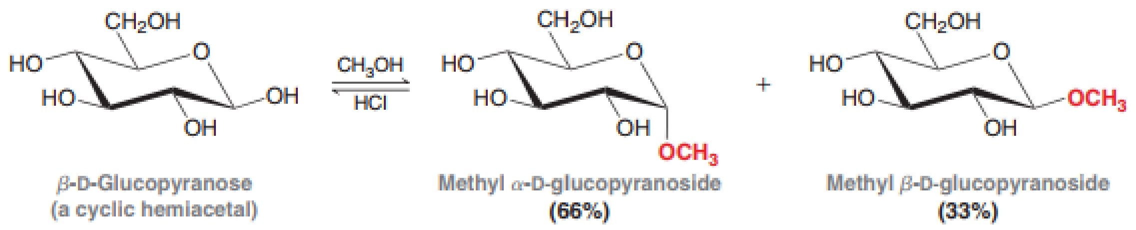
Glycosides in nature

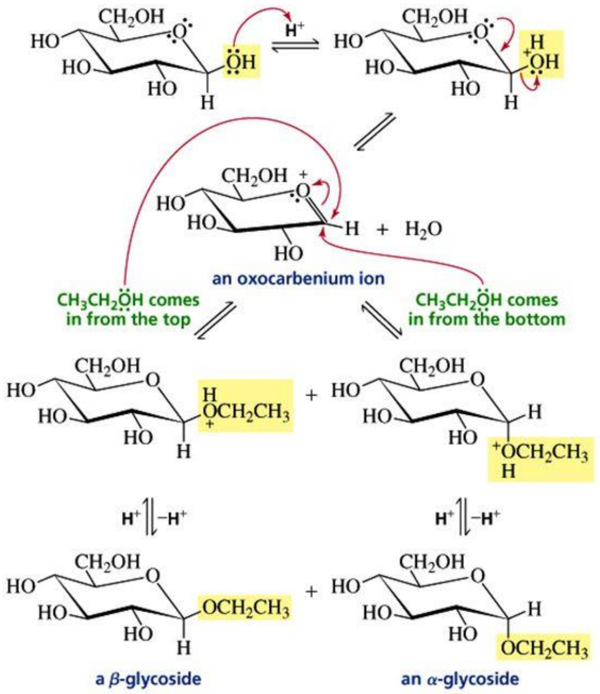
Earlier, we have seen that the cyclic hemiacetal (or hemiketal) formed by monosaccharide can react with alcohol, thiols, and amines to form an *O*-, *S*-, or *N*-acetal (or ketal). The acetal (or ketal) of sugar is called a **glycoside**, and the purpose of attaching these compounds to a carbohydrate is often to improve solubility or transport across membranes - to expel a toxin from the cell, for example.

The bond between the anomeric cabon and alkoxy oxygen is called glycosidic bond and the glycosides are named by replacing the "ose" ending of sugar's name with "oside". The reaction of single anomer leads to the formation of two stereoisomers i.e. α- and β-glycosides. If the OR bond is down, it is an α-glycoside; if up, a β-glycoside.



The mechanism of the reaction shows why both glycosides are formed. The OH group bonded to anomeric carbon becomes protonated in the acidic solution, and a nonbonding pair of electrons on the ring oxygen helps expel a molecule of water. The anomeric carbon in the resulting oxonium ion is sp^2 hybridized, causing that part of the molecule to be planar. When the alcohol comes in from the top of the plane, the β-glycoside is formed; when the alcohol comes in from bottom of the plane, the α-glycoside is formed.

Mechanism of Glycoside Formation



Because glycosides are acetals (or ketals), they are not in equilibrium with the open-chain aldehyde (or ketone) in aqueous solution. Thus they cannot be oxidized by reagents such as Ag^+ or Br_2. Glycosides therefore are non-reducing sugars. On the other hand the hemiacetals (or hemiketals) are in equilibrium with open chain sugars and thus reducing in nature.

Disaccharide

If the hemiacetal group of monosaccharide uses an alcohol group of another monosaccharide to form an acetal, the glycoside that is formed is a disaccharide.

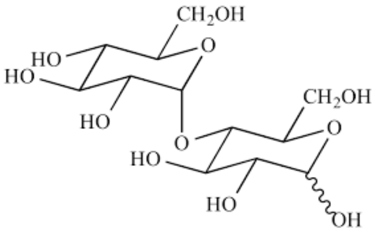
Maltose

Maltose, a disaccharide is used in baby foods and malted milk. It is the principal disaccharide obtained from the hydrolysis of starch by an enzyme in saliva called α-1,4-glucan 4-gluconohydrolase, The enzyme α-1,4-glucan maltohydrolase, found in sprouted barley (malt), convert starch specifically into maltose units. In beer making, malt is used for the conversion of starches from corn or other sources into maltose.

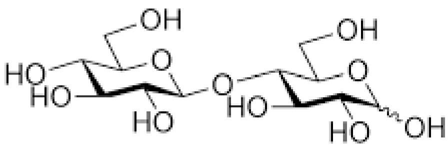
Maltose contains two D-glucose subunits hooked together by an α-1,4'-glycosidic linkage. The linkage is between C-1 of one sugar subunit and C-4 of the other. The 'prime' superscript indicates that C-4 is not in the same ring as C-1. It is an α-1,4'-glycosidic linkage because the oxygen atom involved in the glycosidic linkage is in the α-position. In the disaccharide, the configuration of the anomeric carbon not involved in acetal formation is not specified because maltose can exist in both α– and β–forms. Because maltose can exist in both α– and β–forms, mutarotation occurs when crystals of one form are dissolved in a solvent. Maltose is a reducing sugar because the right-hand subunit is a hemiactal and therefore is in equilibrium with the open-chain aldehyde that is easily oxidized. An enzyme in yeast (a-glucosidase) catalyzes the hydrolysis of maltose into D-glucose units, which is acted upon by other enzymes to yield ethanol.

$$\text{Starch} \xrightarrow[\text{H+ or enzyme}]{H_2O} \text{maltose} \xrightarrow[\text{H+ or enzyme}]{H_2O} \text{D-glucose} \xrightarrow[\text{enzyme}]{} \text{Ethanol}$$

Maltose



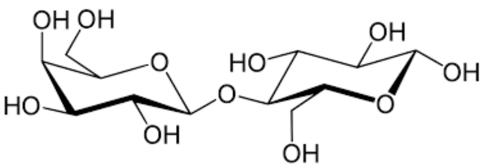
Cellobiose



Cellobiose

A disaccharide obtained from the hydrolysis of cellulose also contains two D-glucose subunits. It differs from maltose in that the two glucose subunits are hooked together by a β-1,4'-glycosidic linkage. It can also exist in α– and β–forms, and is a reducing sugar.

Lactose



Lactose is a disaccharide found in milk. It constitutes 4.5% of cow's milk by weight and 6.5 % of human milk. One of the subunits of lactose is D-galactose, and the other is D-glucose. The D-galactose subunit is acetal and D-glucose subunit is a hemiacetal. The subunits are joined through a β-1,4’-glycosidic linkage. Because one of the unit is hemiacetal, lactose is a reducing sugar and undergoes mutarotation.

Lactose intolerance

Lactose intolerance is due to the lack of the enzyme lactase in the small intestines to break lactose down into D-galactose and D-glucose. Cats and dogs loose their intestinal lactase when they become adults and therefore are no longer able to digest lactose. Consequently when they are fed milk or milk products, the undegraded lactose causes digestive problems such as bloating, abdominal pain, and diarrhea. This is because only monosaccharides can pass into the bloodstream, so lactose has to pass undigested into the large intestine. When humans have stomach flu or other intestinal disturbances, they can temporarily lose their lactase, thereby becoming lactose intolerant. Some humans looses their lactase permanently as they mature. This occurs in approximately 10% of the white population. It is much more common in people whose ancestors came from non-dairy producing countries. For example, only 3% of Danes (from Denmark) but 97% of Thais are lactose intolerant. Such a condition which is also called lactose malabsorption, is usually harmless, but its symptoms can be uncomfortable.

$$\text{Lactose} \xrightarrow[(\beta\text{-galactosidase})]{\text{Lactase}} \text{Glucse + Galactose}$$

Galactosemia

After lactose is degraded into glucose and galactose, the galactose has to be converted into glucose before it can be used by cells. Those who do not have the enzyme that converts galactose into glucose have the genetic disease known as ‘galactosemia’. Without this enzyme, galactose accumulates in the bloodstream and urine. This accumulation can cause mental retardation in infants and even death. Galactosemia is treated by excluding galactose from the diet. (An artificial milk made from soyabeans may be substituted.)

References:

a. Organic Chemistry: Clayden, Greeves, Warren
b. Organic Chemistry: Fessenden and Fessenden
c. Organic Chemistry: Paula, Yurkanis, Bruice