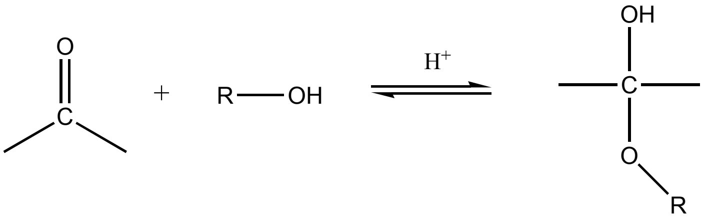
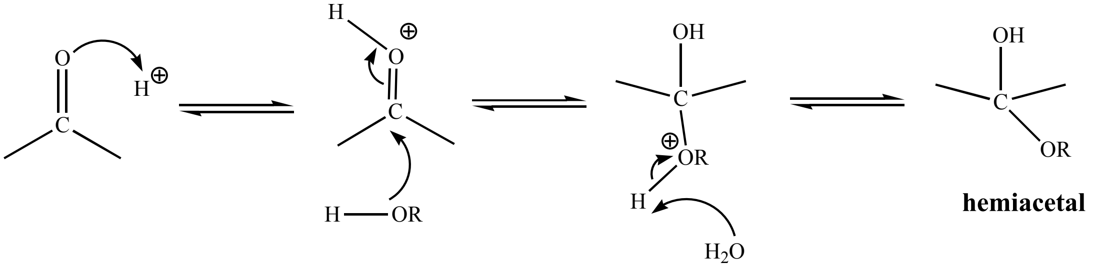
Carbohydrates- Hemiacetal Formation

You know from previous lectures that carbonyl compounds react with all kinds of nucleophiles. Hydration and hemiacetal formation are typical examples.



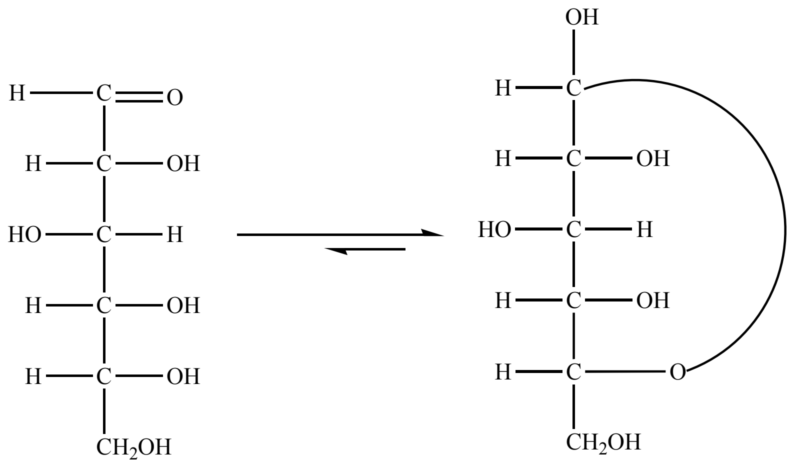
Mechanism (this should be a review from previous lecture):



In nature, formations of 5- and 6-membered rings are favored, and if possible, a molecule will form such a ring when it can.

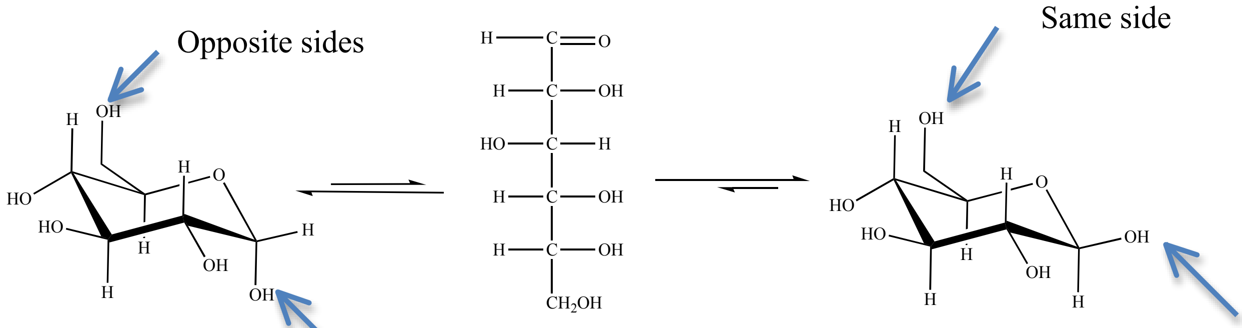
In sugars, the cyclic forms with 5-membered rings are called furanoses, and 6-member rings are called pyranoses. For most aldohexoses, the five membered furanose and six-membered pyranose can be formed. However, with D-glucose the six-membered pyranose usually predominates.

For example, glucose can react internally to form a hemiacetal (an intramolecular cyclization).



D-Glucose **hemiacetal**

The molecule exists predominantly in the cyclic form; however, it is still in equilibrium with a small amount of the acyclic form. The cyclic 6-membered rings exist in energy minimum chair forms (shown in figure below). This is also depicted in the handouts given.



Opposite sides

Same side

α-D-Glucopyranose **D-Glucose** **β-D-Glucopyranose**

The cyclic forms are indicated in the name by combining the simple name of the sugar with "furanose" or "pyranose" to indicate the size of the ring. Therefore, glucose in its 6-membered ring form is called glucopyranose.

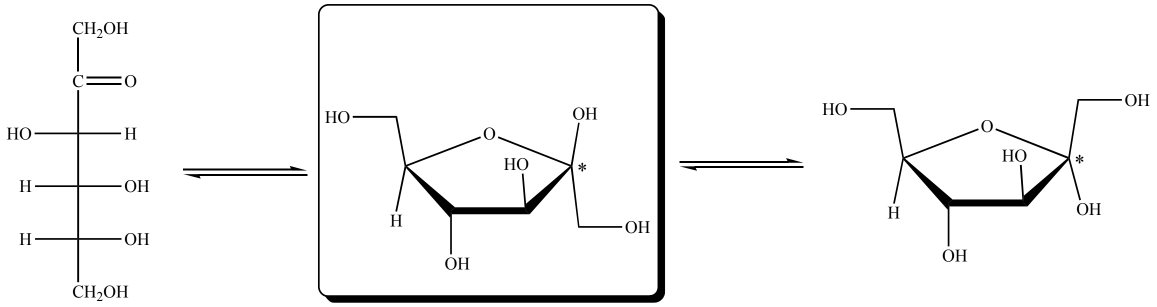
The intramolecular cyclization reaction creates a new stereogenic carbon that can be either R or S configuration, with OH group in equatorial or axial position. The terms $\boldsymbol{\alpha}$ and $\boldsymbol{\beta}$ refer to position of OH at C1 relative to CH_2OH group of C6.

When the OH group attached to C1 is down relative to the CH_2OH group that is up (they are *trans* to each other), The configuration is $\boldsymbol{\alpha}$. When they are on the same side (both are up), the configuration is $\boldsymbol{\beta}$.

The two stereoisomers are interconverting structural isomers called **anomers**. They differ only in stereochemistry at C1 position, which is known as the **anomeric carbon**.

The $\boldsymbol{\alpha}$ and $\boldsymbol{\beta}$ anomers can equilibrate through the linear form.

Formation of a 5-membered ring is possible for D-glucose, but it exist predominantly as the 6-membered ring. Fructose, on the other hand, exists predominantly as 5-membered ring.

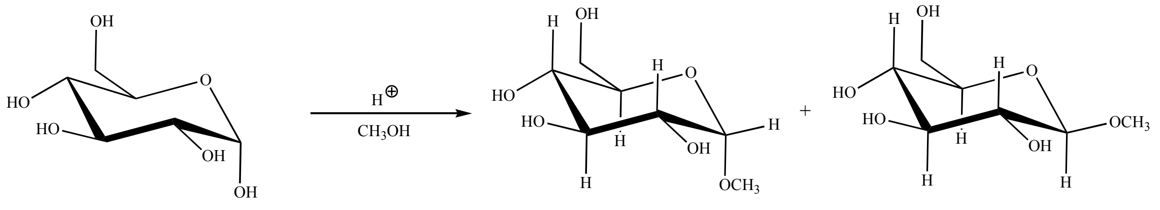


D-Fructose **D-Fructofuranose** **D-Fructofuranose**

D-fructose is a ketohexose (“keto” since it contains ketone). Its cyclized form, D-fructofuranose is a hemiacetal since the anomeric carbon (marked by asterisk) has a free OH group and a OR group attached. An easy way to find the anomeric carbon is to find a carbon with 2 oxygen atoms attached directly.
*Is the fructofuranose highlighted in box an **α** or **β** sugar?*

Answer: It is ***β***. The rule is to find the CH_2OH group (not on the anomeric carbon) and the OH substituent of the anomeric carbon, and see of they are on the same or opposite side. Since the OH group and the CH_2OH group are on the **same** side as each other, the ring is ***β***.

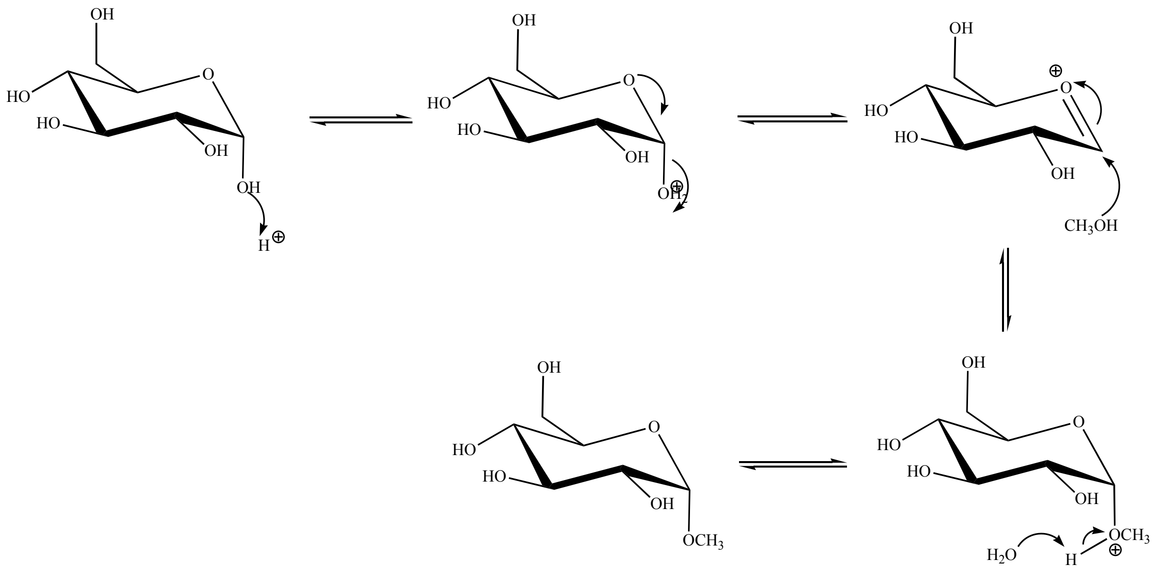
Acetal formation



α-D-Glucopyranose **α-D-Glucopyranoside (favored)** **β-D-Glucopyranoside (minor)**

Treatment with dilute acid and alcohol converts only the OH at the anomeric position into an acetal called a glycoside. Specific glycosides are named by replacing the “ose” of the simple sugar’s name with “oside”. When glucopyranose is reacted, its product is called glucopyranoside.
The ***α*** anomer with the methoxy group in axial position is favored due to the anomeric effect (details about the anomeric effect is beyond the scope of this class).

Mechanism:



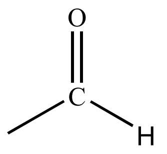
Reducing or non-reducing sugars

We can perform chemical reactions on a sugar to find out if it's a reducing or non-reducing sugar, such as the silver mirror reaction. Silver nitrate in aqueous ammonia is allowed to react with sugar. If a silver mirror is observed, then the sugar is reducing.

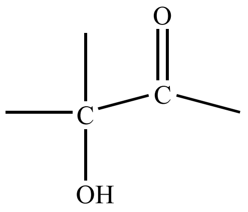
$$Ag(NH_3)_2OH \xrightarrow{\text{Sugar}} Ag^{\bullet}$$

silver nitrate **silver mirror**

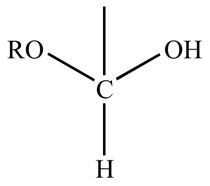
Usually, reducing sugars contain one of the three functional groups:



aldehyde

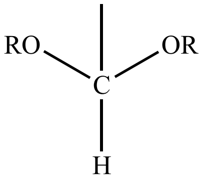


α-hydroxyketone



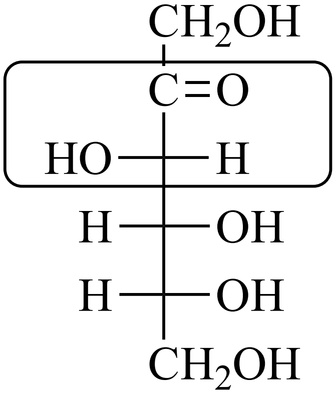
hemiacetal

The non-reducing sugars do NOT contain the above functionality, but may contain an acetal functionality:



acetal

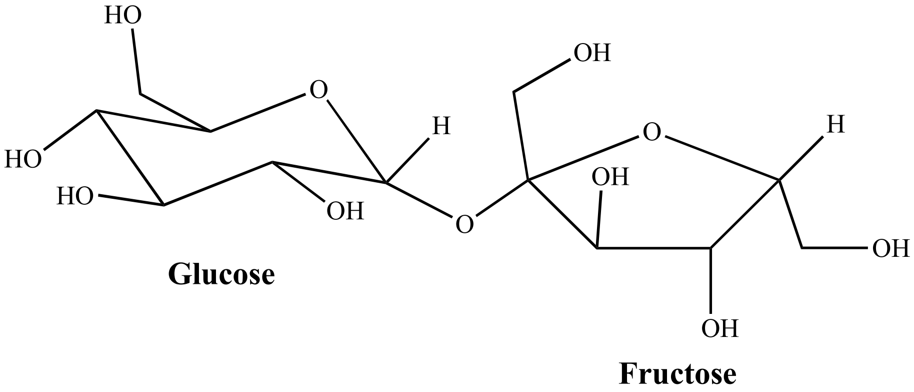
Example:



D-Fructose

Fructose is the sweetest sugar of all (sweetness index 180)

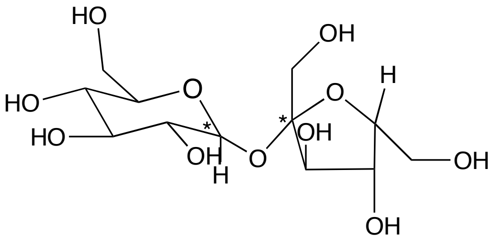
Is it a reducing or non-reducing sugar?
It is reducing since it contains a α-hydroxyl ketone group in open form and the cyclized form is a hemiacetal at anomeric position.
Example: a disaccharide



The structure shown is sucrose (table sugar). It is made up of a glucose and a fructose molecule (sweetness index 100)

Does this molecule have anomeric carbon?
Yes.

Identify the anomeric carbon.
They are highlighted with asterisks.

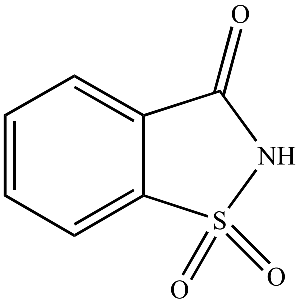


Glucose Fructose

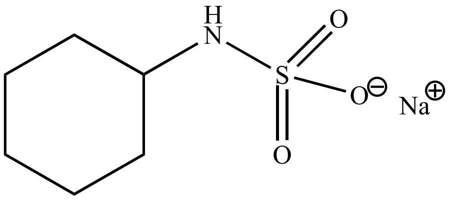
Are they acetals or hemiacetals?
They are acetals. In both cases, the carbon has two OR group attached. There is no free OH group.

Is this sugar reducing or non-reducing?
Non-reducing since the anomeric carbons has acetal groups.

Some artificial sweeteners are shown below:

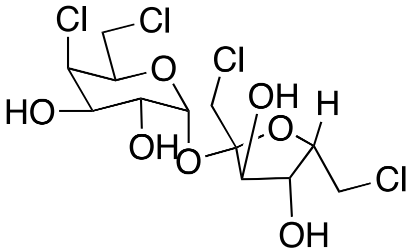


saccharin



sodium cyclamate

Although a small amount tastes a lot sweeter than sugars, these are suggested to be carcinogenic in very large doses.

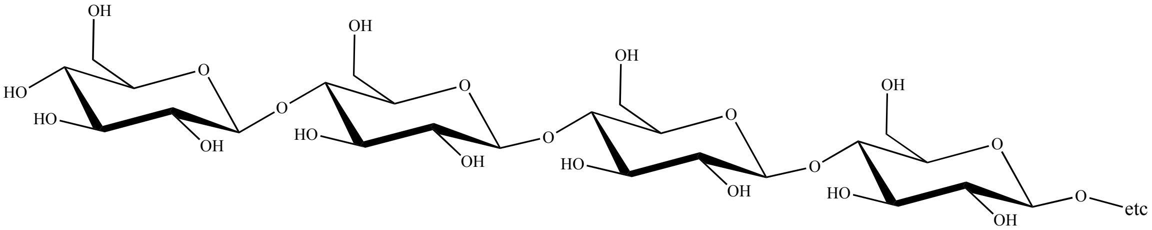


Splenda (sucralose)

Polysaccharides = polymers of sugars

Disaccharides = 2 sugar linked
Trisaccharides = 3 sugar linked
Tetrasaccharides = 4 sugar linked
.
Oligosaccharides = Polysaccharides

Example: Cellulose

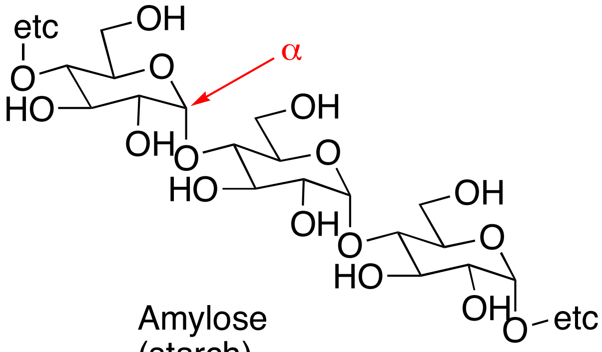


Cellulose is a polymer of simple repeating monosaccharide units (D-glucose).

Polysaccharides

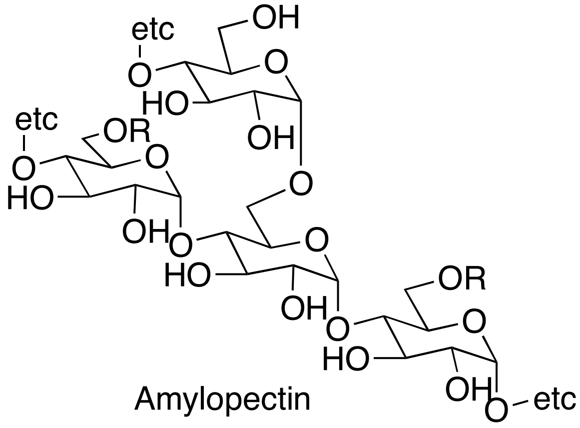
Many mammals cannot digest cellulose directly. Ruminants such as cows or goats have bacteria in their stomach to break it down to its simpler unit. The bacteria have a cellulose hydrolysis enzyme called cellulase which we do not have. Humans cannot metabolize β linkages.

Example: Amylose



In contrast, amylose is a polysaccharide with α linkage between each monosaccharide units. Amylose can be digested by humans. Starch is comprised of approximately 20% amylose.

Example: Amylopectin



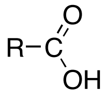
Amylopectin is the other component in starch (~ 80%), which is similar to glycogen.

OUTLINE & SECTION 4

Carboxylic Acids and Derivatives

Carboxylic acids are very important compounds in nature and serve as building blocks for preparing related derivatives such as esters and amides.

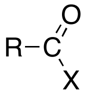
The general formula for a carboxylic acid includes a carbonyl and a hydroxyl group. The carboxylic acid can also be written in different ways and you should take note of these ways.



$R-C(=O)OH \equiv R-COOH \equiv R-CO_2H \equiv HO_2C-R$

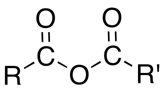
Many derivatives can be derived from carboxylic acids and below they are depicted in order of decreasing reactivity:

Acyl halides where X = F, Cl, Br, I



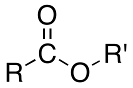
$R-C(=O)X$

Anhydrides where R doesn't have to equal R'

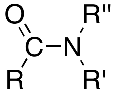


$R-C(=O)-O-C(=O)-R'$

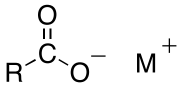
Esters where R doesn’t have to equal R’



Amides where R doesn’t have to equal R’ or R’’



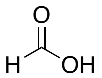
Carboxylate salts where M is usually a metal counter ion



Nomenclature of Carboxylic acids

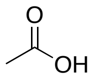
Carboxylic acids are derived from open chain alkanes and are systematically named by replacing the terminal “-e” of the corresponding alkane name with “-oic acid”. The carboxyl group is always numbered C1 in this system. Alternatively, compounds that have a –COOH group bonded to a ring are named with the suffix “-carboxylic acid”. In this system, the carboxylic acid carbon is attached to C1 and is not itself numbered in this system.

For historical reasons having to do with the fact that many carboxylic acids were among the first compounds isolated and purified, there are several common names given to these acids. These common names, along with the systematic names are given below where the common names are given first. (Know the names of the acids below)



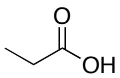
formic acid

methanoic acid



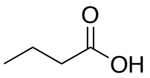
acetic acid

ethanoic acid



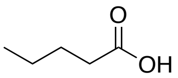
propionic acid

propanoic acid



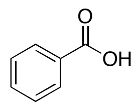
butyric acid

butanoic acid



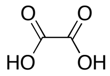
valeric acid

pentanoic acid



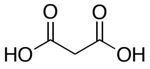
Benzoic Acid

Dicarboxylic acids are also common in nature, know the first 5 common names:



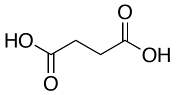
oxalic acid

ethanedioic acid



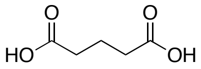
malonic acid

propanedioic acid



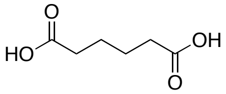
succinic acid

butanedioic acid



glutaric acid

pentanedioic acid



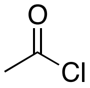
adipic acid

hexanedioic acid

Acid halides, acyl halides

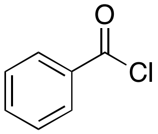
The acid/acyl halides are systematically named by dropping “ic acid” and adding “yl halide”

Examples:

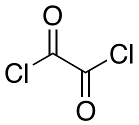


acetyl chloride

ethanoyl chloride



benzoyl chloride

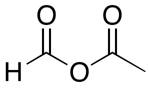


oxalyl dichloride

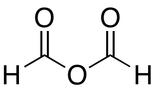
Anhydrides

The anhydrides are named by changing “acid” to “anhydride”.

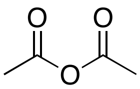
Examples:



formic acetic anhydride

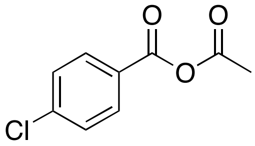


formic anhydride



acetic anhydride

ethanoic anhydride



acetic 4-chlorobenzoic anhydride