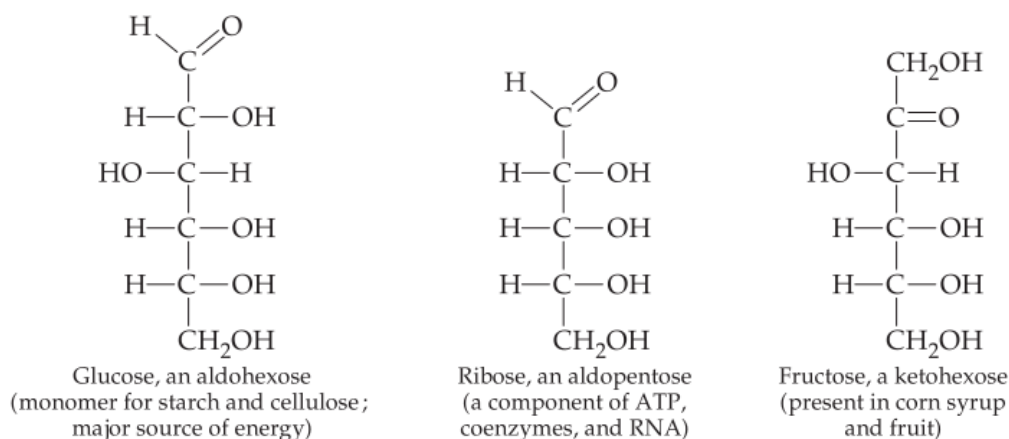# Carbohydrates

Carbohydrates are a large class of naturally occurring polyhydroxy aldehydes and ketones. **Monosaccharides**, sometimes known as **simple sugars**, are the simplest carbohydrates. They have from three to seven carbon atoms, and each contains one aldehyde or one ketone functional group. If the sugar has an aldehyde group, it is classified as an **aldose**. If it has a ketone group, the sugar is classified as a **ketose**. The aldehyde group is always at the end of the carbon chain, and the ketone group is always on the second carbon of the chain. In either case, there is a —CH$_2$OH group at the other end of the chain.

Monosaccharides

An aldose

A ketose
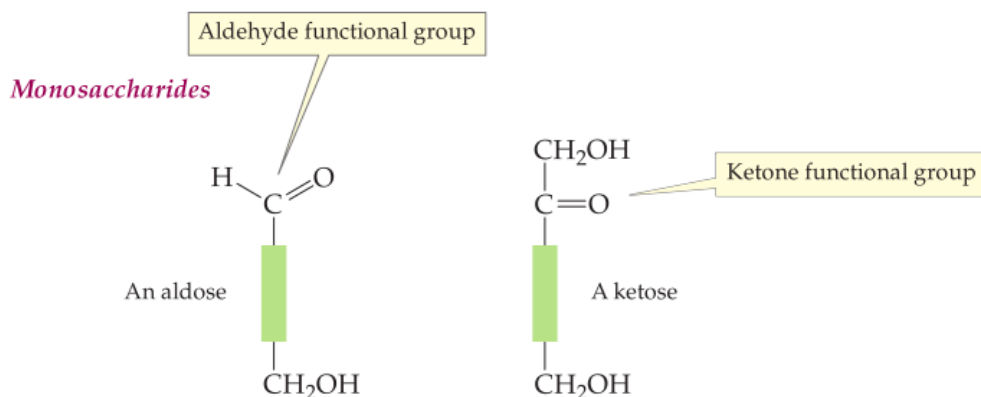
There are hydroxyl groups on all the carbon atoms between the carbonyl carbon atom and the —CH$_2$OH at the other end, and also on the end carbon next to a ketone group, as illustrated in the following three structures. The family-name ending *-ose* indicates a carbohydrate, and simple sugars are known by common names like *glucose, ribose,* and *fructose* rather than systematic names.


Glucose, an aldohexose
(monomer for starch and cellulose;
major source of energy)

Ribose, an aldopentose
(a component of ATP,
coenzymes, and RNA)

Fructose, a ketohexose
(present in corn syrup
and fruit)

The number of carbon atoms in an aldose or ketose is specified by the prefixes *tri-, tetr-, pent-, hex-,* or *hept-*. Thus, glucose is an aldo*hex*ose (*aldo-* = aldehyde, *-hex* = 6 carbons; *-ose* = sugar); fructose is a keto*hex*ose (a 6-carbon ketone sugar); and ribose is an aldo*pent*ose (a 5-carbon aldehyde sugar). Most naturally occurring simple sugars are aldehydes with either 5 or 6 carbons.

Because of their many functional groups, monosaccharides undergo a variety of structural changes and chemical reactions. They react with each other to form **disaccharides** and **polysaccharides** (also known as **complex carbohydrates**), which are polymers of monosaccharides. Their functional groups are involved in reactions with alcohols, lipids or proteins to form biomolecules with specialized functions.

Handedness of Carbohydrates

Glyceraldehyde, an aldotriose and the simplest naturally occurring carbohydrate, has the structure shown below. Because four different groups are bonded to the number 2 carbon atom, this molecule is also chiral.
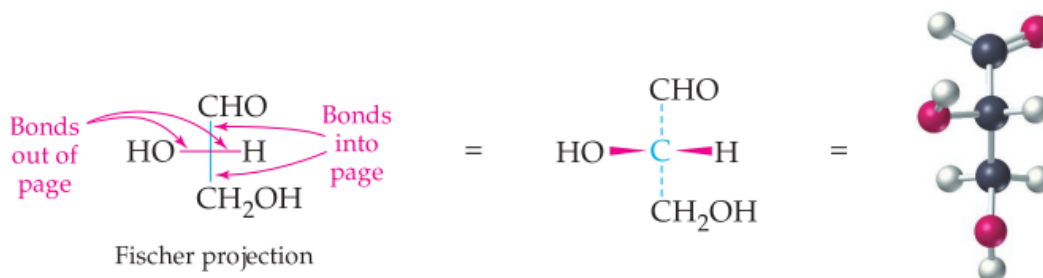

D-Glyceraldehyde
Right-handed

L-Glyceraldehyde
Left-handed
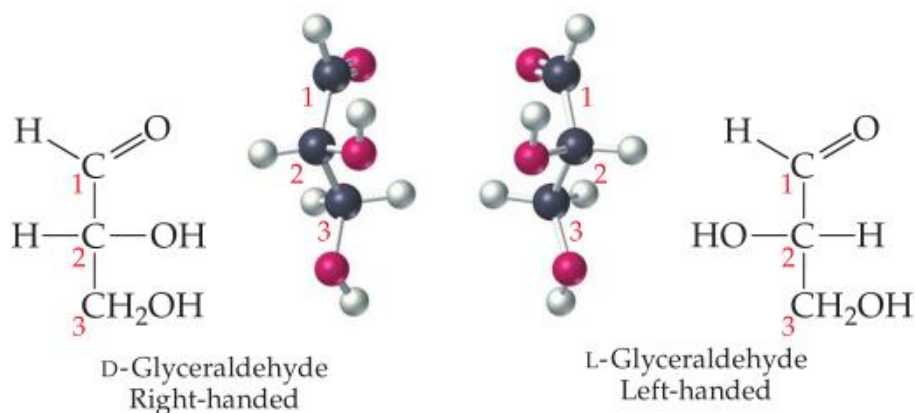
Chiral compounds lack a plane of symmetry and exist as a pair of enantiomers in either a "right-handed" D form or a "left-handed" L form. Like all enantiomers, the two forms of glyceraldehyde have the same physical properties except for the way in which they affect polarized light.


Erythrose

Threose
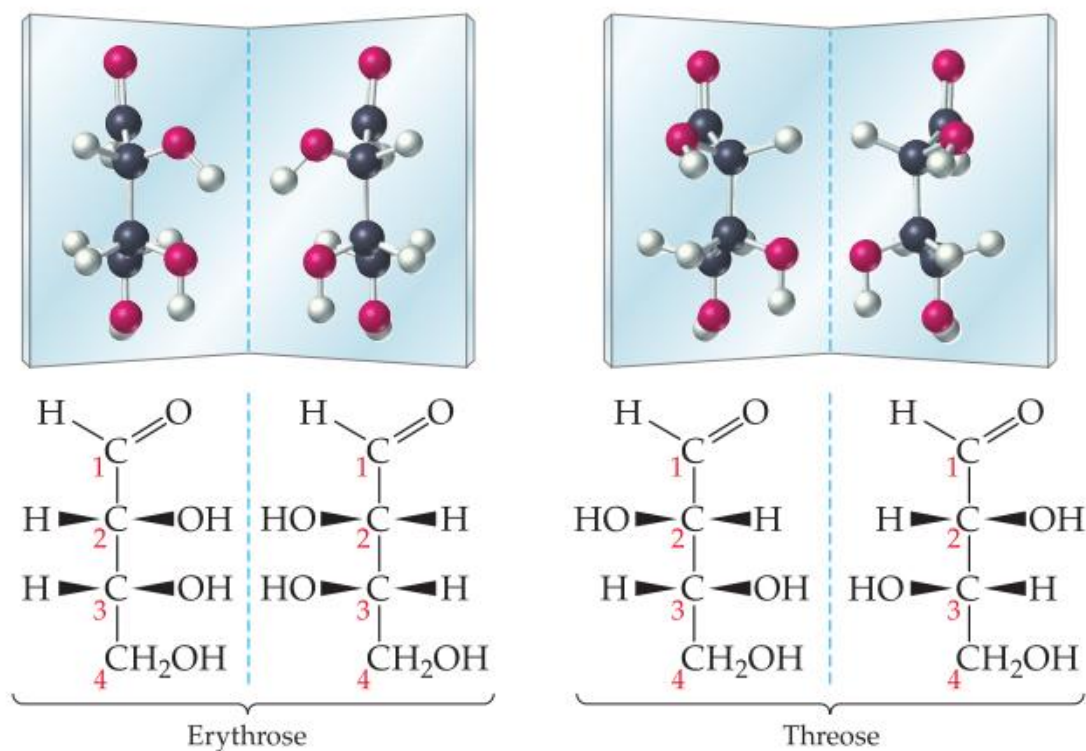
In general, a compound with n chiral carbon atoms has a maximum of 2^n possible stereoisomers and half that many pairs of enantiomers. The aldotetroses, for example, have $n = 2$ so that $2^n = 2^2 = 4$, meaning that four stereoisomers are possible. Glucose, an aldohexose, has four chiral carbon atoms and a total of $2^4 = 16$ possible stereoisomers (8 pairs of isomers). All 16 stereoisomers of glucose are known. (In some cases, fewer than the maximum predicted number of stereoisomers exist because some of the molecules have symmetry planes that make them identical to their mirror images.)

In a Fischer projection, the aldehyde or ketone carbonyl group of a monosaccharide is always placed at the top. The result is that —H and —OH groups projecting above the page are on the left and right of the chiral carbons, and groups projecting behind the page are above and below the chiral carbons. The Fischer projection of one of the enantiomers of glyceraldehyde is therefore interpreted as follows:

Fischer projection of a glyceraldehyde enantiomer

Fischer projection

For comparison, the same glyceraldehyde enantiomer is represented below in the conventional manner, showing the tetrahedron of bonds to the chiral carbon.
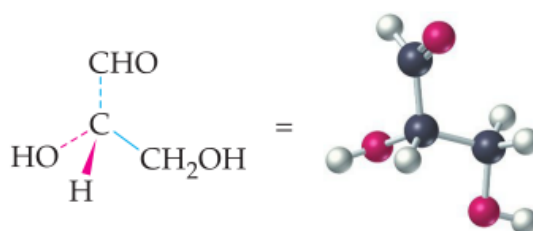

Monosaccharides are divided into two families—the **D sugars** and the **L sugars**—based on their structural relationships to glyceraldehyde. Consistently writing monosaccharide formulas as Fischer projections allows us to identify the D and L forms at a glance. Look again at the structural formulas of the D and L forms of glyceraldehyde.


D-Glyceraldehyde   L-Glyceraldehyde
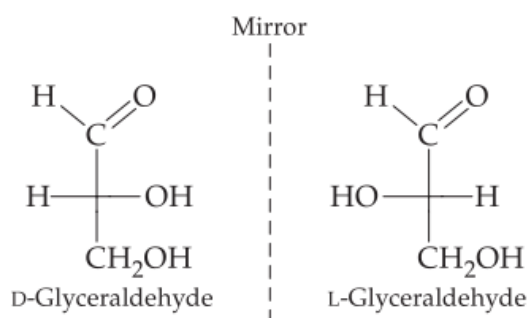
The designations D and L derive from the Latin *dextro* for "right" and *levo* for "left." *In all Fischer projections, the D form of a monosaccharide has the hydroxyl group on the chiral carbon atom farthest from the carbonyl group pointing toward the right, whereas the mirror-image L form has the hydroxyl group on this same carbon pointing toward the left.*
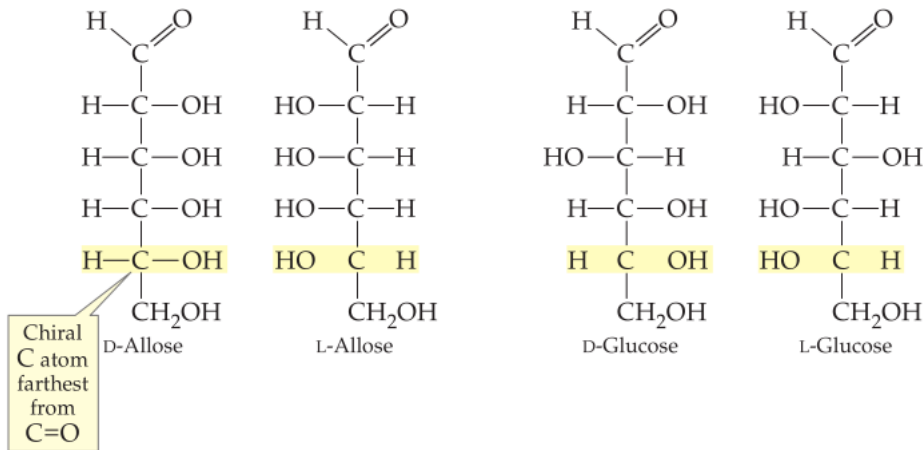
Structure of Glucose and Other Monosaccharides
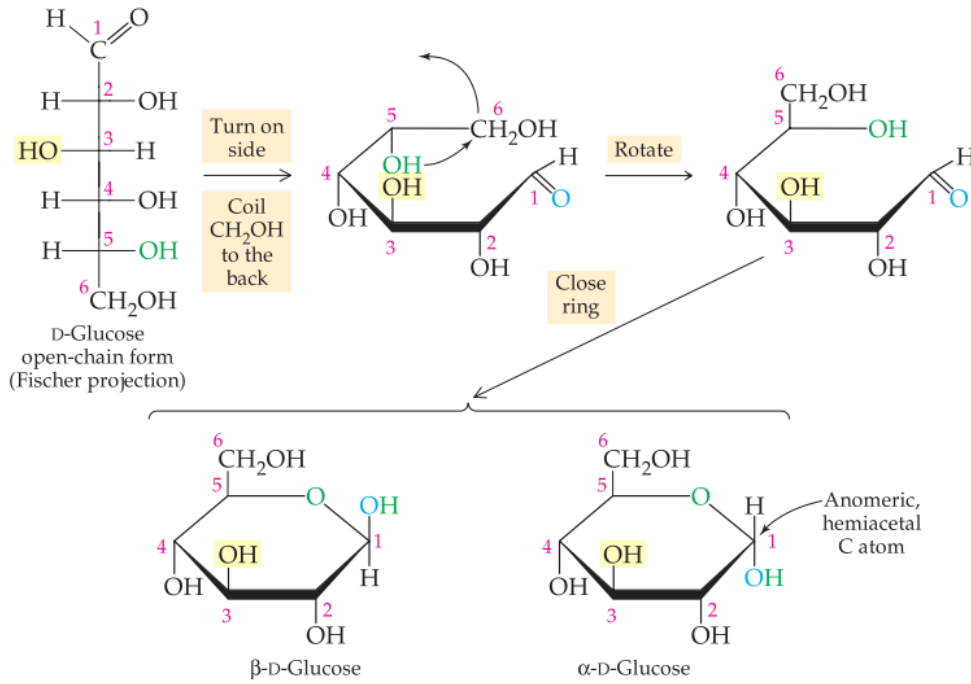
Cyclic monosaccharides that differ only in the positions of substituents at carbon 1 are known as **anomers**, and carbon 1 is said to be an **anomeric carbon atom**. It was the carbonyl carbon atom (C1 in an aldose and C2 in a hexose) that is now bonded to two O atoms. Note that the α and β anomers of a given sugar are not optical isomers because they are not mirror images.
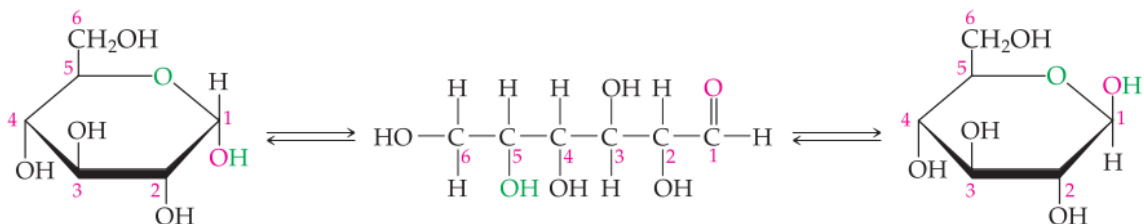
Relative Sweetness of Some Sugars and Sugar Substitutes

| NAME	TYPE	SWEETNESS
Lactose	Disaccharide	16
Galactose	Monosaccharide	30
Maltose	Disaccharide	33
Glucose	Monosaccharide	75
Sucrose	Disaccharide	100
Fructose	Monosaccharide	175
Cyclamate	Artificial	3000
Aspartame	Artificial	15,000
Saccharin	Artificial	35,000
Sucralose	Artificial	60,000

Galactose

D-Galactose is widely distributed in plant gums and pectins, the sticky polysaccharides present in plant cells. It is also a component of the disaccharide lactose (milk sugar) and is produced from lactose during digestion. Like glucose, galactose is an aldohexose; it differs from glucose only in the spatial orientation of the —OH group at carbon 4. In the body, galactose is converted to glucose to provide energy

and is synthesized from glucose to produce lactose for milk and compounds needed in brain tissue.
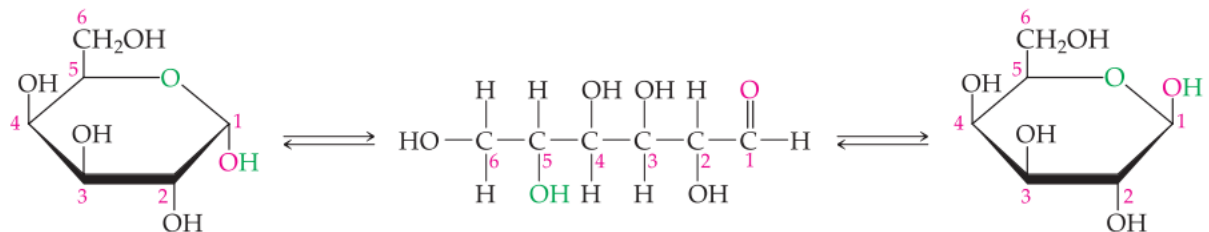

Fructose

D-Fructose, often called *levulose* or *fruit sugar*, occurs in honey and many fruits. It is one of the two monosaccharides combined in the disaccharide sucrose. Fructose is produced commercially in large quantities by hydrolysis of cornstarch to make high fructose corn syrup. Like glucose and galactose, fructose is a 6-carbon sugar. However, it is a ketohexose rather than an aldohexose. In solution, fructose forms five-membered rings:
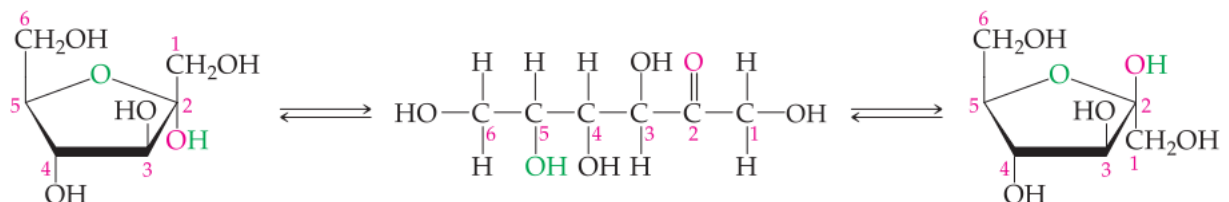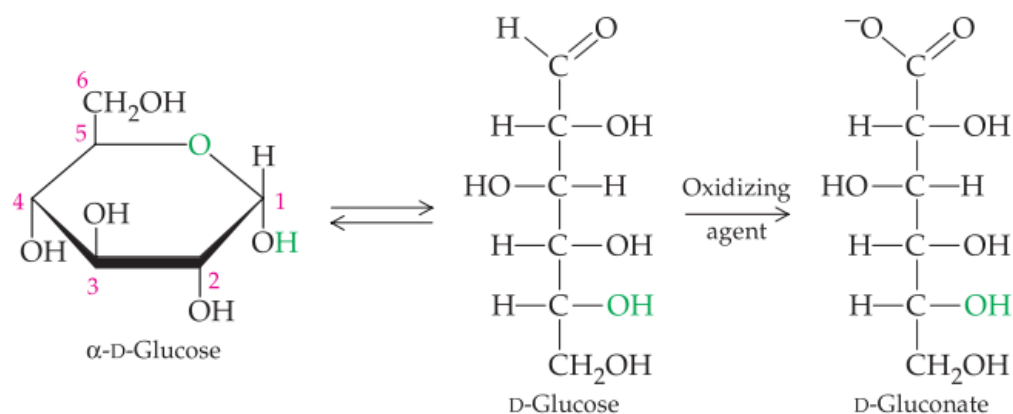

Ribose and 2-Deoxyribose
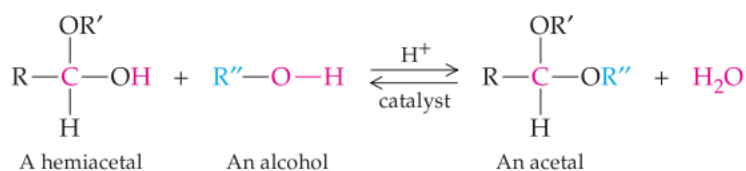Ribose and its relative 2-deoxyribose are both 5-carbon aldehyde sugars.

β-D-Ribose   β-D-2-Deoxyribose
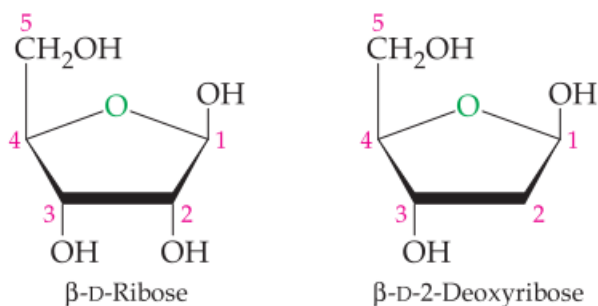
Reactions of Monosaccharides

Reaction with Oxidizing Agents: Reducing Sugars

α-D-Glucose   D-Glucose   D-Gluconate

Reaction with Alcohols: Glycoside and Disaccharide Formation

A hemiacetal   An alcohol   An acetal

Because glucose and other monosaccharides are cyclic hemiacetals, they also react with alcohols to form acetals, which are called **glycosides**. In a glycoside, the —OH group on the anomeric carbon atom is replaced by an —OR group. For example, glucose reacts with methanol to produce methyl glucoside. (Note that a *glu*coside is a cyclic acetal formed by glucose. A cyclic acetal derived from *any* sugar is a *gly*coside.)

Formation of a glycoside

α-D-Glucose   Methyl α-D-glucoside, an acetal
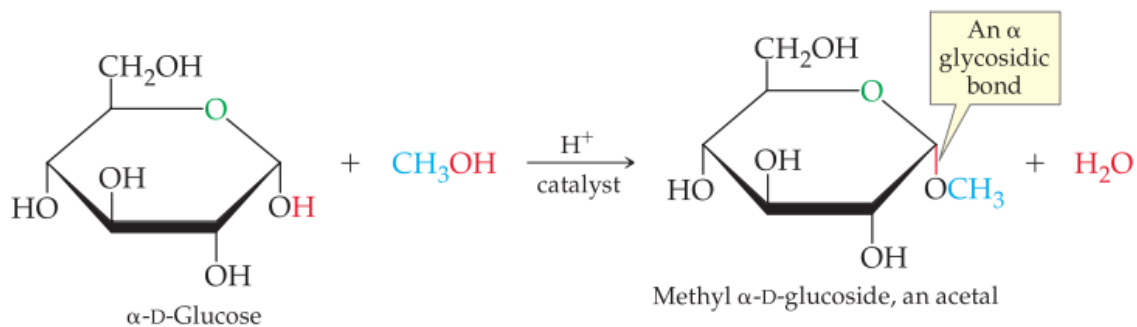
The bond between the anomeric carbon atom of the monosaccharide and the oxygen atom of the —OR group is called a **glycosidic bond**. Since glycosides like the one shown above do not contain hemiacetal groups that establish equilibria with open-chain forms, they are *not* reducing sugars.

In larger molecules, including disaccharides and polysaccharides, monosaccharides are connected to each other by glycosidic bonds. For example, a disaccharide forms by reaction of the anomeric carbon of one monosaccharide with an —OH group of a second monosaccharide.
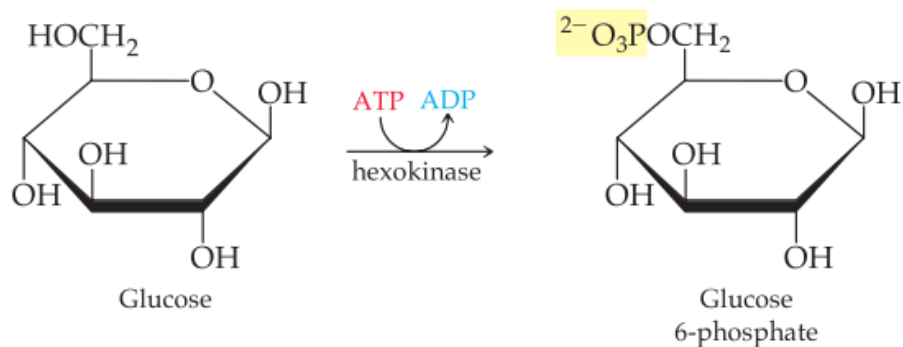
*Formation of a glycosidic bond between two monosaccharides*

An α glycosidic bond
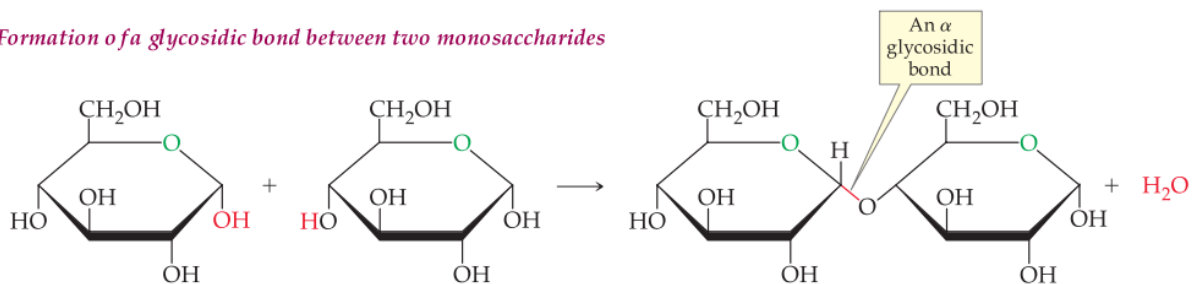
Hydrolysis of a disaccharide
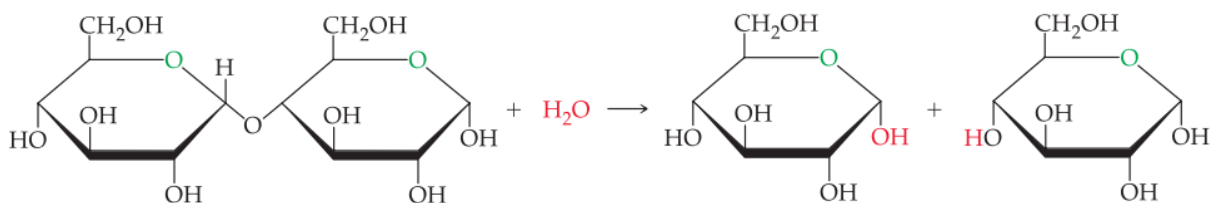
Formation of Phosphate Esters of Alcohols

Glucose →(ATP ADP, hexokinase)→ Glucose 6-phosphate

Disaccharides

Every day, you eat a disaccharide—sucrose, common table sugar. Sucrose is made of two monosaccharides, one glucose and one fructose, covalently bonded to each other. Sucrose is present in modest amounts, along with other mono- and disaccharides, in most fresh fruits and many fresh vegetables. But most sucrose in our diets has been added to something. Perhaps you add it to your coffee or tea. Or it is there in a ready-to-eat food product that you buy, maybe breakfast cereal, ice cream, or a "super-sized" soda, or even bread. Excessive consumption of high-sucrose foods has been blamed for everything from criminal behavior to heart disease to hyperactivity in children, but without any widely accepted scientific proof. A proven connection with heart disease does exist, of course, but by way of the contribution of excess sugar calories to obesity.

Disaccharide Structure

An α-1,4 acetal link

An α-1,4 disaccharide

A β-1,4 acetal link
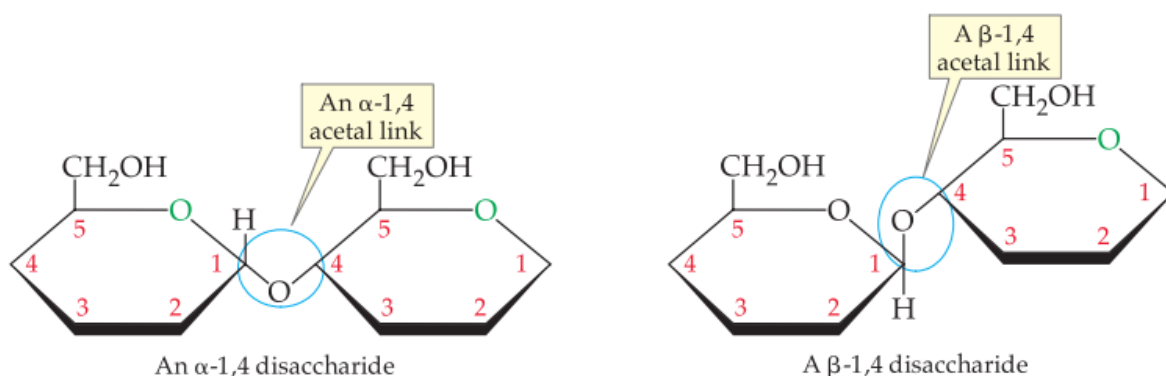
A β-1,4 disaccharide

The three naturally occurring disaccharides discussed in the following sections are the most common ones. They illustrate the three different ways monosaccharides are linked: by a glycosidic bond in the α orientation (maltose), a glycosidic bond in the β orientation (lactose), or a bond that connects two anomeric carbon atoms (sucrose).

Maltose

Maltose, often called malt sugar, is present in fermenting grains and can be prepared by enzyme-catalyzed degradation of starch. It is used in prepared foods as a sweetener. In the body, it is produced during starch digestion by α-amylase in the small intestine and then hydrolyzed to glucose by a second enzyme, maltase.

Two α-D-glucose molecules are joined in maltose by an α-1,4 link. A careful look at maltose shows that it is both an acetal (at C1 in the glucose on the left below) and a hemiacetal (at C1 in the glucose on the right below). Since the acetal ring on the left does not open and close spontaneously, it cannot react with an oxidizing agent. The hemiacetal group on the right, however, establishes equilibrium with the aldehyde, making maltose a reducing sugar.

Glycosidic bond at C1

α-1,4 link

Hemiacetal at C1

α-D-Glucose

α-D-Glucose

Maltose
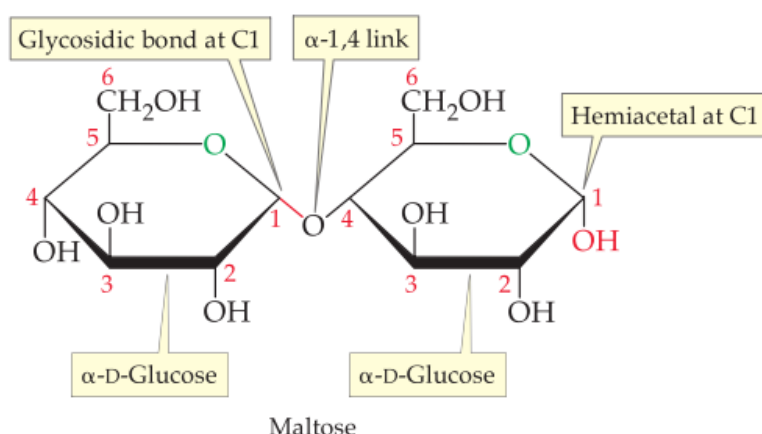
Lactose

Lactose, or milk sugar, is the major carbohydrate in mammalian milk. Human milk, for example, is about 7% lactose. Structurally, lactose is a disaccharide composed of β-D-galactose and β-D-glucose. The two monosaccharides are connected by

a β-1,4 link. Like maltose, lactose is a reducing sugar because the glucose ring (on the right in the following structure) is a hemiacetal at C1.
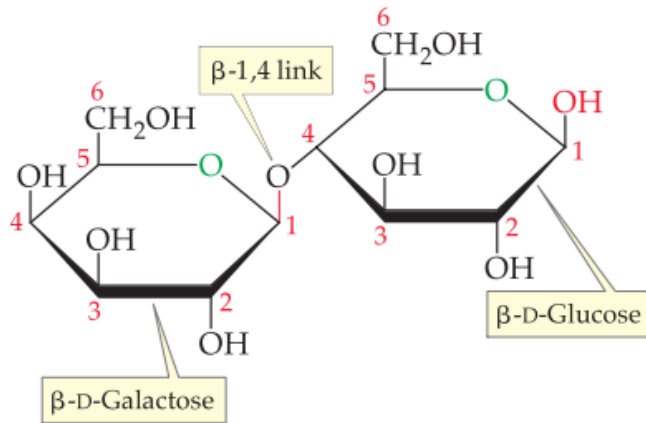

Lactose

Sucrose

Sucrose—plain table sugar—is probably the most common highly purified organic chemical used in the world. Sugar beets and sugarcane are the most common sources of sucrose. Hydrolysis of sucrose yields one molecule of D-glucose and one molecule of D-fructose. The 50:50 mixture of glucose and fructose that results, often referred to as *invert sugar*, is commonly used as a food additive because it is sweeter than sucrose.
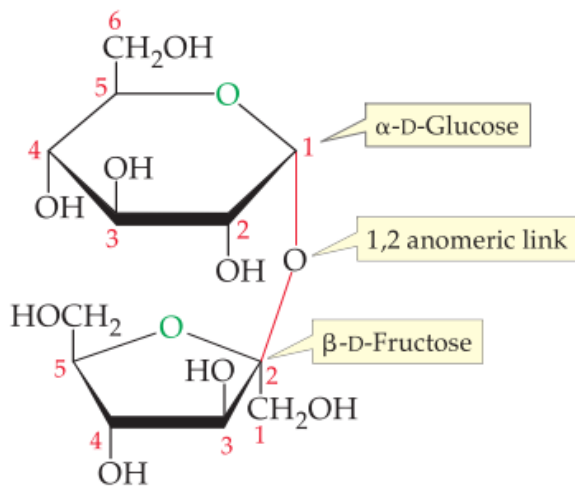

Sucrose

Connective Tissue and Polysaccharides

Hyaluronate repeating unit

Chondroitin 6-sulfate repeating unit
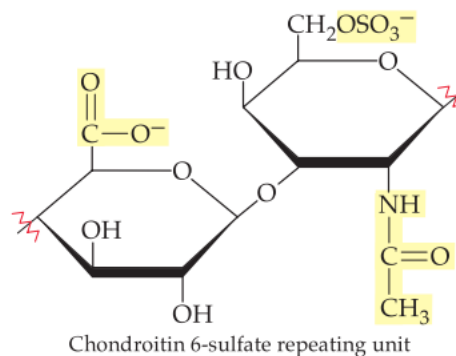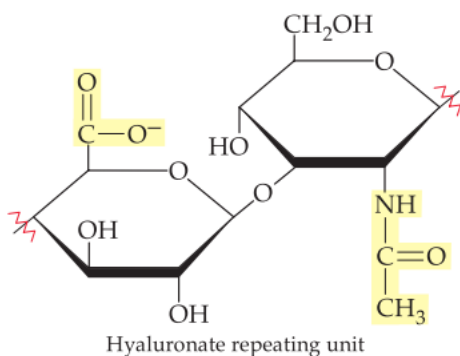
Hyaluronate molecules contain up to 25,000 disaccharide units and form a quite rigid, very viscous mixture with water molecules attracted to its negative charges. This mixture is the *synovial fluid* that lubricates joints. It is also present within the eye. *Chondroitin 6-sulfate* (also the 4-sulfate) is present in tendons and cartilage, where it is linked to proteins. It has been used in artificial skin. Chondroitin sulfates and glucosamine sulfate are available as dietary supplements in health food stores and are promoted as cures for osteoarthritis, in which cartilage at joints deteriorates. They are prescribed by veterinarians for arthritic dogs, and there is anecdotal evidence for benefits in humans.

Heparin

Another of the polysaccharides associated with connective tissue, heparin is valuable medically as an *anticoagulant* (an agent that prevents or retards the clotting of blood). Heparin is composed of a variety of different monosaccharides, many of them containing sulfate groups.
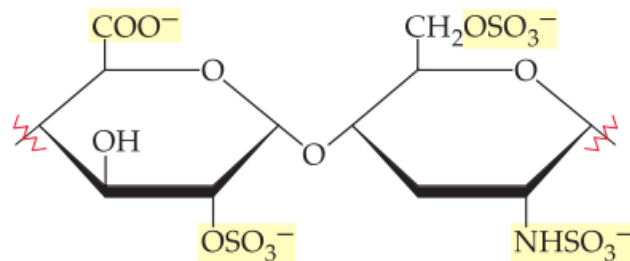

Example of repeating unit in heparin

Notice the large number of negative charges in this heparin repeating unit. Heparin binds strongly to a blood-clotting factor and in this way prevents clot formation. It is used clinically to prevent clotting after surgery or serious injury. Also, a coating of heparin is applied to any surfaces that will come into contact with blood that must not clot, such as the interiors of test tubes used for blood samples collected for analysis or materials in prosthetic implants for the body.

Glycoproteins

Proteins that contain short carbohydrate chains (*oligosaccharide* chains) are known as **glycoproteins**. (The prefix *glyco-* always refers to carbohydrates.) The carbohydrate is connected to the protein by a glycosidic bond between an anomeric carbon and a side chain of the protein. The bond is either a C—N glycosidic bond or a C—O glycosidic bond:
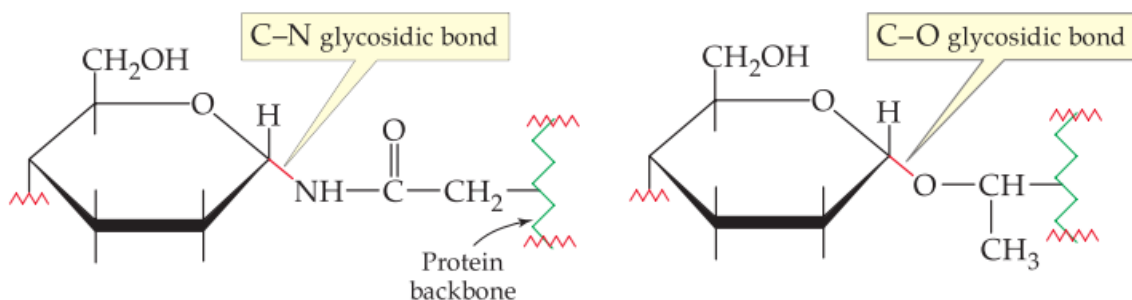

Some Important Polysaccharides

Polysaccharides are polymers of tens, hundreds, or even many thousands of monosaccharides linked together through glycosidic bonds of the same type as in maltose and lactose. Three of the most important polysaccharides are *cellulose, starch,* and *glycogen.* The repeating units making up cellulose and starch are compared in the following structures:

Cellulose repeating unit

Starch and glycogen repeating unit
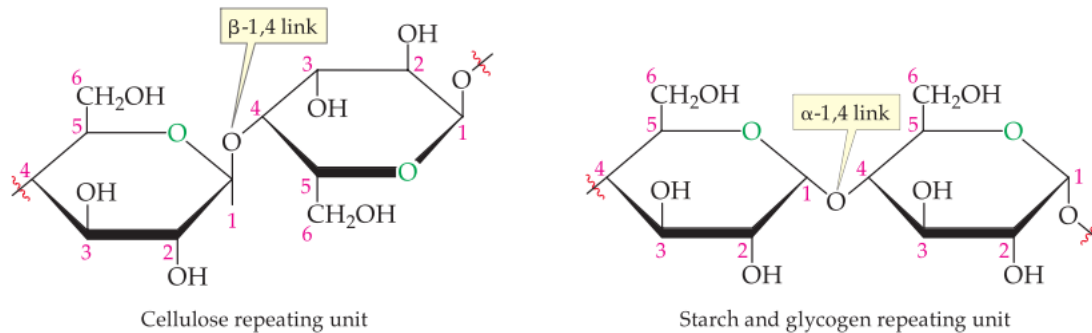
Cellulose

Cellulose is the fibrous substance that provides structure in plants. Each huge cellulose molecule consists of several thousand β-D-glucose units joined in a long, straight chain by β-1,4 links. The bonding in cellulose is illustrated above by the flat hexagons we have used so far for monosaccharides. In reality, because of the tetrahedral bonding at each carbon atom, the carbohydrate rings are not flat but are bent up at one end and down at the other in what is known as the *chair conformation*:


Chair conformation of β-D-glucose
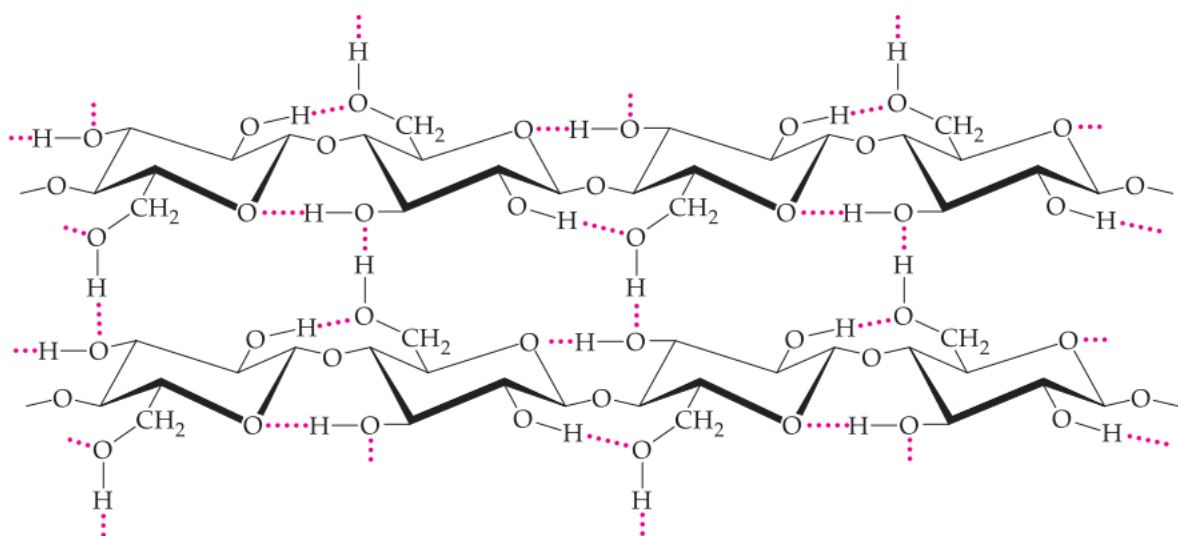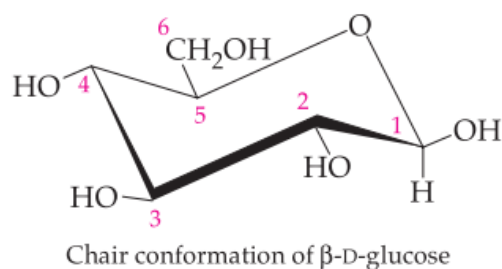
Starch

Starch, like cellulose, is a polymer of glucose. In starch, individual glucose units are joined by α-1,4 links rather than by the β-1,4 links of cellulose. Starch is fully digestible and is an essential part of the human diet. It is present only in plant material; our major sources are beans, the grains wheat and rice, and potatoes.
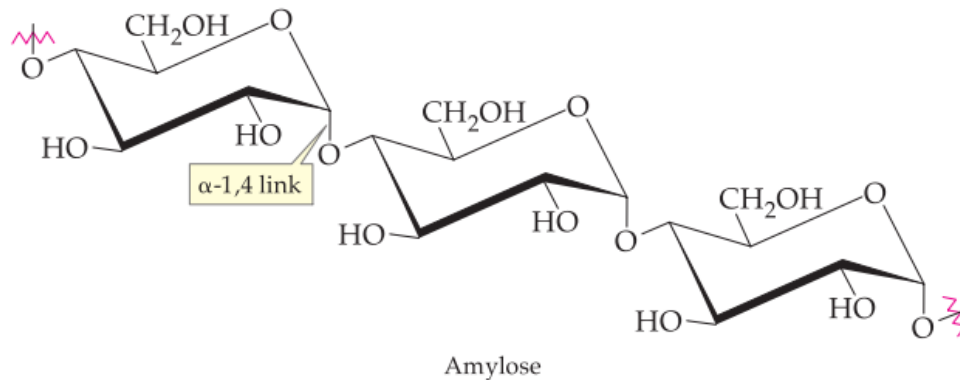
Amylose

Amylopectin, which accounts for about 80% of starch, is similar to amylose but has much larger molecules (up to 100,000 glucose units per molecule) and has α-1,6 branches approximately every 25 units along its chain. A glucose molecule at one of these branch points (shaded below) is linked to three other sugars. Amylopectin is not water-soluble.
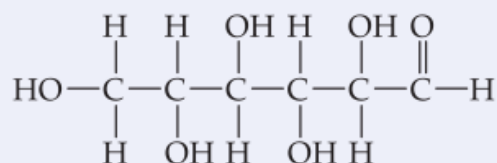
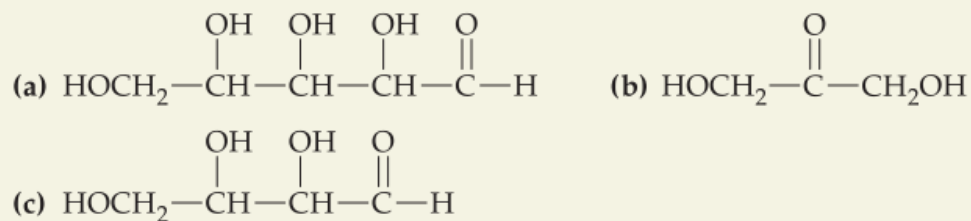*Branch point in amylopectin (also glycogen)*
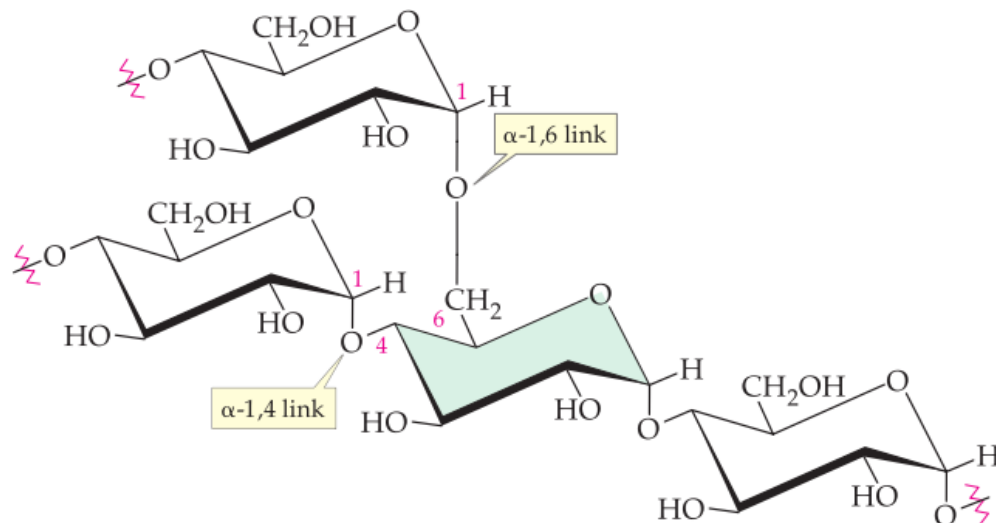
PROBLEM
1.

Classify the monosaccharide shown as an aldose or a ketose, and name it according to its number of carbon atoms.

2.

Classify the following monosaccharides as an aldose or a ketose, and name each according its number of carbon atoms.

(a) HOCH₂—CH—CH—CH—C—H with OH, OH, OH above the three CH carbons and O (double bond) above the C—H carbon

$$\text{(a)} \quad \underset{}{HOCH_2}-\overset{OH}{\underset{|}{CH}}-\overset{OH}{\underset{|}{CH}}-\overset{OH}{\underset{|}{CH}}-\overset{O}{\underset{||}{C}}-H$$

$$\text{(b)} \quad HOCH_2-\overset{O}{\underset{||}{C}}-CH_2OH$$

$$\text{(c)} \quad HOCH_2-\overset{OH}{\underset{|}{CH}}-\overset{OH}{\underset{|}{CH}}-\overset{O}{\underset{||}{C}}-H$$

3.

Notice in structures (a)–(d) below that the bottom carbon and its substituents are written as CH₂OH in every case. How does the C in this group differ in each case from the C atoms above it? Why must the locations of the H atoms and —OH groups attached to the carbons between this one and the carbonyl group be shown?
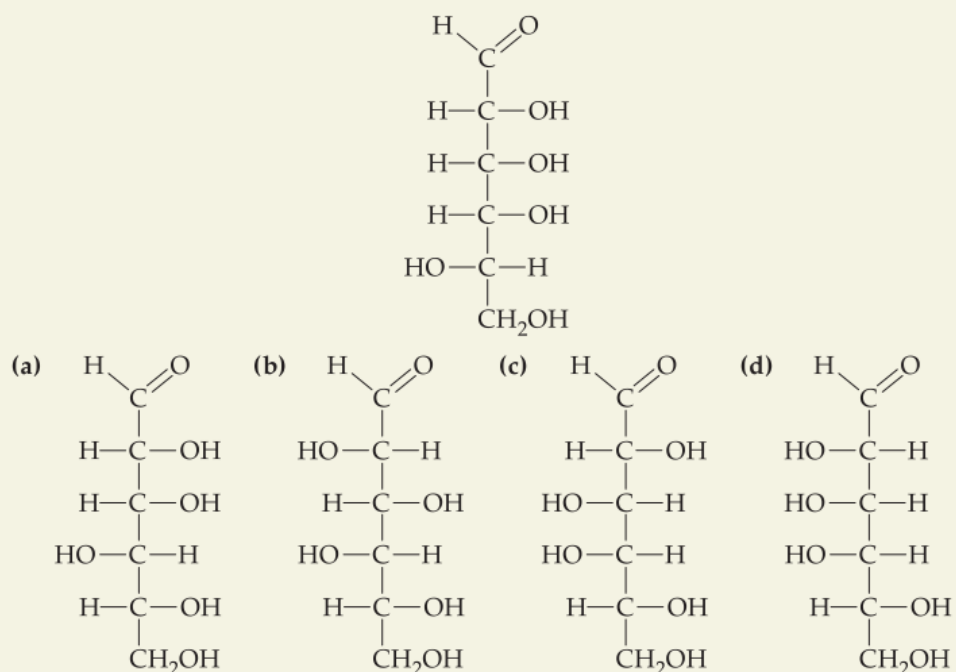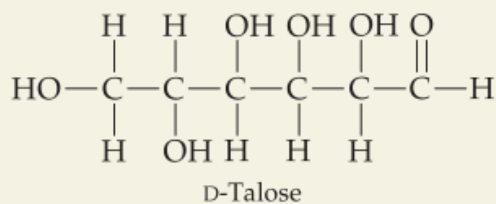

4.

Identify the following monosaccharides as (a) D-ribose or L-ribose, (b) D-mannose or L-mannose.
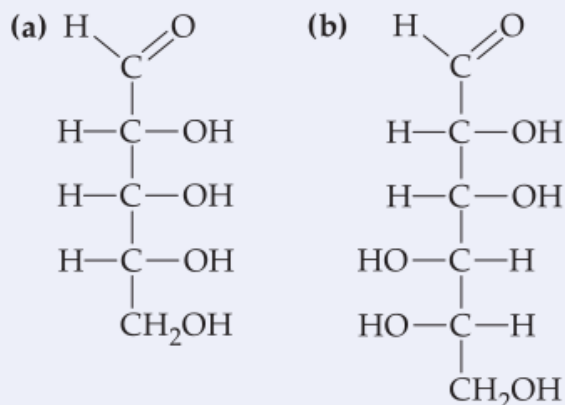
5.

D-Talose, a constituent of certain antibiotics, has the open-chain structure shown below. Draw D-talose in its cyclic hemiacetal form.

$$HO-\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}-\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle OH}{|}}{C}}-\overset{\overset{\displaystyle OH}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}-\overset{\overset{\displaystyle OH}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}-\overset{\overset{\displaystyle OH}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}-\overset{\overset{\displaystyle O}{||}}{C}-H$$

D-Talose

Literature:

1. Fundamentals of general, organic, and biological chemistry/John McMurry, Mary E. Castellion, David S. Ballantine. 6th ed. Prentice Hall: New York, Boston, San Francisco, London, Toronto, Sydney, Tokyo, Singapore, Madrid, Mexico City, Munich, Paris, Cape Town, Hong Kong, Montreal.- 2007. - 901 p.