

## 22

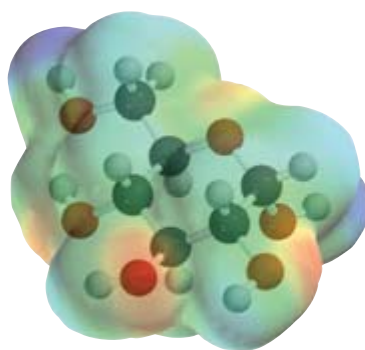
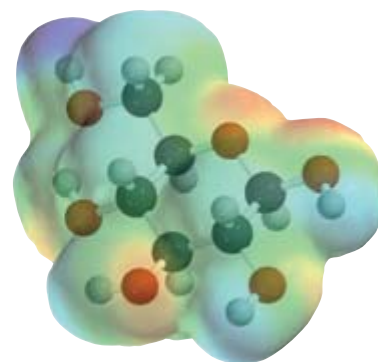
## Carbohydrates

**B**ioorganic compounds are organic compounds found in biological systems. Bioorganic compounds follow the same principles of structure and reactivity as the organic molecules we have discussed so far. There is great similarity between the organic reactions chemists carry out in the laboratory and those performed by nature inside the living cell. In other words, bioorganic reactions can be thought of as organic reactions that take place in tiny flasks called cells.

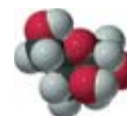
Most bioorganic compounds have more complicated structures than those of the organic compounds you are used to seeing, but do not let the structures fool you into thinking that their chemistry is equally complicated. One reason the structures of bioorganic compounds are more complicated is that bioorganic compounds must be able to recognize each other, and much of their structure is for that purpose—a function called **molecular recognition**.

The first group of bioorganic compounds we will study are the *carbohydrates*—the most abundant class of compounds in the biological world, making up more than 50% of the dry weight of the Earth's biomass. Carbohydrates are important constituents of all living organisms and have a variety of different functions. Some are important structural components of cells; others act as recognition sites on cell surfaces. For example, the first event in all our lives was a sperm recognizing a carbohydrate on the surface of an egg's wall. Other carbohydrates serve as a major source of metabolic energy. For example, the leaves, fruits, seeds, stems, and roots of plants contain carbohydrates that plants use for their own metabolic needs and that then serve the metabolic needs of the animals that eat the plants.

Early chemists noted that carbohydrates have molecular formulas that make them appear to be hydrates of carbon,  $C_n(H_2O)_n$ —hence the name. Later structural studies revealed that these compounds were *not* hydrates because they did not contain intact water molecules, but the term “carbohydrate” persists. **Carbohydrates** are polyhydroxy aldehydes such as D-glucose, polyhydroxy ketones such as D-fructose, and compounds such as sucrose that can be hydrolyzed to polyhydroxy aldehydes or

 $\alpha$ -D-glucose $\beta$ -D-glucose

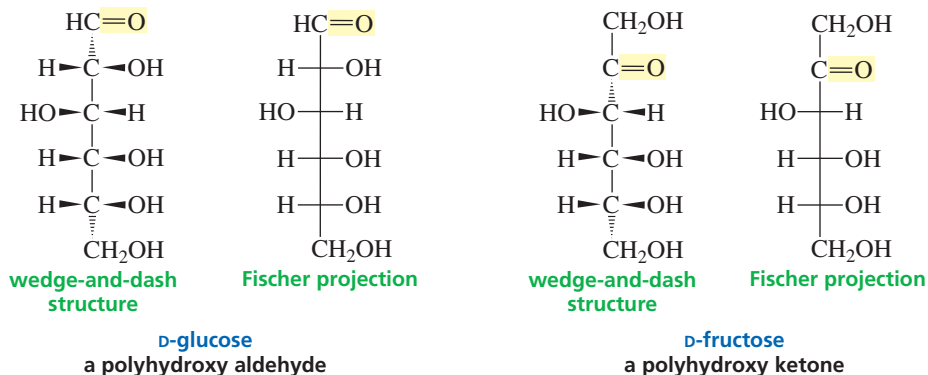
D-glucose



D-fructose

polyhydroxy ketones (Section 22.17). The chemical structures of carbohydrates are commonly represented by wedge-and-dash structures or by Fischer projections. Notice that both D-glucose and D-fructose have the molecular formula  $C_6H_{12}O_6$ , consistent with the general formula  $C_6(H_2O)_6$  that made early chemists think that those compounds were hydrates of carbon.

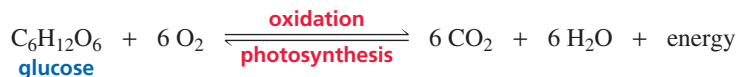
Recall from Section 5.4 that horizontal bonds point toward the viewer and vertical bonds point away from the viewer in Fischer projections.



3-D Molecules:  
D-Glucose;  
D-Fructose

The most abundant carbohydrate in nature is D-glucose. Living cells oxidize D-glucose in the first of a series of processes that provide them with energy. When animals have more D-glucose than they need for energy, they convert excess D-glucose into a polymer called glycogen (Section 22.18). When an animal needs energy, glycogen is broken down into individual D-glucose molecules. Plants convert excess D-glucose into a polymer known as starch. Cellulose—the major structural component of plants—is another polymer of D-glucose. Chitin, a carbohydrate similar to cellulose, makes up the exoskeletons of crustaceans, insects, and other arthropods and is also the structural material of fungi.

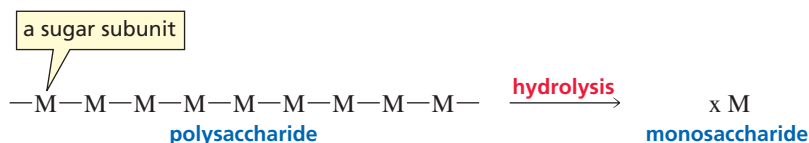
Animals obtain glucose from food—such as plants—that contains glucose. Plants produce glucose by **photosynthesis**. During photosynthesis, plants take up water through their roots and use carbon dioxide from the air to synthesize glucose and oxygen. Because photosynthesis is the reverse of the process used by organisms to obtain energy—the oxidation of glucose to carbon dioxide and water—plants require energy to carry out photosynthesis. Plants obtain the energy they need for photosynthesis from sunlight, captured by chlorophyll molecules in green plants. Photosynthesis uses the  $CO_2$  that animals exhale as waste and generates the  $O_2$  that animals inhale to sustain life. Nearly all the oxygen in the atmosphere has been released by photosynthetic processes.



## 22.1 Classification of Carbohydrates

The terms “carbohydrate,” “saccharide,” and “sugar” are often used interchangeably. “Saccharide” comes from the word for “sugar” in several early languages (*sarkara* in Sanskrit, *sakcharon* in Greek, and *saccharum* in Latin).

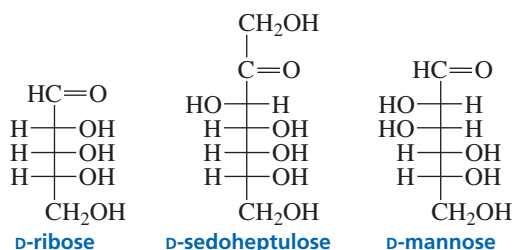
There are two classes of carbohydrates: *simple carbohydrates* and *complex carbohydrates*. **Simple carbohydrates** are **monosaccharides** (single sugars), whereas **complex carbohydrates** contain two or more sugar subunits linked together. **Disaccharides** have two sugar subunits linked together, **oligosaccharides** have three to 10 sugar subunits (*oligos* is Greek for “few”) linked together, and **polysaccharides** have more than 10 sugar subunits linked together. Disaccharides, oligosaccharides, and polysaccharides can be broken down to monosaccharide subunits by hydrolysis.



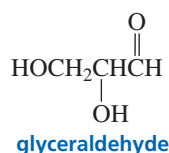
A *monosaccharide* can be a polyhydroxy aldehyde such as D-glucose or a polyhydroxy ketone such as D-fructose. Polyhydroxy aldehydes are called **aldoses** (“ald” is for aldehyde; “ose” is the suffix for a sugar), whereas polyhydroxy ketones are called **ketoses**. Monosaccharides are also classified according to the number of carbons they contain: Monosaccharides with three carbons are **trioses**, those with four carbons are **tetroses**, those with five carbons are **pentoses**, and those with six and seven carbons are **hexoses** and **heptoses**, respectively. A six-carbon polyhydroxy aldehyde such as D-glucose is an aldohexose, whereas a six-carbon polyhydroxy ketone such as D-fructose is a ketohexose.

**PROBLEM 1**

Classify the following monosaccharides:

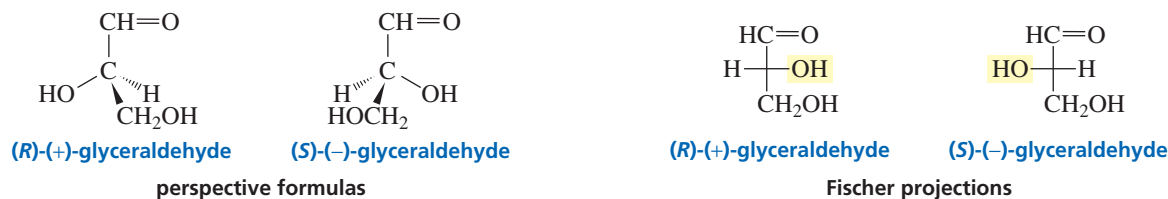
**22.2 The D and L Notation**

The smallest aldose, and the only one whose name does not end in “ose,” is glyceraldehyde, an aldotriose.

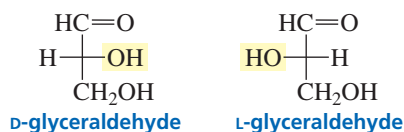


A carbon to which four different groups are attached is an asymmetric carbon.

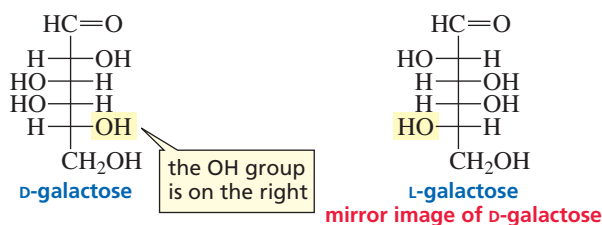
Because glyceraldehyde has an asymmetric carbon, it can exist as a pair of enantiomers.



Emil Fischer and his colleagues studied carbohydrates in the late nineteenth century, when techniques for determining the configurations of compounds were not available. Fischer arbitrarily assigned the *R*-configuration to the dextrorotatory isomer of glyceraldehyde that we call D-glyceraldehyde. He turned out to be correct: D-Glyceraldehyde is *(R)*-(+)-glyceraldehyde, and L-glyceraldehyde is *(S)*-(–)-glyceraldehyde (Section 5.13).

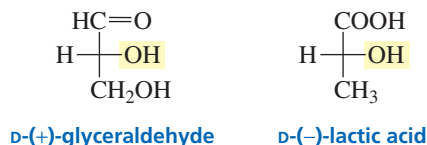


The notations D and L are used to describe the configurations of carbohydrates and amino acids (Section 23.2), so it is important to learn what D and L signify. In Fischer projections of monosaccharides, the carbonyl group is always placed on top (in the case of aldoses) or as close to the top as possible (in the case of ketoses). From its structure, you can see that galactose has four asymmetric carbons (C-2, C-3, C-4, and C-5). *If the OH group attached to the bottom-most asymmetric carbon (the carbon that is second from the bottom) is on the right, then the compound is a D-sugar. If the OH group is on the left, then the compound is an L-sugar.* Almost all sugars found in nature are D-sugars. Notice that the mirror image of a D-sugar is an L-sugar.



Tutorial:  
D and L Notation

Like *R* and *S*, D and L indicate the configuration of an asymmetric carbon, but they do not indicate whether the compound rotates polarized light to the right (+) or to the left (−) (Section 5.7). For example, D-glyceraldehyde is dextrorotatory, whereas D-lactic acid is levorotatory. In other words, optical rotation, like melting or boiling points, is a physical property of a compound, whereas “*R*, *S*, D, and L” are conventions humans use to indicate the configuration of a molecule.



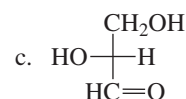
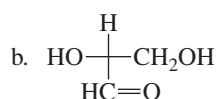
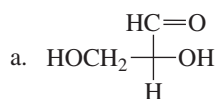
The common name of the monosaccharide, together with the D or L designation, completely defines its structure because the relative configurations of all the asymmetric carbons are implicit in the common name.

### PROBLEM 2

Draw Fischer projections of L-glucose and L-fructose.

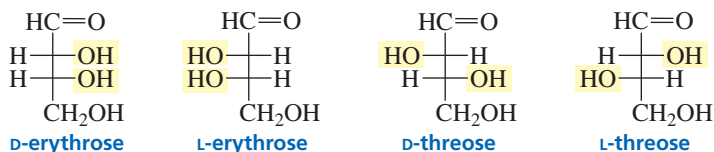
### PROBLEM 3 ♦

Indicate whether each of the following is D-glyceraldehyde or L-glyceraldehyde, assuming that the horizontal bonds point toward you and the vertical bonds point away from you (Section 5.6):



## 22.3 Configurations of Aldoses

Aldotetroses have two asymmetric carbons and therefore four stereoisomers. Two of the stereoisomers are D-sugars and two are L-sugars. The names of the aldotetroses—erythrose and threose—were used to name the erythro and threo pairs of enantiomers described in Section 5.9.



Aldopentoses have three asymmetric carbons and therefore eight stereoisomers (four pairs of enantiomers), while aldohexoses have four asymmetric carbons and 16 stereoisomers (eight pairs of enantiomers). The four D-aldopentoses and the eight D-aldohexoses are shown in Table 22.1.



Movie:  
Configurations of the  
D-aldoses

Diastereomers that differ in configuration at only one asymmetric carbon are called **epimers**. For example, D-ribose and D-arabinose are C-2 epimers (they differ in configuration only at C-2), and D-idose and D-talose are C-3 epimers.

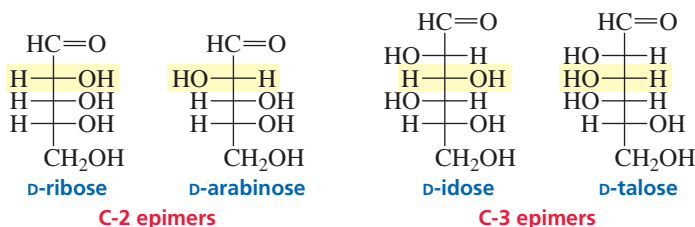
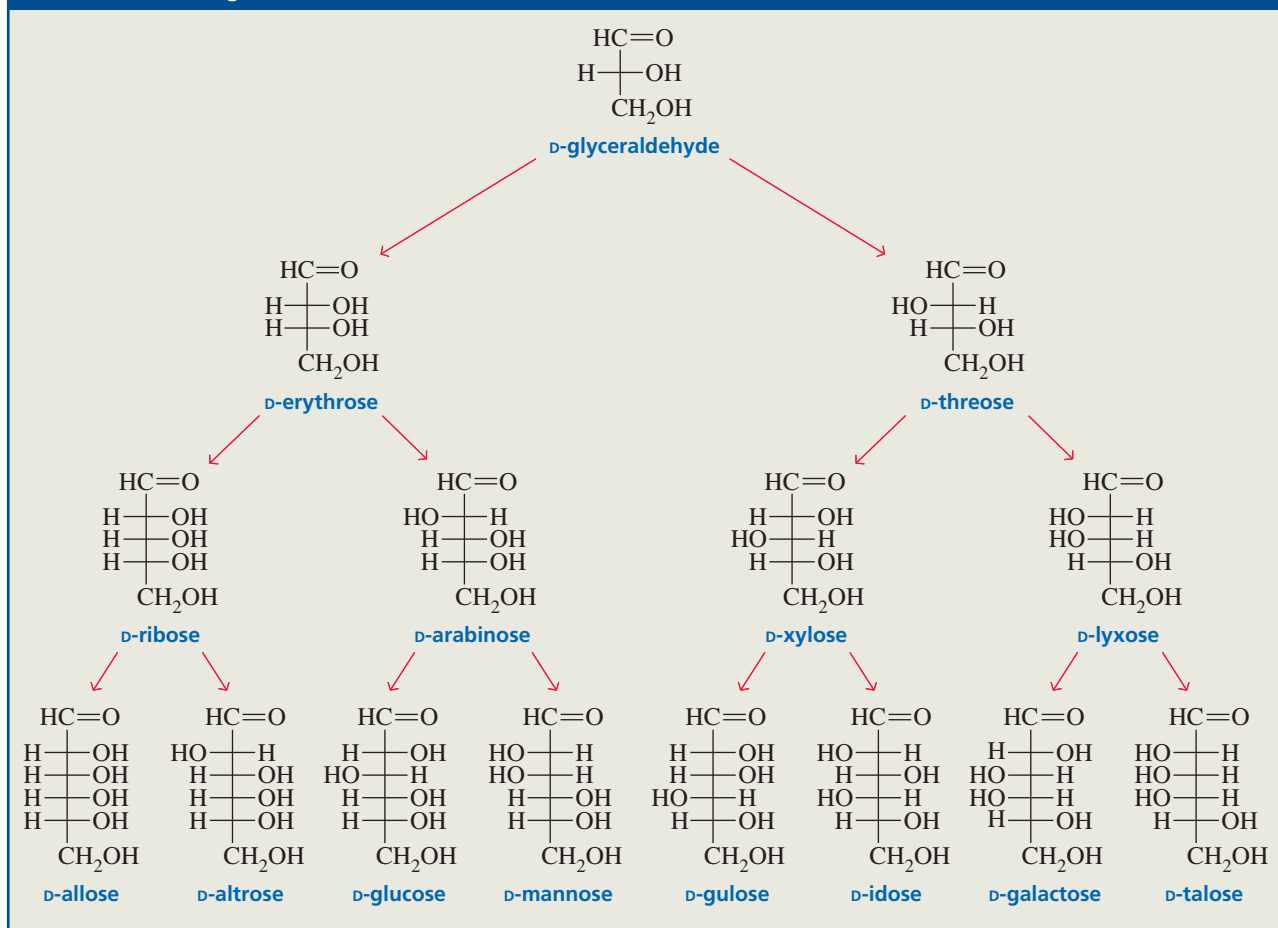


TABLE 22.1 Configurations of the D-Aldoses



D-Mannose is the C-2 epimer of D-glucose.

D-Galactose is the C-4 epimer of D-glucose.

Diastereomers are configurational isomers that are not enantiomers.

D-Glucose, D-mannose, and D-galactose are the most common aldohexoses in biological systems. An easy way to learn their structures is to memorize the structure of D-glucose and then remember that D-mannose is the C-2 epimer of D-glucose and D-galactose is the C-4 epimer of D-glucose. Sugars such as D-glucose and D-galactose are also diastereomers because they are stereoisomers that are not enantiomers (Section 5.9). An epimer is a particular kind of diastereomer.

#### PROBLEM 4 ♦

- Are D-erythrose and L-erythrose enantiomers or diastereomers?
- Are L-erythrose and L-threose enantiomers or diastereomers?

#### PROBLEM 5 ♦

- What sugar is the C-3 epimer of D-xylose?
- What sugar is the C-5 epimer of D-allose?
- What sugar is the C-4 epimer of L-gulose?

#### PROBLEM 6 ♦

Give systematic names to the following compounds. Indicate the configuration (*R* or *S*) of each asymmetric carbon:

- D-glucose
- L-glucose

## 22.4 Configurations of Ketoses

Naturally occurring ketoses have the ketone group in the 2-position. The configurations of the D-2-ketoses are shown in Table 22.2. A ketose has one fewer asymmetric carbon than does an aldose with the same number of carbon atoms. Therefore, a ketose has only half as many stereoisomers as an aldose with the same number of carbon atoms.

#### PROBLEM 7 ♦

What sugar is the C-3 epimer of D-fructose?

#### PROBLEM 8 ♦

How many stereoisomers are possible for

- a 2-ketoheptose?
- an aldoheptose?
- a ketotriose?

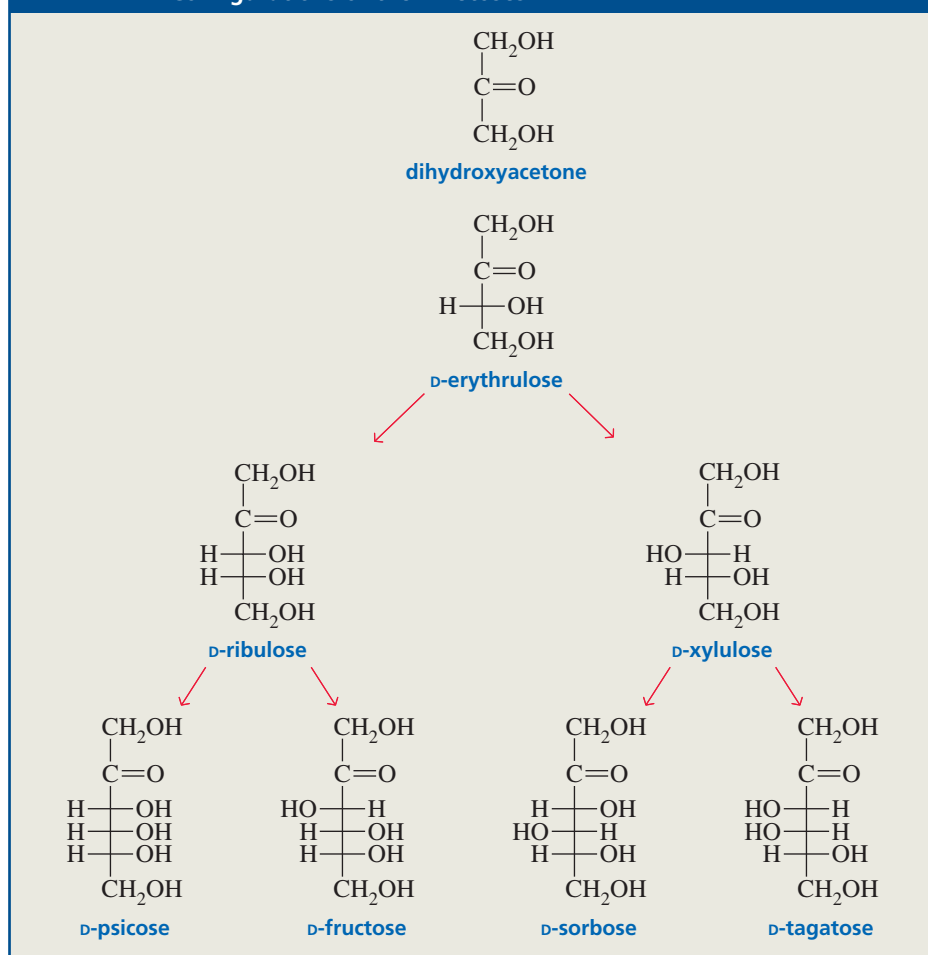
## 22.5 Redox Reactions of Monosaccharides

Because monosaccharides contain *alcohol* functional groups and *aldehyde* (or *ketone*) functional groups, the reactions of monosaccharides are an extension of what you have already learned about the reactions of alcohols, aldehydes, and ketones. For example, an aldehyde group in a monosaccharide can be oxidized or reduced and can react with nucleophiles to form imines, hemiacetals, and acetals. When you read the sections that deal with the reactions of monosaccharides, you will find cross-references to the sections in which the same reactivity for simple organic compounds is discussed. As you study, refer back to these sections; they will make learning about carbohydrates a lot easier and will give you a good review of some chemistry that you have already learned about.

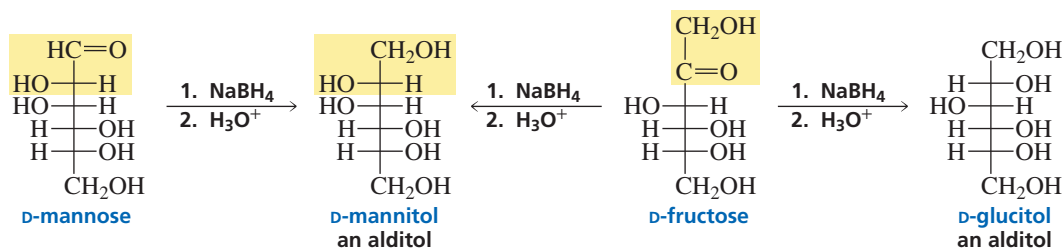
### Reduction

The carbonyl group of aldoses and ketoses can be reduced by the usual carbonyl-group reducing agents (e.g.,  $\text{NaBH}_4$ ; Section 20.1). The product of the reduction is a polyalcohol, known as an **alditol**. Reduction of an aldose forms one alditol. Reduction of a ketose forms two alditols because the reaction creates a new asymmetric carbon in the

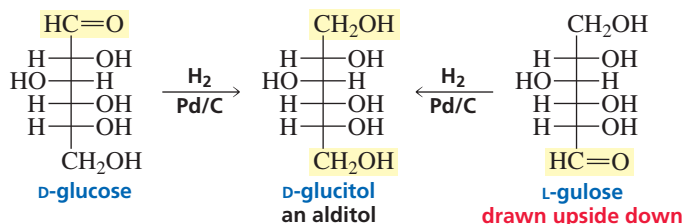
TABLE 22.2 Configurations of the D-Ketoses



product. D-Mannitol, the alditol formed from the reduction of D-mannose, is found in mushrooms, olives, and onions. The reduction of D-fructose forms D-mannitol and D-glucitol, the C-2 epimer of D-mannitol. D-Glucitol—also called sorbitol—is about 60% as sweet as sucrose. It is found in plums, pears, cherries, and berries and is used as a sugar substitute in the manufacture of candy.



D-Glucitol is also obtained from the reduction of either D-glucose or L-gulose.



D-Xylitol—obtained from the reduction of D-xylulose—is used as a sweetening agent in cereals and in sugarless gum.

**PROBLEM 9** ♦

What products are obtained from the reduction of

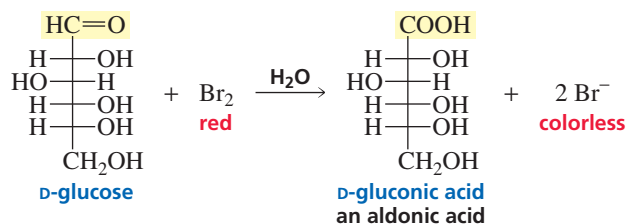
- a. D-idose? b. D-sorbose?

**PROBLEM 10** ♦

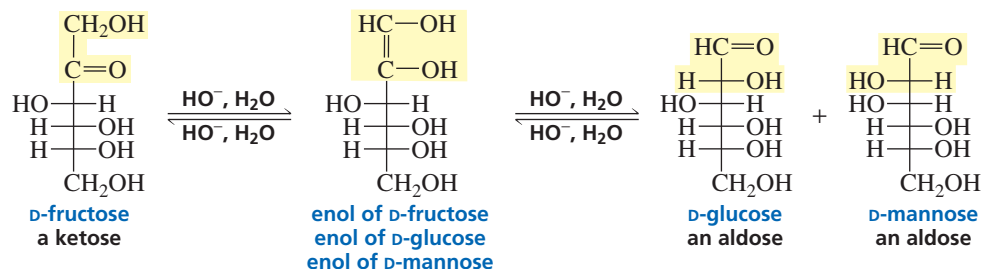
- a. What other monosaccharide is reduced only to the alditol obtained from the reduction of
1. D-talose?
  2. D-galactose?
- b. What monosaccharide is reduced to two alditols, one of which is the alditol obtained from the reduction of
1. D-talose?
  2. D-mannose?

**Oxidation**

Aldoses can be distinguished from ketoses by observing what happens to the color of an aqueous solution of bromine when it is added to the sugar.  $\text{Br}_2$  is a mild oxidizing agent and easily oxidizes the aldehyde group, but it cannot oxidize ketones or alcohols. Consequently, if a small amount of an aqueous solution of  $\text{Br}_2$  is added to an unknown monosaccharide, the reddish-brown color of  $\text{Br}_2$  will disappear if the monosaccharide is an aldose, but will persist if the monosaccharide is a ketose. The product of the oxidation reaction is an **aldonic acid**.



Both aldoses and ketoses are oxidized to aldonic acids by Tollens reagent ( $\text{Ag}^+$ ,  $\text{NH}_3$ ,  $\text{HO}^-$ ), so that reagent cannot be used to distinguish between aldoses and ketoses. Recall from Section 20.3, however, that Tollens reagent oxidizes aldehydes but not ketones. Why, then, are ketoses oxidized by Tollens reagent, while ketones are not? Ketoses are oxidized because the reaction is carried out under basic conditions, and in a basic solution, ketoses are converted into aldoses by enolization (Section 19.2). For example, the ketose D-fructose is in equilibrium with its enol. However, the enol of D-fructose is also the enol of D-glucose, as well as the enol of D-mannose. Therefore, when the enol reketonizes, all three carbonyl compounds are formed.





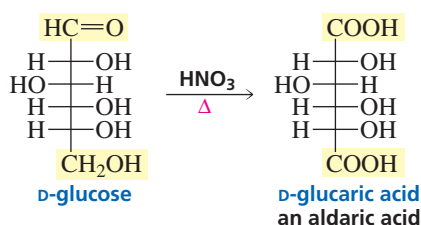
**PROBLEM 11**

Write the mechanism for the base-catalyzed conversion of D-fructose into D-glucose and D-mannose.

**PROBLEM 12** ♦

When D-tagatose is added to a basic aqueous solution, an equilibrium mixture of three monosaccharides is obtained. What are these monosaccharides?

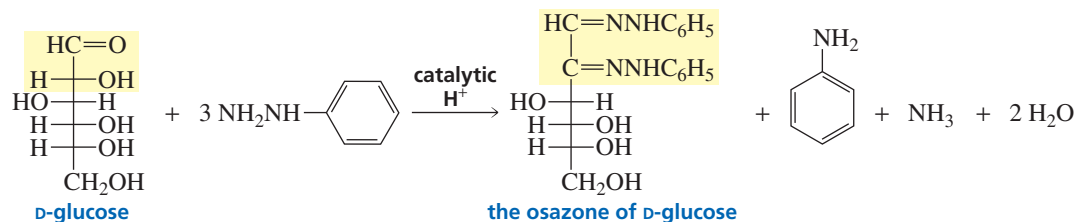
If an oxidizing agent stronger than those discussed previously is used (such as  $\text{HNO}_3$ ), one or more of the alcohol groups can be oxidized in addition to the aldehyde group. A primary alcohol is the one most easily oxidized. The product that is obtained when both the aldehyde and the primary alcohol groups of an aldose are oxidized is called an **aldaric acid**. (In an **aldonic acid**, one end is oxidized. In an **aldaric acid**, both ends are oxidized.)

**PROBLEM 13** ♦

- Name an aldohexose other than D-glucose that is oxidized to D-glucaric acid by nitric acid.
- What is another name for D-glucaric acid?
- Name another pair of aldohexoses that are oxidized to identical aldaric acids.

**22.6 Osazone Formation**

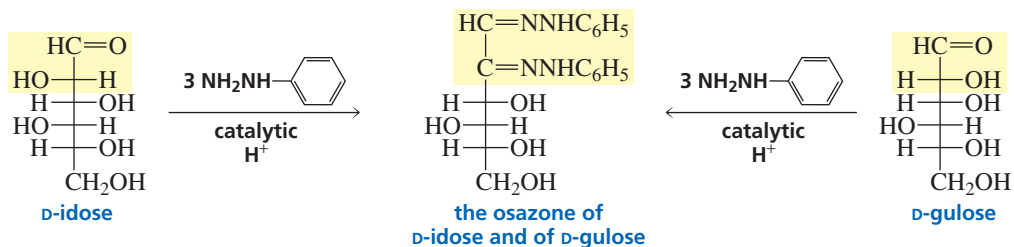
The tendency of monosaccharides to form syrups that do not crystallize made the purification and isolation of monosaccharides difficult. Emil Fischer found that when phenylhydrazine is added to an aldose or a ketose, a yellow crystalline solid that is insoluble in water is formed. He called this derivative an osazone (“ose” for sugar; “azone” for hydrazone). Osazones are easily isolated and purified and were once used extensively to identify monosaccharides.



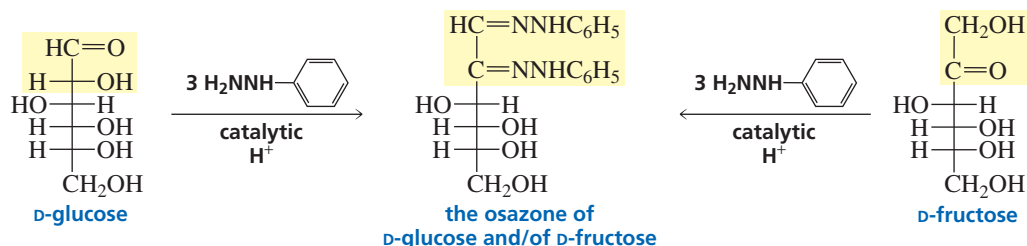
Aldehydes and ketones react with one equivalent of phenylhydrazine, forming phenylhydrazones (Section 18.6). Aldoses and ketoses, in contrast, react with three equivalents of phenylhydrazine, forming osazones. One equivalent functions as an oxidizing agent and is reduced to aniline and ammonia. Two equivalents form imines with carbonyl groups. The reaction stops at this point, regardless of how much phenylhydrazine is present. (Recall that the pH at which imine formation is carried out must be carefully controlled; Section 18.6.)

C-2 epimers form identical osazones.

Because the configuration of the number-2 carbon is lost during osazone formation, C-2 epimers form identical osazones. For example, D-idose and D-gulose, which are C-2 epimers, both form the same osazone.



The number-1 and number-2 carbons of ketoses react with phenylhydrazine, too. Consequently, D-fructose, D-glucose, and D-mannose all form the same osazone.



#### PROBLEM 14♦

Name a ketose and another aldose that form the same osazone as

- D-ribose
- D-altrose
- L-idose
- D-galactose

#### PROBLEM 15♦

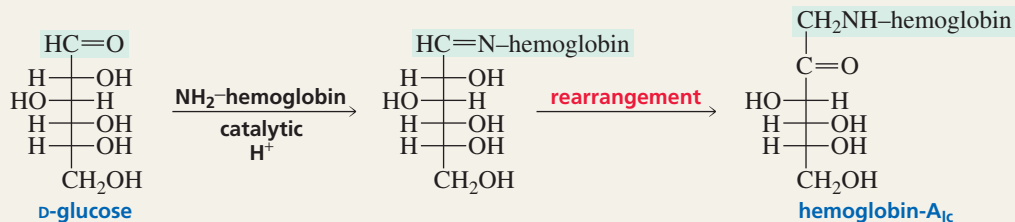
What monosaccharides form the same osazone as D-sorbose?



### MEASURING THE BLOOD GLUCOSE LEVELS OF DIABETICS

Glucose reacts with an  $\text{NH}_2$  group of hemoglobin to form an imine (Section 18.6) that subsequently undergoes an

irreversible rearrangement to a more stable  $\alpha$ -aminoketone known as hemoglobin- $\text{A}_{1\text{C}}$ .



Diabetes results when the body does not produce sufficient insulin or when the insulin it produces does not properly stimulate its target cells. Because insulin is the hormone that maintains the proper level of glucose in the blood, diabetics have increased blood glucose levels. The amount of hemoglobin- $\text{A}_{1\text{C}}$  formed is proportional to the concentration of glucose in the blood, so diabetics have a higher concentration of hemoglobin- $\text{A}_{1\text{C}}$  than nondi-

abetics. Thus, measuring the hemoglobin- $\text{A}_{1\text{C}}$  level is a way to determine whether the blood glucose level of a diabetic is being controlled. Cataracts, a common complication in diabetics, are caused by the reaction of glucose with the  $\text{NH}_2$  group of proteins in the lens of the eye. It is thought that the arterial rigidity common in old age may be attributable to a similar reaction of glucose with the  $\text{NH}_2$  group of proteins.

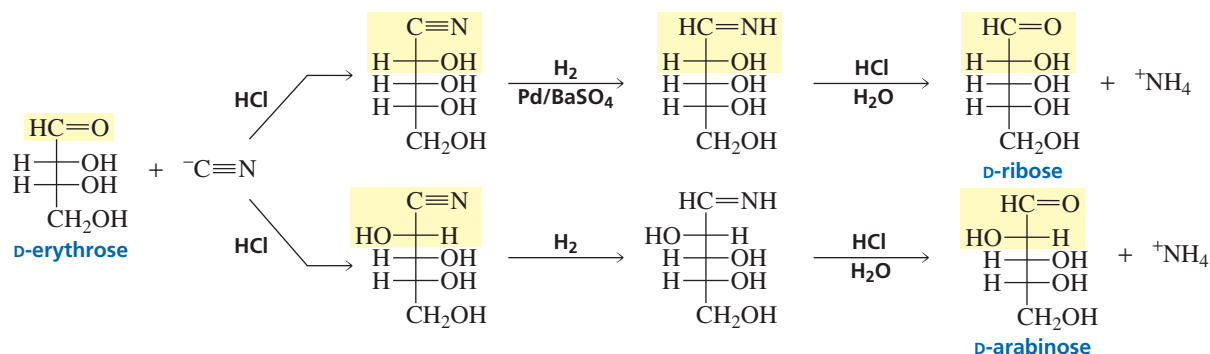
## 22.7 Chain Elongation: The Kiliani–Fischer Synthesis

The carbon chain of an aldose can be increased by one carbon in a **Kiliani–Fischer synthesis**. In other words, tetroses can be converted into pentoses, and pentoses can be converted into hexoses.

In the first step of the synthesis (the Kiliani portion), the aldose is treated with sodium cyanide and HCl (Section 18.4). Addition of cyanide ion to the carbonyl group creates a new asymmetric carbon. Consequently, two cyanohydrins that differ only in configuration at C-2 are formed. The configurations of the other asymmetric carbons do not change, because no bond to any of the asymmetric carbons is broken during the course of the reaction (Section 5.12). Kiliani went on to hydrolyze the cyanohydrins to aldonic acids (Section 17.18), and Fischer had previously developed a method to convert aldonic acids to aldoses. This reaction sequence was used for many years, but the method currently employed to convert the cyanohydrins to aldoses was developed by Serianni and Barker in 1979; it is referred to as the modified Kiliani–Fischer synthesis. Serianni and Barker reduced the cyanohydrins to imines, using a partially deactivated palladium (on barium sulfate) catalyst so that the imines would not be further reduced to amines. The imines could then be hydrolyzed to aldoses (Section 18.6).

**Heinrich Kiliani (1855–1945)** was born in Germany. He received a Ph.D. from the University of Munich, studying under Professor Emil Erlenmeyer. Kiliani became a professor of chemistry at the University of Freiburg.

the modified Kiliani–Fischer synthesis



Notice that the synthesis leads to a pair of C-2 epimers because the first step of the reaction converts the carbonyl carbon in the starting material to an asymmetric carbon. Therefore, the OH bonded to C-2 in the product can be on the right or on the left in the Fischer projection. The two epimers are not obtained in equal amounts, however, because the first step of the reaction produces a pair of diastereomers and diastereomers are generally formed in unequal amounts (Section 5.19).

The Kiliani–Fischer synthesis leads to a pair of C-2 epimers.

### PROBLEM 16 ♦

What monosaccharides would be formed in a Kiliani–Fischer synthesis starting with one of these?

a. D-xylose

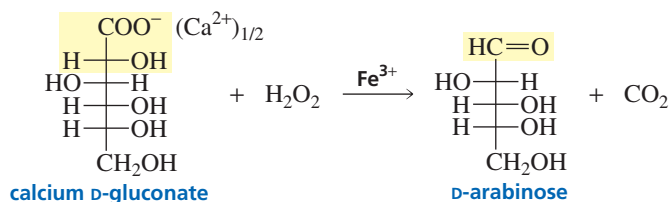
b. L-threose

## 22.8 Chain Shortening: The Ruff Degradation

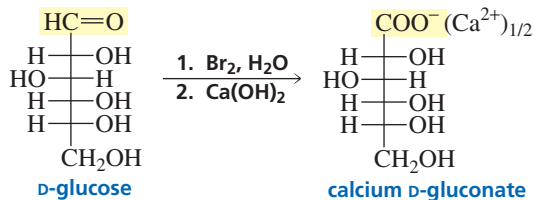
The *Ruff degradation* is the opposite of the Kiliani–Fischer synthesis. Thus, the **Ruff degradation** shortens an aldose chain by one carbon: Hexoses are converted into pentoses, and pentoses are converted into tetroses. In the Ruff degradation, the calcium salt of an aldonic acid is oxidized with hydrogen peroxide. Ferric ion catalyzes the oxidation reaction, which cleaves the bond between C-1 and C-2, forming CO<sub>2</sub> and an aldehyde. It is known that the reaction involves the formation of radicals, but the precise mechanism is not well understood.

**Otto Ruff (1871–1939)** was born in Germany. He received a Ph.D. from the University of Berlin. He was a professor of chemistry at the University of Danzig and later at the University of Breslau.

## the Ruff degradation



The calcium salt of the aldonic acid necessary for the Ruff degradation is easily obtained by oxidizing an aldose with an aqueous solution of bromine and then adding calcium hydroxide to the reaction mixture.



## PROBLEM 17♦

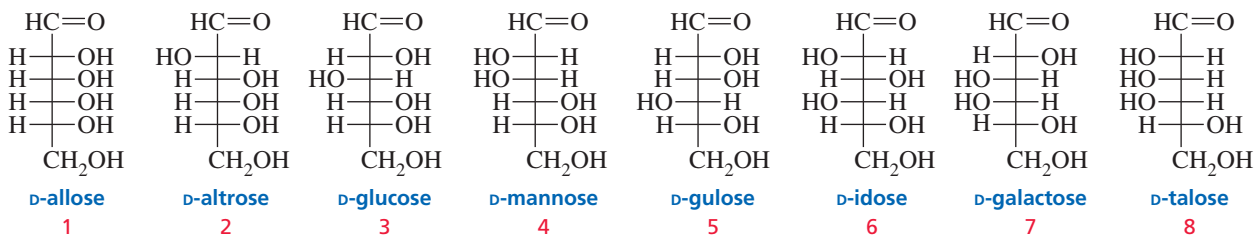
What two monosaccharides can be degraded to

- D-arabinose?
- D-glyceraldehyde?
- L-ribose?

## 22.9 Stereochemistry of Glucose: The Fischer Proof

In 1891, Emil Fischer determined the stereochemistry of glucose using one of the most brilliant examples of reasoning in the history of chemistry. He chose (+)-glucose for his study because it was the most common monosaccharide found in nature.

Fischer knew that (+)-glucose was an aldohexose, but 16 different structures can be written for an aldohexose. Which of them represents the structure of (+)-glucose? The 16 stereoisomers of the aldohexoses are actually eight pairs of enantiomers, so if you know the structures of one set, you automatically know the structures of the other set. Therefore, Fischer needed to consider only one set of eight. He considered the eight stereoisomers that had the C-5 OH group on the right in the Fischer projection (the stereoisomers we now call the D-sugars). One of these would be one enantiomer of glucose, and its mirror image would be the other enantiomer. It was not possible to determine whether (+)-glucose was D-glucose or L-glucose until 1951 (Section 5.13). Fischer used the following information to determine glucose's stereochemistry—that is, to determine the configuration of each of its asymmetric carbons.

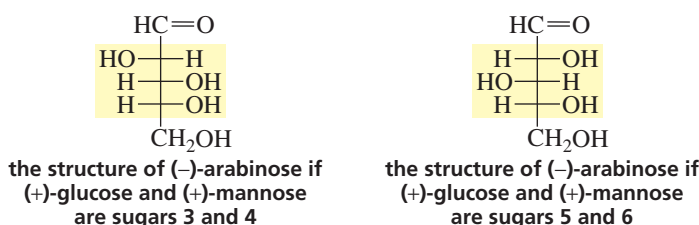


1. When the Kiliani–Fischer synthesis is performed on the sugar known as (–)-arabinose, the two sugars known as (+)-glucose and (+)-mannose are obtained. This means that (+)-glucose and (+)-mannose are C-2 epimers; in other words, they have the same configuration at C-3, C-4, and C-5. Consequently, (+)-glucose

and (+)-mannose have to be one of the following pairs: sugars 1 and 2, 3 and 4, 5 and 6, or 7 and 8.

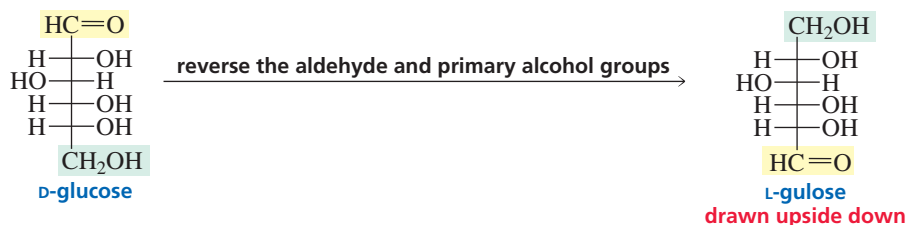
2. (+)-Glucose and (+)-mannose are both oxidized by nitric acid to optically active aldaric acids. The aldaric acids of sugars 1 and 7 would not be optically active because they have a plane of symmetry. (A compound with a plane of symmetry has a superimposable mirror image; Section 5.10.) Excluding sugars 1 and 7 means that (+)-glucose and (+)-mannose must be sugars 3 and 4 or 5 and 6.

3. Because (+)-glucose and (+)-mannose are the products obtained when the Kiliani–Fischer synthesis is carried out on (–)-arabinose, there are only two possibilities for the structure of (–)-arabinose. That is, if (+)-glucose and (+)-mannose are sugars 3 and 4, then (–)-arabinose has the structure shown below on the left; on the other hand, if (+)-glucose and (+)-mannose are sugars 5 and 6, then (–)-arabinose has the structure shown on the right:

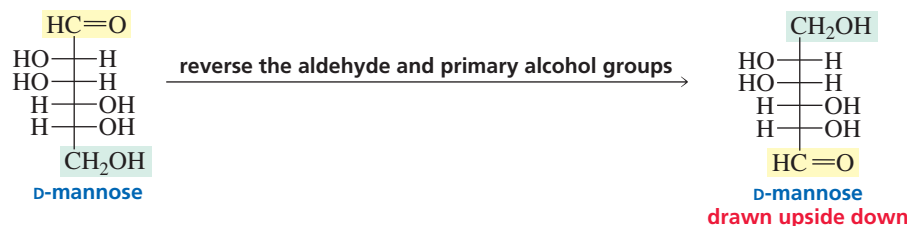


When (–)-arabinose is oxidized with nitric acid, the aldaric acid that is obtained is optically active. This means that the aldaric acid does *not* have a plane of symmetry. Therefore, (–)-arabinose must have the structure shown on the left because the aldaric acid of the sugar on the right has a plane of symmetry. Thus, (+)-glucose and (+)-mannose are represented by sugars 3 and 4.

4. The last step in the Fischer proof was to determine whether (+)-glucose is sugar 3 or sugar 4. To answer this question, Fischer had to develop a chemical method that would interchange the aldehyde and primary alcohol groups of an aldohexose. When he chemically interchanged the aldehyde and primary alcohol groups of the sugar known as (+)-glucose, he obtained an aldohexose that was different from (+)-glucose. When he chemically interchanged the aldehyde and primary alcohol groups of (+)-mannose, he still had (+)-mannose. Therefore, he concluded that (+)-glucose is sugar 3 because reversing the aldehyde and alcohol groups of sugar 3 leads to a different sugar (L-gulose).



If (+)-glucose is sugar 3, (+)-mannose must be sugar 4. As predicted, when the aldehyde and primary alcohol groups of sugar 4 are reversed, the same sugar is obtained.



Using similar reasoning, Fischer went on to determine the stereochemistry of 14 of the 16 aldohexoses. He received the Nobel Prize in chemistry in 1902 for this achievement. His original guess that (+)-glucose is a D-sugar was later shown to be correct, so all of his structures are correct (Section 5.13). If he had been wrong and (+)-glucose had been an L-sugar, his contribution to the stereochemistry of aldoses would still have had the same significance, but all his stereochemical assignments would have been reversed.

AU: OK as changed?



## GLUCOSE/DEXTROSE

André Dumas first used the term “glucose” in 1838 to refer to the sweet compound that comes from honey and grapes. Later, Kekulé (Section 7.1) decided that it should be called dextrose because it was dextrorotatory.

When Fischer studied the sugar, he called it glucose, and chemists have called it glucose ever since, although dextrose is often found on food labels.

### Jean-Baptiste-André Dumas

(1800–1884) was born in France.

Apprenticed to an apothecary, he left to study chemistry in Switzerland. He became a professor of chemistry at the University of Paris and at the Collège de France. He was the first French chemist to teach laboratory courses. In 1848, he left science for a political career. He became a senator, master of the French mint, and mayor of Paris.

### PROBLEM 18 SOLVED

Aldohexoses A and B form the same osazone. A is oxidized by nitric acid to an optically active aldaric acid, and B is oxidized to an optically inactive aldaric acid. Ruff degradation of either A or B forms aldopentose C, which is oxidized by nitric acid to an optically active aldaric acid. Ruff degradation of C forms D, which is oxidized by nitric acid to an optically active aldaric acid. Ruff degradation of D forms (+)-glyceraldehyde. Identify A, B, C, and D.

**SOLUTION** This is the kind of problem that should be solved working backwards. The bottom-most asymmetric carbon in D must have the OH group on the right because D is degraded to (+)-glyceraldehyde. D must be D-threose, since D is oxidized to an optically active aldaric acid. The two bottom-most asymmetric carbons in C and D have the same configuration because C is degraded to D. C must be D-lyxose, since it is oxidized to an optically active aldaric acid. A and B, therefore, must be D-galactose and D-talose. Because A is oxidized to an optically active aldaric acid, it must be D-talose and B must be D-galactose.

### PROBLEM 19

Identify A, B, C, and D in the preceding problem if D is oxidized to an optically inactive aldaric acid, A, B, and C are oxidized to optically active aldaric acids, and interchanging the aldehyde and alcohol groups of A leads to a different sugar.

## 22.10 Cyclic Structure of Monosaccharides: Hemiacetal Formation

D-Glucose exists in three different forms: the open-chain form of D-glucose that we have been discussing and two cyclic forms— $\alpha$ -D-glucose and  $\beta$ -D-glucose. We know that the two cyclic forms are different, because they have different physical properties:  $\alpha$ -D-Glucose melts at 146 °C, whereas  $\beta$ -D-glucose melts at 150 °C;  $\alpha$ -D-glucose has a specific rotation of +112.2°, whereas  $\beta$ -D-glucose has a specific rotation of +18.7°.

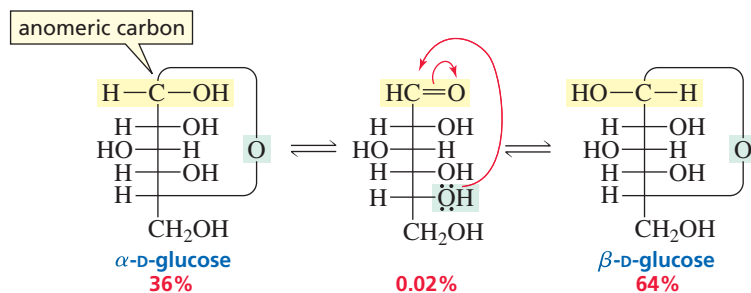
How can D-glucose exist in a cyclic form? In Section 18.7, we saw that an aldehyde reacts with an equivalent of an alcohol to form a hemiacetal. A monosaccharide such as D-glucose has an aldehyde group and several alcohol groups. The alcohol group bonded to C-5 of D-glucose reacts intramolecularly with the aldehyde group, forming a six-membered-ring hemiacetal. Why are there two different cyclic forms? Two different hemiacetals are formed because the carbonyl carbon of the open-chain sugar becomes a new asymmetric carbon in the hemiacetal. If the OH group bonded to the new asymmetric carbon is on the right, the hemiacetal is  $\alpha$ -D-glucose; if the OH group is on



the left, the hemiacetal is  $\beta$ -D-glucose. The mechanism for cyclic hemiacetal formation is the same as the mechanism for hemiacetal formation between individual aldehyde and alcohol molecules (Section 18.7).



Movie:  
Cyclization of a  
monosaccharide



$\alpha$ -D-Glucose and  $\beta$ -D-glucose are called anomers. **Anomers** are two sugars that differ in configuration only at the carbon that was the carbonyl carbon in the open-chain form. This carbon is called the **anomeric carbon**. *Ano* is Greek for “upper”; thus, anomers differ in configuration at the upper-most asymmetric carbon. The anomeric carbon is the only carbon in the molecule that is bonded to two oxygens. The prefixes  $\alpha$ - and  $\beta$ - denote the configuration about the anomeric carbon. Anomers, like epimers, are a particular kind of diastereomers—they differ in configuration at only one carbon atom.

In an aqueous solution, the open-chain compound is in equilibrium with the two cyclic hemiacetals. Formation of the cyclic hemiacetals proceeds nearly to completion (unlike formation of acyclic hemiacetals), so very little glucose exists in the open-chain form (about 0.02%). At equilibrium, there is almost twice as much  $\beta$ -D-glucose (64%) as  $\alpha$ -D-glucose (36%). The sugar still undergoes the reactions discussed in previous sections (oxidation, reduction, and osazone formation) because the reagents react with the small amount of open-chain aldehyde that is present. As the aldehyde reacts, the equilibrium shifts to form more open-chain aldehyde, which can then undergo reaction. Eventually, all the glucose molecules react by way of the open-chain aldehyde.

When crystals of pure  $\alpha$ -D-glucose are dissolved in water, the specific rotation gradually changes from  $+112.2^\circ$  to  $+52.7^\circ$ . When crystals of pure  $\beta$ -D-glucose are dissolved in water, the specific rotation gradually changes from  $+18.7^\circ$  to  $+52.7^\circ$ . This change in rotation occurs because, in water, the hemiacetal opens to form the aldehyde and, when the aldehyde recyclizes, both  $\alpha$ -D-glucose and  $\beta$ -D-glucose can be formed. Eventually, the three forms of glucose reach equilibrium concentrations. The specific rotation of the equilibrium mixture is  $+52.7^\circ$ —this is why the same specific rotation results whether the crystals originally dissolved in water are  $\alpha$ -D-glucose or  $\beta$ -D-glucose. A slow change in optical rotation to an equilibrium value is known as **mutarotation**.

If an aldose can form a five- or a six-membered-ring, it will exist predominantly as a cyclic hemiacetal in solution. Whether a five- or a six-membered ring is formed depends on their relative stabilities. Six-membered-ring sugars are called **pyranoses**, and five-membered-ring sugars are called **furanoses**. These names come from *pyran* and *furan*, the names of the five- and six-membered-ring cyclic ethers shown in the margin. Consequently,  $\alpha$ -D-glucose is also called  $\alpha$ -D-glucopyranose. The prefix  $\alpha$ - indicates the configuration about the anomeric carbon, and “pyranose” indicates that the sugar exists as a six-membered-ring cyclic hemiacetal.



pyran



furan

Fischer projections are not the best way to show the structure of a cyclic sugar, because of how the C—O—C bond is represented. A somewhat more satisfactory representation is given by a **Haworth projection**.

In a Haworth projection of a D-pyranose, the six-membered ring is represented as flat and is viewed edge on. The ring oxygen is always placed in the back right-hand corner of the ring, with the anomeric carbon (C-1) on the right-hand side and the primary alcohol group drawn *up* from the back left-hand corner (C-5). Groups on the *right* in a Fischer projection are *down* in a Haworth projection, whereas groups on the *left* in a Fischer projection are *up* in a Haworth projection.

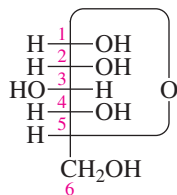
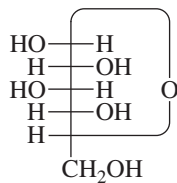
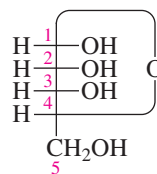
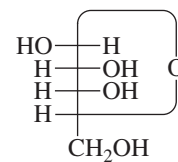
Groups on the *right* in a Fischer projection are *down* in a Haworth projection.

Groups on the *left* in a Fischer projection are *up* in a Haworth projection.

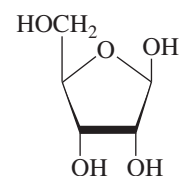
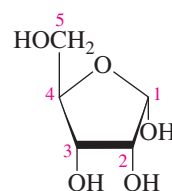
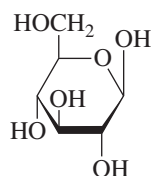
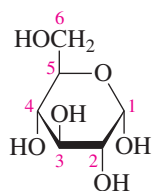
**Sir Walter Norman Haworth**

(1883–1950) was born in England. He received a Ph.D. in Germany from the University of Göttingen and later was a professor of chemistry at the Universities of Durham and Birmingham in Great Britain. He was the first to synthesize vitamin C and was the one who named it ascorbic acid. During World War II, he worked on the atomic bomb project. He received the Nobel Prize in Chemistry in 1937 and was knighted in 1947.

The Haworth projection of a D-furanose is viewed edge on, with the ring oxygen away from the viewer. The anomeric carbon is on the right-hand side of the molecule, and the primary alcohol group is drawn *up* from the back left-hand corner.

 $\alpha$ -D-glucopyranose $\beta$ -D-glucopyranose $\alpha$ -D-ribofuranose $\beta$ -D-ribofuranose

Fischer projections



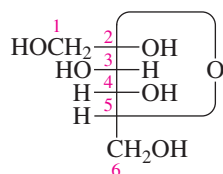
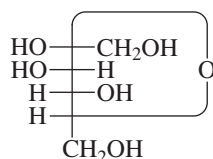
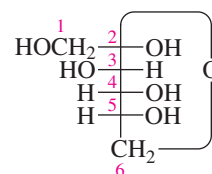
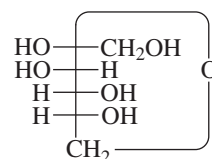
Haworth projections

Ketoses also exist predominantly in cyclic forms. D-Fructose forms a five-membered-ring-hemiketal as a consequence of the C-5 OH group reacting with the ketone carbonyl group (Section 18.7). If the new asymmetric carbon has the OH group on the right in a Fischer projection, the compound is  $\alpha$ -D-fructose; if the OH group is on the left, the compound is  $\beta$ -D-fructose. These sugars can also be called  $\alpha$ -D-fructofuranose and  $\beta$ -D-fructofuranose. Notice that in fructose the anomeric carbon is C-2, not C-1 as in aldoses. D-Fructose can also form a six-membered ring by using the C-6 OH group. The pyranose form predominates in the monosaccharide, whereas the furanose form predominates when the sugar is part of a disaccharide. (See the structure of sucrose in Section 22.17.)

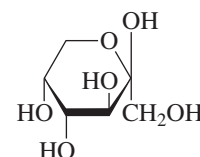
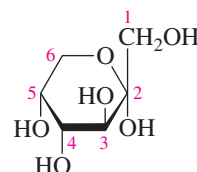
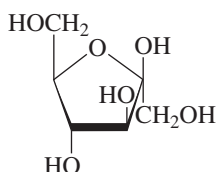
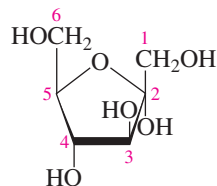


3-D Molecules:

$\alpha$ -D-Glucopyranose;  
 $\beta$ -D-Glucopyranose;  
 $\alpha$ -D-Ribofuranose;  
 $\beta$ -D-Ribofuranose

 $\alpha$ -D-fructofuranose $\beta$ -D-fructofuranose $\alpha$ -D-fructopyranose $\beta$ -D-fructopyranose

Fischer projections



Haworth projections

Haworth projections are useful because they allow us to see easily whether the OH groups on the ring are *cis* or *trans* to each other. Because five-membered rings are close to planar, furanoses are well represented by Haworth projections. However, Haworth projections are structurally misleading for pyranoses because a six-membered ring is not flat but exists preferentially in a chair conformation (Section 2.12).



**PROBLEM 20**

4-Hydroxy- and 5-hydroxyaldehydes exist primarily in the cyclic hemiacetal form. Give the structure of the cyclic hemiacetal formed by each of the following:

- a. 4-hydroxybutanal    c. 4-hydroxypentanal  
b. 5-hydroxypentanal    d. 4-hydroxyheptanal

**PROBLEM 21**

Draw the following sugars, using Haworth projections:

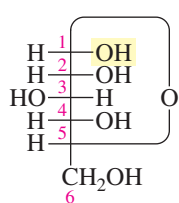
- a.  $\beta$ -D-galactopyranose                          b.  $\alpha$ -D-tagatopyranose                          c.  $\alpha$ -L-glucofuranose

**PROBLEM 22**

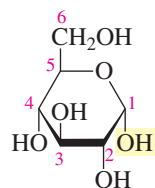
D-Glucose most often exists as a pyranose, but it can also exist as a furanose. Draw the Haworth projection of  $\alpha$ -D-glucofuranose.

## 22.11 Stability of Glucose

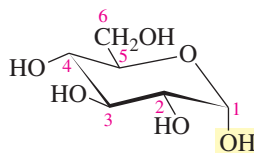
Drawing glucose in its chair conformation shows why it is the most common aldohexose in nature. To convert a Haworth projection into a chair conformation, start by drawing the chair so that the back is on the left and the footrest is on the right. Then place the ring oxygen at the back right-hand corner and the primary alcohol group in the equatorial position. (It would be helpful here to build a molecular model.) The primary alcohol group is the largest of all the substituents, and large substituents are more stable in the equatorial position because there is less steric strain in that position (Section 2.13). Because the OH group bonded to C-4 is trans to the primary alcohol group (this is easily seen in the Haworth projection), the C-4 OH group is also in the equatorial position. (Recall from Section 2.14 that 1,2-diequatorial substituents are trans to one another.) The C-3 OH group is trans to the C-4 OH group, so the C-3 OH group is also in the equatorial position. As you move around the ring, you will find that all the OH substituents in  $\beta$ -D-glucose are in equatorial positions. The axial positions are all occupied by hydrogens, which require little space and therefore experience little steric strain. No other aldohexose exists in such a strain-free conformation. This means that  $\beta$ -D-glucose is the most stable of all the aldohexoses, so it is not surprising that it is the most prevalent aldohexose in nature.



Fischer projection

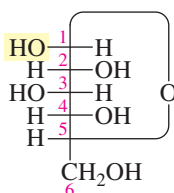


Haworth projection  
 $\alpha$ -D-glucose

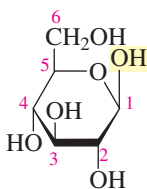


chair conformation

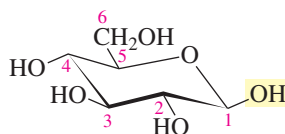
The  $\alpha$ -position is to the right in a Fischer projection, down in a Haworth projection, and axial in a chair conformation.



Fischer projection



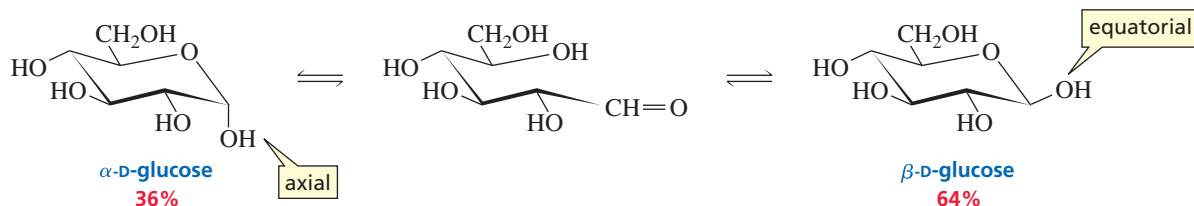
Haworth projection  
 $\beta$ -D-glucose



chair conformation

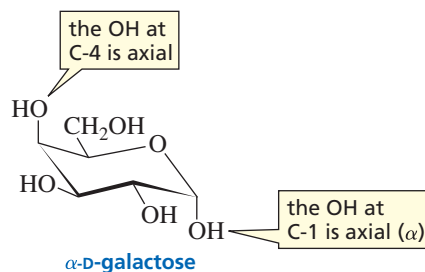
The  $\beta$ -position is to the left in a Fischer projection, up in a Haworth projection, and equatorial in a chair conformation.

Why is there more  $\beta$ -D-glucose than  $\alpha$ -D-glucose in an aqueous solution at equilibrium? The OH group bonded to the anomeric carbon is in the equatorial position in  $\beta$ -D-glucose, whereas it is in the axial position in  $\alpha$ -D-glucose. Therefore,  $\beta$ -D-glucose is more stable than  $\alpha$ -D-glucose, so  $\beta$ -D-glucose predominates at equilibrium in an aqueous solution.

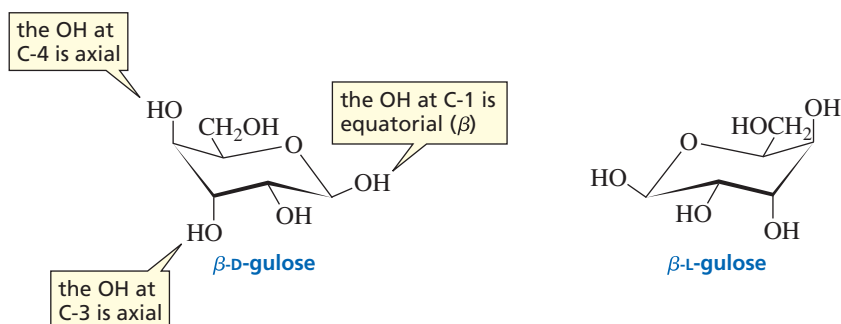


3-D Molecules:  
 $\alpha$ -D-Galactose;  
 $\beta$ -D-Gulose;  
 $\beta$ -L-Gulose

If you remember that all the OH groups in  $\beta$ -D-glucose are in equatorial positions, it is easy to draw the chair conformation of any other pyranose. For example, if you want to draw  $\alpha$ -D-galactose, you would put all the OH groups in equatorial positions, except the OH groups at C-4 (because galactose is a C-4 epimer of glucose) and at C-1 (because it is the  $\alpha$ -anomer). You would put these two OH groups in axial positions.



To draw an L-pyranose, draw the D-pyranose first, and then draw its mirror image. For example, to draw  $\beta$ -L-gulose, first draw  $\beta$ -D-gulose. (Gulose differs from glucose at C-3 and C-4, so the OH groups at these positions are in axial positions.) Then draw the mirror image of  $\beta$ -D-gulose to get  $\beta$ -L-gulose.



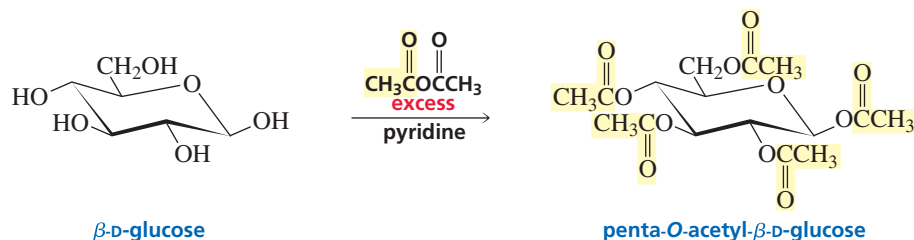
### PROBLEM 23 ♦

Which OH groups are in the axial position in

- $\beta$ -D-mannopyranose?
- $\beta$ -D-idopyranose?
- $\alpha$ -D-allopyranose?

## 22.12 Acylation and Alkylation of Monosaccharides

The OH groups of monosaccharides show the chemistry typical of alcohols. For example, they react with acetyl chloride or acetic anhydride to form esters (Sections 17.8 and 17.9).

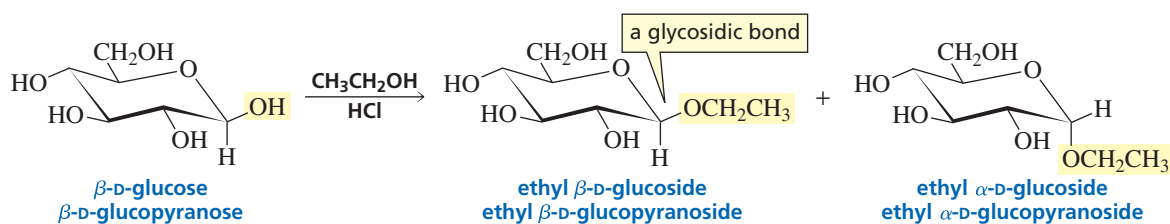


The OH groups also react with methyl iodide/silver oxide to form ethers (Section 10.4). The OH group is a relatively poor nucleophile, so silver oxide is used to increase the leaving tendency of the iodide ion in the  $\text{S}_{\text{N}}2$  reaction.



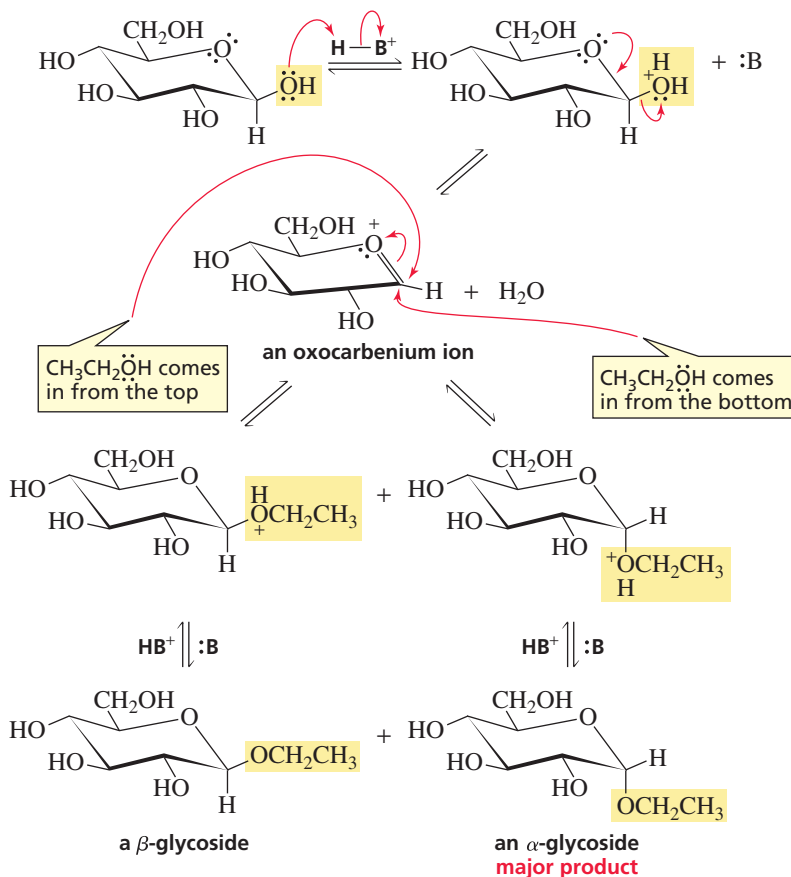
## 22.13 Formation of Glycosides

In Section 18.7, we saw that after an aldehyde reacts with an equivalent of an alcohol to form a hemiacetal, the hemiacetal reacts with a second equivalent of alcohol to form an acetal. Similarly, the cyclic hemiacetal (or hemiketal) formed by a monosaccharide can react with an alcohol to form an acetal (or ketal). The acetal (or ketal) of a sugar is called a **glycoside**, and the bond between the anomeric carbon and the alkoxy oxygen is called a **glycosidic bond**. Glycosides are named by replacing the “e” ending of the sugar’s name with “ide.” Thus, a glycoside of glucose is a glucoside, a glycoside of galactose is a galactoside, etc. If the pyranose or furanose name is used, the acetal is called a **pyranoside** or a **furanoside**.



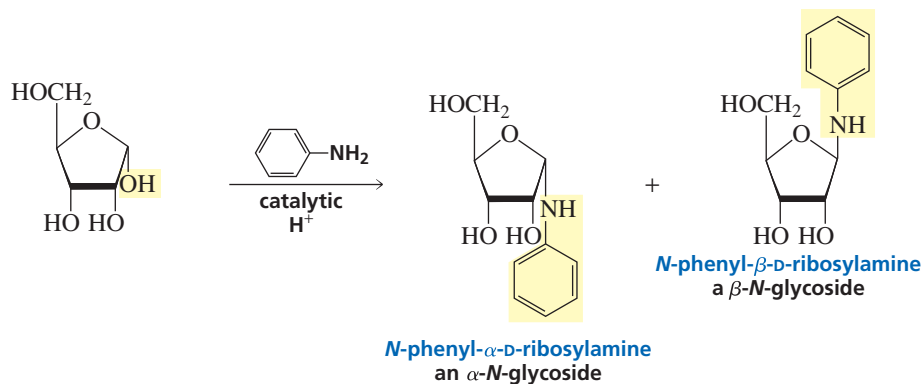
Notice that the reaction of a single anomer with an alcohol leads to the formation of both the  $\alpha$ - and  $\beta$ -glycosides. The mechanism of the reaction shows why both glycosides are formed. The OH group bonded to the anomeric carbon becomes protonated in the acidic solution, and a lone pair on the ring oxygen helps expel a molecule of water. The anomeric carbon in the resulting oxocarbenium ion is  $sp^2$  hybridized, so that part of the molecule is planar. (An **oxocarbenium ion** has a positive charge that is shared by a carbon and an oxygen.) When the alcohol comes in from the top of the plane, the  $\beta$ -glycoside is formed; when the alcohol comes in from the bottom of the plane, the  $\alpha$ -glycoside is formed. Notice that the mechanism is the same as that shown for acetal formation in Section 18.7.

## mechanism of glycoside formation



Surprisingly, D-glucose forms more of the  $\alpha$ -glycoside than the  $\beta$ -glycoside. The reason for this is explained in the next section.

Similar to the reaction of a monosaccharide with an alcohol is the reaction of a monosaccharide with an amine in the presence of a trace amount of acid. The product of the reaction is an *N*-glycoside. An *N*-glycoside has a nitrogen in place of the oxygen at the glycosidic linkage. The subunits of DNA and RNA are  $\beta$ -*N*-glycosides (Section 27.1).



## PROBLEM 24♦

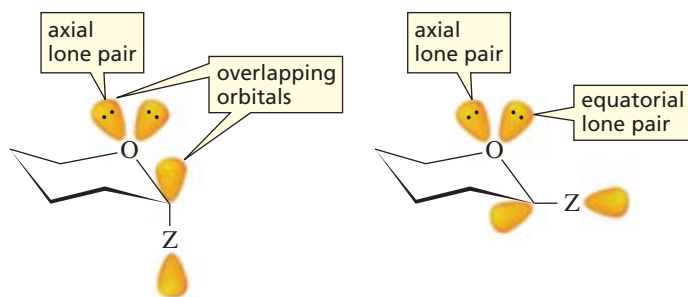
Why is only a trace amount of acid used in the formation of an *N*-glycoside?

## 22.14 The Anomeric Effect

We have seen that  $\beta$ -D-glucose is more stable than  $\alpha$ -D-glucose because there is more room for a substituent in the equatorial position. The relative amounts of  $\beta$ -D-glucose and  $\alpha$ -D-glucose are only 2 : 1, however, so the preference of the OH group for the equatorial position is surprisingly small (Section 22.10). Contrast this to the preference of the OH group for the equatorial position in cyclohexane, which is 5.4 : 1 (Table 2.10 on p. 99).

When glucose reacts with an alcohol to form a glucoside, the major product becomes the  $\alpha$ -glucoside. Since acetal formation is reversible, the  $\alpha$ -glucoside must be more stable than the  $\beta$ -glucoside. The preference of certain substituents bonded to the anomeric carbon for the axial position is called the **anomeric effect**.

What is responsible for the anomeric effect? One clue is that substituents that prefer the axial position have a lone pair on the atom (Z) bonded to the ring. The C—Z bond has a  $\sigma^*$  antibonding orbital. If one of the ring oxygen's lone pairs is in an orbital that is parallel to the  $\sigma^*$  antibonding orbital, the molecule can be stabilized by electron density from oxygen moving into the  $\sigma^*$  orbital. The orbital containing the axial lone pair of the ring oxygen can overlap the  $\sigma^*$  orbital only if the substituent is axial. If the substituent is equatorial, neither of the orbitals that contain a lone pair is aligned correctly for overlap. As a result of overlap between the lone pair and the  $\sigma^*$  orbital, the C—Z bond is longer and weaker and the C—O bond within the ring is shorter and stronger than normal.



## 22.15 Reducing and Nonreducing Sugars

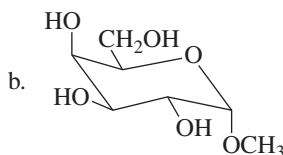
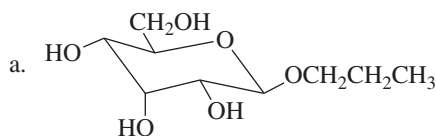
Because glycosides are acetals (or ketals), they are not in equilibrium with the open-chain aldehyde (or ketone) in neutral or basic aqueous solutions. Because they are not in equilibrium with a compound with a carbonyl group, they cannot be oxidized by reagents such as  $\text{Ag}^+$  or  $\text{Br}_2$ . Glycosides, therefore, are nonreducing sugars—they cannot reduce  $\text{Ag}^+$  or  $\text{Br}_2$ .

Hemiacetals (or hemiketals) are in equilibrium with the open-chain sugars in aqueous solution. So as long as a sugar has an aldehyde, a ketone, a hemiacetal, or a hemiketal group, it is able to reduce an oxidizing agent and therefore is classified as a **reducing sugar**. Without one of these groups, it is a nonreducing sugar.

A sugar with an aldehyde, a ketone, a hemiacetal, or a hemiketal group is a reducing sugar. A sugar without one of these groups is a nonreducing sugar.

### PROBLEM 25 SOLVED

Name the following compounds, and indicate whether each is a reducing sugar or a nonreducing sugar:

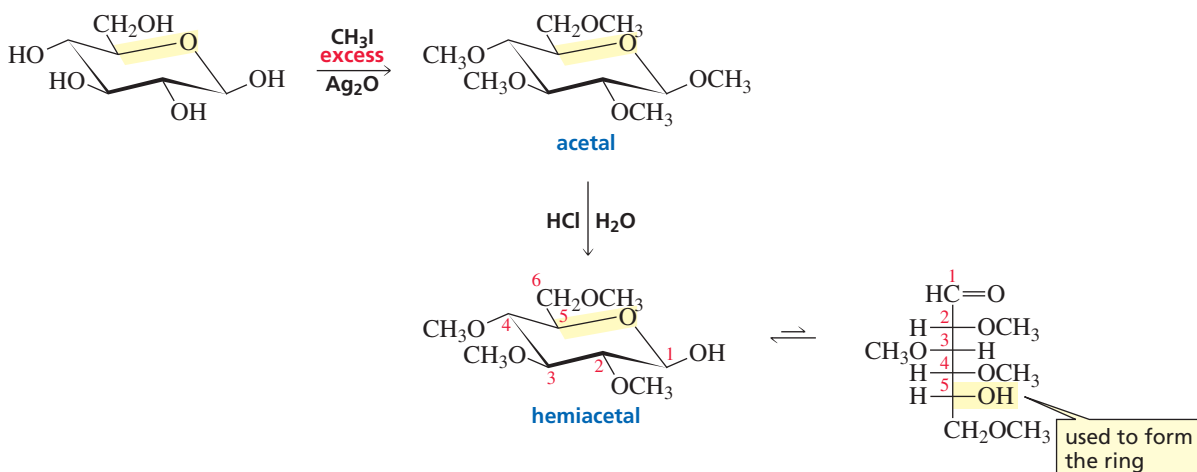




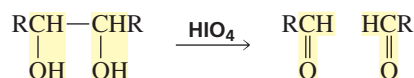
**SOLUTION TO 25a** The only OH group in an axial position in (a) is the one at C-3. Therefore, this sugar is the C-3 epimer of D-glucose, which is D-allose. The substituent at the anomeric carbon is in the  $\beta$ -position. Thus, the sugar's name is propyl  $\beta$ -D-alloside or propyl  $\beta$ -D-allopyranoside. Because the sugar is an acetal, it is a nonreducing sugar.

## 22.16 Determination of Ring Size

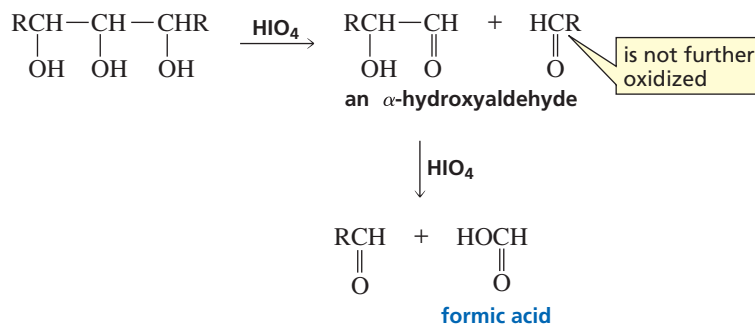
Two different procedures can be used to determine what size ring a monosaccharide forms. In the first procedure, treatment of the monosaccharide with excess methyl iodide and silver oxide converts all the OH groups to OCH<sub>3</sub> groups (Section 22.12). Acid-catalyzed hydrolysis of the acetal then forms a hemiacetal, which is in equilibrium with its open-chain form. The size of the ring can be determined from the structure of the open-chain form because the sole OH group is the one that had formed the cyclic hemiacetal.



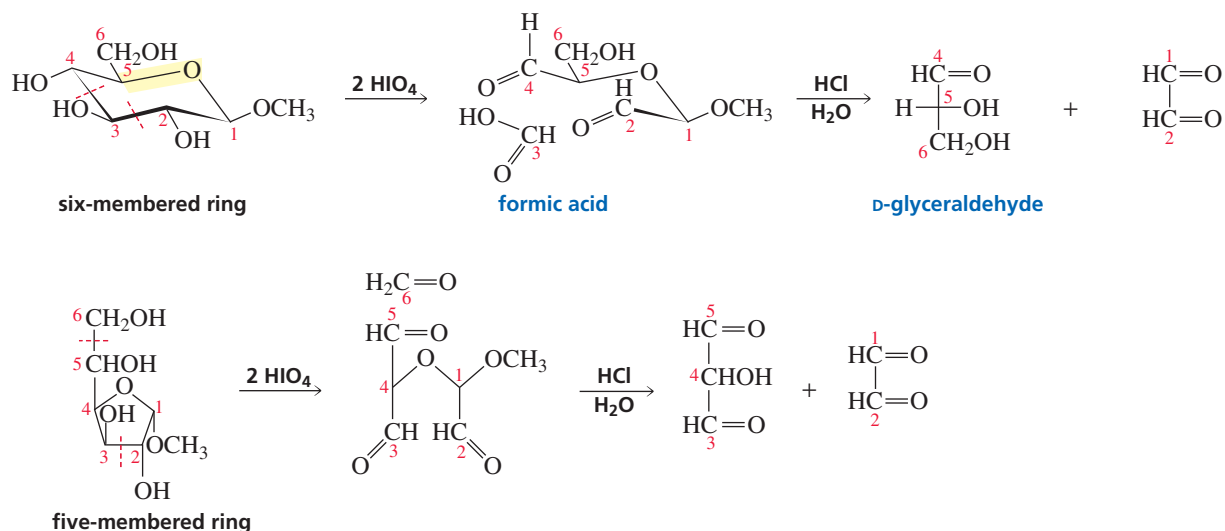
In the second procedure used to determine a monosaccharide's ring size, an acetal of the monosaccharide is oxidized with excess periodic acid. (Recall from Section 20.7 that periodic acid cleaves 1,2-diols.)



The  $\alpha$ -hydroxyaldehyde formed when periodic acid cleaves a 1,2,3-diol is further oxidized to formic acid and another aldehyde.



The products obtained from periodate cleavage of a six-membered-ring acetal are different from those obtained from cleavage of a five-membered-ring acetal.

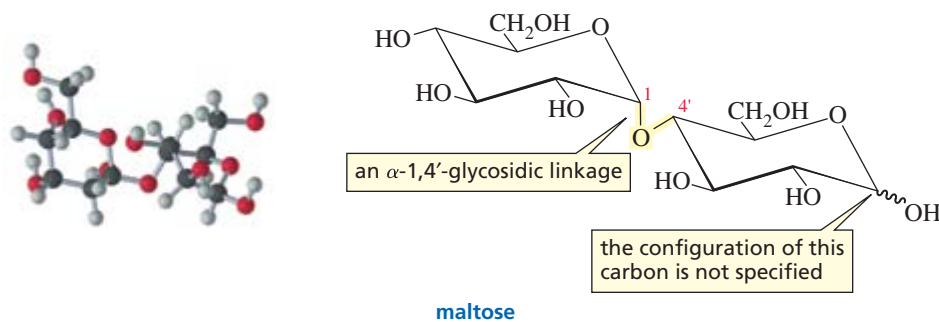


### PROBLEM 26

What kind of aldohexose would form L-glyceraldehyde when its acetal is oxidized with periodic acid?

## 22.17 Disaccharides

If the hemiacetal group of a monosaccharide forms an acetal by reacting with an alcohol group of another monosaccharide, the glycoside that is formed is a disaccharide. **Disaccharides** are compounds consisting of two monosaccharide subunits hooked together by an acetal linkage. For example, maltose is a disaccharide obtained from the hydrolysis of starch. It contains two D-glucose subunits hooked together by an acetal linkage. This particular acetal linkage is called an  **$\alpha$ -1,4'-glycosidic linkage**. The linkage is between C-1 of one sugar subunit and C-4 of the other. The "prime" superscript indicates that C-4 is not in the same ring as C-1. The linkage is an  $\alpha$ -1,4'-glycosidic linkage because the oxygen atom involved in the glycosidic linkage is in the  $\alpha$ -position. *Remember that the  $\alpha$ -position is axial when a sugar is shown in a chair conformation and is down when the sugar is shown in a Haworth projection; the  $\beta$ -position is equatorial when a sugar is shown in a chair conformation and is up when the sugar is shown in a Haworth projection.*





3-D Molecules:

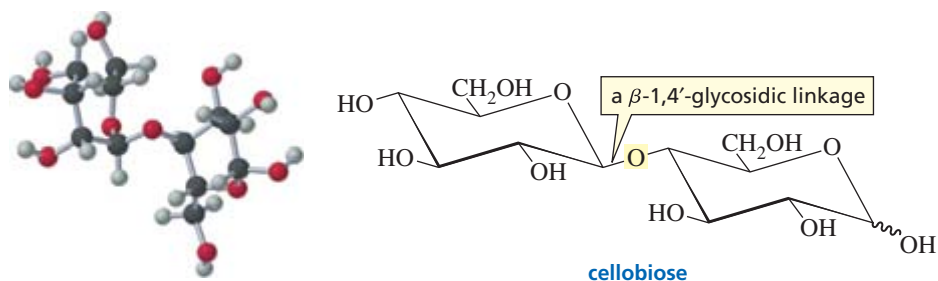
Maltose;

Cellobiose;

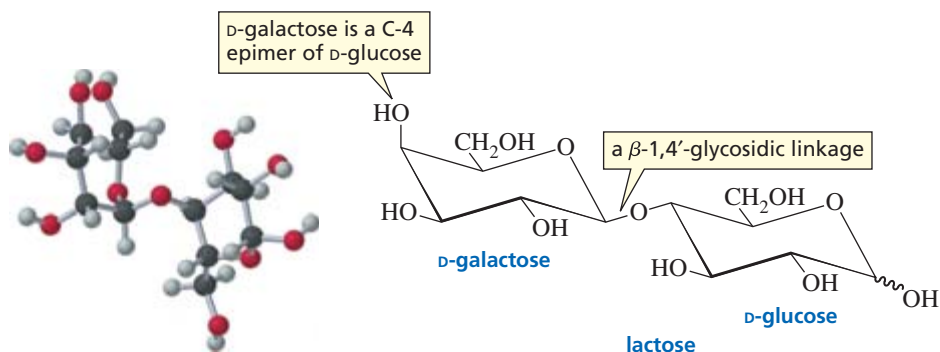
Lactose

Note that the structure of maltose is shown without specifying the configuration of the anomeric carbon that is not an acetal (the anomeric carbon of the subunit on the right marked with a wavy line), because maltose can exist in both the  $\alpha$  and  $\beta$  forms. In  $\alpha$ -maltose, the OH group bonded to this anomeric carbon is in the axial position. In  $\beta$ -maltose, the OH group is in the equatorial position. Because maltose can exist in both  $\alpha$  and  $\beta$  forms, mutarotation occurs when crystals of one form are dissolved in a solvent. Maltose is a reducing sugar because the right-hand subunit is a hemiacetal and therefore is in equilibrium with the open-chain aldehyde that is easily oxidized.

Cellobiose, a disaccharide obtained from the hydrolysis of cellulose, also contains two D-glucose subunits. Cellobiose differs from maltose in that the two glucose subunits are hooked together by a  **$\beta$ -1,4'-glycosidic linkage**. Thus, the only difference in the structures of maltose and cellobiose is the configuration of the glycosidic linkage. Like maltose, cellobiose exists in both  $\alpha$  and  $\beta$  forms because the OH group bonded to the anomeric carbon not involved in acetal formation can be in either the axial position (in  $\alpha$ -cellobiose) or the equatorial position (in  $\beta$ -cellobiose). Cellobiose is a reducing sugar because the subunit on the right is a hemiacetal.



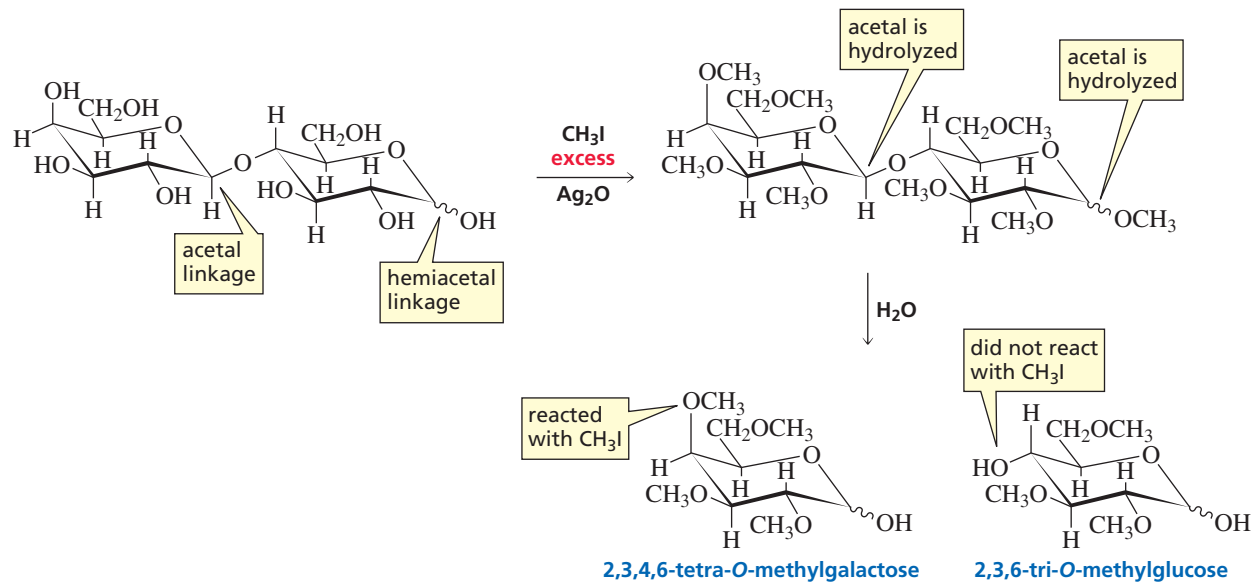
Lactose is a disaccharide found in milk. Lactose constitutes 4.5% of cow's milk by weight and 6.5% of human milk. One of the subunits of lactose is D-galactose, and the other is D-glucose. The D-galactose subunit is an acetal, and the D-glucose subunit is a hemiacetal. The subunits are joined through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



A simple experiment can prove that the hemiacetal linkage in lactose is in the glucose residue rather than in the galactose residue. The disaccharide is treated with excess methyl iodide in the presence of  $\text{Ag}_2\text{O}$  (Section 22.12), and the product is hydrolyzed under acidic conditions. The two acetal linkages are hydrolyzed, but all the ether linkages are untouched. Identification of the products shows that the galactose residue contained the acetal linkage in the disaccharide because it was able to



react with methyl iodide at C-4. The glucose residue, on the other hand, was unable to react with methyl iodide at C-4 because the OH group at that position was used to form the acetal with galactose.



## LACTOSE INTOLERANCE

Lactase is an enzyme that specifically breaks the  $\beta$ -1,4'-glycosidic linkage of lactose. Cats and dogs lose their intestinal lactase when they become adults; they are then no longer able to digest lactose. Consequently, when they are fed milk or milk products, the undegraded lactose causes digestive problems such as bloating, abdominal pain, and diarrhea. These problems occur because only monosaccharides can pass into the bloodstream, so lactose has to pass undigested into the

large intestine. When humans have stomach flu or other intestinal disturbances, they can temporarily lose their lactase, thereby becoming lactose intolerant. Some humans lose their lactase permanently as they mature. Approximately 10% of the adult Caucasian population of the United States has lost its lactase. Lactose intolerance is much more common in people whose ancestors came from nondairy-producing countries. For example, only 3% of Danes but 97% of Thais, are lactose intolerant.



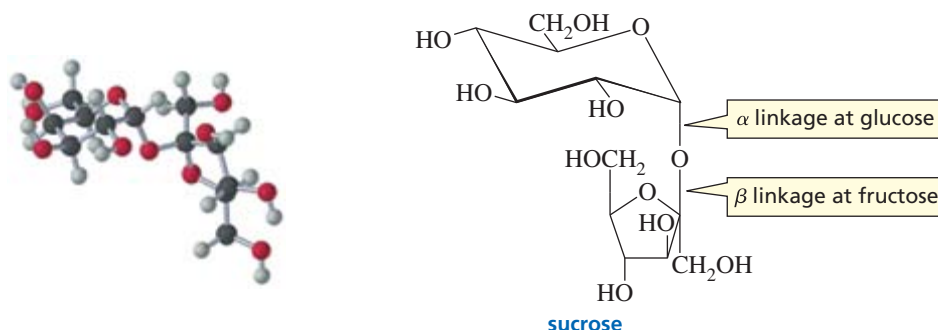
## GALACTOSEMIA

After lactose is degraded into glucose and galactose, the galactose must be converted into glucose before it can be used by cells. Individuals who do not have the enzyme that converts galactose into glucose have the genetic

disease known as galactosemia. Without this enzyme, galactose accumulates in the bloodstream. This can cause mental retardation and even death in infants. Galactosemia is treated by excluding galactose from the diet.

The most common disaccharide is sucrose (table sugar). Sucrose is obtained from sugar beets and sugarcane. About 90 million tons of sucrose are produced in the world each year. Sucrose consists of a D-glucose subunit and a D-fructose subunit linked by a glycosidic bond between C-1 of glucose (in the  $\alpha$ -position) and C-2 of fructose (in the  $\beta$ -position).

Unlike the other disaccharides that have been discussed, sucrose is not a reducing sugar and does not exhibit mutarotation because the glycosidic bond is between the anomeric carbon of glucose and the anomeric carbon of fructose. Sucrose, therefore, does not have a hemiacetal or hemiketal group, so it is not in equilibrium with the readily oxidized open-chain aldehyde or ketone form in aqueous solution.



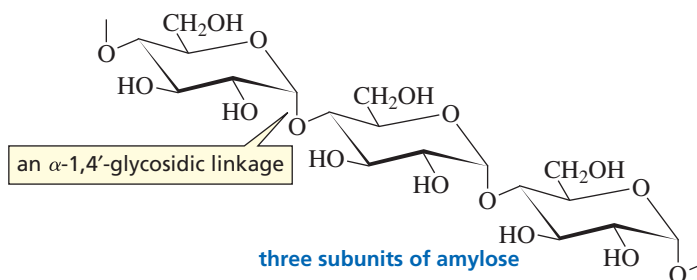
3-D Molecule:  
Sucrose

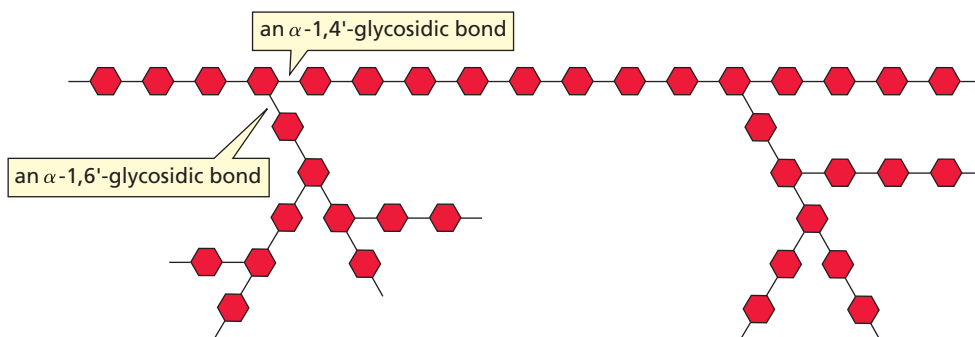
Sucrose has a specific rotation of  $+66.5^\circ$ . When it is hydrolyzed, the resulting equimolar mixture of glucose and fructose has a specific rotation of  $-22.0^\circ$ . Because the sign of the rotation changes when sucrose is hydrolyzed, a 1 : 1 mixture of glucose and fructose is called *invert sugar*. The enzyme that catalyzes the hydrolysis of sucrose is called *invertase*. Honeybees have invertase, so the honey they produce is a mixture of sucrose, glucose, and fructose. Because fructose is sweeter than sucrose, invert sugar is sweeter than sucrose. Some foods are advertised as containing fructose instead of sucrose, which means that they achieve the same level of sweetness with a lower sugar content.

## 22.18 Polysaccharides

Polysaccharides contain as few as 10 or as many as several thousand monosaccharide units joined together by glycosidic linkages. The molecular weight of the individual polysaccharide chains is variable. The most common polysaccharides are starch and cellulose.

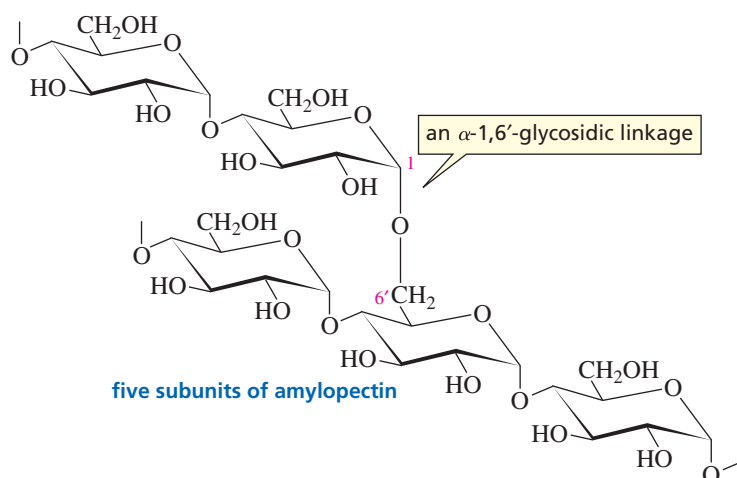
Starch is the major component of flour, potatoes, rice, beans, corn, and peas. Starch is a mixture of two different polysaccharides: amylose (about 20%) and amylopectin (about 80%). Amylose is composed of unbranched chains of D-glucose units joined by  $\alpha$ -1,4'-glycosidic linkages.





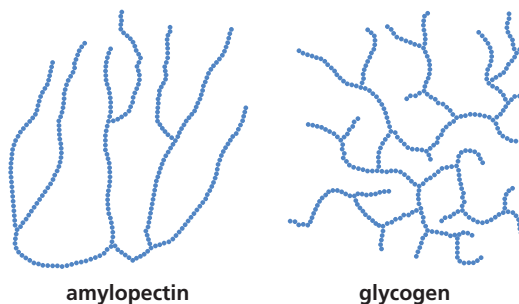
◀ **Figure 22.1**  
Branching in amylopectin. The hexagons represent glucose units. They are joined by  $\alpha$ -1,4'- and  $\alpha$ -1,6'-glycosidic bonds.

Amylopectin is a branched polysaccharide. Like amylose, it is composed of chains of D-glucose units joined by  $\alpha$ -1,4'-glycosidic linkages. Unlike amylose, however, amylopectin also contains  $\alpha$ -1,6'-glycosidic linkages. These linkages create the branches in the polysaccharide (Figure 22.1). Amylopectin can contain up to  $10^6$  glucose units, making it one of the largest molecules found in nature.



Tutorial:  
Identifying glycosidic linkages and numbering pyranose and furanose rings

Animals store their excess glucose in a polysaccharide known as glycogen. Glycogen has a structure similar to that of amylopectin, but glycogen has more branches (Figure 22.2). The branch points in glycogen occur about every 10 residues, whereas those in amylopectin occur about every 25 residues. The high degree of branching in glycogen has important physiological effects. When the body needs energy, many individual glucose units can be simultaneously removed from the ends of many branches.



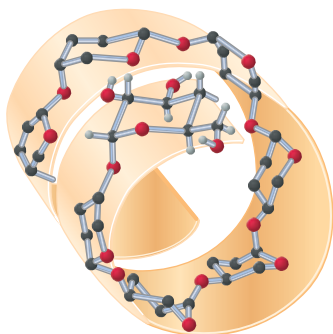
◀ **Figure 22.2**  
A comparison of the branching in amylopectin and glycogen.



### WHY THE DENTIST IS RIGHT

Bacteria found in the mouth have an enzyme that converts sucrose into a polysaccharide called dextran. Dextran is made up of glucose units joined mainly through

$\alpha$ -1,3'- and  $\alpha$ -1,6'-glycosidic linkages. About 10% of dental plaque is composed of dextran. This is the chemical basis of why your dentist cautions you not to eat candy.



▲ **Figure 22.3**

The  $\alpha$ -1,4'-glycosidic linkages in amylose cause it to form a left-handed helix. Many of its OH groups form hydrogen bonds with water molecules.

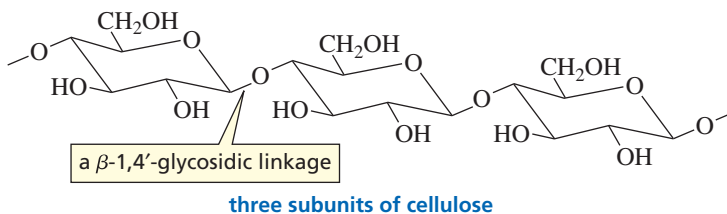


▲ Strands of cellulose in a plant fiber



▲ The shell of this bright orange crab from Australia is composed largely of chitin.

Cellulose is the structural material of higher plants. Cotton, for example, is composed of about 90% cellulose, and wood is about 50% cellulose. Like amylose, cellulose is composed of unbranched chains of D-glucose units. Unlike amylose, however, the glucose units in cellulose are joined by  $\beta$ -1,4'-glycosidic linkages rather than by  $\alpha$ -1,4'-glycosidic linkages.

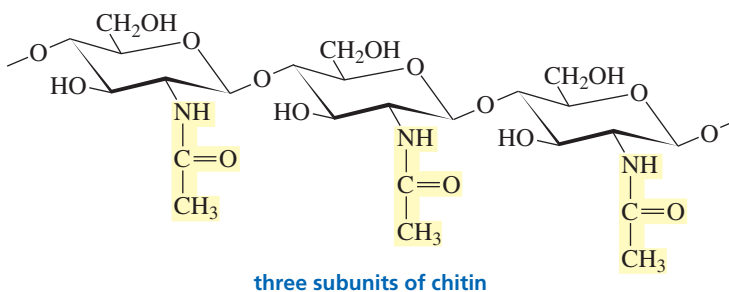


$\alpha$ -1,4'-Glycosidic linkages are easier to hydrolyze than  $\beta$ -1,4'-glycosidic linkages because of the anomeric effect that weakens the bond to the anomeric carbon (Section 22.14). All mammals have the enzyme ( $\alpha$ -glucosidase) that hydrolyzes the  $\alpha$ -1,4'-glycosidic linkages that join glucose units, but they do not have the enzyme ( $\beta$ -glucosidase) that hydrolyzes  $\beta$ -1,4'-glycosidic linkages. As a result, mammals *cannot* obtain the glucose they need by eating cellulose. However, bacteria that possess  $\beta$ -glucosidase inhabit the digestive tracts of grazing animals, so cows can eat grass and horses can eat hay to meet their nutritional requirements for glucose. Termites also harbor bacteria that break down the cellulose in the wood they eat.

The different glycosidic linkages in starch and cellulose give these compounds very different physical properties. The  $\alpha$ -linkages in starch cause amylose to form a helix that promotes hydrogen bonding of its OH groups to water molecules (Figure 22.3). As a result, starch is soluble in water.

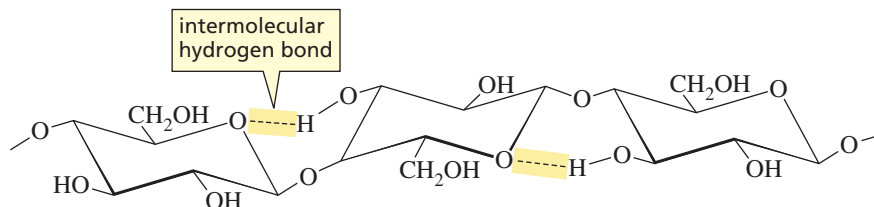
On the other hand, the  $\beta$ -linkages in cellulose promote the formation of intramolecular hydrogen bonds. Consequently, these molecules line up in linear arrays (Figure 22.4), and intermolecular hydrogen bonds form between adjacent chains. These large aggregates cause cellulose to be insoluble in water. The strength of these bundles of polymer chains makes cellulose an effective structural material. Processed cellulose is also used for the production of paper and cellophane.

Chitin is a polysaccharide that is structurally similar to cellulose. It is the major structural component of the shells of crustaceans (e.g., lobsters, crabs, and shrimps) and the exoskeletons of insects. Like cellulose, chitin has  $\beta$ -1,4'-glycosidic linkages. It differs from cellulose, though, in that it has an *N*-acetylamino group instead of an OH group at the C-2 position. The  $\beta$ -1,4'-glycosidic linkages give chitin its structural rigidity.



▲ **Figure 22.4**

The  $\beta$ -1,4'-glycosidic linkages in cellulose form intramolecular hydrogen bonds, which cause the molecules to line up in linear arrays.



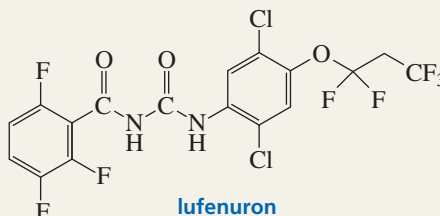
**PROBLEM 27**

What is the main structural difference between

- a. amylose and cellulose?                      c. amylopectin and glycogen?  
 b. amylose and amylopectin?                d. cellulose and chitin?

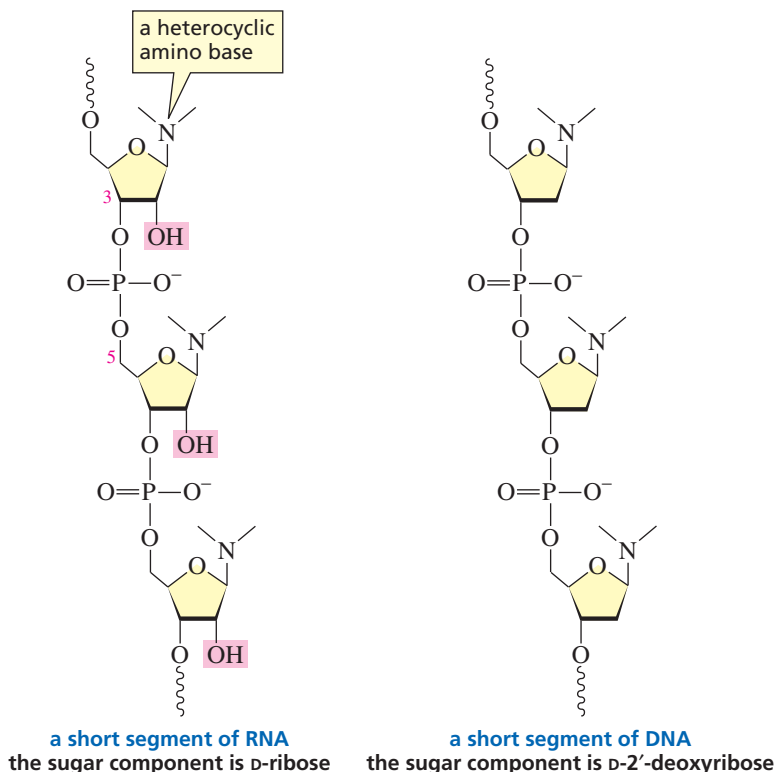
**CONTROLLING FLEAS**

Several different drugs have been developed to help pet owners control fleas. One of these drugs is lufenuron, the active ingredient in Program<sup>®</sup>. Lufenuron interferes with the production of chitin. Since the exoskeleton of a flea is composed primarily of chitin, a flea cannot live if it cannot make chitin.



## 22.19 Some Naturally Occurring Products Derived from Carbohydrates

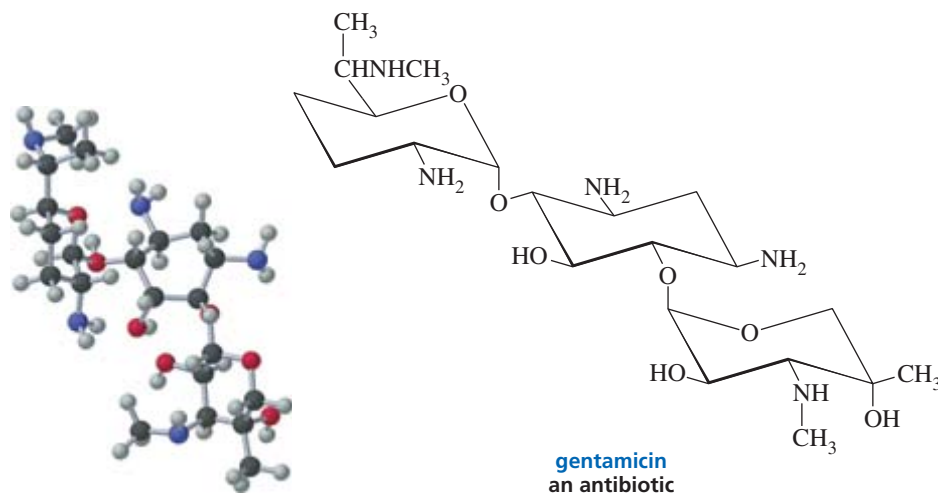
**Deoxy sugars** are sugars in which one of the OH groups is replaced by a hydrogen (*deoxy* means “without oxygen”). 2-Deoxyribose—it is missing the oxygen at the C-2 position—is an important example of a deoxy sugar. Ribose is the sugar component of ribonucleic acid (RNA), whereas 2-deoxyribose is the sugar component of deoxyribonucleic acid (DNA). RNA and DNA are *N*-glycosides—their subunits consist of an amine bonded to the  $\beta$ -position of the anomeric carbon of ribose or 2-deoxyribose. The subunits are linked by a phosphate group between C-3 of one sugar and C-5 of the next sugar (Section 27.1).<sup>1</sup>



<sup>1</sup>In referring to the sugar found in DNA, it is called 2-deoxyribose. In numbering the sugar in a DNA molecule, it is 2'-deoxyribose because the nonprimed numbers refer to positions on the heterocyclic amine components.

3-D Molecule:  
Gentamicin

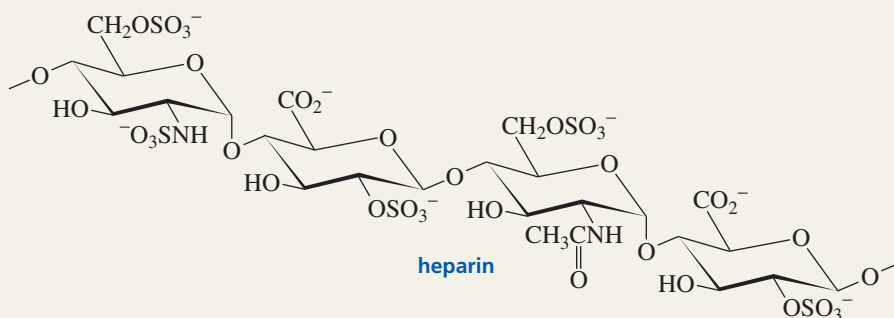
In **amino sugars**, one of the OH groups is replaced by an amino group. *N*-Acetylglucosamine—the subunit of chitin and one of the subunits of certain bacterial cell walls—is an example of an amino sugar (Sections 22.18 and 24.9). Some important antibiotics contain amino sugars. For example, the three subunits of the antibiotic gentamicin are deoxyamino sugars. Notice that the middle subunit is missing the ring oxygen, so it really isn't a sugar.



## HEPARIN

Heparin is an anticoagulant that is released to prevent excessive blood clot formation when an injury occurs. Heparin is a polysaccharide made up of glucosamine, glucuronic acid, and iduronic acid subunits. The C-6 OH groups of the glucosamine subunits and the C-2 OH groups

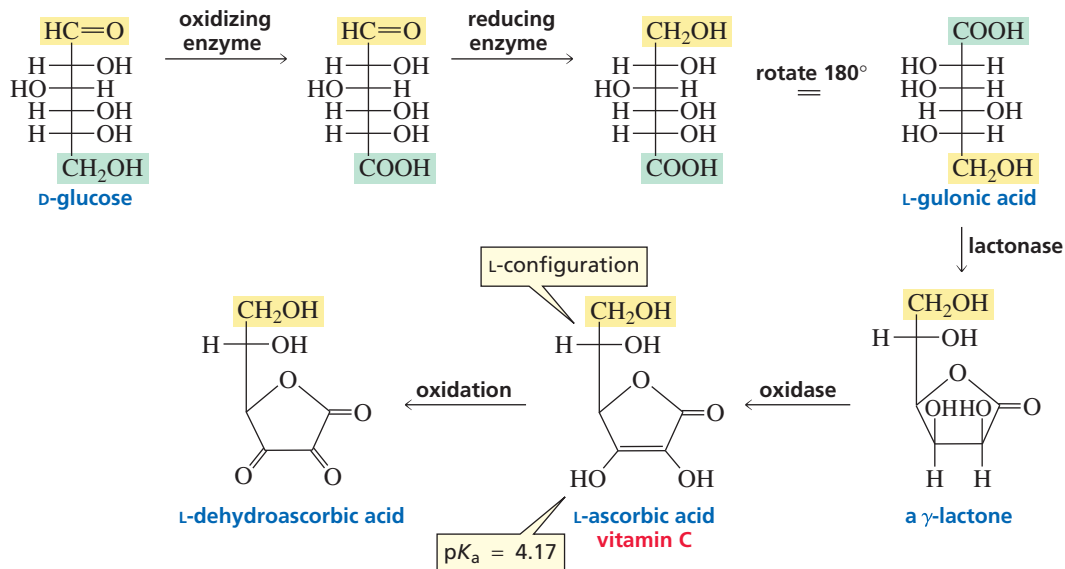
of the iduronic acid subunits are sulfonated. Some of the amino groups are sulfonated and some are acetylated. Thus, heparin is a highly negatively charged molecule, found principally in cells that line arterial walls. Heparin is widely used clinically as an anticoagulant.



L-Ascorbic acid (vitamin C) is synthesized in plants and in the livers of most vertebrates. Humans, monkeys, and guinea pigs do not have the enzymes necessary for the biosynthesis of vitamin C, so they must obtain the vitamin in their diets. The biosynthesis of vitamin C involves the enzymatic conversion of D-glucose into L-gulonic acid—reminiscent of the last step in the Fischer proof. L-Gulonic acid is converted into a  $\gamma$ -lactone by the enzyme lactonase, and then an enzyme called oxidase oxidizes the lactone to L-ascorbic acid. The L-configuration of ascorbic acid refers to the configuration at C-5, which was C-2 in D-glucose.



## the synthesis of L-ascorbic acid



Although L-ascorbic acid does not have a carboxylic acid group, it is an acidic compound because the  $pK_a$  of the C-3 OH group is 4.17. L-Ascorbic acid is readily oxidized to L-dehydroascorbic acid, which is also physiologically active. If the lactone ring is opened by hydrolysis, all vitamin C activity is lost. Therefore, not much intact vitamin C survives in food that has been thoroughly cooked. Worse, if the food is cooked in water and then drained, the water-soluble vitamin is thrown out with the water!



## VITAMIN C

Vitamin C traps radicals formed in aqueous environments (Section 9.8). It is an antioxidant because it prevents oxidation reactions by radicals. Not all the physiological functions of vitamin C are known. What is known, though, is that vitamin C is required for the synthesis of collagen, which is the structural protein of skin, tendons, connective tissue, and bone. If vitamin C is not present in the diet (it is abundant in citrus fruits and tomatoes), lesions appear on

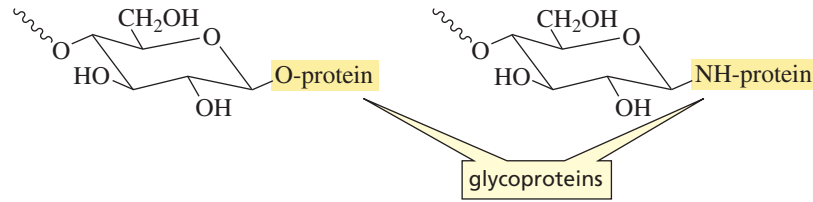
the skin, severe bleeding occurs about the gums, in the joints, and under the skin, and wounds heal slowly. The disease caused by a deficiency of vitamin C is known as *scurvy*. British sailors who shipped out to sea after the late 1700s were required to eat limes to prevent scurvy. This is how they came to be called “limeys.” Scurvy was the first disease to be treated by adjusting the diet. *Scorbutus* is Latin for “scurvy”; *ascorbic*, therefore, means “no scurvy.”

## PROBLEM 28

Explain why the C-3 OH group of vitamin C is more acidic than the C-2 OH group.

## 22.20 Carbohydrates on Cell Surfaces

The surfaces of many cells contain short polysaccharide chains that allow the cells to interact with each other, as well as to interact with invading viruses and bacteria. These polysaccharides are linked to the cell surface by the reaction of an OH or an  $NH_2$  group of a protein with the anomeric carbon of a cyclic sugar. Proteins bonded to polysaccharides are called **glycoproteins**. The percentage of carbohydrate in glycoproteins is variable; some glycoproteins contain as little as 1% carbohydrate by weight, whereas others contain as much as 80%.



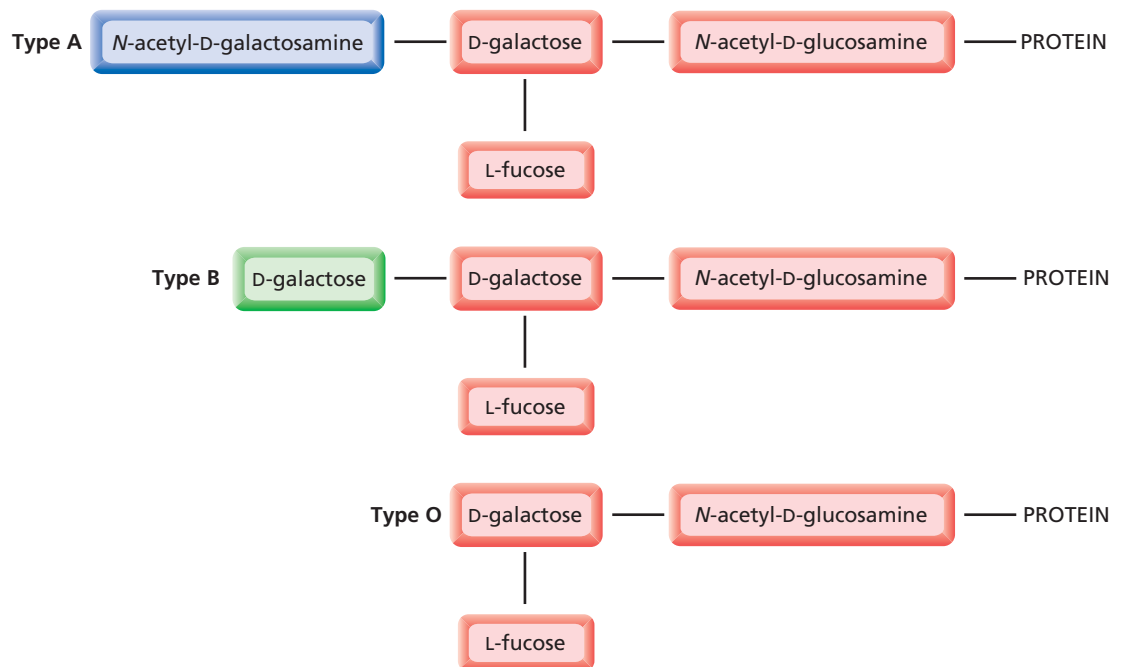
Many different types of proteins are glycoproteins. For example, structural proteins such as collagen, proteins found in mucous secretions, immunoglobulins, follicle-stimulating hormone and thyroid-stimulating hormone, interferon (an antiviral protein), and blood plasma proteins are all glycoproteins. One of the functions of the polysaccharide chain is to act as a receptor site on the cell surface in order to transmit signals from hormones and other molecules across the cell membrane into the cell. The carbohydrates on the surfaces of cells also serve as points of attachment for other cells, viruses, and toxins.

Carbohydrates on the surfaces of cells provide a way for cells to recognize one another. The interaction between surface carbohydrates has been found to play a role in many diverse activities, such as infection, the prevention of infection, fertilization, inflammatory diseases like rheumatoid arthritis and septic shock, and blood clotting. For example, the goal of the HIV protease inhibitor drugs is to prevent HIV from recognizing and penetrating cells. The fact that several known antibiotics contain amino sugars suggests that they function by recognizing target cells. Carbohydrate interactions also are involved in the regulation of cell growth, so changes in membrane glycoproteins are thought to be correlated with malignant transformations.

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Blood type (A, B, AB, or O) is determined by the nature of the sugar bound to the protein on the outer surfaces of red blood cells. Each type of blood is associated with a different carbohydrate structure (Figure 22.5). Type AB blood has the carbohydrate structure of both type A and type B.

**Antibodies** are proteins that are synthesized by the body in response to a foreign substance, called an **antigen**. Interaction with the antibody either causes the antigen to precipitate or flags it for destruction by immune system cells. This is why, for example, blood cannot be transferred from one person to another unless the carbohydrate



▲ **Figure 22.5**

Blood type is determined by the nature of the sugar on the surfaces of red blood cells. Fucose is 6-deoxygalactose.



portions of the donor and acceptor are compatible. Otherwise the donated blood will be considered a foreign substance.

Looking at Figure 22.5, we can see why the immune system of type A people recognizes type B blood as foreign and vice versa. The immune system of people with type A, B, or AB blood does not, however, recognize type O blood as foreign, because the carbohydrate in type O blood is also a component of types A, B, and AB blood. Thus, anyone can accept type O blood, so people with type O blood are called universal donors. Type AB people can accept types AB, A, B, and O blood, so people with type AB blood are referred to as universal acceptors.

### PROBLEM 29

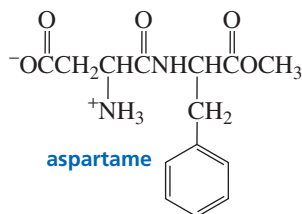
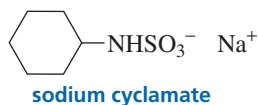
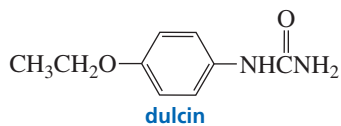
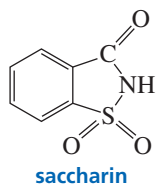
From the nature of the carbohydrate bound to red blood cells, answer the following questions:

- People with type O blood can donate blood to anyone, but they cannot receive blood from everyone. From whom can they *not* receive blood?
- People with type AB blood can receive blood from anyone, but they cannot give blood to everyone. To whom can they *not* give blood?

## 22.21 Synthetic Sweeteners

For a molecule to taste sweet, it must bind to a receptor on a taste bud cell of the tongue. The binding of this molecule causes a nerve impulse to pass from the taste bud to the brain, where the molecule is interpreted as being sweet. Sugars differ in their degree of “sweetness.” The relative sweetness of glucose is 1.00, that of sucrose is 1.45, and that of fructose, the sweetest of all sugars, is 1.65. Developers of synthetic sweeteners must consider several factors—such as toxicity, stability, and cost—in addition to taste.

Saccharin, the first synthetic sweetener, was discovered by Ira Remsen and his student Constantine Fahlberg at Johns Hopkins University in 1878. Fahlberg was studying the oxidation of ortho-substituted toluenes in Remsen’s laboratory when he found that one of his newly synthesized compounds had an extremely sweet taste. (As strange as it may seem today, at one time it was common for chemists to taste compounds in order to characterize them.) He called this compound saccharin, and it was eventually found to be about 300 times sweeter than glucose. Notice that, in spite of its name, saccharin is *not* a saccharide.



Because it has no caloric value, when it became commercially available in 1885, saccharin became an important substitute for sucrose. The chief nutritional problem in the West was—and still is—the overconsumption of sugar and its consequences: obesity, heart disease, and dental decay. Saccharin is also important to diabetics, who must limit their consumption of sucrose and glucose. Although the toxicity of saccharin was not studied carefully when the compound first became available to the public (our current concern with toxicity is a fairly recent development), extensive studies done since



**Ira Remsen (1846–1927)** was born in New York. After receiving an M.D. from Columbia University, he decided to become a chemist. He earned a Ph.D. in Germany and then returned to the United States in 1872 to accept a faculty position at Williams College. In 1876, he became a professor of chemistry at the newly established Johns Hopkins University, where he initiated the first center for chemical research in the United States. He later became the second president of Johns Hopkins.

then have shown saccharin to be a safe sugar substitute. In 1912, saccharin was temporarily banned in the United States, not because of any concern about its toxicity, but because of a concern that people would miss out on the nutritional benefits of sugar.



### THE WONDER OF DISCOVERY

Ira Remsen gave the following account of why he became a scientist:<sup>2</sup> He was working as a physician and came across the statement “Nitric acid acts upon copper” while reading a chemistry book. He decided to see what “acts on” meant. He poured nitric acid on a penny sitting on a table. “But what was this wonderful thing which I beheld? The cent had already changed and it was not small change either. A greenish blue liquid foamed and fumed over the cent and over the table. The air in the neighborhood of the performance became dark red. A great colored cloud arose. This was disagreeable and suffocating—how should I stop this? I tried to get rid of the objectionable mess by picking it up and throwing it out of the window, which I had meanwhile opened. I learned another fact—nitric acid not only acts upon copper but it acts upon my

fingers. The pain led to another unpremeditated experiment. I drew my fingers across my trousers and another fact was discovered. Nitric acid also acts upon trousers. Taking everything else into consideration, that was the most impressive experiment, and, relatively, probably the most expensive experiment I ever performed. I tell of it even now with interest. It was a revelation to me. It resulted in a desire on my part to learn even more about that remarkable kind of action. Plainly the only way to learn about it was to see its results, to experiment, to work in a laboratory.”

<sup>2</sup>L. R. Summerlin, C. L. Bordford, and J. B. Ealy, *Chemical Demonstrations*, 2nd ed. (Washington, DC: American Chemical Society, 1988).

Dulcin<sup>®</sup> was the second synthetic sweetener to be discovered (in 1884). Even though it did not have the bitter, metallic aftertaste associated with saccharin, it never achieved much popularity. Dulcin<sup>®</sup> was taken off the market in 1951 in response to questions about its toxicity.

Sodium cyclamate became a widely used nonnutritive sweetener in the 1950s, but was banned in the United States some 20 years later in response to two studies that appeared to show that large amounts of sodium cyclamate cause liver cancer in mice.

Aspartame was approved by the U.S. Food and Drug Administration (FDA) in 1981. About 200 times sweeter than sucrose, aspartame is sold under the trade name NutraSweet<sup>®</sup> (Section 23.8). Because NutraSweet<sup>®</sup> contains a phenylalanine subunit, it should not be used by people with the genetic disease known as PKU (Section 25.6).

The fact that these four synthetic sweeteners have such different structures, all of which are very different from those of monosaccharides, indicates that the sensation of sweetness is not induced by a single molecular shape.



Tutorial:  
Carbohydrates:  
Common Terms

## Summary

**Bioorganic compounds**—organic compounds found in biological systems—obey the same principles of structure and reactivity as do small organic molecules. Much of the structure of bioorganic compounds is for **molecular recognition**.

**Carbohydrates** are the most abundant class of compounds in the biological world. They are polyhydroxy aldehydes (**aldoses**) and polyhydroxy ketones (**ketoses**) or compounds formed by linking up aldoses and ketoses. D and L notations describe the configuration of the bottom-most asymmetric carbon of a **monosaccharide**; the configurations of the other carbons are explicit in the common name. Most naturally occurring sugars are D-sugars. Naturally occurring ketoses have the ketone group in the 2-position. **Epimers** differ in configuration at only one asymmetric carbon: D-mannose is the C-2 epimer of D-glucose and D-galactose is the C-4 epimer of D-glucose.

Reduction of an aldose forms one **alditol**; reduction of a ketose forms two alditols. Br<sub>2</sub> oxidizes aldoses, but not ketoses; Tollens reagent oxidizes both. Aldoses are oxidized to **aldonic acids** or **aldaric acids**. Aldoses and ketoses react with three equivalents of phenylhydrazine, forming **osazones**. C-2 epimers form identical osazones. The **Kiliani-Fischer synthesis** increases the carbon chain of an aldose by one carbon—it forms C-2 epimers. The **Ruff degradation** decreases the carbon chain by one carbon. The OH groups of monosaccharides react with acetyl chloride to form esters and with methyl iodide/silver oxide to form ethers.

The aldehyde or keto group of a **monosaccharide** reacts with one of its OH groups to form cyclic hemiacetals or hemiketals: Glucose forms  $\alpha$ -D-glucose and  $\beta$ -D-glucose. The  $\alpha$ -position is axial when a sugar is shown in a chair conformation and down when the sugar is shown in a Haworth

projection; the  $\beta$ -position is equatorial when a sugar is shown in a chair conformation and up when the sugar is shown in a Haworth projection. At equilibrium, there is more  $\beta$ -D-glucose than  $\alpha$ -D-glucose.  $\alpha$ -D-Glucose and  $\beta$ -D-glucose are **anomers**—they differ in configuration only at the carbon (**anomeric carbon**) that was the carbonyl carbon in the open-chain form. Anomers have different physical properties. Six-membered-ring sugars are **pyranoses**; five-membered-ring sugars are **furanoses**. The most abundant monosaccharide in nature is D-glucose. All the OH groups in  $\beta$ -D-glucose are in equatorial positions. A slow change in optical rotation to an equilibrium value is known as **mutarotation**.

The cyclic hemiacetal (or hemiketal) can react with an alcohol to form an acetal (or ketal), called a **glycoside**. If the name “pyranose” or “furanose” is used, the acetal is called a **pyranoside** or a **furanoside**. The bond between the anomeric carbon and the alkoxy oxygen is called a **glycosidic bond**. The preference for the axial position by certain substituents bonded to the anomeric carbon is called the **anomeric effect**. If a sugar has an aldehyde, ketone, hemiacetal, or hemiketal group, it is a reducing sugar.

**Disaccharides** consist of two monosaccharide subunits hooked together by an acetal linkage. Maltose has an

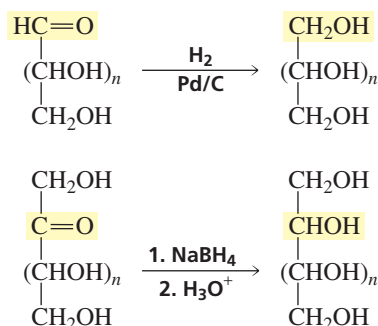
**$\alpha$ -1,4'-glycosidic linkage**; cellobiose has a  **$\beta$ -1,4'-glycosidic linkage**. The most common disaccharide is sucrose; it consists of a D-glucose subunit and a D-fructose subunit linked by their anomeric carbons.

**Polysaccharides** contain as few as 10 or as many as several thousand monosaccharide units joined together by glycosidic linkages. Starch is composed of amylose and amylopectin. Amylose has unbranched chains of D-glucose units joined by  $\alpha$ -1,4'-glycosidic linkages. Amylopectin, too, has chains of D-glucose units joined by  $\alpha$ -1,4'-glycosidic linkages, but it also has  $\alpha$ -1,6'-glycosidic linkages that create branches. Glycogen is similar to amylopectin, but has more branches. Cellulose has unbranched chains of D-glucose units joined by  $\beta$ -1,4'-glycosidic linkages. The  $\alpha$ -linkages cause amylose to form a helix; the  $\beta$ -linkages allow the molecules of cellulose to form intramolecular hydrogen bonds.

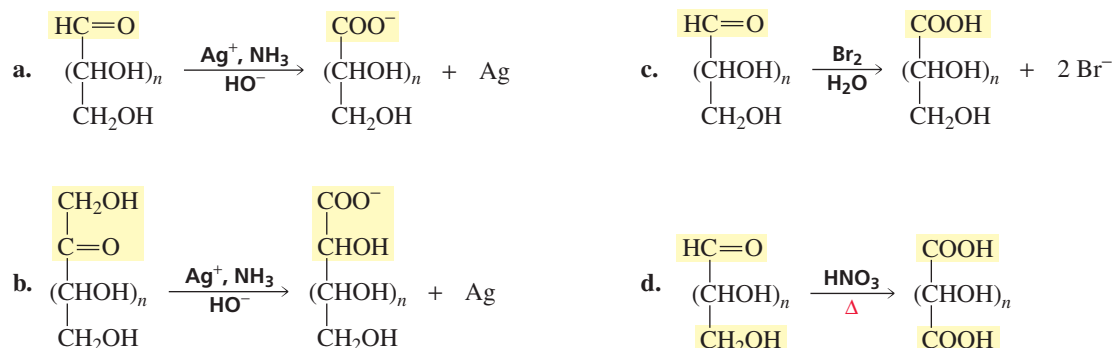
The surfaces of many cells contain short polysaccharide chains that allow the cells to interact with each other. These polysaccharides are linked to the cell surface by protein groups. Proteins bonded to polysaccharides are called **glycoproteins**.

## Summary of Reactions

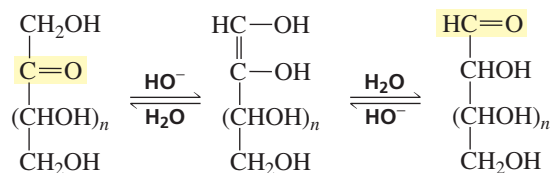
### 1. Reduction (Section 22.5).



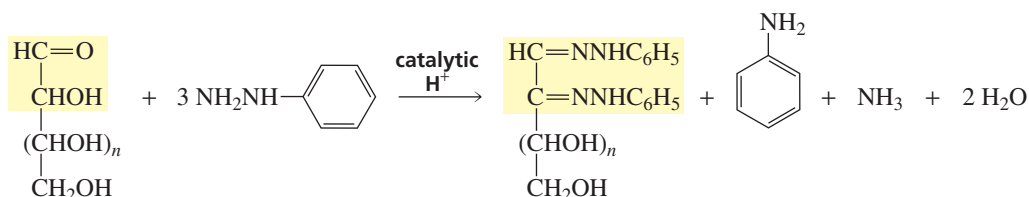
### 2. Oxidation (Section 22.5).



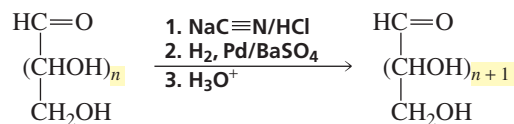
## 3. Enolization (Section 22.5).



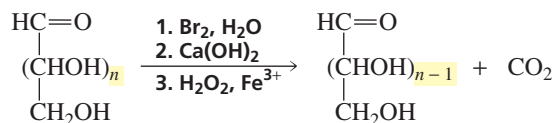
## 4. Osazone formation (Section 22.6).



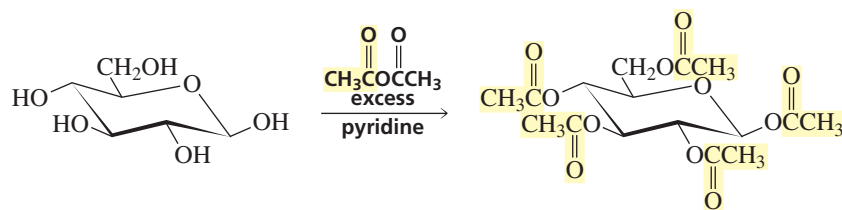
## 5. Chain elongation: the Kiliani–Fischer synthesis (Section 22.7).



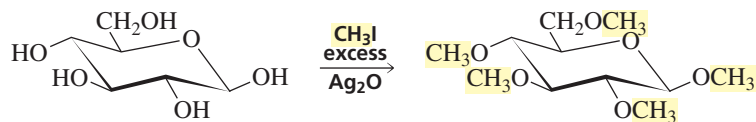
## 6. Chain shortening: the Ruff degradation (Section 22.8).



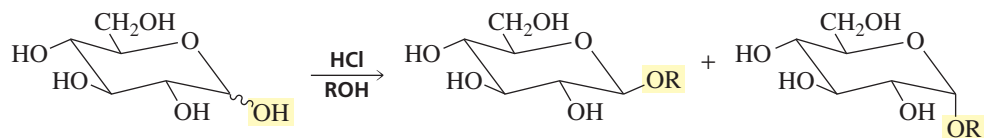
## 7. Acylation (Section 22.12).



## 8. Alkylation (Section 22.12).



## 9. Acetal (and ketal) formation (Section 22.13).



## Key Terms

aldaric acid (p. 929)  
alditol (p. 926)  
aldonic acid (p. 928)  
aldose (p. 923)  
amino sugar (p. 950)  
anomeric carbon (p. 935)  
anomeric effect (p. 941)  
anomers (p. 935)  
bioorganic compound (p. 921)  
carbohydrate (p. 921)  
complex carbohydrate (p. 922)  
deoxy sugar (p. 949)  
disaccharide (p. 922)  
epimers (p. 925)  
furanose (p. 935)

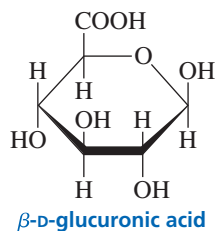
furanoside (p. 939)  
glycoprotein (p. 957)  
glycoside (p. 939)  
*N*-glycoside (p. 940)  
glycosidic bond (p. 939)  
 $\alpha$ -1,4'-glycosidic linkage (p. 943)  
 $\beta$ -1,4'-glycosidic linkage (p. 944)  
Haworth projection (p. 935)  
heptose (p. 923)  
hexose (p. 923)  
ketose (p. 923)  
Kiliani–Fischer synthesis (p. 931)  
molecular recognition (p. 921)  
monosaccharide (p. 922)  
mutarotation (p. 935)

nonreducing sugar (p. 000)  
oligosaccharide (p. 000)  
osazone (p. 000)  
oxocarbenium ion (p. 939)  
pentose (p. 923)  
polysaccharide (p. 922)  
pyranose (p. 935)  
pyranoside (p. 939)  
reducing sugar (p. 941)  
Ruff degradation (p. 931)  
simple carbohydrate (p. 922)  
tetrose (p. 923)  
triose (p. 923)

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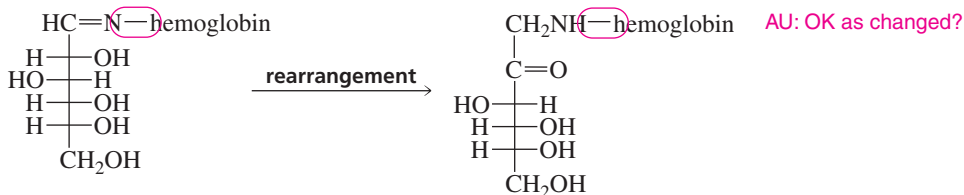
## Problems

30. Give the product or products that are obtained when D-galactose reacts with the following:
- nitric acid
  - Tollens reagent
  - $\text{H}_2/\text{Pd}/\text{C}$
  - three equivalents of phenylhydrazine
  - $\text{Br}_2$  in water
  - ethanol + HCl
  - product of reaction e (above) +  $\text{Ca}(\text{OH})_2$ ,  $\text{Fe}^{3+}$ ,  $\text{H}_2\text{O}_2$
31. Identify the following sugars:
- An aldopentose that is not D-arabinose forms D-arabinitol when it is reduced with  $\text{NaBH}_4$ .
  - A sugar forms the same osazone as D-galactose with phenylhydrazine, but it is not oxidized by an aqueous solution of  $\text{Br}_2$ .
  - A sugar that is not D-altrose forms D-altraric acid when it reacts with nitric acid.
  - A ketose, when reduced with  $\text{H}_2 + \text{Pd}/\text{C}$ , forms D-altritol and D-allitol.
32. Answer the following questions about the eight aldopentoses:
- Which are enantiomers?
  - Which give identical osazones?
  - Which form an optically active compound when oxidized with nitric acid?
33. The reaction of D-ribose with an equivalent of methanol plus HCl forms four products. Give the structures of the products.
34. Determine the structure of D-galactose, using arguments similar to those used by Fischer to prove the structure of D-glucose.
35. Dr. Isent T. Sweet isolated a monosaccharide and determined that it had a molecular weight of 150. Much to his surprise, he found that it was not optically active. What is the structure of the monosaccharide?
36. The  $^1\text{H}$  NMR spectrum of D-glucose in  $\text{D}_2\text{O}$  exhibits two high-frequency (low-field) doublets. What is responsible for these doublets?
37. Treatment with sodium borohydride converts aldose A into an optically inactive alditol. Ruff degradation of A forms B, whose alditol is optically inactive. Ruff degradation of B forms D-glyceraldehyde. Identify A and B.
38. D-Glucuronic acid is found widely in plants and animals. One of its functions is to detoxify poisonous HO-containing compounds by reacting with them in the liver to form glucuronides. Glucuronides are water soluble and therefore readily excreted. After ingestion of a poison such as turpentine, morphine, or phenol, the glucuronides of these compounds are found in the urine. Give the structure of the glucuronide formed by the reaction of  $\beta$ -D-glucuronic acid and phenol.

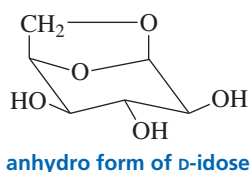


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39. Hyaluronic acid, a component of connective tissue, is the fluid that lubricates the joints. It is an alternating polymer of *N*-acetyl-D-glucosamine and D-glucuronic acid joined by  $\beta$ -1,3'-glycosidic linkages. Draw a short segment of hyaluronic acid.
40. In order to synthesize D-galactose, Professor Amy Losse went to the stockroom to get some D-lyxose to use as a starting material. She found that the labels had fallen off the bottles containing D-lyxose and D-xylose. How could she determine which bottle contains D-lyxose?
41. When D-fructose is dissolved in D<sub>2</sub>O and the solution is made basic, the D-fructose recovered from the solution has an average of 1.7 deuterium atoms attached to carbon per molecule. Show the mechanism that accounts for the incorporation of these deuterium atoms into D-fructose.
42. A D-aldopentose is oxidized by nitric acid to an optically active aldaric acid. A Ruff degradation of the aldopentose leads to a monosaccharide that is oxidized by nitric acid to an optically inactive aldaric acid. Identify the D-aldopentose.
43. How many aldaric acids are obtained from the 16 aldohexoses?
44. Calculate the percentages of  $\alpha$ -D-glucose and  $\beta$ -D-glucose present at equilibrium from the specific rotations of  $\alpha$ -D-glucose,  $\beta$ -D-glucose, and the equilibrium mixture. Compare your values with those given in Section 22.10. (*Hint*: The specific rotation of the mixture equals the specific rotation of  $\alpha$ -D-glucose times the fraction of glucose present in the  $\alpha$ -form plus the specific rotation of  $\beta$ -D-glucose times the fraction of glucose present in the  $\beta$ -form.)
45. Predict whether D-altrose exists preferentially as a pyranose or a furanose. (*Hint*: The most stable arrangement for a five-membered ring is for all the adjacent substituents to be trans.)
46. Propose a mechanism for the rearrangement that converts an  $\alpha$ -hydroxyimine into an  $\alpha$ -aminoketone (Section 22.6).



47. A disaccharide forms a silver mirror with Tollens reagent and is hydrolyzed by a  $\beta$ -glycosidase. When the disaccharide is treated with excess methyl iodide in the presence of Ag<sub>2</sub>O (a reaction that converts all the OH groups to OCH<sub>3</sub> groups) and then hydrolyzed with water under acidic conditions, 2,3,4-tri-*O*-methylmannose and 2,3,4,6-tetra-*O*-methylgalactose are formed.
- Draw the structure of the disaccharide.
  - What is the function of Ag<sub>2</sub>O?
48. All the glucose units in dextran have six-membered rings. When a sample of dextran is treated with methyl iodide and silver oxide and the product is hydrolyzed under acidic conditions, the products obtained are 2,3,4,6-tetra-*O*-methyl-D-glucose, 2,4,6-tri-*O*-methyl-D-glucose, 2,3,4-tri-*O*-methyl-D-glucose, and 2,4-di-*O*-methyl-D-glucose. Draw a short segment of dextran.
49. When a pyranose is in the chair conformation in which the CH<sub>2</sub>OH group and the C-1 OH group are both in the axial position, the two groups can react to form an acetal. This is called the anhydro form of the sugar. (It has lost water.) The anhydro form of D-idose is shown here. In an aqueous solution at 100 °C, about 80% of D-idose exists in the anhydro form. Under the same conditions, only about 0.1% of D-glucose exists in the anhydro form. Explain.



50. Devise a method to convert D-glucose into D-allose.