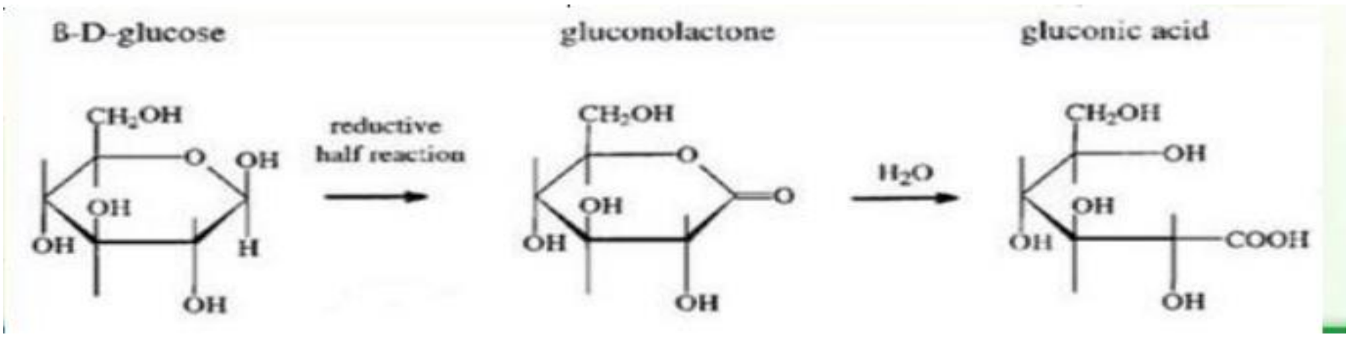
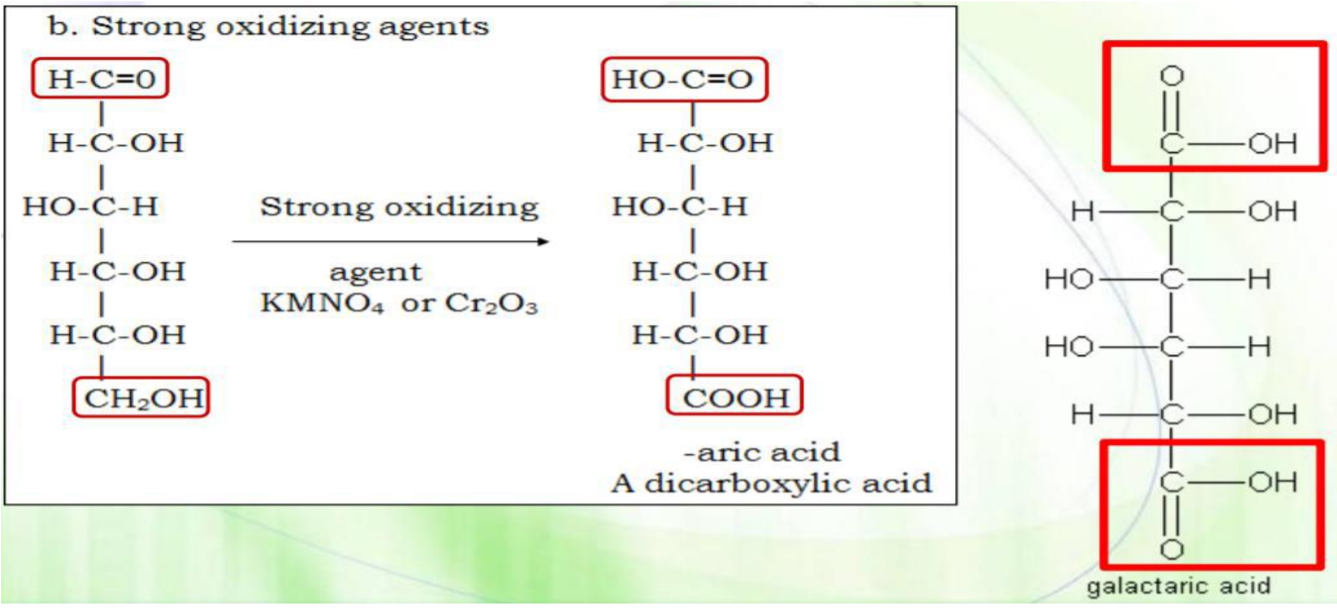


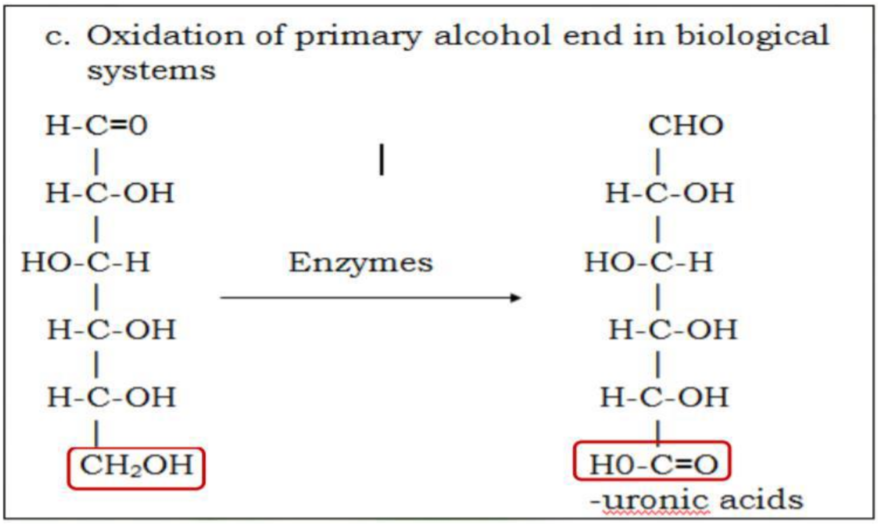
- If we add a weak oxidizing agent, it causes only the aldehyde to be oxidized into carboxylic group.
- Note this reaction is used to test for the presence of aldoses

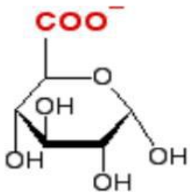
Example 2:



- Adding a strong oxidizing agent oxidizes both, the carbonyl group at the top carbon and the alcohol group at the bottom carbon to become carboxyl groups (carbon 6) to form galactaric acid

Example 3:





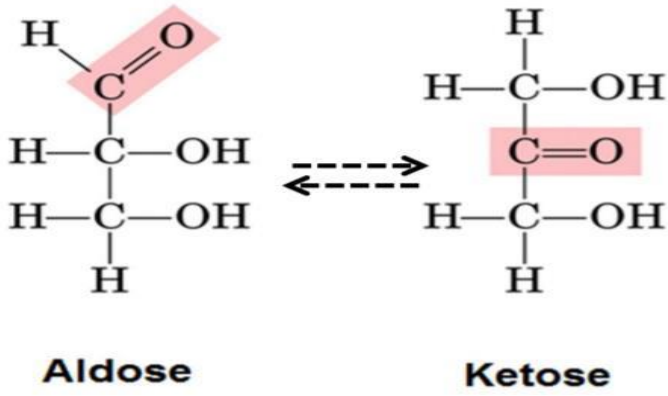
α-D-glucuronate
(D-glucuronic acid, GlcUA)
from oxidation of glucose C6 OH

- Some enzymes can cause oxidation of the primary alcohol attached to carbon #6 only

- Glucose → glucuronic acid

Note:

Can ketoses go through oxidation?
Ketose itself can't be oxidized directly. But ketoses are in equilibrium with their isomers, aldoses and aldoses can be oxidized which ultimately results in an **indirect** oxidation of **ketoses**

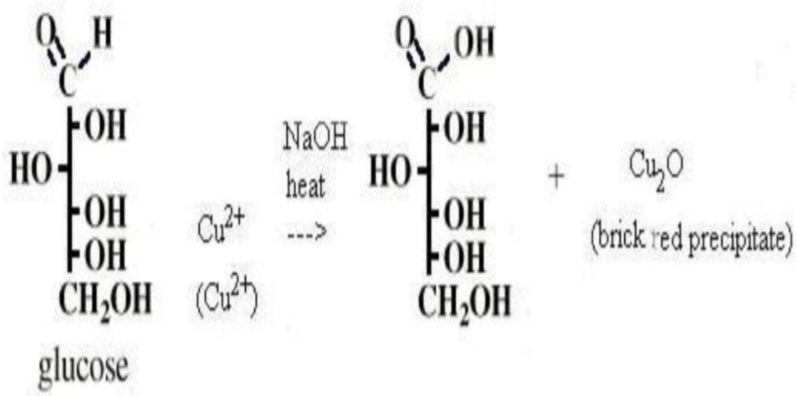


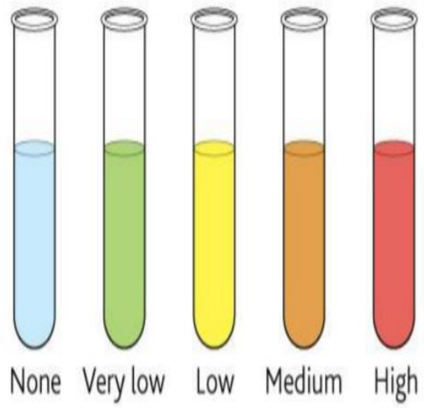
Methods to detect monosaccharides in solutions:

1-Benedict's test:
A chemical reagent that is commonly used to detect the presence of **reducing sugars**. A positive test with Benedict's reagent is shown by a color change from **clear blue to a red** precipitate due to the **reduction of the (Cu_2^+)** in the reagent causing it to precipitate as insoluble red copper(I) oxide (Cu_2O).

- *Cu^{2+} is reduced, glucose is oxidized*
- Depending on the degree of color obtained, we can determine the concentration of the sugar in the solution

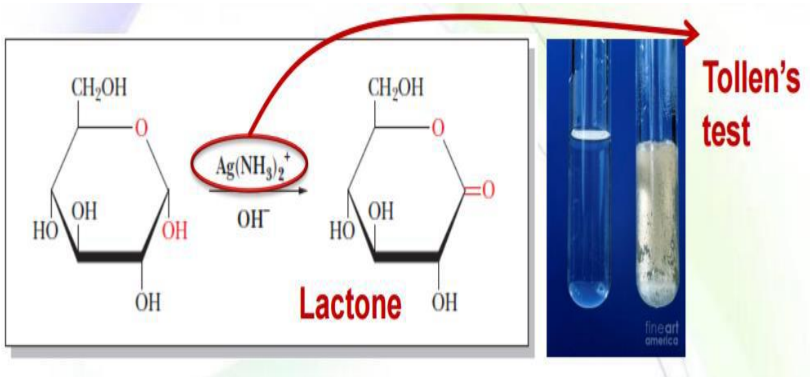
  The more concentrated it is, the redder the solution will be.





2-Tollens test $Ag(NH_3)_2^+$: (SILVER MIRROR)
This test is used to distinguish between aldehyde (oxidizable) and ketone (not oxidizable), silver ions are reduced to produce silver precipitate, and the product is Lactone.

3-Oxidation of cyclic sugars to form lactone:

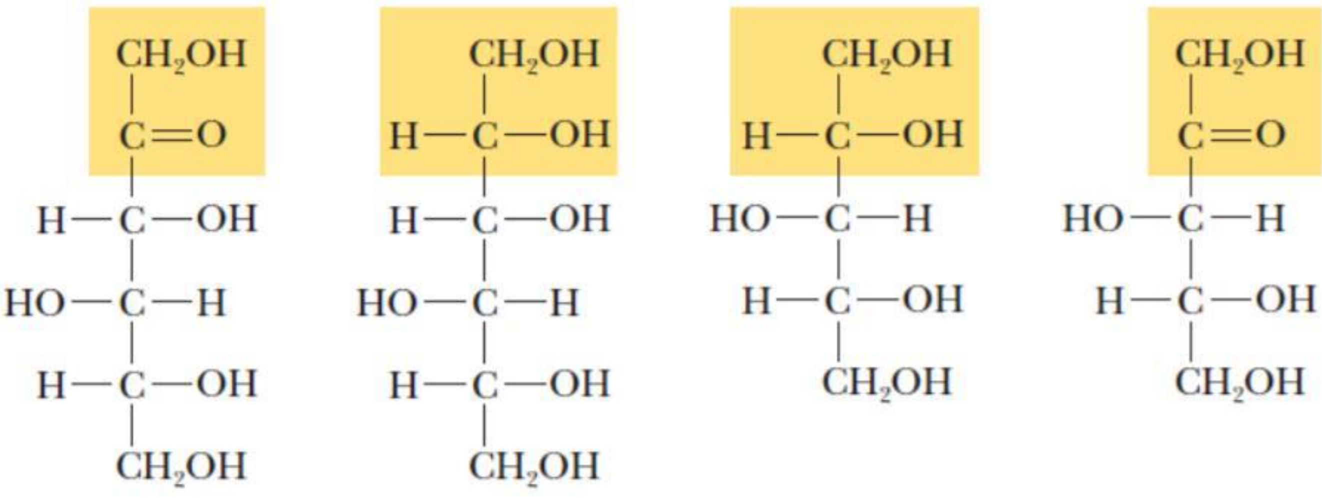


- Using the enzyme glucose oxidase, this is a new method used only for the detection of glucose as the enzyme's active site is specific to glucose
- Vitamin C (aka: ascorbic acid) is an unsaturated lactone (ketone)
- Air oxidation of ascorbic acid, followed by hydrolysis of the ester bond, leads to loss of activity as a vitamin.
- A lack of fresh food can cause vitamin C deficiencies, which in turn, can lead to the disease scurvy.
- ***The doctor mentioned the example of*** *pirates that suffer from teeth decay and gum diseases because collagen is the most abundant protein in our body, and it's essential for our teeth and gum. Vitamin c is essential for the hydroxylation process of collagen (recall: histology course) so any deficiency in vitamin C weakens collagen's structure which essentially causes scurvy.*

2- Reduction of sugars (sugar alcohols):

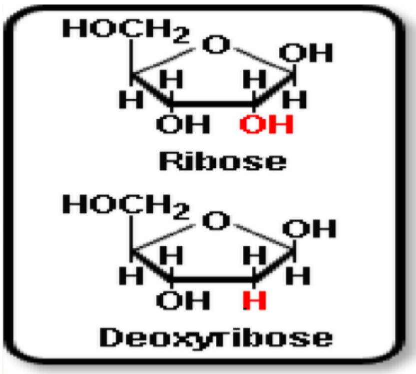
Carboxylic acid→aldehyde→primary alcohols
Ketone→secondary alcohol

- most of these sugar alcohols are used to sweeten the food
- example: sorbitol and xylitol and both important



D-Sorbose D-Sorbitol D-Xylitol D-Xylulose

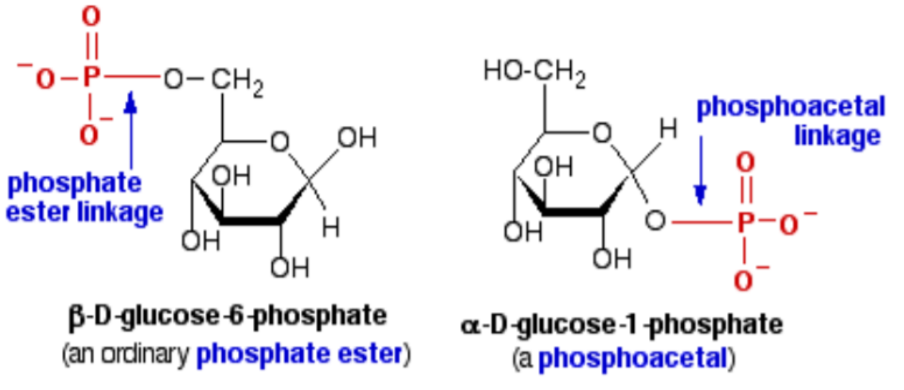
- deoxy sugars (reduced sugars)
  one or more hydroxyl groups are replaced by hydrogen atoms.
  An example: the sugar deoxyribose, a pentose sugar, found in DNA



3-Sugar esters (esterification):

A) Phosphorylation

- Formation of phosphor-esters is an important in metabolic reaction
- Carbons involved are 1 or 6
- Its process is adding a phosphate group to the sugar molecule



- If the phosphate bond is linked to **C#6**, a phosphate **ester** linkage is formed (this carries a lot of energy)
- If the phosphate bond is linked to **C#1**, it is a **phosphoacetal** linkage.

- Importance of phosphate group on the sugar: molecule becomes a high energy molecule so can proceed further in the reaction.

- cell may use phosphorylation to produce ATP $+co_2+H_2o$
- phosphorylation may change glucose to glycogen and when we need ATP breaks it down

B) Glycosides

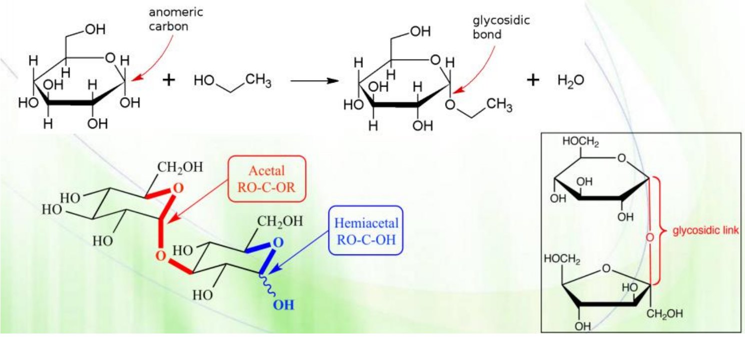
- Its reaction occurs between the hydroxyl group **(at the anomeric carbon)** and an alcohol to form a **glycosidic bond**.
- When the reaction occurs at C#1 in the ring, the ring will not open (so these reactions basically lock the ring) and no mutarotation occurs.
- It stabilizes the ring structure of the sugar molecule
- This reaction is important in the formation of disaccharides, where an anomeric carbon of a monosaccharide forms a glycosidic linkage with another monosaccharide (not necessarily another anomeric carbon though)

This reaction involves: O-glycosides & N-glycosides

O-glycosides:

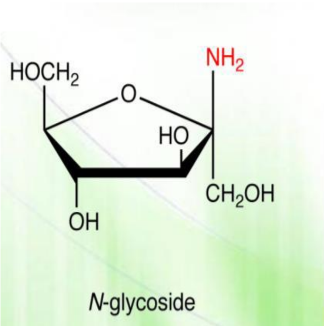
- Each sugar is bonded to an oxygen atom of another molecule

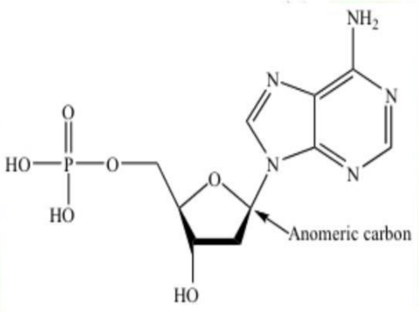
  This occurs when the reaction is with an alcohol (o-glycocidic bonds)



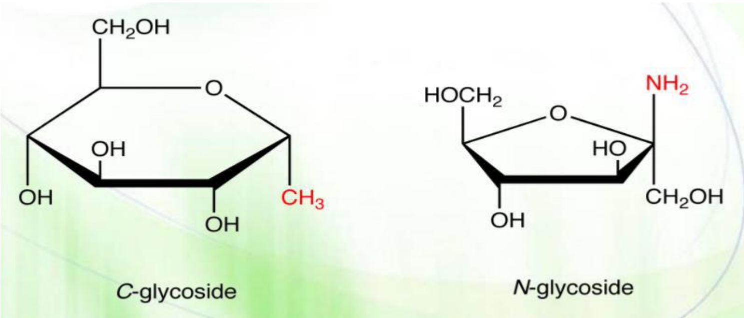
N-glycosides:

- An amino group (–NH_2) or one of its derivatives is substituted for the hydroxyl group in the parent sugar *(n-glycocidic bonds)*
- EX: nucleotides (DNA and RNA)





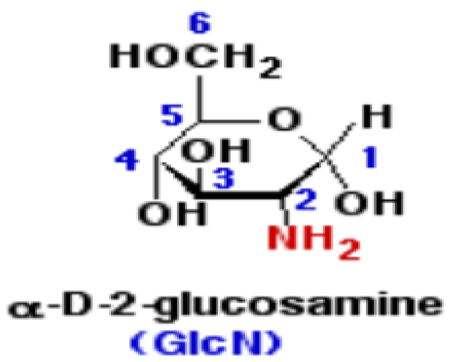
- Note: Glycosides derived from furanoses are called furanosides, and those derived from pyranoses are called pyranosides, regardless if they are N- or O-linked.

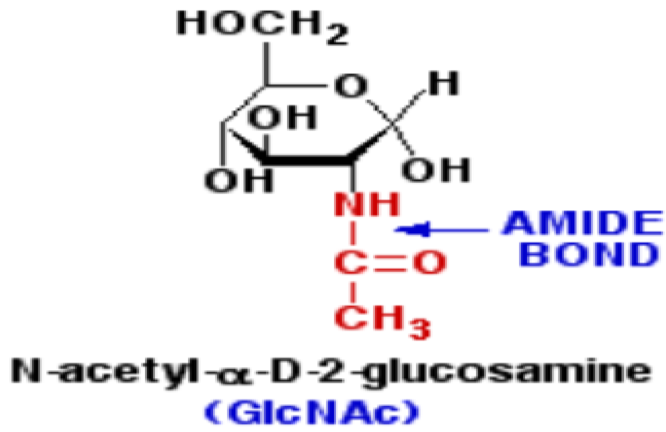


Amino sugars:

- How it differs from N-glycosides: the amino group is *NOT* on the anomeric carbon (this means that anomeric carbon is essentially involved in the formation of N-glycosides)
- Further modification by acetylation.

- *Anomeric carbon: is originally the carbonyl group (the former carbonyl group), it is the asymmetric (chiral) carbon that is formed when a sugar cyclizes, so its aldehyde (or ketone) group reacts with a hydroxyl group (OH) on the same sugar,* *making the carbonyl carbon (carbon 1 for an aldose, carbon 2 for ketoses) asymmetric. It is called anomeric carbon because it can form anomers (α or β)*





And the last topic at this sheet is:

Disaccharides

- They are a type of sugars which consist of 2 monosaccharide monomers joined together by a glycosidic bond, they are very stable and cannot be deformed except by enzymes
- Disaccharides are formed by enzymes called glycosyltransferases
- As mentioned previously, no mutarotation occurs in disaccharides *since they are formed by glycosidic bonds*
- A residue as a definition is each subunit of the compound
  Example: a compound: amino acid +amino acid +amino acid
  Each amino acid is residue
  While outside the compound its only amino acid

Distinctions of Disaccharides

When we want to differentiate between 2 disaccharides and classify a disaccharide, we have certain distinctions to follow:

1. The 2 specific sugar monomers involve and their stereo configurations (D- or L-)
   D: OH, above the ring
   L: OH, below the ring
   - in living organisms D-sugars are mainly present
   - Mostly in nature the sugars exist in the D- stereo configuration
   - in bacteria, L-configurations of the sugars are *present*, but mainly they're in D-configurations
   - In the human body L-sugars can't be metabolized. *Thus, we deal with D-sugars in our books and lectures*

2. The carbons involved in the linkage (C-1, C-2, C-4 or C-6)

- We have to determine which carbons are involved in the glycosidic bond.
- Note that every bond consists of at least one anomeric carbon, but not necessarily two. So, an **anomeric carbon** might bind to any non-anomeric carbon of other compound in the formation of glycosidic bonds.

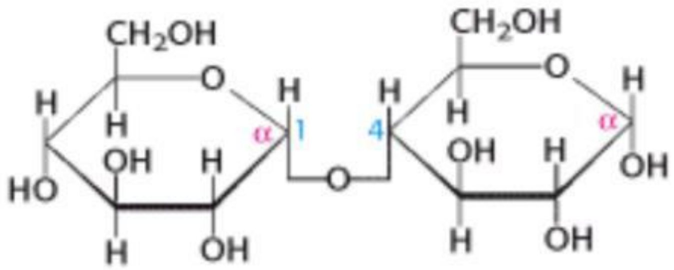
3. The order of the two monomer units, if different (example: galactose followed by glucose)

4. The anomeric configuration of the OH group on carbon 1 of each residue (α or β)

There are many common disaccharide:

1-Maltose:

- It's a sugar made from 2 glucose molecules *(D-glucose)*
- *The OH groups of both monomers at the anomeric carbon are below the ring, therefore they're both α*
- The glycosidic bond is between carbons 1 and 4, respectively *Hence the bond is an α-1,4-glycosidic bond*



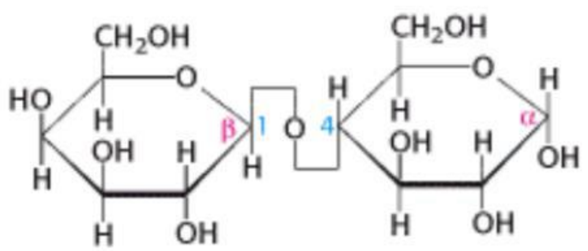
Maltose
(α-D-Glucopyranosyl-(1→4)-α-D-glucopyranose

- It is classified as a reducing sugar as the anomeric carbon is free in the molecule located on the right

Study the figure carefully and understand why we said the previous compound is maltose

2-Lactose:

- It's the sugar found in milk (additional info: The name comes from lac, the Latin word for milk, plus the suffix -ose used to name sugars.)
- Lactose is a disaccharide made up of β-D-galactose and α-D-glucose
- The galactose molecule is a β molecule since the OH group of C#1 is above the ring



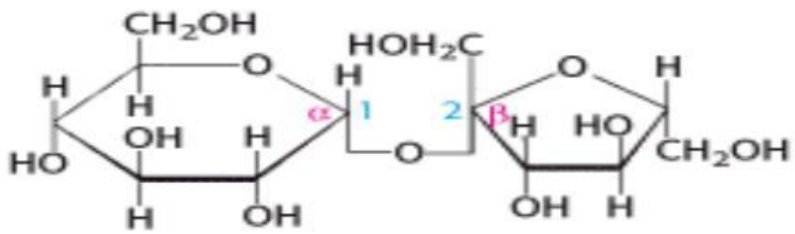
Lactose
(β-D-Galactopyranosyl-(1→4)-α-D-glucopyranose

- The glucose molecule is an α molecule since the OH group of C#1 is below the ring
- Galactose is the C#4 epimer of glucose
- The glycosidic bond is between carbons 1 and 4, respectively
  Hence the bond is a β-1,4-glycosidic bond: the anomeric carbon involved in the glycosidic bond is in the β configuration
- It is classified as a reducing sugar as the anomeric carbon is free in the molecule located on the right.

again, study why the previous compound is lactose

3-Sucrose:

- Sucrose is a disaccharide made up of α-glucose and a β-fructose
- The glucose molecule is an α-molecule since the OH group of C#1 is below the ring



Sucrose
(α-D-Glucopyranosyl-(1 → 2)-β-D-fructofuranose

- The fructose molecule is a β-molecule since the OH group of C-2 is above the ring
- In order to form sucrose in a condensation reaction between α-glucose and a β-fructose, the fructose molecule is flipped sideways
- The glycosidic bond is between carbons 1 and 2, respectively
  Hence the bond is an α,β-1,2- glycosidic bond: 2 anomeric carbons are involved in the glycosidic bond and one is α, the other is β
- It is classified as a non-reducing sugar as both anomeric carbons are involved in the glycosidic linkage

Like this the lecture end the next lecture we will continue talking about sucrose and the other type of sugars ...

REMEMBER: **IF IT WAS EASY EVERYBODY WOULD DO IT**