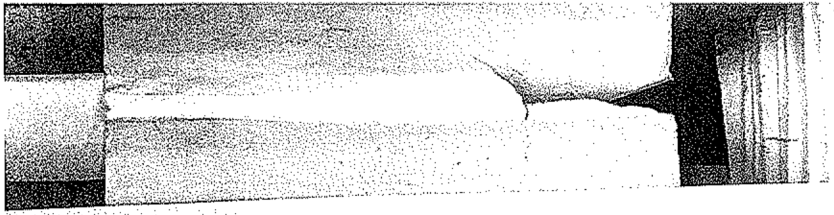
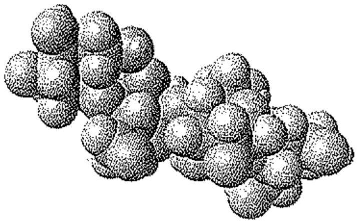




CHAPTER 14

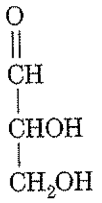
Carbohydrates

14.1 Chemical Nature of Carbohydrates—Polyhydroxy Aldehydes and Ketones

Carbohydrates comprise one of the four major classes of biologically active organic molecules, or biomolecules. (The other classes are lipids, proteins, and nucleic acids.) Simple and complex carbohydrates are the main source of metabolic energy for all the organism's activities, from locomotion to the building of other molecules.

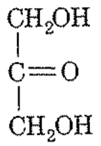
carbohydrate
a polyhydroxy—aldehyde or ketone; the polymers and derivatives of such compounds

The general formula for many common **carbohydrates**—including glucose and fructose ($C_6H_{12}O_6$) and sucrose and lactose ($C_{12}H_{22}O_{11}$)—is $C_n(H_2O)_m$, which would seem to support the old concept that these compounds are hydrates of carbon. However, their true chemical structures are those of polyhydroxy (more than one hydroxy, or —OH groups) aldehydes and ketones. The term *carbohydrate* can also refer to derivatives and polymers of polyhydroxy aldehydes and ketones. Carbohydrates contain a carbonyl group as an aldehyde or ketone as well as more than one alcohol group. The two simplest carbohydrate molecules illustrate this.



$$\begin{array}{c} O \\ \| \\ CH \\ | \\ CHOH \\ | \\ CH_2OH \end{array}$$

Glyceraldehyde
An aldose
A triose
An aldotriose



$$\begin{array}{c} CH_2OH \\ | \\ C{=}O \\ | \\ CH_2OH \end{array}$$

Dihydroxyacetone
A ketose
A triose
A ketotriose

Note that these two compounds have the same molecular formula, $C_3H_6O_3$, and both contain a carbonyl group—one as an aldehyde and the other as a ketone—as well as two alcohol (hydroxy) groups. In addition, they are functional isomers of each other.

14.2 Nomenclature of Carbohydrates

In chemical and biochemical discussions carbohydrates are more frequently referred to as *saccharides*, from the Greek word for something sweet. This term is a misnomer, as many, if not most, saccharides are not sweet. However, this terminology does allow us to talk conveniently about individual carbohydrate units, or **monosaccharides,** as well as their polymer, **oligosaccharides** (two to ten units) and **polysaccharides** (more than ten units).

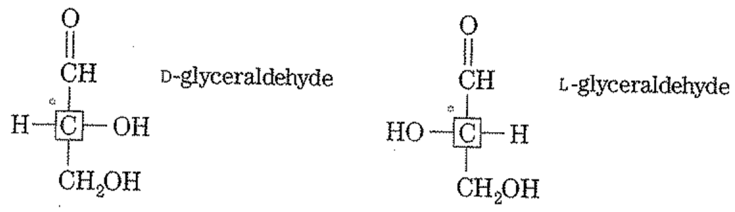
The molecules shown before as well as other carbohydrates can be named according to IUPAC rules of nomenclature. Glyceraldehyde is 2,3-dihydroxypropanal, while dihydroxyacetone would be 1,3-dihydroxypropanone. There are also general ways of naming monosaccharides that, using the suffix *-ose* to indicate a carbohydrate, can specify the carbonyl functional group (**aldose** or **ketose**), the number of carbon atoms (*tri-, tetr-, pent-*), or both (*aldohexose, ketopentose*). In addition, each monosaccharide has its own individual name, which is dependent upon the overall structure of the molecule, as we shall soon see.

monosaccharide	a single carbohydrate unit
oligosaccharide	a polymer of two to ten saccharide units
polysaccharide	a polymer with more than ten saccharide units
aldose	a polyhydroxy aldehyde
ketose	a polyhydroxy ketone

14.3 Structures of Monosaccharides

A. D, L-Aldoses: Open Chain Structures

Glyceraldehyde, the simplest aldose, has one chiral carbon atom and therefore two (2^1) optical isomers (Chapter 7). These are enantiomers, or mirror images.

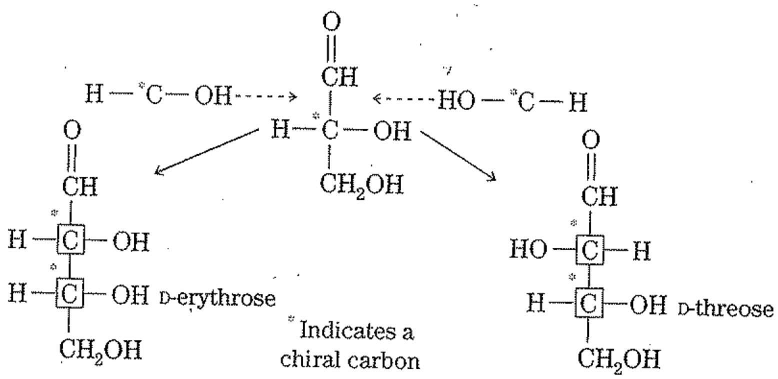


*Chiral center

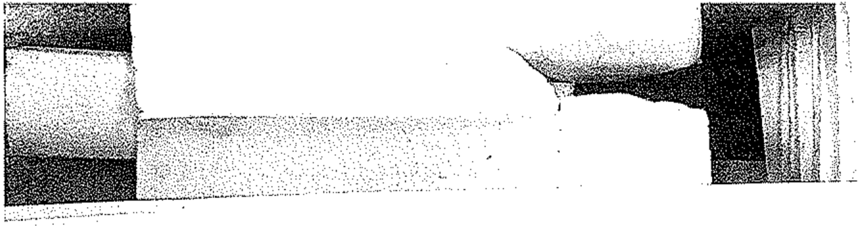
The L- and D- designations refer to the physical placement of the —OH group on the left and right side of the chiral carbon atom, respectively, and have no intended correlation with the direction of the rotation of plane-polarized light.

The structures of monosaccharides with more than three carbons can be drawn by introducing a CHOH group into glyceraldehyde between the carbonyl group and the chiral carbon atom. Notice that the new CHOH will be another chiral atom with the possibility of two orientations, one with the —OH group on the right and one with the —OH group on the left. L- and D- glyceraldehydes will each give rise to two aldotetroses, for a total of four stereoisomers (two chiral centers, 2^2 stereoisomers).

D-sugar
the most common carbohydrates; D- refers to the right-hand orientation of the —OH group on the chiral carbon atom farthest from the carbonyl group



*Indicates a chiral carbon



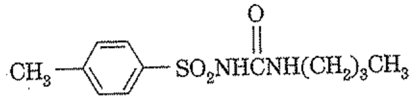
Connections 14.1 www.prenhall.com/bailey

Diabetes

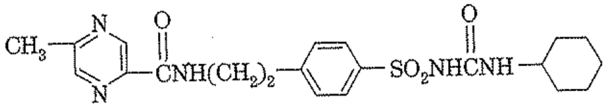
More than 15 million people in the United States currently suffer from the effects of a condition known as *diabetes mellitus*. It may take several forms, all of which result in faulty metabolism of glucose, our primary energy source. Normally, when we ingest food our bodies trigger the release of the endocrine hormone insulin from the beta cells of the pancreas. Insulin, in turn, facilitates the entrance and metabolism of glucose in our cells. If insulin is absent or malfunctions, glucose circulating in the blood increases in concentration. This condition is known as **hyperglycemia.** The kidneys are responsible for cleaning the blood of unnecessary materials and usually reabsorb normal quantities of glucose for metabolism. However, if the blood glucose concentration exceeds the *renal threshold* of 162–180 mg/100 mL (deciliter) in a person who is fasting, glucose will "spill" into the urine and can be detected there by simple tests.

The tragic outcome of this glucose excess is starvation, because the glucose cannot be used by the brain, muscles, and other organs. In addition, all the tissues of the body are being bathed in a concentrated sugar solution that can modify the proteins of the body and severely upset metabolism. Some of the consequences of unchecked diabetes include atherosclerosis (narrowing of the blood vessels), blindness (retinopathy), kidney failure, and coma, all of which could lead to premature death.

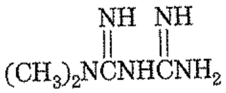
The treatment of diabetes depends upon the type and severity of the condition. Those who produce little or no insulin usually due to the destruction of pancreatic beta cells, have Type 1 (previously called insulin-dependent diabetes mellitus, IDDM) and require daily injections of insulin. Type 2, (noninsulin-dependent diabetes mellitus, NIDDM) in which insulin is produced but is not effective, frequently affects those who are overweight or genetically predisposed. Type 1 diabetes may arise from destruction of the beta cells of the pancreas due to the body's reaction to a virus. Types 1 and 2 may also have genetic or drug-induced causes. Often found in older people who are obese, type 2 is frequently controlled by diet, exercise, and/or the administration of oral drugs such as tolbutamide or glipizide (sulfonylurea class), Metformin® (biguanide class), or miglitol (an antiglucosidase).



Generic drug name: tolbutamide
Trade (proprietary) name: Orinase®

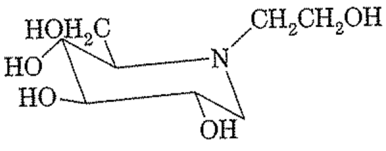


Generic drug name: glipizide
Trade name: Glucotrol®



$$(CH_3)_2N\overset{NH}{\overset{\|}{C}}NH\overset{NH}{\overset{\|}{C}}NH_2$$

metformin (Diabex®)



miglitol

Research into the causes and treatments for diabetes is very active. Biotechnology has produced human insulin, which has fewer side effects than animal types used in the past. The quality and length of life is being increased for millions every day.

Both of these compounds are D-sugars because the chiral carbon farthest from the carbonyl is derived from D-glyceraldehyde. They are related to each other as diastereomers. Recall that diastereomers (section 7.5.B) are distinct chemical entities having different physical properties. More specifically, since D-erythrose and D-threose are different at only one chiral carbon, they are referred to as **epimers.**

epimer
one of two diastereomers that differ in the orientation of groups at only one carbon

There are two chiral carbon atoms in the aldotetroses, which means 2^2 or 4 stereoisomers are possible. Only two are shown. (What are the other two?) Each of these tetroses can be extended to two aldopentoses, and so on. Most of the common naturally occurring monosaccharides have been derived from D-glyceraldehyde. Figure 14.1 illustrates the aldotroses, pentoses, and hexoses derived from D-glyceraldehyde. Since they have in common the D-orientation on the carbon farthest from the carbonyl, they are known as the D-sugars. L-saccharides exist but are not found in great abundance.

The most common aldoses are ribose, glucose, and galactose. Most of the information that follows will use these compounds as examples.

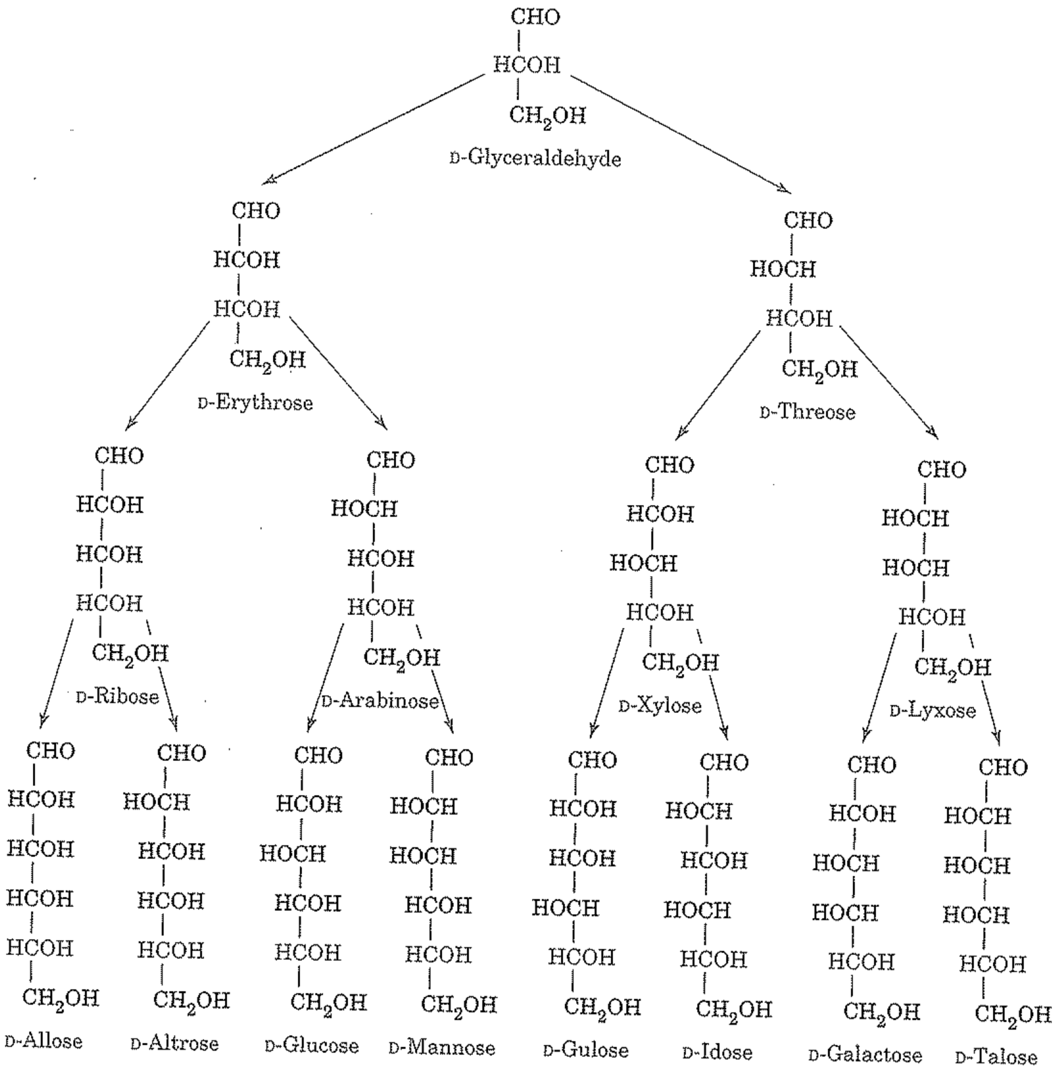


Figure 14.1
The D-aldoses.

GETTING INVOLVED

- ✓ What suffix in a molecular name usually indicates that the structure is a carbohydrate?
- ✓ What functional groups are present in carbohydrate molecules?
- ✓ Draw the structure of an aldopentose; a ketopentose.
- ✓ Now draw the enantiomers of the aldopentose and ketopentose you just made. How are these four structures alike and how are they different?

Problem 14.1

What is the general term that could be used to describe allose? xylose?

Problem 14.2

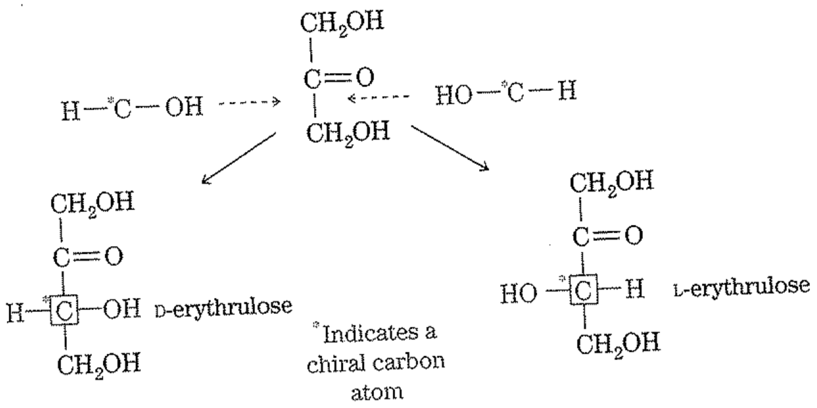
Using Figure 14.1 find an epimer and two diastereomers for D-glucose.

Problem 14.3

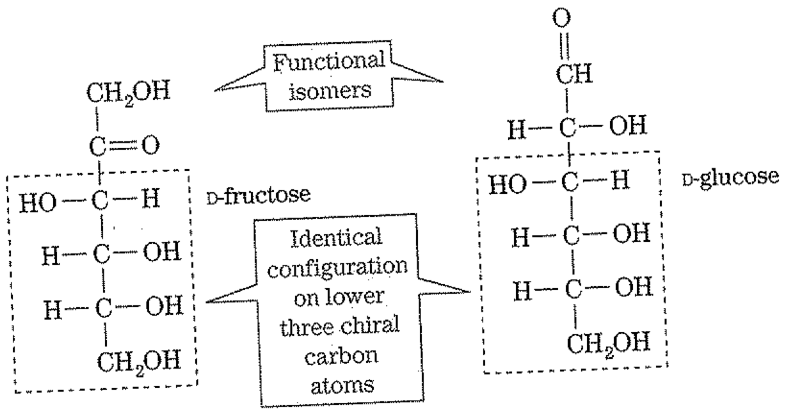
Draw the structures of the aldoheptoses that would arise if you inserted a new chiral carbon atom at position-2 of D-galactose.

B. Ketoses

As yet we have not discussed the structures of ketoses. A family of ketotetroses, ketopentoses, and ketohexoses can be drawn up in the same way as the aldoses, that is, by inserting a chiral carbon atom following the carbonyl group in dihydroxy acetone.



The most common ketose is the ketohexose fructose (fruit sugar). Notice that it is a functional isomer of glucose.



GETTING INVOLVED

- ✓ To draw the family of ketopentoses derived from D-erythrulose, where do you place the new chiral carbon atom?
- ✓ How does the placement of a new chiral carbon in ketoses compare to that for building the aldoses?
- ✓ Identify the chiral carbon atoms in D-fructose and D-glucose.

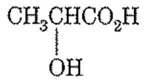
Problem 14.4
Draw the family of ketopentoses derived from D-erythrulose. Which of these are epimers?
See related problem 14.18.

C. Fischer Projections

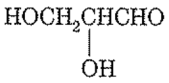
The way in which the previous structures are drawn is called a *Fischer projection;* the most highly oxidized carbon is at the top and the rest of the chain is drawn below with the groups attached to the chiral carbons projected to the left and right in order to simulate the tetrahedral bonding angles of a saturated carbon atom (see section 7.4).

GETTING INVOLVED

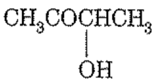
✓ Draw a Fischer projection for each of the following:



$CH_3\underset{\large OH}{\underset{|}{C}}HCO_2H$



$HOCH_2\underset{\large OH}{\underset{|}{C}}HCHO$



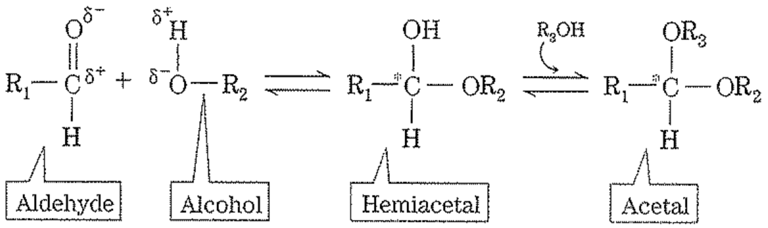
$CH_3CO\underset{\large OH}{\underset{|}{C}}HCH_3$

D. Cyclic Structures—Hemiacetal Formation

In section 11.5.G we saw that the carbonyl group of an aldehyde is polar and can react with a polar alcohol group to form an alcohol-ether known as a **hemiacetal.** The reaction could proceed one step further with another mole of alcohol to form a diether known as an **acetal.** Note that a new chiral carbon atom is formed in the reaction.

hemiacetal
the alcohol-ether product of the reaction between an aldehyde and one mole of an alcohol

acetal
the diether product of the reaction between an aldehyde and two moles of alcohol



*Indicates a chiral carbon center

GETTING INVOLVED

✓ What are the similarities and differences between an acetal and a ketal?

✓ How are hemiacetals formed? acetals?

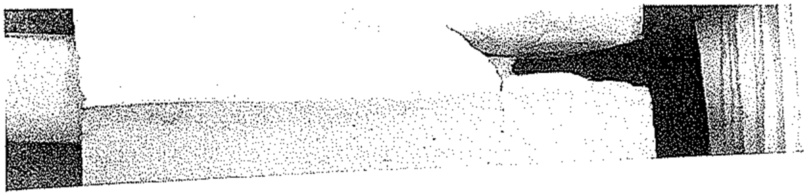
✓ What groups are attached to the new chiral carbon atom in a hemiacetal? in an acetal?

---

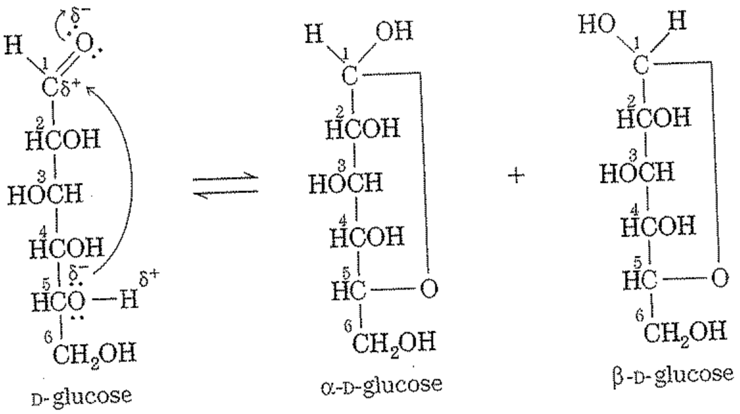
1. ***Ring-Forming Reaction.*** The tetrahedral nature of carbon and the length of the chain in aldopentoses and aldohexoses allow the carbonyl in a monosaccharide molecule to come into close proximity with an alcohol group on the same molecule. The hemiacetal that results from an intramolecular reaction will make a ring, a cyclic hemiacetal. As we saw earlier in section 2.8 on the cyclic structures, five- and six-membered rings are stable. The same holds true for the cyclic hemiacetals with the one difference that one member of the ring is an oxygen.

hemiketal
the alcohol-ether product of the reaction between a ketone and one mole of alcohol

ketal
the diether product of the reaction between ketone and two moles of alcohol



The most prevalent cyclic hemiacetal structure for glucose is a six-membered ring. To form this structure, the carbonyl carbon is the first ring member and the hydroxy group oxygen on the fifth carbon adds to the carbonyl to produce the six-membered ring hemiacetal.



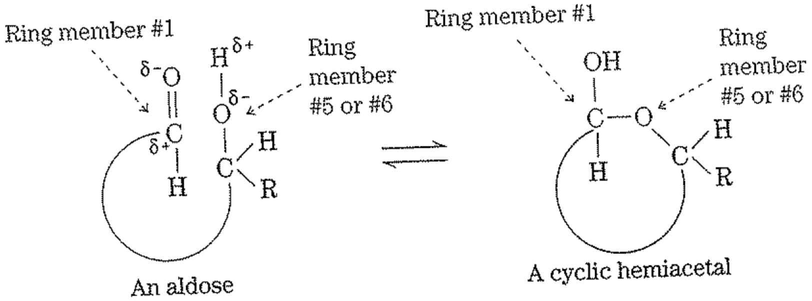
anomer
one of two optical isomers formed at the new chiral carbon produced when an aldehyde forms a hemiacetal or a ketone forms a ketal

α-anomer
the cyclic hemiacetal that has the —OH group on the new chiral carbon below the ring; on the right in a Fischer projection

β-anomer
the cyclic hemiacetal form that has the —OH group on the new chiral carbon above the ring

Notice that a new chiral center has been formed. The symbol **α** or **β** is used to indicate whether the hemiacetal alcohol group is on the right or left, respectively, in the Fischer projection. Specifically, these two new optical isomers (diastereomers) are called **anomers.**

In order to make this connection, the glucose molecule must bend back on itself to form the cyclic structure. The carbonyl carbon is the first member of the ring, while an alcohol oxygen is the last member.



An aldose

A cyclic hemiacetal

GETTING INVOLVED

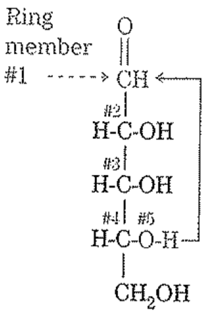
- ✓ How are anomers and epimers alike? How are they different?
- ✓ How are diastereomers related to anomers and epimers?

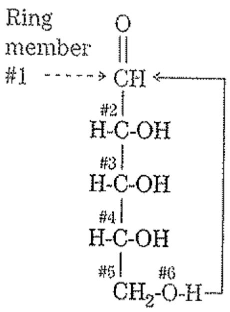
Example 14.1

Draw the five- and six-membered cyclic hemiacetal forms of D-ribose.

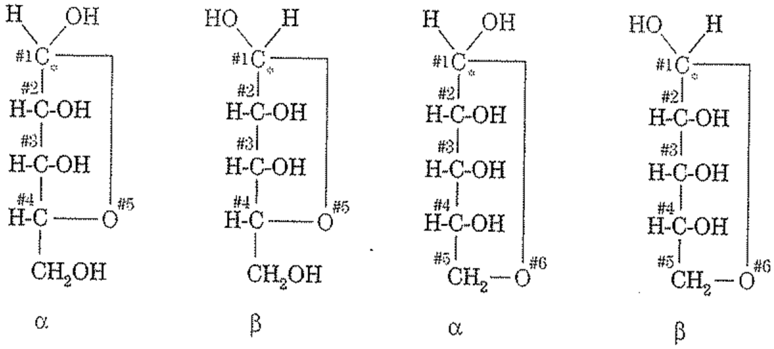
Solution

First draw the Fischer projection D-ribose. Number the members of the proposed ring starting with the carbonyl carbon as #1 and the alcohol oxygen as the last member, #5 or #6, of the ring.





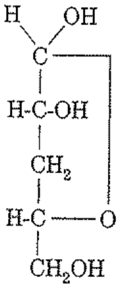
Next, perform the conversion to the hemiacetal.

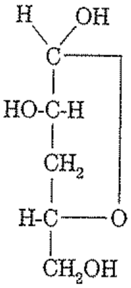


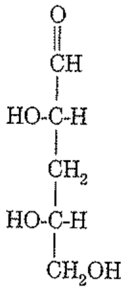
*Indicates the new chiral carbon atom

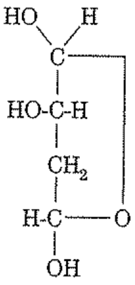
Problem 14.5

Among the four compounds drawn below, which are anomers, which are epimers, and which are diastereomers? Are there any structures which are none of these? Which ones?









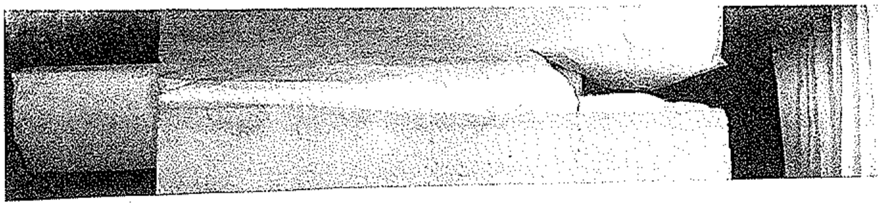
Problem 14.6

Draw the six-membered cyclic hemiacetal forms of D-mannose and D-glucose. Designate the α- and β-anomers.

See related problems 14.19, 14.22, 14.24.

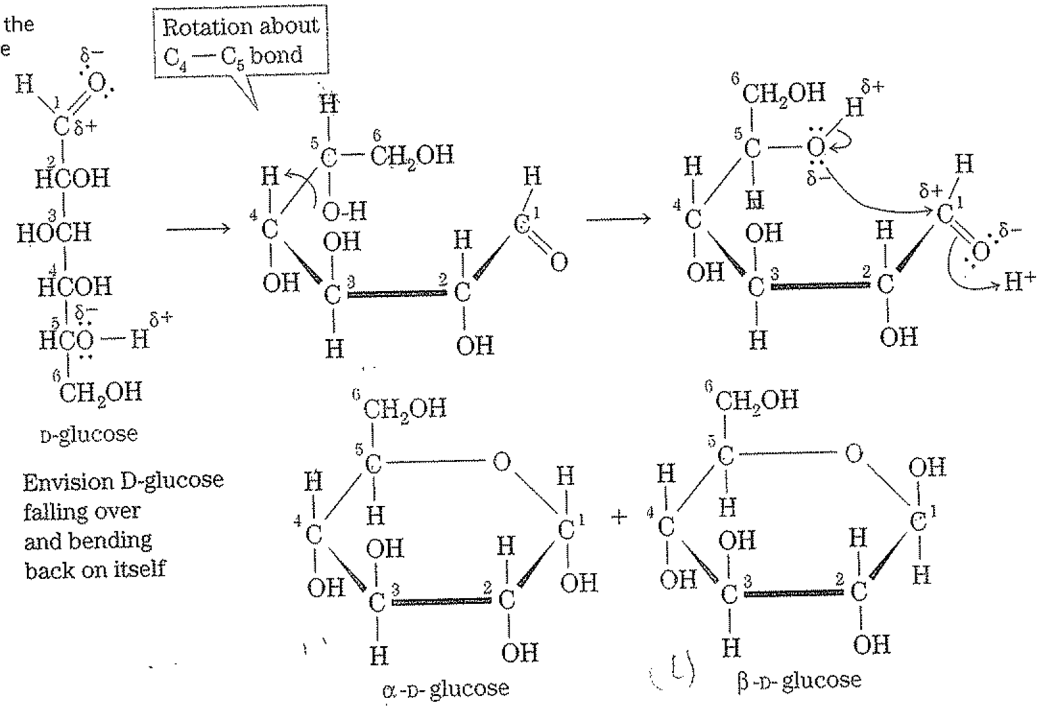
These Fischer projections obviously do not adequately represent the correct bond lengths and atom orientations of the cyclic structures. There are other ways to represent cyclic monosaccharides that may seem more familiar to you.

2. ***Structural Representations: Haworth Structures.*** The cyclic form of a monosaccharide is most frequently represented by using a Haworth formula in



which a planar pentagon or hexagon is viewed as projecting out of the paper toward the reader. In drawing a **Haworth structure,** the hemiacetal carbon is placed on the right end of the ring; for the D-series of monosaccharides, the —CH_2OH is up. Compare, for example, the Fischer and Haworth structures for the α- and β-D-glucose:

Haworth structure
two-dimensional five- or six-membered ring representation of the cyclic form of a monosaccharide; —OH groups that appear on the right in a Fischer projection are drawn down (below the plane of the ring) in a Haworth structure and those —OH groups on the left in a Fischer projection are drawn up

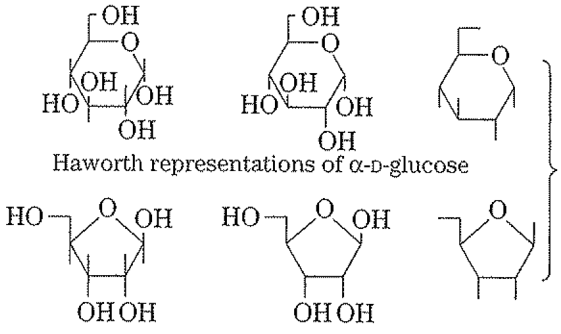


Envision D-glucose falling over and bending back on itself

The —OH groups in the Fischer projection that were on the right (except that on C-6, which is not on a chiral carbon) are drawn downward in the Haworth structure. If the —OH on the new chiral carbon is up, it would be on the left in a Fischer projection, that is, it is β-. This also means that it is on the same side of the ring as the oxygen in the ring. If that group were written down, it would be the α-form. In water solution the α- and β-forms are in equilibrium with the open chain and so can interconvert readily. The cyclic forms, however, predominate in solution.

$$\alpha\text{-form} \rightleftarrows \begin{array}{c}\text{Open chain}\\ \text{aldehyde or}\\ \text{ketone}\end{array} \leftrightarrows \beta\text{-form}$$

Haworth structures can also be drawn as are other cyclic forms, that is, without showing the carbon atoms and using the intersection of bonds to indicate the position of each carbon. The hydrogen atoms may also be assumed, since the cyclic forms have saturated carbons. Because it is the alcohol and hemiacetal groups that are reactive, the figures representing saccharides commonly use a line to indicate an —OH group. Please note that this is used only in carbohydrate chemistry.



Haworth representations of α-D-glucose

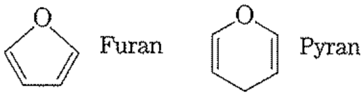
Used only when discussing carbohydrates

Haworth representations of β-D-ribose

Five-membered rings are called **furanose** forms because they resemble the heterocyclic compound furan, while six-membered rings are termed **pyranose** forms because of their resemblance to pyran.

furanose
five-membered ring form of a monosaccharide

pyranose
six-membered ring form of a monosaccharide



GETTING INVOLVED

- ✓ Draw the Haworth structures for the three forms of D-glucose, α-, β-, and open chain, as an equilibrium.
- ✓ Besides being anomers, are the α- and β- forms of a monosaccharide also epimers, diastereomers, and/or enantiomers?
- ✓ How is a furanose version of a monosaccharide the same and how is it different from a pyranose form?
- ✓ Can aldotetroses form both furanose and pyranose rings?

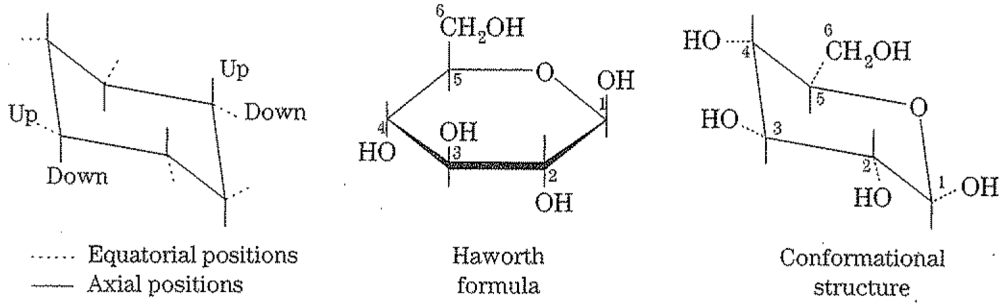
Problem 14.7

Draw the Haworth structures for the five-membered and six-membered cyclic hemiacetal forms of D-arabinose and D-xylose.

---

3. *Structural Representations: Conformational Structures.* Recall that cyclohexane could also be drawn in its **conformational structure,** that is, as a boat and a chair form. This also can be done with cyclic monosaccharides. The chair form is the stable form for sugars as it is for cyclohexane. Placement of the —OH groups will again be up and down, but this time in relation to axial and equatorial positions around the ring. Recall that axial and equatorial alternate as to which is above the ring as you go around it.

conformational structure
relating to carbohydrates, this is the chair form of the cyclic hemiacetal or hemiketal



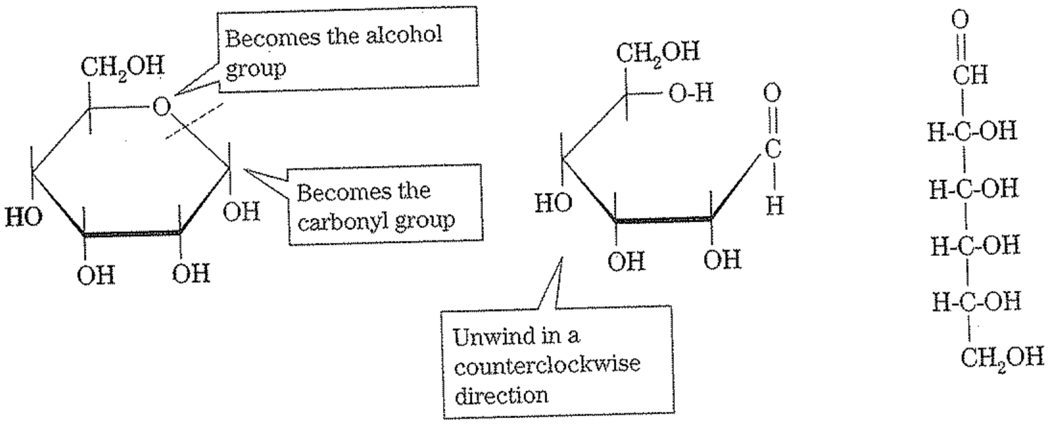
Haworth formula

Conformational structure

Representations of β-D-glucose

It is of interest to note that β-D-glucose is probably the most abundant form of carbon in the biosphere. As you can see from the equatorial placement of all of the substituent —OH groups, it is a very stable structure.

4. ***Converting Cyclic Structures to Open-Chain Fischer Formulas.*** You can convert the cyclic hemiacetals or hemiketals to their open-chain aldose or ketose structures by reversing the reaction that made them, remembering that the oxygen in the ring was contributed by the alcohol group and that the —OH-bearing carbon to which it is attached is part of the carbonyl.



Becomes the alcohol group

Becomes the carbonyl group

Unwind in a counterclockwise direction

5. ***Cyclic Hemiketals and Ketals.*** Ketoses form ring structures in exactly the same way as do aldoses. The difference will lie in the groups attached to the new chiral carbon center.

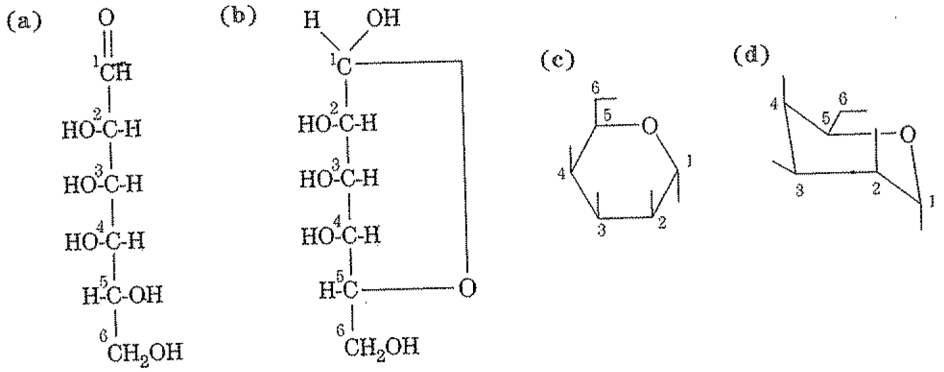
GETTING INVOLVED

- ✓ Can the right and left —OH groups in the Fischer projection of a monosaccharide be correlated directly to up and down positions in the conformational form? Explain the correlation.
- ✓ Compare the cyclic forms of α-D-glucose and α-D-fructose, both in the pyranose Haworth forms. What is the major distinguishing characteristic of an aldose as compared to its corresponding ketose?

Example 14.2

Draw the Haworth and conformational structures for the α-anomer of the six-membered cyclic hemiacetal form of D-talose.

Solution



D-talose

α-D-talose

(a) Begin by drawing the open-chain Fischer projection of D-talose.
(b) Form the hemiacetal linkage for a six-membered ring. Since this is an aldose, the

first carbon, the carbonyl carbon, is the first member of the ring. For the six-membered ring the last atom will be the oxygen on carbon-5. Be sure to draw the α-form.

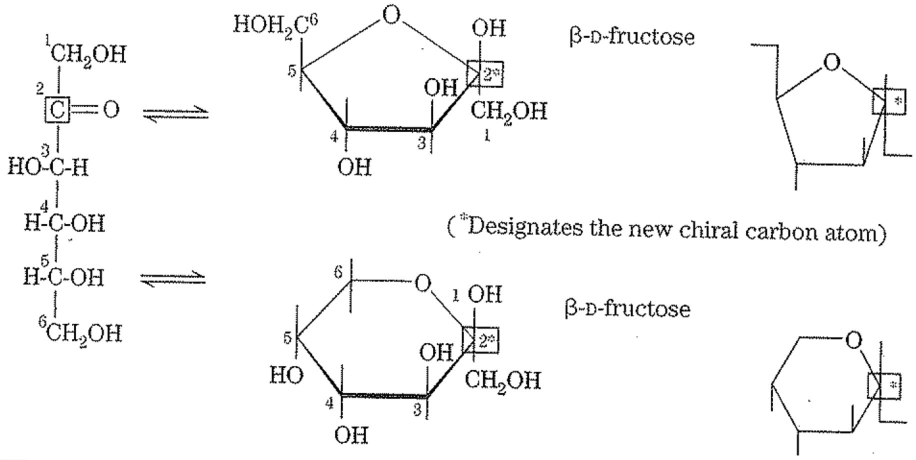
(c) Convert to the Haworth structure. The three remaining —OH groups on chiral carbons are on the left in the Fischer projection and will be drawn up in the Haworth form.

(d) Draw the corresponding conformational structure.

Example 14.3

Draw the Haworth structures for the β-isomer of the five- and six-membered cyclic Haworth structures of D-fructose.

Solution



(*Designates the new chiral carbon atom)

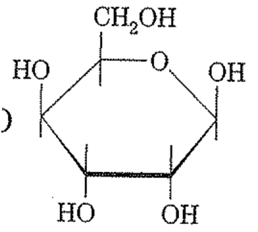
Problem 14.8

Draw the conformational form for the six-membered (pyranose) cyclic hemiacetal structure of D-galactose. Show both α- and β-anomers.

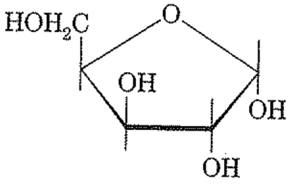
Problem 14.9

Draw the open-chain Fischer projections for the following Haworth forms:

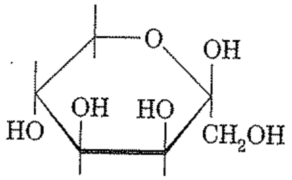
(a)



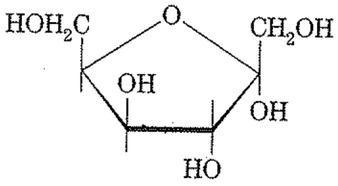
(b)



(c)



(d)



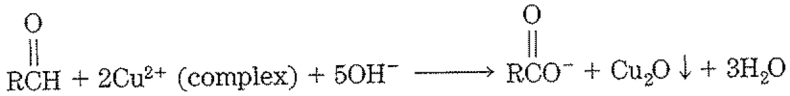
14.4 Some Reactions of Monosaccharides

Since monosaccharides contain carbonyl and alcohol groups, they can undergo the types of reactions that are characteristic of aldehydes, ketones, and alcohols. We will present only a few of these reactions, specifically some of those important to the detection of carbohydrates, their polymerization, and their metabolism.

A. Oxidation of Carbohydrates (Reducing Sugars)

Aldehydes are readily oxidized to carboxylic acids by fairly mild oxidizing agents (section 11.4). Therefore, they are good reducing agents. Aldoses have the same chemical property. If a Cu^{2+} complex is used in basic conditions, a precipitate of copper (I) oxide indicates a reducing agent, or in the case of sugars, a **reducing sugar.** This is known as *Fehling's* (tartrate copper complex) or *Benedict's* (citrate copper complex) *test.*

reducing sugar
carbohydrate that has one or more anomeric carbons available for oxidation by a mild oxidizing agent; that is, the carbon contains an alcohol and an ether group on it

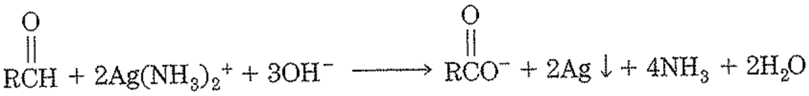


$$\overset{O}{\overset{\|}{RCH}} + 2Cu^{2+}\text{ (complex)} + 5OH^- \longrightarrow \overset{O}{\overset{\|}{RCO^-}} + Cu_2O\downarrow + 3H_2O$$

Aldehyde
or aldose

Red-brown
precipitate

Silver ion (Ag^{1+}) may also be used as the oxidizing agent, in which case elemental silver will plate out on the surfaces that the solution contacts. Known as *Tollens test* or the *silver mirror test,* this reaction was used in the past to make silver-backed mirrors.

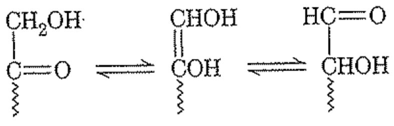


$$\overset{O}{\overset{\|}{RCH}} + 2Ag(NH_3)_2^+ + 3OH^- \longrightarrow \overset{O}{\overset{\|}{RCO^-}} + 2Ag\downarrow + 4NH_3 + 2H_2O$$

Silver mirror

Since both α- and β-anomers of a saccharide are in equilibrium with the open-chain carbonyl, there is no problem in the cyclic forms opening and reacting.

Normal organic ketones do not react with mild oxidizing agents; that is, they give negative Fehling, Benedict, and Tollens tests. However, ketoses are reducing sugars because as 2-oxo compounds with an adjacent alcohol group, they can rapidly tautomerize to aldoses and so be oxidized.



$$\begin{array}{c}CH_2OH\\ |\\ C{=}O\\ \wr\end{array} \rightleftharpoons \begin{array}{c}CHOH\\ \|\\ COH\\ \wr\end{array} \rightleftharpoons \begin{array}{c}HC{=}O\\ |\\ CHOH\\ \wr\end{array}$$

Ketose Enediol Aldose

For many years the Benedict test was a preliminary screen for diabetes because it is positive if excess glucose is spilled into the urine. But because all common aldoses and ketoses give positive reducing sugar tests, more specific tests have been devised to identify the presence of glucose specifically in body fluids as evidence of diabetes, rather than other sugars excreted due to some other form of abnormal metabolism such as fructosemia. Proteins known as enzymes are usually extremely specific in reacting with compounds. The enzyme glucose oxidase has been mixed with dyes and placed on a paper strip (Test-tape®) so that, when dipped into urine, it will record the presence and relative amount of glucose present. This is the basis of the widely used commercial test kit that both takes a sample of blood by pricking the finger and analyzes it.

The oxidized aldose, or carboxylic acid, is named using the specific monosaccharide stem with the ending **-onic acid.** Glucose becomes gluconic acid and galactose becomes galactonic acid.

If the other end of the molecule, the primary alcohol group, is oxidized (without the carbonyl being oxidized), the resulting product is called a **-uronic acid:** glucuronic acid, galactouronic acid.

Are there any **nonreducing sugars?** The answer is yes; if the anomeric group is no longer free to open, it can't be oxidized. This occurs when the molecule reacts with another mole of alcohol to form an acetal or ketal.

-onic acid
a carbohydrate derivative wherein the aldehyde functional group has been oxidized to a carboxylic acid

-uronic acid
a carbohydrate derivative wherein the last, primary alcohol group has been oxidized to a carboxylic acid

nonreducing sugar
a carbohydrate with all of its anomeric carbons bonded to other groups, unavailable for opening to an aldehyde or ketone carbonyl

GETTING INVOLVED

- ✓ What are the key chemical species in the tests for reducing sugars, that is, in Fehling and Benedict test and in Tollens test?
- ✓ How would the testing solutions appear in the presence and absence of a reducing sugar?
- ✓ Draw the structures of gluconic and glucuronic acids. Which structural features are the same and which are different in the two molecules?

Problem 14.10

Under the basic conditions of reducing sugar tests, fructose tautomerizes to an aldose. There are two possible aldoses. What are they?

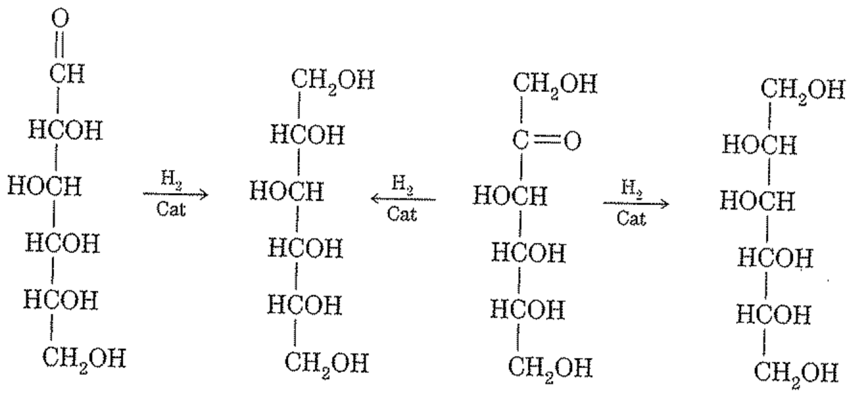
Problem 14.11

Draw the structures of mannuronic acid, xylonic acid, and iduronic acid.

See related problems 14.28, 14.29, 14.30.

B. Reduction of Monosaccharides

The aldehyde or ketone group of a monosaccharide can be reduced purposefully or naturally to produce the corresponding sugar alcohol. Reduced glucose is called *sorbitol,* while fructose can be reduced to sorbitol or *mannitol.*



Glucose Sorbitol Fructose Mannitol

Connections 14.2 www.prenhall.com/bailey

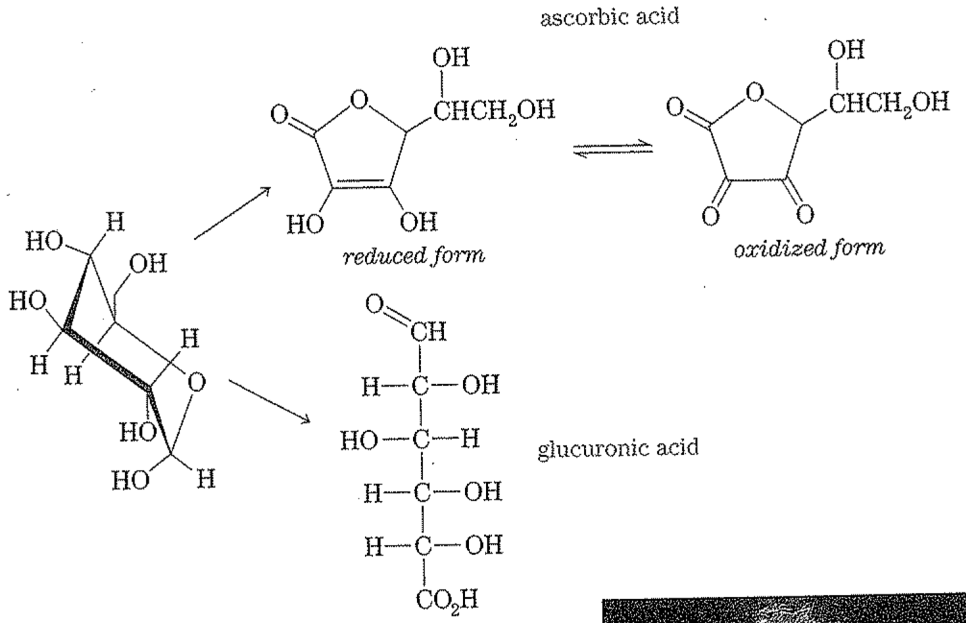
Prevention of Disease and Detoxification

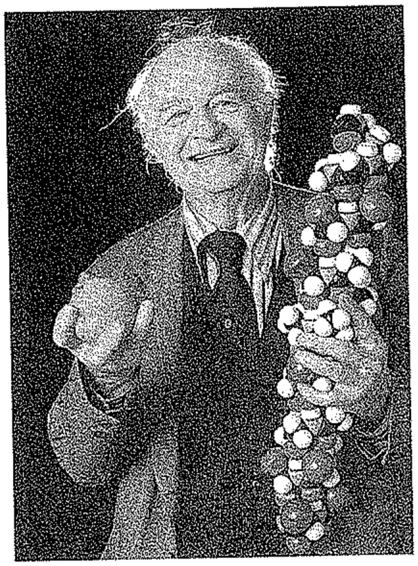
To paraphrase a popular commercial, "Glucose does a body good;" the statement is correct, even if the grammar isn't. Glucose is not only a major body fuel, stored in muscle and liver as its polymeric form, glycogen, but it is also a precursor to oxidation products, ascorbic acid and glucuronic acid, which are essential to metabolism.

Most organisms can produce ascorbic acid through a series of specific enzyme-catalyzed oxidation reactions. Ascorbic acid easily undergoes a reversible oxidation-reduction reaction making it an essential cofactor in metabolism. For example, the formation of collagen and elastin, proteins that comprise our skin, teeth, bones, ligaments, cartilage, and connective tissue, depends upon the oxidation of certain amino acids in those proteins. Ascorbic acid plays an active role in the reactions. In the absence of ascorbic acid, tooth enamel is weakened along with the connective tissue of the gums. Frequent nosebleeds occur as well as bruising; the immune system is generally weakened. This condition is known as scurvy.

Humans, along with other primates, guinea pigs, and the Indian fruit bat, are among the few species that cannot make their own ascorbic acid. Since it must then be provided in the diet, it becomes an essential nutrient or vitamin—vitamin C to be specific. Scurvy was prevalent in the age of sea-faring explorers as it is now in war-torn countries where populations are malnourished. Dietary sources of vitamin C include citrus fruits (lemons, limes, and oranges), strawberries, tomatoes, and green vegetables.

Glucuronic acid, which can be produced by humans, is one of the most important intermediates in the detoxification of the body from regular metabolic wastes as well as foreign toxins including drugs. With its variety of functional groups, it can react, or conjugate, with many kinds of organic molecules to form water-soluble derivatives that can be excreted through the kidneys.





Linus Pauling holding an orange containing vitamin C and an α-helix found in proteins.

Both of these compounds have sweetness and are used as sugar substitutes in candies and chewing gum.

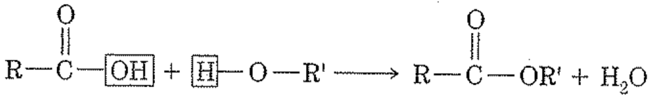
GETTING INVOLVED

Problem 14.12

Xylitol, another sugar substitute, which purportedly can prevent cavities, is produced by the reduction of xylose. Arabitol is the reduction product of arabinose. Draw the structures of xylitol and arabitol. Are they, or the other sugar alcohols, reducing?

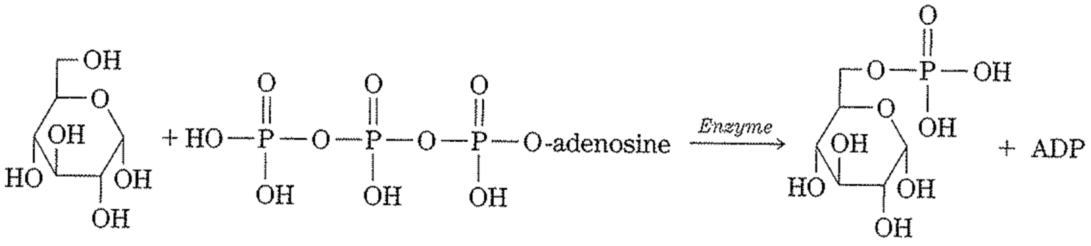
C. Esterification

Since they are alcohols, saccharides can condense with acids to form esters (sections 12.6 and 13.5).



$$\underset{\text{Acid}}{R-\overset{O}{\overset{\|}{C}}-\boxed{OH}} + \underset{\text{Alcohol}}{\boxed{H}-O-R'} \longrightarrow \underset{\text{Ester}}{R-\overset{O}{\overset{\|}{C}}-OR'} + H_2O$$

This can occur with organic or inorganic acids, such as phosphoric and sulfuric acids. These inorganic acids are also found in combined forms such as adenosine triphosphate (ATP).



Glucose ATP Glucose-6-phosphate

Enzymes are necessary to catalyze the condensation. Phosphate derivatives of saccharides are common as metabolic intermediates in all living organisms.

Sulfate esters of carbohydrates can be found in such biochemically important materials as skin, cartilage, and the lens of the eye.

14.5 Disaccharides and Polysaccharides

So far we have looked only at hemiacetal and hemiketal formation. If another mole of alcohol is available, an acetal or ketal can be made. This is the major means by which monosaccharides polymerize into oligo- and polysaccharides, as well as react with other biochemical molecules.

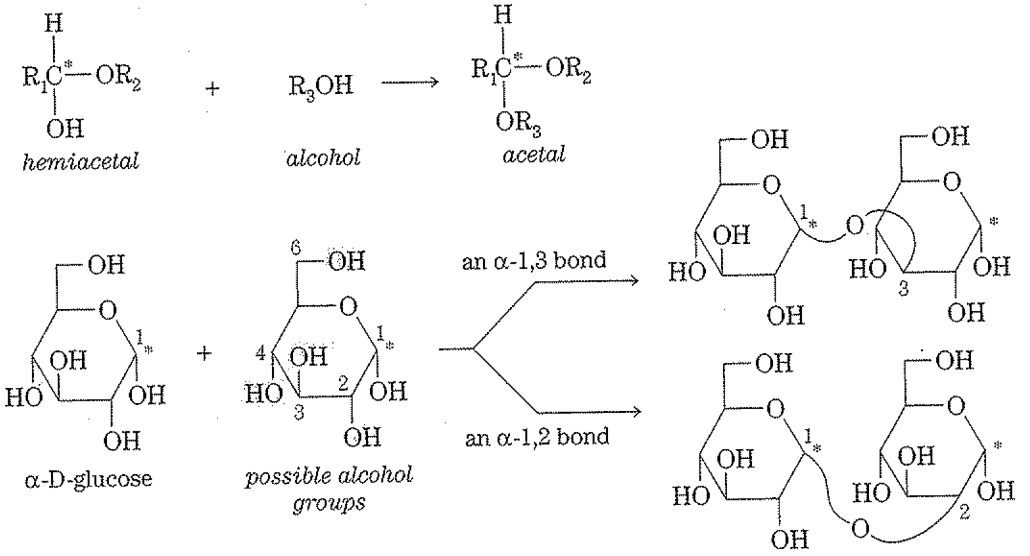
Keep in mind that a second monosaccharide with its —OH groups is a polyol. If the link is made between the anomeric carbon of one unit and an —OH from a second molecule, a polymerization has begun.

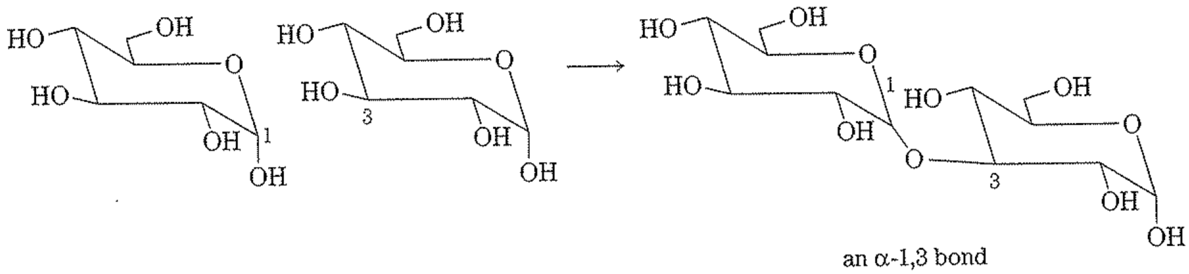
A. Glycosidic Linkages or Bonds

The bond made between two monosaccharide units is called a *glycosidic linkage* or **glycoside bond.** Drawn below are a few of the options open to two molecules of glucose reacting together. Notice that the first glucose unit has its hemiacetal

glycoside bond
acetal or ketal formed from the reaction of a cyclic monosaccharide molecule with another monosaccharide

—OH in the α-position (axial). Once it is linked to an alcohol, the glycoside bond will remain in that α-position and the bond will be an α-glycosidic bond. Does it make a difference whether that first unit has the bond in the α- or β- position? Absolutely. We shall discuss more about this as we proceed with this section.





an α-1,3 bond

Notice that the position of the bond at the anomeric carbon in the first sugar unit can be either α- or β-, which is indicated in the name. The orientation (up or down) of the reacting —OH in the second sugar unit is specified by the identity of the monosaccharide (glucose, galactose, etc.) and the hydroxyl position on the ring.

GETTING INVOLVED

- ✓ Which groups on two monosaccharides react in order to make a glycosidic bond?
- ✓ Considering two α-D-glucose molecules, list the possible glycosidic bond combinations.

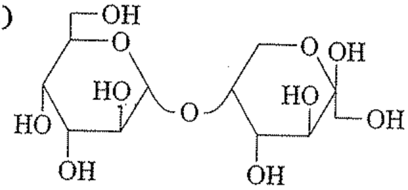
Problem 14.13

Maltose is composed of two glucose units joined in an α-1,4 glycoside bond, while cellobiose has two glucose molecules joined by a β-1,4 bond. Draw the Haworth and conformational structures for the disaccharides maltose and cellobiose. Are these reducing or nonreducing sugars?

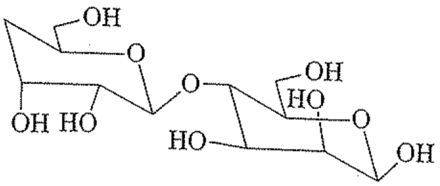
Problem 14.14

Identify the type of glycosidic bond found in each of the following disaccharides. Be sure to specify whether the link is α- or β-.

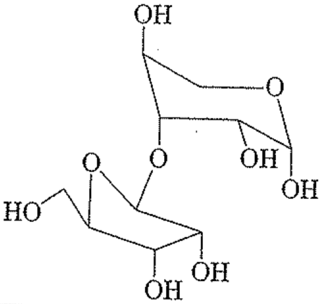
(a)



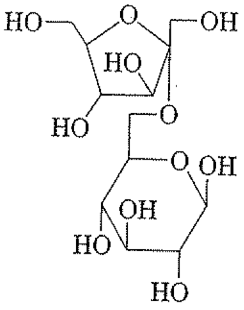
(b)



(c)



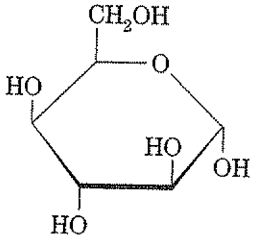
(d)



Problem 14.15

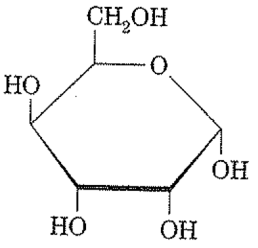
Draw the structures of the disaccharides formed from the following monosaccharide units, using the glycosidic linkages specified.

(a)

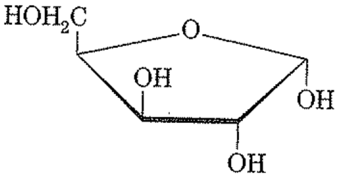


and

α-1,3

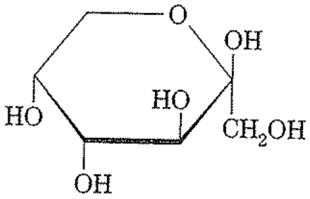


(b)



and

β,α-1,2

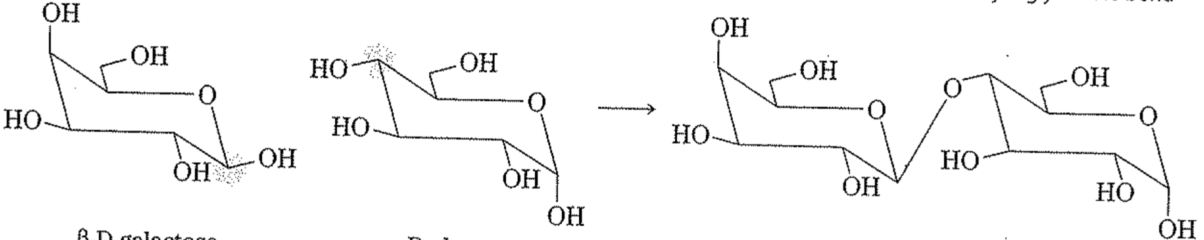


B. Disaccharides

1. ***Lactose: Mother's Disaccharide.*** Found exclusively in the milk of mammals, **lactose** (*lac*, Latin for "milk") makes up 4.5% of cow's milk and 6.7% of human milk. This **disaccharide** is composed of galactose and glucose linked by a β-1,4 glycosidic bond.

lactose
a disaccharide composed of a galactose and a glucose unit joined by a β-1,4 glycosidic bond

disaccharide
two monosaccharide units linked by a glycosidic bond



β-D-galactose

α-D-glucose

β-1,4 bond
α-lactose

Connections 14.3

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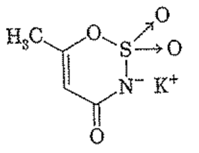
Low-Calorie Sweeteners

Glucose that is not immediately needed for metabolic energy is either stored as glycogen or converted into lipid for storage in adipose (fat) tissue. Lipid deposits can form on the walls of blood vessels, eventually leading to atherosclerosis and an increased risk of stroke or heart attack. Therefore, for health and cosmetic reasons, many persons have attempted to limit their intake of fat and carbohydrates, especially sucrose. In order to satisfy the "sweet tooth" developed by sugared diets, various natural and synthetic materials have been or are being investigated as sugar substitutes or enhancers. Since these sweeteners either are noncarbohydrate in nature or are not absorbed to any extent in the gastrointestinal tract, they are referred to as *low calorie* or, in some cases, *nonnutritive.*

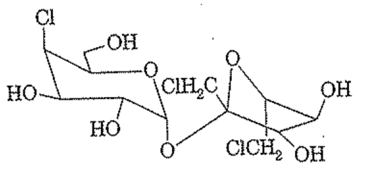
The sugar alcohols, mannitol and sorbitol, although not as sweet as sucrose, have been used for years as low-calorie substitutes. Their ability to be absorbed in the intestine is minimal, but their capacity for hydrogen-bonding has caused them to be associated with unpleasant laxative action if they are consumed in large quantities.

The use of saccharin, which is approximately 300 times sweeter than sucrose, has come into question because it has been shown to promote cancer in laboratory animals under certain conditions—that is, it can enhance the carcinogenicity of other substances. Under the Delaney clause of the Pure Food, Drug, and Cosmetic Act, saccharin is therefore classified as a carcinogen, and foods containing it must display a warning about its effect on laboratory animals.

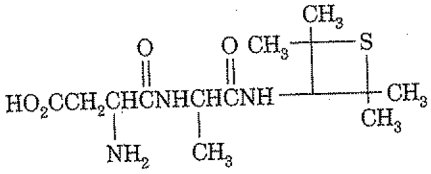
Early in 1983, the Food and Drug Administration approved the use of aspartame (L-aspartyl-L-phenylalanyl-methyl ester) as a low-calorie sweetener. About 200 times sweeter than sucrose, aspartame has found its way into gourmet coffees, diet soft drinks, and many other foods. A dipeptide composed of two amino acids, aspartame illustrates the fact that a molecule need not be a carbohydrate to be sweet. With the patent life on aspartame expiring there are new compounds waiting in the wings to offer it competition, such as fructo-oligosaccharides (FOS) and the L-sugars.



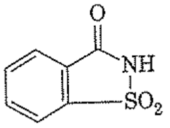
acesulfame-K



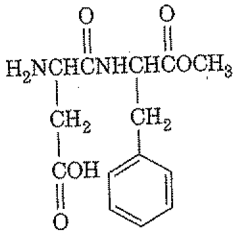
Sucralose (600x the sweetness of sucrose)



Alitame (2000× the sweetness of sucrose)



Saccharin



Aspartame
(Nutrasweet®)

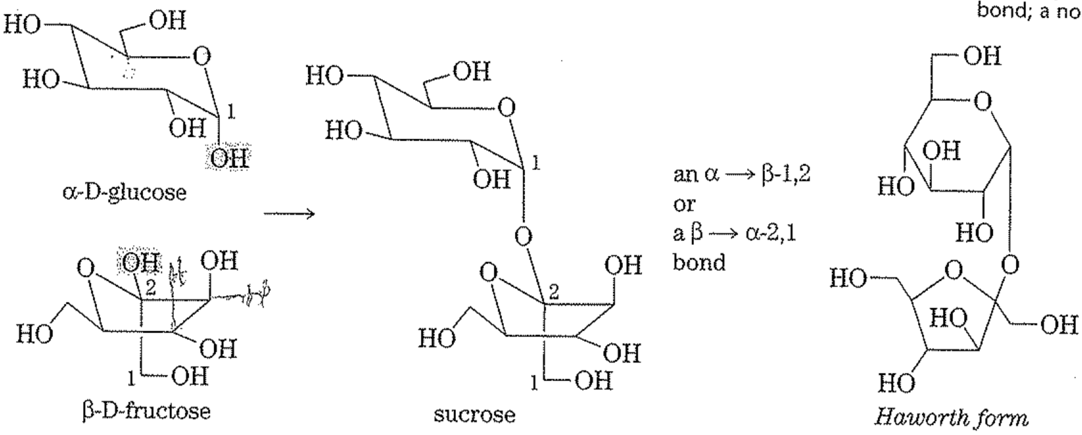
The second unit of lactose, glucose, has its hemiacetal carbon free, and it can therefore open up to the aldose form. Lactose is thus a reducing sugar and will be oxidized by Fehling, Benedict, and Tollens' reagents.

Lactose requires a special enzyme to break its glycosidic bond. This enzyme is called lactase and it is secreted in the intestines of young mammals. As the infant is weaned, the level of lactase being produced decreases markedly. Very low lactase production is characteristic of 70%–80% of the world's adult population. As a result, many adults cannot digest milk and milk products. This condition is known as *lactose intolerance* and can bring about a great deal of gastrointestinal distress due to the fermentation of the undigested lactose by endogenous (natural) intestinal bacteria. In general, persons of northern European ancestry seem to be exempt from this enzyme deficiency. For those suffering from lactose intolerance, already fermented milk products such as yogurt and cheese can be consumed, or milk can be treated with lactase enzyme, which is commercially available (Lactaid®).

In a product called "sweet acidophilus" a bacterium, *Lactobacillus acidophilus*, is added to regular milk. At refrigerator temperatures, the bacteria are fairly inactive. As the ingested milk is warmed in the gastrointestinal tract, they become active and begin to ferment the carbohydrates of the milk. Since the fermentation does not begin until the milk is ingested, the milk is "sweet," not sour like yogurt and sour cream, which have already been fermented. The benefits of "sweet acidophilus" for those suffering from lactose intolerance are in question, since the lactose could still reach the intestine relatively intact.

2. *Sucrose: The Table Disaccharide.* Everyday table sugar is **sucrose.** It is a disaccharide composed of a glucose unit and a fructose unit linked by a glycoside bond between the two anomeric carbons, an α, β-1,2 bond.

sucrose
a disaccharide composed of a glucose unit and a fructose unit joined by an α, β-1,2 glycosidic bond; a nonreducing sugar



Notice that the anomeric carbons of both units are involved in the glycosidic bond, and therefore neither unit can easily open up to the free aldose or ketose. Because of this, sucrose is a *nonreducing sugar;* that is, it will not give a positive Fehling's test.

Sucrose can be isolated from various sources, including sugarcane (15%–20%), sugar beets (10%–17%), fruits, maple sap, seeds, and flowers. As the disaccharide, sucrose is dextrorotatory. Upon hydrolysis, by either acid or enzyme, the optical rotation changes to levorotatory (+66.5° to −20°), as a result of the release of the fructose, also known as **levulose** ($[\alpha]_D^{20} = -92°$) and glucose, or **dextrose** ($[\alpha]_D^{20} = +52°$) units. Since the sign of the optical activity changes from plus to minus, the hydrolysis process is said to cause *inversion* of the optical rotation, and the mixture of the two monosaccharides is called **invert sugar.** Bees contain an enzyme called *invertase,* which causes this conversion during the production of honey. Our bodies have a similar enzyme called *sucrase.*

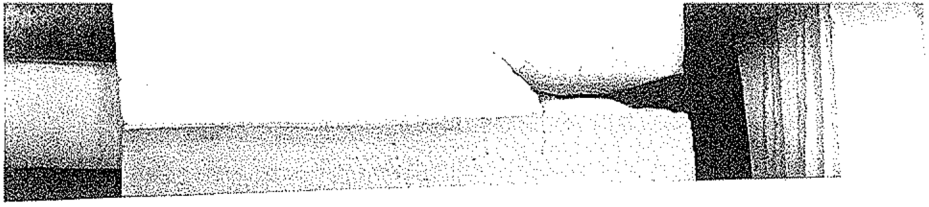
levulose
another name for fructose

dextrose
another name for glucose

invert sugar
a mixture of fructose and glucose produced by the breakdown of sucrose

Sucrose is known to be a cause of extensive tooth decay. The material known as plaque that sticks to our teeth is composed of bacterial colonies of *Streptococcus multans* as well as other types of organisms. The bacteria use sucrose both to produce an adhesive with which they stick to teeth and as a food. The end result of their digestion is lactic acid, which causes the corrosion of the mineral deposits (hydroxyapatite) of the teeth and leads to the destruction of the gums. Since most foods are acidic in nature, brushing and flossing teeth frequently are recommended by dental experts. In addition, foods that contain high concentrations of sucrose, especially ones that also stick to the teeth, should be avoided.

Metabolically, fructose and glucose are broken down in much the same fashion and are used for the body's immediate energy requirements. Otherwise, these saccharides are stored as glycogen or converted enzymatically to lipid (fat) and held in adipose tissue. A large dose of sucrose will most likely end up where we need it least—as excess baggage.

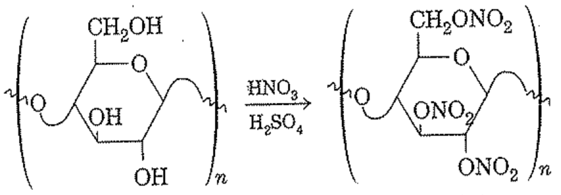


Connections 14.4 www.prenhall.com/bailey

Nitrocellulose and Rayon

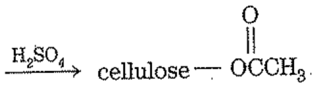
Long before the human mind had any thought of synthetic polymers, nature had come up with cellulose, in the form of cotton, as an ideal natural fiber. It was indeed fitting that one of the first human experiences with synthetic polymers should entail the inadvertent chemical modification of cellulose.

Serendipity smiled on Christian Schönbein in 1846 when he cleaned up a spill of nitric and sulfuric acids with his wife's cotton apron. After rinsing out the apron with water, he hung it to dry in front of a hot stove. To his utter surprise, the cloth flashed up and disappeared, leaving barely a trace. He had accidentally synthesized cellulose trinitrate, or guncotton.



Cellulose Cellulose trinitrate

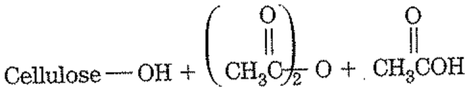
If cellulose is not completely nitrated, another product is formed, called pyroxylin. Pyroxylin and camphor can be combined to form celluloid, a plastic once used for movie film, eyelgass frames, shirt collars, dice, dominoes, and so on. Due to the intrinsic flammability of nitrated cellulose, a good deal of early movie film history has been lost in massive fires. Gradually, of course, this material was replaced by more stable petroleum-based polymers.



$$\xrightarrow{H_2SO_4} \text{cellulose}-\text{O}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{CH}_3$$

The nitration of cellulose converted a very insoluble material, cellulose, into a form that could be dissolved in a solvent and then forced through very small holes to produce a silken thread. However, the material's intrinsic flammability made the resulting fibers short-lived. Less flammable derivatives had to be developed or the solubility of cellulose had to be modified so that it could be formed into threads for cloth.

Acetate rayon is another derivative of cellulose made by acetylating natural cellulose using acetic anhydride. The latter reagent forms ester bonds with the available alcohol groups of the glucose units.



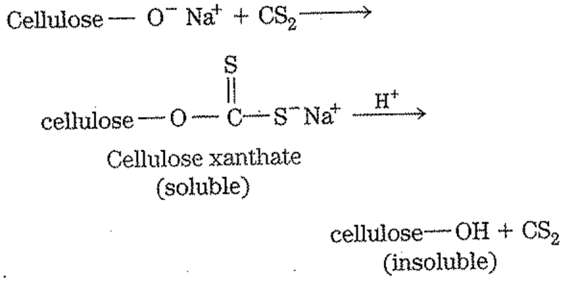
$$\text{Cellulose}-\text{OH} + \left(\text{CH}_3\overset{\text{O}}{\overset{\|}{\text{C}}}\right)_2\text{O} + \text{CH}_3\overset{\text{O}}{\overset{\|}{\text{C}}}\text{OH}$$

Acetic anhydride

The cellulose acetate, in acetone solvent, is extruded through small openings, called spinnerets, to form threads. As the solution leaves the spinneret, hot air flash-evaporates the solvent.

Viscose rayon is actually cellulose that has been derivatized to alter its solubility and then regenerated as it is spun into threads. In the process, carbon disulfide is used to form cellulose xanthate, the sodium salt of which is soluble in basic solution.

The term *viscose* is derived from the fact that the solution of basic cellulose xanthate is very thick, or viscous. An acid bath is used to regenerate the cellulose after it has been forced through the spinnerets. The cellulose thread is used in clothing, carpeting, tire cord, and draperies. If a thin slit rather than spinnerets is used for extrusion, a sheet of cellophane is the result.



$$\text{Cellulose}-\text{O}^-\,\text{Na}^+ + \text{CS}_2 \longrightarrow$$

$$\text{cellulose}-\text{O}-\overset{\text{S}}{\overset{\|}{\text{C}}}-\text{S}^-\text{Na}^+ \xrightarrow{H^+}$$

Cellulose xanthate (soluble)

$$\text{cellulose}-\text{OH} + \text{CS}_2$$

(insoluble)

GETTING INVOLVED

- ✓ The open chain form of an aldose or ketose is required to give a positive test for a reducing sugar. That is, it must have a hemiacetal or hemiketal structure. An acetal or ketal cannot react. Note that acetals and ketals are *diethers*. Show how the glycosidic link in sucrose contains diethers for both glucose and fructose.
- ✓ How are the terms fructose, glucose, levulose, dextrose, and invert sugar related?

C. Polysaccharides

There are as many possible polysaccharide structures as there are combinations of monosaccharides and positions of bonding. Those combinations are limitless. We will briefly consider the most abundant homopolymers, those of glucose.

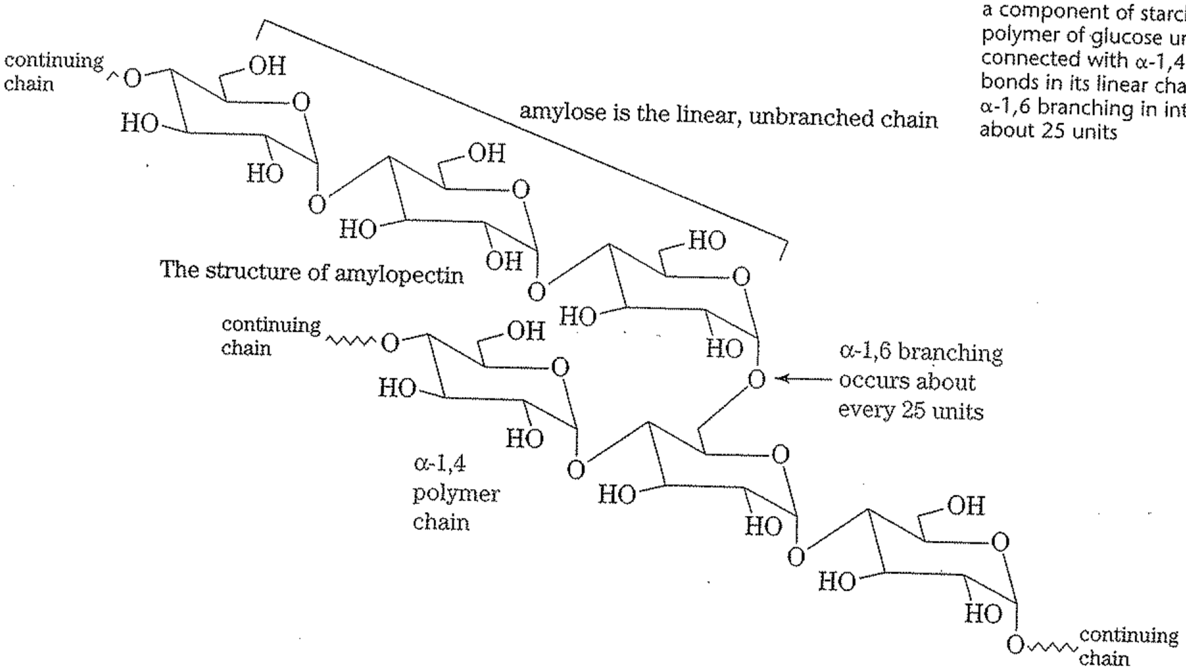
1. ***Starch.*** Plants store their glucose in the form of **starch.** It consists of two related but slightly different polysaccharides, amylose and amylopectin. **Amylose** is polyglucose linked entirely with α-1,4 glycosidic bonds. **Amylopectin** has an amylose-type chain but branches about every 25 glucose units using an α-1,6 glycosidic bond.

Animals possess enzymes that are readily able to cleave the α-bonds in starch and make the glucose available for metabolism.

starch
a natural, complex carbohydrate consisting of the polymers amylose and amylopectin

amylose
a component of starch; linear polymer of glucose units connected by α-1,4 glycosidic bonds

amylopectin
a component of starch; branched polymer of glucose units connected with α-1,4 glycosidic bonds in its linear chains with α-1,6 branching in intervals of about 25 units



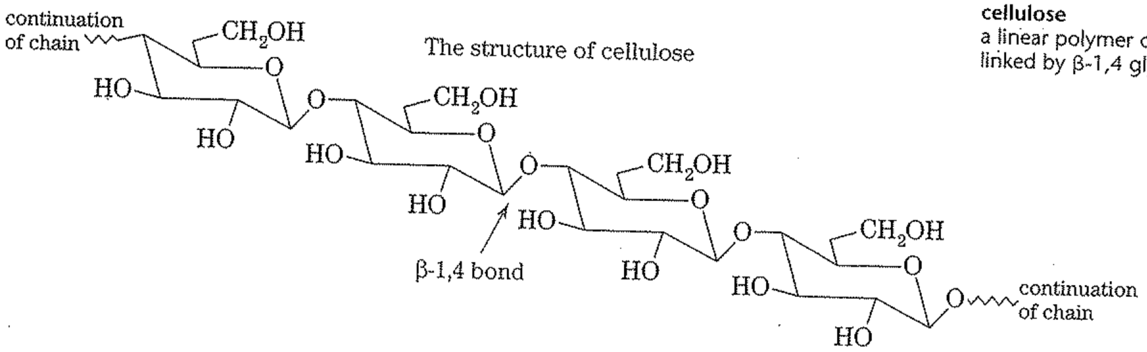
The structure of amylopectin

2. ***Glycogen.*** Animals store glucose using a polymer quite like amylopectin, except that the branching occurs every 8 to 10 glucose units. This adaption produces a more compact structure. A limited amount of **glycogen** is stored in the liver and muscle tissue, where it is a readily available source of energy.

3. ***Cellulose.*** Plants have a rigid exterior that acts as structural support and protection and is composed of a polyglucose-linked β-1,4 called **cellulose.** The

glycogen
branched polymer of glucose units connected with α-1,4 glycosidic bonds in its linear chains with α-1,6 branching in intervals of 8 to 10 units

cellulose
a linear polymer of glucose units linked by β-1,4 glycosidic bonds

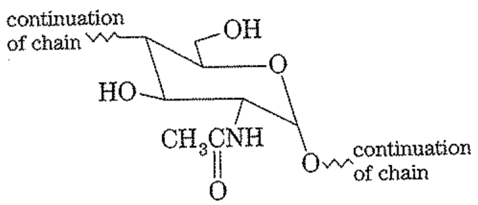


The structure of cellulose

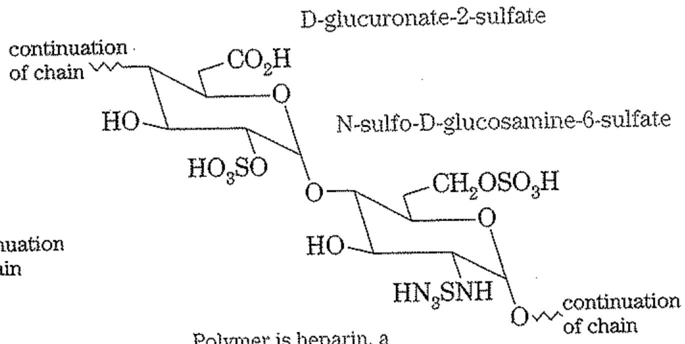
β-bond is not susceptible to animal enzymes, so the cellulose fibers cannot be used as a food source for humans and most animals. However, ruminants such as sheep, goats, and cows have gut bacteria that produce enzymes, cellulases, that digest cellulose, providing glucose for nourishment.

Cellulose is accompanied in its function by other polysaccharides such as hemicellulose (polyxylose) and pectin along with a complex polymer called *lignin.* Cotton, which is more than 90% cellulose, has a tremendous capacity to absorb water because of its large potential for hydrogen bonding.

4. ***Polysaccharide Variations.*** The variations of monomer units as well as of the position and stereochemical orientation of the glycoside bond lead to a tremendous variety of polysaccharides. Add to this the fact that monosaccharide units may be oxidized, derivatized, or otherwise modified, and we have an amazing number of possibilities. A few of these are seen below.



N-acetylglucosamine
Polymer is chitin, structural unit of the exoskeleton of insects and crustaceans.

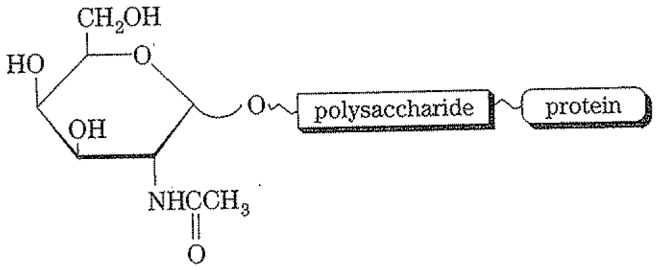


Polymer is heparin, a natural coagulant found in blood.

Blood group types differ in the presence or absence of a galactose unit or a derivatized galactose unit on the nonreducing end of a polysaccharide chain.

Type O

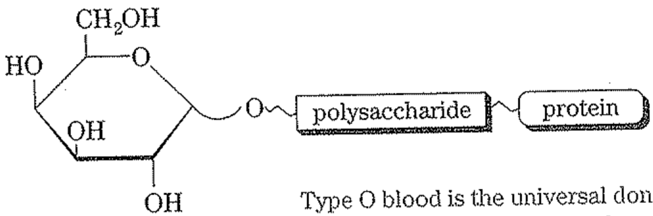
The protein portion is inserted into the red blood cell membrane.



Type A

The immune system recognizes the sugar unit at the left and rejects it if it is wrong. If the left-hand unit is not there as in Type O, the immune system will not respond.

Type B



Type O blood is the universal donor, while type AB is the universal receiver.

ast six polymer units of amylose and glycogen. Be sure to make the correct glycoside bonds.

✓ Can animals digest both starch and cellulose? What structural similarities and differences do these two natural polymers possess?

Problem 14.16

Identify the functional groups in both chitin and heparin. Are these natural polymers acidic or basic?

See related problems 14.26 and 14.27.

Problems

14.17 **Terms:** Distinguish between the members of the following pairs of terms:

- **(a)** hexose, pentose
- **(b)** aldose, ketose
- ~~**(c)** reducing sugar, nonreducing sugar~~
- **(d)** monosaccharide, polysaccharide
- **(e)** α-D-glucose, β-D-glucose
- **(f)** Haworth formula, Fischer projection
- **(g)** amylose, amylopectin
- **(h)** glycogen, cellulose
- **(i)** Type 1 diabetes, Type 2 diabetes
- ~~**(j)** viscose rayon, acetate rayon~~
- ~~**(k)** Fehling's and Tollens' tests~~

14.18 **Structure:** How are the members of the following pairs of saccharides different from each other structurally? Which are reducing, and which are nonreducing? Explain

- **(a)** cellobiose, maltose
- **(b)** lactose, sucrose
- **(c)** α-D-glucose, α-D-galactose
- **(d)** α-D-glucose, α-D-fructose
- **(e)** α-D-xylose, β-D-ribose
- **(f)** maltose, lactose
- **(g)** cellulose, starch

14.19 **Structure:** Draw Haworth formulas for the six-membered ring structures (pyranose forms) of the following:

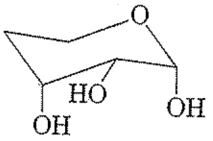
(a) β-D-fructose **(b)** α-D-idose
(c) β-D-talose **(d)** α-D-lyxose

14.20 **Structure** D-2-deoxyribose is found in DNA, our genetic code. Draw the structure of this monosaccharide.

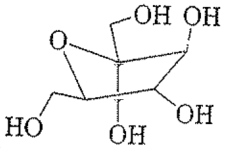
14.21 **Reactions:** Deoxyribose and ribose (RNA) form esters with phosphoric acid in DNA and RNA. Can both of these monosaccharides react to form the same number of ester combinations? Explain.

14.22 **Structure:** Draw the open-chain forms of the following cyclic saccharides:

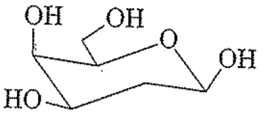
(a)



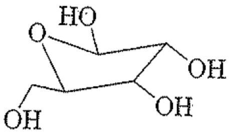
(b)



(c)



(d)

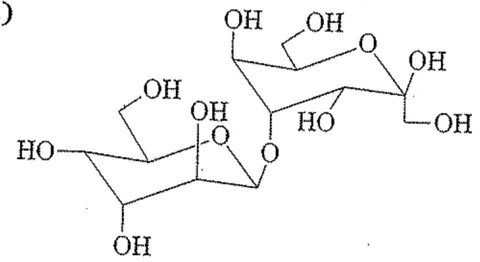


14.23 **Stereoisomers:** Draw the stereoisomers of 3-ketopentose. Which are the enantiomers, diastereomers, and meso compounds?

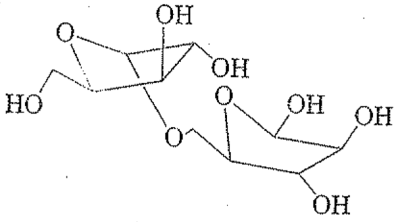
14.24 **Reactions:** Pure α-D-glucose or pure β-D-glucose in the presence of methanol (CH_3OH) and acid will give a mixture of α- and β-methyl glucosides. Why?

14.25 **Structure:** Specify the type of glycosidic bond that appears in each of the following disaccharides. Also identify the general type of monosaccharide units that appear in each, such as aldopentose.

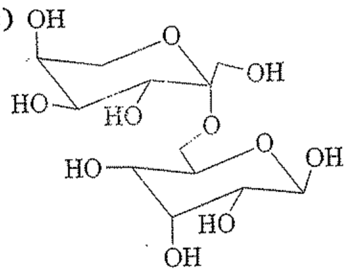
(a)



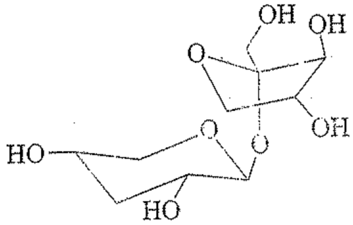
(b)



(c)



(d)



14.26 **Reactions:** Are the disaccharides in the previous question reducing or nonreducing? Explain your answers using the structures.

14.27 **Structure:** Draw the Haworth structures for the following polysaccharides (ring size is indicated in parentheses):

(a) polymannose (pyranose form) linked β-1,3
(b) polyxylose (furanose form) linked β-1,2
(c) polyarabinose (pyranose form) linked α-1,4
(d) polyfructose (furanose form) linked α-2,6 with β-2,4 branching

14.28 **Reactions:** Draw the reactions and products of β-D-galactose in the six-membered ring form with each of the following:

(a) first one mole of methanol and then two moles of methanol
(b) α-D-mannose (six-membered ring also) as a β-1,4-bond
(c) copper (II) in basic solution
(d) α-D-fructose (pyranose) in an α-1,6-bond

14.29 **Reactions:** Why do both glucose and fructose give positive Fehling and Tollens' tests?

14.30 **Reactions:** Is a positive Fehling test for glucose in the urine a direct indication of diabetes? Explain your answer.