

Carbohydrates

CHAPTER 16

16.1 Sugars: Their Structures and Stereochemistry

When the word *carbohydrate* was coined, it originally referred to compounds of the general formula $C_n(H_2O)_n$. However, only the simple sugars, or **monosaccharides**, fit this formula exactly. The other types of carbohydrates, oligosaccharides and polysaccharides, are based on the monosaccharide units and have slightly different general formulas. **Oligosaccharides** are formed when a few (Greek *oligos*) monosaccharides are linked; polysaccharides are formed when many (Greek *polys*) monosaccharides are bonded together. The reaction that adds monosaccharide units to a growing carbohydrate molecule involves the loss of one H_2O for each new link formed, accounting for the difference in the general formula.

Many commonly encountered carbohydrates are polysaccharides, including glycogen, which is found in animals, and starch and cellulose, which occur in plants. Carbohydrates play a number of important roles in biochemistry. First, they are major energy sources (Chapters 17 through 20 are devoted to carbohydrate metabolism). Second, oligosaccharides play a key role in processes that take place on the surfaces of cells, particularly in cell–cell interactions and immune recognition. In addition, polysaccharides are essential structural components of several classes of organisms. Cellulose is a major component of grass and trees, and other polysaccharides are major components of bacterial cell walls.

What is unique about the structures of sugars?

The building blocks of all carbohydrates are the simple sugars called **monosaccharides**. A monosaccharide can be a polyhydroxy aldehyde (**aldose**) or a polyhydroxy ketone (**ketose**). The simplest monosaccharides contain three carbon atoms and are called trioses (*tri* meaning “three”). *Glyceraldehyde* is the aldose with three carbons (an aldotriose), and *dihydroxyacetone* is the ketose with three carbon atoms (a ketotriose). Figure 16.1 shows these molecules.

Aldoses with four, five, six, and seven carbon atoms are called aldotetroses, aldopentoses, aldohexoses, and aldohexoses, respectively. The corresponding ketoses are ketotetroses, ketopentoses, ketohexoses, and ketoheptoses. Six-carbon sugars are the most abundant in nature, but two five-carbon sugars, ribose and deoxyribose, occur in the structures of RNA and DNA, respectively. Four-carbon and seven-carbon sugars play roles in photosynthesis and other metabolic pathways.

We have already seen (in Section 3.1) that some molecules are not superimposable on their mirror images and that these mirror images are **optical isomers (stereoisomers)** of each other. A chiral (asymmetric) carbon atom is the usual source of optical isomerism, as was the case with amino acids. The simplest carbohydrate that contains a chiral carbon is glyceraldehyde, which



Like bread and pasta, fruits and vegetables are sources of carbohydrates, which provide energy.

Chapter Outline

16.1 Sugars: Their Structures and Stereochemistry

- What is unique about the structures of sugars?
- What happens if a sugar forms a cyclic molecule?

16.2 Reactions of Monosaccharides

- What are some oxidation–reduction reactions of sugars?
- What are some important esterification reactions of sugars?
- What are glycosides, and how do they form?
- What are some other important derivatives of sugars?

16.3 Some Important Oligosaccharides

- What makes sucrose an important compound?
- Are any other disaccharides important to us?

16.4 Structures and Functions of Polysaccharides

- How do cellulose and starch differ from one another?
- Is there more than one form of starch?
- How is glycogen related to starch?
- What is chitin?
- What role do polysaccharides play in the structure of cell walls?
- Do polysaccharides play any specific roles in connective tissue?

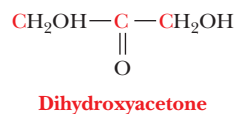
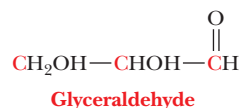
16.5 Glycoproteins

- How are carbohydrates important in the immune response?

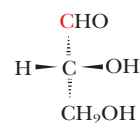
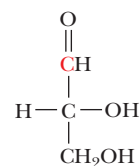
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- 1 A comparison of glyceraldehyde (an aldotriose) and dihydroxyacetone (a ketotriose).



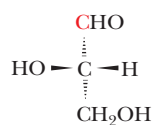
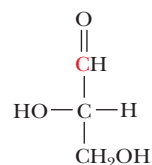
- 2 The structure of D-glyceraldehyde and a space-filling model of D-glyceraldehyde.



D-Glyceraldehyde



- 3 The structure of L-glyceraldehyde and a space-filling model of L-glyceraldehyde.



L-Glyceraldehyde



FIGURE 16.1 The structures of the simplest carbohydrates, the trioses. (Leonard Lessin/Waldo Feng/Mt. Sinai CORE)

can exist in two isomeric forms that are mirror images of each other [Figure 16.1(2) and (3)]. Note that the two forms differ in the position of the hydroxyl group bonded to the central carbon. (Dihydroxyacetone does not contain a chiral carbon atom and does not exist in nonsuperimposable mirror-image forms.) The two forms of glyceraldehyde are designated D-glyceraldehyde and L-glyceraldehyde. Mirror-image stereoisomers are also called **enantiomers**, and D-glyceraldehyde and L-glyceraldehyde are enantiomers of each other. Certain conventions are used for two-dimensional drawings of the three-dimensional structures of stereoisomers. The dashed wedges represent bonds directed away from the viewer, below the plane of the paper, and the solid wedges represent bonds directed oppositely, toward the viewer and out of the plane of the paper. The **configuration** is the three-dimensional arrangement of groups around a chiral carbon atom, and stereoisomers differ from each other in configura-

tion. The *D,L* system to denote stereochemistry is widely used by biochemists. Organic chemists tend to use a more recent one, designated the *R,S* system. There is not a one-to-one correspondence between the two systems. For example, some *D*-isomers are *R*, and some are *S*.

The two enantiomers of glyceraldehyde are the only possible stereoisomers of three-carbon sugars, but the possibilities for stereoisomerism increase as the number of carbon atoms increases. To show the structures of the resulting molecules, we need to say more about the convention for a two-dimensional perspective of the molecular structure, which is called the **Fischer projection** method, after the German chemist Emil Fischer, who established the structures of many sugars. We shall use some common six-carbon sugars for purposes of illustration. In a Fischer projection, bonds written vertically on the two-dimensional paper represent bonds directed *behind* the paper in three dimensions, whereas bonds written horizontally represent bonds directed *in front of* the paper in three dimensions. Figure 16.2 shows that the most highly oxidized carbon—in this case, the one involved in the aldehyde group—is written at the “top” and is designated carbon 1, or C-1. In the ketose shown, the ketone group becomes C-2, the carbon atom next to the “top.” Most common sugars are aldoses rather than ketoses, so our discussion will focus mainly on aldoses. The other carbon atoms are numbered in sequence from the “top.” The designation of the configuration as *L* or *D* depends on the arrangement at the chiral carbon with the highest number. In the cases of both glucose and fructose, this is C-5. In the Fischer projection of the *D* configuration, the hydroxyl group is on the right of the highest-numbered chiral carbon, whereas the hydroxyl group is on the left of the highest-numbered chiral carbon in the *L* configuration. Let us see what happens as another carbon is added to glyceraldehyde to give a four-carbon sugar. In other words, what are the possible stereoisomers for an aldotetrose? The aldotetroses (Figure 16.3) have two chiral carbons, C-2 and C-3, and there are 2^2 , or four, possible stereoisomers. Two of the isomers have

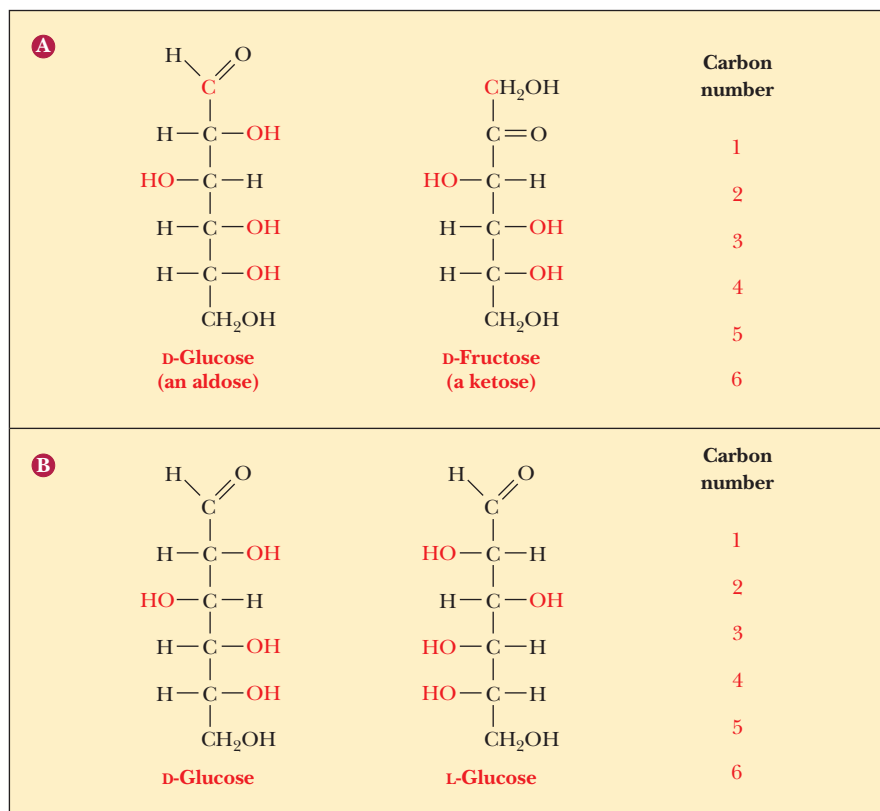
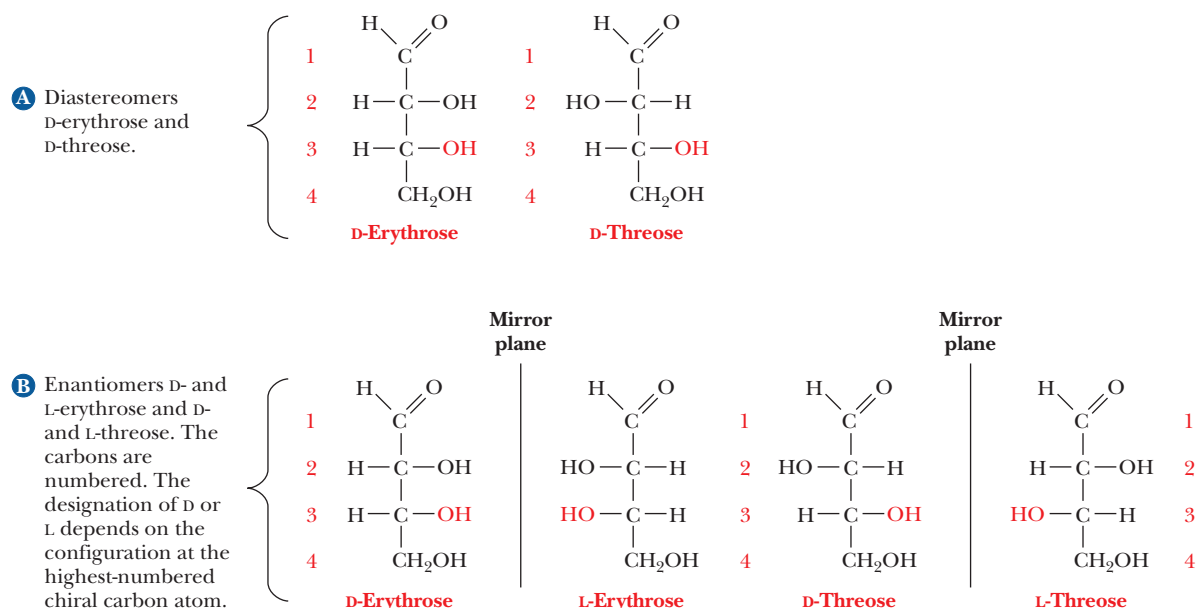


FIGURE 16.2 Numbering of carbon atoms in sugars. (a) Examples of an aldose (D-glucose) and a ketose (D-fructose), showing the numbering of carbon atoms. (b) A comparison of the structures of D-glucose and L-glucose.



■ **FIGURE 16.3** Stereoisomers of an aldotetrose.

the D configuration, and two have the L configuration. The two D isomers have the same configuration at C-3, but they differ in configuration (arrangement of the —OH group) at the other chiral carbon, C-2. These two isomers are called D-erythrose and D-threose. They are not superimposable on each other, but neither are they mirror images of each other. Such nonsuperimposable, non-mirror-image stereoisomers are called **diastereomers**. The two L isomers are L-erythrose and L-threose. L-Erythrose is the enantiomer (mirror image) of D-erythrose, and L-threose is the enantiomer of D-threose. L-Threose is a diastereomer of both D- and L-erythrose, and L-erythrose is a diastereomer of both D- and L-threose. Diastereomers that differ from each other in the configuration at only one chiral carbon are called **epimers**; D-erythrose and D-threose are epimers.

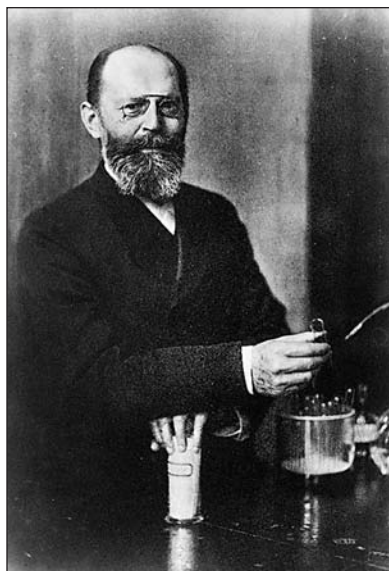
Aldopentoses have three chiral carbons, and there are 2^3 , or 8, possible stereoisomers—four D forms and four L forms. Aldohexoses have four chiral carbons and 2^4 , or 16, stereoisomers—eight D forms and eight L forms (Figure 16.4). Some of the possible stereoisomers are much more common in nature than others, and most biochemical discussion centers on the common, naturally occurring sugars. For example, D sugars, rather than L sugars, predominate in nature. Most of the sugars we encounter in nature, especially in foods, contain either five or six carbon atoms. We shall discuss D-glucose (an aldohexose) and D-ribose (an aldopentose) far more than many other sugars. Glucose is a ubiquitous energy source, and ribose plays an important role in the structure of nucleic acids.

What happens if a sugar forms a cyclic molecule?

Sugars, especially those with five or six carbon atoms, normally exist as cyclic molecules rather than as the open-chain forms we have shown so far. The cyclization takes place as a result of interaction between the functional groups on distant carbons, such as C-1 and C-5, to form a cyclic **hemiacetal** (in aldohexoses). Another possibility (Figure 16.5) is interaction between C-2 and C-5 to form a cyclic **hemiketal** (in ketohexoses). In either case, the carbonyl carbon becomes a new chiral center called the **anomeric carbon**. The cyclic sugar can take either of two different forms, designated α and β , and are called **anomers** of each other.

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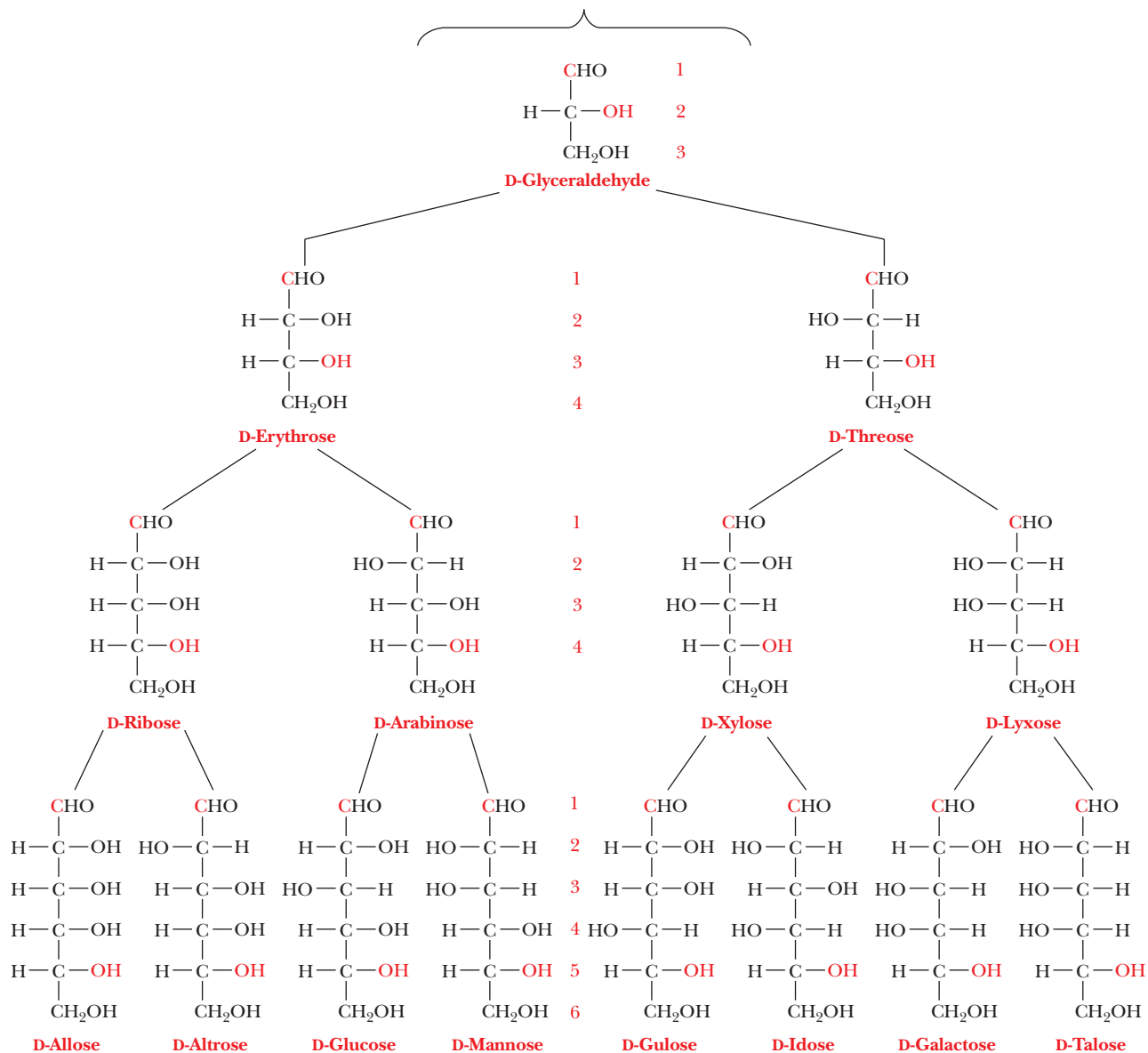
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■ Emil Fischer (1852–1919) was a German-born scientist who won the Nobel Prize in chemistry in 1902 for his studies on sugars, purine derivatives, and peptides.

- A** Aldoses containing from three to six carbon atoms, with the numbering of the carbon atom shown. Note that the figure shows only half the possible isomers. For each isomer shown, there is an enantiomer that is not shown, the L series.



- B** The relationship between mirror images is of interest to mathematicians as well as to chemists. Lewis Carroll (C. L. Dodgson), the author of *Alice's Adventures in Wonderland*, was a contemporary of Emil Fischer.

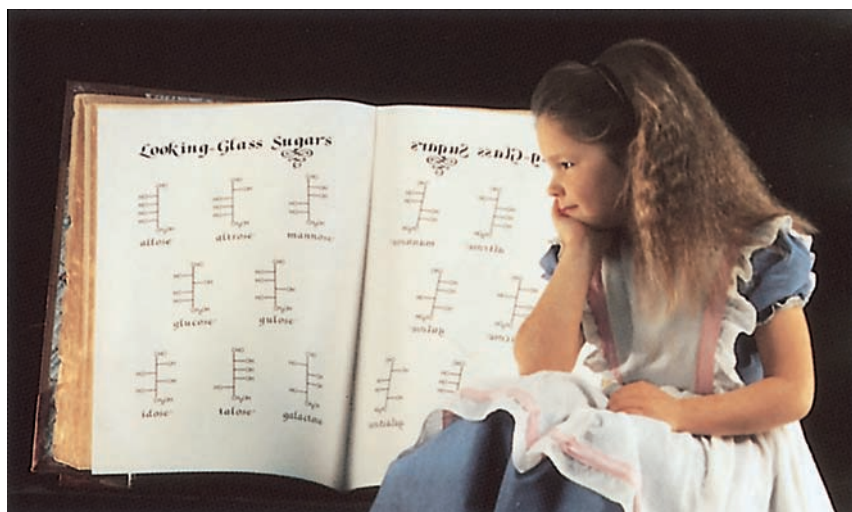
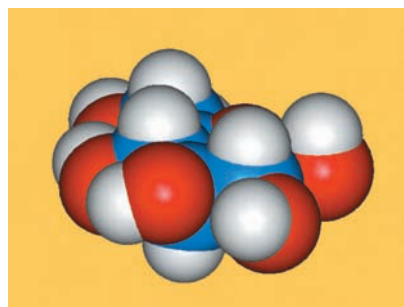
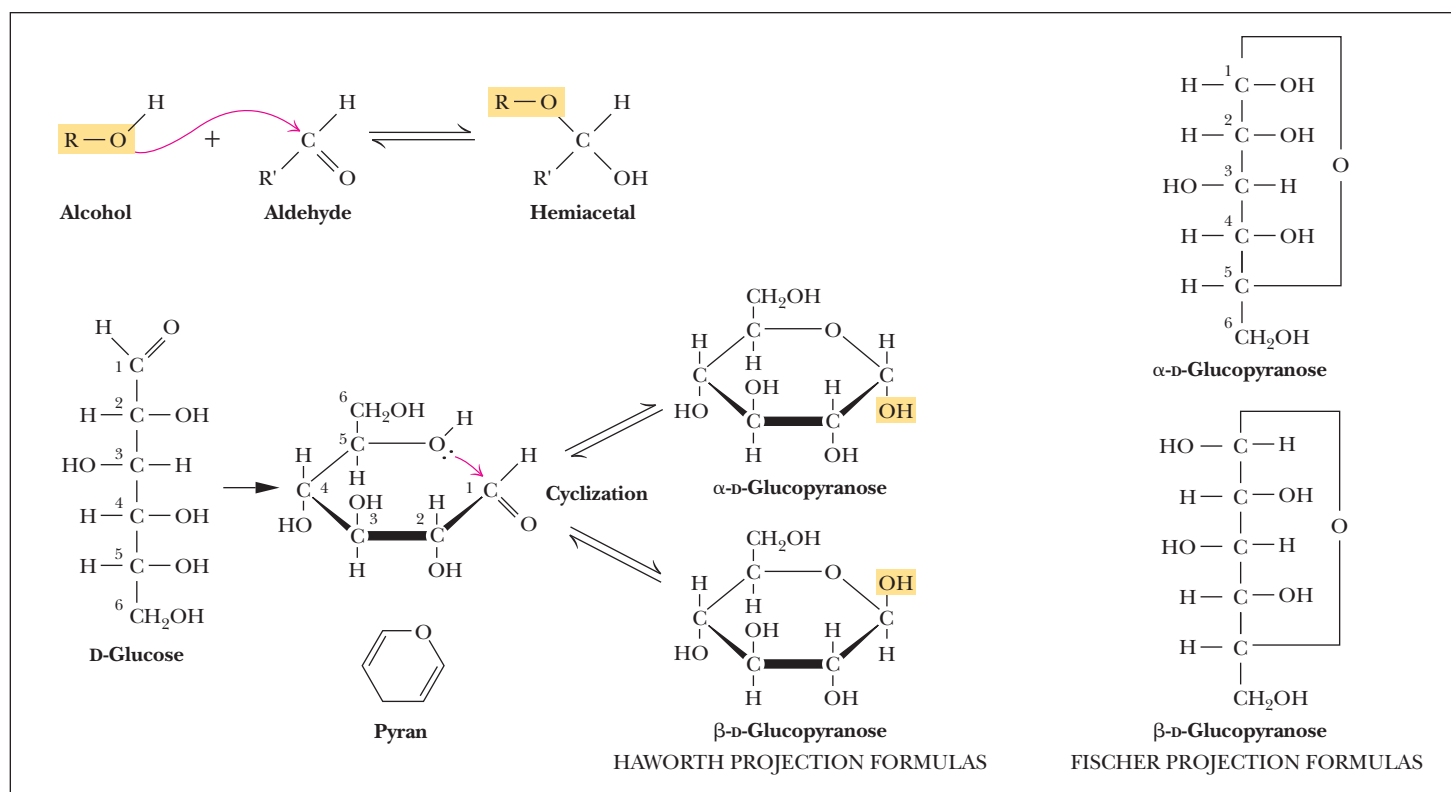


FIGURE 16.4 Stereochemical relationships among monosaccharides.

 β -D-Glucopyranose

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■ **ANIMATED FIGURE 16.5** The linear form of D-glucose undergoes an intramolecular reaction to form a cyclic hemiacetal. Sign in at www.thomsonedu.com/login to see an animated version of this figure.

The Fischer projection of the α -anomer of a D sugar has the anomeric hydroxyl group to the right of the anomeric carbon (C—OH), and the β -anomer of a D sugar has the anomeric hydroxyl group to the left of the anomeric carbon (Figure 16.6). The free carbonyl species can readily form either the α - or β -anomer, and the anomers can be converted from one form to another through the free carbonyl species. In some biochemical molecules, any anomer of a given sugar can be used, but, in other cases, only one anomer occurs. For example, in living organisms, only β -D-ribose and β -D-deoxyribose are found in RNA and DNA, respectively.

Fischer projection formulas are useful for describing the stereochemistry of sugars, but their long bonds and right-angle bends do not give a realistic picture of the bonding situation in the cyclic forms, nor do they accurately represent the overall shape of the molecules. **Haworth projection formulas** are more useful for those purposes. In Haworth projections, the cyclic structures of sugars are shown in perspective drawings as planar five- or six-membered rings viewed nearly edge on. A five-membered ring is called a **furanose** because

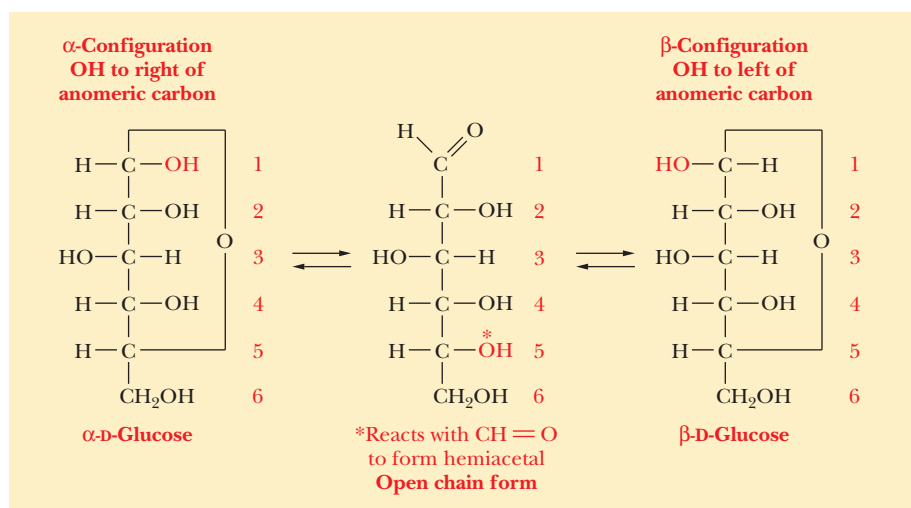
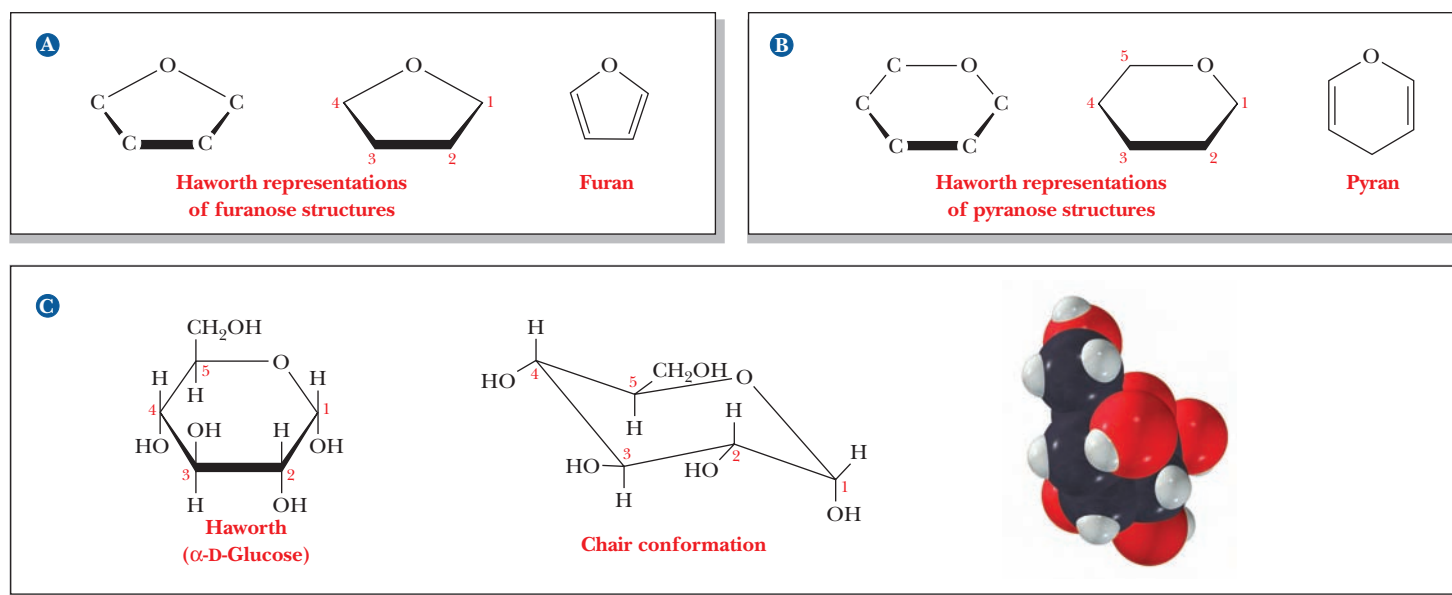


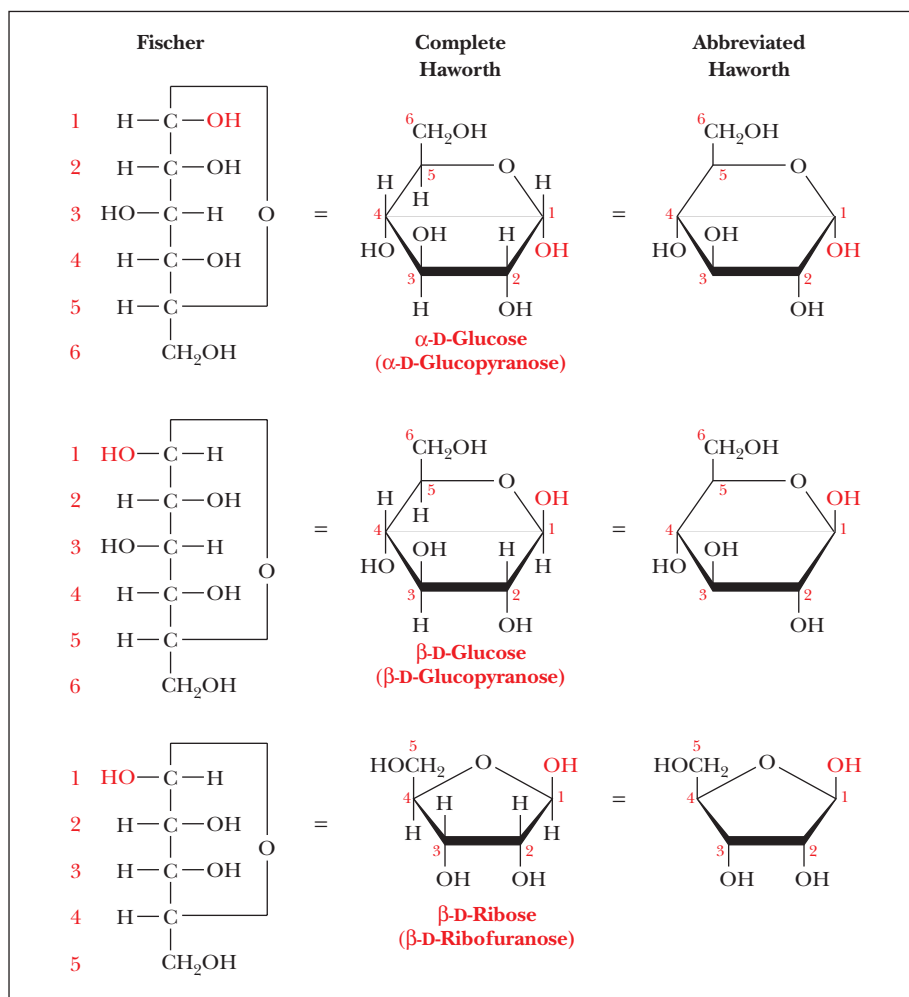
FIGURE 16.6 Fischer projection formulas of three forms of glucose. Note that the α and β forms can be converted to each other through the open-chain form. The configuration at carbon 5 determines the D designation.

of its resemblance to furan; a six-membered ring is called a **pyranose** because of its resemblance to pyran [Figure 16.7(a) and (b)]. These cyclic formulas approximate the shapes of the actual molecules better for furanoses than for pyranoses. The five-membered rings of furanoses are in reality very nearly planar, but the six-membered rings of pyranoses actually exist in solution in the chair conformation [Figure 16.7(c)]. The chair conformation is widely shown in textbooks of organic chemistry. This kind of structure is particularly useful in discussions of molecular recognition. The chair conformation and the Haworth projections are alternative ways of expressing the same information. Even though the Haworth formulas are approximations, they are useful shorthand for the structures of reactants and products in many reactions that we are going to see. The Haworth projections represent the stereochemistry of sugars more realistically than do the Fischer projections, and the Haworth scheme is adequate for our purposes. That is why biochemists use them, even though organic chemists prefer the chair form. We shall continue to use Haworth projections in our discussion of sugars.

For a D sugar, any group that is written to the *right* of the carbon in a Fischer projection has a *downward* direction in a Haworth projection; any group that is written to the *left* in a Fischer projection has an *upward* direction in a Haworth projection. The terminal $-\text{CH}_2\text{OH}$ group, which contains the carbon atom with the highest number in the numbering scheme, is shown in an upward direction. The structures of α - and β -D-glucose, which are both pyranoses, and of β -D-ribose, which is a furanose, illustrate this point (Figure 16.8). Note that, in the α -anomer, the hydroxyl on the anomeric carbon is on the opposite side of the ring from the terminal $-\text{CH}_2\text{OH}$ group (i.e., pointing down). In the β -anomer, it is on the same side of the ring (pointing up). The same convention holds for α - and β -anomers of furanoses.



■ **FIGURE 16.7** Haworth representations of sugar structures. (a) A comparison of the structure of furan with Haworth representations of furanoses. (b) A comparison of the structure of pyran with Haworth representations of pyranoses. (c) α -D-Glucopyranose in the Haworth representation (left), in the chair conformation (middle), and as a space-filling model (right). (Leonard Lessin/Waldo Feng/Mt. Sinai CORE)



■ **FIGURE 16.8** A comparison of the Fischer, complete Haworth, and abbreviated Haworth representations of α - and β -D-glucose (glucopyranose) and β -D-ribose (ribofuranose). In the Haworth representation, the α -anomer is represented with the OH group (red) downward, and the β -anomer is represented with the OH group (red) upward.

Section 16.1 Summary

- Biochemically important sugars usually contain five or six carbon atoms; their structure includes a carbonyl group (either the aldehyde or the ketone form) and several hydroxyl groups.
- Optical isomerism is of paramount importance in the structure of simple sugars. Most of the important sugars found in nature have the D configuration, based on the standard compound D-glyceraldehyde.
- Most sugars exist in cyclic forms with five- or six-membered rings. The cyclization process involves the carbonyl group and gives rise to another chiral center in addition to the ones already present in the sugar molecule. The two possible cyclic isomers, called anomers, are designated α and β .

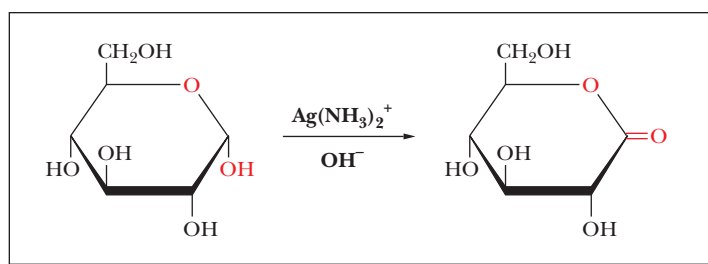
16.2 Reactions of Monosaccharides

What are some oxidation–reduction reactions of sugars?

Oxidation and reduction reactions of sugars play key roles in biochemistry. Oxidation of sugars provides energy for organisms to carry out their life processes; the highest yield of energy from carbohydrates occurs when sugars are completely oxidized to CO_2 and H_2O in aerobic processes. The reverse of complete oxidation of sugars is the reduction of CO_2 and H_2O to form sugars, a process that takes place in photosynthesis.

Several oxidation reactions of sugars are of some importance in laboratory practice because they can be used to identify sugars. Aldehyde groups can be oxidized to give the carboxyl group that is characteristic of acids, and this reaction is the basis of a test for the presence of aldoses. When the aldehyde is oxidized, some oxidizing agent must be reduced. Aldoses are called **reducing sugars** because of this type of reaction; ketoses can also be reducing sugars because they isomerize to aldoses. In the cyclic form, the compound produced by oxidation of an aldose is a *lactone* (a cyclic ester linking the carboxyl group and one of the sugar alcohols, as shown in Figure 16.9). A lactone of considerable importance to humans is discussed in the Biochemical Connections box on page 471.

Two types of reagent are used in the laboratory to detect the presence of reducing sugars. The first of these is Tollens reagent, which uses the silver ammonia complex ion, $\text{Ag}(\text{NH}_3)_2^+$, as the oxidizing agent. A silver mirror is deposited on the wall of the test tube if a reducing sugar is present, as a result of the Ag^+ in the complex ion being reduced to free silver metal (Figure 16.10). A more recent method for detection of glucose, but not other reducing sugars, is based on the use of the enzyme glucose oxidase, which is specific for glucose.



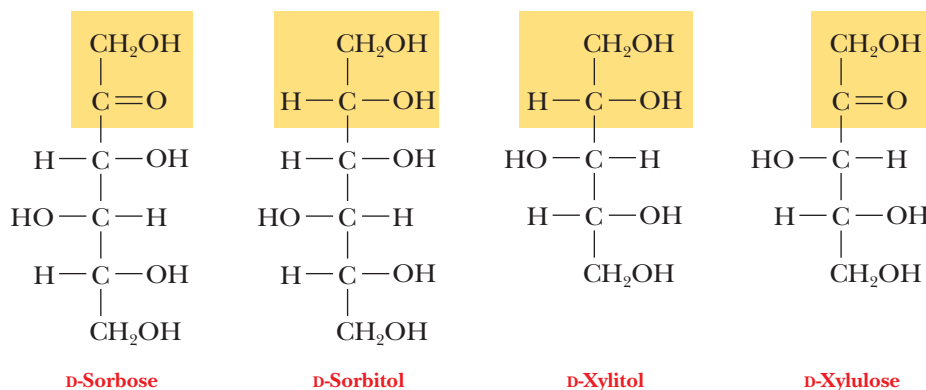
■ **FIGURE 16.9** Oxidation of a sugar to a lactone. An example of an oxidation reaction of sugars: oxidation of α -D-glucose hemiacetal to give a lactone. Deposition of free silver as a silver mirror indicates that the reaction has taken place.



■ **FIGURE 16.10** A silver mirror produced by an aldehyde. After the addition of Tollens reagent to an aldehyde, a silver mirror has been deposited in the inside of this flask.

In addition to oxidized sugars, there are some important reduced sugars. In *deoxy sugars*, a hydrogen atom is substituted for one of the hydroxyl groups of the sugar. One of these deoxy sugars is L-fucose (L-6-deoxygalactose), which is found in the carbohydrate portions of some glycoproteins (Figure 16.11), including the ABO blood-group antigens. The name *glycoprotein* indicates that these substances are conjugated proteins that contain some carbohydrate group (*glykos* is Greek for “sweet”) in addition to the polypeptide chain. An even more important example of a deoxy sugar is D-2-deoxyribose, the sugar found in DNA (Figure 16.11).

When the carbonyl group of a sugar is reduced to a hydroxyl group, the resulting compound is one of the polyhydroxy alcohols known as *alditols*. Two compounds of this kind, xylitol and sorbitol, derivatives of the sugars xylulose and sorbose, respectively, have commercial importance as sweeteners in sugarless chewing gum and candy.

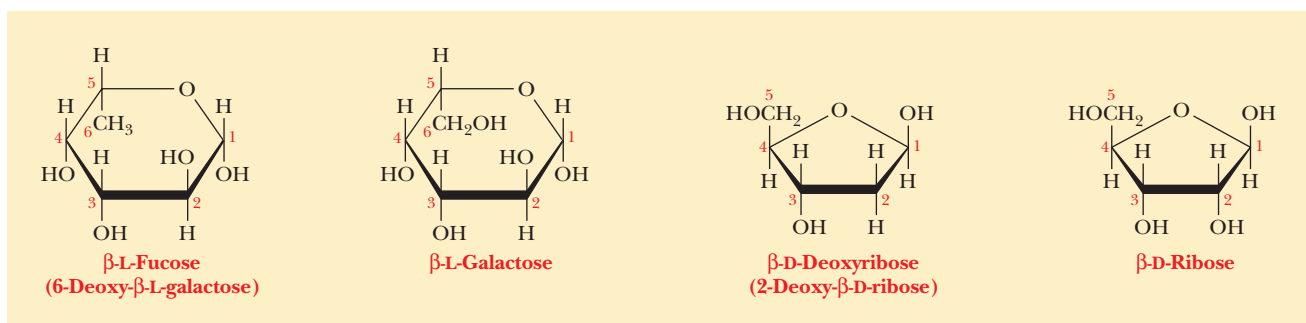


What are some important esterification reactions of sugars?

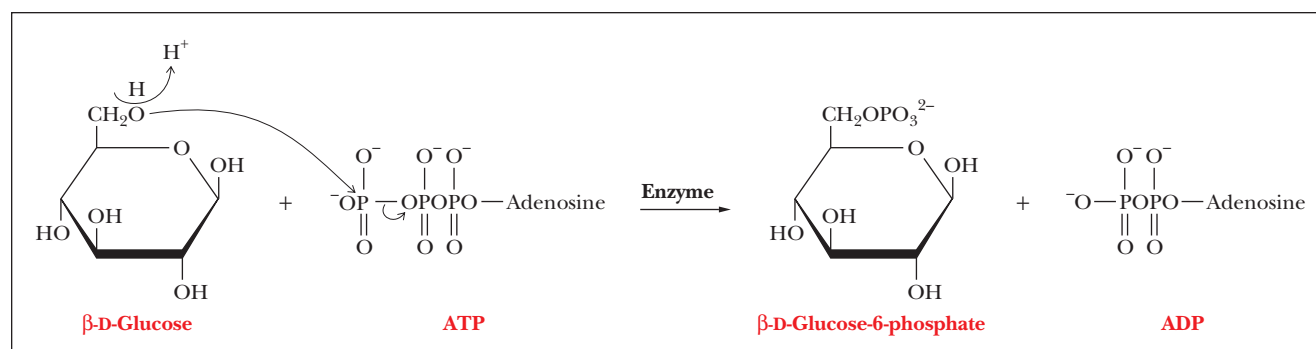
The hydroxyl groups of sugars behave exactly like all other alcohols in the sense that they can react with acids and derivatives of acids to form esters. The phosphate esters are particularly important because they are the usual intermediates in the breakdown of carbohydrates to provide energy. Phosphate esters are frequently formed by transfer of a phosphate group from ATP (adenosine triphosphate) to give the phosphorylated sugar and ADP (adenosine diphosphate), as shown in Figure 16.12. Such reactions play an important role in the metabolism of sugars (Section 17.2).

What are glycosides, and how do they form?

It is possible for a sugar hydroxyl group (ROH) bonded to the anomeric carbon to react with another hydroxyl (R'—OH) to form a glycosidic linkage (R'—O—



■ **FIGURE 16.11** Structures of two deoxy sugars. The structures of the parent sugars are shown for comparison.



■ **FIGURE 16.12** The formation of a phosphate ester of glucose. ATP is the phosphate group donor. The enzyme specifies the interaction with $\text{—CH}_2\text{OH}$ on carbon 6.

R). A glycosidic linkage is *not* an ether (the $\text{R}'\text{—O—R}$ notation is misleading) because glycosides can be hydrolyzed to the original alcohols. This type of reaction involves the anomeric carbon of the sugar in its cyclic form. (Recall that the anomeric carbon is the carbonyl carbon of the open-chain form of the sugar and is the one that becomes a chiral center in the cyclic form.) Stated in a slightly different way, a hemiacetal carbon can react with an alcohol such as methyl alcohol to give a *full acetal*, or **glycoside** (Figure 16.13). The newly formed bond is called a **glycosidic bond**. The glycosidic bonds discussed in this chapter are *O*-glycosides, with each sugar bonded to an oxygen atom of another molecule. (We encountered *N*-glycosides in Chapter 9 when we discussed nucleosides and nucleotides, in which the sugar is bonded to a nitrogen atom of a base.) Glycosides derived from furanoses are called **furanosides**, and those derived from pyranoses are called **pyranosides**.

Glycosidic bonds between monosaccharide units are the basis for the formation of oligosaccharides and polysaccharides. Glycosidic linkages can take various forms; the anomeric carbon of one sugar can be bonded to any one of the —OH groups on a second sugar to form an α - or β -glycosidic linkage. Many different combinations are found in nature. The —OH groups are numbered so that they can be distinguished, and the numbering scheme follows that of

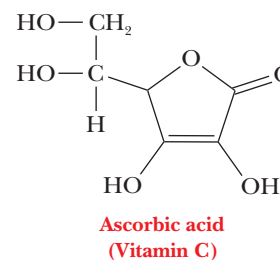
Biochemical Connections *NUTRITION*

Vitamin C Is Related to Sugars

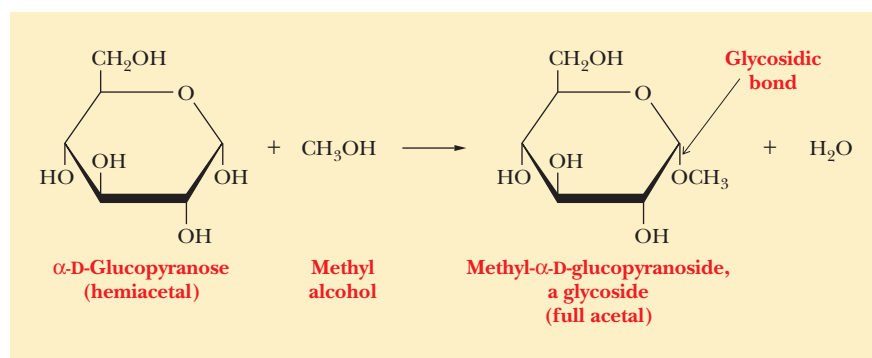
Vitamin C (ascorbic acid) is an unsaturated lactone with a five-membered ring structure. Each carbon is bonded to a hydroxyl group, except for the carboxyl carbon that is involved in the cyclic ester bond. Most animals can synthesize vitamin C; the exceptions are guinea pigs and primates, including humans. As a result, guinea pigs and primates must acquire vitamin C in their diet. Air oxidation of ascorbic acid, followed by hydrolysis of the ester bond, leads to loss of activity as a vitamin. Consequently, a lack of fresh food can cause vitamin C deficiencies, which, in turn, can lead to the disease scurvy (Section 4.3). In this disease, defects in collagen structure cause skin lesions and fragile blood vessels. The presence of hydroxyproline is necessary for collagen stability because of hydrogen-bonded cross-links between collagen strands. Ascorbic acid, in turn, is essential for the activity of prolyl hydroxylase, which converts proline residues in collagen to hydroxyproline. Lack of ascorbic acid eventually leads to the fragile collagen responsible for the symptoms of scurvy.

The British navy introduced citrus fruit into the diet of sailors in the 18th century to prevent scurvy during long sea voyages, and many people still consume citrus fruit for its vitamin C.

Potatoes are another important source of vitamin C, not because potatoes contain a *high* concentration of ascorbic acid but because we eat so many potatoes.



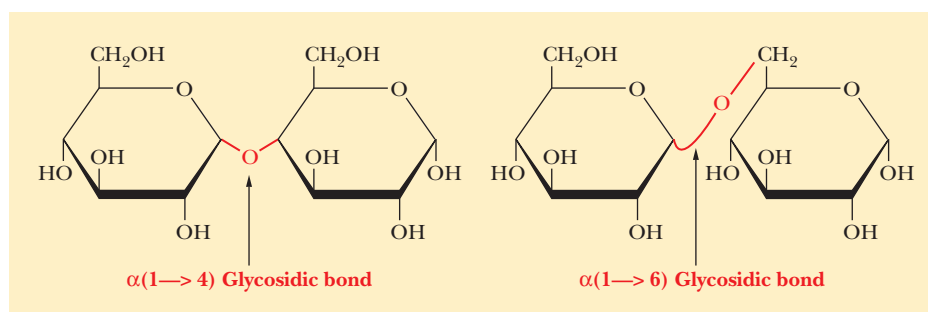
■ **FIGURE 16.13** An example of the formation of a glycoside. Methyl alcohol (CH_3OH) and an α -D-glucopyranose react to form the corresponding glycoside.



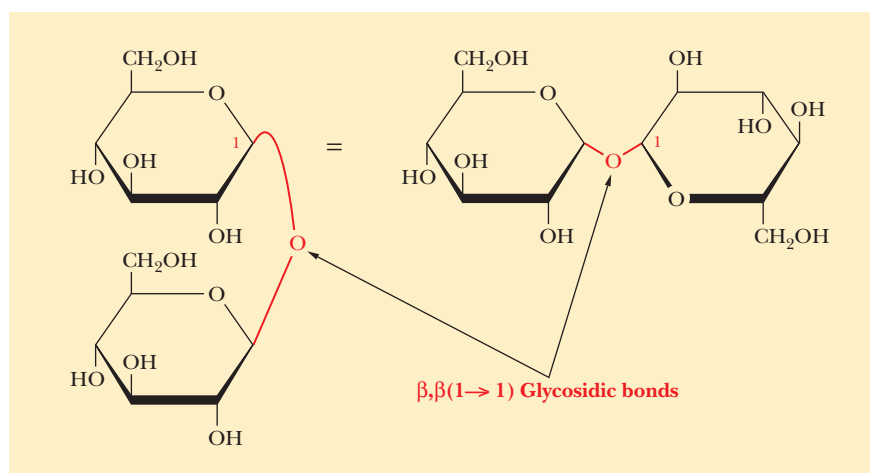
the carbon atoms. The notation for the glycosidic linkage between the two sugars specifies which anomeric form of the sugar is involved in the bond and also specifies which carbon atoms of the two sugars are linked together. Two ways in which two α -D-glucose molecules can be linked together are $\alpha(1 \rightarrow 4)$ and $\alpha(1 \rightarrow 6)$. In the first example, the α -anomeric carbon (C-1) of the first glucose molecule is joined in a glycosidic bond to the fourth carbon atom (C-4) of the second glucose molecule; the C-1 of the first glucose molecule is linked to the C-6 of the second glucose molecule in the second example (Figure 16.14). Another possibility of a glycosidic bond, this time between two β -D-glucose molecules, is a $\beta, \beta(1 \rightarrow 1)$ linkage. The anomeric forms at both C-1 carbons must be specified because the linkage is between the two anomeric carbons, each of which is C-1 (Figure 16.15).

When oligosaccharides and polysaccharides form as a result of glycosidic bonding, their chemical natures depend on which monosaccharides are linked together and also on the particular glycosidic bond formed (i.e., which ano-

■ **FIGURE 16.14** Two different disaccharides of α -D-glucose. These two chemical compounds have different properties because one has an $\alpha(1 \rightarrow 4)$ linkage and the other has an $\alpha(1 \rightarrow 6)$ linkage.



■ **FIGURE 16.15** A disaccharide of β -D-glucose. Both anomeric carbons (C-1) are involved in the glycosidic linkage.



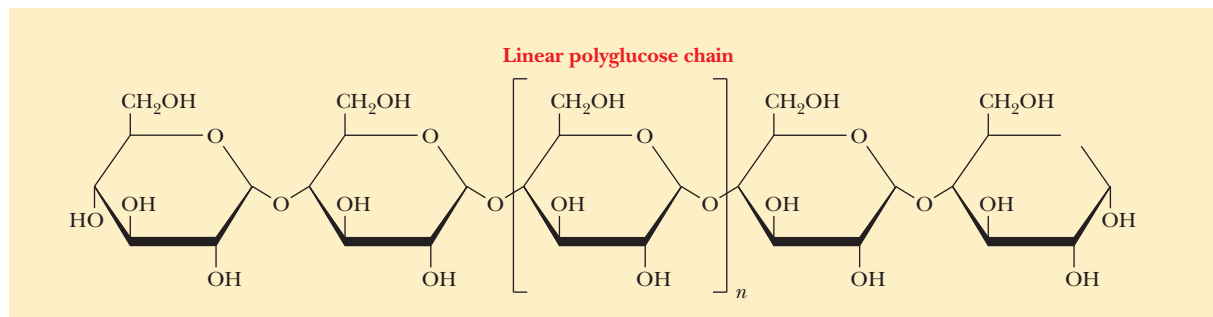
mers and which carbon atoms are linked together). The difference between cellulose and starch depends on the glycosidic bond formed between glucose monomers. Because of the variation in glycosidic linkages, both linear and branched-chain polymers can be formed. If the internal monosaccharide residues that are incorporated in a polysaccharide form only two glycosidic bonds, the polymer will be linear. (Of course, the end residues will be involved in only one glycosidic linkage.) Some internal residues can form three glycosidic bonds, leading to the formation of branched-chain structures (Figure 16.16).

Another point about glycosides is worth mentioning. We have already seen that the anomeric carbon is frequently involved in the glycosidic linkage, and also that the test for the presence of sugars—specifically for reducing sugars—requires a reaction of the group at the anomeric carbon. The internal anomeric carbons in oligosaccharides are not free to give the test for reducing sugars. Only if the end residue is a free hemiacetal rather than a glycoside will there be a positive test for a reducing sugar (Figure 16.17). The level of detection can be important for such a test. A sample that contains only a few molecules of a large polysaccharide, each molecule with a single reducing end, might well produce a negative test because there are not enough reducing ends to detect. The Biochemical Connections box on the next page describes some interesting compounds that contain glycosidic bonds.

What are some other important derivatives of sugars?

Amino sugars are an interesting class of compounds related to the monosaccharides. We shall not go into the chemistry of their formation,

A The linear polyglucose chain occurs in amylose. All glycosidic bonds are $\alpha(1 \rightarrow 4)$.



B The branched-chain polymer occurs in amylopectin and glycogen. Branched-polyglucose-chain glycosidic bonds are $\alpha(1 \rightarrow 6)$ at branch points, but all glycosidic bonds along the chain are $\alpha(1 \rightarrow 4)$.

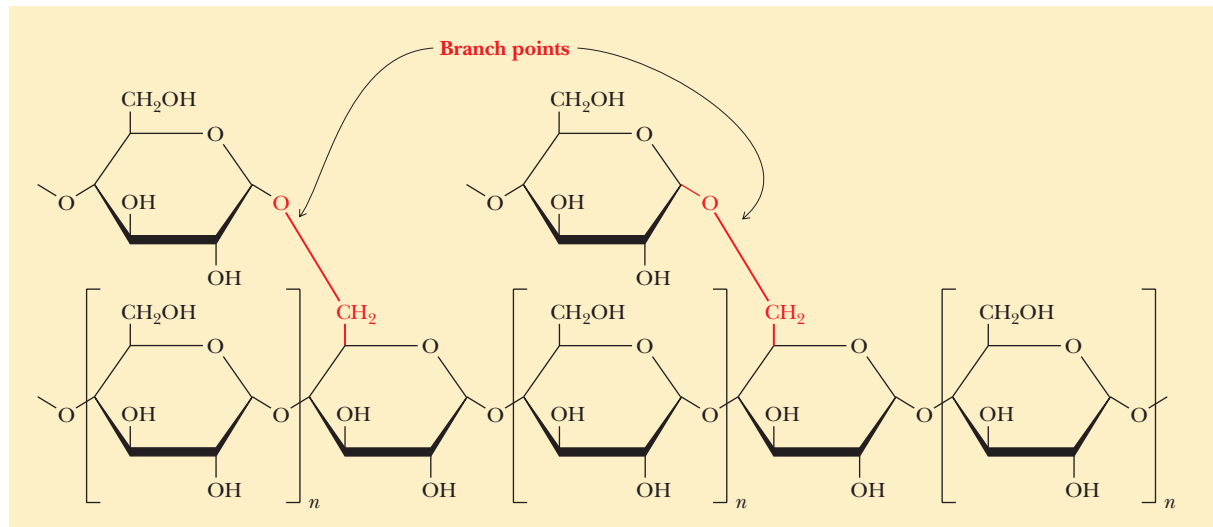
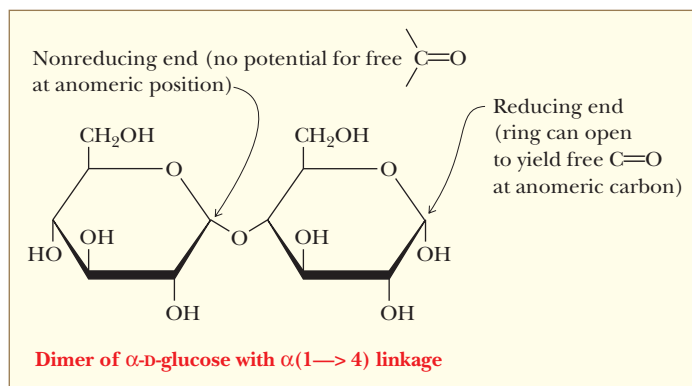


FIGURE 16.16 Linear and branched-chain polymers of α -D-glucose. The linear polyglucose chain.

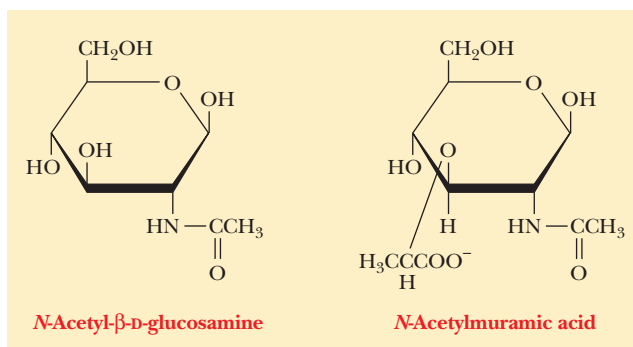


■ **FIGURE 16.17** Reducing sugars.

A disaccharide with a free hemiacetal end is a reducing sugar because of the presence of a free anomeric aldehyde carbonyl or potential aldehyde group.

but it will be useful to have some acquaintance with them when we discuss polysaccharides. In sugars of this type, an amino group ($-\text{NH}_2$) or one of its derivatives is substituted for the hydroxyl group of the parent sugar. In *N*-acetyl amino sugars, the amino group itself carries an acetyl group ($\text{CH}_3-\text{CO}-$) as a substituent.

Two particularly important examples are *N*-acetyl- β -D-glucosamine and its derivative *N*-acetyl- β -muramic acid, which has an added carboxylic acid side chain (Figure 16.18). These two compounds are components of bacterial cell walls. We did not specify whether *N*-acetylmuramic acid belongs to the L or the D series of configurations, and we did not specify the α - or β -anomer. This type of shorthand is the usual practice with β -D-glucose and its derivatives; the D configuration and the β -anomeric form are so common that we need not specify them all the time unless we want to make some specific point. The position of the amino group is also left unspecified because discussion of amino sugars usually centers on a few compounds whose structures are well known.



■ **FIGURE 16.18** The structures of *N*-acetyl- β -D-glucosamine and *N*-acetylmuramic acid.

Section 16.2 Summary

- Sugars can and do undergo oxidation reactions, as well as forming esters.
- Glycosidic linkages are responsible for the bonding of monosaccharides to form oligosaccharides and polysaccharides. The reaction in question takes place when one sugar hydroxyl group forms a bond with another sugar hydroxyl, usually one on an anomeric carbon. Different stereochemical forms are possible in glycosidic linkages, having important consequences for the function of the substances thus formed.

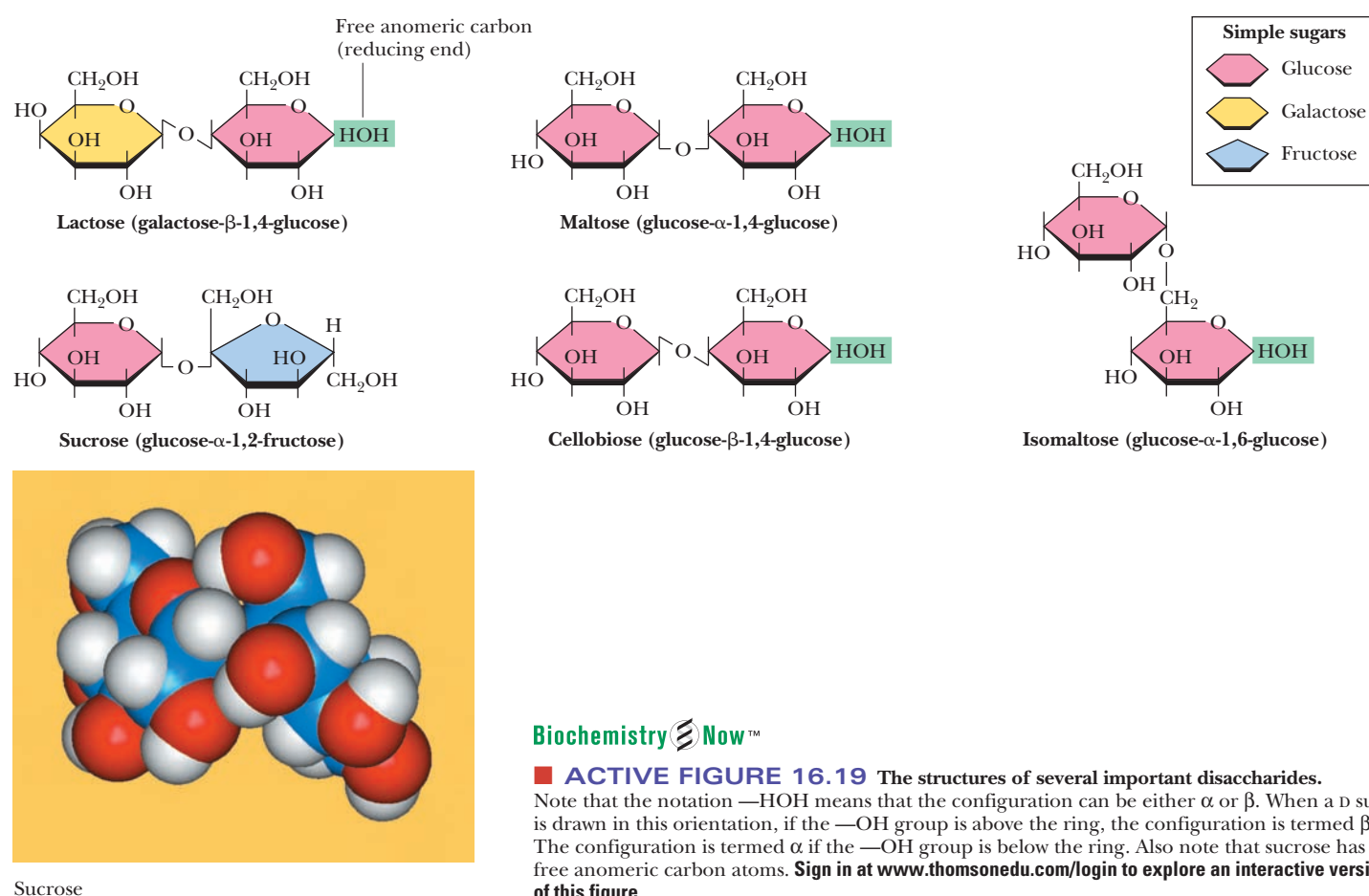
16.3 Some Important Oligosaccharides

Oligomers of sugars frequently occur as **disaccharides**, formed by linking two monosaccharide units by glycosidic bonds. Three of the most important examples of oligosaccharides are disaccharides. They are sucrose, lactose, and maltose (Figure 16.19). Two other disaccharides, isomaltose and cellobiose, are shown for comparison.

What makes sucrose an important compound?

Sucrose is common table sugar, which is extracted from sugarcane and sugar beets. The monosaccharide units that make up sucrose are α -D-glucose and β -D-fructose. Glucose (an aldohexose) is a pyranose, and fructose (a ketohexose) is a furanose. The α C-1 carbon of the glucose is linked to the β C-2 carbon of the fructose (Figure 16.19) in a glycosidic linkage that has the notation $\alpha,\beta(1 \rightarrow 2)$. Sucrose is not a reducing sugar because both anomeric groups are involved in the glycosidic linkage. Free glucose is a reducing sugar, and free fructose can also give a positive test, even though it is a ketone rather than an aldehyde in the open-chain form. Fructose and ketoses in general can act as reducing sugars because they can isomerize to aldoses in a rather complex rearrangement reaction. (We need not concern ourselves with the details of this isomerization.)

When animals consume sucrose, it is hydrolyzed to glucose and fructose, which are then degraded by metabolic processes to provide energy. Humans consume large quantities of sucrose, and excess consumption can contribute to health problems; this fact has led to a search for other sweetening agents. One



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■ ACTIVE FIGURE 16.19 The structures of several important disaccharides.

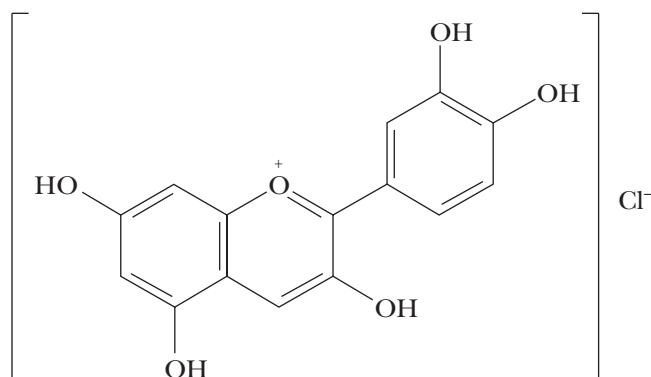
Note that the notation —HOH means that the configuration can be either α or β . When a D sugar is drawn in this orientation, if the —OH group is above the ring, the configuration is termed β . The configuration is termed α if the —OH group is below the ring. Also note that sucrose has no free anomeric carbon atoms. Sign in at www.thomsonedu.com/login to explore an interactive version of this figure.

Biochemical Connections PLANT SCIENCE

Fruits, Flowers, Striking Colors, and Medicinal Uses Too

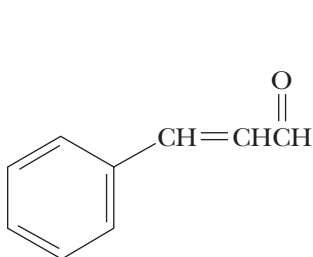
In sucrose, starches, and other sugar polymers, the *O*-glycoside bonds attach sugars to sugars. Other major categories of glycosides are known in which the sugar binds to some other type of molecule. Probably the most common example is the structure of nucleotides (Section 9.2), *N*-glycosides, in which the sugar binds to the nitrogenous, aromatic base, as found in ATP, many vitamins, DNA, and RNA. In glycolipids (Section 8.2) and glycoproteins (Section 16.5), carbohydrates are attached to both lipids and proteins, respectively, by glycoside linkages.

The red and blue colors of some flowers are sugar derivatives, often called anthocyanins. These pigments involve various sugars bonded to the compound cyanidin and its derivatives. These compounds are water soluble because of the polar groups they possess. You may have done an acid–base titration of the pigment from red cabbage or from blueberry juice in a chemistry lab. In contrast, orange, yellow, and green plant pigments tend to be lipid in composition and insoluble in water.

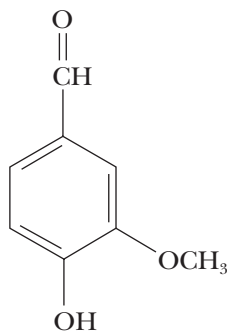


Cyanidin chloride

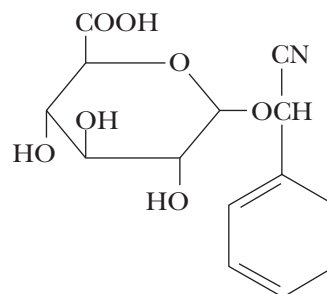
Many flavors involve sugar glycosides. Two familiar ones are cinnamon and vanilla, in which the sugars bond to cinnamaldehyde (3-phenyl-2-propenal) and vanillin, respectively. Both of these compounds are aromatic aldehydes. The distinctive taste of the kernel in a peach or apricot pit (a bitter-almond flavor) is due to laetrile, a controversial substance suggested as a cancer treatment by some.



Cinnamaldehyde



Vanillin



Laetrile

Many medically important substances have a glycosidic linkage as a part of their structure. Digitalis, prescribed for irregular heartbeat, is a mixture of several steroid complexes with sugars attached. Laetrile, a benzaldehyde derivative with a glycosidic linkage to glucuronic acid, was once thought to fight cancer, possibly because the cyanide moiety would poison the fast-growing cancer cells. This treatment is not approved in the United States, and it is likely that the cyanide causes more problems than it solves. The National Cancer Institute maintains a website at <http://www.cancer.gov>; use the search function there to find information about laetrile.



Photodisc Green/Getty Images

■ The foxglove plant produces the important cardiac medication digitalis.

that has been proposed is fructose itself. It is sweeter than sucrose; therefore, a smaller amount (by weight) of fructose than sucrose can produce the same sweetening effect with fewer calories. Consequently, high-fructose corn syrup is frequently used in food processing. The presence of fructose changes the texture of food, and the reaction to the change tends to depend on the preference of the consumer. Artificial sweeteners have been produced in the laboratory and have frequently been suspected of having harmful side effects; the ensuing controversies bear eloquent testimony to the human craving for sweets. Saccharin, for example, has been found to cause cancer in laboratory animals, as have cyclamates, but the applicability of these results to human carcinogenesis has been questioned by some. Aspartame (NutraSweet; Section 3.5) has been suspected of causing neurological problems, especially in individuals whose metabolisms cannot tolerate phenylalanine (see the Biochemical Connections box on page 80).

Another artificial sweetener is a derivative of sucrose. This substance, sucralose, which is marketed under the trade name Splenda, differs from sucrose in two ways (Figure 16.20). The first difference is that three of the hydroxyl groups have been replaced with three chlorine atoms. The second is that the configuration at carbon atom 4 of the six-membered pyranose ring of glucose has been inverted, producing a galactose derivative. The three hydroxyl groups that have been replaced by chlorine atoms are those bonded to carbon atoms 1 and 6 of the fructose moiety and to carbon atom 4 of the galactose moiety. Sucralose is not metabolized by the body, and, consequently, it does not provide calories. Tests conducted so far, as well as anecdotal evidence, indicate that it is a safe sugar substitute. It is likely to find wide use in the near future. We can safely predict that the search for nonfattening sweeteners will continue and that it will be accompanied by controversy.

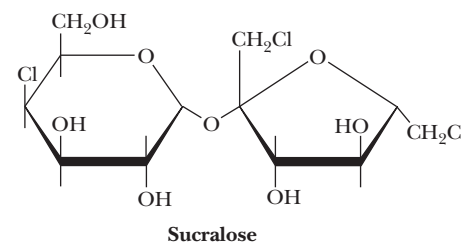
Are any other disaccharides important to us?

Lactose (see the Biochemical Connections box on page 478) is a disaccharide made up of β -D-galactose and D-glucose. Galactose is the C-4 epimer of glucose. In other words, the only difference between glucose and galactose is inversion of configuration at C-4. The glycosidic linkage is $\beta(1 \rightarrow 4)$, between the anomeric carbon C-1 of the β form of galactose and the C-4 carbon of glucose (Figure 16.19). Since the anomeric carbon of glucose is not involved in the glycosidic linkage, it can be in either the α or the β form. The two anomeric forms of lactose can be specified, and the designation refers to the glucose residue; galactose must be present as the β -anomer, since the β form of galactose is required by the structure of lactose. Lactose is a reducing sugar because the group at the anomeric carbon of the glucose portion is not involved in a glycosidic linkage, so it is free to react with oxidizing agents.

Maltose is a disaccharide obtained from the hydrolysis of starch. It consists of two residues of D-glucose in an $\alpha(1 \rightarrow 4)$ linkage. Maltose differs from *cellobiose*, a disaccharide that is obtained from the hydrolysis of cellulose, only in the glycosidic linkage. In cellobiose, the two residues of D-glucose are bonded together in a $\beta(1 \rightarrow 4)$ linkage (Figure 16.19). Mammals can digest maltose, but not cellobiose. Yeast, specifically brewer's yeast, contains enzymes that hydrolyze the starch in sprouted barley (barley malt) first to maltose and then to glucose, which is fermented in the brewing of beer. Maltose is also used in other beverages, such as malted milk.

Section 16.3 Summary

- The disaccharide sucrose is common table sugar. It consists of glucose and fructose linked by a glycosidic bond.
- Lactose, found in milk, and maltose, obtained from starch, are two other common disaccharides.



■ **FIGURE 16.20** The structure of sucralose. Note that sucralose (marketed under the trade name Splenda) differs from sucrose in the substitution of chlorine for three hydroxyls.

Biochemical Connections *NUTRITION*

Lactose Intolerance: Why Do So Many People Not Want to Drink Milk?

Humans can be intolerant of milk and milk products for several reasons. Sugar intolerance results from the inability either to digest or to metabolize certain sugars. This problem differs from a food allergy, which involves an immune response (Section 14.5). A negative reaction to sugars in the diet usually involves intolerance, whereas proteins, including those found in milk, tend to cause allergies. Most sugar intolerance is due to missing or defective enzymes, so this is another example of inborn errors of metabolism.

Lactose is sometimes referred to as milk sugar because it occurs in milk. In some adults, a deficiency of the enzyme lactase in the intestinal villi causes a buildup of the disaccharide when milk products are ingested. This is because lactase is necessary to degrade lactose to galactose and glucose so that it can be absorbed into the bloodstream from the villi. Without the

enzyme, an accumulation of lactose in the intestine can be acted on by the lactase of intestinal bacteria (as opposed to the desirable lactase of the villi), producing hydrogen gas, carbon dioxide, and organic acids. The products of the bacterial lactase reaction lead to digestive problems, such as bloating and diarrhea, as does the presence of undegraded lactose. In addition, the by-products of the extra bacterial growth draw water into the intestine, thus aggravating the diarrhea. This disorder affects only about one-tenth of the Caucasian population of the United States, but it is more common among African-Americans, Asians, Native Americans, and Hispanics.

Even if the enzyme lactase is present so that lactose can be broken down by the body, other problems can occur. A different but related problem can occur in the further metabolism of galactose. If the enzyme that catalyzes a subsequent reaction in the pathway is missing and galactose builds up, a condition known as galactosemia can result. This is a severe problem in infants because the nonmetabolized galactose accumulates within cells and is converted to the hydroxy sugar galactitol, which cannot escape. Water is drawn into these cells and the swelling and edema causes damage. The critical tissue is the brain, which is not fully developed at birth. The swelling cells can crush the brain tissue, resulting in severe and irreversible retardation. The clinical test for this disorder is inexpensive and is required by law in all states.

The dietary therapy for these two problems is quite different. Lactose-intolerant individuals must avoid lactose throughout their lives. Fortunately, tablets like Lactaid are available to add to regular milk, as are lactose- and galactose-free formulas for feeding infants. True fermented food products such as yogurt and many cheeses (especially aged ones) have had their lactose degraded during fermentation. However, many foods are not processed in this way, so lactose-intolerant individuals need to exercise caution in their food choices.

There is no way to treat milk to make it safe for people who have galactosemia, so affected individuals must avoid milk during childhood. Fortunately, a galactose-free diet is easy to achieve simply by avoiding milk. After puberty, the development of other metabolic pathways for galactose alleviates the problem in most afflicted individuals. For people who want to avoid milk, there are plenty of milk substitutes, such as soy milk or rice milk. You can even get your latte or mocha made with soy milk at Starbucks nowadays.



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■ **Dairy substitutes for the lactose intolerant.** These products help those with lactose intolerance meet their calcium needs.

16.4 Structures and Functions of Polysaccharides

When many monosaccharides are linked together, the result is a **polysaccharide**. Polysaccharides that occur in organisms are usually composed of a very few types of monosaccharide components. A polymer that consists of only one type of monosaccharide is a *homopolysaccharide*; a polymer that consists of more than one type of monosaccharide is a *heteropolysaccharide*. Glucose is the most common monomer. When there is more than one type of monomer, frequently only two types of molecules occur in a repeating sequence. A complete characterization of a polysaccharide includes specification of which monomers are present and, if necessary, the sequence of monomers. It also requires that the type

of glycosidic linkage be specified. We shall see the importance of the type of glycosidic linkage as we discuss different polysaccharides, since the nature of the linkage determines function. Cellulose and chitin are polysaccharides with β -glycosidic linkages, and both are structural materials. Starch and glycogen, also polysaccharides, have α -glycosidic linkages, and they serve as carbohydrate-storage polymers in plants and animals, respectively.

How do cellulose and starch differ from one another?

Cellulose is the major structural component of plants, especially of wood and plant fibers. It is a linear homopolysaccharide of β -D-glucose, and all residues are linked in $\beta(1 \rightarrow 4)$ glycosidic bonds (Figure 16.21). Individual polysaccharide chains are hydrogen-bonded together, giving plant fibers their mechanical strength. Animals lack the enzymes, called *cellulases*, that hydrolyze cellulose to glucose. Such enzymes attack the β -linkages between glucoses, which is common to structural polymers; the α -linkage between glucoses, which animals can digest, is characteristic of energy-storage polymers such as starch (Figure 16.22). Cellulases are found in certain bacteria, including the bacteria that inhabit the digestive tracts of insects, such as termites, and grazing animals, such as cattle and horses. The presence of these bacteria explains why cows and horses can live on grass and hay but humans cannot. The damage done by termites to the wooden parts of buildings arises from their ability to use cellulose in wood as a nutrient—owing to the presence of suitable bacteria in their digestive tracts.

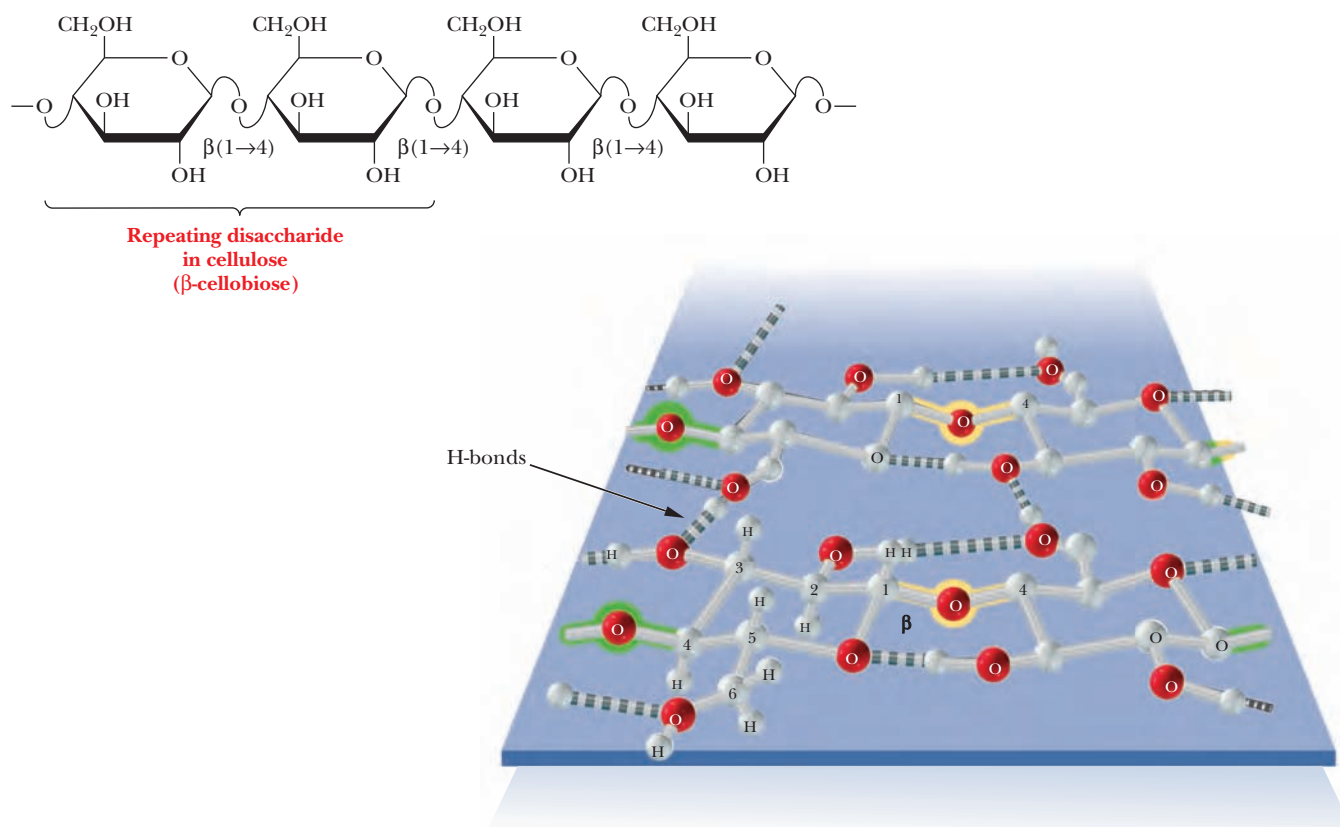
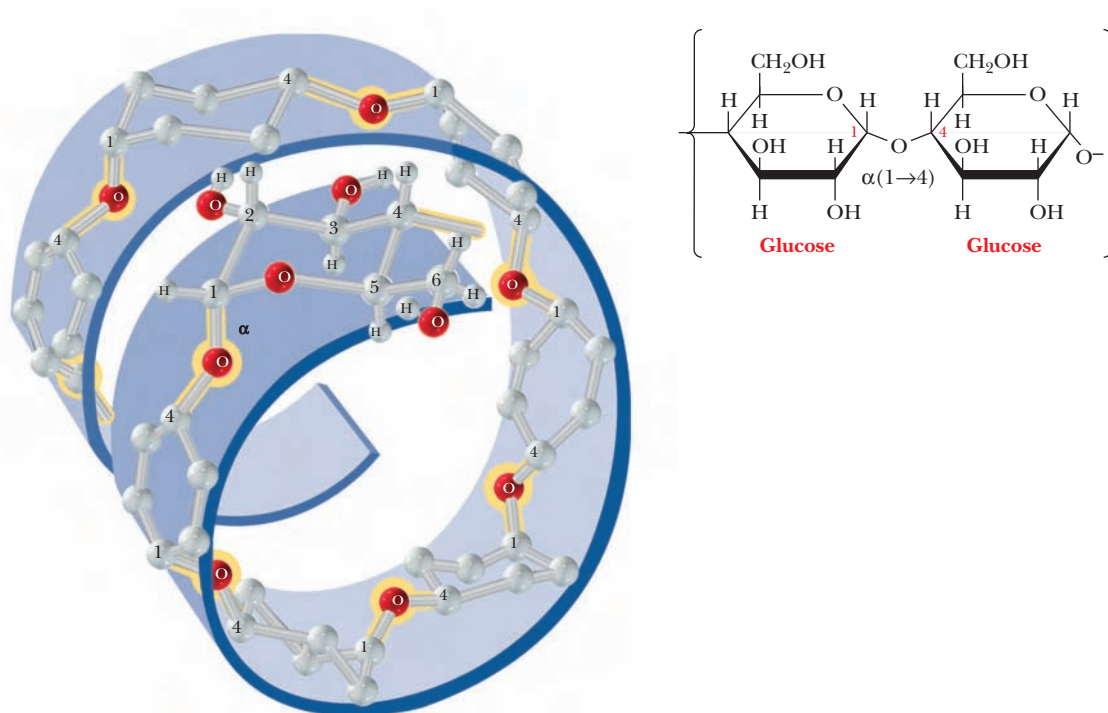


FIGURE 16.21 The polymeric structure of cellulose. β -Cellobiose is the repeating disaccharide. The monomer of cellulose is the β -anomer of glucose, which gives rise to long chains that can hydrogen-bond to one another.



■ **FIGURE 16.22** The structure of starch is based on the α -anomer of glucose. The monomer of starch is the α -anomer of glucose, which gives rise to a chain that folds into a helical form. The repeating dimer has $\alpha(1 \rightarrow 4)$ linkages throughout.



Albert Grant/Photo Researchers, Inc.



William J. Weber/Visuals Unlimited

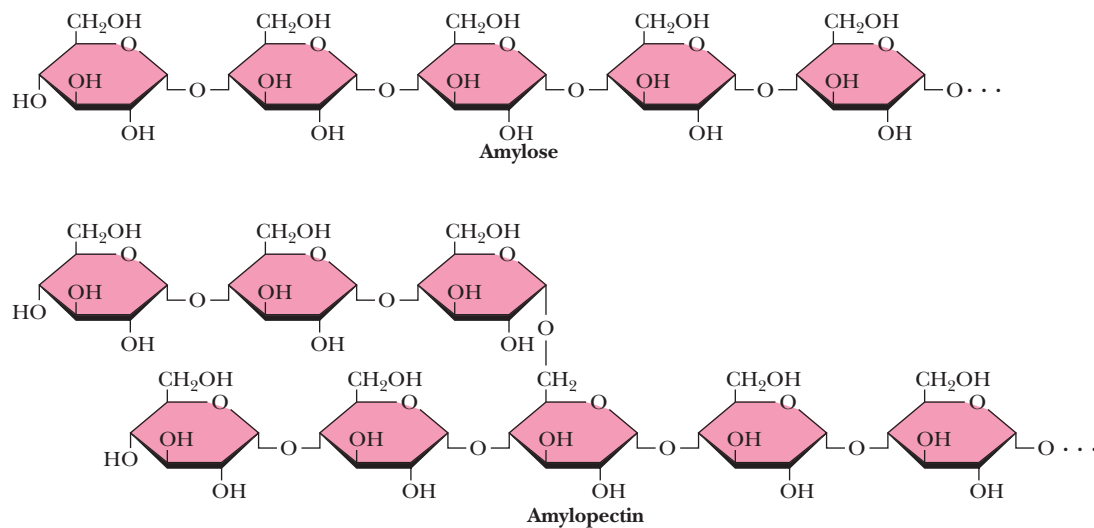
■ **Termites and cattle eating cellulose-containing foodstuffs.** Termites can digest the cellulose in wood, and cattle can digest the cellulose in grass, because bacteria in their digestive tracts produce the enzyme cellulase, which hydrolyzes the β -glycosidic linkage in cellulose.

Is there more than one form of starch?

The importance of carbohydrates as energy sources suggests that there is some use for polysaccharides in metabolism. We shall now discuss in more detail some polysaccharides, such as starches, that serve as vehicles for storage of glucose.

Starches are polymers of α -D-glucose that occur in plant cells, usually as starch granules in the cytosol. Note that there is an α -linkage in starch, in contrast with the β -linkage in cellulose. The types of starches can be distinguished from one another by their degrees of chain branching. Amylose is a linear polymer of glucose, with all the residues linked together by $\alpha(1 \rightarrow 4)$ bonds. Amylopectin is a branched chain polymer, with the branches starting at $\alpha(1 \rightarrow 6)$ linkages along the chain of $\alpha(1 \rightarrow 4)$ linkages (Figure 16.23). The most usual conformation of amylose is a helix with six residues per turn. Iodine molecules can fit inside the helix to form a starch-iodine complex, which has a characteristic dark-blue color (Figure 16.24). The formation of this complex is a well-known test for the presence of starch. If there is a preferred conformation for amylopectin, it is not yet known. (It is known that the color of the product obtained when amylopectin and glycogen react with iodine is red-brown, not blue.)

Because starches are storage molecules, there must be a mechanism for releasing glucose from starch when the organism needs energy. Both plants and animals contain enzymes that hydrolyze starches. Two of these enzymes, known as α - and β -*amylase* (the α and β do not signify anomeric forms in this case), attack $\alpha(1 \rightarrow 4)$ linkages. β -amylase is an *exoglycosidase* that cleaves from the nonreducing end of the polymer. Maltose, a dimer of glucose, is the product of reaction. The other enzyme, α -amylase, is an *endoglycosidase*, which can hydrolyze a glycosidic linkage anywhere along the chain to produce glucose and maltose. Amylose can be completely degraded to glucose and maltose by the two amylases, but amylopectin is not completely degraded because the



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ANIMATED FIGURE 16.23 Amylose and amylopectin are the two forms of starch. Note that the linear linkages are $\alpha(1 \rightarrow 4)$, but the branches in amylopectin are $\alpha(1 \rightarrow 6)$. Branches in polysaccharides can involve any of the hydroxyl groups on the monosaccharide components. Amylopectin is a highly branched structure, with branches occurring at every 12 to 30 residues. **Sign in at www.thomsonedu.com/login to see an animated version of this figure.**

branching linkages are not attacked. However, *debranching enzymes* occur in both plants and animals; they degrade the $\alpha(1 \rightarrow 6)$ linkages. When these enzymes are combined with the amylases, they contribute to the complete degradation of both forms of starch.

How is glycogen related to starch?

Although starches occur only in plants, there is a similar carbohydrate storage polymer in animals. **Glycogen** is a branched-chain polymer of α -D-glucose, and in this respect it is similar to the amylopectin fraction of starch. Like amylopectin, glycogen consists of a chain of $\alpha(1 \rightarrow 4)$ linkages with $\alpha(1 \rightarrow 6)$ linkages at the branch points. The main difference between glycogen and amylopectin is that glycogen is more highly branched (Figure 16.25). Branch points occur about every 10 residues in glycogen and about every 25 residues in amylopectin. In glycogen, the average chain length is 13 glucose residues, and there are 12 layers of branching. At the heart of every glycogen molecule is a protein called glycogenin, which is discussed in Section 18.1. Glycogen is found in animal cells in granules similar to the starch granules in plant cells. Glycogen granules are observed in well-fed liver and muscle cells, but they are not seen in some other cell types, such as brain and heart cells under normal conditions. Some athletes, particularly long-distance runners, try to build up their glycogen reserves before a race by eating large amounts of carbohydrates. When the organism needs energy, various degradative enzymes remove glucose units (Section 18.1). Glycogen phosphorylase is one such enzyme; it cleaves one glucose at a time from the nonreducing end of a branch to produce glucose-1-phosphate, which then enters the metabolic pathways of carbohydrate breakdown. Debranching enzymes also play a role in the complete breakdown of glycogen. The number of branch points is significant for two reasons. First, a more branched polysaccharide is more water soluble. This may not be as important for a plant, but, for a mammal, the amount of glycogen in solution is. There are glycogen-storage diseases caused by lower-than-normal levels of branching enzymes. The glycogen products resemble starch and can fall out of solution, forming glycogen crystals in the muscles and liver.

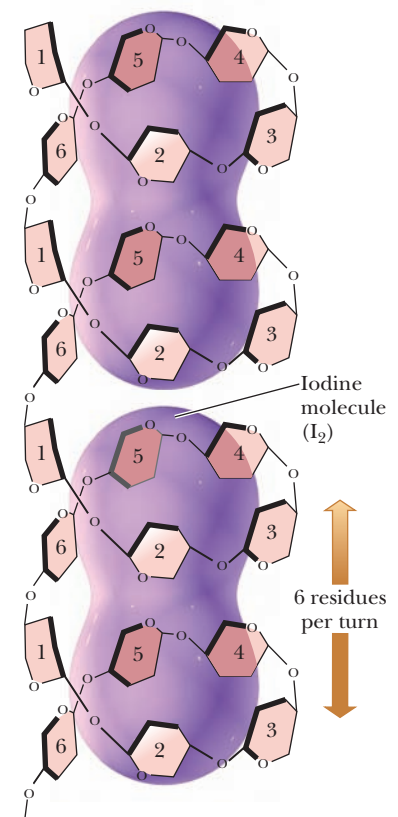


FIGURE 16.24 The starch-iodine complex. Amylose occurs as a helix with six residues per turn. In the starch-iodine complex, the iodine molecules are parallel to the long axis of the helix. Four turns of the helix are shown here. Six turns of the helix, containing 36 glycosyl residues, are required to produce the characteristic blue color of the complex.

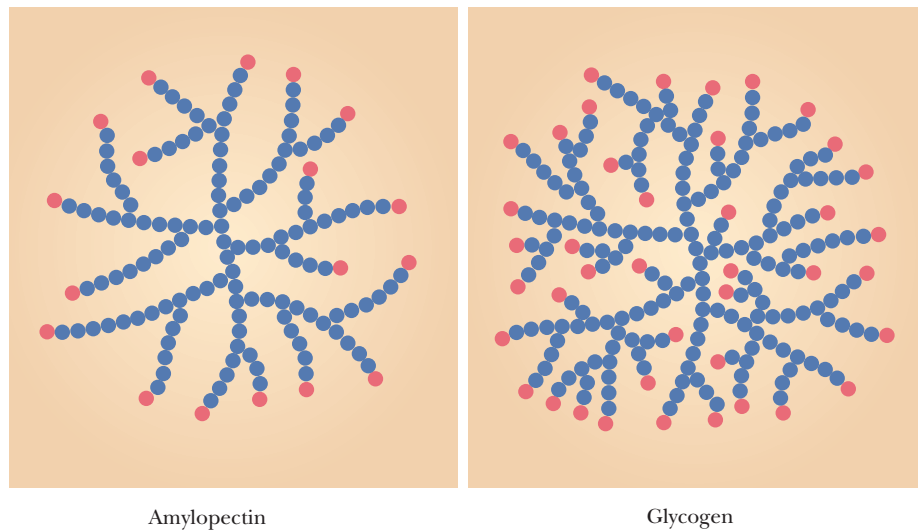
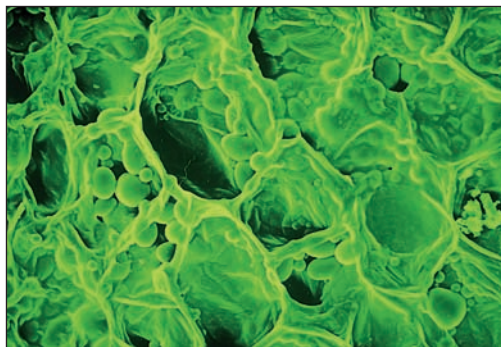
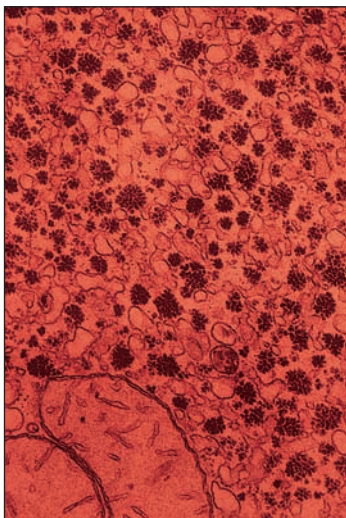


FIGURE 16.25 A comparison of the degrees of branching in amylopectin and glycogen.

Second, when an organism needs energy quickly, the glycogen phosphorylase has more potential targets if there are more branches, allowing a quicker mobilization of glucose. Again, this is not as important to a plant, so there was no evolutionary pressure to make starch highly branched.



Stanley Flegler/Visuals Unlimited



Don Fawcett/Visuals Unlimited

Electron micrographs of starch granules in a plant and glycogen granules in an animal.

What is chitin?

A polysaccharide that is similar to cellulose in both structure and function is chitin, which is also a linear homopolysaccharide with all the residues linked in $\beta(1 \rightarrow 4)$ glycosidic bonds. Chitin differs from cellulose in the nature of the monosaccharide unit; in cellulose, the monomer is β -D-glucose; in chitin, the monomer is *N*-acetyl- β -D-glucosamine. The latter compound differs from glucose only in the substitution of the *N*-acetylamino group ($-\text{NH}-\text{CO}-\text{CH}_3$) for the hydroxyl group ($-\text{OH}$) on carbon C-2 (Figure 16.26). Like cellulose, chitin plays a structural role and has a fair amount of mechanical strength because the individual strands are held together by hydrogen bonds. It is a major structural component of the exoskeletons of invertebrates such as insects and crustaceans (a group that includes lobsters and shrimp), and it also occurs in cell walls of algae, fungi, and yeasts.

What role do polysaccharides play in the structure of cell walls?

In organisms that have cell walls, such as bacteria and plants, the walls consist largely of polysaccharides. The cell walls of bacteria and plants have biochemical differences, however.

Heteropolysaccharides are major components of *bacterial* cell walls. A distinguishing feature of prokaryotic cell walls is that the polysaccharides are cross-linked by peptides. The repeating unit of the polysaccharide consists of two residues held together by $\beta(1 \rightarrow 4)$ glycosidic links, as was the case in cellulose and chitin. One of the two monomers is *N*-acetyl-D-glucosamine, which occurs in chitin, and the other monomer is *N*-acetylmuramic acid (Figure 16.27a). The structure of *N*-acetylmuramic acid differs from that of *N*-acetylglucosamine by the substitution of a lactic acid side chain [$-\text{O}-\text{CH}(\text{CH}_3)-\text{COOH}$] for the hydroxyl group ($-\text{OH}$) on carbon 3. *N*-Acetylmuramic acid is found only in prokaryotic cell walls; it does not occur in eukaryotic cell walls.

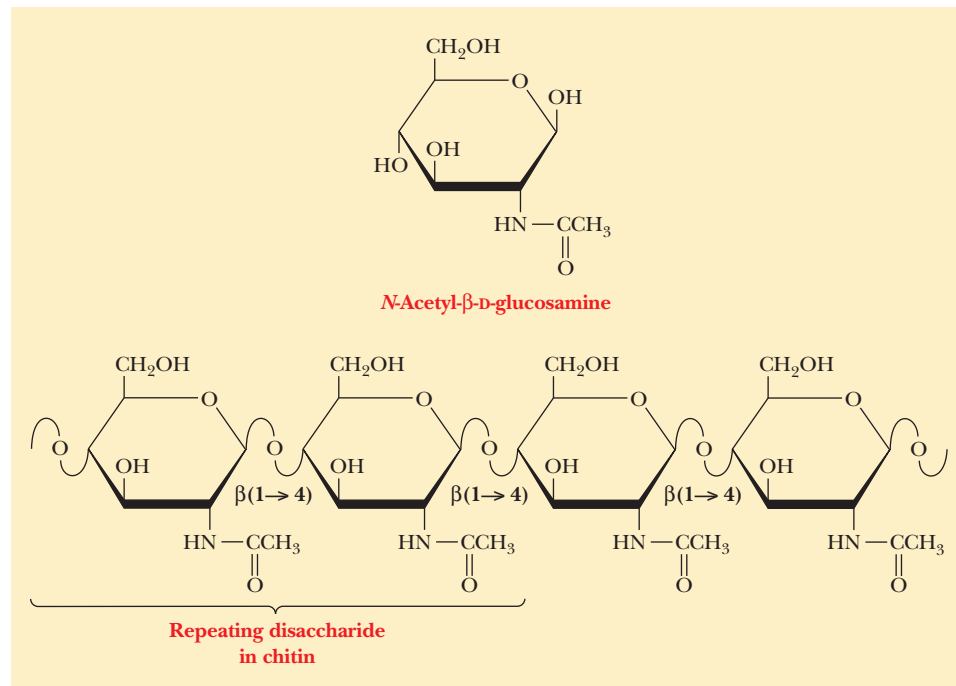


FIGURE 16.26 The polymeric structure of chitin. *N*-Acetylglucosamine is the monomer, and a dimer of *N*-acetylglucosamine is the repeating disaccharide.

Biochemical Connections ALLIED HEALTH

Why Is Dietary Fiber So Good for You?

Fiber in the diet is colloquially called roughage. It is principally made of complex carbohydrates, may have some protein components, and is moderately to fully insoluble. The health benefits of fiber are just beginning to be fully realized. We have known for a long time that roughage stimulates peristaltic action and thus helps move the digested food through the intestines, decreasing the transit time through the gut.

Potentially toxic substances in food and in bile fluid bind to fiber and are exported from the body, thus preventing them from damaging the lower intestine or being reabsorbed there.



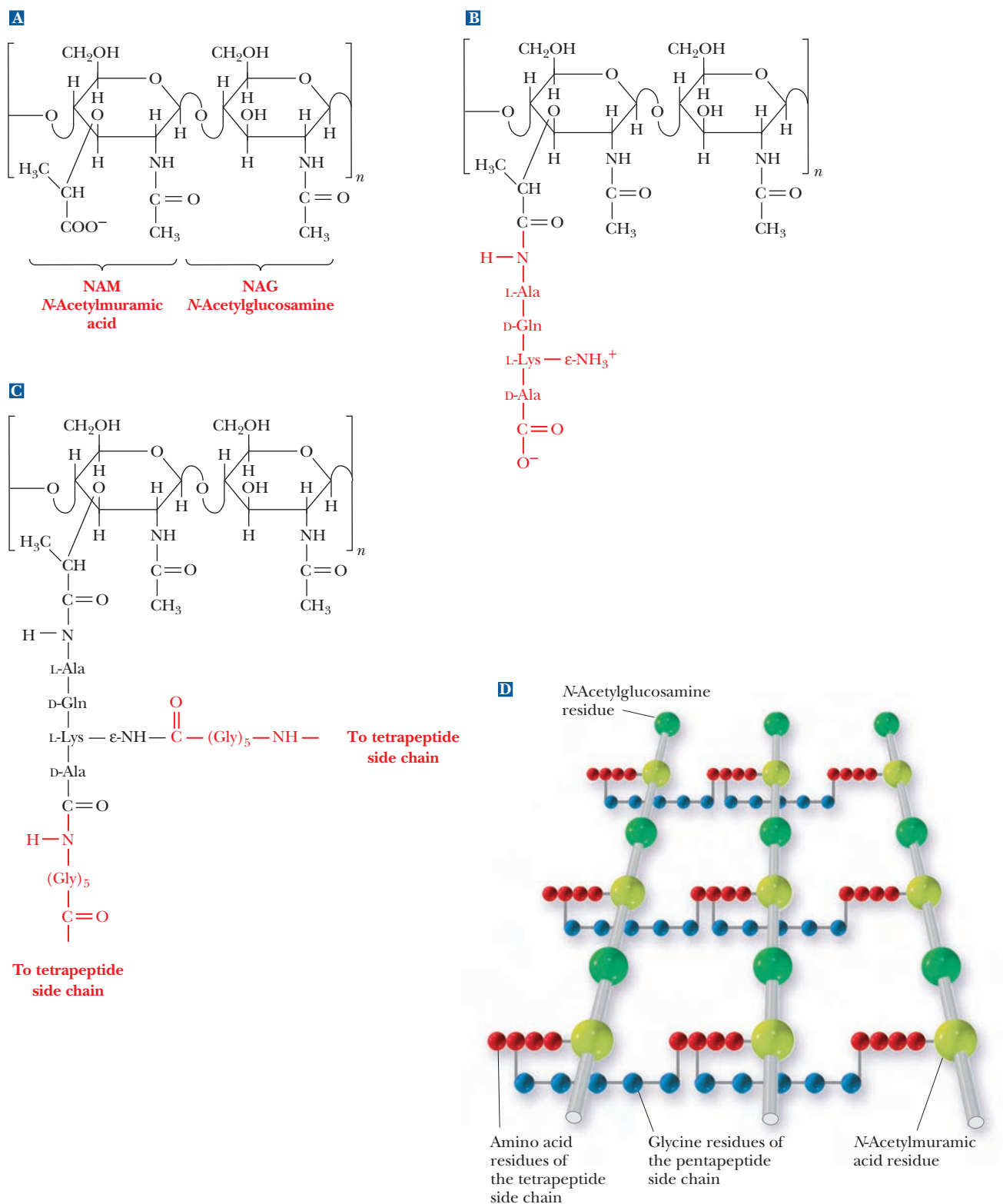
■ Many breakfast cereals advertise their high-fiber content. The presence of fruit adds to the fiber content of such a breakfast.

Statistical evidence indicates that high fiber also reduces colon and other cancers, precisely because fiber binds suspected carcinogens. It is also plausible that the benefit is due to a lack of other items in the high-fiber diet. People on high-fiber diets also tend to take in less fat and fewer calories. Any difference in heart disease or cancer may be due to these other differences.

There has been much publicity about fiber in the diet reducing cholesterol. Fiber does bind cholesterol, and it certainly causes some decrease in the amount in the blood. The reduction, expressed as a percentage, is higher in cases in which the original level of cholesterol is higher. There is, however, no definitive evidence that lowering cholesterol via the ingestion of fiber results in less heart disease.

Fiber comes in two forms: soluble and insoluble. The most common insoluble fiber is cellulose, which is found in lettuce, carrots, bean sprouts, celery, brown rice, most other vegetables, many fruit skins, and pumpernickel bread. Insoluble fiber binds various molecules but otherwise merely forms bulk in the lower intestine. Soluble fibers include amylopectin and other pectins, as well as complex starches. Uncooked and mildly processed foods contain a higher proportion of this type of fiber.

Because of increased surface area, these fibers seem to be more beneficial. Good sources include bran (especially oat bran), barley, and fresh fruits (with skin), brussels sprouts, potatoes with skin, beans, and zucchini. Soluble fiber binds water very well, increasing satiety by helping to fill the stomach.



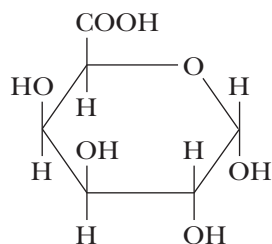
■ **FIGURE 16.27** The structure of the peptidoglycan of the bacterial cell wall of *Staphylococcus aureus*. (a) The repeating disaccharide. (b) The repeating disaccharide with the tetrapeptide side chain (shown in red). (c) Adding the pentaglycine cross-links (shown in red). (d) Schematic diagram of the peptidoglycan. The sugars are the larger spheres. The red spheres are the amino acid residues of the tetrapeptide, and the blue spheres are the glycine residues of the pentapeptide.

The cross-links in bacterial cell walls consist of small peptides. We shall use one of the best-known examples as an illustration. In the cell wall of the bacterium *Staphylococcus aureus*, an oligomer of four amino acids (a tetramer) is bonded to *N*-acetylmuramic acid, forming a side chain (Figure 16.27b). The tetrapeptides are themselves cross-linked by another small peptide, in this case consisting of five amino acids.

The carboxyl group of the lactic acid side chain of *N*-acetylmuramic acid forms an amide bond with the N-terminal end of a tetrapeptide that has the sequence L-Ala-D-Gln-L-Lys-D-Ala. Recall that bacterial cell walls are one of the few places where D-amino acids occur in nature. The occurrence of D-amino acids and *N*-acetylmuramic acid in bacterial cell walls but not in plant cell walls shows a biochemical as well as structural difference between prokaryotes and eukaryotes.

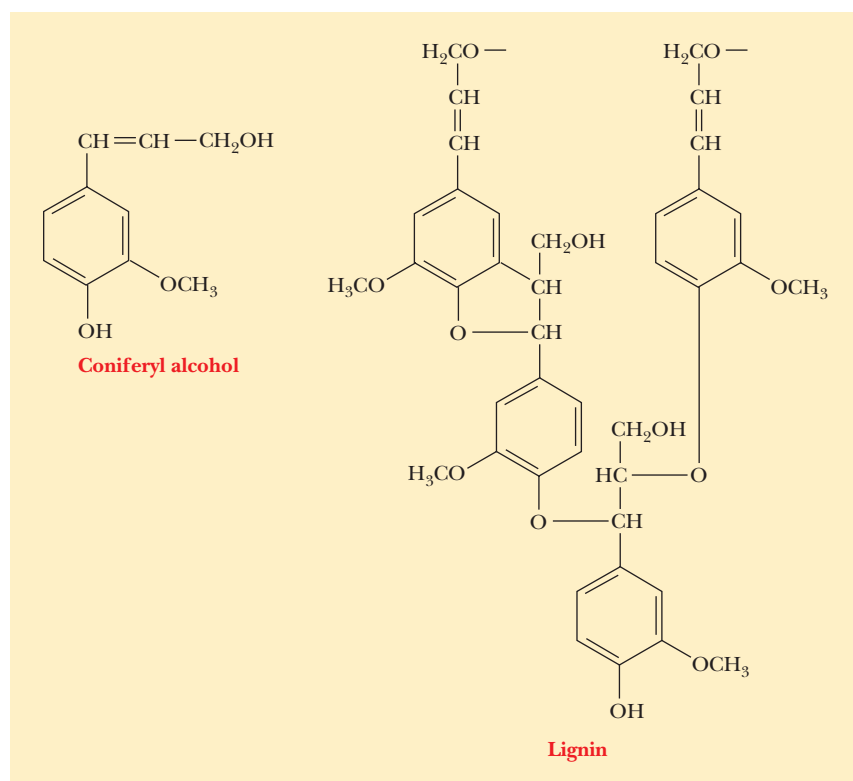
The tetrapeptide forms two cross-links, both of them to a pentapeptide that consists of five glycine residues, (Gly)₅. The glycine pentamers form peptide bonds to the C-terminal end and to the side-chain ε-amino group of the lysine in the tetrapeptide [Figure 16.27(c)]. This extensive cross-linking produces a three-dimensional network of considerable mechanical strength, which is why bacterial cell walls are extremely difficult to disrupt. The material that results from the cross-linking of polysaccharides by peptides is a **peptidoglycan** [Figure 16.25(d)], so named because it has both peptide and carbohydrate components.

Plant cell walls consist largely of **cellulose**. The other important polysaccharide component found in plant cell walls is **pectin**, a polymer made up mostly of D-galacturonic acid, a derivative of galactose in which the hydroxyl group on carbon C-6 has been oxidized to a carboxyl group.



D-Galacturonic acid

Pectin is extracted from plants because it has commercial importance in the food-processing industry as a gelling agent in yogurt, fruit preserves, jams, and jellies. The major nonpolysaccharide component in plant cell walls, especially in woody plants, is **lignin** (Latin *lignum*, “wood”). Lignin is a polymer of coniferyl alcohol, and it is a very tough and durable material (Figure 16.28). Unlike bacterial cell walls, plant cell walls contain comparatively little peptide or protein.



■ **FIGURE 16.28** The structure of lignin, a polymer of coniferyl alcohol.

Do polysaccharides play any specific roles in connective tissue?

Glycosaminoglycans are a type of polysaccharide based on a repeating disaccharide in which one of the sugars is an amino sugar and at least one of them has a negative charge owing to the presence of a sulfate group or a carboxyl group. These polysaccharides are involved in a wide variety of cellular functions and tissues. Figure 16.29 shows the disaccharide structure of the most common ones. Heparin is a natural anticoagulant that helps prevent blood clots. Hyaluronic acid is a component of the vitreous humor of the eye and of the lubricating fluid of joints. The chondroitin sulfates and keratan sulfate are components of connective tissue. Glucosamine sulfate and chondroitin sulfate are sold in large quantities as over-the-counter drugs used to help repair frayed or otherwise damaged cartilage, especially in knees. Many people who are advised that they need knee surgery for damaged ligaments look for improvement first with a two- or three-month regimen of these glycosaminoglycans. Questions exist about the efficacy of this treatment, so it will be interesting to see what future it may have.

Section 16.4 Summary

- Polysaccharides are formed by linking monomeric sugars through glycosidic linkages.
- Starch and glycogen are energy-storage polymers of sugars.
- Cellulose and chitin are structural polymers.
- Polysaccharides are important components of cell walls in bacteria and plants.

16.5 Glycoproteins

Glycoproteins contain carbohydrate residues in addition to the polypeptide chain (Chapter 4). Some of the most important examples of glycoproteins are involved in the immune response; for example, **antibodies**, which bind to and

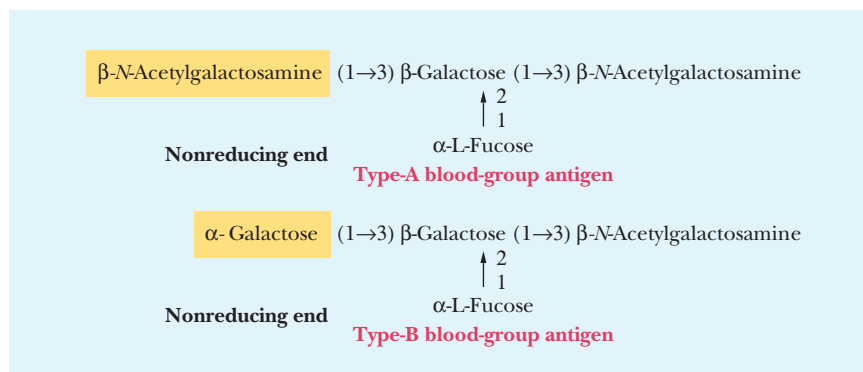
■ **FIGURE 16.29** Glycosaminoglycans, which are formed from repeating disaccharide units, often occur as components of the proteoglycans.

immobilize antigens (the substances attacking the organism), are glycoproteins. Carbohydrates also play an important role as **antigenic determinants**, the portions of an antigenic molecule that antibodies recognize and to which they bind.

How are carbohydrates important in the immune response?

An example of the role of the oligosaccharide portion of glycoproteins as antigenic determinants is found in human blood groups. There are four human blood groups: A, B, AB, and O (see the Biochemical Connections box on the bottom of the following page). The distinctions between the groups depend on the oligosaccharide portions of the glycoproteins on the surfaces of the blood cells called erythrocytes. In all blood types, the oligosaccharide portion of the molecule contains the sugar L-fucose, mentioned earlier in this chapter as an example of a deoxy sugar. *N*-Acetylgalactosamine is found at the nonreducing end of the oligosaccharide in the type-A blood-group antigen. In type-B blood, α -D-galactose takes the place of *N*-acetylgalactosamine. In type-O blood, neither of these terminal residues is present, and, in type-AB blood, both kinds of oligosaccharide are present (Figure 16.30).

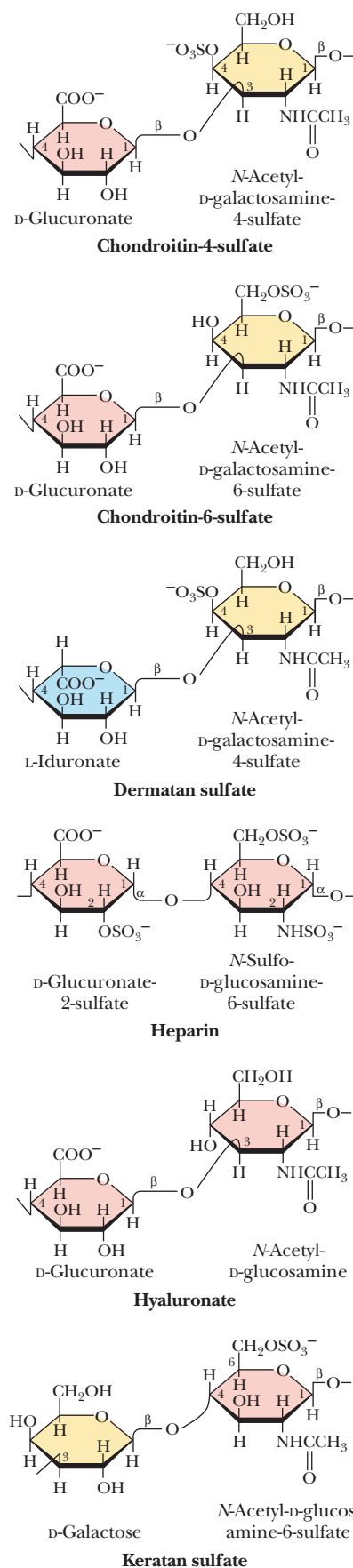
Glycoproteins also play an important role in eukaryotic cell membranes. The sugar portions are added to the protein as it passes through the Golgi on its way to the cell surface. Those glycoproteins with an extremely high carbohydrate content (85%–95% by weight) are classified as **proteoglycans**. (Note the similarity of this term to the word *peptidoglycan*, which we met in Section 16.4.) Proteoglycans are constantly being synthesized and broken down. If there is a lack of the lysosomal enzymes that degrade them, proteoglycans accumulate, with tragic consequences. One of the most striking consequences is the genetic disease known as Hurler's syndrome, in which the material that accumulates includes large amounts of amino sugars (Section 16.2). This disease leads to skeletal deformities, severe mental retardation, and death in early childhood.



■ **FIGURE 16.30** The structures of the blood-group antigenic determinants.

Section 16.5 Summary

- Sugars can be found in specific bonding arrangements in some proteins.
- Glycoproteins frequently play a role in the immune response.



Biochemical Connections *NUTRITION*

Low-Carbohydrate Diets

In the 1970s, the diets that were supposed to be the healthiest were low in fat and high in carbohydrates. “Carbo-loading” was the craze for athletes of all types, genders, and ages, as well as for the average, sedentary person. Thirty years later, things have changed considerably. Now you can go to Burger King and buy a burger wrapped in a piece of lettuce instead of a bun. Why did a



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macromolecule once thought to be healthy become something people want to avoid? The answer has to do with how glucose, the primary monosaccharide of life, is metabolized. Rising glucose levels in the blood cause a subsequent rise in levels of the hormone insulin. Insulin stimulates cells to take up glucose from the blood so that the cells get the energy and blood-glucose levels remain stable. We now know that insulin also has the unfortunate effect of stimulating fat synthesis and storage and inhibiting fat burning.

Some popular recent diets, such as the Zone Diet and the Atkins Diet, are based on keeping the carbohydrate levels low so that insulin levels do not rise and stimulate this fat storage. Current popular diet systems, such as NutriSystem and Weight Watchers, are also marketing their products by focusing on the type and quantity of carbohydrates using a “glycemic index” to distinguish between “good carbs” and “bad carbs.” As with any popular diet, the supporting evidence is not 100% conclusive, but many doctors are suggesting these diets for their patients wishing to lose weight.

In the case of athletes, however, little evidence suggests that a low-carbohydrate diet is effective for athletic performance, because of the extended time needed to replenish muscle and liver glycogen when the athlete is not on a high-carbohydrate diet.

Biochemical Connections *ALLIED HEALTH*

Glycoproteins and Blood Transfusions

If a blood transfusion is attempted with incompatible blood types, as when blood from a type-A donor is given to a type-B recipient, an antigen–antibody reaction takes place because the type-B recipient has antibodies to the type-A blood. The characteristic oligosaccharide residues of type-A blood cells serve as the antigen. A cross-linking reaction occurs between antigens and antibodies, and the blood cells clump together. In the case of a transfusion of type-B blood to a type-A recipient, antibodies to type-B blood produce the same result. Type-O blood has neither antigenic determinant, and so people with type-O blood are considered universal donors. However, these people have antibodies to both type-A and type-B blood, and so they are not universal acceptors. Type-AB people have both antigenic determinants. As a result,

they do not produce either type of antibody; they are universal acceptors.

Transfusion Relationships			
Blood Type	Makes Antibodies Against	Can Receive From	Can Donate To
O	A, B	O	O, A, B, AB
A	B	O, A	A, AB
B	A	O, B	B, AB
AB	None	O, A, B, AB	AB

Summary

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What is unique about the structures of sugars? The simplest examples of carbohydrates are monosaccharides, compounds that each contain a single carbonyl group and two or more hydroxyl groups. Monosaccharides frequently

encountered in biochemistry are sugars that contain from three to seven carbon atoms. Sugars contain one or more chiral centers; the configurations of the possible stereoisomers can be represented by Fischer projection formulas.

What happens if a sugar forms a cyclic molecule?

Sugars exist predominantly as cyclic molecules rather than in an open-chain form. Haworth projection formulas are more realistic representations of the cyclic forms of sugars than are Fischer projection formulas. Many stereoisomers are possible for five- and six-carbon sugars, but only a few of the possibilities are encountered frequently in nature.

What are some oxidation–reduction reactions of sugars? Monosaccharides can undergo various reactions. Oxidation reactions make up one important group.

What are some important esterification reactions of sugars? Esterification of sugars to phosphoric acid plays an important role in metabolism.

What are glycosides, and how do they form? The most important reaction of sugars by far is the formation of glycosidic linkages, which give rise to oligosaccharides and polysaccharides.

What are some other important derivatives of sugars? Amino sugars are the basis of cell wall structures.

What makes sucrose an important compound? Three important examples of oligosaccharides are the disaccharides sucrose, lactose, and maltose. Sucrose is common table sugar. It is a disaccharide formed when a glycosidic bond forms between glucose and fructose.

Are any other disaccharides important to us? Lactose occurs in milk, and maltose is obtained via the hydrolysis of starch.

How do cellulose and starch differ from one another? In polysaccharides, the repeating unit of the polymer is frequently limited to one or two kinds of monomer. Cellulose and starch differ in the anomeric form of

their glycosidic bonds: the α form in starch and the β form in cellulose.

Is there more than one form of starch? Starch exists in two polymeric forms, the linear amylose and the branched amylopectin.

How is glycogen related to starch? Starch, found in plants, and glycogen, which occurs in animals, differ from each other in the degree of branching in the polymer structure.

What is chitin? Cellulose and chitin are polymers based on single kinds of monomer units—glucose and *N*-acetylglucosamine, respectively. Both polymers play structural roles in organisms.

What role do polysaccharides play in the structure of cell walls? In bacterial cell walls, polysaccharides are cross-linked to peptides. Plant cell walls consist primarily of glucose.

Do polysaccharides play any specific roles in connective tissue? Glycosaminoglycans are a type of polysaccharide based on a repeating disaccharide in which one of the sugars is an amino sugar and at least one of them has a negative charge owing to the presence of a sulfate group or a carboxyl group. They play a role in joint lubrication and also in the blood clotting process.

How are carbohydrates important in the immune response? In glycoproteins, carbohydrate residues are covalently linked to the polypeptide chain. Such glycoproteins can play a role in the recognition sites of antigens. A common example is the ABO blood group, in which the three major blood types are distinguished by sugar molecules attached to the protein.

Review Exercises

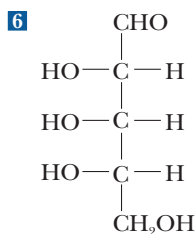
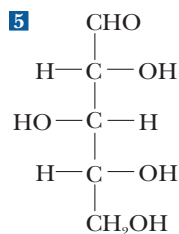
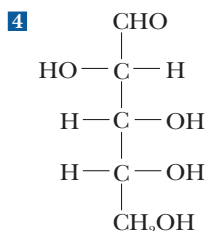
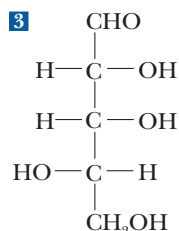
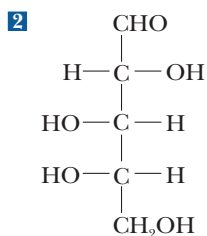
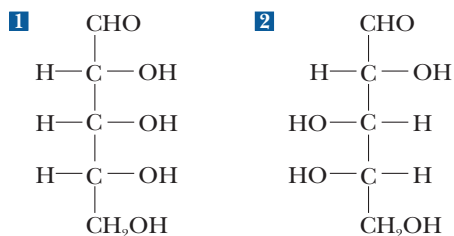
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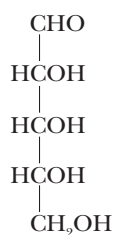
16.1 Sugars: Their Structures and Stereochemistry

- Recall** Define the following terms: polysaccharide, furanose, pyranose, aldose, ketose, glycosidic bond, oligosaccharide, glycoprotein.
- Recall** Name which, if any, of the following are epimers of D-glucose: D-mannose, D-galactose, D-ribose.
- Recall** Name which, if any, of the following groups are *not* aldose–ketose pairs: D-ribose and D-ribulose, D-glucose and D-fructose, D-glyceraldehyde and dihydroxyacetone.
- Recall** What is the difference between an enantiomer and a diastereomer?
- Recall** How many possible epimers of D-glucose exist?
- Recall** Why are furanoses and pyranoses the most common cyclic forms of sugars?
- Recall** How many chiral centers are there in the open-chain form of glucose? In the cyclic form?

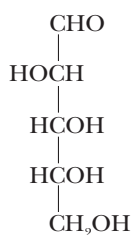
8. **Reflect and Apply** Following are Fischer projections for a group of five-carbon sugars, all of which are aldopentoses. Identify the pairs that are enantiomers and the pairs that are epimers. (The sugars shown here are not all of the possible five-carbon sugars.)



9. **Reflect and Apply** The sugar alcohol often used in “sugarless” gums and candies is L-sorbitol. Much of this alcohol is prepared by reduction of D-glucose. Compare these two structures and explain how this can be.
10. **Reflect and Apply** Consider the structures of arabinose and ribose. Explain why nucleotide derivatives of arabinose, such as ara-C and ara-A, are effective metabolic poisons.



D-Ribose



D-Arabinose

11. **Reflect and Apply** Two sugars are epimers of each other. Is it possible to convert one to the other without breaking covalent bonds?
12. **Reflect and Apply** How does the cyclization of sugars introduce a new chiral center?

16.2 Reactions of Monosaccharides

13. **Recall** What is unusual about the structure of N-acetylmuramic acid (Figure 16.18) compared with the structures of other carbohydrates?
14. **Recall** What is the chemical difference between a sugar phosphate and a sugar involved in a glycosidic bond?
15. **Recall** Define the term *reducing sugar*.

16. **Biochemical Connections** What are the structural differences between vitamin C and sugars? Do these structural differences play a role in the susceptibility of this vitamin to air oxidation?

16.3 Some Important Oligosaccharides

17. **Recall** Name two differences between sucrose and lactose. Name two similarities.
18. **Reflect and Apply** Draw a Haworth projection for the disaccharide gentibiose, given the following information:
- It is a dimer of glucose.
 - The glycosidic linkage is $\beta(1 \rightarrow 6)$.
 - The anomeric carbon not involved in the glycosidic linkage is in the α configuration.
19. **Biochemical Connections** What is the metabolic basis for the observation that many adults cannot ingest large quantities of milk without developing gastric difficulties?
20. **Reflect and Apply** Draw Haworth projection formulas for dimers of glucose with the following types of glycosidic linkages:
- A $\beta(1 \rightarrow 4)$ linkage (both molecules of glucose in the β form)
 - An $\alpha, \alpha(1 \rightarrow 1)$ linkage
 - A $\beta(1 \rightarrow 6)$ linkage (both molecules of glucose in the β form)
21. **Biochemical Connections** A friend asks you why some parents at her child's school want a choice of beverages served at lunch, rather than milk alone. What do you tell your friend?

16.4 Structures and Functions of Polysaccharides

22. **Recall** What are some of the main differences between the cell walls of plants and those of bacteria?
23. **Recall** How does chitin differ from cellulose in structure and function?
24. **Recall** How does glycogen differ from starch in structure and function?
25. **Recall** What is the main structural difference between cellulose and starch?
26. **Recall** What is the main structural difference between glycogen and starch?
27. **Recall** How do the cell walls of bacteria differ from those of plants?
28. **Reflect and Apply** Pectin, which occurs in plant cell walls, exists in nature as a polymer of D-galacturonic acid methylated at carbon 6 of the monomer. Draw a Haworth projection for a repeating disaccharide unit of pectin with one methylated and one unmethylated monomer unit in $\alpha(1 \rightarrow 4)$ linkage.
29. **Reflect and Apply** Advertisements for a food supplement to be taken by athletes claimed that the energy bars contained the two best precursors of glycogen. What were they?
30. **Reflect and Apply** Explain how the minor structural difference between α - and β -glucose is related to the differences in structure and function in the polymers formed from these two monomers.
31. **Reflect and Apply** All naturally occurring polysaccharides have one terminal residue, which contains a free anomeric carbon. Why do these polysaccharides *not* give a positive chemical test for a reducing sugar?
32. **Reflect and Apply** An amylose chain is 5000 glucose units long. At how many places must it be cleaved to reduce the average length to 2500 units? To 1000 units? To 200 units? What percentage of the glycosidic links are hydrolyzed in each case? (Even partial hydrolysis can drastically alter the physical properties of polysaccharides and thus affect their structural role in organisms.)
33. **Reflect and Apply** Suppose that a polymer of glucose with alternating $\alpha(1 \rightarrow 4)$ and $\beta(1 \rightarrow 4)$ glycosidic linkages has just been discovered. Draw a Haworth projection for a repeating tetramer (two repeating dimers) of such a polysaccharide. Would you expect this

polymer to have primarily a structural role or an energy-storage role in organisms? What sort of organisms, if any, could use this polysaccharide as a food source?

34. **Reflect and Apply** Glycogen is highly branched. What advantage, if any, does this provide an animal?
35. **Reflect and Apply** No animal can digest cellulose. Reconcile this statement with the fact that many animals are herbivores that depend heavily on cellulose as a food source.
36. **Reflect and Apply** How does the presence of α -bonds versus β -bonds influence the digestibility of glucose polymers by humans? *Hint:* There are *two* effects.
37. **Reflect and Apply** How do the sites of cleavage of starch differ from one another when the cleavage reaction is catalyzed by α -amylase and β -amylase?
38. **Biochemical Connections** What is the benefit of fiber in the diet?
39. **Reflect and Apply** How would you expect the active site of a cellulase to differ from the active site of an enzyme that degrades starch?
40. **Reflect and Apply** Would you expect cross-linking to play a role in the structure of polysaccharides? If so, how would the cross-links be formed?
41. **Reflect and Apply** Compare the information in the sequence of monomers in a polysaccharide with that in the sequence of amino acid residues in a protein.

42. **Reflect and Apply** Why is it advantageous that polysaccharides can have branched chains? How do they achieve this structural feature?
43. **Reflect and Apply** Why is the polysaccharide chitin a suitable material for the exoskeleton of invertebrates such as lobsters? What other sort of material can play a similar role?
44. **Reflect and Apply** Could bacterial cell walls consist largely of protein? Why or why not?
45. **Reflect and Apply** Some athletes eat diets high in carbohydrates before an event. Suggest a biochemical basis for this practice.
46. **Reflect and Apply** You are a teaching assistant in a general chemistry lab. The next experiment is to be an oxidation–reduction titration involving iodine. You get a starch indicator from the stockroom. Why do you need it?
47. **Reflect and Apply** Blood samples for research or medical tests sometimes have heparin added. Why is this done?
48. **Reflect and Apply** Based on what you know about glycosidic bonds, propose a scheme for formation of covalent bonds between the carbohydrate and protein portions of glycoproteins.

16.5 Glycoproteins

49. **Recall** What are glycoproteins? What are some of their biochemical roles?
50. **Biochemical Connections** Briefly indicate the role of glycoproteins as antigenic determinants for blood groups.

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