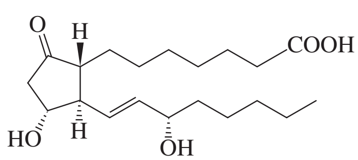
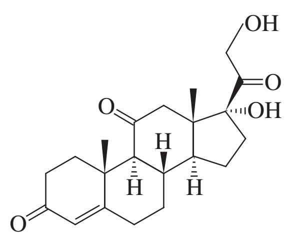
25 The Organic Chemistry of Lipids

Some of the things you will learn in this chapter are the purpose of the large deposit of fat in a whale's head, the difference between a fat and an oil, and why the venom of some snakes is poisonous. You will also see what lemon oil, geranium oil, and peppermint oil have in common and how they are biosynthesized (synthesized in nature).

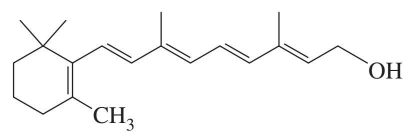
Lipids are naturally occurring organic compounds that are soluble in nonpolar solvents. Because compounds are classified as lipids on the basis of a physical property—their solubility—rather than on the basis of their structures, lipids have a variety of structures and functions, as the following examples illustrate:



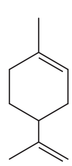
PGE_1
a vasodilator



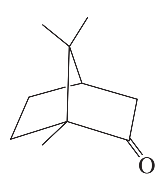
cortisone
a hormone



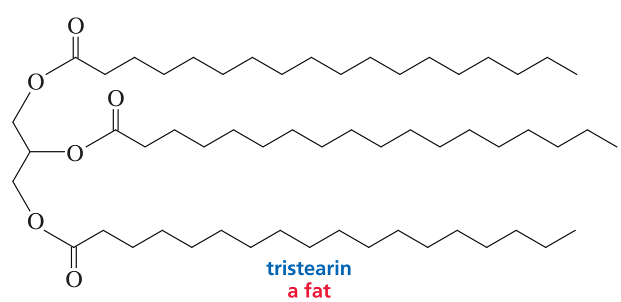
vitamin A
a vitamin



limonene
in orange and lemon oils



camphor
in camphor trees



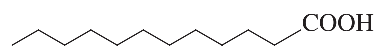
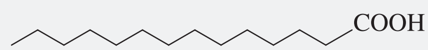
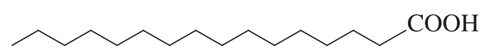
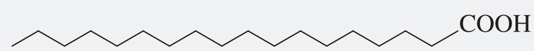
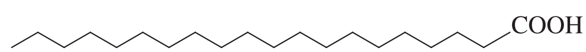
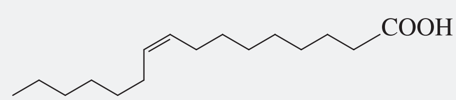
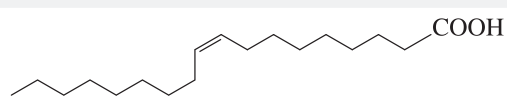
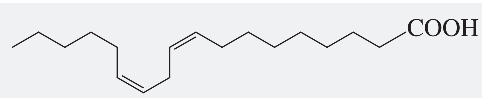
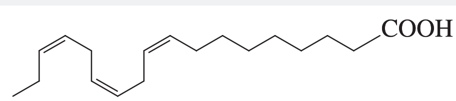
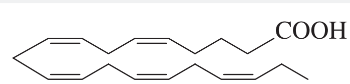
tristearin
a fat

The ability of lipids to dissolve in nonpolar organic solvents results from their significant hydrocarbon component. The hydrocarbon part of a lipid molecule is responsible for its "oiliness" or "fattiness." The word *lipid* comes from the Greek *lipos*, which means "fat."

25.1 FATTY ACIDS ARE LONG-CHAIN CARBOXYLIC ACIDS

The first lipids we will look at are fatty acids. **Fatty acids** are carboxylic acids with long hydrocarbon chains that are found in nature (Table 25.1). They are unbranched and contain an even number of carbons because they are synthesized from acetate, a compound with two carbons. The mechanism for their biosynthesis is discussed in Section 17.20.

Table 25.1 Common Naturally Occurring Fatty Acids

Number of carbons	Common name	Systematic name	Structure	Melting point (°C)
Saturated				
12	lauric acid	dodecanoic acid		44
14	myristic acid	tetradecanoic acid		58
16	palmitic acid	hexadecanoic acid		63
18	stearic acid	octadecanoic acid		69
20	arachidic acid	eicosanoic acid		77
Unsaturated				
16	palmitoleic acid	(9*Z*)-hexadecenoic acid		0
18	oleic acid	(9*Z*)-octadecenoic acid		13
18	linoleic acid	(9*Z*,12*Z*)-octadecadienoic acid		–5
18	linolenic acid	(9*Z*,12*Z*,15*Z*)-octadecatrienoic acid		–11
20	arachidonic acid	(5*Z*,8*Z*,11*Z*,14*Z*)-eicosatetraenoic acid		–50
20	EPA	(5*Z*,8*Z*,11*Z*,14*Z*,17*Z*)-eicosapentaenoic acid		–50

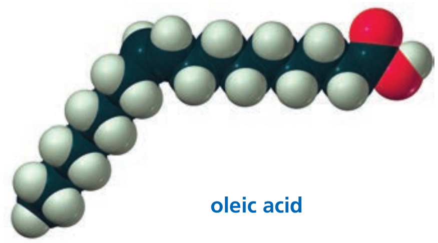
- Fatty acids can be saturated with hydrogen (and, therefore, have no carbon–carbon double bonds).
- Fatty acids can be unsaturated (and have carbon–carbon double bonds).
- Fatty acids with more than one double bond are called **polyunsaturated fatty acids.**
- The double bonds in naturally occurring unsaturated fatty acids have the cis configuration and are always separated by one CH_2 group.

The melting points of saturated fatty acids increase with increasing molecular weight because of increased London dispersion forces between the molecules (Section 3.9). The melting points of unsaturated fatty acids with the same number of double bonds also increase with increasing molecular weight (Table 25.1).

The cis double bond in a fatty acid produces a bend in the molecule, which prevents unsaturated fatty acids from packing together as tightly as saturated fatty acids. As a result, unsaturated fatty acids have fewer intermolecular interactions and, therefore, have lower melting points than saturated fatty acids with comparable molecular weights (Table 25.1).

stearic acid

an 18-carbon fatty acid with no double bonds



oleic acid

an 18-carbon fatty acid with one double bond

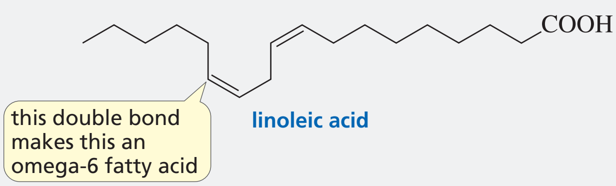
Unsaturated fatty acids have lower melting points than saturated fatty acids.

Omega Fatty Acids

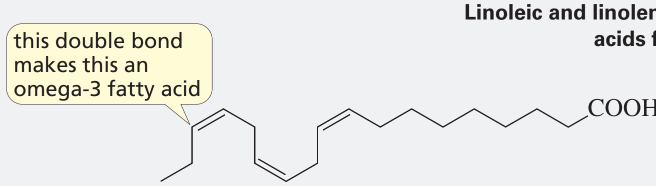
Omega indicates the position of the first double bond in an unsaturated fatty acid, counting from the methyl end. For example, linoleic acid is an omega-6 fatty acid because its first double bond is after the sixth carbon, and linolenic acid is an omega-3 fatty acid because its first double bond is after the third carbon. Mammals lack the enzyme that introduces a double bond beyond C-9, counting from the carbonyl carbon. Therefore, linoleic acid and linolenic acids are *essential fatty acids* for mammals: mammals cannot synthesize them, but because they are needed for normal body function, they must be obtained from the diet.

Omega-3 fatty acids have been found to decrease the likelihood of sudden death due to a heart attack. When under stress, the heart can develop fatal disturbances in its rhythm. Omega-3 fatty acids are incorporated into cell membranes in the heart and apparently have a stabilizing effect on heart rhythm. These fatty acids are found in fatty fish such as herring, mackerel, and salmon.

Linoleic and linolenic acids are essential fatty acids for mammals.



linoleic acid



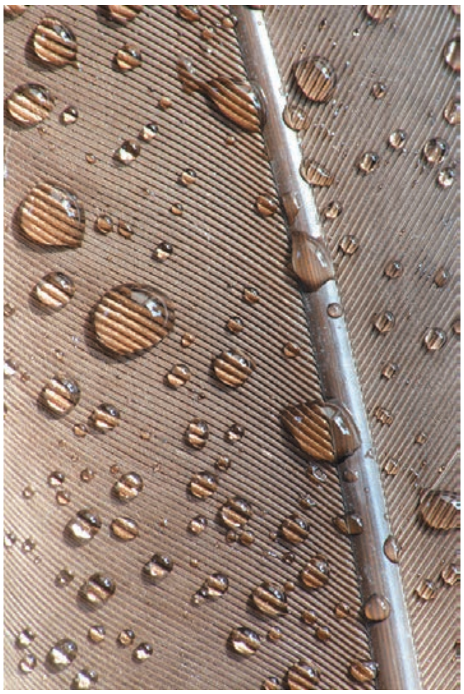
linolenic acid

PROBLEM 1

Explain the difference in the melting points of the following fatty acids:

a. palmitic acid and stearic acid
b. stearic acid and oleic acid
c. palmitoleic and oleic
d. oleic and linoleic

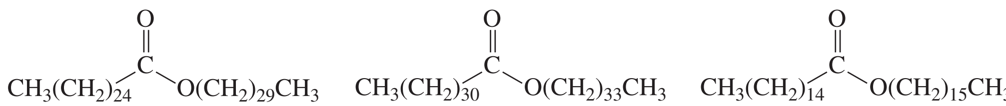
layers of honeycomb in a beehive



raindrops on a feather

25.2 WAXES ARE HIGH-MOLECULAR-WEIGHT ESTERS

Waxes are esters formed from long-chain carboxylic acids (fatty acids) and long-chain alcohols. For example, beeswax, the structural material of beehives, has a 26-carbon carboxylic acid component and a 30-carbon alcohol component. The word *wax* comes from the Old English *weax*, meaning "material of the honeycomb." Carnauba wax is a particularly hard wax because of its relatively high molecular weight; it has a 32-carbon carboxylic acid component and a 34-carbon alcohol component. Carnauba wax is widely used as a car wax and in floor polishes.



major component of beeswax — structural material of beehives

major component of carnauba wax — coating on the leaves of a Brazilian palm

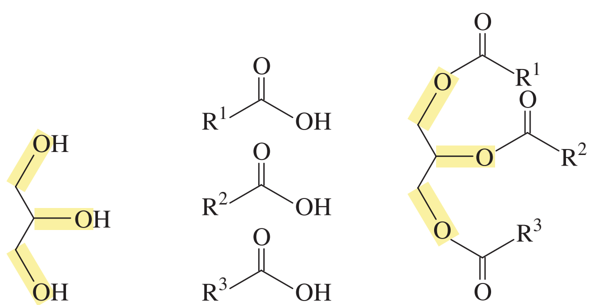
major component of spermaceti wax — from the heads of sperm whales

Waxes are common in living organisms. The feathers of birds are coated with wax to make them water repellent. Some vertebrates secrete wax in order to keep their fur lubricated and water repellent. Insects secrete a waterproof, waxy layer on the outside of their exoskeletons. Wax is also found on the surfaces of certain leaves and fruits, where it serves as a protectant against parasites and minimizes the evaporation of water.

25.3 FATS AND OILS ARE TRIGLYCERIDES

Triglycerides, also called triacylglycerols, are compounds in which each of the three OH groups of glycerol has formed an ester with a fatty acid.

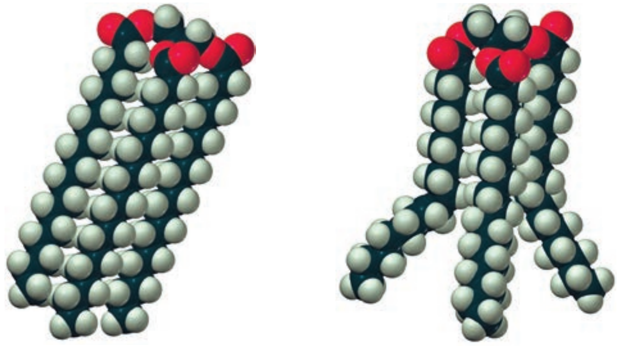
If the three fatty acid components of a triacylglycerol are the same, the compound is called a **simple triglyceride. Mixed triglycerides** contain two or three different fatty acid components and are more common than simple triacylglycerols.



glycerol — fatty acids — a triglyceride, a fat or an oil

Fats and Oils

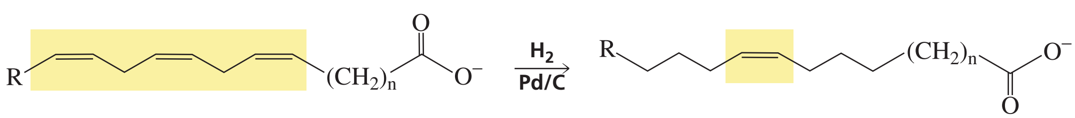
Triglycerides that are solids or semisolids at room temperature are called **fats.** Most fats are obtained from animals and are composed largely of triglycerides with fatty acid components that either are saturated or have only one double bond. The saturated fatty acid tails pack closely together, giving these triglycerides relatively high melting points. They, therefore, are solids at room temperature.



Liquid triglycerides are called **oils.** Oils typically come from plant products such as corn, soybeans, olives, and peanuts. They are composed primarily of triglycerides with unsaturated fatty acids and, therefore, cannot pack tightly together. Consequently, they have relatively low melting points and so they are liquids at room temperature. All triglyceride molecules from a single source are not necessarily identical; substances such as lard and olive oil, for example, are mixtures of several different triglycerides.

Converting Oils to Fats

Some or all of the double bonds of polyunsaturated oils can be reduced by catalytic hydrogenation (Section 5.9). Margarine and shortening are prepared by hydrogenating vegetable oils, such as soybean oil or safflower oil, until they have the desired consistency. The hydrogenation reaction must be carefully controlled, however, because reducing all the carbon–carbon double bonds would produce a hard fat with the consistency of beef tallow. We saw that trans fats can be formed during hydrogenation (Section 5.9).



Vegetable oils have become popular in food preparation because some studies have linked the consumption of saturated fats with heart disease. However, recent studies have shown that *un*saturated fats may also be implicated in heart disease. One unsaturated fatty acid—a 20-carbon fatty acid with five double bonds, known as EPA (Table 25.1) and found in high concentrations in fish oils—is thought to lower the chance of developing certain forms of heart disease.

Once consumed, dietary fat is hydrolyzed in the intestine, releasing glycerol and fatty acids (Section 24.5). We saw that fats and oils can be oxidized by O_2 to form compounds responsible for the unpleasant taste and smell associated with sour milk and rancid butter (Section 12.11).

This puffin's diet is high in fish oil.

PROBLEM 2 ♦

Which has a higher melting point, glyceryl tripalmitoleate or glyceryl tripalmitate?

PROBLEM 3

Draw the structure of an optically inactive fat that, when hydrolyzed under acidic conditions, gives glycerol, one equivalent of lauric acid, and two equivalents of stearic acid.

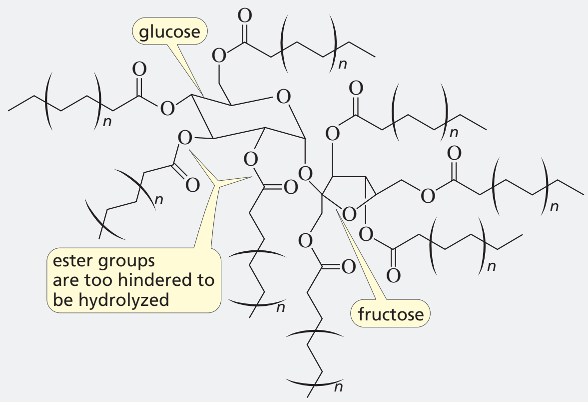
PROBLEM 4

Draw the structure of an optically active fat that, when hydrolyzed under acidic conditions, gives the same products as the fat in Problem 3.

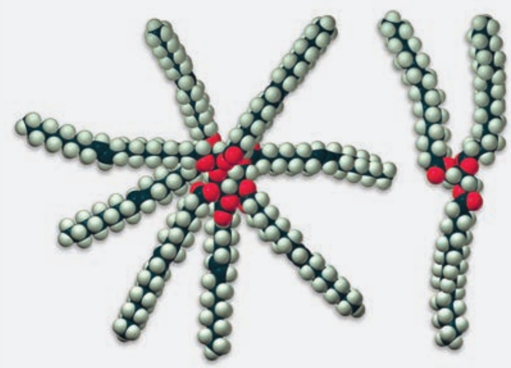
Olestra: Nonfat with Flavor

Chemists have been searching for ways to reduce the caloric content of foods without decreasing their flavor. Many people who believe that "no fat" is synonymous with "no flavor" think this is a worthy endeavor. Procter & Gamble spent 30 years and more than $2 billion to develop a fat substitute they named Olestra (also called Olean). After reviewing the results of more than 150 studies, in 1996 the Federal Food and Drug Administration (page 290) approved the limited use of Olestra in snack foods.

Olestra is a semisynthetic compound. That is, Olestra itself does not exist in nature, but its components do. Developing a compound that can be made from units that are a normal part of our diet decreases the likelihood that the new compound will be toxic. Olestra is made by esterifying all the OH groups of sucrose with fatty acids obtained from cottonseed oil and soybean oil. Therefore, its component parts are table sugar and vegetable oil. Because its ester linkages are too sterically hindered to be hydrolyzed by digestive enzymes, Olestra tastes like fat but it cannot be digested and, therefore, has no caloric value.



Olestra



Olestra a fat

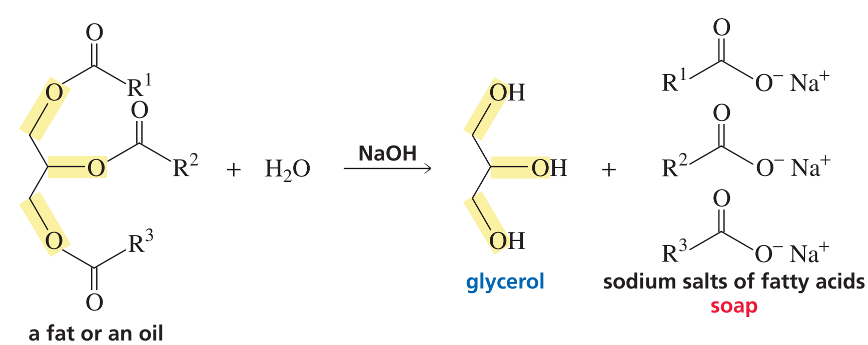
Courtesy of Procter & Gamble Company

Whales and Echolocation

Whales have enormous heads, accounting for 33% of their total weight. They have large deposits of fat in their heads and lower jaws. This fat is very different from both the whale's normal body fat and its dietary fat. Because major anatomical modifications were necessary to accommodate this fat, it must have some important function for the animal. It is now believed that the fat is used for echolocation—emitting sounds in pulses to gain information by analyzing the returning echoes. The fat in the whale's head focuses the emitted sound waves in a directional beam, and the echoes are received by the fat organ in the lower jaw. This organ transmits the sound to the brain for processing and interpretation, providing the whale with information about the depth of the water, changes in the sea floor, and the location of the coastline. The fat deposits in the whale's head and jaw, therefore, give the animal a unique acoustic sensory system and allow it to compete successfully for survival with the shark, which also has a well-developed sense of sound direction.

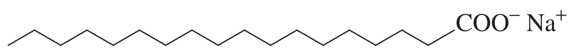
25.4 SOAPS AND MICELLES

When the ester groups of a fat or an oil are hydrolyzed in a basic solution, glycerol and fatty acids are formed. Because the solution is basic, the fatty acids are in their basic forms—namely, RCO_2^-.

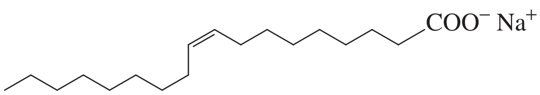


Soap

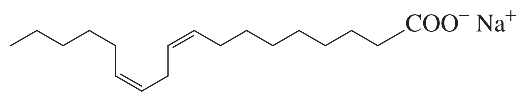
The sodium or potassium salts of fatty acids are what we know as **soap.** Consequently, the hydrolysis of an ester in a basic solution is called **saponification** (the Latin word for "soap" is *sapo*). After hydrolysis, sodium chloride is added to precipitate the soap, which is dried and pressed into bars. Perfume can be added for scented soaps, dyes can be added for colored soaps, sand can be added for scouring soaps, and air can be blown into the soap to make it float in water. Three of the most common soaps are shown below:



sodium stearate



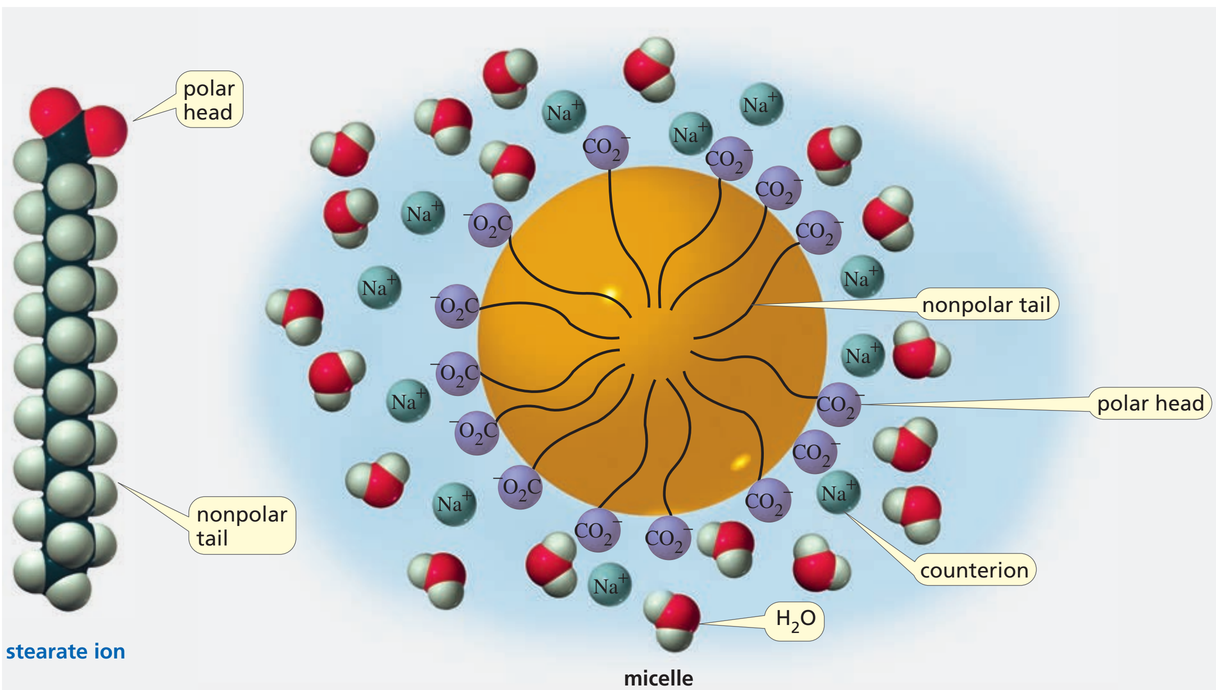
sodium oleate



sodium linoleate

Micelles

Long-chain carboxylate ions do not exist as individual ions in aqueous solution. Instead, they arrange themselves in spherical clusters called **micelles.** Each micelle contains 50–100 long-chain carboxylate ions and resembles a large ball. The polar heads of the carboxylate ions, each accompanied by a counterion, are on the outside of the ball because of their attraction for water, whereas the nonpolar tails are buried in the interior of the ball to minimize their contact with water. The hydrophobic interactions between the nonpolar tails increase the stability of the micelle (Section 21.15).

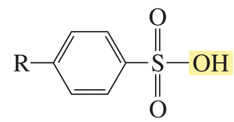


Water by itself is not a very effective cleaner because dirt is carried by nonpolar oil molecules. Soap has cleansing ability because the nonpolar oil molecules dissolve in the nonpolar interior of the micelles and are washed away with the micelle during rinsing.

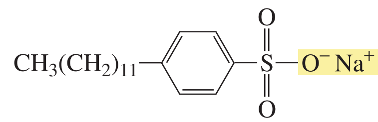
Because the surface of the micelle is charged, the individual micelles repel one another instead of clustering together to form larger aggregates. However, in "hard" water—water containing high concentrations of calcium and magnesium ions—micelles do form aggregates, which we know as "bathtub ring" or "soap scum."

Detergents

The formation of soap scum in hard water led to a search for synthetic materials that would have the cleansing properties of soap but would not form scum when they encountered calcium and magnesium ions. The synthetic "soaps" that were developed, known as **detergents** (from the Latin *detergere*, which means "to wipe off"), are salts of benzenesulfonic acids. Calcium and magnesium salts of benzenesulfonic acids do not form aggregates.



a benzenesulfonic acid



a detergent

After the initial introduction of detergents into the marketplace, it was discovered that those with straight-chain alkyl groups are biodegradable, whereas those with branched-chain alkyl groups are not. Therefore, to prevent detergents from polluting rivers and lakes, detergents are made only with straight-chain alkyl groups.

PROBLEM 5 SOLVED

An oil obtained from coconuts is unusual in that all three fatty acid components are identical. The molecular formula of the oil is $C_{45}H_{86}O_6$. What is the molecular formula of the carboxylate ion obtained when the oil is saponified?

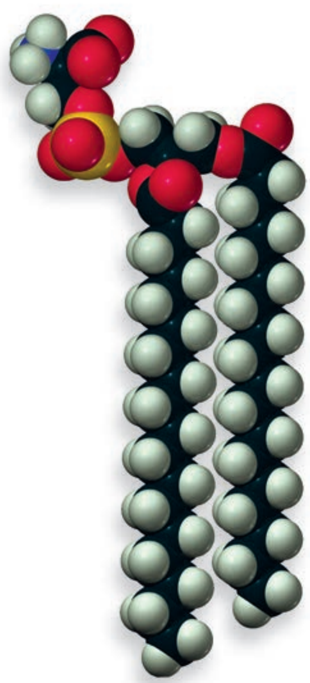
SOLUTION When the oil is saponified, it forms glycerol and three equivalents of carboxylate ion. In losing glycerol, the fat loses three carbons and five hydrogens. Thus, the three equivalents of carboxylate ion have a combined molecular formula of $C_{42}H_{81}O_6$. Dividing by three gives a molecular formula of $C_{14}H_{27}O_2$ for the carboxylate ion.

25.5 PHOSPHOLIPIDS ARE COMPONENTS OF CELL MEMBRANES

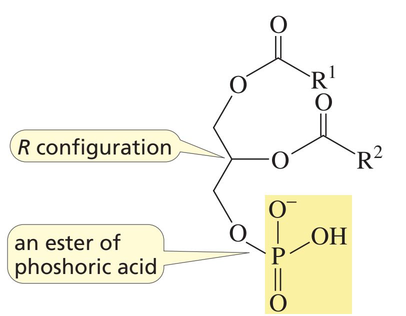
For organisms to operate properly, some of their parts must be separated from other parts. On a cellular level, for example, the outside of the cell must be separated from the inside. "Greasy" lipid **membranes** serve as the barrier. In addition to isolating the cell's contents, membranes allow the selective transport of ions and organic molecules into and out of the cell.

Phosphoglycerides

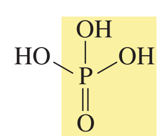
Phosphoglycerides (also called **phosphoacylglycerols**), the major components of cell membranes, belong to a class of compounds called **phospholipids**—lipids that contain a phosphate group. Phosphoglycerides are similar to triglycerides except that a terminal OH group of glycerol is esterified with phosphoric acid rather than with a fatty acid, forming a **phosphatidic acid.** The C-2 carbon of glycerol in phosphoglycerides has the *R* configuration.



phosphatidylserine
a phosphoglyceride



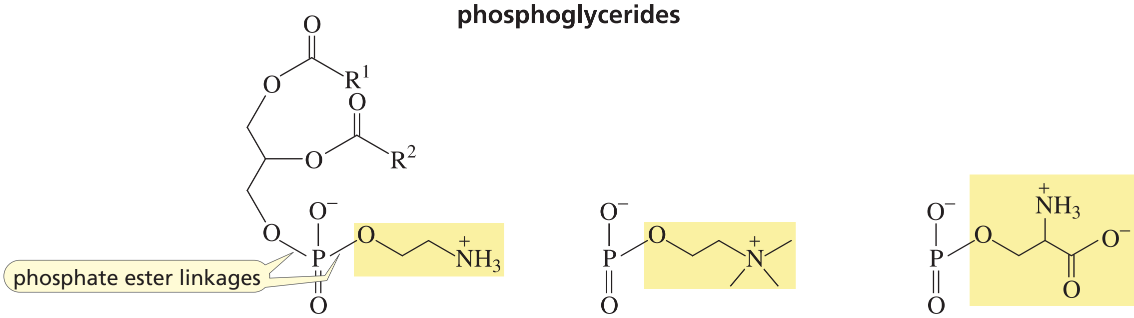
a phosphatidic acid



phosphoric acid

Phosphatidic acids, the simplest phosphoglycerides, are present in only small amounts in membranes. The most common phosphoglycerides in membranes have a second phosphate ester linkage—they are phosphodiesters.

phosphoglycerides



a phosphatidylethanolamine **a cephalin** | **a phosphatidylcholine** **a lecithin** | **a phosphatidylserine**

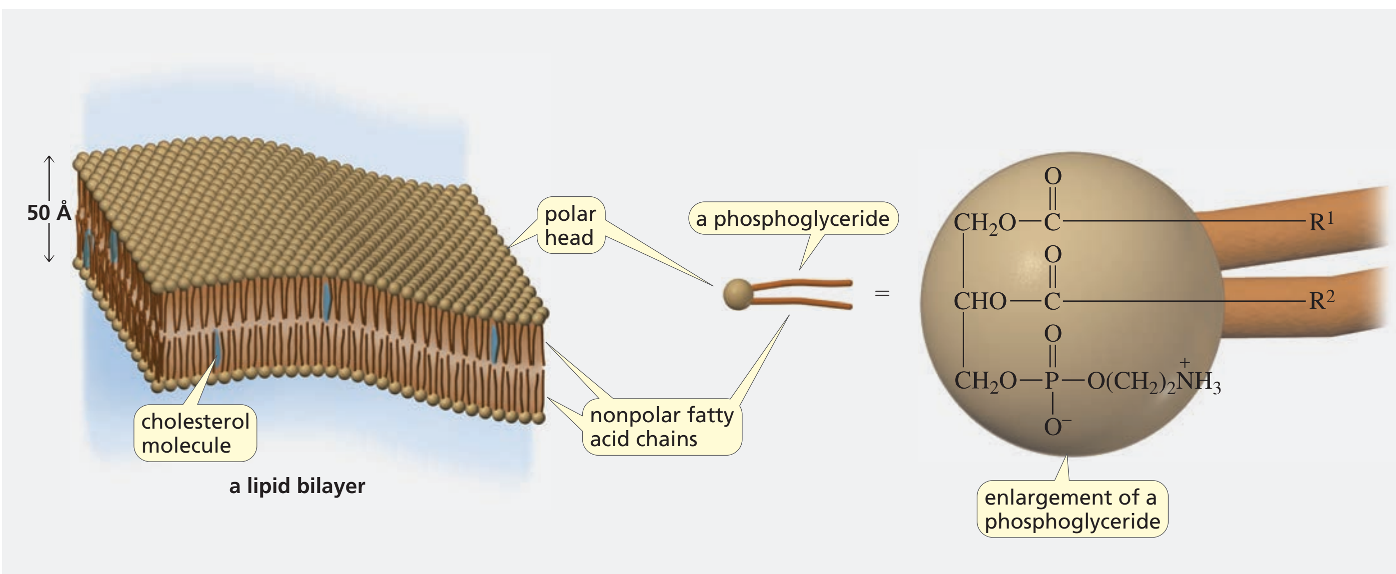
The most common phosphoglycerides in cell membranes are phosphodiesters.

The alcohols most commonly used to form the second ester group are ethanolamine, choline, and serine. Phosphatidylethanolamines are also called *cephalins*, and phosphatidylcholines are called *lecithins*. Lecithins are added to foods such as mayonnaise to prevent the aqueous and fat components from separating.

PROBLEM 6 ♦
Do the identities of R^1 and R^2 in phosphatidic acid affect the configuration of the asymmetric center?

Membranes

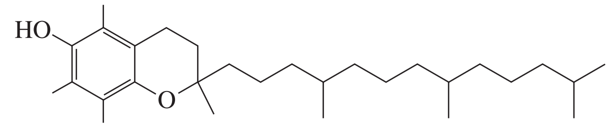
Phosphoglycerides form membranes by arranging themselves in a **lipid bilayer.** The polar heads of the phosphoglycerides are on both surfaces of the bilayer, and the fatty acid chains form the interior of the bilayer. Cholesterol, a lipid discussed in Sections 3.16 and 25.10, is also found in the interior of the bilayer (Figure 25.1). (Compare the bilayer structure with that of the micelles formed by soap in an aqueous solution, described in Section 25.4.)



▲ **Figure 25.1**
Anatomy of a lipid bilayer.

The fluidity (viscosity) of a membrane is controlled by the fatty acid components of the phosphoglycerides. Saturated fatty acids decrease membrane fluidity because their hydrocarbon chains pack closely together. Unsaturated fatty acids increase fluidity because they pack less closely together. Cholesterol also decreases fluidity (Section 25.9). Only animal membranes contain cholesterol, so they are more rigid than plant membranes.

The unsaturated fatty acid chains of phosphoglycerides are susceptible to reaction with O_2, similar to the reaction described on page 554 for fats and oils. This oxidation reaction leads to the degradation of membranes. Vitamin E is an important antioxidant that protects fatty acid chains from degradation through oxidation. Vitamin E, also called α-tocopherol, is classified as a lipid because it is soluble in nonpolar solvents. It is, therefore, able to enter the nonpolar membranes; once there, it reacts more rapidly with oxygen than the phospholipids in the bilayer do (Section 12.11).

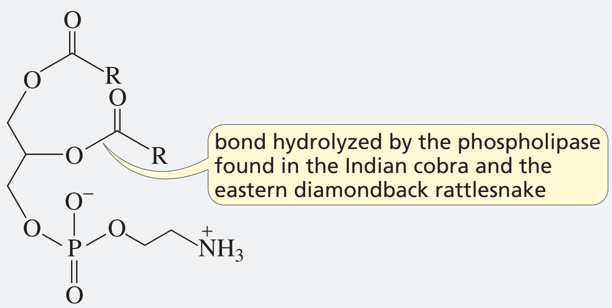


α-tocopherol
vitamin E

There are some who believe that vitamin E slows the aging process. The ability of vitamin E to react with oxygen more rapidly than fats do is the reason it is added as a preservative to many fat-containing foods.

Snake Venom

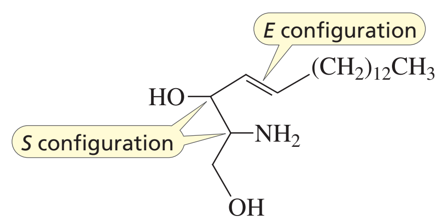
The venom of some poisonous snakes contains a phospholipase, an enzyme that hydrolyzes an ester group of a phosphoglyceride. For example, both the eastern diamondback rattlesnake and the Indian cobra contain a phospholipase that hydrolyzes an ester bond of cephalins, causing the membranes of red blood cells to rupture.



an eastern diamondback rattlesnake

Sphingolipids

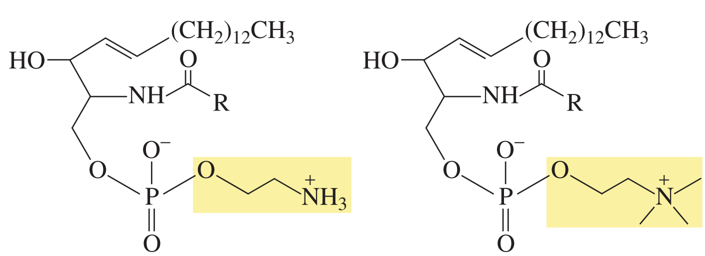
Sphingolipids are another kind of lipid found in membranes. Sphingolipids contain an amino alcohol called sphingosine instead of glycerol. In sphingolipids, the amino group of sphingosine forms an amide with a fatty acid. Both asymmetric centers in sphingosine have the *S* configuration.



sphingosine

Sphingomyelins are the most common sphingolipids. In sphingomyelins, the primary alcohol group of sphingosine is bonded to phosphoethanolamine or phosphocholine, in a manner similar to the bonding in lecithins and cephalins.

sphingomyelins



Multiple Sclerosis and the Myelin Sheath

The myelin sheath is a lipid-rich covering that is wrapped around the brain's neurons—the nerve cells that control our muscles. Composed largely of sphingomyelins, the sheath increases the velocity of nerve impulses. Without the myelin sheath, nerve cells are not able to tell the muscles what to do. Multiple sclerosis is a disease characterized by loss of the myelin sheath, a consequent slowing of nerve impulses, and eventual paralysis.

ADL (adrenoleukodystrophy) is a genetic disease that destroys myelin, causing a decline in brain function as the myelin sheath that surrounds the brain's nerve cells disappears. The defect is in the X chromosome, so the disease affects males. Because women have two X chromosomes, if they inherit an abnormal one, they still have a normal X chromosome that can offset the effect of the mutation.

PROBLEM 7 ♦

Membranes contain proteins. Integral membrane proteins extend partly or completely through the membrane, whereas peripheral membrane proteins are found on the inner or outer surface of the membrane. What is the likely difference in the amino acid composition of integral and peripheral membrane proteins?

PROBLEM 8 ♦

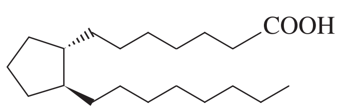
A colony of bacteria accustomed to an environment with a temperature of 25 °C was moved to an identical environment, except that its temperature was 35 °C. The higher temperature increased the fluidity of the bacterial membranes. How can the bacteria regain their original membrane fluidity?

PROBLEM 9

The membrane phospholipids in deer have a higher degree of unsaturation in cells closer to the hoof than in cells closer to the body. Why is this trait important for survival?

25.6 PROSTAGLANDINS REGULATE PHYSIOLOGICAL RESPONSES

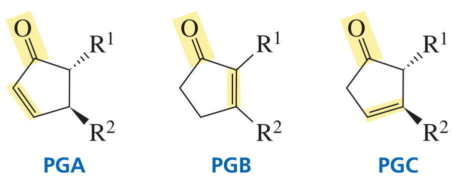
Prostaglandins obtained their names because the first prostaglandins were isolated from the prostate gland. Now, however, we know that prostaglandins are found in all body tissues. They are responsible for regulating a variety of physiological responses, such as inflammation, blood pressure, blood clotting, fever, pain, the induction of labor, and the sleep–wake cycle. All prostaglandins have a five-membered ring with a seven-carbon carboxylic acid substituent and an eight-carbon hydrocarbon substituent. The two substituents are trans to each other.



prostaglandin skeleton

Prostaglandins are classified using the formula PGX, where X designates the functional groups of the compound's five-membered ring.

- PGAs, PGBs, and PGCs all contain a carbonyl group and a double bond in the five-membered ring. The location of the double bond determines whether a prostaglandin is a PGA, PGB, or PGC.



- PGDs and PGEs are β-hydroxy ketones. A subscript indicates the total number of double bonds in the side chains.